ANESTHESIOLOGY

A Comprehensive Board Review for Primary and Maintenance of Certification

- Over 1000 multiple choice questions
- Latest keywords covering all topics tested
- Includes patient safety, ethics, and statistics

Edited by **KAI MATTHES · RICHARD URMAN · JESSE EHRENFELD**

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PREFACE

Passing the anesthesiology board examination is the final hurdle of a long and consuming path through college, medical school, internship, and residency before entering a professional career as an independently practicing anesthesiologist. This pivotal point is probably the most important phase in one's career because many factors may place a heavy burden on the examinee. Peer pressure, job prospects, and monetary factors are frequently on one's mind during these challenging times. In contrast to prior high-stakes examinations during college and medical school, there is limited time to prepare for this test of utmost importance.

Practicing anesthesiologists enrolled in the Maintenance of Certification in Anesthesiology (MOCA) program face a similar time-restraint problem as residents in training studying for the boards based on the daily obligations in the operating room. Wise use of the allocated studying time available is a key step toward mastering the boards.

This book was written in an attempt to provide the best study aid possible with a maximized use of time and focus on what is essential to pass. *Anesthesiology: A Comprehensive Board Review for Primary and Maintenance of Certification* is a high-yield, concise study aid to prepare for the written Anesthesiology Boards and the Maintenance of Certification in Anesthesiology (MOCA) Examination.

More than 1,000 updated, realistic multiple-choice questions written and edited by Harvard Medical School faculty and experts from partnering teaching institutions are tailored to the question content of recent American Board of Anesthesiology (ABA) examinations. The aim of this book is to provide a study guide that is streamlined, while containing adequate depth of knowledge focused on topics frequently asked on the examination. This book has unique learning features distinct from other board review books. To maximize reading efficiency, key messages are repeated and highlighted in bullets. While focusing on the most frequently tested keywords by the ABA, this book also covers new "emerging" topics such as patient safety, statistics, and ethics. Well-chosen illustrations and graphs are used to enhance the learning experience. Also novel is a high-yield summary of the 60 most frequently tested topics and concepts to be reviewed just before taking the boards. In addition to the textbook version, readers are given access to a website with continuously updated content, which also includes a simulated exam.

With this book as guidance, you will be able to efficiently prepare for the written primary certification or recertification anesthesiology board examination.

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1.

INHALATIONAL ANESTHESIA

Jerome Adams, MD, MPH, and Amy Dorwart, MD

1. A 56-year-old, 75-kg man is undergoing general anesthesia for a right colectomy. After induction the patient develops a junctional arrhythmia. Which inhalational anesthetic would most likely be associated with this arrhythmia?

A. Nitrous oxide
B. Desflurane
C. Isoflurane
D. Halothane
E. Sevoflurane

2. Isoflurane is chosen for maintenance of general anesthesia in an elderly patient with severe coronary artery disease. Which of the following is most responsible for maintenance of cardiac output during isoflurane administration?

A. Coronary artery vasodilation
B. Increased systemic vascular resistance
C. Increased venous capacitance
D. Increased heart rate
E. Decreased myocardial oxygen demand

3. Which of the following would result in an INCREASE in the production of Compound A from the interaction between soda lime and sevoflurane?

A. Low soda lime absorbent temperatures
B. Low alveolar partial pressure of sevoflurane
C. Soda lime desiccation
D. High fresh gas flows
E. Short duration of sevoflurane administration

4. A 45-year-old, 100-kg man with coronary artery disease undergoes general anesthesia for resection of his intracranial astrocytoma. Which of the following statements supports the choice of desflurane for anesthetic maintenance in this patient?

A. Desflurane will increase coronary blood flow.
B. Desflurane will increase mean arterial pressure.
C. Desflurane will decrease cerebral blood flow.
D. Desflurane has a low incidence of airway irritation.
E. Desflurane allows for rapid emergence.

5. Induction will be the most rapid with which of the following anesthetic agents?

A. Sevoflurane
B. Isoflurane
C. Enflurane
D. Halothane
E. Desflurane

6. A 22-year-old man is taken to the operating room for repair of his retinal detachment. The ophthalmologist discusses intraocular injection of either air or sulfur hexafluoride (SF6) to facilitate retinal reattachment. Which is true regarding the administration of nitrous oxide to this patient?

A. An intraocular air bubble will expand more quickly during N_2O administration compared to an SF6 bubble.
B. Discontinuing N_2O 15 minutes prior to bubble injection can avoid the risk of gas expansion.
C. An SF6 bubble will slowly shrink in the first 24 hours after injection.
D. N_2O can be safely administered to this patient 1 day after intraocular air injection.
E. N_2O can be safely administered to this patient 5 days after intraocular SF6 injection.

7. A 15-year-old, 55-kg patient with scoliosis undergoes general anesthesia for a posterior spinal fusion. Somatosensory evoked potentials are performed. The addition of 1 MAC of isoflurane will result in which of the following changes to the cortical component of the evoked potentials?

A. Increased amplitude and decreased latency
B. Decreased amplitude and increased latency
C. Increased amplitude and unchanged latency
D. Unchanged amplitude and increased latency
E. Decreased amplitude and decreased latency

8. Which of the following respiratory changes are consistent with the administration of volatile anesthetics?

A. Decrease in $PaCO_2$
B. Decreased respiratory rate
C. Increased tidal volume
D. Increased dead-space ventilation
E. Increased functional residual capacity

9. Desflurane is administered via a heated vaporizer. Heating this volatile anesthetic allows for its accurate administration by which of the following mechanisms?

A. Lowering the partial pressure of desflurane within the vaporizer
B. Raising the partial pressure of desflurane within the vaporizer
C. Lowering the partial pressure of fresh gas flow through the desflurane sump
D. Raising the partial pressure of fresh gas flow through the desflurane sump
E. Minimizing the creation of bubbles within the vaporizer

10. The addition of nitrous oxide is contraindicated in which of the following cases?

A. Thyroidectomy for thyroid nodule
B. Exploratory laparotomy for small bowel obstruction
C. External fixation for femur fracture
D. Strabismus surgery for diplopia
E. Posterior spinal fusion for scoliosis

11. Which of the following is LEAST likely to affect the potency of an inhaled anesthetic agent?

A. Pregnancy
B. Hypernatremia
C. Chronic alcoholism
D. Hypothermia
E. Hyperthyroidism

12. What mechanism is responsible for the fact that the rate of emergence from isoflurane is quicker than the rate of induction?

A. Significant metabolism by cytochrome P-450 isoenzymes
B. Significant transcutaneous losses
C. Significant reductive metabolism
D. Continued uptake of isoflurane into peripheral tissues such as adipose tissue during emergence
E. Ongoing release of isoflurane from peripheral tissues such as adipose tissue during emergence

13. A 50-year-old patient is undergoing general anesthesia maintained with 53% nitrous oxide, 0.9% isoflurane, and 46% oxygen. What is the approximate minimum alveolar concentration (MAC) delivered to this patient?

A. 0.5 MAC
B. 0.75 MAC
C. 1 MAC
D. 1.25 MAC
E. 1.5 MAC

14. Collectively, the brain, heart, liver, kidneys, and endocrine system represent 10% of the total body weight. What percentage of total cardiac output is delivered to these organs?

A. 10%
B. 25%
C. 50%
D. 75%
E. 90%

15. Which inhalational anesthetic undergoes the slowest metabolism?

A. Desflurane
B. Isoflurane
C. Sevoflurane
D. Enflurane
E. Halothane

16. An E compressed O_2 cylinder is used to supply oxygen for a patient during transport. The pressure gauge reads 500 psi. If the oxygen is set at 10 L/min, how long do you have until this cylinder is empty?

A. 3 minutes
B. 15 minutes
C. 45 minutes
D. 120 minutes
E. 150 minutes

17. Which of the following are incorrectly paired?

A. Carbon monoxide toxicity and desflurane
B. High-output renal failure and methoxyflurane
C. Compound A toxicity and sevoflurane
D. Macrocytic anemia and nitrous oxide
E. Fulminant hepatic necrosis and enflurane

18. Volatile anesthetics independently cause skeletal muscle relaxation by interacting with which of the following areas?

A. Cerebral cortex
B. Spinal cord
C. Peripheral nerves
D. Neuromuscular junction
E. Muscle fibers

19. The cerebral metabolic rate for oxygen is INCREASED during the administration of which of the following inhalational anesthetics?

A. Halothane
B. Isoflurane
C. Sevoflurane
D. Desflurane
E. Nitrous oxide

20. Which of the following contributes to the rapid transfer of inhalational anesthetics across the placenta when a general anesthetic is required for a cesarean section?

A. Volatile anesthetics have a high degree of ionization.
B. Volatile anesthetics have low lipid solubility.
C. Volatile anesthetics have a high degree of protein binding.
D. Volatile anesthetics have a low molecular weight.
E. Volatile anesthetics have a small concentration gradient between the maternal and fetal blood.

21. Which of the following best describes how inhalational anesthetic agent exposure results in anesthetic ischemic preconditioning in patients at risk for myocardial ischemia?

A. Decreased myocardial oxygen consumption
B. Coronary vasodilation
C. Decreased afterload
D. Interaction with Na channels
E. Interaction with K channels

22. Which of the following accounts for why nitrous oxide E cylinders have to be weighed to determine the amount of N_2O that is remaining?

A. N_2O is a liquid at normal room temperature and barometric pressure.
B. N_2O exists as both a gas and a liquid at room temperature and barometric pressure.
C. N_2O's critical temperature is below room temperature.
D. N_2O's critical temperature is above room temperature.
E. N_2O has a high vapor pressure.

23. Which of the following factors will increase the rate of an inhalational induction?

A. Hypoventilation
B. Decreased cardiac output
C. High blood-gas partition coefficient
D. Right-to-left intracardiac shunt
E. Endobronchial intubation

24. A patient in septic shock presents to the OR for an exploratory laparotomy. The induction rate of which of the following agents will be most affected by this clinical presentation?

A. Isoflurane
B. Desflurane
C. Sevoflurane
D. Halothane
E. Nitrous oxide

25. Which of the following parameters is most responsible for the potency of an inhalational anesthetic?

A. Vapor pressure
B. Oil-gas partition coefficient
C. Blood-gas partition coefficient
D. Brain-blood partition coefficient
E. Molecular weight

26. The transient hypertension and tachycardia seen with abrupt increases of desflurane are most likely a result of which of the following mechanisms?

A. Diminished baroreceptor reflexes
B. Increased endogenous catecholamines
C. Direct decrease in parasympathetic tone
D. Vasopressin receptor stimulation
E. Acute carbon dioxide elevation

27. Which of the following is the best mechanism to prevent fatal arrhythmias in patients with long QT syndrome who are undergoing general anesthesia?

A. Perioperative beta-blockade
B. Perioperative alpha-blockade
C. Sevoflurane administration
D. Avoidance of lidocaine
E. Perioperative amiodarone

28. The time constant for sevoflurane is approximately 2 minutes. During induction, how long will it take for the brain partial pressure of sevoflurane to approximate the arterial partial pressure of this gas?

A. 2 minutes
B. 6 minutes
C. 12 minutes
D. 24 minutes
E. 36 minutes

29. Which of the following accounts for the transient increase in Pa_{O_2} that occurs when nitrous oxide is initially administered to a patient?

A. Diffusion hypoxia
B. Solubility differences during induction
C. Concentrating effect
D. Concentration effect
E. Second gas effect

30. Which of the following is the most significant factor that determines the rate of both induction and recovery from general anesthesia?

A. Alveolar ventilation
B. Fresh gas flow
C. Blood-gas coefficient
D. Cardiac output
E. MAC of inhalational agent

31. During induction and maintenance with an inhalational anesthetic, which of the following parameters does NOT influence alveolar partial pressure?

A. Cardiac output
B. Alveolar ventilation
C. Inspired volatile anesthetic partial pressure
D. Metabolism of the volatile anesthetic
E. Blood-gas partition coefficient

32. Mask induction is accelerated in neonates compared to adults because of which of the following parameters?

A. Increased cardiac output
B. Increased tidal volume
C. Right-to-left shunt through PDA
D. Increased ratio of minute ventilation/functional residual capacity
E. Increased cerebral blood flow

33. A 62-year-old woman presents for a total abdominal hysterectomy. A sevoflurane vaporizer incorrectly filled with which other volatile agent will result in a nearly accurate anesthetic concentration delivery to the patient?

A. Desflurane
B. Isoflurane
C. Halothane
D. Enflurane
E. Methoxyflurane

34. A bubble-through vaporizer is filled with sevoflurane at sea level. What is the required flow rate of the carrier gas entering the vaporizing chamber in mL/min to achieve a vaporizer output of 40 mL/min?

A. 40 mL/min
B. 150 mL/min
C. 200 mL/min
D. 335 mL/min
E. 500 mL/min

35. A stabilizing agent, thymol, is added to which of the following inhalational agents?

A. Desflurane
B. Isoflurane
C. Sevoflurane
D. Halothane
E. Enflurane

36. The presence of a right-to-left intracardiac shunt results in which of the following?

A. Slows induction, especially with very soluble inhalational agents
B. Slows induction, especially with insoluble inhalational agents
C. Speeds induction, especially with very soluble inhalational agents
D. Speeds induction, especially with insoluble inhalational agents
E. Speeds induction independent of the solubility of the inhalational agent

37. Induction with nitrous oxide is faster than a desflurane induction. Which of the following describes why nitrous oxide has this effect?

A. Lower blood-gas coefficient of nitrous oxide compared to desflurane
B. The concentration effect
C. The second gas effect
D. Higher vapor pressure of nitrous oxide compared to desflurane
E. Higher brain-blood coefficient of nitrous oxide compared to desflurane

38. Administration of which of the following results in the highest blood levels of fluoride?

A. Sevoflurane
B. Isoflurane
C. Desflurane
D. Nitrous oxide
E. Xenon

39. Which of the following statements about volatile anesthetics is FALSE?

A. All volatile anesthetics can trigger malignant hyperthermia.
B. All produce a decrease in uterine blood flow when administered to a gravid patient.
C. All increase tidal volume when administered to a spontaneously ventilating patient.
D. All increase respiratory rate when administered to a spontaneously ventilating patient.
E. All blunt the normal ventilatory response to hypercapnia.

40. Which of the following statements about nitrous oxide is INCORRECT?

A. Produces a dose-dependent decrease in the ventilatory response to CO_2
B. Produces a dose-dependent decrease in the ventilatory response to hypoxia
C. Produces a dose-dependent decrease in tidal volume of spontaneously ventilating patients
D. Can trigger malignant hyperthermia in susceptible patients
E. Can increase CO by means of catecholamine stimulation

41. What is the definition of minimum alveolar concentration (MAC)?

A. The lowest concentration of inhaled anesthetic achieved during the course of a procedure
B. The alveolar concentration of inhaled anesthetic that prevents movement in 50% of patients in response to surgical stimulus
C. The alveolar concentration of inhaled anesthetic that prevents movement in 100% of patients in response to surgical stimulus
D. The alveolar concentration of inhaled anesthetic that prevents spontaneous ventilation in 50% of patients
E. The alveolar concentration of inhaled anesthetic that prevents spontaneous ventilation in 100% of patients

42. Which of the following statements about minimum alveolar concentration (MAC) is INCORRECT?

A. MAC values are measures of potency.
B. MAC values of different anesthetic agents are additive.
C. MAC values mirror brain partial pressures.
D. MAC is the equivalent of a median effective dose (ED_{50}).
E. 0.1 MAC is associated with awakening from anesthesia (MAC awake).

43. All of the following affect minimum alveolar concentration (MAC) EXCEPT

A. A body temperature of 43 degrees Celsius
B. Recent ingestion of amphetamines
C. Pregnancy
D. $PaCO_2$ of 65
E. Hypernatremia

44. Which of the following anesthetics would prevent movement in response to a surgical stimulus in 50% of the population?

A. 4.5% desflurane
B. 0.9% isoflurane
C. 1.5% sevoflurane
D. 80% nitrous oxide
E. 52% nitrous oxide and 1% sevoflurane

45. Properties of desflurane include:

A. Lowest vapor pressure of the volatile anesthetics
B. Lowest potency of the volatile anesthetics
C. Longest duration of action of the volatile anesthetics
D. Highest blood-gas partition coefficient of the volatile anesthetics
E. Most suitable of the volatile anesthetics for inhalational induction

46. Properties of all potent volatile anesthetics include:

A. Increase in tidal volume
B. Prolongation of neuromuscular blocking agents
C. Suitable for inhalational induction
D. Increase in systemic vascular resistance
E. Lowering of respiratory rate

47. Advantages of closed-circuit anesthesia include all of the following EXCEPT

A. Conservation of heat
B. Conservation of humidity
C. Allows faster adjustment of anesthetic concentration
D. Lowered anesthetic pollution
E. Lowered anesthetic cost

48. Which of the following statements about halothane is INCORRECT?

A. It is the most potent of the currently used volatile anesthetics.

B. It causes a dose-dependent decrease in arterial blood pressure.
C. It causes a dose-dependent decrease in cardiac output.
D. It sensitizes the heart to the arrhythmogenic effects of epinephrine.
E. It causes an increase in sinoatrial node conduction.

49. Hypoxic drive may be inhibited by concentrations of halothane in excess of

A. 0.1 MAC
B. 0.5 MAC
C. 1 MAC
D. 2 MAC
E. Hypoxic drive is not inhibited by halothane when used in typical clinical concentrations.

50. You are administering a general anesthetic to a 65-year-old, 150-kg woman for a total abdominal hysterectomy. Her O_2 saturation starts at 100% and slowly decreases over the next hour to 92%. Applying PEEP would improve the patient's hypoxemia by what mechanism?

A. Decreasing dead space
B. Increasing hypoxic pulmonary vasoconstriction
C. Decreasing intrapulmonary shunting
D. Increasing cardiac output
E. Increasing the alveolar concentration of oxygen

51. Significant cardiac effects of desflurane include all of the following EXCEPT

A. Decreased mean arterial pressure
B. Decreased cardiac output
C. Decreased systemic vascular resistance
D. Increased heart rate
E. Decreased myocardial oxygen consumption

52. A 73-year-old man with diabetes, GERD, and a prior echocardiogram showing grade 2+ mitral regurgitation presents for repair of an incarcerated inguinal hernia. Which of the following anesthetic agents is most likely to precipitate worsening mitral regurgitation?

A. Desflurane
B. Halothane
C. Isoflurane
D. Sevoflurane
E. Nitrous oxide

53. Which anesthetic agent does NOT cause myocardial depression?

A. Desflurane
B. Isoflurane
C. Sevoflurane
D. Nitrous oxide
E. All of the above may cause myocardial depression.

54. The use of nitrous oxide is acceptable in which of the following patients?

A. A 35-year-old woman with an incarcerated umbilical hernia
B. A 27-year-old man with chest trauma following a motor vehicle accident
C. A healthy 8-year-old boy presenting for an inguinal hernia repair
D. A 7-year-old girl presenting for tympanoplasty
E. A 56-year-old with emphysema presenting for a femoral-popliteal bypass

55. A 4-year-old girl is anesthetized for an oral surgery procedure as the first case on a Monday morning. Following mask induction with sevoflurane and oxygen, a peripheral IV is placed, neuromuscular blockade is established with rocuronium, and intubation is uneventful and confirmed by end-tidal CO_2. Maintenance of anesthesia is with desflurane 7% and oxygen. Ten minutes after intubation, the patient's blood pressure decreases from a baseline of 90/45 to 70/20 mm Hg, and SpO_2 decreases from 100% to 97%. The blood pressure responds to phenylephrine IV, and the desflurane level is reduced, but the SpO_2 falls to 89%. Which of the following tests is most likely to reveal the cause of the blood pressure and SpO_2 decrease?

A. Arterial blood gas
B. EKG
C. CXR
D. Co-oximetry evaluation
E. Echocardiogram

56. An otherwise healthy 73-year-old man injured his head when he slipped and fell on the ice, and he now presents for evacuation of a subdural hematoma. Which of the following are expected effects of isoflurane for maintenance of general anesthesia?

A. Decreased cerebral blood flow
B. Decreased CMR_{O2}
C. Decrease in SSEP latency
D. Burst suppression of the EEG at 0.5 MAC
E. Increase in SSEP amplitude at 0.5 MAC

57. A 38-year-old woman is undergoing an ORIF of her ankle. Anesthesia is maintained with 60% nitrous oxide, 38% O_2, and 2% sevoflurane. Near the end of the case, nitrous oxide is switched to air and the patient's SpO_2 drops from 99% to 95%. This is most likely explained by

A. An air embolism
B. A pneumothorax
C. The second gas effect
D. Diffusion hypoxia
E. Hypoxic pulmonary vasoconstriction

58. Inhalational anesthetics result in suppression of the normal ventilatory response to hypoxemia primarily through interactions with which of the following?

A. Pulmonary stretch receptors
B. Aortic body chemoreceptors
C. Carotid body chemoreceptors
D. Dorsal group of medullary neurons
E. Ventral group of medullary neurons

59. Which of the following accounts for the reason why nitrous oxide cannot be used alone as a complete anesthetic?

A. Low oil-gas partition coefficient
B. Low blood-gas partition coefficient
C. Critical temperature of 36.5 degrees Celsius
D. Low MAC
E. Lack of analgesic properties

60. Which of the following regarding potent inhalational anesthetics is true in children compared to adults?

A. Volatile anesthetics depress ventilation more in adults than infants.
B. Children are at an increased risk of halothane hepatitis compared to adults.
C. Increased tidal volume in children increases induction rates compared to adults.
D. The MAC of inhalational agents is higher in infants compared to adults.
E. Inhalational anesthetics have a higher blood-gas coefficient in children compared to adults.

61. Compared to young and healthy adults, the elderly experience which of the following when a potent inhaled anesthetic agent is administered?

A. Increased MAC with increasing age
B. Increased myocardial depression
C. Increased speed of recovery
D. Increased tachycardia in response to desflurane
E. Increased cerebral metabolic oxygen rate

62. Which volatile anesthetic will result in the greatest potentiation of nondepolarizing muscle relaxants?

A. Desflurane
B. Isoflurane
C. Sevoflurane
D. Halothane
E. Enflurane

63. Sevoflurane results in a decrease of all of the following parameters EXCEPT

A. Glomerular filtration rate
B. Systemic vascular resistance
C. Cerebral metabolic oxygen rate
D. Portal vein blood flow
E. Cerebral blood flow

64. The decrease in systemic vascular resistance with isoflurane is a result of which of the following mechanisms?

A. Direct inhibition of alpha-1 receptors
B. Increase in histamine release
C. Increase in cutaneous blood flow
D. Increase in skeletal muscle blood flow
E. Direct interaction with calcium channels in vascular smooth muscle

65. A 55-year-old patient with a history of untreated obstructive sleep apnea presents for a total knee replacement. A full cardiac evaluation completed prior to surgery revealed a mean pulmonary artery pressure of 32 mm Hg. Which of the following anesthetic agents should be avoided in this patient?

A. Desflurane
B. Isoflurane
C. Sevoflurane
D. Halothane
E. Nitrous oxide

66. A 12-year-old boy presents to the operating room for an inguinal hernia repair. This patient has a questionable family history of hyperthermia. Which of the following anesthetic agents is most likely to trigger malignant hyperthermia?

A. Desflurane
B. Halothane
C. Sevoflurane
D. Isoflurane
E. Enflurane

67. MAC will be the lowest in which of the following clinical scenarios?

A. A 28-week premature infant presenting for an exploratory laparotomy
B. A term infant presenting for a tracheoesophageal fistula repair

C. A 6-month-old infant presenting for circumcision
D. A 40-year-old woman presenting for a total abdominal hysterectomy
E. A 75-year-old man presenting for a total hip arthroplasty

68. A sevoflurane vaporizer is accidentally filled with the wrong inhalational anesthetic, and the vaporizer output is LESS than the set concentration on the dial. Which of the following inhalational agents was most likely used to fill the sevoflurane vaporizer?

A. Desflurane
B. Isoflurane
C. Halothane
D. Enflurane
E. Methoxyflurane

69. A 55-year-old man presents for a total knee arthroplasty. General anesthesia is maintained with an inhalational agent. Which of the following characteristics is NOT consistent with an ideal anesthetic gas?

A. Inflammability
B. Muscle relaxation
C. Maximal biotransformation
D. Bronchodilation
E. Rapid emergence

70. A 19-year-old girl with Eisenmenger syndrome presents to the operating room for a laparoscopic appendectomy. Inhalational induction with which agent will be most affected (slowest) by this patient's cardiopulmonary physiology?

A. Desflurane
B. Isoflurane
C. Sevoflurane
D. Halothane
E. Enflurane

CHAPTER 1 ANSWERS

1. ANSWER: D

Halothane is a halogenated alkane that is nonflammable due to its carbon–fluoride bonds. Its cardiac effects are important to know. Halothane slows conduction through the SA node, causing both junctional arrhythmias and bradycardia. Halothane interferes with sodium–calcium exchange, resulting in direct cardiac depression and a subsequent dose-dependent decrease in mean arterial blood pressure. Systemic vascular resistance is unchanged. Halothane blunts the baroreceptor reflex that normally results in increases in the heart rate in response to hypotension detected by the aortic arch and carotid baroreceptors. Halothane sensitizes the myocardium to the effects of epinephrine and other endogenous catecholamines. It is recommended to limit concomitant epinephrine doses to less than 1.5 mcg/kg, and to avoid halothane use in patients with pheochromocytoma to avoid arrhythmias.

KEY FACTS: CARDIAC EFFECTS OF HALOTHANE

- **Decreases MAP** by direct cardiac depression and thus a **decrease in CO** but not a decrease in SVR
- Unchanged HR due to **blunting of baroreceptor reflex** that decreases the vagal response to hypotension
- **Decreased myocardial oxygen consumption** because it depresses the myocardium
- Slows conduction through SA node, predisposing patients to **junctional arrhythmias** and **bradycardia**
- Arrhythmias can result from **sensitization of the myocardium to catecholamines.**

ADDITIONAL READINGS

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2. ANSWER: D

Isoflurane anesthesia results in maintenance of cardiac output due to a preserved carotid baroreceptor reflex that senses a decrease in mean arterial pressure (as a result of decreased systemic vascular resistance) and responds by decreasing vagal stimulation to increase the heart rate. It is this increase in heart rate that allows for maintenance of cardiac output in the presence of decreased mean arterial pressure. Isoflurane also causes coronary artery vasodilation, which, in theory, could direct blood flow away from fixed stenotic lesions. This risk of coronary steal syndrome has not been validated in clinical practice.

KEY FACTS: CARDIAC EFFECTS OF ISOFLURANE

- Coronary artery vasodilation
- Decrease in mean arterial pressure due to decreased systemic vascular resistance
- Increase in heart rate due to baroreceptor reflex activation
- Cardiac output is maintained due to an increase in heart rate.

ADDITIONAL READINGS

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3. ANSWER: C

Compound A (trifluoroethyl vinyl ether) is a nephrotoxic end product that results from the interaction of either sevoflurane or halothane with soda lime or barium hydroxide lime. Compound A accumulation is associated with long-duration anesthetics, low fresh gas flow, higher inhaled concentrations of sevoflurane, higher absorbent temperatures, and absorbent desiccation. Compound A has been shown to be nephrotoxic in rats after prolonged exposure. Human studies have not shown an association between Compound A and postoperative elevation in serum creatinine levels. Current recommendations are to maintain fresh gas flows greater than 2 L/min to avoid rebreathing of Compound A.

KEY FACTS: INCREASES IN COMPOUND A ASSOCIATED WITH:

- Long-duration anesthetics
- Low fresh gas flow
- High inhaled concentrations of sevoflurane
- High absorbent temperatures
- Absorbent desiccation

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

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4. ANSWER: E

Desflurane is an excellent choice for anesthetic maintenance in long neurosurgical cases where rapid emergence and prompt neurologic assessment are important. Its low solubility is responsible for both rapid induction and emergence with this agent. Like other volatile anesthetics, desflurane causes a decrease in cerebral metabolic rate and directly increases cerebral blood through cerebral vasodilatation. This increase in cerebral blood flow can result in intracranial pressure elevations, but with desflurane cerebral vasculature remains responsive to changes in $PaCO_2$, so increased intracranial pressure can be prevented by hyperventilation. Desflurane also results in EEG suppression, which can be neuroprotective during episodes of ischemia.

Desflurane is similar to isoflurane in terms of cardiovascular side effects. It results in a decrease in mean arterial pressure primarily though a decline in systemic vascular resistance. A concomitant rise in heart rate maintains a near-normal cardiac output. Desflurane is different from isoflurane in that it does not cause coronary artery vasodilation. Rapid elevations in desflurane concentrations can result in transient hypertension, tachycardia, and elevation in endogenous catecholamines that are more severe than the mild increases in these parameters that can be caused by a rapid elevation in isoflurane concentrations. This can be worrisome, especially in patients with concomitant coronary artery disease. This effect can be attenuated with fentanyl, clonidine, or esmolol.

Desflurane's respiratory effects are similar to other volatile anesthetics (increased respiratory rate, decreased tidal volume, decreased alveolar ventilation, increased resting $PaCO_2$, decreased ventilatory response to $PaCO_2$ and PaO_2). Desflurane is not an ideal induction agent however, because it is associated with a high incidence of airway irritation, laryngospasm, coughing, breath-holding, and salivation.

KEY FACTS: DESFLURANE PHARMACOLOGY

- Neurologic:
  - Rapid emergence due to low blood-gas coefficient (0.42)
  - Decreased CMR_{O2}
  - Increased CBF
  - Vasculature remains responsive to $PaCO_2$ so hyperventilation decreases ICP.
- Cardiovascular:
  - No coronary artery vasodilation
  - Decreased MAP
  - Decreased SVR
  - Increased HR
  - Maintenance of CO
  - Rapid elevations in concentration lead to increases in catecholamines, BP, and HR.
- Respiratory:
  - Pungent, airway irritant, may lead to breath-holding and laryngospasm
  - Increased RR
  - Decreased VT
  - Decreased VA
  - Increased resting $PaCO_2$

ADDITIONAL READINGS

Eger EI, Eisenkraft JB, Weiskopf RB. *The Pharmacology of Inhaled Anesthetics*. Chicago, IL: Baxter Healthcare; 2003.

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5. ANSWER: E

The rate of rise of FA/FI determines the rate of induction. FA is the alveolar concentration and FI is the inspiratory concentration of an inhaled agent. The solubility of an anesthetic agent plays the most significant role in the rate of induction because of its effect on the rate of rise of FA/FI. The blood-gas partition coefficient of a volatile anesthetic indicates its solubility.

An agent with a low blood-gas partition coefficient is minimally soluble in blood, so very little anesthetic agent will be taken up by blood passing the alveoli. This results in a rapid rise in alveolar gas concentrations, and a quicker induction. The exact opposite happens for agents with high blood-gas partition coefficients. These soluble agents are absorbed into the blood, causing the alveolar concentrations to be lower. This will result in a slowed induction due to a slower rate of rise of FA/FI.

Since desflurane has the lowest blood-gas partition coefficient, it is the least soluble agent and will result in the quickest induction.

KEY FACTS: RAPID INDUCTION, ONSET OF VARIOUS GASES

- Blood-gas coefficient indicates its solubility.
- Rate of rise of FA/FI determines the rate of induction.
- Agents with a low blood-gas partition coefficient are less soluble, so less anesthetic agent leaves the alveoli, resulting in an increase in FA/FI and a quick induction.
- Agents with a high blood-gas partition coefficient are more soluble so anesthetic agent leaves the alveoli, resulting in a decrease in FA/FI and a slowed induction.
- Since desflurane has the lowest blood-gas partition coefficient, it is the least soluble agent and will result in the quickest induction.

BLOOD-GAS PARTITION COEFFICIENTS:	
Desflurane	0.42
Nitrous oxide	0.46
Sevoflurane	0.69
Isoflurane	1.46
Enflurane	1.9
Halothane	2.54

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

6. ANSWER: B

Both air and sulfur hexafluoride are injected into the eye by ophthalmologists to flatten the retina and promote healing in retinal detachment procedures. The presence of gas bubbles in the eye has a significant impact on the use of nitrous oxide, both for the anesthetic used during the initial procedure and for subsequent procedures in the near future.

Nitrous oxide is much more soluble than nitrogen in blood so it tends to diffuse from the blood into air-filled spaces such as bubbles in the eye. This can result in rapid expansion and increases in intraocular pressure. It is recommended that nitrous oxide be discontinued for 15 minutes prior to the placement of a gas bubble in the eye to prevent the bubble from expanding as a result of the nitrous oxide diffusion.

If air is used, the bubble will slowly decrease in size and be completely reabsorbed within 5 days of administration. Nitrous oxide should not be administered within 5 days of placement of an intraocular air bubble.

Sulfur hexafluoride, an inert gas, can be used by ophthalmologists instead of air to create a gas bubble in the eye. This gas is much less soluble in blood than nitrous oxide and also less soluble than nitrogen. Slowly over the first 24 hours after placement the bubble will expand as a result of nitrogen from the blood diffusing into the bubble more slowly than sulfur hexafluoride diffuses out of it. This process is very slow and does not result in a significant increase in intraocular pressure. Nitrous oxide administration, however, will result in rapid bubble expansion and increases in pressure. The sulfur hexafluoride bubble is not completely reabsorbed until 10 days after placement, so nitrous oxide administration should be avoided for this time period.

KEY FACTS: N_2O AND EYE SURGERY

- **Air** and **sulfur hexafluoride** can be injected into the eye to promote healing in retinal detachment procedures.
- Nitrous oxide is more soluble than both air and sulfur hexafluoride in the blood.
- Rapid increases in bubble **size** and **intraocular pressure** can occur with N_2O administration.
- **N_2O** should be **discontinued for 15 minutes prior** to the **placement of a gas bubble** in the eye to prevent the bubble from expanding as a result of the nitrous oxide diffusion.
- **Air:** completely reabsorbed within **5 days** of administration, so no N_2O for 5 days
- **Sulfur hexafluoride:** completely reabsorbed within **10 days** of administration, so no N_2O for 10 days

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

7. ANSWER: B

Somatosensory evoked potentials can be performed to assess the function of a patient's central nervous system after possible hypoperfusion or manipulation to either the spinal cord or spinal nerves during surgery. They are performed by applying electrical stimulation to peripheral nerves and recording the subsequent signal, which travels from the patient's peripheral nerve through the posterior column-medial lemniscus pathway and is measured at the patient's scalp.

The most common peripheral nerves that are stimulated include the posterior tibial nerve, median nerve, and ulnar nerve.

The two variables that are carefully analyzed during somatosensory evoked potential monitoring are the latency and amplitude of the waveform. Baseline waveforms are obtained at the onset of the case to compare subsequent waveforms. Increases in latency or decreases in amplitude from baseline indicate neurologic compromise.

The addition of inhalational anesthetics of more than 0.5 MAC can result in dramatic changes to the cortical component of the somatosensory waveform that include BOTH an increase in the latency of response and a decrease in the amplitude of the response. Both of these effects mimic the changes that are seen during episodes of neurologic dysfunction. For this reason it is important to limit inhalational anesthetics to less than 0.5 MAC, and to avoid any abrupt changes in inhaled concentrations of volatile anesthetics during somatosensory evoked potential monitoring.

KEY FACTS: INHALATIONAL ANESTHETIC EFFECTS ON SOMATOSENSORY EVOKED POTENTIALS (SSEPS)

- SSEPs are performed to assess intraoperative **neuronal pathway dysfunction**.

- An electrical stimulus is applied to peripheral nerves and recording electrodes are placed on the scalp
- The most common peripheral nerves that are stimulated include the **posterior tibial nerve**, **median nerve**, and **ulnar nerve**.
- **Increases in latency** or **decreases in amplitude** from baseline indicate neurologic compromise.
- Inhalational anesthetics at concentrations **greater than** 0.**5 MAC result in** decreases in amplitude and increases in latency.

ADDITIONAL READINGS

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8. ANSWER: D

Volatile anesthetics have several effects on ventilation during general anesthesia. As the anesthetic concentration rises, patients experience an increase in respiratory rate and a decrease in tidal volume that results in maintenance of near-normal minute ventilation.

Gas exchange progressively worsens with increasing anesthetic concentrations and $PaCO_2$ rises. This occurs despite minute ventilation being maintained, because dead-space ventilation increases compared to alveolar ventilation due to the decrease in tidal volume.

Functional residual capacity also decreases because patients experience an enhancement in expiratory muscle activity that causes both cephalad displacement of the diaphragm and inward displacement of the ribcage.

Volatile anesthetics blunt both the hypoxic respiratory drive and the hypercarbic respiratory drive.

KEY FACTS: VENTILATORY EFFECTS OF VOLATILE ANESTHETICS

- Increased RR
- Decreased VT
- Decreased FRC
- Increased dead-space ventilation/alveolar ventilation
- Increased $PaCO_2$
- Preserved minute ventilation
- Blunting of hypoxic respiratory drive
- Blunting of hypercarbic respiratory drive

ADDITIONAL READINGS

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9. ANSWER: B

Desflurane's vapor pressure of 660 mm Hg is very close to 760 mm Hg, which is the sea level atmospheric pressure at room temperature. This means that at sea level, desflurane is close to boiling even at room temperature. This fact causes even small changes in either gas temperature or barometric pressure to have a large impact on vaporizer output if desflurane was administered by either a standard measured-flow or variable-bypass vaporizer.

Special desflurane vaporizers have been developed to circumvent this problem. Desflurane is heated to 39 degrees Celsius to raise its partial pressure inside the vaporizer to approximately 1,500 mm Hg. This allows for accurate administration of desflurane despite fluctuations with both atmospheric temperature and pressure. The concentration of desflurane selected on the vaporizer dial will be the concentration of gas that is delivered to the patient.

At high elevations (low atmospheric pressure) the anesthesiologist must manually increase the set desflurane vaporizer concentration to ensure adequate anesthetic administration because the desflurane vaporizer will continue to output the same concentration of desflurane. At higher elevations, the partial pressure of the inhaled agent will be decreased; thus, an increase in the delivered concentration is required to achieve the same anesthetic effect. It is the partial pressure of the anesthetic gas that determines its effect on the patient, not the delivered concentration.

Fresh gas does not flow through the desflurane sump in this type of vaporizer, but instead the desflurane vapor is mixed with the fresh gas flow before it exits the vaporizer.

KEY FACTS: DESFLURANE VAPORIZER

- **Vapor pressure** of desflurane at room temperature is **660 mm Hg,** which is very close to sea level barometric pressure (760 mm Hg) at that same temperature.
- Desflurane is **heated** to 39 degrees Celsius to raise its **partial pressure to approximately 1,500 mm Hg** to ensure a consistent concentration of desflurane released from the vaporizer independent of changes in barometric pressure or temperature.

- **Desflurane vaporizer dial must be set HIGHER at higher elevations** to ensure the same anesthetic effect due to the decrease in partial pressure of the anesthetic gas delivered to the patient at lower barometric pressures.
- **Partial pressure is the important parameter physiologically, not the concentration delivered.**

ADDITIONAL READINGS

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10. ANSWER: B

Nitrous oxide is 34 times more soluble than nitrogen in blood. This means that it can diffuse from the blood into an air-filled cavity much more rapidly than nitrogen (the main component of air) can diffuse out of the space into the blood. This results in rapid expansion of either volume or pressure inside air-filled cavities when nitrous oxide is added to the administered anesthetic. If the air-filled area has a noncompliant wall, the pressure in the space will expand rather than the volume. If the cavity has a compliant wall, the size of the cavity will expand.

Air bubbles in the blood will expand more rapidly than air bubbles in a defined cavity, such as the middle ear. When in the blood nitrous oxide can diffuse directly into the air bubble, whereas in the middle ear, nitrous oxide has to cross several cell membranes prior to entering the air-filled cavity. The rate of increase of either the volume or pressure within an air-filled space is dependent on several factors, including the blood flow to the cavity, the alveolar partial pressure of nitrous oxide, and the duration of nitrous administration. Animal models demonstrate that the volume of a pneumothorax can double in size after 10 minutes of 75% nitrous administration.

KEY FACTS: CONTRAINDICATIONS TO NITROUS OXIDE USE

- Venous air embolism
- Pneumocephalus
- Pneumothorax
- COPD with blebs
- Acute intestinal obstructions
- Tympanic membrane grafting
- Intraocular procedures involving gas bubbles

ADDITIONAL READINGS

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11. ANSWER: E

Minimum alveolar concentration (MAC) is used to describe the potency of volatile anesthetics. It is defined as the alveolar concentration that will prevent 50% of patients from moving in response to a standard surgical stimulation. MAC can be affected by various pharmacologic and physiologic factors.

There is a roughly 6% decrease in MAC per decade of life, demonstrating that MAC decreases with age.

KEY FACTS: ALTERATIONS IN MAC

INCREASED MAC (POTENCY DECREASED)	**MAC UNAFFECTED** (POTENCY UNCHANGED)	**DECREASED MAC** (POTENCY INCREASED)
Young age	Hyperthyroidism	Hypothermia
Hyperthermia > 42 degrees C	Hypothyroidism	Hypoxia: $Pa_{O_2} < 40$ mm Hg
Hypernatremia	Gender	Hypercarbia: $Pa_{CO_2} > 90$ mm Hg
Acute amphetamine use	Duration of anesthetic	Hemoglobin < 4
Acute cocaine use	pH alterations	Severe hypotension
Chronic alcohol abuse		Elderly
Ephedrine		Pregnancy
		Acute alcohol intoxication
		Other medications:
		Barbiturates
		Benzodiazepines
		Cholinesterase inhibitors
		Clonidine
		Dexmedetomidine
		Ketamine
		Lithium

Local anesthetics
Methyldopa
Opioids
Pancuronium
Reserpine
Verapamil

ADDITIONAL READINGS

Eger EI, Saidman LJ, Brandstater B. Minimum alveolar anesthetic concentration: a standard of anesthetic potency. *Anesthesiology*. 1965;26(6):756–763.

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12. ANSWER: D

Emergence coincides with decreasing isoflurane brain partial pressures. There are three primary mechanisms that account for the elimination of inhalation anesthetics: exhalation, metabolism, and transcutaneous loss. There is essentially no transcutaneous elimination of isoflurane and only 0.2% is metabolized in the liver to produce trifluoroacetic acid. Most isoflurane elimination is a result of alveolar ventilation.

Isoflurane, along with the other volatile agents, continues to be absorbed by peripheral tissues such as adipose tissue once its administration is discontinued. This will occur until the alveolar partial pressure of the agent is less than the tissue partial pressure. This allows for a more rapid emergence than induction with inhalational anesthetics. If the administration of an inhalational agent continues for a long duration, the peripheral tissues can become saturated and this phenomenon of quicker emergence than induction does not occur because no further tissue uptake of agent can occur.

KEY FACTS: RECOVERY FROM ISOFLURANE

- Essentially no transcutaneous elimination of isoflurane
- Only 0.2% is metabolized in the liver by cytochrome P-450 to produce trifluoroacetic acid.
- Majority of isoflurane elimination is a result of **alveolar ventilation.**
- **Emergence is quicker than induction** because of volatile agent that continues to be absorbed by peripheral tissues during emergence.
- Administration over a long duration negates this phenomenon because tissues are saturated and no further tissue uptake can occur.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

13. ANSWER: D

Minimum alveolar concentration (MAC) is defined as the alveolar concentration that will prevent 50% of patients from moving in response to a standard surgical stimulation. The MAC values for different anesthetic agents administered at the same time are roughly additive. 1 MAC of nitrous oxide is 105%, so 53% divided by 105% is approximately 0.5 MAC of nitrous oxide. 1 MAC of isoflurane is 1.2%, so 0.9% divided by 1.2% is 0.75 MAC of isoflurane. Since MAC values are additive, 0.5 MAC of nitrous oxide plus 0.75 MAC of isoflurane equals 1.25 MAC.

KEY FACTS: MAC DEFINITION

- Minimum alveolar concentration (MAC) is defined as the alveolar concentration that will prevent 50% of patients from moving in response to a standard surgical stimulation.
- The MAC values for different anesthetic agents administered together are roughly additive.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

14. ANSWER: D

The uptake of anesthetics by the pulmonary circulation is dependent on the concentration gradient between the venous blood and the alveolar gas. This concentration gradient depends upon anesthetic uptake by the peripheral tissues, which are divided into four groups based on perfusion and solubility of the tissues.

The vessel-rich organs are the brain, heart, liver, kidneys, and endocrine system. They make up 10% of the body weight and receive 75% of the cardiac output. This tissue group is the first to become saturated with anesthetic agent due to its small volume and moderate solubility.

The muscle group, receiving 20% of the cardiac output, takes up inhalational agent much more slowly than the vessel-rich group because it has a greater volume: 50% of body weight. Its solubility is similar to the vessel-rich group. Uptake into the muscle group can last for hours.

The fat group receives only 6% of cardiac output, makes up 20% of total body weight, and has a high solubility for anesthetic agent, so it can have sustained uptake for days.

The vessel-poor group is 20% of body weight but receives minimal cardiac output, so uptake of inhalational agent is insignificant.

KEY FACTS: UPTAKE AND DISTRIBUTION OF VOLATILE ANESTHETICS

- **Vessel-rich organs:** brain, heart, liver, kidneys, endocrine system; **10% of the body weigh**t; receive **75% of the cardiac output**; small volume; moderate solubility; rapid saturation
- **Muscle group**: 50% of body weight; receives 20% of the cardiac output; continued uptake as a result of **greater volume**; uptake can last for **hours**
- **Fat group**: 20% of total body weight; receives 6% of cardiac output; high solubility for anesthetic agent so can have **sustained uptake for days**
- **Vessel-poor group**: 20% of body weight; minimal cardiac output; uptake is insignificant

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

15. ANSWER: A

Recovery from anesthesia is accomplished by lowering the concentration of anesthetics in the brain. Inhalational anesthetics are eliminated via exhalation, biotransformation, and transcutaneous loss. Transcutaneous loss of volatile anesthetics is very minimal. Exhalation accounts for the bulk of volatile anesthetic elimination.

There are several parameters that decrease the alveolar concentration of the inhalational agent and speed recovery from the inhaled anesthetic. These include decreased solubility of the anesthetic agent, low absorption by the anesthetic circuit, elimination of rebreathing, high fresh gas flows, increased ventilation, and increased cerebral blood flow.

Desflurane undergoes very little metabolism and less than 0.1% is actually eliminated in this manner. Desflurane is the most slowly eliminated inhaled anesthetic.

Only 0.2% of **isoflurane** is biotransformed into trifluoroacetic acid by the cytochrome P-450 isoenzymes.

5% to 8% of sevoflurane is metabolized by cytochrome P-450 isoenzymes. Fluoride ions can be produced and nephrotoxicity is possible, especially after long anesthetic durations.

Enflurane undergoes oxidative metabolism and may produce fluoride ions, which can lead to high-output renal failure.

Approximately 15% to 40% of halothane is broken down into trifluoroacetic acid, bromide, and chloride by the cytochrome P-450 isoenzymes. **Halothane** is more extensively metabolized than isoflurane and is thus eliminated more rapidly, even though isoflurane is less soluble. Reductive metabolism can also occur with halothane and is evident by elevated fluoride levels.

KEY FACTS: ELIMINATION OF INHALED ANESTHETICS

- Inhalational anesthetics are eliminated via exhalation, biotransformation, and transcutaneous loss.
- Percent Metabolized:
- Halothane 15% to 40%
- Sevoflurane 5% to 8%
- Isoflurane 0.2%
- Desflurane <0.1%
- **Desflurane** is the **most slowly metabolized** inhaled anesthetic.
- **Enflurane** metabolism can produce fluoride ions, which can lead to **high-output renal failure.**
- **Halothane** is eliminated more rapidly than isoflurane because it is more extensively metabolized than isoflurane.
- **Elevated fluoride** levels are indicative of **reductive metabolism of halothane.**

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

16. ANSWER: B

Boyle's law states that for an ideal gas at a stable temperature and fixed mass, the volume of a given quantity of gas is inversely proportional to its pressure.

$$\frac{P1}{V1} = \frac{P2}{V2}$$

This concept allows us to accurately estimate the volume remaining in a compressed gas cylinder using a known

pressure and volume and the current pressure. When an O_2 cylinder is full, it contains 625 L of oxygen at 2,000 psi.

$$\frac{2000 \text{ psi}}{625 \text{ L}} = \frac{500 \text{ psi}}{V2}$$

Solve for V2:

$$V2 = \frac{(500 \text{ psi})\ (625 \text{ L})}{2000 \text{psi}} = 156 \text{ L}$$

If the flow is set at 10 L/minute, then

$$\frac{156 \text{ L}}{10 \text{ L / min}} = 15.6 \text{ minutes}$$

Nitrous oxide exists as both a liquid and gas within the E cylinder, so its volume is not inversely proportional to its pressure. As nitrous oxide gas is expelled from the cylinder, the nitrous that exists as a liquid is vaporized to replace the volume of gas that has been released. This results in a constant pressure within the nitrous cylinder until ALL of the liquid is vaporized.

The pressure gauge of the N_2O cylinder will read a constant pressure of 750 psi until approximately 200-400 L (or 25%) of the original contents (1,590 L) remains. If the N_2O pressure gauge reads 750 psi, then you have between 200 L and 1,590 L of N_2O in the cylinder. The only accurate way to predict the volume remaining in the nitrous oxide cylinder is to weigh it.

E compressed gas cylinders can accumulate frost on the outside as a result of the absorption of heat inside the cylinders during either expansion of a compressed gas like oxygen or vaporization of a liquefied gas like nitrous oxide. Water vapor is most likely to accumulate as frost if flows from these tanks are high.

KEY FACTS: BOYLE'S LAW: VOLUME/ PRESSURE OF E CYLINDER

- **Boyle's law**: the **volume** of a given quantity of gas is **inversely proportional to its pressure**, given a constant temperature and amount.
- A full **O_2** cylinder contains **625 L** of oxygen at **2,000 psi.**
- **Nitrous oxide** is different because it exists as **both a liquid and gas** within the E cylinder.
- The N_2O cylinder pressure gauge will read a constant pressure of **750 psi** until approximately 200-**400 L (or 25%)** of the original **1,590 L** remains.
- E compressed gas cylinders can accumulate **frost** on the outside as a result of the **absorption of heat inside** the cylinders during:
  - Expansion of a compressed gas such as oxygen
  - Vaporization of a liquefied gas such as nitrous oxide

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

17. ANSWER: E

Carbon monoxide can accumulate during desflurane administration as a result of desflurane being degraded by dry CO_2 absorbent into carbon monoxide. Most of this accumulation occurred with the use of barium hydroxide lime, but it can also occur with other types of CO_2 absorbents. The best prevention against carbon monoxide poisoning is to discard desiccated CO_2 absorbents. Limiting fresh gas flow both during cases and between cases will minimize dehydration of the CO_2 absorbents. Carbon monoxide formation can also be seen with sevoflurane and isoflurane degradation in desiccated CO_2 absorbents.

High-output renal failure results from breakdown of methoxyflurane into inorganic fluoride. This causes dose-dependent vasopressin-resistant nephrotoxicity, most commonly seen if fluoride levels are greater than 50 micromoles per liter. Patients develop an inability to concentrate urine, polyuria, hypernatremia, and increased serum osmolarity.

Compound A (trifluoroethyl vinyl ether) is a nephrotoxic end product that results from the interaction of either sevoflurane or halothane with soda lime or barium hydroxide lime. Its accumulation is associated with long-duration anesthetics, low fresh gas flow, higher inhaled anesthetic concentrations, higher absorbent temperatures, and absorbent desiccation. It has been showed to be nephrotoxic in rats after prolonged exposure. Human studies have not shown an association between Compound A and postoperative elevation in serum creatinine levels. Current recommendations are to maintain fresh gas flows greater than 2 L/min to avoid rebreathing of Compound A. Halothane degradation by CO_2 absorbents can also result in the formation of Compound A.

Macrocytic anemia is caused by a deficiency in either vitamin B12 or folic acid that results in inhibition of DNA synthesis in red blood cell production. Nitrous oxide irreversibly oxidizes the cobalt atom in vitamin B12 and renders it inactive. Nitrous oxide results in the inhibition of all vitamin B12-dependent enzymes. Thymidylate synthetase, a vitamin B12-dependent enzyme, is required for DNA synthesis and methionine synthetase is required for myelin formation. Patients with exposure to nitrous oxide are thus at risk for bone marrow suppression, macrocytic anemia, and peripheral neuropathies. Due to interactions with DNA synthesis and the worry about possible teratogenic effects, nitrous should be avoided in pregnancy.

Fulminant hepatic necrosis and less severe hepatic dysfunction have been associated most frequently with

halothane exposure. Halothane undergoes both oxidative metabolism, leading to the formation of trifluoroacetic acid, and reductive metabolism, leading to the production of fluoride ions. The etiology of halothane-induced hepatic dysfunction is most likely a result of immune-mediated damage, but the exact mechanism is unclear. Fulminant hepatic necrosis is most likely in obese middle-aged women who are exposed to multiple halothane anesthetics in a short period of time (4 weeks). Children are less susceptible to developing halothane hepatitis. Although halothane hepatitis is the most tested, hepatic insufficiency can also occur with administration with halothane, sevoflurane, isoflurane, and desflurane.

KEY FACTS: VOLATILE ANESTHETIC TOXICITIES

- **Carbon monoxide** can accumulate due to **desflurane** degradation by **dry CO_2 absorbent,** especially **barium hydroxide**. This can also occur with sevoflurane and isoflurane. Avoid this by **discarding desiccated CO_2 absorbent.**
- **High-output renal failure** can result from **fluoride** levels greater than 50 micromoles per liter produced by methoxyflurane metabolism.
- **Compound A** accumulation results from **sevoflurane** degradation with soda lime or **barium hydroxide** lime. Ensure **fresh gas flows greater than 2 L/min** to avoid rebreathing of Compound A.
- **Macrocytic anemia** can be caused by **nitrous oxide** exposure because it **irreversibly oxidizes the cobalt atom in vitamin B12** and thus inhibits all vitamin B12-dependent enzymes. Nitrous oxide increases the risk of **bone marrow suppression, macrocytic anemia, and peripheral neuropathies**.
- **Fulminant hepatic necrosis** and less severe hepatic dysfunction have been associated with **halothane** exposure. It is most likely in **obese middle-aged women** who are exposed to multiple halothane **anesthetics in a short period** of time.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

18. ANSWER: B

To varying degrees, most volatile anesthetics cause amnesia, unconsciousness, analgesia, and immobility. The dose-related skeletal muscle relaxation resulting from inhalational anesthetics is primarily due to their effect on the spinal cord.

Nitrous oxide, however, is known to increase skeletal muscle tone.

Inhalational anesthetics also potentiate both succinylcholine and nondepolarizing muscle relaxants. Desflurane seems to result in the most potentiation of muscle relaxants compared to the other volatile anesthetics.

KEY FACTS: IMMOBILITY AND INHALATIONAL ANESTHETICS

- Skeletal muscle relaxation during inhalation anesthesia is primarily due to the anesthetic's action on the **spinal cord.**
- **Nitrous oxide**, however, is known to **increase skeletal muscle tone.**
- Volatile anesthetics **potentiate neuromuscular blockade,** with **desflurane** being the most potent.

ADDITIONAL READINGS

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

19. ANSWER: E

Nitrous oxide administration is associated with an increase in the cerebral metabolic rate for oxygen ($CMRO_2$). It also results in cerebral vasodilation, which causes an increase in cerebral blood flow (CBF). These effects can be overcome by the administration of propofol, barbiturates, or opioids when administering nitrous oxide. The increase in cerebral metabolic oxygen consumption is primarily seen when nitrous oxide is administered alone and not in conjunction with another volatile anesthetic.

Administration of all of the other inhalational anesthetic agents listed (halothane, isoflurane, sevoflurane, desflurane) will cause a DECREASE in cerebral metabolic oxygen consumption. Like nitrous oxide, however, they will cause cerebral vasodilation. Normally cerebral blood flow does not increase until concentrations exceed 1 MAC.

KEY FACTS: CEREBRAL EFFECTS OF NITROUS AND OTHER INHALATIONAL AGENTS

- Nitrous oxide, alone:
  - Increases $CMRO_2$
  - Increases CBF
  - Cerebral vasodilation

- Halothane, isoflurane, sevoflurane, desflurane:
  - Decrease CMR_{O2}
  - Increase CBF, if >1 MAC delivered
  - Cerebral vasodilation

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

20. ANSWER: D

When general anesthesia is utilized for a cesarean section, inhalational anesthetics are administered at approximately 0.5 MAC to decrease incidence of maternal recall. The inhalational agent concentration is minimized in an attempt to minimize bleeding as a result of agent-induced uterine relaxation and to minimize fetal exposure to the anesthetic. The placental transfer of volatile anesthetics is rapid because these agents have a low molecular weight, are nonionized, and are highly lipid soluble. The extent to which the fetus is exposed is dependent upon both the maternal blood concentrations of the agent (creating a larger maternal-to-fetus concentration gradient) and the duration of the exposure.

Fetal presentation of increased concentrations of volatile agents normally consists of hypotonia, decreased respiratory drive, and cardiac depression. Treatment is supportive, including assisted ventilation to exhale the anesthetic agents.

KEY FACTS: MATERNAL-FETAL EFFECTS OF INHALATIONAL ANESTHETICS

- At least 0.5 MAC of volatile anesthetic is routinely administered for general anesthesia in the obstetric patient for maternal **amnesia.**
- Volatile anesthetics transfer across the placenta rapidly because of:
  - Low molecular weight
  - Nonionized
  - High lipid solubility
- Minimize agent concentration to lessen uterine relaxation and to reduce fetal exposure to the anesthetic.
- Fetal presentation of anesthetic overdose includes **cardiopulmonary depression** and **hypotonia.**
- Treatment is supportive, including assisted ventilation to exhale the anesthetic agents.

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

21. ANSWER: E

Ischemic preconditioning is the concept that short episodes of ischemia prior to a larger insult will confer protection to the tissues and delay the onset of necrosis. Observations have been made that after the initial insult, there are two time periods during which the patient has cardioprotection. Initially this benefit lasts 1 to 2 hours after the brief period of ischemia. This passes, but later, between 24 hours and 3 days after ischemia, you get another period of time where if a second, more severe insult occurs, the myocardium has some protection from severe necrosis. Volatile anesthetics have been shown to cause pharmacologic preconditioning.

Inhalation anesthetics have several effects on the cardiovascular system that improve the oxygen supply-versus-demand ratio, including directly decreasing myocardial oxygen consumption, causing coronary vasodilation, and decreasing afterload, but none of these explains how these agents cause anesthetic preconditioning.

This mechanism involves activation of mitochondrial ATP-sensitive potassium channels, which ultimately results in decreased calcium levels in the myocyte and confers cytoprotection.

KEY FACTS: ANESTHETIC ISCHEMIC PRECONDITIONING

- **Ischemic preconditioning** describes short episodes of ischemia conferring protection against subsequent more severe episodes of ischemia.
- Volatile anesthetics can result in ischemic preconditioning.
- The mechanism involves activation of **ATP-sensitive potassium channels** that decrease calcium levels in the myocyte.

ADDITIONAL READINGS

Murray CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. *Circulation*. 1986;74:1124–1136.

Noma A. ATP–regulated K+ channels in cardiac muscle. *Nature*. 1983;305:147–148.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

22. ANSWER: D

Nitrous oxide is a colorless, odorless inhalational agent that is a gas at room temperature and ambient pressure. The critical temperature of N_2O is 36.5 degrees Celsius, which is above room temperature. The critical temperature of a substance is the temperature at and above which vapor of the substance cannot be liquefied, no matter how much pressure is applied.

Therefore, N_2O is a gas at room temperature, but it can be easily stored at room temperature as a liquid if enough pressure is applied. In the E cylinder, N_2O exists as both a liquid and a gas because of the pressure applied and the fact that the temperature is below its critical temperature. Oxygen has a critical temperature of minus 118 degrees Celsius, so it can only be stored as a liquid if it is pressurized at a temperature of less than minus 118 degrees Celsius.

In an E cylinder, nitrous oxide exists as both a liquid and gas because the cylinder is pressurized at a temperature that is below its critical temperature. Since both gas and liquid exist in the E cylinder, its volume is not inversely proportional to its pressure. As nitrous gas is expelled from the cylinder, the nitrous that exists as a liquid is vaporized to replace the volume of gas that has been released. This results in a constant pressure within the nitrous cylinder until ALL of the liquid is vaporized. The only reliable method of determining the volume in an E cylinder containing nitrous oxide is to weigh the cylinder. Once the liquid is depleted, the pressure in the cylinder will drop in proportion to the volume in accordance with Boyle's law.

KEY FACTS: N_2O PHYSICAL PROPERTIES: CRITICAL TEMPERATURE

- Nitrous oxide is a colorless, odorless **gas at room temperature** and ambient pressure.
- **Critical temperature** of **N_2O is 36.5** degrees Celsius.
- Critical temperature of a substance is the temperature at and above which vapor of the substance cannot be liquefied, no matter how much pressure is applied.
- N_2O can be easily stored **at room temperature as a liquid if enough pressure is applied.**
- In the E cylinder, N_2O exists as both a liquid and a gas because of the pressure applied and the fact that the temperature is below its critical temperature.
- Because both liquid and gas are contained in an E cylinder, the **only reliable method of determining the volume is to weigh the cylinder.**

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

23. ANSWER: B

The alveolar partial pressure of inhaled anesthetics is used as an indicator of anesthetic depth because it mirrors the anesthetic partial pressure in the brain. There are many factors that influence the alveolar partial pressure of a volatile anesthetic, but it is ultimately determined by the input of the anesthetic into the alveoli and the uptake of the anesthetic into the pulmonary veins. Transfer of volatile anesthetic from the anesthesia machine into the alveoli is based on the inspired partial pressure, alveolar ventilation, and characteristics of the anesthetic circuit. Uptake of the volatile agents into the pulmonary veins depends on cardiac output, solubility of the agent, and alveolar–venous partial pressure difference. Each of these variables is important in the rate of induction.

Increasing inspired partial pressure will increase the rate of induction by delivering more agent to the alveoli. Decreasing the inspired concentration will slow induction.

Increasing alveolar ventilation will increase the rate of induction. Hypoventilation will decrease the rate of induction.

Characteristics of the anesthetic breathing circuit will alter the rate of induction. A large anesthetic breathing circuit will slow the rate of induction, as will low gas inflow rates. Increased solubility of the inhalational agent into the plastic components of the breathing circuit will slow induction.

Increases in cardiac output cause more anesthetic agent to be taken up into the pulmonary veins, resulting in a decrease in the alveolar partial pressure and a slowing of induction. Decreases in cardiac output thus result in an increased rate of induction.

The solubility of the agent, known as its blood-gas partition coefficient, determines the amount of agent that leaves the alveoli by diffusing into the blood. An agent with a low solubility or low blood-gas partition coefficient will not diffuse readily into the blood, the alveolar partial pressure will remain elevated, and the rate of induction is quick. An anesthetic agent with a high blood-gas partition coefficient will diffuse readily into the blood, thus lowering the alveolar partial pressure and causing a slow induction. Hyperthermia will lower gas solubility and will speed induction.

The alveolar–venous partial pressure difference exists due to uptake of inhalational agents by the tissues. Tissues that are highly perfused (brain, heart, liver, kidneys) receive 75% of the cardiac output, and these tissues equilibrate rapidly with the arterial partial pressure. After about 6 to 12 minutes the alveolar–venous partial pressure gradient is very narrow.

Endobronchial intubation is a type of transpulmonary shunt that will slow the rate of induction because venous blood draining nonventilated alveoli will dilute the blood with a higher anesthetic partial pressure from the alveoli that are perfused. This slows induction with an insoluble anesthetic to a greater extent than it will for a soluble agent because with soluble agents the uptake of the agents will partially compensate for the dilutional effect that you see with this type of shunt. Right-to-left intracardiac shunts result in similar effects.

A left-to-right shunt will increase the anesthetic partial pressure in the blood flowing into the alveoli, but this has minimal effect on the overall speed of induction.

Changes with cardiac output and ventilation will have a greater effect on the rate of induction with soluble agents compared to insoluble agents.

KEY FACTS: RATE OF INDUCTION

	INCREASED PA = FASTER INDUCTION	DECREASED PA = SLOWER INDUCTION
Inspired Partial Pressure	High concentration	Low concentration
Alveolar Ventilation	Hyperventilation	Hypoventilation
Breathing Circuit	Small volume	Large volume
Cardiac Output	Decreased	Increased
Blood-Gas Coefficient	Insoluble	Soluble
Temperature/Gas Solubility	Hyperthermia	Hypothermia
Shunts	Transpulmonary	R-to-L intracardiac

- Left-to-right shunts have minimal effects on the speed of induction.
- Inductions with insoluble inhalational anesthetics will be more affected by transpulmonary and endobronchial shunts than soluble anesthetics, although inductions with both will be slowed.
- Changes in CO and alveolar ventilation will have a greater effect on induction times if soluble anesthetic gases are administered compared to insoluble ones.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Stoelting RK, Miller RD: *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

24. ANSWER: D

The depth of an anesthetic is indicated by the alveolar partial pressure of the anesthetic gas. The speed of induction parallels the rate of rise in the alveolar partial pressure compared to the inspired partial pressure. Many factors, such as cardiac output and solubility, affect the speed of induction.

A rise in cardiac output, as occurs in septic shock, results in more uptake of the anesthetic agent into the pulmonary veins, causing a decrease in the alveolar partial pressure. This decrease in alveolar partial pressure compared to inspired partial pressure results in a slowing of the rate of induction. Decreases in cardiac output will have the opposite effect. Less blood flow results in less uptake from the alveoli and an increase in alveolar partial pressure, which causes an increase in the induction rate.

The solubility of the agent also plays a role in the amount of uptake of an inhaled agent into the pulmonary vasculature. An agent with a low solubility will not diffuse readily into the blood, the alveolar partial pressure will remain elevated, and the rate of induction is quick. An anesthetic agent with a high blood-gas partition coefficient will diffuse readily into the blood, be washed away, and lower the alveolar partial pressure, causing a slow induction.

When comparing both of these variables at once, it is clear to see that changing the cardiac output will have a greater effect on the induction time if a soluble anesthetic agent is administered compared to an insoluble agent. Inhalational agents that are insoluble will have very little diffusion into the pulmonary blood compared to soluble agents, so the increases in cardiac output that occur with septic shock will cause more soluble anesthetic to be washed away relative to insoluble agents. Desflurane, being the least soluble agent in the list, will result in the greatest change in rate of induction.

KEY FACTS: VOLATILE AGENT UPTAKE AND THE EFFECT OF CARDIAC OUTPUT

- Induction times parallel the rate of rise in the alveolar partial pressure compared to the inspired partial pressure.
- A **rise in cardiac output**, as occurs in **septic shock**, results in more uptake of the anesthetic agent into the pulmonary veins, causing a decrease in the alveolar partial pressure and a **slowing of induction.**
- **Cardiac output changes** will have a greater **effect on the induction time** if a **soluble anesthetic agent** is administered compared to an insoluble agent.
- **Halothane** is the **most soluble volatile anesthetic agent.**

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

25. ANSWER: B

The oil-gas partition coefficient determines the potency of an inhaled anesthetic. This is inversely related to MAC, which is the minimum alveolar concentration that will prevent 50% of patients from moving in response to a standard surgical stimulation. If an agent has a high potency, it will have a low MAC and a high oil-gas partition coefficient.

An ideal anesthetic agent would have a high oil-gas partition coefficient (high potency) and a low blood-gas solubility coefficient (low solubility).

Inhalation agents in order of most to least potent are as follows: Methoxyflurane < Halothane < Isoflurane < Sevoflurane < Desflurane < N_2O.

KEY FACTS: MAC AND VOLATILE ANESTHETIC POTENCY

- **Oil-gas partition coefficient** determines the **potency** of an inhaled anesthetic.
- Oil-gas coefficient is inversely related to MAC.
- If an agent has a high **potency,** it will have a **low MAC** and a **high oil-gas partition coefficient.**
- Inhalation agents in order of most potent to least potent are as follows: **Methoxyflurane < Halothane < Isoflurane < Sevoflurane < Desflurane < N_2O.**

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

26. ANSWER: B

When administered at less than 1 MAC, desflurane rarely causes a change in either heart rate or mean arterial pressure, but when greater than 1 MAC is delivered, there is a linear, dose-related increase in heart rate.

When the concentration of desflurane is rapidly increased, an abrupt increase in both mean arterial pressure and heart rate is observed that coincides with increased plasma concentrations of epinephrine and norepinephrine. The mechanism for this is most likely an increase in release of these endogenous catecholamines, resulting in activation of the sympathetic nervous system.

This response can be reliably blunted with the administration of esmolol, clonidine, or fentanyl. This effect is also seen in isoflurane administration.

KEY FACTS: DESFLURANE PHARMACOLOGY

- Rapid increases in desflurane concentrations cause abrupt increases in HR and MAP.
- Mechanism: increase in release of these endogenous catecholamines, resulting in activation of the sympathetic nervous system
- Attenuated with esmolol, clonidine, or fentanyl administration
- Can also be seen with isoflurane

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

27. ANSWER: A

Long QT syndrome is a condition involving delayed repolarization following depolarization that results in prolongation of the QT interval to greater than 420 milliseconds. This syndrome is associated with ventricular arrhythmias (torsades de pointes and ventricular fibrillation) that can cause syncope and sudden death.

Inhaled anesthetics have been found to prolong the QT interval, placing any patient with underlying long QT syndrome at risk for clinical deterioration. No inhalational anesthetic has been shown to prevent further prolongation or arrhythmia, but it is recommended that sevoflurane be avoided in such patients.

Perioperative beta-blockade is thought to be the best mechanism to prevent fatal arrhythmias in these patients.

Amiodarone can induce prolonged QT syndrome. Lidocaine has been shown to diminish prolongations in the QT interval.

KEY FACT: INHALATIONAL ANESTHETICS AND LONG QT SYNDROME

- **Long QT syndrome** involves delayed repolarization following depolarization that results in prolongation of the QT interval to greater than **420 milliseconds.**
- Associated with ventricular arrhythmias (**torsades de pointes and ventricular fibrillation**) that can cause **syncope and sudden death**
- **Inhaled anesthetics** prolong the QT interval.
- **Avoid sevoflurane** in patients with long QT syndrome.
- Perioperative **beta-blockade** is the best prevention for fatal arrhythmias in these patients.

ADDITIONAL READINGS

Owczuk R, Wujtewicz MA, Sawicka W, et al. The effect of intravenous lidocaine on QT changes during tracheal intubation. *Anesthesia*. 2008;63(9):924–931.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

28. ANSWER: B

The time that is necessary for equilibration of inhaled anesthetic partial pressures between tissues can be predicted based on time constants.

$$\frac{\text{Inhaled anesthetic amount that can be dissolved by a tissue}}{\text{Time constant}} = \text{Tissue Blood Flow}$$

Time constants of inhaled anesthetics are based on each agent's brain-blood partition coefficient. The time constant for isoflurane is 4 minutes, whereas the time constants for sevoflurane and desflurane are 2 minutes.

It takes three time constants for complete equilibration of any tissue with the arterial partial pressure, so brain partial pressures will equal arterial partial pressures in 12 minutes for isoflurane (4 min × 3) and 6 minutes for sevoflurane or desflurane (2 min × 3).

KEY FACTS: TIME CONSTANTS

- Time constant is the amount of anesthetic agent dissolved by the tissue divided by tissue blood flow.
- Three time constants are required for complete equilibration.
- Sevoflurane: time constant is 2 minutes, so (2 × 3) = 6 minutes.
- Isoflurane: time constant is 4 minutes, so (4 × 3) = 12 minutes.

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

29. ANSWER: E

Second gas effect occurs when the uptake of one gas enhances the rate of rise of alveolar partial pressure of another gas that is administered at the same time. The second gas effect causes an acute increase in the arterial partial pressure of oxygen by 10% when nitrous oxide is initially administered. This is called alveolar hyperoxygenation.

Diffusion hypoxia results from significant volumes of nitrous oxide moving from the blood into the alveoli during the first several minutes after nitrous oxide is discontinued. This large volume of nitrous oxide can result in hypoxia by physically displacing oxygen in the alveoli. Prevention is best accomplished by 100% oxygen administration once the nitrous oxide is turned off.

Concentrating effect occurs when the absorption of one gas into the blood results in concentrating a second gas in the alveoli because loss of the first gas causes an overall decrease in alveolar volume. The same amount of gas within a smaller volume results in an increase in the concentration of the gas. Thus removal of one gas "concentrates" the second gas.

Concentration effect occurs during the initial phases of anesthesia induction when the inspired partial pressure of an anesthetic gas is so high that it causes the alveolar concentration of the gas to rise rapidly. The high inspired concentrations of gas offset the diffusion of inhaled agent into the blood. This results in a quicker induction. Thus, the greater the initial inhaled concentration of gas, the greater the rate of rise of FA/FI, and the quicker rate of induction.

KEY FACT: SECOND GAS EFFECT, CONCENTRATION EFFECT

- **Second gas effect** results from the uptake of a large volume of one gas resulting in an increased rate of rise of alveolar partial pressure of another co-administered gas.
- **Diffusion hypoxia** is when nitrous oxide enters the alveoli after it is discontinued and results in hypoxia by **physically displacing oxygen in the alveoli. Prevention** is best accomplished by **100% oxygen** administration once the nitrous oxide is turned off.
- **Concentrating effect** occurs when one gas is absorbed into the blood, resulting in a **smaller volume for the remaining gas to occupy** and thus "concentrating" the second gas.
- **Concentration effect** occurs when there is **a high inspired gas concentration** that offsets the diffusion of inhaled agent into the blood. The greater the initial inhaled concentration of gas, **the greater the rate of rise of FA/FI**, and the quicker rate of induction.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

30. ANSWER: C

The solubility of volatile agents is dependent on the blood-gas coefficient. This is the most important factor in determining the rate of induction and rate of recovery from inhalational agents.

KEY FACTS: SOLUBILITY OF INHALED ANESTHETICS

- The **blood-gas coefficient** of a volatile anesthetic indicates its **solubility.**
- This is the **most important determinant** in the rate of induction and recovery from inhalational anesthetics.
- High solubility → Greater uptake into blood → Lower alveolar partial pressure → Slower induction/recovery
- Low solubility → Less uptake into blood → Higher alveolar partial pressure → Faster induction/recovery

FROM LEAST SOLUBLE TO MOST SOLUBLE:	BLOOD-GAS PARTITION COEFFICIENT:
Desflurane	0.42
Nitrous oxide	0.46
Sevoflurane	0.69
Isoflurane	1.46
Enflurane	1.9
Halothane	2.54

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

31. ANSWER: D

Metabolism of volatile anesthetics plays a role in recovery but not induction or maintenance of inhalational anesthesia. There are three mechanisms of volatile anesthetic elimination: exhalation, metabolism, and transcutaneous loss. Exhalation accounts for the bulk of volatile anesthetic elimination, and transcutaneous loss is negligible. The extent of metabolism varies between the anesthetic agents.

KEY FACTS: METABOLISM

- Metabolism of volatile anesthetics plays a role in recovery
- Exhalation accounts for the bulk of volatile anesthetic elimination.
- Transcutaneous loss is negligible.
- The extent of metabolism varies between the anesthetic agents.

FROM LEAST METABOLIZED TO MOST:	% METABOLIZED:
Desflurane	<0.1
Isoflurane	0.2
Sevoflurane	5–8
Halothane	15–40

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

32. ANSWER: D

Mask induction in neonates is faster than in adults due to an increase in the ratio of minute ventilation to functional residual capacity. The increase in this ratio allows for an increase in alveolar ventilation that is nearly double the alveolar ventilation in adults. This also accounts for the increased rate of induction during pregnancy.

Increases in cardiac output and the presence of a right-to-left shunt would both decrease the rate of mask induction. Neonates have tidal volumes of approximately 6 mL/kg, which is equal to adult parameters.

KEY FACTS: INHALATIONAL INDUCTION IN NEONATES

- Both neonates and pregnant women experience an increased rate of inhalational induction as a result of an increase in minute ventilation to functional residual capacity ratio.

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

33. ANSWER: D

Modern vaporizers are calibrated to a specific agent's vapor pressure so if a vaporizer is filled with an agent that has a similar vapor pressure, its output would closely match the concentration selected on the dial.

INHALATIONAL ANESTHETICS	VAPOR PRESSURE: MM HG AT 20 DEGREES CELSIUS
Desflurane	670
Halothane	244
Isoflurane	240
Enflurane	172
Sevoflurane	160
Methoxyflurane	23

Since sevoflurane and enflurane have similar vapor pressures, they can be administered at accurate concentrations when filled into the other vaporizer. The same is true for both halothane and isoflurane. These volatile anesthetics can be used interchangeably.

If a vaporizer is filled with an anesthetic gas that has a greater vapor pressure than the gas it was originally calibrated for, the concentration delivered will be HIGHER

than expected by the dial. Examples include a sevoflurane vaporizer filled with desflurane, halothane, or isoflurane.

If a vaporizer is filled with an anesthetic gas that has a lower vapor pressure than the gas it was originally calibrated for, the concentration delivered will be LOWER than expected by the dial. An example includes a sevoflurane vaporizer filled with methoxyflurane.

KEY FACTS: VAPORIZER OUTPUT: VAPOR PRESSURE

- Modern vaporizers are **agent-specific** and calibrated to each volatile anesthetic's **vapor pressure.**
- Filling a modern vaporizer with an agent that has a similar vapor pressure results in the output being similar to the dialed concentration. **Sevoflurane and enflurane** have similar vapor pressures and can be used interchangeably. **Isoflurane and halothane** have similar vapor pressures and can be used interchangeably.

ADDITIONAL READINGS

Block FE Jr, Schulte GT. Observations on use of wrong agent in an anesthesia agent vaporizer. *J Clin Monit Comput*. 1999;15(1):57–61.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

34. ANSWER: B

Four variables are required to determine the flow rate of the carrier gas required to achieve a set vaporizer output.

$$\text{Vaporizer Output} = \frac{(\text{Carrier Gas Flow})(\text{Saturated Vapor Pressure of agent})}{(\text{Barometric Pressure}) - (\text{Saturated Vapor Pressure of agent})}$$

Vaporizer Output: 40 mL/min
Saturated Vapor Pressure: 160 mm Hg
Barometric Pressure at sea level: 760 mm Hg

$$40\,\text{mL/min} = \frac{(\text{Carrier Gas Flow})(160\,\text{mm Hg})}{(760\,\text{mm Hg}) - (160\,\text{mm Hg})}$$

$$= \frac{(\text{Carrier Gas Flow})(160\,\text{mm Hg})}{600\,\text{mm Hg}}$$

$$\frac{(40\,\text{mL/min})(600\,\text{mm Hg})}{160\,\text{mm Hg}} = \text{Carrier Gas Flow}$$

$$= 150\,\text{mL/min}$$

KEY FACTS: VAPORIZER OUTPUT

$$\text{VO} = \frac{(\text{CG flow})(\text{SVP agent})}{(\text{PB} - \text{SVP agent})}$$

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

35. ANSWER: D

Thymol is a preservative added to halothane that helps decrease the rate of spontaneous oxidative decomposition. Halothane is also stored in amber-colored bottles because ultraviolet light quickens its decomposition.

KEY FACTS: HALOTHANE: THYMOL

- **Thymol** is a preservative added to **halothane** that helps decrease the rate of spontaneous oxidative decomposition.
- Halothane is stored in amber-colored bottles.
- Ultraviolet light quickens the breakdown of halothane.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

36. ANSWER: B

Right-to-left intracardiac shunts and transpulmonary shunts ultimately result in dilution of arterial anesthetic partial pressure due to shunted blood containing no anesthetic agent being mixed with the blood that drains ventilated alveoli and contains some inhaled anesthetic agent. This dilutional effect will result in a slower induction.

The extent to which induction is slowed, however, is influenced by the solubility of the inhalational agent. The more insoluble the agent is, the more induction will be slowed by the presence of a right-to-left intracardiac shunt. With more soluble agents, more inhalational agent has been taken up by the blood, and this will partially compensate for the dilutional effect of the shunted blood. For insoluble agents, little agent is taken up by the blood so there is no compensation for the effects of dilution from the shunted blood.

KEY FACTS: INTRACARDIAC SHUNT AND INHALATIONAL UPTAKE

- **Right-to-left intracardiac shunts** and **transpulmonary shunts** (like endobronchial intubations) result in **SLOWING** of induction.
- **Insoluble agents** are more affected by this type of lesion than soluble agents.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

37. ANSWER: B

Nitrous oxide has a higher blood-gas solubility (0.46) compared to desflurane (0.42), but the rate of rise of FA/FI is quicker with nitrous oxide due to the concentration effect.

The concentration effect occurs during the initial phases of anesthesia induction when the inspired partial pressure of an anesthetic gas is so high that it causes the alveolar concentration of the gas to rise rapidly. The high inspired concentrations of gas offset the diffusion of inhaled agent into the blood. This results in a quicker induction. Thus, the greater the initial inhaled concentration of gas, the greater the rate of rise of FA/FI, and the quicker rate of induction.

Since nitrous oxide can be administered at a much higher inhaled concentration compared to desflurane, induction is faster.

KEY FACTS: CONCENTRATION EFFECT: DESFLURANE VS. N_2O ON FA/FI

- Blood-gas solubility of N_20 is 0.46 and that of desflurane is 0.42.
- Rate of rise of FA/FI is quicker in N_2O inhalation compared to desflurane.
- This is a result of the **concentration effect:** high initial inspired concentrations of gas offset the diffusion of the agent into the blood.
- The **greater the initial inhaled concentration of gas,** the **greater the rate of rise of FA/FI,** and the quicker rate of induction.
- Since nitrous oxide can be administered at a much higher inhaled concentration compared to desflurane, induction is faster.

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

38. ANSWER: A

Sevoflurane undergoes metabolism resulting in a temporary rise in serum fluoride concentrations, but it has not been associated with a renal concentrating defect. According to the "fluoride hypothesis," older halogenated agents such as methoxyflurane could cause nephrotoxicity and high-output renal insufficiency due to elevated and prolonged postoperative fluoride levels. This lack of toxicity despite high fluoride levels is thought to be due to sevoflurane's rapid elimination from the body as compared to older agents.

ADDITIONAL READING

Barash PG, Cullen BF Stoelting RK. *Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.

39. ANSWER: C

All of the potent volatile anesthetics serve as triggers for malignant hyperthermia in genetically susceptible patients, produce a dose-dependent decrease in uterine smooth muscle contractility and blood flow, and increase respiratory rate. Volatile anesthetics decrease the tidal volume of spontaneously ventilating patients and decrease the normal ventilatory response to hypoxia and hypercapnia.

KEY FACTS: VENTILATORY EFFECTS OF VOLATILE ANESTHETICS

- Increased RR
- Decreased VT
- Decreased FRC
- Increased dead-space ventilation/alveolar ventilation
- Increased $PaCO_2$
- Preserved minute ventilation
- Blunting of hypoxic respiratory drive
- Blunting of hypercarbic respiratory drive

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK. *Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.

Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

40. ANSWER: D

All volatile anesthetics, as well as nitrous oxide, cause dose-dependent decreases in tidal volume and decrease in

ventilatory responses to CO_2 and hypoxia. Nitrous oxide depresses myocardial contractility in vitro, but in vivo increases in catecholamine release and sympathetic tone result in unchanged or slightly increased CO, heart rate, and arterial blood pressure. Nitrous oxide does not act as a trigger for malignant hyperthermia.

ADDITIONAL READINGS

Barash PG, Cullen BF Stoelting RK. *Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

MHAUS website, http://www.mhaus.org/index.cfm/fuseaction/OnlineBrochures.Display/BrochurePK/8AABF3FB-13B0-430F-BE20FB32516B02D6.cfm. (Accessed July 20, 2011.)

41. ANSWER: B

Minimum alveolar concentration (MAC) is used to describe the potency of volatile anesthetics. The MAC of an inhaled anesthetic is the alveolar concentration that prevents movement in 50% of patients in response to a standardized stimulus (e.g., surgical incision). Roughly 1.3 MAC (e.g., 2% × 1.3 = 2.6% sevoflurane) will prevent movement to surgical stimulus in 95% of patients. MAC is inversely proportional to the lipid solubility (or oil-gas coefficient) of volatile agents. MAC is a useful measure because it mirrors brain partial pressure, allows comparisons of potency between agents, and provides a standard for experimental evaluations.

KEY FACTS: MINIMUM ALVEOLAR CONCENTRATIONS OF VARIOUS VOLATILE AGENTS

- Higher MAC indicates a lower potency of the volatile anesthetic:

Nitrous oxide	105
Desflurane	6
Sevoflurane	2
Isoflurane	1.2
Enflurane	1.7
Halothane	0.75
Methoxyflurane	0.16

ADDITIONAL READINGS

Eger EI, Saidman LJ, Brandstater B. Minimum alveolar anesthetic concentration: a standard of anesthetic potency. *Anesthesiology*. 1965;26(6):756–763.

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

42. ANSWER: E

MAC is a useful measure because it mirrors brain partial pressure, allows comparisons of potency between agents, and provides a standard for experimental evaluations. MAC values for different anesthetics are roughly additive. For instance, 0.5 MAC of sevoflurane (1%) and 0.5 MAC of nitrous oxide (52%) demonstrate a similar amount of CNS depression as 1.0 MAC of isoflurane (1.2%). MAC represents only one point on the dose–response curve: it is the equivalent of median effective dose (ED_{50}). MAC of 0.3 to 0.4 is associated with awakening from anesthesia (MAC awake).

KEY FACTS: MULTIPLES OF MAC

- MAC: prevents movement in response to surgical stimulation in 50% of patients
- 1.3 MAC: prevents movement in response to surgical stimulation in 95% of patients
- 0.3–0.4 MAC: associated with awakening from anesthesia
- 1.5–1.7 MAC: MAC-BAR = the concentration required to block autonomic reflexes to surgical stimulation

ADDITIONAL READINGS

Eger EI, Saidman LJ, Brandstater B. Minimum alveolar anesthetic concentration: a standard of anesthetic potency. *Anesthesiology*. 1965; 26(6):756–763.

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

43. ANSWER: D

Minimum alveolar concentration (MAC) is used to describe the potency of volatile anesthetics. It is defined as the alveolar concentration that will prevent 50% of patients from moving in response to a standard surgical stimulus. MAC can be affected by various pharmacologic and physiologic factors.

There is a roughly 6% decrease in MAC per decade of life, showing that MAC decreases with age.

KEY FACTS: ALTERATIONS IN MAC

INCREASED MAC (POTENCY DECREASED)	MAC UNAFFECTED (POTENCY UNCHANGED)	DECREASED MAC (POTENCY INCREASED)
Young age	Hyperthyroidism	Hypothermia
Hyperthermia >42 degrees C	Hypothyroidism	Hypoxia: Pao_2 < 40 mm Hg

Hypernatremia	Gender	Hypercarbia: $PaCO_2 > 90$ mm Hg
Acute amphetamine use	Duration of anesthetic	Hemoglobin < 4
Acute cocaine use	pH alterations	Severe hypotension
Chronic alcohol abuse		Elderly
Ephedrine		Pregnancy
		Acute alcohol intoxication
		Other medications
		- Barbiturates
		- Benzodiazepines
		- Cholinesterase inhibitors
		- Clonidine
		- Dexmedetomidine
		- Ketamine
		- Lithium
		- Local anesthetics
		- Methyldopa
		- Opioids
		- Pancuronium
		- Reserpine
		- Verapamil

ADDITIONAL READINGS

Eger EI, Saidman LJ, Brandstater B. Minimum alveolar anesthetic concentration: a standard of anesthetic potency. *Anesthesiology*. 1965;26(6):756–763.

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

44. ANSWER: E

Minimum alveolar concentration (MAC) is defined as the alveolar concentration that will prevent 50% of patients from moving in response to a standard surgical stimulation. MAC is a useful measure because it mirrors brain partial pressure, allows comparisons of potency between agents, and provides a standard for experimental evaluations. MAC values for different anesthetics are roughly additive. For instance, 0.5 MAC of sevoflurane (1%) and 0.5 MAC of nitrous oxide (52%) demonstrate a similar amount of CNS depression as 1.0 MAC of isoflurane (1.2%).

KEY FACTS: MAC OF VARIOUS VOLATILE AGENTS

- Higher MAC indicates a lower potency of the volatile anesthetic:

Nitrous oxide	105
Desflurane	6
Sevoflurane	2
Isoflurane	1.2
Enflurane	1.7
Halothane	0.75
Methoxyflurane	0.16

ADDITIONAL READINGS

Eger EI, Saidman LJ, Brandstater B. Minimum alveolar anesthetic concentration: a standard of anesthetic potency. *Anesthesiology*. 1965;26(6):756–763.

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

45. ANSWER: B

Desflurane has the highest vapor pressure of the volatile anesthetics (681 mm Hg at 20 degrees C). The vapor pressure of desflurane is so high that it boils at room temperature at high altitudes, necessitating the use of a special heated vaporizer. The low solubility of desflurane in blood is the reason for its rapid wash-in and wash-out, affording the anesthetist tighter control over anesthetic levels. This is due to desflurane's blood-gas partition coefficient of 0.42, the lowest of the volatile anesthetics. Desflurane is 17 times more potent than nitrous oxide, but only roughly one-fourth as potent as the other volatile agents. Pungency and airway irritation during desflurane induction make it poorly suited for inhalational inductions.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

46. ANSWER: B

All volatile anesthetics increase respiratory rate and decrease tidal volume. Most modern volatile anesthetics are very pungent and broncho-irritating, making coughing, breath-holding, salivation, and laryngospasm likely during an inhalational induction. Sevoflurane is the exception, and it is the

preferred agent for inhalational inductions. Volatile anesthetics all decrease systemic vascular resistance, and all are cardio-depressants to a degree, especially at high doses. All volatile anesthetics cause dose-dependent muscle relaxation, and can potentiate and prolong the action of neuromuscular blocking agents.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

47. ANSWER: C

Closed-circuit anesthesia relies on rebreathing of anesthetic gases and oxygen to maintain low flow rates. Rebreathing conserves both heat and humidity and decreases the amount of waste anesthetic gases, thus lowering pollution. As flow rates are a major determinate of volatile anesthetic cost, the ability to use a lower flow rate during closed-circuit anesthesia affords a less expensive anesthetic. Closed-circuit anesthesia requires a high level of vigilance in order to avoid hypoxia and hypercapnia and to maintain a proper anesthetic dose. As flows are low, adjustments to the anesthetic concentration will take longer. Closed-circuit anesthesia also may require special equipment as some ventilators will not deliver low flows for safety reasons.

KEY FACTS: ADVANTAGES OF CLOSED-CIRCUIT AND/OR LOW-FLOW ANESTHESIA

- Conserves heat
- Conserves humidity
- Lowers anesthetic pollution
- Lowers anesthetic cost
- Allows early detection of circuit leaks

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

48. ANSWER: E

Halothane is the most potent volatile anesthetic in current usage, with a MAC of 0.75. Halothane causes a dose-dependent decrease in blood pressure and cardiac output. This is due primarily to direct myocardial depression and may be accentuated by slowing of sinoatrial node conduction resulting in bradycardia or junctional rhythms (especially in infants). Despite halothane being a coronary artery vasodilator, coronary blood flow actually decreases due to the drop in systemic pressure. Halothane sensitizes the heart to the arrhythmogenic effects of epinephrine, and doses exceeding 1.5 ug/kg should be avoided.

KEY FACTS: CARDIAC EFFECTS OF HALOTHANE

- Decreases MAP by direct cardiac depression and thus a **decrease in CO** but not a decrease in SVR
- Unchanged HR due to **blunting of baroreceptor reflex** that decreases the vagal response to hypotension
- **Decreased myocardial oxygen consumption** because it depresses the myocardium
- Slows conduction through SA node, predisposing patients to **junctional arrhythmias** and **bradycardia**
- Arrhythmias can result from **sensitization of the myocardium to catecholamines**

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

49. ANSWER: A

Halothane is a potent inhibitor of the body's ventilatory response to hypoxia. Hypoxic drive is severely depressed by concentrations of halothane as low as 0.1 MAC.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

50. ANSWER: C

General anesthesia has multiple effects on pulmonary gas exchange. These include increased intrapulmonary shunting, increased dead space, hypoventilation, and inhibition of hypoxic pulmonary vasoconstriction. Various interventions may counteract these effects so as to prevent or correct hypoxemia. PEEP increases FRC and decreases intrapulmonary shunting (remember that shunt is perfusion

without ventilation) by helping to open and maintain the patency of alveoli. The benefits of decreasing shunt outweigh the increase in dead space that PEEP will cause. Too much PEEP can decrease cardiac output however, and a low cardiac output accentuates the effect of shunting on O_2 tensions.

KEY FACTS: GENERAL ANESTHETIC EFFECTS ON PULMONARY GAS EXCHANGE:

- Increases intrapulmonary shunting (largely due to a 15% to 20% reduction in FRC)
- Increases dead space
- Causes hypoventilation/Increases apneic threshold
- Inhibits hypoxic pulmonary vasoconstriction in high doses (>2 MAC)

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

51. ANSWER: B

The cardiovascular effects of desflurane are similar to those of isoflurane, albeit with a greater (though transient) heart rate increase with rapid increases in concentration. Desflurane lowers MAP and minimally depresses myocardial contractility, but an increase in HR along with a decrease in SVR (and the consequent lowered pressure against which the heart must pump) helps to preserve cardiac output (Table 1.1).

ADDITIONAL READINGS

Barash PG, Cullen BF Stoelting RK. *Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.
Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Table 1.1 CARDIOVASCULAR EFFECTS OF VOLATILE ANESTHETICS

	MAP	CO	SVR	HR	O_2 CONSUMPTION
Desflurane	↓↓	↑/↓	↓↓	↑↑	↓
Isoflurane	↓↓	↑/↓	↓↓	↑	↓
Sevoflurane	↓	↓	↓	↑/↓	↓
Halothane	↓	↓	↑/↓	↑/↓	↓↓

52. ANSWER: B

The anesthetic goals of mitral regurgitation are to maintain or increase heart rate and to maintain or decrease SVR. Halothane has minimal effects on SVR, while the other volatile anesthetics tend to decrease SVR. Halothane maintains or causes a dose-dependent decrease in HR, while agents such as desflurane and isoflurane increase heart rate and are preferable in this instance.

ADDITIONAL READINGS

Barash PG, Cullen BF Stoelting RK. *Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.
Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

53. ANSWER: E

All of the volatile anesthetics cause some degree of dose-dependent myocardial depression. **Many individuals do not understand that nitrous oxide has myocardial depressant properties**. When nitrous oxide is given to patients with heart disease, especially in combination with opioids, it can cause lowered blood pressure and cardiac output. Despite depressed myocardial contractility, changes are not usually seen in healthy patients due to N_2O's stimulation of catecholamines.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Tempe D, Mohan JC. Myocardial depressant effect of nitrous oxide after valve surgery. *Eur J Anaesthesiol*. 1997;14(6):672.

54. ANSWER: C

Because nitrous oxide is 35 times more diffusible than nitrogen, it diffuses into air-containing cavities more rapidly than nitrogen can be absorbed back into the bloodstream. This causes either increased volume or pressure in air-filled structures or bubbles, with consequent negative effects. The higher the partial pressure of nitrous oxide, the greater the volume expansion or pressure generated. Seventy-five percent N_2O will double the size of a pneumothorax in 10 minutes. N_2O use has caused blindness after certain types of eye surgery, and hearing loss after certain types of ear surgery.

KEY FACTS: NITROUS OXIDE CONTRAINDICATIONS

- Bowel obstruction: Obstructed bowel is a closed space.
- Emphysema: Blebs can accumulate N_2O and burst.
- Air embolism: If suspected, turn off N_2O immediately.
- Eye surgery when intraocular gases are used: Expansion of gas bubble can cause blindness.
- Middle ear surgery: Accumulation can dislodge a tympanic graft after tympanoplasty.
- Chest wall or head trauma: N_2O can ↑ pneumothorax or ↑ ICP respectively.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Yang YF, Herbert L. Nitrous oxide anaesthesia in the presence of intraocular gas can cause irreversible blindness. *BMJ*. 2002; 325:532–533.

55. ANSWER: D

The potential for ***carbon monoxide (CO) toxicity*** due to the degradation of volatile anesthetics, particularly desflurane, by desiccated carbon dioxide absorbents is well established. Cases occur most typically after periods of ventilator inactivity, commonly on Monday mornings. The affinity between hemoglobin and carbon monoxide is approximately 230 times stronger than that between hemoglobin and oxygen. This decreases the oxygen-carrying capacity of the blood and inhibits the transport, delivery, and utilization of oxygen by the body, causing the many symptoms of CO poisoning.

Diagnosis can be difficult unless CO toxicity is suspected and specifically looked for. This is because symptoms of CO poisoning under anesthesia (hypotension, tachycardia, drops in SpO_2), can mimic other problems. Furthermore, the drops in SpO_2 may be minimal. Pulse oximetry employs two wavelengths of light, 940 nm and 660 nm. An algorithm estimates the oxygen saturation based on this differential absorption. **Pulse oximetry is not adequate to diagnose CO poisoning because COHb and oxyHb both absorb at 660 nm with the same absorption coefficient**. The pulse oximeter therefore overestimates arterial hemoglobin saturation. A co-oximeter or spectrophotometer measures light absorbance at six or more discrete wavelengths. Using the known absorbance spectra of the various hemoglobin species, the co-oximeter calculates the concentration of each species and reports the percentages of reduced, oxygenated, carboxy, and methemoglobin. The **co-oximeter is therefore the test of choice for diagnosis of CO poisoning**. Arterial blood gas measurements may show a metabolic acidosis in severe CO poisoning, but this is a late and nonspecific indicator. Even though the pulse oximeter overestimates arterial hemoglobin saturation, one should definitely include CO poisoning in the differential diagnosis of decreasing intraoperative blood pressure and SpO_2, especially with a history of ventilator inactivity.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

Reddy A, Lasher SC, Fuhrman TM. Carbon monoxide poisoning and SpO_2: a case report. *Internet Journal of Anesthesiology*. 2005;10(1). http://www.ispub.com/journal/the-internet-journal-of-anesthesiology/volume-10-number-1/carbon-monoxide-poisoning-and-spo2-a-case-report.html

56. ANSWER: B

All volatile anesthetics impair brain autoregulation and "uncouple" cerebral blood flow and $CMRO_2$, increasing CBF while decreasing $CMRO_2$. Normally $CMRO_2$ and CBF rise and fall together so as to accommodate escalations and declines in brain O_2 requirements. The inherent danger is that in a patient with elevated intracranial pressure, the use of volatile anesthetics can further increase ICP.

Isoflurane has long been favored for neuroanesthesia because it decreases $CMRO_2$ more than the other volatile agents. At concentrations greater than 2 MAC isoflurane produces an electrically silent EEG. This EEG suppression may provide a degree of protection from cerebral ischemia. Isoflurane is thought by many to increase CSF absorption, which can help to lower ICP in patients with decreased intracranial compliance. It is the only volatile agent with a net favorable effect on CSF dynamics. Finally, though all volatile agents increase CBF, these effects can be attenuated via simultaneous hyperventilation when isoflurane is used. The advantages of decreased O_2 requirements to the point of EEG silence, ICP lowering through impacts on CSF, and the ability to mitigate increases in CBF via hyperventilation make isoflurane the agent of choice in neurosurgical patients with suspected elevated ICP.

KEY FACTS: EFFECTS OF VOLATILE ANESTHETICS ON THE CNS

- Uncoupling of CBF and $CMRO_2$
- Increased CBF (attenuated by hyperventilation, particularly with isoflurane)
- Decreased $CMRO_2$
- Decreased EEG amplitude and increased latency at concentrations >1%
- Increased CSF absorption (with isoflurane only)
- Burst suppression of EEG (only at >2 MAC isoflurane and >4 MAC halothane)

ADDITIONAL READINGS

Miller R. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2005
Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

57. ANSWER: D

Nitrous oxide is extremely insoluble in blood. If it is abruptly discontinued following maintenance of anesthesia, rapid diffusion from the blood into the alveoli can decrease O_2 tension in the lung. This phenomenon is called diffusion hypoxia and can lead to brief periods of decreased O_2 concentration and SpO_2 readings. To prevent diffusion hypoxia 100% O_2 should be administered for 5 to 10 minutes after abrupt discontinuation of N_2O. The timing of the discontinuation of N_2O, the fact that it was replaced with air and not 100% O_2, and the mild drop in SpO_2 readings make "D" the best answer.

The second gas effect describes an abrupt rise in concentration and FA/FI of an accompanying anesthetic during induction with N_2O that is due to a rapid absorption of N_2O from the alveoli.

Hypoxic pulmonary vasoconstriction (HPV) describes an increase in pulmonary vascular resistance in atelectatic lung areas. By shifting blood flow to better-ventilated areas of the lung, HPV optimizes overall gas exchange.

ADDITIONAL READINGS

Duke J. *Anesthesia Secrets*. 3rd ed. Philadelphia, PA: Mosby; 2006.
Miller R. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2005.
Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

58. ANSWER: C

Ventilation is controlled by the interaction of both central and peripheral receptors that respond to changes in Pa_{O_2}, Pa_{CO_2}, pH, and pulmonary stretch. Volatile anesthetics result in a dose-dependent decrease in the response of both the hypercarbic and hypoxemic ventilatory drives.

The carotid bodies are the primary peripheral chemoreceptors that sense changes in Pa_{O_2}, Pa_{CO_2}, pH, and arterial perfusion pressure. The carotid bodies interact with the central respiratory centers through the glossopharyngeal nerves. The carotid bodies are most sensitive to changes in Pa_{O_2} and are the primary way that inhalational anesthetics act to decrease the ventilatory drive to hypoxemia.

Stretch receptors in the lungs act to sense distention and decrease the respiratory drive. Impulses are carried along the vagus nerve, and this does not play a very large role in controlling the respiratory drive in humans.

The dorsal and ventral neurons in the medulla determine basic respiratory rhythm. The dorsal group controls inspiration, and the ventral group determines expiration. Inhalational agents have little effect on these areas of respiratory control.

KEY FACTS: VOLATILE ANESTHETICS AND RESPONSE TO HYPOXEMIA

- Ventilation is controlled by the interaction of both **central and peripheral receptors** that respond to changes in **Pa_{O_2}, Pa_{CO_2}, pH, and pulmonary stretch.**
- **Volatile anesthetics** result in a **dose-dependent decrease** in the response of both the hypercarbic and hypoxemic ventilatory drives.
- The **carotid bodies** are most sensitive to changes in **Pa_{O_2}** and are the primary way that inhalational anesthetics act to decrease the ventilatory drive to hypoxemia.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

59. ANSWER: A

The oil-gas partition coefficient determines the potency of an inhaled anesthetic. The oil-gas coefficient for nitrous oxide is low, indicating its low potency. MAC is inversely related to potency. The MAC of nitrous oxide is 104%, which cannot actually be delivered to a patient because it is greater than 100%. Thus it is the low oil-gas coefficient, the low potency, and the high MAC of nitrous that preclude its use as a sole anesthetic agent.

The critical temperature of N_2O (36.5 degrees Celsius) accounts for the reason that nitrous oxide can be stored as both a liquid and a gas under pressure at room temperature. This is the reason that nitrous oxide cylinders must be weighed to determine their volume.

Nitrous has been found to be useful in dental procedures because it can, even at low MAC, result in significant analgesia.

KEY FACTS: NITROUS OXIDE, NOT A SOLE INHALED AGENT

- Nitrous oxide's **low oil-gas coefficient** indicates its **low potency.** It is the low oil-gas coefficient, the low potency, and the **high MAC** of nitrous that preclude its use as a sole anesthetic agent.

- The **critical temperature of N_2O** (36.5 degrees Celsius) accounts for the reason that nitrous oxide can be stored as both a liquid and a gas under pressure at room temperature. This is the reason that **nitrous oxide cylinders must be weighed to determine their volume.**
- Nitrous has been found to be useful in dental procedures because it can, even at low MAC, result in significant **analgesia.**

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

60. ANSWER: D

It has been well documented that the MAC of inhalational agents is higher in infants compared to adults. The MAC rises during the first year of life and progressively declines (6% per decade) over the remainder of the patient's lifetime. The mechanism is unknown.

Children are at an increased risk of volatile anesthetic overdose because of the increased speed of induction compared to adults. This increase in induction rate is a result of the increased ratio of minute ventilation to functional residual capacity in addition to the lower blood-gas coefficient of inhalational agents in children. Children have a similar tidal volume based on weight compared to adults.

Halothane hepatitis is most likely in obese middle-aged women who are exposed to multiple halothane anesthetics in a short period of time. Children are less susceptible to developing this problem.

KEY FACTS: INHALATION AGENTS: CHILDREN VS. ADULTS

- **MAC** of inhalational agents is **higher in infants** compared to adults.
- MAC rises during the first year of life and progressively declines at a rate of **6% per decade;** mechanism is unknown.
- **Children** are at an increased risk of volatile anesthetic o**verdose** because of the **increased speed of induction** compared to adults.
- Increase in induction rate is a result of the increased **ratio of minute ventilation to functional residual capacity** in addition to the **lower blood-gas coefficient** of inhalational agents in children.
- **Halothane hepatitis** is most likely in obese middle-aged women who are exposed to multiple halothane anesthetics in a short period of time. **Children are less susceptible** to developing this problem.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

61. ANSWER: B

Elderly patients experience an exaggeration in the cardiac depression that is seen with volatile anesthetics. This is important because inhalational agents must be carefully titrated in elderly patients because they often have little cardiac reserve. Careful titration is also important due to the reduction in MAC seen with aging. MAC decreases by 6% for every decade of life.

Decreased pulmonary and hepatic function and an increased volume of distribution account for the prolonged recovery after inhalational anesthetic administration seen in elderly patients. Elderly patients also develop less of a tachycardic response to inhaled agents such as desflurane and isoflurane. Cerebral metabolic oxygen consumption is decreased during inhalational anesthetic administration in patients of all ages.

KEY FACTS: INHALED ANESTHETICS: THE EFFECTS OF AGING

- **Exaggeration** in **cardiac depression** with inhaled agents
- MAC decreases by 6% for every decade of life.
- **Prolonged recovery** after inhalational anesthetic administration due to decreased pulmonary function, decreased hepatic function, increased volume of distribution
- **Less tachycardia** with inhaled agents such as desflurane and isoflurane

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

62. ANSWER: A

Inhaled anesthetic agents tend to potentiate the muscle relaxation that is caused by nondepolarizing muscle relaxants with desflurane providing the most potentiation. Administration of inhaled agents decreases the required doses of nondepolarizers by about 15%.

KEY FACTS: MUSCLE RELAXATION WITH INHALED AGENTS

- Administration of inhaled agents decreases required doses of nondepolarizers by about 15%.

- In order from greatest potentiation to least potentiation: Desflurane > Sevoflurane > Isoflurane > Enflurane > Halothane > Nitrous oxide

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

63. ANSWER: E

Sevoflurane is an inhaled anesthetic with widespread use due to its moderate potency and low solubility. It is an excellent choice for inhaled inductions in both adults and children because of its low blood-gas solubility and due to the fact that it is not pungent and does not cause airway irritation. Sevoflurane, like the other inhaled anesthetic agents, has widespread effects on most organ systems. It results in a decrease in systemic vascular resistance that leads to a decrease in cardiac output. It causes an increase in cerebral blood flow and a decrease in cerebral metabolic oxygen consumption. It is a potent bronchodilator and results in decreases in glomerular filtration rate and portal vein blood flow.

KEY FACTS: SEVOFLURANE PHARMACOLOGY

- Moderate potency and low solubility
- Excellent for inhalational inductions: **nonpungent** and **low blood-gas solubility**
- **Decreased systemic vascular resistance** that leads to a decrease in cardiac output
- **Increased cerebral blood flow**
- **Decreased cerebral metabolic oxygen consumption**
- **Potent bronchodilator**
- **Decreased glomerular filtration rate and portal vein blood flow**

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

64. ANSWER: D

Desflurane, sevoflurane, and isoflurane all result in a decrease in mean arterial pressure by causing a decrease in systemic vascular resistance. Halothane decreases mean arterial pressure through myocardial depression and a decrease in cardiac output. Nitrous oxide has little effect on systemic vascular resistance. Isoflurane administration results in a large increase in skeletal muscle blood flow, and it is this redistribution of the cardiac output that results in the decline of systemic vascular resistance.

KEY FACTS: SVR, INHALED AGENTS

- Desflurane, sevoflurane, and isoflurane: decrease SVR and MAP
- Halothane: decreases MAP by myocardial depression and decreases CO
- Nitrous oxide: no change in SVR, has little effect on systemic vascular resistance
- Isoflurane: decreases SVR due to large increase in skeletal muscle blood flow

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

65. ANSWER: E

This patient most likely has pulmonary hypertension as a result of the chronic obstructive sleep apnea. Normal mean pulmonary arterial pressures are 12 to 16 mm Hg. Pulmonary hypertension is defined as a mean pulmonary artery pressure greater than 25 mm Hg. Pulmonary hypertension is seen in 20% to 40% of patients with obstructive sleep apnea.

Most volatile anesthetics have minimal effects on pulmonary vascular smooth muscle, but nitrous oxide has been shown to produce increases in pulmonary vascular resistance that are worse in patients with underlying pulmonary hypertension. It would be prudent to avoid nitrous oxide in any patient with pulmonary hypertension, especially due to the fact that the other inhaled anesthetic agents will have minimal effect on pulmonary vascular resistance.

KEY FACTS: PULMONARY HYPERTENSION, NITROUS OXIDE

- **Pulmonary hypertension** is defined as a mean pulmonary artery pressure greater than **25 mm Hg**.
- 20% to 40% of obstructive sleep apnea patients have pulmonary hypertension.
- Most volatile anesthetics have minimal effects on pulmonary vascular smooth muscle.
- **Nitrous oxide should be avoided** in these patients because it increases pulmonary vascular resistance.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Sajkov D, McEvoy RD. Obstructive sleep apnea and pulmonary hypertension. *Prog Cardiovasc Dis*. 2009;51(5):363–370.
Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

66. ANSWER: B

Malignant hyperthermia is a rare, genetic, life-threatening condition that is a result of unregulated release of calcium from the sarcoplasmic reticulum. It can be triggered by all volatile anesthetics and by succinylcholine. Halothane is the most potent trigger for malignant hyperthermia compared to the other volatile anesthetics.

KEY FACTS: MALIGNANT HYPERTHERMIA

- Rare, genetic, **life-threatening** condition
- Result of **unregulated release of calcium** from the sarcoplasmic reticulum
- Triggers include all inhalational anesthetics and **succinylcholine**
- **Halothane is the most potent trigger** for malignant hyperthermia compared to the other volatile anesthetics.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

67. ANSWER: E

Minimum alveolar concentration (MAC) is defined as the alveolar concentration that will prevent 50% of patients from moving in response to a standard surgical stimulation. It is independent of sex. MAC decreases by about 6% per decade of life.

KEY FACTS: MAC

- 1.0 MAC Prevents movement in response to surgical stimulus in 50% of patients
- Steadily declines by **6% per decade of life**

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.
Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

68. ANSWER: E

Volatile anesthetics are vaporized in agent-specific vaporizers prior to administration to the patient. Modern vaporizers are calibrated to their specific agent's vapor pressure, so that their output accurately coincides with the concentration set on the vaporizer dial and is independent of temperature and total fresh gas flow.

Filling modern vaporizers with the incorrect anesthetic agent will result in concentration outputs that are different than selected on the vaporizer dial if the two agents have dissimilar vapor pressures. Since modern vaporizers are calibrated to a specific agent's vapor pressure, if a vaporizer is filled with an agent that has a similar vapor pressure, its output would closely match the concentration selected on the dial.

INHALATIONAL ANESTHETICS	VAPOR PRESSURE: MM HG AT 20 DEGREES CELSIUS
Desflurane	670
Halothane	244
Isoflurane	240
Enflurane	172
Sevoflurane	160
Methoxyflurane	23

Since halothane and isoflurane have similar vapor pressures, they can be administered at accurate concentrations when filled into the wrong vaporizer. The same is true for both sevoflurane and enflurane.

If a vaporizer is filled with an anesthetic gas that has a greater vapor pressure than the gas it was originally calibrated for, the concentration delivered will be HIGHER than expected by the dial. Examples include a sevoflurane vaporizer filled with desflurane, halothane, isoflurane, or enflurane.

If a vaporizer is filled with an anesthetic gas that has a lower vapor pressure than the gas it was originally calibrated for, the concentration delivered will be LOWER than expected by the dial. An example includes a sevoflurane vaporizer filled with methoxyflurane.

KEY FACTS: VAPORIZER OUTPUT: VAPOR PRESSURE

- Modern vaporizers are **agent-specific** and calibrated to each volatile anesthetic's **vapor pressure.**
- Filling a modern vaporizer with an agent that has a similar vapor pressure results in the output being similar to the dialed concentration.
- **Sevoflurane and enflurane** have similar vapor pressures and can be used interchangeably.
- **Isoflurane and halothane** have similar vapor pressures and can be used interchangeably.
- Filling a modern vaporizer with an agent that has a **HIGHER vapor pressure** results in a **HIGHER concentration** than what is set on the dial being

delivered to the patient (e.g., sevoflurane filled with desflurane, halothane, isoflurane, or enflurane).
- Filling a modern vaporizer with an agent that has a **LOWER vapor pressure** results in a **LOWER concentration** than what is set on the dial being delivered to the patient (e.g., sevoflurane filled with methoxyflurane)

ADDITIONAL READINGS

Block FE Jr, Schulte GT. Observations on use of wrong agent in an anesthesia agent vaporizer. *J Clin Monit Comput*. 1999;15(1):57–61.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

69. ANSWER: C

Biotransformation refers to the metabolic process by which the body transforms a drug. Most drugs are processed by making them more water soluble and therefore excretable in urine. An ideal inhalational anesthestic agent would not undergo any biotransformation / metabolism.

KEY FACTS: IDEAL INHALATIONAL ANESTHETIC AGENT

- Predictable rapid onset and emergence
- Muscle relaxation
- Hemodynamic stability
- Bronchodilation
- Does not trigger malignant hyperthermia
- Does not induce nausea and vomiting
- Inflammable
- Lack of biotransformation
- Estimation of concentration at site of action

ADDITIONAL READING

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2006.

70. ANSWER: A

Eisenmenger syndrome occurs when chronic left-to-right intracardiac shunt results in prolonged pulmonary hypertension and elevated right heart pressures. Over time, this causes a permanent reversal in blood flow, creating a right-to-left intracardiac shunt. Right-to-left intracardiac shunt results in dilution of the arterial anesthetic partial pressure due to shunted blood containing no anesthetic agent being mixed with the blood that drains ventilated alveoli and contains some inhaled anesthetic agent. This dilutional effect will result in a slower induction. In the presence of a right-to-left intracardiac shunt, insoluble agents will be more affected than soluble agents. With more soluble agents, more inhalational agent has been taken up by the blood, and this will partially compensate for the dilutional effect of the shunted blood. For insoluble agents, little agent is taken up by the blood, so there is no compensation for the effects of dilution from the shunted blood, resulting in slower induction.

KEY FACTS: INTRACARDIAC SHUNT AND INHALATIONAL UPTAKE

- **Eisenmenger's complex**: right-to-left intracardiac shunting after chronic left-to-right shunting results in chronic pulmonary hypertension and elevated right heart pressures
- **Right-to-left intracardiac shunts** and **transpulmonary shunts** (like endobronchial intubations) result in **SLOWING** of induction.
- **Insoluble agents** are more affected by this type of lesion than soluble agents.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. Stamford, CT: Appleton & Lange; 2006.

2.

PULMONARY PHYSIOLOGY

Todd Kerensky, MD, and Stephanie Jones, MD

1. Anatomic dead space begins at the mouth and/or nose and ends at the

A. Lobar bronchi
B. Respiratory bronchioles
C. Terminal bronchioles
D. Alveolar ducts
E. Alveolar sacs

2. Anatomic dead space for a 70-kg man is approximately

A. 140 mL
B. 240 mL
C. 350 mL
D. 500 mL
E. 630 mL

3. A patient with a normal dead-space-to-tidal-volume ratio (V_D/V_T) of 30% is breathing 12 times per minute with a tidal volume of 500 mL. The patient then suffers a pulmonary embolism with the resultant increase of V_D/V_T to 50%. To maintain constant alveolar ventilation, the patient will

A. Decrease tidal volume to 340 mL
B. Increase respiratory frequency to 16 breaths per minute
C. Decrease respiratory frequency to 8 breaths per minute
D. Maintain current tidal volume
E. Maintain current respiratory frequency

4. Please fill in the gaps. Surfactant _____ surface tension, _____ compliance of the lung, _____ work of breathing, and is produced by _____ in the lung.

A. Decreases, increases, decreases, endothelial cells
B. Increases, increases, decreases, type 2 alveolar epithelial cells
C. Decreases, decreases, decreases, type 1 alveolar epithelial cells
D. Increases, decreases, increases, type 1 alveolar epithelial cells
E. Decreases, increases, decreases, type 2 alveolar epithelial cells

5. All of the following can be measured with a spirometer EXCEPT

A. Vital capacity
B. Tidal volume
C. Functional residual capacity
D. Inspiratory capacity
E. Forced expiratory volume in 1 second (FEV_1)

6. At any given pressure, lung volumes during deflation will be

A. Greater than lung volumes during inflation
B. Less than lung volumes during inflation
C. Equal to lung volumes during inflation
D. Independent of transpulmonary pressure
E. Independent of surface tension

7. Which of the following factors affect dynamic compliance of the lung?

A. Tidal volume
B. Airway resistance
C. Respiratory rate
D. All of the above
E. None of the above

8. The relationship between pressure within a sphere and the tension in the wall is described by

A. Laplace's Law
B. Dalton's Law
C. Boyle's Law
D. Poiseuille's Law
E. Fick's Law

9. Which of the following factors would promote a change from turbulent to laminar airflow in a straight tube?

A. Increasing average velocity of gas flow
B. Increasing the radius of the tube
C. Decreasing the density of the gas
D. Decreasing the viscosity of the gas
E. Independent of the Reynolds number.

10. Which of the following airway types contributes LEAST to overall airway resistance?

A. Large airways (>2 mm in diameter, first eight airway generations)
B. Medium-sized airways (lobar and segmental)
C. Medium-sized airways (subsegmental bronchi)
D. Small airways (bronchioles, <2 mm in diameter)
E. All contribute equally.

11. Which of the following neurohumoral factors has the LEAST effect of increasing airway resistance?

A. Acetylcholine
B. Prostacycline
C. Serotonin
D. Thromboxane A_2
E. cAMP

12. The ratio of carbon dioxide eliminated to oxygen consumed by the lungs is called

A. Respiratory quotient
B. Dead-space-to-tidal-volume ratio
C. Alveolar ventilation
D. Alveolar carbon dioxide equation
E. Metabolic Equivalent

13. Distribution of ventilation in the lung in a spontaneously breathing patient is

A. Greatest at the apex
B. Greatest in the mid-lung zone
C. Greatest at the base
D. Greatest in the upper two-thirds of the lung
E. Evenly distributed

14. Which of the following interventions would most likely increase hypoxic pulmonary vasoconstriction?

A. Increase of pulmonary arterial P_{O2}
B. Decrease of alveolar P_{O2}
C. Increase of pulmonary arterial P_{CO_2}
D. Increase of alveolar P_{CO_2}
E. Decrease of alveolar P_{CO_2}

15. The following muscles of respiration are used for inspiration EXCEPT

A. Diaphragm
B. Scalene muscles
C. External intercostal
D. Internal intercostal
E. Sternocleidomastoid

16. Please fill in the gaps. Increasing lung volumes will _____ airway length and will _____airway diameter, with net effect of _____ airflow resistance.

A. Increase, increase, decreased
B. Increase, not change, increased
C. Decrease, decrease, decreased
D. Not change, increase, decreased
E. Not change, decrease, decreased

17. In individuals with normal lungs, residual volume is determined by:

A. Outward force generated by inspiratory muscles equal to inward recoil of the chest wall
B. Inward force generated by inspiratory muscles equal to outward recoil of the chest wall
C. Inward force generated by expiratory muscles equal to outward recoil of the chest wall
D. Outward force generated by expiratory muscles greater than inward recoil of the chest wall
E. Inward force generated by inspiratory muscles greater than outward recoil of the chest wall

18. Vital capacity consists of

A. Functional residual capacity + inspiratory capacity
B. Expiratory reserve volume + inspiratory reserve volume
C. Expiratory reserve volume + inspiratory capacity
D. Tidal volume + inspiratory reserve volume
E. Functional residual capacity + expiratory reserve volume

19. A 30-year-old man is in the preoperative holding area with a heart rate of 70 beats per minute and an estimated stroke volume of 70 mL. He is breathing 10 times per

minute with a tidal volume of 500 mL and an estimated dead space of 100 mL. What is this patient's ventilation/perfusion ratio?

A. 0.5
B. 0.8
C. 1.0
D. 1.2
E. 1.5

20. The ventilation/perfusion ratio throughout the lung can be described as

A. Highest at the apex
B. Highest in the middle of the lung
C. Highest at the base
D. Highest in lower two-thirds of the lung
E. Constant throughout the lung

21. You are caring for a 25-year-old otherwise healthy patient in the PACU who is currently breathing room air with an oxygen saturation of 85%. A blood gas study reveals an arterial P_{O2} of 55 mm Hg and an arterial P_{CO_2} of 70 mm Hg. Which of the following is the most likely cause of this patient's hypoxemia?

A. Right-to-left intracardiac shunt
B. Hypoventilation
C. Atelectasis
D. Pulmonary embolism
E. Intrinsic lung disease

22. Which of the following would INCREASE diffusion of a gas across the alveolar–capillary surface?

A. Decreased alveolar surface area
B. Decreased molecular weight of the gas
C. Decreased partial pressure difference of the gas
D. Decreased solubility of the gas
E. Decreased temperature of the gas

23. According to the Bohr effect, the affinity of hemoglobin for oxygen is INCREASED with

A. Increased temperature
B. Increased 2,3-DPG
C. Decreased 2,3-DPG
D. Decreased P_{CO_2}
E. Decreased pH

24. Which of the following will increase the P_{50} of hemoglobin?

A. Decreased 2,3-DPG
B. Decreased temperature
C. Decreased pH
D. Increased concentration of fetal hemoglobin
E. Decreased concentration of adult hemoglobin

25. Please fill in the gaps. Oxygen is primarily transported in the blood _____, while carbon dioxide is primarily transported_____.

A. Dissolved in plasma; chemically bound to amino acids
B. Bound to hemoglobin; dissolved
C. Dissolved in plasma; as bicarbonate ions
D. Bound to hemoglobin; as bicarbonate ions
E. Bound to hemoglobin; chemically bound to amino acids

26. What is the approximate oxygen content in blood if the blood gas study reveals a Pa_{O_2} of 95 mm Hg with a hemoglobin concentration of 10 g/dL and an oxygen saturation of 98%?

A. 0.3 mL O_2/dL blood
B. 1.0 mL O_2/dL blood
C. 1.3 mL O_2/dL blood
D. 10 mL O_2/dL blood
E. 13 ml O_2/dL blood

27. The P_{50} for normal adult hemoglobin is:

A. 5 mm Hg
B. 15 mm Hg
C. 20 mm Hg
D. 27 mm Hg
E. 35 mm Hg

28. For an acute respiratory acidosis an increase in Pa_{CO_2} of 20 mm Hg will result in a decrease in pH of

A. 0.04 units
B. 0.08 units
C. 0.12 units
D. 0.16 units
E. 0.24 units

29. A patient's blood gas study and metabolic profile reveal pH = 7.36, Pa_{CO_2} = 20 mm Hg, Na = 136, Cl = 102, HCO_3^- = 14. What is the patient's expected Pa_{CO_2}?

A. 24 ± 2
B. 24 ± 4
C. 29 ± 2
D. 29 ± 4
E. 34 ± 2

30. Which of the following best describes the acid–base status of the patient in Question 29?

A. Metabolic acidosis
B. Anion-gap metabolic acidosis
C. Anion-gap metabolic acidosis and respiratory alkalosis
D. Respiratory acidosis
E. Metabolic alkalosis

31. For a chronic respiratory acidosis an increase in $PaCO_2$ of 30 mm Hg will result in a decrease in pH of

A. 0.06 units
B. 0.08 units
C. 0.09 units
D. 0.16 units
E. 0.24 units

32. A patient breathing 100% oxygen has an alveolar–arterial (A-a) gradient of 200 mm Hg. This patient's estimated transpulmonary shunt is

A. 5%
B. 10%
C. 15%
D. 20%
E. 25%

33. Which of the following remains in the lung after a tidal volume breath is expired?

A. Expiratory reserve volume
B. Residual volume
C. Functional residual capacity
D. Inspiratory capacity
E. Total lung capacity

34. Which is the site of greatest airway resistance?

A. Trachea
B. Largest bronchi
C. Medium-sized bronchi
D. Small bronchi
E. Alveoli

35. In patients with chronic obstructive pulmonary disease (COPD)ipratopium acts by

A. Competitive inhibition of cholinergic M3 receptors
B. Noncompetitive inhibition of cholinergic M3 receptors
C. Noncompetitive inhibition of cholinergic M2 receptors
D. Competitive inhibition of B_2 receptors
E. Competitive inhibition of B_1 receptors

36. Please fill in the gaps. In patients with severe kyphoscoliosis, FEV_1/FVC is expected to be _____ and vital capacity to be _____.

A. Decreased; decreased
B. Unchanged; decreased
C. Increased; increased
D. Decreased; unchanged
E. Unchanged; unchanged

37. The effects of obesity on pulmonary lung volumes are

A. Decreased functional residual capacity and increased expiratory reserve volume
B. Increased inspiratory capacity and decreased tidal volume
C. Decreased functional residual capacity and decreased expiratory reserve volume
D. Decreased inspiratory capacity and decreased tidal volume
E. Unchanged vital capacity and expiratory reserve volume

38. A 21-year-old man with a history of asthma develops audible wheezing and a flow–volume curve suggestive of diffuse airway obstruction several minutes after tracheal intubation. Which of the following is appropriate intraoperative management?

A. Increased inspiratory concentration of inhaled agent
B. Skeletal muscle relaxation
C. Increased inspired oxygen concentration
D. Inhaled sympathomimetic agents
E. All of the above

39. An 8-year-old girl underwent surgical drainage of a peritonsillar abscess with adenoidectomy to relieve existing airway obstruction. Upon extubation, she is developing wheezing, tachypnea, and hypoxemia with frothy pink fluid in the endotracheal tube. Postoperative chest x-ray reveals diffuse, bilateral interstitial pulmonary infiltrates. What is the most likely cause of these clinical symptoms?

A. Acute asthma
B. Negative-pressure pulmonary edema
C. ARDS
D. Congestive heart failure
E. Aspiration of gastric contents

40. What is the most appropriate initial therapy for the clinical situation described in Question 39?

A. Inhaled beta agonists
B. Supportive, with increased oxygen concentration and mechanical ventilation with PEEP if necessary
C. Gastric lavage
D. Antibiotics
E. Chest physical therapy

41. What can be done to avoid this clinical situation?

A. Preoperative management with corticosteroids and inhaled beta agonists
B. Preoperative administration of a proton-pump inhibitor
C. Applying continuous positive pressure during anesthesia
D. Inotropic support with digoxin
E. Preventing upper airway obstruction

42. Which of the following is NOT an absolute indication for one-lung ventilation?

A. Presence of a bronchopleural fistula
B. Massive hemorrhage of one lung
C. Pneumonectomy
D. Presence of a bronchocutaneous fistula
E. Unilateral lung lavage

43. Which of the following pulmonary function test results is characteristic of obstructive pulmonary disease?

A. FEV_1 normal, FEV_1/FVC ratio increased, FRC normal
B. FEV_1 decreased, FEV_1/FVC ratio decreased, FRC decreased
C. FEV_1 normal, FEV_1/FVC ratio increased, FRC increased
D. FEV_1 increased, FEV_1/FVC ratio unchanged, FRC increased
E. FEV_1 decreased, FEV_1/FVC ratio decreased, FRC increased

44. A 29-year-old man is being taken to the operating room for surgical management of a comminuted femur fracture sustained in a motor vehicle accident. The patient is intubated and a postintubation chest x-ray reveals that the tip of the endotracheal tube is 2 cm above the carina and there is a small left apical pneumothorax. Mean arterial pressure is sustained in the 60s. Which of the following anesthetics is contraindicated?

A. Total intravenous anesthesia with propofol and fentanyl
B. 1 MAC sevoflurane
C. 1 MAC isoflurane
D. 1 MAC halothane
E. 0.5 MAC desflurane and 0.5 MAC nitrous oxide

45. Which of the following is the only one responding to decreases in P_{O2}?

A. Dorsal respiratory group
B. Ventral respiratory group
C. Central chemoreceptors
D. Peripheral chemoreceptors
E. Botzinger complex

46. A 50-year-old man is undergoing a laparoscopic cholecystectomy. His cardiac output is 6 L/min, hemoglobin concentration is 10 g/dL, and oxygen saturation is 100% on room air. Calculate this patient's oxygen delivery in mL/min.

A. 900 mL/min
B. 800 mL/min
C. 700 mL/min
D. 600 mL/min
E. 500 mL/min

47. You are taking care of an 80-year-old woman in the ICU after total right hip replacement. The hospital is located at sea level. Blood gas analysis reveals an arterial oxygen tension of 70 mm Hg and an arterial carbon dioxide tension of 40 mm Hg. She is intubated and receiving 11 breaths a minute of air (FiO_2 0.21). What is this patient's A-a gradient?

A. 10 mm Hg
B. 20 mm Hg
C. 30 mm Hg
D. 40 mm Hg
E. The A-a gradient cannot be calculated with the information given.

48. Based on the patient and data given in Question 47, what is the most likely cause of this patient's A-a gradient?

A. Ventilation/perfusion mismatch
B. Hypermetabolism
C. Overfeeding
D. Organic acidosis
E. This is a normal A-a gradient for this patient.

49. Which of the following factors influences blood viscosity?

A. Hematocrit
B. Temperature

C. Flow velocity
D. Vessel diameter
E. All of the above

50. Please fill in the blank. Using the Hagen-Poisseuille equation, which describes steady flow through rigid tubes, a 2-fold decrease in the radius of the tube will result in a _____ in flow.

A. 4-fold increase
B. 4-fold decrease
C. 8-fold increase
D. 16-fold increase
E. 16-fold decrease

51. The work of breathing in a 60-year-old patient with pulmonary fibrosis is

A. Increased due to work needed to overcome elastic resistance
B. Decreased due to less work needed to overcome elastic resistance
C. Increased due to work needed to overcome flow resistance
D. Decreased due to less work needed to overcome flow resistance
E. Not different from a patient without the disease

52. The difference between fetal hemoglobin and adult hemoglobin is that it contains

A. Beta chains
B. Gamma chains
C. Delta chains
D. Mu chains
E. Sigma chains

53. A 68-year-old long-time smoker with chronic bronchitis reports for preoperative evaluation. He is breathing deeply and slowly at nine times per minute. As a result of chronic bronchitis this patient's work of breathing is

A. Increased due to work needed to overcome elastic resistance
B. Decreased due to less work needed to overcome elastic resistance
C. Increased due to work needed to overcome flow resistance
D. Decreased due to less work needed to overcome flow resistance
E. Not changed

54. Which of the following modes of ventilation *requires* patient-generated effort to trigger a ventilator breath?

A. Assist-control ventilation
B. Pressure-control ventilation
C. Pressure-support ventilation
D. Inverse-ratio ventilation
E. Pressure-control–volume-guarantee ventilation

55. Which of the following mechanisms is NOT the effect of ventilation using positive end-expiratory pressure (PEEP)?

A. Decreased venous return
B. Decreased ventricular compliance
C. Increased right ventricular outflow impedance
D. Decreased pulmonary vascular resistance
E. Left ventricular afterload reduction

56. A 42-year-old woman was intubated in the ICU because of respiratory distress after being admitted for treatment of abdominal sepsis. Shortly after starting antibiotics she acutely developed respiratory distress. A chest x-ray before intubation revealed equally distributed bilateral lower lobe infiltrates, which were further defined with a CT scan of her chest. The CT scan demonstrated bilateral consolidation confined to the posterior lung regions. Which of the following diagnostic criteria support the clinical diagnosis of ARDS in this patient?

A. $Pa_{O_2}/Fi_{O_2} > 200$ mm Hg
B. Pulmonary artery occlusion pressure ≤ 18 mm Hg
C. 10% neutrophil concentration of lung lavage fluid
D. Absence of predisposing condition
E. Gradual onset

57. The patient described in Question 56 is clinically diagnosed with ARDS. Which of the following management strategies improves survival in ARDS?

A. Bronchodilators
B. Low-volume ventilation
C. Diuretics
D. Prostaglandin E_1
E. End-expiratory plateau pressure > 30 cm H_2O

58. A 67-year-old man with metastatic prostate cancer is admitted to the ICU for treatment of deep venous thrombosis and pulmonary embolism. His oxygen saturation on admission is 90%. Blood gas analysis reveals a Pa_{O_2} of 60 mm Hg and a Pa_{CO_2} of 60 mm Hg. A random sample of expired gas is evaluated and the mean exhaled P_{CO_2} is 30 mm Hg. Please calculate the ratio of dead space volume to tidal volume (V_D/V_T).

A. 30%
B. 40%
C. 50%

D. 60%
E. FiO_2 is needed to calculate V_D/V_T

59. A 90-kg man is admitted to the ICU after partial colectomy for surgical management of colon cancer. He also has a history of congestive heart failure with an ejection fraction of 40%, mild chronic obstructive pulmonary disease (COPD), and anemia. On admission to the ICU his oxygen saturation is 90% on room air. A radial arterial line and an internal jugular central venous line were placed perioperatively. An arterial blood gas study reveals PaO_2 of 55 mm Hg and $PaCO_2$ of 40 mm Hg. Venous blood for labs is drawn from the tip of the central line and reveals a venous P_{O2} of 30 mm Hg. Which of the following factors is most likely contributing to this patient's hypoxemia?

A. Obesity hypoventilation syndrome
B. Opiate-induced hypoventilation
C. Hypothermia
D. Decreased cardiac output
E. COPD exacerbation

60. Which of the following tests of lung function can help differentiate emphysema from chronic bronchitis?

A. Decreased FVC
B. Decreased FEV_1
C. Decreased FEV_1/FVC ratio
D. Decreased diffusion capacity for carbon monoxide (D_LCO)
E. None of the above

61. A marathon runner is training for her next race. She moves from sea level (barometric pressure 760 mm Hg) to high altitude (barometric pressure 500 mm Hg). What is the difference in the partial pressure of oxygen between sea level and the runner's new training location at altitude (500 mm Hg)?

A. 35 mm Hg
B. 44 mm Hg
C. 54 mm Hg
D. 70 mm Hg
E. 82 mm Hg

62. What is the effect on the pulmonary artery pressure of training at altitude?

A. Increase in pulmonary artery pressure due to hypoxic vasoconstriction
B. Increase in pulmonary artery pressure due to thromboxane A_2
C. Increase in pulmonary artery pressure due to endothelin
D. Decrease in pulmonary artery pressure due to nitric oxide
E. No change in the pulmonary artery pressure because cardiac output does not change

63. The immediate respiratory response to altitude is:

A. Hyperventilation as a response to hypoxia sensed by central chemoreceptors
B. Hyperventilation as a response to hypoxia sensed by peripheral chemoreceptors
C. Hyperventilation as a response to hypercarbia sensed by central chemoreceptors
D. Hyperventilation as a response to hypercarbia sensed by peripheral chemoreceptors
E. Hypoventilation as a response to hypocarbia sensed by central chemoreceptors

64. After 2 weeks of training at altitude, which of the following are physiologic adaptations?

A. Increase in tidal volume
B. Increased pulmonary vascular resistance
C. Increased hemoglobin
D. Increase in 2,3-DPG
E. All of the above

65. A 60-year-old woman is tachypneic and has marked dyspnea on exertion. Her oxygen saturation is 97% via a pulse oximeter (SpO_2) on her finger. Is it possible for this patient to be hypoxic?

A. No; since the pulse oximeter reads 97%, she cannot be hypoxic.
B. No, because pulse oximeters are just as reliable as measurement of SaO_2 in the laboratory.
C. Yes; pulse oximeters may differ by as much as 25% when compared to actual measurement of SaO_2.
D. Yes; the patient may have been exposed to carbon monoxide.
E. Yes; her white nail polish may result in an elevated SpO_2 reading.

66. To evaluate for possible carbon monoxide toxicity, a sample of arterial blood is sent to the laboratory for analysis. The SaO_2 from the laboratory is 98%. Based on this result, can the patient still be hypoxic?

A. No; the SaO_2 confirms the pulse oximeter reading and the chance of both tests being wrong is minimal.
B. No; SaO_2 is greater than 95%, and this is sufficient to rule out hypoxia.
C. Yes; it is most likely that the patient is hypoxic because arterial blood gas analysis is frequently inaccurate.

D. Yes; oxygen delivery to the tissues may be impaired by severe anemia, vascular disease, or poisoning of the mitochondria with cyanide or other toxins.
E. Yes, but a co-oximeter will not provide any additional information.

67. Which of the following will increase the ventilatory response to carbon dioxide?

A. Hyperventilation
B. Morphine
C. Inhaled anesthetics
D. Hypoxia
E. All of the above

68. Which of the following sets of pulmonary function test results would you expect in a patient with emphysema?

A. Decreased FEV_1, decreased FEV_1/FVC, decreased D_LCO
B. Decreased FEV_1, normal FEV_1/FVC, normal D_LCO
C. Normal FEV_1, decreased FEV_1/FVC, decreased D_LCO
D. Decreased FEV_1, normal FEV_1/FVC, decreased D_LCO
E. Decreased FEV_1, decreased FEV_1/FVC, normal D_LCO

69. Which of the following statements about the West zones of the lung are INCORRECT?

A. In Zone I, there is no pulmonary blood flow.
B. In Zone II, pulmonary blood flow is determined by the arterial-to-alveolar pressure difference.
C. In Zone III, alveolar pressure is greater than venous pressure.
D. In Zone III, pulmonary blood flow is determined by the arterial-to-venous pressure gradient.
E. In Zone IV, decreased pulmonary blood flow is explained by increasing interstitial pressure.

CHAPTER 2 ANSWERS

1. ANSWER: C

Conducting airways do not participate in gas exchange because they contain no alveoli. The conducting airways begin at the mouth and/or nose and end at the end of the terminal bronchioles. Respiratory bronchioles do participate in gas exchange.

ADDITIONAL READINGS

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West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:2–6.

2. ANSWER: A

In adults anatomic dead space is approximately 2 mL/kg. Dead space may be measured using Fowler's method, in which the subject takes a single breath of 100% oxygen and then exhales. The nitrogen concentration is measured continuously. As exhalation begins there is no nitrogen exhaled because the conducting airways contain 100% oxygen. As gas begins to empty from the alveoli, nitrogen levels rise steadily up to a plateau. The anatomic dead space is the volume of gas exhaled from the start of exhalation to the midpoint of the rising phase of the exhaled nitrogen.

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Stoelting R, Hillier S. *Pharmacology & Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:778.

West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:19–21.

3. ANSWER: B

The patient's minute ventilation (V_T) can be calculated, 500 mL × 12 breaths/min = 6 L/min.

Dead space (V_D) can then be calculated, $V_T \times (V_D/V_T)$; thus, 6 L/min × 30% = 1.8 L.

Alveolar ventilation is determined by **subtracting dead space from tidal volume**.

V_T of 6 L/min minus V_D of 1.8 L yields alveolar ventilation of 4.2 L/min.

Pulmonary embolism increases physiologic dead space because the alveoli affected by the embolism will continue to be ventilated but not perfused. This decreases the number of lung units participating in gas exchange, thus increasing dead space and the V_D/V_T.

To maintain an alveolar ventilation of approximately 4 L/min the patient would need to maintain a minute ventilation of 8 L/min [alveolar ventilation (4 L/min) = V_T (8 L/min) – $0.5 \times V_T$ (8 L/min)].

The other answer choices would decrease or not change minute ventilation, making them incorrect choices.

ADDITIONAL READINGS

Nunn A. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia, PA: Elsevier; 2005:121.

4. ANSWER: E

Surfactant is a mixture of phospholipids, lipids, fatty acids, and proteins produced by type 2 alveolar epithelial cells. Surfactant decreases surface tension and increases compliance of the lung, thereby decreasing work of breathing.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:26–29.

5. ANSWER: C

Spirometry is unable to measure functional residual capacity (FRC), residual volume (RV), and total lung capacity (TLC). FRC may be measured using the inert gas dilution technique or body plethysmography. FRC is the volume of gas in the lung at the end of quiet expiration and is normally 35 mL/kg or approximately 2.5 L in adult men. FRC is composed of expiratory reserve volume (ERV) and RV. Induction of anesthesia and placement of an endotracheal tube is associated with a decrease in FRC of approximately 450 mL, or 15% to 20%. This decrease in FRC will promote atelectasis and hypoxemia if FRC decreases below closing capacity (Fig. 2.1).

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:51–55.

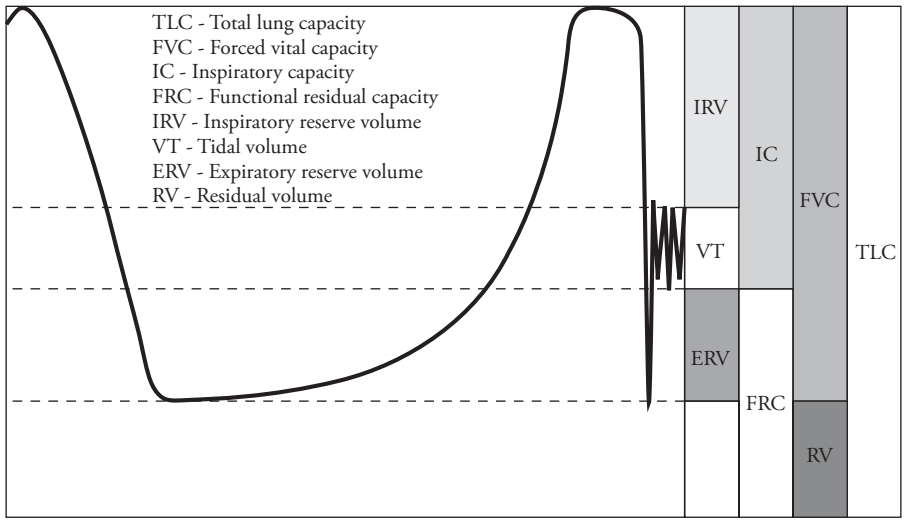

Figure 2.1 The four basic lung volumes are: inspiratory reserve volume (IRV), tidal volume (VT), expiratory reserve volume (ERV), and residual volume (RV). The four basic lung capacities are total lung capacity (TLC), forced vital capacity (FVC), inspiratory capacity (IC), and functional residual capacity (FRC). (Source: Mason RJ, Broaddus VC, Martin TR, et al. *Murray and Nadel's Textbook of Respiratory Medicine*. 5th ed. Philadelphia, PA: Saunders; 2010, Fig. 24–24.)

Gal T. *Respiratory Physiology in Anesthetic Practice*. Baltimore, MD: Williams & Wilkins; 1991:43–44.
Mason RJ, Broaddus VC, Martin TR, et al. *Murray and Nadel's Textbook of Respiratory Medicine*. 5th ed. Philadelphia, PA: Saunders; 2010.
Stoelting R, Hillier S. *Pharmacology & Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:776–777.

6. ANSWER: A

The compliance of the lung is greater during deflation than during inflation. This behavior is called *hysteresis*. Hysteresis means that more than expected pressure is required during inflation, yet less than expected recoil pressure is present during deflation of the lungs. This is largely due to the effects of surface tension, which increases the energy needed to recruit alveoli during inspiration (Fig. 2.2).

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2009.
Nunn A. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia, PA: Elsevier; 2005:30–31.
West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:96.

7. ANSWER: D

Dynamic compliance is the change in lung volume divided by the distending pressure measured during the course of breathing, as compared to static compliance, which is measured in a nonmobile lung. Dynamic compliance is very closely related to static compliance in normal individuals. However, there are three factors that will influence dynamic but not static compliance: tidal volume, airway resistance, and respiratory rate. At larger tidal volumes the larger change in alveolar surface area induces increased surfactant at the alveolar surface, which increases dynamic compliance compared to static compliance. Alveolar units with

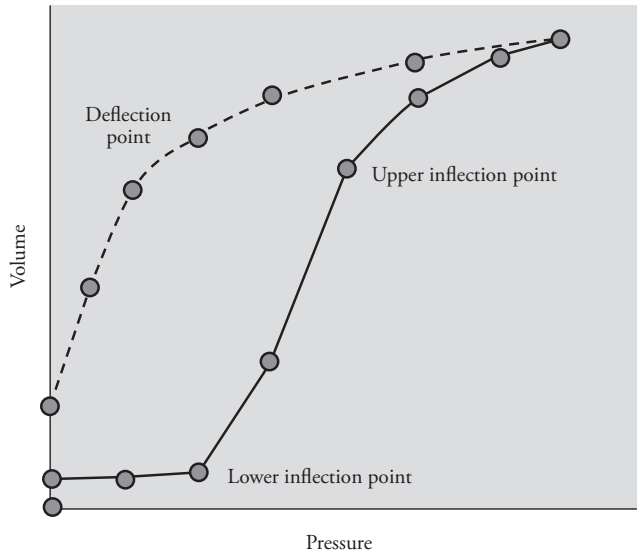

Figure 2.2 Pressure–volume relationship of the lung, showing the inflation (*solid line*) and the deflation limb (*dashed line*). Note the clear difference in lung volume between both limbs at identical pressure (hysteresis). (From van Kaam AHLC. Neonatal mechanical ventilation. In Papadakos PJ, Lachmann B, eds. *Mechanical Ventilation: Clinical Applications and Pathophysiology*. Philadelphia, PA: Elsevier; 2008.)

increased airway resistance require increased filling time in order to achieve the same volume compared to other alveolar units with the same compliance but less airway resistance. The alveolar units with increased resistance are referred to as having long time constants. As respiratory rate increases, the alveolar units with long time constants will have insufficient time to fill and will not participate in dynamic compliance. Therefore, as airway resistance and respiratory rate increase, dynamic compliance decreases compared to static compliance.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:41–43.

8. ANSWER: A

Elastic recoil of the lung is influenced by the surface tension at the air–liquid interface of the alveoli. The relationship between this surface tension and the pressure within a sphere, such as an alveoli, can be described by Laplace's Law.

According to ***Laplace's Law*** the pressure within the sphere (P_s) is equal to two times the wall tension (T) divided by the radius of the sphere (r).

$$P_s = \frac{2T}{r}$$

Dalton's Law states that the partial pressure of a gas in a gas mixture is the pressure that the gas would exert if it occupied the total volume of the mixture in the absence of the other components.

Boyle's Law states that for an ideal gas at constant temperature, the pressure varies inversely with the volume.

Poiseuille's Law describes the flow rate of a liquid in a straight circular tube. Flow rate is proportional to the driving pressure and the radius of the tube to the fourth power and is inversely related to the viscosity of the fluid and the length of the tube.

Fick's Law describes the volume of gas per unit time that diffuses across a tissue sheet; it is directly related to surface areas of the tissue, diffusion constant of the gas, and partial pressure difference of the gas on each side of the tissue and is inversely related to tissue thickness, where the diffusion constant of the gas is the solubility of the gas divided by the square root of the molecular weight.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:25, 35, 67–68, 114–115.

9. ANSWER: C

The nature of gas flow through a straight cylinder can be determined using the Reynolds number (R_e). When the Reynolds number is less than 2,000, flow is predominantly laminar, whereas when the Reynolds number is greater than 4,000, flow is turbulent. Between R_e 2,000 and 4,000, both types of flow exist.

The ***Reynolds number*** is a dimensionless value and can be calculated:

$$R_e = \frac{2rvd}{n},$$

where r is the radius of the cylinder, v is the average velocity, d is density of the gas, and n is the viscosity of the gas. Therefore, R_e will be lower with decreasing the density of the gas, which would promote a change to laminar flow. The density of helium is the lowest of any gas except hydrogen, which is why it may be used in combination with oxygen, as Heliox, to treat upper airway obstruction or stridor.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:35.

Nunn A. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia, PA: Elsevier; 2005:41.

10. ANSWER: D

Small airways with a diameter of less than 2 mm contribute to approximately 20% of the total airway resistance. This apparent paradox is explained by the large number of small airways. At each new generation of airway branching the radius of the airway decreases, which increases the resistance. However, at each airway branching there is an exponential increase in the number of small airways that exist in parallel.

Resistance in an individual airway can be quantified using ***Poiseuille's law***:

$$\text{Resistance}(R) = \frac{8nl}{\pi r^4},$$

where n is the viscosity, l is the length, and r is the radius.

Airways exist in parallel and therefore are added as reciprocals.

$$1/R_{small} = 1/R_1 + 1/R_2 + 1/R_3 \ldots$$

The total airway resistance (R_{aw}) is the sum of the individual resistances in the large, medium, and small airways.

$$R_{aw} = R_{large} + R_{medium} + R_{small}$$

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:35–38.

West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:110.

11. ANSWER: E

Airway resistance is regulated by neurohumoral agents and autonomic neural input via their effects on the smooth muscle surrounding the airway. Stimulation of the parasympathetic nervous system causes airway smooth muscle constriction. Various neurohumoral agents will also cause smooth muscle constriction, including histamine, acetylcholine, thromboxane A_2, serotonin, prostacycline, and leukotrienes. Cyclic AMP has a direct bronchodilating effect.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:40–41.

12. ANSWER: A

The ***respiratory quotient*** is the ratio of carbon dioxide eliminated to oxygen consumed by the lungs. This ratio varies between 0.7 and 1.0 based on inputs to metabolism. When carbohydrates are consumed as energy, the ratio is 1 because 6 molecules of oxygen are consumed to make 36 ATP and 6 molecules of carbon dioxide. When fat is converted to ATP, 23 molecules of oxygen are consumed while 16 molecules of carbon dioxide are produced, which gives a respiratory quotient of 0.7. The respiratory quotient is assumed to be 0.8 for use in the alveolar gas equation.

Dead-space-to-tidal-volume ratio measures the ratio of the volume that does not participate in gas exchange to the volume of a normal breath. Alveolar ventilation is the rate at which carbon dioxide is removed from the alveolus and is the volume of gas that participates in gas exchange. The alveolar carbon dioxide equation expresses the relationship between carbon dioxide production and alveolar ventilation.

The Metabolic Equivalent (MET) is a concept expressing the energy cost of a given physical activity. As an example, watching television is a MET of 1; jumping rope is a MET of 10.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:67–71.

13. ANSWER: C

Distribution of ventilation is not even throughout the lung. Alveoli at the base receive a larger percentage of ventilation. At functional residual capacity, the basal alveoli are on the steeper portion of the pressure–volume curve and are therefore more compliant than apical segments because these alveoli are smaller due to larger (less negative) pleural pressures at the base. Therefore, they receive a larger volume for a given change in pressure (Fig. 2.3).

ADDITIONAL READINGS

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Stoelting R, Hillier S. *Pharmacology & Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:774.

14. ANSWER: B

Hypoxic pulmonary vasoconstriction (HPV) occurs in small pulmonary arterial vessels in response to a decrease of both pulmonary arterial P_{O2} as well as alveolar P_{O2}. Both pulmonary arterial and alveolar P_{O2} stimulate HPV; however, there is a larger influence from decreasing alveolar P_{O2}. Regional HPV helps divert pulmonary blood flow away from regions of the lung in which P_{O2} is low and is important in helping to maintain ventilation/perfusion relationships throughout the lung. An increased pulmonary or alveolar P_{CO_2} can also increase HPV but to a lesser extent than pulmonary or alveolar Pa_{O_2}.

ADDITIONAL READINGS

Nunn A. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia, PA: Elsevier; 2005:101.

15. ANSWER: D

The forces generated by the muscles of inspiration are needed to inflate the lung. These muscles principally include the diaphragm and the external intercostal

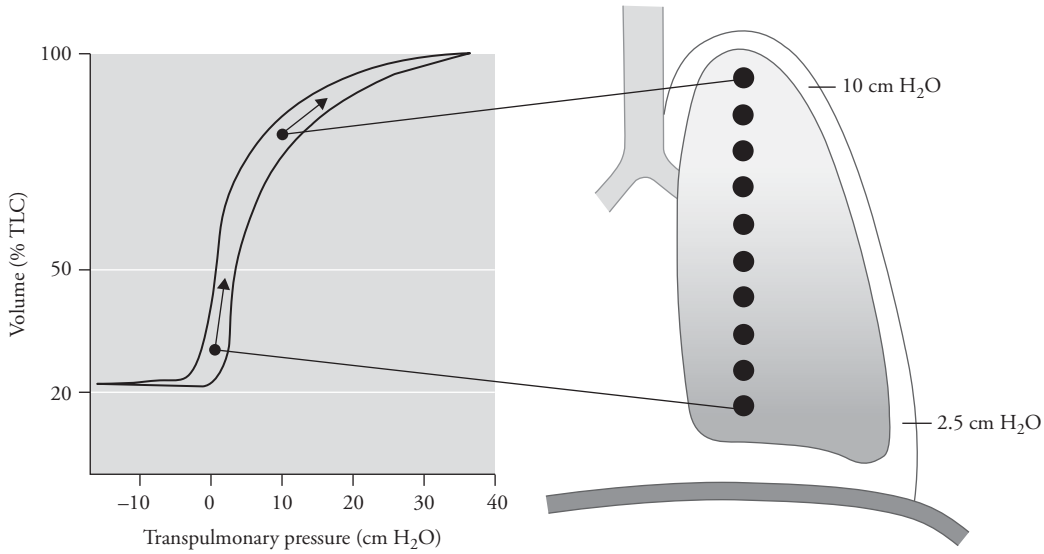

Figure 2.3 Pressure–volume relationships of the lung. Note the curved relationship, which is typical of an elastic structure. Note also the lower (more sub-atmospheric) pleural pressure in the upper regions. Regional transpulmonary pressure (mouth minus pleural pressure) is thus higher for apical lung units than for basal ones in an upright subject. This results in different positions of the upper and lower lung regions on the pressure–volume curve. The consequence will be that the lower lung regions expand more for a given increase in transpulmonary pressure than the upper units do. Thus, ventilation goes preferably to the lower lung regions. (Source: Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2009, Fig. 15–3.)

muscles, which pull the ribs up and forward during inspiration. Accessory muscles of respiration, including the scalene muscles and the alae nasi, which elevate the sternocleidomastoid and cause nasal flaring respectively, help with respiratory efforts during exercise or significant airway obstruction. The pharyngeal muscles, the genioglossus, and the arytenoid muscles help maintain upper airway patency and are included as muscles of inspiration. Expiration, on the other hand, is passive during normal quiet breathing but becomes active with exercise. The muscles of the abdominal wall, including the internal and external obliques, transversus abdominis, and rectus abdominis, are used during active expiration in conjunction with the internal intercostal muscles, which pull the ribs down and inward.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:10–12.

16. ANSWER: A

Increasing lung volume will increase airway length as well as increase airway diameter. The net effect of this change is to decrease airflow resistance because, according to Poiseuille's law, resistance is proportional to changes in the length of a tube and inversely proportional to the fourth power of the radius. Thus, a small increase in the diameter of the airways will make a larger reduction in airway resistance than a small increase in length.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:39–40.

17. ANSWER: C

The residual volume in young healthy lungs is reached when two competing forces are equal to one another. This occurs when the inward force generated by the muscles of expiration equals the outward recoil of the chest wall when residual volume is reached.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:23.

18. ANSWER: C

Please refer to Figure 2.1 of Question 5. Vital capacity is the volume expired after a maximal inspiration followed by

maximal expiration. Vital capacity comprises inspiratory capacity, which is the volume of maximal inspiration (tidal volume plus inspiratory reserve volume), and expiratory reserve volume, which is the volume of maximal expiration.

ADDITIONAL READINGS

West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:15.

19. ANSWER: B

The ventilation/perfusion (V/Q) ratio can be quantified for the entire lung given some knowledge of the patient's alveolar ventilation and cardiac output. Alveolar ventilation can be calculated by subtracting the dead space volume from the tidal volume and multiplying this difference by the respiratory rate. The cardiac output can be calculated by multiplying the stroke volume by the heart rate. In this example, alveolar ventilation is 4 L/min and cardiac output is 4.9 L/min, giving a V/Q ratio of 0.8.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:101–102.

20. ANSWER: A

In the normal, upright lung both ventilation and perfusion increase from the apex to the base. The base of the lung receives more ventilation than the apex because alveoli are smaller and more compliant, and it receives more perfusion than the apex because there is greater intravascular pressure and lower resistance at the base. Moving inferiorly down the lung there is a greater increase in perfusion than ventilation. Therefore, the ventilation/perfusion ratio is greatest at the apex and lowest at the base (Fig. 2.4).

ADDITIONAL READINGS

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West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:64–68.

21. ANSWER: B

Interpreting this patient's blood gas study is helpful in determining the etiology of the hypoxemia. Knowing that the patient is breathing room air, we are able to calculate the expected P_{AO_2} using the alveolar gas equation: expected

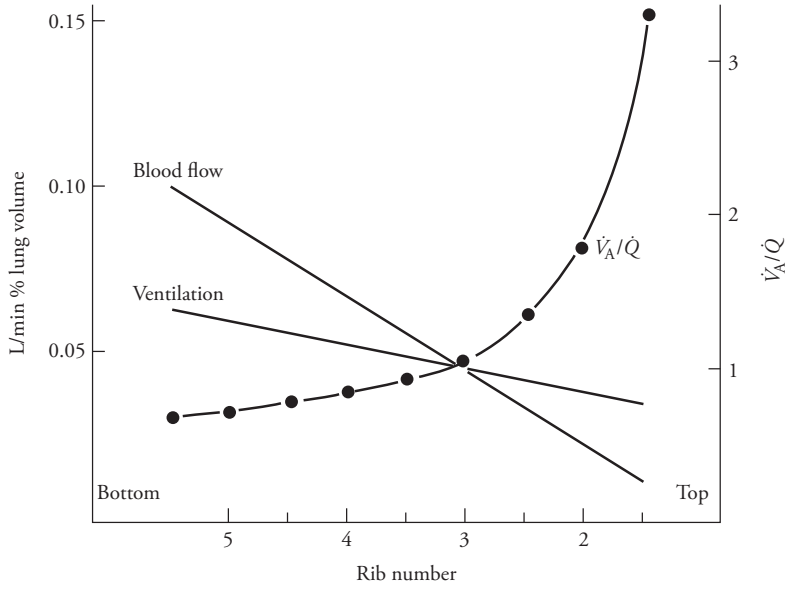

Figure 2.4 Distribution of ventilation, blood flow, and ventilation/perfusion ratio in the normal, upright lung. Straight lines have been drawn through the ventilation and blood flow data. Because blood flow decreases more rapidly than ventilation with distance up the lung, the ventilation/perfusion ratio rises, slowly at first, then rapidly. (From West JB. *Ventilation/Blood Flow and Gas Exchange*. 4th ed. Oxford, England: Blackwell Scientific; 1985.)

$Pa{O_2} = (P_B - P_{H2O}) \times FiO_2 - (PaCO_2/R)$. Assuming arterial PCO_2 equals alveolar PCO_2 and a respiratory quotient of 0.8, this patient's expected PaO_2 is 62.5 mm Hg. We can then evaluate the patient's alveolar–arterial (A-a) gradient. In this case the A-a gradient is 62.5 − 55 = 7.5 mm Hg. This is a normal A-a gradient, adjusted for age using the formula (Age + 10)/4. Given a normal A-a gradient, it is most likely that this patient's hypoxemia is secondary to hypoventilation. Another potential cause of hypoxemia in the setting of a normal A-a gradient is decreased FiO_2. The other causes of hypoxemia all cause a widened A-a gradient.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:102–111.

West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:71–72.

22. ANSWER: B

Fick's law of diffusion states that the diffusion of a gas across a sheet of tissue is proportional to the surface area of the tissue (*A*), the diffusion constant for the specific gas (*D*), and the partial pressure difference on each side of the tissue (*P*1-*P*2), and is inversely related to the tissue thickness (*T*).

$$\text{Diffusion of gas } \alpha = [A \times D \times (P_1\text{-}P_2)]/T,$$

where D = solubility/$\sqrt{}$molecular weight

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:114–115.

23. ANSWER: D

The ***Bohr effect*** refers to changes in hemoglobin's affinity for oxygen with changes in PCO_2 and pH. The affinity of hemoglobin for oxygen increases with a decrease in PCO_2 and/or an increase in pH. This effect enhances oxygen uptake in the lung and the reverse enhances oxygen delivery in the tissues.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:123.

24. ANSWER: C

The P_{50} represents the partial pressure at which hemoglobin is 50% saturated with oxygen. When the oxygen dissociation curve shifts to the right, the P_{50} increases. A decrease in the pH will shift the oxygen dissociation curve to the right and therefore increase the P_{50}. Increasing the concentration of fetal hemoglobin will shift the oxygen dissociation curve to the left because fetal hemoglobin has greater affinity for oxygen than adult hemoglobin (Fig. 2.5).

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:122–125.

25. ANSWER: D

The primary means of transporting oxygen is bound to hemoglobin with a minimal contribution made by dissolved

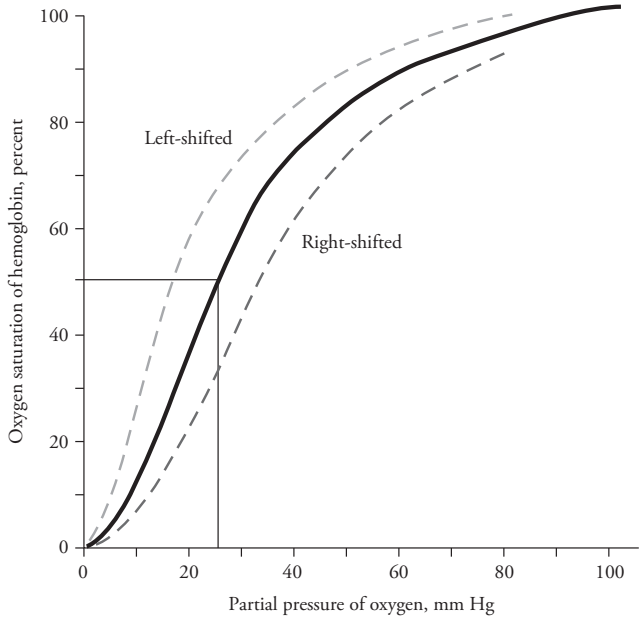

Figure 2.5 Hemoglobin–oxygen dissociation curve. Depicted here is the oxyhemoglobin dissociation curve for normal adult hemoglobin (Hemoglobin A, *solid line*). Note that hemoglobin is 50% saturated with oxygen at a partial pressure of 27 mm Hg (i.e., the P_{50} is 27 mm Hg) and 100% saturated at a P_{O2} of approximately 100 mm Hg. Depicted here are curves that are "left-shifted" (*blue line*, representing increased oxygen affinity) and "right-shifted" (*red line*, decreased oxygen affinity). The effect of right or left shifting of the curve is most pronounced at low oxygen partial pressures. In the examples shown, the right-shifted curve means that hemoglobin can deliver approximately 70% of its attached oxygen at a P_{O2} of 27 mm Hg. In contrast, the left-shifted hemoglobin can deliver only about 35% of its attached oxygen at this P_{O2}. A high proportion of fetal hemoglobin, which has high oxygen affinity, shifts this curve to the left in newborns.

oxygen. The presence of hemoglobin increases the oxygen-carrying capacity of the blood by about 65-fold. Carbon dioxide is transported either physically dissolved, chemically bound to amino acids, or as bicarbonate ions, with the major contribution coming from the bicarbonate ions. When carbon dioxide diffuses from the tissue into plasma it quickly dissolves and then again diffuses from the plasma into red blood cells, establishing an equilibrium. In red blood cells carbon dioxide is quickly converted to bicarbonate ions via a reaction catalyzed by carbonic anhydrase and the bicarbonate ions diffuse out of the cell in exchange for chloride ions.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:119–130.

26. ANSWER: E

The oxygen content in blood is the volume of oxygen contained per unit volume of blood. Oxygen is carried in the blood bound to hemoglobin, and as dissolved oxygen. The total oxygen content in blood is the sum of the bound oxygen and the dissolved oxygen. The oxygen bound to hemoglobin can be calculated because the oxygen-binding capacity for hemoglobin is 1.34 mL of oxygen per gram of hemoglobin.

Therefore, oxygen bound to hemoglobin = (1.34 mL O_2/g Hgb) (10 g Hgb/dL) (98% saturation/100) = 13.1 mL O_2/dL blood.

The dissolved O_2 content can also be calculated by multiplying the Pao_2 by the solubility of oxygen, which is 0.00304 mL O_2/dL blood.

Dissolved O_2 content = 95 mm Hg × 0.00304 mL O_2/dL blood) = 0.3 mL O_2/dL blood.

Total oxygen content = oxygen bound by hemoglobin + dissolved oxygen.

In this example, total oxygen content = 13.1 mL O_2/dL + 0.3 mL O_2/dL = 13.4 mL O_2/dL blood.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:121–122.

27. ANSWER: D

The P_{50} is the partial pressure at which hemoglobin is 50% saturated with oxygen. For normal adult hemoglobin the P_{50} is 27 mm Hg. As the hemoglobin dissociation curve shifts to the right in response to increasing temperature, increasing Pco_2, increasing 2,3-DPG, or decreasing pH, the P_{50} increases. As the hemoglobin dissociation curve shifts to the left (hypothermia, alkalosis, decreasing 2,3-DPG), the P_{50} decreases.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:122–123.

28. ANSWER: D

For a purely acute respiratory acidosis, the pH will change 0.08 units for every 10-mm Hg change in the $Paco_2$. For a purely chronic respiratory acidosis, the pH will change 0.03 units for every 10-mm Hg change in the $Paco_2$. For respiratory disorders that are a combination of acute and chronic, then the pH response will be between 0.03 units and 0.08 units for every 10-mm Hg change in the $Paco_2$.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:137–138.

29. ANSWER: C

30. ANSWER: C

The patient's blood gas and metabolic information indicates that the patient is acidemic because the pH is less than 7.38. In this case the primary disturbance is a metabolic acidemia because the HCO_3^- is less than 24 mEq/L. The next step is to determine whether an anion gap exists. In this case the anion gap is 20 (136 − 102 − 14). We now know that we have an anion-gap metabolic acidemia and can evaluate whether the respiratory system has responded appropriately to compensate for the acidemia.

We can assess the compensation using ***Winter's formula***, which states:

$$\text{Expected } Paco_2 = 1.5 \times HCO_3^- + 8 \pm 2$$

In this example the expected $Paco_2$ = 29 ± 2 mm Hg. The measured $Paco_2$ on the blood gas study is 20 mm Hg, which is less than the expected range calculated using Winter's formula. In this instance the respiratory system has compensated for the metabolic acidemia by

hyperventilation, resulting in a respiratory alkalosis with decreased $PaCO_2$.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:291–296.

31. ANSWER: C

In chronic respiratory acidosis the pH will change 0.03 units for every 10-mm Hg change in $PaCO_2$. This is in contrast to acute respiratory acidosis, in which the pH will change 0.08 units for every 10-mm Hg change in $PaCO_2$. The ability of the kidneys to compensate for chronic respiratory acidosis by excreting acids and retaining filtered bicarbonate accounts for this difference between acute and chronic respiratory conditions.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:137–138.

32. ANSWER: B

When the arterial P_{O2} is greater than 150 mm Hg, the degree of venous admixture can be estimated as approximately 1% for every 20-mm Hg increase in the A-a gradient. In this example, 200 mm Hg would equate to a transpulmonary gradient of 10%.

ADDITIONAL READINGS

Stoelting R, Miller R. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2007:326.

33. ANSWER: C

The remaining lung volume after a tidal volume breath is the functional residual capacity, which is the expiratory reserve volume plus the residual volume.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:18.

34. ANSWER: C

In the normal lung most of the resistance to airflow occurs in the first eight airway generations, with the greatest resistance at the medium-sized bronchi.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:36–38.

35. ANSWER: A

Ipratropium is a competitive inhibitor of cholinergic M3 receptors and is thus more effective at producing bronchodilation in patients with chronic bronchitis and emphysema than beta agonists, which are more effective in asthmatics.

ADDITIONAL READINGS

Stoelting R, Hillier S. *Pharmacology & Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:271–272.

36. ANSWER: B

Mild to moderate kyphoscoliosis is associated with restrictive ventilatory defects or decreased vital capacity and total lung capacity. The degree of restrictive lung disease is directly proportional to the severity of the kyphoscoliosis, and postoperative respiratory failure is most likely in patients with a vital capacity of less than 45% predicted and a scoliotic angle of more than 110 degrees.

ADDITIONAL READINGS

Hines R, Marschall K. *Stoelting's Anesthesia and Co-Existing Disease*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2008:180–181.

37. ANSWER: C

Obesity results in a restrictive ventilatory defect that is thought to be secondary to increased weight on the thoracic cage and abdomen, and increased intrathoracic adipose tissue. This ventilatory defect results in decreased functional residual capacity (FRC), decreased expiratory reserve volume, and decreased total lung capacity. These

effects are accentuated by the supine position and general anesthesia. The FRC may decrease to the point of small airway closure, which can result in ventilation/perfusion mismatching and right-to-left shunting with subsequent arterial hypoxemia.

ADDITIONAL READINGS

Hines R, Marschall K. *Stoelting's Anesthesia and Co-Existing Disease*. 5th ed. Philadelphia, PA: Churchill Livingstone; 2008:301.

38. ANSWER: E

Treatment of intraoperative bronchospasm in an asthmatic after tracheal intubation may include several techniques to minimize the effects of diffuse airway obstruction. Initial therapy may include increasing the depth of anesthesia by increasing concentrations of inhaled anesthetics. Sevoflurane and isoflurane produce bronchodilation in those with obstructive airway disease. Skeletal muscle relaxation is helpful because vigorous expiratory efforts worsen airway obstruction. Relaxation also helps to determine if the increased airway pressures are due to bronchospasm or straining and coughing on the endotracheal tube. If the cause of the increased airway pressures is indeed bronchospasm, the decreased airway caliber will cause decreased ventilation to lung units relative to perfusion. This ventilation/perfusion mismatch can cause arterial hypoxemia; thus, it is helpful to increase the inspired oxygen concentration during acute bronchospasm. The cornerstone of treatment is inhaled sympathomimetics, most commonly albuterol because it is a selective beta-2 agonist. Other pharmacologic treatment options include atropine, glycopyrrolate, and corticosteroids, although these agents are more valuable as prophylaxis rather than acute treatment.

ADDITIONAL READINGS

Gal T. *Respiratory Physiology in Anesthetic Practice*. Baltimore, MD: Williams & Wilkins; 1991:63–65.

Stoelting R, Hillier S. *Pharmacology & Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:63–64.

39. ANSWER: B

40. ANSWER: B

41. ANSWER: E

The clinical symptoms described are most likely caused by ***negative-pressure pulmonary edema (NPPE)***. This may be caused by the higher negative intrapleural pressures generated in order to overcome the airway obstruction, which causes disruption of the capillary walls of the pulmonary microvasculature. Relief of the obstruction leads to decreased airway pressures, increased venous return, increase in pulmonary hydrostatic pressure, and ultimately pulmonary edema. In an attempt to avoid this clinical syndrome, continuous positive pressure to the airway can be employed, and in fact continuous positive-pressure ventilation (and possibly PEEP) may be needed as a therapeutic measure if supportive measures with increased oxygen concentration are insufficient to maintain adequate oxygenation. The use of diuretics in the treatment of NPPE is controversial.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:1308–1309.

42. ANSWER: C

Absolute indications for one-lung ventilation include life-threatening complications in which the healthy lung must be protected from the diseased lung in instances of hemorrhage or infection. The presence of a bronchopleural or bronchocutaneous fistula is also an absolute indication for one-lung ventilation to prevent the presence of a low-resistance pathway for the delivered positive-pressure volumes. Pneumonectomy is a relative indication for facilitating surgical exposure.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:1042–1403.

43. ANSWER: E

In obstructive pulmonary disease, the amount of air exhaled (forced vital capacity [FVC]) is reduced. Furthermore, the amount of air exhaled during the initial 1 second ($FEV_{1.}$ is reduced and is reduced to a greater degree than the entire FVC. Therefore, patients with obstructive pulmonary disease exhibit a decreased FEV_1/FVC ratio. Functional residual capacity (FRC) as well as total lung capacity (TLC) in patients with obstructive pulmonary disease can be increased due to gas trapping (Fig. 2.6).

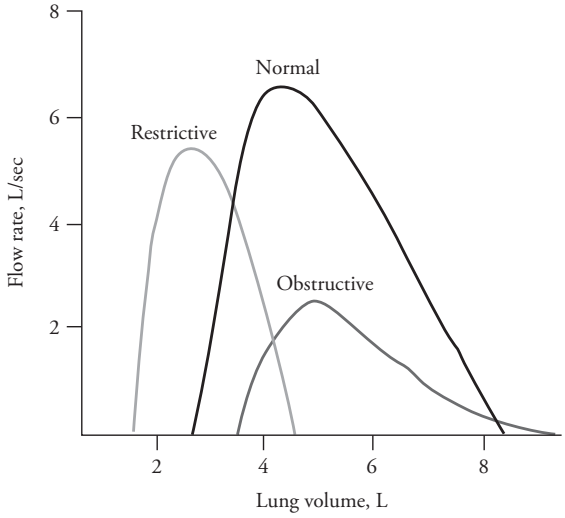

Figure 2.6 Sample flow–volume curves during a maximal forced expiration in a normal person and in patients with obstructive and restrictive lung disease. The normal expiratory portion of the flow–volume curve is characterized by a rapid rise to the peak flow rate, followed by a nearly linear fall in flow as the patient exhales toward residual volume. With obstructive disease, maximal expiration begins and ends at higher lung volumes and lower flow rates than normal. With restrictive disease, the lung volumes and flow rates are reduced but the flow in relation to lung volume is actually higher than normal. (Source: Up-to-date, 2010.)

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:250, 291–296.

44. ANSWER: E

The combined inhaled anesthetic of desflurane and nitrous oxide would be contraindicated in a trauma patient with an apical pneumothorax because nitrous oxide may expand air-filled spaces. Nitrous oxide expands air-filled spaces until the partial pressure of nitrous oxide in the air-filled space equals that in the blood and alveoli.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:423–424.

45. ANSWER: D

Control of respiration has been linked to two groups of nuclei located in the medulla. The dorsal respiratory group is responsible for the pacemaker of the respiratory system and for generating the basic rhythm of ventilation. The counter-control of respiration is located in the ventral respiratory group, which acts as the center of coordination for expiration. Chemoreceptors help the respiratory system respond to changes in the chemical composition of the fluid surrounding the receptors. Central chemoreceptors sense and respond to changes in the pH of the surrounding cerebrospinal fluid (CSF). As the hydrogen-ion concentration or P_{CO_2} increases, the pH of the CSF decreases. This decrease in pH of the CSF is sensed by the central chemoreceptors, triggering an increase in ventilation. Central chemoreceptors are very sensitive to changes in hydrogen-ion concentration, but they do not respond to hypoxia. Hypoxia is sensed only by the peripheral chemoreceptors, located in the carotid and aortic bodies. The peripheral chemoreceptors are the only chemoreceptors capable of responding to decreases in P_{O2}.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:147–152.
Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:238–239.

46. ANSWER: B

Oxygen delivery to the tissues may be calculated by multiplying the cardiac output by the oxygen content of arterial blood. The oxygen content may be calculated by multiplying the oxygen-binding capacity of hemoglobin by the hemoglobin concentration and then multiplying by the oxygen saturation of hemoglobin. In this example:

Oxygen content = 1.34 mL of oxygen/g Hgb × 10g Hgb/100 mL of blood × 1.0 = 0.134 mL of oxygen/mL of blood

Oxygen delivery = cardiac output × oxygen content

Oxygen delivery = 6,000 mL of blood/min × 0.134 mL of oxygen/mL of blood = 804 mL of oxygen/min

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:21–27.

47. ANSWER: C

The A-a gradient is the difference between the calculated alveolar gas and the measured arterial blood.

For this patient the ***alveolar gas equation*** is used to calculate the P_{AO_2}. In this case:

$$P_{AO_2} = FiO_2 \times (P_B - P_{H2}O) - (P_{aCO_2}/R)$$

$$P_{AO_2} = 0.21 \times (760 - 47) - (40/0.8) = 100 \text{ mm Hg}$$

The patient's measured arterial oxygen tension is 70 mm Hg.

The A-a gradient is 100 mm Hg − 70 mm Hg = 30 mm Hg.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:371–372.

48. ANSWER: E

The normal A-a gradient increases with age. The normal range of A-a gradient for an 80-year-old patient is 25 to 38 mm Hg. Ventilation/perfusion mismatch, hypermetabolism, overfeeding, and organic acidosis are potential causes of hypoxemia in patients who truly have an increased A-a gradient after accounting for age as well as inspired oxygen concentration.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:371–372, 375–381.

49. ANSWER: E

Viscosity is a measure of how much a fluid, in this case whole blood, will resist changes in flow rate. As the viscosity of whole blood increases, a greater force must be applied to the fluid to change its flow rate. There are three major factors that influence the viscosity of whole blood. Hematocrit is a major determinant of blood viscosity because it is the cross-linking of circulating red blood cells that influences viscosity. Therefore, as hematocrit decreases, as in anemia, there is an associated decrease in blood viscosity, which will decrease the force needed to initiate a change in flow rate. Temperature will also affect viscosity. As the temperature decreases, as in cooled red blood cell products for transfusion, the viscosity of the fluid will increase. Flow velocity itself also influences the viscosity of whole blood. As blood flows faster in smaller blood vessels, the viscosity of blood decreases. This effect occurs because the velocity of plasma increases more than the velocity of erythrocytes, which increases the relative plasma volume. This effect, also known as the Fahraeus-Lindqvist effect, leads to a reduction in hematocrit in small arterioles (<200 microns in diameter) and capillaries relative to the hematocrit of large feed arteries.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:14–17, 671.

50. ANSWER: E

The ***Hagen-Poisseuille equation*** describes steady flow through rigid tubes, where flow (Q) is proportional to the pressure gradient along the length of the tube (ΔP) as well as the fourth power of the radius of the tube (r^4). Flow is inversely proportional to the viscosity (μ) of the fluid and the length (L) of the tube.

The Hagen-Poisseuille equation states

$$Q = \Delta P \times (\pi\ r^4/8\ \mu L)$$

Thus, if the radius of the tube is halved, this will result in a 16-fold decrease in the flow, because flow is proportional to the fourth power of the radius.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:12–13.

51. ANSWER: A

Work of breathing may be split into elastic work and nonelastic work or resistive work. The work spent overcoming the elastic recoil of the chest wall and lung parenchyma, as well as the work against the surface tension of the alveoli, is referred to as the elastic component of the work of breathing. The other component of total work of breathing is the work spent overcoming the resistance to flow, which is referred to as the flow resistance component. In a patient with pulmonary fibrosis the compliance of the lung parenchyma is decreased. This decreased lung compliance increases the work needed to overcome the elastic component of work of breathing, and thus work of breathing is increased in these patients.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:46–48.

52. ANSWER: B

Fetal hemoglobin is composed of two alpha and two gamma chains. The resulting change in structure increases the affinity of fetal hemoglobin for oxygen, which facilitates oxygen transport across the placenta to the fetus.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:119.

53. ANSWER: C

The work of breathing may be split into elastic work and nonelastic work or resistive work. The work spent overcoming the elastic recoil of the chest wall and lung parenchyma, as well as the work against the surface tension of the alveoli, is referred to as the elastic component of the work of breathing. The other component of total work of breathing is the work spent overcoming the resistance to flow, which is referred to as the flow resistance component. This patient has chronic bronchitis, which increases work of breathing by increasing work required to overcome the increased flow resistance created by chronic bronchitis.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:46–48.

54. ANSWER: C

Pressure-support ventilation is the only ventilator mode listed that requires that the patient initiate a breath for the ventilator to provide support. Therefore, pressure-support ventilation is used only to provide support of spontaneous breathing. When the patient generates the negative pressure of inspiration, a valve opens and the ventilator delivers a breath at a set pressure, which can be altered at the ventilator. In comparison, assist-control ventilation can both assist a patient-generated inspiratory effort and control ventilation altogether if the patient is not breathing spontaneously. Therefore, assist-control ventilation does not require a patient-generated effort, but it will assist patient-generated efforts if they are present. Pressure-control ventilation uses constant pressure to inflate the lungs rather than constant volume. Ventilation is completely controlled by the ventilator and does not require patient-initiated breaths. Inverse-ratio ventilation is pressure-control ventilation in which the inspiratory time is prolonged by decreasing inspiratory flow rates. Inverse-ratio ventilation does not require patient-initiated breaths because it functionally acts like pressure-control ventilation.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:473–481.

55. ANSWER: D

Positive end-expiratory pressure (PEEP) is often used to improve oxygenation of ventilated patients by recruiting alveoli that have collapsed due to decreased lung compliance. PEEP may have deleterious effects on cardiac output by reducing venous return, reducing ventricular compliance, and increasing right ventricular outflow impedance. PEEP also increases positive intrathoracic pressures, which will decrease the pressure gradient for the return of venous blood to the right side of the heart. This mechanism is particularly pronounced in hypovolemic patients. PEEP also induces positive pressure around the outer surface of the heart, which decreases ventricular compliance. During diastole this decreased ventricular compliance may lead to decreased filling of the ventricle. Lastly, PEEP also provides positive pressure around the pulmonary vasculature, which may compress pulmonary blood vessels, increasing pulmonary vascular resistance. Increased pulmonary vascular resistance can particularly impede right ventricular outflow. Over time this will tend to distend the right ventricle and may push the intraventricular septum toward the left ventricle, which reduces left ventricular filling during diastole. While the positive pressure surrounding the heart is deleterious in that it may reduce ventricular compliance during diastole, during systole it reduces left ventricular afterload by effectively increasing the contractility of the left ventricle.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:460–461, 484–485.

56. ANSWER: B

Diagnostic criteria for ***acute respiratory distress syndrome (ARDS)*** include the following five clinical features:

1. Acute onset
2. Presence of a predisposing condition

3. Bilateral infiltrates on frontal chest x-ray
4. Pa_{O_2}/Fi_{O_2} < 200 mm Hg
5. Pulmonary artery occlusion pressure ≤ 18 mm Hg or no clinical evidence of left atrial hypertension

The composition of lavage fluid is not a diagnostic criteria for ARDS, but it can be used as a technique to help exclude or confirm a diagnosis. The percent neutrophil count in the lung lavage fluid can be quantified. In normal subjects the percentage of neutrophils is low, typically less than 5%, while in those with a diagnosis of ARDS the percentage of neutrophils can be as high as 80%. A high neutrophil percentage is indicative of inflammation, which is characteristic of ARDS, but it may also be due to other pathologic states, including pneumonia.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:422–426.

57. ANSWER: B

Low-volume ventilation in patients with ARDS is a technique used to decrease ventilator-induced lung injury in patients with ARDS. Mechanical ventilation with tidal volumes of 6 mL/kg and end-inspiratory plateau pressure less than 30 cm H_2O helps decrease mortality in ARDS compared to conventional tidal volumes of 12 mL/kg. Steroids have been shown to decrease mortality during the fibroproliferative phase, which begins 7 to 14 days after the onset of ARDS. The other therapeutic modalities (bronchodilators, diuretics, and prostaglandin E_1) have not been shown to improve survival.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:426–433.

58. ANSWER: C

The dead-space-to-tidal-volume ratio can be calculated using the ***Bohr equation***:

$$V_D/V_T = (Pa_{CO_2} - Pe_{CO_2})/Pa_{CO_2}$$

Pe_{CO_2} is mean exhaled P_{CO_2} of a random sample of expired gas.

In this example, (60 − 30)/60 = 0.5, or 50%.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:370–371.

59. ANSWER: D

The source of hypoxemia can be broadly characterized into three potential categories: hypoventilation, ventilation/perfusion (V/Q) mismatch, and oxygen delivery or uptake imbalance. In determining which category this patient's hypoxemia falls into, we can evaluate both the A-a gradient and the mixed venous oxygen tension (PvO_2). Hypoventilation from either obesity hypoventilation syndrome or opiate-induced hypoventilation will not cause an elevated A-a gradient or a change in PvO_2. Using the alveolar gas equation the PA_{O_2} is 100 mm Hg, while the Pa_{O_2} is 55 mm Hg. The calculated A-a gradient is then 45 mm Hg, which is elevated. By evaluating the PvO_2 we are able to determine whether the cause of hypoxemia is purely a V/Q mismatch or whether there is an added insult of oxygen delivery or uptake imbalance. If the PvO_2 is normal (40 mm Hg or higher), then the hypoxemia is likely due to a V/Q mismatch. If the PvO_2 is less than 40 mm Hg, then there is a component of decreased oxygen delivery or imbalance in oxygen uptake. In this case the PvO_2 = 30 mm Hg. This imbalance can be due to causes that decrease oxygen delivery, such as decreased cardiac output or anemia. The imbalance may also be due to increased oxygen uptake by the tissues, such as in a hypermetabolic state. In this case the patient has a history of congestive heart failure as well as anemia, which may be both contributing to a decreased oxygen delivery. Decreased cardiac output and V/Q mismatch are possible causes for the hypoxemia in this patient; however, it would be worth evaluating this patient's hemoglobin concentration to evaluate for another potential cause of decreased oxygen delivery.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:371–379.

60. ANSWER: D

The best test to differentiate emphysema from chronic bronchitis is measurement of the diffusion capacity for carbon monoxide (D_LCO). The D_LCO measures the surface area engaged in diffusion of gases. Emphysema destroys alveolar

and capillary walls and therefore decreases the surface area available for diffusion of gases. The $D_L CO$ will be decreased in patients with emphysema but normal in those with chronic bronchitis. The other tests (FVC, FEV_1, and FEV_1/FVC ratio) cannot differentiate emphysema from chronic bronchitis because both are obstructive lung diseases and will alter those test results similarly.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:61–62.

61. ANSWER: C

Dalton's law states that the total pressure of a mixture of gases is equal to the sum of the partial pressures of the individual gases contained in the mixture. As a result:

$$P_{O2} = F_{O2} \times P_B$$

In this case the difference in the partial pressure of oxygen between sea level and at altitude is:

$$P_{O2} = (0.21. \times (760 \text{ mm Hg} - 500 \text{ mm Hg})$$

$$P_{O2} = 54 \text{ mm Hg}$$

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:68–69.

62. ANSWER: A

The result of the lower partial pressure of oxygen at altitude is hypoxemia. Hypoxemia from any cause will result in hypoxic vasoconstriction, which will increase pulmonary artery pressure. A higher pulmonary artery pressure will increase the afterload of the right ventricle. Thromboxane A_2 and endothelin are both pulmonary vasculature vasoconstrictors but are not related to the mechanism of vasoconstriction at altitude. Nitric oxide is a potent vasodilator but is not related to the runner's move to higher altitude.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:94–96, 191–192.

63. ANSWER: B

Hypoxia while training at altitude is due to the decreased atmospheric barometric pressure. This resulting hypoxemia is sensed immediately by peripheral chemoreceptors, the only chemoreceptors capable of sensing changes in arterial partial pressures of oxygen. Once the peripheral chemoreceptors sense hypoxemia they stimulate respiratory drive to maintain oxygenation.

64. ANSWER: E

Acclimatization to high altitude occurs over the course of 2 to 6 weeks. As a result of decreased PaO_2, peripheral chemoreceptors continue to stimulate respiratory drive and increase tidal volume. Hypoxemia secondary to high altitude also stimulates hypoxic pulmonary vasoconstriction, resulting in increased pulmonary vascular resistance. Early during the acclimation process, hypoxemia stimulates renal production of erythropoietin, which stimulates erythropoiesis. Red blood cell production increases hematocrit, which increases the oxygen-carrying capacity of blood. To help facilitate off-loading of oxygen from blood to the tissues, 2,3-DPG, a product of glycolysis, is produced and results in a rightward shift of the oxyhemoglobin dissociation curve.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:191–192.

65. ANSWER: D

Pulse oximetry is a bedside technique that measures light absorption from different structural conformations of hemoglobin based on whether the hemoglobin is oxygenated (HbO_2), deoxygenated (Hb), methemoglobin (met Hb), or carboxyhemoglobin (COHb). The pulse oximeter reads light absorption at 660 nm because deoxygenated hemoglobin absorbs more light at this wavelength than oxygenated hemoglobin. The pulse oximeter then measures light absorption at 940 nm, where the opposite is true: oxygenated hemoglobin absorbs more light than deoxygenated hemoglobin. The oximeter is then able to take the ratio of HbO_2 to the total hemoglobin (HbO_2 + Hb). This works nicely and accurately under most clinical situations because met Hb and COHb account for less than 5% of the total hemoglobin in most clinical situations. However, if a patient was exposed to a significant

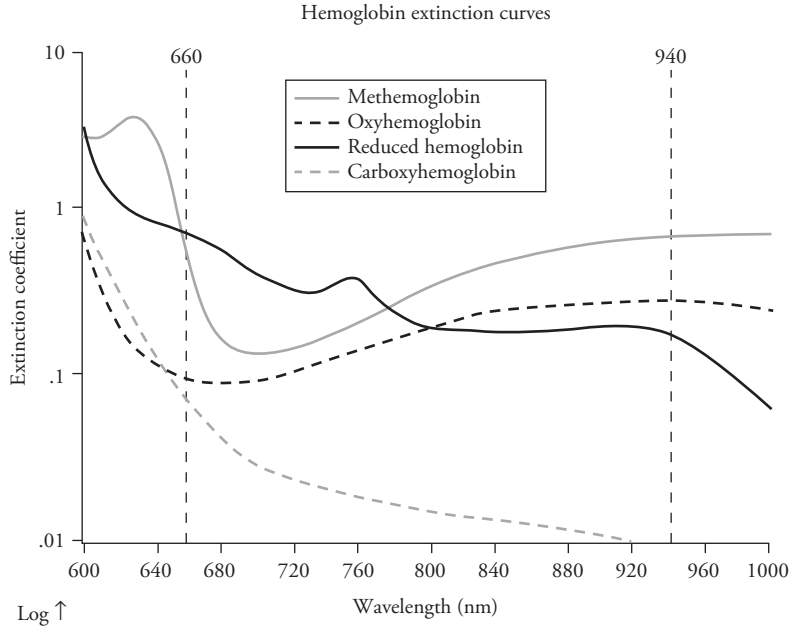

Figure 2.7 Hemoglobin extinction curves. (Source: Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2009, Fig. 38–29.)

amount of carbon monoxide, the pulse oximeter would not be able to differentiate COHb from HbO_2, because each absorbs approximately the same amount of light at 660 nm. Therefore, it is possible to falsely assume there is adequate oxygenation when a patient is exposed to carbon monoxide (Fig. 2.7).

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:126–127.

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:385–388.

66. ANSWER: D

SpO_2 and SaO_2 are measures of oxygen saturation and do not confirm adequate delivery, uptake, or use of oxygen by the tissues. It is possible to have a normal oxygen saturation but still have inadequate delivery or use of oxygen by the tissues, as would occur with other potential causes of hypoxia. These other causes should be considered in this patient and include vascular disease, arterial-venous shunt, severe anemia, or poisoning of the mitochondrial electron transport chain. Co-oximetry measures absorption at several wavelengths to distinguish oxyhemoglobin from carboxyhemoglobin and to determine the oxyhemoglobin saturation (e.g., the percentage of oxygenated Hb compared to the total amount of hemoglobin). In the case of carbon monoxide poisoning, the co-oximeter will detect this Hb and will report the oxyhemoglobin saturation as markedly reduced.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:126–127.

67. ANSWER: D

Control of ventilation is dependent on peripheral and central chemoreceptors, which monitor blood and cerebrospinal fluid for changes in carbon dioxide, oxygen, and pH. The most closely regulated of these is carbon dioxide, and respiratory function is altered almost immediately to maintain $PaCO_2$ close to 40 mm Hg. The ability to alter minute ventilation in response to changing carbon dioxide levels is called the ventilatory response to CO_2. The ventilatory response to CO_2 is increased by hypoxia. As $PaCO_2$ levels increase, there is an increase in alveolar ventilation. This ventilatory response to changes in CO_2 is amplified by hypoxia. The other answer choices all decrease the ventilatory response to carbon dioxide.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:156–157.

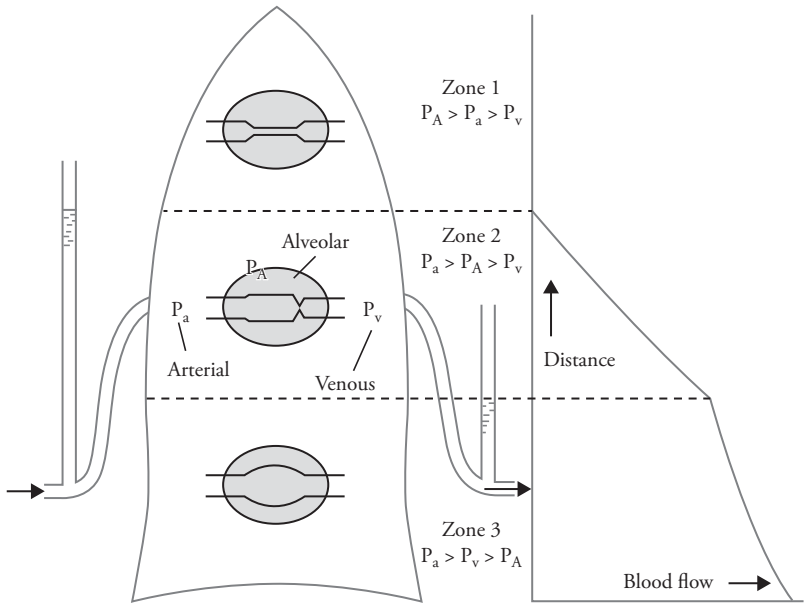

Figure 2.8 Three-zone model designed to account for the uneven topographic distribution of blood flow in the lung. (Source: Mason RJ, Broaddus VC, Martin TR, et al. *Murray and Nadel's Textbook of Respiratory Medicine*. 5th ed. Philadelphia, PA: Saunders; 2010, Fig. 4–11. Redrawn from West JB, Dollery CT, Naimark A. Distribution of blood flow in isolated lung: Relation to vascular and alveolar pressures. *J Appl Physiol*. 1964;19:713–724.).

68. ANSWER: A

Emphysema is an obstructive pulmonary disease characterized by premature airway closure. In obstructive pulmonary diseases such as emphysema there is a decreased FEV_1 as well as a decreased FEV_1/FVC ratio. This is in contrast to restrictive lung disease, in which FEV_1 and FVC are proportionally decreased, which results in a normal FEV_1/FVC ratio. Emphysema is also characterized by destruction of alveolar and capillary walls, leading to a reduction in available surface area for gas diffusion, decreasing $D_L CO$.

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:57–62.

69. ANSWER: C

In an upright individual, blood flow to the alveolar capillaries increases from the top to the bottom of the lung. The vertical distribution of blood flow could accordingly be explained by the influence of gravitation on vascular, alveolar, and interstitial pressure. According to West and colleagues, the lung is classically split into three lung zones based on the differences between arterial, alveolar, and venous pressure seen in each zone. In Zone I, the apex of the lung, alveolar pressure exceeds pulmonary arterial and venous pressure. In this area, pulmonary capillaries are flattened by the larger alveolar pressures and no pulmonary blood flow exists. In Zone II, arterial pressure is greater than alveolar pressure, which is greater than venous pressure. Since alveolar pressure is greater than venous pressure, it is in fact the arterial-to-alveolar pressure

Table 2.1 WEST LUNG ZONES

Zone I	**$P_A > P_a > P_v$** **Alveolar pressure (P_A) exceeds pulmonary arterial (P_a) and pulmonary venous (P_v) pressure, which results in essentially no perfusion.**
Zone II	**$P_a > P_A > P_v$** **Pulmonary arterial pressure (P_a) exceeds alveolar pressure (P_A), which in turn exceeds venous pressure (P_v).**
Zone III	**$P_a > P_v > P_A$** **Both arterial pressure (P_a) and venous pressure (P_v) exceed alveolar pressure (P_A). The difference between arterial and venous pressure creates the driving force through this zone. Pulmonary artery catheters are most frequently located in the zone.**
Zone IV (not shown in the figure 2.8 above)	**$P_a > P_{ISF} > P_v > P_A$** **In the bottom of the lung, recently referred to as Zone IV, there is a decrease in blood flow that is explained by increasing interstitial pressure. The increased interstitial pressure in this area compresses extra-alveolar vessels and makes them narrower.**

difference that determines blood flow to this zone of the lung. At the lower part of the lung, Zone III, venous pressure becomes greater than alveolar pressure and blood flow is determined by the arterial venous pressure gradient. Recently, a zone of reduced blood flow, known as Zone IV, is seen in the lowermost region of the upright human lung. In Zone IV, there is a decrease in blood flow that is explained by increasing interstitial pressure. The increased interstitial pressure in this area compresses extra-alveolar vessels and makes them narrower. This zone becomes smaller as lung volume is increased (Fig. 2.8 and Table 2.1).

ADDITIONAL READINGS

Cloutier M. *Respiratory Physiology*. Philadelphia, PA: Mosby Elsevier; 2007:88–90.

Mason RJ, Broaddus VC, Martin TR, et al. *Murray and Nadel's Textbook of Respiratory Medicine*. 5th ed. Philadelphia, PA: Saunders; 2010.

Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2009.

West J. *Respiratory Physiology—The Essentials*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:42–45.

3.

ANESTHESIA AND DISEASE STATES, PART I

Jutta Novalija, MD, PhD, Vikram Khatri, MD, Srinivasan G. Varadarajan, MD, and Christine M. Zainer, MD

1. Which of the following is NOT a criterion for diagnosing acute respiratory distress syndrome (ARDS)?

A. Acute onset of pathology
B. PaOP ≤ 18 mm Hg
C. Diffuse bilateral radiographic opacities
D. Requirement for controlled mechanical ventilation
E. Pa_{O_2}:Fi_{O_2} ratio < 200 mm Hg

2. A 50-year-old man was diagnosed with ARDS after a Whipple procedure for cancer of the head of the pancreas. The patient was intubated overnight for respiratory support. Which ventilator setting would most likely NOT be used to treat this patient?

A. Tidal volume < 6 mL/kg of IBW
B. Use of PEEP to prevent ventilator induced lung injury
C. Pplat ≤ 30 cm H_2O
D. Lower respiratory rate to reduce repeated stretch injury
E. Target Pa_{CO_2} of 35 mm Hg

3. A 50-year-old woman with severe portal hypertension is scheduled for a transjugular intrahepatic portosystemic shunt (TIPS) procedure under general anesthesia. Which induction agent most likely has the same dosing and effect profile in this patient when compared to a normal healthy individual?

A. Ketamine
B. Etomidate
C. Propofol
D. Midazolam
E. Thiopental

4. A 50-year-old woman has end-stage liver disease due to primary biliary cirrhosis with a Model for End-Stage Liver Disease (MELD) score of 25. While undergoing a transjugular intrahepatic portosystemic shunt (TIPS) procedure, she becomes hypotensive. You suspect hemorrhage in the liver capsule. Resuscitation includes 12 units FFP, 15 PRBC, 2 packs of platelets, and 20 units of cryoprecipitate. The patient continues to bleed. You decide to administer recombinant factor VII. The mechanism of action of factor VII includes all EXCEPT

A. Co-factor to tissue factor
B. Inhibited by antithrombin III–heparin complex
C. Factor X activation
D. Extrinsic pathway activation
E. Factor IX activation

5. A 65-year-old woman with compensated cirrhosis is scheduled to undergo laparoscopic cholecystectomy. Preoperative evaluation finds a twofold rise in serum total bilirubin, AST, ALT, and alkaline phosphatase (ALP). All of the following conditions would raise ALP levels EXCEPT

A. Bone metastasis
B. Obstructive jaundice
C. Paget's disease
D. Osteoporosis
E. Hyperparathyroidism

6. A 50-year-old woman with severe portal hypertension is scheduled to undergo general anesthesia for a TIPS procedure. Which cardiovascular physiologic changes would you expect?

A. Decreased heart rate
B. Increased SVR
C. Increased hepatic blood flow
D. Increased renal blood flow
E. Increased mixed venous oxygen content.

7. A 50-year-old man is undergoing lung volume reduction surgery for severe emphysema. You notice that the mean arterial pressure (MAP) is gradually decreasing, followed by a drop in oxygen saturation. No change in the capnography waveform is noted, although the value is lower. You suspect that auto-PEEP is the cause for these findings. What ventilator parameters would you choose to help avoid this?

A. Higher tidal volume
B. Higher inspiratory flows
C. Higher I:E ratio
D. Higher respiratory rate
E. Add PEEP of 10 cm H_2O to the circuit

8. Which spirometry finding is NOT expected in a 73-year-old man with clinical signs and symptoms of emphysema?

A. Decreased FEV_1 (forced expiratory volume in one second)
B. Decreased FVC (forced vital capacity)
C. Decreased FEV_1/FVC ratio
D. Decreased FRC (functional residual capacity)
E. Increased TLC (total lung capacity).

9. All the following may benefit patients with COPD in the perioperative period EXCEPT

A. Nebulized anticholinergics
B. Smoking cessation
C. Antibiotics for respiratory infection
D. Lung expansion maneuvers
E. Preoperative exercise program

10. A 73-year-old man is undergoing epigastric hernia repair. He has a long smoking history and a recent diagnosis of COPD. You are considering a spinal anesthetic with avoidance of general anesthesia. Which of the following physiologic changes may occur with neuraxial anesthesia?

A. Increased atelectasis
B. Decreased respiratory rate
C. Increase in functional residual capacity (FRC)
D. Increase in expiratory reserve volume (ERV)
E. Increased intrathoracic blood volume

11. A 50-year-old woman with end-stage liver disease due to primary biliary cirrhosis with a MELD score of 25 is scheduled for liver transplantation. Her blood group is A-positive. An AB-negative blood group liver donor becomes available. You are concerned about the compatibility of the transplant. With what type of packed red blood cells can you transfuse this patient?

A. Blood type A only
B. Blood type B only
C. Blood type O only
D. Blood type AB only
E. Blood types O and A

12. A 45-year-old man is undergoing urgent liver transplantation due to fulminant hepatic failure. The surgeon asks you to prepare for venovenous bypass (VVB). Which of the following statements about VVB is CORRECT?

A. Cutdown access of the axillary vein is required.
B. It is a standard of practice in conventional liver transplant.
C. Outcomes are better if it is used.
D. Piggyback transplant technique is almost always done without it.
E. There is no need for a perfusionist.

13. Which airway-management difficulties can be expected in a morbidly obese patient compared to a patient with a normal body habitus?

A. Increased incidence of difficult mask ventilation
B. Increased incidence of difficult intubation
C. Normal incidence of difficult mask ventilation
D. Normal incidence of difficult ventilation
E. Increased incidence of difficult mask ventilation and intubation

14. A 140-kg man is scheduled for bariatric surgery. You choose succinylcholine to facilitate intubation followed by cisatracurium for maintenance of relaxation. Which body weight calculation would you use to determine the dose of each of the muscle relaxants?

A. TBW dose of succinylcholine, TBW dose of cisatracurium
B. IBW dose of succinylcholine, IBW dose of cisatracurium
C. TBW dose of succinylcholine, IBW dose of cisatracurium

D. IBW dose of succinylcholine, TBW dose of cisatracurium
E. IBW plus 25% of the dose of both succinylcholine and cisatracurium

15. A morbidly obese patient without other comorbidities would likely have which of the following physiologic findings?

A. Decreased blood volume
B. Decreased cardiac output
C. Decreased stroke volume
D. Decreased LVEDP
E. Left ventricular hypertrophy

16. Which is an expected finding on a pulmonary function test (PFT) in a morbidly obese patient without lung disease or a history of smoking?

A. Increased FEV_1/FVC ratio
B. Decreased functional residual capacity (FRC)
C. Decreased D_LCO
D. Decreased residual volume (RV)
E. Increased FVC

17. All of the following statements regarding renal blood flow (RBF) are correct EXCEPT?

A. It is approximately 20% of cardiac output.
B. It reaches normal adult values by 3 years of age.
C. It is directly related to MAP.
D. There is low resistance present in the renal circulation.
E. It is lower in women than men.

18. A 20-year-old man with a head injury from an MVA is scheduled for craniotomy and evacuation of a subdural hematoma. When you arrive in the ICU to evaluate patient you find his Foley bag is full of clear urine, HR is 120 bpm, BP is 90/60, and serum sodium is 154 mEq/L. What is the most likely cause for the findings?

A. Diabetes Insipidus
B. Traumatic renal injury
C. Mannitol administration
D. Dehydration
E. Left heart failure

19. A 42-year-old woman with end-stage renal disease secondary to type 1 diabetes mellitus is scheduled to undergo renal transplant. On preoperative assessment she has a history of congestive heart failure and is in atrial fibrillation. Her medications include digoxin, insulin, and calcium. She receives dialysis three times a week. Anesthetic considerations include all of the following EXCEPT

A. Digoxin level must be checked prior to OR.
B. Fentanyl and its congeners have a better safety profile.
C. Increased induction dose of thiopental is needed.
D. Avoid desflurane for maintenance of anesthesia.
E. Intraoperative hypertension can be safely treated with esmolol.

20. All of the following factors play a role in the formation of abdominal ascites EXCEPT

A. Decreased sodium retention
B. Decreased oncotic pressure
C. Hypoabuminemia
D. Increased nitric oxide (NO) and vasodilation
E. Increased portal venous pressure

21. In adults under general anesthesia, which one of the following is the best-preserved temperature regulatory mechanism?

A. Vasoconstriction
B. Shivering
C. Sweating
D. Behavioral thermoregulation
E. Nonshivering thermogenesis

22. Which mechanism for heat loss is most significant in anesthetized surgical patients?

A. Convection
B. Radiation
C. Conduction
D. Evaporation
E. None of the above

23. Causes of hypothermia during epidural anesthesia include the following, EXCEPT

A. Loss of heat to environment
B. Vasodilation
C. Redistribution of heat to the periphery
D. Loss of vasoconstriction response to cold
E. Injection of room-temperature medication through the epidural catheter

24. Mild hypothermia (reduction of core temperature by 2 to 3 degrees C) may cause all of the following EXCEPT

A. Impairment of immune function
B. Blunting of the sympathetic nervous system
C. Increased blood loss during hip arthroplasty
D. Increased incidence of perioperative myocardial ischemia
E. Increased length of postanesthesia care unit (PACU) stay

25. The clinical and biochemical manifestations of excess thyroid hormone are referred to as

A. Hyperthyroidism
B. Thyrotoxicosis
C. Thyrotoxic crisis
D. Thyrotoxicosis factitia
E. Thyroid storm

26. Thyrotoxicosis can cause

A. Increase of basal metabolic rate as much as 60% to 100%
B. Decreased intracellular glucose
C. Decreased tidal volume
D. Decreased cardiac output
E. Vasoconstriction

27. Which of the following statements about the evaluation of the patient with thyroid disease is correct?

A. The thyroid gland completely encircles the trachea and esophagus.
B. Chest x-ray and/or CT of the neck are not necessary in patients with large goiters.
C. Pulmonary function tests are helpful to diagnose tracheal obstruction.
D. After removal of the goiter, patency of the airway is not a concern for extubation.
E. None of the above

28. Which of the following statements about malignant hyperthermia is INCORRECT?

A. Hyperthyroidism and malignant hyperthermia can manifest with hyperthermia and tachycardia intraoperatively.
B. Malignant hyperthermia is associated with profound hypercarbia.
C. Muscle rigidity is a typical sign of malignant hyperthermia but not of thyroid storm.
D. Creatinine phosphokinase levels are decreased in thyroid storm and increased during malignant hyperthermia.
E. Thyroid storm progresses much more slowly than malignant hyperthermia.

29. Following a total thyroidectomy, a 38-year-old woman develops hyperthermia and tachycardia in the recovery room. After several other differential diagnoses are ruled out, thyroid storm is suspected. Which of the following treatment options is initiated first?

A. Volume, electrolyte, and glucose replacement
B. Cooling blankets, ice packs, and aspirin to decrease the temperature
C. Iodide to inhibit thyroid hormone synthesis
D. Bisoprolol to inhibit the peripheral conversion of T_3 to T_4
E. Surgical decompression

30. A 34-year-old woman is presenting with respiratory distress on POD 1 following a thyroidectomy. The most likely explanation of her condition is

A. Bilateral recurrent laryngeal nerve injury
B. Hypocalcemic tetany
C. Respiratory failure
D. Tracheal compression by hematoma
E. Thyroid storm

31. Which of the following statements regarding pheochromocytoma is true?

A. Most pheochromocytomas are bilateral tumors localized in the adrenal glands.
B. The left adrenal gland is more commonly affected than the right.
C. Approximately 40% of adults have solitary tumors.
D. Pheochromocytoma may originate in extra-adrenal sites and most of these tumors are located in the abdomen.
E. Usually pheochromocytoma is part of one type of the multiple endocrine neoplasia (MEN) syndrome.

32. Which of the following drugs used during the preoperative period has contributed to a significant decrease in mortality from pheochromocytoma?

A. Short-acting beta blockers
B. ACE inhibitors
C. Phosphodiesterase inhibitors
D. Alpha-adrenergic receptor blockers
E. Water-soluble benzodiazepines

33. A 58-year-old man has been diagnosed with a pheochromocytoma in his right adrenal gland. The preferred vasodilator for preoperative treatment of hypertension and paroxysms associated with pheochromocytoma is

A. Nitroprusside
B. Clonidine
C. Labetalol
D. Phentolamine
E. Phenoxybenzamine

34. All of the following are reasonable goals prior to anesthesia in a patient with pheochromocytoma EXCEPT

A. Preoperative treatment with phenoxybenzamine for usually 10 to 14 days or longer until blood pressure and paroxysmal symptoms are resolved

B. Resolution of nonpermanent ST-T wave changes on the electrocardiogram
C. Stable blood pressures not greater than 156/90 mm Hg for at least 48 hours prior to surgery
D. Premature ventricular contractions should not exceed 1 every 5 minutes.
E. No orthostatic blood pressure changes on standing

35. Anesthetic management of a patient with pheochromocytoma might include all the following EXCEPT

A. Deep anesthesia during intubation and skin incision, asking surgeon's progress regarding securing venous supply for the tumor
B. Beta blockade prior to alpha-receptor antagonist therapy
C. Nitroprusside for hypertension
D. Pulmonary artery catheterization
E. Prehydration

36. In the perioperative period, drug treatment of a patient with pheochromocytoma may include all of the following EXCEPT

A. Prazosin
B. Propranolol
C. Diltiazem
D. Magnesium
E. Hydrocortisone

37. A 58-year-old man is in the recovery room after undergoing laparoscopic resection of a pheochromocytoma. The LEAST likely expected postoperative complication is

A. Hypotension
B. Hypertension
C. Hypoglycemia
D. Hyperglycemia
E. Sedation

38. A 17-year-old patient was treated with dantrolene (total 6 mg/kg) intraoperatively due to signs and symptoms of malignant hyperthermia (MH). Which of the findings below would be an indication for an additional dose of dantrolene (2 mg/kg) in the PACU?

A. Patient is drowsy.
B. Urine output is 1 mL/kg.
C. Temperature is 38 degrees C.
D. EKG shows frequent arrhythmias.
E. Serum potassium is 4 mEq/L.

39. Complications after the acute episode of MH may include all of the following EXCEPT

A. Disseminated intravascular coagulation
B. Recurrence of symptoms of MH
C. Renal failure
D. Muscle weakness
E. Polycythemia

40. The most specific early sign of MH is

A. Increased temperature
B. Myoglobinuria
C. Muscle rigidity
D. Hyperkalemia
E. Elevated creatine kinase

41. A 24-year-old man undergoing appendectomy develops signs and symptoms of MH. The following are drugs recommended in the management of an acute MH episode, EXCEPT

A. Dantrolene
B. Furosemide
C. Verapamil
D. Sodium bicarbonate
E. Insulin

42. You are discussing the diagnostic options with the family of a 24-year-old man after he experienced an episode of MH. Which statement about the halothane-caffeine contracture test is CORRECT?

A. It has a low sensitivity and high specificity.
B. The muscle biopsy has to be performed close to the testing site.
C. It is available in more than 200 testing center across the U.S.
D. It is based on DNA testing.
E. It is simple and inexpensive.

43. Which of the following statements about masseter muscle rigidity (MMR) is INCORRECT?

A. MMR is often called masseter spasm.
B. Myoglobinuria is common in individuals with MMR.
C. MMR occurs in patients of all ages.
D. If MMR occurs, surgery should be postponed if possible.
E. If MMR is suspected, dantrolene should be given to prevent signs of MH.

44. Which of the following statements about cocaine is CORRECT?

A. It inhibits the reuptake of norepinephrine, dopamine. and serotonin.
B. It decreases blood pressure.

C. It decreases heart rate.
D. It decreases myocardial oxygen demand.
E. It functions as a local anesthetic by blocking calcium channels.

45. Potential complications secondary to cocaine use include all of the following EXCEPT

A. Ventricular cardiac dysrhythmias
B. Seizures
C. Myocardial ischemia
D. Thrombosis
E. Pneumonia

46. A 21-year-old man with acute cocaine intoxication is undergoing thoracic exploration after a gunshot wound. Which drug should be avoided in this patient?

A. Nitroglycerin
B. Midazolam
C. Ketamine
D. Sodium nitroprusside
E. Labetalol

47. A 62-year-old man who presents for a hip replacement has a 40 pack-year smoking history. All of the following statements regarding his history of smoking are true EXCEPT

A. Smokers are more likely to experience respiratory or airway complications.
B. Smoking increases macrophage function.
C. Smoking negatively affects coronary flow reserve.
D. Smoking causes vascular endothelial dysfunction, hypertension, and ischemia.
E. Smokers require longer hospital stays than nonsmokers.

48. A patient stops smoking 1 day before surgery. Beneficial effects of short-term abstinence from cigarette smoking include

A. Decreased sputum production
B. Decreased airway resistance
C. Improved ciliary function
D. Restoration of P_{50} for hemoglobin
E. Improved wound healing

49. A 24-year-old woman with a history of asthma is scheduled for an orthopedic procedure under general anesthesia. Which of the following is LEAST likely to prevent bronchospasm?

A. $Beta_2$ agonist nebulizer in the preoperative holding area
B. $Beta_2$ agonist inhaler before patient is lying down on the operating table
C. Use of laryngeal mask airway instead of endotracheal tube
D. Transtracheal lidocaine before intubation
E. Administration of opioids before intubation

50. Which of the following statements about advanced chronic bronchitis is INCORRECT?

A. Airflow resistance is increased.
B. Dead-space ventilation is decreased.
C. Ventilation/perfusion mismatch in underventilated lung areas
D. Increased $PaCO_2$
E. Alveolar hypoventilation

51. A 32-year-old man develops hypoxia in the postanesthesia care unit after general anesthesia with an endotracheal tube. Negative-pressure pulmonary edema is suspected. Which of the following statements about negative-pressure pulmonary edema is correct?

A. Potential causes are postextubation laryngospasm and obstructive sleep apnea.
B. The edema is exudative.
C. A chest x-ray does not show any abnormal findings until 24 hours after the incident.
D. Diuretics are first-line treatment.
E. Frail and elderly patients are predisposed to developing postobstructive pulmonary edema.

CHAPTER 3 ANSWERS

1. ANSWER: D

According to the joint American–European Congress Consensus Conference in 1994, the ALI/ARDS definition for epidemiologic and research purposes were

1. Acute onset of pathology
2. Pulmonary occlusion pressure (PaOP) ≤ 18 mm Hg
3. Diffuse bilateral radiographic opacities
4. PaO_2:FiO_2 < 200 mm Hg (26.7 kPa)

The committee defined acute lung injury (ALI) as "a syndrome of inflammation and increased permeability that is associated with a constellation of clinical, radiological and physiologic abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension."

PaO_2:FiO_2 < 200 mm Hg (26.7 kPa) is classified as **ARDS. PaO_2:FiO_2 200 to 300 mm Hg** is considered to be **ALI**.

It was agreed that there would not be a cutoff for the P_{O2} value or radiologic appearance.

Mechanical ventilation is NOT a criterion for diagnosis of ALI or ARDS as it is variable in use and is sometimes withheld.

PaOP is not expected to be measured in all cases but would be useful in cases with a high index of suspicion for cardiogenic pulmonary edema.

2. ANSWER: E

Mechanical ventilation in patients with ARDS has been transformed by the findings of the ARDS Network study. There was a higher mortality and number of days on the ventilator in the traditional, higher-tidal-volume group. Since then, a lung protective strategy is being employed in all modern ICUs.

The lung protective ventilation strategy is based on recognition of these concepts:

- Avoidance of overstretch
- Avoidance of repeated opening and closing of alveoli
- Prevention of baro- and volu-trauma to alveoli
- Use of PEEP and recruitment maneuvers to recruit and maintain open alveoli, and allowing ventilation to occur beyond the inflection point

These measures help contain the damage to the already fragile alveolar–capillary interface and also minimize the trauma caused by artificial ventilation itself.

Allowing the carbon dioxide to rise in plasma following a reduction in minute ventilation by lower tidal volumes and respiratory rate has been found NOT to be detrimental. **Humans tolerate hypercapnia** rather well if not contraindicated by conditions such as raised ICP or pulmonary hypertension.

By allowing CO_2 to rise slowly acid–base status is maintained by renal compensation. There is some evidence that hypercapnia might have a therapeutic and cellular protective effect. No consensus exists as to its routine use or the level of permissive hypercapnia.

ADDITIONAL READINGS

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3. ANSWER: E

Thiopental is a barbiturate with an effect duration that is determined mainly due to redistribution, while having a large volume of distribution (Vd) and **insignificant hepatic metabolism.** Therefore, in a patient with liver disease the pharmacokinetic profile is almost identical to that of a healthy individual.

The other drugs referenced are more dependent upon clearance via hepatic metabolism and may have a more prolonged clinical effect in the setting of liver failure (Tables 3.1 and 3.2).

ADDITIONAL READINGS

Table adapted from *Oxford American Handbook of Anesthesiology*, Oxford University Press, USA; 1 edition. 2008: 146.

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4. ANSWER: B

Table 3.3 lists alterations in the hemostatic system that are observed in patients with liver disease.

Hemostatic Milieu in Liver failure

Factor VII has the shortest half-life of all the factors produced by the liver and it is the first to become deficient in liver disease, vitamin K deficiency, or warfarin therapy. It is central

Table 3.1 LIVER FAILURE AND PHARMACOLOGIC EFFECTS OF DRUGS

HEPATIC FAILURE PHYSIOLOGY	PHARMACOLOGIC EFFECT
Decreased portal flow	Decreased first-pass metabolism
Hypoalbuminemia	Increase in free drug fraction
Ascites and sodium and water retention	Increase in Vd
Biotransformation enzymes	Altered activity
Reduced liver cell mass	Reduced activity
Obstructive jaundice	Decreased biliary excretion
Encephalopathy	Exaggerated sedative effect
Reduced plasma cholinesterase activity	

Table 3.2 ANESTHETIC AGENTS IN PATIENTS WITH LIVER DYSFUNCTION

DRUG CLASS	SAFE	CAUTION	CONTRAINDICATED
Premedication	Lorazepam	Midazolam, diazepam	
Induction	Propofol, thiopental, etomidate		
Maintenance	Desflurane, sevoflurane, isoflurane, nitrous oxide	Enflurane	Halothane
Muscle relaxants	Cis atracurium	Pancuronium, vecuronium, succinylcholine	
Opioids	Remifentanil	Fentanyl, alfentanil, morphine, meperidine	
Analgesics		APAP, NSAIDs, dexmedetomidine	

Table 3.3 ALTERATIONS IN THE HEMOSTATIC SYSTEM IN PATIENTS WITH LIVER DISEASE

CHANGES THAT IMPAIR HEMOSTASIS	CHANGES THAT PROMOTE HEMOSTASIS
Thrombocytopenia	Elevated levels of vWF
Platelet function defects	Decreased levels of ADAMTS-13
Enhanced production of nitric oxide and prostacyclin	Elevated levels of factor VIII
Low levels of factors II, V, VII, IX, X, and XI	Decreased levels of protein C, protein S, antithrombin, alpha$_2$ macroglobulin, and heparin co-factor II
Vitamin K deficiency	Low levels of plasminogen
Dysfibrinogenemia	
Low levels of alpha$_2$ antiplasmin, factor XIII, and TAFI	
Elevated t-PA levels	

Table Adapted from Lichtman M, Beutler E, Kaushansky K, et al. *Williams Hematology*. 7th ed. New York, NY: McGraw-Hill; 2005.

to the classical extrinsic pathway by being bound by tissue factor (TF). It also plays a role in the intrinsic pathway as evidenced by its usefulness in patients with hemophilia A and B. It also has activity suggesting direct platelet aggregation and factor IX and X activation. It is not affected by the heparin/ATIII complex, unlike other vitamin K-dependent factors.

Typically a prolonged PT with normal aPTT would indicate deficiency or abnormality of factor VII.

Clinical uses of the factor VII are in

- Hemophilia, especially with inhibitors of the exogenous factors VIII and IX
- Congenital absence of factor VII
- Reversal of warfarin
- Reversal of direct factor X inhibitors
- Platelet dysfunction

Normally these patients are able to maintain adequate hemostasis, and spontaneous bleeding is infrequent except from mechanical causes such as esophageal varices, but undergoing a surgical procedure disrupts that state of balance, and there is significant morbidity and mortality from undergoing major abdominal surgery. Correction of PT and platelet function should be considered before elective surgery.

One has to be acutely aware of all the derangements in complex surgeries like liver transplantation. Not only do different phases of the surgeries pose unique problems, but maintaining hemostasis is extremely challenging for the anesthesiologist (Table 3.4).

5. ANSWER: D

Laboratory testing for quantification and prognostication of liver disease is dependent on various parameters as no single test is very specific or sensitive.

Liver tests can be divided along the lines of measuring

- Hepatic synthetic function: albumin, PT
- Hepatocellular integrity: AST, ALT, blood ammonia
- Excretory function: alkaline phosphatase, bilirubin

Elevated Bilirubin:

- **Conjugated (direct)** = hepatocellular dysfunction, intrahepatic cholestasis, or extrahepatic biliary obstruction
- **Unconjugated (indirect)** = hemolysis or with congenital or acquired defects in bilirubin conjugation
- **Total** = sum of the above. Clinical jaundice = bilirubin ≥ 3 mg/dL

Albumin: A low albumin level is indicative of poor hepatic function, although other protein-losing conditions should be ruled out. The albumin level is not a good index in acute disease because of the long half-life of albumin. In cirrhosis it is useful to know the serum and ascitic albumin gradient (SAAG).

Serum and ascitic albumin gradient (SAAG) = (concentration of serum albumin) minus (concentration of ascitic fluid albumin)

Low SAAG < 1.1 g/dL (exudate): bacterial peritonitis, malignancy, nephrotic syndrome, pancreatitis, tuberculosis

High SAAG > 1.1 g/dL (transudate): cirrhosis, CHF, myxedema, portal vein thrombosis, Budd-Chiari syndrome

Serum Transaminases: Poor correlation with extent of dysfunction or prognosis.

AST is present in many tissues, including the liver, heart, skeletal muscle, and kidneys.

ALT is more specific to the liver.

Minor elevations (<3×) are common and nonspecific large elevations indicate hepatitis and hepatic necrosis.

AST/ALT ratio is >2 in alcoholic disease, <1 in viral hepatitis.

Table 3.4 PHASES OF LIVER TRANSPLANTATION

SURGICAL COURSE	PROBLEM	STRATEGY
Pre-anhepatic	Surgical bleeding	PRBC, plasma replacement
Anhepatic	Decreased clearance of activated clotting factors, hyperfibrinolysis, DIC	Cryoprecipitate, Amicar, EACA
Reperfusion	Heparin, TF and t-PA release, hypothermia, acidosis, hemodilution, low platelets and factor levels	Protamine, FFP, platelets, cryoprecipitate, Amicar, EACA, temperature control
Neo-hepatic phase	Temporary hypercoagulable state, increased level of PAI-1, risk of portal thrombosis	Avoid normalization of parameters.

SOURCE: Lichtman M, Beutler E, Kaushansky K, et al. *Williams Hematology*. 7th ed. New York, NY: McGraw Hill; 2005, and Cullen BG, Stoelting RK, Barash PG. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:1096–1097.

Blood Ammonia: Elevations usually reflect severe hepatocellular damage and disruption of urea synthesis. No correlation to grade of encephalopathy.

Serum Alkaline Phosphatase (ALP)

Alkaline phosphatase is produced by multiple organ systems and is excreted in the bile, and therefore any elevation reflects the excretory function and patency of the biliary tree.

The half-life of ALP is about 1 week, and up to twice the normal value can be nonspecific. Higher values are indicative of intra- or extrahepatic obstruction.

The ALP level is normal in osteoporosis.

ALP level is decreased in hypophosphatasia, a rare, inherited metabolic disease with decreased tissue nonspecific alkaline phosphatase and defective bone mineralization.

Gamma-glutamyltransferase or gamma-glutamyl transpeptidase (GGT)

The main value of GGT over ALP is in verifying that ALP elevations are in fact due to biliary disease; the ALP level can also be increased in certain bone diseases, but the GGT level is not.

GGT is elevated by large quantities of alcohol ingestion. Isolated elevation or disproportionate elevation compared to other liver enzymes (such as ALP or ALT) may indicate alcohol abuse or alcoholic liver disease.

The tests above may be completely normal in patients with early compensated alcoholic cirrhosis.

Derangements of the coagulation profile are discussed elsewhere.

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Harrison TR, Wilson JD, Isselbacher KJ, et al. *Harrison's Principles of Internal Medicine*. 12th ed. New York, NY: McGraw-Hill Professional; 1990:1991.

6. ANSWER: E

The cardiovascular system undergoes profound changes in patients with advanced liver disease as a result of

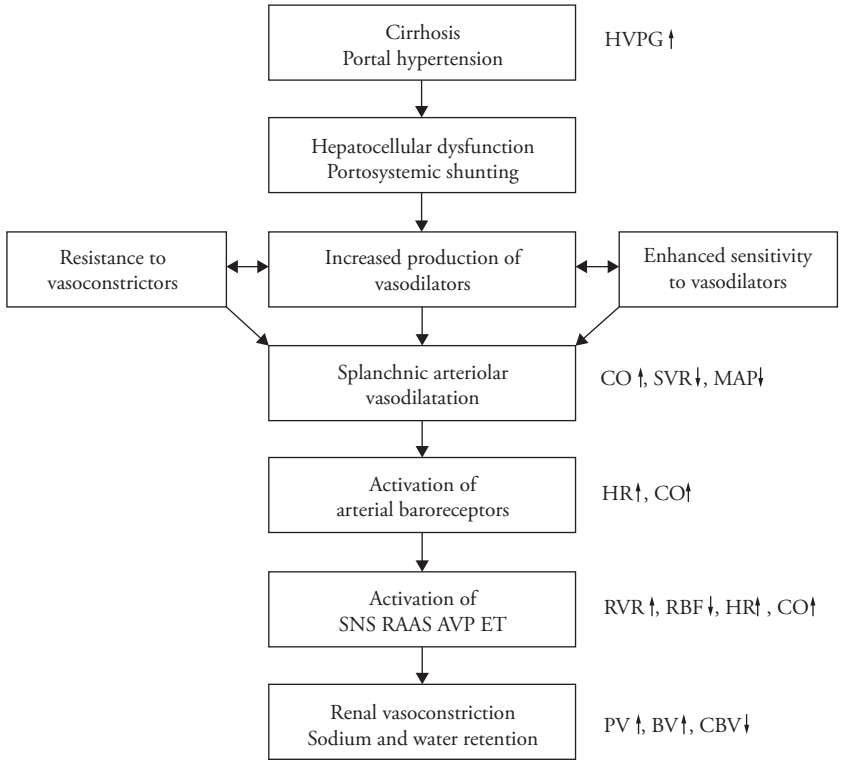

Figure 3.1 Splanchnic and peripheral arteriolar vasodilation with reduced systemic and splanchnic vascular resistance leads to a reduced effective arterial blood volume (CBV), and hence to activation of vasoconstrictor systems. The hemodynamic and clinical consequences are increases in portal pressure (HVPG), cardiac output (CO), heart rate (HR), and plasma (PV) and blood (BV) volumes, and increased renal vascular resistance (RVR) and decreased renal blood flow (RBF), low systemic vascular resistance (SVR) and arterial blood pressure (MAP), and fluid and water retention. The development of the hyperdynamic circulation may increase portal inflow and further aggravate portal hypertension in a vicious cycle. SNS, sympathetic nervous system; RAAS, renin–angiotensin–aldosterone system; AVP, arginine vasopressin; ET, endothelin. (Source: Møller S, Henriksen JH. Cardiovascular complications of cirrhosis. *Gut.* 2008;57:268–278; doi:10.1136/gut.2006.11217)

combined humoral, neurologic, and hemodynamic changes (Fig. 3.1).

Hemodynamic changes that may occur during anesthesia in patients with liver disease:

- Decreased SVR (increased arteriovenous shunting and peripheral vasodilation)
- Increased cardiac output
- Maintained or reduced blood pressure
- Increased blood volume with maldistribution
- Splanchnic hypervolemia, central hypovolemia
- Increased O_2 content in mixed venous blood
- Decreased difference in O_2 content between arterial and venous blood
- Diminished responsiveness to catecholamines
- Increased blood flow to extrahepatic, pulmonary, muscular, and cutaneous tissues
- Decreased total hepatic blood flow
- Maintained hepatic arterial blood flow
- Decreased portal venous blood flow
- Maintained or decreased renal blood flow.
- Depressed cardiac function from cardiomyopathy.

Adapted from Cullen BG, Stoelting RK, Barash PG. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:1091, Table 39–34.

These findings are not a rule, however, and depressed cardiac function can be seen with conditions such as cirrhotic cardiomyopathy, alcoholic cardiomyopathy, or infiltrative cardiac involvement due to hemochromatosis.

Procedures such as draining of ascites and liver transplants can cause severe hypotension.. If the ascites is tense, the splanchnic beds may be compressed by the pressure. Removal of the ascites may result in greater venous capacitance and hypotension. The blood pressure response is unpredictable in a mechanically ventilated patient. Occasionally, removal of ascites improves hemodynamics due to reduction in high airway pressure in a patient with massive tense ascites hampering venous return. Often there is no change in hemodynamics.

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Møller S, Henriksen JH. Cardiovascular complications of cirrhosis. *Gut*. 2008;57:268–278; doi:10.1136/gut.2006.11217

7. ANSWER: B

Dynamic hyperinflation is a hallmark feature in advanced emphysema. Patients lose the elastic recoil of the alveoli by loss of elastic tissue and surfactant. Incomplete emptying of alveoli prior to the next inspiration causes the lung to reset at higher resting volumes and pressure. Air trapping reflects a pressure known as PEEPi (intrinsic PEEP). Newer anesthesia machines have flow loops to identify the phenomenon.

Mechanical ventilation can worsen PEEPi, leading to respiratory and hemodynamic consequences such as barotrauma, reduced cardiac output, and impaired gas exchange.

Cardiorespiratory effects of positive-pressure ventilation. positive pressure ventilation (PPV), PEEP, and PEEPi may compromise cardiovascular function through several mechanisms:

1. Increased mean intrathoracic pressure reduces venous return and therefore reduces CO.
2. Hyper-expanded lungs may cause tamponade of the heart, especially the thin-walled right ventricle.
3. Increased PVR and shunting of blood to nonventilated lung causes hypoxia.
4. Dilation of the RV reduces LV diastolic compliance via interdependenc.

All of the above can cause reduced oxygen delivery and a mismatch between supply and demand.

Reasonable maneuvers to minimize PEEPi are

1. Low tidal volume
2. Reduce respiratory rate
3. Low I:E ratio
4. Increase inspiratory flows to deliver tidal volume in a short time to reduce the I:E ratio and increase expiratory time. The increase in expiratory time is the most important maneuver to minimize PEEi. This may increase peak inspiratory pressures, which reflect the airway but not the alveolar pressures.

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8. ANSWER: D

Chronic obstructive pulmonary disease (COPD) is a pathophysiologic state of obstruction to airflow in the expiratory phase. Maneuvers forcing air out, such as FEV_1 and FVC, are reduced in patients with COPD. FVC is reduced to a lesser extent; therefore, the ratio FEV1/FVC is decreased in this disease. Loss of elasticity (inward force of lung tissue) due to a loss of surfactant function and distension of lung tissue

Table 3.5 GOLD CLASSIFICATION OF COPD (BASED ON POST BRONCHODILATOR FEV_1)

Stage I: Mild	**$FEV_1/FVC < 0.70$** **$FEV_1 \geq 80\%$ predicted**
Stage II: Moderate	**$FEV_1/FVC < 0.70$** **FEV_1 50–80% predicted**
Stage III: Severe	**$FEV_1/FVC < 0.70$** **FEV_1 30–50% predicted**
Stage IV: Very Severe	**$FEV_1/FVC < 0.70$** **$FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted and chronic respiratory failure**

increases lung compliance $\delta V/\delta P$. Therfore lung volume and hence the capacities (sum of two or more lung volumes) are increased. This explains the physical and radiologic appearance of a barrel chest, flat diaphragm, and air trapping.

Table 3.5 shows the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification from the National Heart, Lung, and Blood Institute and World Health Organization initiative on COPD.

ADDITIONAL READINGS

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9. ANSWER: E

Preoperative care of a patient aims at optimizing existing lung function, so the reversible components of COPD such as bronchospasm, infections, and smoking cessation should be aggressively addressed. The most effective measures are smoking cessation, bronchodilators, and treatment of acute infections with antibiotics. Smoking should be stopped 6 to 8 weeks prior to the surgery. A lesser duration of cessation increases sputum production, although there is some evidence of benefit to avoid smoking at least 12 hours prior to surgery due to a reduction in carbon monoxide levels in that period. Bronchodilator drug regimens should be continued throughout the perioperative period. Exercise and rehabilitation programs for COPD have not been conclusively shown to reduce perioperative complications or alter disease progression. A study published in *Chest* in 2001 reported no evidence of benefit for respiratory maneuvers (such as preoperative incentive spirometry) but also no harm. An economic analysis was not performed, but it seems to be a standard of care.

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10. ANSWER: C

An understanding of the physiologic changes, especially respiratory changes, with neuraxial and general anesthesia is important to anesthetic management decisions.

KEY FACTS: NEUROAXIAL ANESTHESIA EFFECTS IN THE ABSENCE OF GENERAL ANESTHESIA

- Preservation of FRC due to lower diaphragm position
- Reduced expiratory volume—may hamper sputum and secretion clearing
- Paralysis/weakness of accessory muscles
- Poor feedback from chest wall; feeling of dyspnea and therefore increased respiratory rate
- Preserved gas exchange and respiratory drive
- No change in sensitivity to Pa_{O_2} or P_{CO_2}
- Hypotension
- Low intrathoracic blood volume
- However, high block can reduce lung volume and have variable effects on ventilatory control.

KEY FACTS: GENERAL ANESTHESIA EFFECTS

- Reduction in FRC
- Depression of respiratory drive
- Impaired mechanics of ventilation
- Impaired gas exchange
- Atelectasis
- Ventilation/perfusion (V/Q) mismatch
- Increased dead-space ventilation
- Reduced hypoxic pulmonary vasoconstriction (HPV)

There are no clearly defined indications for neuraxial anesthesia, as the outcomes of techniques have not been significantly different. However, a subset of patients undergoing specific surgical procedures may benefit from neuraxial anesthesia in terms of reducing perioperative pulmonary complications and morbidity.

ADDITIONAL READINGS

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Wong DH, Weber EC, Schell MJ, et al. Factors associated with postoperative pulmonary complications in patients with severe chronic obstructive pulmonary disease. *Anesth Analg*. 1995;80:276–284.

11. ANSWER: E

Liver transplants can be identical, compatible, and incompatible. The ABO blood group forms the primary immunologic barrier to the transplant. Superior survival is noted in patients with identical or compatible transplants. Incompatible transplants may be performed in case of emergencies such as acute fulminant hepatitis, donor scarcity, and so forth. Tissue typing for HLA matching is not required, and preformed cytotoxic HLA antibodies do not preclude liver transplantation. These transplants may have a hyperacute rejection intra- or postoperatively. Intraoperatively and postoperatively, plasma must be given that is compatible with the recipient's red blood cells but also has no antibodies against the donor liver (Table 3.6).

ADDITIONAL READINGS

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UNOS: http://www.unos.org/policiesandbylaws/policies.asp?resources=true

12. ANSWER: D

The ***piggyback technique of transplantation*** has almost discontinued the practice of VVB. For a VVB, percutaneous lines are placed by the anesthesiologist before the incision to decrease the incidence of lymphoceles. Right internal jugular vein or subclavian vein catheters (9 to 20 French sizes) are generally placed with ultrasound guidance. Large-bore intravenous catheters are also used as volume lines. A small catheter can be placed in the femoral vein prior to the start of the surgery and can be used to upgrade to a larger catheter if bypass is needed after testing the cross-clamping of the IVC. VVB is no longer a standard of practice even in conventional liver transplantation as there is no difference in outcome. Some centers still use VVB only in selected patients—for instance, in fulminant hepatic failure (FHF),

Table 3.6 IDENTICAL/COMPATIBLE TRANSPLANTS

DONOR	RECIPIENT	CELLS	PLASMA	WHOLE BLOOD
O	O	O	O, A, B, AB	O
O	A	O, A	A, AB	A
O	B	O, B	B, AB	B
O	AB	O, A, B, AB	AB	AB
A	A	O, A	A, AB	A
A	AB	O, A, B, AB	AB	AB
B	B	O, B	B, AB	B
B	AB	O, A, B, AB	AB	AB
AB	AB	O, A, B, AB	AB	AB
Incompatible Transplants				
Donor	Recipient	Cells	Plasma	Whole Blood
A	O	O	A, AB	not allowed
B	O	O	B, AB	not allowed
AB	O	O	AB	not allowed
AB	A	O, A	AB	not allowed
AB	B	O, B	AB	not allowed

severe portal hypertension, or volume overload, or in patients who cannot tolerate the cross-clamping of the IVC intraoperatively. If VVB used, a perfusionist is required to manage the pumps and flow rates and so forth.

Potential advantages of using VVB:

- Maintaining the cerebral flow, especially in FHF cases
- Preserving the cardiac and pulmonary flow
- Maintaining renal flow and kidney function
- Maintaining hemodynamic stability during the anhepatic phase
- Providing a longer anhepatic phase for better surgical performance
- Reduction of intraoperative blood loss

Potential disadvantages of using VVB:

- Pulmonary or air emboli, thrombosis
- No evidence of maintaining normal perfusion of abdominal organs
- No evidence of preservation of renal function
- Longer operative and warm ischemic times
- Higher rate of postreperfusion syndrome—hypothermia
- Risk of bleeding due to hemolysis and fibrinolysis in bypass tubing
- Nerve injury, lymphocele, hematoma, wound infection
- Higher transplant cost

Advantages of liver transplantation technique without VVB as published by different authors:

- Obviating the need for VVB
- More hemodynamic stability without a large-volume fluid infusion
- Less impact on renal function
- Shorter anhepatic phase and warm ischemic and operative times
- Lower blood product use
- Less postoperative ventilation requirement
- Shorter length of intensive care unit and hospital stays
- Lower operation and hospital charges

ADDITIONAL READINGS

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Table adapted from Hamidreza Fonouni et al. The official journal of the International Hepato Pancreato Biliary Association, 1477–2574, 10(3): 196–203.

13. ANSWER: A

There is a sufficient amount of literature about airway management in obesity.

Traditionally five independent factors have been identified as **predictors of difficult mask ventilation:**

1. Age > 55 years
2. BMI > 26 kg/m^2
3. Lack of teeth
4. Presence of a beard
5. History of snoring

According to Kheterpal et al., neck radiation changes, male sex, sleep apnea, and Mallampati III or IV are also significant predictors of difficult mask ventilation, but obesity, snoring, and lack of teeth were not considered predictors. Recently, prospective and retrospective studies have found that there is no relation of BMI and intubation success or failure in properly positioned patients. Proper positioning of morbidly obese individuals requires supporting the upper back and head so that a horizontal line exists between the sternal notch and the external auditory meatus.

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14. ANSWER: A

The key facts of pharmacokinetics of drugs in obese individuals are

1. Increased blood volume
2. Increased cardiac output
3. Decreased body water
4. Increased lean body mass
5. Increased muscle mass
6. Increased volume of distribution for lipophilic drugs
7. Altered protein binding
8. Increased renal clearance
9. Normal hepatic clearance
10. Increased pseudocholinesterase activity

The loading dose is based on the Vd and maintenance dosing depends on clearance. Lipophilic drugs have an increased Vd, while the Vd of hydrophilic drugs is not substantially altered. Therefore, lipophilic drugs are generally dosed based on the total body weight (TBW), whereas hydrophilic drugs are dosed based on ideal body weight (IBW).

Lean body mass, which is about 120% to 140% of the IBW, is a better predictor for dosing of hydrophilic drugs

because hepatic clearance is closely related to lean body mass (LBM).

Clearance of the drug is also affected by the Vd, as drugs with a large Vd would take a longer time to clear from the body, and vice versa.

Succinylcholine is affected by an increase in plasma cholinesterase activity in proportion to body weight, therefore requiring an increase in absolute dose based on TBW. **Cisatracurium** and **atracurium** are drugs that are not metabolized by way of organ-dependent mechanisms; therefore, **TBW should be used for dosing.**

Based on the discussion above, Ebert et al. indicate that muscle relaxants **(rocuronium, vecuronium)** should be dosed to **IBW** plus an additional 25%. Repeat doses should be based on the state of neuromuscular blockade desired and achieved (Table 3.7).

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Ebert TJ, Shankar H, Haake RM. Perioperative considerations for patients with morbid obesity. *Anesthesiol Clin*. 2006;24(3):621–636.

15. ANSWER: E

Obese individuals have physiologic changes with many implications for anesthetic management. These include

- **Blood volume, stroke volume, and cardiac output increase** to provide circulation to adipose tissue.
- Asymmetric **left ventricular hypertrophy** secondary to ventricular dilatation results in diastolic function.
- Increased incidence of **hypotension** on **induction**
- A combination of pulmonary hypertension may develop over time with obstructive sleep apnea (OSA) and hypoventilation. Increased cardiac output leads to right heart failure.
- Ischemic heart disease may further impair cardiac function.

ADDITIONAL READINGS

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16. ANSWER: B

Pulmonary function tests obtained in a "healthy" obese population usually report the following:

Decreased FRC: This is the first and most noticeable change, mostly due to reduction in expiratory reserve volume (ERV) and chest compliance. This leads to ventilation/perfusion (V/Q) mismatching and shunting, which worsens in the supine position. These patients require more time to preoxygenate and denitrogenate their lungs and are more likely to have rapid desaturations on induction of anesthesia.

FVC and FEV_1 are normal or both are decreased, therefore preserving a **normal FEV_1/FVC ratio.**

IC (inspiratory capacity) is increased, preserving TLC (total lung capacity) and VC (vital capacity) in mildly obese patients, but as the weight increases, progressive reductions in ERV lead to reductionin the TLC in these parameters.

D_LCO: Gas exchange is preserved to normal values. This is a good test if additional pathology is suspected.

Obese individuals have more perioperative pulmonary complications, raising the question whether morbidly obese patients should have routine PFTs. There is insufficient evidence that they are cost-effective unless indicated for lung volume reduction surgery, lobectomy, or pneumonectomy.

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Table 3.7 DRUG DOSING IN OBESITY

DRUG CLASS	IBW-BASED DOSING	TBW-BASED DOSING
Hynotics	Propofol	Benzodiazepines, barbiturates, propofol (maintenance)
Muscle relaxants	Rocuronium, vecuronium	Succinylcholine, atracurium, cisatracurium
Opiates	Remifentanil, sufentanyl (maintenance)	Fentanyl, sufentanyl (loading)
Local anesthetics	Lidocaine (epidural)	Lidocaine

17. ANSWER: C

A thorough understanding of renal physiology is important to prevent renal injury. The kidney, like the brain and myocardium, has the capacity to autoregulate blood flow. Between the range of MAP 60 to 160 mm Hg, renal blood flow, and consequently the glomerular filtration rate (GFR), remains constant.

Human kidneys usually filter a large amount of plasma and then reclaim almost all of it, leaving behind the waste product. The kidneys have a high metabolic oxygen demand due to high absorptive function.

Renal vessel architecture is in a parallel arrangement, offering very low resistance to blood flow. Developmentally humans reach the adult stage of RBF as a percent of cardiac output by 3 years of age. After reaching adulthood, RBF progressively decreases with age and is only about half that of a young adult at an age of 90 years. Women tend to have lower RBF even after correcting for total body surface area.

Predominantly renin-angiotensin, renal prostaglandins, endothelium-derived relaxing factor (EDRF), and sympathetic tone play a role in maintaining RBF and therefore GFR. Surgical patients under anesthesia might have reduced cardiac output and high sympathetic tone, reducing RBF and contributing to the possibility of perioperative dysfunction.

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18. ANSWER: A

Urine formation is a complex process and various factors influence the final concentration and volume of the urine formed. Kidneys and other organs have mechanisms to ensure that the total body water and osmolality are tightly controlled.

Osmoreceptors in the hypothalamus regulate the release of ADH (vasopressin) from the pituitary. Small changes in serum osmolality can change urine output by large amounts. It is common after head injury to have disorders of ADH secretion. In ***diabetes insipidus***, decreased ADH secretion increases the permeability of the distal collecting tubules to water, producing large amounts of dilute urine, leading to **intravascular dehydration, hypernatremia, and increased serum osmolality.**

Other extrarenal factors involved in the regulation of intravascular and urine volumes are aldosterone and brain/atrial peptides. Natriuretic peptides, both atrial and brain (ventricular), are released in response to increases in intravascular volume. They have multiple sites and modes of action for reducing blood volume and sodium retention.

Traumatic renal injury could have similar findings as in the clinical case presented above, but this is commonly associated with hematuria. Mannitol effect/toxicity usually is manifested by hyponatremia associated with high serum osmolarity. Dehydration may explain the hemodynamic variables in the example, but not the dilute urine. Patients with heart failure usually demonstrate an increased intravascular volume with hyponatremia, and low RBF, GFR, and urine output due to decreased cardiac output.

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19. ANSWER: D

Basic principles of pharmacology in renal disease are as follows (Tables 3.8 and 3.9):

- Decreased gastrointestinal absorption of drugs
- Decreased first-pass hepatic metabolism

Table 3.8 USE OF STANDARD ANESTHETIC AGENTS IN PATIENTS WITH RENAL FAILURE

DRUG CLASS	SAFE	LIMIT OR REDUCE DOSE	DO NOT USE
Premedication		Lorazepam, midazolam, temazepam	
Induction	Propofol, thiopental[1], etomidate	Ketamine	
Maintenance	Isoflurane, desflurane, halothane, propofol	Sevoflurane	Enflurane, methoxyflurane
Muscle relaxants	Succinylcholine[2], cisatracurium	Vecuronium, rocuronium	Pancuronium
Reversal agents	Atropine, glycopyrrolate, neostigmine, edrophonium		
Opioids	Alfentanil, remifentanil	Fentanyl, morphine	Meperidine
Local anesthetics		Bupivacaine, lidocaine	
Analgesics	APAP		NSAIDs

[1] Thiopental plasma free drug fraction increases from 15% to 28%, other kinetics are unchanged.

[2] Normal plasma cholinesterase activity, but hyperkalemia may limit use.

Table 3.9 USE OF VASOPRESSORS AND ANTIHYPERTENSIVE DRUGS IN PATIENTS WITH RENAL FAILURE

DRUG CLASS	SAFE	REDUCE OR LIMIT DOSE	DO NOT USE
Beta blockers	Esmolol, labetalol, propranolol		
Calcium channel blockers	Nifedipine, verapamil, diltiazem		
Diuretics		Thiazides, lasix	
Others	Nitroglycerin	Hydralazine, Sodium nitroprusside, milrinone	

- Decreased plasma protein binding of drugs
- Increased drug availability of free drug for metabolism by the liver
- Glucuronidation, sulfated conjugation, and oxidation are generally unchanged.
- Increased distribution volume (Vd) of drugs that are water-soluble or highly protein-bound
- Decreased renal clearance or excretion of the drugs
- Drugs that are biotransformed are less affected compared to drugs that are excreted.

Reversal agents and **anticholinergic drugs** given to reverse muscle relaxation have equal prolongation of effect, so they can be used in **normal doses.**

Renal failure complicates the use of opiates. It is crucial to find out whether the drug has active metabolites or not, and if the active metabolite is dependent on the kidneys for excretion.

Morphine and **meperidine** have metabolites that are active and **dependent on the kidneys for excretion.**

Synthetic and semisynthetic opioids are not subject to the same process and therefore are less of a problem in renal failure patients.

If **local anesthetics** are used, it is prudent to **decrease the dose** due to less protein binding and a lower threshold for seizures.

Enflurane and methoxyflurane produce a significant amount of inorganic fluoride. Other inhaled anesthetics are safe, although the manufacturer of sevoflurane recommends not using less than 2 L/min fresh gas flow. There is evidence that lesser flows are as safe.

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Table adapted from *Oxford American Handbook of Anesthesiology*. Oxford University Press, 2008: 133.

20. ANSWER: A

Formation of ascites has been difficult to understand. To date three hypotheses have been proposed: the arterial underfilling hypothesis, the overflow hypothesis, and more recently the peripheral arterial vasodilation hypothesis.

While the first two hypotheses propose that the formation of ascites is due to an interaction of plasma volume and renal retention of sodium, the third hypothesis proposes that an increase in portal pressure leads to nitric oxide formation, causing vasodilation. Since the body lacks volume receptors and depends upon pressure receptors to report volume status, even in states of hypervolemia compensatory mechanisms are triggered, leading to the accumulation of even more fluid.

Water distribution in the body is tightly regulated. Movement of fluid across cell membranes is a function of the cell wall, which has active and passive regulatory mechanisms/structures. Osmolarity of the extra- and intracellular components is a major factor.

Since osmolarity of the extracellular compartments is the same due to free passage of ions and simple molecules across the endothelium, oncotic forces play a major part in the regulation of fluid between plasma and interstitial compartments and is governed by ***Starling's law***:

$$J_V = K_F([P_C - P_I] - \Sigma[\pi_C - \pi_I],$$

where

- $[P_c - P_i] - \sigma[\pi_c - \pi_i]$ is the net driving force
- K_f is the proportionality constant
- J_v is the net fluid movement between compartments

By convention, outward force is defined as positive and inward force as negative. The solution to the equation is known as the net filtration or net fluid movement (J_v). If positive, fluid will tend to *leave* the capillary (filtration). If negative, fluid will tend to *enter* the capillary (absorption). This equation has a number of important physiologic implications, especially when pathologic processes grossly alter one or more of the variables.

According to Starling's equation, the movement of fluid depends on six variables:

1. Capillary hydrostatic pressure (P_c)
2. Interstitial hydrostatic pressure (P_i)
3. Capillary oncotic pressure (π_c)
4. Interstitial oncotic pressure (π_i)

5. Filtration coefficient (K_f)
6. Reflection coefficient (σ)

A decrease in synthetic function of the liver along with malnutrition decreases the serum protein concentration and therefore the only gradient in favor of retention of the fluid intravascularly.

The equation is very useful for explaining what is happening at the capillary but has very limited clinical usefulness. Mostly this reflects the impossibility of easily measuring all six variables in actual patients.

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21. ANSWER: C

The thermoregulatory threshold, below which humans actively regulate body temperature, is decreased during general anesthesia and is less effective under anesthesia. Compared to the other homeothermic mechanisms, **sweating is the best-preserved mechanism under general anesthesia.** The threshold for sweating is only slightly increased and the effectiveness of sweating is well preserved under general anesthesia. Under general anesthesia the thresholds for shivering and vasoconstriction are markedly reduced and less effective than normal when activated. Nonshivering thermogenesis does not occur in anesthetized adults and is inhibited in infants.

22. ANSWER: B

Convection is heat lost by currents, such as from drafts and the infusion of cold blood and fluids.

Radiation is heat exchange from one surface to another. In the anesthetized patient heat is lost from the skin or mucosa to the colder environment of the operating room. Heat loss due to **radiation** is proportional to the fourth power of the absolute temperature difference between surfaces and the **most important mechanism** for heat loss.

Conduction is the heat exchanged by direct molecular contact, such as from the skin to the cold operating table.

Evaporation is heat lost by the movement of molecules from the liquid to the gas phase. This may occur during cold skin preparation and irrigation solutions.

Other reasons for heat loss during anesthesia are redistribution from the core to the periphery.

23. ANSWER: E

Vasodilation results in redistribution of core temperature to the periphery. Lack of vasoconstrictor response to cold, secondary to epidural anesthesia, also contributes to heat loss from the core. Heat loss to the environment plays a part but is not a major factor in causing hypothermia. Shivering is abolished in the anesthetized dermatomes, but occurs above the block in response to the drop in core temperature. Most patients shivering under epidural anesthesia do not feel cold because the epidural local anesthetic inhibits tonic cutaneous cold receptor input to hypothalamic thermoregulatory centers. Warming the skin for 2 hours before epidural anesthesia reduces shivering and the drop in core temperature following epidural anesthesia.

The rate of heat loss is similar during general or regional anesthesia, but rewarming is slower after regional anesthesia because residual vasodilation and paralysis impede heat generation and retention.

24. ANSWER: B

In the setting of ***hypothermia***, cellular immune responses are compromised and postoperative infection rates increase. Wound infections can result from a direct impairment of immune function secondary to vasoconstriction with a decreased oxygen delivery to tissues.

Platelet sequestration, decreased platelet function, and reduced clotting factor function contribute to **coagulopathy.**

Postoperative hypothermia **increases sympathetic nervous system activity** with increased epinephrine and norepinephrine levels, elevates peripheral vascular resistance, and decreases venous capacitance.

During emergence, hypothalamic regulation generates shivering to increase endogenous heat production. Oxygen consumption and CO_2 production can increase 200%. Associated increases in minute ventilation and cardiac output might precipitate myocardial ischemia in patients with coronary artery disease or respiratory failure in patients with limited reserve.

Hypothermia complicates and prolongs care in the PACU. Average PACU stay is increased by 40 to 90 minutes for hypothermic patients. A decrease in the minimal alveolar concentration of inhalation anesthetics (5% to 7% per 1 degree C cooling) accentuates residual sedation. Low perfusion and impaired biotransformation might increase the duration of neuromuscular relaxants and sedatives.

KEY FACTS: HYPOTHERMIA

Mild hypothermia (>32–36 degrees C)
- **Shivering (increased oxygen demand)**
- **Increased sympathetic response**
- **Myocardial ischemia**
- **Coagulopathy, platelet dysfunction—Increase in blood loss by 10% for each degree C**
- **MAC decreases about 5% per degree C.**
- **Decreased drug metabolism**
- **Impaired immune system—incidence of infections increases two- to three-fold**

Moderate hypothermia (28 to 32 degrees C)
- **Associated with cardiac dysrhythmias**

Severe hypothermia (≤28 degrees C)
- **Interferes with cardiac rhythm generation and impulse conduction. On ECG, the PR, QRS, or QT interval lengthens, and J waves appear.**
- **Spontaneous ventricular fibrillation occurs at temperatures <28 degrees C.**

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25. ANSWER: B

Hyperthyroidism is thyroid gland hyperactivity with increased synthesis and secretion of thyroid hormone.

Thyrotoxicosis refers to the clinical and biochemical manifestations of excess thyroid hormone. It affects 2% of women and 0.2% of men in the general population.

Thyrotoxic crisis or thyroid storm is a life-threatening complication of hyperthyroidism characterized by a severe, sudden exacerbation of thyrotoxicosis.

Thyrotoxicosis factitia *refers* to thyrotoxicosis without true hyperthyroidism (e.g., ingestion of thyroid hormone, ectopic thyroid hormone production) and is associated with decreased synthesis of thyroid hormone.

26. ANSWER: A

Thyrotoxicosis can cause an **increase of the basal metabolic rate** as much as 60% to 100% when large quantities of thyroid hormones are secreted.

Thyroid hormone **stimulates cellular glucose** use by increasing glucose absorption from the gastrointestinal tract, glycogenolysis, gluconeogenesis, insulin secretion, and cellular uptake of glucose.

It increases free fatty acid availability by increasing lipid mobilization from adipocytes and decreases plasma levels of cholesterol, phospholipids, and triglycerides by increasing the rate of cholesterol secretion into the bile.

Increased levels of thyroid hormones cause increases of oxygen consumption and carbon dioxide production with a **compensatory increase in respiratory rate and tidal volume.**

Thyroid hormone is believed to have a direct effect on the heart by increasing heart rate and contractility, with resultant **increases in cardiac output.**

Increased cellular metabolism and production of metabolic end products result in vasodilation and enhanced tissue blood flow.

27. ANSWER: C

The thyroid gland incompletely encircles the trachea and esophagus. Glandular enlargement can cause tracheoesophageal compression with symptoms such as dyspnea and dysphagia. Acute respiratory insufficiency secondary to bilateral vocal cord paralysis from recurrent laryngeal nerve compression has been reported by patients with intrathoracic goiter.

Chest x-ray and CT of the neck are helpful in evaluating tracheal position and airway obstruction.

Pulmonary function testing is a noninvasive method used to evaluate patients with airway obstruction. Flow-volume loops are generated by inhaling to total lung capacity, exhaling to residual volume, and then inhaling back to total lung capacity. Differing patterns in flow-volume loops can distinguish intrathoracic versus extrathoracic airway obstruction. A large goiter creates a **fixed** lesion of the upper airway and produce plateaus in both the inspiratory and expiratory part of the flow-volume loop (Fig. 3.2). This finding differs from **variable extrathoracic lesions** (often caused by vocal cord paralysis, vocal cord neoplasms, and neoplasm in the neck). Here only the inspiratory limb of the flow-volume loop plateaus. During inhalation, the generation of negative intrathoracic pressure pulls the extrathoracic airway closed. During exhalation, airflow maintains the patency of the airway.

Variable intrathoracic lesions (endobronchial tumors, tracheomalacia) produce plateau of the expiratory cycle only. Inhalation is unimpaired because negative intrathoracic pressure will stent the airway open. During exhalation, positive intrathoracic pressure narrows the airway and results in plateau of the expiratory limb of the flow-volume loop. These patients will have preserved forced vital capacity but marked reductions of forced expiratory volume in 1 second.

Airway patency is always a concern after thyroidectomy. After the resection of a large goiter nerve damage and tracheomalacia have to be considered. If tracheomalacia

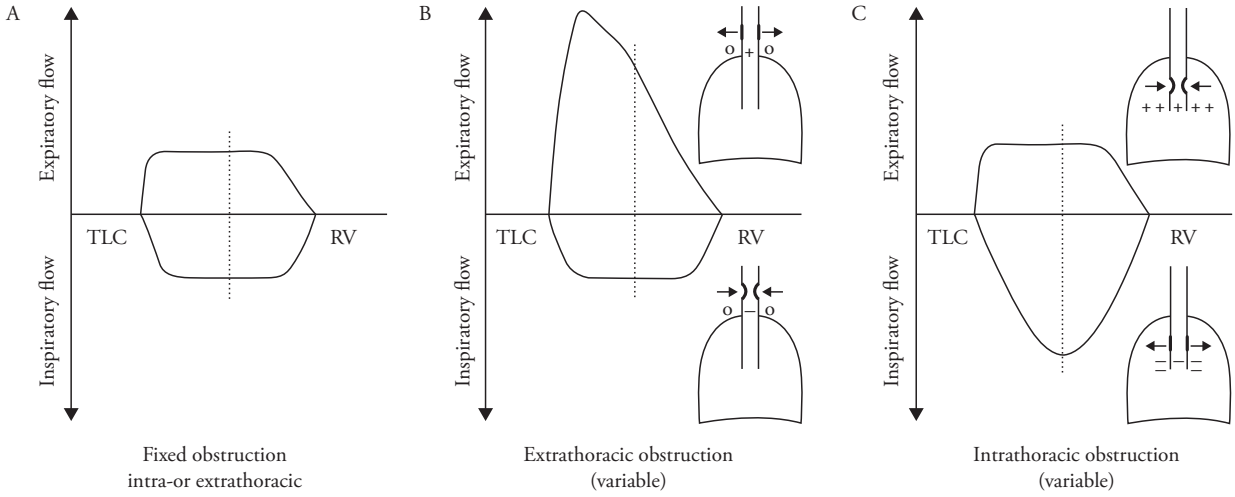

Figure 3.2 Flow-volume curves in fixed and variable obstruction.
(SOURCE: Gurvitch DL. Thyrotoxicosis. In: Yao FF, ed. *Yao's and Artusio's Anesthesiology*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008)

is suspected, direct visualization of airway patency is suggested. The fiberoptic bronchoscope can be used to assess for airway collapse and vocal cord movement as the endotracheal tube and bronchoscope together are slowly pulled back. If tracheal collapse is noted, the endotracheal tube and bronchoscope should be immediately re-advanced.

28. ANSWER: E

Thyroid storm and malignant hyperthermia can present with similar intraoperative and postoperative signs and symptoms (i.e., hyperpyrexia, tachycardia, hypermetabolism). Differentiating between the two may be extremely difficult. The preoperative detection of thyrotoxicosis (tremors, diaphoresis, fatigue, tachypnea, tachycardia, fever, an enlarged thyroid) is very important.

Many of the clinical manifestations of malignant hyperthermia and thyroid storm are compensatory mechanisms for hyperthermia. However, **malignant hyperthermia will result in metabolic acidosis, profound hypercarbia, and muscle rigidity,** which are not present during thyroid storm.

Hyperthyroidism decreases the level of creatinine phosphokinase to about half the normal level, whereas creatinine phosphokinease levels are increased during malignant hyperthermia.

Thyroid storm and malignant hyperthermia progress rapidly and intervention is urgent.

29. ANSWER: A

Supportive measures to treat thyroid storm include replacing fluids to restore intravascular volume, glucose, and electrolytes.

A reduction of temperature can be achieved with acetaminophen, cold lavage of body cavities, cooling blankets, ice packs, and reduction of ambient temperature. **Aspirin should not be used as an antipyretic.** It displaces thyroid hormones from binding proteins, thereby raising free hormone levels. Inotropes, diuretics, and supplemental oxygen may be needed for acute congestive heart failure. Magnesium can be used to reduce the severity and incidence of cardiac arrhythmias.

Iodide can be used to inhibit thyroid hormone synthesis. However, iodide therapy should be delayed after beginning antithyroid drug therapy. Antithyroid drugs reduce the secretion and production of thyroid hormones and prevent iodide binding in the thyroid within the hour.

Catecholamines contribute to the symptoms of thyrotoxicosis. Beta blockers are effective in attenuating the manifestations of excessive sympathetic activity. Beta blockers alone do not inhibit hormone synthesis, but specifically propranolol does impair the peripheral conversion of T_4 to T_3 over 1 to 2 weeks. Any beta blocker may be used, but preoperatively propranolol (in doses titrated to effect) plus potassium iodide (two to five drops every 8 hours) is frequently used before surgery to decrease cardiovascular symptoms and reduce circulating concentrations of thyroid hormones. Preoperative preparation usually requires 7 to 14 days. Rate control may improve congestive heart failure due to poorly controlled paroxysmal atrial fibrillation. Impaired left ventricular function secondary to hyperthyroidism may not be corrected with the use of beta blockers. If a hyperthyroid patient with clinically apparent disease requires emergency surgery, beta blockers should be titrated to achieve a heart rate of less than 90 beats per minute. Beta blockers do not prevent thyroid storm. If beta blockers are contraindicated, other sympatholytic drugs may be useful (reserpine [depletes catecholamine stores] or guanethidine [inhibits catecholamine release]).

There are no signs of hematoma formation. Therefore, surgical decompression is not the correct choice.

30. ANSWER: B

Bilateral recurrent laryngeal nerve injury (secondary to trauma or edema) causes stridor and laryngeal obstruction as a result of unopposed adduction of the vocal cords and closure of the glottic aperture **presenting immediately after extubation.** Endotracheal intubation is usually required, possibly followed by tracheostomy. Unilateral recurrent nerve injury often goes unnoticed because of compensatory overadduction of the uninvolved cord. However, anesthesiologists often test vocal cord function before and after this surgery by asking the patient to say "e" or "moon." Unilateral nerve injury is characterized by hoarseness and bilateral nerve injury by aphonia. Selective injury to the adductor fibers of both recurrent laryngeal nerves leaves the abductor muscles relatively unopposed, and pulmonary aspiration is a risk. Selective injury to the abductor fibers leaves the adductor muscles relatively unopposed, and airway obstruction can occur.

The intimate involvement of the parathyroid gland with the thyroid gland can result in inadvertent hypocalcemia after thyroid surgery. **Hypocalcemia secondary to inadvertent excision of parathyroid tissue manifests within the first 3 days postoperatively,** commonly after 24 hours. The patient may complain of oral numbness and tingling of the hands and feet. If calcium is not supplemented, the patient can develop stridor and airway obstruction secondary to muscle weakness. Severe hypocalcemia can also be associated with seizures and tetany.

Causes of respiratory failure following a thyroidectomy include hemorrhage, respiratory obstruction, tracheomalacia, and pneumothorax that will commonly manifest in the first hours after the surgery; they are less likely after 24 hours. Signs of airway obstruction require emergent evaluation. Hematomas can cause compressive airway obstruction and restrict venous and lymphatic drainage of tracheal mucosa. Hematoma evacuation requires opening and drainage of incision sites. However, tracheal obstruction from mucosal edema may persist. Patients should be intubated early before airway edema from compromised lymphatic and venous return occurs. Initially patients should be positioned upright at 45 degrees to facilitate venous drainage. Steroid and racemic epinephrine though nebulization should be used to decrease laryngeal edema. If dyspnea worsens, the patient should be intubated. If dissection is carried down to the mediastinum, pneumothorax must be ruled out as a cause of postoperative respiratory deterioration.

The anesthesiologist should be prepared to manage thyroid storm, especially in patients with uncontrolled or poorly controlled disease who present for emergency surgery. **Thyroid storm would manifest most likely intraoperatively** during manipulation of the thyroid gland.

KEY FACTS: DRUGS TO TREAT HYPERTHYROIDISM AND THYROID STORM

Acetaminophen	**Reduction of body temperature**
Antithyroid drugs	**Reduction of the secretion and production of thyroid hormones and prevention of iodide binding**
Beta blockers	**Attenuation of excessive sympathetic activity**
Glucocorticoids	**Reduction of thyroid hormone secretion and the peripheral conversion of T_4 to T_3**
Guanethidine	**Inhibition of catecholamine release**
Inotropes, diuretics	**May be needed for acute congestive heart failure**
Iodide	**Inhibition of thyroid hormone synthesis**
Magnesium	**Reduction of severity and incidence of cardiac arrhythmias**
Propranolol	**Impairment of peripheral conversion of T_4 to T_3**
Reserpine	**Depletion of catecholamine stores**

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31. ANSWER: D

Most (85% to 90%) pheochromocytomas are solitary tumors localized to a single adrenal gland, usually the right side. Approximately 10% of adults and 25% of children have bilateral tumors. The tumor may originate in extra-adrenal sites (10%), anywhere along the paravertebral sympathetic chain; however, 95% are located in the abdomen, and a small percentage are located in the thorax, urinary bladder, or neck. Malignant spread of these highly vascular tumors occurs in approximately 10% of cases.

In approximately 5% of cases, this tumor is inherited as a familial autosomal dominant trait. It may be part of the polyglandular syndrome referred to as *MEN type IIA* or *IIB* (E). Type IIA includes medullary carcinoma of the thyroid, parathyroid hyperplasia, and pheochromocytoma; Type IIB consists of medullary carcinoma of the thyroid, pheochromocytoma, and neuromas of the oral mucosa. Pheochromocytomas may also arise in

association with von Recklinghausen neurofibromatosis or von Hippel-Lindau disease (retinal and cerebellar angiomatosis). The pheochromocytoma of the familial syndromes is rarely extra-adrenal or malignant. Bilateral tumors occur in approximately 75% of cases. When these patients present with a single adrenal pheochromocytoma, the chances of subsequent development of a second adrenal pheochromocytoma are sufficiently high that bilateral adrenalectomy should be considered. Every member of a MEN family should be considered at risk for pheochromocytoma.

32. ANSWER: D

The reduction in perioperative mortality rates from a high of 45% to between 0% and 3% with the excision of pheochromocytoma followed the introduction of alpha antagonists for preoperative therapy. **Perioperative blood pressure fluctuations, myocardial infarction, congestive heart failure, cardiac dysrhythmias, and cerebral hemorrhage all appear to be reduced in frequency when the patient has been treated before surgery with alpha blockers** and the intravascular fluid compartment has been re-expanded. Extended treatment with alpha antagonists is also effective in treating the clinical manifestations of catecholamine myocarditis. However, alpha-blocker therapy has never been studied in a controlled way, and some groups question its necessity in light of the availability of potent titratable vasodilators for intraoperative use.

33. ANSWER: E

Alpha-adrenergic blockade is initiated once the diagnosis of pheochromocytoma is established. **Phenoxybenzamine, a long-acting (24 to 48 hours), noncompetitive presynaptic ($alpha_2$) and postsynaptic ($alpha_1$) blocker**, has traditionally been used at doses of 10 mg every 8 hours. Increments are added until the blood pressure is controlled and paroxysms disappear. Most patients need between 80 and 200 mg/day. The absorption after oral administration is variable, and side effects are common. Certain cardiovascular reflexes such as the baroreceptor reflex are blunted, and postural hypotension is common. **Selective competitive $alpha_1$ blockers, such as doxazosin, terazosin, and prazosin, have also been used effectively.** Because postural hypotension can be pronounced with the commencement of therapy, the initial 1-mg dose is given at bedtime. Postural changes are also seen with maintenance therapy. A comparison of patients with pheochromocytoma receiving phenoxybenzamine or prazosin has shown both drugs to be equally effective in controlling the blood pressure. Although the optimal period of preoperative treatment has not been established, most clinicians recommend beginning alpha-blockade therapy at least 10 to 14 days before the proposed surgery. During this time, the contracted intravascular volume and hematocrit return toward normal and the blood pressure is stabilized. Despite the real possibility of hypotension after vascular isolation of the tumor, most clinicians continue alpha blockers up until the morning of surgery.

34. ANSWER: E

The major goal of the perioperative management of patients with a pheochromocytoma is to block the responses to catecholamines released by the tumor. Administration of alpha-adrenergic blockers has been the cornerstone of management. **If adrenergic blockade is not achieved at the time of surgery, it is reasonable to delay the procedure until the patient shows an appropriate degree of alpha blockade.** Answers A through D are reasonable goals to assess the effect, but orthostatic hypotension would be an expected side effect of alpha blockade. On the other hand, it has been suggested that the blood pressure on standing should not be less than 80/45 mm Hg.

35. ANSWER: B

Beta-adrenergic blockade is occasionally added after alpha blockade has been established. This addition is considered in patients with persistent tachycardia or cardiac dysrhythmias that may be caused by nonselective alpha blockade or epinephrine-secreting tumors. **Beta blockers should not be given until adequate alpha blockade** is ensured to avoid the possibility of unopposed alpha-mediated vasoconstriction. There is no clear preoperative advantage of one beta antagonist over another, although the short half-life of esmolol may allow better control of heart rate and arrhythmias in the perioperative setting. Labetalol, a beta-adrenergic antagonist with alpha-blocking activity, is effective as a second-line medication but can increase blood pressure when this drug is used alone.

The circulating blood volume is decreased in many patients with pheochromocytomas. Therefore, many clinicians support the idea of administering volume before surgery while patients receive alpha blockade. However, one must be very careful with patients who have decreased myocardial function to avoid congestive heart failure. Many other clinicians believe volume loading is no longer necessary when the patient has been on alpha blockers for 2 weeks or more, assuming the volume has been restored.

36. ANSWER: E

Alpha blockers are given before beta blockade. Using beta blockers first may inhibit $beta_2$-mediated vasodilation, producing unopposed alpha-mediated vasoconstriction and a hypertensive crisis. Phenoxybenzamine is the most popular alpha blocker in the preoperative period, but prazosin and phentolamine (as a constant infusion) are also commonly used. Phenoxybenzamine has been most widely used because of its relatively long duration of action and ease of administration. It irreversibly alkylates $alpha_1$-adrenergic receptors on vascular smooth muscle, thereby making them nonfunctional, and it may cause postural hypotension and reflex tachycardia. These may be avoided with the careful administration of fluid volume as well as beta blockers. Be sure not to initiate beta blockade until the alpha blockers have been started; otherwise, congestive heart failure may be precipitated. Many believe that beta blockers should be used only when tachycardia or arrhythmias exist.

Prazosin has been used but does not seem to adequately prevent perioperative hypertensive episodes. Prazosin, magnesium sulfate, beta blockers, ACE inhibitors, and calcium channel blockers have been used in combination with phenoxybenzamine to attain hemodynamic stability.

Alpha-methyl-paratyrosine inhibits tyrosine hydrolase. It may be given orally, gradually increasing the dose. This may decrease the catecholamine synthesis by 40% to 80%. It is very effective, but may cause diarrhea, sedation, fatigue, anxiety, or agitated depression or tumors.

Sedation is considered by many clinicians to be important before surgery for pheochromocytoma. Sedation may decrease the need to use high doses of antihypertensive agents before surgery.

37. ANSWER: D

Postoperative hypotension is often seen after the excision of the tumor. This may be due to hypovolemia and/or persistent fatigue of the vasoconstrictor mechanism. Once the excess catecholamines are diminished after the removal of the tumor, the response by the vascular bed to maintain pressure may be sluggish. Hypotension is rarely seen in patients who have been adequately volume-expanded and alpha-blocked preoperatively. If it does occur, it should be treated with volume administration and vasoconstriction using phenylephrine or norepinephrine.

Persistent hypertension after removal of a pheochromocytoma occasionally signifies that a residual pheochromocytoma tumor is present. Plasma catecholamine levels may not decrease to normal levels for many days after removal of the tumor.

These patients are prone to significant hypoglycemia, which alone can make a patient somnolent. In more severe cases, hypoglycemia may cause loss of consciousness and respiratory arrest. The hypoglycemia results from the fact that suppression of beta-cell function disappears after removal of the tumor, and hence the plasma insulin level rises. Neoglycogenesis and glycogenolysis, which have sustained the high blood sugar, are no longer present. Therefore, one should consider switching infusions to glucose-containing intravenous fluids after removal of the tumor and monitor the glucose levels very closely for at least 24 hours postoperatively.

As with most surgeries, blood loss is expected and can be substantial in pheochromocytoma resections.

For the first 48 hours after surgery, these patients may be very somnolent. This is possible due to the sudden removal of activating catecholamines. Frequently this results in decreased narcotic requirements (Table 3.10).

Table 3.10 DRUG USED IN THE MANAGEMENT OF PHEOCHROMOCYTOMA

Phentolamine	Nonselective alpha blocker	Short duration of action, ~5 min
Phenoxybenzamine	Nonselective alpha blocker	Preoperative, long half-life; may accumulate
Doxazosin (terazosin dosing similar)	Selective $alpha_1$ blocker	Preoperative, first-dose phenomenon; may cause syncope
Propranolol	Nonselective beta blocker	Preoperative, should never be given without first creating alpha blockade
Atenolol	Selective $beta_1$ blocker	Preoperative, long-acting drug eliminated; unchanged by kidney
Esmolol	Selective $beta_1$ blocker	Short-acting; elimination half-life ~9 min
Labetalol	Alpha blocker and beta blocker	Preoperative, a much weaker alpha blocker than beta blocker; may cause hypertensive response
Nitroprusside	Direct vasodilator	Powerful vasodilator; short-acting
Nitroglycerin	Direct vasodilator	Short-acting vasodilator, coronary vasodilator
Magnesium sulfate	Direct vasodilator and membrane stabilizer	May potentiate neuromuscular blockade
Nicardipine	Calcium channel antagonist	

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38. ANSWER: D

The clinical course and recurrence of signs of MH determine repeat or further treatment with dantrolene.

The guidelines for the dose and duration of dantrolene therapy after resolution of acute MH are empirical. It would seem prudent to continue dantrolene, 1 mg/kg every 6 hours intravenously, for at least 24 to 36 hours, but more may be given if signs of MH reappear. Arterial blood gas analysis, temperature (usually to 38 degrees C), muscle tone, EKG, arrhythmias, electrolytes, and urine output should be monitored. **Of the presented options, only frequent arrhythmias would be an indication that the symptoms of MH are reappearing.**

Some recommend conversion of dantrolene therapy from intravenous to oral form (4 mg/kg per day or more) with continuation for several days. The MH hotline should be contacted to report the case, verify treatment, and provide appropriate follow-up for the patient and family.

39. ANSWER: E

Disseminated intravascular coagulation (DIC) has often been described in cases of MH, probably resulting from release of thromboplastins secondary to shock and core temperature above 41 degrees C and/or release of cellular contents on membrane destruction.

As many as 25% of patients may experience acute recrudescence, a relapse within hours of the first episode.

Renal failure secondary to myoglobinuria may occur within hours after the episode begins. Dantrolene vials contain 20 mg dantrolene and 3 g mannitol with sufficient sodium hydroxide to yield a pH of approximately 9.5. Dantrolene should be reconstituted with sterile water (not saline) for injection. Diuresis and alkalization of the urine should be continued after the initial treatment to produce more than 1 mL/kg/hr urine output.

Significant muscle weakness and pain may follow MH, resulting from muscle destruction along with dantrolene administration. Recovery of strength may require weeks to months.

40. ANSWER: C

The increased muscle metabolism in MH is initially aerobic, resulting in increased oxygen consumption, hypercarbia, respiratory acidosis, and heat production. As adenosine triphosphate (ATP) is depleted, metabolism becomes anaerobic, resulting in lactic acid production, metabolic acidosis, and further heat production. In the presence of hyperthermia, acidosis, and ATP depletion, the cell loses the ability to maintain the integrity of its membrane. Rhabdomyolysis leads to the release of potassium, myoglobin, and creatine kinase. **Hypercarbia is the earliest and most sensitive sign of MH; generalized muscle rigidity is the most specific sign.**

KEY FACTS: MALIGNANT HYPERTHERMIA

Early Signs:	Late Signs:
Tachycardia	Increased temperature
Tachypnea	Skin mottling
Muscle rigidity	Myoglobinuria
Arrhythmias	Hyperkalemia
Hypercarbia	Elevated creatine kinase
	Mixed acidosis

41. ANSWER: C

Dantrolene is a direct skeletal muscle relaxant that binds to the RYR1 receptor, thereby blocking the release of calcium from the sarcoplasmic reticulum. It is the drug of choice in the treatment of MH. Be aware that the preparation that is mostly available is poorly soluble and takes some time to prepare. A more soluble version recently become available.

Diuresis with furosemide and mannitol (3 g are part of dantrolene drug mix) is important to prevent renal failure secondary to myoglobinuria. Diuresis and alkalization of the urine should be continued after the initial treatment to produce more than 1 mL/kg/hr urine output.

Dysrhythmia control usually follows hyperventilation, dantrolene therapy, and correction of acidosis. **Calcium channel blockers should not be used in the acute treatment of MH.** Verapamil can interact with dantrolene to produce hyperkalemia and myocardial depression. Lidocaine can be given safely during an MH crisis.

In fulminant cases with significant metabolic acidosis, sodium bicarbonate is indicated. Insulin is commonly used in the management of hyperkalemia in combination with glucose, bicarbonate, and hyperventilation. If hyperkalemia is associated with significant cardiac effects, calcium chloride, 1 gram or 10 mg/kg, should be given. Hypokalemia commonly results during therapy of MH. However, potassium

replacement should be undertaken very cautiously, if at all, because potassium may retrigger an MH episode.

KEY FACTS: TREATMENT OF MALIGNANT HYPERTHERMIA

- Call for help and the MH cart with dantrolene.
- Notify surgeon.
- Discontinue volatile agents and succinylcholine.
- Hyperventilate with 100% oxygen at flows of 10 L/min or more. Circle system and CO_2 absorbent do not need to be changed.
- Halt the procedure as soon as possible; if emergent, use nontriggers.
- Administer dantrolene 2.5 mg/kg through large-bore intravenous line. Repeat until there is control of the signs of MH. Sometimes more than 10 mg/kg (up to 30 mg/kg) is necessary. Dissolve the 20 mg in each vial with at least 60 mL sterile preservative-free water for injection. Prewarming the sterile water will speed solubilization of dantrolene. The crystals also contain NaOH for a pH of about 9; each bottle has 3 g mannitol for isotonicity.
- Give bicarbonate for metabolic acidosis.
- Cool the patient with a core temperature above 39 degrees C. Lavage open body cavities. Apply ice to surface. Infuse cold saline IV.
- Dysrhythmias usually respond to treatment of acidosis and hyperkalemia. Avoid calcium channel blockers, which may cause hyperkalemia or cardiac arrest in the presence of dantrolene.
- Hyperkalemia should be treated with hyperventilation, bicarbonate, glucose/insulin, calcium.
- Follow ET_{CO2}, electrolytes, blood gases, CK, core temperature, urine output and color (Foley), urine myoglobin, and coagulation studies. Venous blood gases may document hypermetabolism better than arterial values.
- Postacute care: Observe the patient in an ICU for at least 24 hours. Give dantrolene 1 mg/kg every 4 to 6 hours or 0.25 mg/kg/hour by infusion for at least 24 hours. Follow vital signs and lab studies as above.
- Counsel the patient and family regarding MH and further precautions.
- Consider calling the MH Hotline: 1–800–644–9737.
- Malignant Hyperthermia Association of the United States website http://www.mhaus.org/

42. ANSWER: B

The most accurate diagnostic test for MH is the exposure of biopsied skeletal muscle to halothane, caffeine, and more recently ryanodine or chlorocresol. The test is highly sensitive, close to 100%, but up to 20% of positive results may be false positives. **Nevertheless, the value of the test resides in ruling out MH susceptibility with certainty.** In attempts to further improve the specificity and sensitivity of the contracture test, other agents have been tested for their effect on skeletal muscle. Ryanodine binds to and activates the calcium-release channel of the sarcoplasmic reticulum. Chlorocresol is an activator of ryanodine. Ideally contracture tests using these substances would afford maximum specificity for MH, and early studies supported this concept.

Testing is usually completed within about 5 hours of biopsy to ensure adequate viability of the muscle preparations. Therefore, it is essential that the biopsy be performed no more than 1 hour away from the testing laboratory.

Because the test is invasive and costly and requires strict adherence to specific requirements, there are only approximately 10 testing centers in North America.

DNA testing for MH susceptibility is an alternative diagnostic tool to assess a patient's risk for MH.

43. ANSWER: E

Rigidity of the jaw muscles after administration of succinylcholine is referred to as ***masseter muscle rigidity (MMR)***, masseter spasm, or trismus. MMR may even occur after induction with any anesthetic agent, intravenous or inhalation, before succinylcholine administration. Repeat doses of succinylcholine do not relieve MMR, nor do nondepolarizing relaxants. A peripheral nerve stimulator usually reveals flaccid paralysis.

If the anesthetic is discontinued, the patient usually appears to recover uneventfully. However, within 12 hours, myoglobinuria often occurs and CK elevation is detectable. Therefore, if MMR occurs, urine should be examined for myoglobin. Patients experiencing MMR should be hospitalized for at least 24 hours.

Although MMR probably occurs in patients of all ages, it is more common in children and young adults, particularly following gas anesthesia induction.

Should MMR occur, elective surgery should be postponed and the patient should be observed in an ICU setting for 24 hours, seeking myoglobinuria specifically. In the case of an emergency surgical procedure, the anesthetic should be converted to a "nontriggering" technique and the patient observed for early signs of MH. Dantrolene and other MH treatment procedures should be made available.

Dantrolene administration is advised only if there is generalized rigidity and/or signs of hypermetabolism.

KEY FACTS: TRISMUS OR MASSETER SPASM WITH SUCCINYLCHOLINE (ACCORDING TO MHAUS)

- **Early sign of MH in many patients**
- **If there is limb muscle rigidity, begin treatment with dantrolene.**
- **For emergent procedures, continue with nontriggering agents; consider dantrolene. Dantrolene administration is advised only if there is generalized rigidity and/or signs of hypermetabolism.**
- **Follow CK and urine myoglobin for 36 hours at least. Check CK immediately and at 6-hour intervals until returning to normal.**
- **Observe in PACU or ICU for at least 12 hours.**

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44. ANSWER: A

Cocaine blocks the reuptake of catecholamines into the presynaptic nerve terminals. This occurs in both central and peripheral nervous systems and causes the accumulation of catecholamines in synaptic clefts. The result is increased receptor stimulation (alpha receptor, beta receptor, and dopamine) via an indirect sympathomimetic action. Inotropes must be used with care in patients abusing cocaine, as cardiovascular responses (arterial and left ventricular pressure, contractility, and heart rate) will all be potentiated by the concurrent administration of alpha receptor, beta receptor, or dopamine agonists. Cocaine shifts the dose–response curve of norepinephrine to the left and enhances its maximal effects.

Cocaine increases blood pressure, raises heart rate, and can cause paranoia, anxiety, seizures, angina, and may cause myocardial infarction (even in patients without coronary artery disease).

Cocaine is also a local anesthetic and competitively blocks the fast voltage-sensitive sodium channels of nerve cells, and by preventing the fast inward Na1 current, it prevents the depolarization of the cell membrane. Cocaine decreases both the rate of depolarization and amplitude of the action potential and causes a slowing of conduction.

45. ANSWER: D

Acute cocaine administration is known to cause coronary vasospasm, myocardial ischemia, myocardial infarction, and ventricular cardiac dysrhythmias, including ventricular fibrillation. **Associated systemic hypertension and tachycardia further increase myocardial oxygen requirements at a time when coronary oxygen delivery is decreased by the effects of cocaine on coronary blood flow.** Cocaine use can cause myocardial ischemia and hypotension that lasts as long as 6 weeks after discontinuing cocaine use. Excessive sensitivity of the coronary vasculature to catecholamines after long-term exposure to cocaine may be due in part to cocaine-induced depletion of dopamine stores.

Cocaine may produce hyperpyrexia, which can contribute to seizures. There is a temporal relationship between the recreational use of cocaine and cerebrovascular accidents.

Thrombocytopenia associated with cocaine abuse may influence the selection of regional anesthesia. Other side effects of cocaine use to look out for are lung damage, pulmonary edema, and pneumonia, which have been observed in patients who smoke cocaine. In pregnancy cocaine causes a dose-dependent decrease in uterine blood flow. Cocaine-abusing parturients are at higher risk of spontaneous abortion, abruptio placentae, and fetal malformations.

Long-term cocaine abuse is associated with nasal septal atrophy, agitated behavior, paranoid thinking, and heightened reflexes. In the absence of acute intoxication, long-term abuse of cocaine has not been shown to be predictably associated with adverse anesthetic interactions, although the possibility of cardiac dysrhythmias remains a constant concern.

46. ANSWER: C

Management of anesthesia in patients acutely intoxicated with cocaine must consider the vulnerability of these patients to myocardial ischemia and cardiac dysrhythmias. Any event or drug likely to increase already enhanced sympathetic nervous system activity must be carefully considered before its selection. For this reason ketamine should be avoided in the management of cocaine-addicted patients. It seems prudent to have nitroglycerin readily available to treat signs of myocardial ischemia associated with tachycardia or hypertension. Unexpected agitation during the perioperative period may reflect the effects of cocaine ingestion. Increased anesthetic requirements may be present in acutely intoxicated patients, presumably reflecting increased concentrations of catecholamines in the central nervous system.

A beta blocker should not be given alone because unopposed alpha-adrenergic stimulation can cause a further increase in systemic vascular resistance. Patients with chronic cocaine intoxication are less of a problem, but they are still at risk for dysrhythmias (avoiding halothane, pancuronium, atropine, and sympathomimetics still seems like a good idea). Chronic cocaine exposure increases the halothane minimum alveolar concentration (MAC) in dogs and the isoflurane MAC in sheep, and acute ingestion may antagonize the sedative effects of benzodiazepines in humans.

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47. ANSWER: B

The incidence of specific respiratory events (reintubation, laryngospasm, bronchospasm, aspiration, hypoventilation, hypoxemia, and others) during anesthesia was found to be 5.5% in smokers compared to 3.3% in nonsmokers. The relative risk was 2.3 times higher than normal in young smokers and 6.3 times higher in obese smokers. Reduction in smoking within 1 month of surgery was not associated with a decreased risk for postoperative pulmonary complications.

Pulmonary macrophage activity is decreased in smokers.

Increase in excitability leads to more frequent contractions and again an increase in oxygen consumption. An increase in coronary vascular resistance leads to a decrease in coronary blood flow. Carbon monoxide also binds with cytochrome oxidase and myoglobin and inactivates mitochondrial enzymes in the cardiac muscle. The result is a decrease in the intracellular oxygen transport and usage and a negative inotropic effect. These mechanisms lead to chronic tissue hypoxia. The body compensates with an increase in red blood cells. The result is an improvement of the oxygen availability at the expense of increased plasma viscosity.

Nicotine in smoke stimulates the adrenal medulla to secrete adrenaline, resets the carotid body and aortic receptors to maintain a higher blood pressure, and stimulates autonomic ganglia, increasing sympathetic tone. The result is an increase in systolic and diastolic blood pressure, an increase in heart rate, and an increase in peripheral vascular resistance. These increase the myocardial contractility, leading to an increase in oxygen consumption by the cardiac muscle. The half-life of nicotine is 30 to 60 minutes. Three to four hours of abstinence results in insignificant side effects due to nicotine and a significant improvement of the myocardial oxygen supply/demand ratio.

Exposure to tobacco, directly or through "second-hand" smoke, increases the risk for many perioperative complications. **Smokers are more likely to experience wound infections, respiratory or airway complications (including oxygen desaturation), and severe coughing.** Smoking decreases macrophage function, negatively affects coronary flow reserve, and causes vascular endothelial dysfunction, hypertension, and ischemia. Smokers require longer hospital stays than nonsmokers do and often need postoperative intensive care admission.

48. ANSWER: D

Irritants in smoke increase mucous secretions. The mucus becomes hyperviscous, with altered elasticity. The sputum volume takes 2 to 6 weeks to return to normal. There is some improvement in tracheobronchial clearance after 3 months.

Laryngeal and bronchial reactivity is increased. Cigarette smoke is known to disrupt the epithelial lining of the lung, causing an increase in pulmonary epithelial permeability. This loss of epithelial integrity allows irritants to penetrate the epithelium more easily and stimulate the subepithelial irritant receptors, resulting in increased reactivity. Smoking leads to small-airway narrowing, causing an increased closing volume. Pulmonary surfactant is also decreased. These lead to small-airway disease. It takes 5 to 10 days for laryngeal and bronchial reactivity to settle. There is improvement in small-airway narrowing after 4 weeks, and marked improvement is seen after 6 months. One must be careful in stopping smoking in asthmatics as the asthma may worsen.

Cilia become inactive and are destroyed by ciliotoxins. The result is impaired tracheobronchial clearance. Following smoking cessation, ciliary activity starts to recover within 4 to 6 days.

In smokers, the amount of COHb in the blood ranges from 5% to 15%. In nonsmokers, it is only about 0.3% to 1.6%. The affinity of carbon monoxide for hemoglobin (Hb) is 200 times that of oxygen. Thus, the amount of Hb available for combining with oxygen is drastically reduced. It also shifts the oxyhemoglobin curve to the left due to its high affinity for Hb, a change in shape of the oxyhemoglobin curve from a sigmoidal to a more hyperbolic curve by carboxyhemoglobin, and depletion of 2,3-diphosphoglycerate by carbon monoxide.

The left shift of the oxyhemoglobin curve makes it difficult for tissues to extract oxygen from the hemoglobin. The result is a decrease in the oxygen available to the tissues.

The half-life of carboxyhemoglobin depends chiefly on pulmonary ventilation. At rest, the half-life is about 4 to 6 hours. With strenuous exercise, due to rapid breathing, it is decreased to 1 hour. **During sleep, when the breathing is slow, its half-life is prolonged to about 10 to 12 hours. If one breathes 100% oxygen,** its half-life is reduced to 40 to 80 minutes, and with hyperbaric oxygen, it is even further reduced to 23 minutes. Recently, it has been found that its half-life is longer in male patients than female patients. Thus, on advising patients before anesthesia, these variations should be noted. During the daytime, abstinence for 12 hours is sufficient to get rid of carbon monoxide. If an operation is scheduled for the next morning, the patient should not smoke the previous evening.

Preoperative smoking cessation intervention in patients who underwent knee and hip replacement decreased rates of surgical site infection from 23% in the conventional group to 4% in those who stopped smoking weeks before surgery.

KEY FACTS: SMOKING

- **Smoking increases the risk for pulmonary complications two to six times compared to nonsmokers.**
- **Smoking increases heart rate, SVR, coronary vascular resistance, risk for myocardial ischemia, pulmonary vascular resistance, and blood viscosity.**
- **Smoking increases COHb, mucous secretions, and airway reactivity and decreases FEV_1/FVC and ciliary clearance.**

Smoking Cessation

- **For a minimum of 12 to 24 hours prior to surgery will reduce the COHb and nicotine levels to that of nonsmokers**
- **For more than 8 weeks will reduce postoperative pulmonary complications**
- **For more than 2 years decreases the risk of myocardial infarction**

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49. ANSWER: D

In patients with reactive airways, several choices can help prevent bronchospasm. Patients should be pretreated with inhaled $beta_2$ agonists (e.g., albuterol) or anticholinergic agents (e.g., ipratropium) preoperatively, especially if tracheal intubation is planned. The patient may self-administer an inhaler at the time of transfer to the operating room. If tracheal intubation can be avoided, the use of a laryngeal mask airway or similar device can decrease the risk for bronchospasm, but this does not guarantee that bronchospasm will not develop. **Propofol, ketamine, or volatile anesthetics cause bronchial dilation and are the induction agents of choice.** Barbiturates may provoke bronchospasm. Adjuvants to increase the depth of anesthesia and blunt airway reflexes before intubation such as intravenous lidocaine or opioids may be useful. However, laryngotracheal lidocaine may be less useful, because lidocaine topically applied to the trachea may itself transiently increase airway resistance.

KEY FACTS: PREVENTION OF BRONCHOSPASM

- Optimize preoperative symptom control (corticosteroids?).
- Preoperative anxiolysis as necessary
- Inhaled $beta_2$ agonists or muscarinic antagonists immediately before induction
- Consider alternatives to endotracheal intubation and general anesthesia.
- Minimize airway instrumentation as feasible.
- Induction with propofol, ketamine, or volatile agent
- Use volatile anesthetics early and often (avoid desflurane).
- Adequate depth of anesthesia before airway instrumentation
- Intravenous lidocaine and opioids as adjuncts for endotracheal intubation

KEY FACTS: MANAGEMENT OF INTRAOPERATIVE BRONCHOSPASM

- Deepen anesthesia with a volatile agent.
- Consider propofol, ketamine, and lidocaine to further deepen anesthesia.
- Inhaled $beta_2$ agonists (many doses may be necessary for adequate drug delivery)
- Avoid aminophylline.
- Parenteral corticosteroids to avoid recurrence
- Adjust ventilation to minimize barotrauma and gas trapping (limit peak pressure and prolong expiratory phase).
- Epinephrine may be necessary to provide adequate stimulation of airway beta adrenoreceptors, especially if anaphylaxis triggered bronchospasm.

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50. ANSWER: B

Airflow resistance is normally around 1 cm H_2O/L/sec. With obstructive lung disease it is increased to about 5 cm H_2O/L/sec in mild to moderate asthma and bronchitis and greater than 10 cm H_2O/L/sec in more severe cases.

Patients with obstructive lung disease, including asthma, chronic bronchitis, and emphysema, have increased dead-space ventilation. Some regions are poorly ventilated secondary to the airway obstruction.

Table 3.11 CHRONIC BRONCHITIS VERSUS EMPHYSEMA

FEATURE	CHRONIC BRONCHITIS	EMPHYSEMA
Mechanism of airway obstruction	Decreased airway lumen due to mucus and inflammation	Loss of elastic recoil
Dyspnea	Moderate	Severe
Pa_{O_2}	Marked decrease ("blue bloater")	Modest decrease ("pink puffer")
Pa_{CO_2}	Increased	Normal to decreased
Diffusing capacity	Normal	Decreased
Hematocrit	Increased	Normal
Cor pulmonale	Marked	Mild
Prognosis	Poor	Good

Source: Modified from Kurup V. Respiratory diseases. In: Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-Existing Disease*. 5th ed. Philadelphia, PA: Saunders; 2008:169.

In these patients' lungs some regions are underventilated in relation to their perfusion, which is called a ventilation/perfusion mismatch (signified by low Va/Q ratios).

This forces inspired air to other regions, which may be ventilated in excess of their perfusion. Such opposite Va/Q mismatch (signified by high Va/Q ratios) has the same effect on gas exchange as an increase in dead space does and is also measured as dead space. Patients with advanced chronic bronchitis may have a Va/Q ratio as high as 0.8 to 0.9.

Patients with a high Va/Q ratio would have to ventilate some 30 to 50 L/min to maintain normal Pa_{CO_2}. Pa_{CO_2} eventually rises due to relative alveolar "hypoventilation." Erroneously, it is often said that bronchitic patients are hypoventilating, but in fact they are hyperventilating (Table 3.11).

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51. ANSWER: A

Negative-pressure pulmonary edema may follow relief of acute upper airway obstruction (postobstructive pulmonary edema) caused by postextubation laryngospasm, epiglottitis, tumors, obesity, hiccups, or obstructive sleep apnea in spontaneously breathing patients.

The pathogenesis of negative-pressure pulmonary edema is related to the development of high negative intrapleural pressure by vigorous inspiratory efforts against an obstructed upper airway. High negative intrapleural pressure decreases the interstitial hydrostatic pressure, increases venous return, and increases left ventricular afterload. It has also been shown that the negative pressure leads to intense sympathetic nervous system activation, hypertension, and central displacement of blood volume. Together these factors produce acute pulmonary edema (transudate) by increasing the transcapillary pressure gradient.

The time to the development of symptoms after relief of airway obstruction ranges from a few minutes to as long as 2 to 3 hours. Typical signs are tachypnea, cough, and failure to maintain oxygen saturation above 95%. As they are not specific they may be diagnosed as pulmonary aspiration or pulmonary embolism. Hypoxemia is accompanied by bilateral fluffy infiltrates on the chest radiograph, but radiographic evidence of pulmonary edema resolves within 12 to 24 hours.

Treatment is supportive and maintenance of a patent upper airway and administration of supplemental oxygen are often sufficient treatment. This form of pulmonary edema is typically transient and self-limited. Mechanical ventilation may occasionally be needed for a brief period. **Diuresis is controversial as potentially can further decrease the intravascular volume and cause hypotension.**

Muscular healthy patients are at increased risk of postobstructive pulmonary edema because of their ability to generate significant inspiratory force.

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4.

ANESTHESIA AND DISEASE STATES, PART II

Christopher Plambeck, MD, Vikram Khatri, MD,
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1. A 35-year-old HIV-positive patient who is undergoing a prolonged electrophysiology ablation procedure under monitored anesthesia care using midazolam and fentanyl demonstrates a delayed arousal from the sedation. Which of the following antiretroviral medication classes is most likely contributing to the prolonged effects of the sedatives?

A. Nucleoside reverse transcriptase inhibitors
B. Nucleotide reverse transcriptase inhibitors
C. Protease inhibitors
D. Integrase inhibitors
E. Entry inhibitors

2. What is the correct mechanism by which the nucleoside reverse transcriptase inhibitor class of HIV antiretrovirals inactivates HIV?

A. Prevents cleavage of polyprotein
B. Inactivates enzyme by preventing conformational change
C. Prevents fusion of virus to cell membrane
D. Blocks integration of viral DNA into host genome
E. Prevents DNA polymerization

3. A 74-year-old man with a history of hypertension, diabetes mellitus type 2, and mild chronic renal insufficiency is undergoing a mitral valve repair. Which of the following pharmacologic therapies is most likely to be protective against an acute kidney injury?

A. N-acetylcysteine
B. Dopamine
C. Fenoldopam
D. Mannitol
E. Furosemide

4. An infant born at 27 weeks is exhibiting the signs and symptoms of respiratory distress syndrome. Which of the following therapies is NOT beneficial in preventing bronchopulmonary dysplasia in the premature infant?

A. Increasing FiO_2 to obtain $SpO_2 > 95\%$
B. Nasal continuous positive airway pressure
C. Mild permissive hypercapnia
D. Antenatal steroid administration
E. Surfactant

5. A 32-year-old African-American man with a history of cholelithiasis and sickle cell disease is to undergo an elective laparoscopic cholecystectomy. Which of the following prophylactic preoperative transfusion strategies is indicated to minimize the risk of postoperative sickle cell-related complications in this patient?

A. No prophylactic transfusion
B. Intravenous hydration only
C. Transfuse to hemoglobin of 8 mg/dL
D. Transfuse to hemoglobin of 10 mg/dL
E. Exchange transfusion (HgSS < 30%)

6. In patients with diabetes mellitus, the duration of action of which of the following insulin-replacement therapies is the longest?

A. Insulin lispro
B. Neutral protamine Hagedorn (NPH)
C. Regular insulin
D. Insulin glargine
E. Insulin aspart

7. Which of the following is true regarding the management of diabetic ketoacidosis?

A. Administration of dextrose-containing fluids is contraindicated.
B. Intravenous insulin is given until normoglycemia is obtained.
C. Phosphate therapy is routinely administered to correct hypophosphatemia.
D. Potassium supplementation is frequently required.
E. Sodium bicarbonate is usually given to correct the metabolic acidosis.

8. A 54-year-old woman with end-stage renal disease has no detectable twitches by train-of-four upon completion of a prolonged intra-abdominal operation using rocuronium as the muscle relaxant. Which of the following best explains the prolonged effect of rocuronium in this renal failure patient?

A. No change from healthy patients
B. Kidney is primary site for elimination.
C. Active metabolite requires renal elimination.
D. Increased volume of distribution
E. Decreased renal clearance

9. Which of the following statements regarding the regulation of hepatic blood flow is INCORRECT?

A. The hepatic arterial buffer response (HABR) is controlled by adenosine.
B. Hepatic blood flow is provided 75% from the hepatic artery and 25% from the portal vein.
C. Portal venous pressure is controlled by $alpha_1$ and $alpha_2$ receptors.
D. Halothane increases hepatic arterial vascular resistance.
E. Vasopressin increases splanchnic arterial resistance and decreases portal venous resistance.

10. Which of the following laboratory tests would be most useful in the assessment of acute hepatic synthetic function?

A. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)
B. Serum bilirubin
C. Serum albumin
D. Prothrombin time
E. Alkaline phosphatase

11. Which source serology imposes the highest risk of contracting hepatitis B from a needlestick injury?

A. HBsAg negative/anti-HBc positive
B. HBsAg positive/HBeAg positive
C. HBsAg positive/HBeAg negative
D. HBsAg negative/anti-HBs positive
E. Anti-HBs negative/anti-HBc negative

12. The following are the serologic test results for a patient with hepatitis B virus: HBsAg positive, total anti-HBc positive, IgM anti-HBc negative, anti-HBs negative. The likely interpretation of these serologic test results is

A. Recent immunization (less than 18 days ago)
B. Acute infection
C. Acute resolving infection
D. Chronic infection
E. False positive

13. The CDC guidelines recommend which of the following postexposure prophylaxis methods following a percutaneous exposure to blood from a patient positive for the hepatitis C virus?

A. No prophylaxis required
B. Immunoglobulin
C. HCV vaccination
D. Ribavirin
E. Interferon

14. Which of the following laboratory test results would be most useful in differentiating an *acute* hepatitis C infection from a chronic infection?

A. ALT greater than 10 times normal
B. Positive IgM anti-HCV
C. Positive anti-HCV (EIA)
D. Positive anti-HCV (RIBA)
E. Positive HCV-RNA

15. Prolonged exposure to which anesthetic agent may cause hepatomegaly?

A. Propofol
B. Etomidate
C. Thiopental
D. Sevoflurane
E. Fentanyl

16. While suturing the central line in a patient with a known history of asymptomatic HIV you accidentally prick your finger. A review of the patient's lab data reveals low viral titers and a high CD4 count. According to CDC guidelines, what is the recommendation for postexposure prophylaxis for HIV infection?

A. No prophylaxis required
B. Single-dose, three-drug prophylaxis
C. One-drug regimen for 28 days

D. Two-drug regimen for 28 days
E. Three-drug regimen for 28 days

17. Based on the findings of the recent NICE-SUGAR trial, what is the recommended blood glucose target for insulin therapy in critically ill adults?

A. Less than 81 mg/dL
B. Less than 108 mg/dL
C. Less than 150 mg/dL
D. Less than 180 mg/dL
E. Less than 200 mg/dL

18. All of the following are true regarding the hyperosmolar hyperglycemic state EXCEPT?

A. Occurs in type 2 diabetes mellitus
B. Serum ketones may be present
C. Higher serum glucose than in DKA
D. Lower mortality compared to DKA
E. Occurs more commonly in the elderly

19. A 43-year-old man with end-stage renal disease has been on a ventilator in the ICU for several days with vecuronium used for muscle paralysis. After discontinuation of the vecuronium infusion, he exhibited prolonged residual paralysis. Which of the following best explains the prolonged effect of vecuronium in the renal failure patient?

A. No change from healthy patients
B. Kidney is primary site of elimination.
C. Active metabolite requires renal elimination.
D. Increased volume of distribution
E. Decreased protein binding

20. Hepatic disease may prolong the duration of action of all the following neuromuscular blockers EXCEPT

A. Succinylcholine
B. Pancuronium
C. Vecuronium
D. Rocuronium
E. Cisatracurium

21. A 75-year-old man is oliguric 3 hours following open AAA repair. Which of the following biomarkers is the LATEST indicator of an acute renal injury?

A. Creatinine
B. Cystatin C
C. NGAL
D. IL-18
E. KIM-1

22. The following factors contribute to the requirement for a reduced dose of thiopental during the administration of an anesthetic to an elderly patient EXCEPT

A. Decreased lean body mass
B. Increased body fat
C. Decreased total body water
D. Decreased albumin levels
E. Increased brain sensitivity

23. Which of the following is a likely cause of a postoperative unconjugated hyperbilirubinemia?

A. Volatile anesthetics
B. Cardiogenic shock
C. Blood transfusions
D. Acute viral hepatitis
E. Hepatic congestion

24. Halothane hepatotoxicity is a historically significant cause of postoperative liver dysfunction. Which of these statements is TRUE regarding halothane hepatitis?

A. Repeat exposure increases risk.
B. Increased incidence with preexisting liver disease
C. Recovery common despite marked elevation of transaminases
D. Does not occur in pediatric patients
E. Formation of hapten adduct responsible for mild form of disease

25. On postoperative day 1 following a combined mitral valve annuloplasty and aortic valve replacement, the patient has a urine output of 0.2 mL/kg/hr. A review of the laboratory results reveals a serum creatinine of 3.2 mg/dL (baseline 0.9 mg/dL). Based on the RIFLE criteria, what is the correct severity classification of the acute renal failure?

A. Risk
B. Injury
C. Failure
D. Loss
E. End-stage kidney disease

26. A 42-year-old, 135-kg man is in the recovery room following completion of a 6-hour hand-assisted laparoscopic left nephrectomy for a renal mass. He is complaining of pain in his right lower back and buttock. The patient has produced only 20 mL of tea-colored urine in the past hour. What is the appropriate initial treatment for this postoperative oliguria?

A. Normal saline
B. Mannitol
C. Sodium bicarbonate

D. Furosemide
E. Hemodialysis

27. To best minimize the occurrence of a compartment syndrome in the lower extremities in a patient undergoing general anesthesia in the lithotomy position, anesthetic management might include

A. Normovolemic hemodilution
B. Trendelenburg position
C. Hip flexion of more than 100 degrees
D. Periodic lowering of extremities
E. Controlled hypotension

28. Which combination of anesthetic drugs is most likely to provoke a carcinoid crisis?

A. Propofol and succinylcholine
B. Etomidate and vecuronium
C. Thiopental and rocuronium
D. Propofol and cisatracurium
E. Thiopental and succinylcholine

29. Laboratory findings in a patient with chronic diarrhea (without shock symptoms) are likely to include all of the following EXCEPT

A. Hyponatremia
B. Hypokalemia
C. Anion gap
D. Hyperchloremia
E. Metabolic acidosis

30. What transfusion reaction does a positive direct antiglobulin (Coombs) test confirm?

A. Hemolytic
B. Nonhemolytic
C. Septic
D. Anaphylactoid
E. Transfusion-related acute lung injury (TRALI)

31. Which of the following is contraindicated in patients with Duchenne muscular dystrophy?

A. Hyperbaric spinal
B. Sevoflurane
C. Alfentanil
D. Thiopental
E. Succinylcholine

32. Anesthesia for extracorporeal shock-wave lithotripsy with a third-generation lithotripter may include all EXCEPT

A. General anesthesia with nondepolarizing neuromuscular blockade
B. Epidural to T6 level
C. General anesthesia with LMA
D. Saddle block
E. Intravenous sedation

33. The factor most likely responsible for fluoride-induced nephrotoxicity of methoxyflurane is

A. Baseline renal function
B. Mean plasma fluoride concentration
C. Low total fresh gas flow
D. Hepatic biotransformation
E. Intrarenal metabolism to inorganic fluoride

34. Which inhalational anesthetic is MOST likely to be associated with fluoride-induced renal tubular nephrotoxicity?

A. Enflurane
B. Sevoflurane
C. Halothane
D. Isoflurane
E. Methoxyflurane

35. A medication that does NOT increase gastric fluid pH is

A. Pantoprazole
B. Ranitidine
C. Sucralfate
D. Famotidine
E. Sodium citrate

36. Anesthetic management of a patient with hemoglobin SS disease would most likely NOT include

A. Perioperative forced-air warming
B. Fluid restriction
C. Exchange transfusion
D. High inspired oxygen concentration
E. Regional anesthesia

37. Which is most likely to inhibit hypoxic pulmonary vasoconstriction?

A. Sevoflurane
B. Propofol
C. Desflurane
D. Nitroprusside
E. Ketamine

38. Adverse effects of hyperglycemia do NOT include

A. Difficult intubation
B. Increased blood viscosity

C. Intracellular edema
D. Infection
E. Hyperphosphatemia

39. Which anesthetic technique is preferable in patients at risk for postoperative ileus?

A. General anesthesia with volatile agent
B. Spinal anesthetic (level T12)
C. Lumbar epidural (level T4)
D. Saddle block
E. Total intravenous anesthesia

40. The maximum local anesthetic dose of lidocaine for tumescent liposuction using epinephrine 1:1,000,000 is

A. 5 mg/kg
B. 7 mg/kg
C. 10 mg/kg
D. 30 mg/kg
E. 55 mg/kg

41. What is the metabolic condition most likely associated with large amounts of normal saline infusion in an otherwise healthy patient?

A. Metabolic alkalosis
B. Non–anion gap metabolic acidosis
C. Anion gap metabolic acidosis
D. Increased strong ion difference
E. Compensatory respiratory acidosis

42. Which of the following drugs is NOT associated with methemoglobinemia?

A. Benzocaine
B. Lidocaine
C. Bupivacaine
D. Prilocaine
E. Nitroglycerin

43. What is the active metabolite of morphine most likely to have a clinical effect in renal failure patients?

A. Normeperidine
B. Morphine-3-glucuronide
C. Normorphine
D. Morphine-6-glucuronide
E. Codeine

44. Which drug is expected to have a normal response in a patient with myotonic dystrophy?

A. Succinylcholine
B. Methohexital
C. Rocuronium
D. Morphine
E. Etomidate

45. A 65-year-old patient with Parkinson's disease who is taking levodopa, carbidopa, amantadine, and selegiline sustained a closed fracture of his proximal humerus after a fall, and he is scheduled for ORIF of his proximal humerus the next day. He has a history of GERD. BP = 104/60. ECG shows normal sinus rhythm with HR = 70. Laboratory tests are within normal limits. Patient refuses regional anesthesia. Which of the following medications should be avoided?

A. Carbidopa
B. Metoclopramide
C. Succinylcholine
D. Ketamine
E. Glycopyrrolate

46. An accepted minimum requirement for patient management in clinical practice is a

A. Guideline
B. Standard
C. Statement
D. Law
E. Policy

47. Primary hyperaldosteronism is distinguished from secondary hyperaldosteronism by the finding of

A. Hypertension
B. Hypokalemia
C. Alkalosis
D. Low renin level
E. Edema

48. The classic metabolic derangements in a patient with a history of pyloric stenosis and severe vomiting are:

A. Hypernatremic, hypokalemic, hypocalcemic metabolic acidosis
B. Hypernatremic, hypokalemic, hypercalcemic metabolic alkalosis
C. Hypernatremic hyperkalemic, hyperchloremic metabolic acidosis
D. Hyponatremic, hypokalemic, hypochloremic metabolic alkalosis
E. Hyponatremic, hypokalemic, hyperchloremic metabolic acidosis

49. A 5-week-old boy with a 3-day history of vomiting is admitted to the hospital, a nasogastric tube is placed,

and the baby is scheduled for pyloromyotomy. The most appropriate initial management would be:

A. Identification and correction of severe metabolic abnormalities
B. Proceeding with immediate rapid-sequence induction and balanced anesthesia for surgery
C. Type and cross-match
D. Chest x-ray
E. Insertion of a Salem sump and suctioning in the supine and right and left lateral positions

50. A 6-week-old infant with subglottic stenosis requires a dilation via tracheostomy. Anesthetic management is LEAST likely to include

A. Suctioning of the airway and assisted ventilation
B. Placement of a small-diameter tube beyond the obstruction
C. Inhalational agents
D. Shortened expiratory times
E. Inhalational induction

51. A patient with a tracheoesophageal fistula (TEF) in the distal trachea and a blind esophageal pouch is having a ligation of the TEF and primary esophageal anastomosis via right thoracotomy. Oxygen saturation drops and peak airway pressures increase; positive-pressure ventilation is difficult. The surgeon releases traction on the trachea/lung and is unable to palpate the endotracheal tube (ETT) in the fistula. O_2 saturation drops to 60% and breath sounds are markedly diminished. Suction catheter is difficult to pass and you note thick mucus and clots. The next most appropriate action would be to

A. Place an arterial line
B. Administer albuterol
C. Advance the ETT until resistance is met
D. Replace the ETT
E. Ask the surgeon to occlude the gastrostomy tube

52. Factors that increase the release of antidiuretic hormone (ADH) include all of the following EXCEPT

A. Stimulation of atrial baroreceptors
B. Adrenergic stimulation
C. Increase in blood osmolarity
D. Positive-pressure ventilation of the lungs
E. Histamine release

53. A 28-year-old woman is scheduled to undergo excision of scar covering both the front and back of her torso from a burn injury 2 years ago. With regard to the effect of burn injury on neuromuscular blockade, the following statements are true EXCEPT

A. Succinylcholine can cause dangerous hyperkalemia.
B. There is no correlation between the magnitude of burn injury and hyperkalemic response.
C. Succinylcholine can be used after 1 to 2 years after the burn injury heals.
D. There will be increased sensitivity to nondepolarizing muscle relaxants.
E. Upregulation of extra-junctional receptors is associated with resistance to nondepolarizing relaxants.

54. A 56-year-old woman with longstanding anemia (Hb 7 g/100 mL) is undergoing hysterectomy under general anesthesia. Compensatory mechanisms for her chronic anemia might include:

A. Increased cardiac output
B. Increased coronary blood flow
C. A decrease in mixed venous oxygen saturation
D. A decrease in oxygen-hemoglobin affinity
E. All of the above

55. Which of the following statements pertaining to carbon monoxide (CO) is FALSE?

A. Affinity of CO to Hb is 200 times greater than that of O_2
B. Shift in Hb dissociation curve to the left
C. Desflurane produces the most CO.
D. Baralyme produces more CO than soda lime in CO_2 absorbers.
E. Pulse oximetry detects CO poisoning.

56. The edrophonium (Tensilon) test can be used to identify all of the following conditions EXCEPT

A. Cholinergic crisis
B. Eaton-Lambert syndrome
C. Myasthenia gravis
D. Myasthenic crisis
E. All of the above

57. All of the following statements regarding obesity are true EXCEPT

A. Preoperative pulmonary function tests and room air blood gas analysis are always indicated in a morbidly obese patient with obstructive sleep apnea.
B. A patient with a supine room air SpO_2 of 90% may need further respiratory and cardiac workup.
C. Neck circumference is a single best predictor of difficult intubation.
D. Pulmonary residual volume and closing capacity are unchanged.
E. Sleep apnea in obese individuals is usually obstructive.

58. A 34-year-old man with type 1 diabetes is undergoing incision and drainage of an abscess in the left foot under general anesthesia. Definitive signs of intraoperative hypoglycemia that will allow for correct diagnosis include which of the following?

A. Diaphoresis and lacrimation
B. Hypotension and bradycardia
C. Hypertension and tachycardia
D. Respiratory failure
E. None of the above

59. Following a surgical procedure to remove a gallstone from the common bile duct, a 63-year-old woman with type 2 diabetes and jaundice goes into acute renal failure in the immediate postoperative period. A laboratory finding that supports a diagnosis of acute tubular necrosis in this patient is

A. Urinary sodium concentration > 30 mEq/L
B. Urine to plasma creatinine ratio < 20:1
C. Urinary osmolality equal to plasma osmolality
D. Casts and cellular debris in urine sediment
E. All of the above

60. A 60-year-old male smoker with advanced COPD is undergoing cystoscopy and clot evacuation under sedation with propofol, midazolam, and fentanyl. Physiologic changes expected when his Pa_{2CO2} climbs to 90 mm Hg are all of the following EXCEPT

A. Bronchodilation
B. Pulmonary vasodilation
C. Increased QT interval
D. Sympathetic stimulation
E. Shift of oxy-Hb curve to the right

61. The radiologic image shown in Figure 4.2 is commonly associated with which of the following conditions?

A. Laryngotracheobronchitis (croup)
B. Foreign body in the trachea

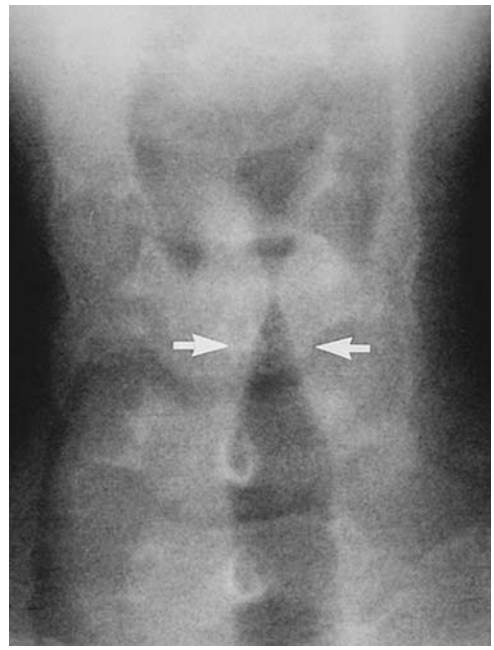

Figure 4.2 Source: Salour M. Radiology. 2000;216: 428–429.

C. Supraglottitis
D. Tracheitis
E. None of the above

62. An 18-year-old, otherwise healthy boy is undergoing strabissimus surgery on the left eye under general endotracheal anesthesia. A few minutes into surgery, the heart rate suddenly drops from 87 bpm to 34 bpm and the BP drops from 132/84 mm Hg to 86/48 mm Hg. The immediate next step in the treatment is to

A. Turn off the volatile anesthetic agent
B. Administer 100% oxygen
C. Administer atropine intravenously at 0.007 mg/kg
D. Instruct the surgeon to stop surgery immediately
E. Instruct the surgeon to inject lidocaine near the eye muscle

CHAPTER 4 ANSWERS

1. ANSWER: C

The antiretroviral therapies that are given to HIV patients are fraught with numerous side effects. Most have general unpleasant effects such as nausea, vomiting, diarrhea, fatigue, rash, and headache. In those taking protease inhibitors, metabolic abnormalities may occur that may cause elevations in cholesterol, triglycerides, and glucose. Also a lipodystrophy syndrome may cause a maldistribution of adipose tissue. Mitochondrial toxicity may result with the nucleoside/nucleotide reverse transcriptase inhibitors that can cause hyperlactatemia, lactic acidosis with hepatic steatosis, peripheral neuropathy, pancreatitis, and peripheral lipoatrophy. Bone marrow suppression causing anemia or neutropenia is also a concern with some antiretroviral therapies.

Of potential interest to the anesthesiologist is the altered pharmacokinetics that may occur with some sedatives by the protease inhibitor class of antiretrovirals. **Protease inhibitors cause inhibition of the cytochrome P-450 3A4 enzyme and can contribute to delayed metabolism of fentanyl and midazolam.** A pharmacokinetic study with healthy volunteers treated with ritonavir (protease inhibitor) demonstrated a reduction in the clearance of fentanyl by 67%. The initial volume of distribution of fentanyl was unchanged, so if only a small amount of fentanyl is given for a brief period no change in drug administration is probably required. However, in patients receiving protease inhibitors who require prolonged procedures or a transdermal patch for chronic pain conditions, the inhibitory effect on fentanyl clearance must be considered.

In a separate study that assessed the pharmacodynamic and pharmacokinetic effects of saquinavir (protease inhibitor) on patients given midazolam, there was also a significant delay in drug clearance and prolongation of the clinical sedation. This study showed that saquinavir decreased the clearance of midazolam by 56% and increased the elimination half-life from 4.1 hours to 9.5 hours. The effect on midazolam clearance, like fentanyl, needs to be considered when the sedative is given for prolonged periods such as the above ablation procedure or in the ICU setting as an infusion. The authors recommended a reduction in midazolam dose by 50% when administering a prolonged infusion.

Of note, the class of antiretrovirals known as nonnucleoside reverse transcriptase inhibitors (e.g., efavirenz) has also been implicated in numerous drug interactions. This class may inhibit or induce the CYP3A4 enzyme depending on the specific drug. The clinical effect of drugs such as methadone, fentanyl, and midazolam needs to be considered in any patient taking this class of antiretroviral agents as well.

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2. ANSWER: E

Inhibition of the viral replication process is the target of many of the HIV antiretroviral agents. The first agents developed were the nucleoside reverse transcriptase inhibitors (NRTIs). HIV is an RNA virus that must be transcribed by the infected host into DNA by the enzyme reverse transcriptase. Reverse transcriptase is a DNA polymerase that uses the HIV RNA to create a DNA:RNA hybrid. Inside the cell the NRTIs are nucleoside analogs that are biologically activated by phosphorylation, allowing them to compete with endogenous nucleosides for incorporation into the DNA chain. The NRTIs lack the 3′ hydroxyl group required on a deoxynucleotide for linking of additional nucleosides to the growing DNA chain. **The NRTIs prevent the polymerization of DNA from viral RNA by the enzyme reverse transcriptase.** Many of the side effects of this class of antiretrovirals relate to the mitochondrial toxicity that develops as a result of its inhibition of DNA polymerase-γ, a principal enzyme in the synthesis of mitochondrial DNA.

A second class of antiretrovirals, called nonnucleoside reverse transcriptase inhibitors (NNRTIs), impedes HIV viral replication by a noncompetitive inhibition of reverse transcriptase. These drugs bind to the catalytic site of reverse transcriptase and prevent a required conformational change in the enzyme, rendering it inactive. The development of resistance to these antiretrovirals by HIV is common.

After the DNA:RNA hybrid is formed it is then copied into a double-stranded DNA copy of the HIV genome. This DNA is then incorporated into the human DNA genome via the enzyme HIV integrase. The virus then utilizes the host to create new viral particles. A new class of antiretrovirals called integrase inhibitors targets this enzyme.

After the translation of viral DNA, a polyprotein of structural and functional proteins is created. To complete the viral replication process and form functional, mature virions it is necessary for the enzyme HIV protease to cleave this polyprotein into separate proteins. The protease inhibitor class of antiretroviral drugs prevents cleavage of the polyprotein, and the virions that are subsequently released are immature and noninfectious.

The fusion inhibitor called enfuviritide (T-20) is the only drug of this class that prevents the entry of HIV into the cell in a multistep process that leads to the fusion of the virus and cell membrane. The viral envelope protein gp120 binds to CD4 on the cell membrane. A conformational change occurs, exposing gp41, which facilitates the fusion of the virus to the cell. Enfuviritide inhibits the conformational changes required for viral entry by binding gp41, thus preventing infection.

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3. ANSWER: C

Fenoldopam mesylate is a potent short-acting dopamine-1 agonist that decreases systemic vascular resistance and increases renal blood flow via DA-1 receptor-mediated vasodilation. It selectively increases renal cortical and outer medullary blood flow. Recent randomized controlled trials have reported a reduction in acute renal failure (ARF) and decreased need for dialysis in patients receiving fenoldopam intraoperatively during cardiac surgery. There have been a few contradictory studies in the literature. However, in those studies showing a positive effect, the best results were at a fenoldopam dose of 0.1 mcg/kg/min or greater. This may be explained by a recent study by Meco and Cirri in which they quantified various measures of renal blood flow. They found that significant increases of renal blood flow and decreases in the resistances of the renal circulation began at the 0.1-mcg/kg/min dose and increased in a dose-dependent fashion to a maximum response at 0.3 mcg/kg/min. This may explain why some studies that used smaller doses did not find any favorable results from using fenoldopam. The incidence of hypotension and use of vasoconstrictors may be increased when using fenoldopam.

ARF is a far-too-frequent complication of cardiac surgery, with a reported incidence of up to 30% to 50% in more complicated procedures. There is a significant increase in morbidity and mortality associated with ARF. The mortality rate is 1% to 5% in those who develop ARF and up to 24% or higher for those who require dialysis. Patients undergoing cardiac surgery often have comorbidities that increase their risk of postoperative renal injury such as advanced age, congestive heart failure, diabetes, and preexisting renal disease. Furthermore, cardiopulmonary bypass is a risk factor for kidney injury due to hypoperfusion, nonpulsatile flow, and inflammation. Thus, many pharmacologic therapies have been studied with the goal of having an effect on preventing ARF in this high-risk patient population.

N-acetylcysteine (NAC) is a thiol compound with antioxidant and vasodilatory properties that has been studied extensively in the prevention of contrast-induced nephropathy. NAC has also had some favorable data in reducing cardiac surgery-related ARF in animal models. A systematic review of 10 randomized, controlled trials found that the prophylactic administration of NAC during cardiac surgery did not reduce the incidence of ARF, hemodialysis, length of ICU stay, or death.

"Renal-dose" ***dopamine*** has long been used as a renoprotective agent. It induces a dopaminergic stimulatory effect at low does and causes splanchnic and renal vasodilation. Dopamine has a natriuretic effect by inhibiting sodium reabsorption in the proximal tubules. However, the current evidence-based opinion is that it does not prevent ARF and should not be used for this purpose. The use of dopamine may be harmful by causing tachycardia and myocardial ischemia due to its adrenergic effects.

Mannitol is an osmotic diuretic that is commonly added to the cardiopulmonary bypass prime with the belief that it may decrease renal injury. The theorized renoprotective effects of mannitol are due to its ability to flush nephrotoxic substances from the tubules, scavenge free radicals, and improve medullary blood flow. Clinical studies have not shown any protective effect from mannitol, and it may even be harmful in diabetic patients.

Furosemide is a loop diuretic that is often used clinically in the setting of oliguria. Loop diuretics act at the medullary thick ascending loop of Henle and inhibit the $Na^+/K^+/Cl^{2-}$ pump. It is theorized that this inhibition could offer a protective effect by reducing oxygen demand of the renal tubular cells. It has not been shown in clinical trials to be effective in the prevention or treatment of ARF. It may offer symptomatic benefit by converting the patient from an oliguric to a nonoliguric state and diminish volume overload. In the setting of intravascular hemolysis, which is not uncommon with prolonged cardiopulmonary bypass, furosemide may be harmful because it can induce an aciduria. The acidic urine can precipitate nephrotoxic casts in the setting of hemoglobinuria and contribute to ARF.

In the recent review by Park et al., the authors reviewed 70 randomized controlled trials that studied various strategies used to prevent or treat ARF during cardiac surgery. Fenoldopam, nesiritide, and off-pump CABG demonstrated the greatest efficacy in preventing ARF. There was no benefit to dopamine or NAC. Some recent data have shown a benefit to sodium bicarbonate as a renoprotective agent. Larger, multicenter trials are needed to confirm the findings of the smaller clinical trials. A common problem with analyzing the literature on acute kidney injury has been the lack of standardization for the definition of ARF. The recently

published RIFLE or ARF criteria should help facilitate this standardization for future research.

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4. ANSWER: A

Bronchopulmonary dysplasia (BPD) is a chronic lung disease that is typically associated with extreme prematurity. The classic form of BPD is a severe form of lung injury that was due primarily to exposing immature lungs to high inspired oxygen concentrations and aggressive mechanical ventilation. Since the introduction of antenatal steroids, postnatal surfactant, and the use of far less aggressive ventilatory strategies, this severe form of the disease is uncommon. Today, a milder form called "new" BPD is the more common presentation and occurs most frequently in neonates younger than 30 weeks and less than 1,200 grams. These infants usually have mild respiratory failure and spend less time on respiratory support. New BPD is characterized by increased lung fluid, diffuse inflammation, and a decrease in alveolar and pulmonary vascular development. The pathophysiology of the new form of BPD is representative of an arrest in lung development due to prematurity compared to that of fibrosis and over-inflation due to lung injury typical of the more severe classic BPD. The current NIH consensus criteria for diagnosing BPD separate infants into those born before or after 32 weeks. Those infants who have required some form of oxygen supplementation for at least 28 days are diagnosed with BPD. For those born before 32 weeks an assessment is made at 36 weeks gestational age or time of discharge to determine oxygen requirements. They are then diagnosed as having mild (breathing room air), moderate (requiring less than 30% O_2), or severe (requiring more than 30% O_2) BPD. Those infants born after 32 weeks are assessed for oxygen requirements at the 56th postnatal day or time of discharge. Infants with BPD may require supplemental oxygen at home for months or even years.

The modern ventilatory strategies used to prevent and manage BPD in premature infants are focused on minimizing the degree of mechanical respiratory support needed to achieve adequate gas exchange. **Excessive use of oxygen therapy exposes the premature infant to retinopathy of prematurity and also may contribute to a worsening of BPD. The current recommendations are to keep the SpO_2 between 87% and 92% in the early phase of treatment of respiratory distress syndrome and between 89% and 94% if BPD has been established.** Studies have demonstrated that mild hypercapnia ($PaCO_2$ 45 to 55 mm Hg) is safe in the early stages of treatment and may reduce ventilatory needs at 36 weeks. The recommended ventilatory strategy is one that avoids baro/volutrauma. This is achieved with a more rapid rate, low tidal volume (3 to 6 mL/kg), low PIP (10 to 20 cm H_2O), and moderate PEEP (4 to 5 cm H_2O). The use of early surfactant and early therapeutic nasal CPAP has been associated with a lower use of mechanical ventilation in premature infants. The ongoing SUPPORT (Surfactant Positive Airway Pressure and Pulse Oximetry Trial) trial is being done to compare CPAP versus surfactant administered to extremely premature infants and the resulting effect on preventing the development of BPD or improving survival. The study also uses pulse oximetry to determine the relative outcomes of infants exposed to oxygen to obtain either a lower SpO_2 (85% to 89%) or a higher SpO_2 (91% to 95%).

It is important to note that strategies to minimize BPD begin before the neonatologist manages the patient. The prevention of premature delivery and the use of antenatal corticosteroids are useful interventions to assist with lung maturation. In addition, it is important to avoid over-aggressive ventilation during resuscitation of the infant in the delivery room.

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5. ANSWER: D

Sickle cell disease (SCD) is an inherited hemoglobinopathy due to a mutation of the beta-globin gene resulting in the formation of hemoglobin S (HgSS). About 0.2% of the

African-American population have SCD and 8% have sickle cell trait. SCD is an autosomal recessive disease that is the result of a single amino acid substitution that replaces a negatively charged glutamic acid for a neutral valine at position six of the beta chain. This structural change results in a hemoglobin molecule that becomes unstable and insoluble when deoxygenated. Hemoglobin S polymerization results, causing a distortion in the shape of the red blood cell. As a result of the adhesiveness of these sickled cells and the associated endothelial dysfunction resulting from freely circulating hemoglobin and iron of ruptured sickle cells, occlusion of the microvasculature occurs. This may result in vaso-occlusive crises that include pain crisis, acute chest syndrome, stroke, and end-organ injury. The risk of sickle cell-related complications in the perioperative period has been reported to be about 15%, with a mortality of 0.3% to 1.1%. Cholecystectomy is considered a moderate-risk procedure and has a reported incidence of perioperative SCD complications of 10% to 20%. **The general classic recommendations for the anesthetic care of the SCD patient include avoiding dehydration, hypoxemia, hypothermia, acidosis, or stasis of blood flow to minimize the formation of sickled red blood cells.** Prophylactic blood transfusion had been historically a widespread therapy for sickle cell patients preoperatively by either exchange transfusion or simple transfusion. The idea is to administer hemoglobin A to improve oxygen-carrying capacity and diminish the blood viscosity by diluting the HgSS. The goal of the exchange transfusion is to reduce the proportion of HbSS to less than 30%. **A simple transfusion simply targets a specific hemoglobin level, usually up to 10 mg/dL.** The Preoperative Transfusion in Sickle Cell Disease Study Group (1995) demonstrated no benefit in exchange transfusion (HbSS less than 30%) compared to simple transfusion (Hgb 10 mg/dL). The exchange transfusion group did have twice the iatrogenic transfusion-related complication rate. In 1997, Habekern published the results of 364 patients who had undergone a cholecystectomy, and he demonstrated no benefit of an exchange transfusion compared to a simple transfusion strategy. A nonrandomized arm of the study showed higher SCD-related complications in a nontransfused group (32%) compared to those patients who received any transfusion (19%). In 1999, a report by Vichinsky et al. examined 138 orthopedic surgeries and randomized the patients into exchange transfusion, simple transfusion, and no transfusion arms. The authors did not detect any clinical benefit to preoperative transfusions except for the occurrence of acute chest syndrome, which was lowest in the simple transfusion group. No published data exist that support the use of aggressive preoperative hydration to reduce the incidence of postoperative SCD complications.

Firth and Head, in their extensive review on the anesthetic management of SCD, have proposed clinical guidelines for the use of perioperative prophylactic erythrocyte transfusions. The authors recommend that a transfusion goal of a hematocrit of 30% may be beneficial when the clinical assessment is that the patient is at moderate or high perioperative risk of complications related to their SCD. The risk of transfusion-related complications outweighs any potential benefit in those at low risk. They do not recommend using an exchange transfusion in reducing the hemoglobin S level below 30%. The authors clearly note that the efficacy of the recommendations has not been clearly demonstrated by randomized studies. Thus, our patient undergoing a moderate-risk cholecystectomy may benefit from having his hemoglobin raised to 10 mg/dL by a simple transfusion.

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6. ANSWER: D

It is well established that maintaining tight glycemic control in diabetic patients is important in lowering the risk of microvascular and macrovascular complications of diabetes, including retinopathy, nephropathy, peripheral neuropathy, and cardiovascular disease. The American Diabetes Association has recommended that diabetic patients try to achieve a hemoglobin A1c of 7.0% or less. Insulin therapy is required in all type 1 diabetics and many type 2 diabetics. Insulin is administered in a manner that attempts to mimic physiologic insulin secretion. A prandial dose is given before a meal to treat postprandial hyperglycemia and a basal dose is given to treat fasting hyperglycemia. A combination of insulin with varying durations of action is given either separately or in mixed formulations, usually as multiple subcutaneous injections or via an infusion pump. The ideal basal insulin replacement would reproduce the fairly steady-state release of endogenous insulin that occurs in nondiabetics. The prandial insulin administered should emulate the rapid rise that normally occurs after a meal, peaking within 1 hour and returning to basal levels within 3 hours. In current use today are recombinant human insulins or insulin analogs of rapid, intermediate, or long durations of action. The insulin analogs are modifications created by changing amino acids in the insulin molecule to change its pharmacokinetic properties. It is important for the anesthesiologist to be familiar with the various formulations and their onset, peak, and duration of action.

RAPID-ACTING INSULIN

Lispro (Humalog)/Aspart (NovoLog): Lispro and aspart are insulin analogs that have a very rapid onset of action (5 to

15 minutes). These prandial insulin therapies have an earlier peak and shorter duration of effect than regular insulin. The amino acids changes made to these molecules prevent the normal tendency of insulin to form hexamers once injected into the tissue, thus allowing for a more rapid absorption. The effect of these rapid insulin analogs more closely resembles that of the endogenous prandial insulin response of nondiabetics. There are fewer episodes of hypoglycemia associated with these medications compared to regular insulin.

Regular: Regular human insulin is given as prandial insulin replacement and has an onset of action of 30 to 60 minutes, peaking at 2 to 3 hours, and a duration of 8 to 10 hours. It has a slower onset and a longer duration of effect compared to the natural insulin response to a meal. This can lead to postprandial hyperinsulinemia and increase the risk of hypoglycemia.

INTERMEDIATE-ACTING INSULIN

Neutal Protamine Hagedorn: NPH is an intermediate-acting human insulin that is given as basal insulin replacement. NPH differs substantially from natural basal insulin secretion because it has a broad peak effect (at 4 to 10 hours) and lasts less than 18 hours. It must be injected twice daily to ensure adequate insulin levels. The broad peak effect increases the risk of hypoglycemia, especially at night.

LONG-ACTING INSULIN

Glargine (Lantus): Glargine is an insulin analog with a long duration of action that is given as basal insulin therapy. It forms microprecipitates at the neutral pH of the tissues, creating a depot of insulin that is slowly absorbed from the subcutaneous tissues. Administered once daily, it has an onset of action of about 1 hour and lasts about 24 hours without any significant peak effect. Glargine reproduces physiologic basal insulin secretion more effectively than NPH. There is less hypoglycemia with glargine compared to NPH (Table 4.1 and Fig. 4.1).

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7. ANSWER: D

Diabetic ketoacidosis (DKA) is a metabolic abnormality in diabetic patients that is identified by hyperglycemia, ketoacidosis, dehydration, and electrolyte abnormalities. It is due to a deficiency in insulin and an excess of counterregulatory hormones such as glucagon, catecholamines, cortisol, and growth hormone. Hyperglycemia results from increased gluconeogenesis, accelerated glycogenolysis, and impaired glucose utilization by the peripheral tissues. Free fatty acids from increased lipolysis are oxidized in the liver to form ketone bodies. DKA is often precipitated by infection (urinary tract infection, pneumonia) or insufficient insulin administration. It may also be triggered by other factors such as myocardial infarction, cerebrovascular accident, acute pancreatitis, trauma, burns, and certain drugs.

Initial therapy for DKA includes crystalloid resuscitation with isotonic fluids and administration of insulin to reverse the production of ketoacidosis. Once normoglycemia is achieved it often is necessary to give dextrose-containing fluids while continuing insulin until the metabolic acidosis resolves. Although hypophosphatemia may develop in the course of treatment, phosphate therapy is not routinely recommended, as severe hypocalcemia may result. It may be

Table 4.1 DURATION OF ACTION OF STANDARD INSULINS AND INSULIN ANALOGS

INSULIN	ONSET OF ACTION	PEAK ACTION	EFFECTIVE DURATION
Standard			
Regular	30–60 min	2–3 hr	8–10 hr
NPH	2–4 hr	4–10 hr	12–18 hr
Zinc insulin (Lente)	2–4 hr	4–12 hr	12–20 hr
Extended zinc insulin (Ultralente)	6–10 hr	10–16 hr	18–24 hr
Analogs			
Lispro	5–15 hr	30–90 min	4–6 hr
Aspart	5–15 hr	30–90 min	4–6 hr
Glargine	2–4 hr	None	20–24 hr

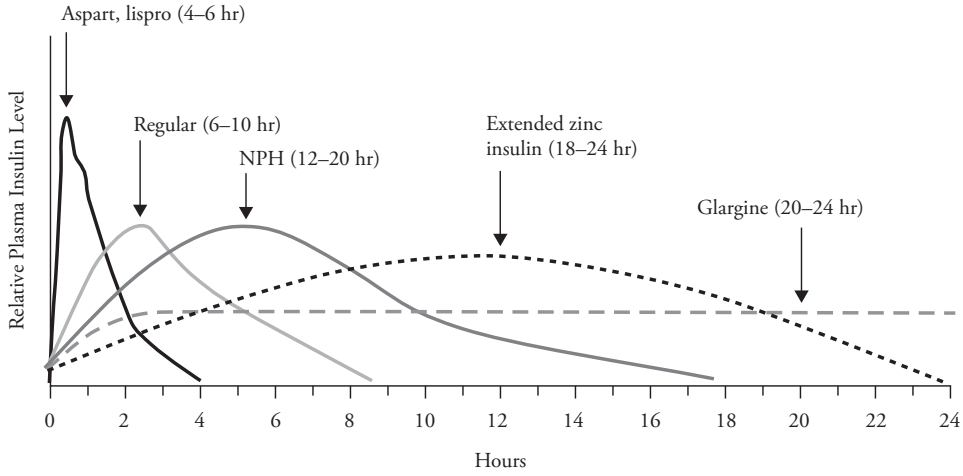

Figure 4.1 Pharmacokinetic profiles of insulin and insulin analogues. Source: Hirsch IB. Insulin analogs. *N Engl J Med.* 2005;352:174–183.

considered in those patients with cardiac compromise, anemia, or respiratory depression. DKA patients may present with elevated serum potassium levels due to the severe acidosis, hypertonicity, and insulin deficiency. **Despite this measured hyperkalemia they are usually suffering from total body potassium depletion. Potassium supplementation is frequently required during treatment as fluids and insulin lower the serum potassium level.** It is necessary to monitor potassium levels every 2 to 4 hours to prevent symptomatic hypokalemia. The administration of bicarbonate therapy is controversial. Insulin is the primary mechanism to correct the acidosis by reversing the production of ketone bodies. Potential concerns regarding bicarbonate therapy include paradoxical CNS acidosis, hypokalemia, increased ketosis, and worsening the serum hypertonicity. Sodium bicarbonate may be necessary if the pH is less than 6.9 to avoid the cardiovascular effects of acidosis.

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8. ANSWER: E

In patients with end-stage renal disease there can be a prolongation in the clinical effect of rocuronium. The primary reason for this effect is likely due to decreased renal clearance of the drug in patients with renal failure. It is important to understand that the recovery from a single dose of a nondepolarizing neuromuscular blocker is mainly due to redistribution. Those drugs dependent upon the kidney for elimination (e.g., pancuronium) exhibit a much prolonged response after repeat administration. Rocuronium is primarily dependent upon biliary excretion of the parent compound, **although up to 33% may be excreted via the kidney in a 24-hour period.** There may be a dose dependency to the pharmacokinetics of rocuronium. The route of excretion through the hepatic and biliary system may be rate-limited, thus increasing the significance of the renal route of elimination at higher doses. Only a small fraction of rocuronium is metabolized, and that compound has relatively little pharmacologic activity.

In an article by Robertson et al., the authors studied the clinical effects of a single 0.6-mg/kg bolus of rocuronium in 17 renal failure patients and 17 healthy controls. The onset of paralysis was the same in both groups. The clinical duration was increased from 32 minutes in the controls to 49 minutes in the renal failure patients. The time to return to a train-of-four ratio of 0.7 was also increased from 55 minutes to 88 minutes. The clearance of rocuronium was reduced by 39% in the renal failure patients. The volume of distribution was unaffected by renal failure. Although published evidence is not available, the authors postulated that in the setting of renal failure an increased plasma concentration and limited redistribution of rocuronium may be due to altered receptor sensitivity or saturation of nonspecific rocuronium sites with endogenous compounds. These effects could be related to a high urea level, concurrent medications, or abnormal electrolytes, or related to underlying disease states causing the renal failure.

In a study by Kocabas et al., the authors compared the pharmacologic effects of a 0.6-mg/kg dose of rocuronium in 40 renal failure patients and 40 healthy controls. Each group in this study was equally divided between elderly and young-adult patients. This study found similar prolongation of the duration of action of rocuronium in the renal failure groups. The train-of-four ratio of 0.7 was 56 minutes versus 88 minutes in the young-adult group and 75 minutes versus 119 minutes in the elderly group.

Earlier studies of the pharmacokinetics and pharmacodynamics of rocuronium in the renal failure patient did not consistently shown any significant prolongation in the duration of action. The studies by Robertson and Kocabas differ from previous studies in that propofol was used instead of isoflurane to avoid any potentiation of the muscle relaxant by the volatile anesthetic. It is possible that use of the volatile anesthetic in the earlier studies contributed to the different clinical findings.

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9. ANSWER: B

Hepatic blood flow is derived from the portal venous system and the hepatic artery. **The portal vein provides about 75% of the total hepatic blood flow, the hepatic artery only about 25%.** Each source provides about 50% of the oxygen to the liver. The regulation of hepatic blood flow is an interaction of various intrinsic and extrinsic control mechanisms.

The ***hepatic arterial buffer response (HABR)*** is a novel intrinsic mechanism in which a decrease (or increase) in portal venous flow will be compensated by an increase (or decrease) in hepatic arterial flow. The synthesis and removal of adenosine from periportal regions is involved in the HABR mechanism. Adenosine is a vasodilator that will accumulate during periods of low portal venous flow and thus lower arteriolar resistance and increase hepatic artery flow. Conversely, increased portal venous flow washes out the adenosine and thereby lowers hepatic arterial blood flow. Since the hepatic artery blood contains more oxygen, the HABR helps to maintain liver tissue oxygen delivery during periods of decreased portal venous flow.

Pressure autoregulation of hepatic artery flow is maintained in the postprandial liver, but not during the fasting state, in which the metabolic demands of the liver are decreased. Autoregulation is not involved in the portal circulation.

The splanchnic circulation represents a very important reservoir that can increase circulatory blood volume during periods of increased demand or hypovolemia. The hepatic and splanchnic arterial bed is controlled by $alpha_1$, $alpha_2$, and $beta_2$ receptors, and the portal venous beds are controlled by $alpha_1$ and $alpha_2$ receptors. Sympathetic stimulation can shift blood from the splanchnic circulation to the systemic circulation by causing vasoconstriction (alpha), decreasing splanchnic venous capacitance (alpha), and minimizing the intrahepatic vascular resistance ($beta_2$). $Beta_1$ stimulation is not involved in the regulation of hepatic blood flow.

Halothane is well known for its adverse effects on the liver. In addition to the risk of halothane hepatitis, this volatile anesthetic can also decrease hepatic blood flow by increasing hepatic artery vascular resistance. The modern volatile anesthetics decrease portal venous flow due to a decrease in cardiac output and mean arterial pressure, but partially compensate for this by increasing hepatic arterial flow and preserving the HABR mechanism. Halothane appears to disrupt this compensatory mechanism.

Vasopressin will increase splanchnic arterial resistance but will decrease portal venous resistance. Vasopressin may have a use in the treatment of portal hypertension due to its ability to reduce portal venous pressure.

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10. ANSWER: D

ALT and AST are enzymes present in hepatocytes and are released during hepatocellular injury. The serum activities of these enzymes are increased in liver diseases such as hepatitis, cirrhosis, or alcoholic liver disease. Thus, ALT and AST are useful for screening for hepatocellular damage and not to assess hepatic synthetic capacity.

Bilirubin is a product of hemoglobin catabolism that undergoes conjugation in the liver and is then excreted in the bile. An increase in serum bilirubin may be due to nonhepatic factors (e.g., hemolysis, Gilbert syndrome), hepatic factors (hepatocellular injury), or biliary obstruction. Measurement of the amount of direct (conjugated) or indirect (unconjugated) bilirubin will assist in the diagnosis of the cause of the hyperbilirubinemia. The presence of direct bilirubin is associated with liver and biliary disease.

Serum albumin is a marker for the synthetic function of the liver, but it does not accurately reflect acute synthetic capacity. Albumin has a half-life of 2 to 3 weeks and thus may be normal in the setting of acute hepatic synthetic dysfunction. It may also be decreased in the setting of malnutrition or protein-losing disease states.

Prothrombin time is prolonged in hepatic dysfunction by impairing the synthesis of the vitamin K-dependent clotting factors prothrombin (II), VII, IX, and X. The

plasma half-life of these factors is very short (hours). The **prothrombin time (or INR) is therefore very reflective of acute changes in hepatic synthetic function.** The INR is currently used in conjunction with bilirubin and creatinine in the Model for End-stage Liver Disease (MELD) score by UNOS to allocate organs for liver transplantation.

Alkaline phosphatase is an enzyme that is involved in the hydrolysis of organic phosphate esters and is found in the liver, bones, intestines, kidneys, and placenta. In regards to liver disease it is a useful test to evaluate for cholestasis or biliary obstruction. The enzyme is synthesized by the biliary epithelium and is released during bile duct obstruction. The circulating half-life of alkaline phosphatase is about 1 week. The measurement of gamma-glutamyltransferase, an enzyme also found in hepatic and biliary epithelial cells, may help in distinguishing between hepatic and other sources of alkaline phosphatase.

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11. ANSWER: B

A percutaneous exposure to the blood of a patient puts the healthcare worker at risk for infection from viral pathogens. The risk of infection from HBV is high compared to HCV or HIV because the virus replicates at a high titer. To gauge the risk of acquiring HBV it is important to know the serologic markers of the contamination source as well as the vaccination status of the exposed person. HBV produces several antigens that can be detected in the serum. These antigens and the antibodies that may develop toward them are useful markers to diagnose an acute versus chronic infection, or any immunity. The HBV surface antigen (HBsAg) is an early serologic marker of infection and if present for greater than 6 months identifies a chronic infection. The HBV e antigen (HBeAg) is a marker for active viral replication and infectivity and can persist in a chronic infection for years. Detecting the presence of antibodies to the HBsAg and HBV core antigen (HBcAg) is also clinically useful.

HBsAg negative/anti-HBc positive: After recovering from the acute phase of HBV infection there may be a "window" phase in which HBsAg is no longer detected and the anti-HBs suggesting developed immunity has not yet developed. During this period the only sign of previous infection may be the development of IgM and then IgG antibodies to the HBV core antigen. Anti-HBc by itself does not imply immunity, but the risk of transmitting an infection is probably low. The HBsAg titers may be below the detection limit of the commercial serologic test. This could also represent a false-positive test for anti-HBc.

HBsAg positive/HBeAg positive: According to CDC guidelines, the risk of acquiring HBV is greatest if the patient is HBsAg positive/HbeAg positive. The risk for transmission of clinical hepatitis is 22% to 31%. HBsAg and HBeAg being present together represent a period of high infectivity as HBV DNA levels are at their highest. The HBeAg reflects active viral replication. This could signify the early phase of acute HBV infection or the chronic phase of the disease. The anti-HBc IgM would be present during the acute infection.

HBsAg positive/HBeAg negative: A chronic HBV infection without the presence of HBeAg and the presence of anti-HBe represents a period of lower infectivity as the HBV DNA levels are not as high. The risk for hepatitis transmission is only 1% to 6%.

HBsAg negative/anti-HBs positive: This represents a patient with immunity to HBV, either from immunization or acquired immunity from prior infection. A patient with immunity from previous natural infection would also have the anti-HBc present.

Anti-HBs negative/anti-HBc negative: This serology would occur in a patient who has not been exposed to HBV or immunization. This person would be HBsAg negative as well. This patient should be offered immunization. Of note, it takes on average 30 days (range 6 to 60 days) for HbsAg to become positive after exposure, so it is theoretically possible that this patient could have been recently exposed and still have a negative serology. A test for HBV DNA can reveal HBV exposure 10 to 20 days before the serum is positive for HBsAg.

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12. ANSWER: D

Testing for serologic markers is used to differentiate the various phases of HBV infection. After exposure to the HBV virus, the patient will develop serologic markers to HBsAg and anti-HBc. The IgM anti-HBc develops during the acute

phase of the illness and is followed by the IgG antibodies, which are represented by the total anti-HBc. The anti-HBc will then always be present.

Recent Immunization: After having received the vaccination for HBV a patient may have a transient period (less than 18 days) in which HBsAg will be detectable. The immunity is confirmed by the development of anti-HBs. The presence of anti-HBc will distinguish immunity that is acquired from exposure to the actual HBV from that acquired from vaccination. Immunity from the HBV vaccination will not demonstrate the anti-HBc marker.

Acute Infection: An acute infection to HBV will demonstrate a positive HBsAg, total anti-HBc, and IgM anti-HBc, but a negative anti-HBs. The presence of the IgM anti-HBc is what distinguishes an acute infection from a chronic infection.

Acute Resolving Infection: In patients who resolve the acute infection there is often a window period when the only markers are those to anti-HBc (total or IgM). The HBsAg is either absent or below detectable levels. The presence of anti-HBs, which may develop slightly later, will convey an immune state. Patients for whom the HBsAg marker remains positive for greater than 6 months are identified as having a chronic infection.

Chronic Infection: Patients who remain chronically infected will have a persistently positive HBsAg and anti-HBc. The IgM anti-HBc will be negative as it typically is detected only in the acute phase. However, even in the chronic phase during periods of active replication it is possible to detect the IgM antibody, but it is usually below detectable limits. The anti-HBs will not be present in the chronically infected patient.

False Positive: If the only serology detected is the anti-HBc, this may represent a false positive in a never-infected individual. The HBsAg will be negative. This may also represent a previously infected but immunized individual whose anti-HBs levels have waned. Likewise, it could represent a chronically infected patient who has very low levels of HBsAg that have fallen below detectable limits. Testing for HBV DNA may be helpful in this situation (Table 4.2).

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Centers for Disease Control and Prevention. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of adults. *MMWR*. 2006;55:4–5.

13. ANSWER: A

The average risk of acquiring HCV after a percutaneous exposure from a known source is estimated to be about 1.8%. The risk varies by route of exposure, with an injury with a hollow-bore needle carrying a higher risk. Transmission occurs rarely from an exposure to mucous membranes. Unfortunately, unlike exposures to HBV and HIV, there is **no proven therapy that is recommended as postexposure prophylaxis (PEP) for HCV.** Immunoglobulin has been studied as PEP for HCV, but although it prolonged the incubation period of HCV, it ultimately did not prevent the infection. Ribavirin and interferon are currently therapies that are used for chronic HCV infection, but so far there are insufficient data to support their use as PEP. As always, the practice of universal precautions is your best defense against HCV. The current CDC recommendation for postexposure management is intended to achieve an early diagnosis of HCV seroconversion and referral for treatment. They recommend having a baseline and 6-month test for HCV antibodies and to monitor ALT. Some advocate testing for HCV RNA at periodic intervals and then treating the early HCV infection with interferon. No vaccination for HCV currently exists.

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14. ANSWER: A

In the U.S. nearly 2% of the population is infected with the ***hepatitis C virus (HCV)***. Many patients are unaware of their exposure to an infection with HCV because they are asymptomatic during the acute phase of the illness. While some will resolve their infection spontaneously, many patients will become chronically infected with the disease. In those with a chronic HCV infection, 20% may progress to cirrhosis, with a 4% incidence of hepatocellular carcinoma. The ability to diagnose the infection in the acute stage is beneficial as treatment has been shown to have a higher response rate when started in the acute phase of the illness.

There are no universally established diagnostic criteria for an acute HCV infection. Only about 25% to 30% of acutely infected patients will develop symptoms. Patients may present with a flu-like illness, fever, jaundice, or dark-colored urine suggestive of hepatitis. They may also have nonspecific complaints such as fatigue, nausea, vomiting, loss of appetite, or abdominal pain. The clinical illness will present about 6 to 8 weeks after infection and may last about 3 to 12 weeks. Fortunately, fulminant acute hepatitis C is very rare.

Table 4.2 **TYPICYAL INTERPRETATION OF SEROLOGIC TEST RESULTS FOR HEPATITIS B VIRUS INFECTION**

SEROLOGIC MARKER				
HBsAg*	TOTAL ANTI-HBC†	IGM§ ANTI-HBC	ANTI-HBC¶	INTERPRETATION
–**	–	–	–	Never infected
+††§§	–	–	–	Early acute infection; transient (up to 18 days) after vaccination
+	+	+	–	Acute infection
–	+	+	+ or –	Acute resolving infection
–	+	–		Recovered from past infection and immune
+	+	–	–	Chronic infection
–	+	–	–	False-positive (i.e., susceptible); past infection; "low-level" chronic infection;¶¶ or passive transfer of anti-HBc to infant born to HBsAg-positive mother
–	–	–	–	Immune if concentration is ≥ 10 mIU/mL after vaccine series completion;*** passive transfer after hepatitis B immune globulin administration

* Hepatitis B surface antigen

† Antibody to hepatitis B core antigen

§ Immunoglobulin M

¶ Antibody to HBsAg

** Negative test result

†† Positive test result

§§ To ensure that an HBsAg-positive test result is not a false positive, samples with reactive HBsAg results should be tested with a licensed neutralizing confirmatory test if recommended in the manufacturer's package insert.

¶¶ Persons positive only for anti-HBc are unlikely to be infectious except under unusual circumstances in which they are the source for direct percutaneous exposure of susceptible recipients to large quantities of virus (e.g., blood transfusion or organ transplant).

*** Milli-international units per milliliter

SOURCE: Centers for Disease Control and Prevention. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of adults. *MMWR*. 2006;55:4.

A clinical challenge of hepatitis C is trying to distinguish between acute and chronic infections. After the initial exposure to the virus it is possible to detect HCV RNA within 1 to 2 weeks. Seroconversion takes about 2 to 6 months, so detecting anti-HCV is less reliable than HCV RNA for establishing an early diagnosis. Unless the patient has a known exposure, such as from an occupational needlestick injury, it is unlikely that there would be any diagnostic studies done at this time. In contrast to HBV, there is no reliable test to detect an IgM antibody to HCV that would easily identify an acute infection. Anti-HCV does not offer immunity against HCV, so it will be present even in those with chronic disease. However, about 3% of chronically infected patients never seroconvert to form antibodies.

An enzyme immunoassay (EIA) is used to screen for the antibody to HCV. As a screening test it is designed to have a very high sensitivity and thus may be falsely positive in healthy patients. A recombinant immunoblot assay (RIBA) can then be used to confirm a HCV infection. This assay has a high sensitivity, making it useful as a confirmatory test for the presence of anti-HCV. If these tests are performed very early in the infection before the antibodies develop, or if the patient is immunocompromised, they may be falsely negative although the patient is truly infected. It is necessary to test also for HCV RNA to verify the diagnosis. The confirmation of the presence of anti-HCV is useful to determine if someone has ever been exposed to the virus, but isn't very useful in differentiating an acute versus a chronic infection. If

a patient has resolved an acute infection but did not become chronically infected, he or she will still have anti-HCV.

The development of increased liver enzymes occurs between 2 and 8 weeks after exposure. In the acute infection, ALT can increase to 10 to 20 times normal. HCV RNA usually peaks at about 6 to 10 weeks. The resolution of clinical symptoms coincides with the reduction of ALT and HCV levels. The acute HCV infection lasts for about 6 months, and about 20% to 40% will have a spontaneous resolution. The remainder will progress to having chronic HCV. The persistence of HCV RNA after 6 months defines a chronic infection. Chronically infected patients may have fluctuations in their ALT levels and also their HCV RNA levels. The liver enzymes do not typically spike as high as in the acute infection. It is also possible that at times the ALT may be normal and the HCV RNA may be below detectable levels, so repeat testing is necessary when monitoring a chronic infection.

The most precise way to determine an acute infection is highly dependent upon historical information. The patient needs to report a recent event that put him or her at risk of exposure (e.g., needlestick). It is also useful to have prior laboratory results that were negative for HCV. In the absence of this information, the detection of a grossly elevated ALT level is probably the most useful laboratory test to differentiate an acute infection from a chronic infection. Either phase of the illness is most likely to be positive for HCV RNA and anti-HCV. If the HCV RNA is positive with a negative anti-HCV, this could represent an early acute infection or a chronic infection that has failed to undergo seroconversion.

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15. ANSWER: A

An enlarged liver due to hepatic steatosis is one feature that is frequently seen in patients who are diagnosed with the ***propofol infusion syndrome (PRIS)***. This disorder was first recognized in the 1990s after the deaths in children who were exposed to prolonged, high-dose infusions of propofol and suffered from metabolic acidosis, heart failure, hypotension, and hepatomegaly. It has subsequently also been seen in adults and patients exposed to shorter durations of propofol. Patients with PRIS often develop a progressive lactic acidosis, hyperlipidemia, rhabdomyolysis, and cardiac instability. These patients often have a bradycardia with a right bundle branch block with ST elevations in V1–V3 (much like the Brugada syndrome) that may deteriorate into more severe ventricular arrhythmias or asystole. There is an association with propofol infusions at doses greater than 4 mg/kg/hr for a duration of more than 48 hours. The proposed mechanism for this disorder is a propofol-mediated inhibition of the mitochondrial respiratory chain and an impairment of mitochondrial fatty acid metabolism. An imbalance of energy utilization occurs, which results in cellular dysfunction and subsequent necrosis of cardiac and peripheral muscle cells. Suggested risk factors for the development of PRIS include pediatric patients, severe critical illness of CNS or respiratory systems, exogenous catecholamine or glucocorticoid administration, inadequate carbohydrate intake, and subclinical mitochondrial disease. The treatment of this disorder is to discontinue propofol and to provide cardiorespiratory supportive care. Some patients have benefited from hemodialysis to treat the acidosis. The best therapy is prevention by recognition of the early signs of PRIS, such as an unexplained metabolic acidosis, lipemia, or the characteristic ECG changes and then intervening before the more severe manifestations occur.

The hepatomegaly in PRIS may be due to several mechanisms, including heart failure-induced hepatic congestion, fatty infiltration from the high lipid content of the propofol formulation, or an increase in circulating fatty acids from enhanced lipolysis in the critically ill patient.

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16. ANSWER: D

A percutaneous inoculation of HIV carries a seroconversion rate of about 0.3%. Features that are associated with a higher rate of transmission include hollow-bore needles, advanced HIV in source patient, a deep puncture, and visible blood on the surface of the needle or scalpel that caused the contamination. Mucous membrane or nonintact skin exposures have a lower incidence of transmission at only 0.09% or less. To determine the necessity for postexposure prophylaxis (PEP) after an occupational exposure one must first determine the characteristics of the source. The CDC categorizes the source patients into five separate groups: (1) asymptomatic HIV infection with low viral load, (2) symptomatic HIV infection, AIDS, acute seroconversion, or high viral load, (3) unknown HIV status, (4) unknown source (needle from disposal unit), and (5) known

HIV-negative status. Also, the degree of the exposure as severe or less severe (i.e., solid needle or superficial injury) is considered in determining the appropriate PEP. The CDC states that PEP is generally not warranted in unknown-status HIV groups unless the source is in a high-risk HIV category. **If the injury is less severe and the source is in the asymptomatic HIV group, then a two-drug regimen is recommended. If the exposure is of the more severe type or if the source is in the higher-risk HIV group, then the three-drug regimen should be given.** PEP should begin within hours of the exposure. Prophylaxis may be of limited benefit after 24 to 36 hours. No optimal regimen currently exists for PEP. The drug regimens include two nucleoside reverse transcriptase inhibitors, plus a protease inhibitor if a third drug is needed. A balance between efficacy, side effects, and cost needs to be considered when choosing the appropriate PEP. It is also important to know of any antiviral resistance in the source. CDC resources, PEPline, or local expert consultants can be useful in helping determine the best treatment. The therapy should be continued for 28 days or until the HIV-negative status of the source can be confirmed. After an exposure from an unknown source, a rapid ELISA for HIV antibodies as well as for testing hepatitis B and C virus should be done. The exposed individual should have an initial HIV screening performed and rechecked at 6 weeks, 3 months, and 6 months to look for seroconversion. The best protection against HIV infection is the use of universal precautions and to use care to minimize needlestick injuries. The CDC report details six cases of occupational exposure in which the healthcare provider acquired HIV despite PEP (Table 4.3).

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17. ANSWER: D

Since the landmark study by Van den Berghe et al. in 2001, the application of intensive blood glucose control in critically ill patients has been a focus of hospital protocols and government regulating bodies in the belief that outcomes would be improved. The application of intensive glucose control has been expanded to the perioperative management of patients as well. In 2009, the Normoglycemia in Intensive Care Evaluation—Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study sought to test the hypothesis that intensive glucose control would reduce mortality at 90 days in critically ill patients. This multicenter, randomized trial assigned over 6,000 patients into two glucose target groups:

Table 4.3 **RECOMMENDED HIV POSTEXPOSURE PROPHYLAXIS (PEP) FOR PERCUTANEOUS INJURIES**

	INFECTION STATUS OF SOURCE				
EXPOSURE TYPE	**HIV-POSITIVE CLASS 1***	**HIV-POSITIVE CLASS 2***	**SOURCE OF UNKNOWN HIV STATUS†**	**UNKNOWN SOURCES§**	**HIV-NEGATIVE**
Less severe¶	**Recommend basic 2-drug PEP**	**Recommend expanded ≥3-drug PEP**	**Generally. no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors†† **	**Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV- infected persons is likely**	**No PEP warranted**
More severe§§	**Recommend expanded 2-drug PEP**	**Recommend expanded ≥3-drug PEP**	**Generally: no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors†† **	**Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV- infected persons is likely**	**No PEP warranted**

* HIV-positive, class I—asymptomatic HIV infection or known low viral load (e.g., <1,500 ribonucleic acid copies/mL). HIV-positive, class 2—symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.

†FOR example, deceased source person with no samples available for HIV testing

§ For example, a needle from a sharps disposal container

¶ For example, solid needle or superficial injury

** The recommendation "consider PEP" indicates that PEP is optional: a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

†† If PEP is offered and administered and the source is later determined to be HIV-negative, PEP should be discontinued.

§§ For example, large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient's artery or vein

SOURCE: CDC. *MMWR*. 2005;54(No. RR-9):3.

intensive control (81 to 108 mg/dL) and conventional control (144 to 180 mg/dL). The primary outcome measure was death from any cause within 90 days. The intensive control group had an increased risk of mortality (27.5%) compared to the conventional group (24.9%). Also, the incidence of severe hypoglycemia (less than 40 mg/dL) was significantly higher in the intensive control group (6.8%) compared to the conventional control group (0.5%). There was no significant difference in the number of days in the hospital or ICU, days on mechanical ventilation, or need for renal replacement therapy between the groups. The conclusion offered by this study was not to recommend the use of intensive glucose control in critically ill patients due to the increased mortality and higher incidence of hypoglycemia, but rather to **use a blood glucose target of less than 180 mg/dL.** An excellent recent review by Akhtar et al. also recommends that a perioperative glucose target of less than 180 mg/dL is reasonable as there is insufficient evidence to recommend more intensive control.

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18. ANSWER: D

Hyperosmolar hyperglycemic state (HHS) and ***diabetic ketoacidosis (DKA)*** are acutely life-threatening conditions associated with diabetes mellitus. HHS is defined by a state of severe hyperglycemia, hyperosmolality, and dehydration but, unlike DKA, the absence of significant ketoacidosis. **The mortality for HHS is high (5% to 20%) compared to the lower mortality of DKA (<5%).** There is a relative insulin deficiency in HHS that is inadequate for optimal glucose utilization by tissues but provides enough insulin to prevent the lipolysis and ketone body formation seen in DKA. The state of insulin deficiency and increased counterregulatory hormones seen in HHS leads to hyperglycemia by decreasing glucose utilization, increasing gluconeogenesis, and increasing glycogenolysis. The hyperglycemic state causes an osmotic diuresis that contributes to the dehydration and hyperosmolality. The most common precipitating factor for HHS is infection. Any stressful condition, such as myocardial infarction, trauma, cerebrovascular accident, pancreatitis, certain drugs, or insulin noncompliance, can trigger HHS. These patients are more likely to be older, obese patients with type 2 diabetes, in contrast to younger, type 1 diabetics who have DKA. Of note, however, HHS may be the initial manifestation of type 2 diabetes for some patients. Elderly patients, who may have restricted water intake due to being bedridden or having decreased thirst response, are at high risk of severe dehydration. The severe dehydration, older age, and concurrent comorbidities together account for the increased mortality in HHS. HHS is typically a process that evolves over days to weeks, unlike DKA, which may occur in a shorter time frame (less than 24 hours). In either hyperglycemic crisis, the patient may present with a history of polyuria, polydipsia, dehydration, weakness, and change in mental status. The physical signs are representative of the severely dehydrated condition of the patient. Profound lethargy and coma are found more frequently in HHS. There is a linear relationship between osmolality and the degree of mental obtundation. The effective serum osmolality ($2[Na^+]$ + glucose/18) is typically greater than 320 mOsm/kg. Patients with HHS have much more severe hyperglycemia (greater than 600 mg/dL) than in DKA. This results in very severe dehydration. Since there is sufficient insulin to prevent clinically significant ketoacidosis, these patients usually have a pH greater than 7.30 and bicarbonate greater than 18 mEq/L. If ketosis is present it is usually mild. The treatment of HHS is volume repletion, insulin therapy, electrolyte replacement, and treating any underlying precipitating cause. The patient is maintained on insulin and the serum glucose is kept between 250 and 300 mg/dL (adding dextrose if needed) until the patient is mentally alert and the hyperosmolar state is corrected. Although rare in adults, too rapid a correction of hyperosmolality may contribute to causing cerebral edema.

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19. ANSWER: C

Nondepolarizing muscle relaxants are commonly used in the ICU to facilitate mechanical ventilation. It has been reported in the literature that very prolonged residual neuromuscular blockade may occur after the termination of vecuronium in patients with both normal and impaired renal function. Although ICU patients are exposed to numerous conditions that may impair neuromuscular recovery, such as antibiotics, acidosis, and electrolyte abnormalities, the metabolism of vecuronium to its major

metabolite, 3-desacetylvecuronium, has particular significance. Vecuronium is eliminated from the body by both renal excretion (25%) and hepatic mechanisms. About 12% of the clearance of vecuronium is by deacetylation in the liver and greater than 40% is by biliary excretion of the parent compound. **The 3-desacetylvecuronium metabolite has about 70% to 80% the potency of vecuronium. It also has a slower clearance rate and longer duration of action. 3-desacetylvecuronium is highly dependent upon the kidney for elimination,** and it thus can accumulate in ICU patients with renal failure and contribute to a prolonged neuromuscular blockade.

Segredo et al.'s retrospective study of 16 patients who had prolonged neuromuscular blockade after several days of vecuronium use in the ICU found an association with metabolic acidosis, elevated plasma magnesium, female sex, renal failure, and high plasma concentrations of 3-desacetylvecuronium. The same authors also published a case report of two renal failure patients with extremely prolonged paralysis after long-term vecuronium use in the ICU. In each case, the 3-desacetylvecuronium levels remained elevated above the threshold for paralysis despite near-undetectable vecuronium levels.

The pharmacologic effect of vecuronium in renal failure patients was also studied by Lynam et al. This study revealed that after a single bolus injection of 0.1 mg/kg of vecuronium, the clinical duration was longer in the renal failure group (98 minutes) compared to the control group (54 minutes). The prolongation was due to a decreased renal clearance of vecuronium. It was noted that the volume of distribution was similar between those with and without renal failure. Vecuronium does not undergo significant protein binding.

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20. ANSWER: E

Hepatic disease may affect the pharmacology of neuromuscular blocking agents and prolong their clinical effects. This may occur by changing the pharmacokinetics of the drug by increasing the volume of distribution or may impair the metabolism of the paralyzing agent. The clinical effect of succinylcholine is prolonged in hepatic failure by a reduction in plasma cholinesterase activity. The prolongation of the duration of action of pancuronium, vecuronium, and rocuronium is due to the decreased plasma clearance of the drugs. Hepatic disease results in an increase in the volume of distribution of the relaxants, which may require larger initial doses to achieve the desired clinical effect, but this will also result in a prolonged recovery. Pancuronium is predominately eliminated by the kidney, but 15% undergoes deacetylation by the liver and is excreted into the bile. The 3-hydroxypancuronium compound has half the clinical potency of the parent drug. In patients with cirrhosis the volume of distribution of pancuronium is increased by 50% and the elimination half-life increases from 114 to 208 minutes. There is a risk of prolonged block and recurarization when using pancuronium in a patient with liver failure. Vecuronium undergoes significant biliary excretion, but up to 30% may be excreted in the urine. Only about 12% of vecuronium is metabolized in the liver to clinically active 3-hydroxyvecuronium. The clinical response to a single dose of vecuronium in the setting of severe hepatic disease depends on the clinical dose administered. A small dose of vecuronium (0.1 mg/kg) has a slower onset and a shorter duration of action. Its clinical effect is terminated predominately by redistribution. Larger doses (0.2 mg/kg) overcome the increased volume of distribution and have similar onset of action as in healthy patients, but the duration of action is significantly prolonged (90 minutes vs. 65 minutes). At larger doses, hepatic clearance plays a larger role in recovery from paralysis. Rocuronium is primarily eliminated in the liver by biliary excretion (70%). The remainder is excreted in the urine. Only a small fraction undergoes liver metabolism, with a metabolite that is a weak neuromuscular blocker. The volume of distribution of rocuronium may be increased up to 75% in hepatic failure, resulting in a prolonged onset and duration of action. **Cisatracurium is metabolized primarily by Hofmann elimination and does not require the liver for elimination.** In fact, the clearance of cisatracurium has been shown to be increased in patients with hepatic disease due to the enhanced volume of distribution. Hofmann elimination, an organ-independent metabolic process, occurs simultaneously in both the central and peripheral compartments of distribution.

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21. ANSWER: A

Acute renal failure (ARF) is a common complication in critically ill patients and is a frequent complication of major vascular and cardiac procedures. Current diagnostic tests for acute kidney injury rely on less-than-ideal markers, such as creatinine and BUN. These markers represent a failure in glomerular filtration and require hours or days after the onset of ARF before accumulating in the blood. Newer biomarkers may detect the early stages of ARF before any reduction in GFR. Urine may contain these markers that are indicators of an ischemic or nephrotoxic injury to renal cells. The goal is to have a test, analogous to the release of troponin in myocardial injury, that can allow the diagnosis of ARF before the onset of more significant renal failure. Some of the clinical biomarkers are representative of tubular dysfunction and enter the urine due to impaired reabsorption or catabolism of the filtered molecule. Others are intracellular tubular enzymes that are released into the urine by either exocytosis or leakage. The potential clinical utility of biomarkers includes the earlier detection and treatment of ARF, aiding in the differential diagnosis, prognostication, and improving outcomes.

Creatinine is an amino acid compound that is produced from the catabolism of creatine. It is released into the plasma at a fairly constant rate, is freely filtered by the kidney, and is not reabsorbed. About 10% to 40% of creatinine is cleared by tubular secretion and thus has the potential to obscure any initial decline in GFR. The serum creatinine level and the detection of oliguria are the currently used measures in the diagnosis of ARF based on the RIFLE or ARF criteria. Serum creatinine is useful for estimating kidney function in patients with chronic kidney disease but is less useful in the early stages of acute kidney injury. Due to the intrinsic reserve of the kidney, GFR must decrease almost 50% before any significant rise in serum creatinine occurs. A rise in creatinine may not occur until 48 to 72 hours after the inciting ARF. Serum creatinine is therefore a poor marker for detecting early ARF. Its concentration is also influenced by nonrenal confounders such as body mass, race, gender, drugs, and protein consumption. Since the rise in serum creatinine lags significantly behind the renal injury, it has limited usefulness in the immediate postoperative period.

Cystatin C is a cysteine protease inhibitor that is produced and released into the plasma at a constant rate by all nucleated cells. It is freely filtered by the glomerulus, completely metabolized by the proximal tubules, and not secreted. Unlike creatinine, it is believed not to be affected by age, gender, or body mass. In ARF it is filtered intact into the urine when proximal tubular injury prevents its metabolism. In the ICU setting, a 50% increase in serum cystatin C predicted ARF 1 to 2 days before any rise in serum creatinine. In postoperative studies of ARF, cystatin C was elevated after 6 to 12 hours and was a more sensitive marker of small changes in GFR than creatinine. An elevated urinary cystatin C was found in one study to be highly predictive of the subsequent need for acute renal replacement therapy.

Neutrophil gelatinase-associated lipocalin (NGAL) is an immunologic protein that is bound to gelatinase from neutrophils and is a urinary biomarker for ARF. NGAL is normally expressed at low levels in several tissues, including the kidney. The gene expressing NGAL has been found to be upregulated in the proximal tubular cells early after an ischemic event to the kidney. In cardiac surgery, NGAL has been shown to be present in the urine only 2 hours after cardiopulmonary bypass and is very predictive of the development of ARF. Serum and urine NGAL has been shown to identify ARF in various clinical situations, including cardiac surgery, critical care, and contrast nephropathy. A limitation of NGAL is that it may be influenced by infection and preexisting renal disease.

Interleukin-18 (IL-18) is a pro-inflammatory cytokine that is activated in injured proximal tubules and is a urinary biomarker of ischemic ARF. It is detectable 4 to 6 hours after an ischemic event. Urine IL-18 concentrations are significantly more elevated in patients with acute tubular necrosis (ATN) than other causes of ARF (prerenal, chronic kidney disease). IL-18 plays a role in the pathophysiology of sepsis and thus may have a limited role in predicting ARF in this patient population.

Kidney Injury Molecule-1 (KIM-1) is a sensitive and specific indicator of injury to the proximal tubules. It is an immunoglobulin transmembrane protein that has an increased expression following acute ischemic or nephrotoxic injury to the kidney. In a study of patients who had undergone cardiopulmonary bypass, KIM-1 levels increased slightly at 2 hours postoperatively, with a greater than 100% rise by 24 hours. The available data suggest that the diagnostic utility of urinary KIM is best 12 to 24 hours after the renal insult. KIM-1 is predominately elevated in ATN. Urinary KIM-1 may be useful in distinguishing ischemic ARF from prerenal azotemia or chronic kidney disease.

Uncertainty still exists regarding these newer biomarkers in terms of whether they possess the accuracy to diagnose acute kidney injury and how they compare across diverse patient populations. The validity of applying the clinical data to broad patient populations has yet to be established. Many of the studies focused on specific populations and often excluded those with chronic renal disease. There have also been variations in the ability of the biomarkers to diagnose between early ARF and established ARF, or to provide risk stratification of ARF. It is likely that in the future a panel of available serum (NGAL, cystatin C) and urinary (NGAL, IL-18, KIM-1) biomarkers will be available to aid in the diagnosis and management of ARF.

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22. ANSWER: E

As patients age, several factors affect the pharmacokinetic properties of the anesthetic agents that are administered. The decrease in lean body mass and total body water that occurs can decrease the central and rapidly equilibrating compartments. This will increase the concentration of the initial bolus of thiopental given to the elderly patient. The increased body fat will increase the total volume of distribution of this lipophilic drug and may prolong the clinical effect. This factor is less important with single-dose administration than if it were given by an infusion. Elderly patients have decreased levels of albumin, which can increase the serum concentration due to decreased protein binding. However, unlike propofol, opioids, and the volatile anesthetics, there is no increased sensitivity to thiopental (or etomidate) in the elderly population. **The most significant reason for a reduction in the induction dose of thiopental is the decreased initial volume of distribution of the drug.**

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23. ANSWER: C

Determining the correct etiology for postoperative jaundice can be assisted by distinguishing the type of hyperbilirubinemia. The differential diagnosis of an unconjugated hyperbilirubinemia differs from that of a conjugated hyperbilirubinemia. Bilirubin is a product of heme metabolism that is carried by albumin in its unconjugated form to the liver. The liver conjugates bilirubin to glucuronic acid by an enzymatic reaction, forming the water-soluble conjugated bilirubin. The conjugated bilirubin is then secreted into the bile. In the postoperative period, a new-onset unconjugated hyperbilirubinemia is most likely due to an overproduction of bilirubin that exceeds the liver's capacity to conjugate the compound. The liver can handle up to three times the typical bilirubin production of 250 mg/day. Hemolysis due to either drug-induced or mechanically induced red blood cell destruction can occur in the perioperative period. **In addition, multiple blood transfusions can increase the level of unconjugated bilirubin** because about 10% of the transfused autologous blood may undergo hemolysis within the first day after transfusion. The reabsorption of hematomas that may occur during surgery also can cause an unconjugated hyperbilirubinemia.

Jaundice due to hepatocellular injury or either intrahepatic or extrahepatic cholestasis will cause an increase in conjugated bilirubin. Ischemic liver injury, viral hepatitis, hepatic congestion, anesthetic effects (halothane), TPN, or drug-induced hepatitis may cause hepatocellular injury. Surgery-related complications, such as retained common duct stone or bile duct injury, may cause postoperative jaundice due to extrahepatic cholestasis. Patients with conjugated hyperbilirubinemia will often have other abnormal liver function test results appropriate to the diagnosis, such as elevated transaminases or alkaline phosphatase.

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24. ANSWER: A

The hepatotoxicity that is associated with volatile halogenated anesthetic agents has been known since the use of chloroform in 1847. Within 2 years of the introduction of halothane into clinical practice in 1956 reports of hepatic injury, often fatal, were published in the medical literature. In 1966, a retrospective analysis of more than 850,000 anesthetics was performed to compare halothane to other general anesthetics. This "National Halothane Study" could not definitively link halothane and hepatic toxicity, but recommended that if unexplained fever or jaundice occurred following a halothane exposure it should be avoided in the future.

There are two clinical forms of halothane-associated liver injury. A mild form that results in only subclinical elevations of liver enzymes occurs quite commonly, about 20% of exposures. A reductive biotransformation of halothane occurs that causes a self-limited, transient, focal hepatic necrosis. This injury may result from a single

anesthetic exposure. Studies have demonstrated that levels of glutathione-S-transferase, an enzyme distributed predominately in centrilobular hepatocytes, are elevated in 35% to 50% of patients exposed to halothane. The second form of halothane hepatotoxicity is an immune-mediated disorder that can cause a fulminant, massive centrilobular hepatic necrosis and may have a mortality greater than 50%. Marked elevations of ALT, AST, bilirubin, and alkaline phosphatase may occur after about 5 to 7 days from halothane exposure. Fortunately, the incidence is rare and has been cited at a rate between 1:10,000 and 1:35,000. The risk of halothane hepatitis is linked to repeat exposure to the anesthetic. The mechanism of injury is related to the oxidative metabolism of halothane to create a trifluoroacetyl (TFA) metabolite by CYP2E1. This reactive metabolite binds irreversibly to various liver microsomal proteins, forming a hapten–protein adduct. This adduct is immunogenic and antibodies are formed against the TFA antigen. Upon subsequent halothane exposure, a cytotoxic T-cell response occurs that leads to cell death.

It is well known that halothane should be avoided in adults due to the higher risk of halothane hepatitis. Although it is extremely rare, the literature does cite reports of halothane hepatotoxicity in pediatric patients. Retrospective studies from the U.K. and U.S. place the incidence at 1:82,000 and 1:200,000. It is not clear why children are at decreased risk for halothane hepatotoxicity, as they metabolize the drug similarly and have competent immune systems. The incidence of halogenated anesthetic-induced hepatotoxicity correlates with the degree that the molecule undergoes oxidative metabolism by CYP2E1: halothane (20%) > enflurane (2.5%) > isoflurane (0.2%) > desflurane (0.01%). All of these anesthetics have the potential to form immunogenic protein adducts, and case reports suggesting a link to liver injury have been published. Cross-sensitivity between these anesthetic agents exists. Patients who had been previously anesthetized with halothane have had hepatic necrosis when exposed to a newer agent. The antibodies created by one anesthetic can cross-react with the antigens produced by an alternate anesthetic. It is interesting to note that sevoflurane does not undergo oxidative metabolism to form a TFA–protein adduct. About 3% to 5% of sevoflurane undergoes biotransformation to form hexafluoroisopropanol (HFIP). This compound undergoes further biotransformation to form HFIP-glucuronide, which is readily excreted in the urine. Only one case of hepatic failure has been linked to sevoflurane, but the mechanism of injury remains unexplained. Due to the potential for cross-sensitization, if a patient has a history of postoperative hepatitis following a halogenated anesthetic, these agents should be avoided in the future.

As discussed, **the prominent risk factor for halothane hepatotoxicity is having multiple exposures to the drug,** but other risk factors exist. For unclear reasons, the disease occurs twice as frequently in female patients. It also occurs more frequently in middle-aged patients, with far fewer cases in children before puberty. The risk is reported to be greater in obese patients. Interestingly, there is no evidence that suggests that patients with preexisting liver disease from other causes have an increased incidence of halothane hepatitis. There may be a genetic predisposition to halothane hepatitis. The differential diagnosis for postoperative jaundice and abnormal liver function test results is long and includes etiologies besides the volatile anesthetics such as viral hepatitis, blood transfusions, and sepsis. There are also many perioperative events that might contribute to liver injury, such as surgical trauma, hypotension, hypoxia, and other drug-induced mechanisms. Thus, anesthetic-induced hepatotoxicity should be a diagnosis of exclusion. If there has been a postoperative hepatitis within 28 days following an anesthetic, not attributable to any other cause, it is possible to test the patient for TFA antibodies to help confirm the suspected diagnosis.

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25. ANSWER: C

Despite the fact that ***acute renal failure*** is a common condition in the intensive care unit, there have not been uniformly accepted diagnostic criteria in the literature until recently. In 2004, the Acute Dialysis Quality Initiative (ADQI) group published consensus criteria on the diagnosis of acute kidney injury. These RIFLE criteria are an acronym to classify acute kidney injury into three increasing-severity classes (**R**isk, **I**njury, and **F**ailure) and two outcome classes (**L**oss and **E**nd-Stage Kidney Disease). The severity classes are based on serum creatinine and urine output criteria. The outcome criteria are defined by duration of loss of kidney function. The term "acute kidney injury," instead of acute renal failure, has been proposed to cover the entire spectrum of renal impairment from minor changes in renal function to the need for renal replacement therapy.

A patient can fulfill the criteria for the appropriate severity class based on either serum creatinine or urine output criteria. The most severe possible classification is then chosen. The *Risk* of renal dysfunction classification is determined by either an increase in serum creatinine 1.5 times

baseline (or a decrease in GFR of greater than 25%) or by a urine output of less than 0.5 mL/kg/hr for 6 hours. If the serum creatinine increases to 2 times baseline (or a decrease in GFR of greater than 50%) or the urine output is less than 0.5 mL/kg/hr for 12 hours, the acute kidney injury is classified as *Injury*. The criteria for *Failure* requires a three-fold increase in creatinine or a 75% decrease in GFR. An elevation of the serum creatinine above 4 mg/dL also defines Failure. The urine output criteria for Failure requires a urine output of less than 0.3 mL/kg/hr for greater than 24 hours or anuria for 12 hours. For patients who do not have baseline measurements of renal function a theoretical serum creatinine is calculated for the patient on the assumption that he or she has a normal GFR. The Modification of Diet in Renal Disease (MDRD) formula can provide an estimate of serum creatinine relative to an estimated GFR of 75 mL/min per 1.73 m^2 based on age, race, and gender. Persistent acute renal failure (Loss) is defined as the need for renal replacement therapy for more than 4 weeks, while End-Stage Kidney Disease is the need for dialysis for more than 3 months.

In a study of over 5.000 critically ill patients, the incidence of acute kidney injury was 67%, with 12% achieving the maximum class of Risk, 27% Injury, and 28% Failure. Over half the patients who initially fulfilled the Risk criteria eventually met the criteria for Injury or Failure. The mortality rate based on maximal RIFLE classification achieved was 8.8% for Risk, 11.4% for Injury, and 26.3% for Failure. Patients without acute kidney injury had a mortality rate of 5.5%. To further highlight the importance of classifying acute kidney injury, while only about 14% of patients who reach RIFLE-Failure will require renal replacement therapy, they have a five-fold increase in hospital mortality compared to ICU patients without acute kidney injury.

Although the RIFLE criteria have since been validated by a large number of studies, an alternative set of criteria has been proposed by the Acute Kidney Injury Network (AKIN). This group proposed that the Risk category be broadened to include an increase in creatinine of at least 0.3 mg/dL, even if it does not reach the 1.5 times baseline threshold. They cite evidence that even small increases in serum creatinine are associated with adverse outcomes. However, this has not been validated in patients with chronic kidney disease. They also established a 48-hour window for documenting an elevation of serum creatinine to more clearly define that the kidney injury is in fact acute. Finally, any patient who is treated with renal replacement, regardless of creatinine or urine output, should be classified as Failure. In the AKIN criteria, the R, I, and F designations are replaced with numerical stages 1, 2, and 3 to be more in line with chronic renal disease classification schemes. The outcome criteria of Loss and End-Stage Kidney Disease were removed. The AKIN criteria were shown in a study by Barrantes et al. to predict hospital mortality, need for renal replacement therapy, and prolonged hospital stay (Table 4.4).

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Table 4.4 ACUTE KIDNEY INJURY NETWORK CRITERIA AND RIFLE CRITERIA

ACUTE KIDNEY INJURY NETWORK CRITERIA			RIFLE CRITERIA		
	CREATININE/GFR	URINE OUTPUT		CREATININE/GFR	URINE OUTPUT
Stage 1	Increased Cr 0.3 mg/dL or Cr 150% baseline	<0.5 mL/kg/hr for >6 hr	Risk (R)	Increased Cr 1.5× or GFR decreased <25%	<0.5 mL/kg/hr for >6 hr
Stage 2	Cr 200%–300% baseline	<0.5 mL/kg/hr for >12 hr	Injury (I)	Increased Cr 2× or GFR decreased <50%	<0.5 mL/kg/hr for 12 hr
Stage 3	Cr > 300% of baseline or >4 mg/dL with 0.5-mg/dL acute increase	<0.3 mL/kg/hr for 24 hr or anuria for 12 hr	Failure (F)	Increased Cr 3× or GFR decreased <75% or Cr 4 mg/dL with 0.5-mg/dL acute increase	<0.3 mL/kg/hr for 24 hr or anuria for 12 hr
			Loss (L)	Persistent acute renal failure > 4 wk	
			End-Stage Kidney Disease (E)	Persistent loss > 3 mo	

For illustration and comparison, both AKIN (preferred descriptive criteria for AKI) and RIFLE criteria are provided.

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26. ANSWER: A

Rhabdomyolysis is the result of skeletal muscle necrosis causing the release of cell contents, including electrolytes, myoglobin, creatine kinase, and sarcoplasmic proteins, into the circulation. It may occur from traumatic and nontraumatic causes and manifests as limb weakness, myalgia, edema, and myoglobinuria. Laboratory diagnosis includes an elevated serum creatine kinase level and the presence of urine myoglobin. The pathogenesis of rhabdomyolysis is related to direct sarcoplasmic injury or depletion of myocyte ATP, leading to an unregulated increase in intracellular sodium and calcium due to Na^+/K^+-ATPase and Ca^{2+}-ATPase dysfunction. The influx of intracellular sodium results in osmotic swelling of the cells. Calcium-dependent intracellular proteases and phospholipases are activated and lead to degradation of the myocyte. The reperfusion of ischemic muscle that occurs after trauma results in additional injury by the infiltration of the damaged muscles by neutrophils. A serious complication of rhabdomyolysis is acute kidney injury as a result of myoglobinuria. Acute kidney injury has been reported to occur in 13% to 50% of cases of rhabdomyolysis. Myoglobin may appear in the urine when the renal threshold for serum myoglobin of 0.5 to 1.5 mg/dL has been surpassed, but does not produce a visibly apparent red-brown discoloration of the urine until the serum myoglobin level reaches 100 mg/dL. The mechanism of renal injury in rhabdomyolysis is multifactorial. Myoglobin may precipitate in the distal renal tubules when it interacts with the Tamm-Horsfall protein. This interaction is increased in acidotic urine. Myoglobin also causes direct cytotoxicity to the proximal tubules by the formation of the hydroxyl free radical ferric oxide (Fe^{3+}). Renal vasoconstriction and volume depletion from fluid sequestration into damaged muscle also contribute to renal injury. There is no direct correlation between creatine kinase values and renal injury, but it usually occurs with creatine kinase levels above 20,000 U/L, though it has been reported when creatine kinase levels were as low as 5,000 U/L. Hyperkalemia is an early manifestation of rhabdomyolysis and may be life-threatening. Hypocalcemia may also occur as a result of calcium entering the injured muscle and precipitating as calcium phosphate. During the recovery period, hypercalcemia may result from the mobilization of this calcium.

In acute kidney injury due to rhabdomyolysis, the patient is severely volume-depleted as a result of the sequestration of fluid into the damaged muscle tissue. The necrosis and inflammation that occur result in the influx of a large amount of fluid into the affected tissue. **The most important step in management of rhabdomyolysis-induced oliguria is aggressive hydration with normal saline to achieve a urine output goal of 3 mL/kg/hr.** There is a theoretical advantage to the alkalinization of the urine with sodium bicarbonate to increase the urine pH above 6.5. The precipitation of myoglobin with the Tamm-Horsfall protein in the distal tubules is reduced. Also, alkalinization inhibits the redox cycling of myoglobin and lipid peroxidation reactions that cause injury to the renal tubules. A disadvantage of alkalinization is that it can worsen hypocalcemia. Diuretics should be used only in patients in whom the volume deficits have been corrected. Mannitol is an osmotic diuretic that may be useful in increasing renal blood flow to flush myoglobin out of the renal tubules, minimizing nephrotoxicity. Mannitol may also help remove the excess fluid from the necrotic muscle based on osmotic gradients. Mannitol also acts as a free radical scavenger. Several studies have failed to demonstrate a benefit to adding sodium bicarbonate and mannitol in comparison to normal saline administration. Despite the lack of evidence-based data, they are still both included as secondary therapies in treatment algorithms for rhabdomyolysis. Loop diuretics, too, have not been shown to be beneficial. There is some concern over their use because they acidify the urine. Hemodialysis is indicated only for the usual reasons of hyperkalemia, acidosis, uremia, and volume overload. Myoglobin is not removed effectively by dialysis due to the size of the protein.

The most common causes of rhabdomyolysis are illicit drugs, alcohol abuse, medications (statins), trauma (crush injury), seizure, and immobility. Genetic disorders of lipid and carbohydrate metabolism may also cause rhabdomyolysis. The most likely cause of rhabdomyolysis in this patient is that he was positioned for a long time in the lateral position. There have been numerous case reports in the literature of position-related rhabdomyolysis in surgical patients. The surgical positions most at risk for causing rhabdomyolysis are the lateral decubitus, lithotomy, sitting, and prone positions. Prolonged pressure on the soft tissues decreases the compartment size and increases tissue pressure. When tissue pressures are within 10 to 30 mm Hg of diastolic pressure, the muscle tissue becomes ischemic. After about 4 hours of ischemia, myonecrosis may occur. Rhabdomyolysis often becomes evident postoperatively as reperfusion of the muscle leads to tissue edema and the development of a compartment syndrome. Risk factors for position-related rhabdomyolysis include male gender, morbid obesity, prolonged duration of surgery, volume depletion, preexisting renal disease, diabetes, and hypertension. The anesthesiologist can help decrease the risk of developing rhabdomyolysis

Table 4.5 **STEPS IN THE PREVENTION AND TREATMENT OF RHABDOMYOLYSIS-INDUCED ACUTE KIDNEY INJURY**

- **Check for extracellular volume status, central venous pressure, and urine output.***
- **Measure serum creatine kinase levels. Measurement of other muscle enzymes (myoglobin, aldolase, lactate dehydrogenase, alanine aminotransferase, and aspartate aminotransferase) adds little information relevant to the diagnosis or management.**
- **Measure levels of plasma and urine creatinine, potassium and sodium, blood urea nitrogen, total and ionized calcium, magnesium, phosphorus, and uric acid and albumin; evaluate acid–base status, blood cell count, and coagulation.**
- **Perform a urine dipstick test and examine the urine sediment.**
- **Initiate volume repletion with normal saline promptly at a rate of approximately 400 mL/hr (200 to 1,000 mL/hr depending on the setting and severity), with monitoring of the clinical course or of central venous pressure.**
- **Target urine output of approximately 3 mL/kg/hr (200 mL/hr).**
- **Check serum potassium level frequently.**
- **Correct hypocalcemia only if symptomatic (e.g., tetany or seizures) or if severe hyperkalemia occurs.**
- **Investigate the cause of rhabdomyolysis.**
- **Check urine pH. If it is less than 6.5, alternate each liter of normal saline with 1 liter of 5% dextrose or 0.45% saline plus 100 mmol of bicarbonate. Avoid potassium- and lactate-containing solutions.**
- **Consider treatment with mannitol (up to 200 g/day and cumulative dose up to 800 g). Check for plasma osmolality and plasma osmolal gap. Discontinue if diuresis (>20 mL/hr) is not established.**
- **Maintain volume repletion until myoglobinuria is cleared (as evidenced by clear urine or a urine dipstick testing result that is negative for blood).**
- **Consider renal-replacement therapy if there is resistant hyperkalemia of more than 6.5 mmol/L that is symptomatic (assessed by electrocardiography), rapidly rising serum potassium, oliguria (<0.5 mL urine/kg/hr for 12 hours), anuria, volume overload, or resistant metabolic acidosis (pH < 7.1).**

* In the case of the crush syndrome (e.g., earthquake, building collapse), institute aggressive volume repletion promptly before evacuating the patient.

SOURCE: Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med*. 2009;361:62–72.

by maintaining adequate hydration, avoiding hypotension, and adequately padding pressure points (Table 4.5).

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27. ANSWER: D

Compartment syndrome is characterized by ischemia, hypoxic edema, and increased tissue pressure within a fascial compartment. Muscle damage with rhabdomyolysis occurs and nerves may be damaged. There are four compartments of the lower extremity; the anterior compartment with the most rigid fascia is most often affected. Classic findings are pulselessness, pallor, paresthesia, and pain. However, tissue-level destruction may be occurring despite intact distal pulses and adequate capillary refill. Primary symptoms include pain and edema of the extremity. If suspected, prompt consultation with orthopedic surgeons must be obtained.

Compartment syndromes have been reported in patients under general anesthesia in the lower and upper extremities.

Factors contributing to compartment syndrome include

- Hypotension
- Hypotension combined with elevation of extremity
- Vascular obstruction due to retractors or positioning devices
- Excessive flexion of hips or knees
- External compression from wrappings, straps, extremity holders, or arms of surgical assistants
- Tight drawsheets keeping arms at sides (anterior interosseous bundle compression with neuropathy or compartment syndrome)
- Prolonged lithotomy position (>5 hours)
- Lateral decubitus positioning—arm compartment syndromes (1:8,720)
- Lithotomy positioning—leg compartment syndromes (1:9,711)

The incidence with general anesthesia and supine positioning is 1:92,441. For long cases where legs are elevated, it is recommended to periodically lower the legs to body level.

For patients in the lithotomy position, forced adduction, abduction, or stretching of hip adductors should be avoided and hips should not be flexed more than 60 degrees from the horizontal. For patients in the lateral decubitus position, a chest roll, termed an "axillary roll," should be placed just below the axilla on the chest wall so that the body weight is supported by the roll, without pressure on the axillary contents, thus avoiding neurovascular compromise. The arms should NOT be abducted greater than 90 degrees from the torso and the pulse should be monitored in the dependent arm.

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28. ANSWER: E

Carcinoid tumors occur in gastrointestinal (GI) tissues but most often in bronchus, jejuno-ileum, or colon/rectum tissues derived from the endoderm. They are slow-growing benign tumors capable of metastasizing and producing a variety of GI peptides. Diagnosis is often delayed due to vague symptomatology. 5-hydroxy-indole-acetic-acid (5-HIAA), a metabolite of serotonin, can be measured in the urine. ***Carcinoid syndrome*** occurs in 20% of patients with carcinoid tumors and has two common manifestations: flushing and diarrhea. An overproduction of GI peptides reaching the systemic circulation occurs. Serotonin is responsible for diarrhea, hypotension, or hypertension. Histamine release causes flushing. Both serotonin and histamine cause bronchoconstriction. Histamine is most likely produced by gastric carcinoids. Bradykinin produces flushing, hypotension, and bronchospasm. ***Carcinoid triad*** is flushing, diarrhea, and carcinoid heart disease, usually manifested as right-sided tricuspid or pulmonic valvular fibrosis resulting in tricuspid regurgitation, but valvular stenosis can be present. Coronary vasospasm, myocardial failure and arrhythmias may occur. ***Carcinoid crisis*** is a life-threatening complication of carcinoid syndrome, occurring spontaneously or provoked by tumor manipulation, embolization, stress, chemotherapy, or some medications. Symptoms and signs are flushing, diarrhea, abdominal pain, tachycardia, hypertension, or hypotension. Anesthetic management may include administration of somatostatin (GI peptide that reduces hormone production with a half-life of 3 minutes) and octreotide (somatostatin analog with a half-life of 2.5 hours), H1 and H2 blockers, avoidance of stress, and aprotinin (kallekrien inhibitor) for hypotension if octreotide is ineffective during carcinoid crises. Ondansetron, a serotonin inhibitor, is a useful antiemetic. High levels of serotonin may be associated with delayed awakening. Epidural analgesia is not contraindicated but requires cautious management if sympathetic block is present and use of octreotide instead of sympathomimetics for hypotension. Preoperative preparation with octreotide should continue on the day of surgery (50 to 500 mcg sc or 10 to 100 mcg IV over 1 hour preop). It may be given IV for carcinoid crises (infusion 50 to 100 mcg/hr; 25 to 100 mcg bolus).

KEY FACTS: AGENTS ASSOCIATED WITH CARCINOID CRISIS

May Provoke Mediator Release:

Succinylcholine, mivacurium, atracurium, d-tubocurarine, epinephrine, norepinephrine, dopamine, isoproterenol, thiopental, histamine-releasing opioids

Not Known to Provoke Mediator Release:

Propofol, etomidate, vecuronium, cisatracurium, rocuronium, sufentanil, alfentanil, fentanyl, remifentanil

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29. ANSWER: C

Diarrhea can lead to volume depletion and electrolyte abnormalities, including hyponatremia and hypokalemia. Usually a **non–anion gap metabolic acidosis** will result from bicarbonate losses, with patients typically becoming hyperchloremic.

Clostridium difficile is the most common cause of in-hospital diarrhea. It is a gram-positive, anaerobic, spore-forming bacterium associated with antibiotic therapy, especially broad-spectrum antibiotics that alter normal bowel flora. Toxins A and B produced by the bacterium cause diarrhea in one-third of patients colonized. Asymptomatic colonization is prevalent in hospitalized patients (approximately 20% in elderly patients). Treatment includes fluid and electrolyte correction, metronidazole or vancomycin (oral if possible), and probiotics (e.g., *Saccharomyces boulardii*, *Lactobacillus rhamnosus*). Colonic dilation and perforation can occur and patients may present for subtotal colectomy and ileostomy or cecostomy or colostomy. Patients may be extremely ill and unstable hemodynamically. Decreased intestinal motility, associated with opioids, may increase toxin release. Contact, isolation, and proper handwashing techniques should be followed with care to avoid contamination of stethoscopes, clothing, or other repositories that may spread the bacterium.

Other causes of diarrhea in perioperative patients include enteral nutrition (2% to 53% of patients) due to hyperosmolar or contaminated feedings and too-rapid administration. Other etiologies include other infectious

causes, hypoalbuminemia, lactose intolerance, and gastrointestinal diseases such as inflammatory bowel disease and carcinoid tumors.

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30. ANSWER: A

A ***direct antiglobulin test*** demonstrates that a red blood cell (RBC) antibody is attached to transfused donor RBCs and thereby confirms a hemolytic transfusion reaction (HTR). Recipient RBCs are examined for surface immunoglobulins and complement and the presence of antibodies that react with donor cells. A positive direct antiglobulin test will confirm both acute and delayed hemolytic transfusion reactions.

If an acute HTR is suspected, blood should be stopped, paperwork rechecked, the blood bank notified, and the following labs sent:

- Serum haptoglobin
- Plasma and urine hemoglobin
- Direct antiglobulin
- Bilirubin
- Return of unused blood and repeat compatibility testing
- Baseline coagulation tests (platelet count, PT, PTT, fibrinogen, fibrin degradation products)

See Table 55–8, Treatment of a Hemolytic Transfusion Reaction, in Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2010, p. 1754.

Signs and symptoms of an acute HTR are as follows (adapted from Table 55–7 in Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2010, p. 1753):

- Fever (common)
- Fever and chills (common)
- Chest pain
- Hypotension*
- Nausea
- Flushing
- Dyspnea
- Hemoglobinuria*
- Bleeding diathesis*

*Indicates symptoms likely under anesthesia, since other symptoms may be masked.

HTR can occur with as little as 10 mL of blood. Death is unlikely if treated but renal failure and DIC are possible. Hemoglobin, as acid hematin, precipitates in the distal renal tubules and causes blockage. Urine output should be increased to 75 mL/hr with fluids and diuretics and the urine alkalinized. As little as 50 mL of incompatible blood can exceed haptoglobin binding capacity. Plasma with 2 mg/dL of hemoglobin is pink or light brown; 100 mg/dL is red; 150 mg/dL indicates hemoglobinuria. Complement is activated in a HTR and results in vasoactive amine and histamine release.

A ***delayed hemolytic transfusion reaction*** will also be confirmed by a positive direct antiglobulin (Coombs) test. In these reactions a drop in hematocrit may be noted after the transfusion, with evidence of hemolysis within 1 to 2 weeks. RBC destruction occurs extravascularly (spleen and reticuloendothelial system) with less severe symptoms. The recipient had very low antibody levels, probably due to previous transfusions or pregnancy, that were not detected during compatibility testing. Re-exposure to these antibodies with transfusion leads to an anamnestic response with eventual lysis of the foreign RBCs. While acute HTRs usually involve the ABO system, delayed HTRs usually involve the Rh, Kell, Duffy, and Kidd systems.

Nonhemolytic transfusion reactions may result in febrile reactions due to pyrogenic cytokines released by donor leukocytes, resulting in chills, fever, headache, myalgias, nausea, and nonproductive cough shortly after transfusion. A ***direct antiglobulin test*** would differentiate between a nonhemolytic and hemolytic reaction. Fever may be a sign of bacterial contamination or ***septic transfusion reaction*** along with other signs of sepsis. Blood cultures should be obtained.

Anaphylactoid reactions are not IgE-mediated and are probably due to a reaction of a foreign protein. Urticaria is a common symptom. ***Anaphylactic reactions*** are due to transfusion of IgA to patients who are IgA-deficient and have formed anti-IgA. RBC destruction does not occur. Symptoms occur rapidly after a few milliliters and include laryngeal edema, dyspnea, hypotension, shock, and chest pain.

Transfusion-related acute lung injury (TRALI) is noncardiogenic pulmonary edema occurring within 1 to 2 hours and becoming more severe by 6 hours after transfusion. All blood products, including FFP, are implicated.

It is characterized by an ARDS-like picture: acute onset, P/F ratio less than 200, absence of left atrial hypertension, and bilateral pulmonary edema. Most patients recover within 96 hours but TRALI is now the leading cause of infusion-related mortality. TRALI was the most frequent transfusion-related cause of death reported to the FDA between 2003 and 2005, with an estimated incidence of 1/1,300 to 1/5,000 in the U.S. and between 5% and 25% mortality. The blood bank should be notified to identify the donor.

An ***indirect antiglobulin test*** is part of the third phase of the cross-matching process and involves the addition of antiglobulin sera to test tubes of recipient serum mixed with donor RBCs and to which albumin or low-ionic-strength salt solution has been added. This phase detects antibodies such as the Rh, Kell, Kidd, and Duffy blood group systems.

See Table 10–2, p. 210 ("Adverse Reactions and their Incidence") in Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

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31. ANSWER: E

Muscular dystrophies include a variety of diseases, all with abnormalities of the muscle membrane. All of the dystrophies have in common a progressive but variable loss of muscle function, with cardiac and smooth muscle also affected. The types of muscular dystrophy are usually classified according to their clinical expression and include Duchenne, Becker, Emery-Dreifuss, limb-girdle, oculopharyngeal, fascioscapulohumeral (Landouzy-Dejerine), distal, and congenital muscular dystrophy.

Duchenne muscular dystrophy (most common, 1:3,500 male births) is a sex-linked recessive trait clinically evident in boys but with subclinical abnormalities in carrier girls. The defect is a lack of production of an important membrane-stabilizing protein, dystrophin, in the muscle cell membrane. Diagnosis is between 2 and 5 years of age (74% by age 4) with progressive muscle weakness and patients usually wheelchair-bound by age 12. Other findings are pseudohypertrophy of calves and macroglossia (30%), kyphoscoliosis, and mental retardation. Death in early adulthood (thirties) is usually due to pulmonary (pneumonia) or cardiac (heart failure) dysfunction.

Anesthetic management involves avoiding drugs that affect skeletal muscle and paying attention to increased risks of aspiration due to delayed gastric emptying, abnormal swallowing, and respiratory insufficiency due to weak respiratory muscles and restrictive lung disease. Cardiac muscle degeneration may result in cardiomyopathy and mitral regurgitation. Characteristic ECG findings are sinus tachycardia, short PR interval, deep Q waves in limb leads, and tall R waves in V_1. Patients are susceptible to myocardial depressant effects of drugs. **Succinylcholine should be avoided because of its potential for rhabdomyolysis and hyperkalemia.** Nondepolarizing agents may have an increased maximal effect and duration. Short-acting opioids are preferable given the potential for respiratory depression. Even though the risk of developing malignant hyperthermia is not considered to be increased in Duchenne patients, they may develop disease-related cardiac complications, or rarely, a malignant hyperthermia-like syndrome characterized by rhabdomyolysis, which may also occur postoperatively. Neuraxial anesthesia can be considered as an alternative to general anesthesia.

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32. ANSWER: D

Extracorporeal shock-wave lithotripsy (ECSWL) results in pain from shock-wave impact and propagation through skin and viscera. General anesthesia, spinal or epidural to T6 level, or conscious sedation is an appropriate technique. First-generation lithotripters with water-bath immersion generated greater pain and required general or regional anesthesia. Conscious sedation may be an option with use of second- or third-generation, nonimmersion lithotripters. Nerve damage has been reported with epidural anesthesia and air injection. Local anesthetic flank infiltration with or without intercostal blocks along with IV sedation has been

used successfully. Epidural catheters should be taped to avoid the shock-wave path and absorption of the energy blast.

Absolute contraindications to ECSWL are obstruction distal to the renal calculi, bleeding, anticoagulation, or pregnancy. Relative contraindications are large calcified aortic or renal artery aneurysms, untreated urinary tract infections, pacemaker or AICD implants, and morbid obesity. Patients with pacemakers or AICDs should have the functional status of the device confirmed, availability of a magnet and programming device, alternative pacing capability, and positioning so that the pacemaker or AICD is not in the path of the shock wave. AICDs should be deactivated for the procedure.

With immersion techniques the cardiovascular changes are increased central venous blood volume, central venous pressure,, increased pulmonary artery blood flow and pulmonary artery pressures. Central venous pressure and pulmonary artery pressure increases are linearly related to the depth of immersion and may increase by 10 to 14 mm Hg with immersion to the clavicle. Respiratory changes include decreased vital capacity, functional residual capacity, and tidal volume with increased respiratory rates.

Hematuria is common and IV hydration is recommended. Subcapsular hematoma occurs in 0.5% of cases, rarely requiring transfusion. Flank pain is possible. Ureteral obstruction may occur from stone fragments collecting in the ureter, known as *steinstrasse* or "stone street." A stent may be needed to relieve ureteral obstruction. Other complications have included sepsis, adjacent organ damage (pancreatitis and gastrointestinal injury), and brachial plexus injuries from improper positioning. In children or patients less than 48 inches tall, Styrofoam sheets may be used to shield the lung from injury with immersion techniques. Arrhythmias, which previously occurred in 10% to 14% of patients, are rare given the current grounding systems and synchronization of the shock waves during the refractory period of the heart.

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33. ANSWER: E

34. ANSWER: E

Fluoride toxicity due to free inorganic fluoride causing injury to renal collecting tubules presents as high-output renal insufficiency. While various mechanisms are involved, the **most significant cause is thought to be production of inorganic fluoride from intrarenal metabolism of methoxyflurane.**

While the duration of systemic fluoride concentration (area under the curve for serum fluoride) is thought to be more important than peak fluoride concentration, correlations of peak levels of inorganic fluoride show that levels above 150 μm/L are associated with polyuric renal failure, while levels below 50 μm/L rarely cause injury. With methoxyflurane, inorganic fluoride levels of 50 to 80 μm/L were associated with moderate injury, 80 to 120 μm/L with severe injury, and above 120 μm/L with death. Methoxyflurane at 1 MAC for 2 hours can generate peak fluoride levels of more than 100 μm/L and is no longer used.

Enflurane rarely generates levels above 25 μm/L, and reports of renal dysfunction are few. Isoflurane generates less than 4 μm/L, and halothane and desflurane do not show increased fluoride ion concentrations and are not considered nephrotoxic.

Although sevoflurane may be associated with inorganic fluoride levels above 50 μm/L, there is no correlation with polyuric renal failure. Sevoflurane is primarily metabolized in the liver, not the kidney. It is less soluble than methoxyflurane and hence more rapidly eliminated from the body, with the result that fluoride concentrations fall rapidly after surgery. Evidence of subclinical renal injury in some studies includes transient loss of renal concentrating ability and elevation of *N*-acetyl-β-glucosaminidase (NAG, a marker of renal tubular damage) in some sevoflurane patients with inorganic fluoride levels of more than 50 μm/L. However, these changes resolved in 6 days.

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35. ANSWER: C

Gastric fluid pH is normally acidic. Stress ulcer prophylaxis that increases gastric fluid pH increases the risk of ventilator-associated pneumonia (VAP). Proton pump inhibitors (protonix) and H2 receptor antagonists (ranitidine, famotidine) increase gastric fluid pH. These medications may be used to increase gastric fluid pH prior to induction of anesthesia to minimize the likelihood of acid aspiration syndrome if gastric contents are aspirated.

Sucralfate is a complex salt of aluminum hydroxide and sucrose sulfate that forms a cytoprotective barrier against pepsin penetration. It does not increase gastric fluid pH and has been associated with decreased mortality compared to treatment with drugs that increase gastric pH. It is considered as an alternative to acid-suppressing agents when needed for prevention or treatment of duodenal or gastric ulcers. Nosocomial pneumonia may be less frequent with sucralfate than antacids. Concomitant administration of antacids may interfere with its action. Aluminum absorption may occur, so caution should be used in renal disease patients.

Sodium citrate is a nonparticulate antacid (15 to 30 mL of 0.3-mol solution, pH ~8.4) that when given 15 to 30 minutes before anesthetic induction reliably increases gastric fluid pH.

Metoclopramide does not reliably change gastric fluid pH but may decrease gastric fluid volume and increase lower esophageal sphincter tone if given 15 to 30 minutes prior to induction of anesthesia.

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36. ANSWER: B

Sickle cell disease is an inherited hemoglobinopathy that results in the formation of deformed red cells (sickling) due to aggregation of the variant hemoglobin in response to a low oxygen concentration. Sickle cell syndromes result from a mutation in the sixth amino acid, changing valine to glutamic acid in the beta-globin gene. The sickle shape is due to aggregation of the deoxygenated Hgb molecules in a longitudinal axis. Factors predisposing to sickling include hypoxemia, vascular stasis, vasoconstriction, hypothermia, and decreased cardiac output. Perioperative management goals include a target hematocrit of 30%. Exchange transfusion may sometimes be necessary to maintain adequate oxygen-carrying capacity. The goals of exchange transfusion are a hematocrit of 30%, a decrease in the concentration of Hgb S to 30% to 40%, and an increase of Hgb A to 40%. Please refer to the answer to question 5 in this chapter for more detail.

Anesthetic management includes drugs and techniques to minimize the likelihood of hypoxemia, vascular stasis, and reduced cardiac output. Regional techniques have been used successfully but may best be avoided if hypoxemia or significant blood loss is anticipated. Perioperative supplemental oxygen should be used and consideration should be given to the use of nonopioid analgesics, along with judicious use of opioids if needed. Tourniquets should be used only if essential (Table 4.6).

KEY FACTS: CONDITIONS PREDISPOSING TO SICKLING IN PATIENTS WITH HGB SS

- **Hypoxemia**
- **Vascular crisis**
- **Vasoconstriction**
- **Hypothermia**
- **Decreased cardiac output**

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Table 4.6 **SICKLE CELL DISEASE VARIANTS**

HGB S VARIANTS	HGB SS (SICKLE CELL DISEASE)	HGB SC (SICKLE CELL THALASSEMIA)	HGB AS (SICKLE TRAIT)
Hgb (g/dL)	7–8	9–12	13–15
Life expectancy (yrs)	30	Reduced	Normal
Sickling propensity	++++	++	+
Clinical signs/symptoms	Vaso-occlusive crises Hepatomegaly Splenic infarcts Skin ulcers	Vaso-occlusive crises Necrosis of the femoral head Retinal thromboses	Few with physiologic conditions (sickling with Hgb sat <20%)
% Prevalence in African-Americans	0.2	0.3	8–10

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37. ANSWER: D

Hypoxic pulmonary vasoconstriction (HPV) reflex is the increase in pulmonary vascular resistance (PVR) that occurs in areas of atelectasis with a resultant shift of blood flow away from poorly to well-ventilated regions, thus decreasing shunt fraction and maintaining oxygenation. HPV occurs in response to P_{AO2} less than 100 mm Hg and is maximal at 30 mm Hg. Decreased P_{VO2} mixed venous oxygen tension is a weaker stimulus for HPV, causing pulmonary vasoconstriction and the stimulus in atelectatic lung. Hypercapnea-induced acidosis increases PVR, especially during hypoxia, and local increases in acidosis and hypercarbia may increase HPV. During one-lung ventilation, HPV occurs within 30 minutes, with a slower maximal response over 2 hours.

All volatile anesthetics attenuate HPV by direct vasodilatory effects and other autonomic and humoral mechanisms. These mechanisms may involve calcium-activated or voltage-sensitive K^+ channels, arachidonic acid metabolism, nitric oxide, endothelial-derived vasodilating factors, and Ca^{2+} homeostasis. Intravenous anesthetic agents are not considered HPV inhibitors. Isoflurane, sevoflurane, and desflurane are weaker inhibitors of HPV than halothane and enflurane.

Indirect effects via alterations in pulmonary perfusion may also occur. Pulmonary blood flow and pressures affect HPV. Pulmonary arterial (PA) flow varies inversely with the effectiveness of HPV, hence a decrease in CO will oppose the direct inhibition of HPV by the volatile agents. Increased PA pressures may result in distention of constricted pulmonary vessels and reverse HPV. Alternatively, reflex pulmonary and systemic vasoconstriction due to hypotension may increase PVR, resulting in a shift of pulmonary blood flow to hypoxic lung regions.

While in vitro studies show the inhibitory effects of volatile agents on HPV, in vivo effects of inhaled anesthetics are relatively mild. Studies with halothane and isoflurane show 20% inhibition of HPV at 1 MAC. A relatively small 2% to 3% increase in shunt fraction has been shown with 20% HPV inhibition at 1.5 MAC isoflurane. Volatile anesthetics are safe for use during one-lung ventilation and may protect against ischemia–reperfusion injury.

Factors that increase PA pressures and antagonize the effect of increased pulmonary vascular resistance caused by HPV may inhibit HPV. Indirect factors that inhibit HPV include hypothermia, volume overload, mitral stenosis, thromboembolism, large hypoxic lung segments, and vasoconstrictors. **Vasodilators such as nitroprusside, nitroglycerin, and hydralazine increase pulmonary shunting and directly inhibit HPV.** Other inhibitors of HPV include infection, surgical trauma to the lung, hypocarbia, and metabolic alkalemia. Thoracic epidural analgesia has little direct effect. The effect of concomitant pulmonary disease is unclear, but it may result in worse anesthetic-induced gas exchange abnormalities.

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38. ANSWER: E

Hyperglycemia promotes nonenzymatic glycosylation reactions with the formation of abnormal proteins that have adverse consequences. These include decreased elastance and tensile strength of wounds. Stiff joints may occur, such as atlanto-occipital fixation, making intubation difficult. Hepatic macroglobulin production is increased, causing increased blood viscosity and intracellular edema due to the production of large nondiffusable molecules (e.g., sorbitol). Tight control of blood glucose reduces chronic complications (retinopathy, nephropathy, neuropathy). Perioperative control of blood glucose levels may decrease other complications, such as infections.

Hyperglycemia decreases chemotaxis and phagocytic activity of granulocytes. Blood glucose levels of approximately 150 mg/dL maintain the ability of immunoglobulin complex formation. Glucose levels above 150 to 250 mg/dL have adverse effects on CNS recovery. Glucose levels should be less than 200 mg/dL if cerebral ischemia is likely. Glucose-induced osmotic diuresis may result in hypophosphatemia due to loss of phosphate in the urine (Table 4.7).

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Table 4.7 HYPERGLYCEMIA AND GLUCOTOXITY

Abnormal protein formation—nonenzymatic glycosylation reactions
Weakens endothelial junctions
Decreases elastance
Decreased wound healing and tensile strength
Stiff joint syndrome (atlanto-occipital fixation)
Increased macroglobulin production
Increased blood viscosity
Intracellular edema (e.g., sorbitol—large, nondiffusible molecule production)
Vasodilation
Impaired autoregulation and autonomic dysfunction
Increased infection—impaired white blood cell function
Decreased chemotaxis/phagocytosis of granulocytes
Poorer neurologic outcomes after ischemic events
Endothelial dysfunction (increased risk of myocardial ischemia)
Osmotic diuresis—dehydration
Delayed gastric emptying
Hypophosphatemia
Proteolysis

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39. ANSWER: C

Intestinal motility is inhibited by preganglionic sympathetic fibers (T8–L3) via the celiac, superior, and inferior mesenteric ganglia. Norepinephrine is the neurotransmitter of postganglionic neurons to the smooth muscle in the gastrointestinal (GI) tract mediated by $beta_2$ receptors. Adrenergic neurons reduce the rate of gastric emptying and are normally inactive. During abdominal surgery, handling of the gut results in reflex firing of adrenergic nerves, thereby inhibiting intestinal activity and resulting in an ileus. Sympathetic block during midthoracic neuraxial anesthesia eliminates this inhibition and results in active peristalsis and relaxed sphincters.

The predominant tone in the gastrointestinal tract is parasympathetic. Parasympathetic cholinergic stimulation causes smooth muscle contraction in the wall of the GI tract, relaxation of the sphincters, and an increase in secretions. Bowel tone and peristalsis are decreased with a loss of parasympathetic tone. In patients with spinal cord lesions, the cranial parasympathetics are still active and increased activity in the enteric plexus may compensate, although colonic dilation and impaction may occur. Acetylcholine is the neurotransmitter.

GI motility is mediated via excitatory and inhibitory motor neurons acting on the circular layer of smooth muscle in both the sphincteric and nonsphincteric areas of the GI tract**. Adrenergic $alpha_1$ receptor stimulation causes sphincter contraction.**

Other than norepinephrine and acetylcholine, nonadrenergic, noncholinergic neurotransmitters controlling intestinal motility include nitric oxide, substance P, vasoactive intestinal polypeptide, and several other peptide hormones.

KEY FACTS: INTESTINAL MOTILITY

Adrenergic $alpha_1$ receptor stimulation—Sphincter relaxation

Adrenergic $beta_2$ receptor stimulation—Smooth muscle inhibition

Norepinephrine—Postganglionic sympathetic neurotransmitter

Cholinergic response —Vagus-end organ ganglia—Smooth muscle contraction—Predominant

Acetylcholine—Parasympathetic neurotransmitter

ADDITIONAL READING

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40. ANSWER: E

Liposuction using the tumescent technique involves subcutaneous infiltration of large volumes of a dilute lidocaine solution and epinephrine and removal of relatively smaller volumes of fat (less than 3,000 cc). The infiltrate solution is Ringer's lactate or normal saline with lidocaine 0.025% to 0.1% and epinephrine 1:1,000,000 using 1 to 4 cc of infiltrate for every 1 cc of fat removed. Blood loss is approximately 1% of the total aspirate. Serum lidocaine levels peak in 12 to 14 hours and decline over the following 6 to 14 hours, similar to a sustained-release medication in a single-compartment clearance model. Epinephrine is added to decrease systemic absorption. Office liposuction is generally limited to 5,000 cc of total aspirate. Semi-tumescent techniques involve greater filtration volumes and more disruption to the subcutaneous tissues, with a greater risk of fluid absorption and fluid overload. **The recommended maximum dose of lidocaine is 55 mg/kg, as per the guidelines of the American Academy of Dermatology.** Medications that inhibit the cytochrome 3A4 or 1A2 system by which lidocaine is also metabolized have the potential to result in lethal levels, so preoperative evaluation is important. It has been suggested that lidocaine may impair

alveolar epithelial fluid clearance; this, along with increased intravascular volume, may explain some liposuction-related deaths. In 2000, the overall mortality rate was 19.1 per 100,000; deaths included pulmonary and fat emboli, infection, hemorrhage, viscus perforation, and "anesthesia causes," and mortality was associated with larger-volume aspirations. Anesthesia for office-based liposuction includes general and IV sedation, according to the ASA Guidelines for Sedation and Analgesia, although neuraxial techniques are discouraged due to the possibility of hypotension and increased fluid requirements.

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41. ANSWER: B

Infusion of large amounts of ***0.9% sodium chloride, normal saline (NS) solutions*** can result in a ***hyperchloremic metabolic acidosis***. In uncomplicated patients this is a non–anion gap acidosis that usually does not need further treatment.

In other patients, chronic diarrhea leads to hyperchloremic metabolic acidosis for which lactate solutions are corrective. If vomiting losses are severe and lead to hypovolemic shock, lactic acidosis may occur. Chronic vomiting with gastric losses can lead to hypochloremic metabolic alkalosis with compensatory respiratory acidosis, for which normal saline is corrective.

The ***strong ion difference*** (SID) is the net positive charge minus the net negative charge or the total charges of the strong cations minus the strong anions. The SID affects the hydrogen ion concentration and acid–base status. Normal SID is positive (40 to 44 mEq). Acidosis is due to a decrease in SID (i.e., more anions than cations). SID = $[(Na^+ + Mg^{2+} + Ca^{2+} + K^+) - (Cl^- + A^-]$. Metabolic acidoses are caused by decreased SID or increased A_{tot} (weak ion concentrations that affect acid–base status, i.e., primarily albumin and phosphate). Chloride is the main anion in extracellular fluid. NS has a greater concentration of chloride than extracellular fluid. Hyperchloremia due to normal saline infusion leads to a net increase in anions, and hence a decrease in SID and metabolic acidosis. However, it is usually a non–anion gap metabolic acidosis. Metabolic acidoses without an anion gap usually do not require treatment. Anion gap metabolic acidoses require investigation and treatment (e.g., lactate acidosis, ketoacidosis, renal failure, toxins). Acute normovolemic hemodilution with 5% albumin and 6% hetastarch, both formulated in NS, may also be associated with hyperchloremic metabolic acidosis. NS is iso-osmotic and isotonic and may be preferred to lactated Ringer's solution in the presence of brain injury, hypochloremic metabolic alkalosis, hyponatremia, or renal failure.

Hyperchloremic Metabolic Acidosis—Characteristics

- **0.9% sodium chloride solution: 154 mEq of Na^+ and Cl^-; SID = 0**
- **↓ SID**
- **SID = $[(Na^+ + Mg^{2+} + Ca^{2+} + K^+) - (Cl^- + A^-)]$**
- **Non–anion gap acidosis**
- **AG = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$**
- **Chloride gain**

Physiologic Changes with Metabolic Acidosis

- **↓ myocardial contractility/cardiac output/perfusion**
- **Inactivation of calcium channels/inhibition release of norepinephrine**
- **Vasodilation; maldistribution of blood flow**
- **↑ postoperative nausea and vomiting**
- **Hyperchloremia—↓renal flow, ↓ GFR, ↓ splanchnic perfusion**
- **Hyperchloremia—modulates renin release**

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42. ANSWER: C

Methemoglobinemia occurs following oxidation of hemoglobin to methemoglobin. Methemoglobin does not bind oxygen or carbon dioxide, resulting in loss of oxygen-carrying capacity. Neonates are at greater risk of methemoglobinemia because fetal hemoglobin is more readily oxidized.

Oxidant drugs include prilocaine, benzocaine, Cetacaine, lidocaine, nitroglycerin, phenytoin, and sulfonamides. Methemoglobinemia can be caused by large doses of prilocaine (typically 600 mg in adults). Prilocaine (Citanest) is metabolized in the liver to *O*-toluidine, which oxidizes hemoglobin to methemoglobin. EMLA cream (eutectic mixture of lidocaine 2.5% and prilocaine 2.5%, formulated as an oil-in-water emulsion) contains prilocaine. ***Benzocaine*** (Americaine) is a topical local anesthetic (200 mg/mL).

The treatment is methylene blue (1 to 2 mg/kg IV over 5 minutes, not to exceed 7 to 8 mg/kg). Methylene blue is reduced to leukomethylene blue, which then acts as an

electron donor and reduces methemoglobin to hemoglobin. Therapeutic effects are observed within 20 to 60 minutes. The effect may be short-lived because the methylene blue may be cleared before all the methemoglobin is reduced to hemoglobin, especially if adipose stores of drugs are present, requiring increased plasma levels of methylene blue.

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43. ANSWER: D

Morphine is metabolized primarily by conjugation in the liver into water-soluble metabolites, morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G), which are excreted via the kidney. Extrahepatic conjugation in the kidney accounts for approximately 40% of the metabolism of morphine. The major metabolite, 75% to 85%, is M3G, with 5% to 10% metabolized as M6G. A small amount, 5%, is demethylated to normorphine, and codeine may be formed. M3G is present within minutes after IV injection. The majority of metabolites are renally excreted, with 7% to 10% excreted in bile. 1% to 2 % is present unchanged in urine. Although metabolized in a ratio of 9:1, M3G is inactive. **M6G is an active metabolite, mu agonist that has analgesia and respiratory depressant properties.**

In renal failure, water-soluble metabolites accumulate. Even metabolites with minimal activity may have a pharmacologic effect. The volume of distribution may be increased in patients with renal failure, also contributing to a prolonged elimination half-life.

Morphine may also have exaggerated effects in patients taking monoamine oxidase inhibitors, as these drugs impair glucuronide conjugation.

Normeperidine is a renally excreted, neurotoxic metabolite of meperidine that can cause seizures. Meperidine is best avoided in renal failure patients.

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44. ANSWER: C

Myotonic dystrophy is an autosomal dominant disorder characterized by myotonia (persistent contracture after muscle contraction or electrical stimulation), progressive muscle weakness and wasting due to abnormal calcium metabolism. The most common form is known as Steinert's disease or MD1, with an incidence of 1:8,000. Weakness and wasting are prominent in cranial and distal limbs, including vocal cord musculature and sternocleidomastoid muscles. Other symptoms are expressionless facies due to facial weakness, ptosis, dysarthria, dysphagia, periodic myotonia, myopathy, insulin resistance, cardiac conduction defects (first-degree AV block is common), mitral valve prolapse (20% of patients), cataracts, neuropsychiatric problems, and testicular atrophy and frontal balding in males.

Anesthetic considerations include the potential for pulmonary complications, cardiomyopathy, conduction abnormalities, and abnormal responses to anesthetic drugs. Specifically, diminished cough reflexes, central and peripheral hypoventilation, poor gastric motility, aspiration, hypersomnolence, central sleep apnea, and increased sensitivity to the depressant effects of benzodiazepines, opioids, and barbiturates may predispose to pulmonary complications. Succinylcholine may cause prolonged contractions. Elimination of nondepolarizing agents, or if necessary use of short-acting nondepolarizing agents, is preferred. Myotonic triggers may be hypothermia, shivering, electrical and mechanical stimuli. Etomidate, propofol, methohexital, and neostigmine can provoke myotonic reactions. Treatments include muscle infiltration of local anesthetic, phenytoin, procainamide, and quinine (300 to 600 mg IV). Procainamide and quinine may have cardiac conduction effects. Pregnancy can result in exacerbation of symptoms due to high progesterone levels, and cesarean section may be necessary with uterine muscle dysfunction.

KEY FACTS: MYOTONIC DYSTROPHY—ANESTHETIC CONSIDERATIONS

- Pulmonary: cranial muscle weakness, aspiration, hypoventilation
- Cardiac conduction abnormalities (first-, second-, or third-degree AV block; cardiomyopathy)
- Increased sensitivity to depressant medications, opioids
- Normal response to nondepolarizing muscle relaxants
- Prolonged contractions with succinylcholine
- Myotonia with hypothermia, shivering, medications, electrical/mechanical stimuli

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45. ANSWER: B

Parkinson's disease is a degenerative disease of the basal ganglia in which decreased dopamine secretion from substantia nigra results in decreased inhibition of the extrapyramidal system by dopamine and unopposed stimulation by acetylcholine. The classic triad is resting tremor (pill-rolling), bradykinesia, and muscle rigidity (cogwheel). Other symptoms include masklike facies, difficulty speaking and swallowing, oculogyric crises, seborrhea, diaphragmatic spasms, bladder dysfunction, papillary abnormalities, dementia and depression. Autonomic symptoms include orthostatic hypotension, excessive salivation, and temperature regulation difficulties.

Treatments include levodopa, carbidopa, anticholinergics, bromocriptine, amantadine, and selegiline. Pergolide, no longer in use, increased the risk of mitral and aortic regurgitation, and a history of its use necessitates evaluation for murmurs, ECG, and possibly an echocardiogram. Levodopa (dopamine precursor) causes dystonic and myoclonic movements and may cause psychiatric symptoms (agitation, hallucinations, mania, paranoia) along with nausea and vomiting, cardiac arrhythmias, and autonomic instability (hypotension). Carbidopa (peripheral decarboxylase inhibitor) decreases the side effects of levodopa. Selegiline (type B monoamine oxidase [MAO] inhibitor) inhibits degradation of dopamine and may have adverse interactions with opiates (e.g., meperidine), which may also worsen rigidity. (Selegiline is not associated with the hypertensive crises possible in patients taking type A MAO inhibitors when consuming tyramine-containing foods, such as cheese and wine.) Amantadine (glutamate receptor antagonist) may help control symptoms and may be neuroprotective. Bromocriptine is a dopamine receptor agonist. Another dopamine agonist, apomorphine, can be given IV or SC if the oral route is not available.

Anesthetic considerations include increased risk of aspiration, upper airway obstruction, increased secretions, hypotension, mental confusion, and neuroleptic malignant syndrome. Routine Parkinson's disease medications should be continued as the interruption of treatment for more than 6 to 12 hours can result in exacerbation of symptoms and ventilation difficulties. Neuroleptic malignant syndrome (fever, rigidity, altered mental status, and autonomic instability) is possible with abrupt discontinuation of levodopa. **Drugs that interfere with dopamine should be avoided, such as metoclopramide, butyrophenones, and phenothiazines.** Because the effects of propofol on motor function are unpredictable, it may be avoided during stereotactic operations. Ketamine has been used successfully, but exaggerated sympathetic responses should be considered. Opioids (alfentanil and fentanyl) have produced dystonic reactions. Inhalation agents have been used without adverse events. There is no contraindication to muscle relaxants.

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46. ANSWER: B

According to the American Society of Anesthesiologists:

*"**Standards*** provide rules or minimum requirements for clinical practice. They are regarded as generally accepted principles of patient management. Standards may be modified only under unusual circumstances, e.g., extreme emergencies or unavailability of equipment."

*"**Guidelines*** are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints and are not intended to replace local institutional policies. In addition, practice guidelines are not intended as standards or absolute requirements, and their use cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by a synthesis

and analysis of the current literature, expert opinion, open forum commentary, and clinical feasibility data."

"***Statements*** represent the opinions, beliefs, and best medical judgments of the House of Delegates. As such, they are not necessarily subjected to the same level of formal scientific review as ASA Standards or Guidelines. Each ASA member, institution, or practice should decide individually whether to implement some, none, or all of the principles in ASA statements based on the sound medical judgment of anesthesiologists participating in that institution or practice."

"ASA Standards, Guidelines and Statements provide guidance to improve decision-making and promote beneficial outcomes for the practice of anesthesiology. They are not intended as unique or exclusive indicators of appropriate care. The interpretation and application of Standards, Guidelines and Statements takes place within the context of local institutions, organizations and practice conditions. A departure from one or more recommendations may be appropriate if the facts and circumstances demonstrate that the rendered care met the physician's duty to the patient."

Although not considered standards of care, juries may still be influenced by guidelines, which are increasingly being used as evidence of standard of care.

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47. ANSWER: D

Primary hyperaldosteronism (Conn syndrome) is distinguished from secondary hyperaldosteronism by the finding of low renin levels due to inhibition by high levels of aldosterone. Secondary hyperaldosteronism involves high renin levels. However, renin may also be suppressed in essential hypertension, and renin levels do not distinguish this from hyperaldosteronism. A nonedematous patient with hypertension and persistent hypokalemia, not taking potassium-wasting medications, should be evaluated for hyperaldosteronism. High urine excretion of potassium (more than 30 mEq/d) also suggests primary hyperaldosteronism. Conn syndrome is present in 0.5% to 1% of patients with no other cause of hypertension and results from an adenoma or bilateral adrenal hyperplasia. (Chronic ingestion of licorice may result in similar findings.) Electrolyte abnormalities include hypokalemic alkalosis. Underlying ischemic heart disease may be present. Polyuria due to hypokalemic nephropathy and inability to concentrate urine, muscle weakness, hypomagnesemia, and abnormal glucose tolerance may also be present. Primary aldosteronism may also occasionally be associated with acromegaly, pheochromocytoma, or primary hyperparathyroidism. Treatment includes spironolactone, an aldosterone antagonist, and may require 1 to 2 weeks before response along with other antihypertensives. Low serum potassium levels may reflect large total-body potassium deficits and slow correction is preferable, at least over 24 hours. Anesthetic management should take into consideration the effects of hypokalemia on nondepolarizing muscle relaxants (potentiates blockade), effects of hyperventilation on potassium levels (decreases), and the potential for increased volume status of patients given their underlying disease or decreased volume status given their preoperative treatment with diuretics. Steroids are probably unnecessary, but an infusion of cortisol 100 mg/24 hr may be warranted if bilateral surgical excision of adrenal tumors is performed.

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48. ANSWER: D

49. ANSWER: A

Pyloric stenosis due to hypertrophy of the muscularis layer of the pylorus occurs in the second to sixth week of life in 1:500 live births, more frequently in boys, and results in nonbilious vomiting developing over a period of days to weeks. An olive-shaped mass is palpable between the right upper quadrant and midline and is diagnosed on ultrasound examination or rarely by barium swallow and x-ray. **While a surgical disease, the condition does not warrant emergent correction if severe metabolic derangements and hypovolemia are present.** These should be corrected first. The classic metabolic derangements are due to a loss of stomach contents containing sodium, potassium, chloride, hydrogen ions, and water. This results in electrolyte abnormalities of hyponatremia, hypokalemic, hypochloremic metabolic alkalosis with a compensatory respiratory acidosis. Volume resuscitation is with a balanced salt solution initially, and the goals of electrolyte correction prior to surgery are as follows: sodium more than 130 mEq/L, potassium at least 3 mEq/L, chloride more than 85 MEq/L and increasing, and urine output at least 1 to 2 mL/kg/hr with normal skin turgor. Due to volume depletion, polycythemia may be present.

Immediately prior to anesthesia, even if a nasogastric tube is in place, a fresh wide-bore orogastric tube should be placed and suctioned in the right and left lateral and supine positions to remove up to 98% of gastric contents, especially if a barium study has been done. Induction of anesthesia can be accomplished with rapid-sequence induction with cricoid pressure or awake endotracheal intubation. Local infiltration of the incision site is recommended and extubation should be done when fully awake. Some centers recommend pulse oximetry and apnea monitoring for the first 12 hours postoperatively because of reports of new-onset apnea.

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50. ANSWER: D

Subglottic stenosis can cause life-threatening obstruction of the airway. Lesions include congenital stenosis, webs, vascular rings, or hemangiomas. Infants younger than 3 months of age should be evaluated for noninfectious etiologies of airway obstruction if presenting with "croup."

Webs form incomplete fibrous membranes and usually present with stridor or respiratory distress shortly after birth. Endotracheal intubation may stent open the airway, and a cricothyroidotomy and tracheostomy may be necessary. Hemangiomas of the airway may increase in size after birth, causing obstruction or bleeding. Their presence elsewhere on the body of an infant in respiratory distress is a clue that they may be present in the airway, necessitating careful, gentle intubation or tracheostomy.

Congenital subglottic stenosis is treated with tracheostomy and serial dilatations. Complications of dilatations include pneumomediastinum, pneumothorax, and airway disruption.

Anesthetic management includes the use of inhalation inductions, assisted ventilation, gentle manipulation of the airway, placement of smaller-diameter tubes beyond the obstruction if possible, prolonged expiratory times to avoid gas trapping, and cricothyroidotomy and tracheostomy. Neonates or preterm infants are at risk for hypoventilation during inhalation inductions due to decreased respiratory drive with inhalation agents, displacement of alveolar oxygen because of increased CO_2, decreased functional residual capacity, and decreased intercostal muscle function. Work of breathing is increased with increased airway resistance due to the narrow lumen.

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51. ANSWER: D

Tracheoesophageal fistula (TEF) is a congenital anomaly often associated with the VATER association (**V**ertebral abnormalities, imperforate **A**nus, **T**racheo-**E**sophageal fistula, **R**adial aplasia, **R**enal abnormalities) and VACTERL association (**VATER** and **C**ongenital heart disease and **L**imb abnormalities). Esophageal atresia is present in 90% of TEF cases. The most common form (85%) is a dilated proximal esophageal pouch and fistula between the esophagus and distal trachea; next is esophageal atresia alone; third is the H-type, with a fistula between the trachea and an intact esophagus. With a blind esophageal pouch, the classic presentation is a neonate who spits up the first feeding and has excessive secretions and in whom a gastric tube cannot be passed.

Treatment may include gastrostomy tube placement under local or general anesthesia to accomplish feedings, keep the stomach drained, and avoid distention and gastric rupture in the event of a large fistula and the need to use positive-pressure ventilation.

Anesthetic management includes awake intubation under topical anesthesia and IV sedation. Inhalation induction minimizing peak inspiratory pressures and avoidance of muscle relaxants is also possible. The right mainstem bronchus is intentionally intubated, and then while auscultating, the tube is pulled back until breath sounds are heard over the left chest. The purpose is to position the tip of the ETT just above the carina but just below the fistula opening to the trachea. Extreme care is needed to avoid ETT displacement. Leak of ventilation gases through the fistula opening and into the stomach may result in inadequate ventilation to the lung.

If a gastrostomy tube is in place, it should remain vented to avoid gastric distention from any gases that may be passing through the fistula opening, especially if positive-pressure ventilation is necessary. In some cases a Fogarty catheter may be passed retrograde from stomach via the gastrostomy tube and then passed into the esophagus to occlude the fistula opening from below.

Difficulty with ventilation may be due to traction on the trachea and lung during the surgery, and therefore close

communication with the surgeon is necessary. Tube displacement into the fistula opening should be considered, and the surgeon may be able to palpate the tip of the ETT in the fistula. Rarely, in the event of occlusion of the ETT by clot or secretions that cannot be suctioned, the ETT may have to be immediately replaced.

Anesthetic considerations include associated cardiac or other abnormalities, history of respiratory distress, aspiration pneumonias, epidural analgesia via caudal approach for postoperative analgesia, and the need for postoperative ventilation. Extubation at the end of surgery is desirable to avoid positive-pressure ventilation and pressure on suture lines but may not be possible due to excessive secretions or pulmonary atelectasis.

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52. ANSWER: A

Factors regulating ADH release: ADH is released from the posterior pituitary in response to stimulation of osmoreceptors in the hypothalamus when there is even a 1% increase in blood osmolarity. ADH release can also be brought about by anxiety, nausea, pain, stress, exercise, cigarette smoking, morphine, beta-adrenergic stimulation, positive-pressure ventilation of the lungs, elevated partial pressure of arterial CO_2, hyperthermia, and any condition that results in the release of histamine.

ADH acts on the collecting ducts of the kidneys to promote water reabsorption. High levels of ADH lead to small volumes of concentrated urine.

Release of ADH is *inhibited* by stimulation of stretch (baro) receptors in the atrium and possibly the pulmonary veins from an increase in blood volume. Other actions of ADH are as follows:

1. Increase in blood pressure by vasoconstriction
2. Promotion of hemostasis by an increase in the level of circulating von Willebrand factor and factor VIII

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53. ANSWER: D

Effect of burn injury on neuromuscular blockade: 24 to 48 hours following a burn injury, there is an upregulation of both fetal ($\alpha_2\beta\gamma\delta$) and mature ($\alpha_2\beta\varepsilon\delta$) nicotinic acetylcholine receptors (nAchRs), causing resistance to nondepolarizing muscle relaxants and increased sensitivity to succinylcholine. This abnormal function of muscle membranes lasts until the growth of normal skin is complete and any infection has been resolved.

The upregulation of nAChRs also results in an exaggerated hyperkalemic response to the administration of succinylcholine. Serum K^+ levels can go up to 13 mEq/L and can cause ventricular tachycardia, fibrillation, and cardiac arrest. There is, however, no correlation between the magnitude of burn injury and the hyperkalemic response.

A safe guideline for the use of succinylcholine following burn injury is not to use the drug after the first 24 hours until 1 to 2 years after the injury has healed.

KEY FACTS: SUCCINYLCHOLINE AND BURN INJURY

- There is increased sensitivity to succinylcholine and resistance to nondepolarizing muscle relaxants in patients with burn injury.
- Hyperkalemia caused by succinylcholine in burn patients can lead to fatal ventricular arrhythmias and cardiac arrest.
- There is upregulation of both fetal and mature nAChRs after 24 to 48 hours following burn injury.
- **It is best to avoid succinylcholine after the first 24 hours following burn injury until 1 to 2 years after the burn injury.**

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54. ANSWER: E

Compensatory mechanisms for chronic anemia are as follows:

1. **Increase in cardiac output:** Systemic vascular resistance (SVR) is determined by vascular tone

and viscosity of blood. As the hematocrit drops, blood viscosity goes down, reducing SVR, thereby increasing stroke volume and cardiac output. Plasma volume is also increased in chronic anemia, contributing to reduced viscosity of blood.

2. **Redistribution of cardiac output:** In chronic anemia, blood flow to organs with normally high O_2 extraction ratios (ER), like the heart and brain, is disproportionately increased. This is the main compensatory mechanism of a healthy heart to the reduced oxygen-carrying capacity of anemia. Coronary blood flow can increase four to six times normal values to help with the increase in cardiac work associated with the increase in cardiac output.
3. **Increased O_2 extraction:** As the hematocrit drops, the whole-body ER increases as a result of increased O_2 extraction in multiple tissue beds, reducing mixed venous O_2 saturation. Because of its highest ER, the heart is at greatest risk under conditions of normovolemic anemia.
4. **Reduced oxygen-hemoglobin affinity:** The oxygen-hemoglobin dissociation curve is shifted to the right with increased P_{50} as a result of increased 2,3-diphoshoglycerate (2,3-DPG). This facilitates release of oxygen at the tissue level.

ADDITIONAL READINGS

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55. ANSWER: E

The toxicity of CO is due to tissue hypoxia caused by its 200- to 250-fold affinity to Hb compared to O_2 and the shift of the Hb dissociation curve to the left, resulting in less release of O_2 to the tissues. At the intracellular level CO causes uncoupling of oxidative phosphorylation in the mitochondria and reduces ATP synthesis, resulting in metabolic acidosis. Binding of CO to intracellular pigments and oxidative stress may contribute to toxicity to multiple organ systems.

Pulse oximetry cannot distinguish between oxy- and carboxy-hemoglobins, and pulse oximeter readings may be normal in the face of CO poisoning. The cherry-red color of the blood occurs only above CO levels of 40% and could be masked by hypoxia and cyanosis. Measurement of CO level is made with CO-oximeters.

The diagnosis of CO poisoning is made by history and corroborated by measurement of CO in blood. The CoHb concentration is stable in anticoagulated blood for several days. There may not be a correlation between actual COHb measurements and the severity of symptoms; this may be due to lower intracellular pO_2, leading to slower elimination of CO from its intracellular binding sites. Presence of fetal Hb may result in overestimation of COHb values.

High levels of CO can produce neuropsychiatric symptoms; death may ensue at levels above 50% to 60%. Late neurologic sequelae can occur after initial lucidity. Hyperbaric oxygen therapy at 2.5 to 3 atm may reduce the neuropsychiatric symptoms and drastically reduce the blood half-life of CO from 4 hours to 30 minutes; it is currently recommended for patients with COHb levels above 30%.

Desflurane produces the most CO from its interaction with CO_2 absorbents, followed by enflurane and isoflurane. Sevoflurane and halothane release negligible amounts of CO. Factors influencing CO production are the choice of the volatile anesthetic agent, its concentration, type of CO_2 absorbent, its moisture content and temperature. Barium hydroxide releases more CO than sodium hydroxide. Fully hydrated or rehydrated absorbents do not release significant amount of CO (Table 4.8).

Table 4.8 SYMPTOMS OF CO TOXICITY

BLOOD CO LEVEL (%)	SYMPTOMS
<15–20	Headache, dizziness, occasional confusion
20–40	Nausea, vomiting, disorientation, visual impairment
40–60	Agitation, combativeness, hallucinations, coma and shock
>60	Death

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56. ANSWER: B

Myasthenia gravis (MG) is an autoimmune disorder characterized by easy fatigability and weakness of skeletal muscles. The presence of anti-nAChr antibodies results in a decrease of acetylcholine receptors at the neuromuscular junctions. MG can manifest at any age; its prevalence is 0.25 to 2 per 100,000 people. nAChr antibodies are present in 80% of patients with MG (seropositive). Antibodies

to muscle-specific receptor kinase (MuSK) have been found in 70% of the seronegative MG patients. Respiratory failure may result when the thoracic and diaphragmatic muscles are affected; there is an increased risk of aspiration pneumonia with involvement of the bulbar muscles. Diagnosis is confirmed clinically by the Tensilon test: improvement in muscle strength following intravenous injection of edrophonium (Tensilon). The Tensilon test is also used to differentiate a **myasthenic crisis** from a **cholinergic crisis**. A myasthenic crisis is brought about by insufficient dosage of cholinesterase inhibitors; a cholinergic crisis is a result of overdosage of anticholinesterases. Both conditions result in similar signs: worsening muscle weakness, sweating, and salivation. The presence of muscle fasciculation, bronchospasm, abdominal cramps, and small pupils may also help differentiate a cholinergic crisis from a myasthenic crisis.

Treatment of MG comprises anticholinesterase medication, thymectomy, immunosuppression, and plasmapheresis in addition to supportive therapy. Thymectomy neither cures MG nor prevents it, suggesting that the nAChr antibodies are produced elsewhere.

Patients with MG exhibit *resistance* to succinylcholine, due to the reduction in the number of nAChrs. On the other hand, the duration of action of succinylcholine may be prolonged in MG patients due to reduced butyrylcholinesterase activity after plasmapheresis or administration of pyridostigmine, or both. MG patients are also susceptible to phase 2 block following even a single dose of succinylcholine.

Because of the decreased number of nAChrs, patients with MG are highly *sensitive* to nondepolarizing muscle relaxants. However, these drugs are not contraindicated in MG. It will be prudent to avoid long-acting muscle relaxants and to carefully titrate the dose of intermediate-acting ones with the use of nerve stimulators. Pyridostigmine therapy may result in diminished sensitivity to nondepolarizers and can make reversal of residual neuromuscular blockade difficult at the end of the surgical procedure. The latter may be due to the fact that cholinesterase activity was maximally inhibited from chronic therapy with pyridostigmine.

Eaton-Lambert syndrome (ELS) is an acquired autoimmune disorder also characterized by skeletal muscle weakness and fatigability. The main differences, in addition to the presence of specific antibody titers, between ELS and MG are as follows:

- In ELS the autoantibodies target presynaptic voltage-gated Ca^{2+} channels and also maybe synaptotagmin, another presynaptic component of the neuromuscular junction (NMJ). The end result is a reduction in the release of acetylcholine (ACh). In MG, on the other hand, the antibodies are targeted against nAChrs in the postsynaptic region of the NMJ.
- Improvement in muscle strength occurs after exercise in ELS, whereas muscle strength improves after rest in MG. This is due to summation of presynaptic Ca^{2+} signals in ELS, resulting in improved release of ACh.
- Anticholinesterases are not of much therapeutic use in ELS.
- 60% of patients with ELS have an associated paraneoplastic response, more often to small cell carcinoma of the lung.
- In ELS, response to high-frequency stimulation results in facilitation of the electromyographic response, as opposed to fade in MG.
- In ELS the NMJs in diseased nerve endings show normal Ach contents and architecture.
- Patients with ELS show increased sensitivity to *both* depolarizing and nondepolarizing muscle relaxants, and their sensitivity to nondepolarizers is even greater than that of MG patients. Neostigmine is not of much use by itself in reversal of residual neuromuscular blockade in ELS. The addition of 4-aminopyridine has been found useful.

KEY FACTS: MYASTHENIA GRAVIS

- The presence of postsynaptic anti-nAChr antibodies results in a decrease of acetylcholine receptors at the neuromuscular junctions.
- 80% of patients are seropositive, 20% seronegative.
- Skeletal muscle weakness occurs in response to exercise, improving with rest.
- **The Tensilon test can be used to identify MG and also differentiate myasthenic from cholinergic crisis; definitive diagnosis is made by antibody titer.**
- There is resistance to succinylcholine, but the duration of action may be prolonged due to plasmapheresis and/or pyridostigmine therapy.

KEY FACTS: EATON-LAMBERT SYNDROME

- The presence of antibodies to presynaptic voltage-gated Ca^{2+} channels results in a decrease of Ach release.
- Exercise results in improvement in muscle strength.
- Anticholinesterases are not of much therapeutic use in ELS.
- There is a strong association with neoplasm.
- Patients are sensitive to both depolarizing and nondepolarizing muscle relaxants.
- Patients with ELS are more sensitive to nondepolarizers than patients with MG.

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57. ANSWER: A

KEY FACTS: RESPIRATORY CHANGES IN OBESITY

- Morbid obesity is a major and most common risk factor for obstructive sleep apnea (OSA).
- OSA predisposes to difficult endotracheal intubation during anesthesia.
- **Neck circumference is the single best predictor of difficult intubation.**
- Chest wall and lung compliance are reduced, the former by fat accumulation on the thorax and the latter by the increased blood volume required to perfuse adipose tissue and by polycythemia due to chronic hypoxemia.
- Functional residual capacity (FRC), vital capacity, and total lung capacity (TLC) are reduced. FRC reduction is primarily due to the reduction in expiratory reserve volume (ERV). Residual volume and closing capacity (CC) are unchanged. Reduced FRC can approach CC, resulting in closure of smaller airways, atelectasis, V/Q mismatch, right-to-left shunting, and arterial hyoxemia. Forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) are usually within normal limits.
- Chronic OSA can result in obesity hypoventilation syndrome (OHS): daytime hypoxemia (P_{O_2} less than 65 mm Hg), sustained hyperrcapnia (P_{CO_2} greater than 45 mm Hg), ultimately leading to Pickwickian syndrome, central apneic events at night, daytime somnolence, pulmonary hypertension, right ventricular hypertrophy, and failure (cor pulmonale). This condition is associated with increased perioperative morbidity and mortality. These patients rely mainly on hypoxic drive for ventilation, similar to patients with severe COPD.
- Simple obesity increases O_2 consumption and CO_2 production, resulting in increased cardiac output and alveolar ventilation.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006: Chapter 36, 1040–1042.

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58. ANSWER: E

Intraoperative hypoglycemia is extremely difficult to diagnose clinically and could be missed or misinterpreted if one does not entertain suspicion of it when providing care for diabetic patients.

Symptoms of hypoglycemia are absent under general anesthesia, and some of the signs may be obscured. Central nervous system symptoms and signs of hypoglycemia include sluggishness, headache, confusion, irritability, seizures, and coma. In the cardiovascular system, there could be initial stimulation of the sympathetic system resulting in tachycardia and hypertension, in addition to diaphoresis and lacrimation—signs very similar to signs of inadequate depth of anesthesia. Advanced diabetic autonomic neuropathy and beta blockade may obscure the signs of sympathetic stimulation of hypoglycemia. Intraoperative hypoglycemia can also manifest as bradycardia, hypotension, and respiratory failure.

KEY FACTS: HYPOGLYCEMIA

- Intraoperative hypoglycemia is difficult to diagnose clinically.
- Hypoglycemia could easily be misinterpreted as "light anesthesia."
- Symptoms are absent under deep sedation and general anesthesia.
- Symptoms may be masked by beta-blockade therapy and diabetic autonomic neuropathy.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006: Chapter 41, 1148.

59. ANSWER: E

A common cause of ***acute tubular necrosis (ATN)*** is prolonged renal hypoperfusion. Other causes include contrast dyes and nonsteroidal anti-inflammatory drugs. Treatment is mainly supportive.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1096.

Miller RD. *Miller's Anesthesia*. 6th ed. New York, NY: Churchill Livingstone, 2004:761.

60. ANSWER: B

The effect of hypercapnia is a direct depression of both myocardium and vascular smooth muscle. However, the sympathetic stimulation caused by increasing CO_2 tends to mask the cardiovascular depression. **Hypercapnia results in bronchodilation but is a potent pulmonary**

Table 4.9 LABORATORY DIFFERENTIATION FROM URINARY FINDINGS BETWEEN PRERENAL AZOTEMIA, HEPATORENAL SYNDROME, AND ATN

	PRERENAL AZOTEMIA	HEPATORENAL SYNDROME	ACUTE TUBULAR NECROSIS
Urinary sodium concentration	<10 mEq/L	<10 mEq/L	>30 mEq/L
Urine to plasma creatinine ratio	>30:1	>30:1	<20:1
Urinary osmolality	Greater than plasma osmolality by at least 100 mOsm	Greater than plasma osmolality by at least 100 mOsm	Equal to plasma osmolality
Urinary sediment	Normal	Unremarkable	Casts and cellular debris

SOURCE: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1096.

vasoconstrictor. The increase in QT interval is even more significant during general anesthesia using halothane, enflurane, and isoflurane as these agents have been shown to increase QTc by themselves, resulting in an increased risk of torsades de pointes.

Hypercapnia causes a shift in the oxy-Hb curve to the right, facilitating release of O_2 at the tissue level. But as the CO_2 level increases, alveolar and arterial O_2 levels may fall if the concentration of nitrogen and other inert gases remains constant.

Hypercapnia increases bicarbonate resorption by the kidneys to compensate for the respiratory acidosis. Hypercapnia also increases the efflux of potassium from cells into the plasma. The incidence of oculocardiac reflex is also increased in the presence of hypercapnia. Increasing CO_2 also results in increased cerebral blood flow and a rise in ICP and IOP.

As the CO_2 increases well above 100 mm Hg the sympathetic stimulation ceases, resulting in respiratory depression and respiratory arrest. CO_2 narcosis occurs when $PaCO_2$ increases above 90 to 120 mm Hg.

ADDITIONAL READING

Miller RD. *Miller's Anesthesia.* 6th ed. New York, NY: Churchill Livingstone; 2004; Chapter 17, 717–718.

61. ANSWER: A

Although the **steeple sign seen in Figure 4.2** is usually associated with a diagnosis of **laryngotracheobronchitis or croup** in children, it is by no means characteristic of that condition. Croup usually affects children between the ages of 6 months and 6 years. **Other conditions that can produce a steeple sign on a radiograph of the upper airway are epiglottitis, thermal injury, angioneurotic edema, and bacterial tracheitis.** In croup, the lateral x-ray film of the upper airway will reveal a normal epiglottis and subglottic narrowing of 1 to 1.5 cm, in contrast to the findings in epiglottitis.

Diagnosis of croup, a viral infection, is made clinically, and radiographic films of the upper airway are used to exclude other causes of stridor that mimic croup, such as foreign body aspiration, esophageal foreign body, congenital subglottic stenosis, epiglottitis, or subglottic hemangioma. In a case of croup, a lateral neck film and posteroanterior (PA) chest radiograph should be obtained as appropriate. Findings include a normal aryepiglottic area, slightly ill-defined tracheal air shadows in a lateral neck radiograph, narrowing on inspiration greater than that on expiration, and slight distention of the hypopharynx. Fixed subglottic obstructions such as papillomas, foreign bodies, hemangiomas, and subglottic stenoses cause narrowing of the airway that does not change with the phase of respiration and are asymmetric in appearance, whereas croup causes symmetric changes in the air column. The PA chest x-ray is most useful to rule out a radiopaque foreign body. In cases of croup, the normally squared shoulders of the subglottic tracheal air shadow will appear more like a steeple, a pencil tip, a nail, or an hourglass.

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Salour M. The steeple sign. *Radiology*. 2000;216:428–429.

62. ANSWER: D

Oculocardiac reflex (OCR) is also known as the **Aschner phenomenon**, **Aschner reflex**, or **Aschner-Dagnini reflex.** It occurs in response to pressure on the globe of the eye or any traction on the surrounding structures, resulting in bradycardia, cardiac arrhythmias, or even asystole (1 in 2,200 strabismus surgeries). In nonanesthetized patients, it can result in sweating, nausea and/or vomiting, and chest discomfort or palpitations. OCR can occur even from

stimulation of an empty orbit after enucleation of the globe or during surgery on the maxilla innervated by the trigeminal nerve, leading to the assumption that OCR may be a part of a larger trigemino-cardiac reflex. The reflex is initiated by stretch receptors present in the extraocular muscles. The pathway for the OCR is as follows:

> Eye stretch receptors → Short and long ciliary nerves → Ciliary ganglion → Ophthalmic division of trigeminal nerve → Gasserian ganglion (sensory nucleus of cranial nerve V in the floor of the fourth ventricle) → Motor nucleus of vagus nerve in the floor of the fourth ventricle → Parasympathetic outflow via vagus nerve → Heart

Increased $Paco_2$ and hypoventilation have been shown to significantly increase the incidence of bradycardia during surgery to correct strabissimus. OCR has been known to fatigue with sustained and repeated stimulation. Premedication with atropine, gentle handling of ocular and surrounding tissues, and maintaining normocapnia tend to reduce the occurrence and severity of OCR.

Immediate release of traction or pressure on the eye is the first step in treatment, followed by administration of intravenous atropine or glycopyrrolate. The latter tends to produce less tachycardia than atropine. Local injection of a local anesthetic or even a retrobulbar block of the ciliary ganglion may help stop recurrent episodes of OCR. However, OCRs have been known to occur during the execution of a retrobulbar block.

KEY FACTS: OCR

- OCR can result in bradycardia, cardiac arrhythmias, asystole, and hypotension.
- Pathway is through ciliary nerves, trigeminal nerve and ganglion to motor nucleus of vagus nerve.
- Premedication with atropine and gentle manipulation of the eye reduce the incidence of OCR.
- Hypercarbia increases the incidence of OCR.
- Treatment consists of removing stimulation or pressure on the eye, intravenous atropine, and injection of local anesthetic locally.

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5.

PEDIATRIC ANESTHESIA

David R. Moss, MD

1. A 14-kg, 3-year-old boy is scheduled for bilateral inguinal herniorrhaphy. With which of the following coexisting diseases would a total intravenous anesthetic technique be most appropriate?

A. Duchenne muscular dystrophy
B. Central core disease
C. Mitochondrial myopathy
D. Becker muscular dystrophy
E. Myotonia congenita

2. A 1-month-old boy is brought to the emergency room with projectile nonbilious vomiting. An olive-shaped mass is palpated in the epigastrium and the diagnosis of pyloric stenosis is confirmed with ultrasonography. Which of the following electrolyte disturbances would be LEAST likely?

A. Hyperchloremia
B. Metabolic alkalosis
C. Hyponatremia
D. Hypokalemia
E. Hypoglycemia

3. For which of the following patients with a history of recent oral intake would ASA fasting guidelines recommend delaying the start of surgery?

A. 6-year-old for tonsillectomy who drank apple juice 2 hours ago
B. 1-month-old for circumcision who had breast milk 4 hours ago
C. 14-year-old with testicular torsion who ate a turkey sandwich 4 hours ago
D. 6-month-old for cleft lip repair who had infant formula 4 hours ago
E. 16-year-old for anterior cruciate ligament reconstruction who ate a light breakfast 6 hours ago

4. On a per-kilogram basis, which of the following respiratory parameters remains unchanged in transitioning from infant to adult?

A. Oxygen consumption
B. Alveolar ventilation
C. Closing capacity
D. Tidal volume

5. Which of the following characteristics is more typical of the infant rather than adult airway?

A. Larynx that is located more caudad in the neck
B. Smaller tongue relative to the oral cavity
C. Narrowest portion of the airway is at the level of the vocal cords.
D. Vocal cords have a more caudad anterior attachment.
E. Epiglottis is relatively broader.

6. Which of the following syndromes is most likely associated with difficult airway management on the basis of mandibular hypoplasia?

A. Apert syndrome
B. Klippel-Feil syndrome
C. Pierre-Robin sequence
D. Beckwith-Wiedemann syndrome
E. Hurler syndrome

7. A newborn is delivered at 28 weeks gestation via cesarean section to a 16-year-old G1P0 mother with severe preeclampsia. One minute after delivery the baby is limp and cyanotic with irregular respirations, unresponsive to stimulation, with a pulse of 80. What is the initial Apgar score in this patient?

A. 1
B. 2

C. 3
D. 4
E. 5

8. Which of the following does NOT increase the risk of postoperative vomiting in a prepubescent child?

A. Female gender
B. Strabismus surgery
C. Age 3 or more
D. Duration of surgery 30 minutes or longer
E. History of postoperative vomiting in parents or siblings

9. Which of the following represents an advantage gained by using an uncuffed rather than a cuffed endotracheal tube in a pediatric patient less than 8 years old?

A. Less likely to change tube size to achieve appropriate fit
B. Ability to use lower fresh gas flow
C. Decreased OR contamination
D. Relatively larger internal diameter may be used.
E. Ability to ventilate with higher pressures

10. A 3-month-old born at 32 weeks gestational age requires surgical repair of an inguinal hernia. Preoperative hemoglobin is 9 g/dL. Which of the following recommendations for this patient's perioperative care would be LEAST appropriate?

A. Postpone surgery until postconceptual age of at least 54 weeks.
B. Administer caffeine.
C. Use a regional rather than general anesthetic technique.
D. Refer to a tertiary-care center.
E. Transfuse packed red blood cells prior to surgery.

11. Which of the following is more typical of gastroschisis rather than omphalocele?

A. Higher incidence
B. Coexisting congenital anomalies
C. Lateral abdominal wall defect
D. Prematurity
E. Peritoneal covering

12. A 2-day-old, 2.5-kg boy was born at 38 weeks gestation with a congenital diaphragmatic hernia (CDH). The patient was intubated after birth, has a nasogastric tube, arterial and venous access, and is awaiting corrective surgery. Which of the following ventilatory strategies is most appropriate?

A. Spontaneous ventilation, pressure support with PIP < 25, to minimize barotrauma
B. Spontaneous ventilation, pressure support with PIP < 25, to avoid hypercapnia
C. Spontaneous ventilation, pressure support with PIP > 25, to avoid hypercapnia
D. Controlled ventilation, pressure control with PIP > 25, to avoid hypercapnia
E. Controlled ventilation, pressure control with PIP < 25, to minimize barotrauma

13. Which of the following descriptions of tracheoesophageal fistula (TEF) represents the vast majority of cases?

A. Esophageal atresia without fistula
B. Esophageal atresia with proximal fistula
C. Esophageal atresia with distal fistula
D. Esophageal atresia with proximal and distal fistula
E. Tracheoesophageal fistula without esophageal atresia (H-type)

14. A 3-day-old, 3-kg neonate with type C tracheoesophageal fistula (TEF) presents to the OR for primary repair. After suctioning the upper esophageal pouch and placing the patient in a semi-upright position, which of the following induction techniques is most appropriate?

A. Rapid-sequence intubation with propofol and succinylcholine
B. Inhalation induction with sevoflurane
C. Awake tracheostomy under local anesthesia
D. Awake fiberoptic intubation
E. IV induction with propofol and pancuronium

15. A 4-month-old born at 28 weeks gestational age requires surgery to repair an inguinal hernia. A spinal anesthetic is planned. Compared to a healthy adult, which of the following is true regarding spinal anesthesia in this patient?

A. The spinal cord terminates higher relative to the spinal column.
B. The dural sac terminates higher relative to the spinal column.
C. There is a greater risk of bradycardia.
D. The duration of surgical anesthesia is shorter.
E. There is a greater risk of hypotension.

16. Which of the following events in early life is the LEAST significant in making the transition from a fetal to a neonatal circulation?

A. Decrease in pulmonary vascular resistance (PVR)
B. Initiation of alveolar ventilation
C. Closure of the ductus arteriosus

D. Closure of the foramen ovale
E. Closure of the ductus venosus

17. A 3-month-old infant with uncorrected tetrology of Fallot (TOF) is awaiting surgical repair. While his diaper is being changed, the baby starts crying and breathing rapidly. The infant becomes cyanotic and a code is called. Vital signs are P 160, BP 50/30, SpO_2 60%. Which of the following interventions would be LEAST appropriate at this time?

A. Administering sodium bicarbonate
B. Administering morphine
C. Administering epinephrine
D. Administering phenylephrine
E. Administering esmolol

18. A 2-week-old neonate born at 26 weeks gestation weighs 1.5 kg. Which of the following is the best estimate of circulating blood volume?

A. 105 mL
B. 120 mL
C. 135 mL
D. 150 mL
E. 200 mL

19. A 3-year-old is undergoing strabismus surgery. Anesthesia is induced with sevoflurane and nitrous oxide, a peripheral IV is placed, rocuronium is given, and the patient is intubated. While applying traction to the lateral rectus muscle, the patient develops junctional bradycardia at 30 bpm. Which of the following neuromuscular structures did NOT contribute to the bradycardia?

A. Abducens nerve
B. Trigeminal nerve
C. Vagus nerve
D. Long ciliary nerve
E. Lateral rectus muscle

20. Compared to a healthy adult, which of the following best describes the use of succinylcholine in a healthy 1-year-old?

A. The intubating dose is unchanged.
B. Fasciculations are more pronounced.
C. It should not be administered routinely.
D. It should not be administered intramuscularly.
E. The duration of action is longer.

21. A 2-week-old born at 32 weeks comes to the operating room for ligation of a patent ductus arteriosus (PDA). Which of the following BEST explains why uptake of sevoflurane with an inhalation induction is more rapid in this patient than in a healthy 6-year-old?

A. Right-to-left shunting
B. Left-to-right shunting
C. Higher alveolar ventilation to FRC ratio
D. Lower blood-gas partition coefficient of sevoflurane
E. Lower proportion of vessel-rich tissues

22. A 2-week-old (birth weight 1.2 kg) born at 28 weeks gestation develops lethargy, fever, vomiting, and bloody stools while in the NICU. The abdomen is distended and tender but there is no evidence of perforation on the abdominal radiograph. Vital signs are BP 59/32, P 168, R 35, T 38.6, SpO_2 93% on room air. The diagnosis of necrotizing enterocolitis is suspected. Which of the following measures would be LEAST appropriate at this time?

A. Administer broad-spectrum antibiotics.
B. Explore the bowel in the OR.
C. Discontinue enteral feedings.
D. Nasogastric decompression
E. Administer IV fluids.

23. Compared to a healthy adult, which of the following hematologic findings is most likely in a healthy term neonate?

A. Lower concentration of fetal hemoglobin (HbF)
B. Higher concentration of 2,3-diphosphoglycerate
C. Right-shifted hemoglobin-oxygen dissociation curve
D. Suppressed erythopoiesis
E. Increased red blood cell life span

24. Which of the following studies is most important in the preoperative evaluation of a 14-year-old child with Duchenne muscular dystrophy and scoliosis scheduled for posterior spinal fusion?

A. In vitro contracture testing
B. Echocardiogram
C. Pulmonary function tests
D. Liver function tests
E. Chest x-ray

25. Which of the following muscle relaxants, when given as a standard intubating dose, is most likely to have a prolonged duration of action in infants compared to adults?

A. Succinylcholine, 1 to 2 mg/kg
B. Pancuronium, 0.1 mg/kg
C. Cisatracurium, 0.2 mg/kg
D. Rocuronium, 0.6 mg/kg
E. Vecuronium, 0.1 mg/kg

26. Which of the following blood gases is most likely to have originated from the umbilical vein?

A. pH 7.35, pCO_2 40, PO_2 30
B. pH 7.28, pCO_2 50, PO_2 20
C. pH 7.35, pCO_2 40, PO_2 80
D. pH 7.28, pCO_2 50, PO_2 60
E. pH 7.40, pCO_2 40, PO_2 80

27. A 2-month-old, 4-kg infant with a nonrestrictive ventricular septal defect is brought to the OR for surgical repair. Which of the following perioperative interventions will most likely precipitate hypotension?

A. Pulmonary artery banding
B. Hypoventilation to an ET_{CO2} of 45
C. Decreasing the Fi_{O2} to 21%
D. Inhalation induction with 8% sevoflurane
E. 50 mcg/kg of fentanyl prior to incision

28. A 3-year-old child is scheduled for removal of a benign skin growth on her left forearm. On preoperative evaluation her mother tells you she has had a cold for the past week. She describes symptoms of rhinorrhea, nasal congestion, and nonproductive cough. Which of the following is most likely to DECREASE the risk of perioperative respiratory complications?

A. Inhalation induction with sevoflurane
B. Delaying the case 2 weeks
C. Using an LMA for airway management
D. Removing the airway device deep
E. Pretreatment with albuterol

29. A 4-year-old girl presents to the emergency room with inspiratory stridor. Which of the following findings is most consistent with a diagnosis of acute epiglottitis?

A. Gradual onset over days
B. Steeple sign on chest x-ray
C. Dysphagia and drooling
D. Barking cough
E. Low-grade fever

30. A 2-year-old child with a history of congenital heart disease requires dental extraction. Which of the following conditions necessitates the use of antibiotic prophylaxis for infective endocarditis?

A. Unrepaired ventricular septal defect (VSD)
B. VSD, surgically closed 4 months ago
C. Atrial septal defect (ASD), closed with a device in the cardiac cath lab 8 months ago
D. Unrepaired aortic stenosis
E. Dextro-transposition of the great arteries status post arterial switch operation in infancy

31. A 6-year-old boy with cerebral palsy and spastic quadriplegia presents to the OR for lower-extremity contracture release. Which of the following perioperative considerations is most likely in this patient?

A. Hyperkalemia after succinylcholine
B. Intraoperative hypothermia
C. Higher anesthetic requirements
D. Coagulopathy
E. Improved ability to assess postoperative pain

32. A full-term 3-kg neonate is born with a myelomeningocele. Corrective surgery is planned to reduce the risk of infection and further neurologic injury. Which of the following conditions is LEAST likely to be present (or later develop) in this patient?

A. Latex allergy
B. Arnold-Chiari malformation
C. Congenital heart disease
D. Hydrocephalus
E. Bladder dysfunction

33. A 12-year-old boy with obstructive sleep apnea underwent adenotonsillectomy 8 hours ago. He is restless, agitated, and spitting up blood. The ENT surgeon wants to take him back emergently to the operating room. Which of the following maneuvers would be LEAST appropriate for this anesthetic?

A. Awake fiberoptic intubation
B. Aggressive volume resuscitation prior to induction
C. Rapid-sequence induction
D. Orogastric aspiration prior to extubation
E. Awake extubation

34. A 5-year-old girl with sickle cell disease presents to the OR for laparoscopic cholecystectomy. She has a history of recurrent bone and abdominal pain. Her preoperative hemoglobin level is 7.4 g/dL. Which of the following is most likely to increase the risk of postoperative complications in this patient?

A. Blood transfusion
B. Respiratory alkalosis
C. Ventilation with 100% FiO_2
D. Epidural analgesia
E. Minimizing IV fluids

35. A 1-week-old, 4-kg neonate born full term presents to the operating room for duodenal atresia repair. Preoperative hematocrit is 38%. At the end of the surgery you estimate an intraoperative blood loss of 75 mL.

Assuming maintenance of euvolemia, what is the likely postoperative hematocrit?

A. 34%
B. 30%
C. 26%
D. 22%
E. 18%

36. A 31-year-old G1P0 delivers vaginally at 39 weeks. The newborn comes out limp and cyanotic with agonal respirations. The heart rate is 80 bpm. After moving the child to a radiant heat source, suctioning the airway, and drying and stimulating the baby, which of the following is the most appropriate next step?

A. Provide chest compressions.
B. Endotracheal intubation and tracheal suctioning
C. Administer IM epinephrine.
D. Obtain IV access and administer 10 cc/kg crystalloid.
E. Provide positive-pressure ventilation.

37. Which of the following physiologic parameters is lower in a healthy 3-month-old compared to an adult (normalized for weight)?

A. MAC for sevoflurane
B. Oxygen consumption
C. Glomerular filtration rate (GFR)
D. Blood volume
E. Total body water

38. Which of the following mechanisms best explains why infants, relative to adults, are more predisposed to hypothermia?

A. Lower skin surface area to body mass ratio
B. Increased keratin content in skin
C. Higher thermoneutral temperature
D. More effective thermoregulatory response
E. Diminished metabolism of brown fat

39. Which of the following complications of prematurity is minimized by maintaining a low-normal oxygen saturation (i.e., 80% to 90%)?

A. Necrotizing enterocolitis
B. Respiratory distress syndrome
C. Patent ductus arteriosus
D. Intraventricular hemorrhage
E. Retinopathy

40. While you are on a medical mission trip to a country with limited resources for surgery, a 5-year-old boy with an isolated cleft palate presents to the operating room for primary closure. Which of the following is most accurate for this patient?

A. Isolated cleft palate is more common than cleft lip.
B. Speech is unlikely to be affected.
C. The patient should be evaluated for cardiac abnormalities.
D. Airway obstruction is more likely now than it would have been at 6 months.
E. Infiltration with local anesthesia is usually sufficient for analgesia.

41. Which of the following findings is most likely to be encountered in a neonate with persistent pulmonary hypertension of the newborn (PPHN)?

A. Left-to-right shunt through the patent ductus arteriosus (PDA)
B. Differential cyanosis
C. Low PVR
D. Reverse differential cyanosis
E. Metabolic alkalosis

42. A 6-year-old boy with Down syndrome presents to the OR for tonsillectomy and adenoidectomy. Which of the following coexisting conditions is LEAST likely in this patient?

A. Chronic kidney disease
B. Cardiac defects
C. Airway obstruction
D. Atlanto-axial instability
E. Subglottic stenosis

43. A 4-year-old boy with midshaft hypospadias is scheduled for repair. As part of the anesthetic, a single-shot caudal will be administered after induction, but prior to incision. Which of the following is most accurate with respect to this neuraxial block?

A. Significant hypotension is likely in the absence of fluid loading.
B. Test dosing with epinephrine is highly sensitive for intravascular placement.
C. The cephalad extent of the block is influenced primarily by local anesthetic concentration.
D. The sacrococcygeal ligament must be punctured.
E. The dural sac terminates at S3–4.

44. A 3-month-old patient with congenital methemoglobinemia presents to the OR for direct laryngoscopy and

rigid bronchoscopy for evaluation of stridor. Which of the following local anesthetics is contraindicated?

A. Bupivacaine
B. Ropivacaine
C. Lidocaine
D. Mepivacaine
E. Prilocaine

45. A 7-year-old girl presents to the OR for biopsy of an anterior mediastinal mass. She has had progressive dyspnea over the past 2 weeks and 3 days of worsening swelling of her arms and face. She also has a history of gastroesophageal reflux disease, for which she is maintained on pantoprazole. You are told that biopsy under local anesthesia is not feasible. Which of the following considerations for induction of general anesthesia is LEAST appropriate?

A. Availability of rigid bronchoscopy
B. Availability of cardiopulmonary bypass
C. Rapid-sequence intubation
D. Availability of help to turn the patient lateral or prone
E. Intubation without the use of muscle relaxants

46. Which of the following statements about the functional residual capacity (FRC) of a spontaneously breathing awake neonate is true?

A. On a mL/kg basis, it is smaller than that of an adult.
B. It is reliably greater than the closing capacity.
C. It represents the volume at which chest wall recoil equals lung recoil.
D. It is determined by dynamic rather than passive factors.
E. It is equivalent to the residual volume plus tidal volume.

47. Which of the following diseases is associated with resistance to depolarizing neuromuscular blockade?

A. Myasthenic syndrome
B. Myasthenia gravis
C. Myotonic dystrophy
D. Duchenne muscular dystrophy
E. Multiple sclerosis

CHAPTER 5 ANSWERS

1. ANSWER: B

Malignant hyperthermia (MH) is a rare hypermetabolic complication of exposure to any of the volatile anesthetics and/or succinylcholine. Rhabdomyolysis, lactic acidosis, hyperthermia, DIC, and fatal arrhythmias may develop precipitously unless treatment with dantrolene (2.5 mg/kg) is promptly initiated. Susceptibility to MH is usually the result of an inherited mutation in the ryanodine receptor, which regulates calcium release from myocyte sarcoplasmic reticulum. **The only two coexisting diseases that have a high concordance with MH are central core disease and King-Denborough syndrome.** Less convincingly, Evans myopathy has also been associated.

Duchenne muscular dystrophy has been associated with rhabdomyolysis after volatile anesthetic exposure due to skeletal muscle instability rather than true MH. A nontriggering technique is easily justified to avoid this risk, and succinylcholine is absolutely contraindicated due to the risk of life-threatening hyperkalemia.

Mitochondrial myopathies and myotonia congenita are not associated with susceptibility to MH. Becker muscular dystrophy is related to Duchenne muscular dystrophy but symptoms are generally milder. There is no increased risk of MH.

ADDITIONAL READINGS

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Gurnaney H, Brown A, Litman RS, et al. Malignant hyperthermia and muscular dystrophies. *Anesth Analg*. 2009;109:1043–1048.

2. ANSWER: A

Pyloric stenosis typically presents between 2 and 6 weeks of age with an incidence of 1:500 live births, affecting more male than female infants. The hypertrophied pylorus can often be palpated as an olive-shaped mass between the midline and right upper quadrant. The gastric obstruction leads to projectile, nonbilious vomiting and electrolyte imbalance from loss of gastric fluids containing hydrogen, chloride, sodium, and potassium. The renal response to vomiting is to retain hydrogen ions in exchange for potassium. Further depletion of sodium and potassium leads to the secretion of acidic urine, worsening the metabolic alkalosis. **The classic metabolic acid–base disturbance is a hypochloremic, hypokalemic, hyponatremic metabolic alkalosis with a compensatory respiratory acidosis.** With further fluid loss prerenal azotemia may lead to severe dehydration, hypovolemic shock, and metabolic acidosis. Hypoglycemia may be present due to malnutrition.

Pyloric stenosis is a medical emergency. Definitive treatment is pyloromyotomy, often performed laparoscopically. Prior to surgical intervention, it is vital that the neonate is sufficiently resuscitated with fluids and electrolytes. Patients should have stomach contents aspirated with an orogastric tube before induction of anesthesia to minimize the risk of pulmonary aspiration. Because of this risk, induction is usually performed as a rapid sequence. If the intubation is anticipated to be difficult, an awake intubation should be considered.

ADDITIONAL READINGS

Guzzetta PC, Randolph JG, Anderson KD, et al. Surgery of the neonate. In: Avery GB, ed. *Neonatology: Pathophysiology and Management of the Newborn*. Philadelphia, PA: JB Lippincott; 1987:944–984.

Touloukian RJ, Higgins E. The spectrum of serum electrolytes in hypertrophic pyloric stenosis. *J Pediatr Surg*. 1983;18:394–397.

3. ANSWER: D

Fasting recommendations prior to surgery and anesthesia aim to balance the risk of aspiration during induction against the potential of dehydration, discomfort, and hypoglycemia. In the past, long periods of preoperative fasting were recommended, but recently it has been demonstrated that clear liquids are rapidly eliminated from the stomach and actually stimulate peristalsis, thereby decreasing gastric volume and acidity. **Emergency surgery, as for testicular torsion, demands emergent anesthesia** regardless of NPO status (Table 5.1).

Table 5.1 **PREOPERATIVE FASTING RECOMMENDATIONS IN INFANTS AND CHILDREN**

Clear liquids	**2 hours**
Breast milk	**4 hours**
Infant formula or light meal	**6 hours**
Solids	**8 hours**

ADDITIONAL READINGS

Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

4. ANSWER: D

Oxygen consumption and alveolar ventilation are twice as high in infancy than adulthood. The closing capacity is

approximately half of TLC in infancy (and may be higher than FRC. but decreases to a third of TLC in adulthood before increasing again. **FRC and tidal volume are unchanged throughout life,** but the mechanics of maintaining FRC are different in infants in comparison to adults (Fig. 5.1 and Table 5.2).

5. ANSWER: D

An infant's larynx is more cephalad in the neck, at the level of C3–4 (vs. C4–5), making airway obstruction by the relatively larger tongue more likely. **The narrowest part of the infant airway is at the level of the cricoid cartilage as opposed to the rima glottidis in adults.** The epiglottis of an infant is narrower and stiffer than that of an adult, and omega-shaped. The vocal cords have a more caudad attachment anteriorly, whereas in adults they are perpendicular to the trachea. This makes it more likely that an endotracheal tube gets "hung up" on the anterior wall of the trachea during intubation. Rotating the tube often overcomes this problem (Fig. 5.2).

ADDITIONAL READINGS

Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

6. ANSWER: C

Difficulty with mask ventilation and/or endotracheal intubation may occur due to distortion of anatomic relationships in the airway. Under normal conditions the tongue and soft tissue are displaced into the anterior mandibular space, allowing direct visualization of the laryngeal inlet. **Mandibular hypoplasia, as occurs in the Pierre-Robin sequence (micrognathia, glossoptosis, cleft palate), may easily result in airway obstruction and difficult intubation due to a small anterior mandibular space.** Glossoptosis refers to abnormal posterior displacement or retraction of the tongue.

Apert syndrome is associated with maxillary hypoplasia and choanal stenosis. These patients are generally mouth-breathers and prone to obstruction when their mouths are closed. Their mandibles are normal-sized and laryngoscopy is not typically difficult.

Klippel-Feil syndrome is associated with limitation of neck flexion and extension due to fused cervical vertebrae, making laryngoscopy difficult. Mask ventilation is usually not problematic.

Beckwith-Wiedemann syndrome patients have a large protuberant tongue that may obstruct the airway. Perioperatively, these patients are at risk for hypoglycemia due to pancreatic hyperplasia. Omphalocele and congenital heart disease are also associated.

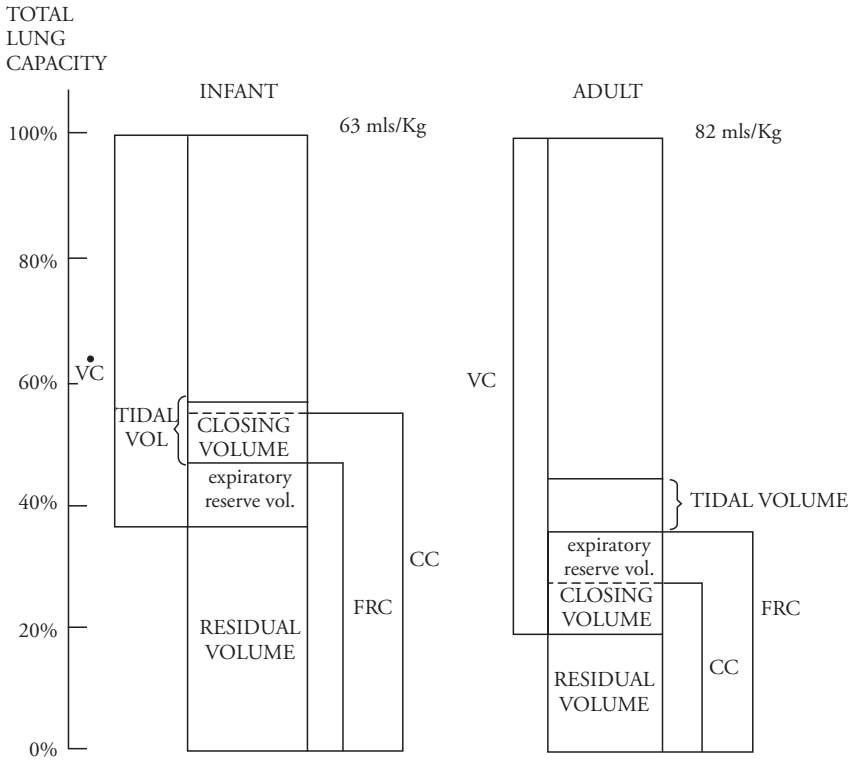

Figure 5.1 Static lung volumes of infants and adults.

Adapted from Fig. 43–9. (Reprinted with permission from Smith CA, Nelson NM. *Physiology of the Newborn Infant*. 4th ed, p. 207. Springfield, IL: Charles C Thomas; 1976. LWW)

Hurler syndrome, as with other mucopolysaccharidoses, may cause airway difficulty because of infiltration of pharyngeal and laryngeal soft tissues, as well as a short neck.

ADDITIONAL READINGS

Nargozian C. The airway in patients with craniofacial abnormalities. *Pediatr Anesth*. 2004;14:53–59.

Table 5.2 **COMPARISON OF NORMAL RESPIRATORY PARAMETERS IN INFANTS AND ADULTS**

RESPIRATORY PARAMETER	INFANT	ADULT
Respiratory frequency	30–50	12–16
Tidal volume (mL/kg)	7	7
Dead space (mL/kg)	2–2.5	2.2
Alveolar ventilation (mL/kg/min)	100–150	60
Functional residual capacity (mL/kg)	27–30	30
Oxygen consumption (mL/kg/min)	7–9	3

Adapted from Barash PG, Cullen BF, Stoelting RK, eds. Clinical Anesthesia. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

7. ANSWER: B

The Apgar score is a widely used assessment of neonatal well-being immediately after delivery. **There are five categories, and a score of 0 to 2 may be given in each.** It is helpful to use the letters in Apgar to recall the categories (Table 5.3).

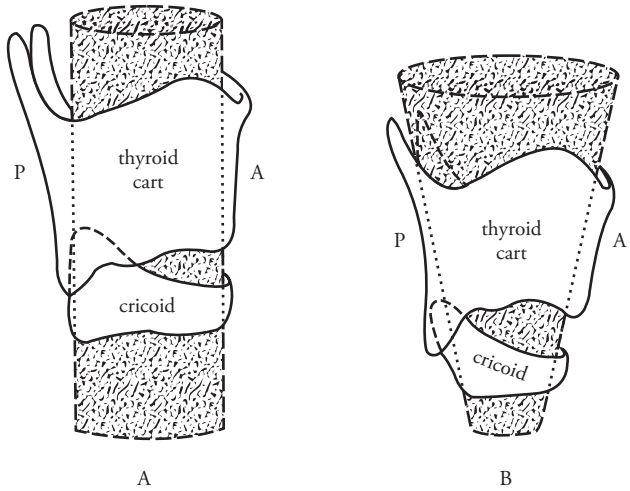

Figure 5.2 Configuration of the adult (A. versus the infant (B. larynx. The adult larynx has a cylindrical shape. The infant larynx is funnel-shaped because of the narrow, undeveloped cricoid cartilage.

Adapted from Barash. Clinical *Anesthesia*. Fig. 43–7. (Reprinted with permission from The Pediatric Airway. In Ryan JF, Coté CJ, Todres ID [eds]: *A Practice of Anesthesia for Infants and Children*. 2nd ed, p. 61. Orlando, FL: Grune & Stratton; 1992.)

8. ANSWER: A

The risk factors for postoperative vomiting (postoperative nausea is not well studied in pediatrics) are different than in adults. **Gender differences have not been shown to be a major factor until after puberty.** Based on a large observational study, a pediatric risk score for vomiting has been validated. The presence of zero, one, two, three, or four risk factors (choices B–E. was associated with incidences of 9%, 10%, 30%, and 55%. Strabismus surgery independently conferred the greatest risk.

ADDITIONAL READINGS

Eberhart LH, Geldner G, Kranke P, et al. The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients. *Anesth Analg*. 2004;99:1630–1637.

9. ANSWER: D

Uncuffed endotracheal tubes have historically been used in children due to the theoretical risk of pressure injury and resultant edema of the tracheal mucosa with cuffed tubes. Comparative studies using modern cuffed tubes (high volume, low pressure) have not shown a difference in postoperative complications, although cuffed tubes must be slightly smaller due to the volume occupied by the cuff. Uncuffed tubes make it more likely to need to change tube size to achieve an appropriate fit (leak at 20 to 25 cm H_2O). They **require higher fresh gas flows** (may not be a problem with modern anesthesia delivery systems) and **contribute to OR contamination** from anesthetic gas. Controlled ventilation is limited by the inspiratory pressure at which the leak occurs.

ADDITIONAL READINGS

Khine HH, Corddry DH, Kettrick RG, et al. Comparison of cuffed and uncuffed endotracheal tubes in young children during general anesthesia. *Anesthesiology*. 1997;86:627–631.

10. ANSWER: E

The former preterm infant (gestation age less than 37 weeks) is at risk for postoperative respiratory depression and apnea after anesthesia. **Elective surgery should be postponed whenever possible until after 54–60 weeks postconceptual age (PCA),** at which point respiratory control is mature and no special measures need be taken in the otherwise healthy ex-premie. If surgery must be performed (most commonly for inguinal hernia or laser photocoagulation of

Table 5.3 APGAR SCORE CRITERIA

ACRONYM	ASSESSMENT	SCORE OF 0	SCORE OF 1	SCORE OF 2
*A*ppearance	Skin color	Blue or pale all over	Blue at extremities, body pink (acrocyanosis)	No cyanosis; body and extremities pink
*P*ulse	Heart rate	Absent	<100	≥100
*G*rimace	Reflex irritability	No response to stimulation	Grimace/feeble cry when stimulated	Cry or pull away when stimulated
*A*ctivity	Muscle tone	None	Some flexion	Flexed arms and legs that resist extension
*R*espiration	Breathing	Absent	Weak, irregular, gasping	Strong, lusty cry

the retina) referral to a tertiary-care center with the ability to closely monitor the baby postoperatively for respiratory events is prudent. A minimum of 12 hours of monitoring is recommended for ex-preterm infants less than 46 weeks PCA. At least 6 hours of monitoring is recommended for infants less than 54 weeks PCA, though institutional practices differ. IV caffeine, 10 mg/kg, has been shown to be an effective prophylactic. A regional anesthetic technique (spinal, caudal) avoids the need for muscle relaxation and opioids, agents thought to be associated with postoperative apnea. Anemia (Hb less than 10 g/dL), independent of PCA, has also been shown to increase the risk of apnea but. there is no evidence to suggest that preemptive transfusion of packed red blood cells lowers that risk.

ADDITIONAL READINGS

Walther-Larsen S, Rasmussen LS. The former preterm infant and risk of post-operative apnoea: recommendations for management. *Acta Anaesthesiol Scand*. 2006;50:888–893.

11. ANSWER: C

Both omphalocele and gastroschisis are abdominal wall defects that can be diagnosed prenatally.

Omphalocele is about twice as common and occurs more frequently in premature infants. Associated anomalies (cardiac, gastrointestinal, genitourinary, Beckwith-Wiedemann syndrome) are more often found in conjunction with omphalocele. ***Gastroschisis*** results from occlusion of the omphalomesenteric artery during gestation, causing herniation of uncovered viscera through an abdominal wall defect lateral to the midline.

ADDITIONAL READINGS

Liu LM, Pang LM. Neonatal surgical emergencies. *Anesthesiol Clin North Am*. 2001;19(2):265–286.

12. ANSWER: A

CDH occurs in 1/2,500 births and is usually left-sided. Morbidity and mortality result from pulmonary hypoplasia and associated pulmonary vascular disease. Corrective surgery is often delayed in order to stabilize the patient in the neonatal ICU. Ventilatory and inotropic support is frequently required. **"Gentle" ventilation strategies that preserve spontaneous ventilation with low inspiratory pressure support (less than 25 cm H_2O) minimize lung distention and barotrauma and correlate with improved survival.** High inspiratory peak pressures can lead to pneumothorax of the contralateral lung. Despite increasing pulmonary vascular resistance, permissive hypercapnia is considered acceptable as long as the pH remains greater than 7.25 and $PaCO_2$ is less than 60 mm Hg. Rescue strategies such as high-frequency oscillatory ventilation (HFOV) and extracorporeal membrane oxygenation (ECMO) with or without inhaled nitric oxide (iNO) may be required if this approach fails.

ADDITIONAL READINGS

Brown RA, Bosenberg AT. Evolving management of congenital diaphragmatic hernia. *Pediatr Anesth*. 2007;17:713–719.

13. ANSWER: C

TEF occurs in 1 in 4,000 births. **85% of cases are Gross type C (i.e., esophageal atresia with distal fistula).** The diagnosis may be suspected prenatally by the presence of polyhydramnios. Clinical features occur early and include excessive salivation, coughing, choking, and cyanosis with feeding. Aspiration of gastric contents can cause pneumonitis and respiratory distress. Associated congenital anomalies are common, particularly cardiac (tetralogy of Fallot, ventricular septal defect, atrial septal defect, patent ductus

arteriosus). Other potential anomalies are found in the acronym VACTERL (vertebral, anal, cardiac, TEF, renal, limb).

ADDITIONAL READINGS

Gayle JA, Gomez SL, Baluch A, et al. Anesthetic considerations for the neonate with tracheoesophageal fistula. *Middle East J Anesthesiol*. 2008;19(6):1241–1254.

14. ANSWER: B

Airway management for the patient with TEF must take into account the high risk of inadvertently ventilating the fistula, causing massive gastric distention as well as ineffective alveolar ventilation and hypoxia. Muscle relaxants should probably be avoided until the endotracheal tube is properly positioned below the fistula. **A technique that maintains spontaneous ventilation is ideal.** Awake intubation is a viable alternative but may be relatively difficult.

ADDITIONAL READINGS

Gayle JA, Gomez SL, Baluch A, et al. Anesthetic considerations for the neonate with tracheoesophageal fistula. *Middle East J Anesthesiol*. 2008;19(6):1241–1254.

15. ANSWER: D

Spinal anesthesia is an excellent alternative to general anesthesia for select surgical procedures. It may have particular application in preterm infants (e.g., for inguinal hernia repair) to minimize the risk of postoperative apnea to which these patients are prone. There may be benefit in avoiding general anesthetics in neonates for fear of neurotoxicity, but this has not been conclusively demonstrated. Single-shot spinals do, however, impose a time limit on the surgical team and are not a technique for slow surgeons or a surgical procedure of unpredictable duration. **Infants have a higher CSF volume (4 mL/kg) than adults (2 mL/kg) and for this reason require relatively higher doses of local anesthetic for an equivalent block.** The rates of CSF production and absorption are also higher in infants that contributes to the shorter duration.

Hemodynamic stability is typical of infant spinals, and there are no reports in the literature of significant hypotension or bradycardia in children under 5 years of age. Because SVR is low at birth and increases progressively with age, the sympathectomy of a spinal block has much less of a hemodynamic effect in infants and young children.

The spinal cord terminates at the level of L3 at birth and reaches its permanent position at L1 by 1 year of age. The dural sac likewise terminates lower at S3 and then migrates to S1 in later years.

ADDITIONAL READINGS

Pullerits J, Holzman RS. Pediatric neuraxial blockade. *J Clin Anesth*. 1993;5:342–354.

16. ANSWER: E

Fetal circulation is characterized by a parallel circuit in which both ventricles supply blood to the systemic circulation. Oxygenated blood returns to the fetus from the placenta via the umbilical vein. Half that blood bypasses the liver via the ductus venosus to reach the inferior vena cava ($SO_2 = 70\%$), where it is preferentially directed across the foramen ovale from the right to the left atrium. Venous blood from the head and upper body ($SO_2 = 40\%$) returns to the right atrium via the superior vena cava, enters the RV, and is ejected out the PA, 90% of which is shunted across the ductus arteriosus to the aorta. At birth, the initiation of alveolar ventilation has the effect of increasing Pao_2, reducing PVR, and functionally closing the ductus arteriosus. LA pressure increases above RA pressure, effectively closing the foramen ovale. **Closure of the ductus venosus occurs by 1 week but is not significant for establishing neonatal circulation.**

ADDITIONAL READINGS

DiNardo JA, Avara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Malden, MA: Wiley-Blackwell; 2007.

17. ANSWER: C

"Tet spells" in the patient with uncorrected TOF are life-threatening and require immediate intervention. Infundibular spasm worsens an already compromised right ventricular outflow tract (RVOT), resulting in right-to-left shunting, hypoxia, and cyanosis. Paroxysmal hyperpnea is the initial finding and compounds the problem. Hyperpnea increases oxygen consumption, causing hypoxia and acidosis, which decrease SVR. Treatment consists of administering 100% oxygen and compressing the femoral arteries by placing the patient in a knee–chest position so as to increase SVR and reduce the magnitude of the shunt. A crystalloid bolus will raise preload, increase the RV chamber size and increase the diameter of the RVOT. Bicarbonate

is effective at temporarily correcting the severe metabolic acidosis and normalizing SVR. Phenylephrine increases SVR and reduces shunt magnitude. Esmolol or propranolol may reduce infundibular spasm by decreasing contractility and allow for improved filling with a slower heart rate. **Epinephrine, like other beta agonists, is a poor choice as it will increase contractility, further narrowing the already compromised RVOT.**

ADDITIONAL READINGS

DiNardo JA, Avara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Malden, MA: Wiley-Blackwell; 2007.

18. ANSWER: D

Circulating blood volume increases on an mL/kg basis with decreasing age and is highest in low-birth-weight, preterm, and critically ill infants. An accurate estimation of circulating blood volume is of critical importance when the potential for blood loss is high (Table 5.4).

Table 5.4 BLOOD VOLUME BY AGE

AGE	ESTIMATED BLOOD VOLUME (ML/KG)
Preterm infant	100
Full-term neonate	90
Infant	80
School age	75
Adults	70

ADDITIONAL READINGS

Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children.* 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

19. ANSWER: A

The ***oculocardiac reflex (OCR)*** may occur during ophthalmologic surgery when traction on the extrinsic ocular muscles causes a trigeminovagal reflex resulting in sinus or junctional bradycardia, AV block, or even asystole. The afferent pathway is the ophthalmic branch of the trigeminal nerve (via the long and short ciliary nerves). The efferent pathway is the vagus nerve (X) which releases acetylcholine at the SA node. The abducens nerve provides motor innervation to the lateral rectus muscle but contains no sensory fibers.

Bradycardia usually resolves abruptly with release of traction on the extraocular muscles. Anticholinergic prophylaxis with atropine or glycopyrrolate may minimize the risk but is rarely practiced. Hypercarbia has been shown to increase the risk of bradycardia, so it may be advisable to support ventilation in order to maintain normocapnia.

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.
Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children.* 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

20. ANSWER: C

According to the FDA, the use of **succinylcholine in infants and children should be reserved for emergency intubation** and instances where immediate securing of the airway is necessary, such as laryngospasm, a difficult airway, or a full stomach, or for intramuscular use when a suitable vein is inaccessible. These recommendations were made because of the risk of fatal hyperkalemic arrest in young boys with undiagnosed muscular dystrophy. Concomitantly, there has been a decrease in the incidence of malignant hyperthermia.

The intubating dose is higher in infants (2 mg/kg) owing to its rapid distribution into a relatively larger extracellular fluid (ECF) volume. Fasciculations may be absent. Despite the fact that infants less than 6 months old have half the level of pseudocholinesterase, the duration of action is not prolonged (6–8 minutes).

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.

21. ANSWER: C

Uptake of volatile agents (FA/FI) is faster in infants than older children and adults due to the higher ratio of alveolar ventilation to FRC. This ratio is 5:1 in neonates compared with 1.5:1 in adults. A PDA typically causes left-to-right shunting, which would have minimal effect on uptake. A right-to-left shunt would slow uptake as pulmonary venous blood is diluted with systemic venous blood. The blood-gas partition coefficient is slightly lower in neonates for halothane and isoflurane but is unchanged for sevoflurane. Infants have

a larger proportion of vessel-rich tissues such as brain, liver, and heart, which also contributes to a more rapid uptake.

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.

22. ANSWER: B

Necrotizing enterocolitis occurs most often in premature neonates. Hypoperfusion of an immature gut and premature oral feeding are contributory. Early signs include feeding problems, lethargy, hyperglycemia, bloody stools, and fever. **Medical management and stabilization is the mainstay of treatment in the absence of intestinal perforation or refractory sepsis.** Cardiovascular status should be optimized with fluid, blood products, and vasopressors as necessary. Enteral feeds should be discontinued and the abdomen decompressed. Broad-spectrum antibiotics should be started to cover enterococci, staphylococci, and coliforms.

If surgery is necessary (approximately 50% of cases), one should anticipate a critically ill patient with varying degrees of hypotension, anemia, thrombocytopenia, coagulopathy, and lactic acidosis. Blood and fluid losses as well as coagulopathy may require large volumes of blood products and fluids to control bleeding and maintain an acceptable volume status. Inotropic support will likely be necessary and arterial pressure monitoring is essential.

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.

Liu LM, Pang LM. Neonatal surgical emergencies. *Anesthesiol Clin North Am*. 2001;19(2):265–286.

23. ANSWER: D

There are significant differences in hematologic parameters between neonates and older children or adults. Fetal hemoglobin (HbF) is synthesized principally in the fetal liver and remains the predominant type of hemoglobin at birth, representing 70% to 80% of hemoglobin. Production of HbF falls over the first few months of life and declines to less than 2% by 1 year. The level of 2,3-DPG is low at birth but increases over the first few months. Both fetal hemoglobin (more avid oxygen binding) and a low 2,3-DPG level contribute to a relatively left-shifted hemoglobin-oxygen dissociation curve. **Erythropoiesis is suppressed after birth,** and together with a reduced red blood cell life span (60 vs. 120 days) gives rise to a physiologic anemia of infancy that reaches a nadir at 8 to 12 weeks. In premature babies, the drop in hemoglobin occurs earlier and is more pronounced.

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.

24. ANSWER: B

Duchenne muscular dystrophy is an X-linked recessive genetic disorder characterized by rapidly progressive muscle weakness and wasting. The disease is caused by a mutation in the gene that encodes the protein dystrophin. There is a high incidence of scoliosis, which together with respiratory muscle weakness puts these patients at high risk for respiratory failure and pneumonia. **Cardiomyopathy is the major cause of death and an echocardiogram is essential for evaluating the degree of cardiac failure.** There is no association with malignant hyperthermia (MH), but there is a risk of anesthetic-induced rhabdomyolysis (AIR) and a nontriggering technique is justifiable.

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.

25. ANSWER: E

There are significant differences in the pharmacokinetics of muscle relaxants in infants versus adults owing to differences in ECF volume and maturity of the neuromuscular junction. ECF is greatest at birth (45% of body weight) and then declines to adult values of 19%. Because muscle relaxants are highly ionized, this increase in ECF results in an increase in the volume of distribution. However, the neuromuscular junction of infants is two to three times more sensitive to the effects of nondepolarizing muscle relaxants such that dose requirements do not vary significantly with age. With succinylcholine, there is no increased sensitivity and so a larger dose must be given to compensate for the increase in ECF. Duration of action of succinylcholine is similar to or somewhat less than that in adults.

The duration of action of both rocuronium and vecuronium is prolonged in infants, but the effect is more significant with vecuronium. A standard intubating

dose of 0.1 mg/kg produces a more than 90% block that lasts an hour in neonates compared with only 18 minutes in children.

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.

26. ANSWER: A

The normal umbilical cord has two arteries (carrying blood from fetus to placenta) and one vein (carrying blood from placenta to fetus). The vein can be identified by its larger size and thinner wall. Standard values of umbilical venous and arterial gases are important for analyzing disturbances that may occur following delivery in compromised neonates.

27. ANSWER: D

Ventricular septal defects (VSDs) are the most common congenital cardiac defect in children, occurring in 1.5 to 3.5 per 1,000 births and accounting for 20% of pediatric congenital heart disease. A large nonrestrictive VSD causes significant left-to-right shunting with ensuing right-sided volume overload and congestive heart failure. If left uncorrected, pulmonary vascular disease and irreversible pulmonary hypertension will develop, causing shunt reversal and cyanosis (Eisenmenger syndrome). Anesthetic management for this patient who presents for early repair must focus on minimizing left-to-right shunting and preventing further deterioration of an already compromised heart. Interventions that increase pulmonary vascular resistance (PVR) such as PA banding and hypoventilation will favorably reduce Qp:Qs, the ratio of pulmonary to systemic blood flow. Maintaining an FiO_2 close to 21% after securing the airway will minimize any decrease in PVR due to hyperoxia. A high-dose narcotic technique is frequently utilized in cardiac anesthesia because of its favorable hemodynamic profile and ability to blunt the cardiovascular response to surgical stimulation (which would increase PVR). **Inhalation with 8% sevoflurane, as is often performed in pediatric anesthesia, is unadvisable in patients with a large VSD.** These patients may have very limited cardiac reserve owing to RV volume overload, and the myocardial depressant effect of high-concentration sevoflurane may precipitate overt heart failure and hypotension. IV access should optimally be secured prior to induction and may be facilitated by generous premedication. Inhalation induction may be acceptable in selected patients, but generally the minimum concentration to facilitate vascular access should be used.

28. ANSWER: C

Anesthesia for the child with an active or recent upper respiratory infection (URI) requires special attention. **Those with fever, purulent rhinitis, productive cough, or rhonchi probably benefit from postponement of elective surgery.** Many children present with mild symptoms and the decision to proceed or cancel is highly dependent on individual circumstances and practitioner experience. A large prospective study has confirmed that children with an active or recent URI (within 4 weeks) are at higher risk for adverse perioperative respiratory complications such as laryngospasm, bronchospasm, arterial desaturation, and postintubation croup. **Independent risk factors that have been shown to increase the risk are copious secretions, use of an endotracheal tube (ETT) in a child less than 5, history of prematurity, nasal congestion, parental smoking, history of reactive airway disease, and surgery involving the airway.**

There is no significant difference between mask and IV induction techniques, although propofol appears to blunt airway reflexes to a greater degree than sevoflurane and may be preferable if IV access is convenient..

Postponing may not significantly reduce the risk unless surgery is delayed at least 4 weeks. It is quite possible that the child may have another URI at that point, and thus many practitioners will agree to proceed under these less-than-ideal circumstances.

Use of the ETT is associated with the highest risk (particularly in younger children) and is best avoided to minimize stimulation of the airway. Whether the airway device (LMA or ETT) is removed deep or awake does not appear to make a significant difference.

Pretreatment with albuterol has not been extensively studied, and it is unclear whether it is beneficial.

ADDITIONAL READINGS

Tait AR, Voepel-Lewis T, Burke C, et al. Risk factors for perioperative adverse respiratory events in children with upper respiratory tract infections. *Anesthesiology*. 2001;95:299–306.

29. ANSWER: C

The differential diagnosis for pediatric respiratory distress includes croup, acute epiglottitis, foreign body aspiration, subglottic stenosis, bacterial tracheitis, retropharyngeal abscess, obstructive laryngeal papillomatosis, and asthma exacerbation, among others. History, physical exam, and chest x-ray will aid the diagnosis.

Croup is most commonly due to a viral infection causing laryngotracheobronchitis and subglottic edema. It has a gradual onset, usually following an upper respiratory

infection (URI), and presents with low-grade fever, stridor, barking cough, and hoarseness. **A steeple sign may be seen on chest x-ray (narrowing of the subglottic air shadow).** Symptoms are generally self-limiting, and conservative measures such as breathing humidified oxygen are most often sufficient. Racemic epinephrine and corticosteroids may be considered.

Acute epiglottitis, by contrast, is much less common but potentially fatal if left alone. The causative organism is typically ***Haemophilus influenzae*** **type B,** to which there is now widespread vaccination. **Onset is abrupt,** with high fevers, severe sore throat, dysphagia, and **drooling** (because of pain on swallowing) in a toxic-appearing child. Because the edema is supraglottic, the usual presentation is of a child sitting up, leaning forward with the mouth open and tongue protruding so as to improve airflow. On a lateral neck x-ray, a "thumb sign" is commonly found secondary to the swelling of the epiglottis. The child must have the airway secured in a controlled environment (i.e., OR), and no attempt should be made to examine the pharynx or larynx without airway resuscitation equipment immediately available should obstruction develop.

ADDITIONAL READINGS

Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children.* 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

30. ANSWER: B

The indications for infective endocarditis (IE) prophylaxis have become more restricted in the most recent guidelines, as the risks of routine antibiotic administration outweigh the risk of developing IE in many situations.

The following cardiac conditions associated with an increased risk of adverse outcome from endocarditis warrant prophylaxis:

- Prosthetic cardiac valve
- Previous IE
- Congenital heart disease (CHD)
- Unrepaired cyanotic CHD, including palliative shunts and conduits
- Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure
- Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
- Cardiac transplantation recipients who develop cardiac valvulopathy

ADDITIONAL READINGS

Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis, guidelines from the AHA. *Circulation*. 2007;116:1736–1754.

31. ANSWER: B

Cerebral palsy (CP) describes a heterogeneous group of nonprogressive motor impairment syndromes caused by a cerebral insult in the immature brain. Three broad categories exist: spastic (70%), dyskinetic (10%), and ataxic (10%). Affected children are often cognitively impaired, with communication and behavior difficulties, and may have visual or hearing loss. Seizure disorders, as well as gastrointestinal (e.g., gastroesophageal reflux disease), respiratory, and urinary tract disorders, frequently coexist. These patients often require orthopedic surgery to release contractures that develop at major joints.

Patients with CP are particularly susceptible to intraoperative hypothermia due to hypothalamic dysfunction and disordered temperature regulation as well as reduced muscle bulk. Anesthetic requirements are lower than in healthy children. Succinylcholine does not cause hyperkalemia because the muscles were never denervated. Coagulopathy is not typically present, and in fact epidural analgesia is an excellent technique since postoperative pain assessment may be challenging.

ADDITIONAL READINGS

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Wongprasartsuk P, Stevens J. Cerebral palsy and anaesthesia. *Paediatr Anaesth*. 2002;12:296–303.

32. ANSWER: C

Patients with ***myelomeningocele*** have a primary failure of neural tube closure. Maternal folic acid supplementation has significantly reduced the incidence of neural tube defects. The majority of defects occur in the lumbosacral area and may cause neurologic injury below the defect (bowel, bladder, neuromuscular dysfunction). The Arnold-Chiari malformation (downward displacement of the cerebellar tonsils and medulla through the foramen magnum) is identified in most infants with this lesion, creating the potential for hydrocephalus and elevated intracranial pressure. Placement of a ventriculoperitoneal shunt is generally performed in a separate surgery.

Surgery is conducted in the first 24 hours of life to minimize the risk of infection and further neurologic

compromise. **Because many of these patients develop a neuropathic bladder and require self-catheterization, it is prudent to avoid latex products to minimize the risk for development of a latex allergy.**

There is no association with congenital heart disease.

ADDITIONAL READINGS

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Stoelting RK, Miller RD, eds. *Basics of Anesthesia*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2007.

33. ANSWER: A

Bleeding following tonsillectomy may occur within a few hours of surgery or at 7 to 10 days postoperatively. Early signs of blood loss include pallor, slow capillary refill, and tachycardia. Late signs, suggestive of significant blood loss, include restlessness, confusion, and hypotension. Resuscitation with crystalloid, colloid, or blood is crucial prior to induction of anesthesia, as cardiovascular collapse may occur after induction in a hypovolemic patient. **Rapid-sequence induction is most often utilized as these patients are at high risk for aspiration.** There is likely to be a large quantity of swallowed blood in the stomach, which is highly emetogenic. Avoidance of positive-pressure facemask ventilation is ideal. Two Yankauer suction devices should be immediately available as well as a variety of laryngoscopes and endotracheal tubes, in anticipation of a potentially difficult laryngoscopy. The patient should have the stomach emptied prior to conclusion and be fully awakened before extubation.

An awake fiberoptic intubation would be a poor choice because the patient is already uncooperative, the view will likely be obscured with blood, and there is an urgency to secure the airway so that bleeding may be controlled surgically.

ADDITIONAL READINGS

Bingham R, Lloyd-Thomas AR, Sury MRJ, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. New York, NY: Oxford University Press; 2008.

34. ANSWER: E

Sickle cell disease is the result of homozygous expression of the SS gene. Hemoglobin S (HbS) has a decreased affinity for O_2 and polymerizes under conditions that promote deoxygenation (hypoxia, acidosis, hyperthermia) or poor perfusion (dehydration, hypothermia), deforming red blood cells and compromising microcirculation causing organ infarction. Bone, spleen, kidney, brain, and lung may be affected by this process and there is a high risk of postoperative complications. In particular, postoperative pain may be worse than in patients without the disease.

Preoperative blood transfusion is controversial but often utilized to correct anemia, dilute HbS red cells, compensate for blood loss, and prevent complications such as stroke. It has been shown that simple transfusion (to a target Hb of 10 g/dL) is as effective as aggressive exchange transfusion used to lower the fraction of HbS.

Dehydration and high altitudes can worsen cell sickling.

ADDITIONAL READINGS

Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

Firth PG, Head CA. Sickle cell disease and anesthesia. *Anesthesiology*. 2004;101:766–785.

35. ANSWER: B

There are two ways to make this calculation. Both require knowledge of the patient's estimated blood volume. For term neonates, 90 cc/kg is appropriate, and therefore the blood volume is 360 mL. One can make use of the ***estimated allowable blood loss equation***:

$$EABL = EBV \frac{(Hct_i - Hct_f)}{Hct_{avg}}$$

Alternatively, one can estimate that 75 mL is slightly more than 20% of the EBV. Hence the hematocrit would be reduced by 20%—that is, 38% − 7.6% = 30.4%.

36. ANSWER: E

Neonatal resuscitation guidelines outline the methodology for assessment and initial resuscitation of newborns. Ideally, neonatal resuscitation should be anticipated and planned for, with expert help immediately available. If any of the following are present resuscitation steps should commence immediately after delivery: preterm delivery, meconium-stained amniotic fluid, poor respiratory effort, weak muscle tone. **The first step is to provide warmth, clear the airway (position and suction), and dry and stimulate the baby while continuously assessing respiratory effort, color, and heart rate.** If the baby is pink and breathing with a heart rate above 100, only observation is necessary. **In the absence of adequate respirations**

or a heart rate above 100, positive-pressure ventilation is the most important next step. The primary measure of adequate initial ventilation is prompt improvement in heart rate. **If after 30 seconds of positive-pressure ventilation the heart rate is less than 60, chest compressions should be initiated** at a ratio of 3:1, with 90 compressions and 30 breaths occurring in 1 minute using a two-thumb/encircling-hands technique.

Endotracheal intubation is indicated if tracheal suctioning for meconium is required (i.e., a depressed [not vigorous] baby with meconium aspiration), if bag-mask ventilation is ineffective, when chest compressions are performed, when endotracheal administration of medications is desired, or in special circumstances such as congenital diaphragmatic hernia or low birth weight.

Drugs are rarely indicated in resuscitation, but both epinephrine and volume expansion should be considered if compressions and ventilation fail.

After 10 minutes of continuous and adequate resuscitative efforts, discontinuation of resuscitation may be justified if there are no signs of life.

ADDITIONAL READINGS

American Heart Association. Guidelines 2005 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, Part 7: Neonatal Resuscitation. *Circulation*. 2005:112:IV-188-IV-195.

37. ANSWER: C

GFR is low at birth but increases rapidly in the first few months of life. It reaches normal adult-indexed values by 2 years of age.

Oxygen consumption is twice that of an adult. MAC for sevoflurane is at a maximum between 1 and 6 months and then decreases with age. Blood volume is highest in preterm infants, than decreases with age (see Question 18). Total body water is 75% of total body weight in infants compared to 50% to 60% in adults. Also, the ratio of extracellular fluid (ECF) to intracellular fluid (ICF) is 1:1 in infants, compared with 1:2 in adults. The adult distribution of body water is reached by age 10.

38. ANSWER: C

Infants are at greater risk for ***perioperative hypothermia***. They have a higher body surface area (skin) to mass ratio but less subcutaneous fat to provide tissue insulation. The most significant mechanism for heat loss is radiation, which is affected by both body surface area and the temperature difference between skin and environment. Evaporative heat losses are also greater as a result of decreased keratin in the skin.

The ability to regulate temperature (thermoregulatory response) is much more limited than in adults and easily overwhelmed by environmental factors. The thermoneutral temperature is the ambient temperature at which oxygen demand (and heat production) is minimal. That temperature is 28 degrees C for an unclothed adult but 32 degrees C for a neonate and 34 degrees C for a preterm infant. Oxygen consumption correlates most closely with the skin to environment temperature gradient. The ability to generate heat is reduced, although the primary mechanism, nonshivering thermogenesis, from the metabolism of brown fat, is much more significant in infants than in adults.

ADDITIONAL READINGS

Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

39. ANSWER: E

Retinopathy of prematurity occurs only in premature infants, and the severity of disease is inversely proportional to birth weight and gestational age. Supplemental oxygen has been implicated as one iatrogenic factor that can increase the likelihood of disease occurrence or progression. Both hyperoxia itself and fluctuations in oxygen saturation appear to be causative. Other factors include mechanical ventilation, TPN, and blood transfusion. It has been demonstrated that targeting an SpO_2 of 80% to 90% decreases the incidence of severe retinopathy in premature infants. The risk decreases after 44 weeks postconceptual age.

ADDITIONAL READINGS

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40. ANSWER: C

Cleft lip, with or without a ***cleft palate***, is more common than an isolated cleft palate. The incidence is highest in the Asian community. Velopharyngeal incompetence (failure of the soft palate to seal the nasopharynx, allowing air to escape into the nose) and poor tongue articulation lead to speech problems. Ideally, repair should occur before 12 months so that speech develops normally. Many countries do not have the resources or access for early surgical repair, and so these patients may suffer from ridicule, bullying, and social exclusion at school.

Coexisting congenital anomalies and syndromes are common in patients with isolated cleft palate. The most frequently associated syndrome is the **velocardiofacial**

syndrome (VCFS), in which cardiac anomalies occur in conjunction with airway malformations (laryngomalacia, laryngeal web, vascular ring) and developmental delay. Preoperative assessment must include identification of cardiac abnormalities (to the extent resources exist).

Other syndromes predispose the patient to difficult intubation and airway obstruction in infancy. Cleft syndromes associated with micrognathia include Pierre Robin, Treacher Collins, Stickler, and Nager syndromes. Significant pharyngeal airway obstruction is a relative contraindication to surgery because it will be exacerbated by palatal closure. Obstruction in these cases generally improves with age.

Infiltration with local anesthesia is ineffective for postoperative analgesia due to the rich nerve supply of the palate. Opioids are generally required but need to be used carefully to avoid postoperative airway obstruction, which is more likely in patients with preexisting airway obstruction.

ADDITIONAL READINGS

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41. ANSWER: B

The pulmonary vasculature of the neonate is more muscularized than in older children and therefore more sensitive to hypoxia, hypercapnia, acidosis, and other noxious stimuli known to increase PVR. In the setting of birth asphyxia, pneumonia, meconium aspiration, or sepsis, the normal transition from fetal to adult circulation (which depends on a reduction in PVR) may be impaired, leading to a persistent fetal circulation. In a neonate with ***persistent pulmonary hypertension***, there is elevated pulmonary arterial pressure and elevated right atrial pressure, and therefore deoxygenated blood shunts right to left through the PDA, which further exacerbates the problem. Metabolic acidosis ensues and myocardial contractility is impaired.

Differential cyanosis refers to cyanosis of the lower but not upper body due to shunt reversal (i.e., right to left) through a PDA. Reverse differential cyanosis is the opposite: cyanosis of the upper but not lower body. This is much less common but can occur in the setting of congenital heart disease, most often D-transposition of the great arteries (LV connects to PA so oxygenated blood shunts left to right across the PDA).

42. ANSWER: A

Children with ***Down syndrome*** are at higher risk during general anesthesia. Multiple organ systems may be involved. Airway concerns relate to the relatively large and protuberant tongue, which predisposes to obstruction. In addition, the larynx and cricoid cartilage are relatively small (subglottic stenosis) and may necessitate the use of a smaller endotracheal tube. **Atlanto-axial instability occurs in 12% to 32% of cases and should be suspected in a symptomatic patient** (abnormal gait, clumsiness, fatigue with ambulation, complaints of numbness or weakness in an extremity) who is at risk for dislocation during extension. Cardiac defects are common (40% to 50%) and include AV septal defects (also known as endocardial cushion defects), ventricular septal defect (VSD), tetralogy of Fallot, and patent ductus arteriosus (PDA). Bradycardia during inhalational induction with sevoflurane is more common in these patients. Renal anomalies are unusual.

43. ANSWER: D

The ***caudal epidural block*** is the most commonly performed regional block in children. In conjunction with general anesthesia, caudal blocks decrease postoperative opioid requirements and blunt the endocrine stress response to surgery. They are relatively simple to perform and have wide applicability to many pediatric surgical procedures. The sacral hiatus is identified by palpation of the sacral cornua or by drawing an equilateral triangle on the skin with the base connecting the two posterior superior iliac spines and the apex identifying the hiatus. **Puncture of the sacrococcygeal ligament signifies entry of the catheter or needle tip into the epidural space.** The risk of dural puncture is highest in young infants, where the dural sac terminates at the S3–4 level. By age 1, however, the dural sac terminates at the S1–2 level as in adults.

Hypotension is much less likely in children following neuraxial block than in adults. This may be due in part to the low SVR at baseline in this population. Fluid loading is usually unnecessary. Test dosing with epinephrine is controversial, but many studies have demonstrated that in the absence of pretreatment with atropine, test dosing is not a sensitive detection method for intravascular injection. The cephalad extent of the block depends primarily on the volume of local anesthetic. The Armitage formula is simple to remember and reliable: 0.5 cc/kg is sufficient to cover the lumbar-sacral dermatomes, while 1 cc/kg is necessary for thoracic and upper lumbar regions.

ADDITIONAL READINGS

Pullerits J, Holzman RS. Pediatric neuraxial blockade. *J Clin Anesth*. 1993;5:342–354.

44. ANSWER: E

While unavailable in the United States as an injected local anesthetic, prilocaine together with lidocaine make

up EMLA cream (eutectic mixture of local anesthetics), which is frequently used in children for skin topicalization. **Hepatic metabolism of prilocaine yields o-toluidine, which can produce methemoglobinemia.** Neonates are particularly susceptible due to decreased activity of methemoglobin reductase. It is contraindicated in children with congenital methemoglobinemia.

ADDITIONAL READINGS

Coté C, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

45. ANSWER: C

Anterior mediastinal masses may be lymphoma (lymphoblastic lymphoma or Hodgkin disease), teratomas, thymoma, or thyroid/parathyroid tumors. Symptoms such as dyspnea or superior vena cava syndrome suggest airway and vascular compression, respectively. Tissue diagnosis is critical for prompt treatment. In such cases, biopsy under local anesthesia is probably safest. However, if general anesthesia is required, maintenance of spontaneous ventilation with an inhalation induction is crucial. Keeping the child in a partial or even full right lateral decubitus position may help maintain airway patency and reduce compression. Intubation should be undertaken without muscle relaxants under deep anesthesia. If airway or vascular compression occurs, the patient should be rapidly turned on her side or prone. Rigid bronchoscopy and even cardiopulmonary bypass may be needed in severe circumstances. Rapid sequence induction should be avoided, as maintenance of spontaneous ventilation is preferred.

46. ANSWER: D

The FRC of a neonate is nearly identical on a mL/kg basis (30 mL/kg) to that of an adult, but the mechanical factors on which it is based differ considerably. In adults FRC is the passive volume at which chest wall recoil is equal and opposite to lung elastic recoil. In neonates and infants, the chest wall compliance is so high (i.e., elastic recoil of the chest is low) that if a recoil equilibrium were reached it would be 10% of TLC instead of the observed value of 40%. **In infants, FRC is dynamically rather than passively maintained by a cessation of exhalation at a lung volume in excess of its relaxation volume (laryngeal braking).** Closing capacity is greater in an infant on a mL/kg basis than in a young adult. It declines during childhood and adolescence and increases thereafter throughout adult life. FRC may be less than closing capacity in young infants, predisposing to small airway collapse and air trapping. FRC is the sum of residual volume and expiratory reserve volume.

ADDITIONAL READINGS

Coté CH, Todres ID, Lerman J, eds. *A Practice of Anesthesia for Infants and Children*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2009.

47. ANSWER: B

Myasthenia gravis is an autoimmune disorder of neuromuscular transmission. Antibodies against the acetylcholine receptor at the neuromuscular junction result in a reduction of the number of the functional receptors, with a decreased safety margin of neuromuscular transmission. Major symptoms are muscle weakness and fatigability, relieved by rest. Anticholinesterase treatment provides symptomatic improvement in most patients. **A resistance (decreased potency) is observed with the use of depolarizing muscle relaxants because the number of available receptors at the endplate is reduced.** High doses of succinylcholine may be required for rapid-sequence tracheal intubation, but phase II block is frequent even after a single dose. The sensitivity to and the duration of action of nondepolarizing muscle relaxants are increased, reducing the intraoperative requirements. The need for anticholinesterase drugs is decreased in the first 48 postoperative hours. These drugs must be restarted carefully and titrated to avoid the risk of cholinergic crisis.

Lambert-Eaton myasthenic syndrome is characterized by a proximal fatigability, relieved by exercise. It can occur as a solitary lesion but in 50% of cases is associated with small-cell lung cancer. The production of anti-calcium voltage-dependent channel antibodies implies a presynaptic neuromuscular blockade with abnormal acetylcholine release. **The response to succinylcholine appears to be normal or moderately increased. The sensitivity to nondepolarizing muscle relaxants is increased.** Reversal agents have a poor response or no effect.

Myotonic dystrophy designates a group of hereditary degenerative diseases of skeletal muscles characterized by persistent contracture of skeletal muscles after their stimulation, resulting from abnormal calcium metabolism. As in Duchenne muscular dystrophy, succinylcholine is formally contraindicated because of the risk of lethal hyperkalemia. A myotonic crisis can be triggered by succinylcholine, hypothermia, surgical manipulations, electrocautery, or certain drugs such as clofibrate, propranolol, neostigmine, or potassium. The use of nondepolarizing muscle relaxants, if clinically needed, requires monitoring the neuromuscular blockade. Reversal agents can precipitate skeletal muscle contraction by facilitating depolarization of the endplate.

Table 5.5 RESPONSE TO DEPOLARIZING MUSCLE RELAXANTS, NONDEPOLARIZING MUSCLE RELAXANTS, AND ANTICHOLINESTERASES IN THE SETTING OF MUSCLE DISORDERS

DISEASE	RESPONSE TO SUCCHINYLCHOLINE	RESPONSE TO NONDEPOLARIZING NEUROMUSCULAR BLOCKADE	RESPONSE TO ANTICHOLINESTERASES
Myasthenia gravis	Resistance, unpredictable response; may result in phase II block, but not contraindicated	Increased sensitivity	May cause weakness
Lambert-Eaton myasthenic syndrome	Normal or increased sensitivity	Increased sensitivity	Poor response
Myotonic dystrophy	Contraindicated (causes exacerbation of disease)	Careful use of nondepolarizing muscle relaxants (if required)	May cause myoclonus
Duchenne muscle dystrophy	Contraindicated (rhabdomylosis, hyperkalemia, cardiac arrest)	Increased sensitivity	Normal response

Duchenne muscular dystrophy is the most common childhood muscular dystrophy (3 per 10,000 births). The disease is caused by an X-linked recessive gene and is often undiagnosed until the age of 3 to 5 years. The initial symptoms involve the proximal muscle groups of the pelvis. Kyphoscoliosis may develop and skeletal muscle atrophy predisposes to long-bone fractures. Elevated plasma creatinine kinase concentrations result from muscle fiber necrosis. Pulmonary complications and congestive heart failure are the main causes of death, which occurs between the ages of 15 and 25 years. Succinylcholine is formally contraindicated because of the risk of rhabdomyolysis and lethal hyperkalemia. Sensitivity to nondepolarizing muscle relaxants is increased.

Multiple sclerosis is an idiopathic disease of suspected autoimmune cause in which the body's immune response attacks a person's central nervous system (brain and spinal cord), leading to demyelination. Succinylcholine should be avoided as it may cause hyperkalemia. The response to nondepolarizing muscle relaxants and reversal agents appears to be normal (Table 5.5).

ADDITIONAL READINGS

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6.

OBSTETRIC ANESTHESIA

Adrienne Kung, MD, and Philip Hess, MD

1. Uterine contractility tone is affected by anesthetic agents and techniques in all of the following ways EXCEPT

A. Uterine tone is not affected by muscle relaxants.
B. Volatile inhalation agents have a dose-dependent relaxant effect.
C. Uterine tone is reduced by epidural local anesthetic sympathetic blockade, which is why labor is longer with epidural analgesia.
D. Opioids do not have any effect on uterine contractions.
E. Nitrous oxide has minimal effect on uterine contractions and tone.

2. Common clinical events that affect uterine blood flow in the term parturient during labor and delivery include all of the following EXCEPT

A. Uterine blood flow is decreased in most parturients when supine due to aortocaval compression.
B. Uterine blood flow can be increased in about 15% of parturients when supine due to the uterine arteries taking off above the level of compression of the aorta.
C. Uterine blood flow decreases when maternal systolic blood pressure drops below 80 mm Hg.
D. Effective epidural analgesia can increase uterine blood flow in the parturient with severe preeclampsia by up to 80%.
E. Maternal hypocapnia from hyperventilation causes uterine artery vasoconstriction, resulting in decreased blood flow.

3. A 26-year-old G1P0 parturient at term delivers a 3,500-g boy vaginally. After 30 minutes the obstetrician grows concerned that the placenta has not yet delivered. The patient is transferred to an operating room and positioned for manual extraction of the placenta. After the placenta is removed, the obstetrician notices brisk uterine bleeding. All of the following medications would be contraindicated in the specific condition identified EXCEPT

A. Methylergonovine, 200 micrograms IM: Severe preeclampsia
B. Carboprost (15-methyl-PGF2α), 250 micrograms IM: History of severe asthma
C. Oxytocin, 10 units IV: Uncorrected maternal hypovolemia
D. Misoprostol, 1,000 micrograms: Maternal fever
E. All of the above are appropriate contraindications.

4. A 20-year-old G1P0 parturient at 32 weeks gestation with no medical problems was in a high-speed motor vehicle accident. She was wearing a seatbelt and has only abrasions on her face and chest. On arrival to the emergency department she is awake and alert. Maternal vital signs are BP 100/60, HR 120, RR 20. Fetal heart rate evaluation shows a persistent fetal bradycardia in the 70-bpm range. A large-bore IV is placed and the patient is taken to the operating room. The most appropriate anesthetic choice would be

A. Etomidate 0.2 mg/kg, succinylcholine 1.5 mg/kg, both IV
B. Propofol 2 to 3 mg/kg, succinylcholine 1.5 mg/kg, both IV
C. Spinal injection of bupivacaine, 12 mg, and fentanyl, 25 mcg
D. Spinal injection of bupivacaine, 12 mg, without fentanyl
E. Inhalational mask induction with preserved spontaneous ventilation until anesthetized to avoid emergent tracheal intubation in a trauma patient

5. A 32-year-old G3P2 parturient with no medical comorbidities with a 29-week twin gestation presents with regular contractions. She is stable and in no apparent distress. On exam she is noted to have a closed cervix. The obstetrician decides to administer terbutaline to stop contractions. Side effects of this therapeutic regimen might include all of the following EXCEPT

A. Maternal supraventricular tachycardia
B. Maternal hyperglycemia
C. Maternal pulmonary edema
D. Maternal hyperkalemia
E. Fetal tachycardia

6. An 18-year-old G1P0 parturient with a history of systemic lupus was diagnosed with mild preeclampsia at 27 weeks gestation. She remained stable on weekly evaluations. Now, at 32 weeks gestation, she experienced the start of contractions in the middle of the night. After evaluation, the obstetrician decides to initiate tocolysis with a 4-g bolus of magnesium sulfate, followed by an infusion of 2 g/hr. The following morning the patient is lethargic and has an oxygen saturation of 85%. In addition to oxygen by facemask and discontinuing the magnesium infusion, appropriate initial therapy would include

A. Ordering an echocardiogram to rule out peripartum cardiomyopathy
B. Furosemide, 40 mg IV
C. Evaluation for evidence of myocardial ischemia, including EKG and serum troponin levels
D. Sublingual nitroglycerin tablets, until an infusion of nitroglycerin can be initiated
E. Calcium gluconate, 500 mg IV

7. Risk factors for postpartum hemorrhage include all of the following EXCEPT

A. The relative dilution of clotting factors due to plasma volume expansion during gestation
B. Previous postpartum hemorrhage
C. Protracted prolonged labor
D. Retained products of conception
E. Multiple previous uterine surgeries

8. The chronological order of the stages of labor is as follows:

A. Latent phase, transition, active phase, second stage, fetal descent, neonatal delivery, third stage, placental delivery
B. First stage, latent phase, active phase, second stage, transition, fetal descent, neonatal delivery, third stage, placental delivery
C. Latent phase, transition, active phase, second stage, neonatal delivery, third stage, placental delivery
D. Latent phase, active phase, transition, fetal descent, second stage, neonatal delivery, third stage, placental delivery
E. None of the above

9. Considerations in the management of the parturient with retained placenta after a vaginal delivery include all of the following EXCEPT

A. Anesthesia can be provided by epidural medications.
B. Blood products may be required and should be requested early if bleeding appears significant.
C. Retained placenta is always an emergency that requires neuraxial or general anesthesia as quickly and safely as possible.
D. If significant blood loss has occurred and has not been corrected, epidural local anesthetics are contraindicated.
E. Intravenous nitroglycerin, 50 to 100 micrograms, can be used to relax the cervical os if it has contracted after delivery of the neonate.

10. A 23-year-old G1P0 with no major medical comorbidities presents with severe preeclampsia at 34 weeks gestation. On admission her blood pressure is 165/95 mm Hg and reflexes are hyperactive with clonus. She is started on magnesium for seizure prophylaxis, which results in normalization of reflexes and reduction of blood pressure. Within 30 minutes, a persistent fetal bradycardia is identified and a stat cesarean delivery is called.. The patient undergoes general anesthesia with propofol, 2 mg/kg; succinylcholine, 1.5 mg/kg; and endotracheal intubation. At the end of surgery, the patient has not had a return of twitches. The most likely cause for prolonged muscle paralysis is

A. The patient has true cholinesterase deficiency.
B. Pregnancy induces production of atypical pseudocholinesterase.
C. Prolongation of neuromuscular blockade is due to the aminoglycoside antibiotic (gentamicin) she received for prophylaxis of group B streptococcus.
D. The prolongation of neuromuscular blockade is due to the magnesium sulfate she received for seizure prophylaxis.
E. The dilution of serum proteins in pregnancy means that the dose of succinylcholine must be reduced.

11. Several issues must be assessed prior to placing neuraxial anesthesia or analgesia in a patient with

severe preeclampsia. All of the following are correct EXCEPT

A. The sympathectomy from neuraxial labor analgesia results in decreased uteroplacental blood flow, which always compromises the fetus.
B. Severe preeclampsia is associated with thrombocytopenia.
C. Severe preeclampsia is associated with the development of coagulopathy.
D. Patients with preeclampsia are at risk for placental abruption.
E. Spinal anesthesia results in an incidence and degree of hypotension less than that in women who do not have preeclampsia.

12. A 24-year-old G3P2 with no medical history presents in normal labor with a vertex fetus at term. She started having painful contractions after breakfast but waited 6 hours before coming to the hospital. All of the following statements about her NPO status and the risk of aspiration are correct EXCEPT

A. She would be at risk for aspiration of gastric contents if general anesthesia were required.
B. She has remained NPO for greater than 6 hours after her last meal; therefore, her stomach is empty and she is not at increased risk of gastric aspiration.
C. The risk of gastric aspiration is increased in the parturient regardless of NPO status.
D. Rapid-sequence induction with cricoid pressure would be appropriate if this patient required general anesthesia.
E. Gastric aspiration can occur at both induction and emergence of anesthesia.

13. Preeclampsia is most often associated with all of the following physiologic characteristics EXCEPT

A. Decreased uteroplacental blood flow
B. Increased systemic vascular resistance
C. Hyperdynamic cardiac function
D. Increased central venous and pulmonary artery wedge pressures
E. Increased systemic blood pressure

14. Which of the following end-organ dysfunction would be UNEXPECTED in a patient with severe preeclampsia?

A. Splenomegaly
B. Hepatic subcapsular hematoma
C. Proteinuria
D. Subarachnoid hemorrhage
E. Pulmonary edema

15. Normal pulmonary function in the term parturient can be described most accurately by which one of the following statements?

A. Minute ventilation is decreased due to the decreased excursion of the diaphragm from the impingement of the gravid uterus.
B. Minute ventilation is similar to the normal, nonpregnant levels due to an increase in respiratory rate.
C. There is evidence of a moderate to severe restrictive physiology as evidenced by flow-volume loop analysis and the ratio of forced expiratory volume in 1 second to forced vital capacity (FEV_1:FVC).
D. The increased minute ventilation results in decreased maternal arterial carbon dioxide concentration ($PaCO_2$).
E. Due to the impingement of the gravid uterus on the diaphragm, the term parturient is nearly 100% dependent on intercostal and accessory muscles for ventilation.

16. Which of the following medications does NOT significantly cross the placenta to accumulate in the fetal circulation?

A. Etomidate
B. FentanylC. Esmolol
D. Succinylcholine
E. Lidocaine

17. Medications that produce neuromuscular blockade when administered to the parturient do not result in clinically significant paralysis of the fetus because

A. The placental barrier reduces the serum concentration of these medications to only 10% to 20% of the maternal serum concentration.
B. The fetal muscles are resistant to all neuromuscular blocking medications because the neuromuscular endplate of striated muscle is immature.
C. The rapid metabolism of these medications in the fetal liver results in very low serum concentrations in the fetus.
D. Succinylcholine does not cross the placenta, but the steroid-based nondepolarizing medications (vecuronium, pancuronium, etc.) do cross and result in clinically significant weakness.
E. None of the above is correct.

18. The factors that determine uteroplacental transfer of medications include all of the following EXCEPT

A. The ionic charge of the molecule
B. The size of the uteroplacental surface area
C. The concentration difference between the mother and the fetus

D. The maternal blood pressure
E. The size of the molecule

19. Normal maternal physiologic changes at term can be most correctly described as

A. A decrease in minute ventilation due to reduction of pulmonary functional residual capacity from the gravid uterus
B. An increase in systemic vascular resistance in response to an increase in cardiac output
C. Peripheral edema resulting from an systolic ventricular dysfunction with a concomitant increase in central venous pressure and pulmonary capillary wedge pressure
D. A decrease in serum hemoglobin concentration despite increased red cell production
E. None of the above is correct.

20. Potential complications of the long-term use of nonsteroidal anti-inflammatory medications in the pregnant woman include all of the following EXCEPT

A. Fetal oligohydramnios
B. Premature in utero closure of the ductus arteriosus
C. Maternal peptic ulcers
D. Gestational hypertension
E. Maternal renal dysfunction

21. The normal changes that support the fetal transition to neonatal physiology include all of the following EXCEPT

A. Expansion of the collapsed lungs with air
B. Closure of the foramen ovale
C. Decreased pulmonary vascular resistance
D. Increased systemic vascular resistance
E. Patent ductus arteriosus

22. A healthy mother delivers a term fetus via uncomplicated normal vaginal delivery. At birth, the neonate is flaccid, cyanotic, and not responsive. After delivery to the warming table, the most appropriate initial step in resuscitation is

A. Immediate laryngoscopy and endotracheal intubation
B. Umbilical vein catheterization and administration of epinephrine
C. Intraosseous administration of isotonic crystalloid
D. Vigorous stimulation by drying the neonate with towels followed by assessment of its status
E. Oropharyngeal suction and mask ventilation with 100% oxygen followed by chest compressions when a second person is available

23. A term healthy parturient in active labor with lumbar epidural analgesia has recurrent decelerations. The obstetrician determines that the fetal heart rate pattern warrants conservative management at this time, but mentions his concern that a cesarean delivery may be required if the pattern does not improve. The most appropriate action by the anesthesia provider is to

A. Assess the effectiveness of the epidural catheter, including quality of analgesia and dermatomal sensory blockade
B. Administer ephedrine to improve uterine artery blood flow
C. Remove the epidural catheter and convert to intramuscular analgesia with opioids
D. Eliminate any opioid from the epidural solution to avoid fetal narcosis
E. Administer 3% chloroprocaine, 15 to 20 mL, in anticipation of the cesarean delivery

24. A full-term newborn boy delivered vaginally is limp and cyanotic; he has a heart rate of 80, gasping respirations, and no response to suctioning. His Apgar score at 1 minute of life would be

A. 1
B. 2
C. 3
D. 4
E. 5

25. Magnesium sulfate affects neuromuscular blockade and the neuromuscular junction in all of the following ways EXCEPT

A. Inhibits the release of acetylcholine at the neuromuscular junction
B. Decreases the sensitivity of the neuromuscular junction to acetylcholine
C. Depresses the excitability of the muscle fiber membrane
D. Increases the potency and duration of vecuronium, rocuronium, and mivacurium
E. Increases the duration of a single intubating dose of succinylcholine

26. All of the following statements concerning lung volume changes in pregnancy are true EXCEPT

A. Functional residual capacity (FRC) begins to fall at the fifth month of pregnancy and is decreased to 80% of that of prepregnancy capacity by term.
B. Vital capacity is significantly decreased by term pregnancy.

C. A 25% reduction in expiratory reserve volume and a 15% reduction in residual volume account for the change in FRC.
D. Inspiratory capacity increases by 15% during the third trimester because of the increases in tidal volume and inspiratory reserve volume.
E. The decrease in FRC is due to elevation of the diaphragm caused by the enlarging uterus.

27. A 38-year-old G3P2 parturient with a history of cocaine abuse presents at 38 weeks gestation. The patient had bleeding in early pregnancy and elevated blood pressures at 28 weeks gestation. On admission she has vaginal bleeding and continuous abdominal pain even between contractions. Her cervix is dilated to 1 cm. The potential complications associated with this parturient's underlying physiology include all of the following EXCEPT

A. Hemorrhagic shock
B. Disseminated intravascular coagulation (DIC)
C. Intrauterine growth retardation
D. Placenta accreta
E. Acute renal failure

28. A 31-year-old G2P1 at 23 weeks gestation presents to the emergency department with acute appendicitis. All of the following statements about the anesthetic management of an open appendectomy in the parturient are true EXCEPT

A. The parturient should have uterine displacement in the operating room to prevent aortocaval compression.
B. Medications with anticholinesterase effects are contraindicated because they may increase uterine tone and precipitate preterm labor.
C. The decision to monitor the fetal heart rate continuously should be considered but is individualized depending on each case, the ease of monitoring, and the site of surgery.
D. Induction could include thiopental, fentanyl, and succinylcholine.
E. Pregnant women are at risk for acid aspiration after 18 to 20 weeks gestation; pharmacologic precautions may be warranted.

29. Which of the following drugs has a rapid transfer across the placenta primarily due to its lipophilic characteristics?

A. Heparin
B. Glycopyrrolate
C. Thiopental
D. Succinylcholine
E. Rocuronium

30. During the second stage of labor at 38 weeks gestation, fetal heart late decelerations are noted. Meconium-stained fluid is identified upon delivery. The newborn is breathing spontaneously, is vigorous, and has a heart rate of 130. The most appropriate management would be

A. Immediate intubation with endotracheal suctioning
B. Expectant management with empiric antibiotics
C. Steroids to treat pulmonary inflammation
D. Routine oral/nasal suctioning with expectant management
E. Endotracheal suctioning followed by radiographic films once suctioning is cleared

31. During the electronic fetal heart rate monitoring of a 34-week-gestational-age fetus, decelerations beginning 10 to 30 seconds after the beginning of uterine contractions and ending 10 to 30 seconds after the end of uterine contractions are noted. Possible causes for this include all of the following EXCEPT

A. Aortocaval compression
B. Maternal hypotension
C. Excessive uterine tone
D. Fetal hypoxemia
E. Intermittent umbilical cord compression

32. A term neonate is born by an emergency cesarean section performed for fetal bradycardia. At birth, a double nuchal cord is noted and the neonate has no spontaneous respirations. Following warming and nasopharyngeal suctioning, the neonate remains apneic with a heart rate of 80. Positive-pressure ventilation is then provided for 30 seconds, with no improvement in the oxygenation, heart rate, or spontaneous activity. The most appropriate next step would be

A. Chest compressions at a rate of 90 compressions/minute
B. Epinephrine 0.01 mg/kg through an umbilical venous line
C. 100 mL of isotonic crystalloid solution through an umbilical venous line
D. Observational care with blow-by oxygen
E. Gentle endotracheal intubation with positive-pressure ventilation

33. All of the following statements regarding fetal hemoglobin as compared with adult hemoglobin are true EXCEPT

A. Hemoglobin F has a greater oxygen affinity than adult hemoglobin.
B. The P_{50} of fetal blood is approximately 27 mm Hg.

C. In fetal blood, hemoglobin F is approximately 75% to 84% of total hemoglobin.
D. The shift in fetal blood oxygen affinity can be explained by a decreased interaction between hemoglobin F and 2,3-DPG.
E. Fetal hemoglobin can be detected for up to 3 months after birth.

34. All of the following statements are true concerning anesthesia for nonobstetric surgery in the parturient EXCEPT

A. Beginning at 18 to 20 weeks gestation, left uterine displacement should be used to prevent aortocaval compression.
B. Scientific evidence supports the avoidance of nitrous oxide during pregnancy, especially after the 6th week of pregnancy.
C. Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used until the second half of pregnancy, at which time they should be used with caution.
D. The second trimester is the optimal time to perform surgery because the risk of preterm labor is lowest during that time.
E. Most structural abnormalities resulting from exposure to teratogenic agents occur between day 31 and day 71 after the first day of the last menstrual period.

35. Risk factors for the development of preeclampsia in the parturient include all of the following EXCEPT

A. Diabetes mellitus
B. Vascular/connective tissue disease
C. Nulliparity
D. Obesity
E. Smoking

36. A 32-year-old G5P4 at 37 weeks presenting for a third repeat cesarean section is found on ultrasound to have placenta previa. The risk of placenta accreta in this patient is

A. Similar to that in the general obstetric population
B. Approximately 10%
C. Increased only if an endometrial strip is visible on ultrasound
D. Approximately 60%
E. At least 95%; all placenta previa is associated with accreta

37. A 36-year-old G3P2 is presenting for repeat cesarean section with a suspected placenta accreta. After a team discussion with the patient, it was agreed that if significant hemorrhage were to occur the obstetric team would perform a cesarean hysterectomy. All of the following statements regarding appropriate anesthetic management are true EXCEPT

A. Two large-gauge intravenous catheters and cross-matched packed red blood cells should be available.
B. The blood loss in an elective cesarean hysterectomy is comparable with an emergent cesarean hysterectomy.
C. Anesthetic options include continuous spinal anesthesia, combined spinal-epidural anesthesia, continuous epidural anesthesia, and general anesthesia.
D. In the event of conversion to general anesthesia from neuraxial anesthesia, the intravascular volume deficit may be underestimated and care should be taken in the selection and dosing of induction agents.
E. The choice of anesthetic technique has little influence on the degree of blood loss.

38. Pain during the first stage of labor

A. Results from the stimulation of visceral afferents that innervate the lower uterine segment and cervix and enter the spinal cord at L4 and L5 segments
B. Can lead to high concentrations of catecholamines. Labor analgesia reduces plasma concentrations of epinephrine and its associated effects on the myometrium.
C. Can be reliably treated by a pudendal block
D. Can be reliably treated by a paracervical block
E. Is necessary for the course of labor to proceed efficiently

39. During the course of an epidural placed for labor analgesia the parturient becomes agitated, is not able to speak, and loses consciousness. The patient is profoundly hypotensive. Possible causes for this clinical scenario include all of the following EXCEPT

A. Unrecognized placement of the catheter in the subarachnoid space
B. Overdose of local anesthetic in the epidural space
C. Migration of the epidural catheter into a epidural vein
D. Subdural injection of local anesthetic
E. Seizure from eclampsia

40. All of the following symptoms and signs may be associated with a postdural puncture headache EXCEPT

A. Tinnitus
B. Cerebral edema

C. Cranial nerve VI palsy
D. Seizures
E. Diplopia

41. Which of the following statements about the use of volatile anesthetics during general anesthesia for cesarean section is INCORRECT?

A. Volatile anesthetics reduce blood pressure, which may result in reduced uterine blood flow.
B. Volatile agents cross the placenta and equilibrate rapidly with fetal tissues.
C. High levels of volatile agents may build up in the neonatal fat and can redistribute to the neonatal circulation, causing a secondary depression of ventilation.
D. End-tidal level of halogenated agents greater than 1 to 1.5 times the minimum alveolar concentration may reduce the effect of oxytocin on uterine tone.
E. The minimum alveolar concentration in pregnancy is higher than in nonpregnant women.

42. Pregnant patients have a higher aspiration risk due to all of the following EXCEPT

A. The upward displacement of the stomach and esophagus results in a reduction of tone of the lower esophageal barrier.
B. Gastric emptying of liquid and solid materials is slowed during pregnancy.
C. Esophageal peristalsis is slowed during pregnancy.
D. Gastric emptying is slowed during labor.
E. Pregnancy is a risk factor for difficulty during intubation.

43. A 32-year-old G1 at 33 weeks gestation has a platelet count of 80,000/mm^3 at a routine doctor's visit, with no prior platelet counts as comparison. Her vital signs are within normal limits and she currently denies signs of easy bruising or bleeding of her gums while brushing her teeth. What is the likely diagnosis?

A. Idiopathic/autoimmune thrombocytopenic purpura (ITP/ATP)
B. Gestational thrombocytopenia
C. Preeclampsia
D. Thrombotic thrombocytopenic purpura
E. Disseminated intravascular coagulopathy

44. A 25-year-old G1 presents in labor. During the anesthesia consult, it is found that she has von Willebrand disease (vWD) type I. Labs drawn 2 days ago show a factor VIII level of 20%. She is in pain and is requesting an epidural. What is the most appropriate next step?

A. Initiate epidural placement because pregnancy is a hypercoagulable state and lessens the severity of vWD.
B. Offer a remifentanil IV PCA.
C. Offer a remifentanil IV PCA and initiate DDAVP infusion.
D. Offer a remifentanil IV PCA and initiate cryoprecipitate.
E. Offer a remifentanil IV PCA and initiate Humate-P.

45. Infants born to mothers with myasthenia gravis (MG)

A. Are unaffected, as maternal antibodies to the acetylcholine receptor are IgM antibodies and do not cross the placenta.
B. Are affected approximately 75% of the time.
C. May need to take immunosuppressant therapy for a minimum of 2 to 3 weeks.
D. May need to take anticholinesterase therapy for 2 to 3 weeks.
E. Are unaffected immediately after birth but become symptomatic after 4 to 6 weeks.

46. While sitting a parturient up in preparation to place an epidural for labor analgesia, you notice a skin dimple in the patient's lumbar area. Which of the following diagnoses would make you most comfortable to proceed with the epidural placement?

A. Meningocele
B. Spina bifida occulta
C. Occult spinal dysraphism
D. Myelomeningocele
E. Tethered cord syndrome

47. Which of the following choices correctly identifies the level at which the spinal cord and the dural sac end for adults and for children?

A. L1/S3—L3/S2
B. L3/S3—L1/S2
C. L1/L1—L3/L3
D. L1/S2—L3/S3
E. L3/L3—L1/L1

48. Which of the following statements about cardiovascular changes during pregnancy is INCORRECT?

A. Stroke volume increases by 20% to 50%.
B. Cardiac output increases by 30% to 50%.
C. Central venous pressure increases by 3 to 5 mm H_2O.
D. There is a 20% decrease of systemic vascular resistance.
E. There is a 30% decrease of pulmonary vascular resistance.

CHAPTER 6 ANSWERS

1. ANSWER: C

The uterus is composed of smooth muscle and as such does not have a neuromuscular endplate. Thus, neuromuscular blockers have no effect on myometrial contractility. On the other hand, many anesthetic agents have significant effects on uterine tone and contractility. The volatile agents have a dose-dependent relaxant effect on uterine muscle. In fact, high alveolar concentrations of volatile agents are used to maintain uterine quiescence during fetal surgery. Opioids and nitrous oxide have minimal effect on uterine contractility. While local anesthetics, in high concentrations or when injected directly to the myometrium, have mixed effects (both increased basal tone and decreased contractile force have been reported), clinically relevant serum concentrations have no effect. While the course of labor under the influence of labor epidural is somewhat controversial, local anesthetics used in low concentrations for labor analgesia certainly have no influence.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:128–130, 256.

Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:263.

2. ANSWER: B

Uterine blood flow increases progressively during pregnancy and reaches a mean value of 500 to 700 mL by term. Blood flow through the uterine vessels is high and has low resistance; this change in resistance occurs most dramatically after 20 weeks of gestation. Uterine blood flow lacks autoregulation (vessels are maximally dilated during pregnancy), and uterine artery flow is therefore dependent on maternal blood pressure and cardiac output. Consequently, factors that alter blood flow through the uterus will adversely affect the fetal blood supply. Uterine blood flow is determined by the following relationship:

Uterine blood flow = (Uterine artery pressure minus uterine venous pressure)/uterine vascular resistance

Uterine blood flow decreases during periods of maternal hypotension, which can occur as a result of hypovolemia, hemorrhage, aortocaval compression, and sympathetic blockade. Similarly, uterine hypercontractility (or conditions that increase the frequency or duration of uterine contractions) and changes in uterine vascular tone, as seen in hypertensive states, may also adversely affect blood flow.

The supine position reduces uterine blood flow. After approximately 20 weeks of gestation, the gravid uterus grows large enough to compress the major intrapelvic and intra-abdominal vessels when the mother is supine. This is termed ***aortocaval compression***, and the result is that the uterus compresses both the venous drainage and most of the arterial supply. The uterine arteries also respond to elevation of maternal catecholamines by constricting, thereby increasing resistance and reducing flow. The exaggerated response to catecholamines that occurs in preeclampsia reduces uterine blood flow significantly and can compromise the well-being of the fetus. Epidural analgesia results in a reduction of maternal catecholamine concentrations and improved uterine artery blood flow.

The compression of the aorta does not increase uterine blood flow in parturients. Only the ovarian arteries arise above the level of compression, but these arteries represent a small volume of blood flow.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:40–41.

3. ANSWER: D

Maternal fever is not a sufficiently dangerous condition that would lead to avoiding misoprostol in this setting. The side effects of misoprostol include fever and shivering, which in very large doses can resemble rigors and sepsis. The other choices are conditions where the medication should be avoided in favor of alternatives. Methylergonovine causes intense vasoconstriction in the patient with preeclampsia. This has led to complications, including myocardial infarction and cerebrovascular accidents. Carboprost causes bronchial constriction, which can trigger an asthmatic attack. Finally, oxytocin causes significant vasodilation, especially when given intravenously as a single large dose.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:820.

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy*. 3rd ed. New York, NY: Springer-Verlag; 2004:115–116.

Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:573.

4. ANSWER: A

This patient may have two contraindications to neuraxial anesthesia: coagulopathy and hypovolemia. The patient was

in a high-speed motor vehicle accident. Although externally she appears to be stable, there is evidence that she may have significant internal injuries. One of the complications of trauma to the abdomen includes placental abruption, which leads to fetal bradycardia. Placental abruption may be associated with a rapidly progressive coagulopathy, including thrombocytopenia, elevation of prothrombin time (PT) and partial thromboplastin time (PTT), and depletion of fibrinogen. In the absence of coagulation studies that document normal coagulation, a regional anesthetic would be contraindicated.

Pregnancy is associated with an elevation of maternal heart rate. However, tachycardia found in the setting of potential abdominal trauma should raise suspicion for occult abdominal injury and bleeding. This represents a second contraindication to neuraxial anesthesia.

An inhalational mask induction is contraindicated because of the risk of pulmonary aspiration. This patient is at increased risk of aspiration since she is in her third trimester having an emergency trauma surgery.

Etomidate and propofol are both acceptable induction agents in parturients. However, intravascular volume depletion presumed from the tachycardia makes etomidate the better option.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:816.

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy*. 3rd ed. New York, NY: Springer-Verlag; 2004:92.

5. ANSWER: D

Terbutaline is a beta$_2$-adrenergic receptor agonist used for treatment of asthma. Terbutaline is also used as a short-term tocolytic in the treatment of hypertonic uterine contractions and preterm labor. Side effects include maternal tachycardia, nervousness, tremors, headache, hyperglycemia, hypokalemia, and pulmonary edema. Fetal side effects include tachycardia, neonatal hypoglycemia, and hyperinsulinemia.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:766–767.

6. ANSWER: E

Magnesium sulfate has three uses in obstetrics: as seizure prophylaxis for patients with preeclampsia, as a fetal neuroprotective agent in cases of imminent preterm delivery, and as a tocolytic agent to terminate preterm contractions, Magnesium sulfate has been shown to be superior to other antiepileptic medications for the prevention of eclampsia. Magnesium is administered as a continuous infusion to maintain serum levels at 5–8 mg/dL. It is eliminated by the kidneys.

Severe preeclampsia is associated with renal impairment, which can lead to reduced elimination of serum magnesium. Therefore, in patients with severe preeclampsia, the effects and serum concentration of magnesium must be monitored. The screening test for magnesium concentration is the assessment of tendon reflexes. Side effects of magnesium toxicity include depressed reflexes, sedation, hypotension, respiratory depression, flaccid paralysis, and cardiovascular collapse. In addition to supplemental oxygen, the immediate treatment of respiratory depression due to magnesium toxicity is reversal with calcium gluconate.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:769.

Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:646–647.

7. ANSWER: A

Postpartum hemorrhage is a complication of 3% to 5% of all deliveries and is one of the most common causes of maternal mortality worldwide. While the remaining conditions are all well-known risk factors for postpartum hemorrhage, the relative dilution of clotting factors is not a true answer. Pregnancy is associated with an expansion of the plasma volume, which leads to a physiologic dilution anemia and a decrease in some plasma proteins. However, pregnancy is most often associated with a slightly hypercoagulable state, which is believed to help prevent life-threatening hemorrhage during delivery.

ADDITIONAL READING

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy*. 3rd ed. New York, NY: Springer-Verlag; 2004:113.

8. ANSWER: D

The stages of labor are

1. Latent phase
2. Active phase

3. Transition
4. Fetal descent
5. Second stage
6. Neonatal delivery
7. Third stage
8. Placental delivery

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:365

9. ANSWER: C

Retained placenta is a complication of delivery that can be associated with abnormal placentation and prematurity, among other causes. Retained placenta is commonly defined as a third stage (neonatal delivery to placental delivery) that exceeds 30 minutes. However, by 60 minutes, approximately half of these cases would deliver spontaneously. Anesthetic management of a patient with retained placenta could include extension of an epidural analgesic to provide anesthesia. General anesthesia is rarely required. In some cases, the uterine musculature contracts significantly, preventing the manual separation of the placenta. In this case, uterine relaxants such as nitroglycerin or volatile anesthetics can be used.

If the placenta has started to separate from the endometrium, then significant bleeding can occur. In this case the management of a retained placenta may become an emergency. Neuraxial anesthesia should be used with caution in a bleeding parturient and is contraindicated in a patient with uncorrected hypovolemia.

ADDITIONAL READING

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy*. 3rd ed. New York, NY: Springer-Verlag; 2004:121–122.

10. ANSWER: A

The extremely prolonged blockade in this patient signifies a true ***pseudocholinesterase deficiency***, which may be accentuated by pregnancy. Pregnancy decreases the concentration of serum pseudocholinesterase by approximately 25%. This can result in a slight prolongation of succinylcholine but is not clinically significant. No dose adjustment is required and this does not result in an increased risk of phase II block. Magnesium binds to the prejunctional motor nerve endings. This blocks the entry of calcium, thereby decreasing the release of acetylcholine and decreasing sensitization of the motor endplate to activation. This results in prolongation of nondepolarizing muscle relaxants, but not succinylcholine. Pregnancy cannot induce atypical pseudocholinesterase; this is a genetically determined condition. Finally, this patient was not stated to have received antibiotics; gentamicin is not the accepted prophylaxis for group B streptococcus.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:28–29.

11. ANSWER: A

Neuraxial labor analgesia can result in a ***sympathectomy*** when local anesthetics are used. If conducted carefully, however, this does not necessarily result in a significant decrease in blood pressure and perfusion pressure, which would compromise the fetus. By decreasing uterine vascular resistance, the sympathectomy can actually increase placental blood flow in women with severe preeclampsia. For reasons not completely understood, preeclamptic patients have a lower incidence of hypotension than normotensive patients after spinal anesthesia.

Preeclampsia is a severe and potentially life-threatening disease of pregnancy. This disease is associated with multiple physiologic derangements, including hypertension, renal disease, and, when severe, thrombocytopenia and coagulopathy. The incidence of placental abruption is also increased, which can lead to hypovolemia and coagulopathy, which are contraindications for neuraxial techniques.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:991–995.

12. ANSWER: B

Gastric emptying is not delayed during pregnancy or in early labor, but is delayed in advanced labor. Despite the period of NPO, patients who are in pain have delayed gastric emptying. This results in increased residual volume, which increases the risk of aspiration if general anesthesia were required.

Death from maternal aspiration was historically one of the more common causes of anesthesia-related death. Death from aspiration is now very uncommon, possibly from the increased use of regional anesthesia, administration of antacids, cricoid pressure, and NPO status during advanced labor.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:526.

Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:18.

13. ANSWER: D

Preeclampsia is a common obstetric complication affecting approximately 7% of all pregnant women. Preeclampsia can be either mild or severe; the severe form is associated with end-organ damage. The systemic hemodynamics of preeclampsia include an increased systemic vascular resistance and hypertension. On initial presentation, women with severe preeclampsia are often volume-depleted, with decreased central and pulmonary venous pressures. Furthermore, with volume resuscitation, these women generally display hyperdynamic cardiac function with increased cardiac output. While cardiac dysfunction with increased central and pulmonary venous pressures can be found in some women, this is not the most common finding.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:983.

Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:505, 512.

14. ANSWER: A

Preeclampsia is a vascular disorder that is progressive through gestation. Severe preeclampsia is a diagnosis that includes evidence of end-organ injury or damage. The most common finding is proteinuria. However, severe preeclampsia is associated with major organ failure, including cerebral hemorrhage, coagulopathy, hepatic subcapsular hematoma, and pulmonary edema. (Table 6.1).

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:987–988.

Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:503–509.

Table 6.1 **FACTORS THAT DIFFERENTIATE MILD FROM SEVERE PREECLAMPSIA**

	MILD	SEVERE
Systolic arterial pressure	<160 mm Hg	≥160 mm Hg
Diastolic arterial pressure	<110 mm Hg	≥110 mm Hg
Urinary protein	<5 g/24 hr	≥5 g/24 hr
	Dipstick + or 2+	Dipstick 3+ or 4+
Urine output	>500 mL/24 hr	≤500 mL/24 hr
Headache	No	Yes
Visual disturbances	No	Yes
Epigastric pain	No	Yes
Right upper quadrant abdominal pain	No	Yes
Pulmonary edema	No	Yes
Cyanosis	No	Yes
HELLP syndrome	No	Yes
Platelet count	>100,000/mm^3	<100,000/mm^3

SOURCE: Miller's Anesthesia, Table 69–8. From Birnbach DJ, Gatt SP, Datta S, ed. Anesthetic and Obstetric Management of High-Risk Pregnancy. 3rd ed. New York, NY: Springer-Verlag; 2004. S (eds): *Textbook of Obstetric Anesthesia*. New York, Churchill Livingstone, 2000, p 543.

15. ANSWER: D

Pregnancy results in significant changes to the maternal pulmonary system. Early in gestation the minute ventilation increases under the influence of hormones. By term gestation the minute ventilation increases approximately 40% to 50% due to an increase in tidal volume, as opposed to an increase in respiratory rate. This results in a decrease in maternal arterial carbon dioxide tension; however, maternal serum pH remains normal due to a decrease in physiologic buffers. The flow-volume loop, FEV_1, and FEV_1/FVC ratio remain unchanged during pregnancy. The parturient is almost completely dependent upon the diaphragm, not the intercostal or accessory muscles, for ventilation.

ADDITIONAL READING

Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:12–13.

16. ANSWER: D

To a variable extent, all medications cross the placenta and enter the fetal circulation. However, the degree to which this occurs depends on the diffusion characteristics of the medication. Drugs that easily pass through the blood–brain barrier to enter the brain will also easily pass the placental barrier. Characteristics that reduce passage of a medication to the fetus include molecular weight, charge, and lipid solubility. Medications that have a low serum concentration due to a high percentage of protein binding, to a low nonionized fraction, or to a small dose being administered will tend not to cross to the fetus.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:63.

17. ANSWER: A

The medications that are used to produce neuromuscular block are equally effective in the neonate, with the exception that the volume of distribution is increased. The medications do not, however, cross the placenta in a clinically relevant amount, resulting in minimal effect on the fetus/neonate. Although some of the medications are steroid-based, their large size and charge prevent passage into the fetal circulation.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:63.

18. ANSWER: D

The degree to which medications cross the placenta depends on the diffusion characteristics of the medication. Drugs that easily pass through the blood–brain barrier to enter the brain will also easily pass the placental barrier. Characteristics that reduce passage of a medication to the fetus include molecular weight, charge, and lipid solubility. Medications that have a low serum concentration due to a high percentage of protein binding, to a low nonionized fraction, or to a small dose being administered will tend to not cross to the fetus.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:63.

19. ANSWER: D

Pregnancy is associated with many physiologic alterations. Briefly, cardiac output is increased, but systemic vascular resistance is decreased, generally resulting in a decrease in blood pressure during the second trimester. Although the gravid uterus does impinge on the diaphragm, the chest diameter is increased, and there is an increase in the tidal volume. This results in an increase in minute ventilation. Finally, both the red cell mass and the plasma volume are increased, with the increase in plasma volume greater than the increase in red cell mass. This results in a physiologic anemia of pregnancy, with adequate oxygen delivery.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:16–22.
Norris MC, ed. *Obstetric Anesthesia*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 1999:4–15.

20. ANSWER: D

Nonsteroidal anti-inflammatory drugs (NSAIDs) are occasionally used during pregnancy. The most common short-term use was for tocolysis of preterm contractions.

The medication used for this was indomethacin. The use of NSAIDs in the third trimester requires frequent fetal monitoring. More than single or short-term use is discouraged during pregnancy to avoid fetal complications. Because prostaglandins are crucial to the dilation of the renal arterioles and the ductus arteriosus, NSAIDs are deleterious to the flow of these vessels. Chronic use of NSAIDs can lead to renal artery constriction causing oligohydramnios, and to spasm of the ductus arteriosus. Similarly, NSAID use can have deleterious effects in the mother, including peptic ulcers and renal dysfunction.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:765.

21. ANSWER: E

The ***transition from fetal to neonatal physiology*** is the crucial step that supports the life of the neonate once the placental circulation has been removed. In the fetal circulation and the oxygenated blood is provided by the placenta and travels via the inferior vena cava to the right heart. The venous (oxygenated) blood then largely bypasses the nonfunctional pulmonary system through two conduits: the foramen ovale and the ductus arteriosus. Transition to neonatal circulation requires the venous (deoxygenated) blood to enter a functional pulmonary system to become oxygenated. Expansion of the collapsed lungs with air decreases the pulmonary vascular resistance, promoting pulmonary blood flow. The blood then returns to the high-pressure left atrium, causing the foramen ovale to close. The constriction and clamping of the umbilical cord stops umbilical artery blood flow, increasing systemic arterial resistance. This decreases ductus arteriosus blood flow.

Patent ductus arteriosus blood flow continues initially, but the ductus closes within the first days after birth. A patent ductus arteriosus may occur in hypoxic states and is considered abnormal.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:156–158.

22. ANSWER: D

The steps of ***neonatal resuscitation*** are defined by the guidelines set forth by the American Academy of Pediatrics. The fetal–neonatal transition requires the neonate to begin respirations. If this is unsuccessful, the fetus will go into primary, then secondary apnea. When a neonate is born unresponsive it is not clear whether it is in primary or secondary apnea. Vigorous stimulation, warmth, and clearing of the oral airway will give the neonate a stimulus to breath. If this is successful, supportive care with supplemental oxygen is all that may be required. If the neonate remains unresponsive, then positive-pressure ventilation may be required.

ADDITIONAL READING

Kattwinkel J, ed. *Neonatal Resuscitation Program Textbook*. 5th ed. American Academy of Pediatrics; 2006. (original publication: American Heart Association and American Academy of Pediatrics. 2005 American Heart Association Guidelines for CPR and ECC of pediatric and neonatal patients: neonatal resuscitation guidelines. *Pediatrics.* 2006;117;e1029–1038.)

23. ANSWER: A

The appropriate action in this situation is to evaluate the effectiveness of the epidural catheter. Most (95%) epidural catheters used for labor can be used successfully for cesarean anesthesia. The predictors of failure of the epidural catheter for cesarean anesthesia include breakthrough pain during labor.

This parturient has hypotension associated with a sympathectomy due to regional anesthesia. Hypotension can reduce uterine artery blood flow, which can lead to hypoperfusion of the placenta. This will proceed to fetal hypoxia and alterations of fetal heart rate control. Late heart rate decelerations associated with hypotension after regional anesthesia should be treated by increasing blood pressure. Removal of the epidural catheter and conversion to intramuscular analgesia would not be appropriate in a patient who may need to proceed to urgent or emergent cesarean delivery. Extension of the epidural catheter to produce cesarean anesthesia would be the safest method of providing anesthesia. If the epidural catheter were removed the patient would likely need general anesthesia. General anesthesia is associated with considerable risk to the parturient. Elimination of any opioid from the epidural solution is incorrect because the amount of opioid delivered by epidural anesthesia is insufficient to cause fetal narcosis. Giving chloroprocaine would be incorrect because this would produce cesarean anesthesia in a patient in whom surgery has not yet been ordered. The patient would require continual monitoring with ASA standard monitors.

24. ANSWER: B

The Apgar scoring system is a standardized, objective method of assessing a newborn's clinical status. It is based

Table 6.2 APGAR SCORE CRITERIA

ACRONYM	ASSESSMENT	SCORE OF 0	SCORE OF 1	SCORE OF 2
*A*ppearance	Skin color	Blue or pale all over	Blue at extremities; body pink (acrocyanosis)	No cyanosis Body and extremities pink
*P*ulse	Heart rate	Absent	<100	≥100
*G*rimace	Reflex irritability	No response to stimulation	Grimace/feeble cry when stimulated	Cry or pull away when stimulated
*A*ctivity	Muscle tone	None	Some flexion	Flexed arms and legs that resist extension
*R*espiration	Breathing	Absent	Weak, irregular, gasping	Strong, lusty cry

on five parameters that are assessed at 1 and 5 minutes of birth: heart rate, respiratory effort, muscle tone, reflex, irritability, and color. A total score of 8 to 10 is normal, 4 to 7 indicates moderate impairment, and 0 to 3 indicates the need for immediate resuscitation (Table 6.2).

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:159–160.

25. ANSWER: E

Magnesium sulfate does affect the neuromuscular junction in all the ways described. However, because succinylcholine is rapidly metabolized by pseudocholinesterase, the increase in duration is not clinically evident. The onset and duration of a single intubating dose are not inordinately prolonged when administered concurrently with a magnesium sulfate infusion. A routine intubating dose of 1 to 1.5 mg/kg should be used during rapid-sequence induction.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:997.

26. ANSWER: B

The vital capacity is not significantly changed during pregnancy. The enlarging uterus compromises residual volume, while vital capacity is maintained by expansion of the chest wall. In addition, total lung capacity is usually preserved or minimally decreased.

To accommodate the increased oxygen demand and requirement for carbon dioxide elimination, pregnancy is associated with an increase in the respiratory minute volume, mostly due to an increased tidal volume. Because of difficulties in performing clinical research on pregnant women, few investigations into respiratory changes in pregnancy have been conducted. Unfortunately, many of the findings quoted in the literature are inconsistent and often based on older techniques that were applied to a very limited number of subjects (Table 6.3).

The breathing pattern changes during pregnancy, with more diaphragmatic respiration as pregnancy progresses because of the effects of the gravid uterus and limitation of thoracic cage movement.

The rapid development of hypoxia as a result of decreased FRC, increased oxygen consumption, and airway closure may be minimized by administration of 100% oxygen for 3 to 5 minutes before the induction of anesthesia. In an emergency setting, four maximal-capacity breaths with 100% oxygen should be sufficient.

Capillary engorgement of the mucosa and edema of the oropharynx, larynx, and trachea may result in a difficult intubation. Any manipulation of the upper airway such as suctioning, insertion of airways, or laryngoscopy may cause edema, bleeding, and upper airway trauma. Because of the particularly friable mucosa of the nasopharynx, instrumentation of the nose should be avoided if at all possible. In performing intubation of a pregnant patient, a smaller-than-usual endotracheal tube (size 6.0 to 7.0) should be used and repeated attempts at laryngoscopy minimized.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:20.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010, Chapter 69.

Table 6.3 RESPIRATORY CHANGES DURING PREGNANCY

INCREASED	DECREASED	UNCHANGED
Minute ventilation, by 45% due to increase in tidal volume by 50%	Functional residual capacity, by 20%–80%	Respiratory rate
Carbon dioxide production	$PaCO_2$, 30 mm Hg by the 12th week of gestation	Closing capacity
Sensitization to carbon dioxide (due to progesterone)	FRC/CC ratio: faster small-airway closure	Vital capacity
Faster desaturation		Total lung capacity

27. ANSWER: D

Placental abruption complicates 0.4% to 1% of pregnancies. Known risk factors for placental abruption include hypertension, preeclampsia, advanced maternal age, parity, maternal and paternal tobacco use, cocaine use, trauma, premature rupture of membranes, chorioamnionitis, bleeding in early pregnancy, and a history of abruption with previous gestation. Classically, the presentation consists of uterine pain, often between contractions, increased uterine activity, and finally fetal compromise. Vaginal bleeding may not be present. The major complications that occur are hemorrhagic shock, acute renal failure, coagulopathy, and fetal compromise or demise. Abruption is also the most common cause of DIC in pregnancy

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:815.

28. ANSWER: B

Anticholinesterase medications used in appropriate doses have no effect on uterine tone and do not induce preterm contractions. Uterine displacement should be used after 18 to 20 weeks of gestation to prevent uterine compression of the aorta and vena cava. A hip wedge should be placed prior to induction of anesthesia. Similarly, because of the potential increased risk of aspiration during pregnancy, nonparticulate antacids should be administered prior to induction. Finally, fetal heart rate monitoring is a decision that can be difficult. In this particular operation, continuous monitoring would be impractical.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:353.

29. ANSWER: C

Factors affecting drug transfer across the human placenta include lipid solubility, protein binding, tissue binding, pKa, pH, and blood flow. Thiopental is very lipid-soluble and quickly appears in the umbilical venous blood after maternal injection, with mean fetal/maternal ratios between 0.4 and 1.1. Glycopyrrolate, heparin, and muscle relaxants do not cross the placenta.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:63.

30. ANSWER: D

Meconium-stained delivery is associated with an increased risk for depression at birth, meconium aspiration syndrome, and bronchopulmonary dysplasia. Only between 5% and 20% of deliveries are complicated by meconium-stained amniotic fluid, but meconium aspiration syndrome develops in 5% of these. Routine oropharyngeal suctioning at delivery has not proven to be beneficial, and randomized controlled trials have suggested that vigorous neonates do not need aggressive airway cleansing with endotracheal intubation. The most severe complication, bronchopulmonary dysplasia, is thought to be an in utero event and not caused by aspiration of particles at delivery. Meconium is considered sterile, so antibiotics are unwarranted.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:148.

31. ANSWER: E

Late decelerations begin 10 to 30 seconds after the beginning of uterine contractions and end 10 to 30 seconds after the end of uterine contractions. Late decelerations result from **uteroplacental insufficiency** or fetal **hypoxemia**. Studies suggest that late decelerations might represent a response to hypoxemia and may result from loss of sympathetic activity and decompensation of myocardial circulation.

In contrast, intermittent ***umbilical cord compression*** can lead to **variable decelerations**, which vary in shape and duration from contraction to contraction.

KEY FACTS: FETAL HEART MONITORING

Late decelerations	Uteroplacental insufficiency Aortocaval compression Increased uterine tone
Variable decelerations	Umbilical cord compressions Fetal anemia Maternal use of narcotics

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:149–150.

32. ANSWER: E

The first steps of neonatal resuscitation in a neonate who is not breathing spontaneously with good tone are to provide warmth, clear the airway, and stimulate. If the infant remains apneic with a heart rate under 100, positive-pressure ventilation should be provided. If the heart rate remains under 100 and positive-pressure ventilation via facemask is not demonstrating adequate chest rise or there is uncertainty regarding adequate ventilation, endotracheal intubation is indicated. Chest compression and epinephrine should be given if the heart rate is less than 60 (Fig. 6.1).

33. ANSWER: B

The P_{50} of human fetal blood is approximately 19 to 21 mm Hg, in contrast to the 27 mm Hg found in adult blood. The difference in affinity for oxygen is largely the result of high concentrations of hemoglobin F in fetal blood. The shift in fetal blood affinity for oxygen is due to decreased interaction between hemoglobin F and 2,3-DPG, which normally acts to lower oxygen affinity by binding to and stabilizing the deoxygenated oxygen tetramer.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:76.

34. ANSWER: B

Beginning at 18 to 20 weeks gestation, left uterine displacement should be used to prevent aortocaval compression. Third-trimester use of NSAIDs may be associated with premature closure of the fetal ductus arteriosus, pulmonary hypertension, and oligohydramnios. Elective surgery should be avoided during pregnancy, especially during the first trimester because that is the period of organogenesis. Organogenesis occurs between days 31 and 71. The second trimester is the optimal time to perform surgery. Scientific evidence does not support the avoidance of nitrous oxide, particularly after the 6th week of gestation.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:353.

35. ANSWER: E

Preeclampsia is associated with several risk factors. Demographic risk factors include advanced maternal age and African racial background; obstetric risk factors include nulliparity, having a new partner as the father, family or previous history of preeclampsia, placental abruption, and fetal abnormalities including growth restriction; medical risk factors include obesity, diabetes, renal or vascular diseases, and hypertension. Interestingly, cigarette and tobacco use is associated with a reduction in risk.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:976–978.

36. ANSWER: D

Placenta accreta is defined as adherence to the myometrium without invasion or passage through the uterine muscle. Abnormal placentation can present in the form of accreta, increta (invasion into the myometrium), or percreta

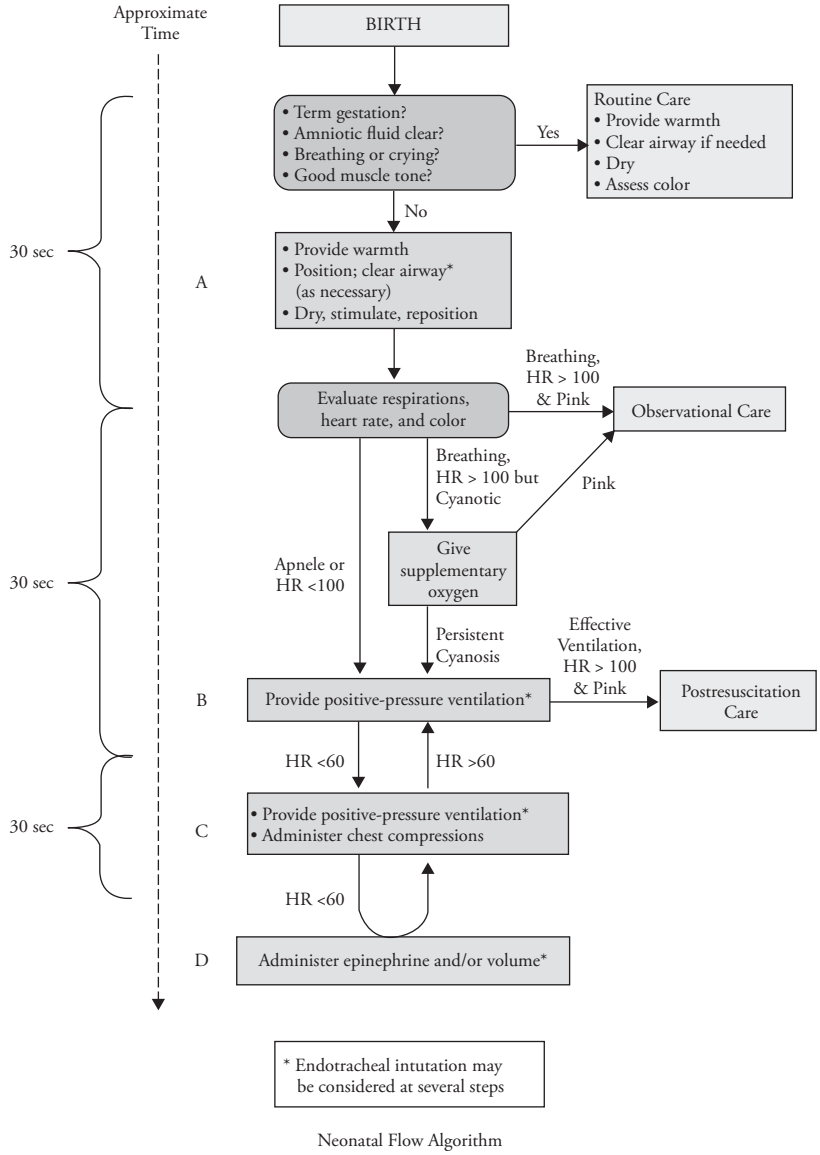

Figure 6.1 Neonatal care algorithm. The algorithm details the immediate steps taken during the first minutes of life of the newborn.

SOURCE: Part 13: Neonatal Resuscitation Guidelines. *Circulation*. 2005;112:IV-188–IV-195; originally published online November 28, 2005.

(invasion through the serosa). The incidence of abnormal placentation and accreta increases with increasing number of prior cesarean deliveries, likely because of the presence of a scar in the endometrium. With abnormal placentation, the endometrial strip is absent on ultrasound examination. These patients should have adequate preparation for transfusion and should be counseled about the potential of hysterectomy and blood transfusion (Table 6.4).

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:824.

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy*. 3rd ed. New York, NY: Springer-Verlag; 2004:102.

37. ANSWER: B

Cesarean delivery in a patient with ***placenta accreta*** is often complicated by significant blood loss, and the team should be prepared and equipped for massive transfusion. Careful communication is required between the obstetric, nursing, and anesthetic teams. The patient should be counseled regarding the potential need for transfusion and general anesthesia. Emergency hysterectomy is associated with increased blood loss compared with elective hysterectomy. The average blood loss for emergent obstetric hysterectomy is significantly greater (2,500 mL), with an average transfusion requirement of 6.6 units of packed red cells; in elective procedures (mean blood loss 1,300 mL), the average replacement was 1.6 units of packed red cells.

Table 6.4 **RISK OF PLACENTA ACCRETA IN PATIENTS WITH CURRENT PLACENTA PREVIA**

NUMBER OF PRIOR CESAREAN DELIVERIES	% OF PATIENTS WITH PLACENTA ACCRETA
0	3
1	11
2	40
3	61
>4	67

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:826.

38. ANSWER: B

Pain during the first stage of labor results from the stimulation of visceral af Carboprost (15-methyl-PGF2), ferents that innervate the lower uterine segment and cervix and enter the spinal cord at T10 to L1. An epidural, lumbar sympathetic, or cervical block may provide analgesia for the first stage of labor. Effective labor analgesia reduces maternal catecholamine concentrations to baseline, nonlabor levels. The paracervical block has the highest failure rate, the shortest duration, and the highest complication rate. Fetal bradycardia is the most worrisome complication of the paracervical nerve block. A pudendal nerve block primarily relieves pain in the second stage of labor.

Pain during the second stage of labor results from distention of the lower vagina, vulva, and perineum. The pudendal nerve, which includes somatic nerve fibers from the anterior primary divisions of the second, third, and fourth sacral nerves, represents the primary source of sensory innervation for the lower vagina, vulva, and perineum.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:501.

39. ANSWER: E

High or total spinal anesthesia results in agitation, profound hypotension, dyspnea, inability to speak, and loss of consciousness. Answers A and D provide etiologies for high spinal anesthesia. A second explanation for this patient's presentation is local anesthetic toxicity. This could be due to excessive medication being administered in the epidural space, or being injected directly into a vein. While a seizure from eclampsia might result in loss of consciousness, this complication would be associated with hypertension, not profound hypotension.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:462.

40. ANSWER: B

Postdural puncture headache resulting in CSF leak may lead to serious complications. The most common of these is traction-induced neuropraxia of the cranial nerves. Ocular symptoms such as diplopia may result from cranial nerve VI palsy. Auditory symptoms such as tinnitus and hypacusis may also be associated with cranial nerve VIII. Seizure is a very rare symptom that may be due to cerebral vasospasm caused by cerebral hypotension from the dural puncture. Cerebral edema of the white matter regions of the posterior circulation is commonly associated with posterior reversible encephalopathy syndrome (PRES). PRES is associated with preeclampsia, uremia, hemolytic-uremic syndrome, and exposure to immunosuppressant drugs, but not dural puncture.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:683.

41. ANSWER: E

Goals for ***anesthetic maintenance during general anesthesia for cesarean section*** include adequate oxygenation, appropriate depth of anesthesia to maintain maternal comfort, minimal effects on uterine tone, and minimal adverse effects on the neonate. All halogenated agents produce dose-sensitive relaxation of the myometrium. Following delivery of the neonate, the concentration of a volatile agent is typically reduced to minimize effects on uterine tone. Although volatile agents may build up in fetal tissues, in emergency

situations delivery usually occurs before sufficient quantities of the anesthetic cross the placenta. Prolonged exposure, as might be seen in a complex surgery, could result in secondary depression of the neonate. Volatile agents may decrease maternal blood pressure, but the response to laryngoscopy and intubation typically offsets this hypotension. The minimum alveolar concentration in pregnancy is reduced in comparison to nonpregnant women.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:549.

42. ANSWER: B

Although it was previously believed to be true, current research shows that gastric emptying of liquid and solid materials is not altered during pregnancy, but may be during labor. Esophageal peristalsis and intestinal transit, however, are slowed during pregnancy, and this has been attributed to the activity of progesterone. The majority of women experience gastric reflux near term gestation, which is a symptom of reduced lower esophageal barrier pressure. This is caused by the mechanical displacement of the stomach and esophagus by the gravid uterus.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:23–24.

43. ANSWER: B

Pregnancy is associated with enhanced platelet turnover and consumption, referred to as ***gestational thrombocytopenia***. Likely, increased platelet production compensates for the greater activation, allowing the platelet count to remain within normal limits. However, 7% to 8% of healthy parturients have platelet counts below 150,000, and 0.9% have a platelet count less than 100,000. While a platelet count below 100,000 is less likely in gestational thrombocytopenia and more likely with ITP/ATP, the incidence of ITP/ATP is 0.01%, making it a less likely diagnosis. Had the platelet count been low prior to pregnancy, ITP/ATP would have been the more likely diagnosis.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:22–23, 951.

44. ANSWER: C

The ***von Willebrand factor*** plays two important roles in coagulation: (1) it forms a complex with factor VIII, decreasing its excretion and (2) it mediates platelet adhesion by binding to platelets. While it is true that pregnancy confers protection in patients with vWD by increasing levels of factor VIII, prophylactic treatment with DDAVP should be initiated in those with factor VIII levels below 25%. If there is no response to DDAVP, fresh frozen plasma (FFP) or cryoprecipitate should be given. Those not responsive to FFP or cryoprecipitate should be given Humate-P, a pasteurized factor VIII concentrate. The goal during labor is a factor VIII level of 50% of normal, which is increased to 80% of normal for cesarean deliveries.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:953.

45. ANSWER: D

Neonatal myasthenia gravis occurs in approximately 16% of infants of mothers with MG, as these maternal IgG antibodies cross the placenta. The infants may exhibit symptoms such as hypotonia or respiratory difficulty for 2 to 3 weeks, at which point the maternal IgG antibodies will have metabolized.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:1060.

46. ANSWER: B

Spina bifida occulta occurs when there is failed fusion of the neural arch without herniation of the meninges or neural elements. The lesion usually occurs at one level, typically

Table 6.5 CARDIOVASCULAR CHANGES IN PREGNANCY

PARAMETER	CHANGE	AMOUNT (%)
Heart rate	Increased	20–30
Stroke volume	Increased	20–50
Cardiac output	Increased	30–50
Contractility	Variable	?10
Central venous pressure	Unchanged	
Pulmonary capillary wedge pressure	Unchanged	
Systemic vascular resistance	Decreased	20
Systemic blood pressure	Slight decrease	Midtrimester 10–15 mm Hg, then rises
Pulmonary vascular resistance	Decreased	30
Pulmonary artery pressure	Slight decrease	

SOURCE: Miller's Anesthesia, Table 69.1. From Birnbach DJ, Gatt SP, Datta S, ed. Anesthetic and Obstetric Management of High-Risk Pregnancy. 3rd ed. New York, NY: Springer-Verlag; 2004. S (eds): *Textbook of Obstetric Anesthesia*. New York, Churchill Livingstone, 2000, p 34.

at L5–S1, which is below the level at which most neuraxial techniques are performed. However, patients with isolated single-level vertebral arch anomalies with normal spinal cords usually do not exhibit superficial signs such as skin dimples or tuft of hair. In tethered cord syndrome, the spinal cord is attached to tissue either at the level of the conus medullaris or anywhere else along the spinal cord. This attachment limits the movement of the spinal cord and can cause stretching of the spinal cord, sometimes to levels below L1, increasing the chance of accidentally piercing the spinal cord should a spinal or inadvertent dural puncture be performed. Occult spinal dysraphism is associated with a low-lying, posteriorly located, tethered spinal cord.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:1046.

47. ANSWER: D

In adults, the spinal cord ends at L1 and the dural sac at S2. In children, the spinal cord ends at L3 and the dural sac at S3.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. Clinical Anesthesiology. 3rd ed, McGraw-Hill/Appleton & Lange, 2001, p. 293.

48. ANSWER: C

During pregnancy, the heart rate, stroke volume, and cardiac output are increased. The systemic and pulmonary vascular resistance is decreased. The central venous pressure during pregnancy is commonly unchanged (Table 6.5).

7.

REGIONAL ANESTHESIA

Pedram Aleshi, MD, and Harold Fong, MD

1. Compared to opiate-only epidural infusion, use of a combination of local anesthetic and opioid epidural infusion leads to:

A. Increased incidence of motor blockade
B. Increased incidence of pruritus
C. Increased incidence of breakthrough pain
D. Decreased incidence of hypotension
E. Increased incidence of respiratory depression

2. The perioperative use of a thoracic epidural with a local anesthetic solution is associated with

A. The spinal reflex inhibition of the gastrointestinal (GI) tract remaining unaffected
B. Similar pulmonary complications as intrapleural and intercostal block
C. Attenuating spinal reflex inhibition of diaphragmatic function
D. No effect in size of myocardial infarction compared to lumbar epidural
E. No change in coronary blood flow

3. A 58-year-old woman with a recent diagnosis of end-stage renal disease is scheduled for creation of an upper-extremity fistula just proximal to the elbow. Her medical history includes insulin-dependent diabetes, hypertension, and a 80 pack-year history of smoking. Which of the following is TRUE?

A. An axillary block would be the best option since it has least likelihood of complications, including pneumothorax.
B. An interscalene block would be best to cover all sensory nerves to the upper arm, including the intercostobrachial nerve.
C. A supraclavicular block is performed at the level of the cords and can effectively block the brachial plexus for the upper arm.
D. An infraclavicular block is performed at the distal trunks and can be used to provide adequate sensory block for the surgery.
E. The surgery can be performed with sedation and local infiltration of anesthesia provided by the surgeon.

4. All of the following nerves at the ankle are terminal branches of the sciatic nerve EXCEPT

A. Posterior tibial nerve
B. Sural nerve
C. Saphenous nerve
D. Deep peroneal nerve
E. Superficial peroneal nerve

5. A 32-year-old G1P0 parturient at 36 weeks with a history of complete spinal cord transaction that occurred 6 months ago resulting in paraplegia presents to labor and delivery. Which of the following is TRUE?

A. A labor epidural is not indicated if patient has a T5-level transaction if she has no motor or sensory function below T5.
B. Autonomic hyperreflexia does not develop if the lesion is below spinal dermatome T7.
C. Use of succinylcholine is contraindicated.
D. Hypertension, flushing, and headaches are likely signs of preeclampsia in this patient.
E. Because of lack of sensory connection to the cortex, a full bladder is well tolerated in this patient.

6. All of the following nerves can be blocked in the axilla EXCEPT

A. Axillary nerve
B. Musculocutaneous nerve
C. Median nerve
D. Ulnar nerve
E. Intercostal brachial nerve

7. An axillary block is performed for a surgical procedure involving the hand. Which of the following is INCORRECT when evaluating the adequacy of the block for surgery?

A. Median nerve block can be evaluated by testing the lateral aspect of the ring finger.
B. Radial nerve block can be evaluated by testing the posterolateral aspect of the hand.
C. Ulnar nerve block can be evaluated by testing the medial aspect of the ring finger.
D. Median nerve block can be evaluated by testing the medial aspect of the palm.
E. Radial nerve block can be evaluated by testing the lateral aspect of the dorsum of the hand.

8. With respect to bupivacaine toxicity, which of the following is TRUE?

A. CNS stimulation is often followed by CNS depression via blockade of inhibitory pathways.
B. The ratio of dose required to induce cardiovascular collapse(CC) to the dose required for CNS effects [CC/CNS] is higher for bupivacaine than for lidocaine.
C. Succinylcholine administration to a patient with a tonic clonic seizure may contribute to metabolic acidosis.
D. Hyperventilation may lead to more CNS toxicity.
E. Combined metabolic and respiratory acidosis may further exacerbate CNS toxicity.

9. Given equal-volume infiltrations for local anesthesia, which of the following would be associated with a higher risk for inducing cardiac arrhythmias?

A. 0.5% racemic bupivacaine
B. 0.5% R(+) bupivacaine
C. 0.5% S(−) bupivacaine
D. 0.5% levo-bupivacaine
E. 0.5% ropivacaine

10. After receiving a local anesthetic injection for a sciatic nerve block, a patient develops tinnitus, circumoral paresthesia, and dizziness. Assuming equal-volume amounts, which of the following is MOST likely to have caused these symptoms?

A. 0.75% bupivacaine
B. 2% lidocaine
C. 0.75% levobupivacaine
D. 0.75% ropivacaine
E. 2% mepivacaine

11. Which of the following statements regarding the cardiotoxicity of lidocaine is INCORRECT?

A. Lidocaine has a negative inotropic action on cardiac muscle in a dose-dependent fashion.
B. Lidocaine has antiarrhythmic properties while bupivacaine exhibits arrhythmogenic properties.
C. Bupivacaine depresses rapid depolarization in Purkinje fibers but lidocaine speeds up rapid depolarization.
D. High local anesthetic concentrations can lead to an increased PR interval and width of the QRS complex.
E. Lidocaine cardiac toxicity may be observed in cases involving tumescent anesthesia.

12. A 58-year-old man with advanced-stage pancreatic cancer is requesting evaluation in the pain clinic for palliation. Which of the following is INCORRECT?

A. The celiac plexus contains afferent and efferent fibers from T5–T12 roots.
B. The plexus is blocked just anterior to the T8 vertebral body.
C. The celiac plexus innervates most of the abdominal viscera.
D. A celiac plexus block perioperatively can decrease body stress and endocrine response to surgery.
E. Complications include aspiration of blood, urine, or CSF from the needle.

13. Which of the following statements is TRUE regarding cervical plexus block?

A. Phrenic nerve blockade is a rare complication of deep cervical plexus block.
B. The superficial cervical plexus innervates the sternocleidomastoid muscle.
C. A deep cervical plexus block is performed at the C4, C5, and C6 levels.
D. A superficial cervical plexus block is performed at the anteromedial aspect of the sternocleidomastoid muscle.
E. The only major blood vessels at risk during a deep cervical plexus block are the carotid artery and the jugular vein, and both can easily be avoided.

14. All of the following statements are TRUE regarding cocaine EXCEPT

A. Cocaine acts as a sodium channel blocker.
B. Cocaine causes release of catecholamines, leading to hypertension and tachycardia.
C. Cocaine is an aminoester.
D. Cocaine blocks reuptake of catecholamines, leading to cerebrovascular accidents, myocardial infarctions, and arrhythmias.
E. Cocaine is metabolized by hepatic carboxylesterases.

15. Which of the following statements is TRUE regarding differential nerve sensitivity to local anesthetics?

A. Small nonmyelinated C fibers are most susceptible to local anesthetic blockade.
B. Large myelinated Aα and Aβ are most susceptible to local anesthetic blockade.
C. Small myelinated B fibers are most susceptible to local anesthetic blockade.
D. Fibers carrying proprioception are more susceptible than fibers carrying cold sensation.
E. Small nerve fibers are more susceptible than larger fibers.

16. Which of the following is NOT a side effect of neuraxial opioids in the obstetric patient?

A. Neurotoxicity
B. Pruritus
C. Hypotension
D. Respiratory depression
E. Reactivation of oral HSV infection

17. All of following statements are TRUE regarding plica mediana dorsalis EXCEPT

A. It is a midline connective tissue band visualized on epiduroscopy.
B. It extends from the dura mater toward the ligamentum flavum.
C. It may lead to difficult catheter insertion.
D. It may lead to unilateral epidural block.
E. It may lead to unilateral spinal block.

18. The subdural space

A. Exists between the dura mater and arachnoid mater
B. Contains CSF
C. Exists between the dura mater and ligamentum flavum
D. Can be easily found in all patients
E. Will produce reliable anesthesia and analgesia

19. Which of the following cardiopulmonary changes is NOT TRUE of a T8 epidural level produced by a local anesthetic-only epidural solution?

A. Decreased stroke volume and cardiac output
B. Decreased mean arterial pressure
C. Decreased peripheral vascular resistance
D. Decreased resting minute ventilation
E. Unchanged dead space

20. Which of the following is FALSE for the effects of neuraxial block on thermoregulation?

A. Spinal anesthesia increases temperature threshold for sweating.
B. Spinal anesthesia decreases temperature threshold for vasoconstriction.
C. Spinal anesthesia decreases temperature threshold for shivering.
D. Intravenous administration of lidocaine, with equivalent plasma levels; alters thresholds for vasoconstriction and shivering similar to epidural administration of lidocaine.
E. The intensity of shivering is decreased by neuraxial anesthesia.

21. Epidural blockade with 0.25% bupivacaine at mid- to high thoracic levels would be expected to

A. Reduce minute ventilation
B. Increase the respiratory rate
C. Increase the work of breathing
D. Lower P_aO_2
E. Reduce expiratory reserve volume

22. A 56-year-old man is receiving epidural analgesia after a laparotomy and resection of a pancreatic lesion. Which of the following is TRUE regarding the use of opiates in the epidural solution?

A. Use of opiates in the epidural solution leads to a higher incidence of respiratory depression compared to a patient-controlled intravenous administration of opiates.
B. Both fentanyl and hydromorphone infusion in equipotent doses provide the same analgesic potency in a lumbar epidural for this patient.
C. The analgesic site of action for continuous infusion of a hydrophilic opioid is systemic.
D. A bolus of hydrophilic opiate will provide a more rapid onset of analgesia than a bolus of a lipophilic opiate.
E. A single bolus of fentanyl 100 mcg in the epidural space is an appropriate step in treating breakthrough pain in this patient.

23. All of the following are TRUE regarding an epidural test dose EXCEPT

A. Hemodynamic changes that occur after an epinephrine-containing test dose solution lead to decreased uteroplacental perfusion in an obstetric patient.
B. Injection of 15 mcg of epinephrine should yield a 15- to 20-bpm rise in heart rate if the catheter is intravascular.
C. Injection of 1 mL of air and hearing a mill-wheel murmur over the right heart with a Doppler is an appropriate test for intravascular injection.
D. Aspiration from a single-orifice catheter is more sensitive in detecting an intravascular epidural catheter compared to a multi-orifice catheter.
E. Injection of lidocaine 100 mg without epinephrine is an appropriate test dose to detect intravascular and/or intrathecal catheter placement.

24. All of the following are TRUE regarding neuraxial anesthesia EXCEPT

A. Neuraxial anesthesia blunts the body's stress response to surgery.
B. Neuraxial anesthesia leads to increased bleeding due to vasodilation.
C. Neuraxial anesthesia decreases the incidence of postoperative thromboembolic events.
D. Neuraxial anesthesia decreases perioperative morbidity and mortality in high-risk patients.
E. Neuraxial anesthesia can be used to extend analgesia into the postoperative period.

25. A 22-year-old athlete is scheduled for an anterior cruciate ligament reconstruction in an ambulatory surgery center. He would like to avoid general anesthesia. Which of the following will lead to a most complete analgesia and speedy recovery and discharge?

A. Spinal anesthesia with bupivacaine and morphine sulfate (Duramorph)
B. Femoral and obturator nerve block
C. Femoral and popliteal nerve block
D. Fascia iliaca block
E. Sciatic and femoral block

26. Which of the following statements is TRUE regarding a femoral nerve block?

A. The femoral nerve is located below both the fascia lata and fascia iliaca.
B. Stimulation of the sartorius muscle will lead to reliable anesthesia in the femoral nerve distribution.
C. The femoral nerve is approximately 1 cm medial to the femoral artery.
D. A femoral nerve block can provide complete anesthesia for a femoral fracture.
E. The needle entry point for a fascia iliaca block is at the intersection of the lateral two-thirds and the medial one-third of the line connecting the pubic tubercle and anterior superior iliac spine (inguinal ligament).

27. Which of the following is NOT a branch coming off from the T5 intercostal nerve?

A. Posterior cutaneous branch
B. Anterior cutaneous branch
C. Medial cutaneous branch
D. Lateral cutaneous branch
E. Gray ramus communicans

28. Which of the following will provide the most reliable analgesia for a chest tube placed in the midaxillary region?

A. Walking off cephalad from the rib and injecting 3 to 5 mL of local anesthetic at the angle of the rib posteriorly
B. Walking off cephalad from the rib and injecting 3 to 5 mL of local anesthetic 3 to 5 cm anterior to the insertion site
C. Walking off caudad from the rib and injecting 3 to 5 mL of local anesthetic just lateral to the sternum
D. Walking off caudad from the rib and injecting 3 to 5 mL of local anesthetic at the angle of the rib posteriorly
E. Walking off caudad from the rib and injecting 3 to 5 mL of local anesthetic just anterior to the insertion site

29. After successful placement of a brachial plexus block at the interscalene level for shoulder surgery, the surgeon informs you that he will need to operate on the hand also. An additional injection of local anesthetic at which of the following locations will most likely ensure adequate analgesia for the entire operation?

A. Adjacent to the brachial artery at the level of the elbow
B. At the groove formed by the olecranon and medial condyle of the humerus
C. At the level of the wrist, lateral to the radial artery near the tendons of the extensor pollicis brevis and extensor pollicis longus
D. At the upper arm, into the body of the coracobrachialis muscle
E. At the elbow level, 2 cm lateral to the biceps tendon

30. Which of the following factors and its effect on postoperative gastrointestinal (GI) motility are paired INCORRECTLY?

A. Use of epidural analgesia—Increased motility
B. Nitrous oxide—Decreased motility
C. Volatile anesthetics—Increased motility
D. Intravenous local anesthetics—Increased motility
E. Splanchnic nerve blockade—Increased motility

31. A 68-year-old, 80-kg man presents for surgery to release trigger fingers of the third and fourth digits of his right hand. The surgeon's time estimate for the surgery is 60 to 90 minutes. In performing IV regional anesthesia, injection of which of the following will provide safe and reliable surgical anesthesia for the hand?

A. 10 mL of 0.5% bupivacaine
B. 10 mL of 1% lidocaine
C. 10 mL of 0.25% bupivacaine
D. 20 mL of 0.125% bupivacaine
E. 50 mL of 0.5% lidocaine

32. Five minutes after intravascular injection of local anesthetic for an IV regional technique for hand surgery, the surgeon is notified that the equipment he needs is not available. It will take approximately 1 hour to get the instruments in the operating room. Which of the following options is appropriate for tourniquet management of this patient?

A. Deflate the tourniquet and perform an axillary block.
B. Deflate the tourniquet after 30 minutes and perform general anesthesia.
C. Deflate the tourniquet and perform general anesthesia.
D. Maintain the tourniquet and wait for the instruments.
E. Inject more lidocaine into the anesthetized hand to allow the block to last longer.

33. According to the guidelines for neuraxial anesthesia published by the American Society of Regional Anesthesia and Pain Medicine, which of the following statements concerning neuraxial anesthesia and anticoagulation is FALSE?

A. Patients receiving fractionated low-molecular-weight heparin (LMWH) preoperatively at thromboprophylactic doses should have the drug held for 12 hours before performing a neuraxial block.
B. There is no significant added risk of spinal hematomas for patients taking aspirin to undergo a neuraxial block.
C. Clopidogrel should be discontinued for 1 week, and ticlopidine for 2 weeks, prior to placing a neuraxial block.
D. Patients receiving thrombolytic therapy should wait 12 hours before receiving a neuraxial block.
E. There is no contraindication to performing a neuraxial block for patients on unfractionated heparin dosed at 5,000 units twice a day.

34. Which of the following shows the correct sequence of local anesthetics from least potent to most potent for peripheral nerve blockade?

A. Prilocaine < lidocaine < mepivacaine < bupivacaine
B. Mepivacaine < lidocaine < bupivacaine < ropivacaine
C. Mepivacaine < lidocaine < ropivacaine < bupivacaine
D. Lidocaine < mepivacaine < prilocaine < bupivacaine
E. Prilocaine < mepivacaine < lidocaine < bupivacaine

35. Which of the following is TRUE regarding regional anesthesia in pediatrics?

A. Pediatric patients have an increased volume of distribution.
B. Pediatric patients have increased protein binding of local anesthetics.
C. Pediatric patients have increased enzymatic activity and breakdown of local anesthetics.
D. Pediatric patients have decreased systemic absorbance of local anesthetics.
E. Adding epinephrine to local anesthetics is not as effective in prolonging blocks compared to adults.

36. Which of the following statements is FALSE?

A. Commercially available premixed solutions of local anesthetics with epinephrine are more basic in order to preserve the potency of epinephrine.
B. Epinephrine added to ropivacaine will intensify blockade but not prolong the duration of an epidural block.
C. Epinephrine can more effectively prolong the effects of lidocaine and 2-chloroprocaine than bupivacaine.
D. The addition of epinephrine can more effectively decrease plasma lidocaine and 2-chloroprocaine levels than plasma bupivacaine levels.
E. Epinephrine contributes to analgesia in the neuraxis due to its presynaptic adrenergic receptor activity.

37. Which of the following statements is FALSE?

A. Addition of 1 mL of 8.4% $NaHCO_3$ (sodium bicarbonate) to 9 mL of 2% lidocaine will increase the speed of onset of a neuraxial block.
B. Alkalinization of bupivacaine will decrease the time of onset of an epidural block.

C. Alkalinization of ropivacaine does not result in a faster onset of block.
D. Alkalinization of ropivacaine is less likely to result in precipitation than alkalinization of bupivacaine.
E. Alkalinization of a local anesthetic solution increases the un-ionized fraction of anesthetic.

38. A patient who previously developed profound hypotension, tachycardia, and bronchospasm after receiving procaine could develop a similar reaction if he were to receive

A. 2-chloroprocaine
B. Lidocaine
C. Ropivacaine
D. Mepivacaine
E. Any other local anesthetic

39. Blockade of all of the following combinations of nerves EXCEPT which one will provide adequate anesthesia for surgery of the entire foot?

A. Femoral, sciatic
B. Popliteal, saphenous
C. Sural, saphenous, deep peroneal, superficial peroneal, posterior tibial
D. Obturator, sciatic, sural, posterior tibial
E. Common peroneal, tibial, femoral

40. Extravasation of a large amount of intravenous fluid was noticed at a peripherally placed IV catheter at the antecubital fossa. An hour later, the patient complains of tingling in his thumb and index and middle fingers, as well as weakness on thumb opposition. Which nerve is most likely injured?

A. Radial nerve
B. Ulnar nerve
C. Musculocutaneous nerve
D. Recurrent branch of the median nerve
E. Median nerve

41. A patient in the intensive care unit is to undergo a bedside bronchoscopic procedure. His nasopharynx was lubricated with viscous lidocaine and the oropharynx was sprayed twice with 20% benzocaine solution. Fifteen minutes into the procedure, the patient becomes cyanotic and oxygen saturation by pulse oximetry has dropped from 97% to 70%. His blood pressure has been unchanged but he has become slightly tachycardic. Soon the patient develops tachypnea and appears to be in significant respiratory distress. His trachea is immediately intubated, and an inspired oxygen fraction of 1.0 is delivered. His oxygen saturation improves to 85%, but an arterial blood gas analysis shows an arterial oxygen tension of 390 mm Hg. Which of the following would most likely confirm your diagnosis?

A. A stat portable chest x-ray
B. Co-oximetry analysis of an arterial blood gas
C. CT of his chest
D. Continued bronchoscopy will reveal the etiology of his respiratory failure.
E. A transesophageal echocardiogram

42. Which statement regarding methylparaben is FALSE?

A. Most allergic reactions to methylparaben are IgE-mediated.
B. Cross-sensitivity between methylparaben and ester-type local anesthetics does occur.
C. Antimicrobial activity from methylparaben and similar preservatives is temperature-dependent.
D. Methylparaben in combination with lidocaine has greater bactericidal activity than lidocaine alone.
E. Methylparaben alone is a less effective antimicrobial agent than when combined with a local anesthetic.

43. Which combination of nerves, when blocked, will provide adequate anesthesia for knee surgery?

A. Lumbar plexus
B. Femoral nerve, lateral femoral cutaneous nerve, sciatic nerve
C. Lumbar plexus, obturator nerve, lateral femoral cutaneous nerve
D. Femoral nerve, sciatic nerve, obturator nerve
E. Femoral nerve, lateral femoral cutaneous nerve, popliteal fossa

44. Which of the following solutions, given through a L3–4 epidural catheter, will result in a block of longest duration?

A. 10 mL of 0.5% bupivacaine
B. 10 mL of 3% 2-chloroprocaine with epinephrine
C. 10 mL of 0.5% ropivacaine
D. 10 mL of 2% lidocaine
E. 10 mL of 2% mepivacaine with epinephrine

45. In regards to the oculocardiac reflex (OCR), which of the following statements is FALSE?

A. The afferent pathway involves the ophthalmic division of the trigeminal nerve, and the efferent pathway is mediated by the vagus nerve.
B. The ciliary and gasserian ganglions are involved in the pathway.
C. Deep anesthesia potentiates this pathway and should be avoided.

D. The OCR can occur during placement of a retrobulbar block.
E. The OCR can result in ventricular fibrillation and nodal rhythms.

46. All of the following are complications of pediatric caudal anesthesia EXCEPT

A. Infections with the use of a caudal catheter
B. A postdural puncture headache
C. Seizures
D. Total spinal anesthesia
E. Profound hypotension with a caudal injection to the T6 level

47. Compared to adults, in the pediatric patient

A. The dural sac ends at a lower level
B. The CSF volume per kilogram of body weight is less
C. "Loss of resistance" is usually more prominent during placement of an epidural
D. The upper limit to local anesthetic dosing is greater than in adults
E. Volume of distribution of local anesthetic is smaller than in adults

48. Which of the following combinations of nerves, when blocked, will facilitate an awake fiberoptic nasotracheal intubation?

A. Trigeminal, glossopharyngeal, superior laryngeal
B. Facial, glossopharyngeal, superior laryngeal, recurrent laryngeal
C. Trigeminal, glossopharyngeal, recurrent laryngeal
D. Lingual, glossopharyngeal, superior laryngeal
E. Maxillary, glossopharyngeal, superior laryngeal

49. In regards to phenol and alcohol as neurolytic agents, which of the following statements is correct?

A. Injection with phenol is more painful than injection with alcohol.
B. Peripheral neurolysis with alcohol, but not phenol, can lead to denervation pain.
C. Alcohol neurolysis is more intense.
D. Alcohol has a biphasic action as a local anesthetic and a neurolytic.
E. Neurolysis with phenol is usually permanent.

50. Which of the following statements about peripheral nociceptors is INCORRECT?

A. Nociceptors are present at the free nerve endings of C and Aδ fibers.
B. The amount of neural activity in nociceptive efferents does not depend on intensity and duration; it is an all-or-none response.
C. Skin rubbing and vibration may decrease the nociceptive neuronal activity.
D. Sensitization of nociceptors occurs by repeated noxious stimuli.
E. Primary hyperalgesia is associated with a lowered pain threshold and spontaneous pain.

51. Which of the following statements is CORRECT?

A. A prodrome of dermatomal pain usually precedes the appearance of a rash.
B. The majority of patients with herpes zoster will develop postherpetic neuralgia (PHN).
C. Symphathetic nerve blocks can reliably reduce pain in patients with herpes zoster and PHN.
D. Antiviral agents such as acyclovir can reliably reduce pain in patients with herpes zoster and PHN.
E. Amitriptyline is effective for treatment of acute herpes zoster pain.

52. Regional anesthesia at which of the following locations would provide adequate analgesia for surgery at the ankle?

A. Injection lateral to the femoral artery, and injection inferolateral to the pubic symphysis
B. Injection in the fascial plane between the vastus medialus and sartorius, and injection at the popliteal fossa
C. Injections in the intermuscular fascial planes between the adductor brevis and adductor longus, and between the adductor brevis and adductor magnus
D. Injection medial to the femoral artery, and injection at the popliteal fossa
E. Injection in the psoas compartment, and injection between the vastus medialis and sartorius

53. Regional anesthesia at which of the following locations would provide adequate analgesia for surgery at the elbow?

A. Injection lateral to the subclavian artery above the first rib
B. Injection medial to the subclavian artery above the first rib
C. Injection between the sternocleidomastoid and anterior scalene at the level of the cricoid cartilage
D. Injection beneath the middle scalene muscle at the level of the cricoid cartilage
E. Injection around the axillary vein and beneath the pectoralis major and minor muscles using the infraclavicular approach

54. Which of the following blocks would NOT be expected to provide adequate analgesia during the first stage of labor?

A. Paracervical block
B. Pudendal block
C. Caudal block
D. Paravertebral lumbar sympathetic block
E. Continuous spinal block

55. After placement of a retrobulbar block by an ophthalmologist, you notice that the patient has lost consciousness, is unarousable, and is not making any respiratory effort. Which of the following is most likely to account for this situation?

A. Inadvertent intra-arterial injection
B. Stimulation of the oculocardiac reflex (OCR)
C. Retrobulbar hemorrhage
D. Brainstem anesthesia
E. Too much intravenous sedation was administered prior to block placement

56. To perform a sciatic nerve block via a posterior approach, which of the following structures need to be identified?

A. Greater trochanter, sacral hiatus, posterior superior iliac spine
B. Greater trochanter, sacral hiatus, iliac crest
C. Greater trochanter, sacral hiatus, anterior superior iliac spine
D. Greater trochanter, ischial tuberosity, sacral hiatus
E. Anterior superior iliac spine, pubic tubercle

57. Which of the following nerves provides sensory innervation to the lateral forearm?

A. The radial nerve
B. The median nerve
C. The medial cutaneous nerve of the forearm
D. The lateral cutaneous nerve of the forearm
E. The intercostobrachial nerve

58. Which cord(s) of the brachial plexus is responsible for sensory innervation of the skin over the extensor surface of the forearm to the wrist?

A. Anterior cord
B. Lateral cord
C. Medial cord
D. Posterior cord
E. Lateral and posterior cords

59. Spinal anesthesia can have all of the following expected effects on cardiovascular physiology EXCEPT

A. Hypotension
B. Bradycardia
C. Decreased right-sided filling pressures
D. Decrease in total peripheral resistance
E. An increase in preload

60. Which of the following statements is FALSE concerning postdural puncture headaches (PDPH)?

A. It happens more commonly in patients with increased age.
B. It usually resolves spontaneously for most patients.
C. Bedrest, analgesics, and caffeine can produce relief of symptoms.
D. It is more common in parturients.
E. The headache is usually worsened by head elevation and occurs in a fronto-occipital distribution.

61. Spinal anesthesia to a T4 level would be expected to cause

A. A decrease in dead space
B. An increase in $PaCO_2$
C. Dyspnea due to hypoxemia
D. A decrement in active exhalation
E. Impairment in diaphragmatic function

62. A patient receives a spinal dose of 2 cc of 0.75% bupivacaine in dextrose at the L3–4 level and then lies supine. 5 minutes later, his heart rate decreases from 80 bpm to 45 bpm, and his BP decreases from 120/80 to 70/45. Appropriate therapeutic maneuvers at this point would include any of the following EXCEPT

A. Ephedrine 10 mg IV
B. Phenylephrine 100 mcg IV
C. Intravenous fluid bolus and Trendelenburg position
D. Epinephrine 5 mcg IV
E. Epinephrine 10 mcg IV

63. While performing a stellate ganglion block, which of the following potential complications is most likely to happen?

A. Injection into the basilar artery
B. Injection into the vertebral artery
C. Injection into the carotid artery
D. Injection into the internal jugular vein
E. Injection into the subclavian artery

64. Which of the following is TRUE regarding a paramedian approach to neuraxial block?

A. A paramedian approach is generally less painful compared to a midline approach.
B. The needle insertion point is approximately 3 to 5 cm lateral to midline.
C. A paramedian approach requires less patient cooperation to reduce lumbar lordosis.
D. The L4–5 has the largest interlaminar space in the lumbosacral region and is used in the Taylor variation of the paramedian technique.
E. The paramedian approach is generally more difficult because a smaller opening is available to access the epidural and intrathecal space.

65. A 67-year-old man is 4 hours status post bilateral hip replacement. The procedure was done with a combined spinal and epidural technique. The epidural catheter remains in place and was bolused with 15 mL of bupivacaine 0.25%. Within 2 minutes the patient becomes hypotensive and becomes unresponsive. Which of the following maneuver is NOT appropriate in this setting?

A. Place patient in Trendelenburg position.
B. Administer Intralipid.
C. Administer ephedrine.
D. Endotracheal intubation
E. Administer epinephrine.

66. After administration of an uneventful spinal anesthetic for a total knee replacement, the patient is positioned and draped. The patient denies pain with the surgical test but expresses pain upon surgical incision. Which of the following would NOT be an appropriate next step in the management of this patient?

A. Administration of 60% nitrous oxide with oxygen through a mask
B. Administration of incremental intravenous ketamine 0.1 to 0.25 mg/kg
C. Conversion to general anesthesia
D. Reassurance of the patient that analgesia is adequate since it was tested before the incision
E. Small boluses of intravenous fentanyl

67. An intrathecal injection of bupivacaine 15 mg in dextrose is likely to result in a higher-than-expected level of anesthesia for all of the following patients EXCEPT

A. A 30-year-old term parturient
B. A 24-year-old woman with a BMI of 40
C. A 50-year-old man with a large abdominal tumor
D. A 45-year-old woman with significant abdominal ascites
E. A 35-year-old man with myasthenia gravis

68. Which of the following statements is FALSE?

A. The adult subarachnoid space extends from the foramen magnum to S2.
B. Injection of local anesthetic below the L1 level in adults should avoid direct trauma to the cord.
C. Injection of local anesthetic below the L2 level in children should avoid direct trauma to the cord.
D. Injection of local anesthetic below the L3 level in children should avoid direct trauma to the cord.
E. The subarachnoid space extends from the foramen magnum to S3 in children.

69. You are performing a spinal for a cesarean delivery through a midline approach. The needle should pass through all of the following structures prior to visualizing CSF EXCEPT

A. Posterior longitudinal ligament
B. Ligamentum flavum
C. Supraspinous ligament
D. Intraspinous ligament
E. Dura mater

70. When performing a subarachnoid block using the midline technique, which of the following is the most correct sequence of structures encountered with the spinal needle before finding CSF?

A. Skin, subcutaneous tissue, intraspinous ligament, epidural space, ligamentum flavum, dura
B. Skin, subcutaneous tissue, supraspinous ligament, intraspinous ligament, ligamentum flavum, epidural space, dura, pia
C. Skin, subcutaneous tissue, intraspinous ligament, ligamentum flavum, epidural space, dura, pia
D. Skin, subcutaneous tissue, supraspinous ligament, intraspinous ligament, ligamentum flavum, epidural space, dura, arachnoid
E. Skin, subcutaneous tissue, supraspinous ligament, intraspinous ligament, ligamentum flavum, epidural space, dura, pia, arachnoid

71. A patient undergoes transurethral surgery of the prostate under spinal anesthesia with lidocaine. The patient recovers well in the postoperative period, with return of sensory and motor responses, and is then discharged home 3 hours after his surgery. The next morning, he notices significant pain in his buttocks and bilateral legs

down to the knee. Which of the following conditions is he most likely to have?

A. Meralgia paresthetica
B. An intrathecal hematoma
C. Cauda equina syndrome
D. Transient neurologic symptoms
E. An abscess is developing near the subarachnoid space due to inadequate sterile precautions prior to block placement.

72. While you are performing an awake fiberoptic intubation, the patient starts coughing when your bronchoscope contacts the posterior side of the epiglottis. Which of the following maneuvers will most likely correct this problem?

A. Bilateral injections of 2 mL of 1% lidocaine into the base of the anterior tonsillar pillar
B. An injection of 4 mL of 4% lidocaine through the cricothyroid membrane into the trachea
C. Bilateral injections of 2 mL of 1% lidocaine at the level of the thyrohyoid membrane just below the greater cornu of the thyroid cartilage
D. Placing local anesthetic-soaked swabs against the inferior aspects of the palatoglossal folds
E. Bilateral injections of 10 mL of 1% lidocaine at the posterior border of the sternocleidomastoid at and near the level of C4

73. Tourniquet use during total knee arthroplasty can result in which of the following?

A. A decreased incidence of wound complications
B. Decreased pain in the postoperative period
C. Acute pulmonary edema upon tourniquet release
D. Quicker recovery of muscle power postoperatively
E. Lack of electromyographic changes postoperatively

74. Which of the following statements is TRUE regarding ultrasound and resolution of the image?

A. Increasing the gain will lead to improved resolution.
B. Increasing the frequency will lead to improved resolution.
C. Decreasing the frequency will lead to improved resolution.
D. Decreasing the gain will lead to improved resolution.
E. Neither gain nor frequency has any effect on the resolution of the image.

75. Which of the following statements is FALSE when comparing ultrasound-guided nerve block with the nerve stimulation technique?

A. Identification of the nerves and other anatomic structures provides an advantage for using ultrasound.
B. Observation of the needle and the spread of local anesthetic is possible using ultrasound.
C. Studies have shown that a decreased volume of injected local anesthetic is needed if using an ultrasound technique compared to a nerve stimulator technique.
D. Randomized clinical trials have shown that complication rates are lower with the use of an ultrasound technique.
E. Performing a nerve block with a nerve stimulator can be more painful for patients compared to an ultrasound technique.

76. When performing an interscalene block with an ultrasound with an in-plane posterior approach, the needle can be visualized going through which of the following structures?

A. Middle scalene muscle
B. Anterior scalene muscle
C. Adjacent to the phrenic nerve
D. Sternocleidomastoid muscle
E. Adjacent to the internal jugular vein

77. A 23-year-old woman just had a stat cesarean section under general anesthesia for fetal bradycardia. She is having severe incisional pain despite intravenous opiates and she is concerned about opiates and breastfeeding. Injection of a local anesthetic in which of the following spaces will lead to reliable analgesia for this patient?

A. Injection deep to the transversus abdominis muscle
B. Injection just superficial to the external oblique muscle
C. Injection in the plane between the external oblique and internal oblique muscles
D. Injection in the midline just cephalad to the incision
E. Injection between the transversus abdominis muscle and the internal oblique muscle

78. Indications for a neurolytic block include all of the following EXCEPT

A. Pain is severe and intractable
B. Intolerable side effects of parenteral analgesics
C. Pain mechanism is primarily neuropathic in nature
D. Pain must be relieved by a diagnostic block
E. Pain is limited to one or two dermatomes

79. Which of the following choices is correct regarding intrathecal neurolytic injection?

A. Both ethanol and phenol are hyperbaric relative to CSF.
B. Both ethanol and phenol are hypobaric relative to CSF.
C. Both ethanol and phenol are isobaric relative to CSF.
D. Ethanol is hypobaric and phenol is hyperbaric relative to CSF.
E. Ethanol is hyperbaric and phenol is hypobaric relative to CSF.

80. Which statement about intrathecal neurolytic blocks is INCORRECT?

A. This block is very useful for extensive and poorly localized pain.
B. Major side effects are skeletal muscle weakness as well as rectal and bladder sphincter dysfunction.
C. Analgesia can last for weeks to months.
D. Neurolytic agents destroy axons through Wallerian degeneration.
E. Intrathecal neurolysis can be repeated as necessary if the pain returns.

81. Which order of systemic local anesthetic toxicity is correct?

A. Intercostal > caudal > epidural > sciatic > brachial plexus
B. Epidural > caudal > intercostal > brachial plexus > sciatic
C. Intercostal > caudal > epidural > brachial plexus > sciatic
D. Caudal > intercostal > brachial plexus > epidural > sciatic
E. Intercostal > caudal > epidural > sciatic > brachial plexus

CHAPTER 7 ANSWERS

1. ANSWER: A

By adding a local anesthetic to the opiate in the epidural infusion, there is a decreased requirement of the opioid concentration, which will lead to overall decreased opioid use. This leads to decreased opiate side effects such as pruritus, nausea, and respiratory depression. The local anesthetic, on the other hand, can cause motor blockage and sympathectomy, which leads to an increased incidence of hypotension. Motor blockade and sympathectomy are not seen with opiate-only epidural infusion. Finally, the combination of opiates and local anesthetics leads to superior analgesia, including improved dynamic pain relief, leading to decreased breakthrough pain.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2767.

2. ANSWER: C

By inhibiting sympathetic outflow and attenuating spinal reflex inhibition of the GI tract, epidural analgesia can facilitate the return of GI tract motility. It has been shown that thoracic epidural analgesia with a local anesthetic decreases the incidence of pulmonary infections and complications compared with epidural opioids alone, wound infiltration with local anesthetic, intercostal blocks, and intrapleural analgesia. Thoracic epidural analgesia reduces splinting behavior and attenuates the spinal reflex inhibition of diaphragmatic function. It also decreases the severity and size of myocardial infarction, as well as attenuation of sympathetically mediated coronary vasoconstriction and improvement in coronary blood flow to areas at risk.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2770.

3. ANSWER: E

An axillary block is not suitable for surgery of the upper arm. An interscalene block is performed at the level of the trunks and is the most proximal block of the brachial plexus, which is derived from C5–T1 nerve roots. The intercostobrachial nerve innervates the medial aspect of the upper arm and is derived from T2, and hence is not blocked with any brachial plexus block. A supraclavicular block is performed at the level of distal trunks/proximal divisions and NOT at the level of the cords. An infraclavicular block is performed at the level of the cords and NOT the trunks. Surgery for this patient can be performed by sedation and local infiltration by the surgeon. Interscalene, supraclavicular, and infraclavicular blocks could all provide adequate analgesia for this procedure as well.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1640–1646.

4. ANSWER: C

The saphenous nerve is a terminal branch of the femoral nerve. All the other nerves listed are terminal branches of the sciatic nerve.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1659.

5. ANSWER: B

A review of 300 patients with ***spinal cord injury*** has shown that autonomic hyperreflexia does not develop if the lesion is below T7. The trigger could be a cutaneous, proprioceptive, or visceral stimulus (full bladder is a common trigger) that leads to sympathetic discharge without upper-level inhibition. This results in hypertension, bradycardia, and headaches. Vasodilation occurs above the level of the lesion, resulting in flushing of the head and neck. The patient may develop these symptoms without experiencing any pain. An epidural is recommended to blunt the sympathetic discharge. The intermediate period, often quoted between 3 days to 6 months, is the period when marked hyperkalemia occurs as a result of succinylcholine administration.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Elsevier Churchill Livingstone, 2004:1044.

6. ANSWER: A

In the axilla, the radial, ulnar, and median nerves are often traveling with the axillary artery and are blocked individually or sometimes together. The musculocutaneous nerve can be blocked as it runs in the coracobrachialis muscle. The intercostobrachial nerve (T2), which is not part of the brachial plexus, can be blocked in the axilla by injecting a subcutaneous band of local anesthetic on the medial surface of the arm in the axilla. This aids with pain as a result of tourniquet application. There is no motor innervation with the intercostobrachial nerve. The axillary nerve is one of five terminal branches of the brachial plexus, but is not blocked in the axilla.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1640–1648.

7. ANSWER: D

A median nerve block covers the palmar aspect of the thumb and index finger, the middle finger, and the lateral aspect of the ring finger, including the lateral palmar surface. The medial palmar surface as well as the medial aspect of the ring finger and the little finger is innervated by the ulnar nerve. The radial nerve innervates the lateral aspect of the dorsum of the hand and the proximal thumb and index and middle finger.

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1640–1648.

8. ANSWER: E

Hypercapnia increases cerebral blood flow and allows more bupivacaine to be delivered to the brain. Combined respiratory and metabolic acidosis decreases plasma protein binding of bupivacaine, which leads to a higher concentration in the plasma, leading to further exacerbation of toxicity. CNS stimulation occurs first as the inhibitory pathways are blocked first, allowing uninhibited discharge of neurons in the cerebral cortex. This is followed by CNS depression as both inhibitory and excitatory neurons are inhibited. The CC/CNS ratio is lower for bupivacaine, meaning there is a smaller difference in doses required to cause CNS toxicity and cardiovascular toxicity. This smaller difference leads to a concern that CNS toxicity is not always detected prior to devastating cardiac toxicity. Tonic clonic seizures may lead to severe skeletal muscle contractions, leading to acidosis. Administration of succinylcholine will prevent this from occurring.

KEY FACTS: LOCAL ANESTHETIC TOXICITY SYMPTOMS

- Numbness of tongue
- Tinnitus
- Lightheadedness, dizziness
- Visual and auditory disturbances
- Shivering
- Muscular twitching
- Seizures
- Unconsciousness
- Convulsions
- Coma
- Respiratory arrest
- Cardiac arrest

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Elsevier Churchill Livingstone, 2004:593–595, 1676.

9. ANSWER: B

All local anesthetics cause a dose-dependent prolongation of cardiac conduction, as evidenced by increased PR intervals and QRS durations on the EKG. This is related to persistent blockade of sodium channels, which predisposes the heart to re-entrant arrhythmias. Since the dissociation constant of bupivacaine is almost 10 times greater than that of lidocaine, bupivacaine is more likely than lidocaine to cause cardiac depression. Local anesthetics also affect potassium channel conduction, prolonging the QTc interval and enhancing inactivation of sodium channels. The dextrorotatory (R+) isomer of bupivacaine is 7 times more potent in blocking potassium channels than the levo-rotatory (S–) isomer. Cardiac toxicity is also related to the lipid solubility and potency of local anesthetics. R(+) bupivacaine has the highest cardiotoxic potency. Racemic bupivacaine is less cardiotoxic (a mixture of R and S), followed by S(−) bupivacaine, then ropivacaine. Ropivacaine is a single levorotatory isomer. Levo-bupivacaine is the same as S(−) bupivacaine. The "R" and "S" prefixes specify the characteristics of a specific chiral center while the "D" and "L" refer to the physical property of rotating polarized light clockwise or counterclockwise, respectively.

ADDITIONAL READING

Casati A, Putzu M. Bupivacaine, levobupivacaine and ropivacaine: are they clinically different? *Best Pract Res Clin Anesthesiol*. 2005;19:247–268.

10. ANSWER: A

The patient is exhibiting signs of ***CNS toxicity***, most likely from local anesthetic administration. A double-blind crossover study of volunteers showed no difference between levo(S–)bupivacaine and ropivacaine in terms of time to first onset of CNS symptoms and mean total volume of study drug administered at the onset of symptoms. Other studies have shown that 10% to 25% larger doses of levobupivacaine and ropivacaine than bupivacaine can be administered before signs of CNS toxicity occur. Lidocaine and mepivacaine are less likely than bupivacaine to produce CNS and cardiac toxicities.

ADDITIONAL READING

Casati A, Putzu M. Bupivacaine, levobupivacaine and ropivacaine: are they clinically different? *Best Pract Res Clin Anesthesiol*. 2005;19:247–268.

11. ANSWER: C

Both lidocaine and bupivacaine depress rapid depolarization in Purkinje fibers; however, lidocaine depresses the depolarization to a lesser extent and has a more rapid rate of recovery. These effects lead to pro- versus anti-arrhythmic properties of lidocaine and bupivacaine. All local anesthetics have a dose-dependent negative inotropic effect on cardiac myocytes and lead to prolonged conduction time, leading to an increased PR interval and widened QRS. Large doses of dilute lidocaine used in tumescent anesthesia (35 to 55 mg/kg) may lead to cardiac toxicity and death.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Elsevier Churchill Livingstone, 2004:591, 593–595.

12. ANSWER: B

The celiac plexus contains fibers from T5–12 and has no somatic fibers. A ***celiac plexus block*** is performed at the L1 level just anterior to the L1 vertebral body and leads to autonomic blockade, leading to decreased stress and endocrine response to surgery. The plexus innervates most of the abdominal visceral organs. Its side effects/complications include diarrhea, hypotension, inadvertent injection into the intrathecal and epidural space, as well as puncture of kidneys, ureters, aorta, vena cava, and bowel.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1669–1670.

13. ANSWER: C

The cervical plexus is made up of C4–6 nerve roots. A superficial cervical plexus block only affects sensory nerves and is done posterior to the sternocleidomastoid muscle. A deep cervical plexus block is done at the transverse processes of C4, 5, and 6 and frequently leads to phrenic nerve paralysis (C3–5) as well as paralysis of other muscles in the neck, including the sternocleidomastoid. Vertebral artery injection is a major vascular complication that may occur during the deep cervical plexus block; it may lead to CNS depression, seizures, and stroke. Spinal and epidural injections are also possible.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:720–721.

14. ANSWER: B

Cocaine is a local anesthetic, and all local anesthetics are sodium channel blockers. There are two major classes of local anesthetics, aminoesters (cocaine, procaine, and tetracaine) and aminoamides (lidocaine, mepivacaine, ropivacaine, and bupivacaine).

All amides are more stable in solution. ***Aminoesters*** are hydrolyzed by plasma esterases, except cocaine, which is metabolized by hepatic carboxylesterases. ***Aminoamides*** undergo enzymatic breakdown in the liver. Cocaine prevents reuptake of catecholamines, leading to hypertension, tachycardia, angina, myocardial infarctions, and strokes. It does NOT cause release of catecholamines.

KEY FACTS: AMIDE AND ESTER LOCAL ANESTHETICS

Amide local anesthetics	Two "i"s in the name (lidocaine) Metabolized in the liver Clearance: bupivacaine < mepivacaine < lidocaine < etidocaine < prilocaine
Ester local anesthetics	Metabolized by pseudocholinesterase (cocaine is an exception) PABA derivative Duration prolonged in liver disease, neonates, and atypical cholinesterase carriers

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:913, 923, 933.

15. ANSWER: C

Different fibers have different susceptibility to local anesthetic blockade. Small myelinated B fibers are most susceptible, followed by small myelinated axons Aγ (motor) and Aδ (sensory). Next are large myelinated axons Aα (efferent to muscles) and Aβ (proprioception), and finally the least susceptible are the small nonmyelinated C fibers. The thought that local anesthetics block the smallest fibers first is incorrect.

KEY FACTS: NERVE FIBERS

A-alpha	Motor function
A-beta	Proprioception
A-gamma	Muscle tone
A-delta	Pain (myelinated), touch, temperature
B	Autonomic system (preganglionic)
C	Autonomic system (postganglionic), pain, temperature (unmyelinated)

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:917, 921–992.

16. ANSWER: A

Neuraxial opioids can lead to sensory changes, as well as nausea and vomiting, pruritus, hypotension, respiratory depression as well as urinary retention. In one study, reactivation of oral HSV was found to occur in 10% of parturients who received epidural morphine and in only 1% of patients who did not receive epidural morphine. Parenteral opioids also cause delayed gastric emptying. Intrathecal administration of fentanyl produces greater delays in gastric emptying compared to epidural fentanyl administration. Neurotoxicity is not associated with intrathecal or epidural administration of opioids; however, concentrated local anesthetic (lidocaine) in the intrathecal space is associated with transient neurologic symptoms.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:266–270.

17. ANSWER: E

Plica mediana dorsalis has been visualized in epiduroscopies and epidurographies, but its clinical significance has been debated. When present, it extends from the dura mater toward the ligamentum flavum, and thus it can cause problems with threading the catheter or lead to a unilateral block. It will not result in a unilateral spinal block since it does not extend beyond the dura and is not present in the intrathecal space. Again, it does not appear to have major clinical significance.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:690–691.

18. ANSWER: A

The potential space between the dura mater and arachnoid mater is called the subdural space. It does not contain CSF, but may contain a very small amount of serous fluid. Accidental subdural injection may occur during both attempted epidural and intrathecal injection and characteristically leads to a patchy block. It has been estimated to occur in less than 1% of intended epidural injections. The space between the dura mater and ligamentum flavum is the epidural space.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:691.

19. ANSWER: D

Mid-thoracic-level epidural anesthesia with local anesthetic-only solution leads to decreased stroke volume, cardiac output, mean arterial pressure, and peripheral vascular resistance. If the solution contains epinephrine as well as local anesthetic, stroke volume and cardiac output both increase; however, the drop in peripheral vascular resistance and mean arterial pressure is more dramatic. A mid-thoracic-level epidural block produces no change in lung volumes, resting minute ventilation, dead space, or shunt fraction.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:705–707.

20. ANSWER: D

Both spinal and epidural anesthesia increase the sweating threshold and decrease the threshold for vasoconstriction and shivering. This is unrelated to plasma levels of local anesthetics, as both spinal anesthesia and epidural anesthesia produce the same effect, and administration of intravenous lidocaine equivalent to plasma levels obtained from an epidural infusion does not produce the same effect. Epidural anesthesia also decreases the maximum intensity of shivering as well as the gain of shivering as the body temperature decreases.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1539–1541.

21. ANSWER: E

Even with a high thoracic epidural block, lung volumes (tidal volume, vital capacity) and resting minute ventilation are mostly unchanged. In patients dependent on accessory muscle function to maintain adequate ventilation, a thoracic epidural could affect forced expiratory maneuvers. However, in a study by Gruber et al. involving patients with end-stage chronic obstructive pulmonary disease undergoing lung-volume-reduction surgery, thoracic epidural analgesia (T2–T8) with 0.25% bupivacaine did not adversely affect minute ventilation, tidal volume, respiratory rate, P_aO_2, P_aCO_2, peak inspiratory and expiratory flow rates, and work of breathing. Historically, high spinal and epidural blockade have been shown to lead to reductions in vital capacity, inspiratory capacity, and expiratory reserve volume.

ADDITIONAL READINGS

Gruber EM, Tschernko EM, Kritzinger M. The effects of thoracic epidural analgesia with bupivacaine 0.25% on ventilatory mechanics in patients with severe chronic obstructive pulmonary disease. *Anesth Analg*. 2001;92:1015–1019.

Freund FG, Bonica JJ, Ward RJ. Ventilatory reserve and level of motor block during high spinal and epidural anesthesia. *Anesthesiology*. 1967;28:834–837.

22. ANSWER: E

Neuraxial opiates lead to respiratory depression in a dose-dependent manner; however, the incidence of respiratory depression is no more than with intravenous administration. Fentanyl and other lipophilic opiates provide less cephalad spread compared to hydromorphone and morphine and would be less useful in a lumbar epidural in this patient with a thoracic-level incision. The analgesic site of action for hydrophilic opiate infusions is primarily spinal. The analgesic site of action for lipophilic drugs depends on the mode of administration. It's been shown that epidural infusion of these drugs has primarily a systemic effect, while single boluses act primarily on the spine. A lipophilic opiate injection has a more rapid onset than a hydrophilic opiate in the epidural space; because of this, a single bolus of fentanyl 25 to 100 mcg is an appropriate step in treating breakthrough pain in this patient.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2765–2770.

23. ANSWER: D

The most commonly used test dose is perhaps the lidocaine solution containing epinephrine. Injection of 15 mcg of epinephrine will often lead to a rise in heart rate by 15 to 20 bpm. In the obstetric patient, the pain from uterine contractions may lead to an increase in heart rate and false-positive test results. Also, injection of epinephrine, if the catheter is indeed intravascular, will lead to decreased uteroplacental perfusion; however, these changes in perfusion are transient and perhaps of less duration compared to the decreased perfusion from uterine contractions. Injection of 1 mL of air and using a Doppler to listen for mill-wheel murmur over the right heart is an appropriate test for detecting

an intravascular catheter. A multi-orifice catheter is 98% sensitive in identifying intravascular location. With a single-orifice catheter, aspiration reportedly fails to detect 34% to 81% of intravascular catheters. A lidocaine 100 mg injection without epinephrine is a large enough dose to produce dizziness, tinnitus, and perioral numbness if the catheter is intravascular, and an intrathecal catheter should produce a profound spinal anesthesia and is considered an appropriate test dose. The same is true for 25 mg of bupivacaine without epinephrine. The goal is to inject a subtoxic dose of a local anesthetic to cause symptoms with intravascular and intrathecal injections without causing systemic toxicity or a total spinal.

ADDITIONAL READINGS

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:239–240.

Norris MC, et al. Does epinephrine improve the diagnostic accuracy of aspiration during labor epidural analgesia? *Anesth Analg.* 1999;88:1073–1076.

24. ANSWER: B

Neuraxial anesthesia has been shown to decrease intraoperative blood loss, as well as decrease the body's stress response, decrease the incidence of thromboembolic events, and decrease perioperative morbidity and mortality. Both spinals and epidurals can be used to extend analgesia into the postoperative period. Injecting morphine into the intrathecal spaces as well as the epidural space prolongs analgesia beyond the intraoperative period. In addition, an epidural catheter may be used in the postoperative period to provide analgesia.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:689.

25. ANSWER: E

Spinal anesthesia will lead to complete analgesia for the surgery; however, in the outpatient setting, bupivacaine may lead to prolonged difficulty with voiding. Also, Duramorph is reserved for inpatients, as there may be a delayed-onset (12–16 hours) respiratory depression. Femoral and obturator nerve blocks will cover the anteromedial aspect of the knee but not the posterior, which comes from the sciatic nerve. A nerve block in the popliteal fossa will likely not cover the pain. The sciatic nerve must be blocked more cephalad, above the bifurcation into the tibial nerve and the common peroneal nerve. A fascia iliaca block will also miss the posterior aspect of the knee.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1652–1659.

26. ANSWER: A

The femoral nerve is located 1 cm lateral to the femoral artery, which is lateral to the femoral vein. The nerve is located deep to the fascia lata and fascia iliacus (two "pops") and can be blocked by performing a fascia iliaca compartment block. Stimulation of the sartorius muscle will not provide reliable anesthesia in the femoral distribution. A quadriceps twitch/patellar retraction is required for reliable anesthesia. A properly placed femoral block should provide anesthesia for a patellar fracture, but not necessarily a femoral fracture, as the femoral nerve supplies only the anterior thigh, but not lateral, medial, or posterior thigh. For a fascia iliaca block, the intersection of the medial two-thirds and the lateral one-third of the line is used (well away from the femoral artery).

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1652–1655.

27. ANSWER: C

Each intercostal nerve has four branches. The gray ramus communicans passes anterior to the sympathetic ganglion. The posterior cutaneous branch supplies the skin and paravertebral area; the lateral cutaneous branch arises in the mid-axillary region and sends branches anteriorly and posteriorly. The anterior cutaneous branch travels anteriorly along the thorax and terminates at midline. T1 fibers contribute to the brachial plexus and T2 and T3 contribute branches to the intercostobrachial nerve.

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1667–1668.

28. ANSWER: D

The neurovascular bundle travels just underneath the rib in the intercostal space. The block should be done by walking caudad off the rib to ensure injection around the nerve. The nerve travels around the thorax from posterior to anterior. A block done anterior to the chest tube will not provide analgesia for the chest tube. By injecting 6 to 8 cm from midline posteriorly and just below the rib, the entire distribution of the corresponding intercostal nerve will be anesthetized.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1668.

29. ANSWER: B

A brachial plexus block performed at the interscalene level is most useful for surgeries at the shoulder level as well as procedures at or proximal to the elbow. Inadequate analgesia is most likely to occur in the ulnar distribution. To ensure adequate analgesia, an ulnar nerve block can be performed as a supplement. The ulnar nerve traverses a groove formed by the olecranon and medial condyle of the humerus, and can be blocked here. Choice A would result in a selective median nerve block, which would be unnecessary given an already established interscalene block. Choice C refers to a selective radial nerve block. Choice D refers to a musculocutaneous nerve block. Choice E also refers to a selective radial nerve block.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:726–732.

30. ANSWER: C

Epidural and spinal local anesthetics as well as IV lidocaine, parasympathetic stimulation, splanchnic nerve blockade, cholinergic agonists, and anticholinesterases have been shown to improve postoperative GI motility. Sympathetic stimulation, pain, opiates, nitrous oxide, volatile anesthetics, and catecholamines (administered and endogenous) have been shown to decrease postoperative GI motility. Nitrous oxide has a more prolonged effect, while volatile anesthetic effects are much shorter in duration.

ADDITIONAL READING

Steinbrook RA. Epidural anesthesia and gastrointestinal motility. *Anesth Analg*. 1998;86:837–844.

31. ANSWER: E

Injecting 50 mL of 0.5% lidocaine (3 mg/kg) will provide adequate surgical anesthesia for this patient. Although bupivacaine is longer-acting, because of potential cardiotoxicity and death associated with bupivacaine, intravenous administration of bupivacaine is not recommended by experts. 10 mL of 1% lidocaine is unlikely to produce adequate anesthesia for surgery.

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1648–1649.

32. ANSWER: B

Immediate deflation of the tourniquet may likely lead to lidocaine toxicity (CNS, cardiac). It is recommended to wait at least 25 minutes before deflating the tourniquet to allow transfer of lidocaine into local tissue and decrease plasma concentrations. Performing an axillary block immediately may additionally expose the patient to more local anesthetic and lead to toxicity. Using a different local anesthetic agent will not help since it is believed that different drugs are additive in terms of their toxic dose. Maintaining the tourniquet will likely lead to wearing off of anesthesia, as IV regional techniques are recommended for surgery lasting less than 90 minutes.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1648–1649.

33. ANSWER: D

According to the American Society of Regional Anesthesia and Pain Medicine, neuraxial techniques should be avoided in patients who have received fibrinolytic or thrombolytic therapy, and there are insufficient data to clearly outline the length of time until neuraxial techniques can be safely performed without an increased risk of spinal hematomas.

Nonsteroidal anti-inflammatory drugs do not pose an added risk to patients undergoing neuraxial procedures, provided the patients are not expected to receive other anticoagulation therapies (such as oral anticoagulants, fractionated or unfractionated heparin) in the immediate postoperative period. The other statements are true.

ADDITIONAL READINGS

Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (third edition). *Reg Anesth Pain Med*. 2010;35:64–101.
www.asra.com

34. ANSWER: A

Increased lipid solubility increases the potency of local anesthetics. For amide local anesthetics, mepivacaine and prilocaine have similar lipid solubility. Lidocaine is more lipid-soluble than mepivacaine, followed by ropivacaine, then etidocaine. Bupivacaine is the most lipid-soluble of the amide local anesthetics. For ester local anesthetics, tetracaine is the most lipid-soluble, chloroprocaine is intermediate, and procaine is the least. The relative potency of local anesthetics largely follows this pattern, with the exception that mepivacaine is considered more potent than lidocaine when used in peripheral nerve blockade: prilocaine 0.8, lidocaine 1, mepivacaine 2.6, ropivacaine 3.6 = bupivacaine 3.6.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:458–459.

35. ANSWER: A

The increased amount of extracellular fluids in pediatric patients leads to an increased volume of distribution. Low plasma protein content leads to an increased plasma concentration of unbound molecules. Enzymatic immaturity leads to slower metabolism, which may be important in pediatric patients on local anesthetic infusions. Increased cardiac output and heart rate generally lead to increased regional blood flow and increased systemic absorption and shorter duration. For this reason, the addition of epinephrine leads to a more prolonged block and the efficacy of epinephrine in prolonging the block is higher.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2520, Table 81–1.

36. ANSWER: A

Commercially available premixed solutions of local anesthetics with epinephrine are more acidic in order to preserve the potency of epinephrine. The lower pH will slow the time of onset of blockade. Thus, adding epinephrine to local anesthetic solutions at the time of use is preferred. Epinephrine is more effective at prolonging the duration of shorter-acting local anesthetics such as lidocaine and 2-chloroprocaine, and is also more effective at decreasing their plasma levels by vasoconstriction of the epidural venous plexus and reducing blood flow. Epinephrine added to ropivacaine will intensify blockade but will not prolong the duration of an epidural block.

ADDITIONAL READING

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:134–139.

37. ANSWER: D

Local anesthetics are weak bases. They are prepared for use in the form of their hydrochloride salts, which improves water solubility (thereby allowing for more concentrated storage), and this in turn is responsible for the solution's acidity. Alkalinization of this solution by adding sodium bicarbonate increases the un-ionized fraction of the local anesthetic, which enables a quicker time to onset of the block. 1 mL of sodium bicarbonate can be added to 9 mL of lidocaine or mepivacaine to achieve this goal. 0.1 mL of sodium bicarbonate added to 10 mL of bupivacaine will also decrease the time of onset of block, as will the addition of 0.3 mL of sodium bicarbonate to 2-chloroprocaine. Studies have shown that alkalinization of ropivacaine does not routinely result in a faster onset of block, and is actually not recommended due to an increased risk of precipitation of solution.

ADDITIONAL READINGS

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:137–139.
Ramos G, et al. Does alkalinization of 0.75% ropivacaine promote a lumbar peridural block of higher quality? *Reg Anesth Pain Med*. 2001;26:357–362.

38. ANSWER: E

True IgE-mediated immunologic reactions to local anesthetics are rare, but they appear to be more common with ester local anesthetics that are metabolized to para-aminobenzoic acid (PABA). There is a potential for cross-allergenicity when patients receive other derivatives of PABA, such as other ester local anesthetics or methylparaben. Methylparaben is a preservative used in multidose vials to prevent microbial growth. Thus, it is possible for patients with a history of ester local anesthetic allergy to develop true allergic reactions to amide local anesthetics if the solution contains methylparaben. Further, antioxidants such as bisulfites contained in solution can also cause an IgE-mediated reaction.

ADDITIONAL READINGS

Becker DE, Reed KL. Essentials of local anesthetic pharmacology. *Anesth Prog.* 2006;53:98–109.

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:117.

39. ANSWER: D

Five nerves provide sensation to the foot: saphenous, superficial peroneal, deep peroneal, sural, and posterior tibial. The saphenous nerve is a continuation of the femoral nerve and supplies sensation to the anteromedial surface of the foot. It is most likely to be located anterior to the medial malleolus. The superficial peroneal nerve is a branch of the common peroneal nerve. It enters the ankle just lateral to the extensor digitorum longus at the level of the lateral malleolus and provides cutaneous sensation to the dorsum of the foot and all five toes. The deep peroneal nerve, also a branch of the common peroneal nerve, is most consistently located just lateral to the flexor hallucis longus at the level of the medial malleolus. It innervates toe extensors as well as provides sensation to the dorsum of the first and second digits (the webspace of the first and second toes). The posterior tibial nerve continues from the tibial nerve and enters the foot posterior to the medial malleolus and provides sensation to the heel, the medial sole, and part of the lateral sole of the foot. The sural nerve continues also from the tibial nerve and provides sensation to the lateral foot. It is located between the Achilles tendon and the lateral malleolus.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: 743–745.

40. ANSWER: E

The median nerve is formed by the C5–C7 roots from the lateral cord, as well as the C8–T1 roots from the medial cord. Inside the cubital fossa, the median nerve travels medial to the brachial artery. At the level of the hand, the median nerve innervates sensation to the palmar surface of the thumb, the index and middle fingers, the lateral half of the fourth finger, as well as small distal portions of the dorsal surface of the thumb and index and middle fingers. The median nerve also supplies motor to the abductor pollicis brevis, the opponens pollicis, and the first and second lumbricals. If the nerve injury is higher than the level of the elbow, forearm muscles can also be affected (pronator teres, flexor carpi radialis, flexor carpi sublimis).

ADDITIONAL READING

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:373–377.

41. ANSWER: B

The patient has significant methemoglobinemia from the topical benzocaine spray. Methemoglobin is formed when the heme iron of unoxygenated hemoglobin is oxidized to the ferric (Fe^{3+}) state. In this oxidized state, hemoglobin cannot perform its basic function of binding and transporting oxygen. Methemoglobin normally accounts for 1% of all circulating hemoglobin, but the level can be elevated from genetic etiologies and from external oxidizing agents such as benzocaine and prilocaine (the topical anesthetic EMLA cream consists of prilocaine and lidocaine). As methemoglobin rises to 10% of all hemoglobin levels, cyanosis ensues. Fatigue, anxiety, and tachycardia are evident at levels between 20% and 50%, and death can occur at even higher levels. These symptoms occur due to hemoglobin's decreased oxygen-carrying capacity. Diagnosis of methemoglobinemia is suggested by an oxygen-unresponsive drop in oxygen saturation by pulse oximetry (since hemoglobin is unable to bind oxygen) despite a normal or high oxygen tension on arterial blood gas analysis. Chocolate-colored cyanosis can also be seen. Some literature reports suggest that SpO_2 typically plateaus at 85% during methemoglobinemia, but lower SpO_2 values have also been observed and should not deter one from considering methemoglobinemia in the differential. The diagnosis would be confirmed by measuring methemoglobin levels by co-oximetry. The treatment is methylene blue 1 to 2 mg/kg IV over 10 minutes. This allows methemoglobin to be reduced back to hemoglobin.

ADDITIONAL READINGS

Clary B, et al. Methemoglobinemia complicating topical anesthesia during bronchoscopic procedures. *J Thorac Cardiovasc Surg*. 1997;114:293–295.

Moore TJ, et al. Reported adverse event cases of methemoglobinemia associated with benzocaine products. *Arch Intern Med*. 2004;164:1192–1196.

42. ANSWER: A

Methylparaben (methyl ester of p-hydroxybenzoic acid) is the most common preservative used in local anesthetics. It can be found in formulations of chloroprocaine, lidocaine, bupivacaine, and mepivacaine. Methylparaben shows greater bactericidal activity at 37 degrees C than at room temperature. In addition, methylparaben in combination with a local anesthetic is more effective than when either drug is used alone. Methylparaben is a structurally similar compound to p-aminobenzoic acid (PABA), a metabolite of procaine and benzocaine that is a known antigen. Since methylparaben can be metabolized to PABA, in theory it can confer some cross-sensitivity to other ester-type local anesthetics that are metabolized also to PABA. Most allergic reactions to local anesthetics and additives (methylparaben) are the non-IgE-mediated anaphylactoid type. True IgE-mediated anaphylaxis from these agents is less common.

ADDITIONAL READINGS

Kajimoto Y, et al. Anaphylactoid skin reactions after intravenous regional anaesthesia using 0.5% prilocaine with or without preservative: a double-blind study. *Acta Anaesthesiol Scand*. 1995;39:782–784.

Larson CE. Methylparaben—an overlooked cause of local anesthetic hypersensitivity. *Anesth Prog*. 1977;24:72–74.

Reichart MG, and Butterworth J. Local anesthetic additives to increase stability and prevent organism growth. *Techn Regional Anesth Pain Manage*. 2004;8:106–109.

43. ANSWER: D

Adequate anesthesia for knee procedures can be provided by blockade of the femoral, sciatic, and obturator nerves. The femoral nerve supplies the anteromedial surfaces of the thigh and knee. The lateral femoral cutaneous nerve exits the lumbar plexus at the L2–3 level and supplies cutaneous sensation for the lateral thigh. The obturator nerve is also a component of the lumbar plexus and is responsible for sensation to the medial thigh and hip joint, and motor innervation to the thigh adductor muscles. It is commonly performed as a complement to additional blocks performed for knee surgery. The sciatic nerve originates from the lumbosacral trunk, involving nerve roots from L4–5 and S1–3. It supplies sensation to the posterior hip and knee, motor to the hamstrings and to all lower-extremity muscles distal to the knee, as well as all sensation distal to the knee except along the anteromedial aspect (by the saphenous).

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*, 4th ed. New York, NY: McGraw-Hill;343–349.

44. ANSWER: A

Epidural blockade with 0.5% bupivacaine will have at least a 160- to 220-minute duration. 0.5% ropivacaine is expected to have up to a 3-hour duration. 2% mepivacaine with epinephrine will have a 160- to 200-minute duration (90 to 160 minutes without epinephrine). 2% lidocaine without epinephrine should last from 80 to 120 minutes (120 to 180 minutes with epinephrine). 3% 2-chloroprocaine will have a 45- to 60-minute duration without and a 60- to 90-minute duration with epinephrine.

ADDITIONAL READING

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:243.

45. ANSWER: C

The OCR is thought to be triggered by traction on extraocular muscles and pressure on the globe. The afferent limb of this pathway involves transmission from the ciliary ganglion to the ophthalmic division of the trigeminal nerve, to the gasserian ganglion, and to the main trigeminal sensory nucleus in the fourth ventricle. The efferent limb is mediated via the vagus nerve, resulting in bradycardia, nodal rhythms, ectopic beats, fibrillation, and even asystole. A retrobulbar block does not reliably prevent this reflex. In fact, massaging the eye after placement of a retrobulbar block can stimulate the OCR. A slowly expanding retrobulbar hematoma (for example, after placement of a block) can also elicit this reflex. Hypoxia, hypercarbia, and light anesthesia have been described as potentiators of this reflex. A higher incidence of OCR is seen during strabismus surgery. Administering anticholinergic premedications such as atropine and glycopyrrolate, as well as maintaining adequate oxygenation, ventilation, and depth of anesthesia, may lower the likelihood of occurrence of OCR, although these methods may not be consistently effective.

ADDITIONAL READING

Choi SR, et al. Effects of different anesthetic agents on oculocardiac reflex in pediatric strabismus surgery. *J Anesth*. 2009;23:489–493.

46. ANSWER: E

Although bacterial colonization rates are higher with caudal than epidural catheters, infection rates have not been found to be higher. The overall infection rate with caudal catheters appear to be low. Postdural puncture headaches are uncommon if care is taken to avoid advancing the needle too far into the sacral canal. Seizures can occur with intravascular injections of local anesthetics. Total spinal anesthesia is possible if a large intrathecal injection is made. Significant changes in heart rate, blood pressure, or cardiac index are not seen with a caudal injection to the T6 level. Even when a thoracic epidural is combined with general anesthesia, healthy pediatric patients usually maintain hemodynamic stability.

ADDITIONAL READINGS

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:730–731.

Silvani P, Camporesi A, AgostinoMR, et al. Caudal anesthesia in pediatrics: an update. *Minerva Anestesiol*. 2006;72:453–459.

Tsuji MH, et al. Left ventricular functions are not impaired after lumbar epidural anaesthesia in young children. *Paediatr Anaesth*. 1996;6:405–409.

47. ANSWER: A

The dural sac ends at S4 in the young pediatric population, compared to S2 in adults. CSF volume per kilogram of body weight is greater in pediatric patients. Loss of resistance is usually more subtle than in adults because the subcutaneous tissues and vertebral ligaments are less densely packed in infants. The recommended limit to local anesthetic dosing is similar in adults and children. Lower plasma protein binding in young patients leads to a proportionately higher free drug concentration in the blood. However, the volume of distribution is significantly greater in children.

ADDITIONAL READING

Dalens B. Regional anesthesia in children. *Anesth Analg.* 1989;68: 654–672.

48. ANSWER: A

The nasal cavity is completely innervated by branches of the trigeminal nerve. The anterior nasal cavity is supplied by a branch of the ophthalmic nerve, and the remaining parts by the maxillary nerve branches. The glossopharyngeal nerve supplies the posterior third of the tongue and is also responsible for the afferent arc of the gag reflex, whereas the motor innervation of the pharynx is by efferents from the vagus nerve. The superior laryngeal nerve (a branch of the vagus) divides into an internal and an external branch. The internal branch supplies sensation to the larynx above the vocal cords. The external branch supplies motor to the cricothyroid muscle. The rest of the laryngeal musculature, as well as infraglottic sensation, is supplied by the recurrent laryngeal nerve. This area can be blocked by a translaryngeal approach.

ADDITIONAL READING

Simmons ST, Schleich AR. Airway regional anesthesia for awake fiberoptic intubation. *Reg Anesth Pain Med.* 2002;27:180–192.

49. ANSWER: C

Pain from malignancy that is intractable to routine treatments may warrant the use of neurolytic nerve blocks. This method is often considered when life expectancy is short. Other factors to consider include the patient's general condition, the type of pain, risks of the procedure, and response to prior conservative therapies. Peripheral nerve destruction with both alcohol and phenol can lead to denervation pain that is as severe or worse than the underlying pain. This is why neuraxial locations are preferred for neurolytic injection. Injection of alcohol is painful, but the neurolytic effects are more intense and the block can be evaluated quite quickly. Phenol has a biphasic action because it has both local anesthetic and neurolytic properties. Neurolytic nerve blocks are not permanent and pain can return within several weeks to months.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 5th ed. New York, NY: Churchill Livingstone; 2000:2366–2367.

50. ANSWER: B

Tissue damage activates nociceptors at the free nerve endings of C and Aδ fibers located in various body tissues. The amount of neural activity in nociceptive afferents is influenced not only by the intensity and duration of stimulation, but also by the microenvironment of the nociceptors. With repeated stimulation, these nerve endings display

enhanced sensitivity, a lowered threshold to stimulation, and a prolonged and exaggerated response to stimulation. Nociceptive activity can be enhanced by repeated noxious stimuli, lowering of the threshold by pain-producing substances, and segmental reflex responses provoked by tissue injury. Inhibition of this activity may be produced by counter-irritation in the skin by rubbing, vibration, electrical stimulators, and acupuncture. Primary hyperalgesia is the effect of tissue injury producing sensitization that is characterized by a lowered pain threshold, spontaneous pain, and increased sensitivity to suprathreshold stimuli.

ADDITIONAL READINGS

Raj PP. *Pain Medicine: A Comprehensive Review*, 2nd ed. Philadelphia, PA: Mosby, Inc.; 1996; 12–13.

51. ANSWER: A

Acute herpes zoster represents reactivation of the varicella-zoster virus. The virus infects dorsal root ganglia, where it remains latent until reactivation. A prodrome of dermatomal pain usually precedes the appearance of a rash. Antiviral agents can reduce the duration of the rash and accelerate healing. Oral analgesics are adjunctive measures to treat pain associated with acute zoster. The majority of adults do not develop PHN. However, immunocompromised patients and the elderly are more likely to develop PHN. Sympathetic nerve blocks are said to be effective in reducing pain in patients with acute zoster, and may even reduce the incidence of PHN, but evidence for its use in established PHN is less convincing. Antidepressants such as amitriptyline, as well as anticonvulsants, opioids, TENS, and transdermal lidocaine, can provide analgesia for PHN.

ADDITIONAL READINGS

Kathleen Hempenstall, Turo J Nurmikko, Robert W Johnson, Roger P A'Hern, Andrew SC Rice. Analgesic therapy in postherpetic neuralgia: a quantitative systematic review. *PLoS Med*. 2005;2:e164.

Wu CL, Marsh A, Dworkin RH. The role of sympathetic nerve blocks in herpes zoster and postherpetic neuralgia. *Pain*. 2000;87:121–129.

52. ANSWER: B

For surgeries at the ankle, the femoral nerve (lateral to the femoral artery) and the sciatic nerve need to be blocked. Commonly, the saphenous nerve, which is a distal branch of the femoral nerve and provides sensory to the medial aspect of the lower leg and foot, can be blocked in the distal medial thigh in the fascial plane between the vastus medialis and sartorius muscles. Ultrasound-guided imaging can enable visualization of the fascial plane. The sciatic nerve can be blocked at the gluteal region, or more distally at the popliteal fossa using ultrasound-guided techniques. At the popliteal fossa, the sciatic nerve divides into the common peroneal and tibial nerves. Blockade of the femoral and obturator nerves (choice A) would not provide adequate coverage of the ankle. The obturator nerve passes through the obturator foramen to the medial aspect of the thigh, and divides into anterior and posterior branches. The anterior branch of the obturator nerve lies in the fascial plane between the adductor brevis and adductor longus. The posterior branch lies between the adductor brevis and adductor magnus. Choice D is incorrect because the femoral nerve lies lateral to the femoral artery. Injection in the psoas compartment (choice E) will result in blockade of the lumbar plexus, but will miss the sciatic nerve, which lies in the sacral plexus.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: 740–744.

53. ANSWER: A

The brachial plexus can be blocked for surgeries at the elbow, usually at the infraclavicular, supraclavicular, or interscalene level. The brachial plexus is formed from C5–T1, with nerve roots exiting the neural foramen to enter the interscalene groove between the anterior and middle scalene muscles, posterior to the sternocleidomastoid muscle. The primary ventral rami of C5 and C6 form the upper trunk above the subclavian artery. C7 forms the middle trunk, and C8–T1 form the lower trunk. At the supraclavicular level, the brachial plexus and subclavian artery lie over the first rib. Nerves in the supraclavicular region appear hypoechoic and lie lateral to the subclavian artery. At the infraclavicular level, the cords of the brachial plexus are located around the axillary artery. The lateral cord lies superior and lateral, the posterior cord lies posterior, and the medial cord lies posterior and medial to the axillary artery. The axillary vein typically lies caudad and medial to the axillary artery, and the pectoralis major and minor muscles lie anterior to the brachial plexus at this level.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: 726–732.

54. ANSWER: B

During the first stage of labor, pain is primarily referred through the T10–L1 dermatomes. In the second stage of labor, the lower sacral segments S2–4 (pudendal nerve) are involved also due to the distention of the vaginal vault and perineum. Analgesia for the first stage of labor can be provided by epidural, spinal, combined epidural and spinal, continuous spinal, paracervical, caudal, and paravertebral lumbar sympathetic blocks. Paracervical blocks are not commonly performed, however, due to a higher incidence of poor neonatal outcome from uterine artery constriction and fetal asphyxia. A paravertebral lumbar sympathetic block carries less risk of fetal bradycardia than a paracervical block, but technical difficulties and risk of intravascular injection also make this technique less favorable than central neuraxial blocks (epidural or spinal).

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: 1159–1160.

55. ANSWER: D

A variety of anesthetic options are available for ophthalmologic procedures, including general anesthesia, retrobulbar block, peribulbar block, sub-Tenon's block, and topical anesthesia. Up until the mid-1990s, retrobulbar blocks were the most commonly used regional anesthetic technique. Due to a better safety profile, peribulbar blocks and topical anesthesia have become more commonly used since that time. There are several potential complications involved with performing a retrobulbar block. The OCR can be elicited, resulting in bradycardia and even cardiac arrest. Intra-arterial injection can result in seizures and other signs of local anesthetic CNS toxicity. Retrobulbar hemorrhage can result in profuse bleeding, proptosis, and a rapid increase in intraocular pressure that can quickly compromise the globe's vascular supply. Inadvertent intrathecal injection can lead to brainstem anesthesia, resulting in loss of consciousness and respiratory effort.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: 983–986.

56. ANSWER: A

To perform a sciatic nerve block using a classical posterior approach, the patient should be positioned laterally, with the side to be blocked uppermost. The superior aspect of the greater trochanter of the hip is identified, and a line is drawn from here to the posterior superior iliac spine. At the midpoint of this line, a perpendicular line is drawn toward the caudad direction. A third line is then drawn between the greater trochanter and sacral hiatus. The point where the second and third lines intersect (usually approximately 5 cm caudad to the first line) will be the point of needle entry, perpendicular to the skin, to elicit nerve responses of the lower leg.

ADDITIONAL READINGS

Allen HW, Liu SS, Ware PD, et al. Peripheral nerve blocks improve analgesia after total knee replacement surgery. *Anesth Analg*. 1998;87:93–97.

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: 740–741.

57. ANSWER: D

The radial nerve arises from the C5–T1 nerve roots. It supplies motor to the triceps, brachialis, brachioradialis, supinator, extrinsic extensors of the wrist and hands, and abductor pollicis longus. The radial nerve provides sensory to the dorsal aspect of the forearm, back of the thumb, and proximal index and middle fingers. The median nerve arises from the C6–T1 nerve roots. It supplies motor to all of the flexors of the forearm except the flexor carpi ulnaris and the part of the flexor digitorum profundus that supplies the medial two fingers (supplied by the ulnar nerve). Forearm muscles innervated by the median nerve include pronator teres, flexor carpi radialis, palmaris longus, flexor digitorum superficialis, flexor pollicis longus, flexor digitorum profundus (lateral half), and pronator quadratus. In the hand, the nerve supplies the first and second lumbricals, opponens pollicis, abductor pollicis brevis, and flexor pollicis brevis. Sensory innervation by the median nerve supplies the lateral aspect of the palm, as well as the palmar side of the thumb, index finger, middle finger, and half of the ring finger. The median nerve also provides sensory innervation to the back of the distal index finger, middle finger, and half of the ring finger. The medial cutaneous nerve of the arm is purely sensory and innervates the area on the medial (ulnar) side of the forearm. The lateral cutaneous nerve of the forearm is a continuation of the musculocutaneous nerve and is purely sensory to the lateral (radial) side of the forearm. The intercostobrachial nerve is the lateral cutaneous branch of the second intercostal nerve. It supplies the skin of the upper half of the medial and posterior aspect of the arm.

ADDITIONAL READING

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:373–385.

58. ANSWER: D

The lateral cord is formed from the anterior divisions of the superior and middle trunks of the brachial plexus. The musculocutaneous nerve, the lateral head of the median nerve, and the lateral pectoral nerves originate from this cord. The anterior division of the inferior trunk forms the medial cord. Nerves arising from the medial cord are the medial pectoral nerves, the medial brachial nerve, the antebrachial cutaneous nerve, the ulnar nerve, and the medial head of the median nerve. The posterior divisions of all three trunks (superior, middle, inferior) of the brachial plexus form the posterior cord. Nerves arising from the posterior cord are the radial nerve, the subscapular nerves, the thoracodorsal nerves, and the axillary nerve. There is no anterior cord. The radial nerve (arising from the posterior cord) is responsible for sensory innervation of the skin over the extensor surface of the forearm to the wrist.

ADDITIONAL READING

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:382–384.

59. ANSWER: E

Spinal anesthesia results in both arterial and venodilation. Venodilation leads to a greater volume in capacitance vessels, and a decrease in preload and right-sided filling pressures. This, as well as a decrease in total peripheral resistance, contributes to hypotension. Although heart rate does not change significantly in the majority of patients receiving spinal anesthesia, significant bradycardia can be seen in 10% to 15% of patients. Blockade of the sympathetic cardioaccelerator fibers at the T1–T4 level accounts for this.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:709.

60. ANSWER: A

PDPH occurs more commonly after spinal anesthesia than epidural anesthesia. The headache is usually absent when the patient is supine, and occurs when the patient assumes a sitting or standing position. The headache is typically in a fronto-occipital distribution. PDPH occurs more often in parturients, and younger rather than older patients, and usually resolves spontaneously. If conservative measures such as bedrest, analgesics, and caffeine do not relieve severe symptoms, an epidural blood patch can be done with approximately a 60% to 90% success rate within 1 to 24 hours of performing the blood patch. Of the patients who fail to respond to an initial blood patch, 90% will respond to a second patch.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:710–711.

61. ANSWER: D

Spinal anesthesia has a relatively small effect on pulmonary function in patients with normal lung mechanics, although it can cause increased dead space due to a decline in cardiac output and increase of the Zone 1 area in the lungs. Even with high spinal anesthesia, arterial blood gas measurements are mostly unchanged. In addition, the phrenic nerve would be spared in a high thoracic spinal, so diaphragmatic function is not impaired. Dyspnea is usually due to the inability to feel the chest wall move during respiration, and ventilation is usually normal if patients are able to speak in a normal voice. The main respiratory effect is that with paralysis of the abdominal and intercostal muscles, forced expiratory maneuvers may be limited.

ADDITIONAL READING

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:206–207.

62. ANSWER: C

Spinal anesthesia leads to both arterial and venodilation, leading to hypotension. If the sympathetic cardiac accelerator fibers at the T1–T4 spinal segments are also blocked, bradycardia can also ensue. Preload depends on patient positioning after spinal anesthesia. Given the propensity for venodilation, elevating the patient's legs above the heart and avoiding the reverse Trendelenburg position can attenuate the decrease in preload and cardiac output. Prehydration or

intraoperative rehydration with intravenous fluids may also help attenuate hypotension. Alpha- and beta-adrenergic agonists can also be used to treat hypotension and bradycardia. Although the Trendelenburg position can improve preload and venous return, patients should NOT be placed head-down within 30 minutes of receiving a hyperbaric spinal anesthetic due to the likelihood of a higher spread toward the cervical levels and above. Further, Trendelenburg positions exceeding 20 degrees can also lead to a decrease in cerebral perfusion due to increases in jugular venous pressure.

ADDITIONAL READINGS

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:205–206.

Sinclair CJ, et al. Effect of the Trendelenburg position on spinal anaesthesia with hyperbaric bupivacaine. *Br J Anaesth*. 1982;54:497–500.

63. ANSWER: B

A stellate ganglion block provides sympatholysis of the upper extremity and can be used for relief of sympathetic dystrophies involving the upper arm and pain from acute herpes zoster infection of the head and neck. The stellate ganglion is a fusion of the lower cervical ganglion with the first thoracic sympathetic ganglion, and it lies lateral to the C7 vertebral body. Potential complications include intravascular injection of local anesthetics, pleural puncture resulting in pneumothorax, subarachnoid injection, signs associated with Horner syndrome, cardiovascular changes, and hoarseness from recurrent laryngeal nerve blockade. Due to its proximity to the stellate ganglion, the vertebral artery is the most likely site of an inadvertent vascular injection while performing this block. A small test dose is prudent before injecting larger volumes of local anesthetic.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:736–737.

64. ANSWER: C

A paramedian approach is useful because it allows access to the epidural and intrathecal space in difficult cases. This approach does not require the patient to fully reduce the lumbar lordosis, so less patient positioning is necessary. This approach also exploits a larger target that is available when needle is inserted in the paramedian approach. The difficulty with the paramedian approach is that it requires the mental image of the anatomy in three planes (vs. two plane in the midline approach). The needle insertion is generally 1 cm lateral and 1 cm caudad to the cephalad spinous process. The needle is then direct toward midline with a 10- to 15-degree angle. The paramedian approach is more painful and requires more local anesthetic infiltration beyond the skin and subcutaneous tissue. The Taylor approach is a variation of the paramedian approach; it uses the L5–S1 interspace, which has the largest interlaminar space in the lumbosacral region.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:232–233.

65. ANSWER: B

The presumed diagnosis here is intrathecal administration of epidural-dose local anesthetic, which leads to a high spinal. The treatment is supportive to correct blood pressure and heart rate, as well as securing the airway (remember the ABCs). The Trendelenburg position improves preload, which may improve cardiac output and blood pressure. Administration of Intralipid is the treatment for intravascular injection of local anesthetic. Although intravascular administration is in the differential diagnosis here, other answers are better choices in this setting.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1633.

66. ANSWER: D

A failed spinal can occur from maldistribution of local anesthetic, or movement of the spinal needle during injection. The visualization of CSF coming back while pulling on the plunger at the end of injection is a reasonable test to verify that the injection was indeed intrathecal. Small doses of fentanyl or ketamine may provide analgesia until enough time has passed for the spinal to be effective. Inhalation of nitrous oxide may also be beneficial. It is always safe to convert to general anesthesia if a regional technique has failed. It is not appropriate to ignore the patient's reporting of pain.

ADDITIONAL READING

Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby, Inc.; 2009:240–241.

67. ANSWER: E

The volume of CSF is inversely correlated with the level of anesthesia achieved with a subarachnoid block. Conditions in which CSF volume is low can result in a block higher than one would normally see. For example, patients with increased intra-abdominal pressure from ascites or large tumors, parturients, and obese patients can all have decreased CSF volume and experience a higher-than-expected level of subarachnoid block.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*, 4th ed. New York, NY: McGraw-Hill;.308–309.

68. ANSWER: C

The subarachnoid space extends from the foramen magnum to S2 in adults, and from the foramen magnum to S3 in children. Injection below L1 in adults avoids direct trauma to the spinal cord, whereas injection below L3 in children serves the same purpose.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*, 4th ed. New York, NY: McGraw-Hill;.304.

69. ANSWER: A

The posterior longitudinal ligament lies posterior to the vertebral bodies but anterior to the dural sac. The needle should pass through these structure in the order listed: skin, subcutaneous tissue/fat, supraspinous ligament, intraspinous ligament, ligamentum flavum, (epidural space), dura mater, and subarachnoid membrane. If the subarachnoid membrane is not penetrated, injection will result in a subdural block.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:689–691.

70. ANSWER: D

The pia mater, a thin layer of connective tissue interspersed with collagen, adheres to the spinal cord and would not be encountered when performing a subarachnoid block.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001: 689–691.

71. ANSWER: D

This patient has transient neurologic symptoms (TNS). This condition involves pain originating in the gluteal region extending to the lower extremities after a subarachnoid block. The intensity of pain varies from mild to severe. It occurs more often when lidocaine is used for the block than other local anesthetics. In some studies, approximately 1 in 7 patients who received lidocaine for an intrathecal block developed TNS. A patient can develop symptoms even after full recovery of sensory and motor responses in the postoperative period. The onset of symptoms is usually within a couple of hours to a day after the block is performed. Symptoms are transient and usually resolve by 5 to 7 days. There is no evidence to show any involvement of neurologic pathology. The dose of lidocaine is more important in causing TNS than the volume used. Meralgia paresthetica refers to paresthesias in the anterolateral thigh resulting from nerve entrapment, typically involving the lateral femoral cutaneous nerve as it courses under the inguinal ligament. Cauda equina syndrome would involve motor weakness as well as bowel and bladder dysfunction.

ADDITIONAL READINGS

Harney D, Patijn J. Meralgia paresthetica: diagnosis and management strategies. *Pain Med*. 2007; 8: 669–677.

Zaric D, Christiansen C, Pace NL, et al. Transient neurologic symptoms after spinal anesthesia with lidocaine versus other local anesthetics: a systematic review of randomized, controlled trials. *Anesth Analg* 2005;100:1811–1816.

72. ANSWER: C

The superior laryngeal nerve (SLN) is a branch of the vagus nerve. The internal branch of the SLN provides sensory innervation to the base of the tongue, epiglottis, arytenoids, and vocal cords. It originates from the SLN lateral to the cornu of the hyoid bone. The external branch of the SLN

supplies motor innervation to the cricothyroid muscle. Other muscles of the trachea, as well as sensation along the trachea, are innervated by the recurrent laryngeal nerve, which can be blocked by a transtracheal injection of local anesthetic through the cricothyroid membrane. The gag reflex is innervated by the glossopharyngeal nerve, which can be blocked at the base of the anterior tonsillar pillar by a local anesthetic injection. Placing anesthetic-soaked swabs at the palatoglossal folds can also be used to block the glossopharyngeal nerve. For surgeries at the neck, the superficial cervical plexus can be blocked at the posterior border of the sternocleidomastoid at C4 with infiltration cephalad and caudally.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:622–623, 723–726.

73. ANSWER: C

Although a tourniquet is commonly used for extremity surgeries due to the advantage of a bloodless field, it is not without potential problems. Postoperative swelling, delay in recovery of muscle strength, pain, limb hyperemia and increased circulatory volume on tourniquet release, and possibly a higher rate of deep venous thrombosis have all been reported in the literature. Some studies have shown an increased or unchanged incidence of wound complications. Electromyographic changes for up to several months has also been shown.

ADDITIONAL READINGS

Smith TO, Hing CB. A meta-analysis of tourniquet assisted arthroscopic knee surgery. *Knee*. 2009;16:317–321.

Wakankar HM, Nicholl JE, Koka R, et al. The tourniquet in total knee arthroplasty, a prospective randomized study. *J Bone Joint Surg Br*. 1999;81:30–33.

74. ANSWER: B

Higher frequency generally leads to better axial resolution because higher frequency leads to shorter wavelength, and the shorter wavelength will allow for better two-point discrimination but lower penetration. Lower frequency leads to a larger wavelength, which will lead to poorer resolution but better penetration.

ADDITIONAL READING

Marhofer P. *Ultrasound Guidance for Nerve Blocks*. New York, NY: Oxford University Press; 2008:4–5.

75. ANSWER: D

Unfortunately, there are no randomized clinical trials showing decreased complication rates of regional anesthesia with the use of ultrasound. Studies have shown that a smaller volume is necessary to achieve a block. Identification of nerves and vasculature is possible with ultrasound, which would provide an advantage. Direct visualization of needle and local anesthetic as it is being injected allows the operator to redirect the needle and optimize the site of injection. Use of a nerve stimulator to perform a block in patients with joint dislocation or fractures is particularly painful.

ADDITIONAL READING

Marhofer P. *Ultrasound Guidance for Nerve Blocks*. New York, NY: Oxford University Press; 2008:17–20.

76. ANSWER: A

In an ultrasound-guided posterior approach to the interscalene block, the needle goes through the middle scalene muscle. The trunks of the brachial plexus are located between the anterior and the middle scalene muscles. The anterior scalene muscle lies anterior to the trunks. The internal jugular vein, the carotid artery, and the phrenic nerve are further anterior to the anterior scalene muscle. The sternocleidomastoid muscle lies anterior and more superficial to the nerve trunks.

ADDITIONAL READING

Marhofer P. *Ultrasound Guidance for Nerve Blocks*. New York, NY: Oxford University Press; 2008:17–20.

77. ANSWER: E

The transversus abdominis plane block can be done blindly or with the use of ultrasound. The injection is done deep to the internal oblique muscle and superficial to the transversus abdominis muscle. The block can be done in the midaxillary line between the lower costal margin and the iliac crest. It can provide analgesia for appendectomy, cesarean section, hernia repair, and abdominal hysterectomy. See the reference for a lot more detail.

ADDITIONAL READINGS

Mukhtar K. Transversus abdominis Plane (TAP) block. *The Journal of NY School Regional Anesth*. 2009;12:28–33.

78. ANSWER: C

Neurolytic blocks are generally reserved for patients with intractable pain that can't be controlled by other conventional methods. It works best for pain that is somatic in origin. Neuropathic pain is not as responsive to neurolytic blocks. A diagnostic block with a local anesthetic solution is generally used first to ensure pain relief before a neurolytic block is done.

ADDITIONAL READING

Loeser JD, ed. *Bonica's Management of Pain*. 3rd ed. Hagerstown, MD: Lippincott Williams & Wilkins, 2001:1967–1990.

Candido K, Stevens RA. Intrathecal neurolytic blocks for the relief of cancer pain. *Best Practice & Research Clinical Anaesthesiol*. 2003;17:407–428.

79. ANSWER: D

Ethanol is hypobaric while phenol is hyperbaric relative to CSF. This allows preferential neurolysis of posterior roots and rootlets with either agent depending on patient position.

ADDITIONAL READING

Loeser JD, ed. *Bonica's Management of Pain*. 3rd ed. Hagerstown, MD: Lippincott Williams & Wilkins, 2001:1978–1979.

80. ANSWER: A

This block is actually contraindicated for extensive and poorly localized pain. Typically motor function is preserved, but muscle weakness and sphincter dysfunction may occur as complications. Analgesia can last for weeks to months, as the axon grows back. Since the destruction is through Wallerian degeneration, the axons can grow back (pain comes back as well), so repeated injections may be necessary.

ADDITIONAL READING

Loeser JD, ed. *Bonica's Management of Pain*. 3rd ed. Hagerstown, MD: Lippincott Williams & Wilkins, 2001:1978–1981.

81. ANSWER: C

The absorption of local anesthetics varies based on the site of injection. The highest systemic local anesthetic concentrations are found with intercostal nerve blocks, followed by caudal blocks, epidurals, brachial plexus blocks, and sciatic nerve blocks.

ADDITIONAL READINGS

Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York, NY: McGraw Hill; 2007:115.

KEY FACTS: LOCAL ANESTHETIC TOXICITY BY SITE

Intercostal > caudal > epidural > brachial plexus > sciatic

8.

ACUTE AND CHRONIC PAIN

Pankaj Mehta, MD, Katherine Zaleski, MD, and Christine Peeters-Asdourian, MD

1. After inguinal hernia surgery under general anesthesia a patient complains of paresthesias in the right hand. Which one of these pairings accounts for the most likely nerve damaged and area of concern?

A. Ulnar nerve—second and third digits
B. Ulnar nerve—fourth and fifth digits
C. Median nerve—first and second digits
D. Median nerve—fourth and fifth digits
E. Ulnar nerve—third and fourth digits

2. A morbidly obese 32-year-old woman undergoes laparoscopic gastric banding under general anesthesia. A few hours after the procedure, she complains of wrist drop and weakness with thumb abduction. Which of these causes would likely explain her clinical scenario?

A. Median nerve damage during technically difficult arterial line placement in the wrist
B. Ulnar nerve damage due to excessively tight arm restraints
C. Musculocutaneous nerve damage due to inadequate padding at the radial head
D. Radial nerve damage due to excessive cycling of her blood pressure cuff
E. Radial nerve damage during antecubital fossa IV placement

3. You are called to the bedside of a diabetic patient who has a continuous epidural catheter in place, 4 days after exploratory laparotomy for a small bowel obstruction. He has appropriate abdominal pain relief but notes significant back pain at the insertion site as well as fever and an inability to move his legs. What is the next step of action?

A. Halve the epidural rate and re-evaluate the patient in 4 hours.
B. Continue the epidural and obtain a stat neurosurgical consult.
C. Stop the epidural and perform stat plain film x-rays.
D. Stop the epidural and perform an emergent MRI.
E. Stop the epidural and administer oral opioids.

4. Which of these mechanisms is responsible for the effect of nonsteroidal anti-inflammatory drugs (NSAIDs) on the peripheral nervous system?

A. NSAIDs work to prevent sensitization of the peripheral nociceptors by affecting prostaglandin formation.
B. Most of the COX-inhibitory activity lies within the R enantiomer.
C. NSAIDs are rapidly absorbed and highly dependent on renal elimination.
D. The toxicity of NSAIDs is unrelated to their plasma half-lives.
E. NSAIDs' ability to affect pain depends on their COX-1 modulatory properties.

5. Which of these guidelines is NOT included in the Federation of State Medical Boards "Model Guidelines for the Use of Controlled Substances for the Treatment of Pain"?

A. Periodic review of medications and implementation of personalized treatment plans for each patient
B. Informed consent and agreement for treatment
C. Proper documentation for opioid efficacy and safety and review of untoward side effects
D. Responsibility of prescribing provider to prescribe opioids for aberrant patients to avoid withdrawal
E. All items above are included in the FSMB guidelines.

6. A 78-year-old woman presents to the pain clinic with vague abdominal pain of 2 months' duration; on further questioning, the description of her symptoms is concerning for abdominal malignancy. Which of these statements is least likely to occur with malignant visceral pain?

A. She complains of a 20-lb unintentional weight loss over the past 6 months that has not improved with dietary supplementation.
B. Pain is highly specific, noted as a periumbilical "burning" pain.
C. Eating causes bouts of severe pain; at times of fasting the pain is more dull in nature.
D. She is able to function with oral NSAIDs during the day but at night complains that the pain intensifies significantly.
E. The patient notes that her pain is continuous, but typically worse at night.

7. A 42-year-old woman has recently been diagnosed with stage 2 orofacial cancer and presents to the pain clinic with continued pain despite 800 mg of ibuprofen three times daily and 1,000 mg of acetaminophen three times daily. Which of these would be considered next step for her pain management according to the World Health Organization (WHO) ladder?

A. Sustained-release oxycodone 10 mg twice daily
B. Neurolytic maxillary nerve block
C. Hydrocodone/acetaminophen 7.5 mg/500 mg three times daily
D. Immediate-release morphine 50 mg three times daily
E. Gabapentin 600 mg twice daily

8. A 58-year-old patient presents to the pain clinic for interventional treatment of a known malignancy. Which of these pairings would be an appropriate treatment for the stated cancer?

A. A neurolytic celiac plexus block used for the treatment of sacral metastases
B. A therapeutic superior hypogastric plexus block used for the treatment of a large pancreatic neoplasm
C. A neurolytic superior hypogastric plexus block used for the treatment of primary mesothelioma
D A neurolytic celiac plexus block used for a pancreatic head neoplasm
E. None of the above

9. A 46-year-old patient status post Morton's neuroma reconstruction presents 1 week later with pain out of proportion to exam. Which of these symptoms is LEAST likely to be associated with complex regional pain syndrome (CRPS), type I?

A. Color change in the affected extremity
B. Poor nail growth and hair loss in the affected extremity
C. Depression and anger in conjunction with physical findings
D. A known injury to a peripheral nerve
E. Diffuse foot pain extending beyond the immediate area of the reconstruction

10. A 67-year-old man presents 2 months after ankle reconstruction with continued severe pain, swelling, and functional loss in the affected foot. His presentation is suspicious for complex regional pain syndrome. Which of these procedures would be effective in targeting the sympathetic fibers to the foot?

A. Celiac plexus block
B. Stellate ganglion sympathetic block
C. Lumbar sympathetic block
D. Ganglion impar sympathetic block
E. Lumbar epidural steroid injection

11. Immediately after undergoing a sympathetic blockade for pancreatic cancer, a patient notices difficulty breathing and is noted to be hypoxic. What is the most likely cause of this clinical presentation?

A. Pneumonia
B. Pulmonary embolism
C. Diaphragmatic paralysis
D. Respiratory depression from procedural sedation
E. Pneumothorax

12. The patient continues to cough and complain of dyspnea despite supplemental O_2 administration per nasal cannula. He is noted to have distended neck veins and tracheal deviation with decreased breath sounds over the left chest. What would be the most appropriate next step?

A. Needle decompression with a 14- to 16-gauge intravenous cannula inserted into the second rib space in the left mid-clavicular line
B. Immediate induction and endotracheal intubation
C. Positive-pressure bag-mask ventilation with cricoid pressure
D. Obtain a chest x-ray and proceed with chest tube insertion at the right fifth intercostal space slightly anterior to the mid-axillary line.
E. Immediate consultation of general surgery

13. A patient has undergone neurolytic celiac plexus block for gastric carcinoma and is now complaining of

weakness and dizziness on standing. After a celiac plexus block, what would be the most common expected side effects?

A. Nausea and vomiting
B. Diarrhea and gastroesophageal reflux
C. Hypotension and diarrhea
D. Hypotension and vomiting
E. Permanent motor paralysis

14. A 43-year-old patient has been prescribed baclofen for acute muscle spasms and low back pain. What is the mechanism of baclofen?

A. It blocks the release of calcium in the sarcoplasmic reticulum.
B. It acts as a GABA-B receptor agonist.
C. It is a centrally acting alpha$_2$ adrenergic agonist.
D. It is a benzodiazepine that has antispastic effect on the spinal cord.
E. It acts on ventral roots of the spinal cord.

15. A 25-year-old patient with acute-onset cervical pain after heavy lifting has been given a prescription for tramadol in the emergency room. Which of these is NOT associated with tramadol administration and ingestion?

A. Tramadol is a schedule II substance, necessitating frequent review and documentation from the prescribing physician.
B. Tramadol has several mechanisms of activity, including μ agonist activity and inhibition of serotonin reuptake.
C. Tramadol 1 to 2 mg/kg has been used successfully in the pediatric population.
D. Tramadol has been associated with seizure activity in those with a history of alcohol abuse.
E. Tramadol is one-tenth as potent as morphine.

16. Which of these statements best describes cocaine's mechanism of action?

A. Prevents dopamine reuptake, resulting in increased neurotransmitter concentrations
B. Promotes dopamine uptake in the neurosynapse, potentiating transmission in the ventral tegmental region
C. Enhances norepinephrine uptake
D. Prevents nitric oxide reuptake, leading to sensitization in the amygdala
E. Decreases dopamine concentrations in the brain

17. A 25-year-old man presents in the trauma bay after sustaining a gunshot wound to the left abdomen. He is tachycardic and hypotensive and noted to have a rapidly expanding abdomen, with concern for hemoperitoneum. A urine drug screen is positive for cocaine metabolites. Which of these statements about cocaine use in anesthesia is FALSE?

A. The addition of epinephrine to cocaine to promote vasoconstriction during local anesthesia is superfluous.
B. Ephedrine is indicated treatment for hypotension in chronic cocaine addicts.
C. Cocaine can facilitate the development of epinephrine-induced cardiac dysrhythmias under halothane anesthesia.
D. Patients with a history of cocaine abuse may exhibit bradycardia with severe hypovolemia.
E. Cocaine has both local anesthetic and vasoconstrictive properties.

18. A 56-year-old woman with a 20-year history of diabetes mellitus presents to an outpatient surgery center for carpal tunnel release. Which of these statements is correct regarding metabolic causes of peripheral neuropathies?

A. Carpal tunnel syndrome occurs more than twice as frequently in the diabetic population.
B. Along with associations with acute lymphocytic lymphoma, amyloidosis can contribute to a severe, progressive polyneuropathy involving motor fibers.
C. Thallium ingestion may lead to an insidious, chronic polyneuropathy.
D. AIDS-related polyneuropathy typically presents as allodynia in the feet with normal electromyographic (EMG) studies.
E. Diseases characterized by inflammation, such as rheumatoid arthritis, can exert pressure on the median nerve but rarely cause carpal tunnel syndrome.

19. A 20-year-old G1P0 undergoes an emergency cesarean section under general anesthesia due to fetal distress. Which of fentanyl's pharmacokinetic properties would place the fetus at risk for opioid-induced respiratory depression?

A. Fentanyl has decreased plasma binding, increasing the free fraction of the drug.
B. Fentanyl exhibits increased lipid solubility, promoting placental transfer.
C. Fentanyl is 90% ionized at pH 7.4 and thus crosses membranes rapidly.
D. Fentanyl is highly hydrophilic, promoting placental transfer.
E. Fentanyl induces histamine-mediated respiratory depression.

20. Which of these symptoms are not associated with the diagnosis of fibromyalgia?

A. Painful tender points at the muscle–tendon junction
B. Subjective swelling
C. Depression
D. Insomnia
E. Irritable bowel syndrome

21. A 32-year-old G1P0 at 24 weeks presents to the pain clinic with headaches and muscle fatigue. She has been taking acetaminophen but would like to know if there are any other medications that she can take while pregnant. Which of these statements is FALSE about pain management during pregnancy?

A. Acetaminophen is a category C medication, as animal studies have shown adverse fetal effects.
B. Ergotamine is contraindicated in pregnancy as it may be teratogenic.
C. Back pain is very common in pregnancy secondary to widening of the pelvic joints.
D. During maternal steroid therapy, less than 1% of the maternal dose of prednisone or prednisolone is recovered in breast milk.
E. Opioids are excreted into breast milk.

22. A 56-year-old man taking chronic opioids for arachnoiditis complains of abdominal fullness with constipation, which he thinks is a side effect of his medications. Which of these statements is INCORRECT regarding opioid-induced bowel dysfunction?

A. Constipation is the most common dose-dependent side effect of opioids.
B. Minimal to no tolerance develops to opioid-induced constipation.
C. Lack of constipation may suggest the dose is being diverted.
D. Lactulose as a stimulating laxative may help alleviate symptoms.
E. Methylnaltrexone may be helpful in reducing opioid-induced constipation.

23. Taking into account the multisystem effects of ketorolac, which of these patients would be at LEAST risk following postoperative ketorolac administration?

A. A 85-year-old man with a history of chronic renal failure, post cholecystectomy repair
B. A 20-year-old boy post open reduction and internal fixation of a traumatic tibial plateau fracture under general anesthetic
C. A 45-year-old woman with a history of gastric ulcers post liposuction under general anesthetic
D. A 60-year-old man post thoracotomy for right upper lobe resection under general endotracheal anesthesia
E. A 57-year-old woman presents for three-level lumbar fusion.

24. Which of these statements is FALSE concerning the risk of renal dysfunction in patients taking NSAIDs?

A. Nonaspirin NSAIDs cause a reversible platelet inhibition that resolves once the drug is eliminated from the body.
B. The most common side effects are renal, presenting as hematuria and dysuria.
C. Allergic nephritis can appear within 2 to 14 days after NSAID ingestion.
D. Minimal-change nephrotic syndrome has been reported in 10% to 20% of patients on NSAIDs.
E. NSAID-induced nephrotoxicity may be worsened by concomitant sepsis.

25. A 5-kg, 1-month-old boy is undergoing hypospadias repair under general anesthetic with isoflurane. He has had a preoperative caudal epidural block placed with 15 cc of 0.25% bupivacaine. 5 minutes into the case ventricular tachycardia is noted on the EKG. Which of the following statements would have contributed to this adverse outcome?

A. Isoflurane is more arrhythmogenic than sevoflurane in infants.
B. Metabolism and elimination of local anesthetics may be delayed in neonates.
C. Infants with hypospadias are at higher risk for intrinsic arrhythmias.
D. Neonates exhibit a lower half-life of local anesthetics due to differences in relative plasma volume.
E. Bupivacaine typically causes central nervous system effects at low concentrations.

26. What property is responsible for the relative differences in potency between bupivacaine and lidocaine?

A. Lipid solubility
B. Concentration
C. pKa
D. Protein binding
E. None of the above

27. A 28-year-old manual laborer has been on short-term disability for 3 months secondary to low back pain that developed after lifting a heavy bag of mulch at work. He smokes two packs of cigarettes per day but is otherwise healthy. A lumbar MRI was negative at the time of injury, and his PCP diagnosed lumbar strain and has prescribed increasing doses of hydrocodone/acetaminophen 10/500 in response to persistent pain complaints. The patient

now reports taking 8 tablets per day and says that this is the only thing that helps, even though he feels he is getting "immune" to the drug. He still reports 10/10 pain, and has had multiple ER visits and early refill requests for his opioids. He has refused to do physical therapy, saying it makes his pain worse, and becomes angry at the suggestion of trialing any other medications for his pain. Controlled drug database screen demonstrates that he filled a prescription for 10 tablets of hydrocodone/acetaminophen 10/500 from another provider in the ER yesterday. A urine drug screen performed today in the office is negative for opioids. What is the most likely diagnosis?

A. Opioid abuse
B. Opioid diversion
C. Pseudoaddiction
D. Opioid tolerance
E. Opioid-induced hyperalgesia

28. A 48-year-old patient with low back pain and chronic left L5 radiculopathy status post lumbar fusion is reporting a lack of efficacy from his medication regimen, which has been unchanged for 2 years. He is working and had been highly functional up until a few months ago. He is taking gabapentin 600 mg TID, celecoxib 100 mg po BID, and sustained-release oxycodone 40 mg BID. He reports his typical pain seems worse, and his scar and other areas are becoming increasingly sensitive to touch. Repeat imaging of the lumbar spine shows no new pathology. He has been compliant with physical therapy without effect. After increasing his oxycodone to 60 mg po BID, he notes that his pain is no better, and even with less activity, seems to be getting worse. What is the LEAST appropriate course of action?

A. Increase his oxycodone to 80 mg BID.
B. Transition to methadone 20 mg BID.
C. Increase his gabapentin to 1,200 mg TID.
D. Discontinue his oxycodone by taper.
E. Spinal cord stimulation

29. Opioid-induced hyperalgesia is primarily mediated by excitation of which of the following receptors?

A. NMDA receptors in CNS
B. Peripheral NMDA receptors
C. CNS μ-opioid receptors
D. Peripheral μ-opioid receptors
E. None of the above

30. The diagnosis of complex regional pain syndrome (CRPS) requires all of the following EXCEPT

A. Exclusion of another etiology for the symptoms
B. Relief of pain by sympathetic blockade
C. Pain in a nondermatomal distribution
D. Pain out of proportion to inciting event
E. Predominance of vasomotor, sudomotor, and/or trophic findings

31. Two weeks after arthroscopic knee surgery, a patient reports excruciating pain from the medial aspect of her knee down to her medial malleolus. She has allodynia and numbness in the same distribution. Her knee is swollen with normal range of motion. There is no fever or erythema. Her calf and ankle are nontender. Her surgeon finds no operatively correctable reason for her pain. Hydrocodone is ineffective in relieving her pain. What is the next best step in management?

A. Schedule for a lumbar sympathetic block.
B. Order physical therapy.
C. Trial of high-dose opioids
D. Trial of gabapentin
E. Sciatic nerve block with local anesthetic and steroid

32. Which of the following is not typical of chronic, or stage III, CRPS?

A. Atrophic skin with brittle nails
B. Limited range of motion in affected extremity
C. Decreased sympathetic outflow to extremity
D. Decreased reactivity of adrenergic receptors in affected limb
E. Patchy subchondral osteopenia in affected limb on plain radiographs

33. Which of the following is likely to be the LEAST effective pharmacologic treatment of a patient with CRPS?

A. IV bisphosphonates
B. Oral corticosteroids
C. Amitriptyline
D. Gabapentin
E. High-dose vitamin C

34. The primary goal in treatment of CRPS is

A. Abolition of pain
B. Prevention of functional loss in the extremity
C. Management of anxiety and depression that worsen pain
D. Reduction of sympathetic outflow to the extremity
E. Prevention of spread of symptoms to the contralateral extremity

35. A 55-year-old patient with CRPS type I of the left lower extremity, in remission for 5 years, developed a recrudescence of his symptoms 3 months ago, after a knee

arthroscopy in the affected limb. He has not responded to pharmacologic management and is having difficulty with physical therapy secondary to the pain. All of the following are appropriate in this context EXCEPT

A. Lumbar sympathectomy with phenol
B. Lumbar sympathetic block with local anesthetic
C. Epidural with clonidine
D. Intravenous regional anesthesia with clonidine
E. Trial of thoracic spinal cord stimulation

36. A man hits the tip of his finger with a hammer. He experiences a sharp pain and immediately withdraws his hand, experiences a dull residual ache in the entire finger, and then rubs his finger briskly, which seems to make it feel better. What receptors are responsible for each of these four sensations, in the order they were experienced?

A. Aδ, Aα, C, Aβ
B. Aβ, C, Aδ, Aα
C. Aδ, Aα, Aβ, C
D. Aα, Aδ, C, Aβ
E. C, Aα, Aδ, Aβ

37. Which area of the brain does NOT play a role in the emotional/affective (as opposed to the sensory/discriminative) experience of pain?

A. Anterior cingulate cortex (ACC)
B. Insula
C. Dorsolateral prefrontal cortex (DLPFC)
D. Spinothalamic tract
E. Spinolimbic tract

38. A 28-year-old woman with TMJ and predominantly right-sided chronic headaches reports that, while having her ears pierced, the right piercing hurt exponentially more than the left one did. What is the best term to describe this response?

A. Hyperalgesia
B. Allodynia
C. Hyperpathia
D. Hyperesthesia
E. Paresthesia

39. Peripheral sensitization of nociceptors occurring after tissue injury can involve all of the following substances EXCEPT

A. Bradykinin
B. Substance P
C. Prostaglandins
D. Serotonin
E. Glutamate

40. Which of the following statements about visceral pain is INCORRECT?

A. Visceral pain is typically described as crampy and diffuse.
B. There are a larger number of visceral afferent nerves than somatic afferent nerves.
C. Visceral afferents terminate in the spinal cord in the same location as somatic afferents.
D. Visceral afferents are insensitive to heat or cutting stimuli.
E. Visceral afferents run with sympathetic fibers, traveling in the sympathetic chain on their way to the dorsal root ganglion, where their cell bodies reside.

41. After receiving a new medication for low back pain, a patient taking fluoxetine for depression develops fever, diaphoresis, nausea, vomiting, agitation, and tremors. Which medication was the most likely precipitant of these symptoms?

A. Tramadol
B. Methadone
C. Pregabalin
D. Carbamazepine
E. Gabapentin

42. A 28-year-old woman describes pain in the right side of her face after extraction of a lower molar. She has a history of TMJ, depression, and migraines accompanied by photophobia and aura. She is otherwise healthy. She notes that the entire right side of her face feels numb, and she reports a patchy sensory deficit to light touch throughout. She has constant pain at baseline, with additional shooting pain that occurs 10 to 15 times a day into her right jaw, ear, and neck without any inciting event. The most likely diagnosis is

A. Glossopharyngeal neuralgia
B. Trigeminal neuralgia
C. Trigeminal neuropathic pain
D. Atypical facial pain
E. Postherpetic neuralgia

43. A 55-year-old woman with unilateral intermittent lancinating facial pain radiating to the jaw presents to your clinic for pain management. Which medication is the most appropriate first-line therapy?

A. Gabapentin
B. Carbamazepine
C. Hydrocodone
D. Amitriptyline
E. Oxcarbazepine

44. A 50-year-old man with controlled hypertension developed trigeminal neuralgia (TGN) 3 months ago, and was found on imaging to have vascular compression of the trigeminal nerve at the level of its entry into the pons. He has been refractory to medical management. Which intervention is the next best step?

A. Microvascular decompression with craniotomy
B. Gamma-knife stereotactic radiosurgery at the pontine entry zone
C. Percutaneous thermal radiofrequency ablation of trigeminal ganglion
D. Percutaneous chemoablation of the trigeminal ganglion with phenol
E. Nucleus caudalis dorsal-root entry zone lesion (DREZ)

45. After a left lumbar sympathetic block for complex regional pain syndrome, a patient reports she cannot feel or move her left thigh. What is the most likely cause?

A. Epidural spread of local anesthetic
B. Acute genitofemoral neuralgia
C. Spread of local anesthetic to the lumbar plexus
D. Hematoma compressing the femoral nerve
E. Anterior spinal cord infarct

46. A 30 year-old healthy man reports burning pain and numbness in his right groin and testicle after a laparoscopic inguinal herniorrhaphy with mesh. He has a sensory deficit to ice in the area of his anterior scrotum and an absent cremasteric reflex. He denies any leg pain, numbness, or weakness. His pain should be relieved by deposition of local anesthetic in which area?

A. 2 cm lateral and inferior to the anterior superior iliac spine (ASIS), deep to the fascia lata
B. Lateral to the pubic tubercle periosteum
C. 2 cm medial and superior to the ASIS, deep to the fascia of the internal oblique muscle
D. 2 cm lateral and inferior to the pubic tubercle, deep to the fascia of the adductor longus and brevis
E. Immediately lateral to the femoral artery at the inguinal crease

47. What is the most reliable method to assess achievement of adequate stellate ganglion blockade?

A. Horner syndrome
B. Hoarseness
C. Ipsilateral increase in hand temperature
D. Nasal congestion
E. Fluoroscopic confirmation of needle placement

48. The stellate ganglion is located posteriorly to the vertebral artery at which vertebral level?

A. C5–C6
B. C6–C7
C. C7–T1
D. T1–T2
E. T2–T3

49. A patient becomes tachycardic and begins coughing during stellate ganglion blockade, as the needle is advanced in an oblique approach to the uncinate process of C7. What is the next step in evaluation and/or treatment?

A. Order a chest x-ray.
B. Reassure the patient that this is normal.
C. Reposition the patient.
D. Administer more sedation.
E. Administer seizure prophylaxis.

50. A patient with Raynaud's Syndrome develops severe vasospasm in both upper extremities and is referred for stellate ganglion blocks. Bilateral blockade is performed. Within a few minutes, the patient begins to exhibit stridor and desaturates to 75% despite 6 L oxygen via nasal cannula. With bag-valve mask ventilation, synchronized to her respiratory effort, she is able to oxygenate and ventilate on room air. What has most likely occurred?

A. Bilateral phrenic nerve paralysis
B. Epidural spread of local anesthetic
C. Total spinal anesthesia
D. Bilateral recurrent laryngeal nerve paralysis
E. Paratracheal hematoma

51. A patient with endometriosis is experiencing pain unresponsive to pharmacologic management. Which of the following blocks is most appropriate?

A. Superior hypogastric plexus
B. Inferior hypogastric plexus
C. Pudendal nerve
D. Ilioinguinal nerve
E. Sacral plexus

52. During a superior hypogastric plexus block for management of pelvic pain, the patient reports a paresthesia going down her leg and into her foot. What nerve is most likely to have been irritated?

A. L4 nerve root
B. L5 nerve root
C. S1 nerve root
D. Sciatic nerve
E. Superior hypogastric plexus

53. Six months after an episode of acute herpes zoster, a patient reports persistent pain in her T8 dermatome, although the rash is now healed. What is the LEAST appropriate management?

A. Topical lidocaine
B. Prednisone
C. Amitriptyline
D. Opioids
E. Gabapentin

54. Which of the following interventional treatments for the rash shown in (Fig. 8.2), if performed, is LEAST likely to provide analgesia?

A. Cervical epidural steroid injection
B. Stellate ganglion block
C. Interscalene block
D. T1–2 intercostal nerve block
E. Intrathecal methylprednisolone

55. A 2-week-old, 2.5-kg child arrives in the OR for repair of an incarcerated inguinal hernia. Caudal anesthesia is performed with 2.5 cc of 0.25% bupivacaine with 1:200,000 epinephrine, after a negative test dose of 0.5 cc of the same local anesthetic solution. Five minutes later, the infant, who is awake, is noted to be twitching and has developed a cardiac dysrhythmia on his ECG. What risk factor most likely contributed to this outcome?

A. Overdose of bupivacaine
B. Decreased hepatic metabolism and protein binding of local anesthetic
C. Use of epinephrine
D. Excessive volume of local anesthetic
E. Methylparaben preservative in the bupivacaine solution

56. Two minutes after performance of an interscalene block with 30 cc of 0.25% bupivacaine and 100 mcg of clonidine, a healthy 40-year-old, 80-kg man reports perioral numbness and tinnitus, which then rapidly progresses to tonic clonic seizure activity. After you obtain an adequate airway and IV access, he is still exhibiting some seizure activity, but his oxygen saturation is 100% on 100% FiO_2. His blood pressure is 75/30, and heart rate is 130 with frequent PVCs. What is the next appropriate step?

A. 2 mg of midazolam
B. 1 mg of epinephrine
C. 100 cc bolus of 20% Intralipid
D. 40 U of vasopressin
E. 100 mcg of phenylephrine

57. What property of a local anesthetic is most responsible for its duration of action?

A. Lipid solubility
B. Protein binding
C. pKa
D. Intrinsic vasodilator activity
E. Concentration

58. A 28-year-old woman is scheduled to undergo ORIF of a forearm fracture under general anesthesia, with an axillary block placed preoperatively for postoperative analgesia. What adjuncts added to local anesthetic are least likely to prolong the duration of her sensory blockade?

A. Clonidine
B. Dexamethasone
C. Morphine
D. Epinephrine
E. All of the above will prolong the duration of the blockade.

59. Which patient is the best candidate for a lumbar epidural steroid injection?

A. A 72-year-old woman who reports new onset of right lower-extremity pain from her back into her big toe in the past month. MRI demonstrates severe central spinal stenosis at L4–5 with multilevel degenerative disk disease, ligamentum flavum hypertrophy, and facet arthropathy.
B. A 41-year-old man with axial low back pain for 20 years, unchanged, refractory to pharmacologic management, with MRI demonstrating multilevel degenerative disk disease
C. A 64-year-old man with back and right leg pain, status post L4–5 laminectomy 6 months ago, with persistent right L5 radiculopathy, documented by EMG/NCV study
D. A 28-year-old woman, injured lifting a box at work a week ago, with back pain radiating to her groin and into her buttocks bilaterally. MRI demonstrates mild disk bulge at L5–S1, with no annular tear, nor any central canal stenosis or neuroforaminal stenosis.
E. None of these patients is a good candidate for lumbar epidural steroid injection.

60. Which is true regarding opioid analgesia in the neonate?

A. Neonates do not experience pain.
B. Peripheral, spinal, and supraspinal pain-transmission pathways are fully formed at birth.

C. Neonatal opioid requirements are less than in a 2-year-old.
D. Cognitive and behavioral function is decreased in neonates given opioids compared to those who did not receive opioids in the neonatal period.
E. Neonatal abstinence syndrome in children of opioid-dependent mothers should be treated, in most cases, with opioids.

61. A 38-year-old otherwise healthy woman taking Suboxone (buprenorphine and naloxone) for opioid addiction therapy presents after a work-related crush injury to her hand requiring emergent surgery. She received no premedications prior to surgery, followed by an uneventful general anesthetic maintained with sevoflurane, and fentanyl. She presents to the postanesthesia care unit with a respiratory rate of 4 breaths per minute, with a P_{CO_2} of 65 on arterial blood gas analysis. Her urine drug screen was otherwise unremarkable. You give her 0.04 mcg of naloxone without any noticeable improvement. Which of the following is the next most appropriate pharmacotherapy?

A. Give a single equipotent dose of the μ-opioid receptor antagonist naltrexone.
B. Titrate additional doses of the μ-opioid receptor antagonist naloxone.
C. Give a single equipotent dose of the selective μ-opioid receptor antagonist cyprodime.
D. Titrate the benzodiazepine antagonist flumazenil to physiologic response.
E. Give an equipotent dose of the selective delta opioid receptor antagonist naltrindole.

62. A 45-year-old man arrives in the postanesthesia care unit (PACU) after an uneventful laparoscopic appendectomy. He has a history of opioid addiction for which he now takes sublingual buprenorphine. He has been off his buprenorphine for 2 weeks and has been maintained temporarily on long-acting oxycodone. Restarting his home dose of buprenorphine in the PACU 6 hours after surgery would most likely result in

A. Opioid-induced respiratory depression
B. Improved analgesia
C. Opioid withdrawal
D. Reduced opioid-induced pruritus
E. Salivation, increased urination, loose stools

63. A 35-year-old man taking chronic buprenorphine for opioid addiction treatment presents after a gunshot wound to the abdomen for emergent exploratory laparotomy. After an uneventful operation, he is found to exhibit persistent respiratory depression and excessive sedation. Concomitant use of which of the following premedications most likely exacerbated this patient's symptoms?

A. Proton-pump inhibitor
B. Metoclopramide
C. Midazolam
D. Clindamycin
E. Dexamethasone

64. A 54-year-old woman with a history of hypertension (controlled), breast cancer (currently in remission for 5 years), and obesity (BMI 31) is being treated in your pain clinic for plantar fasciitis. Today she complains of lower back pain, which she believes was brought on by shoveling snow 2 months ago. It is a constant, dull 4/10 pain with radiation in a right L1–2 nerve root distribution, does not vary by time of day, and is partially relieved with acetaminophen. Sensory and motor exams are normal. The best course of action is:

A. Trial of physical therapy and anti-inflammatory therapy, return to clinic in 1 month
B. Trial of lumbar epidural steroid injection, return to clinic in 1 month
C. Lateral and posterior plain films (x-ray) of lumbar spine as soon as possible
D. MRI of lumbar spine as soon as possible
E. Expectant therapy

65. A 74-year-old man with metastatic lung cancer is being treated in hospice for pain. Until now, his pain has been successfully managed with ibuprofen 400 mg four times per day and hydrocodone/acetaminophen 5/500mg (Vicodin) every 4 to 6 hours, with oxycodone 5 mg every 2 to 3 hours for breakthrough pain. Gastrointestinal upset from the ibuprofen has been treated with omeprazole, and constipation from the opioid therapy is being treated with docusate and senna. His hematocrit is stable at 34% and serum creatinine is 1.1 (baseline 1.0). His current pain regimen is no longer adequate. In accordance with the WHO analgesic ladder for cancer pain, you recommend which of the following?

A. Increase breakthrough medication to oxycodone 10 mg every 2 to 3 hours. Consider adding adjuvants such as antidepressants or anticonvulsants.
B. Replace scheduled Vicodin with a long-acting opioid such as controlled-release morphine in equivalent dose, and titrate to patient comfort. Consider adding adjuvant therapy such as antidepressant or anticonvulsant medication.
C. Replace "weak" opioid (Vicodin) with "strong" opioid (e.g., morphine) and eliminate NSAID (ibuprofen) to limit risk of gastrointestinal and renal toxicity.

D. Add "strong" opioid such as controlled-release morphine 20 mg twice per day and leave other medications unchanged.
E. Substitute acetominophen for ibuprofen. Leave opioid medications and dosing unchanged.

66. You are managing analgesia for a 73-year-old man undergoing outpatient treatment for metastatic renal cell carcinoma. He is currently taking controlled-release morphine (MS Contin) 60 mg PO twice per day with hydromorphone (Dilaudid) 2 to 4 mg PO every 3 to 4 hours PRN breakthrough pain. During your evaluation, his daughter, who is the healthcare proxy, expresses concern about the sedating effect of these drugs and their addictive potential. She asks if there are any alternatives. You explain to her that

A. You would advise limiting opioid use because of their addictive potential.
B. Physical dependence is one of the warning signs of addiction in chronic opioid therapy.
C. Methadone is less addictive than other opioids.
D. Psychostimulants (e.g., caffeine, amphetamine) may themselves have an analgesic effect.
E. You deny any sedating effects of these drugs.

CHAPTER 8 ANSWERS

1. ANSWER: B

Perioperative ulnar neuropathy is a surprisingly common and potentially preventable perioperative injury. According to the American Society of Anesthesiologists Closed Claims Study Database, ulnar injury accounts for roughly one-third of all nerve injury claims. A review of over 1 million patients by Prielipp et al. found the incidence of ulnar neuropathy to be 1 per 2,729 patients. 9% of these had bilateral neuropathies. Factors associated with persistent ulnar neuropathy included male gender and a duration of hospitalization of more than 14 days ($p < 0.01$). Neuropathy was more likely to develop in very thin and obese patients than in patients with average body habitus. Neither the type of anesthetic technique nor the patient position was found to be associated with this neuropathy.

The ulnar nerve is responsible for sensation over the dorsal and palmar aspects of the fifth and half of the fourth finger with some variation. The motor supply is to the intrinsic muscles of the hand as well as the finger and wrist flexors.

The median nerve innervates the entire palmar aspect of the thumb through fourth digit (half), and the dorsal tips (distal to the PIP [proximal interphalangeal] joint) of the same fingers. Its motor supply is to the forearm pronators and the muscles of the thumb, as well as some of the hand intrinsics. Injury most often occurs as the nerve passes through the carpal tunnel. Injury is manifested as thenar muscle wasting, numbness in the distribution described above, and paresthesias in the distribution of the nerve.

ADDITIONAL READINGS

Prielipp RC, Morell RC, Butterworth J. Ulnar nerve injury and perioperative arm positioning. *Anesthesiol Clin North Am*. 2002;20(3):589–603.

Warner MA, Warner ME, Martin JT. Ulnar neuropathy. Incidence, outcome, and risk factors in sedated or anesthetized patients *Anesthesiology*. 1994;81(6):1332–1340.

2. ANSWER: D

Patient positioning is often a compromise between the posture necessary for surgical exposure and the anatomic and physiologic arrangement that the patient can tolerate. The brachial plexus is a source of injury. According to a review of the American Society of Anesthesiologists (ASA) Closed Claims Database from 1999, 670 (16% of 4183) claims were for anesthesia-related nerve injury. The most frequent sites of injury were the ulnar nerve (28%), brachial plexus (20%), lumbosacral nerve root (16%), and spinal cord (13%). Ulnar nerve (85%) injuries were more likely to have occurred in association with general anesthesia, whereas spinal cord (58%) and lumbosacral nerve root (92%) injuries were more likely to occur with regional techniques. Ulnar nerve injury occurred predominately in men (75%) and was also more apt to have a delayed onset of symptoms (62%) than other nerve injuries. Spinal cord injuries were the leading cause of claims for nerve injury that occurred in the 1990s.

Radial nerve compression can occur as the nerve passes dorsolaterally around the middle and lower portions of the humerus in the musculospiral groove. This can occur during periods of pressure from the vertical bars of an anesthesia screen or from frequent cycling of a blood pressure cuff. The radial nerve is responsible for wrist extension and thumb abduction as well as sensation to the "snuff box," the webspace between the thumb and index finger. Medial nerve dysfunction may be a result of trauma to the antecubital fossa, such as during a difficult intravenous catheter placement. The mechanism for ulnar neuropathy is often compression at the cubital tunnel by the cubital tunnel retinaculum with elbow flexion, or, in elbow extension, compression of the ulnar nerve around the medial epicondyle.

KEY FACTS: ANESTHESIA COMPLICATIONS: NERVE INJURY

- According to the ASA Closed Claims Database, the most frequent sites of injury were the ulnar nerve (28%), brachial plexus (20%), lumbosacral nerve root (16%), and spinal cord (13%).
- Neuropathy is more likely to develop in very thin and obese patients than in patients with average body habitus.
- Medial nerve dysfunction may be a result of trauma to the antecubital fossa, such as during a difficult intravenous catheter placement or long periods of frequent cycling of a blood pressure cuff.

ADDITIONAL READINGS

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Cheney FW, Domino KB, Caplan RA, Posner KL. Nerve injury associated with anesthesia: a closed claims analysis. *Anesthesiology*. 1999;90(4):1062–1069.

3. ANSWER: D

Epidural abscess is a rare but potentially catastrophic complication of neuraxial anesthesia. Most epidural abscesses present days to weeks after neuraxial blockade, in contrast to localized skin infections, which typically present sooner, with more local tissue edema and drainage. Most

patients with spinal epidural abscesses have other comorbidities such as diabetes, alcoholism, malignancy, or an immunocompromised state. If an epidural abscess is suspected, immediate evaluation with MRI is warranted. If confirmatory, an urgent laminectomy and decompression would be the definitive treatment. Antibiotic therapy, pending microbiology results, should be initiated to cover both *S. aureus*, the most common pathogen, as well as gram-negative bacilli due to the risk of catastrophic consequences.

Benzon et al. relate that the pathology of an epidural abscess most often results from one of five mechanisms: "(1) direct inoculation of bacteria either at the time of epidural catheter insertion or by contaminated injection/infusion; (2) contiguous spread from a nearby site of infection; (3) spinal instrumentation/neurosurgery; (4) lymphatic spread from a paraspinous lesion; or (5) hematogenous spread, which is thought to be the most common mechanism."

KEY FACTS: BACK PAIN: EPIDURAL ABSCESS

- Most epidural abscesses present days to weeks after neuraxial blockade, in contrast to localized skin infections, which typically present sooner with more local tissue edema drainage.
- Risk factors include diabetes, alcoholism, malignancy, or an immunocompromised state.
- If an epidural abscess is suspected, immediate evaluation with MRI is warranted.

ADDITIONAL READINGS

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Darouiche RO. Spinal epidural abscess. *N Engl J Med*. 2006; 355(19):2012–2020.

4. ANSWER: A

NSAIDs are characterized by their ability to inhibit the COX enzyme. The most commonly known mechanism of action is the prevention of sensitization of the peripheral nociceptors by diminishing prostaglandin formation. As different NSAIDs block COX to different degrees, membrane stabilization has also been suggested as a mechanism of action. COX-1 produces prostaglandins that regulate renal, vascular, and gastric homeostasis, while COX-2 affects pain. NSAIDs have multiple sites of action in the central nervous system as well. They have been shown to reduce hyperalgesia evoked by substance P and NMDA. Most of the COX-inhibitory activity lies within the S form. NSAIDs are metabolized in the liver with little dependence on renal elimination. The toxicity may be related to their plasma half-lives; the greater the half-life, the greater the risk of toxicity.

KEY FACTS: BREAKTHROUGH PAIN: NSAIDS

- NSAIDs prevent the sensitization of the peripheral nociceptors by diminishing prostaglandin formation.
- COX-1 produces prostaglandins that regulate renal, vascular, and gastric homeostasis, while COX-2 affects pain.
- NSAIDs are metabolized in the liver with little dependence on renal elimination.

ADDITIONAL READINGS

Barash P, Cullen B, Stoelting R. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.

Benzon H, Raja H, Fishman S, et al. NSAIDs and COX-2 selective inhibitors. In: *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005:141–158.

5. ANSWER: D

Opioids are a common component of pain-management plans throughout the United States; as the use has increased, more stringent guidelines have been put in place to help avoid diversion and misuse as complications of therapy. Opioid use in chronic nonmalignant pain (CNMP) has been controversial, in part due to these issues. Generally, opioids are used as a second-line therapy once nonopioid medications or other therapeutic interventions have failed. In 1998 the House of Delegates of the Federation of State Medical Boards of the United States established and adopted the "Model Guidelines for the Use of Controlled Substances for the Treatment of Pain." Section III outlines these guidelines: 1. Evaluation of the Patient—a complete medical history and physical exam must be conducted and documented in the medical record; 2. Treatment Plan—this should outline objectives that will determine treatment success and should be individualized for each patient; 3. Informed Consent and Agreement for Treatment—risks and benefits should be discussed and an agreement (with monitoring details such as urine drug screens) should be implemented; 4. Periodic Review—at reasonable intervals a physician should review the plan and evaluation toward initially stated objectives; 5. Consultation—the physician should be willing to refer the patient to other providers as necessary; 6. Medical Records—records should contain documentation of the previous guidelines and should be readily available for review; 7. Compliance with Controlled

Substances Laws and Regulations—the physician should be licensed within the state and comply with federal and state regulations.

Regarding patients who have been aberrant, the physician must determine the appropriate course of action on a case-by-case basis. There are no guidelines stating that opioids must be prescribed to a patient to avoid withdrawal.

KEY FACTS: BREAKTHROUGH PAIN: OPIOID PRESCRIBING

- Chronic opioids are used as a second-line therapy once nonopioid medications or other therapeutic interventions have failed.
- The Federation of State Medical Boards of the United States has established guidelines for the use of controlled substances: patient evaluation, treatment plan, informed consent, periodic review of the plan, consultation, appropriate documentation, and compliance with state and federal laws are all included.
- There are no guidelines stating that opioids must be prescribed to a patient to avoid withdrawal.

ADDITIONAL READINGS

Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

http://www.fsmb.org/. Model Guidelines for the Use of Controlled Substances for the Treatment of Pain, 1998.

6. ANSWER: B

In assessing cancer pain patients, it is important to get a focused history and physical to include all symptoms a patient may be experiencing. For most cancer pain patients, there are multiple factors contributing to the overall picture, and it is important to note whether the presentation is chronic or acute and also whether the symptoms are related to cancer progression, related to therapeutic intervention (medication side effects), or completely unrelated to their disease (another comorbidity). The severity and temporal profile of each complaint should be assessed. Change in constitutional symptoms, such as unintentional weight loss, is suspicious for malignancy.

Most visceral pain is described as crampy and difficult to localize as there is a lack of specificity for innervation as compared with somatic pain, which presents as sharp, throbbing pain that is easily localized. Most cancer pain is continuous with variation in intensity, often worse at night. Cancer pain is often associated with paroxysms of pain with certain movements.

KEY FACTS: CANCER PAIN: DIAGNOSIS

- Most visceral pain is described as crampy and difficult to localize as there is a lack of specificity for innervation.
- Any time a change in constitutional symptoms occurs (weight loss, appetite or sleep changes, changes in bowel habits), malignancy should be considered.
- Most somatic pain presents as sharp, throbbing pain that is easily localized.
- Most cancer pain is continuous with variation in intensity, often worse at night.

ADDITIONAL READINGS

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Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

7. ANSWER: C

The use of oral analgesics is considered essential to management of cancer pain. In 1988 the WHO first promoted the Canadian three-step ladder for cancer pain management. It provides a template that can be used according to the severity of the patient's pain (Fig. 8.1).

Step 1 includes acetaminophen and NSAIDs. These are available without prescription and are used as first-line therapy for mild pain. Step 2 includes "weak" opioids available as combinations with acetaminophen or aspirin such as hydrocodone/acetaminophen and oxycodone/

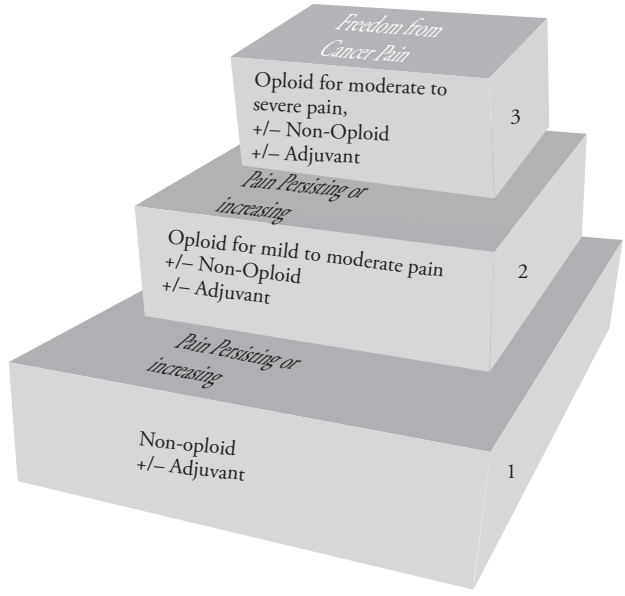

Figure 8.1 WHO's Pain Relief Ladder. Source: http://www.who.int/cancer/palliative/painladder/en/

acetaminophen, which have a ceiling amount due to the safe amount of acetaminophen that can be administered. Step 3 is used for severe pain or when the medications from Step 2 are ineffective in controlling pain. Step 3 includes fentanyl and hydromorphone. Interventions are not noted on the WHO ladder but are informally referenced as "Step 4."

KEY FACTS: CANCER PAIN: MANAGEMENT

- The WHO three-step ladder can be considered for cancer pain management.
- Step 1 includes acetaminophen and NSAIDs.
- Step 2 includes "weak opioids." Step 3 is used when Step 2 medications are ineffective. It is not necessary to try all medications in the previous steps before moving to the next tier.

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Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

8. ANSWER: D

Neurolytic visceral nerve blocks can be performed for both cancer and noncancer pain; however, due to the regrowth of axons and the risk for development of central pain mechanisms (denervation dysthesia), these are not commonly performed for nonmalignant pain. Also, pain in cancer patients is often mediated through multiple mechanisms, which may involve a combination of somatic and neuropathic pain. Thus, visceral nerve blocks are often used in conjunction with medications and other therapies.

The celiac plexus is located in the retroperitoneum at the level of the T12 and L1 vertebrae. The technique sometimes involves placing bilateral needles. The plexus itself can be approached anteriorly or posteriorly; however, the classic technique involves needle placement anterior to the body of L1. Alternatively, a splanchnic nerve block can be performed at the anterolateral surface of T12 and/or T11. The celiac plexus provides autonomic supply to the liver, pancreas, gallbladder, stomach, spleen, kidneys, intestines, and adrenal gland.

The superior hypogastric plexus is located in the retroperitoneum, extending from the fifth lumbar vertebral body to the upper third of the first sacral vertebral body. A superior hypogastric plexus block can be utilized in cancer of the pelvis.

KEY FACTS: CANCER PAIN: MANAGEMENT

- Neurolytic visceral nerve blocks can be performed for cancerous and noncancer pain; however, due to the regrowth of axons and the risk for development of central pain mechanisms (denervation dysthesia), these are not commonly performed for nonmalignant pain.
- The celiac plexus is located in the retroperitoneum at the level of the T12 and L1 vertebrae.
- The celiac plexus provides autonomic supply to the liver, pancreas, gallbladder, stomach, spleen, kidneys, intestines, and adrenal gland and is blocked for pain control in pancreatic cancer and chronic pancreatitis.

ADDITIONAL READINGS

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Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

9. ANSWER: D

CRPS is a term that describes a phenomenon that was previously called reflex sympathetic dystrophy. ***Complex*** describes the varied nature of the syndrome, as some patients present with greatly differing states of involvement. ***Regional*** implies that the symptoms are often nondermatomal, and often extend beyond the area of initial injury. ***Syndrome*** notes the constellation of symptoms associated with the injury. As "sympathetic" dysfunction may or may not be present, it has been removed from the revised definition. Most patients exhibit pain out of proportion to exam, a variable clinical course, sensory changes, trophic and inflammatory changes, and some type of motor involvement. A psychological component such as anxiety and depression is often present as well.

The exact mechanism for CRPS is unknown. However, it is theorized that an initial injury activates nociceptors that subsequently develop adrenergic sensitivity; this activity maintains the central nervous system in a sensitized state. Continued input from ectopic generators or coupling between sensory afferent fibers and sympathetic fibers maintains the state of hyperexcitability.

ADDITIONAL READINGS

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Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

10. ANSWER: C

Peripheral sympathetic blocks have been used in the treatment of complex regional pain syndrome (CRPS) or for cases suspicious for sympathetic involvement. Patients exhibiting symptoms of CRPS may exhibit sensory changes such as allodynia and hyperalgesia; autonomic dysfunction with swelling, color change, or decreased temperature; motor impairment; psychological issues such as anxiety or depression; and trophic and inflammatory changes such as poor nail and hair growth.

The indications for lumbar sympathetic blocks include sympathetically mediated pain in the lower extremities, vascular insufficiency syndromes, and for management of neuralgic pain after trauma or limb amputation. The lumbar sympathetic chain lies along the anterolateral surface of the L2 and L3 vertebral bodies. Celiac plexus blockade is used for visceral pain, including the gallbladder, stomach, and pancreas. The stellate ganglion block targets the cervicothoracic ganglion. Indications include head or facial pain, neck pain, Raynaud's disease, circulatory pain, and CRPS of the hand or arm. The ganglion impar is the termination of the sympathetic chains, located just anterior to the sacrococcygeal junction. Indications include sympathetically mediated perineal pain.

KEY FACTS: CRPS DIAGNOSIS

- CRPS type I was previously called reflex sympathetic dystrophy.
- Most patients exhibit a variable clinical course, sensory changes, trophic and inflammatory changes, and some type of motor involvement. A psychological component such as anxiety and depression is often present as well.
- The proposed mechanism for CRPS is initial adrenergic sensitivity; continued input from ectopic generators or coupling between sensory afferent fibers and sympathetic fibers maintains the state of hyperexcitability.
- Peripheral sympathetic blocks are indicated for treatment in CRPS. The stellate and lumbar sympathetic ganglia are blocked for arm/hand and leg/foot CRPS, respectively.

ADDITIONAL READINGS

Barash P, Cullen B, Stoelting R. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.

Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

11. ANSWER: E

Visceral pain from pancreatic cancer is mediated by the celiac plexus. The plexus lies at the level of the T12 and L1 vertebrae, anterior to the crura of the diaphragm, and encases the anterolateral abdominal aorta. It is composed of both sympathetic and parasympathetic nerve fibers and provides autonomic supply to the liver, pancreas, gallbladder, stomach, kidneys, spleen, intestines, and adrenal glands. Neurolytic blocks are performed for carcinomas of these organs. A meta-analysis done in 1995 by Eisenberg et al. on neurolytic celiac plexus blocks showed partial to complete pain relief in 90% of patients 3 months after treatment and 70% to 90% of patients up to death.

Even under fluoroscopy or CT guidance, complications may occur with this procedure. Pneumothorax is a known complication of the block if the needle placement is too cephalad; however, pneumonia is unlikely to present this acutely during a procedure. This patient is at risk for pulmonary embolism given his cancer diagnosis, but it would be unlikely to be associated with the celiac plexus blockade. Diaphragmatic paralysis is a complication of phrenic nerve blockade after an interscalene brachial plexus block.

ADDITIONAL READINGS

Benzon H, Raja H, Fishman S, et al. Neurolytic visceral sympathetic blocks. In: *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005:542–549.

Waldman S. *Atlas of Interventional Pain Management*. 3rd ed. New York, NY: Elsevier; 2009.

12. ANSWER: A

This patient has developed a tension pneumothorax after a ***celiac plexus block***. Distended neck veins, tracheal deviation, tachypnea, hypoxia, and hypotension are all ominous signs. Additionally, he may present with anxiety . Hemodynamic decompensation is an indication for immediate needle decompression. Immediate endotracheal intubation may be avoided if the decompression is successful. Positive-pressure ventilation may be necessary if the patient continues to decline. A chest x-ray is appropriate but may delay treatment if tension pneumothorax is clinically suspected.

KEY FACTS: CELIAC PLEXUS BLOCK: COMPLICATIONS

- The celiac plexus lies at the level of the T12 and L1 vertebrae, anterior to the crura of the diaphragm, and encases the anterolateral abdominal aorta.
- Pneumothorax is a known complication of the block if the needle placement is too cephalad.
- If pneumothorax is suspected, hemodynamic decompensation is an indication for immediate needle decompression.

- The technique for needle decompression is using a 14- to 16-gauge intravenous cannula inserted into the second rib space in the left mid-clavicular line.

ADDITIONAL READINGS

Leigh-Smith S, Davies G. Indications for thoracic needle decompression. *J Trauma*. 2007;63(6):1403–1404.

13. ANSWER: C

Despite using fluoroscopic or CT guidance, complications may arise with celiac plexus blockade. Diarrhea due to the sympathetic blockade of the bowel is common, occurring in up to 50% of patients. Orthostatic hypotension may occur in 1% to 3% of patients after the block for up to 5 days. Treatments for both include increased fluid intake and bedrest. Loperamide or other antidiarrheal agents may also be used. Given the risk of diarrhea, this block should be avoided in patients with bowel obstructions. Other complications include backache from needle trauma, retroperitoneal hemorrhage, vascular injury, thoracic duct injury, and transient motor paralysis thought due to spasm of the lumbar segmental arteries that perfuse the spinal cord.

KEY FACTS: CELIAC PLEXUS BLOCK: SIDE EFFECTS

- Due to sympathetic blockade during celiac plexus block, common side effects include diarrhea and orthostatic hypotension.
- Procedure-related hypotension may be ameliorated by administering preprocedural IV fluids.
- Loperamide or other antidiarrheal agents may be used for the treatment of block-induced diarrhea.

ADDITIONAL READINGS

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Waldman S. *Atlas of Interventional Pain Management*. 3rd ed. New York, NY: Elsevier; 2009.

Yan B, Myers R. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. *Am J Gastroenterol*. 2007;102: 430–438.

14. ANSWER: B

Baclofen is a GABA-B receptor agonist; it binds to presynaptic GABA receptors in the dorsal horn of the spinal cord. By binding to GABA-B receptors, it decreases the release of excitatory neurotransmitters at the spinal cord level. It is often used to treat spasticity of spinal cord origin. Usual starting dose is 5 mg three times daily, titrated upward to a maximum daily dose of 80 to 100 mg. It is rapidly absorbed and only a small amount crosses the blood–brain barrier. Baclofen can also be administered intrathecally, which provides a faster route to the CSF and also may avoid systemic side effects as compared with oral administration. Rare complications of intrathecal baclofen administration include sedation, orthostatic hypotension, and pump-related complications. Intrathecal baclofen withdrawal can present with hallucinations, psychosis, hyperthermia (classically cyclic fevers), seizures, tachycardia, muscle rigidity, or autonomic dysfunction. It can resemble both sepsis and neuroleptic malignant syndrome.

KEY FACTS: CHRONIC PAIN MEDICATIONS: COMPLICATIONS OF BACLOFEN

- Baclofen is a GABA-B receptor agonist; it binds to presynaptic GABA receptors in the dorsal horn of the spinal cord.
- Rare complications of intrathecal baclofen administration include sedation, orthostatic hypotension, and pump-related complications. Intrathecal baclofen withdrawal can present as a septic-type picture.

ADDITIONAL READINGS

Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

15. ANSWER: A

Tramadol is a weak opioid agonist at the μ receptor but also has properties of inhibition of norepinephrine and serotonin reuptake. It is one-tenth as potent an analgesic as morphine and has fewer respiratory effects than morphine. It is not a schedule II narcotic, and was initially thought to have little abuse potential. However, this may not be completely true for a small population of patients. It has been used successfully in pediatric pain, osteoarthritis of adults, fibromyalgia, and diabetic neuropathy. Side effects include sedation, nausea, headache. Caution should be used in patients taking other selective serotonin reuptake inhibitors (SSRIs) or other selective serotonin and norepinephrine inhibitors (SNRIs). Patients with a history of alcohol abuse are at higher risk for seizures.

KEY FACTS: CHRONIC PAIN MEDICATIONS: COMPLICATIONS OF TRAMADOL

- Tramadol is a weak opioid agonist at the μ receptor but also has properties of inhibition of norepinephrine and serotonin reuptake.
- Caution should be used in patients taking other selective serotonin reuptake inhibitors (SSRIs) or other selective serotonin and norepinephrine inhibitors (SNRIs).
- Patients with a history of alcohol abuse are at higher risk for seizures.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

16. ANSWER: A

Cocaine is a prevalent drug of abuse in the American population. In the early 2000s, more than 23 million Americans were estimated to have used cocaine at some time in their lives. Cocaine effectively blocks the transporter that allows reuptake of dopamine from the synapse, leading to increased dopamine concentrations in the brain. Dopamine also blocks both norepinephrine and serotonin uptake, leading to increased postsynaptic concentrations of these excitatory neurotransmitters.

ADDITIONAL READINGS

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Lakoski J, Galloway M, White F. *Cocaine Pharmacology, Physiology, and Clinical Strategies.* Boca Raton, FL: CRC Press; 1992.

17. ANSWER: B.

Cocaine's mechanism of action involves preventing the reuptake of multiple neurotransmitters (dopamine, serotonin, and norepinephrine), thus increasing their postsynaptic concentrations. Chronic use of cocaine leads to postsynaptic receptor downregulation. Direct-acting vasoconstrictors may be more effective in these cases than the indirect-acting ephedrine. Although in acute intoxication cocaine causes tachycardia and hypertension, in chronic abuse patients may exhibit bradycardia during severe hypovolemia.

Cocaine also has local anesthetic properties and is the only local anesthetic that inherently produces vasoconstriction. Therefore, the addition of epinephrine would be superfluous. Animal studies have shown that after pretreatment with epinephrine, cocaine facilitates the development of epinephrine-induced cardiac dysrhythmias during halothane anesthesia. Cocaine is contraindicated in hypertensive patients or in patients on monoamine oxidase inhibitor therapy or tricyclic antidepressants. Sympathomimetics can exacerbate the effects of cocaine and should not be used in patients who have been abusing the drug, especially during periods of acute intoxication.

KEY FACTS: COCAINE: MECHANISM OF ACTION

- Cocaine prevents the reuptake of multiple neurotransmitters—dopamine, serotonin, and norepinephrine—at the synapse, thus increasing their postsynaptic concentrations.
- Cocaine also has local anesthetic properties and is the only local anesthetic that inherently produces vasoconstriction.
- Cocaine is contraindicated in hypertensive patients or in patients on monoamine oxidase inhibitor therapy or tricyclic antidepressants.
- Sympathomimetics can exacerbate the effects of cocaine.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.

Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.

18. ANSWER: A

Peripheral polyneuropathy in diabetics is associated with multiple causes. Likewise, it can have multiple presentations, ranging from distal sensory loss that usually begins in the lower extremities to truncal neuropathy that may mimic a myocardial infarction. Entrapment neuropathies are known to be more frequent in diabetics than in nondiabetics.

Amyloidosis refers to a range of clinical conditions characterized by the deposition of amyloid proteins in various tissues throughout the body. It can be primary or familial in nature. Primary amyloidosis (AL) involves overproduction of proteins by plasma cells and is often treated with chemotherapy. Amyloidosis can also be a result of multiple myeloma (AA), familial, or associated with other chronic illnesses. As the neuropathy progresses, sensorimotor function is affected and there is loss of reflexes.

Thallium ingestion is associated with an acute onset of gastrointestinal symptoms. Confusion, psychosis, and convulsions may occur within seven days of exposure. One of the earliest findings, within 2 to 3 days, is a rapidly progressive peripheral neuropathy. Alopecia is noted within weeks after the exposure.

As many as 30% of patients with AIDS may develop painful neuropathy. Allodynia may occur, resulting in affected gait. Other neurologic symptoms include paresthesias in a "stocking-and-glove" distribution and autonomic dysfunction. EMG studies often reveal evidence of denervation.

Disease states that are characterized by inflammation, such as rheumatoid arthritis or infections, can exert pressure on the median nerve, leading to exacerbation of carpal tunnel. Additionally, alterations in the balance of body fluids during pregnancy or menopause or due to kidney failure may also increase the pressure within the carpal tunnel and lead to median nerve irritation. Of note, carpal tunnel associated with pregnancy typically resolves without treatment after the pregnancy has concluded.

KEY FACTS: DYSESTHESIA: PERIPHERAL NEUROPATHY

- In patients with diabetic neuropathy, the metabolic abnormalities include (1) accumulation of sorbitol, (2) auto-oxidation of glucose, resulting in reactive oxygen molecules, and (3) inappropriate activation of protein kinase C.
- Patients typically present with alterations in sensation, in a "stocking-and-glove" distribution.
- Neuropathy secondary to amyloidosis is caused by deposition of amyloid proteins in tissues; this can be a result of multiple myeloma.
- As many as 30% of patients with AIDS may develop painful neuropathy and allodynia.

ADDITIONAL READINGS

Benzon H, Raja H, Fishman S, et al. Diabetic and other peripheral neuropathies. In: *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005:418–425.

Dobbs MR. *Clinical Neurotoxicology: Syndromes, Substances, Environments*. Philadelphia, PA: Saunders Elsevier; 2009.

19. ANSWER: B

The placenta offers only a partial barrier to transport of drugs from mother to fetus. The factors that influence placental transfer include the physicochemical properties of the drug, maternal drug concentrations in the plasma, and the hemodynamic and anatomic properties of the placenta. Depression of the neonate can occur and it is important to note the dosage and timing of maternal opioids in regard to the time of birth. The nonionized moiety of a drug is more lipophilic than the ionized one. Opioids are weak bases, with a low degree of ionization. Fentanyl is highly lipophilic and highly bound to albumin; in animal models it crosses the placenta much more rapidly than meperidine. Chronic maternal use of opioids can lead to fetal dependence; neonatal naloxone administration can lead to a life-threatening neonatal abstinence syndrome. Compared to morphine, fentanyl tends to provoke less histamine-mediated pruritus and bronchoconstriction.

KEY FACTS: FENTANYL BINDING IN PREGNANCY

- The factors that influence placental transfer include the physicochemical properties of the drug, maternal drug concentrations in the plasma, properties of the placenta, and hemodynamic events within the fetomaternal unit.
- The nonionized moiety of a drug is more lipophilic than the ionized one.
- Fentanyl is highly lipophilic and highly bound to albumin and thus crosses the placenta more than meperidine.

ADDITIONAL READINGS

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Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.

20. ANSWER: D

Fibromyalgia is a syndrome characterized by diffuse pain along with fatigue, emotional distress, and other associated features such as headaches and irritable bowel syndrome. The pain often accompanies a state of heightened soft tissue tenderness. The diagnosis as per the American College of Rheumatology (1990) involves the following criteria: (1) chronic widespread pain (CWP) of at least 3 months' duration, present above and below the diaphragm, on both sides of the body, plus axial pain; and (2) painful tender points (TPs) in at least 11 out of 18 characteristic locations.

Patients are typically female, with higher levels of psychological illness. Associated conditions include irritable bowel syndrome, migraine headaches, and TMJ disorders. Ulcerative colitis is not commonly associated with fibromyalgia. The goal of treatment is to emphasize functional improvement and quality of life rather than "cure." Medications are often used in the treatment of fibromyalgia. Care plans should be evaluated often due to the risk that side effects may worsen the patient's fatigue.

KEY FACTS: FIBROMYALGIA: DIAGNOSTIC CRITERIA

- Fibromyalgia is a syndrome characterized by musculoskeletal pain along with fatigue, emotional distress, and other associated features such as headaches and irritable bowel syndrome.
- The diagnosis as per the American College of Rheumatology (1990) involves the following criteria: (1) chronic widespread pain (CWP) of at least 3 months' duration, present above and below the diaphragm, on both sides of the body, plus axial pain; and (2) painful tender points (TPs) in at least 11 out of 18 characteristic locations.
- The goal of treatment is most importantly to emphasize functional improvement and quality of life rather than "cure."

ADDITIONAL READINGS

Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

21. ANSWER: A

Pain during pregnancy is very common and treatment should be carefully examined, as many medications have teratogenic side effects and interventional treatment options are limited due to the deleterious effects of radiation on the developing fetus. The U.S. FDA requires labeling of drugs using the Pregnancy Category System. While 20 to 30 commonly used drugs are proven human teratogens, over 70 are listed as category X (teratogenic) and all new medications are listed as category C. Acetaminophen is considered category B; it is also considered the safest medication for nursing mothers. Ergotamine is contraindicated in pregnancy (category X) as it may be teratogenic and can also cause uterine contractions. During lactation, the amount of drug that the infant receives is dependent on maternal dose and dosing interval as well as the pharmacodynamic properties of the drug itself. Overall, the safest drug should be chosen; otherwise, the mother should take the medication just after nursing. Less than 1% of prednisone or prednisolone is recovered in breast milk and even at high doses is unlikely to suppress infant adrenal function. Although opioids are excreted into breast milk, the amounts are minimal and therefore thought to be compatible with breastfeeding.

KEY FACTS: PREGNANCY: PAIN MEDICATION

- The U.S. FDA requires labeling of drugs using the Pregnancy Category System (see Table 32.1 in Benzon). While 20 to 30 commonly used drugs are proven human teratogens, over 70 are listed as category X (teratogenic) and all new medications are listed as category C.
- Acetaminophen is considered category B; it is also considered the safest medication for nursing mothers.
- During lactation, the amount of drug that the infant receives is dependent on maternal dose and dosing interval as well as the pharmacodynamic properties of the drug itself.

ADDITIONAL READINGS

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22. ANSWER: D

Constipation is the most common dose-dependent side effect of opioids. μ-opioid receptors mediate analgesia, respiratory depression, euphoria, sedation, and gastrointestinal dysmotility. Because minimal gastrointestinal tolerance develops with opioids, it should be an expected side effect of treatment. Lack of side effect may suggest the dose is inadequate or there may be an issue of diversion of medications. Morphine and other opioids also affect gastric and pancreatic secretions via the different receptor sites throughout the spinal cord and muscle. Although tone in the bowel is increased, propulsive activity is decreased.

There are many medications used in the treatment of opioid-induced constipation. Laxatives soften stool by affecting water and electrolyte transfer. Lactulose is an osmotic laxative, which is minimally absorbed; it increases stool propulsion but can cause flatulence and abdominal cramping. Senna and bisacodyl are stimulating laxatives that work directly on the myenteric plexus.

Methylnaltrexone (Relistor) is a newer drug that is indicated for opioid-induced constipation. The drug is a peripherally acting μ-opioid antagonist that can reverse a number of opioid side effects, including constipation, without affecting analgesia or leading to withdrawal.

KEY FACTS: INTESTINAL MOTILITY: DRUG EFFECTS

- Constipation is the most common dose-dependent side effect of opioids.
- μ-opioid receptors mediate analgesia, respiratory depression, euphoria, sedation, and gastrointestinal dysmotility.
- Because minimal gastrointestinal tolerance develops with opioids, it should be expected as a side effect of treatment.

ADDITIONAL READING

Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

23. ANSWER: D

Ketorolac is currently the only parenteral NSAID available for clinical use in the United States. It has been useful in providing postoperative pain relief both on its own and also as an adjunct with opioid medications. The anti-inflammatory properties alone are significant and the analgesia it provides is 50 times that of naproxen. It also has antipyretic effects 20 times those of aspirin. However, there are side effects noted that should be taken into account prior to administration. There are case reports of postoperative prolonged bleeding time due to ketorolac administration. Also, there is a risk of NSAID renal toxicity, especially in the setting of reduced renal blood flow from anesthesia and blood loss during surgery. Nonselective NSAIDs can also cause gastropathy with gastroduodenal ulcers. Both COX-1 and COX-2 receptors have been shown to play a role in bone healing and osteogenesis. Although studies have failed to show any impact of NSAIDs on fracture healing, in animal studies and retrospective human lumbar fusion studies it has been suggested that perioperative NSAID use could reduce the rate of successful fusion.

ADDITIONAL READINGS

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24. ANSWER: B

The most frequent adverse reaction to NSAIDs is dyspepsia; renal impairment is the next most common, although the effects are often unrecognized. Renal impairment has been noted to appear in up to 18% of patients using ibuprofen. In healthy individuals, NSAIDs have no adverse effects on renal function. This does not hold true for patients with congestive heart failure, liver disease, diabetes mellitus, and other conditions that lead to decreased levels of renal blood flow. NSAID-induced nephrotoxicity can be heightened with concomitant hypovolemia, diabetes mellitus, sepsis, or a combination with other nephrotoxic agents.

Although aspirin causes irreversible inhibition of COX, the large release of uninhibited platelets that occurs in response to the physiological stress of surgery tends to normalize clinically significant bleeding times sooner than expected. Non-aspirin NSAIDs have been shown to induce a reversible platelet inhibition. Due to the inaccuracies of the bleeding time test it is not often performed to quantitate the effect.

KEY FACTS: KETOROLAC AND POSTOPERATIVE RISKS

- The anti-inflammatory properties of ketorolac are significant and the analgesia it provides is 50 times that of naproxen.
- However, there are reports of prolonged bleeding time due to ketorolac administration. Also, there is a risk of NSAID renal toxicity, especially in the setting of reduced renal blood flow from anesthesia and blood loss during surgery.
- The most frequent adverse reaction to NSAIDs is dyspepsia; renal impairment is the next most common, although the effects are often unrecognized.

ADDITIONAL READINGS

Benzon H, Raja H, Fishman S, et al. *Essentials of Pain Medicine and Regional Anesthesia*. 2nd ed. New York, NY: Elsevier; 2005.

Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.

25. ANSWER: B

Local anesthetic toxicity in infants and children is a rare phenomenon in anesthetic practice despite the increasing use of regional anesthesia in this patient population. Larger relative volumes of local anesthetics are used in infants and neonates as compared with adults and older children. Neonates exhibit delayed metabolism and elimination of local anesthetics, and decreased protein binding in these patients also leads to an increase in unbound drug. The neonatal liver is also immature and has a significantly lower ability to oxidize and reduce local anesthetics compared with the adult liver. Older children absorb local anesthetic more rapidly than in adults; thus, higher drug levels have been found during comparison.

KEY FACTS: LOCAL ANESTHETIC TOXICITY IN INFANTS: SIGNS

- Larger volumes of local anesthetics are used in neonates compared with adults and children.
- Neonates exhibit delayed metabolism and elimination of local anesthetics, and decreased protein binding in these patients also leads to an increase in unbound drug.

ADDITIONAL READINGS

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Yaffe SJ, Aranda JV. *Neonatal and Pediatric Pharmacology: Therapeutic Principles in Practice*. Philadelphia, PA: Lippincott Williams & Wilkins; 2010.

26. ANSWER: A

The potency of a drug refers to the dose required to produce a given effect. It is usually expressed as the amount needed to produce a given effect in 50% of subjects—the ED_{50}. Lipid solubility is the primary determinant of intrinsic local anesthetic potency. Lipid solubility is also important in the redistribution of the drug. High partition coefficients mean that the drug passes easily into the lipid membrane. Speed of onset is related to the pKa; a lower pKa increases tissue penetration and shortens onset of action as there are more lipid-soluble nonionized particles. Protein binding is implicated in the duration of action; high protein binding increases the duration of action.

KEY FACTS: LOCAL ANESTHETIC POTENCY: LIPID SOLUBILITY

- Lipid solubility is the primary determinant of intrinsic local anesthetic potency.
- Speed of onset is related to the pKa.
- Protein binding is implicated in the duration of action.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.
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27. ANSWER: B

Opioid misuse and diversion is rapidly becoming an epidemic in the United States. Hydrocodone and oxycodone are reported to sell for $1/mg on the street, making sale of the medications lucrative, particularly for patients in difficult economic times. Although short-acting opioids may be detected in a urine drug screen for only 1 to 3 days after ingestion, the fact that this patient received 10 hydrocodone the day before the visit makes it unlikely that he would have had a negative urine drug screen if he were taking the medications as prescribed for pain. Conversely, if he had been abusing them, ingestion of all of the prescribed tablets would likely provide a level of hydrocodone above the level of detection less than 24 hours later.

This patient does have risk factors for opioid abuse, however, and it should be considered. Often abuse and diversion go hand in hand. Young age, male gender, and tobacco abuse are three of this patient's risk factors. Other red flags for opioid misuse and/or diversion include multiple early refills, multiple ER visits, refusal to consider other treatment options, anger, and catastrophizing. Other risk factors not mentioned in this scenario include a history of polysubstance abuse. Other than marijuana, prescription opioids are the most commonly abused illicit substance, more than cocaine, heroin, and methamphetamine combined. Among new users of illicit substances ages 12 to 17, more are likely to try prescription opioids to get high than any other drug, including marijuana. Up to 8% of patients in some states report using prescription opioids for nonmedical purposes, so this should always be considered in patients who are not getting better and have risk factors for opioid misuse.

When patients repeatedly take more opioids than prescribed, the diagnosis of pseudoaddiction should also be considered. However, pseudoaddictive aberrant behavior will cease with increased dosing of opioids, once the pain becomes better controlled.

Opioid tolerance and hyperalgesia are possibilities with chronic use of opioids. Opioid tolerance is marked by initial analgesia that seems to wane over time. Whether or not this decreased effect is secondary to increased pain-generating activity in a more functional patient, disease progression, or a biochemical tolerance is somewhat controversial. However, this patient has never reported adequate analgesia, so tolerance is less likely. Opioid-induced hyperalgesia (OIH) may be difficult to distinguish from opioid tolerance, but as opposed to tolerance, patients with OIH develop worsening pain with increased opioid dosing, while those with tolerance should improve. Many addicts may ultimately develop pain secondary to OIH, so this is certainly in the differential for this patient. Detoxification from opioids would be the preferred route for addiction and OIH. However, this patient had a negative urine drug screen and no clinical signs of withdrawal, again making abuse and/or OIH less likely than diversion in this scenario.

KEY FACTS: LOW BACK PAIN, TREATMENT

- Opioid misuse and diversion should be considered in patients with early refills, multiple ER visits, abnormal urine drug screens, catastrophizing behavior, and pain out of proportion to the inciting event, and those with a history of substance abuse.
- Tolerance and opioid-induced hyperalgesia are common in patients taking chronic opioids and should be considered if patients are not responding appropriately to therapy.

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Silverman S. Opioid-induced hyperalgesia: clinical implications for the pain practitioner. *Pain Physician*. 2009;12:679–684.

28. ANSWER: A

Opioid-induced hyperalgesia (OIH) demonstrated extensively in the laboratory setting, in both acute and chronic timeframes, but there are also reports of clinical correlation. For instance, significant pain reduction has been demonstrated in patients who have been detoxified from high-dose opioids. A number of case reports also demonstrated a worsening sensitivity to pain with escalating opioid dosing.

This patient is opioid-tolerant and physically (though not psychologically) dependent after 2 years of therapy; therefore, increasing his opioids is an appropriate first step to address this possibility. However, an opioid-tolerant patient will typically report increased analgesia and functionality with the dose increase, as opposed to an increase in pain. Increase in pain in this scenario, coupled with worsening allodynia on the scar, suggests a central sensitization of nociceptive pathways, which is thought to be the mechanism of OIH. Increasing opioids further is not likely to help in this scenario.

Since tolerance is characterized by decreasing efficacy of a drug, caused by central desensitization of opioid receptors, it can be overcome by increasing the dose. However, unlike tolerance, OIH cannot be overcome by increasing dosage since OIH is a form of pain sensitization induced by the drug that occurs within the CNS. Pain is worsened with increased opioid dosing and is improved by reducing or eliminating the opioid.

If OIH is suspected, modulation of the CNS pathways propagating excitatory neurotransmission should be attempted. This can be accomplished by NMDA receptor blockade, as with the transition to methadone. Increase in gabapentin may also modulate the $alpha_{2D}$ subunit of the calcium channel and block excitatory neurotransmission at the dorsal horn of the spinal cord, thus improving the central sensitization in hyperalgesic states.

The most common indication for spinal cord stimulation is postlaminectomy pain with radiculopathy. The patient has been highly functional and compliant with a stable medication and therapy regimen, and is experiencing worsening pain that has been refractory to pharmacologic manipulation. In this scenario, neuromodulation to facilitate inhibitory pathways at the level of the dorsal horn may improve the patient's pain and focal hyperalgesia.

Detoxification from opioids is another viable option in the setting of a clinical suspicion of OIH, and pain has been clinically reported to improve after detoxification from opioids as the sole intervention. Many patients may be resistant to this idea, especially if nothing else is offered "in its place." However, especially in patients with decreasing function despite increased opioid dose, and in those with other unsavory side effects from opioids, like constipation, pruritus, fatigue, sedation, low testosterone/libido, and urinary retention, detoxification in the setting of hyperalgesia may be the first-line approach.

KEY FACTS: OPIOID TOLERANCE

- Tolerance is characterized by decreasing efficacy of a drug, caused by central desensitization of opioid receptors. It can be overcome by increasing the dose.
- However, unlike tolerance, OIH cannot be overcome by increasing dosage, since OIH is a form of central pain sensitization. Pain from OIH is worsened with increased opioid dosing and is improved by reducing or eliminating the opioid.

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29. ANSWER: A

Sensitization to pain can occur in several areas of the nervous system. Peripheral sensitization involves mediators of inflammation and has been well documented in the setting of peripheral nerve injury. Central sensitization, on the other hand, occurs proximally in the CNS even though the nociceptive stimulus is often a peripheral injury. In the spinal cord, wide-dynamic-range neurons become sensitized through a variety of mechanisms, which may be mediated by neurotransmitters such as calcitonin-gene-related peptide, vasoactive intestinal peptide (VIP), cynorphin (DYN), cholecystokinin (CCK), neuropeptide Y (NPY), and *N*- methyl-d-aspartate (NMDA). The excitatory neurotransmitter NMDA plays a central role in the development of opioid-induced hyperalgesia (OIH). The current data suggest that opioid-induced desensitization (pharmacologic tolerance) and sensitization (OIH),

while distinct processes, may share common cellular mechanisms mediated in part through activation of the central glutamatergic system. NMDA receptors become activated by glutamate and other excitatory neurotransmitters, and when inhibited, prevent the development of tolerance and OIH.

KEY FACTS: OPIOID TOLERANCE

- OIH is a type of central sensitization.
- As with all central sensitization states, the neurotransmitter NMDA is central to its development, via activation of central excitatory pathways.

ADDITIONAL READINGS

Silverman SM. Opioid-induced hyperalgesia: clinical implications for the pain practitioner. *Pain Physician*. 2009;12:679–684.

30. ANSWER: B

A group of pain physicians met in Budapest in 2003 to form a consensus group in order to better define and delineate criteria for the clinical diagnosis of CRPS. The resulting "Budapest Criteria," as published by Harden et al., are as follows: "General Definition of the Syndrome: ***CRPS*** describes an array of painful conditions that are characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings. The syndrome shows variable progression over time.

To make the clinical diagnosis, the following criteria must be met:

1. Continuing pain, which is disproportionate to any inciting event
2. Must report at least one symptom in three of the four following categories:
   Sensory: Reports of hyperesthesia and/or allodynia
   Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
   Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry
   Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Must display at least one sign at time of evaluation in two or more of the following categories:
   Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement)
   Vasomotor: Evidence of temperature asymmetry (>1°C) and/or skin color changes and/or asymmetry
   Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
   Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. There is no other diagnosis that better explains the signs and symptoms

For research purposes, diagnostic decision rule should be at least one symptom in all four symptom categories and at least one sign (observed at evaluation) in two or more sign categories."

The pathogenesis of CRPS is unclear but appears to involve the formation of a reflex pathway after an inciting event. This pathway follows the routes of the sympathetic nervous system and probably involves central and cortical feedback to produce peripheral vascular disturbances. The pain sensation in response to injury may lead to increased sensitivity of injured axons to epinephrine and other substances released by local sympathetic nerves.

The name "CRPS" evolved from the nomenclature of reflex sympathetic dystrophy (RSD), as it became apparent that there are types of CRPS in which the pain is sympathetically maintained and those in which the pain is sympathetically independent. Although autonomic dysfunction likely plays a predominant role at the central level in the pathophysiology of CRPS, not all pain will be responsive to peripheral sympathetic blockade. The term "sympathetically maintained pain" (SMP) is considered to be a variable phenomenon associated with a variety of disorders, including CRPS types I and II.

Two types of CRPS have been recognized:

Type I corresponds to patients with CRPS without a definable nerve lesion and represents about 90% of clinical presentations.

Type II was formerly termed "causalgia" and refers to cases where a definable nerve lesion is present.

KEY FACTS: CRPS

- The diagnosis of CRPS requires sensory, vasomotor, sudomotor/edema, and motor/trophic signs and symptoms, with pain out of proportion to inciting event, not explained by another diagnosis.

- ***CRPS type I*** has no definable nerve lesion and is the most common type of CRPS.
- ***CRPS II*** is also known as causalgia.

ADDITIONAL READINGS

Harden R, Bruehl S, Stanton-Hicks M, Wilson P. Proposed new diagnostic criteria for complex regional pain syndrome. *Pain Med*. 2007;8(4):326–331.

31. ANSWER: D

This patient has a ***saphenous neuralgia***, with neuropathic pain and sensory deficit in the distribution of the saphenous nerve. This can occur from damage to the nerve from an incision or trocar, entrapment of the nerve in a suture or scar, or development of a neuroma. Given the acuity of the injury, and the absence of any other issues like a surgical site hematoma or deep venous thrombosis, an injury to the nerve is the most likely etiology of the patient's pain. Swelling in the knee and limited range of motion are normal in the acute postoperative period. Although physical therapy is important for rehabilitation of the knee, it is unlikely to improve the pain in her leg.

This, however, is not CRPS, as it does not meet the clinical criteria outlined in Question 30. Nor are there indications of regional sympathetic dysfunction that could be contributing to the pain and amenable to a sympathetic nerve block.

As the saphenous nerve is derived from the femoral nerve, a sciatic nerve block would not be helpful. However, a saphenous nerve block or scar injection with corticosteroids might be useful both diagnostically and therapeutically in this setting, where there is likely to be ongoing inflammation and peripheral sensitization contributing to the pain.

Given that this is neuropathic pain and has been unresponsive to opioids, the next best approach is a trial of an antineuropathic agent like gabapentin.

KEY FACTS: NEUROPATHIC PAIN: TREATMENT

- Consider peripheral neuralgia as a cause of persistent postsurgical pain that is unresponsive to opioids.

ADDITIONAL READINGS

Dworkin RH, O'Connor AB, Backonja M, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain*. 2007;132(3):237–251.

32. ANSWER: D

Three clinical stages of CRPS have been described. The clinical existence and utility of "staging" has been recently questioned, and if anything, understanding of CRPS is evolving into categorization based on "warm" and "cold" variants. Nevertheless, the traditional explanation of stages is as follows.

Stage 1—Pain develops in a limb either following an injury or spontaneously. CRPS type I is the most common type. It occurs in 90% of cases and has no known inciting injury or event. CRPS II, or causalgia, occurs in the setting of a defined injury, such as a trauma or fracture. The essential features include burning throbbing aching pain, sensitivity to touch or cold, and edema. The distribution of the pain is not compatible with a single peripheral nerve, trunk, or root lesion. Vasomotor disturbances can occur, producing color and temperature variations. The radiograph of the affected limb is usually normal but may show patchy demineralization.

Stage 2—The second stage is characterized by disease progression and may last for 3 to 6 months. Progressive soft-tissue swelling, thickening of the skin and periarticular tissues, and muscle wasting are characteristic manifestations.

Stage 3—The third stage is characterized by joint contractures, limited range of motion, further trophic skin changes, and brittle nails. Severe bone demineralization can be seen on radiographic studies. Independent of stage, there is decreased, rather than increased, sympathetic outflow to the affected limb; autonomic manifestations previously ascribed to sympathetic overactivity are currently suspected to be due to catecholamine hypersensitivity, which may result in a cool, cyanotic extremity. Despite decreased endogenous sympathetic mediators in the periphery, application of exogenous catecholamines or anything triggering increased sympathetic outflow to the periphery, like cold temperatures, will result in an exaggerated effect and increased pain.

Among the mechanisms proposed for the persistent pain and allodynia is release of inflammatory mediators and pain-producing peptides by peripheral nerves. One theory is that these are then transported up the nociceptive axon into the dorsal horn of the spinal cord, where these excitatory neuropeptides facilitate further release of more excitatory neuropeptides peripherally in a feed-forward cycle.

There are also data to support a role for neuropeptides and for inflammation or other immunologic abnormalities in the pathophysiology of CRPS. Genetic factors have also been implicated. There is also some evidence of cortical restructuring in patients with persistent pain from CRPS.

KEY FACTS: COMPLEX REGIONAL PAIN SYNDROME (CRPS): : EARLY AND LATE STAGES

- Although somewhat arbitrary and controversial, CRPS has been described as having stages.

- Stage 1 CRPS, sometimes referred to as "warm" CRPS, is the acute phase where the classic vasomotor signs and edema with allodynia are more prominent.
- Stage 2 CRPS is an intermediate stage, with progression of motor trophic changes.
- Stage 3 CRPS, also referred to as "cold" CRPS, features reduced sympathetic outflow to the extremity, although there is sympathetic hyperreactivity.

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33. ANSWER: E

Few of the pharmacologic ***treatments for CRPS*** have been studied in well-designed, randomized, placebo-controlled trials. Much of clinical practice is based on utilization of medications with known efficacy in other neuropathic pain states, such as diabetic peripheral neuropathy or postherpetic neuralgia. Topical agents like capsaicin, clonidine, and lidocaine are also commonly employed secondary to the low-risk side-effect profile and reported efficacy in some patients with neuropathic pain and CRPS. Most experts suggest initial therapy with anticonvulsant and/or antidepressant agents with known efficacy in other chronic neuropathic pain. Examples of such commonly used medications are gabapentin, pregabalin, amitriptyline, and NSAIDs. As with other neuropathic pain states, the use of opioids is somewhat controversial; however, since the primary goal of CRPS treatment is to allow sufficient pain control for critical rehabilitative physical therapy, opioids are commonly used in patients with CRPS, especially if treatment with antineuropathic agents has been ineffective.

Corticosteroids have been used orally, IV, peripherally, and neuraxially for the management of CRPS. Oral prednisone in divided doses, particularly in the acute stage of CRPS with inflammatory features, is a reasonable option backed by limited evidence.

The most thoroughly studied therapy has been the bisphosphonate-type compounds, which target the process of bone resorption. The use of intranasal calcitonin, intravenous clodronate and intravenous alendronate has resulted in improvement in functionality in patients with CRPS. Expert recommendations suggest consideration of this type of therapy in patients with CRPS who have been refractory to other pharmacologic therapy. Side effects of bisphosphonates include hypocalcemia, osteonecrosis of the jaw, and GI ulceration.

A large multicenter study that randomized patients with wrist fracture to prophylactic therapy with either vitamin C or placebo reported that significantly fewer patients developed CRPS after 50 days of vitamin C therapy. However, there is currently no evidence that treatment with vitamin C after development of CRPS is useful in pain management or functional recovery.

KEY FACTS: COMPLEX REGIONAL PAIN SYNDROME (CRPS): MANAGEMENT

- CRPS is typically initially treated like neuropathic pain, with anticonvulsants, antidepressants, topical agents, and NSAIDs, with or without opioids.
- Acutely, there is some evidence for use of oral steroids.
- Bisphosphonates may be helpful if other agents fail.
- Vitamin C may be useful prophylactically, but not after onset of symptoms.

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34. ANSWER: B

Prevention is the best "treatment" of CRPS. Early mobilization after trauma, injury, or surgery may reduce the risk of developing CRPS. Once CRPS is established, the results of physical and occupational therapy are conflicting; however, it is clear that the most devastating outcomes of CRPS result from immobilization and loss of function of the affected limb, which can become contracted

and atrophic from disuse. As pain and allodynia are both characteristic of CRPS and exceedingly difficult to abolish while the syndrome persists, the primary goal in the management of CRPS should be to provide enough pain reduction that the patient can participate in successful rehabilitative therapy to prevent functional loss DESPITE the pain.

The role of anxiety, depression, posttraumatic stress disorder, and other mood or personality disorders in the development and maintenance of CRPS is controversial. However, it is clear that the pain and distress associated with CRPS can exacerbate and maintain a state of ongoing pain and distress, whether preexisting or not. This is particularly true in the setting of a syndrome whose pathophysiology is thought to involve autonomic dysregulation, central sensitization, and possible cortical restructuring. Therefore, it is recommended that patients with CRPS avail themselves of cognitive-behavioral therapy, coping skills training, mindfulness, or any other supportive psychological care to reduce anxiety, sleep disturbance, and the effect of distress on the autonomic and central nervous systems.

As discussed above, reduction of sympathetic outflow to the affected extremity is part of the natural progression of most CRPS cases; however, hypersensitivity of the denervated extremity to sympathetic agonists may be present in some cases of sympathetically maintained pain in the setting of CRPS. Blockade of these hypersensitive, re-entrant, excitatory, adrenergic pain pathways may be a part of interventional treatment for CRPS, but it is not the primary goal in the management of the entity.

Spread of CRPS to other extremities has been described and may reflect ongoing CNS dysregulation of the autonomic and nociceptive pathways. The risk factors for this are unknown, but again, management of CRPS is primarily geared toward reducing neuropathic pain in order to allow mobilization and rehabilitation of all affected extremities.

KEY FACTS: COMPLEX REGIONAL PAIN SYNDROME (CRPS): MANAGEMENT

- The primary goal of treatment with CRPS is to control pain enough to facilitate rehabilitation of the affected extremity, in order to prevent functional loss.
- Strategies include interventional management, medications, and cognitive therapies to allow ongoing physical therapy.

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35. ANSWER: A

Interventional management of CRPS is indicated for the purpose of diminishing pain to allow rehabilitative therapy for functional improvement. Each of these procedures has been described as a treatment for CRPS, particularly when there is a sympathetically maintained component to the pain. Most of the studies of interventions for CRPS are fraught with methodologic shortcomings, making conclusive recommendations difficult.

IV regional anesthesia with phenoxybenzamine, prazosin, guanethidine, ketorolac, methylprednisolone, bretylium, and other adrenergic blockers has been utilized with variable success in the treatment of CRPS. TENS units, peripheral nerve stimulators, and tender point injections have also been described as effective in case reports or small series.

Many studies have explored the use of clonidine, through oral, transdermal, peripheral, and neuraxial delivery, as an $alpha_2$ agonist to induce a sympathectomy with the goal of reducing pain in CRPS. Hypotension and sedation are known side effects with use of this medication. Some data support use of IV regional anesthesia with clonidine, and epidural administration has been shown in at least one small placebo-controlled study to be more effective than control.

Spinal cord stimulation, in a randomized trial, reduced pain and improved health-related quality of life more than physical therapy alone for up to 2 years, but no significant difference in pain was present during the period from 3 to 5 years following implantation. However, many pain practitioners propose early utilization of this neuromodulatory technique to facilitate rehabilitation in the case of a failure of pharmacologic management and sympathetic nerve blocks.

Sympathetic nerve blocks with local anesthetic have been the traditional initial interventional approach to management of CRPS. A temperature change in the hand after stellate ganglion block for upper-extremity CRPS, or in the foot after a lumbar sympathetic block, demonstrates the presence of a temporary sympathectomy; if pain relief accompanies this sympathectomy, CRPS is thought to have a sympathetically maintained component, and a series of blocks should result in increasing pain relief.

There have been several studies of neurolytic sympathectomy for CRPS, whether by radiofrequency ablation, chemical sympathectomy with alcohol or phenol, or surgical destruction. Although there are some data supporting this approach, there is a significant risk of worsening pain

and sympathetic dysfunction, like hyperhidrosis, in patients with CRPS, or central sensitization, who have undergone neurolytic sympathectomy for neuropathic pain syndromes. In this patient, who has demonstrated remission of CRPS with more conservative treatment in the past, neuromodulatory techniques are a better first choice than neurolytic techniques.

KEY FACTS: COMPLEX REGIONAL PAIN SYNDROME (CRPS): MANAGEMENT

- IV regional anesthetics, neuraxial and peripheral nerve blocks, sympathetic nerve blocks, and spinal cord stimulation have all been utilized as interventional management strategies for CRPS.
- In general, neuromodulatory techniques are preferred over neurolytic techniques for initial interventional management.

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36. ANSWER: A

Nociceptors in the skin are almost exclusively Aδ or C fibers, and are further categorized based on responses to temperature, mechanical, or chemical stimuli. In general, cutaneous Aδ fibers transmit sharp, well-localized, fast pain sensations. Aδ fibers are 2 to 5 mcm in diameter and are thinly myelinated, conducting "first pain" with a velocity of 20 m/sec.

In contrast to the sharp pain signals of Aδ fibers, the unmyelinated C fibers transmit delayed, dull, poorly localized aching pain. C fibers are 0.2 to 1.5 mcm in diameter and are unmyelinated. They conduct "second pain," which is prolonged, burning, and unpleasant, at a speed of 0.5 m/sec.

A-β fibers are the large and heavily myelinated fibers, at 5 to 12 mcm, that transmit awareness of light touch at rates of 30 to 70 m/sec. They are also thought to activate inhibitory interneurons in the dorsal horn of the spinal cord, which, when activated, may dull nociceptive pain from the Aδ and C fiber excitatory input into the dorsal horn of the spinal cord.

Aα are the fastest, most highly myelinated fibers, at 12 to 20 mcm; when activated in a spinal reflex, they transmit the motor component of the withdrawal reflex at a rate of 70 to 120 m/sec, such that the spinally mediated reflex occurs almost simultaneously with the experience of pain.

KEY FACTS: NOCICEPTIVE AFFERENT NEURONS

In order of decreasing speed of transmission, which is related to decreasing myelination:

- Aα fibers transmit the motor component of the withdrawal reflex.
- A-β fibers transmit awareness of light touch.
- Aδ fibers transmit sharp, well-localized, fast pain sensations.
- Unmyelinated C fibers transmit delayed, dull, poorly localized aching pain.

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37. ANSWER: D

Advances in neuroimaging have linked the function of multiple areas in the brain with the sensation of pain and emotion. These areas (e.g., the ACC, the insula, and the DLPFC) form functional units through which psychiatric comorbidity may amplify pain and disability. Coghill et al. have shown that differences in pain sensitivity between patients can be correlated with differences in activation patterns in the ACC, the insula, and the DLPFC. These areas are part of the spinolimbic (also known as the medial) pain pathway that runs parallel to the spinothalamic tract. Both of these ascending pathways receive direct input from the dorsal horn of the spinal cord.

The spinothalamic tract, leading to the somatosensory cortex, is primarily responsible for the localization and characterization of pain (i.e., the sensory/discriminative aspect).

The spinolimbic tract, leading to limbic structures such as the amygdala, the medial thalamus, and the hypothalamus, is thought to be responsible for the emotional, anticipatory, and motivational aspects of pain. It is also involved in descending pain inhibition at both the cortical and subcortical levels. The disruption or alteration of descending pain inhibition is one of the mechanisms of central sensitization and chronic neuropathic pain. Functional imaging studies such as those performed by Wasan et al. are better elucidating the relationship between these pathways and their relationship with chronic pain states.

KEY FACTS: SOMATIC PAIN PATHWAYS

- The lateral spinothalamic tract is responsible for localization of pain, and is the sensory-discriminative pathway.
- The medial spinolimbic pathway, including the anterior cingulate cortex (ACC), the insula, and the dorsolateral prefrontal cortex (DLPFC), is responsible for the emotional aspects of pain, and is the emotional/affective pathway.

ADDITIONAL READINGS

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38. ANSWER: A

Hyperalgesia is an increased response to a stimulus that is normally painful. Hyperalgesia reflects increased pain on suprathreshold stimulation. For pain evoked by stimuli that usually are not painful, the term "allodynia" is preferred, while "hyperalgesia" is more appropriately used for cases with an increased response at a normal threshold, or at an increased threshold (e.g., in patients with neuropathy).

Allodynia is a painful response to a normally nonpainful stimulus, like light touch. It is important to recognize that allodynia involves a change in the quality of a sensation, whether tactile, thermal, or of any other sort. The original modality is normally nonpainful, but the response is painful.

Hyperpathia is a painful syndrome characterized by increased reaction to a stimulus. It may occur with allodynia, hyperesthesia, hyperalgesia, or dysesthesia. Faulty identification and localization of the stimulus, delay, radiating sensation, and after-sensation may be present, and the pain is often explosive in character. This can be seen with repetitive needle passes in a patient with allodynia for example, where after a period of time, the patient becomes unable to tolerate any stimulus at all secondary to explosive pain in the entire region.

Hyperesthesia is increased sensitivity to any stimulus, excluding the special senses. Hyperesthesia may refer to various modes of cutaneous sensibility, including touch and thermal sensation without pain, as well as to pain. The word is used to indicate both diminished threshold to any stimulus and an increased response to stimuli that are normally recognized.

Paresthesia is an abnormal sensation, whether spontaneous or evoked, but is not perceived as unpleasant. This is to be compared to dysesthesia, which is an unpleasant abnormal sensation, whether spontaneous or evoked. Special cases of dysesthesia include hyperalgesia and allodynia. A dysesthesia should always be unpleasant and a paresthesia should not be unpleasant.

KEY FACTS: SOMATIC PAIN PATHWAYS

- Hyperalgesia is an increased response to a stimulus that is normally painful.
- Allodynia is a painful response to a normally nonpainful stimulus.
- Hyperpathia is a painful syndrome, characterized by increased, explosive reaction to a stimulus.
- Hyperesthesia is increased sensitivity to any stimulus, excluding the special senses.
- Paresthesia is an abnormal sensation, whether spontaneous or evoked, but is not perceived as unpleasant; dysesthesia is an abnormal sensation perceived as unpleasant.

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39. ANSWER: E

Tissue injury stimulates nociceptors, causing the sensation of pain. It also liberates multiple substances from the various cell types in the vicinity of the injury. Injured cells release adenosine triphosphate (ATP), protons, kinins, and arachidonic acid. Mast cells release histamine, serotonin, prostaglandins, and bradykinin. Cytokines and nerve growth factor are released by macrophages. Substance P is also liberated following repetitive C-fiber (afferent, unmyelinated, "second pain") activation. It is thought that release of these substances decreases the threshold for activation of the nociceptors to which they are exposed, a process called peripheral sensitization. The decrease in pH seen in injured tissue acts to further decrease the threshold. Peripheral sensitization

effectively increases the afferent input in the dorsal horn of the spinal cord and the ascending sensory tracts, increasing the amount of excitatory neurotransmitters such as glutamate and aspartate that are released. These excitatory neurotransmitters, in turn, activate NMDA, AMPA, kinate, and glutamate receptors, setting off second-messenger cascades that lower excitation thresholds and facilitate continual activation and hyper-activation (wind-up) of pain pathways. This process is known as central sensitization, and is believed to be responsible for the heightened response to both painful and nonpainful stimuli in patients who suffer from chronic pain states.

KEY FACTS: SOMATIC PAIN PATHWAYS

- Peripheral sensitization involves release of adenosine triphosphate (ATP), protons, kinins, arachidonic acid, histamine, serotonin, prostaglandins, bradykinin, cytokines, nerve growth factor, and substance P.
- Activation of peripherally sensitized nociceptors results in release of glutamate and other excitatory amino acids in the dorsal horn.
- NMDA, kinate, and glutamate receptors are involved in central sensitization
- "Wind-up" involves summation of excitatory input, leading to increased excitability of second-order neurons in the dorsal horn, and can contribute to central sensitization.
- The dorsal horn is the "gate" where excitatory and inhibitory inputs are processed.

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40. ANSWER: B

Visceral pain originates from internal structures such as the organs of the gastrointestinal tract and the heart. It is mediated by the autonomic nervous system. As there is a lack of specificity of innervation, and considerable neuronal crossover, visceral pain is typically difficult to localize or describe, and may encompass an area that is much larger than might be expected for a single organ. Visceral pain involving hollow visci is often characterized as crampy.

Only 2% to 15% of the afferent neurons entering the spinal cord are visceral. These neurons travel with sympathetic fibers to the sympathetic chain, with cell bodies in the dorsal root ganglia, and then synapse in lamina I–V of the dorsal horn, often traveling both cranially and caudally several levels in the dorsal horn before synapsing. This nonspecificity widens the receptive field and often results in what is perceived to be diffuse nociceptor activation. And since the visceral afferents synapse in the dorsal horn at the same location as somatic afferents, visceral pain is often perceived by the brain to be referred to a somatic location, like the jaw or arm in the case of a myocardial infarction. This is known as viscerosomatic convergence.

Visceral afferents are exquisitely sensitive to distention, ischemia, chemical irritation, traction, and stretching, but are insensitive to heat and to cutting. Central sensitization can occur with irritation or compromise of visceral afferents similar to that of somatic nociceptor central sensitization; irritable bowel syndrome, for example, is thought to be a neuropathic pain state arising from hyperalgesia of the visceral afferents.

KEY FACTS: PERIPHERAL NERVOUS SYSTEM: NOCICEPTIVE AFFERENT NEURONS

- Visceral pain is mediated by autonomic nerve fibers, which account for a minority of all afferent neurons.
- Viscerosomatic convergence refers to referral of visceral pain to somatic structures secondary to co-localization of afferents in the dorsal horn; as these visceral afferents travel cranially and caudally prior to synapsing, visceral pain is often described as diffuse.
- Visceral afferents are sensitive to distention, ischemia, traction, and stretching, but insensitive to heat and cutting.

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Thomas J, Ferris F, von Gunten C. Approach to the management of cancer pain. In: Benzon H, ed. *Essentials of Pain Medicine and Regional Anesthesia*. New York, NY: Elsevier online, 2004; Chapter 63.

41. ANSWER: A

Serotonin syndrome is associated with the use of combinations of agents that can increase CNS serotonin levels. Serotonin syndrome should be suspected in patients who develop an abrupt change in mental status accompanied by autonomic and neurologic symptoms. Fever, shivering, diaphoresis, nausea, vomiting, diarrhea, myoclonus, tremor, ataxia, confusion, agitation, and hallucination are common findings.

Treatment includes cessation of the medication, symptom management, and administration of anti-serotonergic drugs like cycloheptadine.

Although tramadol's mechanism of action is incompletely understood, it acts at μ-opioid receptors, as well as by inhibiting reuptake of norepinephrine and serotonin. In

overdose, or in cases of drug interactions with other SSRIs, SNRIs, TCAs, or MAO inhibitors, it can result in seizures and/or serotonin syndrome.

KEY FACTS: SEROTONIN SYNDROME

- Tramadol, in addition to its action at μ-opioid receptors, also has properties of serotonin and norepinephrine reuptake inhibition.
- Any combination of medications that increase serotonin levels can lead to seizures and serotonin syndrome in overdose.

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42. ANSWER: D

As adapted from the International Headache Society, the clinical criteria for the diagnosis of ***trigeminal neuralgia*** (TGN) are as follows:

Paroxysmal attacks of pain that last less than 2 minutes

(and)

Pain with at least four of the following characteristics:
- Distribution along one or more divisions of the trigeminal nerve
- Sudden, intense, sharp, superficial, stabbing, or burning in nature
- Severe intensity
- Precipitation from trigger zones by certain daily activities
- An absence of pain between paroxysms
- Absence of neurologic deficit
- Characteristic pattern of attacks in individual patients
- Other cause of pain ruled out on the basis of history, physical exam, and/or imaging if indicated

TGN typically is seen in patients in their late 50s. In roughly half of patients, the mandibular branch (V3) is affected, whereas the maxillary and ophthalmic branches are the sources of one-third and one-sixth of complaints, respectively. It should be noted that trigeminal neuralgia will never cause pain in the V1 and V3 distributions without also causing symptoms in the V2 distribution. An important consideration in the care of a patient who has the clinical syndrome of trigeminal neuralgia is to rule out a structural or autoimmune cause of the pain, such as multiple sclerosis, acoustic neuroma, tumors, and temporal arteritis. Pain that radiates outside of the trigeminal distribution (i.e., into the neck) is not TGN.

Glossopharyngeal neuralgia often presents with throat pain or a feeling of a lump in the throat, sometimes triggered by yawning or swallowing. It is typically not lancinating like TGN.

Vascular causes of headache like temporal arteritis or migraine can mimic TGN, as well as autoimmune or inflammatory disorders like lupus or Tolosa-Hunt syndrome, which is inflammation of the dura around the cavernous sinus. The pain of TMJ can also radiate into the ear and jaw and be triggered by chewing, but it is not associated with sensory deficits and has a nondermatomal pattern.

Another common cause of pain in the distribution of the trigeminal nerve is ***postherpetic facial pain***. This follows a dermatomal outbreak of zoster, which typically is accompanied by a vesicular rash, but in rare cases can occur without a rash, a condition known as zoster sin herpete. Pain tends to be burning and to have many characteristics of classic neuropathic pain. This patient has no history of rash and her pain is in a nondermatomal distribution.

Other than zoster, there are many causes of local injury to the trigeminal nerve, such as facial trauma, fractures of the facial bones, and sinus surgery. Injury to an individual branch of the trigeminal nerve can give rise to neuropathic pain in the trigeminal distribution, sometimes referred to as trigeminal neuropathic pain. This pain may have other features of neuropathic pain, including constant pain, allodynia, and sensory deficit or numbness. This pain typically does not respond to medications or interventions as well as classic TGN. This patient may have had an injury to a branch of V3 during her extraction, but the patchy diffuse sensory deficit and the extension of the pain into her neck make this diagnosis less likely.

After other etiologies have been considered and ruled out, pain in an ill-defined distribution in the face is diagnosed as atypical facial pain. It is likely to be a neuropathic pain state and often has components of both diffuse aching, throbbing, burning pain and associated lancinating components, confusing the diagnosis with TGN. It has a strong preponderance in young women. It often extends past the distribution of the TGN, can be bilateral, and is often associated with other risk factors or markers for central sensitization such as mood disorders, TMJ, irritable bowel syndrome, fibromyalgia, and/or migraine. It is often refractory to treatment.

KEY FACTS: TRIGEMINAL NEURALGIA

- Trigeminal neuralgia characteristically occurs in the V3 or V2 distribution in patients in their late 50s. The clinical criteria for diagnosis are listed above.
- In contrast, atypical facial pain most commonly occurs in young women and has features of neuropathic pain, including continuous burning pain, allodynia, and sensory deficits. It often occurs in patients with other central sensitization syndromes.

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Jackson T, Gaeta R. Neurolytic blocks revisited. *Current Pain and Headache Reports*. 2008;12:7–13.

43. ANSWER: B

An evidence-based review of the pharmacologic treatment of trigeminal neuralgia (TGN) reveals Level A evidence for the use of carbamazepine as a first-line agent; it is typically so effective that response is considered pathognomonic for the diagnosis. The large majority of patients with TGN will have a good clinical response with carbamazepine. Among the nonresponders, almost all will find some pain relief with other medications, including lamotrigine, phenytoin, gabapentin, oxcarbazepine, topiramate, baclofen, and amitriptyline. Severe side effects include agranulocytosis and aplastic anemia, and bloodwork is indicated every 3 months while on therapy.

Oxcarbazepine has been adopted by many practitioners secondary to a more favorable side-effect profile than carbamazepine, with Level B evidence for efficacy. The most common side effect of oxcarbazepine is hyponatremia, so monitoring of sodium levels is indicated. Lamotrigine and baclofen have Level C designations for TGN and may be considered. Lamotrigine carries a risk of Stevens-Johnson syndrome and should be titrated slowly and carefully to effect.

TGN pain is typically poorly responsive to opioids, but opioids may be considered if other neuropathic agents with known efficacy have failed, and functionality improves with opioid therapy.

KEY FACTS: TRIGEMINAL NEURALGIA: PHARMACOTHERAPY

- Carbamazepine is first-line therapy for TGN. Side effects are agranulocytosis and aplastic anemia.
- There is also evidence for oxcarbazepine, baclofen, lamotrigine, and other antineuropathic agents.
- Opioids may be used but are not typically first-line therapy.

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44. ANSWER: A

It is now thought that focal demyelination of the trigeminal nerve caused by localized vascular compression may be the cause of most cases of TGN. This finding has led to the development of microvascular decompression surgery as a definitive treatment for this disorder. It requires a craniotomy and general anesthesia, so the patient's overall state of health must be considered.

Percutaneous rhizotomy of the trigeminal nerve is a less-invasive treatment option that can be achieved in the outpatient setting with fluoroscopic guidance and minimal anesthesia support. The technique most commonly reported is a radiofrequency thermal lesion, but balloon compression and chemical lesioning also have been described.

The success rate (roughly 85%) for complete pain relief at 2 years is comparable for patients undergoing microvascular decompression and rhizotomy; however, long-term pain-free outcomes were superior with microvascular decompression. Anesthesia dolorosa, a painful state of anesthesia with worsening pain, dysesthesia, and recurrence of pain, is more common following rhizotomy, but microvascular decompression carries an increased risk of perioperative morbidity and mortality.

The gamma knife delivers a single high dose of radiation with high precision at the proximal trigeminal root after the patient is placed in a stereotactic frame and the target is defined on the basis of magnetic resonance imaging. Efficacy has yet to be compared with that of microvascular decompression in randomized controlled trials.

The nucleus caudalis DREZ procedure involves a radiofrequency lesion into the trigeminal nucleus extending from the obex to the C2 electrode. It is primarily indicated for postherpetic neuralgia, deafferentation pain, and other atypical facial pain. It has fallen out of favor secondary to rates of postprocedure ataxia approaching 35%, with pain relief reported as excellent in only 34% of patients overall.

KEY FACTS: TRIGEMINAL NEURALGIA: TREATMENT

- Given its efficacy, low incidence of side effects, and durability of complete relief for TGN, microvascular decompression remains the preferred method of interventional treatment in patients who can tolerate craniotomy.

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45. ANSWER: C

A lumbar sympathetic block is performed somewhere between vertebral levels L2 and 4, where the lumbar sympathetic chain lies in the prevertebral space anterolateral to the vertebral bodies.

The psoas muscle originates from the transverse processes of T12–L5 and courses anteriorly and laterally to insert on the lesser trochanter of the femur. A needle placed too laterally or anteriorly may enter the psoas muscle. The lumbar plexus pierces the body of the psoas muscle in its trajectory, and unilateral leg weakness or numbness after a lumbar sympathetic block is most commonly secondary to spread of the local anesthetic into the body of the psoas muscle, rather than in the paravertebral space. The genitofemoral nerve leaves the lumbar plexus proximally and courses on the surface of the psoas muscle at the L2–4 levels; this makes it vulnerable to blockade with diffusion of the local anesthetic. Cases of genitofemoral neuralgia have been reported after attempted application of neurolytic substances to the lumbar sympathetic chain. However, the genitofemoral nerve is a purely sensory nerve and would therefore not result in weakness of the left thigh.

To the left of the upper lumbar vertebral bodies and sympathetic chain, the aorta is anterior; the inferior vena cava is anterior and to the right. Breach of these vessels can lead to retroperitoneal hematoma as a complication. Although the femoral nerve is derived from the lumbar plexus, this occurs distal to the location of a lumbar sympathetic block, and a retroperitoneal hematoma, arising as a complication of anterior placement of the needle and puncture of these vessels, would not compress this nerve.

If the needle is placed too posteriorly, spread of local anesthetic can enter the epidural space through the intervertebral foramen and lead to epidural anesthesia. This would more likely present as bilateral motor or sensory changes in the lower extremities, depending upon the type and dose of injectate reaching the epidural space.

The artery of Adamkiewicz, the single unpaired radicular blood supply to the anterior aspect of the spinal cord, has a great degree of anatomic variability but typically enters the spinal cord somewhere from T9 to T11 on the left. It has been reported as caudal as L2. It is theoretically at risk with passage of a needle along the left side of the vertebral body, as for a lumbar sympathetic block. Vasospasm, embolism, ischemia, or damage to this artery may result in an anterior spinal cord infarct; however, this would typically present as impaired motor, bowel, and bladder function with bilateral loss of pain and temperature below the level of the lesion, with preservation of proprioceptive function.

KEY FACTS: SYMPATHETICALLY MEDIATED PAIN SYNDROMES

- Complications of lumbar sympathetic block include genitofemoral neuralgia, lumbar plexus blockade, epidural spread of local anesthetic, and retroperitoneal hematoma.

46. ANSWER: B

This patient has ***neuralgia of the genital branch of the genitofemoral nerve***. The genital branch enters the inguinal canal through the deep inguinal ring and passes through the inguinal canal (men) or round ligament of the uterus (women). The genital branch of the genitofemoral nerve supplies motor fibers to the cremasteric muscle and sensory fibers to the skin over the scrotum in men and to the mons pubis and labia majora in women. This nerve is commonly injured with tacking of mesh to the periosteum of the pubis during hernia repair, and is blocked with a field block of local anesthetic at the level of the pubic tubercle.

The femoral branch of the genitofemoral nerve separates from the genitofemoral nerve somewhere above the inguinal ligament and accompanies the external iliac artery and below the inguinal ligament remains enveloped by the femoral vascular sheath lateral to the femoral artery. The femoral branch innervates the skin over the femoral triangle.

Answer A refers to the location of the lateral femoral cutaneous nerve. Damage to this nerve results in meralgia paresthetica, with numbness and burning in the lateral thigh. It commonly occurs in obesity and with trauma or ongoing pressure to the nerve at the level of the ASIS, as with a seatbelt or tight clothing. The nerve is blocked lateral and inferior to the ASIS, between the fascia lata and fascia iliaca. As this is a purely sensory nerve, even if damaged, EMG/NCV will be normal.

Answer C refers to the location of the ilioinguinal/iliohypogastric nerves, which are also commonly injured in herniorrhapy. Pain and sensory deficit with these nerves is typically below the umbilicus to the level of the inguinal ligament. The ilioinguinal nerve runs above the inguinal canal, and may also supply some innervation to the upper medial thigh. The nerves lie in the transversus abdominis plane, between the fascia of the internal oblique and the transversus abdominis muscles.

Answer D refers to the location of the obturator nerve, which is a motor nerve to the thigh adductors, with a variable small sensory component medially above the knee. Various block techniques have been described to access the nerve as it emerges from the obturator foramen, or in this case in the thigh, as it has already split into anterior and posterior divisions deep to the adductor longus and adductor brevis, respectively.

Answer E refers to the femoral nerve. This provides sensation to the anteromedial portion of the thigh and knee, as well as to the extensor and abductor muscles of the thigh.

KEY FACTS: NERVE INJURY—HENRIA REPAIR

- The ilioinguinal, iliohypogastric, and the genital branch of the genitofemoral nerve can all be injured during routine herniorrhaphy, leading to chronic pain.
- The genital branch of the genitofemoral nerve can be injured when mesh is tacked to the periosteum of the pubic tubercle and can be blocked with a field block at this same location.

47. ANSWER: C

48. ANSWER: C

The ***stellate ganglion***, also known as the cervicothoracic ganglion, is made up of the confluence of the inferior cervical and upper thoracic sympathethic ganglia. The preganglionic sympathetic fibers originate in the intermediolateral columns of the upper thoracic spinal cord, travel with the ventral spinal nerve root, and exit along white rami communicantes, entering the thoracic ganglia without synapsing and traveling cephalad in the sympathetic chain before synapsing in the cervical or stellate ganglia.

To achieve successful sympathetic denervation of the head and neck, the stellate ganglion is the target to be blocked, as all preganglionic nerves either synapse or pass through the ganglion on their way to the head and neck. The upper extremity receives most of its sympathetic innervation from gray rami communicantes of C6, C7, C8, and T1, which travel via the stellate ganglion to the brachial plexus, although some postganglionic fibers may bypass this pathway to the upper extremity by traveling with intercostal nerves via so-called nerves of Kuntz, which enter the brachial plexus via T2 and T3, without entering the stellate ganglion. This has been postulated as a reason for failure of technically adequate stellate ganglion block to achieve sympathectomy of the upper extremity.

As the vertebral artery is anterior to the stellate ganglion at C7 through T1, and the cupula of the lung is just inferior and lateral to it, it is not possible to safely block the stellate ganglion at this level; most techniques rely upon blocking the ganglion at C6, where the vertebral artery is posterior and protected by the transverse process of C6, or Chassignac's tubercle. A larger volume of local anesthetic is then used to facilitate diffusion along the sympathetic chain, down to the C7–T1 vertebral level. However, if the local anesthetic diffuses in a cephalad direction, it is possible to have a sympathectomy of the head and neck via blockade of the cervical ganglia cephalad to C7, causing Horner Syndrome (ptosis, miosis, anhidrosis, ipsilateral conjunctival injection and nasal stuffiness) without stellate ganglion bloackade. Furthermore, fluoroscopic needle position confirmation of placement does not functionally prove that a technically successful block was performed, or that the upper extremity will exhibit a sympathectomy; fibers could travel via the nerves of Kuntz, for instance, and therefore be resistant to blockade with technically accurate needle placement. Because of the proximity of the recurrent laryngeal nerve, hoarseness is an expected side effect of a volumetric block in the prevertebral area of the neck, but again is not pathognomonic of a stellate ganglion block per se.

Therefore, the best way to gauge sympathectomy of the upper extremity is via assessment of a temperature increase in the hand, secondary to blockade of sympathetic vasoconstrictor activity in the area innervated by the stellate ganglion.

KEY FACTS: STELLATE GANGLION

- The stellate ganglion is made up of the confluence of the inferior cervical and upper thoracic sympathetic ganglia, and sits posterior to the vertebral artery at C7–T1.
- All preganglionic sympathetic nerves either synapse or pass through the ganglion on their way to the head and neck, although some sympathetics to the upper extremity may bypass the stellate ganglion and travel via T1 and T2 to the brachial plexus via nerves of Kuntz.
- Although Horner syndrome and recurrent laryngeal nerve block are side effects of a volumetric stellate ganglion block, the most accurate way to gauge sympathectomy to the upper extremity, and thus stellate ganglion blockade, is a change in temperature in the affected extremity.

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49. ANSWER: A

The cupula of the lung is inferolateral to the stellate ganglion at C7. Tachycardia and coughing during a stellate ganglion block should raise the suspicion for iatrogenic pneumothorax. Although injury to the vertebral artery and inadvertent intravascular injection of local anesthetic are also possibilities given the surrounding anatomy, the patient's symptoms suggest that this is not the case in this scenario.

50. ANSWER: D

Complications from stellate ganglion block result from its proximity to a number of vital structures. As the ganglion lies anteriorly to the transverse process and tubercle of the first rib, pneumothorax is a distinct possibility. In a patient with tachycardia and coughing, with an approach caudal to C6, pneumothorax is a significant risk, and the procedure should be aborted and a chest x-ray obtained provided the patient is hemodynamically stable.

More common side effects are a result of diffusion of local anesthetic onto nearby nerve structures. Horner syndrome results in ipsilateral ptosis, miosis, and anhidrosis, as well as nasal stuffiness and conjunctival injection. The recurrent laryngeal nerve, when blocked unilaterally, can lead to hoarseness and a feeling of a lump in the throat, with subjective shortness of breath. Bilateral blockade would result in the bilateral vocal cord adduction with stridor and complete airway obstruction, despite respiratory effort. The phrenic nerve is also commonly anesthetized in large-volume stellate ganglion blocks, resulting in temporary ipsilateral diaphragmatic paralysis. This should be considered in patients who have contralateral diaphragmatic paralysis, such as after a coronary bypass surgery, or in those with respiratory compromise at baseline. Bilateral blockade would likely result in respiratory arrest given lack of diaphragmatic function. Given the proximity of both the recurrent laryngeal and phrenic nerves to the stellate ganglion, bilateral stellate ganglion blocks are not advised.

The stellate ganglion also lies in proximity to the C6–8 nerve roots and the interscalene portion of the brachial plexus. Injection of local anesthetic into the epineurium at this level can lead to subarachnoid spread and total spinal. Injection of local anesthetic around these nerve roots, or the brachial plexus, can lead to ipsilateral arm weakness. Spread of local anesthetic medially and posteriorly in large volumes can also result in cervical epidural spread leading to respiratory compromise similar to that seen with total spinal. Intubation with respiratory and cardiovascular support may be necessary until the local anesthetic is metabolized.

With advancement past the cervical transverse process at or above C6, or with an anterior approach at C7 or below, the needle may pierce the vertebral artery. If unrecognized, injection of local anesthetic may result in immediate seizures and/or stroke with vertebral artery damage. The carotid artery, laterally, may also be entered, with similar sequelae if unrecognized. Although puncture of the vessels in proximity to the stellate ganglion could theoretically lead to paratracheal hematoma, the needle gauge used is typically so small that this is unlikely in the absence of coagulopathy.

KEY FACTS: STELLATE GANGLION BLOCK: COMPLICATIONS

- Serious complications of stellate ganglion blockade include pneumothorax, vertebral artery injection resulting in seizure or stroke, total spinal from intrathecal spread, or respiratory arrest from cervical epidural spread.
- Spread of local anesthetic to adjacent structures commonly results in Horner syndrome, hoarseness from recurrent laryngeal nerve blockade, and ipsilateral diaphragmatic paralysis from phrenic nerve blockade.
- Given the risk of airway obstruction or respiratory arrest from blockade of recurrent laryngeal and phrenic nerves, respectively, bilateral stellate blockade should not be performed.

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51. ANSWER: A

52. ANSWER: B

Pelvic innervation is convoluted and incompletely understood but involves input from the superior hypogastric plexus, sympathetic chain, parasympathetic fibers derived from S2–4, and the pelvic splanchnic nerves from the sacral plexus (S1–5).

The superior ***hypogastric plexus*** is located in the midline, anterior to the L5 and S1 vertebral bodies, where it is accessible for blockade. The hypogastric nerves are then formed by the bifurcation of the superior hypogastric plexus; the paired hypogastric nerves give rise to the paired inferior hypogastric plexi. The inferior hypogastric plexi are located on the pelvic sidewalls, making this relatively inaccessible for blockade from a percutaneous approach. Interconnecting fibers between the right and left hypogastric nerves constitute a middle hypogastric plexus, although

it is often difficult to differentiate from the superior hypogastric plexus. Visceral plexi associated with the uterus, vagina, rectum, and bladder are derived from the inferior hypogastric plexus.

The pelvic splanchnic nerves arise from the ventral rami S2–S4 and enter the sacral plexus. They travel to their side's corresponding ***inferior hypogastric plexus***, where they contribute to the innervation of the ***pelvic*** and ***genital*** organs. They contain both ***preganglionic*** parasympathetic fibers as well as visceral afferent fibers. The nerves regulate the emptying of the ***urinary bladder*** and the ***rectum*** as well as ***sexual*** functions like ***erection***. The distal third of the transverse colon through the sigmoid and rectum, is innervated by the pelvic splanchnic nerves, and the proximal two-thirds by the vagus.

The ***sacral splanchnic nerves*** arise from the ***sympathetic trunk*** and provide sympathetic preganglionic and postganglionic efferent sympathetic fibers, as well as visceral afferent fibers. They are found in the same region as the ***pelvic splanchnic nerves***.

Of the given choices, there may be innervation to the uterus from the inferior hypogastric plexus, and the pelvic splanchnic nerves derived from the sacral plexus, but these targets are inaccessible for blockade. The superior hypogastric plexus is likely to provide visceral innervation to the uterus, and in fact neurolysis of this plexus has been demonstrated in randomized controlled trials to provide analgesia for midline pelvic pain from endometriosis.

Blockade of the superior hypogastric plexus requires an oblique approach. The needle, placed posteriorly approximately 5 to 7 cm from the midline, must travel caudad to the iliac crest superficially, and then inferior to the L5 transverse process and superior to the sacral ala on its way to the anterior aspect of the L5 and S1 vertebral bodies. The L5 nerve root traverses inferiorly to the L5 transverse process as it exits the neural foramen and courses anterolaterally to join the lumbosacral plexus. Therefore, it is vulnerable to paresthesia with this approach.

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53. ANSWER: B

Postherpetic neuralgia (PHN), like other neuropathic pain states, is often difficult to treat. Pharmacologic therapy includes tricyclic antidepressants (TCAs), anti-epileptic drugs, opioids, and local anesthetics; they have all shown varying degrees of efficacy. Topical capsaicin and tramadol have also been used. Hempenstall et al. performed a meta-analysis to determine the number needed to treat for the various pharmacologic therapies. According to their findings, topical lidocaine and TCAs may be the most efficacious. There is no evidence for the use of oral steroids in the management of PHN.

KEY FACTS: POSTHERPETIC NEURALGIA: RX

- Tricyclic antidepressants and topical lidocaine have been shown to be the most effective treatments for postherpetic neuralgia.
- Oral corticosteroids are not effective for the treatment of postherpetic neuralgia.

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54. ANSWER: D

Although the application of interventional procedures in the alleviation of pain associated with postherpetic neuralgia seems clinically sound, efficacy has yet to be definitively established. There are some data for the efficacy of intrathecal methylprednisolone, but it is not approved by the FDA for intrathecal administration in the United States due to the concern for arachnoiditis caused by the preservatives found in the available formulations.

The PINE study by van Wijck et al. randomized patients with acute herpes zoster to either standard therapy (analgesics and antivirals) or standard therapy with the addition of a single-shot epidural injection with local anesthetic and steroid. The authors found that the single-shot injection may provide a modest pain-reducing effect in the first month following injection, but this effect was not seen at later pain assessments.

The affected dermatomes here are upper cervical, likely C3–4. Somatic and sympathetic blockade of this area could be achieved with an interscalene block, but care should be taken to avoid needle insertion into an area of active blistering. As discussed above, intrathecal methylprednisolone would likely provide some pain relief; however, given safety concerns, this would not be the first-line therapy in the treatment of this patient. The appropriate sympathetic block for the location of the lesions for this patient would be the stellate ganglion. Intercostal nerve blockade would not be effective for zoster in upper cervical dermatomes.

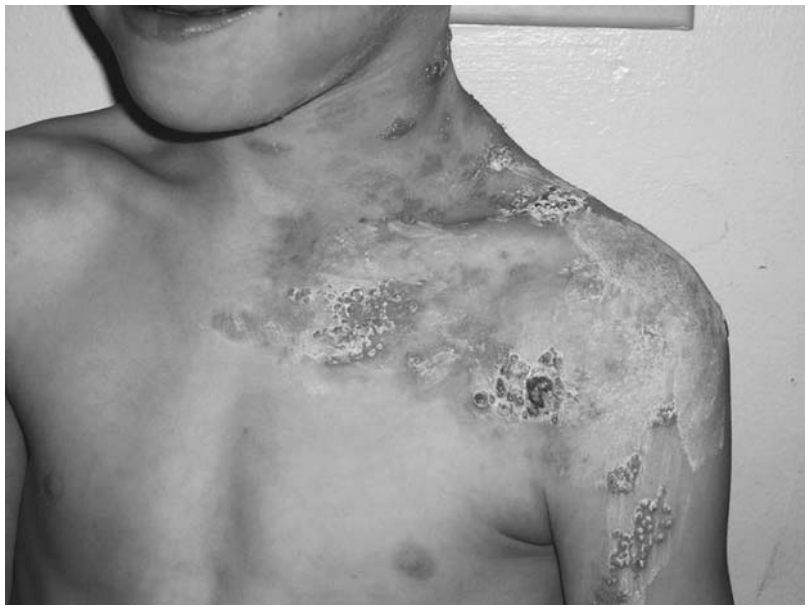

Figure 8.2 http://hardinmd.lib.uiowa.edu/dermatlas/shingles.html Image and content from DermAtlas, Johns Hopkins

KEY FACTS: NEUROPATHIC PAIN: TREATMENT WITH EPIDURAL

- In cases of acute herpes zoster, neuraxial steroids may be effective for pain relief. Intrathecal steroids are not approved for use in the United States by the FDA secondary for concern for arachnoiditis, but have been shown to be efficacious.
- Somatic and/or sympathetic blockade of the affected dermatome is also likely to provide analgesia for acute herpes zoster.
- The role of using nerve blocks in the setting of acute zoster in order to prevent postherpetic neuralgia is controversial.

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55. ANSWER: B

Local anesthetic toxicity is a rare occurrence in the pediatric patient population. Symptoms are the same as those in the adult population, namely seizures, dysrhythmias, cardiovascular collapse, and transient neurologic symptoms. It may be that pediatric patients are at an increased risk of toxicity due to several factors. First, larger volumes are used for epidural anesthesia relative to body mass in pediatric patients than in adults. In the case of this patient, the dose of bupivacaine was appropriate for weight, although at the upper limit of the allowable dose (2.5 mg/kg of bupivacaine). Second, most regional anesthetic procedures in infants and children are performed with the patient heavily sedated or anesthetized. Test doses are not a particularly sensitive marker of intravenous injection in the anesthetized patient, making detection of intravascular local anesthetic injection extremely difficult.

Epinephrine is added to epidural anesthetic solutions to decrease the rate of local anesthetic uptake from the caudal epidural space. The dysrhythmia observed in this patient is unlikely to be caused by the epinephrine, which if injected intravascularly would have caused an isolated, immediate rise in heart rate.

Given this, it is most likely that the local anesthetic toxicity was related to decreased metabolism and elimination of local anesthetic in the neonatal liver. Neonates also have decreased plasma concentrations of alpha(1)-acid glycoprotein, leading to increased concentrations of unbound bupivacaine.

KEY FACTS: LOCAL ANESTHETIC TOXICITY: INFANTS

- The risk of local anesthetic toxicity in neonates and infants may be increased relative to adults because of difficulty in detecting intravascular injection, the relatively larger volumes used for epidural anesthesia, and the performance of blocks with heavy sedation or anesthesia.
- Decreased metabolism and elimination of local anesthetic in the neonatal liver, as well as decreased protein binding, may also contribute to an increased risk of toxicity.

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56. ANSWER: A

When ***local anesthetic toxicity*** occurs, early recognition and immediate application of advanced life support are vital to the patient's survival. The primary goals of management are seizure cessation and the maintenance of hemodynamics. Protocols would be put in place to address the possible need for cardiopulmonary bypass in the event of local anesthetic toxicity.

In the late 1990s, Weinberg et al. observed a patient with carnitine deficiency who was noted to be extremely sensitive to bupivacaine-induced cardiac arrhythmias and hypothesized that bupivacaine induced arrhythmias by inhibiting carnitine-mediated mitochondrial fatty acid uptake, and that pretreatment with a fatty acid infusion prior to administration of bupivacaine might aggravate such arrhythmias. Their initial study results showed the exact opposite, marking the beginning of the development of intravenous lipid emulsions, such as Intralipid, in the treatment of local anesthetic toxicity.

Intralipid is a sterile, nonpyrogenic fat emulsion that is often a component of total parenteral nutrition. It is comprised of soybean oil, egg yolk phospholipids, glycerin, and water for injection. It contains both linoleic and alpha-linolenic acids. Allergic reactions (soybeans, egg yolks), thrombophlebitis, fat embolus, and ARDS are all potential complications of its use. Delayed reactions such as splenomegaly, altered liver function, pulmonary hypertension, and thrombocytopenia have all been associated with long-term use.

The exact mechanism underlying the lipid emulsion reversal of local anesthetic toxicity is unknown. One hypothesis is that the Intralipid acts as a "lipid sink" by creating a lipid phase within the serum that essentially extracts bupivacaine (lipid-soluble) from the plasma, effectively decreasing the amount of exposure of the myocardium to free bupivacaine. An alternate hypothesis is that Intralipid exerts a beneficial energetic-metabolic effect by increasing fatty acid transport at the inner mitochondrial membrane. The recommended dose is a 1-mL/kg bolus of 20% lipid emulsion for local anesthetic-associated cardiac arrest, followed by an infusion of 0.25 mL/kg/min for 10 minutes, while continuing cardiopulmonary resuscitation (CPR). The bolus dose may be repeated, and an infusion may be necessary.

The 2010 American Society of Regional Anesthesia and Pain Medicine (ASRA) practice advisory on local anesthetic toxicity states: "Positive effects of vasopressors in animal models of cardiac arrest have not translated into a clear advantage for their use in the clinical setting. Epinephrine has been associated with suboptimal outcomes in models of various shock states and strong clinical evidence of efficacy in enhancing long-term survival after cardiac arrest is lacking. Furthermore, recent studies suggest that adding vasopressin provides no advantage over epinephrine alone in treating out-of-hospital cardiac arrest. On balance, signs of rapid progression of the toxidrome, or detection of cardiac compromise in terms of either an electrocardiographic abnormality or depressed cardiac output, would constitute reasons for early treatment with lipid. Given the importance of restoring coronary circulation, the positive inotropic and vasopressor effects of epinephrine provide a strong rationale for its use in local anesthetic toxicity, which may be characterized by contractile depression, arrhythmias, and hypotension." Although epinephrine may also be arrhythmogenic, if Intralipid is ineffective, epinephrine administration as part of an ACLS protocol seems warranted.

KEY FACTS: LOCAL ANESTHESIA TOXICITY: MANAGEMENT

- The primary goal of management of local anesthetic systemic toxicity is prevention of acidosis and hypoxia.
- When local anesthetic systemic toxicity occurs, address airway, breathing, and circulation first.
- Seizure suppression is critical to reduce oxygen consumption; benzodiazepines are suggested first.
- IV lipid emulsion, like 20% Intralipid, should be considered in cases of cardiovascular collapse.
- The use of vasopressors is controversial but may be considered if Intralipid is not available or is ineffective.

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57. ANSWER: B

Lipid solubility appears to be the primary determinant of intrinsic anesthetic potency. Highly lipid-soluble agents penetrate the nerve membrane more easily, which is reflected biologically as increased potency.

The protein-binding characteristics of local anesthetic agents primarily influence the duration of action. Anesthetics that penetrate the axolemma and attach more firmly to the membrane proteins tend to possess a prolonged duration of anesthetic activity. Agents such as procaine are poorly bound to proteins and therefore possess a relatively short duration of action. Conversely, tetracaine, bupivacaine, and etidocaine are highly bound to proteins and display the longest duration of anesthesia.

The pKa of a chemical compound may be defined as the pH at which its ionized (BH+) and nonionized (B) forms are in complete equilibrium. The uncharged base form (B) of a local anesthetic agent is primarily responsible for diffusion across the nerve sheath. The onset of anesthesia is directly related to the rate of epineural diffusion, which in turn is correlated with the amount of drug in the base form. The percentage of a specific local anesthetic drug that is present in the base form when injected into tissue whose pH is 7.4 is inversely proportional to the pKa of that agent. For example, lidocaine, which has a pKa of 7.74, is 65% ionized and 35% nonionized at a tissue pH of 7.4. On the other hand, tetracaine, with a pKa of 8.6, is 95% ionized and only 5% nonionized at a tissue pH of 7.4. Local anesthetics like lidocaine, whose pKa is closer to tissue pH, have a more rapid onset time than agents with a high pKa, such as tetracaine.

Finally, the intrinsic vasodilator activity of different local anesthetic agents will influence their apparent potency and duration of action in vivo. The degree and duration of nerve block is related to the amount of local anesthetic drug that diffuses to the receptor site at the nerve membrane. Following injection of a local anesthetic agent, some of the drug will be taken up by the nerve and some will be absorbed by the vascular system. The degree of vascular absorption is related to the blood flow through the area in which the drug is deposited. All local anesthetic drugs, except cocaine, are vasodilator in nature. However, the degree of vasodilatation produced by the various agents differs. The greater vasodilator activity of lidocaine than mepivacaine, for instance, results in greater vascular absorption such that less lidocaine is available for nerve blockade.

KEY FACTS: LOCAL ANESTHETICS: PROLONGATION OF ACTION

- Lipid solubility determines potency. More lipid-soluble = more potent.
- Protein binding determines duration of action. More protein binding = longer duration of action.
- pKa determines onset of action. pKa closer to physiologic pH = more rapid onset, as more drug is available in the nonionized (base) form for diffusion across the nerve membrane.
- Intrinsic vasodilator activity may have various effects on potency and duration. Greater vascular absorption reduces the amount of drug available for action at the nerve.

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58. ANSWER: C

Epinephrine and bicarbonate have long been used as adjuncts to brachial plexus block, epinephrine to prolong duration and bicarbonate to hasten onset.

In at least one prospective, double-blind, randomized controlled trial, the duration of sensory and motor blockade was significantly longer in patients who received dexamethasone in addition to lidocaine for an axillary nerve block. Corticosteroids are often used as an adjunct to local anesthetics, but their mechanism of action is not completely understood. Corticosteroids are known to have a vasoconstrictive effect when applied topically, however, this may not be clinically significant in the acute setting. Corticosteroids also may have a local effect on the nerve, and have been experimentally shown to block nociceptive C fibers, in addition to modulating phospholipase A2 and prostaglandin production. It is unclear in this case whether the synergistic analgesic and anesthetic function is from systemic uptake or local effect in the periphery.

Clonidine is a frequently used adjuvant to local anesthetics. The analgesic properties of clonidine when administered intrathecally or epidurally have been demonstrated; they seem to be attributable to its $alpha_2$ agonist properties. Specific peripheral effects of clonidine appear less obvious because $alpha_2$ adrenoreceptors are not present on the axon of the normal peripheral nerve. The benefit of adding clonidine to local anesthetics for peripheral nerve blocks is less clear, although it is widely believed that clonidine improves the quality and duration of a local anesthetic block. The increased risk of hypotension, fainting, and sedation may limit its usefulness. Clonidine appears to be beneficial in doses up to 150 μg.

At least two randomized controlled trials have explored the efficacy of morphine as an adjunct to local anesthetics in peripheral nerve block. Neither study found any difference in pain relief between the two study arms; however, that by Bourke and Furman did demonstrate lower opioid consumption in the study group who received the blocks with morphine.

KEY FACTS: LOCAL ANESTHETICS: PROLONGATION

- Epinephrine, steroids, and clonidine may increase the duration of peripheral local anesthetic block.

- Bicarbonate does not increase duration, but does hasten onset.
- Opioids do not appear to affect the duration of a peripheral nerve block.

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59. ANSWER: A

Lumbar epidural steroid injections have been used in patients with a variety of causes of low back pain. The optimal steroid (type and/or dose), the site of injection (interlaminar, transforaminal, caudal), and the use of local anesthetic are all variables that remain unclear. Many trials on the subject are flawed by methodologic shortcomings, and difficult to compare due to heterogeneity of patient population, number of injections, outcomes assessed, and the type and dose of steroid used. More than three or four injections per year are usually not recommended because of concerns about potential suppression of the hypothalamic-pituitary-adrenal axis, although there is little objective evidence to support these parameters.

The best evidence for benefit comes from trials for patients with radiculopathy due to a herniated disk; they demonstrate benefit in the short term (less than 3 to 6 months) without strong evidence for benefit thereafter. The evidence does suggest more rapid pain relief with epidural steroids in acute radiculopathy compared with conservative management. Some data suggest that transforaminal injections, which deliver steroid into the anterior epidural space, may be more effective than interlaminar or caudal injections for low back pain, although this remains unproven given a paucity of well-designed trials. Epidural injections by any route for nonspecific axial low back pain, spinal stenosis, or chronic radiculopathy have little robust supportive data.

Of the patients above, patient A is the best candidate, with an acute radiculopathy most likely related to her spinal stenosis. Candidate B has chronic axial low back pain with nonspecific MRI findings and is unlikely to get durable relief from his pain of 20 years' duration with epidural steroids. Candidate C has an EMG-documented chronic radiculopathy, which is not as likely as an acute radiculopathy to respond favorably to epidural steroids. Candidate D's presentation is consistent with acute myofascial strain. Her leg pain is in a nonradicular distribution, which is not explained by her MRI findings, and would be better initially treated with medication and physical therapy.

KEY FACTS: LOW BACK PAIN AND EPIDURAL STEROIDS

- Lumbar epidural steroid injections are most useful in patients with acute radiculopathy, providing short-term benefit (less than 3 to 6 months).
- The use of epidural steroid injections for nonspecific axial low back pain, spinal stenosis, or chronic radiculopathy is controversial, as there is a lack of robust supportive data for long-term efficacy.

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60. ANSWER: C

The neonate's pain-processing pathways are not completely developed at birth and significant maturation in the peripheral, spinal, and supraspinal pain pathways occurs over the early postnatal period. Despite this, the neonate still responds to painful stimuli with behavioral, hormonal, and metabolic signs of stress. Increased morbidity and mortality have been shown in neonates who receive placebo rather than analgesic agents in the perioperative period. Multiple studies have shown that opioids can promote hemodynamic stability, respiratory synchrony, and oxygenation in intubated neonates. Opioid analgesia has also been shown to decrease the incidence of higher-grade intraventricular hemorrhage.

Neonatal abstinence syndrome (NAS) is a constellation of neurologic and hemodynamic symptoms seen in neonates

exposed to certain illicit or prescription substances while in utero. Symptoms include irritability, sleep disorders, seizure, increased reflexes and muscle tone, hyperventilation, vomiting, diarrhea, and diaphoresis. Newborn toxicology screens may be helpful in targeting specific therapy, but supportive, nonpharmacologic therapy including hydration and nutritional support must be instituted regardless of the substance involved. Seizure prophylaxis and opioid (morphine, diluted tincture of opium, and methadone have all been investigated) supplementation should not be delayed if indicated.

KEY FACTS: OPIOID SENSITIVITY: NEONATE

- Neonates feel pain; opioids to reduce pain improve morbidity and mortality.
- Neonates are more sensitive to opioids secondary to ongoing development of nociceptive pathways.
- Maternal opioid use can lead to neonatal abstinence syndrome after delivery. Nonpharmacologic supportive therapy is the standard of care. However, opioid replacement in some neonates with inability to sleep/feed/thrive and/or with seizures is indicated.

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61. ANSWER: B

Buprenorphine, when administered in high doses, has a bell-shaped dose–response curve with a ceiling effect on respiratory depression. Despite the safety margin elicited by the ceiling effect, buprenorphine may result in significant respiratory depression when co-administered with other CNS depressants. Given buprenorphine's strong μ-opioid receptor affinity, μ-receptor antagonists in standard doses are unlikely to reverse opioid-induced respiratory depression. The clinical approach to severe opioid-induced respiratory depression for the co-administration of buprenorphine and opioids is to titrate opioid μ-antagonists, such as naloxone, to effect. Titration of naloxone may require doses in the range of 2 to 10 mg before conferring an effective dose–response. Due to naloxone's relatively rapid half-life, the respiratory effects of buprenorphine outlast the antagonist effects of naloxone, requiring a continuous infusion once reversal is achieved.

Switching to an alternative μ-receptor antagonist, such as cyprodime or naltrexone, in equipotent doses would have little effect on respiratory depression. Similar to the initial bolus of naloxone, any μ-receptor antagonist would likely require titration to effect rather than a single bolus of similar potency to naloxone. A delta opioid receptor antagonist, such as naltrindole, would likely not reverse the effects of the buprenorphine and opioid respiratory depression. Benzodiazepine antagonists may be useful when there is uncertainty of the patient's drug use history; however, in this case the patient's urine drug screen was negative, and no premedications were administered.

KEY FACTS: BUPRENORPHINE

- Buprenorphine is a partial μ-opioid agonist.
- Buprenorphine has a strong μ-opioid receptor affinity and slow dissociation from the receptors.
- Buprenorphine has a ceiling effect on respiratory depression; however, when co-administered with other CNS depressant drugs, severe respiratory depression may result.

ADDITIONAL READINGS

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62. ANSWER: C

Buprenorphine exhibits a high μ-receptor affinity and low intrinsic activity. Buprenorphine's affinity is sufficiently strong that it can block or even displace other opioids from their μ-opioid receptors, resulting in a withdrawal reaction known as precipitated withdrawal. According to the U.S. Department and Health and Human Services Consensus Panel on Buprenorphine Use, "Due to the potential for severe withdrawal, buprenorphine is generally administered once a patient is weaned off opioids and is experiencing mild to moderate opioid withdrawal effects. This may take some time, as sublingual buprenorphine in high doses, such as dosing used for opioid addiction maintenance therapy, has a half life of 20–70 hours (mean of about 37 hours)."

KEY FACTS: BUPRENORPHINE AND PRECIPITATED WITHDRAWAL

- Buprenorphine's high μ-opioid receptor affinity may displace other μ-opioid agonists from their receptors, resulting in precipitated withdrawal.
- High-dose buprenorphine (typically used for opioid maintenance therapy) has a prolonged half life of 20 to 70 hours.

ADDITIONAL READINGS

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63. ANSWER: C

Unlike full μ-opioid agonists, ***buprenorphine*** is a partial μ-opioid agonist. Its subjective and physiologic effects, including respiratory depression, exhibit a ceiling effect with increasing doses. Buprenorphine's effect on respiratory depression levels off at doses higher than 3.0 mcg/kg to approximately 50% of baseline, in contrast to fentanyl, in which dose-dependent respiratory depression results in apnea at comparable doses. This side-effect profile may provide a wider safety margin for use as maintenance therapy in opioid dependence. Despite buprenorphine's safety margin, reports of severe buprenorphine-induced respiratory depression have occurred. These occurrences were primarily associated with the concomitant use of psychotropics or CNS depressants, particularly benzodiazepines.

Buprenorphine is metabolized by cytochrome P-450 3A4 into metabolites with significantly lower potency and affinity for the μ-opioid receptors. It is important to note the possibility of drug interactions with other drugs that induce or inhibit cytochrome P-450 3A4 such as HIV-1 protease inhibitors, erythromycin, carbamazepine, phenobarbital, phenytoin, rifampin, and zileuton.

KEY FACTS: BUPRENORPHINE DRUG INTERACTIONS

- Buprenorphine is a partial μ-opioid agonist.
- Buprenorphine's effects on respiratory depression exhibits a plateau or ceiling effect with increasing doses.
- Severe respiratory depression associated with buprenorphine may result with concomitant use of CNS depressants, particularly benzodiazepines.
- Interactions with buprenorphine may occur with other drugs that induce or inhibit cytochrome P-450 3A4.

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64. ANSWER: D

New-onset back pain that does not improve with time and rest in a cancer patient raises serious concern for metastatic disease. Bone is the tissue most commonly giving rise to cancer pain, and the vertebral column is the most common site of bony metastasis. Up to one-third of cancer patients develop metastases to the spine. Therefore, an MRI is indicated to rule out vertebral metastasis. An x-ray is not sensitive enough to rule out bony metastasis if the index of suspicion is high. Although physical therapy and anti-inflammatory therapy are useful modalities in acute back strain, metastatic disease should be ruled out before initiating these therapies in a cancer patient with this presentation. Likewise, lumbar epidural steroid injection could delay definitive therapy if metastatic disease is not first ruled out.

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65. ANSWER: B

The WHO analgesic ladder is a simple systematic approach to the treatment of cancer pain. The first step utilizes nonopioid analgesics such as NSAIDs and adjuvant drugs. Adjuvant drugs are used for pain (e.g., antidepressants and anticonvulsants) and to control the side effects of the primary analgesic (e.g., omeprazole for gastrointestinal irritation). The second

step utilizes "weak" opioids such as codeine and hydrocodone in addition to nonopioid and adjuvant drugs. The third step replaces "weak" opioids with "strong" opioids. Nonopioid and adjuvant drugs are used in all steps. Nonopioid drugs such as NSAIDs work synergistically with opioids and are important in the treatment of bone pain, which is the most common source of pain in cancer. Care must be taken in order to limit the total dosing of acetominophen especially when a patient is already receiving the drug via another medication such as vicodin or Percocet.

Increasing breakthrough medication alone is not a good strategy, as scheduled medication should be adequate to control pain most of the time. "Weak" and "strong" opioids are a matter of convention, as the agonist action at the μ-receptor of both is in theory limited only by dose. However, "weak" opioids such as codeine and hydrocodone are typically prepared in combination with co-analgesics such as acetaminophen, so their dose escalation is limited. Since this patient is tolerating an NSAID (ibuprofen) with the aid of the adjuvant omeprazole without signs of serious gastrointestinal or renal toxicity, the NSAID should be continued. Although advancing to step 3 in the WHO analgesic ladder by adding a "strong" opioid is advisable at this point, the use of the "weak" opioid hydrocodone (Vicodin) on top of the "strong" opioid morphine is unnecessary and should be discontinued. Acetaminophen could be added back in as an adjuvant drug if desired.

KEY FACTS: CANCER PAIN: MANAGEMENT

- The WHO three-step ladder can be considered for cancer pain management.
- Step 1 includes acetaminophen and NSAIDs.
- Step 2 includes "weak opioids."
- Step 3 is used when Step 2 medications are ineffective.
- It is not necessary to try all medications in the previous steps before moving to the next tier.

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66. ANSWER: D

Addiction is defined as a loss of control over drug use, compulsive use, and use despite harm. It is rare in patients with no history of substance abuse receiving therapy for cancer pain.

Physical dependence is one of the expected pharmacologic effects of chronic high-dose opioid therapy. It is defined by the development of an abstinence syndrome following abrupt discontinuation. It is not a marker of addiction and should not be interpreted as such.

All opioids, including methadone, have the potential for addiction, although addiction is rare in the treatment of cancer. Methadone has a highly variable pharmacokinetic profile due to differences in protein binding, urinary excretion, and induction of metabolism among patients. Because its initial duration of action is much shorter than its half-life, steady state will not be achieved for 2 to 5 days. For these reasons it can be dangerous to administer this drug according to opioid equivalency protocols.

Psychostimulants such as caffeine and amphetamines can be useful in offsetting the sedative effects of opioids. Furthermore, amphetamines have their own analgesic properties.

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9.

CARDIAC ANESTHESIA

Kathleen Chen, MD, and Adam Lerner, MD

1. Which of the following hemodynamic changes is NOT commonly associated with cross-clamping of the infrarenal aorta?

A. Increase in central venous pressure
B. Increase in cardiac output
C. Decrease in pulmonary artery pressure
D. No change in pulmonary artery occlusion pressure
E. Increase in systolic pressure

2. Which of the following statements regarding the use of α-stat and pH-stat management during cardiopulmonary bypass with moderate systemic hypothermia is INCORRECT?

A. pH-stat management requires knowledge of actual patient temperature, whereas α-stat does not.
B. α-stat management results in higher cerebral blood flow than pH-stat management.
C. pH-stat management results in a lower blood pH than α-stat management.
D. α-stat management is based on maintenance of the electrochemical neutrality of the imidazole buffering system.
E. The difference between α-stat and pH-stat management is more pronounced as patient temperature decreases.

3. The most common combination of acid–base disorders seen during cardiopulmonary resuscitation is

A. Respiratory alkalosis and metabolic alkalosis
B. Respiratory acidosis and metabolic acidosis
C. Respiratory alkalosis and metabolic acidosis
D. Respiratory acidosis and metabolic alkalosis
E. None of the above

4. Which of the following conditions would not likely cause an increased difference between pulmonary artery diastolic pressure and left ventricular end-diastolic pressure?

A. Mitral stenosis
B. Primary pulmonary hypertension
C. Hypoxemia
D. Pulmonic stenosis
E. Hypothermia

5. After determining that a patient has no pulse, which one of the following forms of treatment should be used initially for the patient with ventricular fibrillation?

A. CPR
B. Defibrillation
C. Epinephrine IV
D. Lidocaine IV
E. Vasopressin IV

6. Which of the following factors is the LEAST likely explanation for a prolonged activated clotting time (ACT)?

A. Heparin
B. Warfarin
C. Platelet dysfunction
D. Hyperthermia
E. Hemodilution

7. Which of the following therapeutic interventions is NOT indicated in the management of acute, severe aortic regurgitation?

A. Increasing heart rate to 75 to 85 bpm
B. Placement of an intra-aortic balloon counterpulsation device
C. Afterload reduction by titration of vasodilators

D. Inotropic support of reduced contractility
E. Immediate surgical consult

8. Which of the following pharmacologic agents is commonly avoided for effective symptomatic treatment of acute cocaine toxicity?

A. Labetalol
B. Nitroglycerin
C. Nitroprusside
D. Metoprolol
E. Phentolamine

9. During open reduction of a fractured hip, an 80-year-old, 60-kg patient with a history of moderate mitral stenosis develops atrial fibrillation with a ventricular rate of 150 bpm. The patient's blood pressure is 63/37 mmHg. Which of the following is the most appropriate therapeutic intervention?

A. Diltiazem 15 mg IV bolus
B. Heparin 5,000 units and phenylephrine 200 μg IV bolus
C. Transcutaneous pacing at 60 bpm
D. Heparin 5,000 units IV bolus and rapid IV administration of 1 liter of 0.9% normal saline
E. Synchronized cardioversion with 100 joules

10. Which of the following therapeutic interventions is LEAST indicated in the management of acute left ventricular failure?

A. Initiation of intravenous dobutamine
B. Placement of an intra-aortic balloon pump
C. Initiation of intravenous milrinone
D. Initiation of extracorporeal membrane oxygenation (ECMO)
E. Placement of a left ventricular assist device

11. Which of the following is a key hemodynamic goal in the management of patients with acute mitral regurgitation (MR)?

A. Increased afterload
B. Decreased afterload
C. Increased systemic vascular resistance
D. Decreased heart rate
E. Increased preload

12. Which of the following changes in cardiovascular function is NOT generally associated with increasing age?

A. Decreased contractility
B. Increased ventricular filling pressure
C. Increased myocardial stiffness
D. Increased vascular stiffness
E. Increased beta-adrenergic sensitivity

13. Antegrade coronary blood flow occurs during what phase of manual chest compressions?

A. Relaxation phase
B. Compression phase
C. Whenever the pressure in the aorta exceeds the right atrial pressure
D. Whenever the pressure in the right atrium exceeds the aorta pressure
E. Both relaxation and compression phases

14. Which of the following antiemetics does not produce a significant dose-dependent prolongation of the QTc interval?

A. Ondansetron
B. Droperidol
C. Haloperidol
D. Scopolamine
E. Prochlorperazine

15. Which of the following antiplatelet drugs—abcimixab, clopidogrel, and ticlodipine—inhibit platelet aggregation at the ADP receptor site?

A. Abciximab only
B. Clopidogrel only
C. Ticlodipine only
D. Clopidogrel and ticlodipine
E. Abciximab, clopidogrel, and ticlodipine

16. Which of the following hemodynamic parameters should be avoided in a patient with aortic insufficiency?

A. Tachycardia
B. Bradycardia
C. Decreased afterload
D. A and C
E. B and C

17. Which of the following diseases is NOT associated with aortic regurgitation?

A. Marfan syndrome
B. Ehlers-Danlos syndrome
C. Ankylosing spondylitis
D. Primary Sjögren syndrome
E. Syphilis

18. In a patient with severe aortic stenosis, hypertension, and concomitant myocardial ischemia with a heart rate 110 bpm,

BP 160/95 mm Hg, Hct 22%, and oxygen saturation 95%, which of the following therapies is LEAST indicated?

A. Beta blockade to reduce heart rate to 80 bpm
B. Nitroprusside to reduce afterload and diastolic BP to 45 mm Hg
C. Nitroglycerin titrated to a BP of 130/80 mm Hg
D. Increase FiO_2 to increase oxygen saturation to 100%
E. Transfusion with packed red blood cells to Hct of 28%

19. An 80-year-old woman with severe aortic stenosis requires an ORIF of her hip. Her family requests a spinal anesthetic. Your primary concerns associated with this anesthetic technique would NOT include

A. Hypotension secondary to a reduction in preload
B. Hypotension secondary to a fall in reduction in systemic vascular resistance
C. Symptomatic bradycardia
D. Increased risk for postoperative cognitive impairment
E. Use of prophylaxis for deep venous thrombosis

20. During a general anesthetic for a laparoscopic cholecystectomy, a 70-year-old woman with severe aortic stenosis becomes hypotensive, with a blood pressure of 70/33 mm Hg. Which of the following would be the LEAST likely cause for hemodynamic instability in this patient?

A. Development of a junctional rhythm at a rate of 55 bpm
B. Redistribution of splanchnic venous blood during peritoneal insufflation
C. Vagal response with resultant sinus bradycardia to a heart rate of 30 bpm
D. Tachycardia to a heart rate of 110 bpm
E. Inadvertent over-pressurization of the peritoneal cavity to a pressure of 25 mm Hg

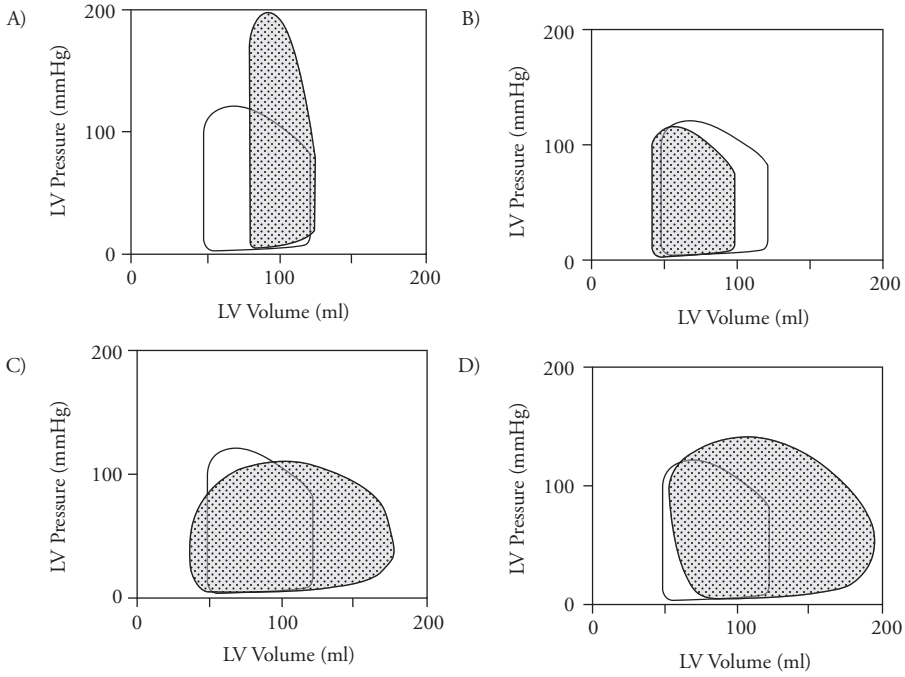
21. After an aortic valve has been replaced for aortic stenosis, left ventricular (LV) end-systolic volume will be

A. Increased, due to increased transvalvular gradient
B. Decreased, due to increased transvalvular gradient
C. Increased, due to reduction in impedance to ventricular ejection
D. Decreased, due to reduction in impedance to ventricular ejection
E. Unchanged

22. Which of the following pharmacologic agents does NOT increase the risk of digoxin-induced arrhythmias?

A. Amiodarone
B. Quinidine
C. Verapamil
D. Rifampin
E. Thiopental

23. Which of the flow–volume loops in Figure 9.1 represents pressure–volume changes typical with severe aortic stenosis?



E) None of the above

Figure 9.1 QUESTION 21

24. Which of the following physical exam maneuvers is used to assess the adequacy of the collateral circulation of the hand?

A. Phalen's test
B. Tinel's test
C. Allen's test
D. Watson's test
E. Kleinman's test

25. An underdamped arterial tracing with a transducer positioned below the level of the patient's heart will result in which of the following blood pressure interpretations relative to the actual reading?

A. Overestimation
B. Underestimation
C. No change due to opposite effects of the two conditions
D. Cannot be determined without knowing patient positioning
E. Cannot be determined without knowing site of arterial cannulation

26. The systolic components of the arterial pressure waveform follow which ECG wave?

A. P wave
B. Q wave
C. R wave
D. S wave
E. T wave

27. Which of the following is an important hemodynamic goal in managing a patient with hypertrophic obstructive cardiomyopathy and known dynamic left ventricular (LV) outflow tract obstruction?

A. Increased myocardial contractility
B. Decreased myocardial contractility
C. Increased heart rate
D. Decreased preload
E. Decreased afterload

28. Which of the following statements regarding the autonomic nervous system is true?

A. The sympathetic nervous system is exclusively an efferent system.
B. The parasympathetic nervous system is limited to the cranial nerves.
C. Acetylcholine is the neurotransmitter of the parasympathetic system, exclusively.
D. The sympathetic nervous system efferents exit through the thoracic and lumbar spinal segments, exclusively.
E. The preganglionic neurotransmitter of the sympathetic nervous system is norepinephrine.

29. Which of the following volatile anesthetics is the most potent depressant of the normal baroreceptor response?

A. Sevoflurane
B. Halothane
C. Isoflurane
D. Desflurane
E. Enflurane

30. Which of the following responses is NOT consistent with beta-adrenergic stimulation?

A. Bronchodilation
B. Increased myocardial contractility
C. Vasodilation
D. Glycogenolysis
E. Decreased plasma renin production

31. A noninvasive blood pressure cuff is placed on both upper extremities in a patient positioned in the right lateral decubitus position. There is a 20-cm difference in the height of the two cuffs. How would the pressure reading from the cuff on the left arm differ from that of the right arm?

A. It will be 20 mm Hg higher.
B. It will be 20 mm Hg lower.
C. It will be 14 mm Hg higher.
D. It will be 14 mm Hg lower.
E. It will be the same.

32. The systolic blood pressure in a noninvasive blood pressure measurement corresponds to

A. Return of blood flow through the artery during cuff inflation
B. Return of blood flow through the vein during cuff inflation
C. Return of blood flow through the artery during cuff deflation
D. Return of blood flow through the vein during cuff deflation
E. The point of maximal cuff pressure fluctuation

33. The hematocrit of a patient on cardiopulmonary bypass is 18%. If the patient is transfused with packed red blood cells and the hematocrit is increased to 30% with no other changes, what would be the expected change in mean arterial blood pressure?

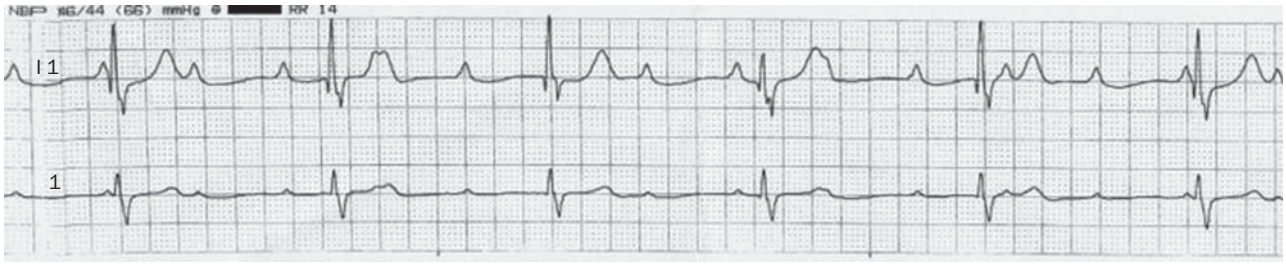


Figure 9.2 QUESTION 34

A. Increased
B. Decreased
C. No change
D. Cannot determine without knowing temperature
E. Cannot determine without knowing flow rate

34. Three days after aortic valve replacement (AVR), a patient is noted to have the ECG shown in Figure 9.2. Of the following, which is the most likely cause of this abnormality?

A. Persistent hyperkalemia
B. Obstruction of blood flow to the posterior interventricular artery
C. Reperfusion injury
D. Sterile pericardial inflammation
E. Acute biatrial enlargement

35. During carotid endarterectomy under general anesthesia, an 80-year-old woman develops sinus bradycardia to a heart rate of 30 bpm and hypotension to a blood pressure of 67/34. Which of the following is the best initial course of treatment?

A. Atropine 0.3 mg IV push
B. Infiltration of the carotid body with 0.5% bupivacaine
C. Initiation of transcutaneous pacing at 70 bpm
D. Immediate cessation of surgical carotid manipulation
E. Naloxone 0.04 mg IV push

36. Upon initiation of cardiopulmonary bypass for a 68-year-old patient undergoing coronary artery bypass grafting, mean arterial pressure decreases from 75 mm Hg to 55 mm Hg. Which of the following would be the most likely cause of this reduction?

A. Hypothermia-induced vasodilation
B. Myocardial ischemia with reduced cardiac output
C. Hemodilution from crystalloid pump prime
D. Reduced left ventricular preload
E. Reduced right ventricular preload

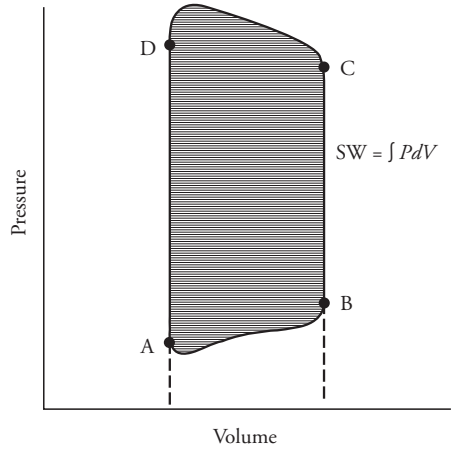


Figure 9.3 QUESTION 37

37. At what point on the cardiac pressure–volume loop shown in Figure 9.3 can preload be determined?

A. Point A
B. Point B
C. Point C
D. Point D
E. Shaded area under the curve

38. An 82-year-old woman with a history of hypertension and coronary artery disease but normal systolic function develops acute-onset pulmonary edema. Her blood pressure is 90/50 with a heart rate of 110 bpm. Which of the following treatments is most appropriate?

A. Dobutamine
B. Dopamine
C. Amiodarone
D. Milrinone
E. Metoprolol

39. Which of the following statements regarding the effects of aging on cardiac function is true?

A. The left ventricle becomes more compliant.
B. The myocardium has an increased sensitivity to beta agonists.

C. Myocardial contractility is unchanged under submaximal demand conditions.
D. Cardiac output is decreased despite increased metabolic demands.
E. Stroke volume remains unchanged.

40. Which of the following statements regarding thermodilution cardiac output measurements in the setting of significant tricuspid regurgitation is true?

A. Cardiac output will be overestimated.
B. Cardiac output will be underestimated.
C. Cardiac output will be accurate.
D. Cardiac output can be accurate, overestimated, or underestimated.
E. Cardiac output will be accurate if a continuous cardiac output catheter is used.

41. In which of the following disease(s) is a cardiac pacemaker NOT indicated?

A. Dilated cardiomyopathy
B. Asymptomatic sinus disease
C. Hypertrophic obstructive cardiomyopathy
D. Long QT syndrome
E. Symptomatic AV node dysfunction

42. Which of the following management strategies is LEAST indicated in the management of cardiac tamponade?

A. Beta blockade to maintain strict heart rate control in the 50- to 60-bpm range
B. Maintenance of spontaneous ventilation until evacuation of pericardium
C. Aggressive volume resuscitation to maintain euvolemia
D. Avoidance of venodilation with nitroglycerin
E. None of the above

43. Which of the following electrophysiologic findings is characteristic of lidocaine cardiotoxicity?

A. PR interval prolongation
B. Increased conduction velocity
C. Reduced phase 4 depolarization
D. Reduced automaticity
E. QRS shortening

44. For a witnessed cardiac arrest, which of the following interventions performed in isolation significantly improves survival outcome?

A. Head tilt, chin lift
B. Mouth-to-mouth ventilation
C. Intubation
D. Chest compressions
E. None of the above

45. Which of the following hemodynamic parameters cannot be obtained in a patient with a pulmonary artery (PA) catheter that has a non-functional balloon?

A. Cardiac output
B. Systemic vascular resistance
C. Pulmonary vascular resistance
D. Stroke volume
E. Mixed venous saturation

46. Which of the following cardiovascular reflexes does NOT cause a decrease in heart rate?

A. Carotid sinus massage
B. Cushing's reflex
C. Oculocardiac reflex
D. Valsalva maneuver
E. Vasovagal reflex

47. Which one of the following parameters in arterial blood modifies the neural output of the carotid body chemoreceptors?

A. Oxygen tension
B. Temperature
C. Carbon dioxide tension
D. Oxygen saturation
E. All of the above

48. Thirty minutes after arrival in the PACU, a 72-year-old man status post carotid endarterectomy is hypertensive to a blood pressure of 190/96 mm Hg. Of the following, which is LEAST likely to be the cause of his hypertension?

A. Surgical denervation of the carotid sinus baroreceptors
B. Impairment of cerebral autoregulation
C. History of hypertension
D. Hyperventilation
E. Hypoxemia

49. Which of the following neurologic structures is involved in the autonomic reflexes associated with the carotid sinus?

A. Glossopharyngeal nerve
B. Vagus nerve
C. Celiac plexus
D. A and B
E. All of the above

50. A 27-year-old man presents for ORIF of his right ankle after falling on ice. On exam, he is noted to be dyspneic and to have prominent rales. Which of the following is most likely the cause?

A. Acute cannabis toxicity
B. Chronic cocaine abuse
C. Salicylate toxicity
D. Acute acetaminophen toxicity
E. Chronic opiate abuse

51. Which of the following describes the typical changes in myocardial oxygen supply and demand associated with congestive heart failure?

A. Increased myocardial oxygen supply and demand
B. Decreased myocardial oxygen supply and demand
C. Increased myocardial oxygen supply and decreased demand
D. Decreased myocardial oxygen supply and increased demand
E. No change

52. Which of the following are NOT characteristic of the effects of cocaine on the heart?

A. Increased PR and QRS intervals on ECG
B. Decreased QT interval on ECG
C. Increased heart rate and blood pressure
D. Increased coronary artery resistance
E. Prolonged ventricular repolarization

53. Which of the following best describes the impact of constrictive pericarditis on a central venous pressure (CVP) waveform?

A. Ventricular dip and plateau
B. Ventricular plateau and dip
C. Ventricular peak and plateau
D. Ventricular plateau and peak
E. Ventricular dip and peak

54. Which of the following has the LEAST impact on coronary blood flow?

A. Heart rate
B. Cardiac output
C. Coronary vascular resistance
D. Diastolic blood pressure
E. Maximum pressure gradient across the aortic valve

55. Which of the following neurologic structures is involved in the autonomic reflexes associated with the carotid sinus?

A. Nucleus of the solitary tract
B. Vagus nerve and cervical plexus
C. Mechanoreceptors with afferent pathway in unmyelinated vagal C fibers
D. Glossopharyngeal and vagus nerve
E. Carotid nerve plexus

56. Which of the following properties is NOT a determinant of coronary blood flow?

A. Perfusion pressure
B. Myocardial intravascular compression
C. Myocardial metabolism
D. Myocardial extravascular compression
E. Neurohumoral control

57. During TEE examination, which of the following findings is NOT consistent with coronary blood flow?

A. Color Doppler exam demonstrating predominant flow during diastole
B. Origination of flow on color Doppler from aortic sinus
C. Blood flow on color Doppler initiating from above the right and left coronary cusps of the aortic valve
D. Biphasic flow pattern on pulse-wave Doppler
E. None of the above

58. Which of the following pharmacologic agents does NOT produce coronary steal?

A. Nitroprusside
B. Dipyridamole
C. Adenosine
D. Sildenafil
E. Isoflurane

59. A 79-year-old woman taking warfarin for atrial fibrillation emergently presents for a craniotomy for subdural hematoma after a fall. Initial laboratory investigation reveals an INR of 6.5. The rest of her coagulation tests were normal. Which of the following treatments is LEAST indicated to control life-threatening hemorrhage in this patient?

A. Vitamin K
B. Recombinant factor VIIa
C. Fresh frozen plasma (FFP)
D. Platelets
E. Prothrombin complex concentrate

60. Thirty minutes after separation from cardiopulmonary bypass and 1 minute after closure of the chest in a 68-year-old woman status post coronary artery bypass grafting and mitral valve repair, 2-mm ST segments are noted in the inferior leads, followed by a sudden onset of

ventricular fibrillation. Which of the following is a possible cause?

A. Hyperkalemia
B. Hypothermia
C. Intracoronary air embolism
D. Atrial pacing during repolarization
E. All of the above

61. During hypothermic cardiopulmonary bypass on a 55-year-old man for aortic valve replacement, an arterial blood gas reveals a Pa_{O_2} of 64 mm Hg despite an FiO_2 of 0.9. Which of the following would LEAST likely explain this result?

A. Inadequate heparin administration
B. Inadequate muscle relaxation
C. Leak in the cardiopulmonary bypass gas circuit
D. Slightly decreased "sweep" speed during bypass
E. None of the above

62. Following separation from cardiopulmonary bypass for mitral valve repair, a 63-year-old woman is found to have an O_2 saturation of 92% despite an FiO_2 of 1.0. Which of the following is an UNLIKELY cause for this finding?

A. Malfunction of expiratory valve
B. Endobronchial location of the endotracheal tube
C. Atelectasis
D. Severe mitral stenosis
E. Severe aortic insufficiency

63. Which of the following parameters is LEAST important in determining adequate cardiopulmonary bypass pump flow and pressure during the aortic cross-clamp phase of a coronary artery bypass grafting procedure?

A. Hematocrit
B. Severity of coronary artery stenoses
C. Temperature
D. Patient size
E. Mixed venous saturation

64. During cardiopulmonary bypass (CPB) for an atrial septal defect repair in a 46-year-old, the mixed venous oxygen saturation monitor is reading 50%. Which of the following is the LEAST likely explanation for this?

A. Pump flows too low for patient temperature
B. Left-to-right shunting through atrial septal defect
C. Inadequate hemoglobin level
D. Malfunction of membrane oxygenator
E. None of the above

65. During routine cardiopulmonary bypass (CPB) during coronary artery bypass grafting on a 63-year-old, the perfusionist suddenly reports massive gas embolism in the arterial cannula tubing. Which of the following maneuvers should be instituted immediately?

A. Cessation of cardiopulmonary bypass
B. Steep Trendelenburg positioning
C. Initiation of retrograde superior vena cava perfusion
D. Deepening of hypothermia
E. All of the above

66. Which of the following statements regarding the effects of aging on the cardiovascular system is FALSE?

A. Myocardial contractility is uncompromised under submaximal demand.
B. Resting cardiac index is decreased.
C. The myocardium atrophies with age.
D. The ventricle undergoes relaxation late in diastole.
E. Passive ventricular filling is reduced.

67. Acute onset of which of the following conditions would be expected to have the LEAST impact on the central venous pressure (CVP) or CVP waveform?

A. Junctional rhythm
B. Atrial fibrillation
C. Right ventricular systolic dysfunction
D. Tricuspid regurgitation
E. Atrial pacing

68. Which of the following statements regarding central venous pressure (CVP) tracings is true?

A. The right atrial "a" wave occurs before the left atrial a wave seen on a pulmonary capillary wedge tracing.
B. The "x" descent is caused by rapid atrial filling after opening of the tricuspid valve.
C. The "c" wave is caused by passive atrial filling.
D. The "v" wave is caused by downward displacement of the tricuspid annulus with the onset of ventricular systole.
E. The "y" descent represents ventricular filling with the onset of diastole.

69. Which of the following statements regarding a DDD pacemaker is true?

A. The pacemaker has both triggered and inhibited responses to sensing.
B. This is the preferred pacemaker mode for avoiding issues with electrocautery interference.
C. Placing a magnet on this pacemaker will likely change its mode to VOO.
D. Rate responsiveness feature is not compatible with this pacemaker mode.
E. This mode should not be used with a junctional rhythm.

70. Which of the following statements regarding thoracic impedance and defibrillation is INCORRECT?

A. Increased pressure on the defibrillator paddles against the skin decreases impedance.
B. Impedance increases after prior defibrillation attempts.
C. Impedance is lower for internal defibrillation paddles compared to external paddles.
D. Impedance is increased during inspiration compared to end-expiration.
E. None of the above

71. Which of the following are NOT determinants of coronary blood flow?

A. Aortic diastolic blood pressure
B. Aortic valve area
C. Myocardial metabolism
D. Heart rate
E. Left ventricular end-diastolic pressure

72. Which of the following statements regarding dominance in coronary circulation is correct?

A. In a right-dominant system the right coronary artery supplies blood to the sinoatrial node.
B. In a right-dominant system the right coronary artery supplies blood to the circumflex artery.
C. In a right-dominant system the right coronary artery supplies blood to the posterior descending artery.
D. In a right-dominant system the right coronary artery supplies blood to the left atrium.
E. Most patients have a balanced supply of both the right and left coronary arteries.

73. Which of the following characteristics of treatment with doxorubicin is mostly associated with the development of heart failure?

A. Time of last treatment
B. Time between each treatment
C. Number of treatments
D. Total dosage
E. Combination with irradiation

74. Which of the following best describes the impact of volatile and intravenous anesthetics on myocardial ion channels?

A. Activate sodium ion channels
B. Inhibit sodium ion channels
C. Activate calcium ion channels
D. Inhibit calcium ion channels
E. Inhibit potassium ion channels

75. Which of the following statements regarding asynchronous pacing is true?

A. Asynchronous pacing should be avoided to prevent ventricular defibrillation.
B. Asynchronous pacing is preferred when bipolar electrocautery is used.
C. In asynchronous pacing, the PR interval changes continuously.
D. Asynchronous pacing requires both atrial and ventricular pacing leads.
E. None of the above

76. Which of the following statements regarding the ECG changes seen with myocardial ischemia and/or infarction is INCORRECT?

A. Subendocardial ischemia may manifest as QT prolongation.
B. T-wave inversion results from reversal of the normal direction of repolarization.
C. Injury and ischemia result in different ECG findings.
D. In left bundle branch block, ST-segment changes cannot be used to help diagnose ischemia.
E. Persistent ST elevation after acute myocardial infarction may be due to a ventricular aneurysm.

77. Which of the following statements regarding the ECG shown in Figure 9.6 is true?

A. Most likely results from disease of the AV node
B. Placement of a permanent pacemaker is likely indicated.
C. Should be treated with amiodarone by IV push
D. Should be treated by synchronized cardioversion if the patient is hemodynamically unstable
E. Frequently seen under anesthesia in otherwise healthy patients

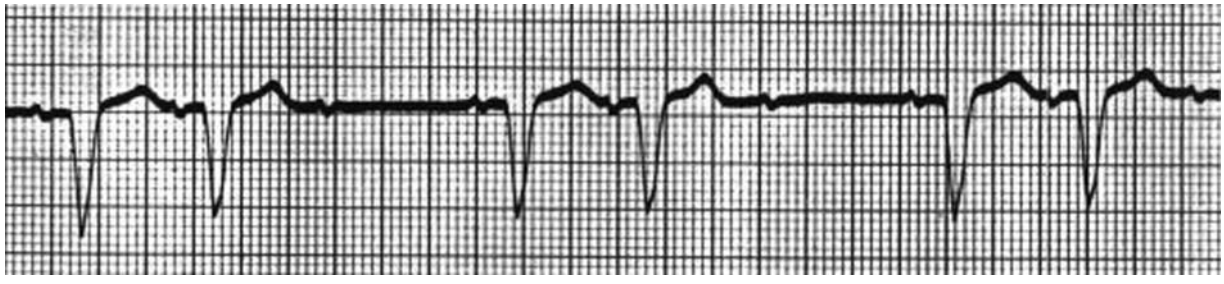


Figure 9.6 QUESTION 77

78. Which of the following ECG findings is consistent with left atrial enlargement?

A. Increased P-wave amplitude
B. Increased P-wave duration
C. Increased P-wave amplitude and duration
D. Terminal P negativity in lead I
E. All of the above

79. A 77-year-old patient status post aortic valve replacement has a suspected air embolus in the right coronary artery. Which of the following ECG changes would be most consistent with this diagnosis?

A. 2-mm ST elevation in leads V_5 and V_6
B. 3-mm ST elevations in leads II, III, and aV_F
C. T-wave inversions in leads I, aV_L, and V_5
D. 1-mm ST depressions in leads V_5 and V_6
E. 2-mm ST depressions in leads I and V_5

80. A healthy 22-year-old undergoing knee arthroscopy develops a junctional rhythm at 70 bpm. Which of the following statements regarding this event is true?

A. This rhythm is likely caused by slowed SA node spontaneous depolarization.
B. This rhythm should be treated with atropine 1 mg by IV bolus.
C. This rhythm will likely lead to hemodynamic instability.
D. This rhythm represents a significant functional abnormality.
E. This rhythm is frequently converted to sinus rhythm by beta-blocker administration.

81. Which of the following statements regarding the ECG of a patient with a normally functioning DDD pacemaker is correct?

A. Atrial and ventricular pacing spikes should always be visible.
B. There should not be any native P waves visible on the ECG.
C. V pacing spikes should be followed by a narrow QRS complex.
D. During complete AV pacing, the PR interval should be the same.
E. The heart rate seen on ECG will match the preprogrammed rate.

82. Which of the following is NOT a likely cause of pulseless electrical activity (PEA)?

A. Ventricular fibrillation
B. Cardiac tamponade
C. Tension pneumothorax
D. Digitalis overdose
E. Pulmonary embolus

83. Five minutes after placement of a right subclavian introducer and pulmonary artery catheter a patient is noted to be pulseless with a heart rhythm of sinus tachycardia at 130 bpm. Which of the following statements regarding management of this patient is most reasonable?

A. Defibrillation should be performed immediately and repeated at two different energy levels.
B. Atropine 1 mg IV should be immediately administered.
C. Epinephrine 1 mg IV should be immediately administered and right-sided pleural decompression or pericardial decompression should be considered.
D. At least 2 units of packed red blood cells should be transfused.
E. All of the above

84. For which of the following conditions is the administration of antibiotics before a dental procedure for endocarditis prevention NOT recommended?

A. Mitral valve prolapse
B. Presence of prosthetic heart valves
C. Status post cardiac transplantation with aortic stenosis
D. Two months after placement of an atrial septal defect closure device
E. None of the above

85. Which of the following treatment options is appropriate for management of obstructive cardiomyopathy?

A. Dobutamine
B. Afterload reduction
C. Fluid bolus
D. Nitroglycerin
E. Phosphodiesterase inhibitors

86. Which of the following can lead to worsened ventricular function in obstructive cardiomyopathy?

A. Mitral regurgitation
B. Hypertrophy of the left ventricle
C. Aortic stenosis
D. Venturi effect
E. All of the above

87. Which of the following coagulation factors is NOT affected by enoxaparin?

A. Antithrombin III
B. Factor Xa
C. Thrombin
D. Factor IXa
E. Factor VIIa

CHAPTER 9 ANSWERS

1. ANSWER: B

Cardiac output is usually decreased in the setting of the placement of an infrarenal aortic cross-clamp. Reductions in cardiac output in the range of 9% to 33% have been described.

The most consistent ***hemodynamic response to cross-clamping the aorta*** at any level is arterial hypertension. This increase in blood pressure is due to the sudden increase in impedance to blood flow through the aorta. This can also result in an increase in systolic ventricular wall tension as well as afterload. The hemodynamic response generally consists of increases in arterial pressure (7% to 10%) and systemic vascular resistance (20% to 32%) with no significant changes in heart rate. With infrarenal aortic cross-clamping, redistribution of blood volume can affect preload and can also depend on coronary circulation. Preload can be dampened due to blood-volume shifts below the clamp to above the clamp. Reports found that patients with severe ischemic heart disease responded to infrarenal aortic cross-clamping with significantly increased central venous (35%) and pulmonary capillary (50%) pressures, whereas patients without coronary artery disease had decreased filling pressures.

KEY FACTS: HEMODYNAMIC CHANGES DURING AORTIC CROSS-CLAMPING

↑ Arterial blood pressure
↑ Segmental wall motion abnormalities
↑ Left ventricular wall tension
↓ Ejection fraction
↓ Cardiac output
↓ Renal blood flow
↑ or ↓ Pulmonary artery occlusion pressure
↑ Central venous pressure
↑ Coronary blood flow

ADDITIONAL READINGS

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Roizen MF, Beaupre PN, Alpert RA, et al. Monitoring with two-dimensional transesophageal echocardiography. Comparison of myocardial function in patients undergoing supraceliac, suprarenal-infraceliac, or infrarenal aortic occlusion. *J Vasc Surg*. 1984;1:300–305.

2. ANSWER: B

The partial pressure of CO_2 in any solution decreases as temperature decreases. Thus, ***the $Paco_2$ of blood decreases as it cools, resulting in an increase in the pH of blood***. In pH-stat blood gas management, the aim is to maintain the pH of blood at 7.4 regardless of temperature. As arterial blood gases are processed at 37 degrees Celsius in the lab, the temperature of blood must be reported so that temperature-corrected results (based on available normograms) can be generated. To maintain pH at 7.4, $Paco_2$ must be increased be increased (e.g., by adding CO_2 to the oxygenator). In α-stat management, the central strategy is maintenance of the electrochemical neutrality of the imidazole buffering system, which occurs naturally as changes in temperature occur. Therefore, in α-stat management, the temperature of the patient is neither reported to the lab nor corrected.

Both pH-stat and α-stat regulation have differing impact on blood flow to the brain and other organs. As temperature decreases, the increased $Paco_2$ with pH-stat management relative to α-stat management leads to increased cerebral blood flow.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:347.

3. ANSWER: B

The poor or absent perfusion and oxygen delivery of cardiac arrest quickly causes a shift in physiologic mechanisms from aerobic to anaerobic glycolysis. This leads to profound metabolic acidosis due to both the generation of significant amounts of lactic acid and decreased carbon dioxide transport from the tissues to the lungs. In combination with the lungs failing to eliminate carbon dioxide, a severe ***combined metabolic and respiratory acidosis results during cardiopulmonary resuscitation (CPR)***. Even if chest compressions are performed perfectly, perfusion pressure still will not be adequate to prevent metabolic acidosis after prolonged cardiopulmonary resuscitation.

Obtaining an arterial blood gas analysis during CPR can accurately measure the subsequent acid-base status. After successful intubation and support of ventilation, hyperventilation is commonly encountered. This can occur unwittingly or as a means to attempt to re-normalize pH and/or to reduce the hyperkalemia that may occur with metabolic acidemia.

ADDITIONAL READINGS

Hennemann PL, Gruber JE, Marx JA. Development of acidosis in human beings during closed-chest and open-chest CPR. *Ann Emerg Med*. 1988;17:672–675.

Von Planta M, Bar-Joseph G, Wiklund L, et al. Pathophysiologic and therapeutic implications of acid-base changes during CPR. *Ann Emerg Med*. 1993;22:404–410.
Von Planta M, Weil MH, Gazmuri RJ, et al. Myocardial acidosis associated with CO_2 production during cardiac arrest and resuscitation. *Circulation*. 1989;80:684–692.

4. ANSWER: D

The distal end of a pulmonary artery catheter is typically directed into a branch of the right pulmonary artery. This is due to the orientation of the natural curvature of the catheter relative to the path of the catheter through the right heart. During diastole, when the balloon on the tip of the pulmonary artery catheter is inflated, a fluid chamber connection from the tip of the pulmonary artery catheter to the left ventricle is established. This is referred to as the pulmonary artery occlusion pressure or "wedge" pressure. This pressure is not equal to but is related to the pulmonary artery diastolic pressure, which is measured when the balloon is deflated.

Any pathology that occurs between the tip of the catheter and the left ventricle will affect and degrade the ***relationship between pulmonary artery diastolic pressure and left ventricular end-diastolic pressure***. Pulmonary artery hypertension from changes in pulmonary vascular resistance, whether from reversible or irreversible causes, will have a negative impact on this relationship. This is due to concurrent pulmonary venous hypertension. The same is true of mitral valve stenosis. In a sense, these lesions prevent a clear "view" of the left ventricle from the pulmonary artery. Pulmonic stenosis, however, occurs proximal to this fluid chamber and will not affect this "view."

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia.* Philadelphia, PA: Elsevier Saunders; 2008: 707.
DiNardo JA, Zvara DA. Monitoring. In: *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd; 2008:54.

5. ANSWER: B

The goal of advanced cardiac life support (ACLS) is to use advanced skills to resuscitate a patient from circulatory dysfunction when basic life support (BLS) support is inadequate. This may include the use of adjuncts to assist in the resuscitation of ventilation and circulation in the patient. ECG monitoring is useful for recognizing life-threatening arrhythmias that may be in need of defibrillation. In adults, one of the most common arrhythmias that leads to cardiac arrest is *ventricular fibrillation*.

Electrical defibrillation is the only consistent therapy for ventricular fibrillation. Factors that contribute to the success of resuscitation in patients in ventricular fibrillation include the duration of fibrillation, the amount of fibrillation time before defibrillation occurs, underlying disease, and metabolic status. Current ACLS guidelines recommend that defibrillation should occur immediately and should not be postponed for any other therapy.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 58.

6. ANSWER: D

The activated clotting time (ACT) is a point-of-care test most commonly used to monitor for heparin effect during cardiovascular surgery. The test consists of adding whole blood to a test tube most often containing either diatomaceous earth (celite) or kaolin. These particulate activators induce thrombus formation, which is timed. Normal ACT values range between 80 and 120 seconds.

The ACT test is useful in that it uses whole blood, can be performed easily at the point of care, and provides results relatively quickly. It is important to realize, however, that ACT is a nonspecific test of coagulation. That is to say, ***a prolonged ACT can be caused by almost anything that decreases coagulation, not just heparin***. While ACT is most affected by the state of the intrinsic coagulation system, the extrinsic system and platelet function also play a role. Therefore, heparin, warfarin, platelet dysfunction, protamine excess, and hemodilution would all be expected to increase ACT. Mild hyperthermia would not be expected to increase ACT, while hypothermia would.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:87.
Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010:1913.

7. ANSWER: B

Aortic regurgitation can be caused by processes that affect the aortic valve leaflets (e.g., rheumatic fever, infective endocarditis, congenital bicuspid aortic valve) or the aortic root and valve-supporting structures (aortic dissection, systemic hypertension, cystic medial necrosis, Marfan syndrome).

With aortic regurgitant lesions, a slightly higher (yet still normal) heart rate range is sought. This is to

compensate for the heart's inability to maintain sufficient forward stroke volume, subsequently placing a greater volume load on the left ventricle. In response, a rise in sympathetic tone increases heart rate and contractility, resulting in a proportional decrease in diastolic time when the regurgitation is occurring. Reduction of diastolic blood pressure in an attempt to decrease regurgitation is also indicated. An intra-aortic balloon pump, which is most often used to increase diastolic blood pressure to improve myocardial oxygen supply and/or to reduce afterload, inflates during diastole. This inflation would increase the severity of aortic regurgitation and likely worsen the patient's status.

ADDITIONAL READINGS

Hensley FA Jr., Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Williams; 2008:323.

8. ANSWER: D

Long-acting beta blockers are generally avoided because of the unopposed alpha-adrenergic receptor-mediated coronary vasoconstriction. However, the use of short-acting beta blockers such as esmolol is NOT contraindicated. Because of its short duration of action, esmolol can be used for the symptomatic treatment of cocaine-induced chest pain. Alpha blockers, nitroglycerin, and labetalol have also been used effectively for symptomatic treatment.

Pharmacologically, cocaine produces prolonged adrenergic stimulation and blocks the presynaptic reuptake of sympathomimetic neurotransmitters, including norepinephrine, serotonin, and dopamine. This inhibition ultimately causes sympathetic cardiovascular effects that result in hypertension, tachycardia, and coronary artery vasospasm—symptoms that can be clinically diagnosed as a myocardial ischemic event. Aortic dissections and ruptured aortic aneurysm have also been reported with acute abuse.

ADDITIONAL READINGS

Kloner RA, Hale S, Alker K, Rezkalla S. The effects of acute and chronic cocaine use on the heart. *Circulation*. 1992;85:407–419.

Lange RA, Cigarroa RG, Flores ED, et al. Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. *Ann Intern Med*. 1990;112(12):897–903.

9. ANSWER: E

Many patients with moderate and severe mitral stenosis develop atrial fibrillation in response to the severe left atrial dilatation that occurs over time. In these patients, ***control of heart rate is dependent on adequate control of the ventricular response rate to the fibrillating atrium***. Medications such as amiodarone, beta blockers, calcium channel blockers, and digoxin are used to control the ventricular response rate by slowing conduction through the atrioventricular node.

Mitral stenosis impedes filling of the left ventricle, making it a preload-dependent lesion. Any process that also impairs filling—particularly if that process occurs acutely—can lead to significant hemodynamic impairment. The onset of rapid atrial fibrillation is an example of an acute insult with two detrimental effects: the loss of effective atrial contractions and their contribution to ventricular filling, and a proportional decrease in diastolic filling time due to increased heart rate. As with any rhythm disturbances that produce hemodynamic instability, rapid cardioversion or defibrillation is indicated.

When cardioverting atrial fibrillation, it is important to synchronize with the QRS complex. This avoids the delivery of an external electrical impulse during repolarization (R-on-T phenomenon), which can induce an unstable ventricular dysrhythmia.

ADDITIONAL READINGS

Fuster V, Ryden LE, Cannom, DS, et al. ACC/AHA/ESC Practice Guidelines. 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for management of patients with atrial fibrillation. *Circulation*. 2011;123:169–367.

10. ANSWER: D

The ***management of acute left ventricular failure*** can represent an extreme challenge. Possible reversible causes, most notably myocardial ischemia, should be directly addressed whenever possible. When such failure is not readily reversible, support can be given through both drug and device therapies. Any available inotrope can be used to improve contractility. Each inotrope has a unique side-effect profile that may make it a better or worse choice in certain situations. Afterload reduction through the use of arteriolar vasodilators and/or via the deflation of an intra-aortic balloon pump is often helpful. A left ventricular assist device (LVAD), which performs the left ventricle's pumping function, may be used when other therapies are inadequate. LVADs are used optimally in situations where the left ventricle is expected to have some recovery of function or as a bridge to possible transplant.

ECMO is used when adequate oxygenation of the blood through the native lung tissue is compromised reversibly (e.g., severe acute respiratory distress syndrome (ARDS)). This therapy has proven to have benefit in the pediatric population more so than in adults.

ADDITIONAL READINGS

Mebazaa A, Pitsis AA, Rudiger A, et. Clinical review: practical recommendations on the management of perioperative heart failure in cardiac surgery. *Crit Care*. 2010;14:201.

11. ANSWER: B

The ideal ***hemodynamic management for a patient with acute MR*** is to promote vasodilation and mild tachycardia. This allows for reduction of afterload and effective forward flow of blood from the left ventricle to the aorta versus regurgitation from the left ventricle to the left atrium. Acute MR can be caused by ruptured chordae tendineae from infective endocarditis and acute left ventricular dysfunction from coronary artery disease. It is important to remember that in acute MR, the left atrium has not undergone the adaptive changes that are seen in chronic MR. Acute processes including elevations in the left atrium and pulmonary vascular pressures can be symptomatically observed with acute pulmonary congestion.

KEY FACTS: HEMODYNAMIC GOALS OF ACUTE MITRAL REGURGITATION

Preload	Increased
Afterload	Decreased
Contractility	Decreased
Rate	Increased
Rhythm	Controlled

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010:4361.

12. ANSWER: E

The ***aging process is associated with changes in the cardiovascular system***, including the heart, blood vessels, and autonomic control. In the heart, left ventricular wall thickening occurs, while myocyte and sinus node cell numbers and the density of conduction fibers decrease. Respectively, these changes translate to increased myocardial stiffness, resulting in increased ventricular filling pressures, decreased contractility, and decreased beta-adrenergic sensitivity. Advanced age also decreases the elasticity of the vasculature due to the gradual deterioration of elastin and collagen matrix in the vascular wall. With an increase in medial and intimal thickness, subsequent increases in the diameter and stiffness of large elastic arteries are observed. Clinically, this translates into elevated mean arterial and pulse pressures.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010:5410–5411.

13. ANSWER: A

Antegrade coronary blood flow occurs exclusively during the relaxation phase of chest compression. Studies show that antegrade coronary blood flow correlated only with a positive "diastolic" or relaxation phase. This flow is a result of the pressure gradient between the aorta and the right atrium at the time of relaxation. In vivo studies with an intracoronary Doppler flow catheter during chest compressions showed that retrograde coronary artery blood flow (flow from the left main coronary artery back into the ascending aorta) occurred during the compression phase, regardless of differing pressure gradients in the heart. Specifically, no antegrade coronary blood flow occurred even when aortic pressures exceeded those in the right atrium during compressions.

ADDITIONAL READINGS

Field JM, Bresler MJ, Mattu A, et al. The Textbook of Emergency Cardiovascular Care and CPR, Lippincott Williams and Wilkins, 2008: 155.

14. ANSWER: D

Scopolamine is a centrally acting anticholinergic and is effective in ameliorating motion sickness. Preoperative placement of a transdermal patch has been shown to reduce the incidence of severe postoperative nausea and vomiting in outpatient gynecologic laparoscopic procedures. Adverse effects of transdermal scopolamine include a high incidence (95% vs. 45% with placebo) of dry mouth, somnolence, mydriasis, and dizziness. However, the scopolamine patch has not been demonstrated to significantly increase the QTc interval.

Antiemetics, including butyrophenone neuroleptic drugs (droperidol and haloperidol), 5-HT3 receptor antagonists (ondansetron, granisetron, and dolasetron), phenothiazines (chlorpromazine and promethazine), and metoclopramide are known to prolong the QTc interval. In most cases, prolongation of the QTc interval is dose-related.

Table 9.1 ANTIPLATELET AGENTS

DRUG	ROUTE	PLASMA HALF-LIFE	MECHANISM	STOP BEFORE PROCEDURE	PROLONGATION OF PT/APTT
Aspirin	Oral	20 min	COX inhibitor	7 days	No/No
Dipyridamole	Oral	40 min	Adenosine reuptake inhibitor	24 hr	No/No
Clopidogrel	Oral	7 hr	ADP receptor inhibitor	5 days	No/No
Ticlodipine	Oral	4 days	ADP receptor inhibitor	10 days	No/No
Abciximab	IV	30 min	GIIB/IIIA inhibitor	72 hr	No/No

ADAPTED from Roberts HR, Monroe DM, Escobar MA. Current concepts of hemostasis: Implications for therapy. *Anesthesiology*. 2004;100:722–730.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010:2559, 2598, 5778–5779.

Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med*. 2004;350:1013–1022.

15. ANSWER: D

Clopidogrel and ticlodipine are antiplatelet drugs that inhibit platelet aggregation at the ADP receptor site (Table 9.1). Limiting platelet activation and aggregation inhibits thrombus formation; thus, antiplatelet drugs are administered to patients who are at high risk for thrombus formation. To review, platelets can be activated most commonly by endothelial cell von Willebrand factor, collagen after tissue injury, thrombin, and ADP activation of platelet surface ADP receptors. These in turn activate coagulation pathways that are the sites of action of the currently available antiplatelet agents. Classes of antiplatelet agents are as follows:

1. Cyclooxygenase inhibitors
2. Glycoprotein IIb/IIIa inhibitors
3. ADP receptor inhibitors
4. Adenosine reuptake inhibitors

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 56.

16. ANSWER: B

Bradycardia should be avoided in patients with aortic insufficiency. Low heart rate means more diastolic time per beat, which increases the likelihood of backflow from the aorta to the left ventricle during diastole. This results in ventricular distention and subsequent elevations in left atrial pressure. Conversely, diastolic time is decreased during ***tachycardia***. ***Ideally, patients with aortic insufficiency should have a full heart and be slightly tachycardic and vasodilated***. Vasodilation reduces the resistance to forward flow, thereby decreasing the potential for backflow into the left ventricle.

KEY FACTS: AORTIC INSUFFICIENCY—HEMODYNAMIC GOALS

Preload	Increased
Afterload	Decreased
Rate	Increased
Rhythm	Controlled

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 31.

17. ANSWER: D

Connective tissue diseases such as Marfan, Ehlers-Danlos syndrome, pseudoxanthoma elasticum, and inflammatory diseases of the aorta such as syphilis, rheumatoid disease, ankylosing spondylitis, and Takayasu aortitis, may produce chronic aortic regurgitation. The aforementioned connective tissue diseases can progressively cause aortic root dilation, dilating the valve annulus, causing poor leaflet apposition, and resulting in regurgitation secondary to pathologic valve remodeling. Patients with Marfan syndrome have a mutated fibrillin gene and commonly have congenital bicuspid aortic valves, highly associated with aortic regurgitation. Inflammatory diseases of the

aorta produce damage to the leaflet and its support structures, resulting in regurgitation due to poor leaflet and valve apposition. Primary Sjögren syndrome has an autoimmune etiology. However, secondary Sjögren syndrome is associated with connective tissue disease and therefore may be associated with aortic regurgitation.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:143.

Vassiliou VA, Moyssakis I, Boki KA, Moutsopoulos HM. Is the heart affected in primary Sjögren's syndrome? An echocardiographic study. *Clin Exp Rheumatol.* 2008;26(1):109–112.

18. ANSWER: B

Patients with severe aortic stenosis are very susceptible to ischemia, which is difficult to detect on an ECG due to baseline left ventricular (LV) pathology. Severe aortic stenosis is associated with:

1. Increased LV size
2. Increased LV strain
3. Increased filling pressures
4. Increased end-diastolic pressure
5. Decreased LV compliance

It is important to optimize coronary perfusion pressure by maintaining elevated LV filling pressures, volume, and/or preload. The increased LV end-diastolic pressure secondary to the reduced LV compliance requires adequate diastolic blood pressures to maintain coronary perfusion. Reducing diastolic blood pressure to 40 mm Hg with nitroprusside in a hypertensive patient will decrease coronary perfusion, possibly compromising adequate myocardial oxygen supply. Furthermore, in severe aortic stenosis, afterload is determined by the stenotic valve and not by systemic vascular resistance (i.e., the arterioles). Therefore, vasodilation with nitroprusside would not be expected to significantly affect afterload. Nitroglycerin can be useful in this situation, but one must remember that minimal reductions in ventricular volume are required; therefore, very low doses of nitroglycerin should be used and they should be carefully titrated to effect. The rest of the intervention choices would be expected to improve myocardial oxygen supply/demand matching. Factors responsible for the myocardial oxygen supply/demand imbalance seen in aortic stenosis are listed in Table 9.2.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:137.

Table 9.2 MYOCARDIAL OXYGEN SUPPLY AND DEMAND—AORTIC STENOSIS

INCREASES IN MYOCARDIAL OXYGEN CONSUMPTION	DECREASES IN MYOCARDIAL OXYGEN DELIVERY
• Mass of myocardium • Left ventricular pressure work • Prolonged ejection phase	• Elevated left ventricular end-diastolic pressure secondary to decreased ventricular compliance • Decreased aortic diastolic pressure • Decreased diastolic coronary perfusion time • Subendocardial vessel compression • High LV systolic:aortic systolic pressure gradient

ADAPTED from DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008: Table 5.2, Myocardial Oxygen Supply and Demand in Aortic Stenosis.

19. ANSWER: D

Spinal anesthesia can produce adverse cardiovascular effects by the mechanism of blocking sympathetic efferents; specifically, blood pressure (hypotension) and/or heart rate (bradycardia) can be altered significantly. These cardiovascular derangements are related to the extent of sympathetic blockade and are the result of both arterial and venodilation. Block height may also increase the risk of cardiovascular changes.

Spinal anesthesia-induced hypotension is a significant concern for a patient with severe aortic stenosis due to its reductions in afterload and cardiac output. Although significant bradycardia has been reported in only 10% to 15% of patients, increased block height has been reported to add to this incidence. A "high spinal" can block sympathetic cardiac accelerator fibers located in the T1–4 spinal segments, resulting in unopposed vagal tone. Loss of venous return due to spinal-induced venodilation can also elicit the Bainbridge reflex, whereby a reduction in atrial stretch causes a decrease in heart rate.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:342, 945–946.

20. ANSWER: B

The central problem in severe aortic stenosis is a noncompliant left ventricular (LV) cavity that is difficult to fill. This noncompliance is the result of LV hypertrophy that develops in response to increased afterload at the stenotic valve. Anything that impedes filling of the LV can lead to

hemodynamic instability if the condition is severe and persists for a significant duration.

With peritoneal insufflation during laparoscopy, splanchnic blood is displaced into the systemic venous circulation, leading to increased preload and cardiac output. Therefore, ***insufflation should improve hemodynamics in a patient with aortic stenosis***. However, over-insuffl ation of the peritoneal cavity can reduce venous return and in that way worsen LV fi lling, leading to instability.

Sinus rhythm is important in aortic stenosis. In the normal LV of a person at rest, left atrial contraction contributes only about 10% of diastolic filling. In comparison, the noncompliant hypertrophied LV in aortic stenosis has a greater dependence on left atrial contraction to fill. Therefore, loss of atrial contraction from a supraventricular tachycardia or junctional rhythm may lead to significant compromise in a patient with aortic stenosis.

Significant bradycardia reduces cardiac output (CO) and diastolic blood pressure and can affect myocardial oxygen supply. The increased LV muscle mass and end-diastolic pressures make these patients prone to myocardial ischemia even in the absence of obstructive coronary artery disease.

Tachycardia proportionally limits diastolic time and thus decreases ventricular filling. In addition, tachycardia increases myocardial oxygen demand in a heart that teeters on the edge of meeting its demand while at slower heart rates.

Over-insufflation of the peritoneal cavity can reduce venous return and in that way worsen LV filling, leading to instability.

KEY FACTS: AORTIC STENOSIS—HEMODYNAMIC GOALS

Preload	Full
Afterload	Maintain coronary perfusion gradient.
Contractility	Inotropic support if persistent hypotension
Rate	Avoid bradycardia (↓CO) and tachycardia (ischemia).
Rhythm	Sinus

21. ANSWER: D

After aortic valve replacement, the obstruction to forward flow is improved drastically. This acute decrease in afterload allows for an increase in LV stroke volume, resulting in a decreased LV end-systolic volume (LVESV). Compliance characteristics in the LV are usually found unchanged up to a year postoperatively due to the delay in myocardial remodeling after aortic valve replacement. It is important to maintain high aortic diastolic perfusion pressures to adequately perfuse the subendocardial tissue at this time. Slower heart rates are better tolerated because of the dramatic reduction in afterload with surgery.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:142–143.

22. ANSWER: E

The crucial dictum to remember in digoxin dosing is that it characteristically has a very low therapeutic index; at toxic levels, symptoms such as anorexia, nausea, and confusion can be observed. More importantly, at these levels conduction disturbances such as sinus bradycardia, junctional tachycardia, premature atrial and/or ventricular contractions, exit blocks, and ventricular tachycardia and fibrillation may be identified on ECG. Metabolic abnormalities can lower the threshold at which these disturbances may occur. Further, interactions with other drugs can affect the metabolism of digoxin. Quinidine, cyclosporine, verapamil, and rifampin are known culprits in increasing the risk of ***digoxin toxicity***. Amiodarone, although known to prevent dysrhythmias, may increase digoxin levels by up to 100% and must be used cautiously in patients who are concurrently prescribed digoxin.

23. ANSWER: A

Aortic stenosis develops chronically due to pressure overload in the left ventricle (LV). In reducing the valvular area and maintaining cardiac output, the gradient is tremendously affected. As a consequence, the LV must generate higher systolic pressures in order to maintain a relatively normal aortic systolic pressure. As the disease progresses, LV afterload increases (pressure) and is compensated by increasing wall thickness, as calculated in the law of Laplace: Myocardial stress = ventricular pressure × radius/(2× wall thickness). In other words, the degree of myocardial thickening occurs as there are increased pressure demands on the ventricle. Figure A demonstrates decreased compliance in the left ventricle as a result of compensatory hypertrophy. ***Thus, patients with aortic stenosis will have higher LV pressures for any given volume in the LV***.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:135–144..

ADDITIONAL READINGS

Longnecker DE, Brown DL, Newman MF, Zapol WM, eds. *Anesthesiology*. New York, NY: McGraw Hill Medical; 2008: Chapter 43.

24. ANSWER: C

Blood pressure can be directly measured via the radial, brachial, axillary, femoral, and dorsalis pedis arteries. The most common site for direct arterial cannulation is the radial artery due to its supporting collateral blood supply from the ulnar artery. The ***Allen's test*** is recommended before cannulation to test the patency of flow from either the radial or ulnar arteries. It can be performed by simultaneously compressing both radial and ulnar arteries for a brief period of time and then releasing pressure on each respective artery to determine if blood flow is compromised at either artery. However, the clinical predictability of the Allen's test is controversial.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:703.

Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: a comprehensive review of recent anatomic and physiologic investigations. *Anesth Analg*. 2009;109(6):1763–1081.

25. ANSWER: A

Direct blood pressure monitoring with an arterial cannula has the advantage of acquiring continuous blood pressure tracings and arterial blood samples. However, it is important to consider the potential errors that can be associated with the catheter-transducer-amplification system. ***The level of the transducer to a reference "zero" point has an impact on pressure measurement***. By convention, the transducer is placed at the level of the right atrium and the reference point for zero is set there. In some situations (e.g., a sitting intracranial procedure), the reference point for zero may be at the level of the auditory meatus to gauge cerebral perfusion pressure more accurately. If the transducer is lowered below the set zero reference point, the blood pressure reading will be an overestimate of actual pressure. The degree of overestimation depends on the distance (in mm Hg) below the reference point the transducer sits. The opposite occurs when the transducer is placed above the reference zero point.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 27, 703.

26. ANSWER: C

Ejection of blood from the left ventricle into the aorta during systole is translated into a systemic arterial pressure waveform that follows the R wave on the ECG. More specifically, ***the R-wave upstroke, peak, and decline correspond to pressure changes of the left ventricle ejecting during systole***.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010:1282.

27. ANSWER: B

Anesthetic management for patients with a dynamic left ventricular outflow tract (LVOT) obstruction is aimed at maintaining a ventricular state that maximizes the size of the LVOT during systole. This includes keeping adequate and abundant preload, slower heart rates that allow for appropriate LV filling, and decreased contractility to keep the interventricular septum away from the LVOT during systole. Atrial pacing to ensure an atrial contraction via transesophageal or pulmonary artery catheter pacing can benefit patients who are preload-dependent (Table 9.3).

Table 9.3 HEMODYNAMIC GOALS—HYPERTROPHIC CARDIOMYOPATHY

Preload	**Full**
Afterload	**Increased**
Contractility	**Decreased, avoid inotropes**
Rate	**Normal**
Rhythm	**Sinus, atrial pacing if required**

ADAPTED from Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Table 31–7.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:1080–1081.

28. ANSWER: D

The ***autonomic nervous system (ANS)*** consists of central and peripheral nervous systems that regulate the "autonomic" or

involuntary actions of cardiac muscle, smooth muscle, glands, and viscera below the conscious level. Commonly known as the "fight-or-flight" response, the ANS is also responsible for organizing changes in the somatic motor and sensory responses in reaction to emotional changes.

The ANS can be broken down into the sympathetic and parasympathetic nervous systems. The center of the sympathetic nervous system is the hypothalamus. Preganglionic neurons exit the spinal cord in the thoracolumbar levels exclusively and synapse with postganglionic neurons in the sympathetic chains situated along both sides of the spine. The exception is in the adrenal medulla, where this synapse also occurs. The parasympathetic nervous system, in contrast, is a craniosacral system.

The ***preganglionic*** neurotransmitter of both the sympathetic and parasympathetic nervous systems is acetylcholine, which acts at nicotinic receptors. The ***postganglionic*** neurotransmitter of the parasympathetic system is acetylcholine, which acts at muscarinic receptors. The neurotransmitter of the postganglionic sympathetic system is norepinephrine except in the sweat glands, where it is acetylcholine acting at muscarinic receptors.

Although the ANS is usually thought of as an efferent system, afferents are abundant.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 15, 327–329.

29. ANSWER: B

The baroreceptor reflex is the main reflex responsible for regulating arterial blood pressure through a negative-feedback loop. The pathophysiology in activation of this reflex is based on the body's autoregulatory system of a preset blood pressure. Stretch receptors located in the carotid sinus and aortic arch increase their firing rate as the vessels expand. In response, the parasympathetic system is activated to decrease heart rate and myocardial contractility. The onset of hypotension (i.e., a decrease in stretching of the vessels) elicits the reverse effect. In patients with chronic hypertension, the autoregulatory set point is usually increased to prevent constant activation of the negative-feedback loop. Of the volatile anesthetics, ***halothane is the most potent inhibitor of the barocepter reflex, namely the heart rate component***.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL, eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 16.

30. ANSWER: E

Beta-adrenergic stimulation is activated by circulating catecholamines released either by the adrenal glands or nerve endings on the myocardium to stimulate cardiac contractility. Both $beta_1$ and $beta_2$ adrenergic receptors are activated in response to stimulation by catecholamines. Both $beta_1$ and $beta_2$ receptors are present in the heart and contribute to increased contractility induced by the catecholamine stimulation. However, in vascular muscle, beta-adrenergic stimulation induces relaxation, and hence vasodilation.

Individually, $beta_1$ receptor stimulation increases plasma renin production and aqueous humor production, whereas $beta_2$ receptor stimulation relaxes smooth muscle, causing bronchodilation, and increases insulin secretion.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008: 132, 222–223.

31. ANSWER: D

Blood pressure is a hydrostatic pressure and is influenced by gravitational force. In general, the right atrium is selected as the zero reference point for pressure measurements. ***Site of measurement above or below this level will affect the pressure measurement relative to this reference point***. Every centimeter difference in height results in a 0.7-mm Hg difference in hydrostatic pressure. Since the left arm is 20 cm higher than the right arm, the pressure reading from the left arm will be 20 × 0.7 or 14 mm Hg lower than the pressure in the right arm.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 27, 703.

32. ANSWER: C

Blood pressure denotes the driving force for perfusion of tissues in the body. In a noninvasive blood pressure measurement, the systolic blood pressures correspond to the points of rapidly increasing oscillations, whereas the diastolic pressures occur during decreasing oscillations. Korotkoff originally described the ***sounds of systolic blood pressure*** as those produced during the return of blood flow through the artery when the blood pressure cuff was deflated.

ADDITIONAL READINGS

Longnecker DE, Brown DL, Newman MF, Zapol WM, eds. *Anesthesiology*. New York, NY: McGraw Hill Medical; 2008: Chapter 29.

33. ANSWER: A

Systemic vascular resistance (SVR) and cardiac output determine blood pressure. Viscosity causes resistance to flow and is a principal determinant (along with vascular tone) of SVR. ***The viscosity of blood is determined primarily by hematocrit; thus, a transfusion will increase blood viscosity and cause a rise in SVR***. Temperature changes also have an impact; as the temperature decreases, viscosity increases. Blood pressure will increase with a rise in hematocrit and blood viscosity, if there are no concomitant decreases in vascular tone, temperature, or cardiopulmonary bypass flow rates.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 16, 379.

34. ANSWER: B

Complete or third-degree heart block is reported in up to 7% of patients undergoing AVR. The atrioventricular node sits in Koch's triangle—an area enclosed by the ostium of the coronary sinus, the membranous portion of the interatrial septum (i.e., tendon of Todaro), and the septal leaflet of the tricuspid valve. This area sits near the aortic valve annulus and can be injured during aortic valve replacement and by disease processes that affect the aortic valve and aortic root. The atrioventricular node receives its blood supply from the posterior interventricular artery. This artery is supplied by the right coronary artery in patients with a right-dominant coronary circulation (approximately 85%) and by the circumflex artery in patients with a left-dominant circulation. Disruption of blood supply from this artery can cause ***infarction of the atrioventricular node and lead to permanent third-degree heart block***, requiring placement of a permanent pacemaker. Ischemia and edema related to surgery can cause temporary third-degree block. In fact, aortic valve surgery has been found to be an independent predictor for pacemaker requirement after surgery.

ADDITIONAL READINGS

Del Rizzo DF, Nishimura S, et al. Cardiac pacing following surgery for acquired heart disease. *J Cardiac Surg*. 1996;11(5):332–340.

Chang AC, Hanley FL, Wernovsky G, Wessel DL, eds. *Pediatric Cardiac Intensive Care*. Baltimore, MD: Lippincott William & Wilkins; 1998: Chapter 1, page 5.

35. ANSWER: D

The carotid sinus is the mediator of bradycardia. These baroreceptors, which receive afferents via the glossopharyngeal nerve and affect heart rate control via the vagus nerve, normally respond to blood vessel stretch stimuli to protect the brain from hypertension. ***The baroreceptor reflex also can be activated when the carotid sinus is surgically manipulated, causing abrupt bradycardia and hypotension***. Cessation of surgical stimulus usually restores heart rate. Pretreatment with atropine or epinephrine can be effective in avoiding bradycardia and can be used when cessation of surgical manipulation does not result in restoration of an adequate heart rate. When atropine is used for treatment of bradycardia, a minimum dose of 0.5 mg is advised, as lower doses actually increase vagal activity via a centrally mediated effect. Infiltration of the carotid bifurcation with a local anesthetic is a controversial intervention to preempt bradycardia. Many studies have found this technique to be ineffective and to result in both postoperative hypotension and hypertension. The carotid body is a chemoreceptor that detects oxygen partial pressure; it has no role in the bradycardic response to surgical manipulation.

ADDITIONAL READINGS

Gottlieb A, Satariano-Hayden P, et al. The effects of carotid sinus nerve blockade on hemodynamic stability after carotid endarterectomy. *J Cardiothorac Vasc Anesth*. 1997;11(1):67–71.

Tang TY, Walsh SR, et al. Carotid sinus nerve blockade to reduce blood pressure instability following carotid endarterectomy: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg*. 2007;34(3):304–311.

36. ANSWER: C

Reduction of arterial pressure is relatively common on initiation of cardiopulmonary bypass. This is most commonly due to the acute reduction of blood viscosity during hemodilution with nonblood priming solutions. Reduction in viscosity is the functional equivalent to a reduction in systemic vascular resistance.

Hematocrit is the primary determinant of blood viscosity. In a situation where blood volume is 5 L and pump prime volume is 1.5 L, there will be a 23% reduction in hematocrit when initiating bypass. Without any other changes in hemodynamic parameters, this will result in a significant reduction in mean arterial pressure.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008: Chapter 14.

37. ANSWER: B

Preload is represented by point B on the curve. If preload is increased, point B may be shifted to the right due to an increase in the length of the end-diastolic muscle fiber, which may increase the speed of muscle shortening recoil as described by Frank-Starling. A normal ***LV pressure–volume loop*** is illustrated in Figure 9.3. Segment AB represents the diastolic pressure–volume relationship. When the left atrial pressure exceeds the left ventricular pressure at point A, the mitral valve opens and ventricular filling occurs. Point B represents end diastole, when isovolumic contraction occurs. This is the point at which the left ventricular pressure exceeds the left atrial pressure and the mitral valve closes. At point C, the pressure in the left ventricle exceeds the aortic pressure and the aortic valve opens. At this point, ventricular contraction proceeds and blood is ejected through the aortic valve. At point D, the aortic pressure exceeds the left ventricular pressure and the aortic valve closes. Segment DA represents isovolumic relaxation, where the left ventricle has constant volume yet rapidly decreasing pressure.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:23–24.

38. ANSWER: E

Systolic ventricular failure occurs when the ventricle does not have the ability to contract, empty, and expel blood normally. Systolic dysfunction manifests as symptoms related to reduced cardiac output such as decreased exercise tolerance, weakness, and fatigue. Pulmonary edema results from volume overload, which causes pulmonary venous back-pressure. It is a chronic issue in systolic failure and is treated with a combination of diuretics and afterload reduction, usually with ACE inhibitors.

In contrast, diastolic heart failure impairs the ventricles' ability to fill normally. Myocardial ischemia prevents the normal reuptake of calcium into the sarcoplasmic reticulum of cardiac muscle, leading to acute increases in myocardial stiffness (i.e., noncompliance). This can cause increased filling pressures, which are transmitted to the pulmonary vasculature, resulting in the acute onset or worsening of pulmonary edema. ***The initial treatment of such patients is best aimed at balancing myocardial oxygen supply and demand***. Beta blockers like metoprolol can be beneficial in this regard. Inotropes would be expected to increase demand. Amiodarone is not indicated in this scenario.

ADDITIONAL READINGS

Aurigemma GP, Gaasch WH. Diastolic heart failure. *N Engl J Med*. 2004;351:1097–1105.
Chatterjee K. Coronary hemodynamics in heart failure and effects of therapeutic interventions. *J Cardiac Fail*. 2009;15:116–123.
Hensley FA Jr., Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Williams; 2008: Chapter 1.

39. ANSWER: C

In the ***aging heart***, myocardial contractility during submaximal demand usually remains uncompromised until the eighth decade of life. The heart does not atrophy with age, but inotropic and chronotropic responses to adrenergic stimulation decrease. The aging heart is limited to a lower maximal heart rate than the "younger" heart, with subsequent increases in stroke volume and left ventricular end-diastolic volume and pressure. Ejection fraction, however, remains unchanged. The fall in metabolic demands is met with a decrease in the resting cardiac index. The aging left ventricle is also thicker and less compliant than the "younger" ventricle; the stiffer ventricle does not completely relax until late in diastole, thus reducing passive ventricular filling. This progressive "diastolic dysfunction" makes the elderly person dependent on ventricular filling time and sinus atrial contractions.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 35, 882.

40. ANSWER: E

Thermodilution cardiac output is inaccurate in the presence of tricuspid regurgitation (TR), which *underestimates* true cardiac output at high cardiac outputs and *overestimates* it at low cardiac outputs. TR may have minimal effect when flow is in the midrange. Recirculation of the cold injectate in the right heart due to TR may lead to an inaccurate assessment of the cardiac output. Continuous cardiac

output (CCO) catheters, which use a thermodilution method, are also inaccurate with regurgitant pathologies. These catheters use a metal heating coil to warm blood and assess temperature change over time at the distal thermistor. The Stewart-Hamilton equation allows for the conversion of the temperature change over time curve to be converted to cardiac output.

$$Q = \frac{V(T_B - T_I)K_1K_2}{T_B(t)^{dt}},$$

where Q = cardiac output, V = volume injected, T_B = blood temperature, T_I = injectate temperature, K_1 and K_2 = computational constants, and $T_B(t)^{dt}$ = change in blood temperature as a function of time.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:57.

Heerdt PM, Blessios GA, Beach ML, Hoque CW. Flow dependency of error in thermodilution measurement of cardiac output during acute tricuspid regurgitation. *J Cardiothorac Vasc Anesth*. 2001;15(2):183–187.

41. ANSWER: B

Indications for permanent pacing are symptomatic sinus node disease, symptomatic AV node disease, long QT syndrome, hypertrophic obstructive cardiomyopathy, and dilated cardiomyopathy. Three-chamber pacing (right atrium, both ventricles) or biventricular pacing is used to treat dilated cardiomyopathy.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008:Chapter 25.

42. ANSWER: A

Cardiac tamponade presents a unique challenge to the anesthesia care team. The elevated pericardial pressures serve as an impediment to the normal filling of all cardiac chambers. As pericardial pressure increases over the pressure within a cardiac chamber, that chamber will collapse. With a circumferential effusion and normal intracardiac pressures, the atria will collapse first, followed by the right ventricle and finally the left ventricle. Chambers will collapse first during that part of the cardiac cycle during which the pressure is lowest—that is, the atria usually during atrial relaxation (i.e., the "x" descent in late diastole and early systole) and the ventricles during diastole. A loculated pericardial effusion, because of its fixed position, may affect only a subset of cardiac chambers. In addition, ventricular interdependence becomes a significant factor in tamponade: the filling of one ventricle occurs at the expense of the other. This is clearly seen during spontaneous ventilation, where, with negative pressure inspiration, the increase in right ventricular filling impedes left ventricular filling, resulting in pulsus paradoxus.

Maintenance of ventricular preload is paramount in management. Any interventions that impede venous return (e.g., hypovolemia, positive-pressure ventilation, increased venous pooling, etc. can have dramatic hemodynamic consequences. The limitations set on venous return make optimization of the other determinants of cardiac output important. Maintaining ventricular contractility and high normal heart rates is also paramount.

KEY FACTS: HEMODYNAMIC CHARACTERISTICS OF CARDIAC TAMPONADE

- Diastolic dysfunction with impaired right heart filling
- Elevated right atrial pressure
- Prominent "x" descent on central venous pressure waveform
- Blunted or absent "y" descent on central venous pressure waveform
- Equalization of diastolic pressures
- Diminished intracardiac chamber volumes
- Diastolic collapse of right atrium and ventricle
- Right ventricular septal shift during late diastole with inspiration
- Decreased blood pressure, cardiac output, and stroke volume
- Increased systemic vascular resistance
- Increased heart rate
- Pulsus paradoxus
- Exaggerated transvalvular flow with respiration

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:293.

43. ANSWER: A

Most local anesthetics have similar effects on the heart, peripheral blood vessels, and autonomic system. In the heart, local anesthetics can cause a decrease in the rate of depolarization of Purkinje fibers and ventricular muscles, where local anesthetics decrease the availability of fast

sodium channels, action potential duration, and the refractory period in cardiac membranes. Peripherally and in the autonomic system, local anesthetics can indirectly block sympathetic and parasympathetic activity.

Local anesthetics at high doses can prolong conduction time in the heart, particularly increasing the PR interval and the duration of the QRS complex. Extremely high doses can even depress spontaneous pacemaker activity in the sinus node, resulting in arrest.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 21, 545.

44. ANSWER: D

Current CPR and Advanced Cardiac Life Support data suggest that eliminating mouth-to-mouth ventilation early in the resuscitation of witnessed fibrillatory cardiac arrest may improve survival. The Belgian CPR Registry supports this notion in documenting similar survival and neurologic outcomes despite initiating full basic life support or only chest compressions. Currently, there is renewed interest in ***uninterrupted chest compressions*** during repeated patient assessment, ventilations, intubation, central line placement, changing rescuers, and defibrillation. Studies have shown that interrupting compressions is detrimental to maintaining myocardial perfusion and, ultimately, to the success of the resuscitation algorithm.

ADDITIONAL READINGS

Cunningham LM, Mattu A, O'Connor RE, Brady WJ. Cardiopulmonary resuscitation for cardiac arrest: the importance of uninterrupted chest compressions in cardiac arrest resuscitation. *Am J Emerg Med*. 2012;30(8):1630–1638.

Longnecker DE, Brown DL, Newman MF, Zapol WM, eds. *Anesthesiology*. New York, NY: McGraw Hill Medical; 2008: Chapter 84.

45. ANSWER: C

Ventricular performance and changes in cardiovascular status can be obtained from a PA catheter. Derivation of vascular resistance requires the measurement of flow or cardiac output and the pressure difference on each side of the vascular bed of interest. To derive pulmonary vascular resistance with a PA catheter, mean PA pressure and PA occlusion pressure measurements are necessary. ***PA occlusion pressure cannot be measured without a functional balloon*** (Table 9.4).

ADDITIONAL READINGS

Hensley FA Jr., Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Williams; 2008: Chapter 3.

46. ANSWER: D

The ***Valsalva maneuver*** results in a reflex increase in heart rate (Table 9.5).

Table 9.4 DERIVED HEMODYNAMIC INDICES

PARAMETER	PHYSIOLOGIC SIGNIFICANCE	FORMULA	NORMAL VALUE
Systemic vascular resistance (SVR)	Reflects impedance of the systemic vascular tree; assumes laminar flow of homogeneous fluid	$80 \times (MAP - CVP)/CO$	700–1,600 dyne·s·cm^{-5}
Pulmonary vascular resistance (PVR)	Reflects impedance of pulmonary circuit	$80 \times (PAM - PCWP)/CO$	20–130 dyne·s·cm^{-5}
Cardiac index (CI)	Index flows to body surface area (BSA), allows for meaningful comparison between patients	CO/BSA	2.5–4.2 L·min^{-1}·m^{-2}
Stroke volume index (SVI)	Reflects fluid status and ventricular performance	CI/HR x1000	40–60 mL·beat^{-1}·m^{-2}
Left ventricular stroke work index (LVSWI)	Estimates work of left ventricle, reflects contractile state	$(MAP - PCWP) \times SVI \times 0.0136$	45–60 g·m·m^{-2}
Right ventricular stroke work index (RVSWI)	Estimates work done by right ventricle and RV performance	$(PAM - CVP) \times SV \times 0.0136$	5–10 g·m·m^{-2}

CO, cardiac output; CVP, central venous pressure; HR, heart rate; MAP, mean arterial pressure; PAM, pulmonary artery mean pressure; PCWP, pulmonary capillary wedge pressure. Modified from Kaplan JA. *Cardiac Anesthesia*. 2nd ed. Philadelphia, PA: WB Saunders, 1987: 203.

Table 9.5 CARDIOVASCULAR REFLEXES

CAROTID SINUS (PRESSORECEPTOR, BARORECEPTOR)	
Anatomy:	Carotid-afferent nerve of Hering (glossopharyngeal)
	Aortic-vagus
	Cardiovascular centers in medulla
Stimulus:	Increased blood pressure
Response:	Inhibition of sympathetic and increase in parasympathetic activity, causing decreased cardiac contractility, heart rate, and vasoconstrictor tone
Other:	Gain determined by pulse pressure
	Reduces arterial pressure fluctuation to one-third of expected threshold 60 torr, limits 175–300 torr
VALSALVA MANEUVER	
Anatomy:	Same as pressoreceptor reflex
Stimulus:	Forced expiration against closed glottis
Response:	Increased venous pressure in head, upper extremities, with decreased right heart venous return causing decreased blood pressure and cardiac output, and reflex increase in heart rate; the tachycardia coupled with coupling of the E and A waves on the mitral transvelocity curve indicates normal left ventricular filling pressures
Other:	Glottic opening increases venous return to right heart, resulting in forceful right and then left ventricular contraction, followed by transient bradycardia
MULLER MANEUVER	
Anatomy:	Decreased pleural pressure increasing left ventricular volume through afterload reduction
Stimulus:	Inspiratory effort against a closed airway
Response:	Right ventricular end-diastolic volume and left ventricular end-diastolic pressure increase, while left ventricular end-diastolic volume is unchanged or decreased, and ejection fraction is unchanged
Other:	Net effect on left ventricular function depends on ventricular interdependence, heart rate, and contractility (position of the heart on diastolic pressure–volume curve)
	Müller maneuver may cause ventricular akinesis due to increased wall stress, increasing myocardial oxygen demand, or increased left ventricular transmural pressure, decreasing motion in nonfunctional ventricular myocardium
VON BEZOLD–JARISCH	
Anatomy:	Ventricular chemoreceptors and mechanoreceptors with afferent pathway in unmyelinated vagal C fibers
Stimulus:	Noxious stimuli to either ventricle associated with myocardial ischemia, profound hypovolemia, coronary reperfusion, aortic stenosis, neuraxial anesthesia associated with sympathetic blockade and "empty" ventricle, or even vasovagal syncope
Response:	Hypotension, bradycardia, parasympathetically induced coronary vasodilation, and inhibition of sympathetic outflow from vasomotor centers
Other:	Reperfusion of previously ischemic tissue elicits reflex
CARDIOGENIC HYPERTENSIVE CHEMOREFLEX	
Anatomy:	Chemoreceptors located between the aorta and pulmonary artery and supplied by the left coronary artery
	Afferent reflex pathway is intrathoracic vagal branches and the efferent path is via phrenic, vagal, and sympathetic routes
Stimulus:	Serotonin
Response:	Arterial pressure increases markedly in 4–6 sec owing to increased inotropy and peripheral vasoconstriction
Other:	Reflex may be responsible for hypertension during angina, myocardial infarction, and after coronary bypass grafting and is abolished by vagotomy, atropine, or local anesthesia of the intertruncal space

(*continued*)

Table 9.5 (CONTINUED)

CUSHING'S REFLEX	
Anatomy:	Increased cerebrospinal fluid (CSF) pressure compresses cerebral arteries
Stimulus:	Cerebral ischemia secondary to increased CSF pressure
Response:	An increase in arterial pressure sufficient to reperfuse the brain
	Intense sympathetic activity causes severe peripheral vasoconstricion as a result of this reflex
BAINBRIDGE ATRIAL REFLEX	
Anatomy:	Primarily mediated through vagal myelinated afferent fibers; activation of sympathetic afferent fibers may also occur
	Increased right atrial pressure directly stretches the SA node and enhances its automaticity, increasing the heart rate
Stimulus:	Increased vagal tone and distention of the right atrium or central veins
Response:	Depends upon the preexisting heart rate
	With preexisting tachycardia, there is no effect
	Volume loading at a slow heart rate causes progressive tachycardia
	Global atrial distention in response to high pressures causes bradycardia, hypotension, and decreased systemic vascular resistance
Other:	Experimental distention of the cavoatrial junctions or other small portions of the atria increases heart rate, but clinical conditions such as heart failure usually do not produce such locally increased atrial pressure
CHEMORECEPTOR	
Anatomy:	Carotid and aortic bodies chemoreceptors whose nerve fibers pass through the nerve of Hering and the vagus nerve to the medullary vasomotor centers
Stimulus:	Decreasing oxygen tension or increased hydrogen ion concentrations
Response:	Increased pulmonary ventilation and blood pressure with decreased heart rate (carotid body chemoreceptors)
	Stimulation of the aortic bodies causes tachycardia
Other:	Normally, the peripheral chemoreceptors are minimally active
OCULOCARDIAC	
Anatomy:	Afferent fibers run with the short or long ciliary nerves to the ciliary ganglion, and then with the ophthalmic division of the trigeminal nerve to the gasserian ganglion
Stimulus:	Traction on the extraocular muscles (especially more on the medial rather than the lateral rectus) or pressure on the globe
Response:	Bradycardia and hypotension as a consequence of this reflex
Other:	Demonstrated in 30–90% of patients undergoing ophthalmic surgery and attenuated by IV atropine
CELIAC (VAGOVAGAL)	
Anatomy:	Vagal stimulation via mesenteric traction, rectal distention, traction on gallbladder, respiratory tract receptors
Response:	Bradycardia, apnea, hypotension with narrowed pulse pressure
Other:	Traction on the mesentery or gallbladder, stimulation of vagal nerve fibers in the respiratory tract, or rectal distention stimulates afferent vagal nerve endings to cause bradycardia, apnea, and hypotension (vagovagal reflex)
	Manipulation around the celiac plexus decreases systolic pressure, narrows pulse pressure, and slightly decreases heart rate

Modified from Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: 878–879.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:878–879.

47. ANSWER: A

The carotid body is a peripheral chemoreceptor located at the bifurcation of the common carotid artery. The neural cells located within it can detect oxygen tension, carbon dioxide tension, temperature, and pH. Oxygen tension is the most potent stimulus to the carotid body, and decreases will lead to ventilatory stimulation. The ***carotid body chemoreceptors*** have nerve fibers that pass through the nerve of Hering and the vagus nerve to the medullary vasomotor centers.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 11, 240.

48. ANSWER: D

Hypertension is commonly seen in the postoperative period after a carotid endarterectomy, especially in patients with poorly controlled preoperative hypertension. Causes of postoperative hypertension include surgical denervation of the carotid sinus baroreceptors, hypoxemia, hypercapnia, bladder distention, and pain. It is important to postoperatively control blood pressure with short-acting drugs due to the possible neurologic and cardiac complications.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 62.

49. ANSWER: D

Autonomic reflexes associated with the carotid sinuses are caused by signals generated from the glossopharyngeal and vagus nerves. Stimulation of the baroreceptors can reflexively cause an increase in vagal tone, producing vasodilation, slowing of the heart rate, and lowering of blood pressure. Increases in vagal tone can occur during episodes of high blood pressure. Effector-receptor sites transmitted from the medullary vasomotor centers are responsible for this inhibition of sympathetic responses.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 12.

50. ANSWER: B

Similar to tricyclic antidepressant medications, cocaine decreases norepinephrine reuptake and can present as fulminant hypertension, tachycardia, and myocardial ischemia in young healthy patients with acute intoxication. It is important to note that management of these patients is similar to those with cardiovascular symptoms seen in patients with pheochromocytoma: vasodilators and beta blockers. However, beta blockers given alone can cause unopposed alpha-adrenergic stimulation and further increase systemic vascular resistance. Patients with **chronic cocaine abuse** are at risk for developing cardiomyopathy. This is independent of the risk of myocardial ischemia and infarction from coronary vasospasm and myocardial oxygen supply/demand mismatch. One hypothesis is that the chronic exposure to the high levels of catecholamines caused by cocaine may lead to cardiomyopathy.

Acetaminophen toxicity is a concern due to its hepatotoxic effects. Salicylate poisoning is notable for its acid–base disturbance and tachypnea and hyperpnea. Aspirin directly stimulates the respiratory center, leading to a respiratory alkalosis while causing a non–anion gap metabolic acidosis.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.

Lange RA, Cigarroa RG, Flores ED, et al. Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. *Ann Intern Med*. 1990;112(12):897–903.

51. ANSWER: D

Congestive heart failure can lead to imbalances in myocardial supply and demand. Myocardial wall tension typically increases due to increased preload. In addition, heart rates are usually elevated in an attempt to maintain cardiac output in the setting of reduced contractility and increased left ventricular end-diastolic pressure. Diminished cardiac output leads to lower systemic diastolic pressures and thus lower coronary perfusion pressure. Increased heart rate also

decreases the time for coronary flow. Heart failure management focuses on agents that decelerate the progression of failure by reducing adverse myocardial remodeling (e.g., ACE inhibitors, beta blockers, and aldosterone antagonists) in combination with other agents that improve symptoms of failure (e.g., diuretics and digoxin).

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008: 868.

52. ANSWER: B

Cocaine is an ester local anesthetic that is most commonly utilized as a topical anesthetic. It causes vasoconstriction at all concentrations by inhibiting the uptake of norepinephrine at premotor neurons. This leads to systemic and coronary vasoconstriction and an increase in heart rate. Cocaine blocks the fast sodium channel of myocardial cells and in this regard is similar to class I antiarrhythmic drugs. This leads to a slowing of conduction and repolarization. On ECG, this is manifest as a widening of the PR, QRS, and QT intervals.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010.

53. ANSWER: A

In constrictive pericarditis, the pericardium acts like a rigid box within which the heart resides. This results in a rapid early filling of the ventricles during diastole that abruptly ends when the limitations of the "box" are encountered. Due to this, ***the central venous waveform demonstrates a steep "y" descent as the rapid early filling of the right ventricle occurs and then abruptly ends***. The "a" wave is also prominent as pressure abruptly increases as atrial contraction occurs. The CVP waveform develops an "m" or "w" shape; the "y" descent is followed by a rapid plateau in pressure that forms a "square root sign" (Fig. 9.4).

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008: Fig. 8.6.

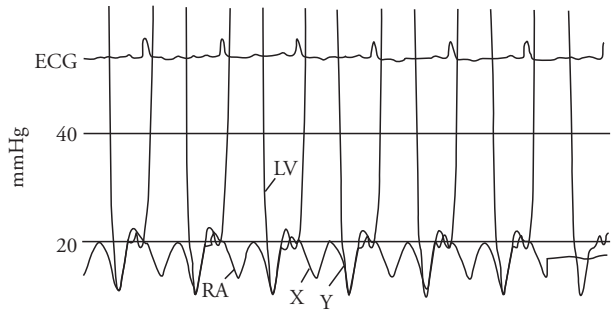


Figure 9.4 Right atrial (RA) and left ventricular (LV) pressure waveforms obtained from patient with constrictive pericarditis. Prominent X and Y descents give characteristic "M" and "W" appearance to the right atrial pressure waveform. Note also that right and left heart pressures are elevated and equal throughout diastole. Reprinted from Lorell BH, Grossman W. Profiles in constrictive pericarditis, restrictive cardiomyopathy, and cardiac tamponade. In: Grossman W, ed. *Cardiac Catheterization and Angiography*. 3rd ed. Philadelphia, PA: Lea & Febiger, 1986, with permission.

54. ANSWER: E

Myocardial oxygen delivery is dependent on coronary blood flow—the carrying capacity of oxygen in the blood. The pressure gradient between the aorta and myocardial tissue dictates coronary blood flow. A gradient for antegrade flow through the coronary circulation of the left ventricle occurs only during diastole. Therefore, aortic diastolic blood pressure represents the "upstream" pressure to drive coronary blood flow. The left ventricular end-diastolic pressure (LVEDP) is the resisting pressure and the difference between the two pressures constitutes coronary perfusion pressure. Since heart rate affects time in diastole proportionally more than time in systole (diastole normally takes up two-thirds of the cardiac cycle), faster heart rates have an impact on coronary blood flow. Increased coronary vascular resistance, from discrete stenosis and/or vasospasm, decreases coronary blood flow at any given coronary perfusion pressure.

The maximum pressure across the aortic valve is affected by cardiac output and the ability of the aortic valve to open. It does not directly affect coronary blood flow.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:349–350.

55. ANSWER: D

Autonomic reflexes associated with the carotid sinuses are caused by signals that travel via the glossopharyngeal and the vagus nerves. Stimulation of the baroreceptors can reflexively cause an increase in vagal tone, producing vasodilation,

slowing of the heart rate, and lowering of blood pressure. Increases in vagal tone can occur during episodes of high blood pressure. Effector-receptor signals transmitted from the medullary vasomotor centers are responsible for this inhibition of sympathetic responses.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 12.

56. ANSWER: B

In normal hearts, the four ***major determinants of coronary blood flow*** are perfusion pressure, myocardial extravascular compression, myocardial metabolism, and neurohumoral control. Coronary blood flow is a function of the pressure gradient across the aortic root and its pressure downstream. Extravascular compression on the heart can cause resistance that increases blood pressure, heart rate, contractility, and preload, ultimately affecting coronary blood flow.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008: Chapter 6.

57. ANSWER: D

Coronary blood flow occurs during diastole. The coronary arteries originate from the aortic sinus with the left main coronary artery ostium above the left coronary cusp and the right main coronary ostium above the right coronary cusp. The ostia and very proximal portions of arteries are best seen in the midesophageal aortic valve short-axis view at an omniplane angle of 40 to 60 degrees. They can also be seen in the midesophageal aortic valve long-axis view at an omniplane angle near 135 degrees. The left circumflex coronary artery can frequently be seen in its cross-section in the midesophageal two-chamber view in the AV groove under the left atrial appendage. The flow pattern is not biphasic, which is typical of pulmonary venous and left ventricular inflow patterns.

58. ANSWER: E

Coronary steal refers to the physiologic condition whereby blood flow is shunted away from areas at risk for ischemia to areas that are not. This happens when the mechanisms that control regional blood flow are overtaken by drugs or other events that indiscriminately dilate the entire coronary vascular bed. Coronary steal can occur in patients with specific coronary artery lesions upon the administration of coronary vasodilators. Approximately one-fourth of patients with coronary artery disease may have these specific coronary lesions. In these patients, the administration of an arteriolar dilator, such as dipyridamole or adenosine, may produce a steal.

An initial study in the mid-1980s suggested that isoflurane may induce coronary steal by shunting flow away from ischemic myocardium. Subsequent studies refuted this claim, suggesting that coronary blood flow to all parts of the heart remained as adequate with isoflurane as with other anesthetics. However, recent evidence suggests that there is actually myocardial protection with isoflurane.

ADDITIONAL READINGS

DiNardo JA, Zvara DA. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford, UK: Blackwell Publishing Ltd.; 2008:99.

Eger E. The pharmacology of isoflurane. *Br J Anaesth*. 1984;56(Suppl 1): 71S–99S.

59. ANSWER: D

Warfarin interferes with hepatic synthesis of vitamin K-dependent coagulation factors: factors II, VII, IX, X, protein C, and protein S. More specifically, warfarin inhibits the carboxylation of glutamic acid residues that are essential for binding coagulation factor activation complexes to phospholipid membranes. Warfarin therapy is monitored using the international normalized ratio (INR) system derived from prothrombin time (PT). In emergency settings where bleeding is life-threatening, vitamin K should be administered (10 mg by slow IV administration), but because the onset of effect is 4 to 6 hours after IV administration, this will not suffice. Prothrombin complex concentrates contain varying amounts of the vitamin K-dependent factors depending on the particular manufacturer. These are concentrated preparations that allow for rapid, low-volume treatment. Recombinant factor VIIa can also be used, with the caveat that there is some evidence of a potential risk of thrombotic complications, such as myocardial infarction. FFP can also be used but amounts in excess of 30 mL/kg may be required. Platelets would not have an impact on the primary problem in this patient and should not be given in the presented scenario.

ADDITIONAL READINGS

Levy JH, Tanaka KA, Dietrich W. Perioperative hemostatic management of patients treated with vitamin K antagonists. *Anesthesiology*. 2008;109:918–926.

60. ANSWER: C

Air is frequently introduced into the cardiac chambers during open chamber procedures. Carbon dioxide is commonly introduced into the surgical field to reduce the amount of air. This occurs because CO_2 is heavier than air and can displace it from the field. CO_2 is much more soluble than air in blood and therefore poses less risk in terms of embolism. Air can also be introduced directly into the coronaries during the grafting process. When air exits the left ventricle in the supine patient it most frequently enters the right coronary artery because the ventricle sits anteriorly. This will manifest as inferior ischemia in a right-dominant coronary circulation (i.e., the right coronary artery supplies the posterior descending artery). Depending on the size of the ***air embolus*** and the status of collateral coronary flow, the clinical syndrome can range from no effect to cardiogenic shock to ventricular fibrillation. Supportive care should be instituted immediately, while initiation of ACLS protocol and return to bypass may be necessary in critical situations. Frequently, mean arterial pressures are increased in an attempt to drive the air distally while waiting for absorption.

Significant hyperkalemia should manifest on ECG as peaked T waves, small P waves, widened QRS complex, and ventricular dysrhythmia. It would not be expected to occur 30 minutes after bypass, as presented in the clinical scenario. Significant hypothermia would also not be expected at this time. Atrial pacing does not cause ventricular fibrillation via an R-on-T phenomenon.

ADDITIONAL READINGS

Sahu MK, Ingole PR, Bisoi AK, Venugopal P. Successful management of a case of massive air embolism from cardiopulmonary bypass with retrograde cerebral perfusion in a child. *J Cardiothorac Vasc Anesth*. 2006;20:80–81.

61. ANSWER: D

"Sweep" speed refers to the flow rates for respiratory gases (air and oxygen) to the membrane oxygenator. This affects $PaCO_2$, where increased sweep speed leads to greater "ventilation," thereby reducing $PaCO_2$. Sweep speed, unless dramatically reduced below reasonable levels, would not explain the arterial blood gas finding demonstrated here.

PaO_2 is usually maintained between 100 and 300 mm Hg by adjusting the FiO_2 to the membrane oxygenator. ***When PaO_2 values are not adequate or near expected levels, the possible causes are inadequate oxygen delivery and increased oxygen demand***. Inadequate delivery can occur from leaks in the gas circuit of the bypass machine, membrane oxygenator malfunctions, or O_2 monitoring problems. Inadequate heparinization can lead to thrombus formation on the oxygenator, leading to a reduced surface for O_2 exchange. Inadequate muscle relaxation can lead to shivering and an increased demand for oxygen. This may be accompanied by low mixed venous oxygen saturations.

62. ANSWER: A

Malfunction of an expiratory valve would lead to rebreathing of expiratory gases and would manifest on gas monitoring as a CO_2 level that does not reach zero during inspiration. It would not be expected to lead to hypoxemia. During cardiopulmonary bypass, the endotracheal tube can move unknowingly from its prebypass position. Expansion of both lungs should be confirmed before removal from bypass. Furthermore, if the lungs are not adequately re-expanded before separation from bypass, profound atelectasis may lead to significant shunting and relative hypoxemia.

Mitral valve repair can lead to acute or worsened mitral stenosis. If severe enough, this can result in pulmonary edema. The noncoronary cusp of the aortic valve lies next to the mitral annulus and can be accidentally tethered by suture during mitral valve repair. This could lead to acute severe aortic regurgitation and pulmonary edema.

63. ANSWER: B

During cardiopulmonary bypass with an aortic cross-clamp in place, the heart is completely isolated from the circulatory circuit. The status of the coronary vasculature is irrelevant during this time. ***Pump flow rates and pressure goals are a balance of providing adequate oxygen delivery to all perfused tissues and maximizing myocardial protection while maintaining a bloodless field for the surgical team***. It is important to remember that cardiopulmonary bypass does not prevent the return of bronchial blood and Thebesian circulation blood to the left heart. Reducing pump flow rates and pressure will reduce this blood flow and reduce warming of the isolated and ischemic heart. Specific flow rates and pressure goals are determined by patient body surface area, hematocrit level, degree of hypothermia, and individual patient issues.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008: Chapter 28.

64. ANSWER: B

Mixed venous oxygen saturation (SvO_2) approaching 50% can be due to compromised oxygen delivery and/or increased oxygen utilization by the tissues. During CPB, levels of SvO_2 at 80% or above are sought. Low pump flows, low hemoglobin levels, and membrane oxygenator malfunction are the most likely causes of low mixed venous oxygen saturation.

ADDITIONAL READINGS

Hensley FA Jr., Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Williams; 2008: 566.

65. ANSWER: E

Massive gas embolism is a rare but disastrous CPB complication. Circumstances that most commonly contribute to these events are inattention to venous reservoir blood level, reversal of left ventricular vent flow, or unexpected resumption of cardiac ejection in a previously opened heart. Rupture of a pulsatile assist device or intra-aortic balloon pump may also introduce large volumes of gas into the arterial circulation. Recommended treatments for massive arterial gas embolism during CPB include immediate cessation of CPB with aspiration of as much gas as possible from the aorta and heart, placing the patient in steep Trendelenburg position, and clearing air from the arterial perfusion line through retrograde superior vena cava perfusion. Once CPB is resumed, maneuvers such as deepening of hypothermia (18 to 27 degrees C) and administration of glucocorticoids and/or anticonvulsants can minimize cerebral edema and resultant seizures.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008: 917–918.

66. ANSWER: C

The aging process is associated with changes in the cardiovascular system, including the heart, blood vessels, and autonomic control; however, it does not atrophy. In fact, the left ventricle wall thickens, myocyte and sinus node cell numbers increase, and the density of conduction fibers decreases. Respectively, these changes translate to increased myocardial stiffness resulting in increased ventricular filling pressures, decreased contractility, and decreased beta-adrenergic sensitivity. Advanced age also decreases the elasticity of the vasculature due to the breakdown of elastin and collagen matrix in the vascular wall. With increases in medial and intimal thickness, subsequent increases in the diameter and stiffness of large elastic arteries are observed. Clinically, this translates to elevated mean arterial pressures and an increase in pulse pressure.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010:5410–5411.

67. ANSWER: E

The acute onset of atrial pacing has the least impact on CVP or its waveform. CVP pressures are essentially equivalent to right atrial pressures and reflect its ventricular preload. Conditions that affect right atrial pressure also influence the CVP pressure trace. The normal CVP waveform consists of three peaks (a, c, and v waves) and two descents (x, y), whose morphology depends on multiple factors including heart rate, conduction disturbances, tricuspid valve dysfunction, normal or abnormal intrathoracic pressure changes, and changes in right ventricular compliance.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 27.

68. ANSWER: A

The "a" wave represents contraction of the atrium (Fig. 9.5 and Table 9.6). In patients with atrial fibrillation, "a" waves are absent. When resistance to the emptying of the right atrium is present, large "a" waves are often observed. Examples include tricuspid stenosis, right ventricular hypertrophy as a result of pulmonic stenosis, or acute or chronic lung disease associated with pulmonary hypertension. Large "a" waves may also be observed when right ventricular compliance is impaired.

The "c" wave is caused by the return of the tricuspid annulus back toward the right atrium during the isovolumic contraction phase.

The "c" wave is followed by the "x" descent, which is caused by the relaxation of the atrium and the apical

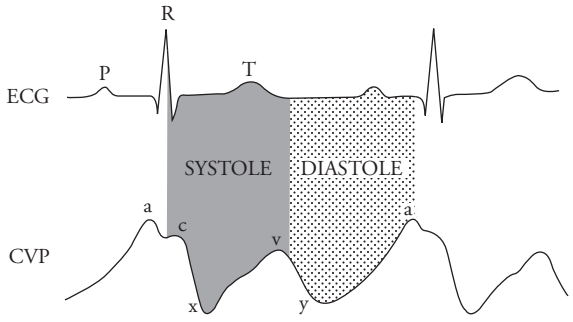


Figure 9.5 The normal central venous pressure trace. Redrawn with permission from Mark JB. Central venous pressure monitoring: Clinical insights beyond the numbers. *J Cardiothorac Vasc Anesth*. 1991;5:163.

displacement of the tricuspid annulus that occurs with the onset of ventricular systole.

The "v" wave is due to the filling of the right atrium during systole. The "y" descent represents rapid atrial filling with the onset of diastole. Tricuspid regurgitation typically produces giant "v" waves that begin immediately after the QRS complex. Large "v" waves are often observed when right ventricular ischemia or failure is present or when ventricular compliance is impaired by constrictive pericarditis or cardiac tamponade. A prominent "v" wave during CVP monitoring may suggest right ventricular papillary muscle ischemia and tricuspid regurgitation. When right ventricular compliance decreases, the CVP often increases with prominent "a" and "v" waves fusing to form an "m" or "w" configuration.

The "v" wave is followed by the "y" descent resulting from diastolic collapse during early ventricular filling.

Using ***pulmonary capillary wedge tracing***, the right atrial "a" wave occurs earlier than the left because the right atrium depolarizes before the left atrium.

Table 9.6 **CENTRAL VENOUS PRESSURE WAVEFORM COMPONENTS**

WAVEFORM COMPONENT	PHASE OF CARDIAC CYCLE	MECHANICAL EVENT
a wave	End diastole	Atrial contraction
c wave	Early systole	Isovolumic ventricular contraction, tricuspid motion toward the right atrium
x descent	Mid-systole	Atrial relaxation, descent of the base, systolic collapse
v wave	Late systole	Systolic filling of the atrium
y descent	Early diastole	Early ventricular filling, diastolic collapse

SOURCE: Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Table 40–3.

69. ANSWER: A

Using the NBG code, the first position of the ***pacemaker code*** refers to the chamber or chambers that can be paced (Table 9.7). The second position refers to the chamber or chambers that can be sensed. The third position refers to the possible responses to sensing. The pacemaker can be inhibited and/or triggered in response to sensed electrical activity.

DDD pacing provides synchronization of the atrium and ventricle. In its default setting, atrial pacing will be in the "inhibited" mode. If there is no sensed atrial event, the pacer will emit an atrial pulse. If an atrial event occurs, either naturally or emitted, the pacing device will ensure that a ventricular event will follow it.

Electrocautery can present a problem to any pacemaker that is actively sensing. Extrinsic electrical impulses from the electrocautery can confuse the pacemaker into "thinking" that native pacemaking and conduction is occurring. This will essentially inhibit the pacemaker and disable its pacing function, potentially resulting in hemodynamic compromise in the pacemaker-dependent patient. Fixed-rate modes (nonsensing modes), such as DOO, AOO, or VOO, are better in this setting. Placing a magnet on a modern pacemaker will place it into a fixed-rate mode, usually DOO in a DDD pacemaker, at a preprogrammed rate.

Rate responsiveness is a feature whereby the pacemaker can sense motion such as would occur with patient exertion and increase its heart rate accordingly. Any external movement (e.g., movement during surgical prep, fasciculations) will cause an increase in the pacemaker rate. This function is best turned off in the operative patient.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 43.

70. ANSWER: B

Impedance is another term for resistance based on the current being used. After multiple defibrillation attempts, impedance is not increased. Factors that decrease transthoracic impedance include paddle pressure applied against the chest wall, size of the paddle and/or electrode, the presence of saline-soaked gauze pads and creams, and most commonly the gel/paste used. In experimental models, transthoracic impedance has been shown to decrease with successive shocks, which may partially explain why the energy is increased in successive shocks when previous shocks at lower energy levels have failed. Transthoracic impedance is higher during inspiration than during exhalation.

Table 9.7 NASPE/BPEG REVISED (2002) GENERIC PACEMAKER CODE (NBG)

POSITION I: PACING CHAMBER(S)	POSITION II: SENSING CHAMBER(S)	POSITION III: RESPONSE(S) TO SENSING	POSITION IV: PROGRAMMABILITY	POSITION V: MULTISITE PACING
O = none	O = none	O = none	O = none	O = none
A = atrium	A = atrium	I = inhibited	R = rate modulation	A = atrium
V = ventricle	V = ventricle	T = triggered		V = ventricle
D = dual (A + V)	D = dual (A + V)	D = dual (T + I)		D = dual (A + V)

THE NBG code is a joint project by the North American Society of Pacing and Electrophysiology (NASPE) (the "N") and the British Pacing and Electrophysiology Group (BPEG) (the "B"). The "G" stands for generic.

SOURCE: Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 43.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Chapter 59, 1545–1546.

71. ANSWER: B

In normal hearts, the four ***major determinants of coronary blood flow*** are perfusion pressure, myocardial extravascular compression, myocardial metabolism, and neurohumoral control. Coronary blood flow is a function of the pressure gradient across the aortic root and its pressure downstream, or in other words the average pressure in the aortic root during diastole. Factors that increase myocardial metabolism (increases in blood pressure, heart rate, contractility, and preload) affect coronary blood flow.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008: Chapter 6.

72. ANSWER: C

Coronary circulation descriptions routinely refer to dominance of a coronary artery, either the right coronary or the left circumflex. This is determined by which artery predominantly supplies blood to the posterior descending coronary artery. The right coronary artery is dominant in 70% of humans, whereas 20% of humans are left dominant. The remaining 10% have equal supply from both coronaries.

73. ANSWER: D

Children with cancer who undergo chemotherapy are subject to cardiotoxic effects that increase cardiovascular risk. Common cardiotoxic agents include 5-fluorouracil, ***doxorubicin***, daunorubicin, and cyclophosphamide. Acutely, ST-segment and T-wave changes and dysrhythmias can be manifested on the ECG. However, chronic cardiotoxic heart failure can develop from cumulative chemotherapeutic dosing. Serious cardiomyopathies can also occur. It is important that these patients undergo thorough preoperative evaluation, including an echocardiogram, prior to chemotherapy.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 83.

74. ANSWER: D

The ion channel in the heart that is most likely significantly affected by anesthetics is the voltage-gated Ca^{2+} channel. Volatile anesthetics decrease the maximal peak current, shorten the duration of the calcium channel current, and increase the rate of inactivation. Overall, the influx of Ca^{2+} influx into the cardiac myocyte is diminished.

Further, intravenously injected anesthetics have been reported to inhibit cardiac Ca^{2+} channels. Thiopental, methohexital, and propofol in excessive doses have been known to block Ca^{2+} currents.

ADDITIONAL READINGS

Kaplan JA. *Essentials of Cardiac Anesthesia*. Philadelphia, PA: Elsevier Saunders; 2008:136.

75. ANSWER: E

Asynchronous pacing is synonymous with fixed-rate pacing. The possible pacemaker modes include DOO, AOO, and VOO. All pacemaker sensing is shut off and the pacemaker will pace the appropriate chambers at the set rate and PR interval. The risk of causing ventricular fibrillation from an R-on-T phenomenon is neither significant nor a clinical concern. This safety was demonstrated by the history of safe use of the first few generations of pacemakers, which were all asynchronous.

Monopolar cautery creates a wide electric field that can confuse a pacemaker with sensing capabilities into "thinking" that native cardiac electrical activity exists. This can result in loss of pacing—a critical event in the pacemaker-dependent patient. Electrocautery interference can be avoided by applying the cautery grounding plate in a location where current is directed away from the pacemaker and its leads. Bipolar cautery does not create such a problematic field since the current flows only between the tips of the device.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005: Appendix: Electrocardiography, p. 1589.

76. ANSWER: D

In the presence of a left bundle branch block, ST elevation greater than 1 mm in leads with a positive QRS deflection and ST depression greater than 1 mm in leads with a dominant S wave (leads V1–V3) are consistent with **myocardial ischemia**.

Repolarization normally occurs in an epicardial-to-endocardial direction. For this reason, subendocardial ischemia does not cause T-wave inversion. Rather, there is an increase in the time for repolarization, which increases the QT interval. In addition, there may be an increase in T-wave amplitude. Transmural ischemia will reverse the direction of repolarization and lead to T-wave inversion.

Injury occurs when ischemia is more severe. Subendocardial injury leads to ST depressions while transmural injury leads to ST elevations. A non–ST-elevation myocardial infarction (NSTEMI) resulting from subendocardial ischemia can result in QT prolongation.

ADDITIONAL READINGS

Engel J, Brady WJ, Mattu A, Perron AD. Electrocardiographic ST segment elevation: left ventricular aneurysm. *Am J Emerg Med*. 2002;20(3):238–242.

Lopes RD, Siha H, Fu Y, Mehta RH, Patel MR, Armstrong PW, Granger CB. Diagnosing acute myocardial infarction in patients with left bundle branch block. *Am J Cardiol*. 2011;108(6):782–788.

Rautaharju PM, Zhou SH, Gregg RE, Startt-Selvester RH. Electrocardiographic estimates of action potential durations and transmural repolarization time gradients in healthy subjects and in acute coronary syndrome patients—profound differences by sex and by presence vs absence of diagnostic ST elevation. *J Electrocardiol*. 2011;44(3):309–319.

77. ANSWER: B

The ECG demonstrates a type 2, ***second-degree AV block (Mobitz II)***. It is characterized by the unexpected loss of AV conduction in the setting of a constant PR interval in conducted impulses that occur both before and after. This rhythm is due to disease of the His-Purkinje system and not the AV node proper. It has the potential to degrade to complete heart block and is therefore an indication for placement of a permanent pacemaker.

78. ANSWER: B

With ***left atrial enlargement***, the P-wave duration is increased as the electrical signal takes longer to spread across the atrium. A P-wave duration of more than 0.11 msec is diagnostic of left atrial enlargement. A double-hump or notched P-wave whose humps are at least 0.04 msec apart can also indicate left atrial enlargement so long as the humps are at least 0.04 msec apart. Right atrial enlargement leads to an increase in P-wave height. A P-wave greater than 2.5 mm in height is diagnostic of right atrial enlargement.

79. ANSWER: B

The right coronary artery supplies blood to the right ventricle. In addition, in 70% of patients, the coronary circulation is right-dominant. This means that the right coronary artery supplies blood to the posterior descending artery and, therefore, the inferior portion of the left ventricle. This is represented on ECG by leads II, III, and aV_F. The sinus node and AV nodal arteries also originate from the right coronary artery. The sinus node artery supplies the right atrial myocardium. In 90% of hearts, the AV branch of the right coronary artery supplies the AV node and the common bundle of His, whereas the remaining 10% of hearts are supplied by the septal perforating branches of the left anterior descending coronary artery. Branches off the AV nodal artery also give rise to the interatrial septum and posterior interventricular septum. Branches of the left anterior descending artery and AV nodal artery give blood

supply to the right bundle branch and the left anterior fascicle. Blood supply to the posterior fascicle is supplied by both the left anterior and posterior descending coronary arteries. For this reason, ***right coronary artery disturbances*** can also lead to a host of conduction abnormalities.

80. ANSWER: E

A junctional rhythm occurs in two basic circumstances. The first is when the normal spontaneous depolarization of the SA node slows below that of the AV node. This can occur through vagal stimulation or from medications. In this situation, the heart rate of the junctional rhythm will generally be in the 40- to 60-bpm range, which is consistent with normal spontaneous depolarization of the AV nodal tissue. The second circumstance occurs when the spontaneous AV node depolarization abnormally increases and overtakes the SA node rate. In this situation the junctional rate is above the 40- to 60-bpm range.

In any event, the normal heart tolerates junctional rhythms well. This is because in a healthy heart, atrial contraction is responsible for only 10% of ventricular filling. Junctional rhythms occur in otherwise healthy patients with some frequency and are well tolerated and require no therapy. Atrial contraction becomes more important when the left ventricle has reduced compliance. If the rhythm is not tolerated, treatment depends on the cause. ***If there is an accelerated junctional rate, beta blockers and/or calcium channel blockers can slow down the AV node and allow the SA node to resume the pacemaker function***. A slowed SA node can be treated with beta agonists or anticholinergics. Atrial pacing can also be used to outpace the junction.

81. ANSWER: D

DDD pacemaker mode is the most commonly encountered mode in patients with permanent pacemakers. This mode allows the greatest flexibility in that both cardiac chambers (right atrium and right ventricle) can be both paced and sensed. Furthermore, the pacemaker can be both inhibited from firing when spontaneous electrical activity is adequate and triggered to fire when normal activity does not occur within a specified range.

The ECG appearance of pacemaker spikes in a patient with a DDD pacemaker will vary depending on the underlying rhythm. If spontaneous activity is normal, no pacing is necessary and no spikes will be seen. If there is inadequate activity of any of the cardiac electrical components, the pacemaker will be stimulated. Therefore, there may be only atrial pacing, only ventricular pacing, or both atrial and ventricular pacing spikes seen. The rate will also depend on underlying activity and can vary. The rate will never fall below the low threshold of the pacemaker if it is functioning properly. When the pacemaker must pace both the atria and the ventricles, the PR interval will consistently correspond to the pacemaker's set PR interval.

82. ANSWER: A

PEA refers to a group of cardiac rhythm disorders characterized by pulselessness in the presence of electrical activity, with the exception of ventricular tachycardia or fibrillation. The criteria of PEA include patients who are pulseless but have organized electrical activity, including abnormal ventricular rhythms, postdefibrillation rhythms, and bradyasystole.

It is important to identify any correctable causes of PEA, which include cardiac tamponade, hypovolemia, tension pneumothorax, hypoxemia, pulmonary embolism, acidosis, hypothermia, medications, and electrolyte abnormalities.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 97.

83. ANSWER: C

In the ***resuscitation of PEA***, the key is determination of etiology and appropriate therapy. Epinephrine can be given to help improve hemodynamics, but until the specific cause is addressed there is little chance of success. Central line placement can be associated with hemorrhage, pneumothorax, pericardial tamponade, and dysrhythmia. Whenever lines are placed and hemodynamic instability ensues, all of these complications must be quickly considered.

ADDITIONAL READINGS

Nordseth T, Olasveengen TM, Kvaløy JT, Wik L, Steen PA, Skogvoll E. Dynamic effects of adrenaline (epinephrine) in out-of-hospital cardiac arrest with initial pulseless electrical activity (PEA). *Resuscitation.* 2012;83(8):946–952.

84. ANSWER: A

The 2007 American Heart Association (AHA) recommendations for the prevention of infective endocarditis stressed the fact that random bacteremic events associated with daily activities (e.g., toothbrushing) are much more likely to cause

endocarditis than dental, gastrointestinal tract, or genitourinary tract procedures. Furthermore, adverse events related to antibiotics seem to outweigh any potentially small benefit.

However, the AHA committee defined specific ***cardiac conditions associated with an increased risk for developing endocarditis***. These specific cardiac conditions include patients with prosthetic heart valves, unrepaired cyanotic congenital heart disease, congenital heart disease repaired with prosthetic devices for 6 months after the procedure, repaired congenital heart disease with residual defects, and cardiac transplantation with valvular heart disease. These are also conditions in which the AHA recommends antibiotic prophylaxis during oral/dental procedures that have a high risk of entraining oral bacteria into the system.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 34.

85. ANSWER: C

Anesthetic management of obstructive cardiomyopathy centers on interventions to decrease the magnitude of the obstruction. Many patients with outflow tract abnormalities have normal to supranormal contractility. Inotropic agents should be avoided or the doses decreased until the dynamic obstruction is relieved. If hyperdynamic, beta blockers can be used since obstruction is exacerbated by hypercontractile states and elevations in heart rate. Increases in outflow tract obstruction occur in hypovolemic patients, so it is important to optimize preload and ventricular filling. Further, afterload reduction should be avoided because it may worsen the obstruction. In fact, increasing afterload decreases the outflow tract gradient. Thus, agents that increase afterload are recommended.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 60.

86. ANSWER: E

Hypertrophic obstructive cardiomyopathy (HOCM) commonly causes hypertrophy of the septum and other areas of the left ventricle. If the basal septum of the left ventricle is affected, the left ventricular outflow tract (LVOT) can be narrowed depending on the shape of the ventricle and the mitral valve. This narrowing can cause obstruction of the outflow tract and subsequently cause mitral valve insufficiency if the basal septum and anterior leaflet of the mitral valve juxtapose in proximity. This creates a pressure gradient across the outflow tract, which leads to obstructive flow to progressive compensatory hypertrophy, which then in turn leads to further narrowing of the outflow tract and worsening of the pressure gradient. The Venturi effect occurs due to increased blood velocity across the narrowed outflow tract during systole and pulls the anterior leaflet of the mitral valve into the outflow tract and at this point causes mechanical obstruction of the LVOT and mitral valve.

ADDITIONAL READINGS

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish J, Young WL. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2010: Chapter 60.

87. ANSWER: E

Low-molecular-weight fractions of heparin are mediated by antithrombin III. The most widely used low-molecular-weight heparin in the United States is enoxaparin. Available agents include certoparin, dalteparin, danaparoid, enoxaparin, reviparin, and tinzaparin. Efficacy differs for each agent. These agents have efficacy against factors IXa, Xa, and XIa. Monitoring is usually not required or performed, but if necessary, the anti-Xa level is the most appropriate test.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:236.

10.

THORACIC ANESTHESIA

William Edward Corcoran, MD, and John Pawlowski, MD, PhD

1. A 56-year-old with a 60 pack-year smoking history presents for surgery with the following lab and pulmonary function test (PFT) results: ABG pH 7.39, $Paco_2$ 45 mm Hg, Pao_2 77 mm Hg, $FEF_{25-75\%}$ 1.69 LPS, FEV_1 58% predicted, FRC 141% predicted, DLCO 59%. This is most consistent with which of the following diagnoses?

A. Emphysema
B. Asthma
C. Chronic bronchitis
D. Acute pneumonitis
E. Asbestosis

2. In a patient in whom one-lung ventilation is not possible, apneic oxygenation is provided. Following 10 minutes of apnea, the Pco_2 would be expected to increase by what amount?

A. 3–12 mm Hg
B. 23–32 mm Hg
C. 33–42 mm Hg
D. 43–52 mm Hg
E. 53–62 mm Hg

3. Which of the following patients with an anterior mediastinal mass cannot safely be given general anesthesia?

A. Moderately symptomatic child with a CT tracheobronchial diameter more than 50% of normal
B. Mildly symptomatic adult with a CT tracheobronchial diameter less than 50% of normal
C. Mildly symptomatic child with a CT tracheobronchial diameter less than 50% of normal
D. Asymptomatic child with CT tracheobronchial diameter more than 50% of normal
E. PFT result indicative of an exacerbation of a variable intrathoracic obstructive pattern when supine

4. Which of the following is consistent with the characteristics of tracheomalacia?

A. Normal FEV_1
B. Flow-volume loop with flattened inspiration, and normal expiration
C. Decreased FIV_1
D. On expiration pleural pressure is greater than airway pressure, resulting in airway collapse and worsening obstruction.
E. On inspiration, atmospheric pressure is greater than airway pressure, resulting in airway collapse and worsening obstruction.

5. Which of the following medications, when administered alone to a patient with an aortic dissection, can increase the risk of propagation of the dissection?

A. Esmolol
B. Nitroprusside
C. Trimethaphan
D. Labetalol
E. Propranolol

6. Which of the following interventions in a patient with a type A aortic dissection with hemopericardium is least likely to be associated with rapid decompensation?

A. Esmolol bolus of 10 mg followed by infusion at 25 mcg/kg/min
B. Percutaneous pericardiocentesis
C. Immediate sternotomy with pericardial opening and relief of cardiac tamponade
D. Labetalol IV bolus of 20 mg followed by infusion at 25 mg/min
E. Diltiazem 10 mg/hr IV

7. Which of the following PFT results are most consistent with an individual with end-stage liver disease and severe ascites?

A. FVC 2.9 L (83%), FEV_1 1.8 L (60%), FEV_1/FVC 61%, $FEF_{25–75\%}$ 0.9 LPS (23%), TLC 4.9 L (100%), DLCO 122%
B. FVC 3.5 L (95%), FEV_1 2.8 L (95%), FEV_1/FVC 80%, $FEF_{25–75\%}$ 2.0 LPS (55%), TLC 6.3 L (99%), DLCO 44%
C. FVC 1.2 L (31%), FEV_1 1.0 L (33%), FEV_1/FVC 85%, $FEF_{25–75\%}$ 1.2 LPS (29%), TLC 2.7 L (50%), DLCO 144%
D. FVC 4.8 L (99%). FEV_1 3.8 L (99%), FEV_1/FVC 76%, $FEF_{25–75\%}$ 4.8 LPS (99%), TLC 6.4 L (99%), DLCO 100%
E. FVC 3.1 L (73%), FEV1 0.7 L (23%), FEV_1/FVC 25%, $FEF_{25–75\%}$ 0.2 LPS (6%), TLC 9.7L (150%), DLCO 19%

8. On postoperative day 2 following right lower lobectomy, an intensive care unit patient develops sudden dyspnea and hypotension and expectorates large amounts of serosanguineous sputum. On examination, the patient has markedly decreased breath sounds on the right. After endotracheal intubation, oxygen saturation decreases and it is not possible to maintain adequate tidal volumes. What is the most appropriate next intervention?

A. Increase PEEP.
B. Insert a chest tube.
C. Increase tidal volume.
D. Insert double-lumen tube with lung isolation of the source of the sputum.
E. Increase the inspiratory time.

9. Which of the following is NOT an absolute indication for one-lung ventilation?

A. Massive hemorrhage
B. VATS
C. Bronchopleural fistula
D. Right middle lobectomy
E. Unilateral lung lavage

10. A right-sided double-lumen tube (DLT) is placed and both the bronchial and tracheal cuffs are inflated. Ventilation is not possible through the tracheal lumen. What can be done to improve ventilation?

A. Advance the tube further into the right mainstem bronchus.
B. Reduce the pressure within the bronchial cuff.
C. Perform a needle thoracostomy to the right lung.
D. Withdraw the tube from the left bronchus and insert into the right bronchus.
E. Reposition the bronchial cuff so as not to occlude the right upper lobe bronchus.

11. Following intubation with a left double-lumen tube, placement is verified after cuff inflation. The endobronchial lumen is clamped and breath sounds are heard only on the left. Where is the distal end of the tube located?

A. Right mainstem
B. Left mainstem
C. In too far on right
D. In too far on left
E. Trachea

12. Left double-lumen tubes are preferable to right double-lumen tubes for both left- and right-sided procedures for which of the following reasons?

A. Increased rigidity of the left mainstem bronchus
B. The angle of the right mainstem bronchus impairs proper placement.
C. The distance from the upper lobe bronchus to the carina is greater on the left than the right.
D. The left main bronchus is larger.
E. Placement on the right is prone to advancement into the bronchus intermedius.

13. Which of the following factors is inversely proportional to the degree of turbulent flow?

A. Linear velocity
B. Diameter
C. Gas viscosity
D. Gas density
E. Reynolds number

14. A child presents to the emergency department with a history of the sudden onset of cough and choking, which has resolved prior to admission. The patient currently complains of an occasional cough, but is in no significant distress. Chest x-ray demonstrates hyperinflation of the right lung and mediastinal shift to the left. Which of the following physical examination findings would be most consistent with this patient's condition?

A. Absent breath sounds on the right
B. Absent breath sounds on the left
C. Wheezing on the right
D. Wheezing on the left
E. Stridor

15. Which of the following conditions increases FRC?

A. Idiopathic pulmonary fibrosis
B. Vasculitis
C. Pneumoconiosis
D. Chronic obstructive pulmonary disease (COPD)
E. Granulomatosis

16. A patient presents with flow-volume loops depicting flattened inspiration and normal expiration. This is consistent with which of the following diagnoses?

A. Tracheomalacia
b. Vocal cord paralysis
C. Tracheal stenosis
D. Tracheal tumor
E. External compression of a trachea by a mediastinal mass

17. Drugs that impair hypoxic pulmonary vasoconstriction (HPV) include

A. Isoflurane
B. Atropine
C. Spinal anesthesia
D. Aspirin
E. Almitrine

18. A 22-year-old patient is undergoing one-lung ventilation in the thoracic intensive care unit following left lung resection surgery and begins to desaturate. Which of the following interventions will likely worsen shunt in this patient?

A. Hypercapnia
B. Hyperthermia
C. Right lateral recumbent position
D. Increased left atrial pressure
E. Acidosis

19. Which of the following regional anesthetic blocks results in the highest blood level of local anesthetics per volume injected of any block in the body?

A. Paravertebral
B. Epidural
C. Superficial cervical plexus
D. Spinal
E. Intercostal

20. Which of the following assessments of respiratory function are the most indicative of postoperative adverse outcomes following lung resection?

A. Predicted postoperative FEV_1 less than 40%
B. Maximal oxygen consumption (VO_{2max}) less than 15 mL/kg/min
C. Preoperative DLCO 18 mL/min per mm Hg
D. PaO_2 less than 60 mm Hg
E. $PaCO_2$ more than 45 mm Hg

21. Which of the following values, assuming a 44% blood flow to the healthy lung determined by radioisotope scanning, indicates the greatest operative risk?

A. FEV_1 1.8 L
B. FEV_1/FVC 50% of predicted
C. Maximum breathing capacity 50% of predicted
D. Maximum VO_{2max} 12 mL/kg/min
E. PaO_2 50 mm Hg

22. Noncardiogenic reperfusion pulmonary edema during single-lung transplant is a result of which of the following mechanisms?

A. Release of free radicals and inflammatory cytokines
B. Transfused biologically active lysophosphatidylcholine that primes neutrophils and degrades cell membranes
C. Decreased compliance of the transplanted lung
D. Passively transfused antibodies that attach HLA antigens and agglutinins lodge in the pulmonary vasculature
E. Preferential perfusion of the transplanted lung

23. Which of the following scenarios results in an increase in compliance of the dependent lung when moving from the supine to the lateral decubitus position?

A. Positive-pressure ventilation, open pneumothorax, anesthetized
B. Spontaneous ventilation, open pneumothorax, anesthetized
C. Spontaneous ventilation, closed chest, anesthetized
D. Spontaneous ventilation, closed chest, awake state
E. Positive-pressure ventilation, closed chest, anesthetized

24. Which of the following is an absolute indication for one-lung ventilation?

A. Minimally invasive cardiac surgery
B. Upper lobectomy
C. Bronchopleural fistula
D. Pneumonectomy
E. Thoracic artery aneurysm repair

25. Which of the following factors is the LEAST likely to predict desaturation during one-lung ventilation?

A. Right-sided thoracotomy
B. Supine position during one-lung ventilation

C. Restrictive lung disease
D. Preoperative PFTs indicative of severe COPD
E. High percentage of ventilation or perfusion to the operative lung on preoperative V/Q scan

26. Following 10 minutes of single-lung ventilation for a pneumonectomy, the patient's oxygen saturation begins to decrease from 100% to 79% on a FiO_2 of 100%. The most appropriate intervention would be which of the following?

A. Change from volatile anesthetic to total intravenous anesthetic.
B. Reinflate deflated lung.
C. Apply continuous positive airway pressure (CPAP) to the deflated lung.
D. Increase positive end-expiratory pressure (PEEP) to nonoperative lung.
E. Recruit ventilated lung.

27. Which of the following maneuvers is the most effective means of increasing PaO_2 during one-lung ventilation?

A. Increasing the inspiratory flow rate
B. Applying positive end-expiratory pressure (PEEP) to the dependent lung
C. Increasing the ventilatory rate
D. Increasing the tidal volume
E. Applying continuous positive airway pressure (CPAP) to the nondependent lung

28. Which of the following criteria is the most predictive of successful weaning from the ventilator?

A. Respiratory compliance = 33 mL/cm H_2O
B. F/Vt less than 100 breaths/min/L
C. $PAO_2/PaO_2 = 0.35$
D. Maximal inspiratory pressure of −30 cm H_2O
E. Minute ventilation more than 10 LPM

29. Prior to thoracotomy surgery, a patient's PFT results reveal a decreased RV, a decreased VC, and an increased FEV_1/FVC. These results are most consistent with which of the following diagnoses?

A. Cystic fibrosis
B. Sarcoidosis
C. Bronchiolitis
D. Bronchiectasis
E. Asthma

30. Which of the following PFT results is most consistent with an individual with severe sarcoidosis?

A. FVC 2.9 L (83%), FEV_1 1.8 L (60%), FEV_1/FVC (61%), $FEF_{25–75\%}$ 0.9 LPS (23%), TLC 4.9 L (100%), DLCO 122%
B. FVC 4.4 L (78%), FEV_1 4.9 L (72%), FEV_1/FVC (94%), $FEF_{25–75\%}$ 4.5 LPS (95%), TLC 5.3 L (79%), DLCO 44%
C. FVC 1.2 L (31%), FEV_1 1.0 L (33%), FEV_1/FVC (85%), $FEF_{25–75\%}$ 1.2 LPS (29%), TLC 2.7 L (50%), DLCO 144%
D. FVC 4.8 L (99%). FEV_1 3.8 L (99%), FEV_1/FVC (76%), $FEF_{25–75\%}$ 4.8 LPS (99%), TLC 6.4 L (99%), DLCO 100%
E. FVC 3.1 L (73%), FEV_1 0.7 L (23%), FEV_1/FVC (25%), $FEF_{25–75\%}$ 0.2 LPS (6%), TLC 9.7L (150%), DLCO 19%

31. Anterior spinal artery syndrome following thoracic aneurysm surgery is characterized by which of the following deficits?

A. Loss of vibration sense and proprioception
B. Muscle flaccidity, hyporeflexia, gait ataxia, and paresthesias
C. Loss of tendon reflex, and loss of pain and temperature sensation in one or two dermatome levels
D. Loss of motor function and pinprick sensation with urinary incontinence
E. Sphincter dysfunction with flaccid paralysis of the bladder and rectum, impotence, and saddle anesthesia

32. In the management of subglottic stenosis, helium–oxygen mixtures (heliox) reduce airway resistance due to which of the following characteristics?

A. Low viscosity
B. High density
C. Low viscosity/density
D. Low density/viscosity
E. High density/viscosity

33. The artery of Adamkiewicz most frequently originates between which of the following levels?

A. T1–T4
B. T5–T8
C. T9–T12
D. L1–L2
E. L3–L5

34. Following a Nissen fundoplication for severe gastroesophageal reflux disease (GERD), a patient is being monitored in the intensive care unit. On postoperative day 3 the patient is continuing to have an unusually large serosanguineous output from his chest tube. The patient is otherwise stable with no further complaints. Testing of the fluid reveals an exudative effusion with dark staining

with Sudan R. Which of the following is the most likely complication?

A. Esophageal perforation
B. Septic pericarditis
C. Fluid overload
D. Thoracic duct injury
E. Splenic injury

35. For an awake intubation, the internal branch of the superior laryngeal nerve is blocked by injection of local anesthetic into a closed space. Which of the following structures does NOT enclose this space?

A. Hyoid bone
B. Cricothyroid membrane
C. Thyroid cartilage
D. Thyrohyoid membrane
E. Laryngeal mucosa

36. By what mechanism does inhaled nitric oxide improve oxygenation in reperfusion injury after lung transplantation?

A. Free radical superoxide scavenging
B. Diuresis
C. Immunosuppression
D. Improved V/Q matching
E. Improved pulmonary compliance

37. Which of the following modes of ventilation delays liberation from the ventilator?

A. ACV
B. SIMV
C. PSV
D. APRV
E. PAV

38. Which of the following lung disorders result in hypoxemia primarily due to V/Q mismatch?

A. Atelectasis
B. Pulmonary edema
C. Acute respiratory distress syndrome
D. Emphysema
E. Pneumonia

39. A patient with emphysema is anesthetized for lung reduction surgery. Tidal volume is 400 mL and end-tidal CO_2 is 33 mm Hg. ABG results are as follows: pH 7.35, $PaCO_2$ 52 mm Hg, PaO_2 277 mm Hg. Calculate the patient's VD/VT ratio.

A. 14%
B. 29%
C. 37%
D. 58%
E. 63%

40. Which of the following factors decreases dead space?

A. Supine posture
B. Emphysema
C. Anticholinergic drugs
D. Neck extension
E. Hypotension

41. Which of the following is an advantage of pressure-limited ventilation versus volume-limited ventilation?

A. Decreased mortality
B. Improved oxygenation
C. Decreased work of breathing
D. Ensures a minimum minute ventilation
E. Allows less alveolar overdistention

42. Which of the following risk factors is the strongest predictor of postoperative pulmonary dysfunction?

A. Dyspnea
B. Smoking
C. Obesity
D. Age greater than 60 years
E. General anesthesia greater than 3 hours

43. Which of the following pulmonary function guidelines indicates an increased risk of morbidity and mortality from lung resection?

A. PaO_2 less than 70 mm Hg
B. RV/TLC more than 50%
C. FEV_1 less than 60% predicted
D. MVV more than 50% predicted
E. FVC less than 70% predicted

44. Which of the following is LEAST likely to result in hypoxia during one-lung ventilation?

A. Nondependent lung vasodilation due to propofol infusion
B. Core temperature decrease from 40 to 30 degrees
C. FiO_2 decrease from 1.0 to 0.5
D. Positioning devices (rolls, pads, chest supports)
E. Prolonged lateral decubitus position

45. Which of the following bronchodilators has the least beta-2 activity?

A. Albuterol
B. Epinephrine
C. Salmeterol

D. Terbutaline
E. Pirbuterol

46. Which of the following is the most common complication of mediastinoscopy?

A. Pneumothorax
B. Phrenic nerve injury
C. Recurrent nerve injury
D. Hemorrhage
E. Infection

47. Which of the following is NOT a reason that airway pressure-release ventilation is potentially superior to conventional ventilation?

A. Promotes alveolar recruitment
B. Improves the Pa_{O_2}/Fi_{O_2} ratio
C. Decreases mean airway pressures
D. Decreases peak airway pressures
E. Decreases amount of sedation required

48. Which one of the following characteristics differentiates intermittent mandatory ventilation (IMV) from assist control (AC)?

A. IMV provides a minimal minute ventilation with a set respiratory rate and tidal volume.
B. IMV does not allow the patient to over-breathe the ventilator.
C. IMV autoregulates the inspiratory time to generate a smaller rise in plateau pressures.
D. IMV increases patient–ventilator synchrony.
E. IMV allows patients to increase minute ventilation by spontaneous breathing, rather than with patient-initiated ventilator breaths.

49. Which of the following interventions is implemented to increase the work of breathing?

A. Use flow triggering.
B. Increase tidal volume.
C. Increase flow rate.
D. Initiate pressure-support ventilation.
E. Decrease pressure-support trigger sensitivity.

50. Performance of needle decompression at the fifth intercostal space in the midaxillary line (MAL) instead of the third intercostal space at the midclavicular line (MCL) increases which of the following risks?

A. Treatment failure
B. Life-threatening hemorrhage
C. Pneumonia
D. Lung damage
E. Atelectasis

51. Evidence of which one of the following findings of tension pneumothorax is consistently seen only in ventilated patients and warrants immediate needle decompression?

A. Great vessel compression
B. Mediastinal shift
C. Chest pain
D. Tachycardia
E. Contralateral hypermobility

52. Which of the following ventilatory strategies is NOT responsible for worsening shunt during one-lung ventilation?

A. Dependent lung PEEP
B. Dependent lung hyperventilation
C. Dependent lung Fi_{O_2} of 0.5
D. Dependent lung Vt 6 to 8 cc/kg
E. Nondependent lung CPAP

53. Which of the following correctly describes a strategy by which ventilator settings are adjusted during one-lung ventilation?

A. Respiratory rate is titrated to maintain physiologic Pa_{CO_2} at 40 mm Hg.
B. Tidal volumes are kept lower than 15 mL/kg to prevent nondependent-lung HPV.
C. Ideal tidal volume is 10 to 12 mL/kg to prevent atelectasis and shunt.
D. Fi_{O_2} is titrated to the lowest level tolerated to avoid absorption atelectasis and oxygen toxicity.
E. Minute ventilation must be increased with the conversion to one-lung ventilation to maintain normocapnia due to V/Q mismatch.

54. A PEEP setting of 5 cm H_2O is a reasonable initial ventilator setting in all but which of the following clinical scenarios?

A. Congestive heart failure
B. Acute respiratory distress syndrome
C. Acute-on-chronic respiratory failure
D. Restrictive lung disease
E. Drug overdose

55. Which of the following branches of the intercostal nerve is NOT blocked by an intercostal nerve block, making the use of this method inadequate for certain thoracotomy incisions?

A. Posterior cutaneous branch
B. Posterior lateral cutaneous branch
C. Anterior lateral cutaneous branch

D. Anterior cutaneous branch
E. Muscular branches

56. Which of the following methods of thoracotomy pain management is associated with a significant incidence of paresthesias and post thoracotomy pain syndrome?

A. Intercostal nerve block
B. Interpleural regional analgesia
C. Transcutaneous electrical nerve stimulation
D. Cryoanalgesia
E. Intrathecal analgesia

57. To improve thoracic epidural analgesia, clonidine is added to a patient's epidural infusion. Which of the following mechanisms explains the mechanism by which clonidine improves epidural analgesia?

A. Opening potassium channels
B. Blocking sodium channels
C. Preventing calcium influx
D. NMDA receptor antagonism
E. Reducing vascular absorption

58. Which of the following adverse events is the most common following unilateral paravertebral nerve block?

A. Failure of the nerve block
B. Pneumothorax
C. Skin hematoma
D. Vascular puncture
E. Pleural puncture

59. Which of the following is true regarding respiratory physiology after lung transplantation?

A. Airway reactivity is increased.
B. Mucociliary clearance is unchanged.
C. HPV is unaffected.
D. Lymphatic drainage is intact.
E. PA pressures are not immediately normalized in individuals with pulmonary hypertension.

60. An 18-year-old boy with scoliosis is undergoing preoperative testing in preparation for spinal fusion. Which of the following is most predictive of the need for postoperative ventilation?

A. Cobb angle of 40 degrees
B. FEV_1 of 2.4 L (60% predicted)
C. Involvement of high anterior thoracic levels requiring one-lung ventilation
D. Vital capacity 40% predicted
E. Anterior spinal fusion

61. Which of the following is the most appropriate next test for the patient with an anterior mediastinal mass, a fixed pattern on flow-volume loops (FVL), and severe tracheal distortion on chest CT?

A. Upright and supine spirometry
B. Chest MRI
C. Flexible fiberoptic bronchoscopy
D. Transthoracic echocardiogram
E. Barium contrast esophagram

62. During confirmation of appropriate placement of a left-sided endobronchial tube, verification of the right upper lobe bronchus entails visualization of which of the following?

A. Apical, anterior, and posterior bronchi
B. Medial and lateral segmental bronchi
C. Superior, medial basal, anterior basal, lateral basal, and posterior basal bronchi
D. Apical posterior, anterior, superior, and inferior bronchi
E. Superior anterior basal, lateral basal, and posterior basal bronchi

63. Which of the following risk factors is the LEAST likely to increase the risk of barotrauma?

A. Asthma
B. Chronic interstitial lung disease
C. Previous ARDS
D. Aspiration
E. ARDS developing during mechanical ventilation

64. Intraoperatively, following induction for a patient with COPD, the patient is noted to have elevated peak airway pressures. An elevation in which of the following is most likely to indicate that the patient would benefit from bronchodilator therapy?

A. Plateau pressure − total PEEP
B. Peak pressure − plateau pressure
C. Change in lung volume × elastance of the respiratory system
D. Change in lung volume/respiratory system static compliance
E. Peak pressure − elastic pressure − PEEP

65. Which of the following is LEAST likely to be a potential complication of ventilation using elevated airway pressures?

A. Pneumoperitoneum
B. Venous air embolus
C. Abdominal compartment syndrome

D. Periorbital edema
E. Increased physiologic shunt

66. During rigid bronchoscopy, ventilation is held. Which of the following is NOT an anticipated physiologic change resulting from the subsequent hypercapnia?

A. Decreased myocardial contractility
B. Increased cerebral blood flow
C. Decreased release of oxygen to tissues
D. Depressed diaphragmatic function
E. Increased brain levels of glutamine

67. Which of the following effects is NOT an expected result of the application of PEEP to a hypoxic patient?

A. Increased FRC
B. Increased tidal volume above closing capacity
C. Improved lung compliance
D. V/Q correction
E. Decreased dead space ventilation

68. For laryngobronchoscopy, high-frequency jet ventilation (HFJV) is chosen as the means of ventilation. Which of the following provides the most important basis for this mode of ventilation?

A. Beer-Lambert law
B. Bohr equation
C. Laplace law
D. Bernoulli principle
E. Pendelluft

69. Fifteen minutes after the initiation of HFJV, an ABG analysis is obtained, demonstrating hypercapnia. Which of the following is NOT an appropriate intervention?

A. Increase driving pressure by 5-psi increments.
B. Increase inspiratory time in 5% increments.
C. Increase frequency in increments of 10 breaths per minute.
D. Add PEEP in 5-cm H_2O increments.
E. Add conventional tidal volume breaths.

70. Which of the following characterizes the most dependent portion of the right lung during one-lung ventilation in the right lateral decubitus position?

A. $P_A > P_V > P_a$
B. $P_A > P_a > P_V$
C. $P_V > P_a > P_A$
D. $P_a > P_V > P_A$
E. $P_a > P_A > P_V$

71. During pneumonectomy with one-lung ventilation, the SpO_2 reading decreases to 80%, but the SvO_2 remains 70%. Which of the following is the most likely explanation?

A. Left-to-right shunt
B. High cardiac output
C. Elevated PaO_2
D. Decreased red cell mass
E. Carboxyhemoglobin

72. Which of the following methods of lung isolation with pneumonectomy has the lowest risk of providing poor lung isolation or surgical complication?

A. Left-sided DLT for a left pneumonectomy
B. Right bronchial blocker for right pneumonectomy
C. Right-sided DLT for left pneumonectomy
D. Left-sided DLT for a right pneumonectomy
E. Right-sided DLT for a right pneumonectomy

73. Following a motor vehicle collision, a decision is made to donate the victim's lungs for transplantation. Complicating the deceased donor's course is an elevated urine output as high as 1,000 mL/hour. In addition to fluid resuscitation, which of the following is the most appropriate management of this condition?

A. Desmopressin 1 U BID until organs are transplanted
B. Insulin 10-U bolus and start infusion to maintain glucose between 80 and 150 mg/dL
C. Carbamazepine 300 mg BID until organs are transplanted
D. Hydrochlorothiazide 25 mg BID until organs are transplanted
E. Vasopressin titration to keep urine output 100 to 200 mL per hour

74. Which of the following is the most common symptom of a pulmonary embolus in patients without preexisting cardiopulmonary disease?

A. Pleuritic pain
B. Dyspnea
C. Cough
D. Wheezing
E. Two-pillow orthopnea

75. Smoking cessation on the day before surgery results in which of the following effects?

A. Decreased postoperative respiratory complications
B. Decreased carboxyhemoglobin concentrations
C. Decreased need for postoperative ventilation
D. Decreased risk of postoperative arrhythmias
E. Decreased sputum volume

76. Which of the following does NOT occur following the removal of the aortic cross-clamp during thoracic aneurysm repair?

A. Release of embolizing thrombotic material
B. Myocardial depression
C. Increased renal blood flow
D. Decreased glomerular filtration rate (GFR)
E. Vasodilation

77. The most appropriate prevention of hypotension prior to removal of the aortic cross-clamp during thoracic aneurysm repair consists of which of the following?

A. Starting inotropic agents 10 minutes before removal of clamp
B. Volume loading with crystalloid or colloidal agents prior to clamp removal
C. Simultaneous vasopressor bolus during clamp removal
D. Reducing anesthetic agents to allow for sympathetic compensation
E. Transfusing to a hemoglobin of 10 mg/dL prior to clamp removal

78. Repair of which of the following thoracic aortic aneurysms (TAAs) results in the greatest risk of postoperative hepatic dysfunction and subsequent coagulopathy?

A. Type I
B. Type II
C. Type III
D. Type IV
E. Type V

79. Which of the following is NOT a risk factor for spinal cord injury after open TAA repair?

A. Type I and II TAAs
B. Emergent operation
C. Intercostal sacrifice
D. Cerebrospinal fluid (CSF) pressure less than 5 mm Hg
E. Intraoperative hypotension

80. The loss of blood supply to anterior spinal cord motor neurons during TAA repair can result in spinal cord infarction, manifested by postoperative paraplegia. Which of the following is NOT a blood supply contributor to the anterior spinal cord?

A. Anterior spinal artery
B. Posterior intercostal artery
C. Anterior segmental medullary artery
D. Deep cervical artery
E. Vertebral artery

81. Which of the following is NOT an effective strategy to prevent airway fires during laser airway surgery?

A. Decreasing fresh gas flows to less than 2 LPM
B. Replacing nitrous oxide with air or helium
C. Using wet sponges in the surgical field
D. Keeping inspired oxygen concentrations as low as possible
E. Limiting laser intensity and duration

82. During laser airway surgery a fire occurs in the airway. According to the ASA operating room airway fire algorithm, which of the following is the recommended initial management in the response sequence?

A. Extinguish fire with a CO_2 fire extinguisher.
B. Stop the flow of all airway gases.
C. Remove all drapes and flammable materials.
D. Pour saline or water into the patient's airway.
E. Remove the endotracheal tube.

83. Which of the following intravenous medications diminishes bronchospasm?

A. Propofol
B. Sodium thiopental
C. Midazolam
D. Etomidate
E. Fentanyl

84. Which of the following medications can treat bronchospasm through direct depression of smooth muscle contractility and inhibition of reflex neural pathways?

A. Ipratroprium
B. Desflurane
C. Zafirlukast
D. Sevoflurane
E. Theophylline

85. Pulmonary vascular resistance is directly proportional to which of the following?

A. MAP – CVP
B. CO
C. PAP – LAP
D. PCWP
E. SVR

86. Absence of alveolar gas plateau on capnography indicates which of the following?

A. Normal capnography
B. Severe COPD
C. Spontaneous respiratory effort

D. Exhausted CO_2 absorbent
E. Incompetent inspiratory valve

87. During one-lung ventilation with inadequate muscle relaxation the patient begins to breathe. The patient is hypercapnic, normoxic, and acidotic. Which of the following is LEAST likely to be responsible for stimulating alveolar ventilation in this patient?

A. Medullary chemoreceptors
B. Carotid bodies
C. Pneumotaxic area
D. Apneustic center
E. Expiratory area

88. While inducing general anesthesia for a tracheal resection, intubation by means of direct laryngoscopy fails with two attempts. According to the ASA Difficult Airway Algorithm, failure of intubation attempts after induction of general anesthesia, with inadequate face mask ventilation, should be followed by which of the following?

A. Invasive airway ventilation
B. Awaken patient
C. Emergency noninvasive airway ventilation
D. LMA placement attempt
E. Return to

spontaneous ventilation

89. Which of the following is changed during epidural anesthesia at midthoracic levels?

A. Lung volumes
B. Resting minute ventilation
C. Dead space
D. Ventilatory response to hypercapnia
E. Shunt fraction

90. Which of the following is most predictive of postoperative respiratory failure?

A. Emergency surgery
B. Thoracic surgery
C. History of COPD
D. Age > 70
E. Neurosurgery

91. Which of the following characteristics or conditions does NOT decrease FRC in a spontaneously breathing individual?

A. Supine positioning
B. Male versus female gender
C. Idiopathic pulmonary fibrosis
D. Obesity
E. Short stature

92. Which of the following statements regarding laryngospasm is CORRECT?

A. Preferred treatment is administration of 1 mg/kg of succinylcholine.
B. The vestibular folds are not affected.
C. Stimulation of the superior laryngeal nerve is responsible.
D. Laryngeal muscles are relatively insensitive to muscle relaxants.
E. The epiglottis is not affected.

93. A patient undergoing a palliative procedure for small cell lung cancer has been diagnosed with paraneoplastic Lambert-Eaton syndrome. Which of the following symptoms is UNLIKELY to be seen in this individual?

A. Autonomic dysfunction
B. Proximal limb weakness
C. Absent reflexes
D. Decremental responses on repetitive nerve stimulation
E. Muscle ache

94. During one-lung ventilation, hypercapnia is a less common complication than hypoxia primarily because of which of the following factors?

A. Amount of surface area available
B. Membrane thickness
C. Pressure difference of gas across the barrier
D. Molecular weight of the gas
E. Solubility of the gas

95. Thoracic aortic aneurysm repair is undertaken in a patient with significant cardiac disease. With a pulmonary artery catheter, the cardiac index is calculated at 1.9 L/min. ABG measurements show a P_{O2} of 100 mm Hg, SaO_2 is 97%, and Hgb is 10 g/dL. What is the oxygen delivery index for this patient (expressed in mL/min/m^2)?

A. 262
B. 142
C. 364
D. 568
E. 622

96. During one-lung ventilation the oxygen saturation decreases to 88%. ABG analysis shows PaO_2 60.0 mm Hg

and Hgb 14.0 g/dL. Assuming a cardiac output of 5.00 LPM, what is the oxygen delivery for this patient?

A. 16.3
B. 148
C. 160
D. 865
E. 1,600

97. During aortic aneurysm repair, with the patient on cardiopulmonary bypass, an ABG is obtained and analyzed at 37 degrees C; it reveals PaO_2 80 mm Hg. The patient's body temperature is 30 degrees C. What is the temperature-corrected PaO_2?

A. 27
B. 47
C. 70
D. 85
E. 97

98. A V_D/V_T of 0.4 to 0.9 corresponds to which of the following scenarios?

A. Normal lung
B. Pulmonary embolus
C. Atelectasis
D. One-lung ventilation
E. Pneumothorax

99. During one-lung ventilation, end-tidal capnography indicates a low expired CO_2, but ABG monitoring shows a markedly elevated CO_2. Which of the following could explain this discrepancy?

A. Pulmonary embolus
B. Elevated carboxyhemoglobin level
C. Hypervolemia
D. Condensation of water vapor in sample tubing
E. Exhausted CO_2 absorbent

100. The potential benefits of delaying a procedure for 24 hours for an individual who smokes include which of the following?

A. Decreased risk of perioperative myocardial infarction
B. Vasopressor effects of nicotine will have dissipated.
C. Reduced mortality risk
D. Improved pulmonary function
E. Reduced sputum production

101. A 56-year-old woman presents for a left thoracotomy and lobectomy to remove a bronchial tumor. Manipulation of the mass during the procedure elicits flushing, tachycardia, increased peak inspiratory pressures, and severe hypotension. Which of the following is the most appropriate intervention to manage this patient's hypotension?

A. Epinephrine
B. Calcium
C. Octreotide
D. Phenylephrine
E. Ephedrine

CHAPTER 10 ANSWERS

1. ANSWER: A

Emphysema is characterized by destruction of lung parenchyma with loss of alveolar radial traction, decreasing the area of effective gas exchange. **These patients tend to preserve arterial oxygen tension and do not retain CO_2 until late in the disease course.** This absence of significant changes is reflected in the ABG presented. This type of ABG result is in contrast to patients with chronic bronchitis, who tend toward decreased arterial oxygen tension and increased arterial carbon dioxide tensions. In long-term cigarette smokers, a low DLCO is typically due to emphysema. The DLCO decrease usually occurs after FEV_1 declines. The DLCO is typically higher than the percentage of predicted FEV_1. DLCO reductions imply impaired alveolar–capillary membrane gas transfer and may be due to abnormal V/Q ratios, alveolar–capillary membrane destruction, or short capillary transit times.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:559.

2. ANSWER: C

An alternative to one-lung ventilation is ***apneic oxygenation***. Adequate oxygenation can be maintained, but its use is limited to 10 to 20 minutes due to progressive respiratory acidosis. **During apnea, P_{CO_2} rises 6 mm Hg in the first minute followed by a rise of 3 to 4 mm Hg during each subsequent minute.**

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:599.

3. ANSWER: C

Anesthetic deaths in children with ***mediastinal masses*** are often the result of more compressible cartilaginous structures of the airway in children. All patients with mediastinal masses should undergo a CT of the trachea and chest. **Children with tracheobronchial compression greater than 50% on a CT scan cannot safely be given general anesthesia**. Other high-risk predictors of airway compromise in children with anterior mediastinal masses include severe symptoms, histologic diagnosis of lymphoma, superior vena cava syndrome, radiologic evidence of major vessel compression or displacement, or pericardial or pleural effusion.

ADDITIONAL READING

Slinger PD, Campos JH. Anesthesia for thoracic surgery. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009: 1874–1876.

4. ANSWER: D

Tracheomalacia results in an intrathoracic obstruction. Intrathoracic obstructions are characterized by an obstruction on exhalation during which pleural pressure exceeds airway pressure and the airway collapses. On inspiration, the airway pressure is greater than pleural pressure, decreasing airway obstruction. Consistent with this, the FIV_1 is normal, FEV_1 is reduced, and the flow volume loop demonstrates a normal inspiratory loop and a flattened expiratory loop. Figure 10.1 depicts tracheomalacia with a collapsing posterior wall occurring in an 11-year-old girl.

ADDITIONAL READING

Triantafillou AN, Kanellas S. Anesthesia for the surgical management of mediastinal mass lesions. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw-Hill; 2001:829.

5. ANSWER: B

Treatment of an ***aortic dissection*** usually includes nitroprusside and beta blockade (esmolol or labetalol). Beta blockade is necessary to decrease the rate of rise of aortic pressure and decrease shear forces. Use of nitroprusside alone without beta blockade may actually increase the aortic pressure rate of rise and increase the risk of propagation of the dissection.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:528.

6. ANSWER: E

All answer choices are appropriate interventions for a patient with an aortic dissection. Cardiac tamponade can complicates management choices A, B, C, & D. Cardiac

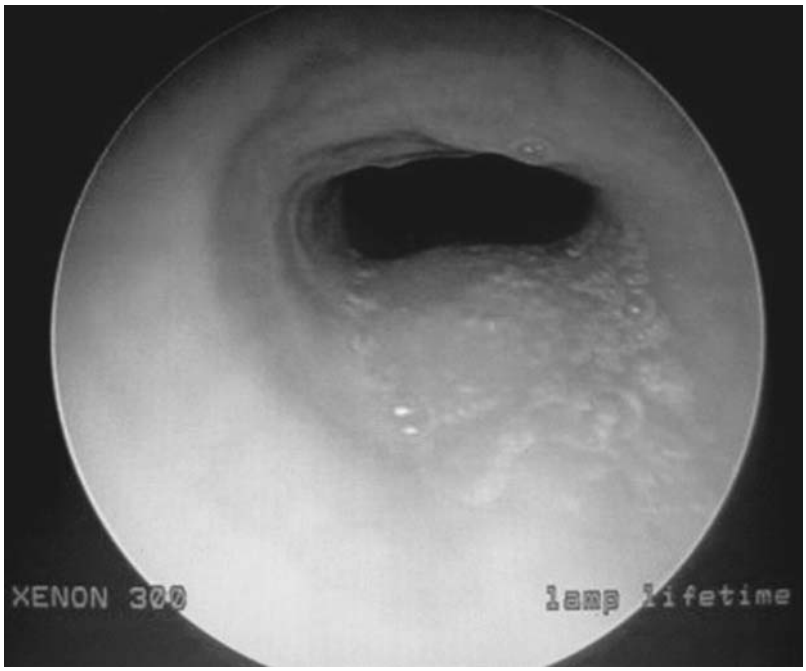


Figure 10.1 Bronchoscopic image showing tracheomalacia with a collapsing posterior wall.

SOURCE: Longnecker DE, Brown DL, Newman MF, Zapol WM. Anesthesiology: http://www.accessanesthesiology.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

tamponade with an aortic dissection should be managed with immediate sternotomy with preparations to institute cardiopulmonary bypass with femoral artery cannulation. Pericardial opening, however, can be followed by hypertension, causing aortic rupture. Efforts to drain this percutaneously can be used as a temporizing measure but are associated with a high mortality and are not recommended. Medical management in patients with cardiac tamponade must also be adjusted because excessive slowing of the heart rate or myocardial depression due to beta blockers can result in cardiogenic shock.

ADDITIONAL READING

Kaplan JA, ed. *Kaplan's Cardiac Anesthesia*, 5th ed., Philadelphia: Elsevier Saunders, 2006: 755.

7. ANSWER: C

The pulmonary function test (PFT) results in answer C would be consistent with a patient with a restrictive defect. FVC and FEV_1 are markedly reduced, but the ratio is normal (85%), so this is not an obstructive process. The TLC is low, making this a restrictive process. DLCO is normal, depicting normal diffusing capacity. An exclusively restrictive process is seen in severe ascites and neuromuscular diseases. Note that typical values for a man, age 40, 75 kg, 175 cm tall, are listed in answer D. The various measurements are described below:

FVC (forced vital capacity)—After a maximal inhalation, this is the volume of air that can be forcibly exhaled until no more can be expired. This value is reduced in obstructive disease due to difficulty exhaling, and reduced in restrictive disease due to smaller starting volumes.

FEV_1 (forced expiratory volume in 1 second)—This is the volume of air that can be forcibly exhaled from the lungs in the first second of a forced expiratory maneuver. This value is typically reduced in obstructive disease due to prolongation of exhalation. It is typically equally reduced with FVC in restrictive disease.

FEV_1/FVC (ratio of FEV_1 to FVC)—This indicates what percentage of the total FVC was expelled from the lungs during the first second of forced exhalation. Because the FEV_1 is reduced to a greater extent compared to FVC in obstructive disease, it is usually low in obstructive pathology. It is usually close to normal or elevated in restrictive disease.

$FEF_{25-75\%}$ (forced expiratory flow between 25% and 75% of forced vital capacity)—This measurement describes the amount of air expelled from the lungs during the middle half of the FVC test. This value is reduced in obstructive disease due to decreased expiratory patency.

TLC (total lung capacity)—The volume of air at the end of maximal inhalation. It is reduced in restrictive lung disease and increased in obstructive lung disease.

DLCO (diffusing capacity of the lung for carbon dioxide)—demonstrates gas uptake through the alveolar membrane and the capillaries. It is reduced in conditions with reduced effective alveolar surface area.

ADDITIONAL READING

Fauci AS, Braunwald E, Kasper DL, Hauser SL. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill Professional, 2008:1588, A-15.

8. ANSWER: B

This patient has a ***bronchopleural fistula***, which is a feared complication of multiple pulmonary conditions, such as infection, malignancy, or surgery (following pneumonectomy or lobectomy). Presentation is often variable. When acute, a life-threatening tension pneumothorax or asphyxial flooding can develop from pleural effusions entering the bronchial tree. When occurring in the first four postoperative days, it is usually secondary to a mechanical failure of stump closure and requires surgical re-exploration. Acute management requires the immediate insertion of a chest tube to manage the tension pneumothorax. During positive-pressure ventilation, air escapes through the fistula as a low-resistance path, resulting in loss of tidal volume. The goal in promoting healing is to decrease flow by limiting tidal volume, shortening the inspiratory time, limiting PEEP, and decreasing the respiratory rate.

ADDITIONAL READING

Lois M, Noppen M. Bronchopleural fistulas: an overview of the problem with special focus on endoscopic management. *Chest*. 2005;128(6):3955–65.

9. ANSWER: D

In practice, a double-lumen tube is commonly used for lobectomy or pneumonectomy. Upper lobectomy and pneumonectomy are relative high-priority indications due to desirability of surgical exposure and a quiet operative field. This, however, is only a relative indication, and middle or lower lobectomies are a relative low-priority indication.

Absolute indications for one-lung ventilation (OLV) include the following: massive bleeding and infection require lung isolation for protection of the uninvolved lung from contamination. Bronchopleural and bronchocutaneous fistulas should be isolated because they provide a low-resistance pathway for delivered tidal volumes. Giant unilateral bullae can rupture under positive pressure. Bronchopulmonary lavage requires unilateral lung protection to prevent drowning of the contralateral lung. Video-assisted thoracoscopy requires a collapsed lung for visualization of the surgical field.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:1042.

10. ANSWER: A

This scenario describes an endotracheal intubation with the endobronchial lumen of a double lumen tube. When a DLT is not inserted far enough, leaving the bronchial lumen above the carina, bilateral breath sounds can be heard when ventilating through the bronchial lumen. The tracheal lumen lies between the two cuffs and gas flow would be obstructed by the proximal (tracheal) and distal (bronchial) cuffs. Proper management would be performed by deflating the cuffs and advancing the tube into the desired mainstem bronchus (the right mainstem bronchus in this case). This type of scenario is depicted in Figure 10.2 using a left-sided tube, labeled "out too far."

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:1046.

11. ANSWER: A

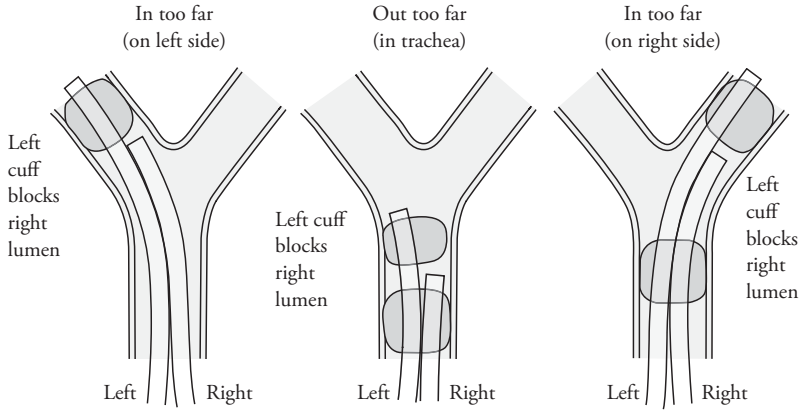
A double-lumen tube may be accidentally passed into the opposite of the desired mainstem bronchus, collapsing the lung opposite to that desired. In this scenario the left tube is placed into the right mainstem bronchus. Upon clamping the endobronchial lumen, which resides in the right lung, ventilation is provided only to the left side via the tracheal lumen, leading to breath sounds heard only on the left.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:1046.

12. ANSWER: C

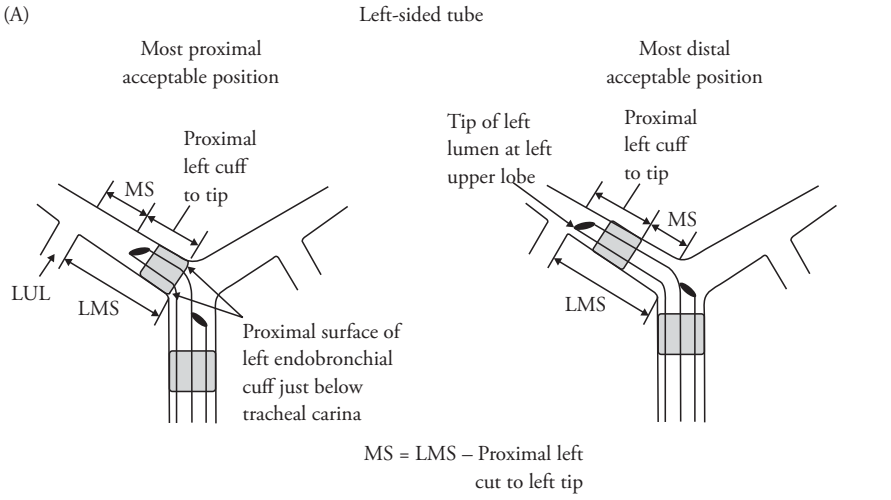
A major difference between the right and left main bronchi is that the orifice of the right upper lobe bronchus is 1 to 2.5 cm from the carina, versus the left upper lobe, which is about 5 cm distal to the carina. Because of anatomic variations, difficulties can often arise when trying to ventilate with right-sided tubes. Although right-sided tubes are designed for left thoracotomies, left-sided tubes are often used regardless of the operative side. Note in Figure 10.3 the larger margin of safety (MS) when using left-sided double-lumen tubes (A) versus right-sided tubes (B). LMS, Length of left mainstem



Procedure	Breath sounds heard		
Clamp right lumen (both cuffs inflated)	Left	Left and right	Right
Clamp right lumen (both cuffs inflated)	None or very ↓↓	None or very ↓↓	None or very ↓↓
Clamp right lumen (deflate left cuff)	Left	Left and right	Right

Figure 10.2 Auscultatory breath sounds of various double-lumen endotracheal tube positions.

SOURCE: Longnecker DE, Brown DL, Newman MF, Zapol WM. Anesthesiology: http://www.accessanesthesiology.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.



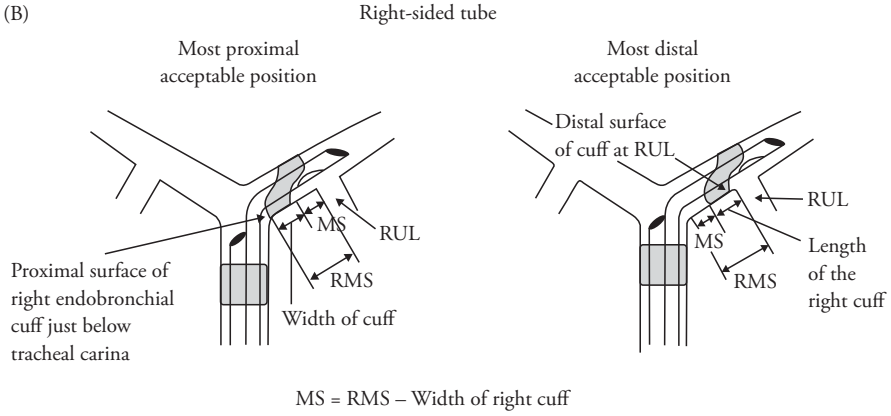


Figure 10.3 Correct position of left and right-sided double-lumen endotracheal tubes.

SOURCE: Longnecker DE, Brown DL, Newman MF, Zapol WM. Anesthesiology: http://www.accessanesthesiology.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

bronchus; LUL, left upper lobe; RMS, length of right mainstem bronchus; RUL, right upper lobe.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill, 2006:590.

13. ANSWER: C

Turbulent flow is characterized by random movement of gas molecules down air passages and occurs at high gas flows, at branch points or changes in airway diameter. It is predicted by the Reynolds number (high values of more than 2,000 produce turbulent flow). The Reynolds number is derived from the ratio of inertial to viscous forces and is proportional to the radius, velocity, and gas density, and inversely proportional to the gas viscosity.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill, 2006:546–548.

14. ANSWER: C

Aspiration of an object resulting in a partial obstruction typically leads to three stages of symptoms: (1) Initial event with violent coughing, choking and gagging; (2) Asymptomatic interval with lodging of the body with reflex fatigue; (3) Complications with obstruction, erosion, or infection. This patient presents with a foreign body in the right bronchus during an asymptomatic interval that is producing a partial obstruction. Air is going into the lung during inspiration but is barely coming out during expiration, producing a right-sided wheeze. Had this been a complete obstruction, creating absent breath sounds on the right, the patient would have a completely collapsed right lung with a mediastinal shift to the right.

ADDITIONAL READING

Behrman RE, Kliegman RM, Jenson HB, eds. Behrman: *Nelson Textbook of Pediatrics*, 17th ed. Philadelphia, PA: Saunders Elsevier, 2004:1411.

15. ANSWER: D

In patients with COPD, emphysema in particular, the loss of elastic lung tissue makes the lung demonstrate less elastic recoil and makes it more prone to being pulled by the outward force of the chest wall. This, in combination with chronic air trapping, results in an increased FRC. Fibrosing diseases such as idiopathic pulmonary fibrosis, pneumoconiosis, granulomatosis, vasculitis, and pulmonectomy all reduce FRC.

ADDITIONAL READING

Hedenstierna G. Respiratory physiology. In Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:363.

16. ANSWER: B

The description of a flow-volume loop with flattened inspiration and normal expiration is that of an extrathoracic obstruction such as vocal cord paralysis or croup. Tracheal tumor or tracheomalacia would result in an intrathoracic obstruction with normal inspiration and flattened expiration. Tracheal stenosis or external compression of the trachea by a mediastinal tumor results in a fixed obstruction with both inspiration and expiration flattened (Fig. 10.4).

ADDITIONAL READING

Triantafillou AN, Kanellas S. Anesthesia for the surgical management of mediastinal mass lesions. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw-Hill, 2001:829.

17. ANSWER: A

Primarily in response to a low alveolar P_{O2}, HPV decreases perfusion to hypoxic areas of the lung. It is inhibited by multiple mediators in the blood and lung parenchyma as well as multiple other factors. Many drugs affect HPV. It is enhanced by epidural and spinal anesthesia, cyclooxygenase inhibition (aspirin, indomethacin), and the respiratory stimulant almitrine. HPV can be inhibited by multiple vasodilating drugs, including sodium nitroprusside, calcium channel blockers, and halogenated anesthetics.

ADDITIONAL READING

Naeije R, Brimioulle S. Physiology in medicine: importance of hypoxic pulmonary vasoconstriction in maintaining arterial oxygenation during acute respiratory failure. *Critical Care*. 2001;5:67–71.

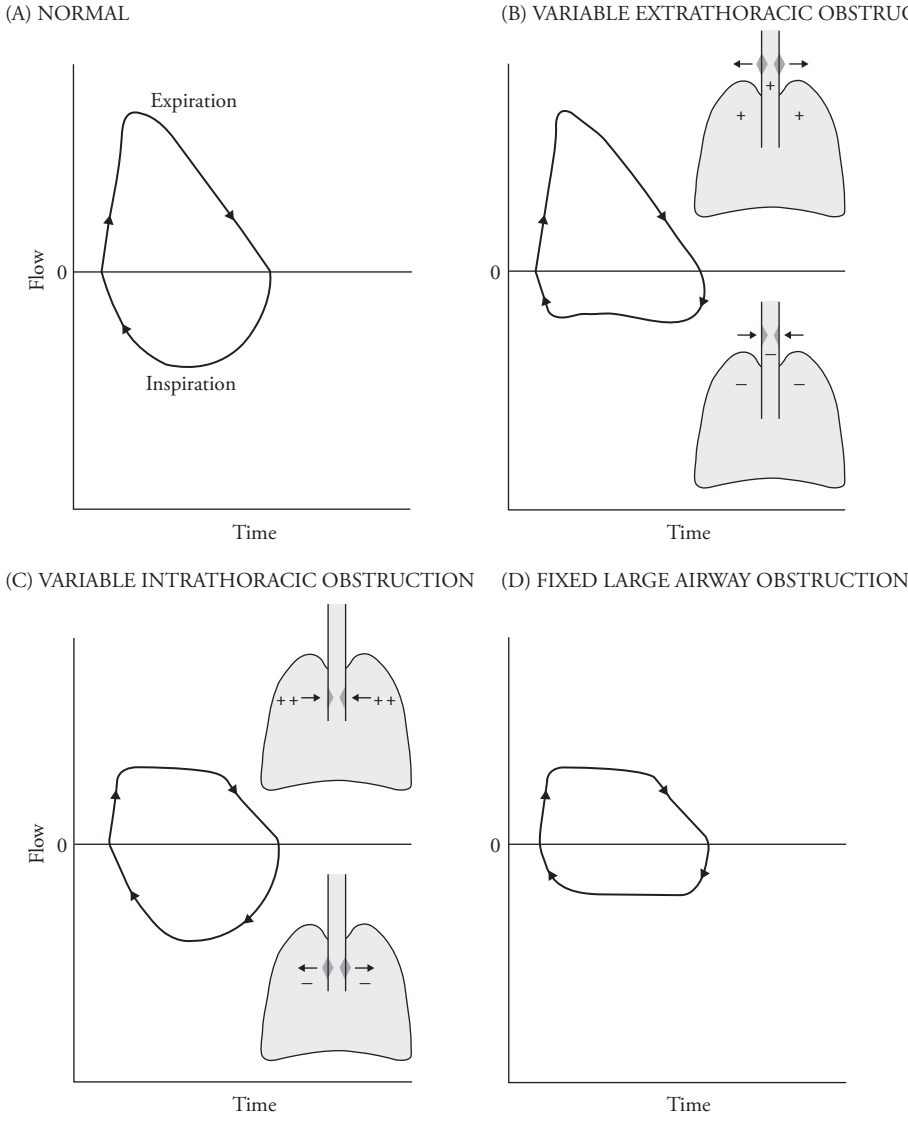


Figure 10.4 Flow-volume loops of variable and fixed airway obstructions.

SOURCE: Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. http://www.accessmedicine.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

18. ANSWER: D

Hypoxic pulmonary vasoconstriction (HPV) of the pulmonary arteries helps to improve V/Q matching by reducing perfusion of poorly oxygenated lung tissue, decreasing shunt. The poorly oxygenated lung tissue in this patient is the nonventilated lung. HPV is active between a P_AO_2 of 40 and 100 mm Hg in the adult and proportional to the degree of hypoxia. Low partial pressure of oxygen inhibits potassium currents, leading to membrane depolarization and calcium entry, which results in smooth muscle contraction. The primary stimulus for HPV appears to be the alveolar P_AO_2, with some influence by the mixed venous P_vO_2. Multiple physiologic variables have been demonstrated to inhibit HPV, which in our patient would worsen shunt. These include alkalosis, hypocapnia, hypothermia, and increased left atrial pressure. The answer choices of hypercapnia, hypertension, hyperthermia, and acidosis all contribute to HPV.

ADDITIONAL READING

Lohser J. Evidence based management of one-lung ventilation. *Anesthesiol Clin*. 2008;26(2):241–272.

19. ANSWER: E

Intercostal nerve blocks are commonly used perioperatively to supplement general anesthesia and for postoperative analgesia following thoracic and upper abdominal surgery.

They result in the highest blood levels of local anesthetic per volume injected of any block in the body.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill, 2006:353–354.

20. ANSWER: B

The VO_{2max} is the most useful predicator of post thoracotomy outcome. Few patients with a VO_{2max} greater than 20 mL/kg/min (which correlates to the ability to climb five flights of stairs) have respiratory complications, while the risk is unacceptably high in those with a preoperative VO_{2max} less than 15 mL/kg/min. The ability to climb two flights of stairs corresponds to a VO_{2max} of 12 mL/kg/min. The patient who cannot climb two flights of stairs is at very high risk of respiratory complications.

ADDITIONAL READING

Slinger PD, Campos JH. Anesthesia for thoracic surgery. In Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:1837.

21. ANSWER: A

For pneumonectomy operability, the most commonly used criterion is a predicted postoperative FEV_1 greater than 800 mL. The percentage of total pulmonary blood flow to each lung is assumed to be proportional to each lung's contribution to FEV_1 and is calculated by multiplying the percentage of blood flow to remaining lung by the total FEV_1 (Table 10.1).

Table 10.1 **PREOPERATIVE LABORATORY CRITERIA FOR PNEUMONECTOMY**

TEST	HIGH-RISK PATIENTS
Arterial blood gas	$PaCO_2$ > 45 mm Hg (on room air)
	PaO_2 < 50 mm Hg
FEV_1	<2 L
(Predicted postoperative FEV_1)	<0.8 L or <40% of predicted
FEV_1/FVC	<50% of predicted
Maximum breathing capacity	<50% of predicted
Maximum $\dot{V}O_2$	<10 mL/kg/min

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; $\dot{V}O_2$, oxygen consumption.

ADDITIONAL READING

Morgan GE Jr., Mikhail MS, Murray MJ. Chapter 24, Anesthesia for Thoracic Surgery. In Morgan GE Jr., Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill, 2006:595.

22. ANSWER: E

Patients with primary pulmonary hypertension who are receiving a single-lung transplant are at an increased risk of noncardiogenic reperfusion pulmonary edema. The transplanted lung has a significantly lower pulmonary vascular resistance than the native lung and is preferentially perfused. This results in unilateral pulmonary edema and respiratory failure.

ADDITIONAL READING

Rosenberg AL, Madhu R, Benedict PE. Anesthetic implications for lung transplantation. *Anesthesiol Clin North Am*. 2004;22:767–788.

23. ANSWER: D

During spontaneous ventilation in the awake state with a closed chest, the dependent lung is on a more favorable, steep part of the compliance curve. When positioned laterally, the dependent hemidiaphragm is pushed higher into the lungs by the abdominal contents. Contraction is more efficient as it assumes a higher position in the chest. During spontaneous ventilation, the diaphragm's ability to contract is maintained and allows an adequate distribution of tidal volume to the dependent lung. With general anesthesia induction, there is bilateral volume reduction with a decrease in FRC; however, the impact is more pronounced in the dependent lung due to compression from the abdomen and mediastinal structures. Both lungs are moved down the S-shaped compliance curve, with the lower lung in a less compliant position and the upper lung moved to the steeper, more favorable part of the compliance curve. Positive-pressure ventilation therefore favors the upper lung because of its better compliance.

In an open chest, the dependent lung is further compromised by a mediastinal shift into the dependent lung due to the negative pressure in the intact hemithorax versus the less negative pressure of the open hemithorax. The open side now has a dramatically reduced compliance. Paralysis further reinforces this with additional compression of the dependent lung by abdominal contents (Fig. 10.5).

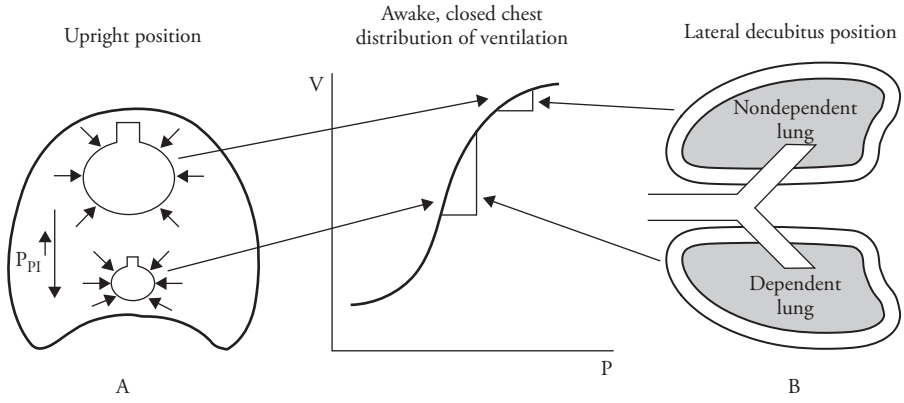


Figure 10.5 Lung compliance in upright and lateral decubitus position.

SOURCE: Longnecker DE, Brown DL, Newman MF, Zapol WM. Anesthesiology: http://www.accessanesthesiology.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:1040–1041.

24. ANSWER: C

Absolute indications for one-lung ventilation include those that could result in life-threatening complications, such as unilateral lavage, massive bleeding, or infection, which could lead to contamination of the opposite lung. Absolute indications also include pathology requiring control of distribution of ventilation. Examples are bronchopleural fistulas, which offer low-resistance pathways to tidal volume during positive-pressure ventilation; bullae, which could rupture under positive pressure; or major bronchial disruption or trauma. Video-assisted thoracoscopic surgery is also typically an absolute indication.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:1042–1043.

25. ANSWER: D

In the majority of cases it is possible to determine which patients are most at risk of desaturation during one-lung ventilation. Right-sided thoracotomy, supine position during one-lung ventilation, restrictive lung disease, and a low Pa_{O_2} during two-lung ventilation in the lateral position before one-lung ventilation all correlate with an increased risk of desaturation. A low Pa_{O_2} during two-lung ventilation in the lateral position before one-lung ventilation is the most significant indicator. The degree of obstructive lung disease correlates **inversely** with Pa_{O_2} during one-lung ventilation. Patients with more severe airflow limitation on their preoperative spirometry will tend to have a better Pa_{O_2} during one-lung ventilation than patients with normal spirometry. In patients at high risk of desaturation, the use of continuous positive airway pressure (CPAP) of 2 to 5 cm H_2O of oxygen to the nonventilated lung or positive end-expiratory pressure (PEEP) to the dependent lung, or both, is often an effective preventive measure.

ADDITIONAL READING

Slinger PD, Campos JH. Anesthesia for thoracic surgery. In Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:1830.

26. ANSWER: B

Severe hypoxemia indicated by a decline in Sp_{O_2} to less than 90% should prompt consideration of reinflating the deflated lung. Patients should not have to suffer prolonged hypoxemia, and a reduction to 79% warrants immediate reinflation. For less severe reductions, other methods should be considered because reinflation (or even CPAP to the deflated lung) will impair surgical access to the lung, particularly during thoracoscopic procedures. Mild hypoxemia should be managed by confirming the position of the lung isolation device, increasing the Fi_{O_2} toward 1.0, providing CPAP to the operative lung (after recruitment), considering reduction in vapor anesthetic and/or total intravenous anesthesia, and ensuring adequate oxygen-carrying capacity (hemoglobin). Lung derecruitment in the ventilated lung is common, easily reversed with recruitment maneuvers, and preventable with appropriate PEEP levels. Low mixed venous oxygen saturation secondary to low cardiac output is another frequent and easily treatable cause of desaturation.

ADDITIONAL READING

Lohser J. Evidence based management of one-lung ventilation. *Anesthesiol Clin*. 2008;26(2):241–272.

27. ANSWER: E

The single most effective maneuver to increase PaO_2 during one-lung ventilation is the application of CPAP to the nondependent lung. Applying CPAP of 5 to 10 cm H_2O after delivering a tidal volume to the nondependent lung allows oxygen uptake to occur by maintaining patency of alveoli. Application of larger amounts of CPAP (15 cm H_2O) is not beneficial and results in overdistention with hemodynamic effects.

Application of PEEP to the dependent lung may be preferable in certain thoracic procedures, such as thoracoscopic procedures, in which application of CPAP to the nondependent lung is not acceptable. This also provides benefit by increasing FRC and improving the V/Q relationship in the dependent lung.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:1052–1053.

28. ANSWER: B

Multiple objective parameters have been studied to predict weaning outcome in order to accurately identify patients ready to wean. As a screening test, a high sensitivity (low false-positive rate) with an acceptable high false-positive rate is desirable. Of the parameters of respiratory compliance, frequency/tidal volume ratio, arterial/alveolar oxygen tension ratio, maximal inspiratory pressure, and minute ventilation, the frequency/tidal volume ratio (also known as RSBI) has the most support. It is simple, quick, and safe and has been prospectively studied in multiple studies with a sensitivity as high as more than 90% in some studies. Flaws in the frequency/tidal volume ratio have been demonstrated, albeit negative studies to date have had methodological flaws. The other indicators listed have shown poor sensitivity and specificity and poor positive and negative predictive values in multiple prospective studies.

ADDITIONAL READINGS

Tanios MA, Nevins, ML, Hendra KP, et al. A randomized controlled trial of the role of weaning predictors in clinical decision making. *Crit Care Med*. 2006;34:2530.

Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med*. 1991;324:1445.

29. ANSWER: B

The hallmark of ***restrictive lung disease***, as seen in patients with sarcoidosis, idiopathic pulmonary fibrosis, pneumoconiosis, or interstitial lung disease, is a decrease in lung volumes such as RV and VC. These disorders can further be subdivided into parenchymal, like the examples listed above, versus extraparenchymal, seen in neuromuscular weakness and chest wall deformity. In pulmonary parenchymal disease RV is decreased, whereas in extraparenchymal disease the RV can be variable. Forced expiratory flow rates are also preserved in restrictive parenchymal disease and tend to be supranormal when compared to the FVC, resulting in an increased FEV_1/FVC ratio. Obstructive disease, as seen in cystic fibrosis, bronchiolitis, bronchiectasis, and asthma, will demonstrate a decreased FEV_1/FVC as well as increased RV.

ADDITIONAL READING

Fauci AS, Braunwald E, Kasper DL, Hauser SL. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill Professional, 2008:1588–1589.

30. ANSWER: B

Sarcoidosis is a chronic granulomatous disease, which in the vast majority of cases affects the lungs. In severe cases this can result in diffuse pulmonary infiltration and fibrosis. PFTs most often demonstrate restrictive disease, with decreased volumes and diffusion capacity. Approximately 5% of patients have airway involvement (lesions involving the epiglottis, aryepiglottic folds, or arytenoids) with airway narrowing and symptoms of dyspnea, throat pain, hoarseness, weak voice, or stridor. This can present as an obstructive pattern on PFTs. Mediastinal adenopathy can result in recurrent laryngeal neuropathy with subsequent vocal cord paralysis. The various measurements are described below:

FVC (forced vital capacity)—After a maximal inhalation, this is the volume of air that can be forcibly exhaled until no more can be expired. This value is reduced in obstructive disease due to difficulty exhaling, and reduced in restrictive disease due to smaller starting volumes.

FEV_1 (forced expiratory volume in 1 second)—This is the volume of air that can be forcibly exhaled from the lungs in the first second of a forced expiratory maneuver. This value is typically reduced in obstructive disease due to

prolongation of exhalation. It is typically equally reduced with FVC in restrictive disease.

***FEV_1/FVC (ratio of FEV_1 to FVC)*—**This indicates what percentage of the total FVC was expelled from the lungs during the first second of forced exhalation. Because the FEV_1 is reduced to a greater extent compared to FVC in obstructive disease, it is usually low in obstructive pathology. It is usually close to normal or elevated in restrictive disease.

***$FEF_{25-75\%}$*—**This measurement describes the amount of air expelled from the lungs during the middle half of the FVC test. This value is reduced in obstructive disease due to decreased expiratory patency.

***TLC*—**The volume of air at the end of maximum inhalation. It is reduced in restrictive lung disease and increased in obstructive lung disease.

***DLCO*—**The diffusing capacity for carbon dioxide. It demonstrates gas uptake through the alveolar membrane and the capillaries. It is reduced in conditions with reduced effective alveolar surface area.

ADDITIONAL READING

Fleisher LA, ed. *Anesthesia and Uncommon Diseases*, 5th ed. Phildapelphia, PA: Saunders Elsevier, 2006:138–139.

31. ANSWER: D

Spinal cord ischemia during aortic clamping can result in paraplegia, particularly in cases with cross-clamping periods longer than 30 minutes. The classic deficit is anterior spinal artery syndrome, damage to the area receiving blood supply by the anterior spinal artery (Fig. 10.6). The syndrome, also known as ventral cord syndrome, is due to damage to the tracts of the anterior two-thirds of the spinal cord (the corticospinal tracts, spinothalamic tracts, and descending autonomic tracts to the sacral centers for bladder control). Symptoms are unpredictable due to anatomic variations in spinal cord blood supply but are typically thought of as the loss of motor function (damage to corticospinal tracts) and loss of pinprick sensation (damage to spinothalamic tracts) with preservation of vibration and proprioception (preservation of the dorsal columns). Answer B describes dorsal column syndrome, symptoms in answer C are consistent with central cord syndrome, and answer E lists the symptoms found in conus medullaris syndrome.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill, 2006:530–531.

32. ANSWER: D

In cases of severe turbulent flow, such as is the case in airway obstruction, heliox is clinically useful due to its ability to increase laminar airflow. The degree of turbulent or laminar flow is predicted by the Reynolds number, described by the following equation:

$$\text{Reynolds number} = (\text{Density})(\text{Flow Velocity})(\text{Length})/\text{Viscosity}$$

Smaller Reynolds numbers are associated with more laminar flow and larger numbers are associated with more turbulent flow. As is evident from the equation, turbulent flow is proportional to density and inversely proportional to viscosity. Of the clinically used gasses, heliox has a significantly lower density-to-viscosity ratio. **Helium–oxygen mixtures decrease turbulent flow and decrease resistance**

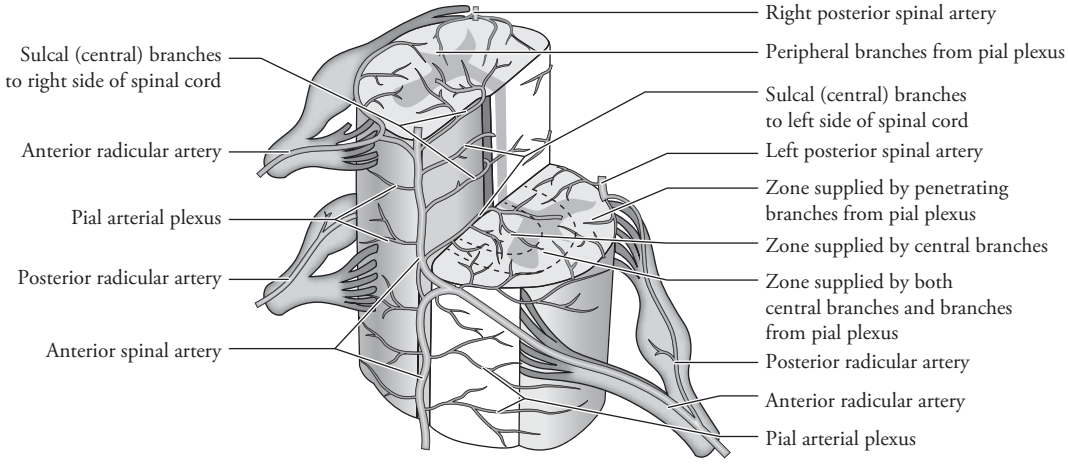


Figure 10.6 Arterial distribution of the spinal cord.

SOURCE: Netter FH. *Atlas of Human Anatomy*. 4th ed. Philadelphia: Saunders Elsevier; 2006: plate 172.

when turbulent flow is present by means of its lower density-to-viscosity ratio. It increases flow for any given pressure gradient or maintains flow for small pressure gradients.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:1219, 2360.

33. ANSWER: C

Paraplegia occurs in approximately 6% of thoracic aorta surgeries, presenting as an anterior spinal artery syndrome. This is usually due to interruption of spinal cord blood flow or prolonged hypoperfusion resulting in spinal cord ischemia. The lower part of the spinal cord is almost exclusively supplied by the artery of Adamkiewicz, which is variable in origin (Fig. 10.7). The origin is between T5 and T8 in 15% of people, between T9 and T12 in 75%, and between L1 and L2 in 10%.

ADDITIONAL READING

Schure A, Ellis J. Thoracic aortic aneurysm. *Complications in Anesthesia*. 2nd ed. 2007:387.

34. ANSWER: D

Chylothorax can occur after injury to the thoracic duct when performing antireflux procedures. This occurs during mobilization of the cardia or crural suture placement. The thoracic duct passes through the aortic hiatus from the abdomen to the lower chest. It then courses anterior to the spine between the aorta and the esophagus. Symptoms typically are prolonged serosanguineous drainage. Milky chyle is typically not present until the diet is liberalized and fat content increases. Diagnosis is with Sudan R staining, which stains the fat globules. It is not usually necessary to obtain cholesterol and triglyceride levels; however, the ratio of cholesterol to triglyceride is typically less than 1. Management is through a low-residue diet and chest tube drainage. If drainage persists after a week with more than 400 mL per 8-hour period, thoracic duct ligation is necessary.

ADDITIONAL READING

Yeo CJ, ed. *Shackelford's Surgery of the Alimentary Tract*. 6th ed. Philadelphia, PA: Saunders, 2007.

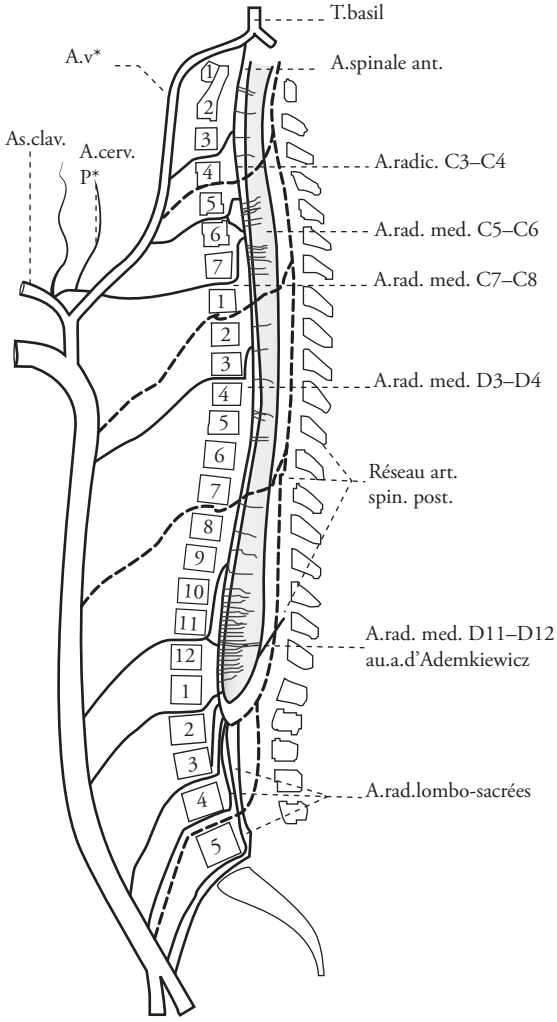


Figure 10.7 Anatomy of blood supply to the spinal cord.

SOURCE: Adapted from Djindjian R. Arteriography of the spinal cord. *Am J Roentgenol Radium Ther Nucl Med*. 1969;107(3):461–478.

35. ANSWER: B

The internal branch of the superior laryngeal nerve provides sensory innervation from the base of the tongue to the vocal cords, including the posterior surface of the epiglottis, the aryepiglottic fold, and the arytenoids. It is a branch of the vagus nerve, which branches into the superior laryngeal nerve at the level of the larynx. The superior laryngeal nerve divides into external and internal branches. The internal branch penetrates the thyrohyoid; the external branch penetrates and innervates the cricothyroid muscle. Within the thyrohyoid, the internal branch of the nerve lies within an enclosed space additionally bounded by the hyoid bone, the thyroid cartilage, and the laryngeal mucosa. As shown in Figure 10.8, a ⅝-in, 25-gauge needle is inserted in an anteroinferomedial direction until the lateral aspect of the greater cornu of the hyoid is contacted. If the needle is then walked downward toward the midline

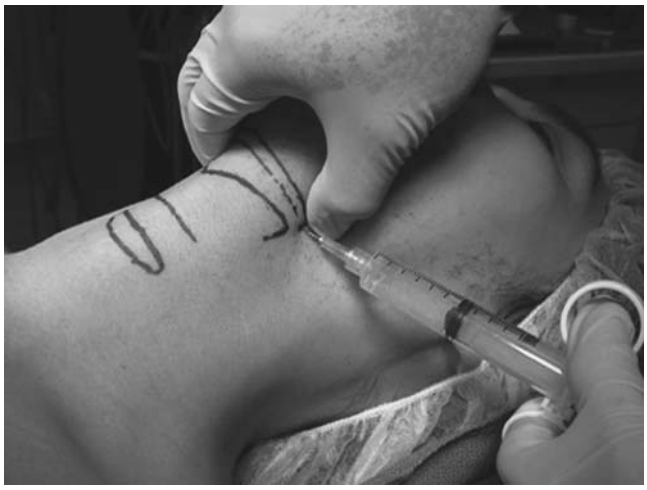


Figure 10.8 Photograph demonstrating the superior laryngeal nerve block.

(1 to 2 mm) off the inferior border of the greater cornu, the thyrohyoid membrane is pierced and the internal branch alone is blocked. Within this space 2 mL of 2% lidocaine is injected bilaterally to anesthetize this nerve, as depicted in Figure 10.8.

ADDITIONAL READINGS

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:1318.

Sutherland L, Misita D, Chapter 19, Regional & Topical Anesthesia for Endotracheal Intubation. In Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York: McGraw-Hill Professional, 2006

36. ANSWER: D

Reperfusion injury, also known as reimplantation injury or primary graft failure, typically occurs in the first 6 hours after transplantation. It is mild in most cases and is usually managed with hemodynamic monitoring, diuresis, and inotropes. In the 15% of cases that are severe, inhaled nitric oxide (iNO), differential lung ventilation, or extracorporeal membrane oxygenation (ECMO) may be necessary. iNO has been shown to improve pulmonary artery pressures and oxygenation in patients with reperfusion injury by delivering nitric oxide to ventilated lung segments only, resulting in selective ventilation and improved V/Q matching.

ADDITIONAL READING

Rosenberg AL, Madhu R, Benedict PE. Anesthetic implications for lung transplantation. *Anesthesiol Clin North Am*. 2004;22:767–788.

37. ANSWER: B

Multiple studies consistently demonstrate delayed liberation from the ventilator with the use of synchronized intermittent mandatory ventilation (SIMV) despite its frequent use for this purpose. It is likely that SIMV leads to respiratory muscle fatigue. This may be due to the reduction of airway pressure that is necessary to activate a demand valve and inadequate gas flow, which increases the work of breathing. Possibly, patient effort is increased due to the inability of the respiratory center to rapidly adapt to intermittent support. Of the various options, literature consistently supports PSV with declining amounts of pressure support as the optimal mode for liberation from the ventilator.

ADDITIONAL READING

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia: Saunders Elsevier; 2009:148–155.

38. ANSWER: D

In COPD, some areas of the lung are poorly ventilated due to obstruction, therefore underventilating them in relation to their perfusion. This is ***ventilation/perfusion (V/Q) mismatch***. This forces more air to other areas, over ventilating them compared to their perfusion. This degree of V/Q mismatch leads to the difficulty in removing CO_2 that is so often seen in these patients. Shunt is the primary mechanism for hypoxemia seen in atelectasis, pulmonary edema, acute respiratory distress syndrome, and pneumonia. Shunting is not seen in COPD without a coexistent complication, such as atelectasis or pneumonia.

ADDITIONAL READING

Hedenstierna G. Respiratory physiology. In Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:362, 374, 276.

39. ANSWER: C

Dead space (V_D) is the part of tidal volume not participating in gas exchange. This is composed of gases in nonrespiratory airways and nonperfused alveoli. V_D/V_T is normally 33% and is derived by the ***Bohr equation***:

$$V_D/V_T = (PaCO_2 - PeCO_2)/PaCO_2$$

Paco$_2$ is the alveolar Co_2 tension approximated by the arterial Co_2 tension. *Peco*$_2$ is the mixed expired Co_2 tension. In this case the calculated V_D/V_T using a $Paco_2$ of 52 and a $Peco_2$ of 33 is 37%.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:552.

40. ANSWER: A

Dead space (V_D) is the part of tidal volume not participating in gas exchange. This is composed of gases in nonrespiratory airways and nonperfused alveoli. Upright posture results in about 150 mL of anatomic dead space (2 mL/kg). This amount decreases when the patient is positioned supine. Many factors increase the amount of dead space, including neck extension, age, positive-pressure ventilation, anticholinergic drugs, decreases in pulmonary perfusion (e.g., pulmonary emboli or hypotension), and diseases such as emphysema.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:552.

41. ANSWER: E

Barotrauma is lung injury resulting from alveolar distention. Accumulating evidence suggests that this, by way of high-tidal-volume ventilation, is the more likely mechanism of alveolar injury than barotrauma. Pressure-limited/pressure-cycled ventilation provides a constant peak airway pressure (the sum of the inspiratory pressure and the applied PEEP), providing more homogeneous gas distribution with less regional alveolar overdistention, decreasing the risk of ventilator-induced volutrauma and lung injury.

ADDITIONAL READING

Prella M, Feihl F, Domenighetti G. Effects of short-term pressure-controlled ventilation on gas exchange, airway pressures, and gas distribution in patients with acute lung injury/ARDS: comparison with volume-controlled ventilation. *Chest*. 2002;122:1382.

42. ANSWER: A

Six risk factors increase the risk of postoperative pulmonary dysfunction, the most common postoperative complication:

1. Preexisting pulmonary disease
2. Thoracic or abdominal surgery
3. Smoking
4. Obesity
5. Age greater than 60 years
6. General anesthesia

The two strongest risk factors are location of surgery and a previous history of dyspnea, which correlates to the severity of preexisting pulmonary disease.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:572.

43. ANSWER: B

Mortality from lung resection is between 2% and 4% due to pulmonary embolism, empyema, bronchopleural fistula, respiratory failure, and pneumonia. An increased risk of complications can be predicted from the following pulmonary function guidelines:

- FVC less than 50% predicted
- FEV_1 less than 50% of FVC or 2 L
- MVV less than 50% predicted or 50 L per minute
- Diffusion capacity less than 50% predicted
- RV/TLC more than 50%
- $Paco_2$ more than 45 mm Hg
- Pao_2 less than 50 mm Hg

ADDITIONAL READING

Yao FF, ed. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:32–33.

44. ANSWER: A

Perfusion of the dependent, ventilated lung is largely due to gravitational effects and nondependent lung hypoxic pulmonary vasoconstriction (HPV); however, hypoxic compartments in the dependent lung can develop, decreasing Pao_2. In the lateral decubitus position mediastinal compression and positional effects due to rolls, pads, supports, etc., can decrease lung volume, decreasing the V/Q ratio and causing atelectasis. The lateral decubitus position can further worsen oxygenation by causing the transudation of fluid to the dependent lung. Preferential perfusion of the dependent

lung can also decrease with dependent lung vasoconstriction due to hypothermia or a decrease in dependent lung FiO_2. Nondependent lung vasodilation (loss of HPV) does not occur with intravenous anesthetics such as propofol.

ADDITIONAL READING

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:71–94.

45. ANSWER: B

Beta-2 sympathomimetic agents are the most useful bronchodilators. Through activation of adenylate cyclase, intracellular cyclic adenosine monophosphate (cAMP) is formed, producing bronchodilation. Beta agonists vary in their receptor selectivity and potency, with the strongest beta-2 agonists being bitolterol, formaterol, pributerol, and salmeterol. Epinephrine and metaproterenol have relatively less beta-2 activity.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:574.

46. ANSWER: D

The mortality rate for mediastinoscopy has been quoted at 0.09% and the morbidity at 1.5%, with the most common complication being hemorrhage. The inferior thyroid venous plexus can complicate mediastinoscopy and produce a significant wound hematoma. In 10% of patients, the right bronchial artery may pass across the trachea and along the anterior aspect of the right bronchus, which makes this artery susceptible to injury from the mediastinoscope. Also at risk are the pulmonary and innominate arteries, aorta, superior vena cava (SVC), and the azygos. If a major vascular structure is perforated, blood loss can be rapid, requiring emergent sternotomy and even cardiopulmonary bypass. Because packing and clamps may be applied to the SVC, lower extremity vascular access may be required.

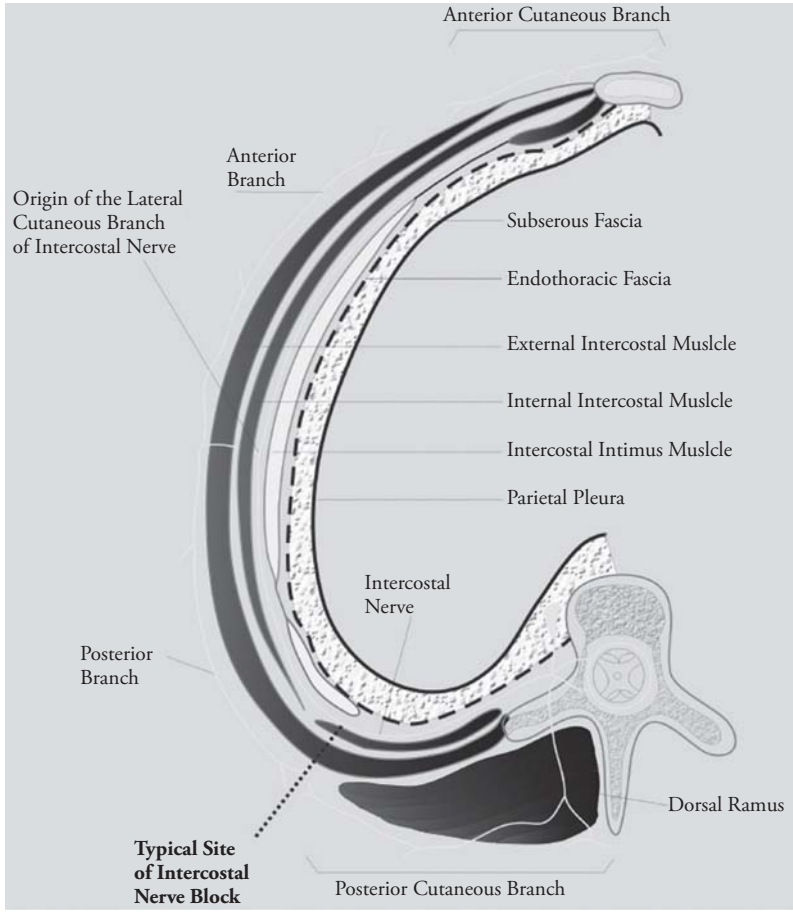


Figure 10.9 Anatomy of the intercostal nerve block.

SOURCE: Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*: http://www.accessanesthesiology.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

ADDITIONAL READINGS

Kaplan JA, Slinger PD, ed. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003.
Yao FF, ed. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:36.

47. ANSWER: C

Airway pressure-release ventilation (APRV) is a novel ventilatory mode, and the literature supports its superiority to conventional modes of ventilation due to its ability to reduce peak airway pressure without compromising oxygenation. During APRV, a high continuous positive airway pressure is delivered for a long duration and then falls to a lower pressure for a shorter duration. Alveolar recruitment is increased by the high continuous positive airway pressure. **APRV may offer advantages by promoting alveolar recruitment and improving oxygenation at lower peak airway pressures**. It allows for a slight elevation in mean airway pressures to overcome closing forces and recruit previously nonaerated, dependent lung units. This mode allows for spontaneous breathing and improves V/Q matching and oxygenation in severe ARDS. It allows for less sedation, improved cardiopulmonary function, and decreased time on ventilatory support. Findings are not universal, however, and mortality has yet to be shown to improve with this mode of ventilation.

ADDITIONAL READING

Dart BW, Maxwell RA, Richart CM, Brooks DK, Ciraulo DL, Barker DE, Burns RP. Preliminary experience with airway pressure release ventilation in a trauma/surgical intensive care unit. *J Trauma Injury Infection Critical Care*. 2005;59:71–76.

48. ANSWER: E

With both IMV and AC, the minimal minute ventilation is set by setting the respiratory rate and tidal volume. Both modes allow the patient to increase the minute ventilation. With IMV mode, minute ventilation is increased by spontaneous breathing, rather than through patient-initiated ventilator breaths, as provided in AC. During AC, each patient-initiated breath receives the set tidal volume from the ventilator. SIMV (synchronized intermittent mandatory ventilation), a variation of IMV, synchronizes ventilator breaths to patient inspiratory effort and increases patient–ventilator synchrony. PRVC (pressure-regulated volume control) is a variation of AC that allows the ventilator to autoregulate the inspiratory time and flow so that a smaller rise in plateau pressure is generated.

ADDITIONAL READING

Hall JB, Schmidt GA, Wood LDH. *Principles of Critical Care*. 3rd ed. New York: McGraw-Hill; 2005.

49. ANSWER: E

Ventilation with pressure-support ventilation is used for active patients capable of triggering the ventilator. Ventilation is determined by inspiratory pressure, PEEP, patient-determined frequency, patient effort, and patient's lung mechanics. When the patient triggers a breath, the ventilator attempts to maintain the inspiratory pressure using whatever flow is necessary. Flow decreases at the end of inspiratory effort or at the onset of elastic recoil when lung volume increases. Inspiratory pressure is maintained until flow decreases by a certain amount or decreases below a certain flow rate (depending on the ventilator). At constant minute ventilation, the work of breathing can be increased by decreasing inspiratory pressure, by decreasing the sensitivity of the trigger, or if the patient's respiratory mechanics change.

ADDITIONAL READING

Hall JB, Schmidt GA, Wood LDH. *Principles of Critical Care*. 3rd ed. New York: McGraw-Hill; 2005.

50. ANSWER: D

Needle decompression performed in the second/third intercostal space, midclavicular line, penetrates pectoral muscles and fat, and in some patients can produce edema and subcutaneous emphysema. This can lead to treatment failure as a typical 14-gauge cannula is only 4.5 cm long and may not be able to penetrate the parietal pleura. The fourth/fifth intercostal space at the midaxillary line has been recommended by ATLS. However, because gas collects at the highest point, and because adhesions are likely in dependent parts of the lung, the site is more prone to lung injury.

ADDITIONAL READING

Leigh-Smith S, Harris T. Tension pneumothorax—time for a re-think? *Emerg Med J*. 2005;22(1):8–16.

51. ANSWER: A

In awake patients, hypotension and tachycardia can be seen with tension pneumothorax; however, decreased cardiac

output is uncommon and if present is often due to other pathology. It is likely not possible to be due to great vessel compression. Great vessel compression is not seen in awake patients due to the inability to achieve that level of intrapleural pressure. This can, however, occur in a ventilated patient. The subsequent decreased cardiac output is consistent and progressive with subsequent hypotension that is preterminal, leading to cardiac arrest.

ADDITIONAL READING

Leigh-Smith S, Harris T. Tension pneumothorax—time for a re-think? *Emerg Med J.* 2005;22(1):8–16.

52. ANSWER: E

Increasing pulmonary vascular resistance in the dependent lung is responsible for the diversion of blood to the nondependent lung that is unable to effectively oxygenate blood. Blood circulating through the nondependent lung returns to the heart, and is sent, deoxygenated, on to the systemic circulation (shunt). Several ventilatory strategies, such as dependent lung PEEP, hyperventilation, hypoventilation, and reduction of the FiO_2, all increase pulmonary vascular resistance in the dependent lung.

Dependent lung PEEP and hyperventilation increases lung volume and compresses the intra-alveolar vessels in the dependent lung, increasing dependent lung pulmonary vascular resistance, diverting blood to the nondependent lung, and worsening shunt. Resulting hypocapnia can also inhibit HPV in the nondependent lung. Decreasing FiO_2 as well as ventilation with low tidal volumes with subsequent atelectasis in the ventilation of the dependent lung causes an increase in the vascular tone in the dependent, normoxic lung, which decreases blood flow from being diverted from the hypoxic to the normoxic lung.

ADDITIONAL READING

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:71–94.

53. ANSWER: B

Ventilation management during the initiation of one-lung ventilation is based on blood flow distribution during one-lung ventilation as well as the risks of hypoxemia. There is a theoretical risk of absorption atelectasis and oxygen toxicity; however, the benefits of ventilation at 100% exceed these risks. A high FiO_2 maintains safe levels of PaO_2 and increases dependent lung vasodilatation, allowing for redistribution of blood from the nondependent lung.

One-lung ventilation has much less of an effect on the $PaCO_2$ than on the PaO_2. The blood flowing through well-ventilated alveoli will release a proportionately greater amount of CO_2 than O_2. Despite this, blood flowing through relatively underventilated alveoli will retain more than a normal amount of CO_2. Tidal volume has been classically taught to be ventilated at 10 to 12 mL/kg. This is because volumes less than 8 mL/kg cause atelectasis and those greater than 15 can increase vascular resistance in the dependent lung and decrease nondependent lung HPV, as well as cause volutrauma in some patients. Tidal volumes of 10 to 12 mL/kg can be inappropriately high and can cause volutrauma. Tidal volume should be initiated at 8 to 10 mL/kg and can then be adjusted to the level that does not cause lung hyperinflation or excessive airway pressure.

Respiratory rate has traditionally been adjusted to maintain a $PaCO_2$ of 40 mm Hg; however, this often requires elevated respiratory rates, which can be associated with dynamic air trapping, hyperinflation, and hemodynamic instability. Permissive hypercapnia has now been advocated to prevent pulmonary hyperinflation.

ADDITIONAL READING

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:71–94.

54. ANSWER: B

The goal for patients with acute hypoxic respiratory failure includes the addition of the least amount of PEEP producing SpO_2 90% with an adequate circulating hemoglobin on a nontoxic FiO_2. PEEP levels of 5 cm H_2O are reasonable in most patients. Patients in acute respiratory distress syndrome (ARDS) suffer from extreme hypoxemia, requiring an initial FiO_2 of 1.0. PEEP should be instituted immediately beginning with 15 cm H_2O and then rapidly titrating PEEP to produce an SpO_2 of 88% and an FiO_2 of no larger than 0.6, using the smallest amount of PEEP necessary. Another notable exception to an initial PEEP of 5 cm H_2O is the scenario of asthma, in which patients have a significant amount of dynamic hyperinflation and auto-PEEP.

ADDITIONAL READING

Schmidt GA, Hall JB. Chapter 36, Management of the Ventilated Patient. In Hall JB, Schmidt GA, Wood LDH, eds. *Principles of Critical Care*, 3e. New York: McGraw-Hill Professional, 2005.

55. ANSWER: A

It is important to understand the anatomy of the intercostal nerve to choose the correct method of analgesia for a particular thoracic procedure. There are three main sensory divisions of the intercostal nerve—the posterior, lateral (which subdivides into posterior and anterior branches), and anterior cutaneous nerves (Fig. 10.9). The posterior cutaneous nerve cannot be blocked by an intercostal nerve block, which makes this method less useful for a traditional posterolateral thoracotomy incision.

ADDITIONAL READING

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:454.

56. ANSWER: D

Cryoanalgesia can be an effective and long-lasting method of pain control, providing 4 weeks to 6 months of intercostal nerve block. Two 30-second freeze cycles are applied to each of the affected nerves. Unfortunately, a detailed study has revealed a significant incidence of paresthesia and post thoracotomy pain syndrome.

ADDITIONAL READING

Yao FF, ed. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:46.

57. ANSWER: A

Clonidine prolongs the duration of epidural sensory and motor blockade by producing conduction blockade through its action of opening potassium channels, thus attenuating A-δ and C-fiber nociception. It increases acetylcholine and norepinephrine in the cerebrospinal fluid and inhibits substance P release and modulates wide-dynamic-range neurons in the dorsal horn of the spinal cord. The sites of action are the α_2-adrenoreceptors on primary afferent, substantia gelatinosa, and brainstem nuclei.

ADDITIONAL READING

Hadzic A. Epidural Space. In Hadzic A. *The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management*. New York: McGraw-Hill; 2007.

58. ANSWER: A

Although an effective means of post thoracotomy analgesia, ***paravertebral nerve blocks*** have a high failure rate (6% to 10%). Vascular puncture, skin hematoma, and pain at the site of injection occur occasionally (3.8%). Pneumothorax (1.1%) and pleural puncture (0.5%) are also occasionally encountered. The pneumothorax incidence is markedly increased, as high as eightfold, when performed bilaterally.

ADDITIONAL READINGS

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:451.
Yao FF, ed. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:46.

59. ANSWER: C

HPV remains intact in the transplanted lung. In episodes of rejection, blood can be shunted from the transplanted lung. Airway reactivity is not increased in the transplanted lung. Mucociliary clearance is impaired, predisposing the recipient to infections. Lymphatic drainage is impaired, predisposing the individual to pulmonary edema. Following transplantation, pulmonary pressures are immediately normalized.

ADDITIONAL READING

Robin ED, Theodore J, Burke CM, et al. Hypoxic pulmonary vasoconstriction persists in the human transplanted lung. *Clin Sci (Lond)*. 1987;72:283–287.

60. ANSWER: D

Thoracic scoliosis results in a narrowed chest cavity with resultant restrictive lung disease with decreased chest wall compliance. Cobb angles greater than 65 degrees usually significantly decrease lung volumes. In these patients, pulmonary function tests must be performed prior to surgery. **Vital capacity of less than 40% of normal is predictive of the need for postoperative ventilation**. Combined spinal fusion (vs. posterior or anterior spinal fusion) is most predictive of postoperative pulmonary complications.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:2254–2256.

61. ANSWER: C

Any patient with an anterior mediastinal mass who has a fixed pattern on FVL and severe tracheal distortion or compression on chest CT requires a more extensive evaluation to rule out airway obstruction. This assessment typically includes an awake, fiberoptic bronchoscopy to view areas of distortion or compression.

Other testing provides additional information in certain situations. Chest MRI is valuable when CT does not clearly delineate anatomic issues or if additional information about the mass and its relationship to other organs is required. Transthoracic echocardiography is useful to define the extent of cardiac involvement, pericardial effusion, impact of the mass on cardiac filling, and other associated abnormalities. Barium contrast esophagram is often an initial test to determine tracheobronchial tree involvement, but it is not helpful at this point following a CT. Upright and supine spirometry may not be any better at predicting complications than symptoms and chest CT, and it should not be routinely obtained in patients with anterior mediastinal masses.

ADDITIONAL READING

Cohen N, ed. *Medically Challenging Patients Undergoing Cardiothoracic Surgery*. Baltimore: Lippincott Williams & Wilkins; 2009:285–299.

62. ANSWER: A

Answers A through E refer to the segmental bronchi of the RUL, RML, RLL, LUL, and LLL. respectively. The RUL bronchus divides into three segments: the apical, anterior, and posterior bronchi (C in Fig. 10.10). A is the only answer that provides three secondary bronchi choices.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:1842.

63. ANSWER: D

Barotrauma is a form of lung injury related to high peak inflation pressures and underlying lung disease. It is more likely to develop in patients with chronic lung disease or patients with ARDS. Multiple studies have demonstrated that a history of ARDS or interstitial lung disease significantly increases the risk for developing barotrauma.

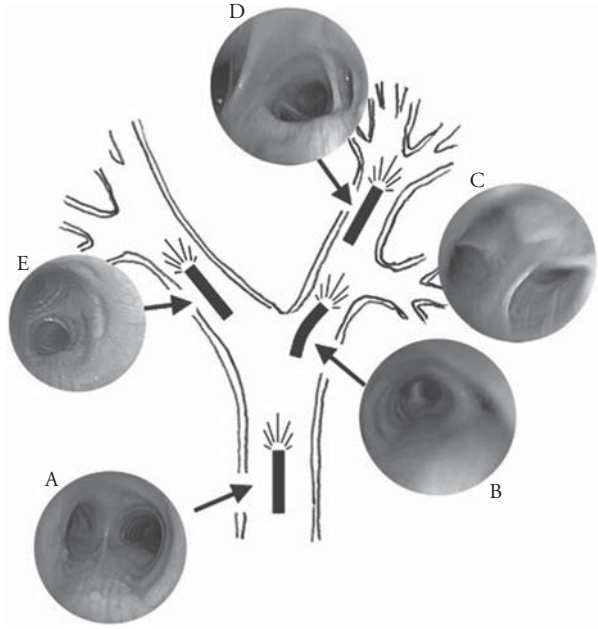


Figure 10.10 Bronchoscopic view of anatomical landmarks.

SOURCE: Longnecker DE, Brown DL, Newman MF, Zapol WM. Anesthesiology: http://www.accessanesthesiology.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

ADDITIONAL READING

Anzueto A, Frutos-Vivar F, Esteban A, Alía I, Brochard L, Stewart T, et al. Incidence, risk factors and outcome of barotrauma in mechanically ventilated patients. *Intensive Care Med*. 2004 April;30(4):612–619.

64. ANSWER: B

When a patient's peak pressure is elevated, dividing its components of airway opening pressure (P_{ao}) can narrow the differential diagnosis. P_{ao} consists of three components: the resistive pressure (P_{res}), the elastic pressure (P_{el}), and peak end-expiratory pressure (PEEP):

$$P_{ao} = P_{res} + P_{el} + \text{Total PEEP}$$

P_{res} refers to the pressure needed to drive gas across the inspiratory resistance. This can be determined by stopping flow and allowing the pressure to fall from its peak to a plateau pressure to measure the flow-related pressure. The difference between peak pressure and plateau pressure is P_{res}, which is typically between 4 and 10 cm H_2O. Elevation of the resistive pressure should lead the physician to suspect high flow, bronchospasm, COPD, secretions, kinked or obstructed tubing, airway edema, airway tumor/mass, or airway foreign body as the source of the peak airway pressure.

$$P_{res} = P_{peak} - P_{plat}$$

P_{el}, the pressure needed to expand the alveoli against the elastic recoil of the lungs and chest wall, is proportional to the elastance of the respiratory system and the tidal volume. It is calculated by the difference between the plateau pressure and PEEP:

$$P_{el} = P_{plat} - PEEP$$

P_{el} indicates excessive tidal volume or increased elastic recoil of the chest wall (pulmonary fibrosis, acute lung injury, or abdominal distention) and can be described by the following:

P_{el} = change in lung volume × elastance of the respiratory system (E_{rs})

Because respiratory system static compliance (C_{rs}) is the inverse of E_{rs} it can also be described as the following:

$$P_{el} = \text{change in lung volume} / C_{rs}$$

ADDITIONAL READING

Hall JB, Schmidt GA, Wood LDH, eds. *Principles of Critical Care*. 3rd ed. New York: The McGraw-Hill Companies; 2005.

65. ANSWER: E

Pulmonary barotrauma refers to the rupture of alveoli due to positive-pressure ventilation with elevated transalveolar pressure. Air then enters the pulmonary interstitium, which then tracks along perivascular sheaths, causing pneumoperitoneum, pneumomediastinum, pneumothorax, and subcutaneous emphysema tracking along the upper chest, neck, and face, appearing as crepitus or edema. Although less likely, venous air embolism can develop as well as severe pneumoperitoneum causing abdominal compartment syndrome.

Physiologic shunt exists when blood flows through inadequately ventilated lung tissue. This is often due to atelectasis with persistent perfusion. Positive-pressure ventilation increases the mean airway pressure, ensuring alveolar patency and decreasing physiologic shunt.

ADDITIONAL READING

Anzueto A, Frutos-Vivar F, Esteban A, Alía I, Brochard L, Stewart T, et al. Incidence, risk factors and outcome of barotrauma in mechanically ventilated patients. *Intensive Care Med*. 2004 April;30(4): 612–619.

66. ANSWER: C

Hypercapnia in an otherwise normal patient results in an increase in cerebral blood flow, depressed myocardial contractility, increased sympathetic stimulation, a propensity toward dysrhythmias, depressed diaphragmatic function, and increased brain glutamine levels, which depress minute ventilation and inspiratory drive. Hypercapnia results in acute respiratory acidosis and a subsequent right shift of the hemoglobin–oxygen dissociation curve, increasing oxygen release to tissues. Severe hypercapnia can also result in hypoxia secondary to oxygen displacement.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006.

67. ANSWER: E

The major effect of PEEP is to increase FRC. PEEP increases tidal ventilation above closing capacity, improves lung compliance, and corrects V/Q abnormalities. There is a resultant decrease in intrapulmonary shunting with subsequent improved arterial oxygenation. PEEP can also increase dead space ventilation.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:1038–1039.

68. ANSWER: D

Jet ventilation uses a small cannula to administer a jet of high-pressure gas delivered at a high frequency. By means of the Bernoulli principle, which states that an increase in the speed of the gas occurs simultaneously with a decrease in pressure by means of the conservation of energy, tidal volume is augmented by surrounding air, which is attracted to the low pressure of the delivered oxygen in the gas jet.

The Beer-Lambert law is the basis of spectrophotometry used by monitoring devices to estimate the concentrations of dissolved substances. The Bohr equation is used to determine the ratio of physiologic dead space to total tidal volume in an individual's lungs. The Laplace law is used to calculate transmural pressure in the heart and is often applied to describe alveoli inflation. Pendelluft describes the movement of gas between alveoli at the end of inspiration

and end of expiration. Pendelluft does provide some contribution to the gas exchange accomplished during HFJV.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:1034–1035.

69. ANSWER: D

In HFJV, a pulsed jet of high-pressure gas delivered through a small cannula entrains air that augments tidal volume. Following initiation of HFJV, an ABG analysis should be obtained. Carbon dioxide elimination is generally proportional to drive pressure. Appropriate interventions for an elevated carbon dioxide level would be to increase the driving pressure in 5-psi increments up to 50 psi, increasing the inspiratory time in 5% increments to a maximum of 40%, increasing the frequency in increments of 10 breaths per minute up to 250 breaths per minute, or adding breaths from another mode of ventilation.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:1034–1035.

70. ANSWER: D

Pulmonary blood flow in the lateral decubitus position results in similar zones to that in the upright position. West zones 1, 2, and 3 are created due to vertical gradients of gravity-dependent blood flow. Pulmonary blood flow increases in the most dependent portions of the lung, resulting in pulmonary artery pressure exceeding pulmonary venous pressure, which exceeds alveolar pressure.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2009:1040.

71. ANSWER: B

Mixed venous oxygen saturation (SvO_2) refers to the hemoglobin saturation measured in the proximal pulmonary artery. When oxygen delivery is inadequate to meet demands, returning venous blood has reduced oxygen content (SvO_2). Oxygen delivery is determined by both cardiac output and the oxygen content of arterial blood. Cardiac output increases in response to sudden decreases in arterial saturation, compensating and resulting in an unchanged SvO_2.

ADDITIONAL READING

Shepherd SJ, Pearse RM. Role of central and mixed venous oxygen saturation measurement in perioperative care. *Anesthesiology*. 2009;111:649–656.

72. ANSWER: D

Lung isolation is generally best accomplished by intubating the nonoperative bronchus with the same sided endobronchial tube. Intubating the operative side requires that the anesthesiologist pull back the tube at the time of cross-clamping and risks disrupting the stump with accidental advancement of the tube. Right-sided DLTs can be troublesome for left pneumonectomies because of short right mainstem bronchi, leading to poor lung isolation and right upper lobe collapse. Bronchial blockers work well for left-sided pneumonectomies but can become dislodged when used for right pneumonectomies because of the short right mainstem bronchus.

ADDITIONAL READING

Kaplan JA, Lake CL, Murray MJ, eds. *Vascular Anesthesia*. 2nd ed. Philadelphia: Elsevier/Churchill Livingstone; 2004:222.

73. ANSWER: E

The most important endocrine problem in the brain-dead donor is central diabetes insipidus, caused by inadequate ADH production. This is most appropriately managed with vasopressin or desmospressin administration with a goal of urine output of 100 to 200 mL per hour. It is also important to maintain euvolemia with appropriate fluid replacement.

ADDITIONAL READING

Wood KE, Becker BN, McCartney JG, et al. Care of the potential organ donor. *N Engl J Med*. 2004;351(26):2730–2730.

74. ANSWER: B

The signs and symptoms of a ***pulmonary thomboembolus*** **(PTE)** can vary considerably. The most common symptom

is dyspnea followed by pleuritic pain. Dyspnea, hypotension, and syncope may indicate a massive PTE. Obstruction of 60% to 75% can result in acute cor pulmonale with marked dyspnea, hypotension, syncope, and cardiac arrest.

ADDITIONAL READING

Thys DM, Hillel Z, Schwartz AJ, eds. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw Hill; 2001:1112–1113.

75. ANSWER: B

Carboxyhemoglobin concentrations in the blood decrease with abstinence of more than 12 hours. The levels associated with smoking, however, have not been related to postoperative complications. Complications for nonsmokers undergoing thoracic surgery are decreased compared to those smoking up to the time of surgery. It is not clear how long smokers must quit prior to surgery to decrease the risk of postoperative complications. Cardiac surgery data suggest a threshold of 8 weeks for a reduction in the risk of postoperative pulmonary complications. Data do indicate a progressive decrease in postoperative complications and mortality with increased duration of smoking cessation.

ADDITIONAL READING

Thys DM, Hillel Z, Schwartz AJ, eds. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw Hill; 2001:791–792.

76. ANSWER: C

Removal of the aortic cross-clamp results in the recirculation of acidotic and lactate-rich blood, causing myocardial depression, hypotension, and vasodilation. Debris is also released, which travels to the viscera or periphery. Due to sympathetic stimulation and renin-angiotensin system stimulation, renal blood flow and GFR are decreased for a prolonged period.

ADDITIONAL READING

Kaplan JA, Lake CL, Murray MJ, eds. *Vascular Anesthesia*. 2nd ed. Philadelphia: Elsevier/Churchill Livingstone; 2004:276–277.

77. ANSWER: B

Following reperfusion of the visceral organs or lower extremities, ischemic washout leads to significant hypotension. Maintenance fluid and blood loss must be replaced. Fluid loading should be started before unclamping, and it is important to be prepared to infuse vasoactive drugs after unclamping to manage the hyperemia that develops.

ADDITIONAL READING

Levine WC, Lee JJ, Black JH, Cambria RP, Davison JK. Thoracoabdominal aneurysm repair. *Int Anesthesiol Clin*. 2005;43(1):39–56.

78. ANSWER: B

Type II TAAs, which extend from the left subclavian artery to below the renal arteries, interrupt visceral perfusion, causing ischemia and end-organ dysfunction. History of hepatitis, acute rupture, and emergency presentation contribute to the risk. Postoperative hepatic dysfunction is manifested by an increase in PT, PTT, and alkaline phosphatase. Visceral perfusion using left atrial femoral bypass is somewhat protective.

Knowledge of the classification of TAA aneurysms is important for both anesthetic management and determination of risk. Crawford classification is based on a type I through IV classification scheme (Fig. 10.11). Type I aneurysms extend from the left subclavian to the diaphragm, type II aneurysms extend from the left subclavian to below the renal arteries, type III aneurysms extend from the midthoracic descending aorta to below the renal arteries, and type IV aneurysms extend from the diaphragm to below the renal arteries.

ADDITIONAL READINGS

Coselli JS, Moreno PL. Descending and thoracoabdominal aneurysm. In: Cohn LH, Edmunds LH Jr, eds. *Cardiac Surgery in the Adult*. New York: McGraw-Hill, 2003:1169–1190.

Levine WC, Lee JJ, Black JH, Cambria RP, Davison JK. Thoracoabdominal aneurysm repair. *Int Anesthesiol Clin*. 2005;43(1):39–56.

79. ANSWER: D

Spinal cord injury after TAA repair occurs in approximately 11% of patients and is related to several variables, including type I and II TAAs, emergent operation, intercostal sacrifice, and intraoperative hypotension. Literature also demonstrates that elevated CSF pressure is a risk factor for delayed spinal cord injury. Overaggressive drainage with CSF pressure less than 5 mm Hg is associated with an elevated risk of subdural hematoma from tearing of bridging dural veins.

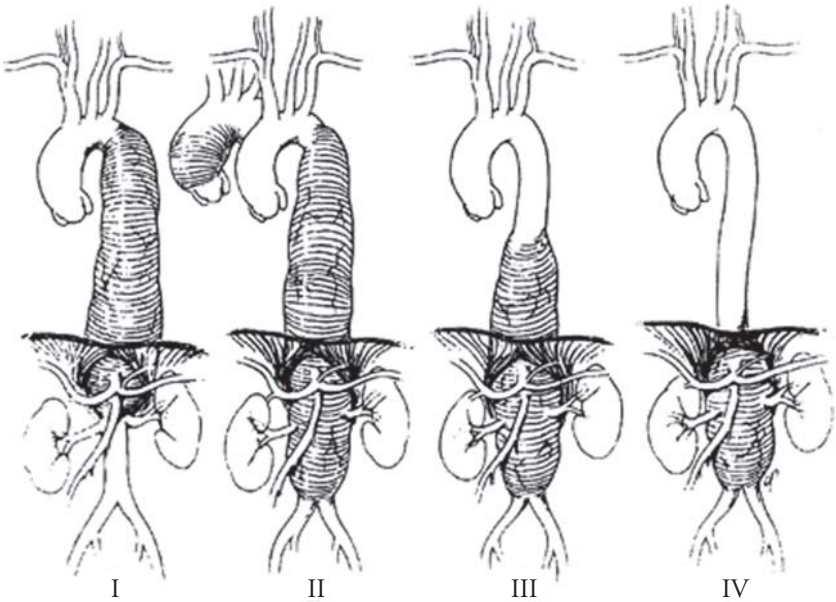


Figure 10.11 Thoracoabdominal aneurysm repair.

ADDITIONAL READING

Levine WC, Lee JJ, Black JH, Cambria RP, Davison JK. Thoracoabdominal aneurysm repair. *Int Anesthesiol Clin*. 2005;43(1):55–56.

80. ANSWER: D

During open or endovascular repair, blood supply to the anterior spinal cord can be compromised, resulting in infarction. The anterior spinal artery runs midline anterior to the spinal cord and supplies blood flow to anterior motor neurons. It is formed from branches of the vertebral artery and is fed by feeder arteries. Posterior intercostal arteries provide anterior segmental medullary arteries (most noteworthy being the artery of Adamkiewicz), which contribute significant perfusion to the anterior spinal artery.

ADDITIONAL READING

Kaplan JA, Lake CL, Murray MJ, eds. *Vascular Anesthesia*. 2nd ed. Philadelphia: Elsevier/Churchill Livingstone; 2004:213–214.

81. ANSWER: A

Preventing OR fires entails minimizing oxidizing agents at the surgical site (oxygen, nitrous oxide), safely managing ignition sources (electrocautery, electrosurgical devices, lasers), and safely managing fuels (alcohol-based skin prepping agents, dry sponges and gauze). A wide range of fuel ignites in the presence of oxidizing agents such as oxygen or nitrous oxide, which can build up in the presence of some drape configurations. Replacing oxygen with air or using oxygen concentrations that are as low as possible, allowing flammable skin-prepping solutions to completely dry before draping, limiting laser intensity and duration, and wetting sponges in the airway are all effective strategies for preventing airway fires.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:839–840.

82. ANSWER: E

According to the ASA Task Force on Operating Room Fires, as quickly as possible, the tracheal tube should be removed along with all other flammable materials in the airway, gases should stop, and saline should be poured into the airway to extinguish embers and cool tissues. If this is unsuccessful for extinguishing the fires, a CO_2 fire extinguisher should be used, the fire alarm should be activated, and the patient should be evacuated from the room and the medical gas supply should be turned off. Their recommendations strongly encourage a predetermined sequence of actions, and the order that one "may wish to consider" is the following: (1) remove the tracheal tube; (2) stop the flow of all airway gases; (3) remove all flammable and burning materials from the airway; and (4) pour saline or water into the patient's airway. The task force acknowledges that stopping gases and removing the tube simultaneously would be

ideal to prevent a blowtorch effect caused by continued gas flow through a burning tracheal tube, but feel that these simultaneous actions are difficult to accomplish.

ADDITIONAL READING

Practice advisory for the prevention and management of operating room fires: a report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology*. 2008; 108:786–801.

83. ANSWER: A

Many thoracic patients are at risk of bronchospasm due to the prevalence of reactive airway disease. Placement of a DLT or bronchial blocker can trigger bronchoconstriction. Management principles include avoiding airway manipulation in a lightly anesthetized patient, using bronchodilating agents, and avoiding histamine-releasing medications. Bronchospasm is diminished with the use of propofol and ketamine. This is not seen with the use of barbiturates, opioids, benzodiazepines, or etomidate.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:1846.

84. ANSWER: D

Volatile anesthetics are effective bronchodilators and have been used successfully to treat status asthmaticus when other treatments have been unsuccessful. They indirectly inhibit reflex neural pathways and directly relax airway smooth muscle by depressing smooth muscle contractility. They may also prevent bronchoconstriction through an additional mechanism involving nitric oxide. Sevoflurane may be the best choice as a volatile bronchodilator as it has a rapid onset, is not pungent, and has a lack of cardiovascular depression. Desflurane results in a transient increase in bronchoconstriction due to a direct effect causing airway irritability. Ipratroprium functions by blocking the action of acetylcholine at parasympathetic sites on bronchial smooth muscle. Zafirlukast is a leukotriene-receptor antagonist. Leukotriene production is associated with airway edema and smooth muscle constriction. Theophylline acts by blocking phosphodiesterase-induced increases in cAMP, which promotes catecholamine stimulation and induces epinephrine release from the adrenal medulla.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2009:265, 434.

85. ANSWER: C

Pulmonary vascular resistance is expressed by the following equation:

$$PVR = [80 \times (\text{Pulmonary Artery Pressure} - \text{Left Atrial Pressure})]/CO$$

The values of mean PAP and PCWP are used for PAP and LAP respectively. The numerator is the pressure difference between input into the pulmonary vasculature and the output from the pulmonary vasculature and the denominator is flow rate. This equation can be thought of conceptually analogous to Ohm's law:

$$V = IR \quad \text{or} \quad R = V/I$$

This can be conceptually translated to

$$\text{Resistance} = \text{Driving Pressure}/\text{Rate of Blood Flow}$$

Therefore, PVR is inversely related to right ventricular cardiac output and directly proportional to the difference between pulmonary artery pressure and left atrial pressure.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:424–425.

86. ANSWER: B

Capnography monitors the elimination of CO_2 into the circuit. The wave is divided into four phases. Phase 0 reflects the period of inspiration, phase 1 represents the CO_2-free gas from the airways from dead space ventilation, phase 2 represents a mixture of anatomic and alveolar dead space, and phase 3 consists of CO_2-containing gas from the alveoli and is depicted as a plateau (Fig. 10.12). The angle between phase 2 and 3 is called the alpha angle and the fall from phase 3 is called the beta angle. Obstruction presents a prolonged phase 2 upstroke and a prolonged phase 3 without a flattened plateau. The alpha angle in between is also increased.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:143.

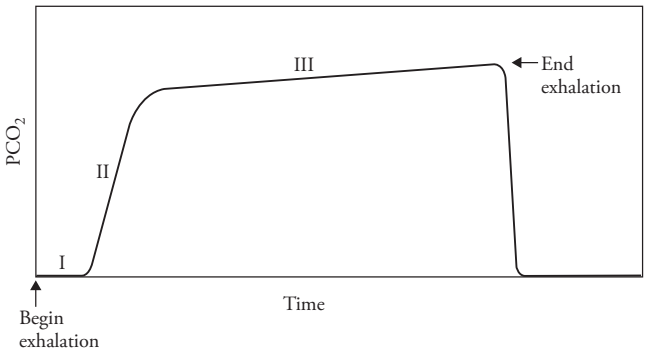


Figure 10.12 Normal capnography curve.

SOURCE: Longnecker DE, Brown DL, Newman MF, Zapol WM. Anesthesiology http://www.accessanesthesiology.com Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

87. ANSWER: B

Responses to hypoxia are primarily mediated by carotid body chemoreceptors, which transmit signals through the glossopharyngeal nerves to the respiratory center in the medulla. The carotid bodies are responsive to changes in P_{CO_2} and hydrogen ion concentration as well. It is the Pa_{O_2}, not the hemoglobin saturation, which stimulates the chemoreceptors. Normally peripheral chemoreceptors become strongly stimulated when the Pa_{O_2} decreases below 60 mm Hg. The response is an increase in minute ventilation. The concentration of volatile agents depressing the hypoxic ventilatory response is lower than that required for loss of consciousness; therefore, the hypoxic response can be attenuated even when the patient is awake and responsive. With high P_{O2} values the majority of the patient's ventilatory response is mediated by the central chemoreceptors.

88. ANSWER: D

According to the ASA Difficult Airway Algorithm (Fig. 10.13), after induction of general anesthesia, with inadequate face mask ventilation, LMA should be considered or attempted. Failed intubation should not be futilely repeated. Changes must be made in the approach to intubating the patient. If the patient is also difficult to ventilate with a mask, alternative airway management techniques must be pursued. LMA is initially recommended, but failure of the LMA should be followed by calling for assistance (including surgical airway assistance) and pursuing other options such as rigid bronchoscopy, Combitube ventilation, or transtracheal jet ventilation.

ADDITIONAL READING

American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2003;98:1269.

89. ANSWER: D

Epidural blocks to midthoracic levels have little to no impact on lung volumes, resting minute ventilation, dead space, arterial blood gas tensions, and shunt fractions. The ventilatory response to hypercapnia is increased by epidural and spinal block. High blocks have more of a significant impact, reducing accessory muscle function, impairing active ventilation, and reducing expiratory reserve volume, peak expiratory flow, and maximum minute ventilation. Epidural blockade can impair cough as well, which can affect those patients who rely on accessory muscles to maintain a clear airway.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2009:434, 947.

90. ANSWER: B

With the use of the National Veterans Administration Surgical Quality Improvement Program, a multifactorial risk index for postoperative respiratory failure was developed. Of the various risk factors, abdominal aortic aneurysm repair was the most predictive of mechanical ventilation greater than 48 hours after surgery or reintubation after postoperative extubation, with an odds ratio of 14.3. This was followed by thoracic surgery, with an odds ratio of 8.14. The other factors listed in the answer choices are also predictive of respiratory failure, but to a much lower degree.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:1107–1108.

91. ANSWER: B

Functional residual capacity (FRC) is the volume remaining at the end of exhalation. This is the point at which the outward chest recoil equals the inward lung recoil. Factors known to alter FRC include the following:

- Body habitus: FRC is proportional to height and is decreased by obesity.
- Sex: FRC is reduced by 10% in females.
- Posture: FRC is decreased in supine positioning.

Difficult Airway Algorithm

1. Assess the likelihood and clinical impact of basic management problems.
   A. Difficult ventilation
   B. Difficult intubation
   C. Difficulty with patient cooperation or consent
   D. Difficult tracheostomy
2. Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management.
3. Consider the relative merits and feasibility of basic management choices:

A.	Awake intubation	VS.	Intubation attempts after induction of general anesthesia
B.	Noninvasive technique for initial approach to intubation	VS.	Invasive technique for initial approach to intubation
C.	Preservation of spontaneous ventilation	VS.	Ablation of spontaneous ventilation

4. Develop primary and alternative strategies.

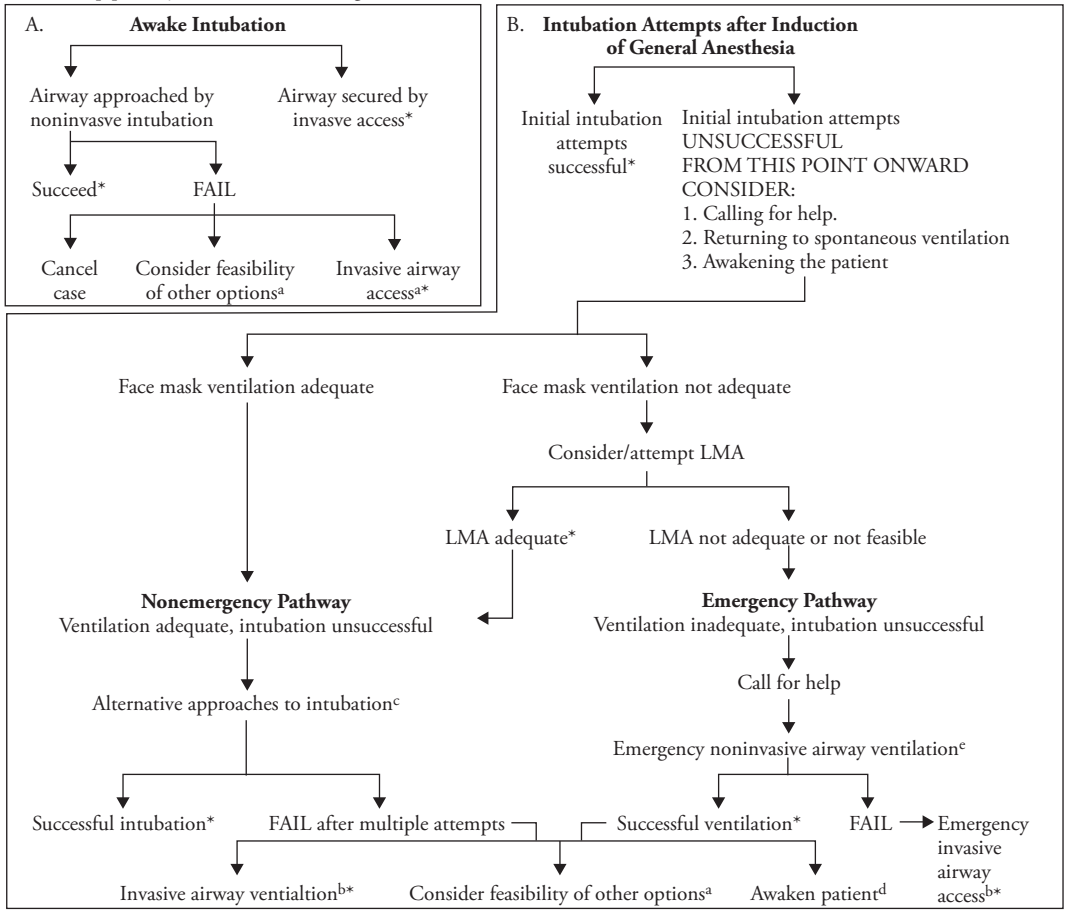


Figure 10.13 Difficult airway algorithm.

SOURCE: Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. http://www.accessmedicine.com Copyright © The McGraw-Hill Companies. All rights reserved.

- General anesthesia: FRC is reduced with the loss of diaphragmatic tone.
- Lung disease: Decreased compliance of the lung and/or chest is a result of restrictive pulmonary disorders and results in a low FRC.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:545–546.

92. ANSWER: C

Laryngospasm is the exaggerated glottic closure reflex produced by the stimulation of the superior laryngeal nerve, and is sustained after removal of the stimulus. It typically occurs during "light" anesthesia after stimulation by the presence of blood, secretions, or debris in the airway and is manifested by stridor with possible progression to complete airway closure. Preventive strategies include IV or topical lidocaine, IV magnesium, or deep extubation.

Management includes removal of the stimulus and splinting the airway open with PEEP or CPAP until the depth of anesthesia lightens. If this fails, deepening anesthesia or muscle relaxation with succinylcholine (0.1 to 0.5 mg/kg) can be used.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:2359.

93. ANSWER: D

Lambert-Eaton myasthenic syndrome (LEMS) can cause weakness similar to myasthenia gravis (MG) but more commonly affects the proximal muscles of the lower extremities. It can be easily differentiated from MG because patients with LEMS have depressed reflexes and autonomic changes and have incremental rather than decremental responses to repetitive nerve stimulation. As many as one-third of patients with LEMS complain of muscle pain.

ADDITIONAL READING

Drachman DB. Myasthenia gravis and other diseases of the neuromuscular junction. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill Professional, 2008:2673–2675.

94. ANSWER: E

Carbon dioxide diffuses from plasma to alveoli and diffuses 20 times faster than oxygen primarily because of its solubility. Diffusion is linearly related to solubility. CO_2 is almost 30 times more soluble in water than O_2, so there is no lung disease that results in any significant impairment in diffusion of CO_2. The amount of gas that diffuses across a membrane is determined by the surface area available for diffusion, the thickness of the membranes, the pressure difference of the gas across the barrier, the molecular weight of the gas, and the solubility of the gas in the tissues that it has to cross.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:369–371.

95. ANSWER: A

Using hemodynamic monitoring and ABG measurements, calculation of oxygen delivery to tissues can be obtained with the oxygen delivery index (DO_2I). This can estimate a deficit in oxygen supply. Studies have demonstrated improved outcome with supranormal levels during resuscitation. 500 to 600 mL/min/m^2 is a normal value in an adult. To calculate this value, the oxygen content of arterial blood must first be obtained. The oxygen content of blood is the sum of what is in solution plus that carried by hemoglobin.

Normal arterial oxygen content is between 16 and 20 mL/dL, and it is expressed by the following equation:

$$O_2 \text{ content} = ([0.003 \text{ mL } O_2/\text{dL blood per mm Hg}] \times PO_2) + (SO_2 \times \text{Hgb gm/dL} \times 1.39 \text{ mL/dL blood})$$

Using the information listed in the question stem, this can be calculated as follows:

$$\begin{aligned} CaO_2 &= (0.003 \times 100) + (0.97 \times 10 \times 1.39) \\ &= 0.3 + 13.5 \\ &= 13.8 \text{ mL/dL} \end{aligned}$$

This value can be calculated using the following equation:

$$DO_2I \text{ (mL/min/m}^2) = CaO_2 \times CI \times 10$$

Using the information provided in the question stem, the DO_2I can be calculated as follows:

$$\begin{aligned} DO_2I &= 13.8 \times 1.9 \times 10 \\ &= 262.2 \text{ mL/min/m}^2 \end{aligned}$$

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:563–564.

96. ANSWER: D

The oxygen delivered to tissues is a function of the oxygen content of blood and the cardiac output delivering that blood to the tissues. The oxygen content of blood is the sum of what is in solution plus that carried by hemoglobin.

Normal arterial oxygen content is between 16 and 20 mL/dL and is expressed by the following equation:

$$O_2 \text{ content} = ([0.003 \text{ mL } O_2/\text{dL blood per mm Hg}] \times PO_2) + (SO_2 \times \text{Hgb gm/dL} \times 1.39 \text{ mL/dL blood})$$

Using the information listed in the question stem, this can be calculated as follows:

$$\begin{aligned} CaO_2 &= (0.003 \times 60) + (0.88 \times 14 \times 1.39) \\ &= 0.18 + 17.12 \\ &= 17.3 \end{aligned}$$

Oxygen delivery can then be calculated with the following equation:

$$DO_2 = Q \times CaO_2$$

where DO_2 = oxygen delivery (mL/min), Q = cardiac output (dL/min), and CaO_2 = oxygen content of arterial blood (mL O_2/dL blood).

It is then calculated as follows, keeping in mind that cardiac output is converted to dL/min:

$$DO_2 = 50.00 \times 17.3 = 865.2 \text{ mL/min}$$

Normal DO_2 is 1,000 mL/min

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2006:563–564.

97. ANSWER: B

Although the actual content of oxygen and carbon dioxide in the blood does not change, the solubility of oxygen and carbon dioxide is inversely proportional to temperature: at lower temperatures, the solubility increases and the partial pressure decreases. For standardization, most ABGs are analyzed at 37 degrees C, regardless of the patient's temperature. There are multiple conversion formulas, but as a guideline, for each degree reduction in temperature, the Pa_{O_2} should be decreased by 5 mm Hg. Another conversion guideline is to reduce Pa_{O_2} by 6% for each degree reduction in temperature.

ADDITIONAL READING

Stoelting RK, Miller RD, eds. *Basics of Anesthesia*. 5th ed. Philadelphia: Churchill Livingston/Elsevier; 2007:324–325.

98. ANSWER: B

A large increase in dead space ventilation is created by the ventilation of nonperfused alveoli, such as that which occurs with a pulmonary embolus. The normal V_D/V_T (dead space-to-tidal volume ratio) is 0.3 and results from anatomic dead space and some degree of normal V/Q mismatch in normal lungs. Elevated measurements range from 0.4 to 0.9. Other patients who suffer from elevated dead space are those with obstructive lung disease such as emphysema, asthma, and chronic bronchitis. This is because obstruction results in underventilated areas in relation to their perfusion (i.e., V/Q mismatch), sending gas to other areas, which results in over ventilated areas, in excess of their perfusion. This opposite V/Q mismatch has the same effect on gas exchange and is also measured as dead space.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:362.

99. ANSWER: A

$P_{ET}CO_2$ underestimates $PACO_2$ by 1 to 5 mm Hg in normal, healthy patients because of a small amount of alveolar dead space. Increasing alveolar dead space widens this gradient. Numerous reasons exist for alveolar dead space, such as reduced cardiac output, pulmonary embolism, obstructive lung disease, smoking, and advanced age. $P_{ET}CO_2$ can overestimate Pa_{CO_2} as well due to such reasons as water vapor in the sample tubing and exhausted CO_2 absorbent.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:1427–1429.

100. ANSWER: B

A significant reduction in perioperative risk by smoking cessation is likely achieved only after a prolonged period of abstinence. However, acute changes occur during the immediate period of abstinence. Any long-term benefit to these changes is unproven and purely speculative. Soon after a patient quits smoking, carboxyhemoglobin levels decrease, potentially improving oxygen delivery; cyanide levels decrease, benefiting mitochondrial metabolism; lower nicotine levels improve vasodilation; and toxins that may have some impact on wound healing will have cleared.

ADDITIONAL READING

Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009:1022.

101. ANSWER: C

Bronchial carcinoids are a rare group of neuroendocrine neoplasms. Like other carcinoid tumors they are composed of peptide- and amine-producing cells. Carcinoids can arise from a number of different sites, though most commonly the gastrointestinal tract. The lung is the second most common site (20% to 30% of all carcinoid tumors).

Carcinoid tumors have the ability to take up and modify amine precursors and synthesize, store, and secrete biologically active neuroamines and neuropeptides. Carcinoid syndrome refers to the systemic release of these substances with symptoms of flushing, diarrhea, and bronchospasm. A carcinoid crisis (acute carcinoid syndrome) is a life-threatening form of carcinoid syndrome that can be triggered by tumor manipulation, resulting in a carcinoid tumor releasing an overwhelming amount of biologically active compounds. As opposed to gastrointestinal carcinoids, bronchial carcinoids do not typically secrete high levels of bioactive peptides. Therefore, these crises occur less often from bronchial tumors. Despite this, bronchogenic carcinoids are capable of releasing a massive amount of mediators, and anesthesiologists should be aware of the appropriate treatment. During a carcinoid crisis patients acutely develop flushing, diarrhea, tachycardia, arrhythmias, hypertension, hypotension, bronchospasm, or myocardial infarction.

Because bronchial carcinoids rarely result in crises, prophylactic treatment is not indicated. If a crisis does occur, octreotide (25- to 100-mcg IV boluses given immediately to effect, with a 50- to 100-mcg/hr infusion if needed) is the appropriate treatment. Management is different from other forms of intraoperative hypotension. Such an episode is typically resistant to fluid resuscitation, and calcium and catecholamines can stimulate further mediator release and result in worsening of the crisis. Carcinoid tumors have somatostatin receptors. Somatostatin is a gastrointestinal regulatory peptide that reduces the production and release of gastropancreatic hormones, thus reducing serotonin release from carcinoid tumors. Therefore, administering somatostatin will reduce the amount of serotonin released by the tumor. Octreotide is a long-acting, synthetic somatostatin analog.

ADDITIONAL READING

Barish PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2009:1227–1228.

11.

VASCULAR ANESTHESIA

Elizabeth Eastburn, DO, and Ruma Bose, MD

1. A 66-year-old man with hypertension and non–insulin-dependent diabetes is scheduled for open repair of a 6 centimeter suprarenal abdominal aortic aneurysm. In the preoperative holding area, his blood pressure is 160/75 mm Hg and heart rate is 80 bpm. After placement of the aortic cross-clamp, his blood pressure is 180/78 mm Hg and heart rate is 115 bpm. Which of the following is the most appropriate perfusion goal during aortic cross-clamping?

A. Current blood pressure and heart rate are acceptable
B. Optimal systolic blood pressure is less than 110 mm Hg
C. Urine output should be greater than 50 cc/hr
D. Preoperative heart rate and blood pressure values are appropriate as long as operating conditions are acceptable
E. Central venous pressure should be maintained between 5 to 8 cm H_2O

2. A 57-year-old man with a history of hypertension presents with shortness of breath and severe chest pain, with radiation to the back. His heart rate in the emergency room is 140 bpm and his blood pressure is 190/100 mm Hg. The best next step in his treatment would be:

A. CT scan of the chest
B. Oxygen, intravenous morphine, heparin infusion
C. Aggressive blood pressure control with nitroprusside and labetalol infusions
D. Intravenous metoprolol and observation
E. Rapid sequence intubation for emergent surgery

3. A 72-year-old woman is undergoing open abdominal aortic aneurysm repair. The surgical repair and anesthetic course have been uneventful. An aortic cross-clamp was placed below the level of the renal arteries. After approximately 45 minutes of clamp time, the surgeon informs you that he is ready to remove it. All of the following intravenous therapies are appropriate next steps except:

A. 2 liter bolus of isotonic crystalloid solution
B. 1 gram infusion of calcium chloride
C. 200 microgram bolus of phenylephrine
D. 40 milligram bolus of furosemide
E. 0.5 liter bolus of 5% albumin

4. Activation of carotid chemoreceptors is greatest with which of the following?

A. Increase in arterial partial pressure of oxygen
B. Decrease in arterial partial pressure of carbon dioxide
C. Decrease in arterial pH
D. Increase in cerebrospinal fluid pH
E. Increase in mean arterial pressure

5. Four days after a left-sided carotid endarterectomy, a 78-year-old woman develops severe left-sided headache and minutes later has a witnessed generalized seizure. In the postoperative period, the patient required sodium nitroprusside infusion for 12 hours to control her blood pressure, which peaked at 180/110 mm Hg. She is now being maintained on metoprolol 50 mg three times daily. Her blood pressure in the emergency department is 190/85 mm Hg. The most likely cause of her seizure is

A. Postoperative respiratory insufficiency
B. Excessive cerebral perfusion
C. Postoperative stroke
D. Aortic dissection
E. Intracranial hemorrhage

6. Which of the following hemodynamic changes would be an expected compensatory response in healthy individuals following carotid body baroreceptor activation?

A. Increased heart rate
B. Increased mean arterial pressure
C. Increased right atrial filling pressure
D. Increased venous capacitance
E. Increased cardiac index

7. A 78-year-old man with NYHA class III congestive heart failure is undergoing emergency exploratory laparotomy for colonic perforation. Intraoperatively, he has systemic hypotension, metabolic acidosis and an elevated blood lactate level. Transesophageal echocardiography shows left ventricular hypokinesis. Dobutamine infusion is begun, with minimal clinical improvement. What is the most likely reason for the poor response?

A. Dobutamine is an inappropriate choice for this profile
B. Cardiac beta-adrenergic receptors are downregulated
C. Systemic catecholamines are depleted
D. Metabolic acidosis affecting enzymatic activity
E. Vasoplegia due to systemic inflammatory response syndrome (SIRS)

8. A 68-year-old man with insulin-dependent diabetes mellitus is in the surgical intensive care unit following a right total hip replacement. His course has been complicated by a pulmonary embolus, and he is currently on an intravenous heparin infusion. His quantitative platelet count on admission was 210,000 and now, on postoperative day 5, it has fallen to 80,000. An ELISA antibody test for heparin-induced thrombocytopenia is positive. The best treatment for this patient is:

A. Stop heparin and start only warfarin
B. Stop all anticoagulants and place an inferior vena cava filter
C. Continue anticoagulation, but change heparin to a direct thrombin inhibitor
D. Continue heparin infusion
E. Transfuse platelets

9. Which of the following physiologic changes would be associated with a subsequent reduction in peripheral blood flow?

A. Core temperature of 37.5 degrees C (from 35.5 degrees C)
B. Point-of-care hematocrit of 40% (from 25%)
C. Right atrial pressure of 8 cm H_2O (from 12 cm H_2O)
D. Infusion of low-molecular-weight colloid solution
E. 2 liter bolus of normal saline

10. A 60-year-old man with hypertension and atrial fibrillation presents with an ischemic stroke in the distribution of the middle cerebral artery. His hematocrit on admission is 29%. Transfusion of packed red blood cells is most likely to have which of the following hemodynamic consequences?

A. Increased cerebral blood flow
B. Decreased cerebral blood flow
C. Decreased renal blood flow
D. Increased coronary blood flow
E. Prevention of coronary ischemia

11. A 50-year-old man with a history of end-stage renal failure secondary to diabetes mellitus is undergoing cadaveric renal transplant. Preoperatively, the hematocrit is 34%, the blood glucose is 121 mg/dL, and the vital signs are within normal limits. Shortly after an occlusive clamp is applied to the right common iliac artery, the systolic blood pressure falls to 85 mm Hg and the patient develops mild tachycardia to 105 bpm. The O_2 saturation is 96% on 50% FiO_2. Central venous pressure is 8 cm H_2O. The most appropriate next step in the management is:

A. Start intravenous phenylephrine infusion at 25 mcg/min
B. 1 liter bolus of normal saline
C. Increase minute ventilation
D. Start intravenous dopamine infusion at 3 mcg/kg/min
E. 12.5 grams intravenous mannitol

12. A 62-year-old woman presents to the neurologic intensive care unit following an acute subarachnoid hemorrhage. She exhibits altered mental status, headache, and nystagmus. An arterial line, a central venous line, and a dural pressure monitor are placed. Currently, her mean arterial pressure is 60 mm Hg, central venous pressure is 20 cm H_2O, and intracranial pressure is 12 mm Hg. The cerebral perfusion pressure is:

A. 48 mm Hg
B. 28 mm Hg
C. 32 mm Hg
D. 40 mm Hg
E. 45 mm Hg

13. A 33-year-old man was recently diagnosed with adrenal pheochromocytoma. He presents for preoperative evaluation with symptoms of headache, palpitation, and dizziness. On examination, his blood pressure is 200/110 mm Hg and his heart rate is 100 bpm. An acceptable first line of treatment is:

A. Esmolol
B. Labetalol

C. Phentolamine
D. Nitroglycerine
E. Diltiazem

14. The above patient is undergoing surgery for excision of his tumor after appropriate preoperative preparation. After adrenal vein ligation, the patient develops hypotension to 70/40 mm Hg. All of the following steps are appropriate at this time except:

A. 1 liter bolus of normal saline
B. Phenylephrine infusion at 50 mcg/min
C. Trendelenburg positioning
D. Dobutamine infusion at 5 mcg/kg/min
E. Transfusion of 2 units packed red blood cells

15. You are caring for a 72-year-old man in the cardiovascular intensive care unit who is postoperative day 2 following coronary artery bypass grafting. The patient is extubated and off vasopressors but has not yet mobilized. You are called urgently to the bedside by a family member, and on arrival you notice the patient is tachypneic and in distress. Jugular venous distention is noticeable. Blood pressure is 75/40 mm Hg, heart rate is 120 bpm, and oxygen saturation is 88% on room air. The family reports the patient was sitting up in bed talking when he became acutely short of breath and "passed out." Which of the following echocardiographic findings is most likely to be seen in this patient?

A. Apical hypokinesis
B. Dilated left ventricle
C. Tricuspid valve insufficiency
D. Aortic valve insufficiency
E. Systolic anterior motion of the mitral valve

16. You are relieving a colleague during a craniotomy performed in the supine position. The patient is a 42-year-old woman with a history of hypertension and frontal lobe astrocytoma. At the time you enter the case, the surgeons are at work dissecting the tumor. After full report, you take over the anesthetic care. The patient is anesthetized with 0.5% end-tidal isoflurane in oxygen and air and continuous remifentanyl and cisatracurium infusions. A 12-French triple-lumen catheter is in the right subclavian vein, and an arterial line is in the left radial artery. Blood loss has been minimal. Approximately 5 minutes after relieving your colleague, you notice an acute decrease in your end-tidal CO_2 concentration from 40 mm Hg to 20 mm Hg. The blood pressure, which had been above 110/55 mm Hg for the entirety of the case, is now 75/40 mm Hg. Which of the following maneuvers would NOT be indicated at this time?

A. Trendelenburg positioning
B. Irrigation of the operative field with normal saline
C. Move the patient into right lateral decubitus position
D. Ensure adequate chemical paralysis
E. Change inspired oxygen to 100%

17. A 70-year-old man with hypertension and stage II chronic kidney disease is undergoing thoracic lobectomy for a left-sided lung mass and is requiring one-lung ventilation, which he tolerates well. Intraoperatively, he develops hypertension requiring the administration of nitroprusside. Which of the following changes is likely to be seen in this patient following nitroprusside administration?

A. Arterial partial pressure of oxygen will increase
B. Arterial partial pressure of oxygen will decrease
C. Gradient between arterial and end-tidal CO_2 will decrease
D. Worsening oliguria
E. Cyanide toxicity with intraoperative nitroprusside

18. You are called to the recovery room to evaluate one of your patients. The patient, a 28-year-old woman, had an uneventful anesthetic for laparoscopic cholecystectomy 3 hours prior and is otherwise healthy. Her urine output has been minimal despite what you consider to be adequate volume replacement. She has made only 30 cc of urine since completion of surgery, and the catheter has been flushed. The intraoperative course was unremarkable, and the last recorded vital signs were blood pressure 132/71 mm Hg and heart rate 81 bpm. She is warm, alert, and comfortable. Which of the following is the most likely cause of the patient's oliguria?

A. Excessive peritoneal insufflation
B. Gross circulating volume depletion
C. Preoperative fluid restriction
D. Intraoperative ureteral injury
E. Surgical stress response

19. A 60 kg, 50-year-old woman with history of tobacco use and uterine fibroids is undergoing open hysterectomy. After 2 hours of operative time, systolic blood pressure is 90 mm Hg, heart rate is 105 bpm, and oxygen saturation is 98%. At this point, the estimated blood loss is 1,000 mL. Which of the following statements is correct?

A. Mean arterial pressure is always a good indicator of renal perfusion
B. Intravenous esmolol is indicated to lower heart rate
C. Colloid is strongly preferred over crystalloid for volume replacement

D. Sympathetic outflow to the renal system would be much higher than normal
E. Intraoperative urine output is a reliable predictor of postoperative renal function

20. Trace the course of systemic arterial blood flow from the left ventricle, assuming there is no significant vascular obstruction. As the distance from the aortic valve increases, which of the following changes is seen?

A. Systolic blood pressure increases
B. Diastolic blood pressure increases
C. Pulse pressure decreases
D. Mean arterial pressure increases
E. Systemic vascular resistance increases

CHAPTER 11 ANSWERS

1. ANSWER: D

The level of ***aortic cross-clamping*** plays an important role in the systemic hemodynamic profile. A clamp placed more proximally will typically result in a more profound hypertensive response. The physiologic changes that occur when an aortic cross-clamp are placed are due to increases in arterial pressure, systemic vascular resistance, and global sympathetic activation. Upon placement of the clamp, sympathetic activation and distal venous recoil result in systemic venoconstriction. The decrease in venous capacity shifts blood volume proximally. Therefore, there is an increase in intracranial, intrapulmonary, and proximal muscle blood volume. This increase in venous return also results in an increase in cardiac preload. A clamp placed more distally may allow this increased blood volume to offload into the splanchnic vasculature with minimal effect on preload.

After application of the aortic cross-clamp there is an acute increase in left ventricular afterload and filling pressures. This can result in myocardial ischemia and left ventricular failure in patients with underlying left ventricular dysfunction or coronary disease. Inotropic support and coronary vasodilators can be used to help offset the hemodynamic changes caused by aortic cross-clamping, but treatment should be focused primarily on measures that decrease afterload (systemic vasodilators) and maintain preload (intravenous fluid administration). Hypotension should be avoided, allowing perfusion pressure to be maintained below the clamp via collateral circulation. This will help prevent tissue ischemia.

Renal failure after aortic surgeries is a major problem. It is most commonly seen after emergency aortic surgery, prolonged cross-clamping periods, clamps placed above the renal arteries, and in patients with preexisting renal dysfunction. The most significant anesthetic consideration is avoidance of prolonged periods of systemic hypotension. Many therapies have been advocated for prevention of postoperative renal failure, such as infusions of dopamine, fenoldopam, or mannitol, but no strong evidence supports any of these therapies. The most important anesthetic consideration for renal protection is the maintenance of systemic perfusion, usually through adequate hydration and support of cardiac function. Intraoperative urine output does not necessarily predict postoperative renal dysfunction.

ADDITIONAL READINGS

Biebuyck JF, Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1060.

Chapter 32, Anesthesia for Vascular Surgery. In Barash P, et al., eds. *Clinical Anesthesia*. 5th ed. Philadelphia: J. B. Lippincott; 2006.

2. ANSWER: C

The primary medical intervention for management of ***acute aortic dissection*** is aggressive blood pressure control and reduction in force of left ventricular ejection. The goal is to reduce shear forces from steepness of the rise of the aortic pressure (dP/dt), ideally resulting in stabilization of the dissection. The plan should be to achieve the lowest blood pressure without compromising end-organ perfusion. Usually, systolic blood pressure is kept between 100 and 120 mm Hg or mean arterial pressure 60 to 75 mm Hg, regardless of the baseline blood pressure. Typically, aortic dissection will require operative intervention, although stabilization of blood pressure should be first priority, and some dissections may be managed with medical therapy only.

Long-acting medications should be avoided due to the potential for acute and prolonged intraoperative hypotension. Nonselective beta-blockers such as labetalol are effective at reducing both systolic blood pressure and dP/dt. Adding a vasodilator such as nitroprusside will further reduce blood pressure. Nitroprusside administered without concurrent use of a beta-blocker may result in increase dP/dt, as contractility may be unaffected or even worsened with acute arterial vasodilatation. Pain can exacerbate the sympathetic response to the dissection, and therefore IV narcotics can assist with aggressive blood pressure management. This would be a secondary consideration in the patient with acute aortic dissection, however. Anticoagulation should be avoided in this patient. Intubation could certainly be indicated in this patient if surgical intervention were planned; however, care should be taken to avoid excessive sympathetic stimulation. Rapid sequence intubation may not be the preferred technique when all factors are taken into consideration.

ADDITIONAL READINGS

Khan IA, Nair CK. Clinical, diagnostic, and management perspectives of aortic dissection. *Chest*. 2002;122:311–328.

Chapter 56, Diseases of the Aorta. In Libby P, et al. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. Saunders, 8th ed, 2007. 1479–1482.

3. ANSWER: D

Profound systemic hypotension is likely to occur with ***removal of an aortic cross-clamp***. This is due to the rapid decrease in afterload, vasodilatation distal to the clamp, and the release of mediators by ischemic tissue. These mediators can cause systemic vasodilatation, hyperkalemia, acidosis, and cardiac depression, and administration of calcium chloride or sodium bicarbonate prior to unclamping can offset the effects. Volume loading or addition of a vasoconstrictor

such as phenylephrine or norepinephrine prior to unclamping may attenuate the resulting hypotension. The most important strategy, however, is gradual release of the clamp, allowing for fluid replacement and slow washout of mediators.

KEY FACTS ANESTHETIC GOALS FOR AORTIC SURGERY

1. Appropriate monitoring based on type of aortic surgery and patient comorbidities. This will likely include an arterial line, a central venous pressure monitor, and possibly a pulmonary artery catheter. Transesophageal echocardiography may also be indicated.
2. Reduction of the systemic stress from the placement and removal of the aortic cross-clamp
3. Measures to prevent spinal cord ischemia should be considered in surgeries involving the thoracic aorta, such as prevention of hypotension, administration of mannitol, or placement of a cerebrospinal fluid drain.
4. Consider strategies for renal preservation.
5. Transfusion of blood products in the setting of massive acute blood loss

ADDITIONAL READINGS

Biebuyck JF, Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1060.

Chapter 32, Anesthesia for Vascular Surgery. In Barash P, et al., eds. *Clinical Anesthesia*. 5th ed. Philadelphia: JB Lippincott; 2006.

4. ANSWER: C

The ***carotid and aortic bodies*** are located in areas of very high blood flow. Both of these areas contain chemoreceptors, for detection of subtle physiologic changes in blood flow and composition. ***Chemoreceptors*** are primarily activated by decreases in Pa_{O_2} and pH and increases in Pa_{CO_2}. The direct effect of activation is an increase in vagal nerve activity, resulting mainly in changes in respiration and blood pressure.

Hemorrhage that leads to hypotension results in a relative reduction in blood flow to the chemoreceptors, ultimately causing cellular hypoxia and activation of the chemoreceptor. This is the mechanism for activation secondary to decreased arterial pH or worsening acidemia. The primary mechanism for response to acute changes in systemic arterial blood pressure is the relative stretch of the baroreceptor fibers, and activation is greatest with increased stretch such as would be seen in increased systemic blood pressure.

ADDITIONAL READING

Barrett KE, Barman SM, Boitano S, Brooks HL. Chapter 33, Cardiovascular Regulatory Mechanisms. In *Ganong's Review of Medical Physiology*. 23rd ed. New York: McGraw-Hill Medical; 2009.

5. ANSWER: B

Cerebral hyperperfusion syndrome is thought to occur when the blood flow to the brain exceeds the metabolic demands. This may occur days after carotid endarterectomy and typically presents as a severe ipsilateral headache, which may progress to signs of cerebral excitability or seizures.

Postoperative hypertension is common after carotid endarterectomy and is associated with adverse events such as stroke or death. Although the mechanism is not fully understood, it appears to be related to increased sensitivity or impaired function of the carotid baroreceptors. Postoperative hypertension is more likely to occur in patients with a preoperative history of uncontrolled hypertension. Conversely, some patients develop postoperative hypotension due to improved flow to the carotid baroreceptors.

ADDITIONAL READINGS

Ellis JE, Roizen MF, Mantha S, et al. Anesthesia for Vascular Surgery. In Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:953–954.

Hirschl M, Kundi M, Hirschl M, et al. Blood pressure responses after carotid surgery: relationship to postoperative baroreceptor sensitivity. *Am J Med*. 1993;94:463–468.

6. ANSWER: D

The carotid sinus is located at or near the bifurcation of the common carotid artery and contains the carotid baroreceptors, which are specialized neural fibers designed to sense stretch at this region of high flow. The afferent limb of the reflex originates at the sinus, and fibers travel to the nucleus tractus solitarius through the glossopharyngeal nerve (CN IX). Baroreceptor activity is increased with increased stretch, which is primarily due to elevations in mean arterial pressure or in systolic pressure. Through vagal activation and inhibition of the sympathetic nervous system, the net result is venous dilation and decreases in heart rate, blood pressure, and cardiac output.

ADDITIONAL READING

Barrett KE, Barman SM, Boitano S, Brooks HL. Chapter 33, Cardiovascular Regulatory Mechanisms. In *Ganong's Review of Medical Physiology*. 23rd ed. New York: McGraw-Hill Medical; 2009.

7. ANSWER: B

Patients with congestive heart failure often have increased sympathetic cardiac function to maintain systemic perfusion in the setting of severely diminished intrinsic function. As a result, there are higher levels of circulating catecholamines. Over time, the increased sympathetic activity and the increased release of catecholamines leads to downregulation of beta-1-adrenergic receptors. The magnitude of downregulation is directly related to the severity of heart failure (and the level of circulating catecholamines is inversely related to prognosis). The downregulation of beta-adrenergic receptors may also result in a decreased responsiveness to exogenous beta-agonist administration, as might be given during aggressive hemodynamic resuscitation.

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8. ANSWER: C

Heparin-induced thrombocytopenia (HIT) is an immune-mediated response caused by antibodies against complexes of platelet factor 4 (PF4) and heparin. This leads to activation of platelets and, in some cases, a prothrombotic state. It typically occurs within 5 to 10 days of new exposure to heparin, but may occur sooner when a patient is re-exposed to heparin. Platelet counts rarely drop below 10,000, and a drop of greater than 50% of normal platelet count should raise suspicion. The thrombotic risk is 30 times greater than in control populations.

The initial test for HIT is the ELISA test for antibodies to heparin–PF4 complexes, and a positive ELISA test, in concert with a high index of suspicion, is usually enough for the diagnosis of HIT, at which point all heparin-containing substances should be withdrawn from the patient. Further diagnostic tests may be conducted, the most specific of which is considered the serotonin-release assay (SRA), which measures serotonin levels as a marker of platelet activity.

After the diagnosis of HIT is made, an alternative anticoagulant must then be started to prevent and treat thrombus formation. Alternative anticoagulants may include factor Xa inhibitors (apixaban, edoxaban, etc.) or direct thrombin inhibitors (lepirudin, argatroban, etc.). These anticoagulants must be continued until the platelet count normalizes (usually about 4 to 14 days), at which point warfarin should be started. Once the patient is appropriately therapeutic on warfarin, the bridging medication can be stopped.

Oral anticoagulation should be continued for 4 to 6 weeks, because the risk of thrombus remains even after the platelet count normalizes. Starting warfarin before normalization of the platelet count can lead to severe skin necrosis due to a decrease in protein C levels. Aspirin and inferior vena cava (IVC) filters are not adequate for the treatment of HIT. Platelet transfusion can be thrombogenic in HIT, and are rarely indicated.

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9. ANSWER: B

Peripheral blood flow is determined by perfusion pressure, blood vessel size, and blood viscosity. Increased blood viscosity has been demonstrated in a number of vascular diseases. Also, declines in body temperature, such as in deep hypothermic cardiac arrest, result in decreased blood flow. Therefore, decreasing blood viscosity will improve systemic blood flow. Several mechanisms can result in lower viscosity and, subsequently, increased blood flow: hemodilution with crystalloids, anemia, and administration of low-molecular-weight dextran.

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10. ANSWER: B

Viscosity of blood is determined predominantly by hematocrit, which is defined as the percentage composition of whole blood composed of erythrocytes. As the hematocrit increases, the blood viscosity increases and blood flow through vessels decreases. This effect of viscosity on blood flow is mainly seen in vessels with larger diameter, which have

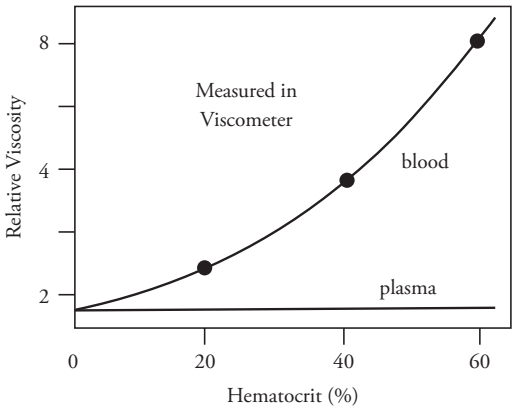

Figure 11.1 Change in viscosity of blood with change in hematocrit.

nonlaminar flow. Viscosity of blood is also affected by body temperature, blood flow, and vessel diameter (Fig. 11.1).

At a hematocrit of 40%, the relative viscosity of blood is 4. At a hematocrit of 60%, the relative viscosity is about 8. Therefore, a 50% increase in hematocrit from a normal value increases blood viscosity by about 100%.

The rate of blood flow through the vasculature also affects viscosity. At very low-flow states in the microcirculation, as during circulatory shock, the blood viscosity can increase quite significantly. This occurs due to increased cell-to-cell and plasma protein-to-cell adhesive interactions that can cause erythrocytes to adhere to one another and increase the blood viscosity.

Normal vasculature can autoregulate blood flow in response to changes in the viscosity of blood; in other words, there is vasodilation in response to increase in viscosity and vice versa. However, vessels supplying ischemic areas lose their ability to autoregulat—for example, in focal ischemic brain injury, blood flow to ischemic areas would decrease with increasing blood viscosity.

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11. ANSWER: B

One of the primary goals of intraoperative management of the kidney transplant recipient is maintenance of adequate perfusion to the transplanted kidney. Immediate graft function is associated with increased graft survival and lower patient mortality. Ensuring adequate intravascular volume status is paramount. Intraoperative hypotension is deleterious to adequate renal perfusion and should be aggressively treated.

Patients with end-stage renal disease are typically hypovolemic at baseline, despite an increase in total body water. Much of this fluid is extravascular. Adequate intraoperative volume replacement (either with crystalloid or colloid) is an important measure for ensuring adequate renal blood flow. Placement of a central venous catheter is suggested as a possible guide for intraoperative volume replacement. Pulmonary artery catheters have also been used. The optimal central venous pressure is typically 10 to 15 cm H_2O.

The use of alpha-1-agonists to treat hypotension should be limited because they may cause further reduction in renal perfusion. Therefore, phenylephrine and ephedrine use should be restricted. Many physicians prefer dopamine receptor-agonists for treatment of intraoperative hypotension refractory to other therapies, but these are not typically first-line steps in managing hypotension.

Adequate diuresis of the transplanted kidney is equally important and is achieved by diuretics (furosemide, mannitol), but these would not be expected to help intraoperative hypotension. Dopamine agonists (dopamine, fenoldopam) may support urine output in conjunction with blood pressure support.

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12. ANSWER: E

Cerebral perfusion pressure is the gradient that exists between the arterial and venous pressures in a comparable location in the vascular tree. Blood flow through the vascular system follows physical principles that dictate movement of fluid in most systems, and it is governed by the principles of Ohm's law: current equals voltage difference divided by resistance.

In the cardiovascular system blood flow equals the pressure gradient divided by the vascular resistance. In blood vessels, the flow is determined by the pressure difference between two points with comparable vascular resistance. For any organ system, perfusion pressure is determined by the pressure difference between the arterial and venous systems supplying that organ.

Cerebral perfusion pressure is determined by calculating the difference between the mean arterial pressure and the greater of the intracranial pressure or the central venous pressure.

$$CPP = MAP - ICP \text{ (or CVP)}$$

A simple conversion is required to change central venous pressure measurements from cm H_2O into mm Hg. Approximately 0.75 mm Hg = 1 cm H_2O; therefore, 20 cm H_2O would equal 15 mm Hg. This conversion should be memorized for arterial line measurements as well ("the arterial line transducer is 20 cm below the heart; what is the true pressure?").

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13. ANSWER: C

Pheochromocytoma is a catecholamine-secreting tumor most often arising from the enterochromaffin cells of the adrenal medulla. The tumor typically secretes epinephrine, norepinephrine, and dopamine, which in turn activate the alpha- and beta-adrenergic receptors. The presenting symptoms often include sudden episodes of headache, diaphoresis, palpitation, and abdominal pain with signs of uncontrolled hypertension and tachycardia.

The diagnostic workup includes 24-hour urine metanephrine levels and radiologic evaluation by CT and MRI of the abdomen. Definitive treatment is surgical excision of the tumor.

The goals of the preoperative evaluation include establishing the baseline end-organ function, optimization of hemodynamics, restoration of intravascular volume, and prevention of further end-organ damage. Alpha-adrenergic antagonists are the mainstay of preoperative medical management of pheochromocytoma. Phenoxybenzamine is a noncompetitive alpha-blocker and is also the most effective in preventing hypertensive episodes. However, it has a longer duration of action and can contribute to postoperative hypotension. Phentolamine is a competitive alpha-blocker that can be given intravenously. Other alpha-blockers such as prazosin, terazosin, and doxazosin are competitive antagonists and have a shorter duration of action. Hypotension due to alpha-blockade can be treated by volume replacement. Serial hematocrit measurements can be a useful guide to the adequacy of alpha blockade and volume replacement, with a 5% drop in hematocrit from baseline value considered adequate.

Beta-blockers are used to treat tachycardia and arrhythmias. However, they should not be used before appropriate alpha-blockade, because this may potentially cause an unopposed alpha-adrenergic response to catecholamines, making hypertension more pronounced.

Combined alpha- and beta-blocking agents can be used, although the minimum ratio of alpha to beta antagonism required is 4:1. Labetalol and carvedilol have an alpha:beta activity of 1:7 and can cause paradoxical hypertension. Therefore, these are not agents of choice in pheochromocytoma.

Calcium-channel-blockers prevent reuptake of calcium into the vascular endothelium and prevent vasospasm and can be used as a supplement to alpha-blockers in patients with uncontrolled hypertension, or those suffering from side effects of alpha-blockers such as postural hypotension. Vascular-specific agents such as nicardipine would be preferable to diltiazem in this instance.

Metyrosine is an analog of tyrosine and inhibits tyrosine hydroxylase, which is the rate-limiting step in catecholamine production. It crosses the blood-brain-barrier and can cause side effects such as sleepiness, anxiety, and depression. Metyrosine is frequently combined with alpha-blockers preoperatively.

Patients with pheochromocytoma can have significant end-organ damage, including cardiomyopathy and heart failure, as a result of longstanding hypertension. They can also present with renal insufficiency, which will affect perioperative management. Careful history and physical examination is important. Further preoperative workup may be required to determine the baseline cardiac and renal function.

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14. ANSWER: D

Intraoperative hypotension is commonly observed after the venous outflow from the adrenal tumor is ligated. The desensitization of sympathetic adrenoceptors from prolonged exposure to high levels of adrenergic hormones plays a role in exacerbating the hypotension. The residual effect of anti-adrenergic agents used perioperatively to treat hemodynamic perturbations also contributes to the hypotension.

Management of intraoperative hypotension includes volume replacement and vasopressors such as phenylephrine or norepinephrine. Normalization of intravascular volume prior to surgery minimizes the occurrence of hypotension. Serial hematocrit measurement is a useful method to check the adequacy of volume replacement and alpha-blockade. A 5% drop in hematocrit from baseline is indicative of adequate volume replacement.

Blood transfusion is recommended when indicated. Dobutamine would not be an ideal choice for management

of hypotension without evidence of heart failure, because it predisposes to arrhythmia and has less affect on the vasoplegia seen after pheochromocytoma resection.

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15. ANSWER: C

Acute pulmonary embolism (PE) is a rare but devastating complication and may occur rapidly and unpredictably. The type of embolism in the intraoperative setting varies depending on the source of origin and the nature of the surgical procedure. Fat embolism is seen in hip arthroplasty during instrumentation of long bones, and in spine surgery. Amniotic fluid embolism may be seen during cesarean section. The risk of air embolism is high when the site of surgery is above the level of the heart. The event described above likely resulted from venous stasis and hypercoagulability following surgery.

The clinical presentation depends on the PE severity. The sudden onset of hypotension, extreme hypoxemia, electromechanical dissociation, or cardiac arrest is seen with massive PE. Patients who are awake often have dyspnea or chest pain, cough, palpitation, wheezing, and rales. Tachypnea and tachycardia are common but nonspecific findings. Signs of pulmonary hypertension caused by PE may include elevated neck veins, a loud P_2, a right-sided gallop, and a right ventricular lift.

Electrocardiographic manifestations such as an S1-Q3-T3 pattern, right bundle-branch block, p-wave pulmonale, or right axis deviation are more common with massive PE, but none are sensitive or specific enough to rely on for diagnosis. The chest radiograph may show gas in the pulmonary arterial system, pulmonary arterial dilatation, focal oligemia (Westermark's sign), or pulmonary edema.

Patients with acute PE usually have hypoxemia, and a sudden or unexplained change in arterial oxygen saturation should raise suspicion. An acute drop in end-tidal carbon dioxide may indicate venous air embolism, but it is also seen in shock states. An increase in end-tidal nitrogen is sensitive for air embolism. Transthoracic doppler can detect small air emboli, resulting in a characteristic mill-wheel murmur on physical exam.

Transesophageal echocardiography is useful in early diagnosis of massive PE. The right ventricle is dilated and hypokinetic, with flattening of the intraventricular septum. There is a distinct regional pattern of right ventricular dysfunction, with akinesis of the mid-free wall but normal motion at the apex. Insufficiency of the tricuspid and pulmonary valves is commonly seen. Overall, echocardiography has a low sensitivity for diagnosing pulmonary embolism, but the efficacy is much better in massive cases. Direct visualization of the thrombus in the pulmonary artery is diagnostic.

The goal for management of PE is primarily to manage the impending cardiovascular collapse by improving forward blood flow, and also to treat the cause, if possible. In this respect, the anesthesia care is often considered supportive and diagnostic rather than therapeutic. Catheter-based mechanical pulmonary embolectomy, local intraembolic thrombolytic therapy, and surgical pulmonary embolectomy are all treatment options. Surgical intervention is often indicated in the presence of right heart thrombi, with or without PE.

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Tapson VF. Acute pulmonary embolism. *N Engl J Med*. 2008;358; 1037–1052.

16. ANSWER: C

The nature of the procedure, the position of the patient, and the clinical signs and symptoms all suggest ***venous air embolism***. The intracranial venous sinuses are frequently interrupted during brain surgery, and occasionally air is entrained into the venous circulation. If enough air is taken in (50 to 75 cc, approximately a stroke volume), then significant cardiopulmonary dysfunction may be seen. However, signs such as the ones described may be seen with lower amounts. Clinically, the patient may exhibit hypotension, tachycardia, and acute drops in end-tidal CO_2 tracing, as well as hypoxemia.

For treatment of acute air embolism, the patient should be placed in Trendelenburg position, ideally in the left lateral decubitus position, which allows air trapped in the right ventricular outflow tract to more easily migrate back toward the venous circulation. This is theoretical, however, and proves to be extremely difficult in practice. However, keeping the patient in the supine position would be preferable to moving to the RIGHT lateral position. 100% inspired oxygen should be initiated because it may help support regions of low blood flow, as well as possibly reducing the size of the entrained air mass. Nitrous oxide, if being administered, should be halted. Irrigation of the operative field, typically with saline solution, may prevent further air entrainment until the problem can be isolated.

Closed-chest cardiac massage forces air out of the pulmonary outflow tract into smaller pulmonary vessels and should improve forward blood flow. Air can be aspirated from the right ventricle via a percutaneously introduced

needle or a central venous catheter. In general, however, these maneuvers are of limited benefit. Use of hyperbaric oxygen has been described in the literature.

ADDITIONAL READING

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17. ANSWER: B

In cases where the total pulmonary circulation is maintained intact, ***one-lung ventilation*** will almost universally reduce the arterial partial pressure of oxygen, due to the shunting that occurs as an unventilated lung sees part of the cardiac output.

Hypoxic pulmonary vasoconstriction plays an important role in maintaining oxygenation during one-lung ventilation by redistributing blood to the ventilated lung, which helps to maintain oxygenation in the event of hypoventilation. This process is not 100% efficient, and some shunting will still occur, resulting in a decline in Pa_{O_2}, and in most cases SpO2 as well.

Hypoxic pulmonary vasoconstriction is attenuated by inhaled anesthetics, hypocapnia, hypothermia, acidosis, and alkalosis. Some medications, such as calcium channel blockers and isoproterenol, may also inhibit the process. Nitroprusside and nitroglycerine are known to directly inhibit pulmonary vasoconstriction, worsening the intrapulmonary shunt.

Due to the presence of the intrapulmonary shunt, we would expect the arterial/alveolar CO_2 gradient to increase or stay the same; a decrease would be most unlikely. No specific effects of one-lung ventilation or nitroprusside infusion would be expected to affect urine output in the case described. Over time, continuous infusion of nitroprusside will predispose patients to development of cyanide toxicity. Renal failure is somewhat protective, however.

ADDITIONAL READING

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18. ANSWER: E

Antidiuretic hormone (ADH) is synthesized in the hypothalamus and released by the posterior pituitary, primarily in response to elevations in plasma osmolality, but also in response to stress. The primary action in humans is reclamation of free water at the distal convoluted tubule and collecting ducts of the nephron. It also has direct effects on arterial blood pressure, through augmentation of peripheral vascular resistance.

Secretion of ADH is also stimulated by hypovolemia and hypotension conditions, which are sensed by stretch receptors in the atrium and aorta. Changes in blood pressure and volume are not nearly as sensitive a stimulator for ADH release as increased osmolality, but they are nonetheless potent in severe conditions such as massive hemorrhage.

ADH release is augmented by several factors in addition to increased plasma osmolality and hypovolemia, such as pain, hypotension, hyperthermia, stress, and nausea and vomiting. ADH release is inhibited by decreased plasma osmolality, ethanol intake, alpha-agonist administration, cortisol secretion, and hypothermia.

The situation described above is a common postoperative recovery scenario, and the stable patient should guide you away from suspecting anything dramatic such as direct or indirect renal injury. Certainly, you must be aware of the catastrophic possibilities, but the oliguria in this case is most likely a result of postsurgical ADH hypersecretion due to surgical stress. This will normalize over time.

ADDITIONAL READING

Stoelting RK. *Pharmacology and Physiology in Anesthetic Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999.

19. ANSWER: D

Renal blood flow determines renal function and represents 20% to 25% of cardiac output even though the kidneys represent only 0.5% of body weight. Renal blood flow is approximately 4 cc/gram/min, compared to 0.7 cc/gram/min for the heart and liver. The majority of the renal blood flow is delivered to the renal cortex and is responsible for flow-dependent functions.

Renal blood flow is maintained by vascular autoregulation, tubuloglomerular balance, and hormonal and neural mechanisms. Intrinsic autoregulation normally occurs between a mean arterial pressure of 50 and 150 mm Hg. As such, mean arterial pressure may not reliably predict renal blood flow. The myogenic response causes the afferent arterioles to undergo vasoconstriction in response to elevated perfusion pressure, thereby decreasing glomerular flow.

The renal system has abundant sympathetic nervous system supply. The afferent arterioles constrict in response to sympathetic stimulation, causing redistribution of blood to nonrenal sites. This has clinical importance because systemic blood pressure may be maintained in the event of hypovolemia even though renal perfusion is decreased.

This patient in the scenario is volume-depleted, likely having lost nearly 25% of circulating volume. As such, we would expect renal sympathetic function to be significantly elevated. The treatment of choice would be to replace intravascular volume deficits with either crystalloid or colloid, and not to artificially suppress heart rate (and cardiac output), with intravenous esmolol. Because many factors, including surgical stress, may affect urine output, its presence or absence is neither sensitive nor specific for approximating renal function, and other markers, such as laboratory tests and clinical examination, should be more heavily relied upon.

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Renin angiotensin system in maintaining effective circulatory blood volume . Modified from Lote CJ, Harper L, Savage COS. Mechanisms of acute renal failure. *Br J Anaesth.* 1996;82–89.

Stoelting RK. *Pharmacology and Physiology in Anesthetic Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins ;.

20. ANSWER: A

Systemic arterial blood pressure represents the force exerted by the blood per unit area on the arterial wall and is the sum of hemodynamic, kinetic, and hydrostatic pressures. Arterial pressure is typically measured at its peak, which is the systolic blood pressure (SBP), and at its trough, which is the iastolic blood pressure (DBP). The SBP is determined by the stroke volume, the velocity of left ventricular ejection or contractility, systemic vascular resistance, the compliance of the aortic and arterial walls, the viscosity of blood, and the left ventricular preload. The blood pressure in the aorta during systole is a clinical indicator of afterload, or the sum of the forces the left ventricle must overcome to eject blood.

Arterial pressure is most accurately measured in the ascending aorta. In the arterial system, the aorta has the highest compliance, due in part to a relatively greater proportion of elastin fibers versus smooth muscle and collagen. This serves the important function of dampening the pulsatile output of the left ventricle. As the pressure wave travels peripherally it is distorted by the relatively increasing resistance of smaller vessels, distance from the heart, and resonance of the pressure waves in the peripheral arteries. The SBP progressively increases with increasing distance from the heart. The DBP decreases and the pulse pressure increases. The mean arterial pressure remains unchanged.

Ultimately, the SBP in the most distal arteries is 10 to 20 mm Hg higher than the central aortic pressure, and the DBP is 10 to 20 mm Hg lower than the central arterial pressure. Mean arterial pressure should remain constant, as it is a function of cardiac output and systemic vascular resistance, which are global values.

ADDITIONAL READING

Monitoring in Anesthesia and Critical Care, New York, Churchill Livingstone 1985 Cardiac Anesthesia; Kaplan, Reich, Konstadt, Fourth Edition.

12.

NEUROANESTHESIA

Tiffany Brainerd, MD, and Mary Ellen McCann, MD, MPH

1. Impending respiratory failure in an otherwise healthy patient in the intensive care unit with acute spinal cord injury can be diagnosed by monitoring the strength of the inspiratory muscles using maximum inspiratory pressure meter, vital capacity measurement, and arterial blood gases. Which of the following measurements would best describe a patient with impending acute respiratory failure?

A. PI max −12 cm H_2O, VC = 6 cc/kg, and ABG on room air 7.40, PaO_2 95 and $PaCO_2$ 40 mm Hg
B. PI max −34 cm H_2O, VC = 10 cc/kg, and ABG on room air 7.40, PaO_2 95 and $PaCO_2$ 40 mm Hg
C. PI max −23 cm H_2O, VC = 9 cc/kg, and ABG on room air 7.21, PaO_2 95 and $PaCO_2$ 60 mm Hg
D. PI max −14 cm H_2O, VC = 5 cc/kg, and ABG on room air 7.21, PaO_2 95 and $PaCO_2$ 60 mm Hg
E. None of the above

2. A 40-year-old man having an appendectomy is induced with propofol and maintained with isoflurane and intermittent doses of fentanyl. Which of the following statements is correct?

A. Burst suppression or an isoelectric EEG usually occurs once the end-expiratory concentration of isoflurane reaches 1 MAC.
B. Opioids such as fentanyl do not affect the EEG.
C. The actions of propofol on the EEG are similar to the actions of etomidate and barbiturates.
D. In general, inhaled anesthetics affect the EEG by decreasing the frequency and decreasing the amplitude of the EEG waves.
E. End-tidal concentrations of isoflurane above 1.5 MAC are associated with spike activity, which in the setting of hypocapnia can lead to frank EEG seizures.

3. A 16-year-old patient with traumatic brain injury and elevated intracranial pressure must be anesthetized for intracranial clot evacuation. Which of the following statements is correct?

A. Nitrous oxide would be a good choice as an adjunctive anesthetic with a volatile anesthetic because it has been demonstrated to decrease cerebral blood flow and cerebral metabolic rate.
B. Approximately 45% of cerebral energy consumption is devoted to electrophysiologic activities and 55% to homeostatic mechanisms during the awake relaxed state.
C. Volatile anesthetic concentrations causing burst suppression mean that the cerebral energy consumption is decreased about 45% from an awake relaxed state.
D. Ketamine is unique among intravenous anesthetics because it causes a decrease in cerebral metabolic rate and an increase in cerebral blood flow.
E. Barbiturates and propofol cause a dose-dependent decrease in cerebral metabolic oxygen consumption and cerebral blood flow.

4. A 57-year-old man is scheduled for clipping of an aneurysm arising at the base of the right anterior communicating artery. Which one of the following statements is correct?

A. The ideal time for this surgery is between 4 and 10 days after subarachnoid hemorrhage because the intravascular clot is most stable at this time and thus the chance of rebleeding during surgery is low.
B. The best management for cerebral vasospasm is volume loading and induced hypotension.
C. The hallmark of cerebral salt-wasting syndrome is volume contraction, hyponatremia, and a urine sodium level of less than 50 mmol/L.
D. Calcium channel blockers have not been shown to be effective in reducing the morbidity associated with subarachnoid hemorrhage.

E. Anesthetic techniques that facilitate brain relaxation and precise control of blood pressure should be used.

5. A 50-year-old man presents in the emergency room with paresthesia of his left lower limb. Which one of the following statements is correct?

A. The major motor pathways involve an upper and lower motor neuron.
B. The descending spinal tracts include the anterior and lateral corticospinal tracts and are involved in sensory perception.
C. The dorsal root ganglia include only neuron cell bodies involved in the autonomic nervous system.
D. In contrast to the descending spinal columns, the ascending spinal columns do remain ipsilateral from the periphery to the cerebral cortex.
E. The nucleus gracilis and nucleus cuneatus are important motor nuclei in the medulla.

6. A 35-year-old woman is scheduled for an excision of a left posterior fossa tumor. Which statement is correct?

A. A reasonable method of neuromonitoring for this case would be the use of bilateral brainstem evoked potentials (BAEPs) because it is possible that intraoperatively the auditory pathways may be damaged.
B. BAEPs are exquisitely sensitive to the effects of volatile anesthetics.
C. The correct order of sensitivity of sensory evoked potentials to the effects of volatile anesthetics is (from most sensitive to least sensitive) visual evoked potentials (VEPs), somatosensory evoked potentials (SSEPs), and BAEPs.
D. Adding nitrous oxide to the volatile anesthetic regimen will cause a decrease in the amplitude and latency of the BAEPs.
E. Intravenous anesthetics affect the waveform of BAEPs more than volatile anesthetics when given in equipotent doses.

7. A 17-year-old boy is scheduled for a fracture stabilization of a left femur injury sustained in a wheelchair accident. This patient also sustained a complete cord transection on the level of C5 2 years ago. Which one of the following statements is correct?

A. Autonomic hyperreflexia occurs during the acute phase of injury but is unlikely 2 years after the injury.
B. Based on the downregulation of adrenergic receptors in patients with high spinal cord transections, these patients require higher-than-normal doses of vasopressors when hypotensive.
C. Light general anesthesia is ideal for patients with spinal cord lesions higher than T5 scheduled for lower abdominal surgery because these patients are insensate and thus do not require anesthesia.
D. Patients with high spinal cord lesions are prone to hypothermia due to vasodilation below the level of the spinal cord lesion.
E. Autonomic hyperreflexia is most commonly heralded by hypertension, tachycardia, diaphoresis, and flushing above the spinal cord lesion.

8. Which of these statements about the autonomous nerve system is INCORRECT?

A. The cranial nerves involved in the parasympathetic nervous system include cranial nerves 3, 7, 9 and 10.
B. The stellate ganglion is a cervical sympathetic ganglion consisting of the middle and inferior cervical ganglions.
C. The adrenal gland can be considered a sympathetic ganglion.
D. The vagus nerve provides parasympathetic supply to the viscera of the neck, thorax, foregut, and midgut.
E. The sympathetic nervous system consists of a chain of ganglia running next to the spinal cord.

9. A 54-year-old man with a 10-year history of insulin-dependent diabetes mellitus is scheduled for inguinal hernia repair. Which statement below is most accurate?

A. As long as it can be demonstrated that his serum glucose is within the normal range during his preoperative surgical visit, this patient is appropriate for day surgery.
B. Diabetic autonomic neuropathy can be detected by eliciting postural hypotension: more than a 30-mm Hg decrease in systolic BP and the 30:15 standing ratio for heart rate is less than 1.03.
C. Gastroparesis found in patients with significant autonomic neuropathy is refractory to treatment with metoclopramide.
D. Although patients with diabetic autonomic neuropathy are at increased risk for painless myocardial ischemia, they are not at increased risk for postoperative cardiorespiratory arrest.
E. One of the reasons that patients with autonomic neuropathies also develop pain syndromes is that the sympathetic system fails first in patients with diabetic autonomic neuropathy, then the parasympathetic system.

10. The processed EEG can be used to monitor a patient's level of consciousness during general anesthesia. Which one of the following statements is correct?

A. The processed EEG is an effective way to monitor focal pathology occurring within the brain.

B. Adding 60% inspired nitrous oxide to an anesthetic regimen usually results in a lower value on processed EEG monitors.
C. Adding neuromuscular blockade can lower processed EEG values.
D. General anesthetics and sedatives are the only drugs used routinely in the operating room that can cause lower values on processed EEG monitors.
E. The actions of ketamine are mediated by the NMDA glutamate receptors, and there is a close correlation between the level of sedation and processed EEG values.

11. A 53-year-old woman presents to the emergency room with severe low back pain and sudden loss of bowel and bladder control. Which of the following statements is correct?

A. Severe low back pain is always a medical emergency and often results in emergency surgery.
B. Low back pain is a very common complaint in patients over 8 years of age.
C. Cauda equina pain is usually unilateral, with accompanying bowel or bladder pain.
D. Pseudoclaudication is seen in patients with spinal stenosis and is relieved by the patient's extending the back to relieve traction on the sciatic nerve.
E. Isolated back pain can be indicative of a serious systemic pathology.

12. A 24-year-old man sustained a closed head injury in a motorcycle accident. An intracranial pressure (ICP) monitor placed in the emergency department demonstrates an ICP of 30 mm Hg. Which of the following statements is true?

A. The first-line treatment for elevated ICP is a barbiturate coma.
B. Even if the barbiturate coma does not reliably decrease the ICP, it is useful because it can be used prophylactically to prevent status epilepticus.
C. Once the loading dose of barbiturate is given, one can expect a sustained drop in ICP in patients whose ICP is responsive to the barbiturate.
D. The goal of barbiturate coma is to decrease the $CMRO_2$ to about 80% of normal.
E. Barbiturates reduce the cerebral metabolic rate, blood flow, and total intracranial blood volume.

13. Barbiturates have been used for cerebral protection in patients for which of the following reasons?

A. Barbiturates reduce cerebral metabolism by antagonizing GABAa receptors in the brainstem.
B. The major inhibitory neurotransmitters in the brain are mediated by glutaminergic-NMDA receptors, and barbiturates activate these receptors.
C. In certain situations, barbiturates may aid in cerebral protection by lowering ICP.
D. A downside of barbiturate coma for cerebral protection is that large doses of barbiturates may increase cerebral perfusion pressure by preferentially decreasing ICP over mean arterial pressure (MAP).
E. The clinical endpoint in treating a patient with brain injury with barbiturates is arterial hypotension of less than 50% normal values for age.

14. A 36-year-old women presents to the emergency room after having taken an overdose of diazepam (Valium). Her respiratory rate is 6 and she is stuporous. Which of the following statements is true?

A. Based on the side-effect profile of flumazenil, care should be supportive in nature.
B. Flumazenil is a noncompetitive benzodiazepine antagonist that can be given to reverse the effects of Valium overdose.
C. Flumazenil has a lower affinity for the benzodiazepine receptors than benzodiazepines.
D. Flumazenil has very little discernible cardiovascular effect when given alone.
E. The onset of action of flumazenil is about 10 minutes, so it is very important to monitor the patient for respiratory depression.

15. A 51-year-old woman is undergoing a craniotomy and craniofacial surgery to remove a tumor on the right side of her face and head extending into her maxillary sinuses and temporal bone. During the procedure she becomes suddenly bradycardic, with a heart rate of 33 bpm. Her anesthetic consisted of remifentanil, propofol, and nitrous oxide. What is the most likely cause?

A. Acute rise in ICP secondary to the retraction of the facial tissues leading to obstruction of venous drainage from the head
B. Accumulation of remifentanil and propofol
C. Rise in ICP due to fluids given intraoperatively
D. Allergic reaction to antibiotic prophylaxis
E. Trigeminal cardiac reflex

16. A 36-year-old man is scheduled for a craniotomy for a right-sided temporal mass. Which of the following statements is correct?

A. Conceptually one should consider the intracranial space as four subcompartments: cells (including the brain), fluid (intracellular and extracellular), cerebrospinal fluid (CSF), and blood.
B. Lumbar CSF drainage will reduce the CSF pressure and therefore is a useful tool in managing supratentorial masses.

C. In this patient, spontaneous breathing during anesthesia is an important sign that the brainstem is being adequately perfused; thus, muscle relaxants should be avoided.
D. Although the anesthesiologist cannot influence the cellular component, he or she can influence the CSF and intravascular component.
E. In patients who demonstrate signs and symptoms of increased ICP, volatile agents are preferred over intravenous anesthetics because of their effects on smooth muscle.

17. A 16-year-old girl who was riding on the back of a motorcycle and not wearing a helmet is involved in an accident. She is found unconscious with an open femur fracture. Which of the following statements is correct?

A. There is no need for concern about traumatic brain injury as long as she regains consciousness prior to femur surgery.
B. Before undergoing femur surgery, it is necessary to do cervical spine films because the likelihood of a cervical spine injury in this scenario is greater than 20%.
C. In traumatic brain injury the baseline cerebral blood flow (CBF) is usually greater than normal.
D. Moderate hypocapnia ($CO_2 < 30$) should be maintained in brain-injured patients to decrease the chance of brain herniation, especially in the first 24 hours.
E. Hypocapnia should be avoided in patients with subarachnoid hemorrhage.

18. A 58-year-old man with an audible left carotid bruit is scheduled for a left carotid endarterectomy. Which of the following statements is correct?

A. The risk of a perioperative stroke is increased roughly threefold in patients with a carotid bruit.
B. Perioperative aspirin therapy is not helpful in preventing morbidity and mortality after carotid endarterectomy because it is associated with postoperative bleeding.
C. Perioperative hypertension and hyperglycemia are associated with increased postoperative morbidity.
D. In patients with both significant carotid and coronary artery disease amenable to surgical treatment, the coronary artery surgery should be performed first.
E. The leading cause of perioperative and late mortality after carotid endarterectomy is stroke.

19. Which one of the following statements about cerebral autoregulation is correct?

A. Cerebral autoregulation begins to become impaired at a mean systemic blood pressure of 50 mm Hg.
B. Anesthetic drugs do not influence the cerebral autoregulation curve.
C. Cerebral blood flow (CBF) = cerebral perfusion pressure / cerebral vascular resistance
D. Chronic hypertension can shift the CBF versus systemic mean blood pressure curve to the left.
E. Hypercapnia will lead to a decrease in CBF.

20. A 63-year-old man is in the PACU after having undergone a left-sided carotid endarterectomy. He had his right side done 18 months before and his postoperative course then was characterized by mild hypoxia in the PACU. Which of the following statements is correct?

A. The afferent of the carotid body is relayed to the medulla oblongata through the vagus nerve.
B. The carotid body is most sensitive to the effects of hypoxia and less sensitive to the effects of hypercarbia.
C. Although this patient is at risk for bilateral carotid body damage, he is not at risk for respiratory failure because of his central chemosensors.
D. The carotid bodies consist of specialized endodermal cells sensing changes in pH.
E. Surgical damage to the carotid body generally occurs late in the postoperative period, and thus it is important to monitor these patients with pulse oximetry and capnographs for at least 24 hours.

21. A 72-year-old woman is in the PACU after having undergone a right-sided carotid endarterectomy. Which one of the following statements is correct?

A. Activation of the carotid body chemoreceptors causes the carotid body reflex to occur, which involves increased ventilation and increased vagal tone.
B. The carotid body chemoreceptors are sensitive to carbon dioxide tension, pH, and arterial oxygen tension.
C. The aortic body chemoreceptors are able to upregulate enough to completely compensate for the inadvertent damage to carotid bodies during carotid endarterectomy.
D. Bilateral damage to the carotid bodies can lead to complete ablation of increased ventilation to hypoxia in the setting of hypercapnia.
E. Patients with ablations of their carotid bodies will always develop a higher resting carbon dioxide level in their blood.

22. A 55-year-old woman is scheduled for a left-sided carotid endarterectomy. She has complete occlusion

of her right carotid artery, which was noted preoperatively. Which one of the following statements is correct?

A. EEG monitoring in some centers is used to determine which patients need selective shunting during this operation.
B. All volatile anesthetics cause similar EEG changes, and thus all can be used interchangeably during carotid endarterectomy.
C. Since most perioperative strokes occur intraoperatively, EEG monitoring is most importantly done in the operating room.
D. Routine use of the BIS monitor has been shown to decrease the incidence of intraoperative stroke during carotid endarterectomy.
E. About a third of all patients undergoing carotid endarterectomy will exhibit EEG signs of ischemia and therefore be candidates for shunting.

23. A 63-year-old man is in the PACU after having undergone a left-sided carotid endarterectomy. He had his right side done 18 months before and his postoperative course then was characterized by mild hypoxia in the PACU. Which of the following statements is correct?

A. The ventilatory response to hypercapnia is more sensitive to the effects of volatile anesthetics than the responses to hypoxia.
B. Inhibition of ventilatory drive occurs when the patient's end-tidal volatile anesthetic concentration is 1 MAC or greater.
C. The chemoreceptor response to hypercapnia has both a slow and a fast component.
D. The mechanisms by which low concentrations of volatile anesthetics attenuate the hypercapnic ventilatory drive are well understood.
E. Halothane causes less hypoxic ventilatory drive suppression than desflurane.

24. Which one of the following statements about cerebral aneurysm clipping is correct?

A. Somatosensory evoked potentials (SSEPs) are more sensitive at detecting postoperative neurologic deficits in the posterior cerebral circulation than the anterior circulation.
B. Clipping cerebral aneurysms has been shown to be safer in terms of morbidity and mortality than intravascular coiling.
C. The risk of vasospasm increases when the cerebral aneurysm clipping occurs in the first 72 hours after subarachnoid hemorrhage because of postoperative inflammation.
D. Elective clipping of unruptured cerebral aneurysms should always be done in patients less than 45 years of age because the risk of rupture is so high.
E. Conditions associated with cerebral aneurysms include polycystic kidney disease, coarctation of the aorta, fibromyodysplasia, and connective tissue disorders.

25. A 52-year-old woman has sudden onset of an excruciating headache. She is being evaluated in the emergency room. Which one of the following statements is correct?

A. A ruptured cerebral aneurysm classically presents with a gradual onset of severe headache, accompanied by nuchal rigidity.
B. The most common site of rupture is within the vertebral artery.
C. Physical examination is usually not helpful in diagnosing subarachnoid hemorrhage.
D. It is extremely rare for patients who have a ruptured cerebral aneurysm to have a prior history of headache.
E. The mortality rate of subarachnoid hemorrhage is up to 40% after 1 week and almost 50% after 6 months.

26. A 30-year-old man is involved in a motorcycle accident and has sustained severe head trauma with no evidence of a cerebral hemorrhage. He is admitted to the intensive care unit for management. Which one of the following statements is correct?

A. Local brain metabolism is made up of two parts: neuronal activity and maintenance activity.
B. In healthy patients there is a redundancy of cerebral blood flow (CBF), so increases in neuronal activity do not increase CBF.
C. The coupling of CBF and cerebral metabolism is mediated solely through nitric oxide.
D. $Paco_2$ and Pao_2 do not affect CBF in patients with an intact blood–brain barrier.
E. When autoregulation is intact and the basal blood pressure is within the normal autoregulation range, the administration of catecholamines should be done cautiously because the CBF may increase and cause deleterious effects.

27. A 72-year-old man is undergoing right-sided carotid endarterectomy. His past medical history is significant for transient ischemic attacks. Which one of the following statements is correct?

A. Jugular bulb venous monitoring is the most accurate method of determining whether there is cerebral ischemia during carotid endarterectomy.

B. Cerebral ischemic monitoring has proven to be cost-effective because it has been shown to decrease the incidence of postoperative morbidity associated with intraoperative cerebral ischemic events.
C. Clinically, if cerebral ischemia is detected intraoperatively, the surgeon may use carotid artery shunting and/or the anesthesiologist may try to optimize cerebral blood flow (CBF) by increasing the mean arterial pressure.
D. One of the advantages of standard EEG monitoring over processed EEG monitoring is that standard EEG monitoring is not affected by the level of anesthesia.
E. Transcranial Doppler ultrasonography is the standard of care in the United States for cerebral ischemia monitoring during carotid endarterectomy.

28. A 60-year-old woman is admitted to the intensive care unit with a left-sided acute stroke. Which one of the following statements is correct?

A. If there is evidence that the stroke is hemorrhagic in nature, a low-normal systemic blood pressure is best to limit further extension of the stroke.
B. Cerebral perfusion pressure is calculated as CPP = MAP + ICP.
C. Nimodipine has been found to be helpful in patients with stroke because it reduces blood pressure and decreases the incidence of vasospasm.
D. One of the management goals of treating patients with acute stroke is to augment cerebral blood flow by maintaining a high-normal cerebral perfusion pressure.
E. Cerebral blood flow and cerebral perfusion pressure are always linearly linked.

29. A 10-year-old boy had a vertebral artery aneurysm coiled one week ago. He is readmitted to the hospital with new-onset headaches. He develops a coughing spell and shortly thereafter is unresponsive. The diagnosis of a subarachnoid hemorrhage (SAH) is made. Which one of the following statements is correct?

A. Cerebral vasospasm is not an important consideration in this case because he is a child.
B. Cerebral vasospasm is usually apparent in the first 72 hours after SAH.
C. Ischemic complications occur in about 15% of all patients with SAH.
D. CT scan is used to predict the size of the SAH and therefore the likelihood of cerebral vasospasm occurring.
E. SAH in general does not impair cerebral autoregulation unless there is intraparenchymal bleeding.

30. The 10-year-old patient with the SAH is found to have a 1.5-mm layer of blood hemorrhaged over his cerebral fissures. Which one of the following statements is correct?

A. Prophylactic treatment of cerebral vasospasm is always necessary.
B. Hypernatremia is a warning sign of impending vasospasm.
C. "Triple H" therapy refers to hypervolemia, hyperoxia, and hemodilution.
D. Clipping aneurysms early is important because it makes it safer to aggressively administer triple H therapy.
E. Selective cerebral calcium channel blockers can be used in conjunction with systemic vasodilators to diminish the vasospasm.

31. A 30-year-old freshwater near-miss drowning victim is admitted in a comatose state to the intensive care unit. Which one of the following statements is correct?

A. For every degree Celsius drop in core body temperature, the $CMRO_2$ drops 7%.
B. Multiple studies have proven that mild hypothermia during aneurysm surgery has decreased morbidity and mortality.
C. Although hypothermia has been shown to decrease $CMRO_2$, hyperthermia has no effect.
D. The best way to measure core body temperature is pulmonary artery, jugular bulb, or bladder temperature.
E. Hypothermia affects only the electrophysiologic function and not the basal component of neuronal functioning.

32. A 24-year-old man is admitted with a closed head injury. He is comatose, with a left pupil that is fixed and dilated. He is found to have a large left-sided subdural clot, which is being evacuated. Which one of the following statements is correct?

A. The correct management of this patient includes emergent intubation and hyperventilation to a $Paco_2$ of 25 mm Hg for 48 hours.
B. After the procedure, hyperventilation should NOT be maintained.
C. There is no evidence that hyperventilation is associated with brain ischemia.
D. The cerebrospinal fluid is equally sensitive to either respiratory or metabolic changes in pH.
E. Indications for instituting hyperventilation perioperatively include an elevated intracranial pressure or a need to improve conditions in the surgical field.

33. A 16-year-old girl is undergoing a 7-hour anesthetic for removal of a tumor near the optic chiasm. Her anesthetic consists of sevoflurane and narcotics. Postoperatively she is noted to have increased urine output. Which one of the following statements is correct?

A. Sevoflurane is less likely to cause renal toxicity than isoflurane.
B. The increased urine output is probably caused by SIADH, which peaks postoperatively.
C. Renal toxicity from inorganic fluoride from halogenated inhaled anesthetics depends on the degree of metabolism of the anesthetic and the blood-gas solubility.
D. Vasopressin levels are usually suppressed in patients with inorganic fluoride renal toxicity.
E. Diabetes insipidus should be suspected in the operating room when the patient's serum osmolality and urine osmolality increase.

34. A 42-year-old woman is having surgery for a brain tumor near the optic chiasm. During the anesthesia, it is noted that her urine output increases to 150 mL/hr and her serum sodium level increases to 146 mEq/L. She has lost minimal blood during the procedure and the anesthesiologist is administering her fluids as normal saline at her maintenance rate. Which one of the following statements is correct?

A. Her elevated sodium level is probably secondary to the fact that she is getting normal saline, which is a hypernatremic solution (153 mEq/L).
B. Diabetes insipidus (DI) should be entertained as a reason for excessive urine output once the patient's urine output increases to 200 mL/hr.
C. Chronic hypernatremia is generally well tolerated.
D. Surgery around the pituitary gland is associated with hypersecretion of ADH, which leads to central DI.
E. Intraoperative management of DI includes the administration of hypertonic solutions to attenuate the pituitary ADH secretion.

35. On postoperative day 1 after right craniotomy after a motorcycle crash, a 16-year-old boy is intubated in the intensive care unit, requiring minimal ventilatory support. In addition to noninvasive monitoring, he has an arterial line in place as well as a Foley catheter. His urine output has been 200 mL/hr for several hours. Urinalysis and blood laboratory results reveal urine osmolality of 121, plasma osmolarity of 300, creatinine of 0.7, serum sodium of 154, serum glucose of 98, and serum potassium of 4.3. What is the appropriate treatment for this patient?

A. DDAVP
B. Mannitol
C. Hypertonic saline
D. Fludrocortisone
E. Fluid restriction

36. An 84-year-old woman is undergoing eye surgery. Preoperative vital signs are NIBP 132/84, heart rate 88, respiratory rate 10, oxygen saturation on room air 99%. Moments after the self-retaining lid retractor is placed, her heart rate falls to 32. After you request removal of the retractor, her heart rate is 74. The afferent and efferent branches of the oculocardiac reflex are, respectively,

A. Vagus and oculomotor nerve
B. Trigeminal and vagus nerve
C. Vagus and vagus nerve
D. Optic and vagus nerve
E. Optic and oculomotor nerve

37. Regarding the function of the respiratory center of the brain, which of the following is a correct statement?

A. Oxygen directly controls the chemosensitive area.
B. The pneumotaxic center stimulates the inspiratory center to initiate respiration.
C. The ventral respiratory group regulates inspiration.
D. The Hering-Breuer reflex terminates inspiration due to bronchiolar stretching.
E. The ventral respiratory group is involved in regulation of inspiration; the dorsal respiratory group regulates expiration.

38. A 37-year-old man with refractory major depression disorder and suicidal ideation is anticipated for electroconvulsive therapy (ECT). Which of the following anesthetic agents has the most likely effect of shortening the seizure duration induced by ECT?

A. Remifentanil
B. Methohexital
C. Propofol
D. Ketamine
E. Etomidate

39. A 59-year-old man with well-controlled hypertension and a history of myocardial infarction one year ago presents for his first electroconvulsive therapy (ECT) procedure. Which of the following is true regarding the anesthetic considerations for ECT?

A. Concomitant administration of caffeine has been shown to decrease seizure duration.
B. Concomitant administration of beta blockers has been shown to increase seizure duration.
C. ECT is categorized as a low-risk procedure according the American Heart Association.

D. ECT is contraindicated in pregnancy.
E. Delirium results in approximately 85% of patients after the procedure.

40. A 21-year-old man with medication-resistant schizophrenia is scheduled for electroconvulsive therapy (ECT). His past medical and surgical history includes a laparoscopic appendectomy at the age of 13. Which physiologic effects would NOT be expected as a result of ECT?

A. Decreased heart rate
B. Increased heart rate
C. Increased blood pressure
D. Decreased salivation
E. Increased intracranial pressure

41. Which of the following anesthetic agents, if delivered in large enough doses, is capable of producing burst suppression on electroencephalography (EEG)?

A. Morphine
B. Propofol
C. Dexmedetomidine
D. Fentanyl
E. Ketamine

42. A 23-year-old man is admitted to the intensive care unit following a motor vehicle collision and after initial evaluation in the emergency department. On exam he opens his eyes to questioning and speaks in full sentences but is disoriented. He does not follow commands and upon sternal rub he reaches to grab the examiner's hand. What is his Glasgow Coma Scale score?

A. 8
B. 9
C. 10
D. 11
E. 12

43. A 20-year-old man who has been in a motor vehicle collision enters the operating room for open reduction and internal fixation of a compound tibia fracture. He ate a full meal approximately 3 hours ago. A cervical collar is in place with midline cervical tenderness on examination, and he has a LeFort III fracture. His past surgical history includes a laparoscopic appendectomy at age 17, after which he was told he was an easy intubation. According to the American Society of Anesthesiology (ASA) recommendations, it is advisable to manage his airway via

A. Awake fiberoptic intubation with patient's assistance in maintaining neck extension
B. Direct laryngoscopy with appropriate "sniffing" position
C. Rapid sequence intubation with in-line stabilization
D. Laryngeal mask airway for duration of case
E. Blind nasal intubation after induction of general anesthesia

44. A 47-year-old woman undergoes craniotomy for aneurysmal subarachnoid hemorrhage (SAH). Which of the following medications is indicated in the immediate postoperative period as prophylaxis against secondary (delayed) ischemia?

A. Nimodipine
B. Metoprolol
C. Doxazosin
D. Phenylephrine
E. Phenytoin

45. An 87-year-old woman with well-controlled Parkinson's disease is experiencing nausea in the postanesthesia care unit after total hip replacement via neuraxial anesthesia. Which of the following antiemetics is contraindicated in this setting?

A. Promethazine
B. Ondansetron
C. Diphenhydramine
D. Scopolamine
E. Metoclopramide

46. An obese 47-year-old-woman with a past medical history including hysterectomy and well-controlled hypothyroidism presents to the preoperative holding area for spinal fusion from T6 to L1 in the prone position. In the preoperative counseling and informed consent process, the patient is informed that she is at increased risk for ocular injury, including blindness, during the procedure because of her:

A. Habitus
B. Gender
C. Prone positioning
D. Hypothyroidism
E. Age

47. A 37-year-old man presents to the operating room approximately 2 hours after being ejected from his car during a motor vehicle collision. He complains that he cannot feel his legs and on examination has complete motor and sensory deficits below T6. Which of the following is a true statement regarding spinal cord injury (SCI) and succinylcholine administration?

A. Use of succinylcholine is contraindicated in this patient at this time.

B. Use of succinylcholine is contraindicated in this patient for future anesthetics.
C. Succinylcholine may lead to hypokalemia in patients with SCI.
D. Succinylcholine administration leads to influx of potassium from extra- to intracellular compartments in patients with SCI.
E. Downregulation of extrajunctional acetylcholine receptors in SCI patients leads to increased dose requirements of succinylcholine.

48. With regard to somatosensory evoked potentials (SSEPs), which of the following agents causes a dose-dependent decrease in amplitude without significant changes in latency?

A. Sevoflurane
B. Etomidate
C. Nitrous oxide
D. Ketamine
E. Fentanyl

49. A 67-year-old woman presents for craniotomy in the sitting position. While the surgeon is sawing through the calvarium, you notice dry, white bone without bleeding. Shortly thereafter you appreciate high-pitched sounds via precordial Doppler and a mill-wheel murmur via precordial stethoscope. Which of the following is consistent with venous air embolism?

A. Increase in blood pressure
B. Increase in end-tidal carbon dioxide
C. Increase in end-tidal nitrogen
D. Increase in cardiac output
E. Decrease in central venous pressure

CHAPTER 12 ANSWERS

1. ANSWER: A

Impending respiratory failure in spinal cord patients is heralded by weakening of the inspiratory muscles. The strength of these muscles conventionally is monitored by measuring the maximum inspiratory pressure, and the PI max should be less (more negative) than −20 cm H_2O, or by a vital capacity measurement, which should be greater than 8 cc/kg in a patient with normal respiratory mechanics. Elective endotracheal intubation and ventilation should be instituted before the ABGs deteriorate. Answer B shows normal measurements seen in patients without any evidence of respiratory failure. The values in answer C demonstrate that the patient has respiratory failure but the motor strength of inspiratory muscles is still intact. One possibility is that the patient has received opioids, which may have suppressed his respiratory drive. The measurements in answer D indicate that the patient is already in respiratory failure with poor respiratory muscle strength, evidenced by the poor PI max, low VC, and respiratory acidosis on the ABG.

ADDITIONAL READING

Cabrera Serrano M, Rabinstein AA. Anticipating mechanical ventilation in Guillain-Barré syndrome. *Eur J Neurol*. 2012 Mar;19(3):452–456.

2. ANSWER: C

The effects of barbiturates, etomidate, and propofol all produce similar EEG patterns (Table 12.1). Initially there is increased fast frontal beta activity (>13-Hz frequency) at low doses, then at moderate doses there is increased frequency of frontal alpha (8- to 13-Hz frequency) spindles, and eventually at very high doses there is diffuse delta (<4-Hz frequency) wave activity, then burst suppression, and finally an isoelectric state. These agents also cause the EEG amplitude to increase with increasing doses.

The typical EEG finding with isoflurane is similar to the one of other potent inhaled anesthetics. Initially, at subanesthetic doses, the EEG pattern is activated with an increase in beta waves frontally. Then, at higher anesthetic doses, the EEG pattern that predominates is alpha (4- to 13-Hz frequency) waves frontally, and then, with doses of isoflurane over 1.5 MAC, theta and delta waves, burst suppression, and an isolectric state is found.

Opioids generally cause a dose-related decrease in frequency and increase in amplitude of the EEG. Epileptiform activity is found in humans and animals who receive very large doses of some opioids. In humans, 20% of patients will demonstrate an increase in sharp wave activity after 30 micrograms/kg of fentanyl and 80% after a dose of 70 micrograms/kg of fentanyl.

The basic pattern of anesthetic-related EEG changes may be described for inhaled volatile anesthetics. These changes are very similar to the changes seen with barbiturates, etomidate, and propofol. Although in subanesthetic doses there is initially an increase in EEG frequency from alpha waves in the awake relaxed state to beta waves in the frontal cortex, once the patient is unconscious, the EEG pattern slows in frequency and increases in amplitude.

Although the volatile anesthetics all follow a basic pattern, there are differences between them. Isoflurane can be associated with isolated epileptiform patterns at 1.5 to 2.0 MAC but is not associated with frank seizures. Sevoflurane shows a similar pattern to isoflurane. The EEG patterns associated with enflurane are similar to sevoflurane and isoflurane except that the epileptiform activity is more common. Frank seizure activity has been seen in patients who are hypoventilated and receiving more than 2.0 MAC enflurane.

3. ANSWER: E

Barbiturates, propofol, and etomidate have similar effects on cerebral blood flow and cerebral metabolic oxygen consumption. Large doses of these drugs cause complete EEG suppression and a corresponding decrease in $CMRO_2$ between 55% and 60%. Further increases in these drugs do not further decrease the cerebral oxygen consumption, suggesting that the major effect of clinically safe doses of these drugs relates to electrical brain function rather than cellular homeostasis.

Nitrous oxide is not always a good choice because experimental data in humans and animals indicate that N_2O causes an increase in cerebral blood flow, which can lead to an increase in intracranial pressure when it is administered alone. When it is administered with intravenous agents such as benzodiazepines, narcotics, barbiturates, and propofol, this effect is modest. However, when it is given in conjunction with volatile anesthetics, moderate increases in cerebral blood flow are noted. The data on the effects of nitrous oxide and cerebral metabolic rate are more equivocal, but recent studies in humans indicate that nitrous oxide does increase the cerebral metabolic rate when administered with either sevoflurane or propofol.

It is important to remember that approximately 60% of cerebral energy consumption is devoted to electrophysiologic activities and 40% to homeostatic cellular function in the awake relaxed state. In patients receiving a nontoxic dose of anesthesia, burst suppression means that the electrophysiologic activities of the brain have ceased. For volatile anesthetics causing burst suppression, studies have shown that maximal reduction in cerebral metabolic rate is obtained

Table 12.1 ANESTHETIC DRUGS AND EEG

DRUG	EFFECT ON EEG FREQUENCY	EFFECT ON EEG AMPLITUDE	BURST SUPPRESSION?
Isoflurane			Yes, >1.5 MAC
Subanesthetic	Loss of alpha, ↑ frontal beta	↑	
Anesthetic	Frontal 4–13 Hz activity	↑	
Increasing dose >1.5 MAC	Diffuse theta and delta → burst suppression → silence	↑→ 0	
Desflurane	Similar to equi-MAC dose of isoflurane	Similar to equi-MAC dose of isoflurane	Yes, >1.5 MAC
Sevoflurane	Similar to equi-MAC dose of isoflurane	Similar to equi-MAC dose of isoflurane	Yes, >1.5 MAC
Nitrous oxide (alone)	Frontal fast oscillatory activity (>30 Hz)	↑, especially with inspired concentration >50%	No
Enflurane			Yes, >1.5 MAC
Subanesthetic	Loss of alpha, ↑ frontal beta	↑	
Anesthetic	↑ frontal 7–12 Hz activity	↑	
Increasing dose >1.5 MAC	Spikes/spike and slow waves → burst suppression; hypocapnia → seizures	↑↑→ 0	
Halothane			Not seen in clinically useful dosage range
Subanesthetic	↑ frontal 10–20 Hz activity	↑	
Anesthetic	↑ frontal 10–15 Hz activity	↑	
Increasing dose >1.5 MAC	Diffuse theta, slowing with increasing dose	↑	
Barbiturates			Yes, with high doses
Low dose	Fast frontal beta activity	Slight ↑	
Moderate dose	Frontal alpha frequency spindles	↑	
Increasing high dose	Diffuse delta → burst suppression → silence	↑↑↑→ 0	
Etomidate			Yes, with high doses
Low dose	Fast frontal beta activity	↑	
Moderate dose	Frontal alpha frequency spindles	↑	
Increasing high dose	Diffuse delta → burst suppression → silence	↑↑→ 0	
Propofol			Yes, with high doses
Low dose	Loss of alpha, ↑ frontal beta	↑	
Moderate dose	Frontal delta, waxing/waning alpha	↑	
Increasing high dose	Diffuse delta → burst suppression → silence	↑↑→ 0	
Ketamine			No
Low dose	Loss of alpha, ↑ variability	↑↓	
Moderate dose	Frontal rhythmic delta	↑	
High dose	Polymorphic delta, some beta	↑↑ (beta is low amplitude)	
Benzodiazepines			No
Low dose	Loss of alpha, increased frontal beta activity	↑	

(*continued*)

Table 12.1 (CONTINUED)

DRUG	EFFECT ON EEG FREQUENCY	EFFECT ON EEG AMPLITUDE	BURST SUPPRESSION?
High dose	**Frontally dominant delta and theta**	↑	
Opiates			**No**
Low dose	**Loss of beta, alpha slows**	↔↑	
Moderate dose	**Diffuse theta, some delta**	↑	
High dose	**Delta, often synchronized**	↑↑	
Dexmedetomidine	**Moderate slowing, prominent spindles**	↑↑	**No**

MAC, minimum alveolar concentration.
*delta =< 4 Hz frequency; theta = 4–7 Hz frequency; alpha = 8–13 Hz frequency; beta => 13 Hz frequency.
SOURCE: Table 46–2. Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 46.

with the occurrence of EEG suppression, which occurs at 1.5 to 2.0 MAC for sevoflurane, isoflurane, and desflurane.

Ketamine like nitrous oxide can cause an increase in the cerebral metabolic rate and cerebral blood flow. Even subanesthetic doses of ketamine (0.2 to 0.3 mg/kg) are associated with increases in the cerebral metabolic rate of about 25%. The concomitant administration of other anesthetic drugs such as propofol, benzodiazepines, isoflurane with nitrous oxide has been shown to attenuate the increase in cerebral metabolic rate and cerebral blood flow associated with ketamine alone.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapters 13 and 27.

4. ANSWER: E

Correct management of surgery for ***intracranial aneurysmal clipping*** includes administering agents that facilitate brain relaxation to make it easier for the surgeon to gain access to the aneurysm. Many institutions use mannitol for this purpose. It is also very important to maintain precise blood pressure control in these patients during surgery. In general, it is important to maintain a high-normal mean arterial pressure to insure that there is adequate cerebral blood flow into recently damaged and marginally perfused areas of the brain. It also may be necessary to briefly decrease the mean arterial blood pressure to minimize hemorrhage during the procedure. Excessive increases in mean blood pressure are contraindicated because of the risk of rebleeding during the procedure.

Most aneurysms are clipped during the first 24 to 48 hours of a subarachnoid hemorrhage (SAH). Although the risk of rebleeding is high during this time because the intravascular clot is unstable, the best postsurgical results are achieved with early surgery. If surgery is not feasible during this time window, then the next best time is 2 weeks after SAH. Cerebral vasospasm peaks between 4 and 10 days after SAH, so this is not an ideal time for surgery. Should cerebral vasospasm occur, the intensive care unit management usually includes maintaining mild hypertension, hypervolemia, and hemodilution ("triple H" therapy). Although prospective studies have not demonstrated efficacy of this triple therapy, the reasoning is that this therapy will maximize cerebral blood flow through vasospastic areas. Furthermore, there is clear evidence that mean arterial hypotension is deleterious to patients with vasospasm.

Cerebral salt-wasting syndrome is heralded by hyponatremia, volume contraction, and a urinary sodium level of more than 50 mmol/L. It is believed to be mediated by the release of natriuretic peptide by the injured brain. Treatment consists of the administration of isotonic solutions to reach a state of normovolemia. This syndrome can be easily confused with inappropriate secretion of antidiuretic hormone (SIADH), which is characterized by normovolemia or hypervolemia and is treated with fluid restriction.

Calcium channel blockers such as nimodipine have been shown to decrease neurologic deficits associated with SAH, but there has not been clear evidence of decreased vasospasm with nimodipine.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 63.

5. ANSWER: A

The ***descending spinal cord tracts*** transmit information from the upper motor neuron to the lower motor neuron.

The lower motor neuron conducts the nerve signal to the efferent spinal root, which is often combined with other efferent spinal roots to form a peripheral nerve. This peripheral nerve carries the motor signal to the relevant muscle.

The descending spinal tracts are motor tracts, not sensory tracts. The main descending spinal tracts consist of the corticospinal tract, which is made up of axons from upper motor neurons from the motor cortex and brainstem. Cortical motor neurons send descending axons through the internal capsule into the medullary pyramids, where the majority of them cross to the contralateral side and descend in the spinal cord as the lateral corticospinal tract. These axons eventually synapse with anterior horn cells in the spinal cord. About 10% of cortical axons do not cross and remain ipsilateral and descend in the ventral corticospinal tract. Most of these cross to the contralateral side of the cord before synapsing with anterior horn cells.

The ***dorsal root ganglia*** include the primary neuron cell bodies of sensory nerves. Sensory nerves involved in touch and vibration send central axons into the spinal cord, where they form the dorsal column. These axons then synapse with one of the dorsal column nuclei found in the medulla oblongata, the ***nucleus gracilis*** (axons from below T6) or the ***nucleus cuneatus*** (axons T6 and above). The axons emanating from these nuclei are known as the internal arcuate fibers, which cross to the contralateral side and synapse with neurons in the VPL (ventral posterior lateral nucleus) of the thalamus. ***Ascending pain fibers*** from the dorsal nuclei enter the cord, ascend one or two levels before synapsing in the substantia gelatinosa of the spinal cord, and then decussate or cross over and then ascend to the brain in the anterior lateral portion of the cord as the spinothalamic tract.

ADDITIONAL READING

Bradley WG, Daroff RB, Fenichel GM, Jankovic J, eds. *Neurology in Clinical Practice*, 5th ed. Oxford: Butterworth-Heinmann; 2007. Chapter 54.

6. ANSWER: C

Brainstem evoked potentials (BAEPs) are the least sensitive modality of sensory evoked potentials clinically used (Tables 12.2 and 12.3). Although the volatile anesthetics will cause an increased latency in BAEPs, this effect is less than is seen with SSEPs and VEPs, and in general it is possible to administer volatile anesthesia to patients in whom BAEPs are measured. For BAEPs, generally only one ear at a time is monitored. Monitoring both ears can lead to false-negative results, meaning that the stimulation of the contralateral ear may cause normal BAEPs in the affected ear, leading to a false sense of security. Sometimes "white" noise is added to the contralateral ear to prevent bone conduction from the stimulated ear to the nonstimulated ear. Adding nitrous oxide to a maintenance volatile anesthetic during the monitoring of BAEPs causes no further change. Likewise, use of nitrous oxide alone causes no change in BAEPs, unless gas accumulates in the middle ear.

Subcortical and spinal ***somatosensory evoked potentials (SSEPs)*** are less sensitive to the effects of volatile anesthetics than cortical SSEPs. Volatile anesthesia will increase the latency times of sensory evoked potentials. With all types of sensory evoked potentials it is very important to maintain a steady level of anesthesia, especially during times of possible nerve injury during surgery. In general, it is possible to adequately monitor SSEPs when patients are receiving less than 1 MAC.

Visual evoked potentials (VEPs) are most sensitive to the effects of volatile anesthesia.

In general, for all types of sensory evoked potentials, intravenous anesthetics affect the evoked potentials less than volatile anesthetics when given in equipotent doses. This effect is less important when monitoring BAEPs because BAEPs are relatively resistant to the effects of volatile anesthesia.

7. ANSWER: D

Patients with ***high spinal cord lesions*** can have difficulties with thermogenesis. There is an inability to shiver below the spinal cord lesion and there may be cutaneous vasodilation below the lesion, leading to hypothermia. It is also possible for hyperthermia to develop because normal sweating is impaired below the spinal cord lesion.

Autonomic hyperreflexia occurs after the acute phase of spinal shock. Autonomic hyperreflexia can occur within weeks to years of spinal cord injury, but 80% of patients susceptible to this syndrome will exhibit this within the first year of injury. Patients with high spinal cord lesions exhibit hyporeflexia for the first 4 days of the injury and then develop hyperreflexia. The normal inhibition of spinal autonomic reflexes by supraspinal feedback ceases after spinal cord transection and can lead to exaggerated sympathetic activity.

There is evidence of supersensitivity of adrenergic receptors in patients with high spinal cord lesions. During autonomic hyperreflexia or mass reflex there is only a modest increase in sympathetic nerve activity and plasma norepinephrine levels, thus leading to speculation that the extremely high blood pressures seen may be due to hypersensitive adrenergic receptors. Quadriplegic patients are extremely sensitive to the effects of angiotensin and catecholamines.

Light anesthesia is not indicated in patients with high spinal cord lesions because significant visceral reflexes can

Table 12.2 ABILITY OF AN INDIVIDUAL ANESTHETIC DRUG TO PRODUCE A CHANGE IN SENSORY AND MOTOR EVOKED POTENTIALS THAT COULD BE MISTAKEN FOR A SURGICALLY INDUCED CHANGE

	SSEPS		BAEPS		VEPS		TRANSCRANIAL MEPS	
DRUG	LAT	AMP	LAT	AMP	LAT	AMP	LAT	AMP
Isoflurane	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Enflurane	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Halothane	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Nitrous oxide*	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Barbiturates	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Etomidate	No	No	No	No	Yes	Yes	No	No
Propofol	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Droperidol	No	No	No	No	—	—	Yes	Yes
Diazepam	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Midazolam	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Ketamine	No	No	No	No	Yes	Yes	No	No
Opiates	No	No	No	No	No	No	No	No
Dexmedetomidine	No	No	No	No	No	ND	ND	No

NOTE: This table is not quantitative in any way. "Yes" or "no" designations indicate whether an individual drug is capable of producing an effect on any portion of the evoked response that could be mistaken for a surgically induced change.

(P): Use of this drug and any dose may render this type of monitoring impossible for a significant period of time.

AMP, amplitude; BAEPs, brainstem auditory evoked potentials; LAT, latency; MEPs, motor evoked potentials; ND, no data available from the literature; SSEPs, somatosensory evoked potentials; VEPs, visual evoked potentials.

* **Increases the effect of the agent(s) with which it is used.**

SOURCE: Table 46–3. Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 46.

Table 12.3 GUIDELINES FOR CHOOSING ANESTHETIC TECHNIQUES DURING PROCEDURES IN WHICH SENSORY EVOKED RESPONSES ARE MONITORED

1. Intravenous agents have significantly less effect than "equipotent" doses of inhaled anesthetics.

2. Combinations of drugs generally produce "additive" effects.

3. Subcortical (spinal or brainstem) sensory evoked responses are very resistant to the effects of anesthetic drugs. If subcortical responses provide sufficient information for the surgical procedure, anesthetic technique is not important, and effects on cortically recorded responses may be ignored.

SOURCE: Table 46–4. Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 46.

be evoked even if the patient feels no pain. These reflexes can be minimized by the use of spinal anesthesia, adequate general anesthesia, or vasodilator drugs such as nitroprusside or nitroglycerine.

Autonomic hyperreflexia is most commonly associated with hypertension, bradycardia, flushing, and diaphoresis above the spinal cord lesion. Bradycardia is often seen because the only intact efferent component of the baroreflex pathways in quadriplegic patients is the vagus. When the systemic blood pressure rises as a result of the mass reflex, the baroreceptor reflex is activated, resulting in bradycardia.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 12.

8. ANSWER: B

The ***stellate ganglion*** is a sympathetic ganglion formed by the fusion of the inferior cervical ganglion and the first thoracic ganglion. It is usually located at the level of C7 anterior to the

transverse process of C7 and just below the subclavian artery. Stellate ganglion blocks may be done to ameliorate the symptoms of Raynaud's disease or complex regional pain syndrome.

The ***parasympathetic nervous system*** consists of cranial nerves and sacral nerves (known as the pelvic splanchnics S2, S3, and S4). The head is supplied by fibers in cranial nerves 3, 7, and 9, which synapse in four cranial ganglia, the ciliary, pterygopalatine, submandibular, and otic. The ciliary ganglion (cranial nerve 3) sends out fibers to the eye, causing the pupil to constrict. The pterygopalatine ganglion (cranial nerve 7) supplies fibers to the lacrimal gland and mucous membranes of the nose and mouth. The submandibular ganglion (cranial nerve 7) supplies fibers to the submandibular and sublingual glands, and the otic ganglion (cranial nerve 9) supplies fibers to the parotid gland.

The ***adrenal glands*** are made up of two layers, cortex and medulla. The cortex synthesizes corticosteroids from cholesterol. The medulla receives preganglionic fibers from the sympathetic nervous system originating in the thoracic spinal cord T5–12. Thus, it can be considered a specialized sympathetic ganglion. However, it differs from other sympathetic ganglia in that it releases its secretions (epinephrine and norepinephrine) directly into the bloodstream.

The ***vagus nerve*** (10th cranial nerve) is known as the wandering cranial nerve. It supplies motor parasympathetics to all organs from the neck down except the adrenal and supplies the gut until the second segment of the transverse colon. Eighty percent of the nerve is made up of efferent fibers from the gastrointestinal system, which relay back to the brain the state of the gastrointestinal system. It contains motor fibers (not part of the parasympathetic system) to several skeletal muscles, including the muscles of the larynx.

The ***sympathetic nervous system*** trunks run from the base of the skull to the front of the coccyx in a chain of ganglia. Efferent fibers travel down the spinal cord and exit into the paravertebral ganglia lying along the spinal cord from T1 to L2. Once a nerve fiber enters a ganglion of the sympathetic trunk, it may travel up or down the trunk to synapse at a different level, it may synapse within the ganglion that it first entered, or it may pass through the ganglion and exit it "unsynapsed" to synapse in a prevertebral ganglion such as the celiac ganglion.

ADDITIONAL READINGS

Hansen JT. *Netter's Clinical Anatomy*, 2nd ed. Philadelphia: Saunders; 2009. Chapter 2.

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 12.

9. ANSWER: B

There are several cardiac tests that can be done to determine whether a patient is exhibiting signs of ***autonomic neuropathy***. Often the resting heart rate is greater than 100 bpm. There is also diminished beat-to-beat variation. Normal variation of a patient at rest and supine while taking deep breaths is 15 bpm. Less than 5 bpm is abnormal, although this index is age-dependent. The normal response to standing up is for tachycardia to peak at 15 seconds and for the heart rate to return to baseline by 30 seconds. This can be evaluated during EKG monitoring, and by measuring the R-R interval. In patients without autonomic neuropathy the max/min ratio should exceed 1.03.

An isolated normal glucose level in a diabetic patient tells the clinician little about how well the diabetes is controlled over time and whether the patient exhibits signs of autonomic neuropathy. Patients with significant neuropathy have a 5-year survival rate of 50% and are at significant risk for intraoperative and postoperative morbidity.

These patients are at risk for silent ischemia and aspiration from gastroparesis. The gastroparesis seen in diabetic autonomic neuropathy is amenable to treatment with metoclopramide. Patients treated with 10 mg po metoclopramide preoperatively had significantly lower residual gastric contents measured than the placebo group. Presumably, patients with gastroparesis and large residual gastric volumes are at increased risk for aspiration on induction. Treatment with metoclopramide has not been shown to decrease this complication in patients with diabetic autonomic neuropathy.

Patients with autonomic neuropathy are at increased risk for cardiorespiratory arrest, in addition to having an increased risk for silent myocardial ischemia. Patients with autonomic neuropathy are more sensitive to the effects of anesthetics, pain medications, or other sedative drugs. Most of the cases of cardiorespiratory arrest postoperatively seemed to be related to respiratory depression or sedative or opioid overdose.

The parasympathetic system usually fails first in the case of diabetic autonomic neuropathy.

ADDITIONAL READINGS

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Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. *Circulation*. 2007;115:387–397.

10. ANSWER: C

The ***processed EEG*** has many limitations compared with the raw EEG. The standard EEG montage consists of 16 channels (or sites of measurements) placed on a patient's head at prescribed intervals, which gives an experienced electroencephalographer the ability to differentiate between different locations of the brain. This permits the monitoring of

focal pathology such as regional ischemia that may occur when the carotid artery is clamped. The processed EEG uses four or fewer channels (one or two per hemisphere), thereby limiting its use as a monitor for focal changes in cerebral function during anesthesia.

The effects of nitrous oxide on the processed EEG are minimal. Seventy percent nitrous oxide has been shown to cause loss of consciousness in healthy volunteers, yet the addition of up to 66% nitrous oxide to patients anesthetized with fentanyl and midazolam infusions for coronary bypass surgery did not result in changes in the processed EEG numbers. Nitrous oxide has also been found not to alter the bispectral index number in volunteers when used as a sole agent.

One of the limitations of some processed EEG monitors is that the addition of neuromuscular blockers can lower the processed EEG values. This phenomenon has been noted in both anesthetized patients and awake volunteers who have been given a full dose of neuromuscular blockers.

The processed EEG cannot be used to characterize the state of unconsciousness in patients anesthetized with ketamine because ketamine, in contrast to most other anesthetic drugs, is associated with a disorganized EEG pattern that is variable in all doses. Electrocortical silence or an isoelectric state cannot occur with anesthetic doses of ketamine, even in patients who are deeply anesthetized. In fact, ketamine is associated with increased epileptiform activity.

Opioids in general will cause a dose-related decrease in the frequency and an increase in the amplitude of the EEG waves. They do not cause burst suppression, and in supraclinical doses they are associated with some epileptiform activity, with 80% of patients showing this after receiving 70 ug/kg of fentanyl.

ADDITIONAL READING

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11. ANSWER: E

The differential diagnosis of ***low back pain*** is broad and includes pelvic inflammatory disease, abdominal aortic aneurysm, prostatitis, ovarian cysts, ectopic pregnancy, urinary tract disease, perforated viscus, large bowel obstruction, prostatitis, and perirectal abscess. However, most of the time, these pathologies do not present with isolated low back pain. It is extremely important to take a detailed history and careful physical examination to exclude the non-musculoskeletal causes of back pain. For laboratory tests one should consider a urinalysis, hCG, erythrocyte sedimentation rate, and CBC to exclude some of these non-musculoskeletal causes.

Low back pain is one of the most common complaints of adults of all ages, but it is extremely uncommon in children. When children complain of back pain, it is more commonly associated with serious disease such as infection and malignancies.

Once non-musculoskeletal causes are excluded, even severe low back pain is usually not an emergency and rarely requires that the patient be admitted for pain management. However, back pain caused by cauda equina syndrome is a medical emergency and often requires immediate surgery. This syndrome presents with a midline mass that impinges on the spinal canal. It can be due to extrusion of nuclear material from spinal disks or tumor, and the classic presentation includes *bilateral* sciatica with bowel or bladder dysfunction.

Spinal stenosis may occur when the intervertebral disk spaces shrink with age. Even minor trauma can cause inflammation and impingement around the nerve roots. The pain is usually bilateral and patients exhibit pseudoclaudication. They have progressive pain bilaterally down the lateral aspect of their legs. This pain is relieved by walking in a stooped position to lessen traction on the sciatic nerves.

ADDITIONAL READING

http://emedicine.medscape.com/article/822462-overview

12. ANSWER: E

Barbiturate coma has been tried in the treatment of status epilepticus, head trauma, ischemic stroke, intracranial hemorrhage, neurosurgical operations, and intracranial aneurysms. The theory is that the barbiturates will reduce the metabolic rate of the brain tissue to about 45% of normal (the amount of metabolism that is needed to maintain cellular integrity) as well as decreasing cerebral blood flow. The decrease in cerebral blood flow is accompanied by a decrease of total blood volume in the head and thus a decrease in ICP. Once the brain swelling is improved, the hope is that there may be less brain damage. However, studies are equivocal about the efficacy of barbiturate coma to improve morbidity and mortality in the above conditions.

The first line of treatment for elevated ICP is fluid restriction and administration of mannitol if the patient's hemodynamic state permits. The therapeutic aim in brain injury is to maintain cerebral perfusion to both injured and noninjured areas of the brain. Increased ICP can be caused by many etiologies, including increased production of cerebrospinal fluid, blockage of egress and resorption of cerebrospinal fluid, intracranial tumors, and brain swelling due

to injury. Mannitol and fluid restriction will cause the brain tissue volume to decrease and thus the ICP to decrease, which may improve perfusion to the brain.

Barbiturate coma usually transiently reduces the ICP in many patients, but after 24 to 72 hours of therapy the effects of the barbiturate may wane. The goal of barbiturate therapy is to reduce the brain waves to an isoelectric state. Barbiturate coma is a last-line treatment for patients in status epilepticus that has proven refractory to other treatments. However, there is no evidence that morbidity and mortality of status epilepticus are affected by barbiturate coma.

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13. ANSWER: C

Barbiturates have been shown to lower ICP by inducing a dose-dependent reduction in cerebral blood flow (CBF) and $CMRO_2$. Large doses of barbiturates cause the EEG to become isoelectric and the $CMRO_2$ to be reduced by 45%. This in turn causes the CBF to drop by about 55% and consequently the cerebral blood volume (CBV) to drop, leading to a lowered ICP. Unfortunately, many studies have shown that treatment with barbiturate coma does not cause a decrease in morbidity or mortality.

Barbiturates are believed to decrease $CMRO_2$ by several mechanisms. They enhance the synaptic actions of the major inhibitory neurotransmitters such as GABAa. Barbiturates at low concentrations decrease the rate of dissociation of GABA on its receptors and in higher concentrations directly bind to the GABA receptors.

They also inhibit the excitatory neurotransmitters such as glutamate and acetylcholine. In addition, they may act by antagonizing glutaminergic NMDA receptors, which cause neuronal excitation and an increase in cerebral metabolism.

Theoretically, the upside of barbiturate treatment for cerebral protection is that although barbiturates can cause myocardial depression, the decrease in arterial blood pressure is usually less than the decrease in ICP. This means that cerebral perfusion pressure is improved after treatment with barbiturates. The clinical endpoint in treatment with barbiturates for cerebral protection is EEG suppression. Once the EEG is suppressed, no further decrease in $CMRO_2$ is achievable with barbiturates. It is important to support the cardiovascular system during barbiturate coma to ensure that there is adequate perfusion to the brain as well as the rest of the body.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 13.

14. ANSWER: D

Flumazenil is a competitive benzodiazepine antagonist that has high affinity and great specificity for the benzodiazepine receptor. It also has minimal intrinsic effect. Its onset of action is about 3 minutes and it is cleared rapidly (more rapidly than all the benzodiazepines), so it is possible that resedation may occur. It is a *competitive* antagonist, so it is possible that its action can be surmounted and overcome by the addition of more benzodiazepine.

Flumazenil reverses the hypnotic and respiratory effects of benzodiazepines more than the amnestic effects. Unlike naloxone reversal for opioids, flumazenil has no negative side effects on the cardiovascular system.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 26.

15. ANSWER: E

The ***trigeminal cardiac reflex*** is manifested by sudden onset of parasympathetic activity, sympathetic hypotension, and apnea or gastric hypermotility during central or peripheral stimulation of any of the sensory branches of the trigeminal nerve. It has been reported to occur during craniofacial surgery, manipulation of the trigeminal ganglion, and surgery for lesions in the cerebellopontine angle, cavernous sinus, and pituitary fossa. Treatment usually consists of having the

surgeon cease manipulating in the relevant area, but in some cases an anticholinergic agent may need to be given. The oculocardiac reflex is a manifestation of this phenomenon.

Other causes of bradycardia during neurosurgery include procedures that may acutely elevate ICP and cause Cushing's triad to be activated (bradycardia, hypertension, and apnea). These include space-occupying lesions compressing brain parenchyma such as tumors, subdural hematomas, subarachnoid hemorrhage, hydrocephalus, and traction by neurosurgery. Other rarer causes include intraoperative seizures and spinal lesions (autonomic hyperreflexia). The best treatment for these causes of bradycardia is to treat the underlying pathology.

Although it is possible to cause an increase in ICP secondary to decreased drainage of venous flow, this is not usually an acute problem. Likewise, although remifentanil and propofol are associated with a decrease in heart rate, this is usually not an acute problem. It is important during neurosurgical cases to not overhydrate patients because this can also lead to an increase in ICP. Anaphylaxis is usually accompanied by a decrease in blood pressure and a reflex increase in heart rate.

ADDITIONAL READINGS

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16. ANSWER: A

Conceptually, the intracranial space, which is a closed space in everyone except young children, can be considered to consist of ***four subcompartments***.

The **cellular compartment** includes the brain (neurons, glia), lesions, and extravascular blood, all of which can be reduced by surgical means only.

The **fluid compartment** consists of intra- and extracellular fluids, and this space can be reduced by the administration of diuretics as well as steroids, which can be helpful in reducing the swelling associated with tumors.

The **CSF** can be reduced pharmacologically (acetazolamide), but only over several days. Intraoperatively, the only feasible way to reduce CSF is to surgically drain it. Lumbar CSF drainage can be used to improve surgical exposure only in situations with no substantial hazard of uncal or transforaminal herniation.

And the last subcompartment to consider is the (**intravascular) blood compartment**. Venous drainage can be improved by positioning the head up, making sure there are no venous obstructions such as tight endotracheal tube ties. Furthermore, placing the head in a neutral position and keeping the patient paralyzed ensures that there is no bucking or coughing during the case. Attention should also be paid to the ventilation settings to minimize the effects of excessive positive end-expiratory pressure.

The anesthesiologist should also be careful to choose an anesthetic technique that minimizes increases in arterial cerebral blood flow (CBF). Most intravenous anesthetic agents, with the exception of ketamine, are associated with both a decrease in cerebral metabolic rate and a reduction in CBF. Volatile agents cause cerebral vasodilation, with the order of vasodilation going from halothane (most), enflurane, desflurane, isoflurane, and sevoflurane (the least). Nitrous oxide is also associated with cerebral vasodilation. The anesthesiologist can acutely diminish CBF by causing hypocapnia, but this may also cause cerebral ischemia. The anesthesiologist and surgeon should discuss prior to the start of the case the optimal concentration of carbon dioxide.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 63.

17. ANSWER: E

Hypocapnia should be avoided whenever possible in patients with ***subarachnoid hemorrhage*** because these patients usually have low CBF to begin with. Traumatic brain injury patients also usually have low CBF in the first 24 hours of injury. In general, the use of hypocapnia should be reserved for specific time-limited episodes in which it is necessary. These include preventing imminent herniation, minimizing retractor pressure, facilitating surgical access, and acutely lowering the ICP to less than 20 mm Hg. In addition, the effects of hypocapnia are not sustained, with the pH of the CSF and extracellular fluids and the CBF returning to normal within 6 to 24 hours of the institution of hypocapnia. Thus, it is important not to abruptly cease hypoventilation of a patient who has been hyperventilated for a prolonged period of time to prevent hyperperfusion.

Any patient who has sustained a period of loss of consciousness due to trauma should concern the anesthesiologist. It is very possible to have delayed deterioration even up to 48 hours after the initial injury. It is believed that patients sustaining contusions in the frontal and medial temporal areas especially are at risk for developing edema, which can result in herniation through the foramen magnum. Patients who have sustained loss of consciousness as a result

Table 12.4 **GLASGOW COMA SCALE**

	1	2	3	4	5	6
Eyes	Does not open eyes	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneously	N/A	N/A
Verbal	Makes no sounds	Incomprehensible sounds	Utters inappropriate words	Confused, disoriented	Oriented, converses normally	N/A
Motor	Makes no movements	Extension to painful stimuli (*decerebrate response*)	Abnormal flexion to painful stimuli (*decorticate response*)	Flexion/ Withdrawal to painful stimuli	Localizes painful stimuli	Obeys commands

SOURCE: Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 63.

of trauma and who require nonneurosurgical emergency surgery should be evaluated by a neurosurgeon and should have neuroimaging studies to determine the extent of their brain injuries. It may be prudent to monitor their ICP intraoperatively, especially in prolonged surgical cases.

The incidence of coincidental cervical spinal injury in patients with traumatic brain injury is 8% to 10% in patients with a Glasgow Coma Scale score of less than 8 (Table 12.4).

18. ANSWER: C

Preoperative hypertension is a known risk factor for both myocardial infarction and stroke. In one study comparing a propofol technique with an isoflurane technique, myocardial ischemia on emergence was associated with a systolic blood pressure of more than 200 mm Hg. The goal of anesthesia in patients undergoing this surgery is to have tight control of their hemodynamic parameters. In general, it is advisable to maintain their blood pressure in their normal preoperative range. Hypotension can lead to hypoperfusion of the ipsilateral brain during this surgery. Likewise, hypertension can lead to problems with myocardial ischemia; in one study 28% of patients undergoing elective carotid endarterectomy had severe correctable coronary artery disease.

In animal models it is known that increased ischemic injury to neural tissue occurs in the presence of hyperglycemia. A recent study from Johns Hopkins found an increased risk of perioperative stroke, transient ischemic attack, myocardial infarction, and death when the operative-day glucose level was greater than 200 mg/dL.

The risk of perioperative stroke is 0.1% in unselected surgical patients, 1% in patients with an asymptomatic carotid bruit, and 3.6% in patients with at least 50% carotid stenosis.

Perioperative aspirin therapy has been shown to be efficacious in reducing the incidence of perioperative myocardial infarction, so it should be continued throughout the surgical treatment. The leading cause of mortality perioperatively and after this surgery is myocardial infarction, not stroke.

In patients with both severe carotid disease and coronary artery disease, it is controversial which should be treated first or whether both diseases should be treated during the same surgery. This management issue is further complicated by the possibility of interventional nonsurgical treatments (stents and angioplasties) done before or after coronary artery disease surgery. Because this issue has not been sorted out by objective data, clinicians should be guided by the relative severity of the patient's vascular disease and the treatment experience of their institution.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 62.

19. ANSWER: C

CBF is determined by the cerebral perfusion pressure divided by the cerebral vascular resistance. Cerebral perfusion pressure is determined by the formula:

$$CPP = MAP - ICP.$$

In general, in humans cerebral autoregulation begins to become impaired at a mean blood pressure of 70 mm Hg. The upper limit of autoregulation is a mean arterial pressure of about 150 mm Hg. Anesthetic drugs and carbon dioxide levels do alter the shape of the curve, with mild hypocapnia (not hypercapnia) causing vasoconstriction but increasing the limits of autoregulation and volatile anesthetics limiting the brain's ability to autoregulate. Chronic hypertension is believed to shift the autoregulation curve to the right, not the left (Fig. 12.1).

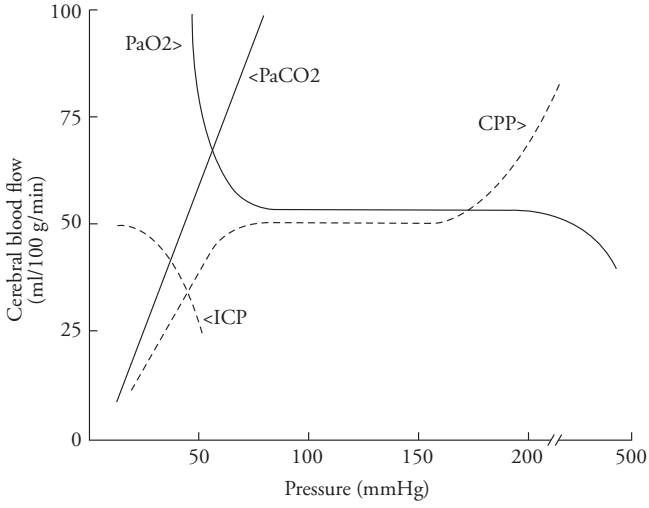

Figure 12.1 Cerebral autoregulation curve.

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Laffey JG, Kavanagh BP. Hypocapnia. *N Engl J Med*. 2002 Jul 4;347(1):43–53.

20. ANSWER: B

The ***carotid body*** is a highly vascular collection of cells derived from neuroectoderm found at the bifurcation of the carotid artery. It is made up of two different types of cells: glomus 1 cells, which are the chemoreceptor cells, and glomus 2 cells, which are the strial cells supporting the chemoreceptor cells. Pa_{O_2} levels less than 100 mm Hg and hypercarbia cause these cells to produce an action potential, which is transmitted by the glossopharyngeal nerve to the medulla oblongata.

The aortic body found along the aortic arch also contains glomus cells, but their action potentials are transmitted to the medulla oblongata through the vagus nerve.

The central chemoreceptors in the brainstem are most sensitive to changes in Pa_{CO_2}, whereas the carotid body cells are more sensitive to changes in Pa_{O_2} than changes in Pa_{CO_2}.

In this patient it is possible that the contralateral carotid body was damaged prior to this procedure. Unilateral damage is usually well tolerated by the patient. However, this patient is at risk for bilateral damage, which can lead to respiratory failure, especially if opioids are given in the postoperative period. Most serious complications (damage to carotid bodies, carotid sinus damage, cranial nerve damage, and hematoma) occur in the first 12 hours postoperatively.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 62.

21. ANSWER: B

The ***carotid body chemoreceptors*** are responsible for about 20% to 30% of the ventilatory drive in the normoxic state. The rest of the ventilatory drive in the normoxic state is caused by the aortic body and central chemoreceptors in the medulla. The medullary receptors are sensitive to changes in the hydrogen ion and not sensitive to changes in arterial carbon dioxide tension or arterial oxygen tension. The sensors in the carotid bodies are sensitive to carbon dioxide tension, pH, and arterial oxygen tension.

Activation of the carotid body sensors is transmitted through the afferent fibers of the glossopharyngeal nerve to the medulla, where it activates a sympatho-excitatory effect in humans leading to a profound increase in blood pressure. The threshold for P_{O_2} activation is about 80 mm Hg, and any elevation in P_{CO_2} above 40 mm Hg will cause the chemosensors to activate in a normal person.

The aortic body may be able to partially compensate for the activity of the carotid bodies. In several studies a residual responsiveness to hypoxemia was found in patients with bilateral resections of the carotid bodies. This effect was magnified in the setting of hypercapnia. Possible explanations of this include upregulation of the aortic bodies, and the possibility of regeneration of carotid chemosensitivity.

Most of the literature looking at the ventilatory response to hypercapnia and hypoxemia has examined patients who have some degree of pulmonary disease, so it is difficult to separate the effects of the carotid bodies from the effects of the pulmonary disease. However, in studies looking at patients with isolated carotid body ablations and no pulmonary disease, some of these patients have had a slight increase in their resting Pa_{CO_2} while others have maintained normocarbic levels.

ADDITIONAL READINGS

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22. ANSWER: A

Many centers currently use ***EEG monitoring during carotid endarterectomy*** as a tool to determine who has

cerebral ischemia and therefore which patients are candidates for intraoperative shunting. The processed EEG or BIS is not as sensitive in detecting regional ischemia compared to the full 16-channel EEG. Up to 20% of patients will exhibit some ischemia during cross-clamping of the carotid, but in patients with known complete occlusion of their contralateral carotid artery, up to 50% will exhibit ischemia.

One of the limitations of EEG monitoring during carotid endarterectomy is that the EEG varies with factors other than ischemia. The level of volatile anesthesia must be maintained at a steady state. Although all of the volatile anesthetics depress the EEG in a similar manner, they differ in terms of regional cerebral blood flow. Isoflurane and sevoflurane preserve regional blood flow better than halothane and enflurane at equi-MAC concentrations and thus are preferred for carotid endarterectomy.

Although EEG can detect ischemia, there is little evidence that the use of routine EEG monitoring during carotid endarterectomy actually leads to fewer perioperative strokes. This may be due in part to the fact that most perioperative strokes occur in the postoperative period.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 62.

23. ANSWER: C

The chemoreflex response to carbon dioxide consists of a slow response, which is believed to be mediated by the central chemoreceptors, and a fast response, which is believed to be mediated by the peripheral chemoreceptors in the carotid bodies.

The ventilatory response to hypoxia is more sensitive to the effects of even low concentrations (0.1 MAC) of volatile anesthetics than the ventilatory response to hypercapnia. It is very dependent on the volatile anesthetic, with the order of anesthetics causing depression being halothane (the most), enflurane, isoflurane, sevoflurane, and desflurane (the least). The precise mechanisms by which low concentrations of volatile anesthetics suppress ventilatory drive have not been determined.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 22.

24. ANSWER: E

Polycystic kidney disease, coarctation of the aorta, fibromyodysplasia, and connective tissue disorders, as well as conditions that result in a high-flow state such as vascular malformations, are associated with ***cerebral aneurysms***. The incidence of these aneurysms is believed to be between 1% and 6% of the population. Five percent to 40% of patients with autosomal dominant polycystic kidney disease have multiple aneurysms. Of patients with intracranial aneurysms, about 10% to 30% have multiple aneurysms, and there is a clear female predilection for having these aneurysms. It is believed that these aneurysms are congenital in nature but take years to manifest themselves, with gradual arterial wall weakening leading to a significant aneurysm.

About 85% of aneurysms are present in the anterior circulation (supplied by the carotids) and 15% in the posterior circulation (the vertebral-basilar arteries). Monitoring by SSEPs during surgery for aneurysmal clipping has been shown to be predictive of postoperative outcome. Most patients without SSEP changes awaken with no neurologic deficits, and most patients who develop persistent SSEP changes awaken with neurologic deficits. Patients who develop changes that resolve with repositioning of the clip can develop transient or permanent neurologic deficits, depending on the duration and nature of their SSEP changes. Intraoperative management can be altered if SSEP changes are detected, such as increasing the mean arterial blood pressure. Unfortunately, SSEP monitoring is usually not a sensitive monitoring device for aneurysms of the posterior circulation.

The advantages of clipping cerebral aneurysms over coiling include that the repair is more durable. Some coiled aneurysms can recanalize and need to be recoiled. However, the morbidity and mortality have been shown to be less during coiling than craniotomy and clipping. The advantage of treating a ruptured aneurysm with either coiling or clipping in the first 72 hours after subarachnoid hemorrhage is that when vasospasm peaks at days 10 to 14, it is safer to treat them with hypertension. There is no evidence that postoperative inflammation after clipping leads to more vasospasm. The decision to treat unruptured cerebral aneurysms is a difficult one because the risk of rupture is not precisely known, but it is generally thought to be lower than estimated earlier (1% to 2%/year) and may be more on the order of 0.5%/year, particularly if the aneurysm is less than 7 mm in diameter. However, the risk of rerupture is as high as 50% in untreated ruptured aneurysm.

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Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 33.

25. ANSWER: E

The presentation of ***ruptured cerebral aneurysm*** classically is a *sudden* onset of headache (peak severity in less than a minute), which may be associated with nuchal rigidity. It often occurs with exertion and events that cause a Valsalva maneuver. Other symptoms that may be seen are fever, nausea, vomiting, seizures, lethargy, and coma. Retinal hemorrhages and focal neurologic findings also point toward subarachnoid hemorrhage. Diagnosis can be made by seeing blood on a noncontrast CT or blood in the cerebrospinal fluid during lumbar puncture. The most common site of rupture is within the circle of Willis.

Many patients (up to 18%) will have sentinel headaches prior to a large bleed. These sentinel headaches may represent a small leak from the aneurysm. The fatality rate with subarachnoid hemorrhage is nearly 50%, and half the survivors are left with severe disabilities.

Neurosurgical evacuation of large quantities of blood may be necessary to reduce compression and reduce the risk of herniation. It is also necessary to clip or coil the aneurysm to reduce the risk of rebleeding. Although waiting until the clot is mature may decrease the immediate risk of rebleeding, it also increases the chance of cerebral vasospasm, so most neurosurgeons prefer to clip or coil the aneurysm in the first few days after the hemorrhage.

ADDITIONAL READING

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26. ANSWER: A

Local and global ***brain metabolism*** is made up of two components. The first component is fixed and is the energy required to maintain the neuronal and glial structures. This represents about 40% of the cerebral metabolic rate. The second part is the neuronal energy, which is variable and depends on neuronal activity. When the EEG is isoelectric, this variable component of neuronal activity is at its lowest.

Cerebral blood flow and the cerebral metabolic rate are tightly coupled over the range of complete autoregulation, which in humans is generally thought to be from 70 mm Hg to 150 mm Hg. A mean arterial pressure of 50 mm Hg is generally considered to be the point where there is not even limited autoregulation and CBF is passively dependent on cerebral perfusion pressure. Therefore, in healthy patients there is not a redundancy of CBF.

Although there is a coupling between CBF and cerebral metabolic rate over the autoregulation range, many factors also can alter CBF, including $PaCO_2$, PaO_2, anesthetic drugs, and systemic vasodilators and vasopressors.

Catecholamines generally do not affect the CBF significantly because when the basal pressure is within the autoregulatory zone, increases in mean arterial pressure result in autoregulation to maintain a constant CBF. When the patient is hypotensive and not in the autoregulation zone, then CBF will decrease as mean arterial pressure decreases.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 13.

27. ANSWER: C

EEG monitoring can detect alterations in signals, which can indicate ischemia. Standard EEG is preferable to processed EEG because the 16 signal points can pinpoint the location of the ischemia more accurately than the processed EEG. Although it has not been proven that cerebral ischemic monitoring affects clinical outcome, it is the most commonly accepted cerebral monitoring modality currently used. The reason to do cerebral ischemia monitoring is to detect cerebral ischemia and then to intervene to ameliorate the ischemia. Options open to the clinical team include carotid artery shunting during carotid cross-clamping and/or increasing the mean arterial pressure to increase the cerebral perfusion pressure. One possible reason that cerebral ischemia monitoring during anesthesia has not proven to decrease the incidence of perioperative stroke is that it has been demonstrated by transcranial Doppler monitoring that up to 70% of patients will have particulate embolization in the first 2 to 3 hours *postoperatively*.

Methods of cerebral ischemia monitoring include

- Stump pressure, which measures the back-pressure of the distal end of the carotid artery and represents the collateral flow through the circle of Willis. Although easy to perform, it is generally not used because it is not very accurate.
- Regional blood flow measurements (rCBF), which can be obtained by injecting radioactive xenon into the ipsilateral carotid artery or intravenously and analyzing the

decay curves of detectors placed over the skull in the area of the cortex supplied by the middle cerebral artery. This technology is expensive to interpret so it is not widely used.

- Somatosensory evoked potentials (SSEPs) are useful in that the sensory cortex is primarily supplied by the middle cerebral artery. When the regional cerebral blood flow is diminished, there is decrease in the latency and amplitude. When there is no regional flow, no signal is detected. Many anesthetic factors affect the SSEPs, including temperature, volatile anesthetics, nitrous oxide, and blood pressure.
- Transcranial Doppler (TCD) is a method to continuously measure mean blood flow velocity. It also has the capability to detect microembolic events, both particulate and air. This modality has not been widely adopted because of technical failures.
- Jugular bulb oxygenation can be directly measured intraoperatively and gives a measure of global cerebral oxygen metabolism. This is a technically challenging technique and thus is not commonly used.
- Near-infrared spectrometry is a measure of the oxygenation saturation of the regional cerebral area through the scalp. It is primarily a measure of the venous saturation because most of the blood in tissues at any time is venous. This is a continuous measure. Its drawbacks include that there is no clinical threshold of decreased cerebral oxygen saturation known to predict the need for intraoperative shunting.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 46.

28. ANSWER: D

Cerebral blood flow (CBF) in healthy brain is autoregulated in the systemic blood pressure range of mean arterial pressure (MAP) 70 to 150 mm Hg. This means that CBF is most closely coupled with the $CMRO_2$ of the brain over this blood pressure range. When the MAP is below or above this range, the CBF has a diminished ability to autoregulate, and when the MAP is 50 mm Hg in humans, there is no ability to autoregulate and the CBF is pressure-dependent and varies linearly with cerebral perfusion pressure (CPP). The same occurs when the MAP is above 150 mm Hg.

The CPP is dependent on both the MAP and the ICP. Based on the equation CPP = MAP − ICP, the CPP can be improved in patients at risk for ischemia by either lowering the ICP or raising the MAP. Therefore, it is important to maintain a high-normal MAP in patients with evidence of cerebral ischemia.

In patients treated with nimodipine after hemorrhagic stroke, a 10% to 20% drop in MAP was associated with a fourfold increase in mortality. Nimodipine, a calcium channel blocker, is believed to decrease the incidence of vasospasm and therefore be helpful in augmenting CBF. However, it can cause hypotension, which should be immediately treated. Hypotension by decreasing the CBF can increase the ischemic penumbra around the stroke area and lead to further disability.

ADDITIONAL READINGS

Bradley WG, Daroff RB, Fenichel GM, Jankovic J, eds. *Neurology in Clinical Practice*, 5th ed. Oxford: Butterworth-Heinmann; 2007. Chapters 51 and 55.29. A 10-year-old boy had a vertebral artery aneurysm coiled one week ago. He is readmitted to the hospital with new-onset headaches. He develops a coughing spell and shortly thereafter is unresponsive. The diagnosis of a subarachnoid hemorrhage (SAH) is made. Which one of the following statements is correct?

A. Cerebral vasospasm is not an important consideration in this case because he is a child.
B. Cerebral vasospasm is usually apparent in the first 72 hours after SAH.
C. Ischemic complications occur in about 15% of all patients with SAH.
D. CT scan is used to predict the size of the SAH and therefore the likelihood of cerebral vasospasm occurring.
E. SAH in general does not impair cerebral autoregulation unless there is intraparenchymal bleeding.

29. ANSWER: D

It is important to obtain a CT to predict the likelihood of the patient developing ***cerebral vasospasm***. Subarachnoid blood clots larger than 5 × 3 mm or a layer of blood greater than 1 mm thick in the basal cisterns or fissures is associated with a higher incidence of vasospasm. Pediatric patients are at risk from the complications of cerebral vasospasm.

Cerebral vasospasm is a late phenomenon, usually occurring 5 days after SAH. This complication occurs in about 24% to 32% of patients with SAH and may last one to two weeks. Cerebral vasospasm is used to refer to ischemic neurologic findings that occur in conjunction with cerebral vessel constriction. Because cerebral autoregulation is usually impaired after a SAH, inadequate cerebral perfusion pressure can result in localized cerebral ischemia and long-term morbidity and mortality.

Cerebral vasospasm is caused by cerebrovascular vasoconstriction that is reversible. The degree of ischemia does not

always correlate with angiography findings because much of the ischemia is found in vessels too small to be seen.

ADDITIONAL READINGS

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Brisman JL, Eskridge JM, Newell DW. Neurointerventional treatment of vasospasm. *Neurol Res*. 2006;28(7):769–776.

30. ANSWER: D

Early clipping or coiling of aneurysm is advised if possible. Although the chance of bleeding intraoperatively is greater because the clot is not as well defined and organized, this is outweighed by the benefits of early clipping, which include a diminished risk of later rebleeding and the ability to aggressively treat cerebral vasospasm.

Currently cerebral vasospasm is treated with two main therapies, either alone or together. Given prophylactically, selective cerebral calcium channel blockers such as nimodipine will reduce the amount of vasospasm. Although there is little to no evidence that these agents reduce angiographic evidence of vasospasm, several large clinical trials have shown a reduction in morbidity and mortality in patients who have received nimodipine.

The other therapeutic mainstay is ***triple H therapy***, which consists of **hypervolemia, hypertension, and hemodilution**. The theory behind this therapy is that a high circulation volume will increase cardiac output and therefore increase mean arterial blood pressure and then cerebral perfusion pressure. Likewise, hypertension will also increase cerebral perfusion pressure in areas of the brain that do not have cerebral autoregulation, and finally that mild hemodilution will decrease the blood viscosity and increase cerebral blood flow. In fragile, elderly patients who may not tolerate hypervolemia, often a pulmonary catheter is placed to safely administer additional fluids. The systolic blood pressure is often increased to the 160s and the hematocrit is maintained between 30% and 35%.

Guidelines have not been established to determine when to institute therapy prophylactically, but many centers will follow patients by transcranial Doppler. Impending vasospasm is often heralded by increased velocity. Also, hyponatremia can herald impending cerebral vasospasm.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 63.

31. ANSWER: A

The ***cerebral metabolic rate*** ($CMRO_2$) decreases about 7% for every degree Celsius drop in temperature. Eventually this will lead to complete suppression of the EEG at about 18 to 20 degrees C. Further reductions in temperature beyond the temperature at which an isoelectric EEG is reached will result in further decreases in $CMRO_2$, which means that hypothermia also can affect the basal component of neuronal functioning, in contrast with general anesthetics. This may be a reason why prolonged circulatory arrest in young children is well tolerated from a neurologic perspective.

In contrast, hyperthermia is associated with an increase in $CMRO_2$ until a temperature of 42 degrees C, which is associated with decreased $CMRO_2$ and permanent neurologic damage.

Despite the theoretical advantages of hypothermia there are not many studies that demonstrate a benefit. One study demonstrated a benefit to maintaining mild hypothermia in patients who are admitted to intensive care units after closed head injuries who already had mild hypothermia. Another study demonstrated improved outcome of patients who were cooled within 4 hours of a cardiac arrest. It may be that the timing of the mild hypothermia is critical to its success.

There are many ways to accurately measure core body temperature, including esophageal, tympanic membrane, pulmonary artery, and jugular bulb measurements. However, bladder temperatures are not accurate.

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32. ANSWER: E

Hyperventilation should NOT be an automatic part of every neuroanesthetic. It should be considered a therapy with benefits as well as risks, and the need for hyperventilation should be discussed with the neurosurgeon prior to the surgery. The usual indications for institution of hyperventilation include the desire to lower the intracranial pressure and the need for the surgeon to have a "relaxed brain" during the surgery.

The benefits of hyperventilation are not sustained and generally last only between 8 and 18 hours after institution. In hyperventilation, the CO_2 levels of the extracellular cerebrospinal fluid rapidly change and through mediators (NO and prostaglandins) decrease the blood flow through cerebral vessels. $PaCO_2$, can rapidly diffuse into the cerebrospinal fluid, but hydrogen ion cannot; thus, respiratory changes alter cerebral blood flow much more than metabolic changes. The effect is greatest in areas of normal to increased flow as well as within the range of physiologic $PaCO_2$. For instance, at a baseline $PaCO_2$, the cerebral blood flow will change 1 to 2 mL/100 g/min for each 1-mm Hg change in $PaCO_2$. However, this effect is diminished below a $PaCO_2$ of 25 mm Hg. The decreased blood flow is time-limited because carbonic anhydrase will work to reduce the concentration of bicarbonate ion in the extracellular cerebrospinal fluid, causing the pH to return to normal.

One of the downsides of hyperventilation is that it is necessary to slowly wean the individual from a hyperventilated state, especially if the patient has been hyperventilated for a prolonged period of time. Because the effects of hyperventilation are not sustained, after about 8 hours the cerebral blood flow is back to baseline levels. Rapid return to normocapnia will cause a rapid increase in cerebral blood flow and could be harmful to the patient.

Another risk is the possibility of brain ischemia, especially in areas of injury. Several studies have demonstrated that patients who were hyperventilated to a level of $PaCO_2$ of 25 mm Hg have a poorer outcome compared with patients hyperventilated to a level of $PaCO_2$ of 35 mm Hg. In addition, there are reports that the jugular venous bulb O_2 tensions are decreased in patients who are vigorously hyperventilated.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 63.

33. ANSWER: C

Inorganic fluoride, a byproduct of the metabolism of halogenated inhaled anesthetics, can cause a nephrogenic diabetes insipidus. The patient, if awake, has increased thirst and urination. Serum osmolality increases and the patient becomes hypernatremic.

There are two types of ***diabetes insipidus*** (DI): central and nephrogenic. Some of the symptoms of DI can be mimicked by excessive fluid intake. A fluid deprivation test is done in awake patients to determine whether they are able to concentrate their urine. If there is still excessive urine production, and increased serum osmolality and hypernatremia, then the patient has DI. The next test is a desmopressin (a synthetic antidiuretic hormone) test. If the urine production decreases, then the patient has central DI; if there is no change, then the patient has nephrogenic DI.

Central DI is associated with neurologic pathology such as trauma, tumor, and cranial surgery, especially surgery occurring around the posterior pituitary gland. Nephrogenic DI can be caused by drugs (amphotericin, lithium), polycystic kidney disease, and sarcoidosis and induced by inorganic fluoride toxicity.

The anesthetic most associated with renal toxicity is methoxyflurane, which is no longer used in clinical practice. This anesthetic was highly metabolized, leading to high levels of fluoride. In addition, these high levels persisted in the serum in part because of a high lipid solubility or blood-gas ratio. Patients with inorganic fluoride levels of less than 50 μmol/L usually showed no evidence of renal injury, those with levels of 50 to 80 μmol/L had moderate injury, and those with levels of 80 to 120 μmol/L had severe injury.

Sevoflurane and enflurane are metabolized more than isoflurane and thus are associated with higher inorganic fluoride levels than isoflurane. However, even though studies have shown that serum fluoride levels in some patients who have had sevoflurane anesthetics have exceeded 50 μmol/L, the high serum levels do not persist due to the relatively low lipid solubility of sevoflurane. Sevoflurane anesthesia has not been associated with nephrogenic DI, although subtle signs of renal impairment have been noted in some studies after a prolonged sevoflurane anesthetic.

ADDITIONAL READINGS

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapters 24 and 54.

34. ANSWER: C

Patients with ***central diabetes insipidus*** have a deficiency of ADH. This deficiency can either be partial or complete. Intraoperatively, patients with known partial DI can usually be managed with mild fluid restriction, which stimulates the pituitary gland to release ADH. Likewise, the stress of surgery is usually sufficient to stimulate the pituitary to release ADH. Plasma osmolality needs to be frequently monitored; if it rises above 290 mOsm/L, it should be treated with aqueous vasopressin.

For patients who have a partial deficiency of ADH, it is not necessary to use aqueous vasopressin perioperatively unless plasma osmolality rises above 290 mOsm/L. Nonosmotic stimuli (e.g., volume depletion) and the stress of surgery usually cause the release of large quantities of ADH perioperatively. Consequently, these patients require

only frequent monitoring of plasma osmolality during this period.

When managing an intraoperative patient with complete absence of ADH, make sure that the patient does not get too much DDAVP and run the risk of SIADH. Patients can be given nasal DDAVP or an intravenous infusion of aqueous vasopressin at a rate of 100 to 200 mU/hr. Frequent plasma osmolality monitoring is important to make sure the patient is not getting fluid-depleted or is retaining fluid. Intraoperative fluids should be isotonic to reduce the risk of water depletion and hypernatremia.

Although normal saline is a slightly hypernatremic solution, it rarely is a cause of hypernatremia. The diagnosis of DI should be considered in a patient who presents with elevated plasma osmolality, hypernatremia, and urinary output of greater than 100 mL/hr.

Chronic hypernatremia is generally well tolerated because the brain is able to regulate its volume. There is no reason to rapidly correct chronic hypernatremia, and in fact it may be harmful because it can lead to brain edema.

ADDITIONAL READING

Miller RD, Fleisher LA, Wiener-Kronish JP, Young WL, Eriksson LI, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Health Sciences; 2009. Chapter 54.

35. ANSWER: A

Posttraumatic diabetes insipidus may be seen in patients after neurosurgery or neurotrauma as well as a result of other etiologies. DI results in the excretion of large amounts of dilute urine and hypernatremia. The two types of DI, central and nephrogenic, may be distinguished by the administration of a desmopressin (DDAVP) stimulation test. In central DI urine output is subsequently decreased and urine osmolarity increased. In the case of nephrogenic DI, no such changes result. DDAVP is therefore therapeutic for central DI. Adequate hydration is also indicated.

Had this patient been experiencing diabetes mellitus, one would expect hyperglycemia in his laboratory studies. SIADH would result in hyponatremia, decreased urine output, and decreased serum osmolality. With well-functioning kidneys, suggested by this patient's normal creatinine, overzealous hydration with normal saline would not be expected to result in the noted derangements. Excessive administration of furosemide would be associated with hypokalemia.

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36. ANSWER: B

Traction of the extraocular muscles or compression of the eyeball may evoke the ***oculocardiac reflex***, resulting in bradycardia. It is mediated afferently by the trigeminal nerve, predominately the ophthalmic division. Efferent mediation is via the vagus nerve. The first step for treatment in the operating room is to eliminate the offending stimulus. If bradycardia persists, an anticholinergic agent such as atropine or glycopyrrolate may be administered.

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37. ANSWER: D

The respiratory center is found in the medulla and pons. The ventilatory rate is indirectly controlled by CO_2 in the form of hydrogen ions in the cerebrospinal fluid bathing the chemosensitive area. The pneumotaxic center, located in the pons, signals the inspiratory center to cease inspiration. The Hering-Breuer reflex results in termination of inspiration by way of bronchiolar stretch receptors. The ventral respiratory group is involved in regulation of expiration; the dorsal respiratory group regulates inspiration.

ADDITIONAL READINGS

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Morgan GE, Mikhail MS, Murray MJ, eds. *Clinical Anesthesiology*, 4th ed. New York City: The McGraw-Hill Companies; 2005.

38. ANSWER: C

Electroconvulsive therapy (ECT) is prescribed for the treatment of schizophrenia, major depression, bipolar disorder,

Table 12.5 **EFFECTS OF INTRAVENOUS ANESTHETIC AND CARDIOVASCULAR DRUGS ON THE DURATION OF ECT-INDUCED SEIZURE ACTIVITY**

	INCREASED	NO CHANGE	DECREASED
Anesthetic Drugs	**Etomidate**	**Methohexital,* ketamine, alfentanil,† remifentanil†**	**Thiopental, thiamylal, lorazepam, midazolam, propofol**
Cardiovascular Drugs	**Aminophylline, caffeine**	**Clonidine, esmolol, labetalol, dexmedetomidine, nifedipine, nicardipine, nitroglycerin, trimethaphan, nitroprusside**	**Diltiazem, lidocaine**

From Ding Z, White PF: Anesthesia for electroconvulsive therapy. *Anesth Analg.* 2002;94:1351.
*Compared with saline, methohexital decreases the seizure duration of ECT.
†Increases seizure time because of an anesthetic-sparing effect.

and other psychiatric disorders when a patient has failed to respond to medical management. Anesthetic considerations include providing for amnesia and analgesia as well as allowing seizures to occur for a sufficient period of time. It has been traditionally thought that ECT-induced seizures had to be at least 20 to 30 seconds in duration to be effective, but more recent outcome studies have put this into question.

Remifentanil and methohexital have little effect on the duration of ECT-induced seizures. Propofol has been shown to shorten the duration of ECT-induced seizures. Ketamine and etomidate have been shown to prolong seizure duration induced by ECT (Table 12.5).

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39. ANSWER: C

Electroconvulsive therapy (ECT) has a large number of psychiatric indications, especially in cases refractory to medical management, patients with comorbidities prohibiting pharmacologic therapy, or psychiatric emergencies threatening life. Pregnancy is NOT a contraindication, nor is stable cardiovascular disease, as ECT is considered a low-risk procedure according to the ACC/AHA 2007 guidelines.

Delirium results in approximately 10% of patients after ECT; the incidence is higher with associated conditions predisposing to delirium, such as advanced age and Parkinson's disease.

Caffeine has been shown to increase seizure duration; beta blockers have been shown to decrease seizure duration.

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40. ANSWER: D

ECT is prescribed for the treatment of schizophrenia, major depression, bipolar disorder, and other psychiatric disorders when a patient has failed to respond to medical management. Typical physiologic effects are the result of initial parasympathetic stimulation followed by predominance of

sympathetic stimulation. Bradycardia, even asystole as well as increased salivation may be seen during parasympathetic stimulation. With a predominance of sympathetic stimulation, tachycardia and hypertension are then seen. Cerebral blood flow is increased with the resultant seizures and concomitant increases in cerebral oxygen consumption and intracranial pressure.

Hypertension and tachycardia may be significant enough to require beta blockade, although routine administration of beta blockers is not recommended. Salivation may be significantly increased as a result of ECT and is frequently abated by pretreatment with antisialagogues.

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41. ANSWER: B

Burst suppression is represented by high-amplitude EEG patterns with intervening low-amplitude activity of less than 10 μv (Fig. 12.2). EEG burst suppression may be caused by some anesthetic agents, ischemic brain damage, and hypothermia. Burst suppression is also often seen as the baseline EEG waveform in premature infants. The combination of medications and/or physiologic states may augment burst suppression.

Of the above-listed anesthetic agents, only propofol is capable of producing burst suppression at high enough doses. Most inhalational agents will produce burst suppression at MAC greater than 1.5. Notable exceptions are halothane and nitrous oxide.

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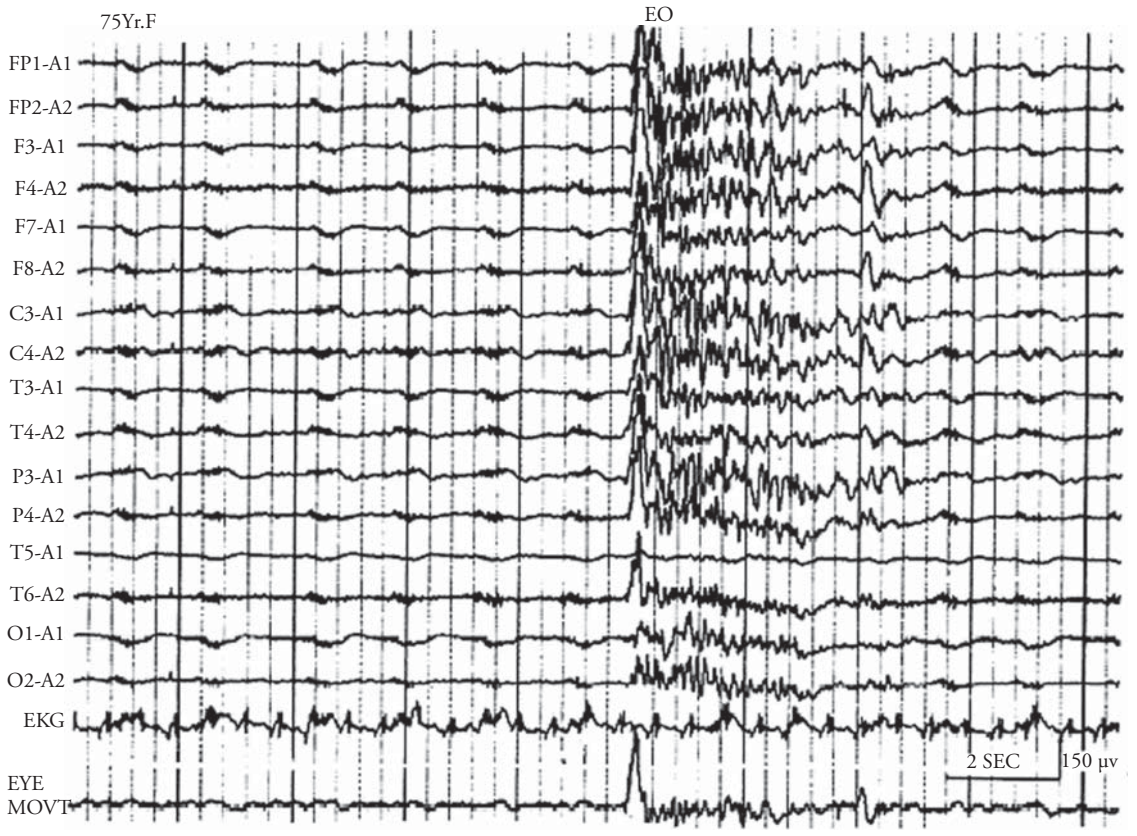

Figure 12.2 Burst suppression EEG.

SOURCE: Semin Neurol © 2003 Thieme Medical Publishers

42. ANSWER: E

The ***Glasgow Coma Scale*** (see Table 12.4) is the most commonly used system for scoring the level of consciousness in patients. It is most commonly applied to trauma patients and patients requiring intensive care. Scores are based upon the patient's best response to testing in three categories: motor, verbal, and eye opening.

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43. ANSWER: C

According to the ASA, rapid sequence intubation is preferred over other forms of intubation provided the neck is not moved (Fig. 12.3). Given the patient's full stomach status, an endotracheal tube is preferred over laryngeal mask airway. Nasal intubation or placement of nasogastric tubes and so forth is contraindicated in the presence of any midfacial fractures or basilar skull fractures.

ADDITIONAL READINGS

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44. ANSWER: A

Nimodipine, a calcium antagonist, is usually started orally or intravenously within 4 to 10 days after surgery for SAH due to ruptured cerebral aneurysm. It has been shown to improve outcomes by decreasing the incidence of ischemia (also referred to as delayed ischemia). Nimodipine was once thought to be effective for this indication by decreasing the incidence of postoperative cerebral vasospasm. However, some studies showing lack of radiographically verifiable evidence of this in comparison to other calcium antagonists have brought the exact mechanism into question.

Metoprolol is a beta antagonist. Doxazosin is a specific $\alpha 1$-adrenergic receptor antagonist. Neo-Synephrine is an $\alpha 1$-adrenergic receptor agonist. Phenytoin is used as an antiepileptic medication.

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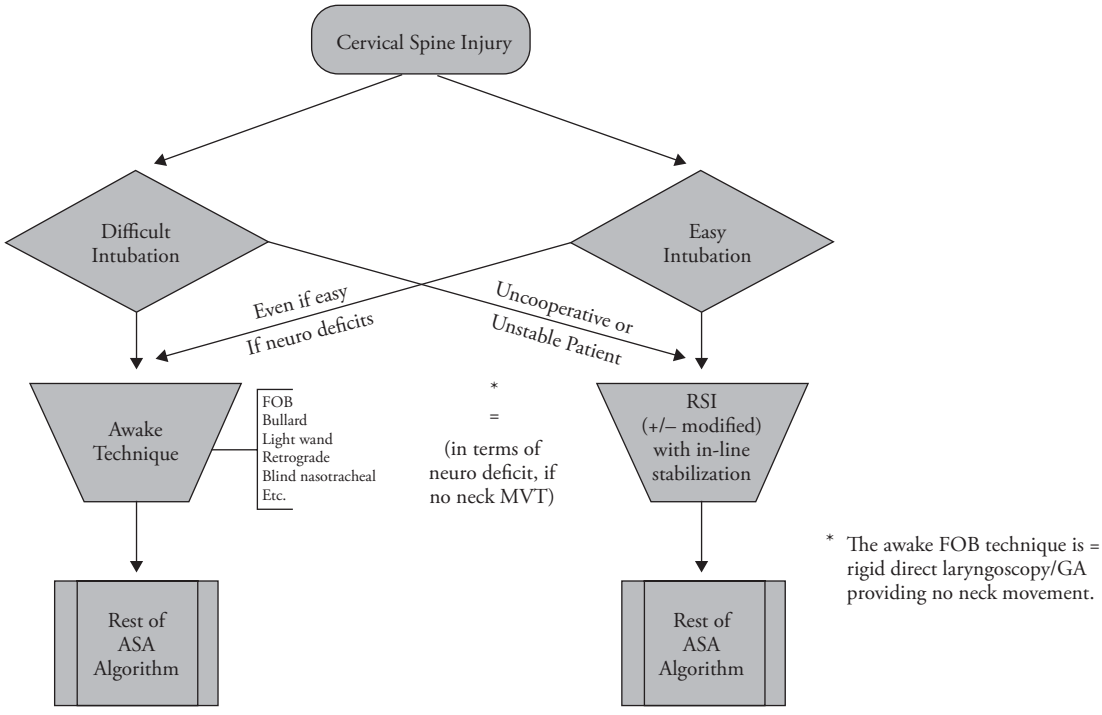

Figure 12.3 Algorithm for intubation of patients with cervical spine injury.

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45. ANSWER: E

Metoclopramide has dopamine-2-receptor antagonist properties, among other pharmacologic mechanisms. Its antagonism at D2 receptors is thought to be implicated in its ability to induce extrapyramidal side effects. This manifests as parkinsonism or, in the case of patients diagnosed with Parkinson's disease, an exacerbation of their underlying symptoms. It has been suggested that elderly patients may be particularly susceptible. Tardive dyskinesia, rigidity, resting tremor, and bradykinesia are possible. Such symptoms in the setting of metoclopramide may be refractory to treatment with typical agents used to treat Parkinson's disease, specifically L-dopa and bromocriptine. Extrapyramidal manifestations associated with metoclopramide generally improve or resolve with cessation of administration of the medication.

Promethazine and diphenhydramine are H1-receptor antagonist. Ondansetron is a serotonin 5-HT3 receptor antagonist. Scopolamine is an anticholinergic.

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46. ANSWER: C

Prone positioning is related to several specific anesthetic risks, including blindness, facial edema, and tongue injury. While positioning the patient it is important to note lack of external pressure on the orbits. Even with well-documented careful attention to this point, case reports reveal blindness can occur. This is especially true in cases of long duration and/or with marked blood loss associated with significant fluid resuscitation. Related factors may involve relative hypoperfusion to the ocular nerve, stressing the importance of maintaining normotension for the duration of the procedure. Neither the patient's habitus, age, gender, nor past medical/surgical history have been shown to be specifically related to increased risk of blindness.

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47. ANSWER: B

Succinylcholine is contraindicated in patients with SCI after approximately the first week from the onset of their injury because of the risk of severe hyperkalemia leading to cardiac arrest. The mechanism is thought to be due to upregulation of extrajunctional acetylcholine receptors and their depolarization. Subsequent efflux of potassium from intracellular stores to the extracellular space results. Because upregulation of the receptors is a process that takes time to occur, it is generally thought that succinylcholine use is not contraindicated within the first week after SCI.

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48. ANSWER: C

Sevoflurane, like all other volatile anesthetics, causes a decrease in amplitude as well as an increase in latency. Nitrous oxide is unique among inhaled anesthetics in that is causes a dose-dependent decrease in amplitude without significant changes in latency. Both etomidate and ketamine increase the latency and amplitude of SSEPs. Opioids such as fentanyl have a minimal effect on SSEPs (Table 12.6).

Table 12.6 EFFECT OF INTRAVENOUS AGENTS ON EVOKED POTENTIALS

AGENT	EFFECT
Propofol	Increases latency and decreases amplitude of SSEPs; decreases amplitude of VEPs
Etomidate	Increases latency and amplitude of cortical SSEPs; increases latency of VEPs
Thiopental	Induction dose may increase latency and decrease amplitude of SSEPs; increases latency and decreases amplitude of VEPs Increasing doses result in dose-dependent increase in latency and decrease in amplitude of cortical SSEPs and progressive increases in latency in BAEPs
Pentobarbital	Increases latency and decreases amplitude of SSEPs and VEPs
Ketamine	Increases latency and amplitude of SSEPs; increases latency and decreases amplitude of VEPs
Midazolam	No change or increase in latency and decrease of amplitude of SSEPs
Diazepam	No change or increase in latency and decrease of amplitude of SSEPs; decreases amplitude of VEPs
Opioids	Minimal change in SSEP waveforms

SOURCE: Table 29.4. Neuromonitoring. In Vacanti C, ed. *Essential Clinical Anesthesia*. Cambridge University Press, 2011.

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49. ANSWER: C

The risk of ***venous air embolism (VAE)*** is increased in cases when the operative field is above the level of the heart. Air is allowed to entrain to the venous vasculature because central venous pressure is less than the pressure at height. Pulmonary vasculature is obstructed by entrained air bubbles, leading to V/Q mismatch, decreased cardiac output, hypotension, increased arterial carbon dioxide (decreased end-tidal carbon dioxide), increased central venous pressure, and increased end-tidal nitrogen. The most sensitive monitor available is transesophageal echocardiography, followed by precordial Doppler. Immediate intraoperative steps for treatment of VAE are largely supportive and include immediately notifying the surgeon in order to flood the operative field with fluid to prevent further entrapment of air. Nitrous oxide, if in use, should be discontinued. If a central venous catheter is in place and properly positioned near the junction of the superior vena cava and right atrium, it can be aspirated in an attempt to remove the offending air.

ADDITIONAL READINGS

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13.

TRANSFUSION THERAPY

Peter Wu, MD, and Rob Hsiung, MD

1. The administration of fresh frozen plasma (FFP) is best indicated for which of the following scenarios?

A. A patient on chronic warfarin with a PT of 1.4 times normal for transurethral prostate resection
B. A patient with an INR of 1.8 awaiting a liver transplant
C. A patient coming to the operating room for an exploratory laparotomy following a gunshot wound
D. A patient with hemophilia A undergoing a total knee replacement
E. 5 hours into a L1–S1 fusion where the surgeon reports excessive oozing and the coagulation panel has not returned

2. Which one of the following patients would you choose to administer platelets to?

A. A pregnant patient with HELLP syndrome expecting to undergo emergent cesarean delivery, platelet count 100×10^9/L
B. A patient with an intracranial hemorrhage on aspirin and clopidogrel requiring decompressive craniectomy, platelet count 200×10^9/L
C. A pregnant patient expecting to deliver vaginally without an epidural, platelet count 55×10^9/L
D. A patient with thrombotic thrombocytopenic purpura (TTP) requiring dialysis catheter placement for plasmapheresis, platelet count 50×10^9/L
E. A patient who is post-cardiopulmonary bypass arriving in the cardiothoracic intensive care unit with an output of 50 cc/h of blood from the chest tube, platelet count 200×10^9/L

3. Which of the following is correct about using DDAVP perioperatively?

A. DDAVP reduces blood transfusions in patients without bleeding disorders.
B. DDAVP treats nephrogenic diabetes insipidus.
C. DDAVP treats factor deficiency in hemophilia B.
D. DDAVP is useful to reduce bleeding in uremic patients.
E. DDAVP can be used in all patients with von Willebrand disease.

4. Halfway through a complex pancreatectomy, the surgeon asks you to administer a couple of liters of Hetastarch because he would like the patient extubated at the end of surgery. Estimated blood loss is 1 L and the patient has already received 6 L of crystalloid. She is 70 kg. Your best response would be which of the following?

A. You tell the surgeon she has already received too much crystalloid to be extubated.
B. You agree to administer Hetastarch because it improves renal function and reduces interstitial fluid edema, which could complicate extubation.
C. You do not agree to administer Hetastarch because it can cause coagulopathy, leading to increased surgical blood loss.
D. You do not agree to administer Hetastarch because the pancreatectomy will impair the patient's ability to handle the hyperglycemia caused by the degradation of Hetastarch to glucose.
E. You agree to administer Hetastarch because there are few to no side effects.

5. A 35-year-old Army captain who presents for a thoracotomy for right upper lobectomy secondary to tuberculosis has a mildly prolonged bleeding time on preoperative blood work drawn 1 week ago. Other lab results include white cell count 6, hematocrit 35, platelets 250K, and INR 1.0. Upon questioning, he denies spontaneous bleeding, easy bruising, excessive bleeding at the dentist, or a family history of bleeding disorders. His medications include atenolol, baby aspirin (stopped

1 week ago), and simvastatin. He does not take herbal supplements. Your physical examination is unremarkable. The surgeon and patient would both like an epidural for postoperative analgesia. The next appropriate step would be to

A. Repeat the bleeding time test. If the bleeding time is prolonged, skip the epidural.
B. Not perform an epidural, as the bleeding risks outweigh the benefits.
C. Perform the epidural, as bleeding times do not predict bleeding tendency and have uncertain value in the perioperative setting.
D. Administer platelets, as the prolonged bleeding time implies abnormal hemostasis.
E. Order a platelet aggregation test. If normal, place the epidural.

6. Which of the following could cause a prolonged partial thromboplastin time (PTT) but not prothrombin time (PT)?

A. Warfarin treatment
B. Thrombocytopenia
C. Disseminated intravascular coagulation (DIC)
D. Von Willebrand disease
E. Factor V deficiency

7. Your patient tells you 10 minutes before his scheduled femoro-femoral bypass grafting that he has von Willebrand disease. He is unable to give you further information. The surgeon requests a general anesthetic. Your next action would be which of the following?

A. Perform a history and physical, and if unremarkable, proceed to surgery.
B. Postpone surgery and obtain a hematology consultation.
C. Administer DDAVP and proceed with surgery.
D. Administer platelets and von Willebrand factor and proceed with surgery.
E. Check PT, PTT, and INR, and if normal, proceed with surgery.

8. Your next patient for femoro-femoral bypass also has a bleeding disorder. Fortunately he has seen a hematologist, who has diagnosed him as having vWD type 3. What is the best treatment for this patient?

A. DDAVP
B. vWF/factor VIII concentrates
C. Cryoprecipitate
D. Fresh frozen plasma
E. Platelets

9. The surgeon asks you to administer Dextran 40 to a patient undergoing carotid endarterectomy. What is the purpose of this?

A. Increase intravascular volume
B. Serve as an anti-inflammatory
C. Affect glucose hemostasis
D. Induce hypertension to maintain cerebral perfusion pressure
E. Act as an anticoagulant

10. Which of the following is NOT a side effect of Dextran 40?

A. Anaphylactoid reaction
B. Interference with blood cross-matching
C. Renal impairment
D. Coagulopathy
E. Hyperglycemia

11. During your aorto-bifemoral bypass graft case, you give the patient 3 L of crystalloid, 1 unit of packed red blood cells, and 500 mL of 5% albumin. Estimated blood loss is 2 L. The patient's vital signs are blood pressure 85/40 mm Hg, heart rate 105, and oxygen saturation 85%. Ventilation requirements are increasing with worsening hypoxia. Current ventilator settings are tidal volume 600 mL, rate 14, FiO_2 1.0, and PEEP +8. Your blood gas analysis reveals a pH of 7.35, $Paco_2$ 35, PaO_2 50, and oxygen saturation of 85%. You suspect this may be transfusion-related acute lung injury (TRALI) and decide not to extubate. What would be the best way to confirm this diagnosis?

A. Leukopenia
B. Obtaining a chest x-ray
C. Inserting a pulmonary artery catheter to obtain PA pressures
D. Sending a specimen to the blood bank for an antibody–antigen cross-match
E. This is not TRALI.

12. You are 3 hours into an aorto-bifemoral bypass with an estimated blood loss of 2 L and your current fluid administration is 6 L of normal saline. Currently the blood pressure is 90/45 mm Hg, pulse is 95 bpm, and central venous pressure is 4 cm H_2O. Appropriate choices for fluid administration include all the following EXCEPT

A. Albumin, because you wish to avoid fluid overload with crystalloid
B. Ringer's lactated solution, as you are worried about hyperchloremic metabolic acidosis with normal saline

C. Any crystalloid, as there is no mortality difference between crystalloid and colloids
D. Administration of crystalloid and blood products to a central venous pressure of 16 and a SVO_2 of 90%
E. Packed red blood cells, if the hemoglobin is 7 g/dL

13. Which of the following therapies carries the least infectious risk?

A. Whole blood
B. Fresh frozen plasma
C. Thawed plasma
D. Platelets
E. Albumin

14. What is the most common noninfectious adverse reaction associated with blood product transfusion?

A. Transfusion-related immunomodulation (TRIM)
B. Transfusion-related acute lung injury (TRALI)
C. Anaphylactic/anaphylactoid reactions
D. Alloimmunization
E. Acute hemolytic transfusion reactions

15. Upon evaluating your patient's epidural placed 3 days ago for a transhiatal esophagectomy, you notice that she is jaundiced with a mild fever of 38 degrees C. Her hemoglobin is 7 mg/dL. She looks well otherwise. She received two units of blood intraoperatively for an estimated blood loss of 700 mL. You suspect that she is having a delayed hemolytic transfusion reaction. Which of the following statements would be true about this patient?

A. You gave her ABO-incompatible blood.
B. The blood bank failed to detect antibodies.
C. The transfused blood was old and largely hemolyzed.
D. This patient is bleeding and will need to be re-explored.
E. This is a very common phenomenon.

16. Which of the following is LEAST likely to be the cause of excessive bilirubin levels from hemolysis of red blood cells in the perioperative period?

A. G6PD deficiency
B. Sickle cell disease
C. Prosthetic cardiac valves
D. Massive blood transfusion
E. Kidney failure

17. Leukoreduction, or the removal of leukocytes from the transfused blood products, reduces the incidence of all of the following EXCEPT

A. Febrile transfusion reactions
B. Cytomegalovirus (CMV) infection
C. Rate of HLA alloimmunization
D. Allergic urticarial transfusion reactions
E. Bacterial transmission

18. Your patient for a total hip replacement under spinal anesthesia received 3 units of packed red blood cells over the past hour and started to scratch her skin repeatedly. You notice that she has developed hives. Her vital signs are stable and unchanged and she is afebrile. Which of the following statements is INCORRECT regarding allergic transfusion reactions?

A. Hypotension, bronchospasm, edema, and angioedema are other possible signs and symptoms
B. Leukoreduction may reduce the rates of allergic reactions.
C. IgA deficiency is often associated with allergic reactions.
D. Most anaphylactic and anaphylactoid reactions have no detectable cause.
E. Transfusion should be discontinued.

19. Thirty minutes after being transfused, your patient in the intensive care unit experiences a drop in blood pressure to 70/30 mm Hg. There is no hematuria or obvious source of bleeding. You are concerned about a transfusion reaction. The last known hemoglobin is 7 mg/dL. Your first action would be which of the following?

A. Start an epinephrine infusion.
B. Transfuse 1 unit of O-negative blood.
C. Give a bolus of 1 mg epinephrine IV.
D. Quickly infuse 1 L of crystalloid.
E. Give 100 mg of hydrocortisone.

20. All of the following laboratory tests may help confirm the presence of hemolysis EXCEPT

A. Tryptase
B. LDH
C. Haptoglobin
D. Bilirubin
E. Hemoglobin

21. All of the following are true pertaining to fevers associated with transfusion of blood products EXCEPT

A. It may represent a hemolytic transfusion reaction.
B. It may represent bacterial contamination.
C. It may be due to cytokines or antibodies to donor leukocytes.
D. Routine premedication can decrease the incidence of fevers.
E. Stopping transfusion is prudent in the absence of hypotension.

22. A 58-year-old, 90-kg man is scheduled to undergo an open repair of a 5.6-cm infrarenal abdominal aortic aneurysm. He is a Jehovah's Witness and refuses any blood products. His past medical history includes coronary artery disease with stable angina and non–insulin-dependent diabetes mellitus. His Hgb level is 14. He asks whether acute normovolemic hemodilution would be an option. Which of the following factors would be the biggest concern in using this technique?

A. His current hemoglobin level
B. His history of coronary artery disease
C. That he has not been started on erythropoietin
D. His being a Jehovah's Witness
E. His history of diabetes mellitus

23. How much blood would be withdrawn from the patient in Question 22 to target a hemoglobin concentration of 10 g/dL?

A. 600 mL
B. 1,200 mL
C. 1,400 mL
D. 1,600 mL
E. 2,400 mL

24. Which one of the following would be a reason to routinely use Cell Saver over allogeneic blood?

A. To reduce the incidence of dilutional coagulopathy in massive transfusion because of the ability of Cell Saver to scavenge coagulation factors and platelets
B. To decrease the use of allogeneic transfusion and possibility of a hemolytic transfusion reaction in surgeries with anticipated large blood loss
C. To avoid transmission of bloodborne pathogens in allogeneic blood transfusion for cesarean sections
D. Transfused Cell Saver red cells survive longer than allogeneic red cells.
E. Transfused Cell Saver red cells have better oxygen transport properties than allogeneic red cells.

25. A type and screen involves all of the following EXCEPT

A. Mixing recipient serum with commercially available O^- red blood cells with phenotypes for common antigens
B. Mixing recipient serum with donor red blood cells
C. Mixing recipient serum with type A and B red blood cells
D. Mixing recipient red blood cells with anti-A and anti-B antibodies
E. Mixing recipient serum with Rh-positive red cells

26. Which of the following is true about a unit of 35-day-old packed red blood cells stored in CPDA-1 from the blood bank that is just about to be transfused?

A. The pH would be close to 7.4 because of the phosphate buffer additive.
B. The K^+ level is more than 70 mEq/L as a result of red blood cell hemolysis.
C. The glucose level would be more than 100 mg/dL because of added dextrose.
D. The Hgb-O_2 dissociation curve is shifted to the right because of decreased 2,3-DPG.
E. The survival of transfused red blood cells is approximately 50% if measured 24 hours after transfusion.

27. The FDA mandates screening donated blood for all of the following infectious diseases EXCEPT

A. HIV
B. Hepatitis B and C
C. HTLV
D. CMV
E. Syphilis

28. A hemodynamically unstable 60-year-old woman is being brought to the operating room for an exploratory laparotomy after suffering a penetrating abdominal wound. A partial cross-match has determined that the patient's blood type is A^+. All of the following blood products could be safely transfused EXCEPT

A. O^+ packed red blood cells
B. O^- whole blood
C. AB^- fresh frozen plasma
D. A^- packed red blood cells
E. B^- platelets

29. An 18-year-old, 70-kg boy with hemophilia A is brought to the operating room for an emergent exploratory laparotomy after suffering blunt trauma to his abdomen in a motor vehicle accident. Factor VIII clotting factor levels are drawn in the emergency department, followed by administration of 3,000 units of factor VIII concentrate. The patient is quickly brought to the operating room and surgery has begun when preinfusion clotting factor levels are reported to be 20% with a low-responding inhibitor. What is the next appropriate step to maintain hemostasis?

A. No additional factor VIII concentrate is needed as the initial dose should increase activity to 100%.
B. Resend factor VIII levels to determine current levels following the initial infusion.
C. Administer another 500 units of factor VIII concentrate.

D. Administer DDAVP to stimulate factor VIII production.
E. Administer a bypassing agent such as recombinant activated factor VII (rFVIIa).

30. Which of the following is a true statement regarding hemophilia A and hemophilia B?

A. Hemophilia A is sex-linked; hemophilia B is autosomally inherited.
B. Hemophilia A prolongs the aPTT; hemophilia B does not.
C. The primary deficiencies in hemophilia A and B are factors VIII and X, respectively
D. DDAVP can be used in mild cases of both hemophilia A and B.
E. Fresh frozen plasma is preferable to cryoprecipitate if factor concentrates are not available for hemophilia B patients.

31. A 1-month-old neonate who was found to have sickle cell disease through the newborn screen is scheduled for surgery. The mother is worried that her daughter will have a sickle cell crisis during the perioperative period. Which of the following statements is correct regarding the newborn child?

A. Keeping the neonate NPO for surgery increases her risk for a vaso-occlusive crisis secondary to relative dehydration.
B. HgbF is the predominant form of hemoglobin at this stage of her life, and complications from sickle cell anemia are unlikely to occur.
C. She is at increased risk for retinopathy of prematurity because a high FiO_2 is needed to prevent HgbS from sickling red blood cells.
D. An exchange blood transfusion is needed to decrease the HgbS concentration to less than 30% prior to surgery.
E. She is susceptible to pneumococcal sepsis because of functional asplenia.

32. A 14-year-old boy with sickle cell anemia is in the postanesthesia care unit complaining of pain in his chest and difficulty breathing following a laparoscopic cholecystectomy. His vital signs are as follows: oxygen saturation 89% on 2 L NC, blood pressure 130/80 mm Hg, heart rate 110 bpm, temperature 38.8 degrees C, and respiratory rate 26. A diagnosis of acute chest syndrome (ACS) is suspected and a chest x-ray is ordered. Which of the following would NOT be helpful in the management of ACS?

A. Antibiotics
B. Simple blood transfusion
C. Furosemide
D. Albuterol nebulizer
E. Hydromorphone

33. An 18-year-old girl is scheduled for an open reduction and internal fixation of a fractured right wrist after slipping on ice. She gives a history of sickle cell anemia. Her Hgb is 8.3. Which of the following anesthetic considerations would be most appropriate for this patient?

A. Use of an intraoperative tourniquet to reduce blood loss
B. Exchange transfusion to increase HgbA and to decrease HgbS to less than 30%
C. Aggressive IV fluid administration to reduce blood viscosity
D. Induced hypotension to reduce bleeding from the operative site
E. Use of a regional-over-general anesthetic because there is an increased risk for acute chest syndrome with general anesthetics

34. During an exploratory laparotomy for a gunshot wound to the abdomen, 12 units of packed red blood cells are rapidly transfused over 1 hour. Although the surgeon has identified the source of injury, he reports having difficulty achieving hemostasis. Which of the following would NOT be a factor in this patient's coagulopathy?

A. Hypothermia
B. Disseminated intravascular coagulation (DIC)
C. Acidosis
D. Dilution of platelets and coagulation factors
E. Citrate toxicity

35. A 63-year-old man is transfused with 10 units of packed red blood cells during a liver transplant following an episode of uncontrolled bleeding. Estimated blood loss is estimated to be 4 L. His blood pressure is 78/50 mm Hg. You suspect citrate toxicity. All of the following are characteristic of citrate toxicity EXCEPT

A. Low ionized calcium level
B. Prolonged QT interval
C. Narrowed pulse pressure
D. Decreased central venous pressure
E. Elevated end-diastolic pressure

36. Which of following statements is INCORRECT regarding advantages of using prothrombin complex concentrates (PCC) over fresh frozen plasma (FFP) in achieving reversal of anticoagulation in an elderly patient?

A. PCC can be administered with much less volume compared to FFP, decreasing the likelihood of volume overload or congestive heart failure.
B. Reversal of anticoagulation is quicker and more complete with PCC compared to FFP.

C. PCC does not have to be ABO-type-specific, whereas FFP does.
D. Vitamin K is not required for long-term anticoagulation reversal with PCC as it is with FFP.
E. There is a decreased risk of viral transmission with PCC compared to FFP.

37. Which of the following products is LEAST likely to reduce perioperative transfusion requirements for a patient undergoing high-risk repeat coronary bypass grafting surgery?

A. ε-aminocaproic acid (ECAC)
B. Desmopressin (DDAVP)
C. Tranexamic acid
D. Recombinant factor VIIa
E. Prothrombin complex concentrates (PCC)

38. Cryoprecipitate contains all of the following EXCEPT

A. Factor XIII
B. Factor VIII
C. Fibrinogen
D. Von Willebrand factor
E. Thrombin

39. A newer generation of Hetastarches, termed the tetrastarches, have all of the following advantages over older Hetastarches EXCEPT

A. Higher molar substitution ratio
B. Lower molecular weight
C. More rapid elimination
D. Decreased accumulation of byproducts
E. Decreased incidence of coagulopathy

40. Which of the following potential blood donors would be deferred?

A. Healthy man taking a baby aspirin daily
B. Patients who are positive for cytomegalovirus (CMV)
C. Foreign travel to India 6 months ago
D. A donor with sickle cell trait
E. History of treated syphilis 2 years ago

41. During a colon resection, you decide to start transfusing your patient with packed red blood cells for excessive blood loss of 1 L. Prior to transfusion, the patient's vital signs are blood pressure 100/61 mm Hg, heart rate 90 bpm, oxygen saturation 98%, and temperature 36.8 degrees C. Following initiation of the first unit of packed red blood cells, the patient becomes hypotensive with a blood pressure of 71/38 mm Hg. The surgeon does not report any major blood loss at the moment. You notice that the urine has become blood-tinged. What are the most appropriate initial actions to treat this patient?

A. Stop the transfusion and open IV fluids wide open to maintain urine output.
B. Administer epinephrine and steroids to combat the allergic transfusion reaction.
C. Stop the transfusion and initiate empiric antibiotics for presumed bacterial contamination.
D. Continue giving the blood as this patient has likely decompensated from excessive blood loss.
E. Send the blood back to the blood bank for a replacement, as it is probably old and hemolyzed.

42. The American Association of Blood Banks (AABB) guidelines for autologous blood donation include all of the following EXCEPT

A. A predonation Hgb of more than 11
B. Age more than 10 years
C. Ability to donate up to 3 days prior to surgery
D. Donation of up to 10.5 mL/kg of blood per session
E. Unused blood cannot be used for other recipients as allogeneic blood

CHAPTER 13 ANSWERS

1. ANSWER: E

Fresh frozen plasma (FFP) is indicated for the treatment of microvascular bleeding when the International Normalized Ratio (INR), aPPT, or PT is greater than 1.5 times normal. Patients undergoing multilevel spine fusion may develop a consumptive coagulopathy due to blood loss and pooling at the surgical site. If clinical suspicion of microvascular bleeding exists, transfusion of FFP is indicated to maintain hemostasis while awaiting the return of laboratory values. While reversing anticoagulation from warfarin is another indication for FFP administration, especially in acute situations like an expanding subdural hematoma, it would only be necessary for a PT greater than 1.5 times normal.

Patients with cirrhosis frequently have elevated INRs of more than 1.5; however, FFP administration is not indicated while waiting for a liver transplantation, as this would cause only a transient improvement in the coagulation profile. FFP maybe indicated in patients awaiting liver transplantation if the INR is very high such that spontaneous intracranial hemorrhage may occur. FFP should not be used as a volume expander or to prophylactically treat coagulopathy in anticipation of massive transfusion. Assessment of clinical hemostasis and/or coagulation studies should help guide treatment in these situations. Patients with hemophilia A should receive specific factor VIII concentrates perioperatively in conjunction with hematology consultation. Cryoprecipitate, not FFP, may be indicated if factor VIII concentrates are unavailable.

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Nuttall GA, Brost B, Connis RT, Gessner JS, Harrison CR, Miller RD, Nickinovich DG, et al. Practice guidelines for perioperative blood transfusion and adjuvant therapies. *Anesthesiology*. 2006;*105*:198–208.

2. ANSWER: B

Bleeding into a closed or noncompliant space such as the brain, eye, and spine demands immediate reversal of anticoagulation. Clopidogrel irreversibly inhibits the $P2Y_{12}$ receptor and thus prevents the cross-linking of platelets to fibrin, the final step in the clotting cascade pathway. Aspirin irreversibly inactivates the cyclooxygenase enzyme and thus blocks the formation of thromboxane A_2 in platelets, further decreasing platelet aggregation. While transfused platelets in a patient on these agents may also be inactivated, their transfusion would be appropriate in the scenario given.

According to the 2006 ASA Task Force Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies, "platelet transfusion is rarely indicated if the platelet count is known to be greater than 100×10^9/L and is usually indicated when the count is below 50×10^9/L in the presence of excessive bleeding." Furthermore, procedures with limited anticipated blood loss, including vaginal deliveries, may be performed with platelet counts less than 50×10^9/L.

Although HELLP syndrome may lead to worsening thrombocytopenia and possible bleeding, transfusion would not be warranted at this time according to the guidelines.

The transfusion of platelets in disseminated intravascular coagulation (DIC) or other consumptive processes featuring active platelet destruction, such as heparin-induced thrombocytopenia (HIT), TTP, and idiopathic thrombocytopenic purpura (ITP), is generally not indicated unless there is uncontrolled bleeding or the platelet count is less than 20K.

Although platelet dysfunction is common after cardiopulmonary bypass, there is no clear indication for platelet transfusion if chest tube output does not suggest active bleeding. The causes for post-cardiopulmonary bypass platelet dysfunction are thought to be multifactorial, including heparin suppression of platelet activation secondary to thrombin inhibition, hypothermia, and the physical shearing stress on platelets during cardiopulmonary bypass.

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3. ANSWER: D

Desmopressin, or DDAVP, is an analog of antidiuretic hormone (ADH). When administered, it stimulates the release of stored von Willebrand factor and factor VIII from the vascular endothelium within 30 to 60 minutes for a continued effect of up to 24 hours. It is indicated for the treatment of central diabetes insipidus, control of bleeding in mild hemophilia A where the factor VIII activity is more than 5%, and certain subtypes of von Willebrand disease. Its use as a treatment for uremic patients in acute or chronic renal failure has been shown to reduce bleeding. It is given as a one-time dose of 0.3 mcg/kg, as repeated doses can cause tachyphylaxis. In addition to DDAVP, erythropoietin, cryoprecipitate, and estrogen have also been shown to help treat uremic bleeding.

DDAVP has not been shown to reduce the need for blood transfusions in patients without bleeding disorders. DDAVP has no effect on increasing levels of factor IX, the

deficient factor in hemophilia B. Use of DDAVP in von Willebrand disease has a variable response. While it is helpful in increasing levels when there is a mild quantitative deficiency of vWF, such as the most common type I subtype, it can be detrimental and cause severe thrombocytopenia in patients with subtype IIB.

Nephrogenic diabetes insipidus has partial to complete resistance to ADH, and thus exogenous administration may not be helpful. Dietary changes, thiazide, and potassium-sparing diuretics and a trial of nonsteroidal anti-inflammatories are the first line of treatment in nephrogenic diabetes insipidus.

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4. ANSWER: C

Hetastarch is a synthetic colloid in the family of hydroxyethyl starches (HES). It is derived from amylopectin-rich starch that undergoes hydroxyethylation to increase its water solubility and protect it from complete metabolism to glucose by amylase. By creating an osmotic gradient within the intravascular space, Hetastarch achieves effective volume expansion using less volume than crystalloid. Its volume expansion properties last for up to 24 hours before excretion by the kidneys.

Hetastarch, a first-generation HES, is manufactured with large molecular weights (480 to 670 kDa) and a high degree of hydroxyethylation (molar substitution) to slow the rate of metabolism and elimination. These two properties, however, also appear to be responsible for its numerous side effects, including coagulopathy, anaphylactic reactions, renal impairment, and accumulation of byproducts. While the mechanism is uncertain, Hetastarch interacts with platelets and decreases factor VIII and von Willebrand factor, thus leading to a von Willebrand-like syndrome. This occurs in a dose-dependent fashion with significant bleeding risk at doses greater than 20 mL/kg. Because this patient is 70 kg, the maximum recommended dose is 1,400 mL. Renal impairment likely occurs from the accumulation of these large molecules within the renal tubules.

Repeated administration can lead to accumulation of Hetastarch byproducts in the reticuloendothelial system and peripheral nerves, which can manifest as pruritus. Subsequent generations of HES, the pentastarches (second) and tetrastarches (third), have decreased molecular weights and molar substitution. Recent studies with the tetrastarches have demonstrated similar volume-expansion properties and much improved safety profiles with little to no effect on hemostasis, renal impairment, or accumulation of byproducts.

Although it remains to be seen whether this patient should be extubated at the end of surgery, there is not a predefined maximum volume of crystalloid that one can administer that would preclude extubation. Hetastarch may impair, not improve, renal function. Furthermore, although there may be less airway interstitial fluid edema with colloid versus crystalloid administration, there is no evidence that extubation would be more successful because of the choice of fluid administration.

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5. ANSWER: C

The ***bleeding time*** is a test to assess platelet function. It is performed by making an actual cut on the forearm and observing the duration of bleeding until hemostasis occurs. A normal bleeding time generally ranges between 2 and 9 minutes. The most common causes of a prolonged bleeding time are aspirin, nonsteroidal anti-inflammatories, or any other cyclooxygenase inhibitors. Other causes include von Willebrand disease, certain vascular diseases such as scurvy, thrombocytopenia, disseminated intravascular coagulation, and hypofibrinoginemia. Heparin and warfarin can also prolong the bleeding time while affecting the results of other coagulation tests.

While a prolonged bleeding time in theory may indicate a vascular defect, platelet function defect, or thrombocytopenia, its role as a diagnostic and predictive test is questionable. A prolonged result is nonspecific and studies have not demonstrated a correlation between bleeding time, bleeding tendency, and blood loss. As such, the bleeding time by itself should not influence the decision to place an epidural.

Suspected bleeding problems can frequently be determined by the history and physical alone. The ASRA Consensus Conference states, "There is no wholly accepted test, including the bleeding time, which will guide antiplatelet therapy. Careful preoperative assessment of the patient to identify alterations of health that might contribute to bleeding is crucial. These conditions include a history of easy bruisability/excessive bleeding, female gender, and increased age." Given this patient's negative history and physical findings, along with aspirin ingestion, which could account for the prolonged bleeding time, it would be unlikely that he has a clinically significant bleeding disorder. Thus, repeating the bleeding time test is unnecessary, as is ordering a further workup with a platelet aggregation test. The platelet aggregation test involves drawing a specimen and using an aggrenometer to measure the turbidity of the plasma. It should be ordered in conjunction with a hematology consult if there is a clinical suspicion that there is a bleeding disorder. Placing a thoracic epidural for thoracotomy provides the benefits of improved analgesia in comparison to intravenous analgesia, and should be used when possible. There is no clear indication for a platelet transfusion as the patient's platelet count is normal and there is no evidence of platelet dysfunction outside of aspirin use.

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6. ANSWER: D

Prothrombin time (PT) measures the extrinsic and final common pathways of the coagulation cascade. The PT, which is normally 11 to 14 seconds (depending on the control), measures the activity of fibrinogen, prothrombin, and factors V, VII, and X. The relatively short half-life of factor VII (4 to 6 hours) makes the PT useful in evaluating hepatic synthetic function of patients with acute or chronic liver disease.

Partial thromboplastin time (PTT) evaluates the intrinsic and common coagulation pathways and adequacy of all coagulation factors except XIII and VII. PTT is usually abnormal if any factor level drops below 25% to 40% of normal, depending on the PTT reagent used. PTT is commonly used to monitor heparin therapy. PTT is increased in deficiency of any individual coagulation factor except XIII and VII, presence of nonspecific inhibitor (e.g., lupus anticoagulant), specific factor inhibitor, von Willebrand disease (PTT may also be normal), hemophilia A and B, DIC, heparin, direct thrombin inhibitor (e.g., hirudin, argatroban), and warfarin.

Warfarin measurement is likely the most common indication for measurement of PT. It is usually reported in conjunction with the International Normalized Ratio (INR), which provides a standardized measurement of PT across different laboratories. Factor VII affects the PT the most. In the perioperative setting, the prolonged PT often is caused by poor or restricted nutritional intake and/or antibiotic treatment causing a deficiency in vitamin K (factors II, VII, IX, and X are vitamin K-dependent). Besides factor deficiency, other causes include the presence of an inhibitor, liver disease (low factor V), amyloidosis (factor X deficiency), and myeloproliferative disease (factor V deficiency). Classically DIC leads to an increased PT, PTT, and fibrin degradation products as well as decreased platelets and fibrinogen (Table 13.1).

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7. ANSWER: B

Von Willebrand disease (vWD) is the most common inherited bleeding disorder, with an estimated incidence of 1 in 100 to 1,000 people. Unlike hemophilia, it affects both males and females. There are three main types of vWD. Type 1 and 2 are inherited in an autosomal dominant fashion, while type 3 is autosomal recessive. An acquired vWD is seen in patients with autoantibodies to von Willebrand factor (vWF) and certain patients with aortic stenosis.

Most patients with vWD have the mildest and most common form, type 1, accounting for approximately 75% of all patients. A thorough history and physical, such as asking about bleeding after tooth extraction and other surgeries, nosebleeds, gingival oozing, hemarthrosis, petechiae, and bruises, can provide most of the risk stratification. An unremarkable history and physical would suggest a milder type of vWD, likely type 1. Patients with type 2 (defective vWF) and type 3 (generally absent vWF and low factor VIII levels) have more severe disease. Answers A and C suggest that the

Table 13.1 COAGULATION STUDIES IN VARIOUS CLINICAL SETTINGS

CONDITION	PT/INR	PTT	BLEEDING TIME	PLATELET COUNT
Warfarin treatment or vitamin K deficiency	Prolonged	Unchanged/Prolonged	Unchanged	Unchanged
Unfractionated heparin treatment	Unchanged	Prolonged	Unchanged	Unchanged
Low-molecular heparin treatment	Unchanged	Unchanged	Unchanged	Unchanged
Disseminated intravascular coagulation (DIC)	Prolonged	Prolonged	Prolonged	Decreased
Von Willebrand disease	Unchanged	Prolonged	Prolonged	Unchanged
Factor V deficiency	Prolonged	Prolonged	Unchanged	Unchanged
Hemophilia	Unchanged	Prolonged	Unchanged	Unchanged
Aspirin treatment	Unchanged	Unchanged	Prolonged	Unchanged
Thrombocytopenia	Unchanged	Unchanged	Prolonged	Decreased
Early liver failure	Prolonged	Unchanged	Unchanged	Unchanged
End-stage liver failure	Prolonged	Prolonged	Prolonged	Decreased
Uremia	Unchanged	Unchanged	Prolonged	Unchanged
Congenital afibrinogenemia	Prolonged	Prolonged	Prolonged	Unchanged
Glanzmann's thrombasthenia	Unchanged	Unchanged	Prolonged	Unchanged

patient has vWD type 1. However, because management would be different based on the different subtypes, further information should be obtained regarding this patient's subtype before proceeding. Thus, further workup with a hematology consultation should be obtained to determine the subtype of vWD. Initial tests to evaluate for vWD may include vWF:RCo, vWF:Ag, and factor VIII activity.

Administering vWF may help, especially if there is also factor VIII with it; however, this patient may not need this treatment. Platelet transfusions will not help in vWD. Similarly, the test of the intrinsic or extrinsic pathways will likely be normal (Table 13.2).

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8. ANSWER: B

Patients with vWD type 3 have a severe deficiency in vWF and factor VIII. vWF/factor VIII concentrates, like Humate-P,

Table 13.2 vON WILLEBRAND DISEASE (VWD) TYPES

vWD TYPE	I	II	III
Defect	Mild to moderate quantitative deficiency in vWF (i.e., ~20–50% of normal levels)	Qualitative abnormalities of vWF and is subdivided into types IIA, IIB, IIN, and IIM	Severe quantitative deficiency in vWF, low factor VIII levels
Inheritance	Autosomal dominant	Autosomal dominant or recessive	Autosomal recessive
Frequency	~70%	~30%	Rare, <1%
Treatment	DDAVP results in rapid increase in circulating levels of vWF:Ag and factor VIII and RCoF activity	Variable response to DDAVP (should not be used in IIb subtype because of possible thrombocytopenia and thrombotic complications); vWF-containing factor VIII concentrates	Factor VIII concentrates

have been used safely and effectively for treatment and prophylaxis of severe vWD disease for the past 20 years. Risks of using these concentrates include the potential for viral and prion transmission (as it is derived from plasma), and the potential for thromboembolic events. Although vWD is often categorized as a platelet disorder, neither the platelet number nor platelet function is reduced. Cryoprecipitate is derived from fresh frozen plasma but with higher concentrations of fibrinogen, vWF, and factor VIII. Thus, if specific factor concentrates were not available, cryoprecipitate is an alternative. Fresh frozen plasma does not contain much vWF or factor VIII, which makes it a poor treatment for vWD type 3. While DDAVP increases the factor VIII activity in vWD type 1, the most common (75%) and mildest form, it would not increase factor levels enough for vWD type 3.

Plasma factor VIII is the most important determinant of surgical and soft-tissue bleeding, and replacement therapy monitoring may be needed every 12 hours.

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9. ANSWER: E

Dextran is a branched-chain polysaccharide of varying chains used medicinally as an antithrombotic or a volume expander. It comes in two formulations, Dextran 40 and 70, based on its molecular weight. Although both formulations can be used as volume expanders, Dextran 40 is more commonly used in vascular and microvascular surgery because of its interaction with platelets, factor VIII, and endothelial cells to decrease platelet aggregation and blood viscosity. These perceived benefits are hypothesized to aid in maintaining graft patency and microcirculation, although its popularity and effectiveness have been questioned. The benefits of increased intravascular volume and induced hypertension are probably not realized at low infusion rates, usually between 30 and 50 mL/hr. Dextran 40 is not related to dexamethasone, a steroid, which has anti-inflammatory properties, nor should it affect glucose control despite its sugar backbone.

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10. ANSWER: E

Dextran has multiple side effects, including anaphylaxis, renal failure, coagulopathy, and interference in cross-matching blood. Dextran-induced anaphylactoid reactions (DIARs) occur in 1% of patients when patients have IgG antibodies that bind to dextran, causing a type III immune-complex–meditated anaphylactoid reaction. These reactions can be significantly reduced by pretreating with 20 mL of Dextran 1, a hapten that binds to the patient's dextran-reactive antibodies. Dextrans can coat the RBC membranes of the recipient, making blood cross-matching less reliable. Renal failure from dextran is hypothesized to be from accumulation of dextran molecules in the renal tubules. Dextran administration can lead to a coagulopathy with decreased platelet–endothelial adhesiveness, decreased factor VIII, and increased fibrinolysis. Hyperglycemia is not commonly seen despite its sugar backbone.

ADDITIONAL READINGS

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Zinderman C, Landow L, Wise R. Anaphylactoid reactions to Dextran 40 and 70: Reports to the United States Food and Drug Administration, 1969 to 2004. *J Vascular Surg* 2006;. *43*(5):1004–1009.

11. ANSWER: D

Transfusion-related acute lung injury (TRALI) is defined as an acute lung injury within 6 hours of transfusion with features of hypoxemia (with a $Pa_{O_2}/Fi_{O_2} < 300$ mm Hg), bilateral pulmonary infiltrates on chest radiograph, and lack of left atrial hypertension. It has been previously described as pulmonary hypersensitivity reaction and noncardiogenic pulmonary edema. Its reported incidence is 1 in 5,000 transfusions, but the actual incidence is unknown because of underreporting and difficulty in distinguishing it from transfusion-associated circulatory overload (TACO).

A "two-hit" hypothesis has been proposed for the etiology of TRALI, with comorbidities such as hematologic malignancies, cardiopulmonary bypass exposure, burns, sepsis, trauma, and massive transfusions being the initial "hit." The second insult is likely immunogenic, where passively transfused antibodies, biologic active lipids, or

plasma breakdown products activate neutrophils that lead to oxidative and nonoxidative destruction of the pulmonary endothelium, causing pulmonary edema.

TRALI can be induced in patients receiving as little as 10 to 15 mL of plasma. It is also more likely in patients who receive platelets compared to fresh frozen plasma and packed red blood cells. Treatment is generally supportive, with the use of lung-protective ventilation strategies and fluid minimization. Leukopenia is often seen, and fever is often associated with TRALI; however, its presence is often missed and is nonspecific by itself. Likewise, a chest x-ray is important in the diagnosis of TRALI, but it cannot distinguish it from other causes of hypoxemia, such as TACO and heart failure. The insertion of a pulmonary artery catheter to measure the pulmonary arterial occlusion pressure, not the pulmonary artery pressure, would be helpful in ruling out left atrial hypertension (where PAOP ≥ 18 mm Hg), and thus a cardiac etiology for the pulmonary insufficiency. Sending a patient specimen back to the blood bank for an antibody–antigen cross-match, especially to identify granulocyte and HLA donor antibodies, would be the best way to confirm the diagnosis of TRALI. Nevertheless, TRALI is still a clinical diagnosis, and ruling out other cardiogenic and volume-induced pulmonary edema is important.

ADDITIONAL READING

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12. ANSWER: D

Although there is a growing movement toward intraoperative goal-directed therapy, as in septic shock, more studies are needed to determine benefit. While the insertion of a pulmonary artery catheter to measure mixed venous oxygen saturation and fluid status is reasonable, resuscitation to predefined supernormal values confers no benefit and may actually be detrimental to the patient. The choice of crystalloid versus colloid administration for fluid resuscitation continues to remain controversial. Extrapolating data from the intensive care unit to the operating room and vice versa can confuse the picture even more. Most large studies, like the SAFE trial, and meta-analyses, like the Cochrane database, suggest that there is no mortality difference in crystalloids versus colloids. Thus, most would choose crystalloids due to the significantly increased expense of colloids. Nevertheless, if the patient is better served with less fluid intake due to other comorbid conditions, colloids may be a reasonable choice, with the understanding that mortality is unlikely different. Hyperchloremic metabolic acidosis can occur in large-volume fluid resuscitation with normal saline; however, it is uncertain whether its occurrence affects clinical outcomes. Switching to Ringer's lactate with less sodium and chloride would be a reasonable choice. Blood would be an appropriate choice for a patient who is anemic and hypotensive with ongoing blood losses.

ADDITIONAL READINGS

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13. ANSWER: E

All blood products can carry infectious risks. Whole blood contains all the components of blood prior to separation. It is rarely used except on the battlefield or in the absence of a blood-banking system. Risks of disease transmission include bacterial, viral, parasitic, and prion diseases. Modern blood donation and banking practices, including screening and storage, have decreased much of the infectious transmission risks associated with blood products. Plasma, whether frozen or thawed, carries the same infectious risks. Platelets carry similar infectious risks. However, because they are stored at room temperature to optimize effectiveness for up to 5 days, platelets are also prone to increased bacterial contamination, including syphilis, compared to blood products stored at lower temperatures.

Albumin is pooled from a large human volunteer population and then undergoes pasteurization for 10 hours at 60 degrees C. This in vitro process essentially kills all enveloped and nonenveloped viruses, including HIV and hepatitis. There have been reports that Creutzfeldt-Jakob disease, a prion disease, could be transmitted through albumin therapy. Albumin does not contain preservatives and is latex-free.

ADDITIONAL READING

Miller RD. Chapter 55, Transfusion Therapy. In Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone, 2009.

14. ANSWER: A

With modern blood-banking practices, the infectious complications of transfusion have decreased to a point where noninfectious complications have become more prominent. The transfusion of blood products have been shown to have immunomodulatory effects since the 1970s, when blood transfusions improved graft survival after kidney transplantation. Transfusion-related immunomodulation (TRIM) may also have some sort of inflammatory effect, but its true clinical scope is uncertain. It is often thought to be a possible reason for cancer recurrence, postoperative infection, virus activation, and in organ dysfunction and mortality. Alloimmunization is the development of antibodies to the transfused blood products. See Table 13.3.

ADDITIONAL READINGS

Drummond JC, Petrovich CT, Lane TA. Chapter 16, Hemostasis and Transfusion Medicine. In Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.

Vamvakas EC, Blajchman MA. Transfusion-related immunomodulation (TRIM): an update. *Blood Rev*. 2007:*21*(6):327–348.

15. ANSWER: B

This case describes a ***delayed hemolytic transfusion reaction***, which usually occurs 3 to 7 days after transfusion. Common clinical signs include mild fever with or without chills, moderate jaundice, and an unexplained decrease in hemoglobin following transfusion. Its incidence is estimated to be less than 1 in 2,000 transfusions. Antibodies formed from either previous transfusion exposure or pregnancy (common) or through primary alloimmunization (less common) increase in the days after a transfusion, which then bind to the transfused red blood cells to form antigen–antibody complexes. These complexes are removed by the reticuloendothelial system with subsequent extravascular hemolysis, leading to increased bilirubin levels and jaundice. Because these antibodies are generally at low titers before transfusion, they are frequently missed by usual cross-matching procedures. Unlike immediate hemolytic transfusion reactions, delayed hemolytic transfusion reactions rarely progress to hemodynamic instability, renal failure, or disseminated intravascular coagulation.

The transfusion of ABO-incompatible blood would result in immediate hemolysis and severe symptoms, mediated via IgM antibodies. Most of the blood released by the blood bank is considered "older" because near-expiring

Table 13.3 NONINFECTIOUS ADVERSE REACTIONS ASSOCIATED WITH BLOOD PRODUCT ADMINISTRATION, IN THE APPROXIMATE ORDER OF THEIR AVERAGE FREQUENCIES IN THE PUBLISHED LITERATURE

ADVERSE REACTION	INCIDENCE	COMMENT
Transfusion related immunomodulation (TRIM)	100%	
Inflammatory response	(?) 100%	Increases with duration of storage
Alloimmunization		
Packed red blood cells	0.5%	
Platelets	10%	Reduced by leukoreduction
Minor allergic reactions (urticaria, flushing)	0.5–4%	Platelets and fresh frozen plasma > red blood cells
Febrile reactions	0.1–2%	Probably reduced by leukoreduction
Delayed hemolytic transfusion reaction (DHTR)	1/2,000	Most often Kell, Kidd, and Rhesus (E) antibodies
Transfusion-related acute lung injury (TRALI)	1/5,000	All plasma containing products; fresh frozen plasma and platelets > packed red blood cells
Anaphylactic/anaphylactoid reactions	1/25,000	Platelets > packed red blood cells IgA deficiency increases risk
Acute hemolytic transfusion reaction (AHTR)	1/25,000	Usually patient ID error; 2% mortality; plasma-incompatible platelets are a rare cause
Graft-versus-host disease (GVHD)	Rare	Immunocompromised patients, especially marrow transplant recipients

From: Drummond JC, Petrovich CT, Lane TA. Chapter 16, Hemostasis and transfusion medicine. In Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*, 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.

blood will be used first. Nevertheless, all blood still must meet the FDA criteria of 75% transfused red blood cells surviving for 24 hours. Consequently, the hemolysis in "old" blood would not be significant enough to cause this patient's jaundice. The patient appears to be stable without evidence of bleeding, and does not need to head back to the operating room for re-exploration. A direct antiglobulin test (Coombs test) should be sent and will be positive in nearly all instances of a delayed transfusion reaction.

ADDITIONAL READINGS

Drummond JC, Petrovich CT, Lane TA. Chapter 16, Hemostasis and Transfusion Medicine. In Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.

Harmening D. *Modern Blood Banking and Transfusion Practices*. Philadelphia, PA: FA Davis Company; 2005.

16. ANSWER: E

The liver usually clears bilirubin from the blood by conjugation, and thus in liver failure, not kidney failure, there is often an increased bilirubin load. All the other disease states (answers A, B, C) can cause hemolysis of red blood cells: metabolic (G6PD deficiency), structural (sickle cell disease), and mechanical (prosthetic valves). Approximately 10% to 25% of transfused red cells can hemolyze within 24 hours. Hence, massive transfusion can result in increased bilirubin levels.

ADDITIONAL READING

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17. ANSWER: D

Leukoreduction is the process of removing white blood cells from blood products. This can be performed prior to storage of blood products or through the use of bedside leukoreduction filters at the time of transfusion. Bedside leukoreduction filters, however, are not as effective or uniform in leukoreduction compared to prestorage techniques. Furthermore, they are not capable of removing cytokines produced by leukocytes during storage that may incite nonhemolytic febrile transfusion reactions.

Urticarial reactions are mild allergic transfusion reactions that occur in as many as 1% to 3% of all transfusions. Although its mechanism is not fully understood, it is thought to be an interaction between IgG and IgE antibodies either in the donor plasma or the recipient and an allergen in the recipient or donor plasma, respectively. This interaction results in a histamine release from mast cells that can range from mild hives, erythema, and pruritus to laryngeal edema, bronchospasm, and angioedema. Leukoreduction has not shown any benefit in reducing the incidence of allergic urticarial transfusion reactions.

In nonhemolytic febrile transfusion reactions, it is hypothesized the recipient has developed antibodies toward transfused leukocytes from prior transfusions, tissue transplantation, or pregnancy. Subsequent transfusions of blood products containing leukocytes may act directly or indirectly through the complement system to produce pyrogens such as interleukin-1 and prostaglandins to cause fever. Thus, one of the major benefits of leukoreduction is reducing the incidence of febrile transfusion reactions.

CMV commonly infects leukocytes to survive and replicate. Hence, leukocytes are a major mode of transmission for the virus. Similarly, leukocytes may harbor bacteria and increase bacterial transmission. The incidence of bacterial sepsis following blood transfusion was shown to drop significantly following the adoption of universal leukoreduction in France. Leukoreduction has also been shown to reduce the rate of HLA alloimmunization, which can increase the likelihood of platelet transfusion refractoriness and other transfusion reactions.

Although initially thought to benefit those who are immunocompromised, leukoreduction appears to offer many universal benefits. Hence, the push for leukoreduction has become greater each year. While universal leukoreduction has been adopted in many countries, including Canada, France, and the United Kingdom, it is not universally performed in the United States.

ADDITIONAL READINGS

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18. ANSWER: B

Leukoreduction decreases the frequency and severity of nonhemolytic febrile transfusion reactions (NHFTRs), not allergic transfusion reactions, following red blood cell and platelet transfusions. Allergic transfusion reactions are a diagnosis of exclusion and generally not life-threatening. It is caused by cytokines and/or recipient antibodies reacting with donor leukocytes in patients receiving frequent

transfusions. Laboratory evaluation for acute hemolytic transfusion reactions, the most serious being the transfusion of ABO-incompatible red blood cells, includes the direct antigen test, urine and plasma hemoglobin, and tests for hemolysis (e.g., LDH, haptoglobin, bilirubin). IgA deficiency is associated with allergic reactions, and knowing a patient has IgA deficiency allows preparation for future blood transfusions. Distinguishing one type of transfusion reaction from another is difficult. Both urticaria and anaphylaxis are due to antibody–allergen interaction causing mast cell degranulation and other mediator responses. It is best to stop the transfusion in case this is an early anaphylactic reaction without hemodynamic compromise. Even under careful exploration, the cause of anaphylaxis may never be known. Thus, careful planning regarding future blood transfusions is warranted.

ADDITIONAL READING

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19. ANSWER: D

This patient likely has an ***anaphylactic or anaphylactoid transfusion reaction***. The first step is to stop the blood transfusion. The second step is to support and treat the patient. Whether or not this is an anaphylactic or anaphylactoid reaction, quickly administering fluids such as crystalloid often stabilizes the situation. Although epinephrine is the treatment for an anaphylactic or anaphylactoid reaction, small initial doses such as 0.3 to 0.5 mL of epinephrine 1:1,000 (300 to 500 mcg) subcutaneously or 5- to 10-mcg IV increments should be administered before escalating to the ACLS dose of 1 mg IV. The same is true for starting an epinephrine infusion, because volume expansion can be performed more quickly than starting an infusion. Despite a low hemoglobin and hypotension, transfusion of blood is unwarranted unless you think this patient is actively bleeding rather than having a transfusion reaction. Giving O-negative blood may worsen the picture and may muddle the investigation as to what happened. While hydrocortisone may be beneficial in treating an anaphylactic or anaphylactoid-type reaction, its benefits will not be realized for several hours.

ADDITIONAL READING

Harmening D. *Modern Blood Banking and Transfusion Practices*. Philadelphia, PA: FA Davis Company; 2005.

20. ANSWER: A

Many of the tests for ***hemolysis***, including LDH, reticulocyte count, haptoglobin, and bilirubin, are nonspecific, and abnormal values only help support clinical suspicion of hemolysis. Often the first clue is anemia, and thus the hemoglobin value is important. Erythrocyte adenylate kinase, a red cell enzyme released from red blood cells, has been shown to be highly sensitive and specific in vitro and in vivo. It can be measured by rapid electrophoresis or immunologic methods but has not been widespread, likely due to availability. There are other tests for hemolysis, including plasma hemoglobin and urine hemosiderin, both of which are not frequently ordered. The gold standard is the chromium red cell survival test, but it is not used because of slow result reporting. Lactate dehydrogenase is often a marker of tissue breakdown or turnover and is abundant in red blood cells. Although elevations of LDH could indicate hemolysis, it serves as a clinical marker for myocardial infarction, tissue turnover, *Pneumocystis* pneumonia, and differentiation of exudates from transudates. Haptoglobin, a serum protein that binds free hemoglobin, is usually decreased in hemolysis. As an acute phase reactant, levels can be elevated in any inflammatory process or stress response. A positive direct Coombs test, a direct antiglobulin test (DAT), would indicate an immunologic process in hemolysis. It is usually weakly positive because the transfused cells are small relative to the patient's blood volume. β-tryptase levels are elevated in most patients with anaphylaxis associated with hypotension. It is released with mast cells along with histamine but it diffuses more slowly, with a half-life of 1.5 to 2.5 hours, as opposed to histamine, which would return back to normal within 30 minutes. Tryptase levels may be elevated if the transfused blood caused anaphylaxis, but this question is looking for tests suggesting hemolysis.

ADDITIONAL READINGS

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21. ANSWER: D

Fever during transfusion should be investigated. It can be relatively abrupt, suggesting a more sinister cause such as an acute hemolytic transfusion reaction or bacterial contamination. Febrile nonhemolytic transfusion reactions (FNHTRs), generally a diagnosis of exclusion, may be another cause. Stopping the transfusion for further investigation is prudent even in the absence of hypotension,

as continued transfusion may lead to less desirable situations, including hypotension and shock. The ASA Committee on Transfusion Medicine recommends stopping transfusions in patients who have a 1 °C or greater temperature rise not explained by the patient's condition (e.g., sepsis). It is no longer recommended that patients routinely receive acetaminophen and diphenhydramine as premedication to treat allergic or febrile nonhemolytic transfusion reactions. It is estimated that routine premedication would need to be done 200 times to prevent one reaction, at the same time increasing the costs and risk of drug side effects. Furthermore, it may delay action if fevers caused by acute hemolytic transfusion reactions are suppressed.

ADDITIONAL READINGS

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Geiger TL, Howard SC. Acetaminophen and diphenhydramine premedication for allergic and febrile nonhemolytic transfusion reactions; good prophylaxis or bad practice? *Transfus Med Rev*. 2007;*21*:1–12.

22. ANSWER: B

Acute normovolemic hemodilution (ANH) is a technique in which the patient's blood is removed while replacing it with an equal intravascular volume of crystalloid or colloid prior to surgery or surgical blood loss. Theoretically, less red blood cell mass and coagulation factors are lost per milliliter of blood compared to nondiluted blood. Absolute contraindications to ANH include severe sepsis, hypovolemia, uncompensated congestive heart failure, and anemia. Relative contraindications include moderate to severe cardiac, pulmonary, renal, or liver disease. The severity of the patient's comorbidities should guide the degree of hemodilution and type of monitoring to perform the technique safely.

A starting hemoglobin of more than 11 to 12 is recommended for ANH. Thus, the patient's current hemoglobin should be adequate. Diabetes mellitus is not a contraindication to ANH. The patient's stable angina implies that there is an increased risk for myocardial ischemia. Withdrawing blood decreases oxygen-carrying capacity, thereby decreasing the margin of safety for adequate oxygen delivery. This, coupled with the increased myocardial demand during aortic cross-clamping, increases the risk of myocardial ischemia and cardiac comorbidity, and would be the biggest concern in using this technique.

Jehovah's Witnesses have been accommodated using ANH as long as the blood that is withdrawn and returned remains in a closed-loop system in continuity with their circulation. Although erythropoietin may stimulate red blood cell production in an effort to raise the patient's hemoglobin level, it is not a prerequisite to performing ANH. Given that the patient's Hgb is within the normal range, increasing it further would not lead to much benefit. Decisions to use ANH and EPO are made on an individual basis for Jehovah's Witnesses. Thus, their use must be clarified prior to using them.

ADDITIONAL READINGS

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23. ANSWER: E

To determine the amount of blood to be withdrawn from this patient, we must first estimate the total blood volume. The estimated blood volume is 80 cc/kg in men and 70 cc/ kg in women. This patient's estimated blood volume would be 80 cc/kg × 90 kg = 7,200 cc. Next, we would use the following formula to calculate maximum estimated blood loss for our target hemoglobin of 10 g/dL:

$$\text{Allowable blood loss} = \text{Hgb}_{\text{starting}} - \text{Hgb}_{\text{Allowed}}/\text{Hgb}_{\text{Avg}} \times \text{Estimated blood volume}$$

$$= 14 - 10/12 \times 7{,}200 = 2{,}400 \text{ ML}$$

The blood is withdrawn via gravity using a large-bore catheter such as a central line into a blood storage bag containing citrate. At the same time volume must be replaced to maintain normovolemia. If crystalloid is used, it is replaced in a 3:1 ratio. With colloid (albumin, Hetastarch, etc.), it is replaced in a 1:1 ratio.

ADDITIONAL READING

Goodnough LT, Monk T. Chapter 57, Autologous Transfusion, Recombinant Factor VIIa, and Bloodless Medicine. In M*iller'* s A*nesthesia.* 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

24. ANSWER: B

Cell Saver, or intraoperative salvage, is a process where blood that is lost on the surgical field is collected and

processed by washing and centrifugation to obtain red blood cells for autotransfusion. It is commonly used in procedures where large amounts of blood are expected to be lost, such as cardiac, major vascular, orthopedic, liver transplantation, or trauma surgery. The advantage of using Cell Saver is to avoid the complications of transfusing allogeneic blood, mainly transfusion reactions, such as hemolytic reactions, and transmission of bloodborne pathogens. During the processing, blood components such as platelets and coagulation factors are lost. Thus, massive transfusion with Cell Saver will also result in a dilutional coagulopathy. Complications from Cell Saver can include air embolism, excessive hemolysis of red blood cells from high vacuum settings, bacterial contamination, and incomplete removal of scavenged debris. It is not routinely used in surgeries where the blood may be contaminated with urine, feces, tumor cells, infectious pathogens, or amniotic fluid. Thus, Cell Saver is not routinely used in cesarean sections, despite its ability to protect against the transmission of bloodborne pathogens using allogeneic blood. The quality of red blood cells appears to be equal to that of allogeneic red cells, with similar oxygen transport and survival properties.

ADDITIONAL READINGS

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Williamson KR, Taswell HF. Intraoperative blood salvage: a review. *Transfusion*. 1991;31:662.

25. ANSWER: B

A ***type and screen*** involves determining the ABO-Rh type of the recipient and screening for antibodies in his or her sera. The sample is first spun down and separated into serum/plasma and red blood cells. The recipient's red blood cells are first mixed with serum containing anti-A and anti-B antibodies to determine ABO blood type. Confirmation of blood type is then performed by mixing the recipient's serum with red blood cells with known A and B antigen.

The Rh type is determined next by mixing anti-D antibodies with the recipient's red cells. If the no agglutination occurs, the patient is Rh-negative. Because anti-D antibodies can be present in someone who is Rh-negative (i.e., a mother being sensitized by fetal red blood cells during a previous childbirth), the recipient's serum is then mixed with Rh-positive red cells to test for its presence.

The antibody screen tests for antibodies in the recipient's serum that may cause a transfusion reaction or reduce survival of transfused red blood cells. It involves mixing the recipient's serum with commercially available O– red blood cells with phenotypes for common antigens such as Kell, Duffy, and Lutheran. A positive antibody test requires further investigation and identification of the specific antibody. The chances of a serious transfusion reaction from typed and screened blood are estimated to be less than 1 in 10,000.

A ***type and cross-match*** involves mixing recipient serum with donor red cells both at room and physiologic (37 degrees C) temperatures. Incubation at physiologic temperature aids in the detection of incomplete antibodies that may bind to red blood cell antigens but do not cause agglutination. Although exceedingly uncommon, these incomplete antibodies can cause hemolytic transfusion reactions. Thus, the cross-match simulates the actual blood transfusion and confirms compatibility of the donor unit.

ADDITIONAL READINGS

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Harmening D. *Modern Blood Banking and Transfusion Practices*. Philadelphia, PA: FA Davis Company; 2005.

26. ANSWER: B

Blood that is stored for 35 days has different characteristics compared to freshly donated blood. The storage solutions, such as CPDA-1, contain agents that help preserve blood. Citrate is added as an anticoagulant, the phosphate to buffer, dextrose as an energy substrate, and adenosine as a building block for ATP synthesis. The FDA criteria for the shelf life of stored blood is defined by more than 70% packed red blood cells surviving in the circulation 24 hours after transfusion. 2,3-DPG levels decrease dramatically after 1 week of storage. These decreased levels shift the Hgb-O_2 dissociation curve to the left, not the right. This increases the Hgb's affinity for oxygen, thereby decreasing its ability to release oxygen to tissues. The plasma concentration of K^+ in a unit of packed red cells can be more than 70 mEq/L as a result of cell lysis. Although phosphate is added to serve as a buffer, a unit of blood becomes more acidic as metabolic byproducts and hemolysis occur during storage (Table 13.4).

ADDITIONAL READING

Miller RD. Chapter 55, Transfusion Therapy. In Miller RD, ed. *Miller'* s A*nesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009

Table 13.4 **PROPERTIES OF WHOLE BLOOD AND PACKED RED CELL CONCENTRATES STORED IN CPDA-1**

	DAYS OF STORAGE		
PARAMETER	0	35 (WHOLE BLOOD)	35 (PACKED CELLS)
pH	7.55	6.73	6.71
Plasma hemoglobin (mg/dL)	0.50	46.00	246.00
Plasma potassium (mEq/L)	4.20	17.20	76.00
Plasma sodium (mEq/L)	169.0	153.00	122.00
Blood dextrose (mg/dL)	440.0	282.00	84.00
2,3-Diphosphoglycerate (μM/mL)	13.20	1.00	1.00
Percent survival*	—	79.00	71.00

SOURCE: Miller RD. Chapter 55, Transfusion therapy. In Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

27. ANSWER: D

The FDA mandates that the following tests be performed on all donated blood in the United States to minimize transmission of infectious diseases:

- Hepatitis B surface antigen (HBsAg)
- Hepatitis B core antibody (anti-HBc)
- Hepatitis C virus antibody (anti-HCV)
- HIV-1 and HIV-2 antibody (anti-HIV-1 and anti-HIV-2)
- HTLV-I and HTLV-II antibody (anti-HTLV-I and anti-HTLV-II)
- Serologic test for syphilis
- Nucleic acid amplification testing (NAT) for HIV-1 and HCV

Although not mandatory, many blood banks also choose to perform the following tests, especially in high-risk areas or patients:

- NAT for West Nile virus (WNV)
- Antibody test for *Trypanosoma cruzi* for Chagas disease
- Antibody test for CMV

ADDITIONAL READINGS

Committee on Transfusion Medicine of the American Society of Anesthesiologists— Brauer SD, Cywinski JB, Downes K, Johnson LN, Kindscher JD, Koehntop DE, McDade W, et al. *Questions and Answers About Blood Management*. 4th ed. Park Ridge, IL: American Society of Anesthesiologists Committee on Transfusion Medicine; 2006–2007.

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28. ANSWER: B

In emergency transfusion scenarios, the order of preference for transfusion of packed red blood cells is

- Type-specific uncross-matched
- O^- uncross-matched
- Type-specific whole blood

If O^- packed red blood cells are unavailable or scarce, then O^+ packed red blood cells can be used in male patients and postmenopausal female patients. Women of childbearing age should avoid O^+ packed red blood cells to avoid Rh-sensitization, which could cause hemolytic anemia of the fetus in subsequent pregnancies. Whole blood is rarely indicated and should be avoided if possible. O^- whole blood contains anti-A and anti-B antibodies, which would react with this recipient's type A red blood cells, causing a hemolytic transfusion reaction. Type-specific whole blood should be used, if needed.

For other blood products, cryoprecipitate does not contain donor antibodies and thus ABO compatibility is not mandatory. Donor antibodies are present in fresh frozen plasma; thus, ABO compatibility is necessary. AB– fresh frozen plasma is the universal donor unit. Although platelets can be transfused without regard to ABO typing, type-specific platelets may increase their survival because platelets can express ABO on their membranes (Table 13.5).

ADDITIONAL READING

Welsby IJ, Bredehoeft SJ. Chapter 85. Blood and Blood Component Therapy. In Longnecker DE, Brown DL, Newman MF, Zapol WM, eds. *Anesthesiology*. New York: The McGraw-Hill Companies; 2008.

Table 13.5 BLOOD PRODUCT COMPATIBILITY

		COMPATIBLE BLOOD PRODUCTS			
PATIENT BLOOD TYPE	ANTIBODIES IN PATIENT'S SERUM	WHOLE BLOOD	PACKED RED BLOOD CELLS	FRESH FROZEN PLASMA	CRYOPRECIPITATE OR PLATELETS
A^+	Anti-B	A^+	A or O	A or AB	All
A^-	Anti-B, +/− Anti-D	A^-	A or O	A or AB	All
B^+	Anti-A	B^+	B or O	B or AB	All
B^-	Anti-A, +/− Anti-D	B^-	B or O	B or AB	All
AB^+	None	AB^+	A, B, AB, or O	AB	All
AB^-	+/− Anti-D	AB^-	A, B, AB, or O	AB	All
O^+	Anti-A and B	O^+	O	A, B, AB, or O	All
O^-	Anti-A and B, +/− Anti-D	O^-	O	A, B, AB, or O	All

29. ANSWER: B

Hemophilia A is a sex-linked inherited bleeding disorder in which factor VIII levels are markedly reduced or nonexistent. Factor VIII is part of the intrinsic blood clotting pathway, which can prolong the PTT depending on the severity of the hemophilia. The severity of bleeding tendency depends on the type of mutation. Hemophilia is classified based on the clotting factor level activity as mild (5% to 40%), moderate (1% to 5%), and severe (1% or less).

For surgery, factor replacement to levels of 80% to 100% is recommended, with continued replacement for up to 2 weeks after surgery. Inhibitors, which are antibodies directed toward factor VIII, can develop in 10% to 15% of patients and can make factor replacement difficult. Their presence is detected using the Bethesda inhibitor assay. Low-responding inhibitor (reported as less than 5 Bethesda Units) indicates a low titer of antibodies and may be overcome by increasing doses of factor concentrate. The presence of a high-responding inhibitor may render factor concentrate therapy ineffective and require bypassing products such as recombinant activated factor VII (rFVIIa), prothrombin complex concentrates (PCC), or activated prothrombin complex concentrate (APCC) to establish hemostasis.

In this clinical scenario, blood should be sent to determine the factor level activity after the initial infusion. The factor VIII dose is calculated using the following equation: [desired factor VIII (units/mL) − initial factor VIII (units/mL)] × plasma volume (mL) = units of factor VIII required. $(1 - 0.2) \times 3{,}430 = 2{,}744$ units. Without the presence of inhibitor, the initial dose of factor VIII would result in a calculated clotting factor level of more than 100%. However, the presence of an inhibitor will likely reduce the initial infusion's effectiveness. Therefore, it is unknown whether an additional 500 units would raise the clotting factor activity to the target level of more than 80%. The clotting factor activity must be continually monitored to determine appropriate levels of factor VIII before administering additional units. DDAVP can be given in mild hemophiliacs to stimulate production of factor VIII to more than three times the current level. However, this would not increase levels to the surgical target of more than 80%. Using a bypassing agent is expensive, and would be a last resort if factor VIII levels do not increase appropriately with factor concentrates, or if the patient continues to hemorrhage profusely.

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30. ANSWER: E

The major difference between ***hemophilia A and B*** (also known as Christmas disease) relates to the deficiency of factor VIII in hemophilia A and factor IX in hemophilia B. Both hemophilia A and B clotting factor genes reside on the X chromosome and thus exhibit a sex-linked inheritance. DDAVP increases factor VIII levels by three- to six fold, but there is no effect on factor IX levels. In situations where factor IX concentrates are not available, fresh frozen plasma would be preferable to cryoprecipitate because it contains the majority of factor IX, whereas cryoprecipitate is rich in

Table 13.6 HEMOPHILIA A AND B

CHARACTERISTICS	HEMOPHILIA A	HEMOPHILIA B
Factor deficiency	VIII	IX
Inheritance	Recessive sex-linked	
Blood test	Prolonged aPTT, normal bleeding time and PT	
Clinical symptoms	Spontaneous epistaxis and joint hemarthrosis, easy bruising, excessive bleeding following trauma	
Treatment	Purified factor VIII concentrates, cryoprecipitate, and DDAVP (mild cases only)	Factor IX concentrates, fresh frozen plasma, prothrombin complex concentrates (PCC)
Incidence of inhibitors	10–15%	1–3%, but >50% of those can develop life-threatening allergic reactions
Bypass agents	Factor VIIa, PCC, and activated PCC (aPCC)	

factor VIII, fibrinogen, and von Willebrand factor. Bypass agents such as factor VIIa can be used for both hemophilias. See Table 13.6 for characteristics and comparisons between the two hemophilia types.

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31. ANSWER: B

Newborn screening for ***sickle cell disease (SCD)*** is recommended by the U.S. Preventive Task Force (USPTF) to establish early education for parents regarding lifelong consequences of SCD and to initiate prophylactic antibiotic treatment with penicillin and vaccination against life-threatening pneumococcal infections by 2 months of age.

At birth, the SCD neonate has a large proportion of fetal hemoglobin (HgbF) compared to normal adult (HgbA) and sickle cell (HgbS) hemoglobin. Thus, neonates are initially "protected" from the complications of SCD, including vaso-occlusive crises and functional asplenia. This protection wanes over the first year as HgbS levels rise and HgbF levels fall. Because of the low percentage of HgbS at birth, an exchange or simple blood transfusion is not indicated prior to surgery. High FiO_2 to prevent sickling of HgbS is also not recommended because of the low percentage of HgbS.

Functional asplenia, a term used to describe the spleen's inability to combat infection despite its physical presence, also tends to occur with an increasing HgbS:HgbF ratio. Although this neonate is susceptible to pneumococcal infection for a variety of reasons (i.e., an immature immune system, surgical contamination), functional asplenia does not occur in the first month of life.

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32. ANSWER: C

Patients with ***sickle cell anemia*** are at increased risk for perioperative complications. ***Acute chest syndrome (ACS)*** is a serious complication with increased morbidity and mortality in patients with sickle cell disease. The exact etiology of ACS is unknown, but multiple etiologies have been proposed, including infection, pulmonary infarction from vaso-occluded pulmonary vessels, fat embolism from infarcted bone marrow, and hypoventilation. Onset of ACS can range from as little as 1 hour to over 1 week following surgery. Laparoscopy does not appear to lessen the incidence for ACS and may actually increase it.

Diagnosis of ACS is based on finding a new infiltrate on chest x-ray and one of the following: fever, cough, sputum production, dyspnea, or hypoxia. Sputum cultures sometimes reveal an infectious source. Treatment is supportive and directed toward maintaining adequate oxygen delivery to tissues and treating the lung pathology. This includes maintaining an adequate hemoglobin level through simple or exchange transfusion, IV fluids, antibiotics to treat infectious causes, and analgesics, such as hydromorphone, for pain control. There is a high association between ACS and asthma, although the relationship is not clear. Hence, many sickle cell patients also benefit from asthma treatments such as albuterol and steroids. Furosemide could lead to dehydration, promote red blood cell sickling, and potentially worsen the ACS episode. If severe enough, exchange transfusion and mechanical ventilation may be needed.

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33. ANSWER: C

Sickle cell anemia is a recessively inherited anemia that is common to people of African descent. A genetic alteration in which valine is substituted for glutamic acid in the beta subunit of the hemoglobin tetramer drastically alters the structure and function of the hemoglobin unit, termed HgbS. When exposed to a deoxygenated and acidic environment, HgbS causes red blood cells to become unstable and sickle. This rigid, hydrophobic structure causes widespread complications affecting almost every organ system through chronic vaso-occlusion, endothelial damage and dysfunction, and decreased red cell survival. Clinically, these patients experience symptoms of painful vaso-occlusive crises, acute chest syndrome, and aplastic crises, which can result in stroke, renal insufficiency, chronic lung disease, and functional asplenia.

Sickle cell patients are at increased risk for complications in the perioperative period. The principles of anesthetic management of sickle cell patients are to optimize oxygen delivery and avoid conditions that would induce HgbS cells to sickle, including hypoxia, acidosis, and hypothermia. Use of an intraoperative tourniquet is relatively contraindicated, as it can promote acidosis and hypoxic conditions that favor sickling in the ischemic limb. Studies have shown that exchange transfusions to decrease HgbS to less than 30% are no more effective than simple transfusion to a target of Hgb of more than 10. Furthermore, simple transfusion of packed red cells to increase Hgb to above 10 has not been shown to reduce complications from sickle cell anemia for minor surgeries. These patients should be treated with aggressive fluid management to prevent dehydration, acidosis, and increased blood viscosity due to sickle cells. Induced hypotension may jeopardize oxygen delivery to tissue and promote acidosis and sickling of red cells. There are no data to show that regional anesthesia is preferable to general anesthesia, although regional anesthesia may improve blood flow through autonomic vasodilation and improve analgesia. General anesthetics have not been shown to increase the incidence of acute chest syndrome compared to regional anesthesia techniques.

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34. ANSWER: E

Massive transfusion (MT) is defined as giving more than 10 units of blood or the patient's total blood volume over a period of 24 hours. Although frequently associated with trauma, MT can occur with any surgery where there is major blood loss. The complications of MT are numerous and interrelated. They can include dilutional coagulopathy, DIC, citrate toxicity, hypothermia, and acidosis.

Citrate toxicity can occur if transfusion of red cells is given more quickly than the liver can metabolize the citrate. Although this may lead to transient hypotension and hypocalcemia, it does not affect hemostasis.

Dilutional coagulopathy occurs secondary to infusion of large amounts of crystalloid and red cells without concomitant replacement of platelets and coagulation factors. Traditionally, blood products such as fresh frozen plasma, cryoprecipitate, and platelets are not administered at the onset of MT because hemostasis can still occur despite this dilutional effect. Trauma exsanguination protocols where a set ratio of packed red cells:fresh frozen plasma:platelets is transfused to combat dilutional coagulopathy are controversial. Proponents for these protocols argue that early goal-directed therapy, similar to the concept used in treating

sepsis, reduces blood loss, averts severe coagulopathy, and improves outcomes. Arguments against these protocols are that products may be overused to prophylactically achieve hemostasis, and expose the patient to increased transfusion risks, such as transfusion-related acute lung injury and bloodborne infections. Given the rapidly changing status of an exsanguinating patient, both clinical assessment of bleeding and laboratory testing should be used to guide hemostatic therapy.

DIC frequently occurs in the setting of major blood loss and subsequent tissue hypoperfusion. As a result, these hypoxic tissues trigger the coagulation cascade by releasing factors that ultimately cause a vicious cycle of clotting formation and lysis. This consumptive cycle ultimately leads to bleeding diathesis by depleting coagulation and fibrinolytic factors. Laboratory studies will reveal high PT/INR and aPTT and a low fibrinogen level.

Hypothermia slows the activity of the coagulation cascade, reduces the synthesis of coagulation factors, increases fibrinolysis, and affects platelet function. Efforts to curb hypothermia include using a blood/fluid warmer, increasing the room temperature to reduce radiant heat loss, and using warm lavage fluid (if needed) and active warming blankets (forced-air or conductive).

A metabolic acidosis can develop during MT for a variety of reasons, including transfusion of acidic blood, tissue hypoperfusion secondary to shock, and IV fluid administration. Acidemia makes enzymes and coagulation factors less effective. When coupled with hypothermia, the coagulation pathway is synergistically impaired.

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35. ANSWER: D

Citrate is used as an anticoagulant by chelating calcium in stored blood. Massive transfusion of red cells introduces large amounts of citrate into the circulation, which can bind free calcium and cause hypocalcemia. Hypocalcemia induced by citrate toxicity generally corrects itself because the liver can rapidly metabolize citrate at the rate of 3 g (contained in 1 unit of packed red blood cells) every 5 minutes. However, in cases where there is liver dysfunction or in low-perfusion states, the patient's ability to metabolize citrate is impaired. Signs of citrate toxicity/hypocalcemia include hypotension, narrow pulse pressure, elevated central venous pressure, and elevated end-diastolic pressure. Exogenous calcium is indicated when the ionized calcium level is low or when there is evidence of cardiovascular compromise (prolonged QT interval or hemodynamic instability). Newer blood banking processes make citrate toxicity a much less likely event, even in massive transfusions.

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36. ANSWER: D

Prothrombin complex concentrates (PCC) are composed of vitamin K-dependent factors II, VII, IX, and X derived from pooled plasma. Because it is derived from plasma, it carries a risk of viral transmission. However, this risk is not as great as with the traditional blood products because it is filtered, heat-inactivated, and/or treated with solvent detergent. PCC does not have to be ABO-type-specific because antibodies and red blood cells are removed during the purification process.

PCC is useful in reversing warfarin anticoagulation and providing replacement factors for factors II, IX (hemophilia B), and X deficiencies. It can also be used as a bypass agent for hemophilia A patients with inhibitors or to aid in achieving hemostasis in cases with major hemorrhage. There are many formulations of PCC on the market today. Although the factor IX levels are standardized across all preparations, the levels of the other factors can vary. The main risk associated with PCC administration is thrombosis, although it is exceedingly rare. To combat this, proteins C and S, antithrombin, and heparin are added to most formulations to reduce thrombogenicity. Hence, PCC is contraindicated in patients with heparin-induced thrombocytopenia and disseminated intravascular coagulation.

A dose of PCC can be reconstituted in as little as 20 cc for the urgent reversal of warfarin anticoagulation, with its effects being seen in as little as 10 minutes. Conversely, FFP must be thawed and usually requires an infusion of at least 2 to 4 units (~200 cc/bag) before reduction of INR is achieved. This large volume of fluid may potentially tip

frail patients into volume overload and/or congestive heart failure. Reversal of anticoagulation with PCC is also more complete, with a higher frequency of normalization of INR less than 1.5 compared to FFP. However, both FFP and PCC provide short-term reversal of anticoagulation because the replacement factors have half-lives in the range of hours. To maintain long-term reversal, vitamin K administration is recommended with both FFP and PCC.

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37. ANSWER: B

Many agents have been used in an attempt to reduce bleeding and transfusion requirements during major surgeries involving large blood loss, including cardiac surgery. These agents can be divided into four main categories: antifibrinolytics, desmopressin, factor VIIa, and PCC. These agents are used either prophylactically to reduce blood loss and transfusion requirements, or as a rescue technique once major blood loss has occurred.

DDAVP is a synthetic analog of vasopressin, an antidiuretic hormone. It is primarily used for patients with mild hemophilia A and von Willebrand disease undergoing surgery to correct the underlying clotting factor deficiencies, as it stimulates the release of von Willebrand factor and factor VIII. However, studies have been inconclusive in demonstrating a decreased transfusion requirement during cardiac surgery. Although it may be helpful in reducing blood loss and transfusion requirements for cardiac surgeries with recent aspirin use, it does not appear to help in other cases.

Antifibrinolytics are pharmacologic agents that act to prevent the breakdown of blood clots. They consist of the lysine analogs (aminocaproic and tranexamic acid) and serine protease inhibitors (aprotinin). The lysine analogs bind to the plasmin complex, inhibiting it from binding to fibrin to degrade the clot. Aprotinin acts to inhibit plasmin, plasma and tissue kallikreins, and activated factor XII. Multiple studies have demonstrated the ability of antifibrinolytics to reduce the need for blood transfusion and decreased blood loss. Aprotinin, however, was withdrawn from the market in 2007 after a major clinical trial (BART) demonstrated an increased incidence of adverse cardiovascular and cerebrovascular events leading to increased mortality following cardiac surgery.

Developed as a bypass agent for hemophilia A and B patients with inhibitors, recombinant factor VIIa is increasingly being used for a variety of off-label indications, including massive blood loss in trauma and cardiac surgery. It works in a variety of ways to stimulate clotting, including (1) activation of factor X to generate thrombin in response to binding to exposed tissue factor from damaged endothelial cells and (2) platelet activation to stimulate further factors to produce fibrin clots. Although its use in cardiac surgery as a prophylactic versus rescue method is still evolving, recombinant factor VIIa has been clearly shown to decrease blood loss and the need for blood transfusion.

PCC contains vitamin K-dependent factors II, VII, IX, and X derived from pooled plasma. Although its main indications include reversal of warfarin anticoagulation and treatment of hemophilia and factor II and X deficiency, PCC is becoming more commonly used in the setting of massive bleeding. Similar to recombinant factor VIIa, PCC is used as a rescue therapy to curtail blood loss after traditional measures have failed. Studies demonstrate improved hemostasis and decreased use of blood products following administration of PCC for cardiac surgery.

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38. ANSWER: E

Cryoprecipitate is derived as a white insoluble precipitate from fresh frozen plasma as it is thawing. It contains large amounts of factor VIII, fibrinogen, von Willebrand factor, and fibronectin. This makes it useful in the treatment of fibrinogen deficiency states (disseminated intravascular coagulation, liver failure, and massive transfusion) and factor VIII (hemophilia A) deficiency when purified factor concentrates are not available. Cryoprecipitate also contains factor XIII, which can be used to treat factor XIII deficiency. It is administered without regard to ABO-type cross-matching. One unit per 10 kg of patient weight increases plasma fibrinogen approximately 50 to 70 mg/dL in the absence of a consumptive/dilutional process, with 70 to 100 mg/dL being the minimal level needed to achieve hemostasis.

Thrombin is not a component in cryoprecipitate. However, when mixed with cryoprecipitate, it forms a fibrin glue that can be used for a variety of purposes, including sealing tissues (dural tears, vascular grafts) and controlling diffuse microvascular bleeding during major surgery such as cardiac and trauma.

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39. ANSWER: A

Tetrastarches are the latest generation of hydroxyethyl (HES) starches on the market. They have a lower molecular weight (less than 200 kDal) and a lower molar substitution ratio (less than 0.4) than older Hetastarches. Although a larger molecular weight and a higher molar substitution ratio were thought to contribute to increased volume-expansion properties through decreased degradation and elimination, they also result in increased side effects of accumulation of byproducts, renal impairment, and alteration of blood coagulation. Newer tetrastarches, despite their lower molecular weights and lower molar substitution, appear to have similar volume-expansion properties without the added side effects.

Recent studies have demonstrated decreased accumulation of byproducts, likely because of its more rapid elimination. Despite being more rapidly eliminated, it is hypothesized that there are more molecules within the same volume administered to compensate, and thus provide similar volume-expansion duration. The incidence of coagulopathy has also been shown to be decreased. Hence, the tetrastarches have an increased maximum recommended dose of 50 mL/kg, compared to 20 mL/kg for the older Hetastarches.

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40. ANSWER: C

Prospective blood donors undergo a thorough screening process consisting of a history, physical, and lab work to ensure that they are able to tolerate blood donation and provide blood that is suitable and safe for transfusion. In general, a prospective donor must be healthy, at least 17 years old, and more than 110 lbs in order to donate. Any chronic health problems must be under good control with treatment.

The donation process starts with a questionnaire that aims to identify any medical conditions or high-risk activity (intravenous drug use, male homosexuality, foreign travel, tattoos) that may cause the donor to be deferred. Once screened, a hemoglobin/hematocrit is obtained along with a brief physical exam with vital signs.

Taking aspirin is not a reason for deferral. However, donors must wait at least 2 days after the last dose for platelet apheresis. Patients who are positive for CMV are allowed to donate blood. Although not mandatory, most blood centers screen for CMV antibodies in donated blood. CMV-positive units can then be diverted away from immunocompromised (transplant recipients, HIV) or neonatal populations because CMV infections could potentially be life-threatening. Inquiry about foreign travel is important to reduce the risk of transmission of certain infectious diseases, including malaria, Creutzfeldt-Jakob disease, and leishmaniasis. India is considered an area with a high prevalence of malaria. Thus, it is recommended that donation occur more than a year after travel to allow for clinical symptoms of infection to manifest. Sickle cell trait is not a reason for deferral. Donors with treated syphilis more than 1 year ago are eligible for donation.

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41. ANSWER: A

With the lack of bleeding at the surgical site and the onset of symptoms soon after the initiation of blood transfusion, this most likely is a transfusion reaction and not just a decompensation from excessive blood loss. The onset of blood-tinged urine suggests that this is an ***immediate hemolytic transfusion reaction*** rather than other transfusion reactions, such as an allergic, anaphylactic, or bacterial contamination reaction. Hence, treating with epinephrine and steroids, or with empiric antibiotics, alone will not likely resolve the reaction. Although older blood can contain up to 30% hemolyzed red blood cells by FDA criteria, this rarely causes a hemoglobinuria because the body usually has the capacity to bind and eliminate free hemoglobin through the reticuloendothelial system. Furthermore, even

if a unit of packed red blood cells with enough hemolysis to cause a hemoglobinuria was transfused, it would not cause hypotension or complications of an immune-mediated hemolytic transfusion reaction.

Immediate hemolytic transfusion reactions occur when incompatible ABO-type blood is given to a patient. The recipient's antibodies and complement attack and hemolyze the transfused red cells within the intravascular space. The liberated contents of the red blood cell can cause widespread damage, including precipitation within renal tubules and activation of the intrinsic clotting and kallikrein systems, causing acute renal failure, disseminated intravascular coagulation (DIC), and hypotension, respectively. In the awake patient, clinical symptoms can include fevers, chills, nausea, and chest pain. However, anesthesia can mask many of these signs. Clues to the diagnosis in the anesthetized patient include hypotension, tachycardia, and hemoglobinuria. Fever and DIC are late findings.

Similar to most other blood transfusion reactions, immediate actions include stopping the blood transfusion and administering liberal IV fluids to maintain urine output. Subsequent management is directed at preventing the main complications of acute renal failure and DIC and confirming the hemolytic transfusion reaction. Mannitol and/or furosemide can be added to maintain urine output if liberal IV fluids alone are inadequate. Alkalinization of urine to a pH of more than 8 with sodium bicarbonate is also recommended to decrease the likelihood of precipitation of red cell contents within the renal tubules. The units of blood should also be returned to the blood bank for further analysis. Laboratory studies on both blood and urine to confirm hemolysis and determine coagulation status are also important.

KEY FACTS: STEPS IN THE TREATMENT OF A HEMOLYTIC TRANSFUSION REACTION

1. Stop the Transfusion.
2. Maintain the urine output at a minimum of 75 to 100 mL/hr by the following methods:
   a. Generously administer fluids IV and possibly mannitol (12.5 to 50 g, given over 5 to 15 minutes).
   b. If IV fluids and mannitol are ineffective, administer furosemide (20 to 40 mg) IV.
3. Alkalinize the urine; because bicarbonate is preferentially excreted in the urine, only 40 to 70 mEq of sodium bicarbonate per 70 kg of body weight is usually required to raise the urine pH to 8, whereupon repeat urine pH determinations indicate the need for additional bicarbonate.
4. Assay urine and plasma hemoglobin concentrations.
5. Determine platelet count, partial thromboplastin time, and serum fibrinogen level.
6. Return unused blood to blood bank for repeat cross-match.
7. Send patient's blood and urine sample to blood bank for examination.
8. Prevent hypotension to ensure adequate renal blood flow.

SOURCE: Miller RD. Chapter 55, Transfusion Therapy. In Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

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42. ANSWER: B

Autologous blood donation is an alternative therapy to traditional allogeneic blood transfusion for elective surgeries. Using one's own blood has many touted advantages over allogeneic blood transfusion, including avoidance of transmission of infectious disease, immunomodulation, alloimmunization, and most transfusion reactions (hemolytic, febrile, allergic, etc.). Despite these advantages, there are real risks associated with it, including bacterial contamination, clerical error, and the possibility of rendering the patient anemic preoperatively. While its use increased in the 1980s, when the risk of viral transmission (especially HIV) was higher with allogeneic blood transfusion, autologous blood use has decreased as allogeneic blood-screening methods have improved. In addition, costs are higher for autologous blood transfusion compared to allogeneic transfusion. Hence, autologous donation should be used judiciously only if there is a high likelihood that it will be needed during surgery, such as total joint replacement, open radical prostatectomy, and cardiovascular surgery.

The AABB recommends that the donor be in good health and able to tolerate removal of blood. Some contraindications include active bacteremia, active seizure disorder, unstable angina, or a recent cardiovascular event. Although the AABB guidelines do not have any age restrictions, the donor's comorbidities and total blood volume need to be weighed against the benefits of autologous donation, especially with the extremes of age. A predonation hemoglobin of more than 11 is required. Donation can occur on a weekly basis up to 3 days prior to surgery. This allows for

restoration of intravascular volume following donation. Donation volume should not exceed 10.5 mL/kg. Patients should be offered iron to aid in hematopoiesis following the induced postdonation anemia. Unused units cannot be shifted into the regular blood bank pool because of the less stringent restrictions placed on autologous blood.

ADDITIONAL READINGS

Goodnough LT. Autologous blood donation. *Critical Care*. 2004;*8*(Suppl 2):S49-S52.

Miller RD. Chapter 55, Transfusion Therapy. In Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

14.

ANESTHESIA EQUIPMENT

Aalok Agarwala, MD, MBA, Rafael Vazquez, MD, and Cuong Vu, MD

1. Which of the following contributes to the dead space in a circle system?

A. CO_2 absorber
B. Breathing bag (reservoir)
C. Length of tubing from unidirectional valves to Y-piece
D. Distance from Y-piece to the terminal bronchioles
E. All of the above

2. Which of the following is the correct arrangement of Mapleson breathing circuit components most efficient for controlled ventilation (from proximal to distal with patient at distal end)?

A. Adjustable pressure-limiting (APL) valve, breathing bag, breathing tube, fresh gas inlet, mask
B. Breathing bag, breathing tube, fresh gas inlet, APL valve, mask
C. Breathing bag, APL valve, breathing tube, fresh gas inlet, mask
D. Fresh gas inlet, breathing bag, breathing tube, APL valve, mask
E. None of the above

3. Which of the following is the LEAST likely cause of postoperative hypoxia?

A. Excessive intraoperative opioid administration
B. Negative-pressure pulmonary edema
C. Hypothermia
D. Hypotension
E. Pain after thoracic surgery

4. Which of the following statements about electrical shock is INCORRECT?

A. If applied directly to the heart, 100 microamps can cause ventricular fibrillation.
B. Macroshock refers to current applied outside of the body.
C. There is greater tissue penetration with lower frequencies, resulting in greater likelihood of cardiac excitation.
D. The larger the area of skin exposed to current, the greater the likelihood of damage.
E. The duration of contact has an effect on the degree of damage.

5. Which of the following statements regarding the dynamics of laminar fluid movement through a tube is INCORRECT?

A. Flow is inversely proportional to the viscosity of the fluid.
B. Flow is directly proportional to the square of the radius of the tube.
C. Flow is inversely proportional to the length of the tube.
D. Flow is directly proportional to the pressure gradient between the two ends of the tube.
E. All of the above statements are true.

6. A 72-year-old woman is undergoing a total hip replacement under general anesthesia. Shortly after the femoral prosthesis is placed, you notice that the patient's end-tidal CO_2 is 24 mm Hg. Which of the following is LEAST likely to be the cause?

A. Hypothyroidism
B. Fat embolus
C. Hypoperfusion
D. Hyperthermia
E. Hyperventilation

7. A low-pressure leak test is performed on the anesthesia machine prior to anesthetizing a healthy 22-year-old woman undergoing urgent laparoscopic appendectomy at 2 a.m. The test fails. Which of the following statements about the low-pressure system of the anesthesia system is INCORRECT?

A. Leaks in the low-pressure system can cause patient awareness.
B. The CO_2 absorber is one of the most common sites of leaks in the low-pressure system.
C. The flowmeters should be turned on when performing a negative-pressure test.
D. The low-pressure portion of the system develops leaks more frequently than other parts.
E. A loose filler cap on a vaporizer can result in failure of the low-pressure leak test.

8. Which of the following can result in anesthetic agent overdose?

A. Overfilling of vaporizers
B. Incorrect volatile agent in the vaporizer
C. Tipped vaporizer
D. Failure of the vaporizer interlock system
E. All of the above

9. A 44-year-old man is undergoing lumbar laminectomy under general anesthesia with sevoflurane and nitrous oxide on a Monday morning. In the middle of the case, you notice that the patient is hypertensive and tachycardic, and notice that the patient is moving his hands. Which of the following is the LEAST likely cause?

A. A tipped vaporizer
B. Empty nitrous oxide cylinder
C. Use of sevoflurane in a vaporizer for isoflurane
D. Entrainment of air into the bellows
E. Isoflurane placed in a halothane vaporizer

10. A 54-year-old man is to undergo an open colectomy under general anesthesia with an epidural catheter placed for postoperative pain control. As the patient is being preoxygenated prior to induction of anesthesia, the line isolation monitor (LIM) alarm sounds. Which of the following statements is INCORRECT?

A. The LIM is useful in protecting against macroshock.
B. The LIM detects a first fault condition in the secondary circuit.
C. The LIM will interrupt the power supply and prevent macroshock from occurring.
D. The alarm signifies excessive current leak, representing a partial conversion of the ungrounded power system to a grounded one.
E. The most appropriate next step is to postpone the surgery or move the patient to another operating room.

11. A 24-year-old woman is undergoing exploratory laparotomy after a ruptured ectopic pregnancy. Soon after induction of general anesthesia, the SaO_2 starts to decrease. Which of the following is LEAST likely to be the cause?

A. Hypoventilation
B. Malpositioned pulse oximeter probe
C. The presence of blue nail polish on the digit with the probe
D. Severe anemia
E. Raynaud's phenomenon

12. In which of the following patients is an inaccurately low pulse oximetry oxygen saturation reading LEAST likely to be present?

A. A 35-year-old woman shivering in the postanesthesia care unit after laparoscopic ovarian cystectomy
B. A 65-year-old man undergoing cystoscopy who just received an injection of methylene blue
C. A 54-year-old man who recently underwent awake flexible bronchoscopy with use of benzocaine
D. A 48-year-old woman undergoing knee replacement with a malpositioned sensor
E. A 12-year-old girl found unconscious in her home with a malfunctioning kerosene space heater

13. Which of the following is the LEAST likely potential cause of barotrauma?

A. Use of the oxygen flush valve during inspiration with certain models of mechanical ventilators
B. Closed APL valve when switching from mechanical to spontaneous ventilation
C. Obstruction of the expiratory limb of the breathing circuit
D. Use of jet ventilation during laryngeal surgery
E. Incompetent ventilator relief valve

14. Which of the following statements about turbulent gas flow is INCORRECT?

A. Flow rate above the critical number is required for turbulent flow to exist.
B. A higher Reynolds number is predictive of turbulent flow.

C. Gas viscosity is more important than gas density in turbulent flow.
D. Constriction in the flow tubing can cause turbulent flow.
E. Resistance is proportional to the square of the flow rate with turbulent flow.

15. A 56-year-old woman undergoes a cystectomy under general anesthesia using 70% nitrous oxide, 29% oxygen, and 1% isoflurane. Within minutes of emergence, she is transported to the postanesthesia care unit (PACU) spontaneously ventilating with oxygen by face mask; however, the anesthesiologist does not realize that the oxygen tank is empty. Vital signs on arrival to the PACU are BP 140/76, pulse 82, RR 18, SpO_2 84%. On exam, she has clear bilateral breath sounds with excellent tidal volumes and appears comfortable. Which of the following is the most likely cause of the patient's low pulse oximeter reading?

A. Negative-pressure pulmonary edema
B. Alveolar hypoventilation
C. Inadequate neuromuscular blockade reversal
D. Diffusion hypoxia
E. Pneumothorax

16. Which of the following statements about American Society of Anesthesiologists (ASA) Standards and Guidelines is true?

A. *Guidelines* provide rules or minimum requirements for clinical practice.
B. *Standards* provide recommendations for clinical practice and represent the opinions, beliefs, and best medical judgments of the ASA House of Delegates.
C. *Guidelines* may be modified only under unusual circumstances, for example extreme emergencies or unavailability of equipment.
D. *Standards* are subject to revision as warranted by the evolution of medical knowledge, technology, and practice.
E. *Guidelines* provide basic recommendations that are supported by a synthesis and analysis of the current literature, expert opinion, open forum commentary, and clinical feasibility data.

17. A patient is undergoing surgery under general anesthesia using an anesthesia machine with a ventilator. Which of the following is the LEAST likely consequence from a hole in the ventilator bellows?

A. Hyperventilation
B. Hypoventilation
C. Barotrauma
D. Oxygen analyzer value will decrease.
E. Oxygen analyzer value will increase.

18. Capnometry is LEAST useful for monitoring which of the following?

A. Accidental extubation
B. Complete airway obstruction
C. Endobronchial intubation
D. Malignant hyperthermia
E. Esophageal intubation

19. A 65-year-old man is undergoing a low anterior resection in Leadville, Colorado (elevation 10,152 feet, atmospheric pressure 523 mm Hg). If the patient is under general anesthesia with isoflurane with a perfectly calibrated variable-bypass vaporizer set to deliver 1%, which of the following statements would be true?

A. Only the percent concentration of isoflurane delivered will be higher than at sea level.
B. Only the partial pressure output of the isoflurane vaporizer will be higher than at sea level.
C. Both the percent concentration delivered and the partial pressure will be higher than compared to sea level.
D. Both the percent concentration delivered and the partial pressure will be lower than compared to sea level.
E. Both the percent concentration delivered and the partial pressure will be approximately equal to those at sea level.

20. Which of the following statements about the oxygen flush valve is FALSE?

A. Use of the oxygen flush valve can cause barotrauma, especially in older anesthesia machines.
B. The flush valve always delivers oxygen to the common gas outlet at 50 psi.
C. Use of the oxygen flush valve can cause dilution of inspired volatile anesthetic.
D. The oxygen flush valve may be used for jet ventilation in certain circumstances.
E. All of the above statements are true.

21. A 78-year-old woman has just undergone an abdominal aortic aneurysm resection under general anesthesia and is to be transported to the intensive care unit intubated. The Ambu bag is connected to the oxygen tank at the foot of the bed. It is a standard E cylinder, and the pressure gauge reads 1,200 psi. How many minutes will you have before the oxygen tank is empty if the oxygen is flowing at 15 L/min?

A. 15 minutes
B. 20 minutes
C. 25 minutes

D. 35 minutes
E. 42 minutes

22. A 25-year-old patient is undergoing a dilation and curettage for retained products of conception and persistent bleeding. The patient is under general anesthesia using nitrous oxide at 2 L/min, oxygen at 1 L/min, and sevoflurane at 1%. There is no nitrous oxide pipeline in this particular operating room, and the E cylinder mounted on the back of the machine has a pressure gauge reading 750 psi. How many minutes can pass before the nitrous oxide tank is empty?

A. 33
B. 330
C. 795
D. 1,590
E. Unable to determine from information given

23. Which of the following is a determinant of anesthetic vapor pressure?

A. Volume of liquid in a container (i.e., vaporizer)
B. Temperature
C. Atmospheric pressure
D. Surface area of the liquid in a container
E. More than one answer is correct

24. All of the following affect the rate of gas flow through a flowmeter EXCEPT:

A. Physical properties of the gas
B. The pressure difference across the constriction in the tube
C. The length of the flowmeter tube
D. The size of the opening within the tube
E. The ambient pressure

25. A 47-year-old man with a history significant for chronic obstructive pulmonary disease presents with progressive stridor and is diagnosed with laryngeal cancer. He is scheduled for suspension microlaryngoscopy using a CO_2 laser. What strategy will be most effective in decreasing the risk of an airway fire?

A. Using a mixture of 70% nitrous with 30% oxygen
B. Using a silicone endotracheal tube wrapped in aluminum tape
C. Diluting oxygen with air to achieve an inspired O_2 concentration of less than 30%
D. Filling the endotracheal cuff with methylene blue
E. Using a mixture of 70% helium with 30% oxygen

26. A 75-year-old woman presents to the preoperative clinic to undergo a left total knee replacement. She has a history of hypertension, well-controlled type 2 diabetes, and osteoarthritis. She has also had a dual-chamber permanent pacemaker placed for syncope related to sick sinus syndrome. She brings with her documentation stating that her pacemaker is AAIR. A recent interrogation reveals she is paced 50% of the time at a rate of 60 bpm. The pacemaker is located in the left infraclavicular region. The ECG is notable for sinus rhythm at 68 bpm. In preparation for surgery, how will the pacemaker be best managed?

A. Proceed with surgery.
B. Ask the surgeon to use bipolar electrocautery intraoperatively.
C. Ask the cardiologist to turn off the rate response.
D. Ask the cardiologist to turn off the pacemaker, as the patient is not pacer-dependent.
E. Place a magnet over the pacemaker.

27. During transport of a patient from the operating room to the surgical intensive care unit, you are no longer able to monitor lead II or V5 on the five-lead ECG. Leads I can only be monitored. What best explains this finding?

A. The ECG cable is not properly seated into the monitor.
B. A 12-lead ECG cable is being used instead of a 5-lead ECG cable.
C. The RA lead connection is faulty.
D. The LA lead has been placed on the right lower limb.
E. The LL lead is making poor contact with the patient.

28. A 46-year-old man with end-stage liver disease from hepatitis C is scheduled for a liver transplant. Physical examination reveals a markedly jaundiced patient. Review of the laboratory data reveals a total bilirubin of 20 mg/dL. How will this condition interfere with the pulse oximeter?

A. It will give a falsely high pulse oximeter measurement.
B. It will give a falsely low pulse oximeter measurement.
C. It will not interfere with the pulse oximeter measurement.
D. Placing the pulse oximeter perpendicular to the nail will decrease interference.
E. The pulse oximeter tracing will be of very poor quality.

29. One hour into an occipital craniotomy, the inspired CO_2 is 4 mm Hg. Anesthetic maintenance is with 70% nitrous oxide and 0.4 MAC of sevoflurane. The calcium hydroxide ($Ca(OH)_2$) soda lime absorbent has changed colors. Upon changing the absorbent you notice the

canister is very warm. What is the most likely explanation for this?

A. Benign exothermic reaction
B. Falsely high oxygen saturation level
C. Postoperative renal failure in the patient
D. Upper airway mucosal injury
E. Damage to the respiratory circuit

30. A 51-year-old woman with a history of obesity, mitochondrial dysfunction, and depression on paroxetine is scheduled to undergo an urgent laparoscopic cholecystectomy. She is extremely anxious about the surgery and concerned about awareness. A general anesthetic using an inhalational volatile agent for maintenance and muscle relaxant without nitrous oxide is planned. Which of the following is a risk factor for intraoperative awareness in this patient?

A. The use of muscle relaxants during the case
B. History of mitochondrial dysfunction
C. History of depression
D. The patient's age
E. Urgent abdominal procedure

31. Which of the following conditions will most likely result in a reading that overestimates the flow through a nitrous oxide variable-orifice flowmeter?

A. Hyperbaric conditions
B. Increased altitude
C. Replacing nitrous oxide with carbon dioxide
D. Decreased temperature
E. Accuracy remains unchanged despite changes in surrounding conditions.

32. At the conclusion of a left video-assisted thoracoscopic surgery (VATS) pleurodesis for chronic pleural effusion, the surgeon requests left lung reexpansion. The patient is placed on manual ventilation, the APL valve is closed to a pressure of 20 cm H_2O, and the reservoir bag is filled using the flush button. The lung is gradually reexpanded, increasing the APL pressure incrementally to 30 cm H_2O and maintaining positive pressure with the reservoir bag. The patient is then placed on the ventilator. Thereafter the end-tidal CO_2 waveform demonstrates a different shape: the expiration plateau phase is prolonged, and there is a downsloping of the curve without reaching zero at inspiration. What best accounts for this?

A. Increased CO_2 production from decreased lung dead space
B. The patient is having bronchospasm.
C. An incompetent inspiratory valve
D. An incompetent expiratory valve
E. Exhaustion of CO_2 absorbent

33. A 29-week-old premature neonate admitted to the neonatal intensive care unit develops bilious vomiting, abdominal distention with a palpable mass, and rectal bleeding. The patient is intubated, resuscitated, and scheduled for an emergent exploratory laparotomy. On transport to the operating room a Mapleson F breathing circuit is used by the anesthesiologist. What advantage do Mapleson systems have over a circle system?

A. Decreased fresh gas flow requirement
B. Preservation of airway humidity
C. Decreased work of breathing
D. Efficient delivery of anesthetic vapors
E. Increased dead space

34. To transport an intubated newborn, the anesthesiologist chooses a Bain circuit instead of a Mapleson D. What is the main advantage of the Bain circuit over the Mapleson D?

A. Less dead space
B. Decreased work of breathing
C. Requires less fresh gas flow for ventilation
D. Decreased circuit resistance
E. Conserves moisture better

35. You are conducting a standard general anesthetic with inhalational agents on a Navy ship when suddenly the oxygen main pipe fails. At what point are you most likely to first observe a decrease in nitrous oxide flow?

A. When the oxygen tank is completely empty
B. When the oxygen pressure falls below 30 psi
C. Immediately when the oxygen pipeline pressure falls below 50 psi
D. When the oxygen supply failure alarm is activated
E. As the oxygen pressure delivery to the nitrous flow meter decreases

36. A 69-year-old woman develops mild hoarseness in the postanesthesia care unit after a left carotid endarterectomy. Her oxygen saturation on room air is 95%. She is noted to have mildly increased work of breathing. An airway examination reveals mild left vocal cord paralysis. How will administration of a 70% helium/30% oxygen gas mixture increase gas flow over a 70% nitrous oxide/30% oxygen gas mixture at a constant flow?

A. The helium/O_2 mixture has a significantly lower density than the N_2O/O_2 mixture.
B. The helium/O_2 mixture has a significantly lower viscosity than the N_2O/O_2 mixture.

C. The helium/O_2 mixture has a significantly greater viscosity than the N_2O/O_2 mixture.
D. The helium/O_2 mixture will decrease the diameter of the airway.
E. The helium/O_2 mixture has a very low diffusion capacity.

37. While in the surgical intensive care unit, a patient who is postoperative day 1 after a tracheal resection and reconstruction begins to develop respiratory distress, with an oxygen saturation of 90%. He is placed on an oxygen facemask at 15 L/min, but his saturation improves only slightly. Which of the following devices is likely to increase his oxygen saturation the most?

A. Simple facemask
B. Nonrebreathing face mask
C. Face tent
D. Partial rebreathing mask
E. Venturi mask

38. During emergence from a mediastinoscopy, the patient, a 60-year-old man with severe chronic obstructive pulmonary disease, is placed on pressure support with an FiO_2 of 1.0 at a flow rate of 12 L/min. He is fully reversed from neuromuscular blockade and breathing at 8 breaths per minute. His end-tidal sevoflurane concentration is 1%. To speed up emergence, the oxygen flush valve is activated and the peak pressures increase acutely. What best accounts for this?

A. Excess oxygen pressure was transmitted during the inspiratory cycle.
B. Excess oxygen pressure was transmitted during the expiratory cycle.
C. The patient has increased airway resistance due to bronchoconstriction.
D. There is a malfunction of the pressure-relief valve.
E. There is a malfunction of the pipeline pressure regulator.

39. You are seeing a 61-year-old man in the preoperative clinic with a history of hypertension and aortic arch aneurysm who will undergo an aortic root replacement. He also has polycythemia vera, with a hematocrit of 65%. If this patient were to receive a nitroprusside infusion, what impact would you expect on blood pressure when compared with a patient with a normal hematocrit?

A. There will be no effect on blood pressure.
B. The blood pressure decrease would be blunted as compared to a normal patient.
C. The blood pressure would be dramatically decreased as compared to a normal patient.
D. The blood pressure would be slightly increased as compared to a normal patient.
E. The blood pressure would be dramatically increased as compared to a normal patient.

40. You are a volunteer performing anesthesia in a small town in Vietnam. The equipment in the hospital, although dated, is fully functional. Upon turning on the anesthesia machine, you immediately hear an alarm. How should you proceed next?

A. Replace the vaporizer.
B. Call engineering to check the oxygen pipeline supply.
C. Replace the oxygen tank.
D. Continue the machine checkout.
E. Unplug the anesthesia machine.

41. While in the recovery room an ASA class 3 morbidly obese patient status post gastric bypass surgery is desaturating to 90% and is placed on a continuous positive airway pressure (CPAP) machine at a pressure of 10 cm H_2O. What will be the resultant physiologic effect?

A. Pulmonary shunting will increase.
B. Functional residual capacity will increase.
C. Cardiac output will decrease.
D. Venous return will increase.
E. It will increase work of breathing.

42. The pressure gauge of a nitrous oxide E cylinder reads 700 psi. At this reading the nitrous oxide volume is approximately

A. 10%
B. 25%
C. 35%
D. 50%
E. 75%

43. A healthy 16-year-old boy was an unrestrained passenger in a motor vehicle accident. He is undergoing an emergent exploratory laparotomy for perforated bowel and ruptured renal capsule. Other injuries include a 15% pneumothorax and a tibial plateau fracture. If 70% nitrous oxide were to be administered as part of the patient's general anesthetic, in which compartment would there be the most dramatic volume expansion?

A. Intestinal loops
B. Pleural cavity
C. Endotracheal tube cuff
D. Middle ear cavity
E. Renal capsule

44. A 37-year-old Jehovah's Witness has suffered a ruptured spleen along with a right renal capsule rupture

in a motor vehicle crash. He undergoes a splenectomy and kidney repair. In the surgical intensive care unit he remains intubated with the following vital signs: BP 70/40 mm Hg, SpO_2 100% on 25 mcg/min of norepinephrine, hemoglobin 5.0, and mixed venous oxygen saturation 50% with a lactic acid level of 4. Blood transfusion is refused and hyperbaric oxygen therapy is planned. How much would his dissolved oxygen content increase if he is treated with 3 atmospheres?

A. 5 g/dL
B. 4 g/dL
C. 3 g/dL
D. 6 g/dL
E. 10 g/dL

45. A 65-year-old man with a history of ischemic cardiomyopathy with an ejection fraction of 35% and type 2 diabetes mellitus type is undergoing hyperbaric oxygen therapy for a chronic nonhealing ulcer at 3 atmospheres. He is most likely at risk for developing which of the following?

A. Hyperpyrexia
B. Heart failure
C. Blindness
D. Deafness
E. Hypothermia

46. Which of the following statements about oxygen analyzers is true?

A. Paramagnetic oxygen analyzers require more frequent calibration than others.
B. Galvanic oxygen analyzers last longer than paramagnetic analyzers.
C. Polarographic analyzers can differentiate inspired versus expired oxygen concentrations.
D. Paramagnetic oxygen analyzers have the fastest response time.
E. Galvanic oxygen analyzers do not require replacement of electrodes.

47. An otherwise healthy 56-year-old man is undergoing an exploratory laparotomy for a small bowel obstruction. Prior to induction, the patient is preoxygenated by facemask using a semiclosed anesthesia circuit and machine flowing 10 L/min of oxygen. After 2 minutes you notice on the monitor that the FiO_2 and FeO_2 are both 21%. What is the most likely reason?

A. Inadequate seal with the facemask
B. An air cylinder is connected to the oxygen inlet.
C. Failure of the oxygen analyzer
D. Failure of the oxygen supply
E. There is a leak in the ventilator bellows.

48. A 34-year-old woman is undergoing a total thyroidectomy. Induction of anesthesia with endotracheal intubation proceeds without any problems. The patient is maintained on 1.2% sevoflurane, 2 L/min of nitrous oxide, and 1 L/min of oxygen. The patient's saturation slowly decreases to 95% after induction, and a glance at the monitor shows that the FiO_2 is 17%. What is the most likely explanation for this finding?

A. Oxygen supply failure
B. Flowmeter leak
C. Oxygen cylinder leak
D. Low gas flow
E. Failure of the flow-proportioning system

49. A 60-year-old man is undergoing a total hip replacement under general anesthesia. Induction of anesthesia and endotracheal intubation proceed without any complications. One hour into the case you notice that $FiCO_2$ is 10 mm Hg and $FeCO_2$ begins to rise to 60 mm Hg. What is the best explanation for this finding?

A. Incompetent expiratory valve
B. Acrylic cement embolus
C. A cracked CO_2 absorbent canister
D. Inadequate tidal volumes
E. Low gas flow

50. Which of the following is NOT a necessary component of the preanesthesia checkout procedures?

A. Ensuring adequate suction
B. Confirming that AC power is available
C. Verifying that the air cylinder is mounted and full
D. Test scavenging system function
E. Verify that the piped gas pressures are at least 50 psi

51. A 27-year-old man undergoing shoulder arthroscopy was found to have third-degree burns from the electrocautery grounding pad. Which of the following would NOT decrease the likelihood of this adverse event?

A. Using shorter bursts of electrocautery
B. Using a larger grounding pad
C. Improving contact of the grounding pad
D. Using a conductive fluid during arthroscopy
E. Ensuring that the grounding pad is not placed in proximity to indwelling hardware

52. Which of the following temperature measurement sites is LEAST likely to reflect brain temperature during hypothermic circulatory arrest?

A. Rectal
B. Nasopharyngeal

C. Pulmonary artery
D. Esophageal
E. All of the above will accurately reflect brain temperature.

53. What is the approximate FiO_2 delivered by nasal cannula with 100% oxygen flowing at 6 L/min?

A. 30%
B. 45%
C. 60%
D. 75%
E. 90%

54. A 54-year-old man with a history of diabetes and end-stage renal disease is undergoing a total hip replacement. At the end of the case he is placed on pressure support ventilation at 10 cm H_2O/5 cm H_20 and is noted to have a respiratory rate of 40. He is then switched to spontaneous ventilation and is noted to be apneic. What is the most likely explanation?

A. Autotriggering of pressure support ventilation
B. Cheyne-Stokes respiration
C. Opioid overdose
D. Hypocapnia
E. Hyperglycemia

55. A 43-year-old woman is undergoing a laparoscopic cholecystectomy. She is receiving 1.2% sevoflurane with 1 L/min N_2O and 0.2 L/min of oxygen. You notice that her saturation is 89%, and you look at the oxygen analyzer that is alarming with an FiO_2 of 17%. What is the most likely cause of her desaturation?

A. Low gas flows
B. Decreased functional residual capacity
C. Failure of the flow-proportioning system
D. Oxygen supply failure
E. Hypoventilation

56. A 34-year-old woman is about to undergo a knee arthroscopy under general anesthesia. After induction you notice that fresh gas flows of 10 L/min are required to inflate the reservoir bag to manually ventilate the patient. Which statement about this anesthetic machine's gas scavenging system is most likely true?

A. Negative pressure relief valve has failed.
B. Positive pressure relief valve has failed.
C. The scavenging system is an open system.
D. The scavenging system is passive.
E. There is no scavenging system.

57. Which of the following statements regarding intermittent mechanical ventilation (IMV) is correct?

A. IMV does not help prevent lung overinflation during periods of tachypnea.
B. Continuous-flow IMV reduces the work of breathing compared to demand-flow IMV.
C. Demand-flow IMV reduces the work of breathing compared to continuous-flow IMV.
D. IMV does not have an effect on cardiac output in patients with normal intravascular volume.
E. IMV increases cardiac output in patients with left ventricular dysfunction.

58. An E cylinder filled with oxygen is reading 1,000 psi. Approximately how long would you be able to run this cylinder at 10 L/min?

A. 10 minutes
B. 20 minutes
C. 30 minutes
D. 50 minutes
E. 100 minutes

59. Which of the following would increase the percent concentration of anesthetic delivered by a desflurane vaporizer?

A. Decreasing the temperature
B. Increasing the temperature
C. Decreasing the vapor pressure
D. Decreasing the altitude
E. Increasing the altitude

60. Which of the following toxic compounds is produced by desflurane flowing through a desiccated soda lime CO_2 absorber?

A. Cyanide
B. Carbon monoxide
C. Compound A
D. Dichloroacetylene
E. None of the above

61. A 56-year-old man with acute respiratory distress syndrome is found cyanotic from being disconnected from the ventilator. What is the most likely reason that this disconnection failed to be detected?

A. Partial occlusion of the ventilator circuit
B. Pressure alarm set too high
C. Decreased moisture in circuit
D. Complete occlusion of the ventilator circuit
E. Ventilator alarm silenced

62. A 57-year-old woman is undergoing a laparoscopic gastric bypass under general anesthesia. During preoxygenation with 10 L/min through the oxygen flowmeter you notice that the patient begins to desaturate. You notice that the FiO_2 is 8% while the $FiNO_2$ is 90%. Which of the following is LEAST likely to improve saturations?

A. Take the mask off and allow the patient to breathe room air.
B. Switch to the auxiliary oxygen outlet on the anesthesia machine.
C. Use the backup or separate oxygen cylinder.
D. Increase the flow of air through the anesthesia machine.
E. Disconnect the oxygen pipeline from the anesthesia machine.

63. Which of the following helps improve the electrical safety of the operating room?

A. Designation as a dry environment
B. Use of a grounded electrical supply
C. Use of an isolated power system
D. Directly grounding the patient
E. All of the above

64. A 2-year-old girl was anesthetized using 8% desflurane and oxygen for an inguinal hernia repair. Her oxygen saturation, which was initially 100%, began to slowly decrease throughout the case to a nadir of 88%. Co-oximetry showed a carboxyhemoglobin concentration of 60%. All of the following would make this event less likely to occur EXCEPT

A. Changing the CO_2 absorber
B. Using sevoflurane instead of desflurane
C. Flushing the circuit with oxygen
D. Using soda lime instead of Baralyme
E. Using low gas flows

CHAPTER 14 ANSWERS

1. ANSWER: D

Dead space is defined as the portion of a tidal volume that does not undergo gas exchange. As dead space increases, in order to maintain a specified alveolar ventilation, the delivered tidal volume must be increased.

A circle system is composed of several components, which together allow lower gas flows, less waste of anesthetic agents, reduced loss of patient heat and humidity, and reduced environmental pollution as compared to Mapleson circuits. These components include a CO_2 absorber, breathing bag reservoir with adjustable pressure-limiting valve, inspiratory and expiratory unidirectional valves, corrugated tubing, and a Y-piece that can attach to a mask or endotracheal tube.

In a circle system, the presence of unidirectional valves limits the contribution of the ventilatory apparatus to the anatomic dead space. Only the area distal to the Y-piece that joins the inspiratory flow to the expiratory flow at the mask or endotracheal tube is significant. This small volume adds to the patient's anatomic dead space, which includes the nose, mouth, oropharynx, and airways from the trachea through the terminal bronchioles.

The CO_2 absorber and breathing bag are proximal to the unidirectional valves in a circle system, and are therefore not exposed to mixing of inspired and expired gases. The unidirectional valves also prevent the mixing of inspired and expired gas proximal to the Y-piece, thereby eliminating the effect of the length of tubing, as exists in the Mapleson circuits. The only relevant addition to the patient's anatomic dead space is the distance from the Y-piece to the patient's airway.

KEY FACTS: DEAD SPACE

- **Dead space** is defined as the portion of a tidal volume that does not undergo gas exchange.
- In a circle system, the presence of unidirectional valves limits the dead space. Only the area distal to the Y-piece adds to the anatomic dead space.

ADDITIONAL READINGS

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Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:31–40.

2. ANSWER: C

Although they are not used as frequently as in the past, ***Mapleson circuits*** are simple, inexpensive, and lightweight (Fig. 14.1). Because there is no CO_2 absorption, and no unidirectional valves are present, rebreathing does occur to some extent, although this can be limited by increasing fresh gas flow. The efficiency of the systems is related to the amount of fresh gas flow required.

Answer A refers to the **Mapleson F** or Jackson-Rees modification of the Mapleson E or Ayre's T-piece. It is essentially a Mapleson E with a breathing bag with APL attached to the proximal end to allow controlled ventilation and gas scavenging. This type of circuit requires fresh gas flows of at least two to three times minute ventilation for spontaneous ventilation, and at least two times minute ventilation for controlled ventilation.

Answer B refers to the **Mapleson B** circuit. This type of circuit requires fresh gas flows of at least two times minute ventilation for spontaneous ventilation, and at least two to two-and-a-half times minute ventilation for controlled ventilation.

Answer C refers to the **Mapleson D** circuit. This circuit is the most efficient Mapleson circuit for controlled ventilation, and is reasonable for spontaneous ventilation. This type of circuit requires fresh gas flows of at least two to three times minute ventilation for spontaneous ventilation, but only one to two times minute ventilation for controlled ventilation.

The **Bain circuit** is a modification of the Mapleson D that allows the fresh gas to run through tubing within the breathing tube, allowing warming of fresh gas as it passes by expired gas. The fresh gas is still added to the circuit in the same place as with the Mapleson D, thereby allowing the Bain circuit to retain the positive aspects of the Mapleson D. Although the modification adds to the size and weight of the apparatus, it results in better retention of heat and humidity.

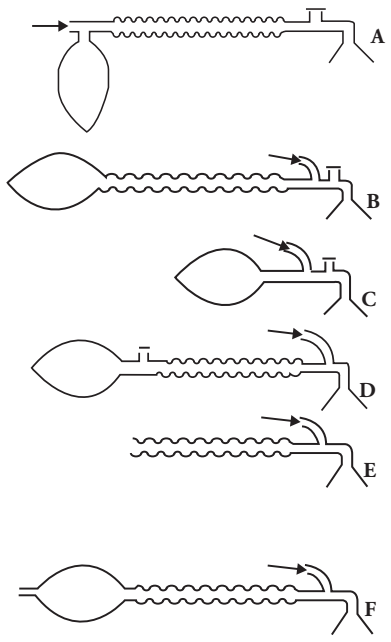

Figure 14.1 The five semiclosed anesthetic systems listed by Mapleson (1954) together with the Jackson-Rees modification of Ayre's T-piece.

SOURCE: Willis BA, Pender JW, Mapleson WW. Rebreathing in a T-piece: volunteer and theoretical studies of the Jackson-Rees modification of Ayre's T-piece during spontaneous respiration. *Br J Anaesth.* 1975;47:1239.

Answer D refers to the **Mapleson A** circuit. This type of circuit requires the least fresh gas flow for spontaneous ventilation, needing only an amount equal to minute ventilation (~80 mL/kg/min). It is the least favorable choice of the Mapleson circuits for controlled ventilation, requiring very high and unpredictable gas flows.

KEY FACTS: MAPLESON CIRCUITS

- The Mapleson D is the most efficient Mapleson circuit for controlled ventilation, and is reasonable for spontaneous ventilation, requiring fresh gas flows of at least two to three times minute ventilation for spontaneous ventilation, but only one to two times minute ventilation for controlled ventilation.
- The Bain circuit is a modification of the Mapleson D that allows the fresh gas to run through tubing within the breathing tube, allowing warming of fresh gas as it passes by expired gas.
- The Mapleson A is the most efficient for spontaneous ventilation, requiring a fresh gas flow of only an amount equal to minute ventilation (~80 mL/kg/min).
- Efficiency for spontaneous ventilation: Mapleson A > D > C > B
- Efficiency for controlled ventilation: Mapleson D > B > C > A

ADDITIONAL READINGS

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3. ANSWER: C

Postoperative hypoxia is common and may be due to a variety of causes.

Excessive intraoperative opioid administration may lead to respiratory depression in the postoperative period. The resulting hypoventilation may be significant enough to result in a decrease in oxygen saturation.

Airway obstruction in the immediate postoperative period may lead to inspiratory effort against a closed glottis or otherwise obstructed upper airway. Especially in the younger, stronger patient, this can lead to development of **negative-pressure pulmonary edema**. Hypoxia can ensue from impaired diffusion of oxygen at the alveoli from this or any other cause of pulmonary edema.

Temperature is one of the factors that can shift the oxygen–hemoglobin dissociation curve. As the curve shifts to the right, hemoglobin loses affinity for oxygen molecules, thereby requiring a higher oxygen content to maintain a given oxygen saturation. Factors that can shift the oxygen–hemoglobin dissociation curve to the right include hyperthermia, high levels of 2,3-DPG, acidosis, and hypercarbia. Factors that shift the curve to the left include hypothermia, low levels of 2,3-DPG, alkalosis, hypocarbia, and high levels of carbon monoxide.

Although it would need to be severe to have a measurable effect in most patients, a decrease in cardiac output can lead to hypoxia. **Hypotension** as a result of low cardiac output can lead to increased shunting, and therefore a decreased mixed venous and arterial oxygen content.

Pain after thoracic surgery could lead to multiple causes of hypoxia, including hypoventilation from splinting, and increased atelectasis resulting in a greater shunt fraction. As more blood flows through nonventilated atelectatic portions of the lung, it reduces the total arterial oxygen content, resulting in hypoxia.

KEY FACTS: CAUSES OF EARLY POSTOPERATIVE HYPOXIA

- Excess opioid administration leading to respiratory depression and hypoventilation
- Bronchospasm, or severe exacerbation of chronic obstructive pulmonary disease (COPD)
- Airway obstruction causing hypoventilation
- Negative-pressure pulmonary edema due to airway obstruction
- Fluid overload, or other causes of pulmonary edema
- Aspiration, or other pneumonia
- Pulmonary embolus, from thrombus, gas, or fat
- Acute respiratory distress syndrome (ARDS)
- Pneumothorax or hemothorax
- Shift in oxygen–hemoglobin dissociation curve
- Atelectasis from surgical or other causes
- Severe anemia
- Severe hypotension or decreased cardiac output, shock
- Cardiac arrhythmias

This list is not exhaustive but provides the majority of causes of early postoperative hypoxia.

ADDITIONAL READINGS

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Sellery GR. A review of the causes of postoperative hypoxia. *Can J Anesthesiol*. 1968;*15*:142–151.

4. ANSWER: D

Electrical shock can occur in any situation that allows a person to come in contact with an electrical source or device. For shock to occur, there must be a circuit with a driving voltage that becomes closed by contact with the person. By Ohm's law (Voltage (V) = Current (I) × Resistance (R)), the current that flows through a person when the circuit, or loop, is closed is related to the resistance offered by the person's skin or other point of contact, and the driving voltage. There are two classifications of electrical shock relevant to the operating room environment: macroshock and microshock.

Macroshock generally refers to current applied outside of the body. A current of 1 milliamp (mA) is perceptible, with 10 mA leading a person to experience tingling or muscle contraction. 15 to 80 mA can cause a painful shock or significant muscle contraction. 100 mA or more can cause ventricular fibrillation.

Microshock refers to current applied to the inside of the body, and is a concern for equipment that is used within the body that comes in contact with the heart, such as central venous catheters and pacemakers. Microshock refers to currents less than 1 mA. The recommended maximum leakage for equipment that comes in contact with the heart is 10 microamps (μA). Currents of 100 μA can cause ventricular fibrillation when directly applied to the heart.

Higher frequencies are protective against tissue penetration; therefore, the higher the frequency, the less likely to cause cardiac excitation.

The area of skin exposed to current is *inversely* related to the amount of damage the current will inflict, as the energy is spread over a greater area and damage at any single point will be less. Therefore, the larger the area of skin exposed, the less likelihood of damage.

The duration of contact with electrical current is proportional to the damage that can be done. The longer the exposure, the greater the damage.

The type of current, whether alternating (AC) or direct (DC), can also affect the degree of damage, with DC requiring higher amounts of current to create the same degree of shock

KEY FACTS: ELECTRICAL SHOCK

- For shock to occur, the person must "close the loop" of an electrical circuit.
- Macroshock refers to currents above 1 mA, and is relevant for current applied outside the body.
- Microshock refers to currents below 1 mA, and is relevant for current applied within the body.
- Duration of contact, frequency, amount of area exposed, and type of current can all affect the degree of damage caused by the shock.

ADDITIONAL READINGS

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Ehrenwerth J, Eisenkraft JB. *Anesthesia Equipment: Principles and Applications*. New York, NY: Mosby; 1993:460–463.

5. ANSWER: B

The principle that describes the laminar flow of a non-compressible homogeneous and viscous fluid through a tube is called ***Poiseuille's law***. This law expresses the relationship between the rate of flow of a liquid in a tube and the pressure gradient in the tube, the radius of the tube, the length of the tube, and the viscosity of the liquid.

$$Q = \frac{\pi r^4 \Delta P}{8 \eta L}$$

Q is flow rate, ΔP is the pressure difference between the two ends of the tube, η is fluid viscosity, and L is the length of the tube.

From the above equation, we see that flow (Q) is inversely proportional to viscosity (η), and the length of the tube (L), and directly proportional to the radius to the fourth power, and the pressure gradient (P) in the tube.

KEY FACTS: POISEUILLE'S LAW

- Flow is directly proportional to the radius to the fourth power, making the radius the most important factor in determining the rate of flow.
- Flow is inversely proportional to viscosity.
- Flow is inversely proportional to the length of the tube.
- Flow is directly proportional to the pressure gradient between the two ends of the tube.

ADDITIONAL READINGS

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6. ANSWER: D

ASA guidelines for basic anesthetic monitoring state that correct position of an endotracheal tube or supraglottic

airway device must be verified by monitoring CO_2 in the expired gas. Furthermore, continuous monitoring of CO_2 must be performed until the device is removed or the patient is taken to a postoperative care location.

Capnography is the recording of CO_2 concentration over time, most commonly done with monitoring of end-tidal (et) CO_2 in expired gas. CO_2 is released from tissues as a metabolic product, carried by blood to the alveoli in the lungs, and excreted via respiration. Changes in any of these components of CO_2 production or transport will lead to changes in the $etCO_2$ concentration.

Hypothyroidism is a state of decreased metabolic activity and therefore decreased CO_2 production. Although it may be unlikely, if the hypothyroidism is severe enough, it may lead to a decreased $etCO_2$ during anesthesia.

Any type of **pulmonary embolus**, whether thrombus, fat, air, or amniotic fluid, will lead to increased dead space in the lungs, and reduced surface area for carbon dioxide transport from the blood to the alveoli, therefore leading to decreased $etCO_2$.

Hypoperfusion, as would occur with severe hypotension, limits the amount of CO_2 than can be picked up from tissues and brought to the lungs, leading to decreased $etCO_2$.

Hyperthermia is a sign of a hypermetabolic state, and as such would lead to increased CO_2 production. This would lead to an increased $etCO_2$ value, not a decreased value.

Hyperventilation increases the CO_2 gradient in the alveoli, leading to greater transport of CO_2 from the blood to the expired gas, and would over a short period of time lead to a decreased $etCO_2$.

KEY FACTS: MEASURING END-TIDAL CO_2

CAUSES OF DECREASED ETCO2	CAUSES OF INCREASED ETCO2
Hypothermia	Hyperthermia (fever, malignant hyperthermia)
Hypothyroidism	Hyperthyroidism, thyroid storm
Pulmonary embolism	Absorption during laparoscopy
Hypoperfusion	Pain, anxiety
Increased patient dead space	Shivering
Hyperventilation	Hypoventilation
Muscle relaxation	Convulsions
Leak in CO_2 detector tubing	Administration of sodium bicarbonate
	Parenteral hyperalimentation (TPN)
	Release of tourniquet or arterial clamp

ADDITIONAL READINGS

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Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. New York, NY: Churchill Livingstone; 2007:58–59.

7. ANSWER: C

The ***low-pressure system*** of an anesthesia machine is the portion of the system that is generally only slightly above atmospheric pressure. This pressure may vary depending on the components of the low-pressure system, including flow control valves, check valves, and back pressure from the breathing system. Other components of the low-pressure system include flowmeters, vaporizers, pressure relief devices, unidirectional valves, the common gas outlet, and hypoxia prevention devices.

Leaks in the low-pressure system can lead to lower-than-intended concentrations of volatile agent being delivered to the patient, and therefore may lead to awareness. In addition, leaks can lead to delivery of a hypoxic mixture by allowing leakage of oxygen in the presence of high concentrations of nitrous oxide.

The CO_2 absorber portion of the breathing system is one of the most common leak sites. Leaks may be due to broken or defective seals or gaskets, absorbent granules preventing adequate seals, or incomplete tightening. Small cracks may also contribute to leaks.

The negative-pressure test is performed using a suction bulb attached to the common gas outlet. If there is a leak in the system, the bulb will inflate. This test may be performed automatically by newer anesthesia machines, but it remains important for anesthesia providers to understand how the test works. Flowmeters must be turned OFF before the test, as the goal is to create a negative pressure in the low-pressure system to assess for leaks. If the flowmeters are on, there will be a positive pressure in the system, thereby negating the validity of the test.

Any leak in the vaporizer can lead to a failure of the leak test, including a loose filler cap. Care must be taken to be sure that vaporizers are mounted properly and that filler and drain caps are tightly secured prior to beginning a leak test.

KEY FACTS: LEAKS IN THE LOW-PRESSURE SYSTEM

- Leaks in the low-pressure system can cause patient awareness.
- The CO_2 absorber is one of the most common sites of leaks in the low-pressure system.
- The flowmeters should be turned off when performing a negative-pressure test.

- The low-pressure portion of the system develops leaks more frequently than other parts.
- Any leak in the vaporizer can lead to a failure of the leak test, including improper mounting, loose filler and drain caps, or other vaporizer leaks.

ADDITIONAL READING

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8. ANSWER: E

Overfilling of vaporizers is more difficult in modern vaporizers because the use of agent-specific filling devices prevents overfilling by coupling air intake into the agent bottle with filling of the vaporizer chamber. This safety mechanism can be overcome, however, if the bottle adapter is slightly unscrewed and the vaporizer is turned on during filling.

Incorrect agent filling is also limited by the agent-specific filling devices commonly used today. However, if the wrong agent is placed in a bottle prior to filling—for example, isoflurane in a sevoflurane bottle—then the wrong liquid can still be introduced to a vaporizer. If an agent with a higher vapor pressure is placed in a vaporizer meant for an agent with a lower vapor pressure—for example, isoflurane liquid placed in a sevoflurane vaporizer—anesthetic overdose can occur.

If a vaporizer full of liquid is tipped, as might happen during transport, the initial concentration of volatile agent delivered when the vaporizer is turned on may be significantly higher than the dialed concentration. Some newer vaporizers (such as the Drager Vapor 2000) now have a "transport" lock that helps to prevent this from occurring.

Vaporizer interlock systems are in place to prevent two vaporizers from being turned on at the same time. If this system is not working properly, two vaporizers may be turned on at the same time, resulting in a potential anesthetic agent overdose.

Other potential causes of anesthetic agent overdose include lack of recognition of a vaporizer inadvertently left on from a prior case and improper vaporizer installation.

KEY FACTS: CAUSES OF ANESTHETIC OVERDOSE

- Overfilling of vaporizers
- Incorrect agent in the vaporizer
- Tipping of a filled vaporizer
- Failure of the vaporizer interlock system
- Inadvertently turned-on vaporizer
- Improper vaporizer installation

ADDITIONAL READINGS

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:418.

9. ANSWER: A

The problem here appears to be inadequate anesthesia, which could be due to a variety of factors. Although some of the factors that may lead to this are related to the patient (e.g., increased anesthetic requirements for chronic alcoholics and users of certain drugs, whether legal or illicit), many of the factors leading to inadequate anesthesia are equipment-related.

Tipping of a filled vaporizer would generally result in a higher, not lower, concentration of volatile agent being delivered to a patient than intended, and may lead to anesthetic overdose.

The nitrous oxide pipeline is subject to a number of potential issues, including leaks, malfunctioning regulators, and depletion of central supply. If nitrous oxide is being delivered by cylinder rather than pipeline, and the cylinder inadvertently runs out during an anesthetic, this could also lead to inadequate anesthesia. There may also be leaks within the anesthesia machine (e.g., the flowmeter), leading to decreased nitrous oxide delivery.

Because it is Monday morning, it is possible that the anesthesia machine being used had high fresh gas flow running through it all weekend, leading to a desiccated CO_2 absorber. Sevoflurane can react with some desiccated CO_2 absorbents so rapidly and extensively that there may be inadequate delivery of agent to the patient. If a significant discrepancy exists between the dialed concentration and the delivered concentration as monitored in the breathing system, one should consider the possibility of sevoflurane being broken down rapidly by the absorbent.

Entrainment of air into the breathing system or ventilator through any sort of leak can result in dilution of anesthetic concentration, thereby leading to inadequate anesthesia.

As discussed before, the placement of an incorrect anesthetic agent in a vaporizer can lead to differences between the intended and actual concentration delivered. If the vapor pressure of the liquid in the vaporizer is lower than the vapor pressure of the intended liquid, as would occur if sevoflurane was placed in an isoflurane vaporizer, there would be a lower concentration delivered to the patient than dialed.

Halothane (244 mm Hg at 20 degrees C) and isoflurane (239 mm Hg at 20 degrees C) have similar vapor pressures and likely would not vary much in the delivered concentration if erroneously switched. However, because the MAC of halothane (0.74) is lower than the MAC of isoflurane (1.15), it is possible that the placement of isoflurane in a halothane vaporizer would result in a lower-than-necessary concentration of isoflurane being delivered.

For example, if the anesthesiologist thought halothane was being used, he or she might turn the dial to 0.75%, expecting approximately 1 MAC. If isoflurane was instead in the vaporizer, 0.75% would still be delivered, but it would be 0.75% isoflurane, resulting in only ~0.65 MAC.

KEY FACTS: CAUSES OF INADEQUATE ANESTHESIA

- Empty vaporizer or gas cylinder
- Pipeline nitrous oxide problems
- Leaks in the ventilator, breathing circuit, anesthesia machine, etc.
- Misfilling of vaporizers
- Use of sevoflurane with desiccated CO_2 absorbent
- Incorrect vaporizer setting
- Malfunctioning vaporizer
- Repeated use of the oxygen flush valve

ADDITIONAL READINGS

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10. ANSWER: C

The line isolation monitor (LIM) alarm sounds when the normally ungrounded operating room power system becomes grounded, such that the patient or operating room personnel are at risk of shock should a second fault or short circuit occur.

The electricity in every operating room is isolated from the main power source by an isolation transformer that has a primary circuit and a secondary circuit. The primary circuit is grounded, but the secondary circuit is not. The LIM monitors both isolated power lines of this secondary circuit, and the alarm sounds when the impedance in the system falls below 25,000 ohms, or when the maximum current that a short circuit could cause exceeds 2 to 5 mA.

All electrical devices that have a power cord, such as electrosurgical cautery units, headlamps, fluid and body warmers, medication pumps, and all other devices in the operating room that need to be plugged in, have a small amount of continuous current leak to ground. This partial grounding increases the risk of shock if a short circuit or fault were to occur.

LIMs are in place to ensure that the ungrounded power source in the operating room is maintained as ungrounded. They are purely monitors and do not interrupt the electrical current. They therefore cannot prevent shock from occurring, only warn against the possibility. The alarm sounds at the first fault, which is not yet a shock hazard. If there is a second fault, the patient or operating room personnel could be exposed to 2 to 5 mA of current, enough to cause one to pull away but not enough to cause significant damage. Given this range of detection, there is no protection against microshock from the LIM.

If a LIM alarm sounds before a surgical procedure has begun, the most appropriate thing to do is to postpone the surgery until the fault is identified and repaired, or until the procedure can be done in another operating room. If the procedure has already begun when the LIM alarm sounds, the offending device that caused the alarm should be found, if possible, by systematically unplugging electrical devices, beginning with the one most recently plugged in.

KEY FACTS: LINE ISOLATION MONITOR

- The line isolation monitor (LIM) alarm sounds when the normally ungrounded operating room power system becomes grounded, placing the patient and operating room personnel at risk of shock with a second fault.
- The LIM alarm sounds when impedance falls below 25,000 ohms, or when the maximum current that a short circuit could cause exceeds 2 to 5 mA.
- LIMs are in place to ensure that the ungrounded power source in the operating room is maintained as ungrounded.
- LIMs are purely monitors and do not interrupt the electrical current.
- Given its range of detection, there is no protection against microshock (<1 mA) from the LIM.
- If a LIM alarm sounds before a surgical procedure has begun, the most appropriate thing to do is to postpone the surgery until the fault is identified and repaired, or until the procedure can be done in another operating room.
- If a LIM alarm sounds after a procedure has begun, the offending device that caused the alarm should be found, if possible, by systematically unplugging electrical devices, beginning with the one most recently plugged in.

ADDITIONAL READINGS

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Litt L. Electrical Safety in the Operating Room. In Miller RD, et al., eds. *Miller's Anesthesia*. Philadelphia, PA: Churchill Livingstone; 2010:3041–3050.

11. ANSWER: D

Although its usefulness is evident, pulse oximetry is subject to certain limitations, as are all monitoring technologies.

The pulse oximeter works by comparing the absorption of two wavelengths of light as they pass through tissue. At the red wavelengths (650 to 750 nm), reduced hemoglobin (without oxygen) absorbs more light than oxyhemoglobin. The opposite is true of the infrared wavelengths (900 to 1,000 nm). The pulse oximeter emits light at both of these wavelengths and measures the absorbance of each. The ratio between the two is used with an empirical algorithm to relate to an arterial oxygen saturation.

Pulse oximetry has a variety of limitations, which include inadequate reading in a variety of clinical situations and patient populations. Failure appears to be more likely in ASA class 3 or greater patients, patients at the extremes of age, certain types of surgery (including orthopedic, vascular, and cardiac), and various physiologic factors such as hypotension, hypothermia, and chronic renal failure. Other limitations include poor function with poor perfusion, inaccuracy with different hemoglobin species (i.e., methemoglobin, carboxyhemoglobin, sulfhemoglobin), reduced accuracy at low saturations, optical interference, electrical interference, and motion artifacts.

In addition, the presence of black, brown, blue, or green nail polish may artificially reduce the reading of the pulse oximeter as these colors may absorb light in the same range as deoxygenated hemoglobin, with green being the worst offender. Red or purple nail polish does not have this effect. Also, synthetic nails or the presence of onychomycosis may interfere with pulse oximeter readings, causing a decreased reading.

In the presence of severe anemia, the oximeter may actually overestimate the oxygen saturation at low saturations, but it is likely to be accurate at normal or high saturations.

Raynaud's phenomenon may cause vasoconstriction in the digits where a probe might be placed, and can cause inaccurately low pulse oximetry readings.

KEY FACTS: SITUATIONS IN WHICH PULSE OXIMETRY MAY BE INACCURATE

- Poor perfusion at measurement site
- Low saturations
- Optical interference from external light
- Motion artifacts
- Potential electrical interference
- Presence of dysrhythmias
- Presence of certain dyes
- Presence of certain colors of nail polish
- Severe hypotension, hypothermia
- Raynaud's syndrome
- Different hemoglobin types (i.e., methemoglobin, carboxyhemoglobin, sulfhemoglobin)
- Strong venous pulsations
- Malpositioned pulse oximetry probe

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12. ANSWER: E

As with any monitoring technology, **Pulse Oximeters** are subject to a variety of limitations.

Pulse oximeters are subject to motion artifact, as occurs in a shivering patient. Motion artifact can lead to both inaccurately high (false-negative) readings and inaccurately low (false-positive or false alarm) readings.

Dyes such as methylene blue, indocyanine green, indigo carmine, nitrobenzene, or lymphazurin can cause falsely low pulse oximeter readings without a true decrease in arterial oxygen saturation. Fingerprinting dye and henna may also lead to falsely low pulse oximeter readings.

Methemoglobinemia can be congenital or acquired, and is an oxidation product of hemoglobin that impairs the unloading of oxygen to tissues. Drugs that cause methemoglobinemia include prilocaine, benzocaine, dapsone, and nitrobenzene, among others. In patients with methemoglobinemia, as compared to functional arterial oxygen saturation, many pulse oximeters give inaccurately low readings for actual saturations above 85% and inaccurately high readings for actual saturations below 85%. These inaccuracies improve with treatment of methemoglobinemia as the metHb fraction decreases.

Pulse oximeter readings are subject to inaccuracy as a result of improper probe positioning or attachment. Although there are reports of inaccurately high readings of oxygen saturations when the actual saturation is low and the probe is malpositioned, the readings can frequently be inaccurately low.

The patient in answer E is most likely suffering from carbon monoxide poisoning. This would lead to the presence of high amounts of carboxyhemoglobin, which absorbs the same spectrum of light as oxyhemoglobin. Because the absorption spectrum is so similar, most pulse oximeters read carboxyhemoglobin as oxyhemoglobin, therefore overestimating the actual oxygen saturation.

ADDITIONAL READINGS

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Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:140–141.

13. ANSWER: E

Barotrauma in the setting of anesthesia and critical care refers to damage caused to tissues as a result of excessively high positive airway pressures. There are a number of causes of barotrauma, which can be categorized as due to excessive inflow, or due to reduced outflow. An incompetent ventilator relief valve leads to hypoventilation because anesthetic gas is delivered into the scavenging system instead of the inspiratory limb.

EXCESSIVE INFLOW

OXYGEN FLUSH VALVE

Malfunction or accidental use of the oxygen flush valve may result in delivery of 35 to 75 L/min of oxygen, depending on the machine being used. Although mechanical malfunction is possible, leaving the valve in the "On" position, it is also possible with some mechanical ventilators to cause barotrauma by using the flush valve during the inspiration phase. This can occur because of the addition of a large volume of oxygen from the flush valve being added to the dialed tidal volume, potentially resulting in excessive airway pressure.

MALFUNCTION OF VENTILATOR CONTROL VALVE

This could lead to unchecked pressure being delivered through the ventilator from the wall gas supply, causing barotrauma.

MISCONNECTION OF OXYGEN TUBING

If tubing meant for an open oxygen mask is connected to an airway device without a mechanism to allow venting, barotrauma can occur. For example, this could occur if tubing directly from the wall or an accessory oxygen port were connected to a cuffed endotracheal tube without venting.

DECREASED OUTFLOW

OBSTRUCTION OF THE EXPIRATORY LIMB

The expiratory limb can be obstructed by external compression (such as the anesthesia machine or other equipment), or by internal obstruction by foreign bodies or water. It may also be obstructed by a manufacturing defect, a misapplied or malfunctioning positive end-expiratory pressure (PEEP) valve, or use of a defective T-piece assembly.

OBSTRUCTION AT THE ADJUSTABLE PRESSURE-LIMITING (APL) VALVE

Malfunction or blockage of the APL valve can result in sustained high positive pressure to the airways, resulting in barotrauma. Forgetting to open the valve when switching from mechanical to spontaneous ventilation can do the same.

OBSTRUCTION OF THE SCAVENGING SYSTEM

Malfunction or incorrect installation of valves in the scavenging system can lead to excessive pressure buildup in the breathing system, resulting in barotrauma.

POSITIVE END-EXPIRATORY PRESSURE

Either unintentional use or malfunction of an integrated PEEP valve or misuse or malfunction of an external PEEP valve can lead to barotrauma.

JET VENTILATION

Jet ventilation, as may be used during laryngeal surgery through special small-diameter endotracheal tubes, or as might be used during emergency cricothyroidotomy, is achieved through delivery of very high pressure for short bursts of time. If there is inadequate time for expiration, or an inadequate pathway for gas to be exhaled, barotrauma can occur.

KEY FACTS: CAUSES OF BAROTRAUMA

- Misuse or malfunction of the oxygen flush valve
- Malfunction of ventilator control valve
- Misconnection of oxygen tubing
- Obstruction of the expiratory limb of the breathing circuit
- Obstruction at the APL valve
- Obstruction of the scavenging system
- Misuse or malfunction of PEEP valves

ADDITIONAL READINGS

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:414–415.
Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:1030.

14. ANSWER: C

Gas flow in breathing systems and the lungs is a combination of laminar flow and turbulent flow. Laminar flow is described by the **Hagen-Poiseuille law (Poiseuille's law)**, and can be described as smooth and orderly with particles moving in parallel with the walls of the tube. Flow rate is faster at the center of the tube and slower at the walls of the tube due to friction.

Turbulent flow is not smooth or orderly, with particles moving in multiple directions. Flow rate is constant across the diameter of the tube, unlike laminar flow. Although the same factors are responsible for determining the rate of laminar gas flow, including the pressure gradient across the tube, the radius of the tube, the length of the tube, and the viscosity of the gas, with turbulent flow *the density of the gas becomes more important than the viscosity*.

Turbulent flow can be generalized or localized. If the flow rate of a gas moving through a tube reaches a certain value, the critical number or critical flow rate, then flow becomes turbulent.

The Reynolds number can be used to predict whether flow will be laminar or turbulent. It is determined by the following equation:

$$\text{Reynolds number} = \frac{\text{Linear Velocity} \times \text{Diameter} \times \text{Gas Density}}{\text{Gas Viscosity}}$$

A low Reynolds number (less than 1,000) is generally representative of laminar flow, whereas a Reynolds number above 1,500 is generally associated with turbulent flow.

Turbulent flow is usually caused by high gas flows, by sharp angles or branching points in tubing, and in response to significant changes in the diameter of a tube (such as upper airway obstruction or constriction).

With laminar flow, resistance is directly proportional to flow rate; however, in turbulent flow resistance is proportional to the square of the flow rate.

KEY FACTS: TURBULENT GAS FLOW

- Laminar flow is smooth and orderly; flow is fastest in the center of the tube.
- Turbulent flow is random; flow is equal throughout the diameter of the tube.
- A higher Reynolds number is predictive of turbulent flow.
- Gas density is more important than gas viscosity in turbulent flow.
- Flow is likely to become turbulent at higher gas flows, with sharp angles or branches in tubing, and with changes in tube diameter.
- Resistance is directly proportional to flow rate with laminar flow and proportional to the square of the flow rate with turbulent flow.

ADDITIONAL READINGS

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:192–193.

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:546–547.

15. ANSWER: D

Causes of postoperative hypoxemia are numerous and include all of the answer choices and many more. In this particular case, however, the most likely explanation is diffusion hypoxia.

Diffusion hypoxia refers to a scenario that can occur due to the rapid elimination of nitrous oxide into the alveoli following a nitrous oxide-based anesthetic. Nitrous oxide diffuses so quickly into alveolar gas that the diluted alveolar gas mixture can have decreased partial pressures of oxygen and carbon dioxide. In a patient breathing room air, this decrease in PAO_2 can lead to arterial hypoxemia. If supplemental oxygen is not provided, diffusion hypoxia can persist for 5 to 10 minutes following the anesthetic, and can therefore contribute to arterial hypoxemia in the PACU.

Other causes of postoperative hypoxemia include atelectasis, V/Q mismatch, pulmonary edema, congestive heart failure, alveolar hypoventilation, aspiration, pulmonary embolus, shivering, sepsis, transfusion-related lung injury, acute respiratory distress syndrome, obesity, and patient conditions such as asthma or chronic obstructive pulmonary disease.

KEY FACTS: DIFFUSION HYPOXIA

- Diffusion hypoxia can occur in the minutes after a nitrous oxide-based anesthetic.
- Supplemental oxygen should be provided to prevent diffusion hypoxia.
- When transporting a patient to the PACU, care should be taken to prevent a disconnection from the oxygen tank and to ensure the tank is not empty.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2009:422.

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:161.
Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. New York, NY: Churchill Livingstone; 2007:568.

16. ANSWER: E

The American Society of Anesthesiologists (ASA) publishes Standards, Guidelines, and Statements to provide guidance to anesthesiologists and anesthesia practices to improve decision making and outcomes for the practice of anesthesiology.

Standards provide rules or requirements for clinical practice and are regarded as generally accepted principles of patient management. There are currently only three published Standards: Standards for Basic Anesthetic Monitoring, Basic Standards for Preanesthesia Care, and Standards for Postanesthesia Care. They may be modified only under unusual circumstances, for example extreme emergencies or unavailability of equipment.

Guidelines are not intended as standards or requirements; they are systematically developed recommendations supported by a synthesis and analysis of the current literature, expert opinion, open forum commentary, and clinical feasibility data. Guidelines may be revised as medical knowledge and technology evolve. They are not meant to replace local institutional policies, and may be modified or rejected as clinical needs or restraints dictate. At the time of writing, there were 11 guidelines published by the ASA on such topics as Ambulatory Anesthesia and Surgery, Delineation of Clinical Privileges in Anesthesiology, the Ethical Practice of Anesthesiology, Regional Anesthesia in Obstetrics, Office-Based Anesthesia, and Expert Witness Qualifications and Testimony.

Statements simply represent the opinions, beliefs, and best medical judgments of the ASA House of Delegates. They are not specifically subject to the same scientific standards of review that standards and guidelines are.

(Paraphrased from ASA website with permission, cited below.)

KEY FACTS: ASA STANDARDS, GUIDELINES, AND STATEMENTS

- *Standards* provide rules or minimum requirements for clinical practice and may be modified only under unusual circumstances.
- *Guidelines* are systematically developed recommendations that may be adopted, modified, or rejected according to clinical needs and constraints and are not intended as standards or absolute requirements.
- *Statements* represent the opinions, beliefs, and best medical judgments of the ASA House of Delegates, and are not necessarily subjected to the same level of formal scientific review as ASA Standards or Guidelines.

ADDITIONAL READING

Standards, Guidelines, and Statements. American Society of Anesthesiologists Website, accessed May 15, 2010: http://www.asahq.org/publicationsAndServices/sgstoc.htm Content used with permission.

17. ANSWER: E

Most anesthesia ventilators are pneumatically powered and electronically controlled, with driving gas of either oxygen, air, or a mixture of both. Some ventilators use a mechanism that can increase the amount of total gas flow delivered while limiting the amount of driving gas, by employing a device called an injector. This device allows air to be entrained while high-pressure oxygen is delivered (the Venturi effect), resulting in an air–oxygen mix.

In any case, a hole in the bellows can result in exposure of the breathing system, and therefore the patient's lungs, to the pressure of the driving gas used to power the ventilator bellows. If that occurs, there exists the possibility of both barotrauma and alveolar hyperventilation.

Depending on the composition of the driving gas, the oxygen analyzer may read an increased or decreased value. If, for example, the driving gas is 100% oxygen, as in Ohmeda machines, the oxygen analyzer would read higher. However, if the machine is a Drager, the driving gas would be an air–oxygen mix, and the oxygen analyzer value may decrease.

KEY FACTS: HOLE IN THE VENTILATOR BELLOWS

- A hole in the bellows can result in hyperventilation or barotrauma.
- The type of driving gas can affect whether the oxygen analyzer value will increase or decrease.
- Ohmeda ventilators use 100% oxygen as the driving gas; Drager ventilators use an air–oxygen mixture.

ADDITIONAL READINGS

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:314.
Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:79–81.

18. ANSWER: C

Capnometry, the measurement of end-tidal carbon dioxide ($etCO_2$), has proved to be useful for a wide variety of indications. It has proved to be so useful, in fact, that the American

Society of Anesthesiologists includes the continual measurement of expired carbon dioxide in their Standards for Basic Monitoring.

Capnometry can be useful for detecting and monitoring altered CO_2 production, or absorption, as with laparoscopic surgery, hyperthermia, hypothermia, increased muscle tone, pain, anxiety, shivering, convulsions, and conditions such as malignant hyperthermia.

Circulatory changes may be detected by capnometry as well, in conditions such as severe hypotension with decreased perfusion, decreased transport of CO_2 to the lungs as with pulmonary embolus, and increased patient dead space conditions.

Capnometry can be useful in detecting respiratory and ventilatory problems as well. It is one of the most reliable monitors for accidental extubation, disconnection, and complete airway obstruction. Capnography, measurement of etCO_2 over time, can also be helpful in partial airway obstruction as occurs in chronic obstructive pulmonary disease. Esophageal intubation is also most reliably detected with etCO_2 monitoring; however, there have been numerous reports of CO_2 being detected despite esophageal intubation.

Endobronchial intubation is not reliably detected by capnometry. Although one might be able to recognize changes in the CO_2 waveform with one-lung ventilation, CO_2 will continue to be detected by capnometry, and given the speed with which CO_2 diffuses from blood to alveolar gas in normal lungs, the value will likely remain relatively constant, even with only one lung ventilated. Hypoxia and increased airway pressures are more likely to be signs of endobronchial intubation.

KEY FACTS: CAPNOMETRY

- Continual measurement of CO_2 is part of the ASA Standards for Basic Monitoring.
- Capnometry can be useful in detecting and monitoring conditions with altered CO_2 production and absorption, significant circulatory changes, and problems with respiration and ventilation.
- Endobronchial intubation is not reliably detected with capnometry.

ADDITIONAL READINGS

American Society of Anesthesiologists. *Standards for Basic Anesthetic Monitoring*, 2011. Retrieved from: http://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:705–709.

19. ANSWER: A

At ***high altitudes***, different types of vaporizers can behave quite differently. Traditional variable-bypass vaporizers can be used at any altitude with little change in the dialed setting of the vaporizer, despite the fact that the actual volume percent delivered is significantly different at higher elevations.

This is because it is the partial pressure of a particular anesthetic in the central nervous system that seems to be responsible for the effect of the agent, rather than the volume percent. The partial pressure of an anesthetic agent required to anesthetize someone does not change with altitude, and if the vaporizer continues to deliver a more or less fixed partial pressure, there is no need for a change in the dialed output.

Most conventional variable-bypass vaporizers already automatically compensate for this requirement by virtue of the fact that the output is really a partial pressure, not a percent, despite the labeling on the dial.

If we are looking at the actual volume percent output of a variable-bypass vaporizer, there is a significant increase with altitude, inversely proportional to the change in barometric pressure. For example, at an elevation of 10,000 feet (~3,000 meters), where atmospheric pressure is about two-thirds that at sea level, the increase in output from an isoflurane vaporizer almost doubles (if set to 1%, output is actually almost 2%).

The result of this increased output is that when using a variable-bypass vaporizer at high altitudes, the altitude can mostly be ignored. Although the percent concentration required for anesthesia increases, the vaporizer will already deliver higher percentages. The partial pressure required for anesthesia is constant, and the delivered partial pressure at altitude is almost the same as at sea level.

The same is not true for other types of vaporizers, such as those used for desflurane. These are dual-circuit, gas/vapor-blending vaporizers whose percentage output remains the same regardless of altitude. When using desflurane with a heated, pressurized vaporizer such as the Ohmeda Tec 6 or Drager D-vapor, the concentration dial will need to be increased in order to deliver adequate anesthesia to the patient at high altitude.

KEY FACTS: HIGH ALTITUDES

- When using a variable-bypass vaporizer at high altitudes, the altitude can mostly be ignored.
- Although the percent concentration required for anesthesia increases, a variable-bypass vaporizer will already deliver higher percentages at higher altitudes.
- The partial pressure required for anesthesia remains constant at high altitude, and the delivered partial pressure at altitude is almost the same as at sea level with variable-bypass vaporizers.
- When using desflurane in a heated, pressurized dual-circuit vaporizer, the percent concentration dial on the vaporizer must be increased to deliver adequate anesthesia.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:667.
Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins, 2008, Chapter 6.

20. ANSWER: B

The ***oxygen flush valve*** provides a communication between the high-pressure oxygen system (as from the pipeline inlet or cylinder pressure regulator) and the low-pressure circuit. Oxygen at very high flows, typically 35 to 75 L/min, is directed to the common gas outlet.

The ultimate result of oxygen flush valve activation depends on the individual anesthesia machine manufacturer and type. Depending on the presence or absence of check valves, the pressure generated, and the location of the check valve in relation to the vaporizers and other components of the anesthesia machine, activation of the oxygen flush may shut off other gas flows, may result in negative or positive pressure in the remainder of the system, and may or may not result in high pressures being directed to the patient.

In older machines that do not decouple fresh gas inflows and that have a one-way check valve between the vaporizers and the flush valve as well as a positive-pressure relief valve that is downstream from the vaporizers but upstream from the outlet check valve, enough positive pressure can be generated to allow the oxygen flush valve to be used for jet ventilation. If these conditions exist, the entire 35 to 75 L/min is directed to the common gas outlet, and pressure of up to 50 psi can be delivered. This also introduces the risk of barotrauma with the use of the oxygen flush valve.

Many machines, however, lack the one-way check valve between the vaporizers and the flush valve, allowing some oxygen flow retrograde into the machine, and reducing the pressure generated at the common gas outlet to as low as 7 psig, depending on the model of anesthesia machine.

Regardless of whether the oxygen flush valve stops the flow of other gases or not, there is likely to be some dilution of volatile agents. Repeated use can lead to inadequate concentrations to maintain anesthesia, and therefore lead to higher theoretical risk for awareness.

KEY FACTS: OXYGEN FLUSH VALVE

- The oxygen flush valve provides a communication between the high-pressure oxygen system and the low-pressure circuit.
- The oxygen flush valve may be used for jet ventilation in certain circumstances.
- Use of the oxygen flush valve can cause barotrauma, especially in older anesthesia machines.
- Repeated use can lead to inadequate concentrations to maintain anesthesia, and therefore lead to higher theoretical risk for awareness.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:660.
Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:100–101.

21. ANSWER: C

A size E compressed gas cylinder containing oxygen weighs approximately 5.90 kg empty and 6.76 kg full. When full, it contains approximately 625 L of oxygen at a pressure of approximately 2,000 psi.

By using Boyle's law, one can estimate the amount of gas remaining in a cylinder. Boyle's law states that for a fixed mass at a given temperature, the product of pressure and volume is constant. Using this relationship, and given that oxygen exists only in a gaseous state within the cylinder, we can estimate the remaining volume in an oxygen cylinder as a proportion of the original volume.

$$1{,}200 \text{ PSI}/2{,}000 \text{ PSI} = X/625 \text{ L}$$

This yields a value of 375 L. If the flow rate is 15 L/min, then there are 25 minutes remaining until the tank is empty (Table 14.1).

ADDITIONAL READINGS

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:9.
Faust RJ, et al. *Anesthesiology Review*. 3rd ed. New York, NY: Churchill Livingstone; 2002:210.
Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. New York, NY: Churchill Livingstone; 2007:188.

22. ANSWER: E

E-size cylinders can be used to store both nonliquefied and liquefied gases. Examples of gases that are nonliquefied include oxygen, air, nitrogen, and helium. When all of the particular agent exists within the cylinder in gaseous form only, the pressure within the cylinder decreases proportionally with the amount of gas remaining. For example, a full E cylinder containing oxygen contains approximately 625

Table 14.1 PROPERTIES OF MEDICAL GAS CYLINDERS

	COLOR				
GAS	U.S.	INTERNATIONAL	PRESSURE AT 70 DEGREES F (PSI)	STATE IN CYLINDER	E CYLINDER CAPACITY (L)
Oxygen	Green	White	1,900–2,200	Gas	625–660
Carbon dioxide	Gray	Gray	838	Liquid <88 degrees F	1,590
Nitrous oxide	Blue	Blue	745–750	Liquid <98 degrees F	1,590
Helium	Brown	Brown	1,600–2,000	Gas	496
Nitrogen	Black	Black	1,800–2,200	Gas	651
Air	Yellow	White and black	1,800	Gas	625

Adapted from Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008.

to 660 L at a pressure of approximately 2,000 psi. If the pressure gauge reads 1,000 psi, there are approximately 312 to 330 L remaining in the cylinder.

In contrast, nitrous oxide and carbon dioxide exist as liquid within E cylinders at normal room temperatures. The pressure within a nitrous oxide cylinder depends on the vapor pressure of the liquid gas, and does not vary proportionally with the remaining agent, until all of the liquid has vaporized and there is only gas remaining in the cylinder.

For nitrous oxide, a full E cylinder contains 1,590 L at a pressure of 745 psi, and weighs approximately 8.8 kg. As the cylinder empties, the pressure remains at 745 psi until there is only about 25% of the initial capacity of gas remaining. At that point, the pressure begins to fall rapidly.

ADDITIONAL READINGS

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:9.

Faust RJ, et al. *Anesthesiology Review*. 3rd ed. New York, NY: Churchill Livingstone; 2002:210.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 5th ed. New York, NY: Churchill Livingstone; 2007:188.

23. ANSWER: B

Vapor pressure is defined as the pressure exerted by a vapor in equilibrium with its liquid or solid phase. More specifically, in anesthesia, it is the pressure exerted by an anesthetic vapor when in equilibrium with its liquid state.

As an anesthetic liquid is kept in a closed container at a constant temperature and pressure, molecules of liquid break away into the gas phase until a dynamic equilibrium is reached, a state in which the number of molecules in the gas phase versus the liquid phase is constant. The molecules on the gas phase will constantly bump into the walls of the container, creating pressure on the walls of the container. This pressure is defined as the saturated vapor pressure.

Under normal ambient pressures in which anesthesia is given, the vapor pressure of a substance depends only on the nature of the substance and the temperature. As temperature increases, vapor pressure increases. Heat causes particles to move faster, gaining more kinetic energy. When particles have greater kinetic energy, they are more likely to evaporate and stay in a gaseous phase as opposed to a liquid phase. In our example of a closed container, there would be a greater number of particles bumping into the container walls, exerting a greater pressure, representing a higher vapor pressure.

Volume of liquid is not relevant to the vapor pressure of the liquid. It does not matter whether there is 1 mL or 1,000 mL in a container: the vapor pressure is the same.

Surface area also does not change the vapor pressure of a specific liquid. A container may be long and narrow or short and shallow; either way the vapor pressure remains the same.

KEY FACTS: VAPOR PRESSURE

- Vapor pressure depends only upon the specific liquid and the temperature.
- Ambient pressure is not a factor within the range of barometric pressures encountered when providing anesthesia.

ADDITIONAL READING

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:122.

24. ANSWER: C

Flowmeters may be mechanical or electronic. Some newer anesthesia machines use electronic flowmeters but still have

a graphical representation of a mechanical flowmeter on the screen. There may also be a mechanical flowmeter for the total gas flow.

Mechanical flowmeters work on the principle that flow past a certain resistance is based on the pressure exerted. Traditional mechanical flowmeters are classified as variable orifice, using an internally tapered vertical glass tube with the smallest diameter at the bottom. Other types of variable-orifice flowmeters include constant-pressure flowmeters, variable-area flowmeters, and Thorpe tubes. When the flow is turned on gas flows past an indicator, known as a bobbin, held within the tube. As flow, and therefore pressure, increases within the lower portion of the tube, the bobbin rises, allowing greater amounts of gas to flow around the edges of the bobbin as it rises within the tube. The bobbin balances within the tube as the pressure of gravity is balanced by the pressure of flowing gas.

The rate of flow through the tube depends on several factors. The pressure drop across the bobbin, which is acting as the constriction within the tube, is a key factor in the flow rate. There is resistance due to friction between the bobbin and the tube wall, which decreases as the bobbin rises and there is an increased diameter within the tube.

The annular opening within the tube will also affect the flow rate. These types of variable-orifice flowmeters are also called constant pressure flowmeters, referring to the fact that regardless of where the bobbin may be in the tube, the pressure drop from one side to the other remains the same. It is just enough pressure to counteract the weight of the bobbin, so as flow increases, the height of the bobbin increases. As the annular opening increases, additional gas escapes around the bobbin, allowing the flow to increase.

The physical characteristics of the gas are relevant to the flow rate. When the flow rate is low, the constriction provided by the bobbin is relatively longer and narrower than when the flow rate is high and the bobbin is high in the tube. At the lower flows, the flow tends to be laminar, and therefore primarily a function of the viscosity of the gas. As flow increases, it becomes more turbulent, and therefore becomes more dependent on the density of the gas, as described by the Hagen-Poiseuille equation.

Temperature and ambient pressure may have an effect on flowmeter function, as flowmeters are specifically calibrated at atmospheric pressure (760 torr, 1 atm) and room temperature (20 degrees C). Temperature and pressure variations will affect the viscosity and density of a gas, and will therefore affect the flow rate of that gas. In general, temperature changes are not clinically significant. It is important to note, however, that in a hyperbaric chamber the actual gas delivered will be less than that indicated by the flowmeter. Conversely, at high altitude, the delivered gas will be greater than indicated by the flowmeter.

The length of the flowmeter tube has no relevance on the flow rate itself, only the range over which different flow rates can be delivered.

KEY FACTS: FLOWMETERS

- Mechanical flowmeters work on the principle that flow past a certain resistance is based on the pressure exerted.
- The pressure drop across the bobbin, which is acting as the constriction within the tube, is a key factor in the flow rate.
- The annular opening also affects flow rate. As the annular opening increases, additional gas escapes around the bobbin, allowing the flow to increase.
- Flow rate is affected by the physical properties of a specific gas, namely its viscosity and density.
- Pressure and temperature changes can affect flow rate as they affect the physical properties of a gas.
- Flowmeters will be inaccurate at high altitudes and in hyperbaric chambers.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins, 2009:655–658.

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:103–104.

25. ANSWER: E

Airway fire is one of the most devastating complications that can result from laser airway surgery, one that can result in severe morbidity and even death. The CO_2 laser is most commonly used for upper airway and proximal trachea surgery, with an incidence of laser-related endotracheal fire or cuff ignition reported to be 0.14% to 1.5%.

During its use, the CO_2 laser emits high energy that can ignite nonmetallic and nonglass objects. Endotracheal tubes can be ignited either directly by the laser or indirectly by heat from nearby tissues, and if this occurs, the tube can effectively become similar to a blowtorch in the trachea, causing significant damage to the trachea.

Numerous strategies have been developed to decrease the likelihood of an airway fire, but none is 100% effective. Strategies include using specialized laser-resistant endotracheal tubes such as the Xomed laser shield tube, metal tubes, and flexometallic tubes. However, these endotracheal tubes have disadvantages in terms of being less flexible, having reduced internal diameters that make ventilation more difficult, and being more expensive. Conventional tubes such as polyvinyl chloride (PVC), red rubber, and silicone tubes are highly combustible; however, PVC tubes combust less readily than both red rubber and silicone tubes, and can be used more safely with laser surgery if wrapped with aluminum. Drawbacks to this technique include leaving areas

of the tube uncovered, especially around the cuff, and the risk of having edges of the aluminum tape that can damage the tracheal mucosa.

Other low-cost and practical techniques to prevent airway fire include placing wet gauze around the endotracheal tube, placing water-soaked pledgets in the subglottic area or around the endotracheal tube cuff portion, and filling the tube cuff with ice-cold saline containing methylene blue to serve as a heat sink and early indicator of cuff laser damage.

Regardless of the type of endotracheal tube selected, as the O_2 concentration increases the risk of a major fire increases significantly. Keeping the FiO_2 as low as possible is a very useful tactic that is easy to execute. There is literature to support either an FiO_2 of less than 40% or an FiO_2 of less than 30%; however, an FiO_2 of less than 30% is preferred. Mixing the oxygen with air or nitrogen to achieve dilution is effective, but the use of helium is ideal as it is less dense than either air or nitrogen and therefore promotes "smooth" laminar flow (with a decreased Reynolds number) and decreases the chance of ignition if the endotracheal tube becomes damaged. It has been demonstrated that helium in a concentration greater than 60% delays ignition of unwrapped PVC tracheal tubes from CO_2 laser energy. It should be noted that nitrous oxide has similar combustibility to 100% oxygen, and volatile anesthetic agents have the potential of being combustible and should be avoided if possible.

KEY FACTS: LASER-RELATED AIRWAY FIRE

- The incidence of laser-related endotracheal fires or cuff ignitions is reported to be 0.14% to 1.5%.
- The CO_2 laser is most commonly used for upper airway and proximal trachea surgery.
- The endotracheal tube may be ignited directly by the laser beam or indirectly by flaming tissues during laser surgery.
- Various techniques may be employed to decrease the risk of airway fire, including using specialized endotracheal tubes to shield the laser energy, decreasing the heat of the tracheal mucosa with moisture, and adding saline and color indicator to the cuff to dissipate heat and indicate cuff damage.
- Various specialized endotracheal tubes are available for laser surgery, including Xomed laser shield tubes, metal tubes, and flexometallic tubes.
- Polyvinyl chloride (PVC) tubes are more resistant to ignition than red rubber and silicone tubes and can be used for laser surgery if wrapped carefully with aluminum.
- The incidence of airway fire increases exponentially with increasing oxygen concentration. The lowest permissible concentration is preferred, ideally less than 30%.
- Oxygen can be diluted in air, nitrogen, or helium, with helium being the least likely to support combustion and the most likely to facilitate gas flow because of its physical profile.
- Avoid nitrous oxide and volatiles if possible as they could support combustion in the presence of oxygen.

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26. ANSWER: C

Cardiac pacemakers are electrical devices used to temporarily or permanently regulate the heart's beating when pacing from the heart's intrinsic pacer cells or conduction system is inadequate. There are numerous devices to pace the heart temporarily or permanently. Temporary devices include transcutaneous, transesophageal, and transvenous pacers. Permanent devices are implantable, placed in a subdermal pocket with wires tracking to either the right atrial endocardium, right or left ventricular endocardium, or all three.

Implantable pacemakers have a universal standardized nomenclature known as the *NGB pacemaker code*. This is a five-letter code that describes and characterizes the function of pacemakers.

The first letter (position I) describes the chamber paced. It is designated as A for *a*trium, V for *v*entricle, or D for *d*ual-chamber pacing; O is the designation for inactivated pacing.

Position II describes the chamber sensed. In a similar fashion, A is designated for *a*trial sensing, V for *v*entricular sensing, and D for *d*ual-chamber sensing; O is the designation for inactivated sensing.

Position III refers to the mode of response to sensing. In inhibited (I), whenever an intrinsic event is sensed the pacemaker will not pulse an output to the chamber(s) sensed (on position II). Triggered event, T, in this position signifies that the pacemaker will pulse an output in response to a sensed event. This mode is mainly used for diagnostic purposes and rarely encountered. The *d*ual, D, designation indicates that the device will respond to a sensed signal (i.e. atrial output) by inhibiting pacer output. It will then track the event through a defined time interval mimicking the PR interval.

If no event is sensed from the ventricle, the pacer will trigger an output to maintain AV synchrony. Conversely, if a ventricular event is sensed within the defined PR interval time, the pacer output is inhibited.

The fourth position (IV) refers to the programmable features of a pacemaker, in particular the ability to regulate pulse firing during periods of physical activity. This may be designated by the letter R, indicating *rate response* or *rate-adapting pacing*. As such, the device is able to sense an increase in activity and increases pulsed output accordingly for chronotropically incompetent patients (patients unable to achieve appropriate heart rate for a given physiologic activity). A pacer can be programmed to sense surrogate indicators of increased physical activity, including vibration/movement, minute ventilation, QT (stimulus-T), and oxygen saturation. O indicates absence of rate modulation and is often omitted in the absence of this feature.

Finally, the position V is used to document if the device has the ability to pace sites in all four chambers, more one than stimulation site in one chamber, or a combination of both abilities. The features are represented by A for atrial/atrium multisite pacing, V for ventricular/ventricle multisite pacing, and D for multisite pacing in both atrium and ventricle.

Perioperative management includes eliciting background information regarding the indication for pacer placement (sinus node dysfunction, AV node dysfunction, AV conduction defect, etc.) and the type and manufacturer of the device. This is important because the asynchronous heart rate can vary depending on the manufacturer when the pacer is placed in an asynchronous mode. A recent interrogation is highly recommended to determine pacemaker capabilities, function, pacing frequency (i.e., pacer dependence), and ECG analysis. The physical location of the pacer on the patient is also important.

The nature of the surgery plays a major role in perioperative management, and it is important to determine the site of the surgery, the duration of the surgery, whether electrocautery will be used, and ease of access to the pacemaker intraoperatively by the anesthesiologist. Monopolar electrocautery interferes with pacemaker functions by mimicking intrinsic output and inhibiting pacing output. Conversely, electrocautery output can increase pacer output if the signal is sensed as intrinsic cardiac output via the AV conduction system, with a resulting increase in ventricular rate. In addition, electrocautery can be sensed as increased physical activity and falsely increase pacer output. Monopolar electrocautery can damage pacer circuitry if it is used in close proximity to the device. Generally, electrocautery used in areas of close proximity dubbed "high-risk zones" pose the greatest risk for pacemaker interference or damage. High-risk zones include the abdomen above the umbilicus, chest, neck, shoulders, and the ipsilateral arm with respect to the device. Bipolar cautery travels less and can be substituted for monopolar cautery if surgery needs to done using electrocautery in the high-risk zone. However, bipolar cautery can be difficult to use for surgeons and is not as precise as monopolar cautery.

In the above scenario, the patient presents for surgery in a low-risk zone. This particular pacer is pacing AAIR (a.k.a "physiologic mode"), designed for patients with intact AV nodal conduction with a chronotropically incompetent heart. This allows for better AV synchrony with improved hemodynamics during periods of rest and activity. In this particular situation, asking the surgeon to use bipolar cautery is not appropriate as the interference from monopolar cautery will be negligible given the surgery is in a low-risk area. Proceeding with general anesthesia without an intervention will most likely result in pacer dysfunction, as the mechanical ventilation will trigger increased pacer output secondary to the perceived increase in physical activity. The patient is paced 50% of the time, and turning the pacer off completely will likely result in decreased cardiac performance during times when the sinus node is not functioning. Placing a magnet over the pacemaker will revert the pacer to an asynchronous mode; in this case it may be DOO or AOO at a set rate depending on the manufacturer. This would deactivate the rate-response mode; however, because the patient is not totally pacer-dependent, there is the risk of a pacer pulse being triggered during repolarization of the myocardium (R-on-T phenomenon), with a resultant possibly lethal cardiac dysrhythmia. Consulting with the cardiologist to inactivate the rate response would be the most appropriate choice.

KEY FACTS: PACEMAKERS

- Careful planning with the surgeon, the anesthesiologist, and the patient's cardiologist is important for appropriate perioperative care of a patient with a pacemaker.
- Indication for pacemaker, pacemaker documentation, physical location, and nature of surgery must all be taken into account for successful perioperative management.
- Pacemakers have a universal NGB code comprising five positions with various letters to indicate function and capabilities: position I = chamber paced, position II = chamber sensed, position III = response to sensed event, position IV = ability to regulate output (rate response), position V = pacing site(s).
- Monopolar electrocautery can interfere with and damage pacemaker function if it is used in the high-risk zone. Bipolar cautery is a viable alternative because it has a lower risk of interference.
- Mechanical ventilation can interfere with the rate-response function and cause false pacemaker triggering in response to a perceived increase in physical activity.
- Placing a magnet over a pacemaker switches a pacemaker to an asynchronous mode where there is pacing but not sensing.

- Patients who are not pacemaker-dependent are at risk of cardiac dysrhythmias with an asynchronous pacemaker.

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27. ANSWER: E

The ECG is used primarily to detect cardiac arrhythmias and myocardial ischemia, and also to detect chamber enlargement, heart block, electrolyte effects, pericardial disease, and pacemaker function. Lead II is used to diagnose arrhythmias because its axis parallels the electrical axis of the heart and the p-wave is most prominent.

The V5 lead allows for anterior myocardial wall monitoring and has been demonstrated to be the most sensitive lead in identifying ischemia, with a single-lead sensitivity of 75%. The combination of lead II and V5 results in a sensitivity of 80% because lead II enables inferior wall analysis. The addition of V4 has shown 96% sensitivity in detecting myocardial ischemia. Thus, 12-lead ECG continuous analysis should be considered in patients at high risk for myocardial ischemia.

The standard five-lead ECG used in the operating room comprises the three basic limb leads, RA, LA, LL, and a precordial lead, V5, appropriately placed at the fifth intercostal space on the anterior axillary line, along with the grounding lead RL. Using these five electrodes, seven different ECG leads can be observed (I, II, III, AVR, AVL, AVF, and V5). The limb leads are known as *bipolar* leads because they represent the potential between two points in relation to the electrical vector activity of the heart. Lead I is formed by the positive potential in the LA and the negative potential of the RA. Lead II is formed by the positive LL electrode and the negative RA electrode. Lead III is formed by the positive electrode in the LL and the negative electrode in the LA. These three limb leads form Einthoven's triangle and serve to measure the electrical activity of the heart, forming the wave deflections seen in typical ECG recording.

In addition to the three bipolar limb leads there are three augmented *unipolar* limb leads. These are termed unipolar leads because there is a single positive electrode that is referenced against a combination of the other limb electrodes (the "zero lead," also referred to as Wilson's Central Terminal). The positive electrodes for these augmented leads are located on the left arm (aV_L), the right arm (aV_R), and the left leg (aV_F). These leads use the same electrodes used for leads I, II, and III and record electrical activity along a single plane, termed the *frontal plane* relative to the heart.

There are also the precordial leads V1 to V6 that record the electrical activity in a plane perpendicular to the frontal plane. These leads are positive electrodes that are placed at different positions in the chest that correspond to different regions of the heart to measure the electrical vector activity along the perpendicular plane. In the operating room the V5 lead is the only lead that is routinely measured in patients at risk for myocardial ischemia because it has approximately 89% of ST-segment information contained in a conventional 12-lead ECG.

Disruption of any one of the bipolar limb leads will consequently disrupt Einthoven's triangle, leaving one lead intact. In the case disruption of the LL electrode will leave lead I intact as RA and LA potential is intact. This will also affect all the unipolar limb leads, as well as the precordial leads.

KEY FACTS: ECG MONITORING

- The ECG monitoring in the operating room, typically comprising 5 leads, allows for the monitoring of 7 of the 12 leads of a full ECG.
- The limb leads I, II, and III are bipolar leads and correspond to the RA, LA, and LL leads respectively. They represent the potential between two points and make up Einthoven's triangle.
- The precordial leads are a set of six positive leads recording electrical activity along regions of the ventricle perpendicular to the frontal plane. In the typical five-lead operating room monitoring setup, the V5 lead is the sole precordial lead recorded.
- The V5 lead is monitored in the operating room because it contains approximately 89% of the ST-segment information of a 12-lead ECG. The V5 lead has a single lead sensitivity of 75% in diagnosing myocardial ischemia. Together with lead II and lead V5 the sensitivity increases to 80%.
- In patients with a high risk of myocardial ischemia, additional V leads should be monitored, in particular the V4 lead, because it increases sensitivity to 96%.
- Disruption of any of the five ECG leads will cause a partial disruption in Einthoven's triangle/frontal plane with a resultant inability to monitor the set of leads that rely on the disconnected lead.

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28. ANSWER: C

The concept of pulse oximetry utilizes the Beer-Lambert law to derive the oxygen saturation of hemoglobin. The Beer-Lambert law relates the transmission of light to the absorption properties of a material, taking into account the distance the light travels through the material. Thus, it is possible to derive the concentration of a material (i.e., gas, liquid) based on its absorptive properties of the transmitted light, the light intensity, and the length, the light travels through the material.

Pulse oximeters have two light-emitting diodes (LEDs) that transmit two different wavelengths, one at 660 nm (red) and another at 940 nm (infrared). These wavelengths correspond to absorption spectra where oxyhemoglobin has a considerably greater absorption (660 nm) than deoxyhemoglobin and where oxyhemoglobin and deoxyhemoglobin have an approximately equal absorption (940 nm, isobestic point). The wavelengths are emitted in an alternative fashion at a frequency of 400 Hz. Ultimately the LEDs emit light onto a pulsatile vascular bed. The nature of the vascular bed is such that there are constant nonpulsatile elements, including soft tissue and blood components, and a major pulsatile element, oxygenated blood. At the two distinct wavelengths the nonpulsatile tissue elements have a constant predictable absorption spectra, whereas the pulsatile elements vary in absorption spectra. Through software processing the nonpulsatile elements are subtracted. A ratio of the wave absorption of the pulsatile and nonpulsatile elements at 660 nm versus pulsatile and nonpulsatile elements at 940 nm is calculated. Oxygen saturation is then computed based on preexisting algorithms, with calibration curves that are specific to each manufacturer from data obtained from healthy volunteers. Low oxygen saturations (less than 80%) are calculated from extrapolations and thus are not very accurate.

Several situations and conditions can influence the pulse oximeter reading. Substances whose absorption profile falls within the pulse oximeter wavelengths interfere with its accuracy. For example, carbon monoxide irreversibly binds to hemoglobin, and at a wavelength of 660 nm mimics oxyhemoglobin such that it can give falsely elevated readings. Methemoglobin increases absorption at 940 nm and produces falsely low oxygen saturation readings. Other conditions that decrease the accuracy of pulse oximetry include low cardiac output state, motion artifact, nail polish (especially blue and green), severe anemia (hematocrit less than 10%), and skin pigmentation. In general pulse oximeters have a standard error of margin of ±4% to 5% above a saturation of 80%. Bilirubin does not affect pulse oximetry readings because its absorption spectrum is at approximately 450 nm.

KEY FACTS: PULSE OXIMETRY

- Pulse oximetry is based on the Beer-Lambert law, as it relates the change in intensity of light through a substance with the distance the light travels through the substance. The concentration and density of a substance can be calculated using algorithms with the knowledge of the absorptive properties of a substance.
- The pulse oximeter uses light-emitting diodes that emit two wavelengths of light, 660 nm and 940 nm, to analyze nonpulsatile and pulsatile elements in a vascular bed. Pulsatile elements are assumed to be oxygenated hemoglobin and nonpulsatile elements include deoxygenated hemoglobin, blood elements, and tissue.
- Through pulse oximeter processing the pulsatile data versus the nonpulsatile data are compared and a ratio is obtained. The ratio is plotted against an algorithm derived from healthy patient data and the corresponding oxygen saturation is obtained.
- Pulse oximeter data are reliable and accurate above a saturation of 80%, but below oxygen saturations of 80% the accuracy is significantly lower, given that these values are extrapolated from calibration curves.
- Inaccurate measurements result from motion artifact, dyshemoglobinemias, endogenous and exogenous color artifacts, such as in certain colors of nail polish and intravenous dyes such as methylene blue and indocyanine green that fall within the 660-nm and 940-nm spectra. Bilirubin, however, does not affect pulse oximetry readings.

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29. ANSWER: A

Soda lime is a substance composed mainly of hydroxide salts (potassium, sodium, and calcium) that is used in CO_2 absorbents to neutralize carbonic acid. Carbonic acid is the product of a reaction between CO_2 and water. It reacts with soda lime to produce water, heat, and calcium carbonate.

The chemical composition of soda lime varies from manufacturer to manufacturer in terms of the percentage of hydroxide salts. Water is needed to initialize the production of carbonic acid and for the soda lime absorbent to function correctly. When there is lack of a water source, as occurs when soda lime is desiccated from normal exhaustion or from high fresh gas flow when the ventilator is not in use, the absorbent is no longer able to function properly and CO_2 is recirculated. The pH indicator that signals exhaustion does not necessarily indicate desiccation. The salts in a desiccated soda lime absorber may begin to degrade volatile agents and produce toxic byproducts and very high temperatures. In particular, the potassium salt (KOH) can react with sevoflurane to produce compound A, formaldehyde, methanol, methyl formate, and dimethoxymethane in a highly exothermic reaction that can cause fire. The temperature from the exothermic reaction does not reach hazardous levels (100 degrees C) with soda lime composed of calcium or sodium salts. However, there have been case reports implicating sevoflurane with desiccated barium hydroxide (Baralyme) CO_2 absorbents.

To date, compound A has not been implicated in increasing the risk of nephrotoxicity in humans. Volatile anesthetics may all react with elements within soda lime or Baralyme to produce carbon monoxide, but this occurs only with desiccated absorbers. Therefore, the concern for falsely high oxygen saturation readings from possible carbon monoxide poisoning is unlikely in this situation because there is exhaustion but not necessarily desiccation. Desflurane is the most likely to result in production of carbon monoxide when it reacts with dry barium hydroxide (i.e., Baralyme), but may also do so with soda lime. Given the concern for toxic byproducts from CO_2 absorbents with strong bases (salts), most modern absorbents have moved away from using strong bases, such as KOH, in favor of less reactive substances such as $Ca(OH)_2$.

KEY FACTS: SODA LIME CO_2 ABSORBENTS

- Soda lime CO_2 absorbents, especially those with KOH, have been implicated in the production of toxic byproducts and dangerous exothermic reactions when desiccated.
- Under normal circumstances CO_2 combines with water to form carbonic acid. This product reacts with the soda lime salts to produce water and calcium carbonate in a mild exothermic reaction.
- Desiccation occurs when the CO_2 absorbent is dry from exhaustion, continual high fresh gas flow through the absorber, and disconnection of the reservoir bag, causing depletion of moisture from the granules.
- A desiccated soda lime absorber lacks the water needed to form carbonic acid; instead the salts, especially the KOH, react with volatiles to produce toxic byproducts and a highly exothermic reaction capable of igniting a fire.
- Sevoflurane reacts with KOH to produce compound A, formaldehyde, methanol, methyl formate, and dimethoxymethane in a highly exothermic reaction.
- Sevoflurane can react with NaOH in soda lime, but the exothermic reaction is mild. When it reacts with barium hydroxide from a Baralyme absorbent, the exothermic reaction can ignite a fire.
- Calcium salts do not react with sevoflurane or other volatiles and the risk of toxic byproducts is unlikely.
- Desflurane can react with dry barium salts (Baralyme) to produce significant levels of carbon monoxide.

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30. ANSWER: A

According to the *ASA Practice Advisory for Intraoperative Awareness and Brain Function Monitoring*, "Intraoperative awareness occurs when a patient becomes conscious during a procedure performed under general anesthesia, processes it into explicit memory and subsequently has recall of specific events during the procedure." This does not include the time before the general anesthetic or during emergence, when arousal is intended. The incidence of this complication ranges from 0.1% to 0.3%. Patient characteristics associated with intraoperative awareness include:

1. Age (less than 40 years)
2. Female sex
3. ASA physical status 4 or 5
4. Drug resistance or tolerance from substance use or abuse (e.g., chronic pain patients using high doses of opioids, patients on high-dose benzodiazepines, and those with cocaine use)
5. Limited hemodynamic reserve
6. History of awareness
7. Difficult intubation

Procedures and surgeries classically associated with recall include cesarean delivery, cardiac surgery, and trauma surgery. Anesthetic techniques are also implicated in recall. These include rapid sequence induction, sub-MAC anesthetic doses, use of muscle relaxants, total intravenous anesthesia (TIVA), and nitrous oxide–opioid anesthesia.

Light anesthetic concentrations and difficult laryngoscopy have also been associated with intraoperative awareness. Preoperative evaluation may be helpful in identifying patients at risk for intraoperative awareness.

Obesity and history of anxiolytic use have not been implicated as risk factors for intraoperative awareness. There is no evidence that patients with mitochondrial disorders or other inborn errors of metabolism have a significantly higher risk of awareness than the normal population.

Preventive techniques for treating patients at high risk for recall center around adequate premedication, using generous doses for anesthetic administration, and ensuring anesthetic delivery. Specifically, these patients should always be administered amnestic premedication (e.g., midazolam, scopolamine). There should be routine equipment checks to ensure anesthetic delivery, adequate dosing of induction agents, and use of MAC doses for volatile anesthetics and propofol dosing. Monitoring of volatile end-tidal concentrations and frequent checks of IV lines should be performed. Multiple modalities to assess depth of anesthesia may be employed, including the use of brain function monitors such as the bispectral index (BIS) monitor.

Use of brain function monitors have been associated with decreased incidence of intraoperative recall; however, routine use is controversial, as awareness has been demonstrated despite the use of these monitors.

If awareness does occur, postoperative management involves counseling and long-term psychological support with a specialist. Long-term complications may include posttraumatic stress disorder.

KEY FACTS: INTRAOPERATIVE AWARENESS

- The incidence of intraoperative awareness ranges from 0.1% to 0.3%.
- Patient factors associated with intraoperative awareness include young age, female sex, ASA patient status 4 or 5, history of drug resistance or tolerance, limited hemodynamic reserve, difficult intubation, and history of awareness.
- Procedures associated with awareness include cesarean section and cardiac and trauma surgery.
- Rapid sequence induction, sub-MAC anesthetic doses, use of muscle relaxants, total intravenous anesthesia (TIVA), and nitrous oxide–opioid anesthesia have been implicated in recall.
- Obesity and history of anxiety are not associated with risk of intraoperative recall.
- Management includes adequate medication with amnestic agents preoperatively, dosing medications liberally, and ensuring anesthetic delivery through frequent checks.
- Brain function monitors can be used as an adjunct to assess depth of anesthesia, but recall has been reported with its use and it remains controversial.
- Intraoperative recall is managed with personal and psychological support.
- Posttraumatic stress disorder is a serious long-term complication of intraoperative recall.

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31. ANSWER: A

Contemporary anesthesia machines incorporate ***variable-orifice flowmeters*** (also known as constant-pressure flowmeters, variable-area flowmeters, or Thorpe tubes) for gas delivery. The main function of these flowmeters is to control and measure gas flow to the common gas inlet using a flow scale superimposed on or beside the flowmeter tube. Each assembly is unique to an individual gas. Variable-orifice flowmeters are characterized by internal tapering of the vertical glass tube with increasing diameter at the top as the indicator elevates. Gas flow is measured as a function of pressure needed to overcome a resistance. The indicator elevates as gas passes through the annular opening between the indicator and the glass tube and floats freely at a position where the downward force caused by gravity is equal to the upward force of the gas pressure at the bottom. The proportionality between pressure and flow is determined by the shape of the tube (resistance) and physical property of the gas (density and viscosity). As gas flow increases, the size of the annular opening around the indicator increases with height allowing for more gas flow. The pressure, however, remains constant at all tube heights.

The rate of flow through the tube depends on:

- Pressure drop across the constriction: Gas flow encounters frictional resistance between the indicator and the tube wall with a resultant pressure drop. The pressure drop is equal to the weight of the float divided by its cross-sectional area and is constant at all positions in the tube.
- Annular size opening: In variable-orifice flowmeters, the annular cross-sectional area varies with varying indicator height. The pressure drop across the indicator, however, remains constant for all positions in the tube. Increasing the flow does not increase the pressure drop, but causes the indicator to rise to a higher position in the tube, thereby providing greater flow area for the gas (hence the name constant-pressure flowmeters). The elevation of the

indicator is a measure of the annular area for flow and, therefore, of the flow.
- Physical properties of the gas: Inherent to variable-orifice flowmeters is the variability in the size of the annular opening and resultant constriction created by the increasing gas flow. The physical property that relates gas flow to the pressure difference across the constriction varies with the size of the constriction. When a low flow of gas passes through the glass tube, the annular opening between the float and the wall of the tube will be narrow and long. At this position, gas flow is predominantly laminar and can be characterized by the Hagen-Poiseuille equation for compressible fluids, whereby flow is a function of viscosity. With high flow the annular opening becomes larger and the gas constriction is shorter; flow is more turbulent as characterized by Graham's law, with flow being a function of gas density.

Because the inherent properties of gases (primarily viscosity and density) vary depending on temperature and pressure, changes in these conditions alter the accuracy of flowmeters. In general, temperature changes need be drastic to have a significant impact on gas characteristics. Changes in pressure, however, can alter the gas properties significantly enough to interfere with flowmeter readings. This is more relevant at high flows, where flow is more related to density than viscosity, because pressure has little effect on viscosity while having a significant effect on density. With decreasing pressure (as in high altitude), the density of a gas decreases and flowmeter readings will underestimate the flow of gas. With increasing pressure (as in a hyperbaric chamber), density increases and flowmeter readings will overestimate the flow of gas. The following equation can be used to estimate changes in flow depending on density changes:

$$F_1 = F_0 \times (d_1/d_0)$$

where F_1 = flow at ambient pressure, F_0 = flow at calibrated scale to sea level, d_1 = density of gas at sea level, and d_0 = density of gas at ambient pressure.

Flowing carbon dioxide gas through a nitrous oxide flowmeter will not significantly affect the accuracy, as both gases have similar properties.

KEY FACTS: VARIABLE-ORIFICE FLOWMETERS

- Variable-orifice flowmeters are characterized by internal tapering of a vertical glass tube with increasing diameter at the top as the indicator elevates.
- Gas flow is measured as a function of pressure needed to overcome a resistance.
- The proportionality between pressure and flow is determined by the shape of the tube (resistance) and the physical property of the gas (density and viscosity).
- As gas flow increases, the size of the annular opening around the indicator increases with height allowing for more gas flow. The pressure, however, remains constant at all tube heights.
- The rate of flow through the tube depends on pressure drop across the constriction (constant), annular size opening (variable at different vertical heights), and physical properties of the gas (density and viscosity).
- Because the inherent properties of gases, such as viscosity and density, vary depending on temperature and pressure, changes in these conditions alter the accuracy of flowmeters.
- Changes in pressure alter gas properties and interfere with flowmeter readings, especially at high flows. With decreasing pressure (as in high altitude), density of a gas decreases and flowmeter readings will underestimate the flow of gas. With increasing pressure (as in a hyperbaric chamber), density increases and flowmeter readings will overestimate the flow of gas.
- In general, temperature changes do not play a significant role because they tend to stay constant during an anesthetic.

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32. ANSWER: C

The function of an inspiratory valve is to prevent backflow of expired CO_2 into the inspiratory limb of a circuit during exhalation. Exhaled CO_2 from the patient travels toward the expiratory limb and through the expiratory valve. An incompetent inspiratory valve will allow for CO_2 produced by the patient to flow both through the expiratory limb and the inspiratory limb of the circuit. This in effect "contaminates" the fresh gas flow originating from the ventilator with CO_2 from exhalation. During the subsequent inspiration, the patient receives fresh gas flow with CO_2 from the prior breath and proceeds to exhale increased CO_2. This results in a linearly prolonged expiratory plateau phase (phase III) on the capnograph (in contrast to the upsloping prolonged expiratory phase seen in obstructive pulmonary disease). Initially, the end-tidal waveform may look elongated, with the inspiratory phase (phase I) of the waveform reaching an end-tidal of zero, but only after a prolonged period. However, as rebreathing continues there is a sloping down of the curve in phase I and full fresh gas inspiration is not

reached (the waveform does not reach an end-tidal CO_2 of zero).

The maneuvers to reinflate the lung result in a decrease in shunt, as lung areas that were being perfused but not ventilated are reexpanded to allow gas exchange. Dead space is not necessarily reduced by reexpansion of a deflated lung, and in fact may be increased.

During bronchospasm, or other obstructive lung pathology, there is a prolonged, upsloping expiratory phase of the capnogram, but in the presence of functioning valves, the end-tidal CO_2 should return to the zero during inspiration.

An incompetent expiratory valve results in an elevated baseline, as exhaled gases are rebreathed during inspiration, a prolonged phase II during initial expiration, and a slanting down during initial inspiration.

Exhaustion of the CO_2 absorbent would result in a progressively elevated baseline and progressively elevated plateau height of the capnogram, as CO_2 rebreathing increases with each breath.

KEY FACTS: INCOMPETENT INSPIRATORY AND EXPIRATORY VALVES

- An incompetent inspiratory valve presents with a characteristic change in the end-tidal waveform that includes a linear elongation of the phase III expiratory plateau, an prolonged phase I inspiratory phase, and a progressive increase in the baseline end-tidal CO_2 at the curve nadir (inspiration never reaches end-tidal CO_2 of zero).
- An incompetent expiratory valve results in an elevated CO_2 baseline.

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33. ANSWER: C

Mapleson systems, also known as carbon dioxide washout circuits or flow-controlled breathing systems, lack unidirectional valves and CO_2 absorbing devices. There are six variations, designated letters A through F, each with unique advantages. The Mapleson F and Mapleson D circuits are popular configurations. Each consists of a reservoir bag, corrugated tubing (Mapleson D), adjustable overflow valve, fresh gas inlet, and the patient connection. There is no separate inspiratory and expiratory limb. These circuits rely on high fresh gas flows to circulate and eliminate CO_2 out of the circuit. Rebreathing will occur when the inspiratory flow exceeds fresh gas flow. Composition of inspired gas will depend on how much rebreathing takes place, and it will vary depending on the use of controlled versus spontaneous ventilation. Monitoring of end-tidal CO_2 is the best method to determine optimal fresh gas flow. The relative simplicity of the systems decreases the resistance and work of breathing, especially during spontaneous ventilation. They also offer a decrease in dead space. Furthermore, they are light, convenient, and inexpensive.

There are drawbacks to Mapleson systems, however. Their delivery of anesthetic vapors is inefficient and can pollute the surrounding atmosphere. Furthermore, these systems are unable to preserve humidity of the inspired gases from high fresh gas flows and lack a humidifying unit.

KEY FACTS: MAPLESON CIRCUITS

- Mapleson circuits are valveless, semiclosed partial rebreathing systems that minimize the work of breathing, especially for infants during spontaneous ventilation.
- Multiple configurations exist, each with certain advantages in terms of efficiency of rebreathing. Mapleson D and F circuits are popular.
- Mapleson breathing circuits rely on high fresh gas flows for delivery of anesthetic vapors and elimination of CO_2.
- Mapleson circuits consist of a reservoir bag, corrugated tubing, APL valve, fresh gas inlet, and the patient connection without separate inspiratory and expiratory limbs.
- Advantages of Mapleson systems include decreased work of breathing (especially during spontaneous ventilation) from the absence of valves, decreased dead space, relative convenience, and low cost.
- Disadvantages include rebreathing of large amounts of CO_2 if fresh gas flows are not adequate, inefficient delivery of anesthetic vapors with subsequent pollution, and loss of humidity with high gas flows.

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34. ANSWER: E

The Bain circuit is a modification of the Mapleson D consisting of the same components, but with fresh gas flow tubing contained within the inspiratory limb directed toward the patient outlet. Fresh gas flow requirements are similar to other Mapleson circuits. However, the Bain circuit has been shown to preserve more heat and humidity as compared to other Mapleson circuits, given that the inspiratory fresh gas flow is heated by close contact with expiratory flow.

A unique hazard of the use of the Bain circuit, however, is occult disconnection or kinking of the inner, fresh gas delivery hose. If this occurs, the entire corrugated limb becomes dead space. This can result in respiratory acidosis unresponsive to increased minute ventilation.

KEY FACTS: BAIN CIRCUIT

- The Bain circuit is a modification of the Mapleson D consisting of the same components, but with fresh gas flow tubing contained within the inspiratory limb.
- Fresh gas flow requirements are similar to other Mapleson circuits.
- The Bain circuit has been shown to preserve more heat and humidity as compared to other Mapleson circuits, given that the inspiratory fresh gas flow is heated by close contact with expiratory flow.

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35. ANSWER: B

The ***fail-safe feature*** of anesthetic machines incorporates a valve that prevents hypoxic mixtures from being delivered to the patient when pressure flow decreases as a result of exhaustion and/or disconnection of the oxygen source. It is the pressure of oxygen gas that drives the opening or closing of the fail-safe valve. As the oxygen pressure decreases, the valve adjusts appropriately to decrease the gas flow of nitrous oxide, completely ceasing nitrous oxide delivery when oxygen pressure falls below a threshold of 20 to 30 psi (depending on the ventilator). The fail-safe valve works in response to specific pressures, not specific gases; theoretically, 100% nitrous oxide can be delivered if pressure were to be maintained by a source other than oxygen to keep the fail-safe valve open and allowing for delivery of nitrous oxide.

Pipeline oxygen pressures range from 40 to 60 psi. The pressure is adjusted to 45 psi by pressure regulators in the ventilator circuit. A fall in pipeline oxygen pressure below 50 psi will not affect delivery of nitrous oxide unless it drops below 30 psi, activating the fail-safe device. An oxygen tank delivers oxygen at 45 psi as dictated by the pressure regulator, when the oxygen main pipeline fails. If the oxygen tank is closed, the pipeline pressure will fall below 30 psi and the fail-safe device will be activated. However, if the oxygen tank is open, the oxygen tank supply will be exhausted to less than 30 psi before the fail-safe device is activated.

The oxygen supply failure alarm, also known as the low-pressure alarm, will be activated (alarm) when a significant increase or decrease in the oxygen supply pressure occurs, as can happen with a sudden loss of cylinder or pipeline pressure in the scenario given. However, the flow of nitrous oxide will not be affected, as this alarm has no impact on the function of the fail-safe device. Oxygen does not flow through the nitrous oxide flowmeter; instead, it is an indirect relationship linked by the fail-safe device.

KEY FACTS: FAIL-SAFE DEVICE

- The fail-safe device incorporates a valve that prevents hypoxic mixtures of nitrous oxide from being delivered to the patient when pressure decreases as a result of oxygen supply failure.
- When oxygen pressure falls below a threshold of 20 to 30 psi, the fail-safe valve decreases or completely ceases nitrous oxide delivery.
- The oxygen supply failure alarm (the low-pressure alarm) will be activated when there is a sudden rise or fall in the oxygen supply pressure (i.e., cylinder or pipeline pressure failure).

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36. ANSWER: A

The ***Reynolds number*** ($Re = \tilde{n}Vd/\grave{\imath}$, where $\tilde{n}$ is the gas density, V is the velocity, d is the diameter of the tube, and $\grave{\imath}$ is the viscosity of the gas) predicts whether flow through a straight, unbranched tube will be laminar or turbulent. At low Reynolds numbers laminar flow occurs, where viscous forces dominate. High Reynolds numbers correspond to turbulent flow, which is affected more by density than viscosity. A helium/oxygen mixture of 70%/30% has about the same viscosity as a 70%/30% nitrogen/oxygen mixture but only one-fifth the density. When turbulent flow predominates, an increase in flow will occur with a helium/oxygen mixture.

Helium has no effect on the diameter of the airways, although theoretically a decrease in airway diameter could improve laminar flow. Finally, diffusion capacity plays no role in flow mechanics.

KEY FACTS: REYNOLDS NUMBER

- Laminar versus turbulent gas flow through a straight tube is predicted by the Reynolds number.
- The Reynolds number is calculated by: $Re = \tilde{n}Vd/\grave{\imath}$, where $\tilde{n}$ is the gas density, V is the velocity, d is the diameter of the tube, and $\grave{\imath}$ is the viscosity of the gas.
- At low Reynolds numbers laminar flow occurs, where viscous forces dominate. High Reynolds numbers correspond to turbulent flow, affected more by density than viscosity.
- A helium/oxygen mixture of 70%/30% has about the same viscosity as a nitrogen/oxygen mixture of 70%/30%, but has a lower density, and therefore a lower Reynolds number, promoting laminar gas flow.

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37. ANSWER: B

The **simple facemask** is the most common style of oxygen mask. It can allow up to 60% oxygen to be delivered with flow set up to 8 L/min. By design, the mask provides a small reservoir that allows oxygen to accumulate in the mask, and allows the patient to secondarily entrain room air through vents on the side of the mask. Given that the reservoir is small and air entrainment is allowed, the FiO_2 that can be achieved with this mask is limited. Flow should be set to a minimum of 5 L/min to flush out expired CO_2 and limit rebreathing. This mask may cause some discomfort if needed for long periods of time.

An **oxygen face tent** is a soft plastic "tent" that can be used in patients who are claustrophobic or otherwise have difficulty tolerating a mask. The primary limiting factor with face tents is that the maximum FiO_2 achieved is approximately 40%, even with flows as high as 15 L/min.

Partial rebreathing and nonrebreathing masks are similar in their construction and both contain a reservoir bag as part of the mask. The partial rebreathing mask allows part of the exhaled breath to fill the reservoir bag, whereas the nonrebreathing mask incorporates a valve to prevent filling of the reservoir bag. The nonrebreathing mask also incorporates a flap to reduce entrainment of room air with inhalation, although this is not complete. Partial rebreathing masks may allow an FiO_2 from 35% to 75% with flows at 7 to 15 L/min. The delivered FiO_2 with nonrebreathing masks can be 40% to 100% with flows of 7 to 15 L/min.

The **Venturi mask**, or air-entrainment mask, is a high-flow system that intentionally allows air entrainment through a number of entrainment ports. It requires a high flow of oxygen and air to work, and can deliver an FiO_2 in the range of 24% to 50% depending on the ratio of oxygen to air desired.

KEY FACTS: OXYGEN DELIVERY DEVICES

- The simple face mask can deliver an oxygen concentration of 40% to 60% with flows of 5 to 10 L/min.
- A partial rebreathing mask allows an FiO_2 of approximately 35% to 75% with flow rates of 7 to 15 L/min.
- A nonrebreathing mask is the most efficient noninvasive oxygen delivery device, delivering an FiO_2 of 90% to 100% with flow rates of 15 L/min.
- A Venturi mask is a high-flow oxygen delivery device that intentionally entrains room air to deliver an FiO_2 of 24% to 50%.

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38. ANSWER: A

The oxygen flush is a direct link between the high-pressure and low-pressure circuits in an anesthesia machine, bypassing the flowmeters and vaporizer. In certain anesthesia machine configurations the flush valve can deliver 100% oxygen at 45 to 50 psi regardless of its source (pipeline or cylinder) with a flow rate of 35 to 75 L/min. However, other ventilators have incorporated pressure-relief valves downstream from the oxygen flush and will deliver a more modest pressure of approximately 7 psi (not suitable for jet ventilation).

In the scenario above, if the O_2 flush flow rate is 60 L/min, 1 L of O_2 would flow into the breathing circuit for every second that the O_2 flush button is held down. During

the inspiratory phase of mechanical ventilation, the gas pressurizes the circuit as the ventilator pressure-relief valve remains closed and the APL valve is out of circuit. In this situation there is momentarily no outlet for excess gases. If the O_2 flush button is pressed during the inspiratory phase of mechanical ventilation, pressure inside the breathing circuit will increase rapidly as 1 L of fresh O_2 is introduced each second into the momentarily closed circuit. This pressure is then transmitted to the lungs, leading to an acute increase in measured airway pressure.

Many contemporary anesthesia machines incorporate an inspiratory pressure limiter or fresh gas decoupling, which works to prevent excess fresh gas inflow from flowmeters or the flush valve from entering the inspired tidal volume. If the oxygen flush button is pressed during the expiratory phase of mechanical ventilation, the bellows will initially fill rapidly to its maximum capacity. After reaching maximum capacity, any pressure in excess of 2 to 4 cm H_2O will be vented through the pressure-relief valve.

KEY FACTS: ANESTHESIA MACHINE OXYGEN CONFIGURATION

- The oxygen flush is a direct link between the high-pressure and low-pressure circuits in an anesthesia machine.
- In certain anesthesia machine configurations the flush valve can deliver 100% oxygen at 45 to 50 psi regardless of its source (pipeline or cylinder) with a flow rate of 35 to 75 L/min.
- Most anesthesia machines have incorporated pressure-relief valves downstream from the oxygen flush that diminish the delivered pressure to approximately 7 psi. In these machines, the oxygen flush is unsuitable for jet ventilation.
- In certain anesthesia machines, if the O_2 flush button is pressed during the inspiratory phase of mechanical ventilation, pressure inside the breathing circuit will increase rapidly as the pressure-relief valve remains closed and the APL valve is out of circuit. This may result in excessive pressure being transmitted to the lungs.
- Contemporary anesthesia machines incorporate an inspiratory pressure limiter or fresh gas decoupling, which prevents excess fresh gas inflow from flowmeters or the flush valve from entering the inspired tidal volume.

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39. ANSWER: B

The consequence of a dramatically elevated hematocrit is an increase in the viscosity of blood. As a result there is an increase in the resistance of blood flow with an increase in pressure drop across blood vessels as described by ***Poiseuille's law***. Poiseuille's law is a physical law that describes the pressure change in a fluid flowing through a cylindrical tube (e.g., large arteries). It can be applied to describe laminar viscous fluids that are incompressible (e.g., blood). The flow must be through a constant circular cross-section that is significantly longer than its diameter (i.e., a pipe or artery). The equation is as follows:

$$\Delta P = 8\eta LQ/\pi r^4$$

where ΔP = the change in pressure, η = is the viscosity constant, L = length of cylinder, Q = flow velocity, and r = radius.

Traditionally, Poiseuille's law is used to describe the impact of varying arterial vessel diameter in relation to blood pressure. Small changes in vessel radius can have a large impact on the degree of blood pressure drop as radius is exponentially related (to the fourth power).

The viscosity constant, η, describes a fluid's resistance to flow. For blood, viscosity is determined primarily by the liquid portion, plasma, which is three times more viscous than water. With an increase in hematocrit, resistance is increased and flow is impaired, leading to hyperviscosity syndrome, in which patients are at risk of compromised tissue perfusion. Plasma proteins can have a similar effect, but to a lesser extent. Changes in temperature can also affect viscosity, especially during deep hypothermic circulatory arrest, where body temperatures may be as low as 18 to 20 degrees C. Increases in temperature decrease viscosity and vice versa. Hemodilution can be theoretically used in these patients to decrease viscosity and improve tissue perfusion.

In the scenario, the patient requires an increase in pressure across his arterial system to compensate for the higher viscosity from the elevated hematocrit. With an arterial dilator, the radius of the vessels would increase, leading to a decrease in the pressure in the arterial system; however, in the patient with polycythemia, this decrease in pressure would be blunted by the increased pressure required to move the more viscous blood forward. As explained by Poiseuille's law, r will increase, leading to a decrease in ΔP, but η is increased, which would lead to an increase in ΔP, blunting the overall change in ΔP.

KEY FACTS: POISEUILLE'S LAW

- Poiseuille's law is a physical law that describes the pressure change in a fluid flowing through a cylindrical tube.
- It can be used to describe the impact of varying arterial vessel diameter in relation to blood pressure.
- Poiseuille's law: $\Delta P = 8\eta LQ/\pi r^4$

- – Where ΔP = the change in pressure, η = is the viscosity constant, L = length of cylinder, Q = flow velocity, and r = radius.
- Small changes in vessel radius can have a large impact on the degree of blood pressure change as pressure is inversely related to the radius exponentially (to the fourth power).
- The viscosity constant, η, describes a fluid's resistance to flow.
- Increasing viscosity increases the pressure required to maintain constant flow across vessels, as described by Poiseuille's law.
- Blood viscosity is determined by the liquid portion, plasma, which is three times more viscous than water.
- An increase in hematocrit increases viscosity and theoretically decreases blood flow through the arterial system, assuming a constant blood pressure.

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40. ANSWER: D

The alarm initially heard on traditional anesthesia machines when they are turned on or off is the oxygen supply failure alarm, also known as the low-pressure alarm. The oxygen supply failure alarm is designed to sense a sudden change in oxygen pressure, be it from the pipeline or oxygen tank. This sudden change can be either an increase or, more importantly, a decrease in pressure. Classically, when the anesthesia machine is initially turned on the oxygen pressure insufflates a canister that calibrates the alarm to a set pressure. In the process of insufflation the gas flows through a whistle. When there is a further increase or decrease in oxygen pressure the whistle blows as the canister fills further or deflates. The oxygen supply failure alarm will not be heard when pressure changes are subtle.

KEY FACTS: OXYGEN SUPPLY FAILURE ALARM

- The oxygen supply failure alarm (a.k.a. the low-pressure alarm) is designed to sense a sudden change in oxygen pressure.
- The sudden change can be a decrease or increase in pressure.
- The oxygen supply failure alarm is normally heard when the anesthesia machine is turned on or off as the alarm apparatus is insufflating and desufflating with oxygen with the corresponding pressure changes.
- If pressure changes are subtle, the oxygen supply failure alarm will not be activated.

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41. ANSWER: B

CPAP is a noninvasive positive-pressure ventilation modality that assists spontaneous ventilation by delivering pressurized gas to the airways via a nasal or oral-nasal mask. This increases transpulmonary pressure and inflates the lungs, stenting open alveoli. Exhalation occurs passively by elastic recoil of the lungs and any active force exerted by the expiratory muscles. This effectively combines spontaneous breathing with the advantages of elevated positive end-expiratory pressure (PEEP) without an increase in the work of breathing. By delivering a constant pressure during spontaneous inspiration and expiration, CPAP increases functional residual capacity (FRC) by expanding collapsed and/or underventilated alveoli, decreases right-to-left intrapulmonary shunt, and improves arterial oxygenation. Also, lung compliance and the work of breathing are both decreased.

CPAP also improves cardiovascular performance by decreasing left ventricular transmural pressure, resulting in a decrease in the left ventricular preload and afterload with an increase in cardiac output. For this reason CPAP is beneficial in patients with acute cardiogenic pulmonary edema. CPAP also decreases venous return by increasing intrathoracic pressure and decreasing the gradient from the systemic venous circulation to the right heart.

CPAP has been used in patients with chronic obstructive pulmonary disease to reduce the work of breathing by counterbalancing intrinsic PEEP. It is also used as an effective treatment for sleep apnea by pneumatically "splinting" the pharyngeal airway and preventing its collapse during sleep.

KEY FACTS: CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

- CPAP delivers a constant pressure during spontaneous inspiration and expiration.
- It increases functional residual capacity by expanding collapsed and/or underventilated alveoli, decreases

right-to-left intrapulmonary shunt, and improves arterial oxygenation.
- Lung compliance and the work of breathing are both decreased with the use of CPAP.
- The benefits of CPAP on cardiovascular performance include decreased left ventricular transmural pressure with a decrease in left ventricular preload and afterload with an increase in cardiac output.

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42. ANSWER: B

Medical gas cylinder tanks are classified alphabetically from A to H based on dimensions and capacities. They contain pressurized gas with a gauge indicating tank pressure. E cylinders are the most commonly used size in the hospital setting for storage of common medical gases, including oxygen, nitrous oxide, air, and carbon dioxide. These tanks are commonly found on anesthesia machines.

The tare weight of an empty E cylinder is 5.9 kg. The capacity and weight of E cylinders vary according to the physical properties of the gas they contain and the amount of that gas. Table 14.2 lists the various capacities and volumes of a typical E cylinder tank according to the gas it contains.

For cylinders containing compressed nonliquefied gases (gases with high vapor pressure), such as oxygen and air, pressure is directly proportional to gas content. For example, if an oxygen tank is half empty, the pressure would read approximately 1,000 psi (half of a full tank pressure of approximately 2,000 psi).

Nitrous oxide and carbon dioxide are different from oxygen and air in that their vapor pressures are relatively lower. Nitrous oxide, for example, has a vapor pressure of approximately 750 psi, above which it will exist at least partially in liquid form. For a partially liquefied gas under pressure, such as nitrous oxide, there exists an equilibrium in the tank between the liquid and gas phases, and pressure alone cannot be used to measure the amount of gas in the tank. As nitrous oxide gas is depleted from a tank, the pressure will remain steady at 750 psi as liquid nitrogen continually vaporizes and replenishes the vapor phase of the equilibrium. When the liquid phase of nitrous oxide is finally depleted, the pressure will start to fall from 750 psi (the pressure inside a full tank of N_2O). This happens when the tank is approximately 75% empty, with only 25% of the full tank remaining. At this point the total amount of volume in the cylinder is 25% of the full volume (1,590 L), approximately 400 L. Once the pressure starts to fall within the tank, nitrous oxide exists solely in the gas phase and cylinder pressure is then directly proportional to nitrous oxide content. To determine the amount of volume in the cylinder at full pressure, the weight of the tank must be determined.

Table 14.2 E CYLINDER CHARACTERISTICS

GAS	OXYGEN	NITROUS OXIDE	AIR
Cylinder tare weight (kg)	5.9	5.9	5.9
Cylinder weight full (kg)	6.8	8.8	
Cylinder pressure (psi)	2,000	745–750	1,800
Cylinder volume (L)	625	1,590	625

KEY FACTS: E CYLINDERS

- E cylinders are the most commonly used size in the hospital setting for storage of common medical gases, including oxygen, nitrous oxide, air, and carbon dioxide.
- The tare weight of an empty E cylinder is 5.9 kg.
- For E cylinders containing nonliquefied gases, such as oxygen or air, the pressure within the tank is directly proportional to the volume of gas in the tank.
- For E cylinders containing liquefied or partially liquefied gases, such as nitrous oxide and carbon dioxide, the tank pressure alone is inadequate to measure volume.
- The measured pressure of an E cylinder containing nitrous oxide will be approximately 745 to 750 psi as long as there is liquid remaining in the tank that is being vaporized to maintain the gas–liquid equilibrium. When all of the liquid is vaporized, the pressure will begin to fall from 750 psi. This occurs when approximately 75% of the total volume of nitrous oxide gas has been depleted. This corresponds to a tank volume of approximately 400 L (25% of the total cylinder volume).
- To determine the volume of an E cylinder containing nitrous oxide with a pressure of 750 psi, the weight of the cylinder must be determined.

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43. ANSWER: B

Nitrous oxide is a nonpolar, highly soluble gas that easily diffuses through membranes. The blood–gas partition coefficient of nitrous oxide is 0.46, making it 34 times more soluble than nitrogen (coefficient 0.014). This dramatically greater solubility as compared to nitrogen results in rapid diffusion of nitrous oxide along its concentration gradient, from the lungs into the blood, and on into air-containing spaces such as the bowel, pleural cavity, and other spaces.

The difference in the blood–gas partition coefficient of nitrous oxide (0.47) and nitrogen (0.014) results in preferential transfer of nitrous oxide into a compliant air-filled cavity faster than nitrogen can exit. This results in rapid expansion of the air-filled space as nitrous oxide from the blood reaches equilibrium with the air-filled space, while nitrogen slowly diffuses out. Due to this phenomenon, use of nitrous oxide during gastrointestinal surgery and in patients with ileus or bowel obstruction is relatively contraindicated, as bowel gas volume can expand two to three times within the first 2 hours of the administration of 75% nitrous oxide, and may cause harmful traction across anastomoses and worsening of obstructive symptoms.

A pneumothorax has been shown to rapidly and dramatically expand in volume with the use of nitrous oxide, doubling in the first 10 minutes and tripling in 30 to 45 minutes when a 75% nitrous oxide/oxygen mixture is used. Other functional disorders such as pneumoperitoneum, pneumopericardium, and pneumocephalus can also be theoretically worsened by nitrous oxide administration; however, the volume–pressure relations vary as these tissues have differing compliances, resulting in a varied impact. Generally speaking, as compliance is greater (as with the pleural cavity and bowel), the volume change will be greater, and as compliance is lower (as within the skull and middle ear), the pressure change will be greater.

The rate at which volume increases take place in gas-enclosed spaces is affected by the solubility of the respired gas in the blood and the blood flow to the space or blood flow/space volume ratio. Other factors that affect the rate of diffusion through any semipermeable membrane include temperature, molecular weight of the respired gas, permeability of the gas through, or the solubility in, the tissue composing the membrane, and finally the pressure gradient of the respired gas across the membrane.

The amount of gas diffusing into air-filled spaces depends on the transport capacity of the blood as given by the blood–gas partition coefficient of nitrous oxide and the membrane characteristics where the diffusion process takes place (i.e., whether the membrane is porous vs. nonporous, silicone vs. latex). For example, lung tissue is both porous and highly compliant, contributing to the rapid increase in size of a pneumothorax when a patient inspires a mixture of oxygen and nitrous oxide. Recent data suggest that nitrous oxide may even diffuse directly from the alveolar gas into the pleural space rather than being transferred by the blood via the circulation, contributing to the observation of rapid expansion.

Other air-filled cavities that can expand include the middle ear compartment, endotracheal tube cuff, and LMA cuff, as well as air-filled balloons of catheters (such as that of a Swan-Ganz catheter). Nitrous oxide can also expand an iatrogenically air-filled cavity such as an intracardiac air embolus. Pressure in air-filled endotracheal tube cuffs has been shown to increase steadily throughout general anesthesia with nitrous oxide, creating excessive pressure even when the initial sealing pressure is satisfactory. The increase in the tracheal cuff pressure mostly occurs during the first hour of anesthesia and can contribute to tissue ischemia. With the advent of high-volume, low-pressure cuffs this has been attenuated, but the phenomenon still exists. The increase in volume in endotracheal cuffs is not as dramatic as compared to pleura or bowel, in large part because the initial volume is so much smaller, and there is a higher corresponding pressure increase.

The middle ear can accumulate nitrous oxide, which can be problematic when the Eustachian tube is not properly working, but as described, this will increase pressure more than it will increase volume.

Renal capsule rupture would result in accumulation of blood within the capsule and would not be affected by administration of nitrous oxide.

KEY FACTS: NITROUS OXIDE SOLUBILITY

- Nitrous oxide is 34 times more soluble in blood than nitrogen.
- This results in preferential transfer of nitrous oxide into a compliant air-filled cavity faster than nitrogen can exit, resulting in expansion of the air-filled space.
- Nitrous oxide rapidly and dramatically accumulates in the pleural space, with the potential to triple the volume of a pneumothorax within 45 minutes when administered at 75%.
- Bowel gas volume will also expand with the use of nitrous oxide, but not as dramatically (two to three times in the first 2 hours of 75% nitrous administration).
- Pneumoperitoneum, pneumopericardium, and pneumocephalus can also be theoretically worsened by nitrous oxide administration, but the volume impact may be less dramatic given the low compliance of tissues.
- Other air-filled cavities that may expand include the middle ear compartment (more deleterious with an occluded Eustachian tube), endotracheal tube cuffs, LMA cuffs, and catheter balloons filled with air.
- The rate at which volume increases take place in gas-enclosed spaces depends on the solubility of the respired gas in the blood, the blood flow to the space, and the blood flow/space volume ratio.

ADDITIONAL READINGS

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44. ANSWER: D

Hyperbaric oxygen therapy (HBOT) involves placing a patient in a pressurized chamber with a 100% oxygen concentration. HBOT may also be administered by using a tight-fitting mask, similar to masks in anesthesia or those used for noninvasive positive-pressure ventilation such as continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BPAP). A nasal catheter may also be used for small children.

Administration of pressurized oxygen has a number of benefits on conditions associated with hypoxia or ischemia. The primary benefit is the resulting hyperoxygenation of blood, which can decrease the size of gas bubbles, activate proliferative factors, and have immunomodulatory effects on host and pathogens. Hyperoxygenation is achieved when oxygen concentration in body fluids is elevated to 10 to 25 times its normal levels.

Clinical applications of this therapy are multiple, with hyperoxygenation of blood being used to treat decompression sickness, carbon monoxide poisoning, central artery occlusion, compromised tissue grafts/flaps, crush injury, and severe blood loss anemia.

Other major applications include treatment of air or gas embolism to decrease bubble size and to promote wound healing in refractory bone and soft tissue infections, because HBOT promotes angiogenesis, fibroblast synthesis, and leukocyte oxidative killing. HBOT has been shown to inhibit bacterial toxin production, specifically clostridial toxin, which has benefits in treating necrotizing fasciitis. It has also been shown to work synergistically with certain antibiotics in treating infections.

Burn patients benefit greatly from this type of therapy because it promotes wound healing, skin graft survival, and treatment of bacterial infections.

The physics behind HBOT is explained by the ideal gas laws: Henry's law, Boyle's law, and Charles' law.

Hyperoxygenation results from **Henry's law,** which states that the amount of gas dissolved in a liquid is directly proportional to the partial pressure of the gas exerted on the surface of the liquid. Therefore, by increasing the atmospheric pressure in the chamber, more oxygen can be dissolved into the blood plasma than would occur at normal atmospheric pressure. The effect of hyperbaric conditions in producing a state of hyperoxygenation can be demonstrated using the formula for arterial oxygen content (CaO_2) of blood:

$$CaO_2\ (mL/dL) = Hb\ (g/dL) \times 1.39\ mL/g \times \text{oxygen saturation} + PaO_2\ (0.003\ mL/dL)$$

Under normal physiologic conditions at an atmospheric pressure of 760 mm Hg (1 atm) and 21% oxygen concentration, the partial pressure of oxygen in the blood is approximately 100 mm Hg (using the alveolar gas equation). Hemoglobin is able to carry 1.39 mL of oxygen per 100 cc (or 10 dL). Assuming a hemoglobin of 15 g/dL and 100% saturation, the blood is able to carry 21.15 mL/dL of oxygen.

If the patient is treated with 3 atmospheres of pressure (3×760 mm Hg = 2,280 mm Hg) with 100% oxygen, the calculated alveolar oxygen tension is 2,183 mm Hg ((2280 mm Hg – 47 mm Hg) × 100% FiO_2 – 0.8/40).

The dissolved oxygen content is 2,183 mm Hg × 0.003 mL/dL = 6.5 mL/dL.

The total arterial oxygen content of the patient's blood is therefore

$$CaO_2 = 5\ g/dL \times 1.39\ mL/g \times 100\% + 2{,}183\ (0.003\ mL)$$
$$= 13.5\ mg/dL$$

At this oxygen content the patient will have enough oxygen to meet the metabolic demands of the brain and heart until his hemoglobin recovers and his body adjusts to the meet the new metabolic demands.

KEY FACTS: HYPERBARIC OXYGEN THERAPY

- HBOT involves placing a patient in a pressurized chamber with 100% oxygen, or requires the use of specialized masks.
- Administration of pressurized oxygen has a number of benefits on conditions associated with hypoxia or ischemia. The primary benefits result from hyperoxygenation of blood.
- Hyperoxygenation results from Henry's law, which states that the amount of gas dissolved in a liquid is directly proportional to the partial pressure of the gas exerted on the surface of the liquid.
- Alveolar oxygen tension varies with changes in pressure, oxygen concentration, metabolism, and alveolar tissue transport. It is calculated by the alveolar gas equation:

$P_{atm} - 47\ mm\ Hg \times FiO_2 - R/PaCO_2$, where P_{atm} is atmospheric pressure, R is the respiratory quotient, usually 0.8, and $PaCO_2$ is the arterial CO_2 content.

- The effect of hyperbaric conditions in producing a state of hyperoxygenation can be demonstrated using the formula for arterial oxygen content (CaO_2) of blood:

$$CaO_2\ (mL/dL) = Hb\ (g/dL) \times 1.39\ mL/g \times \text{oxygen saturation} + PaO_2\ (0.003\ mL/dL)$$

- HBOT can be used to treat severe anemia where blood transfusion is contraindicated as a bridging therapy until the body compensates.

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45. ANSWER: B

Hyperbaric oxygen therapy (HBOT) involves placing a patient within a pressurized chamber containing 100% oxygen or the use of a tight-fitting mask. There are a number of clinical applications, including treatment of decompression sickness, carbon monoxide poisoning, severe blood loss anemia, crush injuries, and air and gas emboli.

HBOT is also helpful in the treatment of nonhealing wound infections, as it promotes angiogenesis, fibroblast synthesis, and leukocyte oxidative killing, as well as inhibiting bacterial toxin production. It has also been shown to work synergistically with certain antibiotics.

The physics behind HBOT lies within the ideal gas laws: Henry's law, Boyle's law, and Charles' law. As described in the previous question, hyperoxygenation results from Henry's law, which states that the amount of gas dissolved in a liquid is directly proportional to the partial pressure of the gas exerted on the surface of the liquid. Therefore, by increasing the atmospheric pressure in the chamber, more oxygen can be dissolved into the blood plasma than would be seen at normal atmospheric pressure.

Boyle's law ($P_1V_1 = P_2V_2$) describes the relationship of pressure and volume of a gas. Specifically, within a closed system at a constant temperature, pressure varies inversely with volume. Therefore, as pressure increases, as would occur under hyperbaric conditions, the volume of a gas would decrease, thereby reducing the hemodynamic perturbation that might come from a large air or other gas embolus.

Charles' law ($V_1/T_1 = V_2/T_2$) describes the relationship between temperature and volume, specifically that temperature and volume are directly related, such that as a gas is heated, it expands in volume. A corollary of this relates temperature to pressure by making use of the ideal gas law ($PV = nRT$). If volume is held constant, as pressure increases, temperature also increases. This direct relationship between pressure and temperature explains why an increase in temperature results from chamber pressurization, and conversely a decrease in temperature results with depressurization. Although body temperature does increase with pressurization in a hyperbaric chamber, it is not significant enough to cause hyperpyrexia (above 40.0 degrees C).

HBOT has a number of effects on the cardiovascular system. There is a decrease in heart rate while stroke volume is maintained, resulting in an overall decrease in cardiac output. Furthermore, systemic vasoconstriction increases afterload. Together these factors can exacerbate heart failure in patients with a history of cardiomyopathy. In the above scenario, the patient with a low ejection fraction is most at risk of developing heart failure.

Other side effects of HBOT include oxygen toxicity, deafness, and visual changes. Oxygen toxicity may be manifested by seizures, a rare side effect whose treatment includes removing the patient from the high oxygen concentration. Deafness can occur but is extremely rare in the absence of Eustachian tube pathology. Although blindness is not a complication of HBOT, cataracts and transient visual disturbances can result from optic disk changes.

KEY FACTS: HYPERBARIC OXGEN THERAPY

- The physics behind HBOT lies within the ideal gas laws: Henry's law, Boyle's law, and Charles' law.
- Henry's law explains the hyperoxygenation of blood plasma, as increased oxygen partial pressure causes more oxygen to be dissolved in plasma.
- Boyle's law explains the inverse relationship between pressure and volume, and therefore explains how HBOT decreases the size of gas emboli.
- Charles' law explains the direct relationship between volume and temperature, and by corollary the direct relationship between pressure and temperature. Increasing pressure results in an increase in temperature, but this change is not significant enough to cause hyperpyrexia with HBOT.
- HBOT decreases heart rate while maintaining stroke volume, resulting in an overall decrease in cardiac output. Afterload increases as a result of vasoconstriction.

This can exacerbate heart failure in patients already at high risk.
- Side effects of HBOT may include seizures due to oxygen toxicity, cataracts, transient visual disturbances, and transient decreases in hearing, especially with Eustachian tube dysfunction.

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46. ANSWER: D

Three types of oxygen analyzers are commonly used in anesthetic practice: galvanic, polarographic, and paramagnetic oxygen analyzers.

Galvanic oxygen analyzers work through the chemical reaction between a cathode and anode electrode separated by a gel. An electrical current is produced by a reaction between the electrodes and oxygen. This current is proportional to the concentration of oxygen. The disadvantages of galvanic oxygen analyzers are that electrodes get exhausted over time and require replacement. They are also not fast enough to determine the difference in oxygen concentration between inspired and expired gases and require frequent calibration.

Polarographic oxygen analyzers work through a mechanism similar to galvanic oxygen analyzers. The difference is in the chemicals used for the electrodes and the fact that polarographic oxygen analyzers use an external battery source that helps speed the chemical reaction, resulting in a slightly faster reaction time compared to galvanic oxygen sensors. However, they suffer from the same disadvantages. Their electrodes get exhausted over time and require frequent calibration. They also are not fast enough to determine the difference in oxygen concentration between inspired and expired gases.

Paramagnetic oxygen analyzers use the magnetic properties of oxygen to determine the oxygen concentration. A dumbbell containing a diamagnetic gas is suspended between two magnets, and changes in oxygen concentration, a paramagnetic gas, cause the dumbbell to rotate. A current is then applied to a spring connected to the dumbbell to resist the rotation. The amount of current needed is thus proportional to the concentration of oxygen. Paramagnetic oxygen analyzers are faster than the other two types of oxygen analyzers. They are fast enough to determine both inspired and expired oxygen concentrations accurately. They also require less frequent calibration and do not have any consumable parts.

KEY FACTS: OXYGEN ANALYZERS

- Galvanic, polarographic, and paramagnetic oxygen analyzers are the most commonly used oxygen analyzers in anesthesia machines.
- Polarographic and galvanic oxygen analyzers require replacement of electrodes and more frequent calibrations and are slower than paramagnetic analyzers.
- Paramagnetic oxygen analyzers determine the oxygen concentration more quickly than the other two types, allowing for determination of both inspired and expired oxygen concentration, without the need for replacement of consumables.

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47. ANSWER: C

Three different types of oxygen analyzers are used commonly in anesthesia: polarographic, galvanic, and paramagnetic oxygen analyzers. Polarographic and galvanic oxygen analyzers use an electrochemical reaction that generates a current proportional to the concentration of oxygen. These oxygen analyzers need to be calibrated to room air, which is set at 21%. Paramagnetic oxygen analyzers work through the magnetic properties of oxygen. These analyzers also use a mechanism that generates a current that is proportional to the concentration of oxygen and also need to be calibrated, although less frequently than the electrochemical analyzers.

Errors in calibration or failures in the oxygen analyzers themselves can result in the failure of detecting the difference between the current generated by the 21% oxygen in room air and that in the inhaled and expired gases themselves and would show up as 21% oxygen, or the concentration in room air.

Answer A is incorrect because even without an adequate seal with the facemask, the inspired oxygen concentration would still be higher than 21% if you are flowing 10 L/min of oxygen.

Answer B is incorrect because the pin index system, which is a geometric yoke system that prevents the wrong cylinder from being attached to the wrong inlet, should prevent an air cylinder from being used where an oxygen cylinder would normally reside.

Answer D is incorrect because the flowmeters are downstream from the oxygen supply and you would be unable to flow 10 L/min through the flowmeters if there was an oxygen supply failure.

Answer E is incorrect because a hole in the ventilator bellows may or may not cause the delivered oxygen concentration to be inaccurate, but would not lead to a reading of 21% if the fresh oxygen flow was 10 L/min.

KEY FACTS: OXYGEN ANALYZERS

- Oxygen analyzers generate a current proportional to the concentration of oxygen.
- Oxygen analyzers require calibration.
- Failure in calibration or failure in the oxygen analyzer can result in the analyzer being unable to detect a difference between room air concentration and that of inspired oxygen.

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48. ANSWER: B

Anesthesia machines are built with multiple safety mechanisms in place that help to prevent delivery of a hypoxic gas mixture. Oxygen is the only gas supply that can pass directly to its flow-control valve. Other gases must pass through fail-safe valves, which close proportionally in the presence of low oxygen pressures to prevent delivery of a hypoxic gas mixture. There is also an oxygen supply pressure alarm downstream from the oxygen supply that is able to detect low oxygen pressures. If there was a failure of the wall oxygen supply, or a problem with oxygen delivery from the oxygen cylinder, this low-pressure alarm would sound, and the machine would not be able to deliver the 1 L/min of oxygen along with the 2 L/min nitrous oxide.

In addition to the low-pressure alarm, depending on the type of ventilator and anesthesia machine, the flow-proportioning system for nitrous oxide would prevent the delivery of nitrous in the absence of adequate fresh oxygen flow. Anesthesia machines all have some form of flow-proportioning system, whether electronic, pneumatic, or mechanical, to limit the delivery of nitrous oxide in the presence of low oxygen flows. These systems typically allow no less than 23% to 25% FiO_2, assuming the components are working correctly, the supply gases are appropriate, and there is no leak downstream from the proportioning system.

Another added protection to prevent delivery of a hypoxic mixture lies in the way the flowmeters are positioned, with the oxygen flowmeter always positioned downstream from the other gases. By doing this, a leak in a flowmeter for another gas does not affect the delivery of oxygen, since it is the last gas added to the mixture.

However, a leak in the oxygen flowmeter can result in the delivery of a hypoxic mixture of gas. If the leak is on the proximal portion of the flowmeter, below the bobbin, the bobbin will show accurately the decreased flows depending on the size of the leak. If, however, the leak is distal to the bobbin on the flowmeter, then the flowmeter will inaccurately show higher flow than is actually reaching the patient. If the flows of the other gases are high enough, the patient is subject to a potentially hypoxic mixture of gas.

Although it is possible to deliver a hypoxic mixture with low gas flows, it would be extremely unlikely at the gas flows described in the question above. To deliver a hypoxic mixture due solely to low gas flows, the amount of oxygen delivered would need to be less than the amount of oxygen consumed by the patient. Given that the typical oxygen consumption for an anesthetized person is 200 to 250 mL/min, a flow of 1 L/min should be more than adequate to prevent this from occurring.

KEY FACTS: OXYGEN FLOWMETERS

- The oxygen flowmeter is positioned downstream from all other gases to prevent an upstream leak of the other gases causing an oxygen leak.
- A leak in an oxygen flowmeter may result in the delivery of a hypoxic mixture of gas.
- Oxygen flowmeter leaks proximal to the bobbin will show accurate flows; however, flowmeter leaks distal to the bobbin will show inaccurate flows (flows will be much lower than what is read on the bobbin).

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49. ANSWER: A

The presence of hypercapnia in a mechanically ventilated patient is important to recognize. Elevated CO_2 has multiple effects on a patient, including increasing intracranial pressure and pulmonary artery pressure as well as hypertension and possible cardiac arrhythmias. There are a number of causes of hypercapnia: increased production, increased absorption, or decreased elimination. Some of these include patient factors such as malignant hyperthermia and inadequate ventilation, surgical factors such as CO_2 insufflation and absorption during laparoscopy, and equipment factors such as the malfunction of one-way valves in the anesthesia machine.

In the scenario presented above, the key to determining which of these factors is responsible is the elevation of inspired CO_2. This points to the rebreathing of expired CO_2, which can occur only because of an equipment issue. The rebreathing of expired CO_2 can result from either the incompetence of the unidirectional flow valves or exhaustion of the CO_2 absorbent.

The anesthetic circuit has two unidirectional flow valves, an expiratory valve and an inspiratory valve. The expiratory valve is a one-way valve that allows expired gas to flow in one direction away from the patient and prevents rebreathing of the expired gas. The inspiratory valve is a one-way valve that allows inspired gas to flow only toward the patient. If either of these valves is incompetent, rebreathing of expired gases, including CO_2, would result as the gases would never reach the CO_2 absorbent canister.

Only the exhaustion of the CO_2 absorbent, and not a crack in the canister, would result in rebreathing of CO_2. A crack in the CO_2 absorbent canister, which is part of the anesthetic circuit, would cause a leak in the anesthetic circuit but would not result in rebreathing.

Inadequate tidal volumes would result in hypoventilation, which would increase the end-tidal CO_2 but would not increase the inspired CO_2.

Low gas flows in the presence of a working CO_2 absorber would not result in rebreathing of CO_2, but would exhaust the CO_2 absorbent more quickly.

An acrylic cement embolus would result in a sudden increase in dead space, leading to a sudden decrease in end-tidal CO_2, and would not result in an increase in inspiratory CO_2.

KEY FACTS: CO_2 REBREATHING

- Rebreathing of CO_2, as demonstrated by an elevated $FiCO_2$, primarily occurs as a result of equipment malfunction.
- Causes of high inspired CO_2 include expiratory or inspiratory unidirectional valve failure and exhaustion of the CO_2 absorbent.
- Expiratory and inspiratory valves allow for the unidirectional flow of gas and prevent rebreathing.

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50. ANSWER: C

Anesthetic machine checks are extremely important. Multiple studies over the past several decades have shown that adverse patient outcomes are associated with improper checking of anesthetic equipment. The Australian Incident Monitoring Study published in 1993 reviewed one of the largest databases of anonymously reported adverse events and found that approximately 21% of these had a lack of machine check as the main contributing factor. A more recent analysis of the anesthetic closed claims database published in 1998 placed anesthetic gas delivery equipment-related adverse events at 2% of all closed claims, with 75% of these due to equipment misuse or improper checking. This decrease in incidence may be in large part due to the fact that most major anesthetic societies have released guidelines on the importance of machine checks and anesthetic checklists.

In 2008 the American Society of Anesthesiologists (ASA) released updated recommendations on preanesthetic checkout procedures (Table 14.3).

In regards to the question above, verifying the presence of auxiliary oxygen cylinders is recommended by the ASA, but the presence of an air cylinder is not required. The other answer choices are all part of the recommended preanesthetic checkout.

KEY FACTS: ANESTHESIA MACHINE CHECKS

- Anesthesia machine checks are important in reducing equipment-related morbidity and mortality
- Preanesthetic checkout procedures are outlined in the ASA recommendations and include verifying an oxygen supply, suction, oxygen alarms, and a leak test.

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Table 14.3 ANESTHESIA MACHINE CHECKOUT PROCEDURES

Verify auxiliary oxygen cylinder and self-inflating manual ventilation device are available & functioning.
Verify patient suction is adequate to clear the airway.
Turn on anesthesia delivery system and confirm that AC power is available.
Verify availability of required monitors, including alarms.
Verify that pressure is adequate on the spare oxygen cylinder mounted on the anesthesia machine.
Verify that the piped gas pressures are at least 50 psig.
Verify that vaporizers are adequately filled and, if applicable, that the filler ports are tightly closed.
Verify that there are no leaks in the gas supply lines between the flowmeters and the common gas outlet.
Test scavenging system function.
Calibrate, or verify calibration of, the oxygen monitor and check the low oxygen alarm.
Verify carbon dioxide absorbent is not exhausted.
Perform breathing system pressure and leak testing.
Verify that gas flows properly through the breathing circuit during both inspiration and exhalation.
Document completion of checkout procedures.
Confirm ventilator settings and evaluate readiness to deliver anesthesia care.

Adapted from *2008 ASA Guideline for Designing Pre-Anesthesia Checkout Procedures*, available at http://www.asahq.org/~/media/For%20Members/Standards%20and%20Guidelines/FINALCheckoutDesignguidelines.ashx

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51. ANSWER: D

Electrocautery works by creating a circuit between the target tissue on a patient and an electrosurgical generator. The current is focused at a narrow point, which results in heat conduction, allowing the instrument to cut and/or coagulate tissue. The excess energy is dispersed through the patient onto a grounding pad that has a much larger surface area than the electrocautery device and is therefore able to disperse the heat as it is taken back to the electrosurgical unit and grounded.

In some cases, burns can be caused due to excessive heat generated by the grounding pad. This can be prevented by decreasing the duration of electrocautery, using a larger grounding pad to disperse the heat over a larger area, and improving contact between the grounding pad and the patient.

Use of conductive fluid (such as saline, as opposed to glycine or distilled water) during arthroscopic procedures creates the need for higher currents to achieve the same desired cutting or coagulation effect, because the current is dispersed by the fluid. This can result in excessive heat generation at the grounding pad site, which can then burn the patient.

Another practice that should be avoided is placing two grounding pads on the same limb, or on opposite limbs, as this can generate a significant amount of heat within close proximity, also resulting in a burn. If two grounding pads are to be used, they should be placed far away from each other. Newer grounding pads able to detect the amount of heat generated by the grounding pad have been created, and some electrosurgical units are capable of switching back and forth between two grounding pads to prevent either one from overheating.

Electrosurgical units can also cause burns by the creation of aberrant conduction pathways in patients who have previously implanted metallic hardware. One way to reduce the risk of burns occurring at or near the sites of implanted hardware is to ensure that the grounding pad are placed away from the implants.

KEY FACTS: ELECTROSURGICAL UNITS

- Electrosurgical unit burns can be caused by excessive heat generated by the grounding pad.
- The risk of grounding pad burns can be reduced by ensuring good contact between the patient and the grounding pad, using a large grounding pad, and avoiding higher-than-necessary currents and long durations of electrocautery.
- If two grounding pads are used, they should be placed away from one another.
- Grounding pad placement should take into account any prior implanted metallic hardware that the patient may have.

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52. ANSWER: A

In an awake patient, core body temperature correlates well with brain temperature. However, under anesthesia, a patient's thermal autoregulatory mechanisms are abolished, and this may result in a temperature gradient across the patient's body.

Temperature is normally regulated by the hypothalamus, which causes peripheral vasoconstriction and shivering in response to hypothermia. These mechanisms are abolished under anesthesia and the vasodilation caused by most anesthetic agents often results in a drop in core body temperature. This decrease is usually 1 to 2 degrees C over the first hour, and without the use of warming devices, gradually an additional 3 to 4 degrees C until reaching a point of equilibrium. This decrease is primarily due to redistribution of core body heat to the periphery as blood vessels dilate, and can be explained by the convective, conductive, evaporative, and radiative loss of heat in the operating room environment.

The lack of temperature regulation under anesthesia can be utilized during surgery in maneuvers such as hypothermic circulatory arrest. The goal of inducing hypothermia in these cases is to provide brain protection by reducing the metabolic demand of tissues during periods of ischemia. However, this makes it very important to monitor temperature in a way that the measured temperature correlates well with the temperature of the brain.

A study by Stone et al. published in *Anesthesiology* measured core temperature at various sites under bypass and correlated them with brain temperatures and found that brain temperatures best matched temperatures measured in the nasopharynx, esophagus, and pulmonary artery. Rectal temperatures have a slow response to temperature changes and do not accurately reflect core temperature or brain temperature. Other inferior temperature monitoring sites include the axillae, bladder, and tympanic membrane.

KEY FACTS: TEMPERATURE REGULATION

- Anesthesia inhibits the body's normal temperature regulatory mechanisms.
- Heat is redistributed during anesthesia from the core to the periphery.
- Nasopharyngeal, esophageal, and pulmonary artery temperatures correlate best with brain temperatures during cardiopulmonary bypass.

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53. ANSWER: B

There are two types of oxygen delivery systems: variable and constant FiO_2 systems. A variable system, also known as a low-flow system, is a system in which the amount of gas delivered may be less than the minute ventilation of the patient. For moments when the minute ventilation exceeds that of the oxygen delivery system, room air may be entrained, thus reducing the amount of FiO_2 delivered. In these systems the amount of FiO_2 delivered varies during the patient's respiratory cycle. Examples of variable FiO_2 systems include nasal cannulae and facemasks without a reservoir.

Constant FiO_2 systems, also known as high-flow oxygen delivery systems, are systems where the amount of oxygen delivered exceeds the minute ventilation of the patient. This allows for a fixed fraction of oxygen to be delivered to the patient. A few examples of a constant FiO_2 system include facemasks with a reservoir (such as nonrebreathing masks) and high-flow oxygen masks.

Nasal cannulae are a type of variable FiO_2 system that uses the nasal pharynx as a small reservoir (approximately 50 mL). Due to the small size of the reservoir, patients easily entrain room air with each breath, making this device a variable FiO_2 or low-flow system. Each liter of oxygen flow through a nasal cannula increases FiO_2 by approximately 3% to 4%. Therefore, at 6 L/min, the maximum FiO_2 is approximately 45%.

KEY FACTS: OXYGEN DELIVERY DEVICES

- Oxygen delivery devices are categorized as variable or constant oxygen delivery systems.
- Nasal cannula is considered a variable oxygen delivery system, with a maximum FiO_2 of about 50%.
- The presence of a reservoir allows for administration of a constant FiO_2. Examples of such systems include the nonrebreather oxygen mask and high-flow oxygen masks.

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54. ANSWER: A

Pressure support ventilation is a mode of ventilation that allows the patient to determine the respiratory cycle duration, respiratory rate, and inflation volume. This mode of

ventilation works by setting a preselected trigger, based either on pressure or flow. When the patient reaches that specific trigger, the ventilator augments the patient's inspiration by delivering a constant preset amount of pressure. When the patient's flow rate drops below 25% of the peak inspiratory flow rate, the ventilator's augmented pressure then ceases, allowing the lungs to deflate.

Pressure support ventilation allows the patient to dictate the duration and frequency of his or her respiratory cycle, which allows for greater synchrony with the ventilator. It also allows the patient to autoregulate his or her own inflation volume and decreases the work of breathing as compared to spontaneously breathing on a ventilator.

Autotriggering occurs when the flow or pressure trigger of the ventilator is reached, resulting in an augmented breath without the patient actually initiating that breath. This can be caused by surgical manipulation, and sometimes even by cardiac oscillations.

In the case described above, the pressure support ventilation is being autotriggered, as can be seen by the patient becoming apneic when the pressure support is turned off. Cheyne-Stokes respiration describes a breathing pattern that alternates between apnea and tachypnea. In this case, the patient is apneic only when the ventilator is switched off, and he does not show the prolonged apnea followed by tachypnea that is characteristic of Cheyne-Stokes breathing. Opioids cause a change in the threshold at which carbon dioxide drives breathing. An opioid overdose would result in respiratory depression with a decrease in respiratory rate, and does not explain the respiratory rate of 40 while on pressure support ventilation. Hypocapnia is usually the result of hyperventilation, but this would not explain an increased respiratory rate on pressure support ventilation. Hyperglycemia does not affect the respiratory rate.

KEY FACTS: PRESSURE SUPPORT VENTILATION

- Pressure support ventilation allows a patient to determine the respiratory cycle duration, respiratory rate, and inflation volume.
- Pressure support triggers can be based on either inspiratory flow or inspiratory pressure.
- Autotriggering occurs when flow or pressure triggers are reached without actually being initiated by the patient.
- Pressure support decreases the work of breathing as compared to spontaneously breathing on the ventilator.

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55. ANSWER: C

Anesthesia machines are equipped with a number of devices intended to prevent the administration of a hypoxic mixture of gas. Older anesthesia machines are equipped with a fail-safe or nitrous oxide shutoff valve. These valves are kept open by a threshold pressure of oxygen, and once oxygen falls below that threshold, these valves close, thereby cutting off the supply of nitrous oxide. This prevents the administration of a hypoxic mixture of gases.

Newer anesthesia machines are equipped with flow-proportioning devices, also called oxygen failure protection devices or balance regulators. These devices may be electronic, pneumatic, or mechanical, and are similar to fail-safe valves in their goal of preventing delivery of hypoxic gas mixtures. However, unlike fail-safe valves, they are capable of allowing a variable amount of nitrous oxide, depending on the oxygen pressure. If the oxygen pressure is too low, these valves also shut off the nitrous oxide supply completely to prevent administration of a hypoxic mixture. These systems typically allow no less then 23% to 25% FiO_2, assuming the components are working correctly, the supply gases are appropriate, and there is no leak downstream from the proportioning system. Failure of these devices could allow a hypoxic mixture of gas to be administered to the patient.

Low gas flows can result in delivery of a hypoxic gas mixture, but only if the delivered oxygen flow fails to meet the patient's oxygen consumption. In this scenario, 200 mL/min of oxygen is being delivered, which may be below the amount that the patient requires. More important is the fact that the flow of nitrous oxide would not be allowed to be 1 L/min if the oxygen flow was only 200 mL/min, unless the flow-proportioning device had malfunctioned or failed.

Although functional residual capacity is reduced during laparoscopic surgery due to increased intra-abdominal pressures, and this can be a cause of both hypoxemia and hypoventilation resulting in hypercarbia, there is no causal relationship between reduced functional residual capacity and an FiO_2 of 17%.

If there was an oxygen supply failure in the presence of a functioning flow-proportioning system, there would also be a decrease in the amount of nitrous oxide that can be administered.

KEY FACTS: FLOW-PROPORTIONING SYSTEMS

- Flow proportioning systems decrease the amount of nitrous oxide that is allowed to be administered

depending on the oxygen flow to prevent the administration of a hypoxic mixture.
- Fail-safe devices differ from flow-proportioning systems in that they completely shut off nitrous oxide once oxygen pressure drops below a certain threshold.
- Flow-proportioning devices may be mechanical, pneumatic, or electronic.

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56. ANSWER: A

Anesthetic gas scavenging systems are located on all modern anesthesia machines. There are two types of scavenging systems, open and closed. The purpose of the anesthetic scavenging system is to vent away the excess gas and anesthetic vapors, which helps reduce air pollution in the operating room. If a patient at a steady state of anesthesia is receiving a total fresh gas flow of 5 L/min, then 4.75 to 4.8 L/min would need to be removed by the scavenging system (5 L minus oxygen consumption of 200 to 250 mL/min), or else this would result in increased pressure in the anesthetic circuit and barotrauma.

Scavenging systems are designated as open when they are open to the atmosphere. This prevents the need for pressure relief valves since excess pressure is vented to the atmosphere. In open systems, negative pressure results in the entrainment of room air, preventing the buildup of negative pressure in the breathing circuit. Closed scavenging systems require both negative and positive pressure relief valves to prevent either excess positive or negative pressure from building up.

Scavenging units can also be classified as active or passive. As described by the nomenclature, passive units allow gas to move through the unit passively, whereas active units require the use of suction. Active units require both a negative pressure relief valve to prevent excess negative pressure buildup and a positive pressure relief valve to relieve excess positive pressure and barotrauma to the patient. Passive units require only a positive pressure relief valve, as there is no risk from negative pressure from the system being attached to vacuum.

Failure of the negative pressure relief valve in a closed scavenging unit would result in excess gas being scavenged from the unit. The negative pressure could also be transmitted to the patient if the fresh gas flows were not high enough. The scenario above demonstrates this phenomenon, manifesting as a high fresh gas flow requirement.

Failure of the positive pressure relief valve would result in excess inflation of the reservoir bag, and potentially in barotrauma if the adjustable pressure-limiting (APL) valve were also closed. The APL valve would be irrelevant if the patient were being mechanically ventilated.

Neither an open nor a passive scavenging system could be responsible for the scenario above, as there is no suction and no reason to have excess gas drawn out of the system, and therefore no need for a negative pressure relief valve.

KEY FACTS: SCAVENGER SYSTEMS

- Scavenger systems vent excess gas from the anesthetic circuit.
- Closed systems require both positive and negative pressure relief valves to prevent administration of positive or negative pressure to the patient.
- Open systems do not require pressure relief valves.
- Active scavenger systems use a vacuum and require both positive and negative relief systems; passive scavenger systems require only a negative relief system.

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57. ANSWER: B

IMV is a mode of ventilation that provides partial ventilation support. It was designed to combat the problem of incomplete emptying of the lungs with rapid breathing during assist control ventilation. IMV allows for either pressure- or volume-controlled ventilation with a set frequency, like assist control, but allows spontaneous breaths in between controlled ventilation breaths. The ability to take spontaneous breaths helps prevent lung overinflation during periods of rapid breathing.

However, during the periods of spontaneous breathing the patient must combat the resistance of breathing through the endotracheal tube and ventilatory circuit, which both make spontaneous breathing more difficult to tolerate. Newer mechanical ventilators are able to provide support during spontaneous breaths.

With demand-flow IMV, a pressurized valve opens once the patient surpasses a threshold negative pressure as the patient is taking a spontaneous breath. The negative pressure

opens a valve that allows gas to flow toward the patient, thus allowing the patient to take a spontaneous breath. This differs from continuous-flow IMV, where there is no valve and gas is able to flow freely during any inspiratory effort that the patient makes.

Demand-flow IMV has the disadvantage that it increases the work of breathing because the patient must be able to provide enough negative pressure to open the inspiratory valve. This valve also increases the work of expiration. Although it avoids these disadvantages of demand-flow IMV, continuous-flow IMV has the disadvantage that it requires continuous gas flows through the circuit.

Cardiac output is affected by all types of positive-pressure ventilation, including IMV. Positive-pressure ventilation may increase or decrease cardiac output, depending on the effects on ventricular preload and afterload. Although positive-pressure ventilation usually results in augmented cardiac function in patients with left ventricular dysfunction, these patients have worsened cardiac output with IMV, and it should generally be avoided in this group of patients.

KEY FACTS: INTERMITTENT MECHANICAL VENTILATION

- IMV allows for spontaneous breaths in between mechanically ventilated breaths.
- IMV has the advantage that it helps prevent lung overinflation during periods of tachypnea.
- Demand-flow IMV increases the work of breathing compared to continuous-flow IMV.
- IMV decreases cardiac output in patients with left ventricular dysfunction and should be avoided in this group of patients.

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58. ANSWER: C

Oxygen cylinders come in many different sizes. E cylinders are the most commonly used in the medical practice. These cylinders can hold a maximum of 660 L at 1,900 to 2,200 psi. A size E compressed gas cylinder containing oxygen weighs approximately 5.90 kg empty and 6.76 kg full.

The amount of time you can use an oxygen tank depends on a few variables, such as how much oxygen is present in the tank and at what rate the oxygen is flowing. This can be calculated using ***Boyle's law***, which states that for a fixed mass at a given temperature, the product of pressure and volume is constant. Using this relationship, and given that oxygen exists only in a gaseous state within the cylinder, we can estimate the remaining volume in an oxygen cylinder as a proportion of the original volume.

$P_1 \times V_1 = P_2 \times V_2$. Where P_1 = initial pressure and P_2 = final pressure and V_1 = initial volume and V_2 = final volume

$$\text{So } P_1/P_2 = V_2/V_1$$

So in this case 1,000 psi/~2,000 psi = V_2/660 L
So V_2 = 330 L
Flow = volume / time or Q = V/t
In this case Q = 10 L/min = 330 L/t
So t = 33 minutes

Boyle's law can be rearranged to the following: $P_2/P_1 = V_2/V_1$ or

$$(P_2 \times V_1/P_1)/Q = t, \text{ where } V_2 = Q \times t$$

A quick way to determine the time remaining would be if we were to round V_1 = 660 L to 600 L and P_1 = 1,900–2200 psi to 2000 psi.

This would make the equation: $P_2/Q \times 0.3 = t$, which is easier to remember.

Using the numbers in the above question, $1000/10 \times 0.3 = 30$ minutes, which is close to 33 minutes.

KEY FACTS: OXYGEN CYLINDER VOLUME CALCULATION

- E cylinders can hold a maximum of 660 L at 1,900 to 2,200 psi.
- Boyle's law relates before-and-after pressures with before-and-after volumes at a constant temperature.
- Time remaining on an oxygen cylinder can be approximated by the equation $P_2/Q \times 0.3$.

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59. ANSWER: B

Desflurane differs from other commonly used volatile anesthetics in that the vapor pressure is much higher than the others, so high in fact that desflurane actually boils at room temperature.

Desflurane vaporizers are unique in that they heat desflurane to a temperature of 39 degrees C, raising the vapor

pressure to 2 atmospheres. Unlike typical variable-bypass vaporizers, no fresh gas flows through these vaporizers. Instead, pure desflurane vapor is released from the vaporizer to mix with fresh gas. The amount of vapor is determined by the total fresh gas flow rate as well as the concentration control dial.

Despite the uniqueness of the desflurane vaporizer, the concentration of desflurane delivered is still dictated by the same rules that can be applied to other volatile anesthetics. Higher temperatures would increase the vapor pressure of a volatile anesthetic, and a higher vapor pressure would mean a higher concentration of volatile anesthetic being emitted from the vaporizer. However, most modern vaporizers have mechanisms to maintain a constant temperature.

In a typical variable-bypass vaporizer, the ratio of carrier gas flow (flow through the vaporizer) as compared to bypass gas flow (flow that bypasses the vaporizer) also determines the concentration of delivered anesthetic. Increasing the amount of carrier gas that flows through the vaporizer or decreasing the amount of gas that bypasses the vaporizer would increase the concentration of delivered anesthetic.

With all volatile anesthetics, as altitude increases, the required percent concentration of anesthetic increases. Although the potency of anesthetics does not change with altitude (because the partial pressure required to produce anesthesia does not change), the concentration required (in %) increases as altitude increases, because a higher percentage of the reduced atmospheric pressure is required to deliver the same partial pressure as at sea level. With variable-bypass vaporizers, the vaporizer automatically compensates for this change, and no adjustment of the dial is necessary (even though the dial may be set to 1%, the delivered percent concentration will be higher, approximately matching the increased need).

This does not hold true for the desflurane vaporizer, however. Because it is pressurized, the desflurane vaporizer delivers an approximately constant percentage of desflurane, regardless of altitude. The implication of this is that if you are using desflurane at high altitudes, you must remember to increase the percentage dialed to achieve the same depth of anesthesia as at sea level.

KEY FACTS: ANESTHESIA VAPORIZERS

- Desflurane has the highest vapor pressure of the commonly used volatile anesthetics.
- Increased temperatures increase vapor pressure, resulting in a higher anesthetic concentration delivered.
- With variable-bypass vaporizers, increasing the ratio of carrier gas to bypass gas increases the concentration of volatile anesthetics delivered.
- High altitudes require an increased percentage concentration to be delivered to achieve the same depth of anesthesia as at sea level.
- Unlike variable-bypass vaporizers, the desflurane vaporizer does not automatically compensate for altitude and needs to be dialed at a higher concentration to achieve the same depth of anesthesia as at sea level.

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60. ANSWER: B

Soda lime CO_2 absorbers contain NaOH, KOH, H_2O, and Ca(OH)2. The reaction with CO_2 is as follows:

$$CO_2 + H_2O \rightarrow H_2CO_3$$

$$H_2CO_3 + 2NaOH \rightarrow Na_2CO_3 + 2H_2O$$

$$H_2CO_3 + 2KOH \rightarrow K_2CO_3 + 2H_2O$$

$$Na_2CO_3 + Ca(OH)_2 \rightarrow 2NaOH + CaCO_3$$

$$\text{Or } K_2CO_3 + Ca(OH_2) \rightarrow 2KOH + CaCO_3$$

However, when soda lime absorbers are desiccated, they can react with volatile anesthetics to produce toxic compounds. The toxic compounds that can be produced include compound A and carbon monoxide. Compound A, also known as fluoromethyl-2,2-difluoro-1-(trifluoromethyl)-vinyl ether, is produced by the reaction of sevoflurane with soda lime at low fresh gas flows. While not demonstrated in humans, Compound A has been shown to be toxic in rats.

All volatile anesthetics flowing through a desiccated soda lime absorber will produce carbon monoxide. Desflurane has one of the highest carbon monoxide productions of the volatile anesthetics.

Another important product of the CO_2 absorbers is heat. Baralyme was taken off the market because it was capable of producing temperatures as high as 400 degrees and was a cause of operating room fires.

Desiccated CO_2 absorbers are not responsible for the production of cyanide. Cyanide toxicity may occur as a complication of prolonged sodium nitroprusside use.

Dichloroacetylene is a neurotoxin that is produced by the reaction between soda lime and trichloroethylene, a chemical solvent and degreaser that was used as a volatile anesthetic from the 1930s through the 1970s, but was phased out of use as halothane became more popular.

KEY FACTS: CO_2 ABSORBERS

- Compound A is a substance shown to be toxic in rats that is produced by sevoflurane reacting with soda lime.
- Soda lime, when desiccated, can produce carbon monoxide with all volatile anesthetics, although desflurane has the highest carbon monoxide production.
- CO_2 absorbers are capable of generating high amounts of heat.

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61. ANSWER: A

Ventilators are equipped with multiple alarms. The most basic of these alarms detects disconnection from the ventilator. The ventilator disconnect alarm is a low-pressure alarm that works by detecting inspiratory pressure. This alarm is generally set slightly below the patient's peak inspiratory pressure. If the patient gets disconnected from the ventilator, this pressure threshold would not be reached and the ventilator would detect this as a disconnection from the ventilator and sound the alarm.

The low-pressure alarms have multiple faults to them. If the ventilator circuit is partially occluded, the pressure in the circuit could be higher due to the occlusion rather than the patient's pulmonary resistance. In this scenario, the ventilator alarm would not trigger because the inspiratory pressure would not drop below the alarm threshold. If the pressure alarm threshold is set too low, then a disconnection could also go undetected. Partial disconnects could also go undetected if the pressure alarm threshold is set too low. Moisture in the circuit could build up around the pressure sensor, which would cause it to detect higher pressures and also not alarm appropriately.

Newer ventilators have other alarms that can help detect ventilator disconnects, including tidal volume alarms, which are able to detect exhaled tidal volumes. The ventilator would alarm if the exhaled tidal volume is low. Capnography is another method used to detect disconnection from the ventilator.

KEY FACTS: VENTILATOR DISCONNECT ALARMS

- Ventilator disconnect alarms work by detecting low inspiratory pressure, low exhaled tidal volumes, or low end-tidal CO_2.
- Partial occlusion or a partial disconnect can result in a failure to detect a ventilator disconnect.

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62. ANSWER: B

Oxygen pipeline crossover is a rare but potentially catastrophic event. Inhalation of pure nitrous oxide leads to rapid desaturation, which if unrecognized can lead to cardiac arrest, central nervous system damage, and death. There are multiple ways that the oxygen pipeline can be crossed with another gas line, including the filling of the wrong the gas in the main supply containers or misconnecting the pipeline at any point as it travels from the facility's main gas containers to the anesthesia machine.

It is important to recognize this event quickly. This is helped with newer gas analyzers that allow for the detection of inspired oxygen and nitrous oxide. Pipeline crossover can easily be recognized during preoxygenation. If nitrous oxide is detected during preoxygenation, then the most likely cause is a pipeline crossover.

Steps that can be taken to administer oxygen during a pipeline crossover include the following: bag-mask ventilation with an oxygen cylinder or room air, disconnecting the oxygen pipeline and opening up the backup oxygen cylinder, and administering 100% oxygen or air.

Opening up the backup oxygen cylinder without disconnecting the oxygen pipeline supply would not prevent the administration of the crossed-over gas because the gas flow will still be preferentially taken from the pipeline supply. Using the auxiliary oxygen outlet would also not prevent the administration of the crossed-over gas because the auxiliary oxygen outlet receives its gas from the oxygen pipeline.

KEY FACTS: OXYGEN SUPPLIES

- Oxygen pipeline crossovers can be spotted by detecting the administration of nitrous oxide when attempting to administer 100% oxygen.

- The auxiliary oxygen supply receives its oxygen from the pipeline oxygen supply.
- Backup oxygen cylinders do not work in the presence of a connected oxygen pipeline with appropriate pipeline pressure.

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63. ANSWER: C

Electrical safety in the operating room is important for the patient as well as all healthcare personnel in the operating room. Electrical shocks can cause muscle paralysis, seizures, and cardiac arrest. Electrical shocks are the result of completion of a circuit between two conductive materials with different voltage potentials. Most electrical supply systems, including the systems found in most homes and businesses, are grounded systems. These systems have a live conductor that is connected to a ground contact, which provides a root mean square potential difference of 120V. When a grounded person contacts the live conductor, that person completes a circuit with a voltage potential difference and receives a shock.

Most operating rooms use isolated power systems. These systems are ungrounded power systems with two live conductors that are isolated from the ground. Because they are isolated from the ground there is not a voltage potential difference between the two conductors. If a grounded patient were to come in contact with one of these conductors, then a shock would not occur because a circuit would not be completed. A grounded patient would need contact with both conductors to complete the circuit. However, if one conductor became grounded through the use of faulty equipment, then a grounded patient could receive a shock if the other conductor was contacted. Intentionally grounding the patient would place the patient at a higher risk of shock in the operating room environment.

The isolated power system provides an extra level of electrical safety in the operating room. Most operating rooms are designated wet environments, which requires the use of isolated power systems because these environments are full of opportunities to be grounded, placing individuals at higher risk for shock in a nonisolated system. Dry environments do not require the use of isolated power systems.

KEY FACTS: ELECTRICAL SAFETY

- Operating rooms use isolated rather than grounded electrical systems.
- Both conductors in an isolated electrical system need to come in contact with an individual to complete a circuit and result in shock.
- If one conductor in an isolated system becomes grounded, contact with the other conductor and the ground would result in a shock.
- Grounded electrical systems require contact with only one conductor and the ground to receive a shock.

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64. ANSWER: C

Carbon monoxide poisoning is an uncommon but known complication of administering inhalation anesthetics. Carbon monoxide is produced by a chemical reaction between a volatile anesthetic and desiccated hydroxide-containing CO_2 absorbers. The amount of carbon monoxide produced can be significant. The most carbon monoxide is produced by the reaction of desflurane with Baralyme. Sevoflurane and isoflurane produce lower amounts of carbon monoxide, and soda lime produces less carbon monoxide than Baralyme.

The typical clinical scenario usually occurs during the first case on Monday morning. If fresh gas flows remain on through an entire weekend, the granules within the CO_2 absorber can become desiccated. This can go unrecognized, resulting in carbon monoxide production during the first case. Only desiccated CO_2 absorbers produce any significant amount of carbon monoxide. In fact, rehydrating a CO_2 absorber reduces the amount of carbon monoxide produced by the CO_2 absorber.

Newer CO_2 absorbers that do not contain hydroxide, and do not produce clinically significant amounts of carbon monoxide. Low flow anesthesia in the presence of a hydrated CO_2 absorber also does not produce clinically significant amounts of carbon monoxide.

Changing the CO_2 absorbent canister can help prevent the production of carbon monoxide. Since the reaction that results in carbon monoxide production occurs only with the reaction of volatile anesthetics with desiccated absorbent

granules, changing the canister helps to prevent carbon monoxide poisoning.

While flushing the circuit with oxygen might drive some carbon monoxide into the scavenging system, it would not prevent carbon monoxide poisoning, and in fact may worsen it by further desiccating the absorbent granules, increasing the likelihood of carbon monoxide production. Low flows, by contrast, would reduce the production, but may not adequately flush out carbon monoxide if it was already being produced.

KEY FACTS: PREVENTION OF CARBON MONOXIDE POISONING IN THE OR

- Carbon monoxide is produced by a reaction between volatile anesthetics and desiccated hydroxide-containing CO_2 absorbent granules.
- Of the modern volatile anesthetics, desflurane produces the most carbon monoxide.
- Baralyme produces more carbon monoxide than soda lime.
- CO_2 absorbers become desiccated with prolonged high fresh gas flows through the circuit or improper maintenance.
- Frequent changing of canisters, lower fresh gas flows, and use of soda lime rather than Baralyme can help prevent carbon monoxide production and poisoning.

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15.

AIRWAY MANAGEMENT

Joe Meltzer, MD

1. Compared to nonsmokers, smokers have an increased rate of

A. All pulmonary complications
B. Infectious pulmonary complications
C. Intensive care unit (ICU) admission after surgery
D. Prolonged mechanical ventilation after surgery
E. All of the above

2. Smoking is an independent risk factor for which of the following events occurring with management of the airway?

A. Oxygen desaturation
B. Lower preoperative oxygen saturation
C. Bronchospasm
D. Dental injury
E. Mucus plugging

3. The rate of failed intubation, or inability to place an endotracheal tube, is approximately 0.05% for surgical patients. The rate of difficult intubation (requiring multiple attempts) is

A. 0.5% to 1%
B. 1% to 4%
C. 4% to 8%
D. 8% to 15%
E. Greater than 15%

4. The modified Cormack-Lehane grading system of the laryngoscopic view and its modifications are used to grade the visualization of the vocal cords, glottis, and epiglottis at the time of laryngoscopy. A grade IIb view as classified by the original Cormack-Lehane system means the operator can visualize

A. More than 50% of the glottic opening
B. Posterior part of the glottis and arytenoids
C. Arytenoids, but not the glottis
D. The epiglottis only, which can be lifted from the posterior pharyngeal wall
E. The epiglottis only, which cannot be lifted from the posterior pharyngeal wall

5. The Mallampati classification focuses on the visibility of oropharyngeal structures when the patient is examined in which of the following positions?

A. Supine, mouth fully open, tongue protruded, with phonation
B. Semirecumbent, mouth fully open, tongue protruded, without phonation
C. Sitting, mouth opened, tongue in neutral position, without phonation
D. Sitting, mouth fully opened, tongue protruded, without phonation
E. Sitting, mouth fully opened, tongue protruded, with phonation

6. Which of the following patient presentations presents with the LEAST risk of difficult intubation?

A. 67-year-old woman, 82 kg, thyromental distance 7 cm, mouth opening 3 cm, Mallampati II, prominent incisors
B. 45-year-old man, 145 kg, thyromental distance 5 cm, mouth opening 6 cm, Mallampati III, short neck with limited extension
C. 56-year-old man, 72 kg, thyromental distance 5 cm, mouth opening 5 cm, Mallampati III, poor dentition
D. 52-year-old man, 45 kg, thyromental distance 5 cm, mouth opening 5 cm, Mallampati II, history of neck radiation, limited submandibular compliance
E. 34-year-old woman, 72 kg, thyromental distance 6 cm, mouth opening 5 cm, Mallampati II, high-arched palate, prominent incisors with two maxillary incisors missing

7. Inability to ventilate will eventually lead to hypoxemia and hypercarbia. The rate of difficult mask ventilation is estimated to be between 0.1% and 5%. Which of the following has NOT been associated with difficult mask ventilation?

A. Lack of teeth
B. Age more than 55 years
C. Presence of beard
D. History of snoring
E. Male sex

8. The development of hypoxemia within 10 minutes of endotracheal intubation must be assumed to be due to esophageal intubation UNLESS

A. The tube can be visualized passing through the vocal cords and there is a normal waveform by capnography
B. Bilateral breath sounds can be auscultated in the presence of chest wall expansion
C. There is normal chest wall compliance with hand-bag ventilation
D. There is an absence of breath sounds over the stomach
E. None of the above

9. Which of the following structures in the infant and adult respectively determine the correct size for an endotracheal tube?

A. Glottis; vocal cords
B. Vocal cords; vocal cords
C. Cricoid cartilage; vocal cords
D. Vocal cords; cricoid cartilage
E. Cricoid cartilage; thyroid cartilage

10. An airway fire is one of the most serious complications of laser surgery. The "fire triad" describes the three necessary components: an oxidizing source (endotracheal tube), an ignition source (laser), and oxygen. To reduce the risk of airway fire during laser surgery, many specialized tubes have been created. Which of the following statements is INCORRECT?

A. Wrapped Teflon/silicon/aluminum tubes (Laser-Shield II Tracheal Tubes) are designed for use with CO_2 and KTP lasers. However, part of the tube and cuff is unprotected, so the tube must be wrapped in cottonoids and kept moist to reduce fire risk.
B. Flexible stainless steel tubes (Laser-Flex Tracheal Tubes) and red rubber tubes wrapped with copper tape (Sheridan Laser Trach Tubes) are designed for use with the Nd-YAG laser but do not hold up well when used with CO_2 or KTP lasers.
C. Laser tube cuffs often contain methylene blue crystals and should always be filled with saline. The methylene blue acts as a marker for cuff rupture or perforation due to laser damage. Also, fluid acts as a heat sink and makes the cuff more difficult to perforate.
D. Positive end-expiratory pressure (PEEP) can reduce the risk of fire in PVC tubes when CO_2 lasers are in use.
E. Nitrogen, air, or helium should be used to reduce the oxygen concentration to the lowest level possible while still providing adequate oxygenation.

11. You are called to the bedside of a patient in the post-anesthesia care unit (PACU) with stridor and moderate respiratory distress who underwent a total thyroidectomy for a multinodular goiter that day. The patient was asymptomatic upon admission to the PACU and had been alert until 15 minutes ago. As you review the chart, obtain a brief history, and examine the patient, the patient's distress worsens and oxygen saturation begins to fall despite receiving 100% inspired oxygen. The most likely cause of her symptoms is

A. Hypocalcemia
B. Bilateral recurrent laryngeal nerve injury
C. Postextubation stridor
D. Bilateral superior laryngeal nerve injury
E. Hematoma

12. Which of the following has the greatest effect on the resistance of a breathing circuit?

A. One-way valves
B. CO_2 absorbent
C. Y-piece
D. Endotracheal tube
E. None of the above

13. You are called to evaluate a patient in the emergency department for severe airway swelling after administration of an angiotensin-converting enzyme (ACE) inhibitor. On examination the patient exhibits inspiratory "crowing" and expiratory stridor. The patient's oxygen saturation is slowly dropping despite the administration of an increased fraction of inspired oxygen. The most appropriate next step is to

A. Administer intravenous epinephrine and give oxygen via a nasal cannula

B. Administer high-dose steroids and request an emergent ENT consult
C. Start an intravenous line and induce general anesthesia in preparation for intubation
D. Assess the patient's airway, call for help, administer topical anesthetic to the airway for an awake fiberoptic intubation with surgical backup for a possible tracheostomy
E. Transfer the patient to the intensive care unit for close monitoring

14. An 85-year-old, 65-kg man is brought to the operating room from a nursing home for an exploratory laparotomy, lysis of adhesions, and possible small bowel resection under general anesthesia. You have chosen propofol as your induction agent. With regard to propofol, which of the following statements is INCORRECT?

A. The appropriate induction dose of propofol for a general anesthetic is 2.0 to 2.5 mg/kg.
B. Because propofol is quickly metabolized, a continuous infusion can be used with little drug accumulation, allowing for rapid emergence from general anesthesia.
C. Propofol has antiemetic effects and can be used to treat postoperative nausea and vomiting.
D. Propofol causes respiratory depression in all patients and pain upon injection in 10% to 50% of patients.
E. Propofol is metabolized by the liver and excreted from the body as glucuronide and sulfate conjugates primarily in the urine. Because clearance of propofol exceeds hepatic blood flow, extrahepatic clearance mechanisms have also been proposed.

15. Awake intubation may be facilitated by administration of local anesthesia to the upper airway and by intravenous sedatives, when safe. Which of the following statements regarding awake intubation is CORRECT?

A. Premedication with cholinergic medications serves to decrease secretions.
B. Topical anesthesia can be administered via atomizers, pledgets, nebulization, or "swish and spit" of solutions containing lidocaine. Absorption is minimal from the mucosa and therefore the toxic dose of local anesthetic is less of a concern.
C. The superior laryngeal nerve supplies sensory fibers to the vocal cords and can be blocked to reduce the risk of vomiting and gagging.
D. Cocaine is the preferred drug for anesthetizing the nasal mucosa.
E. The tracheal mucosa can be anesthetized with a transtracheal block. This can be performed by rapid injection of lidocaine through the cricothyroid membrane during inspiration.

16. A patient is brought to the operating room for exploration of presumed cardiac tamponade on postoperative day 1 after aortic valve replacement. Induction of general anesthesia, placement of an endotracheal tube, and positive-pressure ventilation in the presence of significant cardiac tamponade can potentially cause life-threatening hypotension for all the following reasons EXCEPT

A. Anesthetic-induced hypotension
B. Myocardial depression
C. Decreased venous return
D. Ventricular dysrhythmias
E. Increased intrathoracic pressure secondary to positive-pressure ventilation

17. Prolonged mechanical ventilation has multiple risks, including ventilator-associated pneumonia (VAP) and tracheal stenosis/malacia. Tracheal stenosis/malacia is thought to develop from decreased tracheal capillary blood flow from an overinflated cuff. What is the maximum recommended cuff pressure?

A. 5 to 15 mm Hg
B. 15 to 25 mm Hg
C. 25 to 35 mm Hg
D. 35 to 45 mm Hg
E. 45 to 55 mm Hg

18. A 25-year-old man is brought to the emergency room after a near-drowning. Witnesses saw him dive into a shallow pond while intoxicated. He hit his head, was unable to swim, and was then rapidly pulled from the pond by his family. He never lost consciousness yet appears to have aspirated some pond water. He is complaining of severe weakness in his arms and hands and cannot move his feet. The emergency department physician would like the patient intubated due to marginal oxygen saturation, presumed aspiration pneumonia, and anticipated surgery to stabilize the cervical spine. All of the following are true EXCEPT

A. Cervical alignment with manual in-line stabilization should be maintained during laryngoscopy.
B. An awake fiberoptic intubation should be attempted if the patient is cooperative.

C. The patient's head and neck should be stabilized in a neutral position by a rigid cervical neck collar and standard induction of anesthesia and intubation attempted.
D. Because the injury has already been sustained with neurologic sequelae, proceeding with a standard rapid sequence intubation and direct laryngoscopy is appropriate.
E. The use of succinylcholine is not contraindicated.

19. A patient in the intensive care unit has massive hemoptysis and pulmonary hemorrhage. You are asked to place a double-lumen endotracheal tube for lung isolation. Which of the following is CORRECT regarding lung isolation?

A. Double-lumen tubes are smaller than single-lumen tubes and are therefore more difficult to provide pulmonary toilet through.
B. It is necessary to know which lung is bleeding prior to placement of the double-lumen endotracheal tube in order to know which type of tube to place.
C. A bronchial blocker is equally efficacious for lung isolation during pulmonary hemorrhage.
D. A left double-lumen tube advanced into either the left or right mainstem bronchus will achieve lung isolation.
E. A single-lumen tube advanced into either the right or left mainstem bronchus is equally efficacious for lung isolation during pulmonary hemorrhage.

20. The potential advantage of the LMA-ProSeal over classic LMA is that the Pro-Seal LMA provides

A. Better seal at the epiglottis, thereby allowing for positive-pressure ventilation to be employed.
B. Conduit to permit gastric fluids to bypass the glottis
C. Conduit to facilitate blind or fiberoptic intubation
D. More flexible shaft that is resistant to kinking and thereby facilitates its use during oral, dental, or head and neck surgery
E. Lower-profile design that can easily be inserted into even awake patients

21. When lidocaine is used for topical anesthesia for airway management, which of the following is INCORRECT?

A. Most reports show that systemic absorption of topical lidocaine is limited.
B. Oral lidocaine that is swallowed, as opposed to spit out, can result in very high plasma concentrations because lidocaine is not subject to first-pass metabolism by the liver.
C. Lidocaine applied directly to the trachea results in much higher blood levels than lidocaine applied topically.
D. The toxic dose of intravenous lidocaine is 4 to 5 mg/kg and the toxic level of lidocaine is 5 to 6 mcg/mL.
E. Swallowing lidocaine in the setting of topical airway anesthesia can cause nausea and vomiting.

22. Respiratory gases have an effect on airway function. Which of the following statements is INCORRECT?

A. Hypercapnia causes bronchoconstriction.
B. Hypoxia enhances airway irritability.
C. Nitroglycerine directly relaxes airway smooth muscle.
D. Hypocapnia causes bronchoconstriction.
E. None of the above

23. The recurrent laryngeal nerve may be traumatized during surgery on the thyroid and parathyroid glands. All of the following are true EXCEPT

A. Pressure from the endotracheal tube or LMA can affect the function of the recurrent laryngeal nerve after surgery and anesthesia.
B. The right recurrent laryngeal nerve is injured twice as often as the left due to the higher-riding and larger-sized right lung.
C. Damage to the external branch of the superior laryngeal nerve during thyroidectomy is the most common cause of voice change.
D. When laryngeal spasm occurs, both the false and true cords lie tightly in the midline opposite each other.
E. Bilateral incomplete recurrent laryngeal nerve palsy is more dangerous than bilateral complete nerve injury.

24. Risk factors for aspiration of gastric contents at the time of airway management include all of the following EXCEPT

A. Emergency surgery
B. Higher ASA classification
C. Small bowel obstruction
D. Obesity
E. Inexperienced anesthetist encountering airway problems

25. Cricoid pressure (Sellick's maneuver) can be used in an attempt to

A. Reduce gastric distention during bag-mask ventilation
B. Reduce passive regurgitation of gastric contents

C. Improve laryngoscopic view by applying backward, upward, and rightward pressure
D. Occlude the esophagus against the C6 vertebra
E. All of the above

26. The process of preoxygenation/denitrogenation greatly increases the time to desaturation during intubation. The reasons for failure to achieve an FiO_2 close to 100% include leak, rebreathing of gases, and using systems incapable of delivering highly enriched oxygen. The main causes of circuit leak include all of the following EXCEPT

A. Beards
B. Edentulous patients
C. Nasogastric tubes
D. Incorrect facemask size
E. None of the above

27. Because pregnant women are at high risk for pulmonary aspiration, rapid sequence induction should be used whenever general anesthesia is needed for obstetric or nonobstetric surgery. Which of the following statements is INCORRECT?

A. Maximal preoxygenation can be achieved faster in pregnant than nonpregnant women because of increased alveolar ventilation.
B. Maximal preoxygenation can be achieved faster in pregnant than nonpregnant women because of decreased functional residual capacity.
C. During apnea, pregnant women become hypoxic faster than nonpregnant women due to decreased functional residual capacity.
D. During apnea, pregnant women become hypoxic faster than nonpregnant women due to increased oxygen consumption.
E. After the fifth month of pregnancy, the functional residual capacity (FRC) is decreased by 40% and oxygen consumption is increased by 80%.

28. If rheumatoid arthritis (RA) is severe, airway management may prove difficult. Which of the following may be a sign of a difficult airway in the RA patient?

A. Recent change in voice with stridor
B. A sense of fullness in the throat and tracheal deviation either by palpation or radiography
C. Flexion deformity of the cervical spine with radiculopathy
D. Temporomandibular joint ankylosis
E. All of the above

29. All of the following congenital syndromes are known for their grossly abnormal head and neck anatomy and possible difficult airway EXCEPT

A. Crouzon syndrome
B. Pierre Robin syndrome
C. Treacher Collins syndrome
D. Becker's muscular dystrophy
E. Goldenhar syndrome

30. Shortly after the induction of general anesthesia and during mask ventilation, bile-stained fluid filling the facemask is observed. Your next course of action should be all of the following EXCEPT

A. Turn the patient's head to the side.
B. Call for help.
C. Attempt to clear the pharynx of gastric fluid with a Yankauer suction.
D. Check the patient's vital signs.
E. Place the patient into the reverse Trendelenburg position.

31. During induction of general anesthesia and initial airway management, your patient becomes markedly rigid. Which of the following statements about postintubation rigidity is correct?

A. It is known as generalized hypertonus of skeletal muscle and usually occurs after rapid intravenous boluses of opioid antagonists.
B. It can occur with fentanyl, alfentanil, sufentanil, and remifentanil but most commonly occurs with morphine.
C. It generally involves only the abdominal and thoracic muscles.
D. It is more common in the elderly.
E. It is usually unaffected by muscle relaxants.

32. Negative-pressure pulmonary edema can occur at or around the time of extubation. All of the following statements are correct EXCEPT

A. It may occur in spontaneously breathing patients.
B. The inciting factor is inspiratory effort against a closed glottis, generating a negative intrathoracic pressure in excess of 100 cm H_2O.
C. Rib retraction, laryngospasm, and stridor may lead to this condition.
D. Furosemide should be administered rapidly to facilitate fluid removal.
E. Increases in left ventricular preload and afterload are part of the pathophysiologic development of pulmonary edema.

33. Laryngeal edema

A. Is an important cause of postextubation airway obstruction, especially in neonates and infants

B. Is most common when intubation lasts longer than 1 hour
C. Usually presents with stridor within 30 minutes after extubation, but may start as late as 6 hours after extubation
D. Can often be prevented or minimized with corticosteroid prophylaxis, and can be treated with racemic epinephrine
E. All of the above

34. Which of the following choices of endotracheal tube (ETT) size and position is most appropriate?

A. 12-month-old—3.0 ETT taped at 7 cm at the mouth
B. 2-year-old—4.5 ETT taped at 8 cm at the mouth
C. 3-year-old—4.5 ETT taped at 13 cm at the mouth
D. 6-year-old—6.5 ETT taped at 12 cm at the mouth
E. 10-year-old—7.0 ETT taped at 15 cm at the mouth

35. You are called to intubate an obtunded patient in the emergency department. Upon review of the chart you find one of the documents listed below. Which of these documents holds the greatest weight with regard to your next course of action in terms of intubation?

A. Living will
B. "Do not intubate" order in the chart
C. A healthcare surrogate, such as spouse or next of kin
D. A healthcare proxy/agent/power of attorney for healthcare
E. All are equal.

36. You are called to evaluate a patient in the medical intensive care unit with an ETT cuff leak. Your first course of action should be which of the following?

A. Review the most recent x-ray and order another.
B. Check the patient's vital signs and evaluate for immediate reintubation.
C. Suction the posterior oropharynx.
D. Deflate the pilot balloon.
E. Add additional air to the cuff.

37. You are called to the postanesthesia care unit to emergently intubate a patient for respiratory distress 6 hours postoperatively from a laparotomy. She was extubated without event in the operating room postoperatively. You struggle to intubate her and desaturation forces you to abandon your plan for a rapid sequence intubation. You mask ventilate her for some time with difficulty while you gather airway equipment and wait for help to arrive. You intubate the patient. A portable colorimetric end-tidal CO_2 detector shows color change, and you confirm bilateral breath sounds over each hemithorax and inaudible breath sounds over the stomach. Which of the following statements is correct?

A. Multiple breaths of detectable end-tidal CO_2 are required to confirm ETT placement.
B. The presence of bilateral breath sounds confirms ETT position.
C. Intubation of the esophagus will never produce end-tidal CO_2.
D. Only a chest x-ray can confirm proper ETT position.
E. None of the above

38. During laser surgery on the trachea under general endotracheal anesthesia, dark smoke appears in the bronchoscopic surgical field. The most appropriate initial action is which of the following?

A. Change to high-flow fresh gas flow with air.
B. Stop fresh gas flow.
C. Flood the field with water.
D. Clamp the endotracheal tube.
E. Remove the endotracheal tube.

39. Hypoxemia is defined as a partial pressure of oxygen in arterial blood (Pa_{O_2}) less than _____ mm Hg while breathing room air.

A. 50
B. 60
C. 70
D. 80
E. 100

40. Oxygen saturation varies with Pa_{O_2} in a _____ relationship and is affected by which of the following factors?

A. Linear; temperature, partial pressure of CO_2, barometric pressure, pH, cardiac output
B. Nonlinear; temperature, partial pressure of CO_2 in the arterial blood (Pa_{CO_2}), pH, 2,3-diphosphoglycerate concentration, barometric pressure
C. Nonlinear; temperature, partial pressure of CO_2 in the arterial blood (Pa_{CO_2}), pH, 2,3-diphosphoglycerate concentration
D. Linear; temperature and pH
E. None of the above

41. Retrograde intubation can be a useful technique for the difficult airway. It would be reasonable to consider it in all of the following situations EXCEPT

A. Trismus
B. Ankylosis of the mandible

C. Obese patient with a beard
D. Ankylosis of the cervical spine
E. Maxillofacial trauma

42. The ASA Difficult Airway Practice Guidelines offer tube exchangers as part of an extubation plan for patients who are difficult to intubate. While they can be lifesaving, they also may contribute to reintubation or failed intubation if not properly used. All of the following are true EXCEPT

A. Exchange catheters can be irritating to the airway, leading to uncontrollable coughing or bronchospasm.
B. Barotrauma, mucosal injury, or tension pneumothorax may develop from the catheter or through its use in jet ventilation.
C. The catheter may cause increased work of breathing.
D. The exchange catheter may be dislodged from the trachea during removal of the original endotracheal tube and can migrate into the esophagus, leading to an esophageal intubation.
E. Direct laryngoscopy should always be employed when using an exchange catheter.

43. When extubating a patient after cardiac surgery, all of the following criteria should be satisfied EXCEPT

A. Vital capacity more than 10 to 15 cc/kg
B. Negative inspiratory force more than 25 cm H_2O
C. Respiratory rate less than 25 breaths/minute
D. Rapid Shallow Breathing Index less than 200
E. $PaCO_2$ less than 48 torr, pH 7.32 to 7.45, PaO_2 more than 70 torr on an FiO_2 less than 50%

44. Severe postintubation hypertension should be avoided in all cases. In some patients it is particularly likely to precipitate cardiovascular collapse. Patients with which of the following conditions would tend to BEST tolerate hypertension during airway management in the operating room?

A. Aortic insufficiency
B. Ventricular septal defect
C. Aortic stenosis
D. Coronary artery disease
E. Mitral regurgitation

45. According to the American Society of Anesthesiologists Difficult Airway Algorithm, which actions should be considered after initial intubation attempts are unsuccessful?

A. Calling for help
B. Returning to spontaneous ventilation
C. Awakening the patient
D. Placement of a laryngeal mask airway (LMA)
E. All of the above

46. Which of the following is NOT a suggested use for the laryngeal mask airway?

A. Emergency ventilation when tracheal intubation has failed
B. Assisting a tracheal intubation
C. To protect against aspiration
D. Providing an airway with minimal changes in blood pressure and heart rate
E. To assist in fiberoptic bronchoscopy

CHAPTER 15 ANSWERS

1. ANSWER: E

A higher rate of pulmonary complications has been recognized in smokers since a 1944 prospective study of 1,257 patients undergoing abdominal surgery showed an incidence of pulmonary complications six times higher in smokers than in nonsmokers. More recent studies have supported this trend. Smokers appear to have increased rates of all pulmonary complications, including infection, ICU admission, and prolonged ventilation. The causative factor with the greatest impact on complications appears to be sputum production. In one prospective study of 127 patients undergoing abdominal surgery, chest infection occurred in 83% of smokers with chronic bronchitis, 21% of smokers without chronic bronchitis, and 7% of nonsmokers.

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Moller A, Maaloe R, Pederson T. Postoperative intensive care admittance: The role of tobacco smoking. *Acta Anaesth Scand*. 2001;45: 345–348.

Morton H. Tobacco smoking and pulmonary complications after operation. *Lancet*. 1944;1:368–370.

2. ANSWER: C

Smoking is associated with a higher incidence of perioperative airway complications. The rates of reintubation, laryngospasm, bronchospasm, and hypoventilation are all increased in smokers. Chronic bronchitis further increases risk of these complications. Smoking is also an independent risk factor for bronchospasm.

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3. ANSWER: B

Failed endotracheal intubation is defined as the absence of endotracheal tube placement after multiple attempts.

Difficult endotracheal intubation is described as intubation after multiple attempts and is often the result of difficult laryngoscopy. The best attempt at intubation and laryngoscopy should incorporate the most skilled operator, changing the patient's position, changing the size and type of laryngoscope blade, as well as maneuvers to aid intubation such as cricoid pressure, cricoid manipulation, and bimanual laryngoscopy.

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Cattano D, Pescini A, Paolicchi A, Giunta F. Difficult intubation: An overview on a cohort of 1327 consecutive patients. *Minerva Anesth*. 2001;67:45.

Langeron O, Mazzo E, Huraux C. Prediction of difficult mask ventilation. *Anesthesiology*. 2000;92:1229–1236.

Rose DK, Cohen MM. The airway: Problems and prediction in 18,500 patients. *Can J Anesth*. 1994;41:372–383.

4. ANSWER: B

Yentis and Lee modified the Cormack-Lehane scoring system by dividing the grade II view into IIa (partial view of glottis) and IIb (only arytenoids visible). This modification allows for the definition of difficult laryngoscopy to be refined to include the IIb, III, and IV laryngoscopic views. A grade III view denotes that only the epiglottis is visible in both the original and modified Cormack-Lehane grading systems (Table 15.1 and Fig. 15.1).

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Table 15.1 **CORMACK-LEHANE GRADING OF LARYNGOSCOPY VIEW, INCLUDING SUBCLASSIFICATIONS**

Grade 1	**Most of the glottis is visible**
Grade 2	**Posterior part of the glottis is visible**
Grade 2a	**Arytenoids and partial view of glottis**
Grade 2b	**Only arytenoids visible**
Grade 3	**No part of the glottis and only the epiglottis is visible**
Grade 3a	**Epiglottis *can* be lifted from the posterior pharyngeal wall**
Grade 3b	**Epiglottis *cannot* be lifted from the posterior pharyngeal wall**
Grade 4	**Not even the epiglottis can be seen**

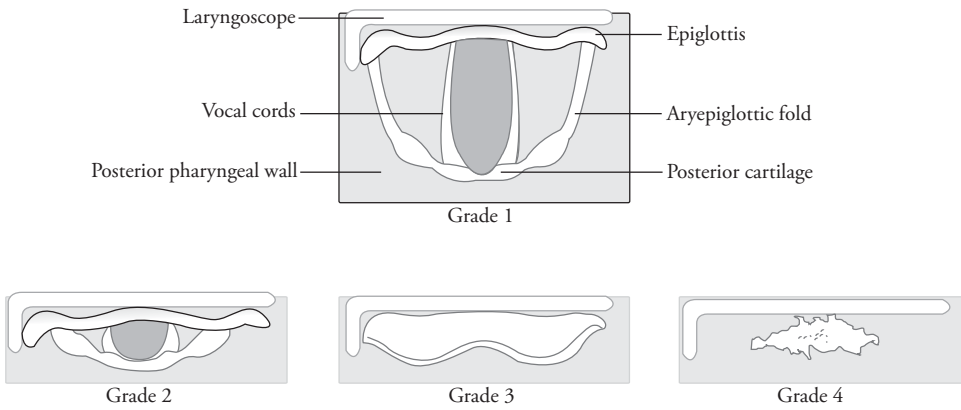

Figure 15.1 Classification of Laryngoscopic Views, Grades 1 through 4.

SOURCE: Miller RD, Eriksson LI, Fleisher LA, et al. *Miller's Anesthesia*, 7th Ed, Churchill Livingstone, 2009. Figure 50-10.

Yentis SM, Lee DJH. Evaluation of an improved scoring system for the grading of direct laryngoscopy. *Anesthesia*. 1998;53:1041–1044.

5. ANSWER: D

Assessment of the Mallampati classification must be made with the patient in the sitting position with the mouth fully opened and the tongue completely protruded. A tongue depressor is not used and the patient should not phonate during the examination (Table 15.2 and Fig. 15.2).

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Wolters Kluwer/ Lippincott Williams & Wilkins; 2009.

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6. ANSWER: C

Airway assessment to predict difficulty with laryngoscopy is based on anatomic features, and values have been selected as probable indicators of difficulty. The combination of mouth opening, jaw protrusion, and head extension is the basis of airway assessment. Mouth opening is measured as the interincisor distance, and an opening of less than 4 cm (two fingerbreadths) has been proposed as an indicator of probable difficult intubation. Prognathic inability of the mandible (the mandibular incisors cannot be brought in line with the maxillary incisors) is associated with difficult intubation. Limited head (more accurately described as occipito-atlanto-axial) extension impairs direct laryngoscopy. It can be measured as the angle between the occlusal surface of the maxillary teeth and the horizontal, with angles of less than 20 degrees suggesting difficult laryngoscopy. The Mallampati test is of limited value on its own but can be combined with an assessment of dentition. The thyromental distance is of limited value as a predictor of difficult laryngoscopy, but examination ensures that the laryngeal cartilage is palpated and submandibular compliance assessed. Dental patterns, such as protruding

Table 15.2 MALLAMPATI/SAMSOON CLASSIFICATION

Class I	**Visualization of soft palate, fauces, entire uvula, and pillars**
Class II	**Visualization of soft palate, fauces, and a portion of the uvula**
Class III	**Visualization of soft palate and base of the uvula**
Class IV	**Visualization of hard palate only**

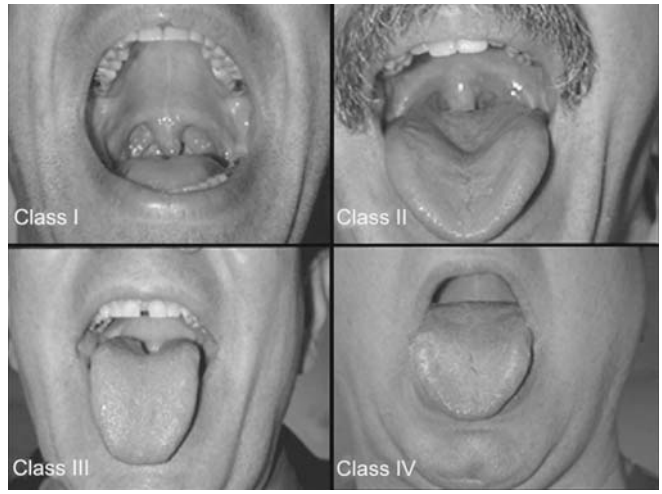


Figure 15.2 Mallampati classification of the airway.

SOURCE: Figure 22–4. Barash PG, Cullen BF, Stoelting RK, et al., Eds, *Clinical Anesthesia,* 6th ed. Lippincott Williams & Wilkins, 2009.

or single or missing maxillary incisors, increase the difficulty of direct laryngoscopy. The examination described by El-Ganzouri and colleagues (assessment of mouth opening, prognathic ability, head extension, thyromental distance, and Mallampati test) has been used with minor modification by others.

No single anatomic factor has been shown to be uniformly predictive of difficult intubation, but multiple nonreassuring factors seem to increase the likelihood of difficult laryngoscopy and therefore intubation. The patient described in answer C has only the Mallampati III as a risk factor, which by itself is not a reliable predictor of difficult intubation.

ADDITIONAL READINGS

El-Ganzouri AR, McCarthy RJ, Tuman KJ, et al. Preoperative airway assessment: Predictive value of a multivariate risk index. *Anesth Analg*. 1996;82:1197–1204.

Lee A, Fan LT, Gin T, et al. A systematic review (meta-analysis) of the accuracy of the Mallampati tests to predict the difficult airway. *Anesth Analg*. 2006;102:1867–1878.

Practice guidelines for the management of the difficult airway: An updated report by the American Society of Anesthesiologist Task Force on Management of the Difficult Airway. *Anesthesiology*. 2003;98:1269–1277.

7. ANSWER: E

The following criteria have been found to be predictive of difficult mask ventilation:

- Age > 55
- BMI > 26 kg/m^2
- Lack of teeth
- Presence of beard
- History of snoring
- Mallampati class III and IV
- Reduced jaw protrusion (mandibular subluxation)

ADDITIONAL READINGS

Kheterpal S, Han R, Tremper KK, Shanks A, Tait AR, Ludwig TA. Incidence and predictors of difficult and impossible mask ventilation. *Anesthesiology*. 2006;105:885–891.

Langeron O, Mazzo E, Huraux C. Prediction of difficult mask ventilation. *Anesthesiology*. 2000;92:1229–1236.

Williamson JA, Webb RK, Szekely S. The Australian Incident Monitoring Study: Difficult intubation: An analysis of 200 incident reports. *Anesth Intensive Care*. 1993;21:602.

8. ANSWER: A

Esophageal intubation is the inadvertent placement of the endotracheal tube into the esophagus at the time of intubation or its displacement into the esophagus later. It can occur due to difficulty either in visualizing the larynx or in passing the endotracheal tube. Changes in patient position may lead to tube displacement. Abnormally low or absent end-tidal CO_2, absent breath sounds, abnormal compliance during hand ventilation, endotracheal tube cuff leak, abdominal distention with ventilation, gastric fluid in the tube or ventilatory circuit, or oxygen desaturation may all be signs of esophageal intubation. If esophageal intubation is suspected, the anesthesiologist must verify the position of the endotracheal tube by confirming a continuous and normal-appearing capnography waveform and by direct laryngoscopy and/or fiberoptic bronchoscopy to visualize endotracheal tube position.

ADDITIONAL READINGS

Gaba DM, Fish KJ, Howard SK. Esophageal Intubation. In: *Crisis Management in Anesthesiology*. Philadelphia, PA: Churchill-Livingstone; 1994:68–70.

9. ANSWER: C

There are many anatomic differences between the infant and adult airway. The infant tongue is larger relative to the oral cavity and therefore tends to obstruct more easily. The larynx itself sits in a more cephalad position, making the angle between the glottic opening and the base of the tongue more acute. This can obscure visualization by direct laryngoscopy. The infant epiglottis is narrower and more difficult to manipulate with a laryngoscope. As opposed to the adult airway, where the narrowest part is at the vocal cords, the infant airway is narrowest at the cricoid cartilage. This can result in successful passage of the endotracheal tube through the vocal cords only to be followed by the inability to pass beyond the cricoid cartilage.

ADDITIONAL READING

Cote CJ, Todres ID, Ryan JF, Goudsouzian NG. *A Practice of Anesthesia for Infants and Children*. 3rd ed. Philadelphia: Elsevier; 2001.

10. ANSWER: B

Flexible stainless steel and copper-covered red rubber tubes as well as Teflon/silicon/aluminum tubes are all designed for use with CO_2 and KTP lasers. The best tubes for use with an Nd-YAG laser are those that are reusable, spiral-wound metal tubes with thick walls (Norton Tube) or the white rubber tubes with a cuff-within-a-cuff (Lasertube).

The CO_2 laser is widely used in upper airway surgery. The beam is invisible so a helium-neon aiming beam is used as a marker. The Nd-YAG laser is transmitted down fiberoptic cables. Because it is taken up by pigment, colored markings on tracheal tubes are more likely to be damaged than clear portions. Blood or mucus on the tube makes it less resistant to this type of laser beam. The KTP laser is also transmitted down fiberoptic cables. It passes through clear substances but is absorbed by hemoglobin. Pigment also reacts instantly with the KTP laser. The risk of airway fires can be minimized by using the following: low fraction of inspired oxygen, laser protocols, endotracheal tube cuffs filled with saline instead of air, protectively wrapped and specially designed tubes, and PEEP.

ADDITIONAL READING

Dorsch JA, Dorsch SE. Tracheal Tubes. In: *Understanding Anesthesia Equipment*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 1999:569–603.

11. ANSWER: E

Hypocalcemia can occur after thyroidectomy and may cause fatigue and respiratory distress due to weakness of the respiratory and pharyngeal musculature. It would not, however, occur suddenly in the recovery room, but is most commonly seen 24 to 48 hours postoperatively. Hypocalcemia is suggested by a positive Chvostek's or Trousseau's sign and is confirmed by laboratory testing. Bilateral recurrent laryngeal nerve injury would result in stridor or complete airway obstruction immediately after extubation. Unilateral recurrent laryngeal nerve injury results in one vocal cord in the paramedian position due to unopposed adduction by the ipsilateral cricothyroid muscle. This can cause mild hoarseness but negligible airway obstruction and minimal aspiration risk. The fact that this patient was speaking normally for some period of time makes any nerve injury less likely. Postextubation stridor also tends to present immediately after extubation and rarely presents after a period of normal speech. Motor branches of the superior laryngeal nerve innervate the cricothyroid muscle and the inferior pharyngeal constrictor muscles and would not be involved in this scenario. The most likely explanation for the patient's symptoms is the development of a hematoma with compression of the airway (Table 15.3).

Table 15.3 RESPIRATORY DISTRESS OR STRIDOR AFTER THYROIDECTOMY/PARATHYROIDECTOMY

ETIOLOGY	TIME OF CLINICAL PRESENTATION
Recurrent laryngeal nerve injury	Immediately after extubation
Hematoma	Minutes to hours postoperatively
Hypocalcemia	24 to 48 hours postoperatively

12. ANSWER: D

Due to its long length and relatively small diameter, the endotracheal tube creates the greatest resistance in a breathing circuit.

ADDITIONAL READING

Dorsch JA, Dorsch SE. Tracheal Tubes. In: *Understanding Anesthesia Equipment*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1999:569–603.

13. ANSWER: D

The patient is exhibiting sign of impending complete airway obstruction due to ***angioedema***. The safest course of action is to perform an awake fiberoptic intubation after topical anesthesia. Observation of the patient or transfer to another location may result in total airway obstruction, hypoxemia, and death. Induction of general anesthesia prior to intubation may result in a lost airway in this high-risk patient.

14. ANSWER: A

The adult dose of propofol for induction of anesthesia is 2 to 2.5 mg/kg. This should be reduced in patients who are older, who are hypovolemic, or who have limited cardiovascular function. In this elderly patient with possible small bowel ischemia, a 2- to 2.5-mg/kg induction dose of propofol would lead to profound hypotension and possibly cardiac arrest. A 2-mg/kg dose of propofol induces general anesthesia in less than 1 minute. Its mechanism of action is likely GABAergic, and it causes decreased cerebral metabolism, cerebral blood flow, and intracranial pressure. It also produces dose-dependant respiratory depression and blunts laryngeal reflexes, thus facilitating airway management by bag-mask ventilation, LMA placement, or laryngoscopy. Propofol is also a very effective antiemetic.

ADDITIONAL READING

Stoelting RK. Nonbarbiturate induction drugs. In: *Pharmacology and Physiology in Anesthetic Practice*. 3rd ed. Philadelphia, PA: Lippincott-Raven; 1999:140–157.

15. ANSWER: E

For ***awake endotracheal intubation***, anticholinergics, not cholinergics, can be used to reduce secretions and speed the onset of topical local anesthetics. While topicalization via atomizers, pledgets, and nebulization can be effective, absorption is variable and difficult to quantify. Exceeding the toxic dose is of concern. Although the superior laryngeal nerve does supply sensory fibers to the vocal cords, blocking it may impair the patient's ability to protect the airway. This can be catastrophic in the setting of vomiting. Due to the abuse potential of cocaine, anesthesia to the nasal mucosa should be provided with a mixture of phenylephrine and lidocaine.

ADDITIONAL READING

Stoelting RK, Miller RD. Airway Management and Tracheal Intubation. In: *Basics of Anesthesia*. 4th ed. New York: Churchill Livingstone; 2000:148–167.

16. ANSWER: D

Reasons for hypotension in patients with cardiac tamponade include decreased systemic vascular resistance due to anesthetics, myocardial depression, and reduced venous return. Many experts recommend pericardiocentesis, if possible, prior to the induction of general anesthesia. This can generally be performed with local anesthesia alone and may make it safer to induce general anesthesia. If pericardiocentesis cannot be done prior to induction, extreme caution must be taken to maintain cardiac output and blood pressure, with vasopressor support as needed. Vigorous positive-pressure ventilation leads to a decrease in cardiac output and can precipitate cardiovascular collapse in tamponade. Ketamine, etomidate, midazolam, and fentanyl all have a relatively stable cardiovascular profile and can be useful drugs for these patients. Surgical support should be available, and having the patient prepped and draped for surgery at the time of anesthetic induction should be considered. Central venous access and continuous arterial blood monitoring should be used.

ADDITIONAL READING

Stoelting RK, Dierdorf SF. Pericardial Diseases. In: *Anesthesia and Co-Existing Disease*. 3rd ed. New York: Churchill Livingstone; 1993:107–112.

17. ANSWER: C

The risk factors for tracheal mucosal injury and tracheal stenosis include prolonged hypotension, infection, prolonged intubation, and cuff pressures exceeding the tracheal capillary blood pressure, resulting in tissue ischemia. The recommended cuff pressure for tracheostomy cuffs is 25 to 35 mm Hg.

ADDITIONAL READINGS

Behringer EC. Tracheal Surgery. In: Youngberg JA, Lake CL, Roizen MF, Wilson RS, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:670–687.

Stoelting RK, Miller RD. Airway Management and Tracheal Intubation. In: *Basics of Anesthesia*. 4th ed. New York: Churchill Livingstone; 2000:148–167.

18. ANSWER: D

The fear of permanent damage to the spinal cord in patients with cervical spine disease during induction, intubation, and positioning is paramount. Neck extension can compress the cervical cord in patient with cervical spine disease. Quadriplegia/paresis has been reported. Attention must be paid to minimizing cervical spine extension and rotation. Cervical alignment with in-line stabilization (assistant stabilizes the patient's head by placing his or her hand alongside the head with fingertips on the mastoid bone, meanwhile holding the occiput down to the bed or backboard) is effective. Alternatively, the patient's head and neck can be stabilized in a neutral position by a rigid cervical neck collar that decreases flexion and extension to 30% of normal and lateral movement to 50% of normal. An awake fiberoptic approach is also very reasonable, as long the patient is cooperative and not at risk of coughing and bucking. It would not be prudent to approach this like any other airway situation and simply induce without mindfulness to the cervical cord and spine. Hyperkalemia in patients with spinal cord injury does not occur until a few days after the injury, so succinylcholine would not be contraindicated in this setting.

ADDITIONAL READINGS

Stoelting RK, Miller RD. Critical Care Medicine and Trauma Patient Management. In: *Basics of Anesthesia*. 4th ed. New York: Churchill Livingstone; 2000:436–448.

Todd MM, Warner DS, Maktabi MA. Neuroanesthesia: A Critical Review. In: Longnecker DE, Tinker JH, Morgan GE, eds. *Principles and Practice of Anesthesiology*. 2nd ed. St. Louis, MO: Mosby; 1998:1607–1658.

19. ANSWER: D

One option for ***lung isolation*** is a left double-lumen tube. With a double-lumen tube it is not necessary to know which

lung is bleeding. If a left double-lumen tube inadvertently enters the right mainstem bronchus, it will provide lung isolation but may occlude the takeoff of the right upper lobe. A double-lumen tube is of benefit during pulmonary hemorrhage due to the ability to suction both lungs and provide pulmonary toilet. Although each lumen (of a double-lumen tube) is often smaller than the lumen of a single-lumen tube, the tube itself has a larger outer diameter than single-lumen endotracheal tubes. Clot may occlude the narrower lumens of double-lumen endotracheal tubes. Endobronchial intubation may isolate one lung from the other but does not allow pulmonary toilet to the bleeding lung. This is also true of bronchial blockers, making them less useful in these situations.

ADDITIONAL READING

Slinger PD. Lung Isolation. In: Youngberg JA, Lake CL, Roizen MF, Wilson RS, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:603–638.

20. ANSWER: B

The ***LMA-ProSeal*** was designed with a principal objective of providing a separate conduit to permit gastric fluids to bypass the glottis and to provide a better seal around the glottis and allow positive-pressure ventilation in a more reliable manner than the LMA classic. The LMA-ProSeal permits access to the stomach using standard gastric tubes, provides a more comfortable fit within the pharynx, reduces leakage of gases into the stomach, and permits the diagnosis of incorrect LMA placement. It is not designed for intubation. It can, as can all LMAs, be placed into awake patients with adequate topicalization. The shaft is not kink-resistant.

ADDITIONAL READING

Ferson DZ, Brain AIJ. Laryngeal Mask Airway. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia: Mosby-Elsevier; 2007:476–501.

21. ANSWER: B

Oral lidocaine produces very low plasma lidocaine concentrations, probably due to first-pass metabolism. Toxic reactions to systemic absorption involve the central nervous system and the cardiovascular system, and can ultimately lead to cardiovascular collapse.

ADDITIONAL READING

Warner DO. Airway Pharmacology. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia, PA: Mosby-Elsevier; 2007:164–212.

22. ANSWER: E

Hypercapnia and hypocapnia both cause bronchoconstriction. It is not known whether hypoxia causes bronchodilation or bronchoconstriction; however, it seems that hypoxia will enhance the action of other airway irritants. Nitrocompounds such as nitroglycerine relax airway smooth muscle.

ADDITIONAL READING

Warner DO. Airway Pharmacology. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia: Mosby-Elsevier; 2007: 164–212.

23. ANSWER: B

The left recurrent laryngeal nerve may be compressed by tumor in the thorax, aortic aneurysm of the aorta. The left nerve is injured twice as frequently as the right. Malignancy in the neck can affect recurrent laryngeal nerve function. The recurrent laryngeal nerve carries both abductor and adductor fibers. The abductor fibers are more vulnerable (Selmon's law). When abductor fibers are damaged bilaterally (incomplete damage to the recurrent laryngeal nerve), the adductor fibers draw the cords toward each other, resulting in a very narrow glottic opening and, potentially, respiratory distress.

ADDITIONAL READING

Krohner RG, Ramanathan S. Functional Anatomy of the Airway. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia: Mosby-Elsevier; 2007:3–21.

24. ANSWER: D

Gastrointestinal obstruction places patients at high risk of aspiration. The sicker the patient, as classified by the ASA, the greater the risk of aspiration pneumonia/pneumonitis. Emergency surgery, hypotension in the awake patient, preoperative opioid use, increased intragastric volume and pressure, as well as decreased lower esophageal barrier pressure

all increase the risk of gastric aspiration. Obese patients were traditionally thought to pose a high risk for aspiration due to increased gastric volume and decreased gastric pH, but this assumption has been challenged in recent literature. Obese patients appear to have a normal lower esophageal pressure.

ADDITIONAL READING

Tasch MD, Stoelting RK. Aspiration Prevention and Prophylaxis: Preoperative Considerations. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia, PA: Mosby-Elsevier; 2007:281–302.

25. ANSWER: E

Sellick's maneuver is a component of a rapid sequence induction in patients with a full stomach. It has been noted to reduce gastric distention during mask ventilation. Although there have been concerns with cricoid pressure in terms of its unproven benefits and possible risks, it is still widely used and may be considered standard of care. Regurgitation of stomach contents is dependent on esophageal pressure, gastrointestinal pathology, intragastric pressure, and the esophageal sphincter pressure as well as the patency of the esophagus. It stands to reason that if cricoid pressure can occlude the esophagus, it may aid in the reduction of regurgitation.

ADDITIONAL READING

Suresh MS, Munnur U, Wali A. The Patient with a Full Stomach. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia, PA: Mosby-Elsevier; 2007:756–782.

26. ANSWER: E

All of the above are sources of air entrainment, thus hindering the ability to preoxygenate.

ADDITIONAL READING

Baraka A, Salem MR. Preoxygenation. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia, PA: Mosby-Elsevier; 2007:303–318.

27. ANSWER: E

Beyond the fifth month of pregnancy, the FRC is decreased by 80% and oxygen consumption increases by 30% to 40%. During apnea, pregnant women become hypoxemic rapidly because of limited FRC and increased consumption. Effective preoxygenation can be achieved in pregnant women with either 3 minutes of tidal breathing or deep breathing for 1 minute.

ADDITIONAL READING

Baraka A, Salem MR. Preoxygenation. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia, PA: Mosby-Elsevier; 2007:303–318.

28. ANSWER: E

Rheumatoid arthritis may involve any joint in the body, including the cervical spine. A change in voice, dysphagia, stridor, or fullness in the throat may indicate laryngeal involvement. Changes in phonation may indicate decreased mobility of the vocal cords, making an endotracheal tube difficult to pass. Temporomandibular joint involvement or cervical spondylosis can make intubation difficult or impossible by direct laryngoscopy. Joint and vertebral destruction can lead to instability of the cervical spine. Neck pain, reduced neck range of motion, and cervical spine arthritis should lead the anesthesiologist to suspect instability. In patients with an unstable neck, laryngoscopy should be performed with in-line stabilization.

ADDITIONAL READING

Ovassapian A, Mesnick PS. Evaluation of the Patient With a Difficult Airway. In: Longnecker DE, Tinker JH, Morgan GE, eds. *Principles and Practice of Anesthesiology*. 2nd ed. St. Louis, MO: Mosby; 1998:219–231.

29. ANSWER: D

Muscular dystrophies, including Becker's and Duchenne's, are not associated with difficult airway scenarios. All of the other syndromes listed can be associated with abnormal head and neck anatomy.

ADDITIONAL READING

Ovassapian A, Mesnick PS. Evaluation of the Patient With a Difficult Airway. In: Longnecker DE, Tinker JH, Morgan GE, eds. *Principles and Practice of Anesthesiology*. 2nd ed. St. Louis, MO: Mosby; 1998: 219–231.

30. ANSWER: E

In the setting of ***postinduction vomiting***, the patient is at risk for aspiration and should be placed in the head-down

position, not the head-up position. Trendelenburg positioning may facilitate drainage and minimize entry of gastric contents into the lungs.

ADDITIONAL READING

Ovassapian A, Meyer RN. Airway Management. In: Longnecker DE, Tinker JH, Morgan GE, eds. *Principles and Practice of Anesthesiology*. 2nd ed. St. Louis, MO: Mosby; 1998:

31. ANSWER: D

Rigidity is known as generalized hypertonus of skeletal muscle and occurs after intravenous boluses of opioids. Morphine can induce rigidity, but it is much more common with fentanyl, alfentanil, sufentanil, and remifentanil. It manifests not only in the abdominal and thoracic musculature but also the neck, extremity, laryngeal, and pharyngeal muscles. The incidence and severity are greatest when large amounts of opioids are given, but it can occur with very small doses as well. The effect usually occurs immediately after induction. Rigidity can also occur at the time of emergence and is more common in the elderly and with the coadministration of nitrous oxide. High inspiratory pressures are often needed for ventilation, leading to decreased venous return and gastric insufflation. Rigidity can be managed with a small dose of a rapidly acting muscle relaxant.

ADDITIONAL READING

Rosow CE, Dershwitz M. Pharmacology of Opioid Analgesic Agents. In: Longnecker DE, Tinker JH, Morgan GE, eds. *Principles and Practice of Anesthesiology*. 2nd ed. St. Louis, MO: Mosby; 1998: 1233–1259.

32. ANSWER: D

Negative-pressure pulmonary edema is caused by a closed glottis in the spontaneously ventilating patient and the generation of a significant negative intrathoracic pressure due to rib retraction from an inspiration attempt. This causes increased left ventricular preload and afterload, as well as altered pulmonary capillary permeability, a hyperadrenergic state, right ventricular dilatation, and increased hydrostatic pressure. The negative pleural pressure can result in fluid entry into the lung. This can also happen when an endotracheal tube becomes occluded, most commonly by a mucus plug, clot, or biting on the endotracheal tube.

ADDITIONAL READING

Hagberg CA, Georgi R, Krier C. Complications of Managing the Airway. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia, PA: Mosby-Elsevier; 2007:1181–1216.

33. ANSWER: E

Laryngeal edema is an important cause of postextubation airway obstruction. It is most common in children and infants. It may result from surgical manipulation, positioning, hematoma, fluid excess, impaired venous drainage, or coexisting conditions such as angioedema. Traumatic intubation is a risk factor, as is prolonged intubation and bucking on the endotracheal tube at the time of emergence. It usually develops rapidly but may be delayed for up to 6 hours. Management depends on the severity of the condition. Therapy consists of humidified gases, racemic epinephrine, head-up positioning, and reintubation with a smaller tube if needed. Steroids may help prevent this condition.

ADDITIONAL READING

Hagberg CA, Georgi R, Krier C. Complications of Managing the Airway. In: Hagberg CA, ed. *Benumof's Airway Management*. 2nd ed. Philadelphia, PA: Mosby-Elsevier; 2007:1181–1216.

34. ANSWER: C

Several different methods of determining the appropriate ETT size in children are available. For patients 1 year of age and older the following formula may be used:

$$(\text{Age of patient} + 4) / 4 = \text{Size of ETT diameter}$$

This formula is valid for uncuffed tubes, which are generally used in children until 8 years of age. Cuffed endotracheal tubes are being used more often, even in children, but care should be used to avoid overinflation of the cuff. In general, a cuffed tube will be 0.5 size smaller than an uncuffed one for any given patient.

For children less than 1 year of age, sizes are as follows:

Premature: 2.5 to 3.0

Full-term neonate: 3.0 to 3.5

6 to 12 months: 3.5 to 4.0

Appropriate size is determined by air leak around the ETT. This should be checked in all children. Generally acceptable leak is 0 to 30 cm H_2O.

The appropriate depth (in cm) of the ETT at the teeth or alveolar ridge can be approximated by **three times the size of the ETT** for oral intubations (if the patient takes the appropriate-size ETT). The oral/nasal mark should be visible at the nares for nasal tubes.

Extension of the head pulls the ETT backward. Flexion of the head pushes the ETT in. Turning the head to the side moves the ETT backward.

ADDITIONAL READING

Vassallo SA, Baboolal HA. Anesthesia for Pediatric Surgery. In: Dunn PF, ed. *Clinical Anesthesia Procedures of the Massachusetts General Hospital*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:515–539.

35. ANSWER: D

The healthcare agent/proxy/power of attorney has the greatest impact on healthcare decisions when patients are obtunded and cannot make decisions for themselves.

36. ANSWER: B

The purpose of the ETT cuff is to facilitate positive-pressure ventilation and prevent aspiration of secretions. When a cuff leak occurs, the first maneuver is always to assess the patient's vital signs and evaluate for possible emergent intervention. Very often practitioners simply add extra air to the cuff; this risks cuff overinflation and mucosal ischemia as well as cuff herniation above the cords. After assessing the patient, the ETT position should be confirmed. Usually an ETT at 20 to 24 cm places the tube in the midtrachea in most adults. When checking a cuff leak, do the following: review the x-rays, obtain a repeat x-ray, suction the posterior pharynx, deflate the balloon to determine how much air is in the cuff, and reinflate the balloon with 3 to 6 mL of air up to a maximum of 10 mL to obtain a seal (if greater than 10 mL is withdrawn there is either overinflation of the cuff or a cuff rupture). Consider direct visualization by direct laryngoscopy or fiberoptic bronchoscopy.

ADDITIONAL READINGS:

Dalencourt G, Martinez EA. Do Not Overinflate the Endotracheal Cuff. In: Marcucci L, Martinez EA, Haut ER, Slonim AD, Suarez JI, eds. *Avoiding Common ICU Errors*. Philadelphia: Lippincott Williams & Wilkins; 2007:267–268.

37. ANSWER: A

Detection of end-tidal CO_2 with a single breath is not sufficient to confirm ETT placement. Gastric insufflation with partially exhaled CO_2 will produce aberrant CO_2 during esophageal intubation. Bicarbonate tablets will also produce end-tidal CO_2 from the stomach. A chest x-ray is commonly used to confirm proper ETT position, but a clinical decision using end-tidal CO_2 and bilateral breath sounds is sufficient to use the ETT for ventilation of the patient.

ADDITIONAL READING

Veloso PM. Do Not Use the Presence of End-Tidal CO_2 to Rule Out Esophageal Intubation. In: Marcucci L, Martinez EA, Haut ER, Slonim AD, Suarez JI, eds. *Avoiding Common ICU Errors*. Philadelphia, PA: Lippincott Williams & Wilkins, 2007:249–250.

38. ANSWER: E

According to the ***Practice Advisory for the Prevention and Management of Operating Room Fires*** (Fig. 15.3), if an airway fire is suspected, the procedure should be stopped and the endotracheal tube removed before the gas flow is stopped. In the advisory, some experts and educators recommend an initial step that involves two simultaneous actions: removing the tracheal tube and stopping the flow of medical gases (e.g., by disconnecting the breathing circuit at the Y-piece or the inspiratory gas limb). The intent is to prevent a "blowtorch" effect caused by continued gas flow through a burning tracheal tube. This "blowtorch" effect can spread fire to other locations on or near the patient, and may cause additional burns on the patient or other members of the operating room team.

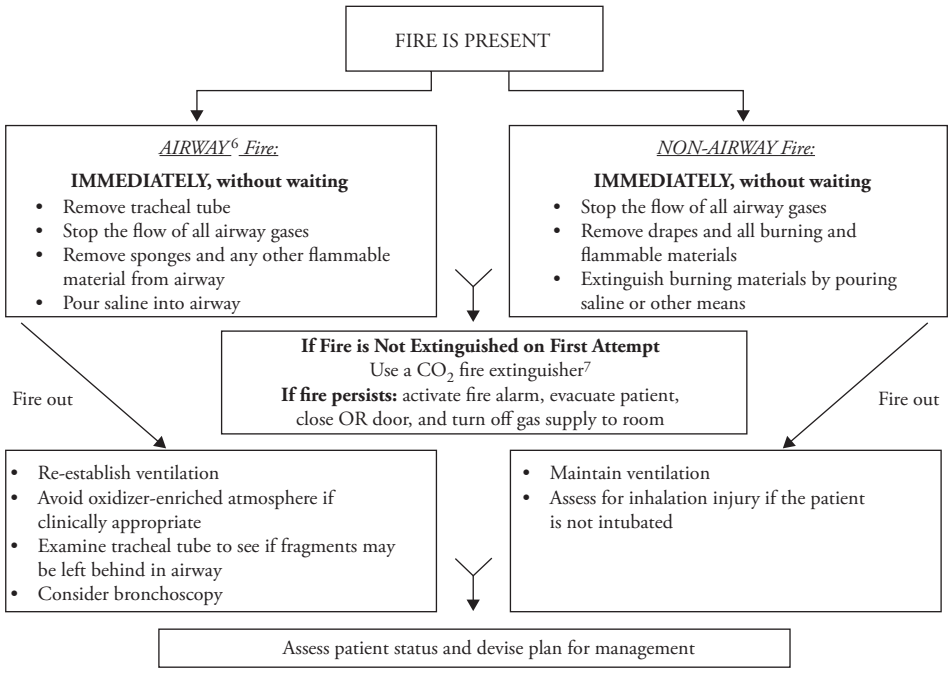
The Task Force has carefully considered this concern and agrees that these simultaneous actions represent an ideal response. However, the Task Force is concerned that, in actual practice, the simultaneous actions may be difficult to accomplish or may result in delay when one team member waits for another. Therefore, the Task Force recommends that the actions take place as fast as possible.

In the setting of a non-airway fire, gases are stopped, drapes and burning material are removed, and fire is extinguished with saline or by other means. The patient is not immediately extubated if a non-airway fire is suspected.

ADDITIONAL READINGS

Morgan GE, Mikhail MS, Murray MJ. Airway Fire Protocol. In: *Clinical Anesthesiology*. 3rd ed. New York: McGraw-Hill; 2002:774.

Practice Advisory for the Prevention and Management of Operating Room Fires. A Report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology*. 2008;108: 786–801.



1 Ignition sources include but are not limited to electrosurgery or electrocautery units and lasers.
2 An oxidizer-enriched atmosphere occurs when there is any increase in oxygen concentration above room air level, and/or the presence of any concentration of nitrous oxide.
3 After minimizing delivered oxygen, wait a period of time (*e.g.,* 1–3 min) before using an ignition source. For oxygen dependent patients, *reduce* supplemental oxygen delivery to the minimum required to avoid hypoxia. Monitor oxygenation with pulse oximetry, and if feasible, inspired, exhaled, and/or delivered oxygen concentration.
4 After stopping the delivery of nitrons oxide, wait a period of time (*e.g.,* 1–3 min) before using an ignition source.
5 Unexpected flash, flame, smoke or heat, unusual sounds (*e.g.,* a "pop," snap or "foomp") or odors, unexpected movement of drapes, discoloration of drapes or breathing circuit, unexpected patient movement or complaint.
6 In this algorithm, airway fire refers to a fire in the airway or breathing circuit.
7 A CO_2 fire extinguisher may be used on the patient if necessary

Figure 15.3 Algorithm for the prevention and management of operating room fires.

SOURCE: Practice Advisory for the Prevention and Management of Operating Room Fires. A Report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology.* 2008;108:786–801.

39. ANSWER: D

Hypoxemia is defined as a Pao_2 less than 80 mm Hg while breathing room air.

ADDITIONAL READING

Rogers P. Respiratory Distress with Arterial Hypoxemia. In: Fink MP, Abraham E, Vincent JL, Kochanek PM, eds. *Textbook of Critical Care*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2005:35–38.

40. ANSWER: C

The arterial oxygen content (Pao_2) is the amount of oxygen in solution in the blood, whereas the oxygen saturation (SaO_2) is the percent of oxyhemoglobin relative to total hemoglobin. The oxygen saturation varies in a nonlinear relationship with the Pao_2. The oxyhemoglobin dissociation curve depends on the pH, temperature, $Paco_2$, and 2,3-DPG concentration. Low pulse oximeter saturation can be seen with a poor waveform or dark blue or black nail polish. Methemoglobinemia can cause a falsely low saturation, whereas carboxyhemoglobinemia can cause falsely elevated O_2 saturation. Because of this variation in the oxygen hemoglobin dissociation curve, the saturation may vary for any given Pao_2.

ADDITIONAL READING

Rogers P. Respiratory Distress with Arterial Hypoxemia. In: Fink MP, Abraham E, Vincent JL, Kochanek PM, eds. *Textbook of Critical Care*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2005:35–38.

41. ANSWER: C

Retrograde intubation requires several steps and a long period of time before oxygenation and ventilation via endotracheal tube can be established. The bearded obese individual would likely be difficult to mask ventilate and therefore not a great candidate for a retrograde intubation.

ADDITIONAL READING

Schaefer JJ, Gonzales R. Difficult Airway Management for Intensivists. In: Fink MP, Abraham E Vincent JL, Kochanek PM, eds. *Textbook of Critical Care*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2005: 1743–1755.

42. ANSWER: E

Airway exchange catheters can be used blindly or in combination with a direct laryngoscopy. Complications using airway exchange catheters include bronchospasm, barotraumas, mucosal injury, pneumothorax, and accidental endotracheal tube dislodgment.

ADDITIONAL READING

Schaefer JJ, Gonzales R. Difficult Airway Management for Intensivists. In: Fink MP, Abraham E Vincent JL, Kochanek PM, eds. *Textbook of Critical Care*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2005: 1743–1755.

43. ANSWER: D

The ***Rapid Shallow Breathing Index*** or RSBI (respiratory rate/tidal volume in liters) should be less than 100, not 200. Prior to extubation a patient should remain awake without aggressive stimulation. Other requirements include the ability to generate adequate negative inspiratory force, tidal volume (about 5 cc/kg), vital capacity (about 10 to 15 cc/kg), and respiratory rate (less than 25 breaths/minute). Blood gas values should be in the acceptable range on minimal ventilatory support.

ADDITIONAL READING

Meade. Weaning parameters are not predictive. *Chest*. 2001;120: 400S-424S.

44. ANSWER: C

Hypertension should be avoided in most anesthetics and can be catastrophic in conjunction with some cardiac conditions. It can be dangerous in all of the listed conditions, although patients with aortic stenosis, may actually benefit from the increased afterload associated with hypertension.

ADDITIONAL READING

Bojar RM. *Manual of Perioperative Care in Adult Cardiac Surgery*. 4th ed. Boston, MA: Blackwell Publishing; 2005.

45. ANSWER: E

The ***ASA's difficult airway algorithm*** states that three useful things to consider after initial intubation attempts are unsuccessful are calling for help, returning the patient to spontaneous ventilation, and awakening the patient. Important next steps are continuing to mask ventilate the patient and considering LMA placement if mask ventilation is unsuccessful.

ADDITIONAL READING

American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice Guidelines for management of the difficult airway: an updated report. *Anesthesiology*. 2003;98:1269–1277.

46. ANSWER: C

Laryngeal mask airways can be used in emergency situations, to assist in tracheal intubation, to provide an airway when trying to avoid a large variation in blood pressure and heart rate, and during fiberoptic bronchoscopy. However, they are in no way a substitute for an endotracheal tube to protect against aspiration, not even when using the ProSeal or Supreme types.

ADDITIONAL READING

Longnecker DE, et al. Airway Management. In: *Anesthesiology*. New York: McGraw Hill Medical; 2008:696.

16.

COMPLICATIONS

Elizabeth Cohen, MD, Amanda Monahan, MD, and Stephen Pratt, MD

1. A 24-year-old man with a grade 3 liver laceration suffered in a motor vehicle crash is coming emergently to the operating room. Heart rate is 125 bpm and blood pressure is 85/63 mm Hg. Which of the following neuromuscular blocking drugs would be the best choice to maintain muscle relaxation during anesthesia?

A. Succinylcholine
B. Atracurium
C. Rocuronium
D. Pancuronium
E. Any of the above

2. A 28-year-old G2P1 otherwise healthy woman is undergoing a repeat cesarean section. Spinal anesthesia consisting of 11.25 mg of bupivacaine, 25 mcg of fentanyl, and 0.25 mg of morphine was administered without difficulty. There was no delay in patient position. Thirteen minutes later, during the separation of the placenta, the patient begins to complain of shortness of breath and numbness in the fifth digit of both hands. Her oxygen saturation remains stable at 99%. What is the most likely cause of her shortness of breath?

A. Amniotic fluid embolism
B. High spinal
C. Pneumonia
D. Hyperventilation
E. Anxiety

3. A 45-year-old man with a medical history significant for obesity, hypertension, and arthritis is undergoing a left total shoulder replacement. An interscalene block was placed for postoperative pain control. Intraoperatively, an endotracheal tube was placed and the patient was placed in the beach-chair position. His mean arterial pressure was greater than 60 mm Hg for the duration of the case. There was no obvious complication intraoperatively. In the postanesthesia care unit, the patient complained of difficulty swallowing and on careful neurologic examination was found to have tongue deviation to the right. Which of the following is LEAST likely to explain these findings?

A. Intraoperative stroke from relative hypotension
B. Stretch injury from positioning
C. Nerve injury from intubation
D. Local anesthetic effect from the interscalene block
E. None of the above

4. Which of the following receptors is most commonly identified as the defective receptor in patients who experience malignant hyperthermia?

A. Ryanodine receptor (RYR)
B. Dihydropyridine receptor (DHPR)
C. Acetylcholine receptor
D. Gamma-aminobutyric acid receptor (GABA)
E. *N*-methyl-D-aspartate receptor (NMDA)

5. A 37-year-old woman with a past medical history significant for gastroesophageal reflux disease (GERD) presents for excision of a breast mass. She takes no medications. In the holding area, you examine her airway and find the following—Mallampati class III, poor mouth opening (2 to 3 cm), short hyomental distance but adequate thyromental distance, poor mandibular prognathism, good dentition, free range of motion of her neck. You decide to perform a rapid sequence intubation. Which of the following medications would be the BEST choice to administer prior to going to the operating room?

A. 10 mg omeprazole IV
B. 10 mg omeprazole PO
C. 30 mL sodium citrate PO
D. 50 mg ranitidine IV
E. 150 mg ranitidine PO

6. A 25-year-old otherwise healthy woman is brought to the operating room for elective shoulder arthroscopy. Upon direct laryngoscopy, you have a grade 4 view and there is a copious amount of light green-yellow fluid in the oropharynx. You suction the oropharynx and place a 7.0 endotracheal tube using an intubating LMA. In the postanesthesia care unit, the patient develops tachypnea with oxygen saturations in the upper 80s on 10 L nonrebreather face mask. The patient is reintubated and a chest x-ray does not show infiltrates. What is the most likely cause of the respiratory distress?

A. Aspiration pneumonia
B. Aspiration pneumonitis
C. Excessive opioids
D. Pulmonary embolus
E. None of the above

7. Which of the following systems is NOT activated during an anaphylactoid reaction?

A. Complement system
B. Kinin-generating system
C. Fibrinolytic system
D. Antigen–mast cell interaction
E. Coagulation system

8. A 52-year-old man presents for an elective cholecystectomy. His past medical history is significant for hypertension, coronary artery disease, status post appendectomy, and an allergy to penicillin. The patient is brought to the operating room, and general anesthesia is induced with fentanyl, lidocaine, propofol, and succinylcholine. His trachea is intubated and he is placed on the ventilator without incident. About 15 minutes after induction, the patient is stable and he is given 2 g of cefazolin. Three minutes later, you notice a new rash on his torso. The peak and plateau pressures on the ventilator have increased. The patient's face appears to be swelling, and his blood pressure has dropped from 130/78 to 85/40 mm Hg. What is your next step?

A. Administer IV fluid bolus and inhaled albuterol.
B. Administer IV fluid bolus and IV ephedrine.
C. Administer IV fluid bolus and IV epinephrine.
D. Administer transtracheal epinephrine and IV phenylephrine.
E. Administer IV fluid bolus, IV hydrocortisone, and IV diphenhydramine.

9. A 57-year-old man presents for elective right craniotomy for resection of a brain mass. General anesthesia is induced uneventfully, and he is placed on the ventilator. What would be an appropriate goal for ventilation of this patient?

A. End-tidal (et) CO_2 of 42 mm Hg
B. etCO_2 of 22 mm Hg
C. etCO_2 of 32 mm Hg
D. PaCO_2 of 32 mm Hg
E. PaCO_2 of 22 mm Hg

10. A 25-year-old man with traumatic brain injury from a motor vehicle crash was brought to the operating room for an open tracheostomy. He has an 8.0 PVC endotracheal tube (ETT) in place. The induction of anesthesia was without complication and the patient's vital signs were stable. The surgical team had dissected neck tissue all the way down to the trachea. The patient was given 100% FiO_2 prior to pulling back the ETT. The surgeon noted a blue flame while cauterizing. Which of the following actions is NOT correct?

A. Immediately remove the ETT.
B. Irrigate the field with normal saline.
C. Shut off all airway gasses.
D. Disconnect the circuit.
E. Leave the ETT in place since a reintubation would be difficult due to the swelling of soft tissue. Irrigate the trachea with water through the ETT.

11. Which of the following types of surgery is NOT associated with an increased risk for intraoperative awareness under general anesthesia?

A. Cardiac surgery
B. Trauma surgery
C. Orthopedic surgery
D. Obstetric surgery
E. All of the above are associated with awareness under general anesthesia.

12. You are taking over care of a 58-year-old woman with acute-on-chronic pancreatitis secondary to prolonged alcohol abuse. Her initial complaint on presentation was severe epigastric pain without radiation. She was admitted to the intensive care unit, made NPO, and started on total parenteral nutrition (TPN) to be continued until her pain completely resolved. After several weeks, her epigastric pain is improving but she complains of new-onset right upper quadrant pain. WBC, AST, and ALT are within normal limits, INR is 1.0, and right upper quadrant ultrasound does not reveal cholelithiasis. Which of the following statements may account for the patient's new symptoms?

A. The patient has cholestasis from prolonged TPN.
B. The patient has acute liver failure from prolonged TPN.

C. The patient has referred pain from her pancreatitis.
D. The patient is seeking additional narcotics.
E. None of the above would explain the patient's symptoms.

13. A 19-year-old boy who was in a motorcycle accident is brought immediately from the trauma bay to the operating room for emergent evacuation of an enlarging subdural hemorrhage identified on CT scan. On arrival to the trauma bay, the patient was intubated with an 8.0 ETT for a Glasgow Coma Scale score of 8. He has two 16-gauge IVs in his antecubital fossae. He has 0.9% normal saline running through one IV; the other is clamped. His vital signs are stable. His FAST scan was negative for intraperitoneal bleeding. He has not received any or blood products. The patient has several extremity fractures that have been stabilized. General anesthesia is induced with etomidate. Prior to the start of the operation, he becomes hypotensive and has oozing around his IV sites. He has several lacerations that have clotted. An esophageal temperature probe is placed and reads 34.0 degrees C. What is the most likely cause of the hypotension and oozing around the IV sites?

A. Massive blood loss
B. Missed injury
C. Unknown clotting disorder
D. Induction of anesthesia
E. Hypothermia

14. Which of the following strategies will most likely increase the body temperature in the setting of intraoperative hypothermia in an adult-size patient?

A. Forced-air warming blanket on the upper body
B. Infusion of 1 L warmed IV fluids (40 degrees C)
C. Switching to low-flow anesthesia
D. Raising the temperature of the operating room by 10 degrees C
E. Applying warmed blankets on the lower extremity

15. A 35-year-old female nurse presents for elective shoulder arthroscopy after traumatic injury. She denies any drug or latex allergies but has several food allergies, including kiwi, avocado, and bananas. She states that she started to develop a red macular rash on her hands while at work last winter. She attributed this to the frequent hand washing and winter weather. However, the hospital changed to latex-free gloves in January and she has not had any issues since that time. Which of the following items should be avoided while caring for this patient?

A. Latex gloves
B. Neoprene gloves
C. Silicone endotracheal tubes
D. Plastic face masks
E. All of the above

16. A 36-year-old, 175-kg woman with a history of hypertension and diabetes mellitus presents for elective open gastric bypass surgery. An epidural is placed in the holding area for postoperative pain control. Given her high risk for development of venous thromboembolism (VTE), which of the following is NOT an appropriate option to prevent a venous embolism?

A. Early ambulation after surgery
B. 5,000 units of subcutaneous heparin prior to surgery and then every 12 hours
C. 175 mg of subcutaneous Lovenox prior to surgery and then every 24 hours
D. Sequential compression device boots during and after surgery until the patient is ambulating
E. 100 mg of aspirin PO for 3 days postoperatively

17. A 42-year-old, 85-kg woman presents for an elective cholecystectomy after recurrent biliary colic. She is overweight but otherwise healthy. She takes no medications and is active. She is brought to the operating room and an uncomplicated induction of general anesthesia with fentanyl, lidocaine, propofol, and succinylcholine is performed. The patient is hemodynamically stable. The procedure begins and the initial umbilical trocar is inserted. The abdomen is insufflated with carbon dioxide. The patient's heart rate suddenly drops 30 bpm. The $etCO_2$ is unchanged. At your request, the surgeon stops insufflation and opens the release valve on the trocar. The patient's pulse returns to baseline. The surgeon resumes the flow of carbon dioxide and the patient's abdomen is insufflated without difficulty. She remains hemodynamically stable for the remainder of the case. What is the most likely explanation for her bradycardia?

A. Profound bradycardic response to propofol
B. Bradycardia secondary to increased intraabdominal pressure
C. Toxic dosage of lidocaine at induction
D. Carbon dioxide embolism
E. Overdose of fentanyl at induction

18. A 17-year-old patient with beta-thalassemia presents for a laparoscopic splenectomy due to splenomegaly and concerns for splenic rupture during football practice. The patient is otherwise healthy and his last transfusion was 3 days prior. His starting Hct is 33. Induction of general anesthesia is uncomplicated and the patient is hemodynamically stable on the ventilator. The surgeon places a Veress needle into the abdomen and begins insufflation. The patient's $etCO_2$ begins to decline rapidly and the abdomen is not expanding evenly despite insufflation of

several liters. What is the most likely cause of the sudden drop in etCO_2?

A. Air embolism
B. Pulmonary embolism from venous thromboembolism (VTE)
C. CO_2 embolism
D. Myocardial infarction
E. None of the above

19. You are taking care of a 67-year-old man in the trauma intensive care unit. He was brought in after a motor vehicle crash in which he sustained an unstable cervical vertebra fracture. His fracture was stabilized and the patient was being monitored in the intensive care unit for frequent neurologic checks. He was started on subcutaneous heparin for deep venous thrombosis prophylaxis, 5,000 units BID. His platelet count had been stable until postoperative day 7, when his morning laboratory studies revealed a platelet count of 46,000. There was no clinical evidence of spontaneous bleeding. A heparin-dependent platelet antibody test was positive. After ruling out other causes of thrombocytopenia, a diagnosis of heparin-induced thrombocytopenia (HIT) is made. What is the appropriate treatment?

A. Discontinue heparin, as continuation could worsen the patient's platelet count.
B. Continue heparin, as the platelet count will likely rebound.
C. Discontinue heparin and start Lovenox.
D. Continue heparin and start aspirin.
E. None of the above

20. You are taking care of a laboring 26-year-old G1P0 otherwise healthy woman who requests epidural labor analgesia. The catheter is placed uneventfully at L4/L5 and is negative for aspiration of blood or cerebrospinal fluid. A test dose of 3 mL of 1.5% lidocaine with epinephrine 1:200,000 was negative for intravascular or intrathecal injection. The patient has been comfortable with a solution of 0.125% bupivacaine, 4 mcg/mL fentanyl, and 0.66 mcg/mL epinephrine running at 8 mL/hr. The baby's head is beginning to descend and the patient requires an additional bolus. After negative aspiration, a 10-mL bolus of 0.25% bupivacaine with 100 mcg of fentanyl is given via the epidural catheter. The patient reports sudden onset of perioral tingling and a funny taste in her mouth. Which of the following interventions is most appropriate?

A. Stop the continuous infusion and replace the epidural catheter.
B. Continue the epidural catheter while monitoring the patient's vital signs every 5 minutes for at least 30 minutes.
C. Proceed with a cesarean section under general anesthesia.
D. Administer lorazepam intravenously.
E. Administer a spinal anesthetic with tetracaine to ensure adequate length for the remainder of her labor.

21. A 25-year-old man was admitted to the hospital after a motorcycle accident in which he sustained several fractures, including a right femur fracture. The patient's other fractures were stabilized externally, and he was observed overnight prior to going to the operating room for open reduction and internal fixation of the right femur. In the holding area, you note the patient to be confused. You take the patient to the operating room and note the oxygen saturation to be 90%. This improves to 94% with 100% FiO_2. You induce anesthesia and place an 8–0 endotracheal tube without complication. As the patient is being positioned, you note a petechial rash on the patient's upper chest and neck. You continue to administer 100% oxygen and send an arterial blood gas sample for analysis. The result is significant for hypoxemia despite 100% FiO_2. What is the most likely diagnosis for this patient?

A. Pulmonary embolism
B. Fat embolism
C. CO_2 embolism
D. Air embolism
E. None of the above

22. Which of the following ventilator settings would be most appropriate in the setting of a fat embolism?

A. Maintain a low tidal volume (TV) of 4 to 6 mL/kg with 5 cm of positive end-expiratory pressure.
B. Maintain a normal TV of 10 to 15 mL/kg.
C. Adjust ventilator settings to maintain a normal pH.
D. Adjust settings to maintain a normal CO_2.
E. High-frequency oscillatory ventilation

23. A 17-year-old boy who was diagnosed with mononucleosis approximately 2 months previously sustained trauma to his abdomen while at football practice. He began complaining of left-sided abdominal pain. He was evaluated in the emergency department and found to have a grade 4 splenic laceration. He is now intubated in the surgical intensive care unit under your care after an open splenectomy. He has received 4 units of packed red blood cells, 2 units of platelets, and 2 units of fresh frozen plasma. When he arrived in the intensive care unit approximately 2 hours ago, he was hemodynamically stable. The nurse informs you that the patient is now febrile and tachycardic. He has developed frothy secretions requiring frequent suctioning. His central

venous pressure has dropped slightly, and urine output has decreased to 20 mL/hr. An arterial blood gas sample was recently sent and the patient was hypoxemic, with a Pao_2/Fio_2 ratio of 250. A chest x-ray shows the endotracheal tube (ETT) approximately 2 cm above the carina and bilateral infiltrates. Which of the following diagnoses would best explain his sudden respiratory distress?

A. Reaction to the blood products
B. Aspiration
C. Pneumonia
D. Malposition of ETT
E. None of the above

24. What is the most appropriate management for transfusion-related acute lung injury (TRALI) in the patient described above?

A. Antibiotics
B. Pulling the ETT back 2 cm
C. Pushing the ETT in 1 cm
D. Ventilatory support
E. Diuretics

25. A 39-year-old woman presents for carpal tunnel release of the left wrist. The patient will receive MAC for the procedure and the surgeon will administer a local block. The tourniquet is inflated and the patient does well throughout the procedure. After closing, the tourniquet is released. Which of the following changes can occur with deflation of the tourniquet?

A. 10% to 15% increase in heart rate
B. 5% to 10% increase in serum potassium
C. Slight increase in $Paco_2$ (1 to 8 mm Hg)
D. Transient metabolic acidosis
E. All of the above

26. A 67-year-old woman with a past medical history of diabetes mellitus, peripheral vascular disease, coronary artery disease status post four-vessel coronary artery bypass grafting, and smoking presents for an endovascular abdominal aortic aneurysm repair. The aneurysm is 6.2 cm and has recently increased 1 cm in size. The patient reports an allergy to contrast dye. Which of the following is the LEAST favorable option to manage this patient?

A. Methylprednisolone PO prior to the procedure to prevent contrast allergy
B. Diphenhydramine IV prior to the procedure to prevent contrast allergy
C. Prednisone PO prior to the procedure to prevent contrast allergy
D. Use of a nonionic, low-osmolality contrast medium
E. Not performing the procedure endovascularly

27. A 72-year-old man with a past medical history significant for diabetes mellitus type 2 well controlled with metformin presents for an angiogram with bilateral lower extremity runoff to evaluate claudication symptoms. The patient will undergo intervention for the stenosis as indicated and be admitted overnight for observation. The patient's baseline creatinine is 1.5 mg/dL and his estimated glomerular filtration rate is 43 mL/min. Which of the following is NOT an acceptable therapy for the prevention of contrast-induced nephropathy?

A. Hold metformin for 48 hours after the procedure or until renal function has returned to baseline.
B. Normal saline 1 mL/kg/hr for 12 hours before and 12 hours after the procedure
C. Normal saline 1 to 2 mL/kg/hr for 3 to 6 hours before and 6 hours after the procedure
D. Sodium bicarbonate 1 to 2 mL/kg/hr for 12 hours before and 12 hours after the procedure
E. Sodium bicarbonate 1 to 2 mL/kg/hr for 3 to 6 hours before and 6 hours after the procedure

28. An 80-year-old man is brought to the operating room for an exploratory laparotomy for small bowel obstruction (SBO). He has had multiple abdominal surgeries in the past for Crohn's disease. A lumbar epidural is placed prior to induction for postoperative pain control. General anesthesia is induced with propofol, fentanyl, and succinylcholine. The cause of the SBO is found to be adhesions, and the patient undergoes lysis of adhesions. Intravenous morphine is administered as an adjunct to the epidural. An esophageal temperature probe was placed at the beginning of the case, and you note that the patient's temperature has dropped from 36.8 to 35.4 degrees C. Which of the following is a potential contributor to the patient's hypothermia?

A. Propofol
B. Morphine
C. Sevoflurane
D. Lumbar epidural
E. All of the above

29. A 67-year-old man undergoes open aortic aneurysm repair. The best predictor of postoperative renal injury is which of the following?

A. Preoperative creatinine clearance
B. Intraoperative urine output
C. Postoperative creatinine clearance
D. Intraoperative blood loss
E. Intraoperative fluid administration

30. A 35-year-old woman is emerging from anesthesia after a laparoscopic appendectomy. She is otherwise

healthy and on no medications. She received 4 mg of midazolam in the holding area prior to surgery, and 4 mg of hydromorphone for pain control during the 90-minute case. At the end of the case the train of four indicated four equal twitches and tetanic contraction was sustained after neuromuscular blockade reversal. She has not started breathing on her own although there is no detectable end-tidal anesthetic gas and she is receiving 100% FiO_2. Which of the following would help to establish a cause of her respiratory depression?

A. Naloxone
B. Flumazenil
C. Dezocine
D. Meptazinol
E. Nalbuphine

31. Multiple EMLA applications were used to secure difficult IV access in a 3-year-old child. The most likely symptom the child may display is

A. Shortened PR interval
B. Pulse oximetry saturation of 85%
C. Cherry-red mucous membranes
D. Masseter spasm
E. Tonic-clonic seizures

32. Following a bolus injection of 20 mL of 0.25% bupivacaine into the following anatomic sites, which would lead to the highest subsequent peak blood levels and potential for toxicity?

A. Caudal
B. Epidural
C. Interscalene
D. Infraclavicular
E. Sciatic nerve

33. 600 mcg of preservative-free morphine is injected into the intrathecal space in a patient undergoing a Whipple procedure. Postoperatively, the patient develops hypoventilation approximately 6 hours following the spinal placement. This may be attributed to

A. Systemic absorption of the initial morphine dose from the cerebrospinal fluid space
B. Intraoperative use of 250 mcg IV fentanyl at intubation
C. Postoperative administration of 5 mg morphine IV by the postanesthesia care unit staff
D. Rostral spread of morphine in the cerebrospinal fluid space
E. Allergic reaction to morphine

34. Treatment of cyanide toxicity from nitroprusside administration may include all of the following except

A. Discontinuation of nitroprusside
B. Amyl nitrate
C. Hydroxycobolamine
D. Dicobalt ethylenediaminetetraacetic acid
E. Sodium thiosulfate
F. Methylene blue
G. Sodium nitrite
H. Pralidoxime chloride
I. Hyperbaric oxygen therapy

35. A craniotomy is performed in a 24-year-old otherwise healthy woman. Control of hypertension is achieved using sodium nitroprusside intraoperatively. Postoperative laboratory values may be notable for

A. Low vitamin B12 levels
B. Metabolic alkalosis
C. Elevated mixed venous oxygen saturation
D. Respiratory acidosis
E. Low SaO_2 values

36. You are called to evaluate a 32-year-old woman two days postpartum. She had an uneventful vaginal delivery with combined spinal epidural analgesia. She now complains of a headache. Blood pressure is 137/83 mm Hg, and the rest of her exam, including the neurologic examination, is unremarkable. Possible causes of headache include

A. Postdural puncture headache (PDPH)
B. Sagittal sinus thrombosis
C. Pregnancy-induced hypertension
D. Tension headache
E. All of the above

37. Which of the following has been shown to most likely decrease the likelihood of PDPH?

A. IV hydration
B. Bed rest
C. Prophylactic blood patch
D. Use of a pencil-point spinal needle (e.g., Sprotte or Whitacre)
E. Prophylactic epidural blood patch

38. Which of the following is NOT associated with or a known complication of PDPH?

A. Fever
B. Nuchal stiffness
C. Diplopia
D. Decreased hearing
E. Intracranial, subdural hemorrhage

39. A healthy 24-year-old woman complains of positional headache 1 day following an uneventful spinal for elective cesarean section. Which of the following needles is associated with the lowest risk of postdural puncture headache?

A. 25-gauge Whitacre
B. 25-gauge Quincke
C. 21-gauge Crawford
D. 18-gauge Tuohy
E. 24-gauge Sprotte

40. Risk factors for perioperative aspiration of gastric contents include all of the following except

A. Emergency surgery
B. Intestinal obstruction
C. Female gender
D. Obesity
E. Head injury

41. A 38-year-old male trauma patient is brought to the emergency department receiving bag-mask ventilation. At the time of rapid sequence intubation, there is a large regurgitation of gastric contents. Which of the following is NOT indicated?

A. Intubation
B. Saline lavage of the trachea to retrieve acidic fluid
C. Positive-pressure ventilation with 100% oxygen
D. Bronchoscopy for retrieval of particulate matter
E. Lateral decubitus and Trendelenburg positioning

42. Which of the following is a known independent predictor of postoperative cognitive decline (POCD)?

A. Inhalational anesthesia
B. Intraoperative hypotension
C. High educational level
D. Previous cerebrovascular accident
E. Long intraoperative time

43. An 86-year-old woman experiences increased confusion and disorientation postoperatively. She complains of "seeing" deceased relatives visiting her room. Which of the following risk factors is NOT considered a risk factor for postoperative delirium?

A. Visual impairment
B. Female gender
C. Sleep deprivation
D. Immobility
E. ICU admission

44. Intravenous administration of 1 liter of lactated Ringer's at room temperature will decrease the body temperature of a 70-kg person by approximately

A. 5 degrees C
B. 2.5 degrees C
C. 1 degree C
D. 0.25 degree C
E. 0.025 degree C

45. The most significant cause of intraoperative heat loss is from

A. Radiant loss
B. Conductive loss
C. Convective loss
D. Evaporative loss
E. Cold IV fluids

46. Which of the following is NOT true regarding perioperative hypothermia?

A. Hypothermia is associated with prolonged muscle relaxation.
B. Hypothermia is associated with increased transfusion requirements.
C. Postanesthesia care unit stay may be prolonged.
D. Hypothermia is associated with a less favorable outcome in patients with traumatic brain injuries.
E. Hypothermia is associated with an increased incidence of wound infections.

47. A 49-year-old man complains of visual disturbance 3 days following a laminectomy fusion surgery. Ischemic optic neuropathy (ION) is suspected. Which are the following is NOT a risk factor for ION?

A. Prone position
B. Long duration of surgery
C. Prolonged hypotension
D. Significant intraoperative blood loss
E. Baseline elevated intraocular pressure

48. A morbidly obese 57-year-old man complains of tingling of the fourth and fifth digits of the hand following open gastric bypass surgery. Which of the following minimizes the risk of this complication?

A. Forearm pronation
B. Forearm supination
C. Large anatomic ulnar tubercle
D. Elbow flexion
E. Elbow extension

49. A 68-year-old man develops right hand weakness and right facial droop on postoperative day 1 following coronary artery bypass grafting (CABG). This phenomenon is most likely

A. Hemorrhagic
B. Thrombotic
C. Hypoperfusion
D. Embolic
E. Positional nerve injury

50. A hypotonic infant with a history of central core disease presents for treatment of a dislocated hip. Which of the following anesthetic agents should be avoided?

A. Nitrous oxide
B. Cisatracurium
C. Droperidol
D. Sevoflurane
E. Long-acting opioids

51. While undergoing surgery for a tonsillar bleed, a 7-year-old boy develops tachycardia, hypertension, and hypercarbia. He is treated with a 2-mg/kg bolus of dantrolene and the procedure is quickly finished. This treatment acts by facilitating

A. Increased uptake of calcium into the sarcoplasmic reticulum
B. Binding of extracellular calcium
C. Decreased release of calcium from the sarcoplasmic reticulum
D. Buffering of metabolic acidosis
E. Antagonism with calcium at the neuromuscular junction

52. A 61-year-old woman with a history of rheumatoid arthritis calls you with complaints of significant hoarse speech 2 days following a laparoscopic cholecystectomy. Two attempts were required for intubation. The most appropriate next step in management is

A. Inform the patient that the hoarseness will resolve within one week.
B. Ask the patient to present to the surgeon who performed the laparoscopic cholecystectomy.
C. Instruct the patient to follow up with her rheumatologist.
D. Send the patient to an interventional pulmonologist for foreign body workup.
E. Arrange for otolaryngology consultation.

53. A 43-year-old man with a BMI of 42 reports a "rough"-feeling tooth postoperatively. Which teeth are at highest risk for dental trauma during intubation?

A. Maxillary central incisors
B. Maxillary canines
C. Mandibular central incisors
D. Maxillary lateral incisors
E. Mandibular lateral incisors

54. An otherwise healthy 39-year-old complains of altered speech and uncomfortable swallowing following a 3-hour orthopedic hand procedure with use of an LMA Classic. Cuff pressures were not measured intraoperatively. What injury is most likely?

A. Vocal cord paralysis
B. Subglottic stenosis
C. Hypoglossal nerve palsy
D. Superior laryngeal nerve palsy
E. Uvula edema

55. A 71-year-old man with a history of peripheral vascular disease undergoes posterior craniotomy in the beach-chair position with a right internal jugular central venous catheter and radial arterial line. Blood pressures intraoperatively were maintained at baseline, oxygen saturations were 99%, and blood gas findings were unremarkable. Twenty minutes postoperatively, the patient remains responsive only to painful stimuli. What etiology is most likely?

A. Inadequate arterial perfusion pressure
B. Hypoglycemia
C. Hypernatremia
D. Impaired venous return
E. Intracranial hemorrhage

56. A patient under general endotracheal anesthesia with rocuronium and propofol TIVA for endoscopic sinus surgery has a rising end-tidal CO_2 with increasing baseline. Ventilatory settings are unchanged. Gas flows are increased and the capnogram remains unchanged. An alarm alerts for "reversed flow." The most likely etiology is

A. Exhausted Baralyme absorbent
B. Malfunctioning expiratory valve
C. Malignant hyperthermia
D. Malfunctioning inspiratory valve
E. Normal finding in closed-circuit anesthesia

57. A positive-pressure leak test will NOT detect anesthesia machine leaks present in the

A. Oxygen cylinder check valve
B. Nitrous oxide cylinder pressure regulator
C. Second-stage oxygen pressure regulator
D. Vaporizer
E. APL valve

58. Which of the following will NOT raise intraocular pressure (IOP)?

A. Etomidate
B. Prone positioning
C. Hypoxia
D. Ketamine
E. Succhinlycholine

59. A preoperative patient characteristic that may NOT increase the risk of postoperative ischemic optic neuropathy (ION) is

A. Diabetes mellitus
B. Hypertension
C. Rheumatoid arthritis
D. Coronary artery disease
E. Cerebrovascular disease

60. Which approach to central venous cannulation is most likely to be associated with the complication of chylothorax?

A. Right external jugular vein
B. Left internal jugular vein
C. Right internal jugular vein
D. Left femoral vein
E. Right subclavian vein

61. A patient with eczema and documented food allergy to avocado and kiwi develops hypotension and bronchospasm during knee arthroscopy under spinal anesthesia. What should be avoided intraoperatively?

A. Iodine skin cleanser
B. Latex gloves
C. Cefazolin antibiotic prophylaxis
D. Vecuronium
E. Dextrane infusion

62. A spinal fusion patient is transfused in the postanesthesia care unit for acute blood loss anemia. Fifteen minutes following initiation of the packed red cells, she develops limited itching and hives, but remains otherwise stable. After stopping the transfusion, the most appropriate initial action is to administer

A. Epinephrine
B. Dexamethasone
C. Diphenhydramine
D. IV fluid bolus
E. All of the above

63. A 15-year-old girl vomits on induction of anesthesia for an elective rhinoplasty. She was chewing gum on arrival to the hospital. What is her recommended fasting period?

A. No fasting required
B. 2 hours
C. 4 hours
D. 6 hours
E. 8 hours

CHAPTER 16 ANSWERS

1. ANSWER: C

Succinylcholine is a depolarizing neuromuscular blocking agent adequate for induction but is not a good choice for maintenance of neuromuscular relaxation. Atracurium causes histamine release, which may cause hypotension in hypovolemic patients. Pancuronium would be a poor choice as it would likely worsen the patient's tachycardia. Rocuronium has the smallest effect on the cardiovascular system and is therefore the best option.

ADDITIONAL READINGS

Morgan G, Mikhail M, Murray M, eds. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2006.

2. ANSWER: B

In this patient, a ***high spinal*** would be the most likely cause of her symptoms. The classic symptoms of high spinal include numbness and/or tingling in the hands and shortness of breath. High spinal can occur up to 20 to 30 minutes after the onset of the block. The patient should be monitored closely to ensure that level of the spinal does not continue to move upward. In the event of continually rising spinal anesthesia, it may be necessary to intubate the patient to assist with ventilation until the anesthetic has worn off. The patient should be reassured.

Anytime a woman complains of shortness of breath during a cesarean section, amniotic fluid embolism should be considered. This patient's oxygen saturation remained stable and she was not complaining of a sense of impending doom. Treatment of amniotic fluid embolism is supportive. Pneumonia due to aspiration is always of concern in pregnant women. However, in this patient, the risk of aspiration is relatively low given the use of neuraxial anesthesia.

Finally, anxiety and hyperventilation could also cause a similar clinical picture, but other causes should be ruled out first.

ADDITIONAL READINGS

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3. ANSWER: D

This patient is presenting with a right-sided lesion; recall that the tongue points toward the lesion. Since the interscalene block was placed on the left, this does not explain the underlying etiology of a right-sided lesion.

An intraoperative stroke would be the most concerning diagnosis and should always be considered after a patient has been in the beach-chair position. In this position, the blood pressure cuff is usually on the arm, which is commonly below the level of the head and could be overestimating the patient's cerebral perfusion pressure. Therefore, one should consider that the patient's cerebral perfusion pressure is slightly less than the cuff pressure. As a result, it may be of benefit to maintain the mean arterial pressure slightly higher than usual to ensure adequate cerebral perfusion.

Stretch injury is also of concern from the beach-chair position. Although we take precautions to ensure the head is properly supported, there is considerable movement with a total shoulder. Diligent monitoring of the patient's position is necessary but often difficult in these cases. Adjustments should be made as often as needed and good communication with the surgeon is essential. In this patient, the stretch injury as the underlying cause would be less likely given the side of the lesion.

Nerve injury is a potential risk with any intubation. Although relatively uncommon, there are case reports to document injury to the hypoglossal and trigeminal nerves. The hypoglossal nerve runs over the most lateral prominence of the first cervical vertebrae, which can be stretched during head extension. It then enters the mouth below the mylohyoid muscle and can be impinged during direct laryngoscopy. Symptoms of injury to this nerve would be deviation of the tongue toward the side of nerve injury.

The lingual branch of the trigeminal nerve enters the mouth deep to the mucosa of the floor of the mouth and can also be injured during direct laryngoscopy. Injury to the lingual nerve will result in loss of sensation over the anterior two-thirds of the tongue on the same side as the nerve injury.

ADDITIONAL READING

Hong S, Lee J. Isolated unilateral paralysis of the hypoglossal nerve after transoral intubation for general anesthesia. *Dysphagia*. 2009;24:354–356.

4. ANSWER: A

Malignant hyperthermia is associated with a defective calcium channel located in the membrane of the sarcoplasmic reticulum. The ryanodine receptor is a calcium-induced calcium channel. Volatile anesthetics and succinylcholine cause the intracellular level of calcium to increase, which activates RYR. In patients with a defective RYR receptor, the calcium channel becomes "locked" open and the intracytoplasmic level of calcium continues to rise. This results in continuous muscle activation and increased metabolism

due to increased ATP consumption and hence the rise in temperature that occurs as a late sign. These factors, in turn, lead to the symptoms associated with malignant hyperthermia, including elevated temperature, metabolic acidosis, and increased CO_2 production.

The dyhydropyridine receptor is also involved in intracellular calcium levels. This gene has been associated with malignant hyperthermia in a few families but has not been as prominent as the causal link between RYR and malignant hyperthermia.

The acetylcholine receptor is directly activated by succinylcholine, which leads to activation of muscle contraction by allowing extracellular Ca^{2+} to flow into the cell and bind to the sarcoplasmic reticulum, allowing the release of large amounts of calcium into the cytoplasm. However, succinylcholine does not enter the cell to act directly on the RYR, causing it to become locked in the open position. Provided that the RYR is intact, the intracytoplasmic calcium could be taken up into the sarcoplasmic reticulum to prevent sustained contraction.

The GABA receptor is thought to play a role in the inhibition of pain in the spinal cord.

The function of the NMDA receptor is still unknown. It is thought to be involved in the cascade of events leading to neuronal cell death. It is also involved in producing long-term depression at central nervous system synapses.

ADDITIONAL READINGS

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Brunton L, Lazo J, Parker K, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. New York, NY: McGraw-Hill Companies, Inc.; 2006.

Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

5. ANSWER: C

This patient has multiple risk factors for ***aspiration pneumonia***. First, the results of the airway examination increase the likelihood that she will be difficult to intubate. Difficult intubation is the leading risk factor for aspiration of gastric contents under anesthesia and subsequent development of aspiration pneumonitis.

Second, the patient has GERD that is not treated with an H_2 blocker or a proton-pump inhibitor. This likely indicates that her lower esophageal sphincter tone is poor and her gastric pH is likely less than 2.5. A pH of 2.5 or greater has the same effect on pulmonary mucosa as distilled water. However, at a pH below 2.5, pulmonary damage will occur with a volume as small as 25 mL.

Given the significant risk of aspiration pneumonia in this patient, an immediate-acting antacid would be the best choice. Sodium citrate would be the best drug to give because its action is immediate. Although omeprazole and ranitidine would both help to increase the gastric pH and thus prevent pulmonary damage, both will take time (10 minutes to 3.5 hours depending on route of administration) to exert their effects. Omeprazole, a proton-pump inhibitor, and ranitidine, an H2 blocker, will prevent additional acid from being secreted into the stomach; however, neither drug will affect the pH of the contents already in the stomach. Thus, sodium citrate is the best choice for an immediate-acting drug that will increase the pH of the gastric contents. Use of omeprazole or ranitidine would be an excellent adjunct to help prevent the gastric pH from dropping after the sodium citrate has left the stomach.

ADDITIONAL READING

Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

6. ANSWER: B

Aspiration pneumonitis would be the most likely cause of this patient's respiratory distress. Aspiration pneumonitis is a chemical injury to the lungs due to the inhalation of sterile gastric contents. It is clear that the patient had reflux of gastric contents into the oropharynx during intubation, which increases her risk of aspiration. Her normal chest x-ray is consistent with a diagnosis of acute aspiration pneumonitis. However, one may also see inhaled food particles on the chest x-ray, usually in the right lower lobe. Aspiration pneumonia is an infectious process used to describe a patient with a history of aspiration of oropharyngeal contents colonized by pathogenic bacteria. Chest x-ray findings will be consistent with pneumonia (infiltrates) and may progress to acute respiratory distress syndrome (ARDS).

The patient is likely not suffering from opioid overdose because she is tachypneic. Opioids will decrease the drive to breathe and result in hypoventilation with low respiratory rates and potentially arrest of respiration, depending on the dose.

Pulmonary embolus should be considered in any patient with respiratory distress in the perioperative period. However, given the difficulties with the intubation, aspiration of gastric contents is more likely.

ADDITIONAL READING

Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

7. ANSWER: D

Anaphylactic and anaphylactoid reactions manifest as the same clinical syndrome, including bronchospasm, increased mucus secretion, vasodilation, edema, increased permeability of vasculature, and even cardiovascular collapse. The difference between the two lies in the way the mast cells and basophils are activated. In anaphylactic reactions, an antigen–antibody complex binds to a mast cell or basophil, resulting in the release of chemical mediators such as histamine, leukotrienes, kinins, and prostaglandins. In an anaphylactoid reaction, the complement, kinin-generating, fibrinolytic, or coagulation system is activated directly, leading to activation of mast cells and basophils, which then release the same chemical mediators as direct immunologic stimulation. The end syndrome is indistinguishable to the clinician, and therefore they are treated the same.

ADDITIONAL READING

Hall J, Schmidt G, Wood L, eds. *Principles of Critical Care*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2005.

8. ANSWER: C

This patient appears to be having an ***allergic reaction*** to cefazolin. These reactions can be caused by a variety of substances including drugs (antibiotics, neuromuscular blockers, anesthetic agents), environmental agents (latex), blood/blood products, and polypetides (protamine). More than 90% of allergic reactions to intravenously administered medications occur within 5 minutes of administration of the drug. It is most likely that this patient is having a reaction to the cefazolin.

The most appropriate initial treatment for anaphylaxis is epinephrine and fluids. Anaphylaxis produces a significant decrease in systemic vascular resistance due to dilation of capillaries and venules. This increased permeability will lead to loss of intravascular volume, which should be replaced with fluids.

Epinephrine is of particular importance because it will affect both the alpha- and beta-adrenergic receptors. The alpha-adrenergic vasoconstrictive effects of epinephrine will help to alleviate the symptoms related to the decreased systemic vascular resistance and increased capillary permeability. This includes hypotension, erythema, urticaria, and angioedema. The beta-adrenergic effects include bronchodilation, positive inotropic effect, and suppression of continued activation of inflammatory mediators from mast cells and basophils.

Epinephrine can be given intravenously, intramuscularly, or via inhalation depending on the patient's access. Adult IM doses are 0.2 to 0.5 mg every 5 to 15 minutes, depending on the severity of the reaction. IV infusions should be titrated to clinical response. Inhalational epinephrine is a last-resort form of dosing. The problems with inhalational epinephrine include inability to achieve a quick significant increase in the plasma epinephrine concentration, perioral paresthesias, bad taste, and gastrointestinal effects.

Diphenhydramine (Benadryl), a nonselective histamine blocker, will also be of benefit by curbing the affect of histamine. However, it is not the first-line therapy in an unstable patient with an anaphylactic reaction. In addition, glucocorticoids will also suppress the immune response, but these will take approximately 24 hours to be fully effective.

ADDITIONAL READINGS

Hall J, Schmidt G, Wood L, eds. *Principles of Critical Care*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2005

Kemp SF, Lockey RF, Simons F, Estelle R, on behalf of the World Allergy Organization ad hoc Committee on Epinephrine in Anaphylaxis. Epinephrine: The drug of choice for anaphylaxis. A statement of the World Allergy Organization. *World Allergy Organization Journal*. 2008;1(7):S18–S26.

9. ANSWER: D

Craniotomies and brain masses present a very delicate management dilemma between maintaining adequate cerebral perfusion pressure and preventing increased intracranial pressure. Several strategies can be employed to maintain proper balance. These include use of diuretics, hyperosmotic solutions such as mannitol, steroids, maintaining adequate mean arterial pressure, head-of-bed elevation, and hyperventilation.

Although controversial, controlled hyperventilation is considered to be effective to temporarily decrease intracranial pressure because a reduction in $PaCO_2$ causes a decrease in cerebral blood flow. Decreased cerebral blood flow results in a decrease in intracranial pressure. However, hypocarbia below a $PaCO_2$ of 25 mm Hg can result in a significant enough decrease in cerebral blood flow that ischemia can occur. Thus, a $PaCO_2$ of 30 to 35 mm Hg is an appropriate goal. This may need to be adjusted based on clinical findings in the surgical field.

It is important that the $PaCO_2$ is checked. $etCO_2$ can differ markedly from $PaCO_2$ due to changes in physiologic dead space during general anesthesia. Thus, frequent arterial blood gas assessments are necessary. It may be possible to correlate the $PaCO_2$ with the $etCO_2$ when the first arterial blood gas sample is checked; however, relying only on $etCO_2$ is not sufficient to ensure appropriate hyperventilation.

ADDITIONAL READING

Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

10. ANSWER: E

Airway fires are a very rare but serious complication during anesthesia and surgery. In the event of an airway fire, the ETT should be immediately removed for several reasons. The high temperature can cause continued thermal damage to the airway. Burning PVC releases toxic chemicals that spread into more distal portions of the airway, worsening damage. Finally, the ETT could potentially collapse, resulting in complete obstruction.

Disconnection of the circuit and discontinuation of all airway gases will remove the oxidizing source of the fire. Irrigation with normal saline will help to extinguish the fire as well as cool the airway to stop additional thermal injury. Once the fire has been extinguished, ACLS guidelines should be followed and an airway may need to be reestablished.

The American Society of Anesthesiologists recommends the following during an airway fire: without any delay, remove the ETT, stop the flow of all airway gases, remove sponges and other flammable material from the airway, and pour saline into the airway.

ADDITIONAL READINGS

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Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

11. ANSWER: C

Orthopedic surgeries are generally not associated with intraoperative awareness under general anesthesia. Cardiac, trauma, and obstetric surgeries tend to be associated with awareness because the patients may be too unstable to tolerate an appropriate depth of anesthesia. For those procedures that are not usually associated with awareness, the common causes include inaccurate labeling or administration of medications.

ADDITIONAL READING

Morgan G, Mikhail M, Murray M, eds. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2006.

12. ANSWER: A

The most likely explanation for new-onset right upper quadrant pain in a patient who has been on prolonged TPN is cholestasis. A HIDA scan would be the most sensitive test to confirm this diagnosis. Although prolonged TPN administration can also cause acute liver failure, this patient's liver enzymes are within normal limits, indicating that there is no destruction of liver cells. In addition, her normal INR decreases the likelihood that her liver function has declined.

Complications that can arise from using TPN include increased morbidity and mortality due to increased infection rates, difficulty with maintaining intravenous access needed for TPN, increased bacteremia, liver failure, cholestasis, and increased systemic inflammation. Several randomized prospective trials have shown that patients with pancreatitis should not receive TPN. As a result of this information, patients with pancreatitis are no longer maintained on TPN.

The randomized prospective studies have shown that the mortality from pancreatitis is significantly decreased if enteral nutrition is started earlier and TPN is avoided altogether. It has been shown that failure to provide enteral nutrition results in villous atrophy and loss of integrity at gap junctions. This has been associated with an increase in systemic inflammatory markers as well as an increase in bacteremia. Both of these findings are thought to worsen the inflammatory response and increase infection rates. The increase in bacteremia can also develop into sepsis, as central access is necessary for prolonged TPN use. The catheter presents a potential landing site for bacteria to colonize and proliferate.

ADDITIONAL READING

Hall J, Schmidt G, Wood L, eds. *Principles of Critical Care*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2005.

13. ANSWER: E

The patient's core body temperature is less than 35 degrees C. ***Hypothermia*** can cause coagulopathy, increased oxygen consumption secondary to shivering, vasoconstriction from increased epinephrine and norepinephrine, decreased oxygen delivery, and if severe enough, decreased heart rate and blood pressure and cardiac irritability leading to ventricular fibrillation.

Massive blood loss, a missed injury, and unknown clotting disorder could also result in hypotension and coagulopathy. However, this patient's vital signs had been stable and no other significant injuries leading to massive blood loss were present. Massive blood loss or a missed injury leading to unidentified blood loss often leads to hypotension and coagulopathy secondary to the blood loss being replaced with crystalloid only or crystalloid and packed red blood cells.

It is unlikely that the patient would have organized clots on lacerations and then begin oozing from his IV sites if he had an underlying clotting disorder. The sudden onset of oozing makes it more likely that this is an acquired disorder rather than a hereditary one.

ADDITIONAL READINGS

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14. ANSWER: A

The primary ways that heat is lost during surgery include evaporative loss from surgical site, redistribution of blood volume to the periphery, impairment of the hypothalamic and autonomic nervous system's thermoregulation, and use of unwarmed anesthetic gases and fluids.

The normal physiologic responses to hypothermia are shivering, cutaneous vasoconstriction, and piloerection. However, this patient is under general anesthesia, which blocks these responses. All of the strategies listed should be employed to raise the patient's body temperature. In addition, low-flow anesthesia and a heat–moisture exchanger in the anesthesia circuit may also be of benefit. Comparative studies have shown that forced-air units used appropriately and with maximum contact surface appear to be most effective to restore normal body temperature in a hypothermic patient.

ADDITIONAL READINGS

Ng SF, Oo CS, Loh KH, Lim PY, Chan YH, Ong BC. A comparative study of three warming interventions to determine the most effective in maintaining perioperative normothermia. *Anesth Analg*. 2003;96(1):171–176.

Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

15. ANSWER: A

All latex products should be avoided in this patient. Although she denies a latex allergy there seems to be an association between latex gloves and her atopy. This patient also has several risk factors that can result in an anaphylactic/anaphylactoid reaction to latex. These risk factors include being a healthcare worker, atopy to latex gloves, and allergies to foods that cross-react to latex, including kiwi, avocado, passion fruit, bananas, chestnuts, and mangos.

Anaphylactic/anaphylactoid reactions to latex are often difficult to recognize because the symptoms may not present for over an hour after exposure. This is different from the usual reaction time of 5 minutes with intravenously injected drugs. Thus, the patient's reaction may be inadvertently attributed to a medication instead of the latex. These reactions also range from a mild contact dermatitis to severe anaphylaxis. Treatment varies based on the severity of the reaction.

ADDITIONAL READING

Morgan G, Mikhail M, Murray M, eds. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2006.

16. ANSWER: E

Deep vein thrombosis is a significant cause of morbidity and mortality in patients during the postoperative period. Early ambulation after surgery and the use of intermittent pneumatic compression boots are both inexpensive and noninvasive methods for reducing the risk of VTE. These two methods are employed on almost all surgical patients. The use of heparin has increased substantially due to the clear improvement of morbidity and mortality with its use. The exact dosing has been investigated by several organizations, resulting in published guidelines to assist the clinician in ordering the best therapy for his or her patient.

In the patient described, the most appropriate VTE prophylaxis according to the current ACCP guidelines (seventh conference) would be 5,000 units of subcutaneous heparin three times daily or 40 mg of subcutaneous Lovenox once daily. However, the above patient has had an epidural placed. Prospective studies have shown three-times-daily dosing of heparin for VTE prophylaxis may lead to increased surgical bleeding. Although there is enough evidence to say that twice-daily dosing of heparin is safe in neuraxial anesthesia; there is not enough evidence at this time to determine whether this holds true for thrice-daily dosing. Therefore, the safest thing for this patient would be to provide twice-daily dosing of 5,000 units of subcutaneous heparin while the epidural is in place. In addition, low-dose anesthetic in the epidural may be preferred to allow for earlier recognition of neurologic complications. Finally, due to the incidence of heparin-induced thrombocytopenia, a platelet count should be obtained prior to removal of the epidural catheter.

ADDITIONAL READINGS

Horlocker T, Wedel D, Rowlingson J, et al. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine

Evidence-Based Guidelines (Third Edition). *Regional Anesthesia & Pain Medicine: January/February*. 2010;35(1):64–101.
Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, Ray JG. Prevention of venous thromboembolism: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004 Sep;126(3 Suppl):338S–400S.

17. ANSWER: B

Bradycardia during insufflation of the abdomen is usually the result of a vagally mediated response to the increase in intraabdominal pressure. Intravenous lidocaine is often used during induction of anesthesia to help blunt the sympathetic response during direct laryngoscopy and ETT placement. Lidocaine is generally safe up to a dose of 2 mg/kg via intravenous injection. At doses above this, several adverse effects can occur, including bradycardia. However, in this patient, the onset of bradycardia was several minutes after the administration of the intravenous lidocaine, making it an unlikely culprit. In addition, the patient's bradycardia resolved with desufflation of the abdomen. This increases the likelihood that the bradycardia is secondary to insufflation.

Propofol can rarely cause a profound bradycardic response. Again, this is less likely given the time between injection of propofol and the timing of the bradycardic response.

An overdose of fentanyl may result in a decreased heart rate, but it is not likely to result in profound bradycardia. Overdose of any narcotic usually results in significant respiratory distress. Because the patient's ventilation is being controlled, it is not possible that she became bradycardic as a result of respiratory distress.

Carbon dioxide embolus will initially present with a rapidly declining etCO_2.

ADDITIONAL READINGS

Barash P, Cullen B, Stoelting R, et al. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, a Wolters Kluwer Business; 2009.
Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

18. ANSWER: C

The most likely cause of the patient's symptoms is ***CO_2 embolism***. Although any of the causes mentioned could lead to a decrease in etCO_2, this situation is most consistent with CO_2 embolism. The blind insertion of the Veress needle has a risk of piercing a vessel, resulting in direct intravascular injection of CO_2. Additional facts that support CO_2 embolism include uneven expansion of the abdomen and failure to achieve full insufflation after infusion of several liters. Air embolism usually occurs in the sitting position with a vein open to air. PE from VTE is unlikely in a young patient who is physically active. The same is true for myocardial infarction.

ADDITIONAL READING

Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

19. ANSWER: A

There are two types of heparin-induced thrombocytopenia (HIT). **HIT type I** usually occurs after 1 to 4 days of heparin therapy. It is usually self-limited and there is often no need to stop heparin therapy. **HIT type II**, however, is a life-threatening condition in which heparin therapy should be discontinued. HIT type II usually develops 5 to 10 days after initiation of heparin therapy due to the development of heparin PF4 antibodies, leading to platelet activation, aggregation, and formation of clots. These clots can cause significant damage, including arterial thrombosis that can lead to limb ischemia, myocardial infarction, and cerebrovascular accidents.

Making a definitive diagnosis of HIT is not always easy. The patient must meet the following criteria: development of thrombocytopenia while on heparin therapy, exclusion of other causes of thrombocytopenia, improved platelet count after discontinuation of heparin, and presence of heparin-dependent platelet antibody.

Despite developing HIT, many patients may still need options for prophylaxis against deep venous thrombosis/pulmonary embolus. There are a few choices, including direct thrombin inhibitors (lepirudin, desirudin) and factor Xa inhibitors (fondaparinux, danaparoid).

ADDITIONAL READINGS

Hassell K. The management of patients with heparin-induced thrombocytopenia who require anticoagulant therapy. *Chest*. 2005;127:1S-8S.
Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

20. ANSWER: A

Local anesthetic toxicity is a potential, albeit rare, complication of any procedure requiring its use. Toxicity can occur with direct vascular injection or with systemic absorption. With the increasing use of regional anesthesia, it is important to be able to recognize the signs of toxicity early.

The signs and symptoms of toxicity may be subtle at first but can rapidly progress to seizures and on to cardiovascular collapse. Initially, patients may experience dizziness or lightheadedness, perioral numbness or tingling, metallic taste, or tinnitus. Continued increases in serum local anesthetic concentration can result in tremors, muscle twitching, generalized tonic-clonic seizures, and loss of consciousness. In the most severe cases, cardiovascular disturbances and collapse from hypotension and vasodilation, or myocardial conduction abnormalities including arrhythmias, bradycardia, and cardiac arrest can occur.

Finally, treatment must be swift and includes immediate cessation of local anesthetic administration. The patient's vital signs should be closely monitored and treated aggressively with fluids and vasopressors if needed. BLS and ACLS algorithms should be followed. However, the clinician should be sensitive to the potential arrhythmogenic properties of epinephrine in the setting of bupivacaine-induced cardiac toxicity. The ASRA consensus guideline recommends reducing individual epinephrine doses to less than 1mcg/kg. Seizure treatments including benzodiazepines, barbiturates, and even propofol should be readily available to treat seizures, should they develop. Lipid emulsion (20%) therapy may be required, at a bolus dose of 1.5 mL/kg followed by 0.25 mL/kg/min. The bolus dose may be repeated for refractory cardiovascular collapse. If the patient will require additional regional anesthesia, as in the case above, the epidural catheter should be replaced when the patient is stable and the blood concentration of the local anesthetic has decreased. In this case, the catheter likely migrated into the vasculature and the negative aspiration was a false negative.

ADDITIONAL READING

Neal JM, Bernards CM, Butterworth JF, et al. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med*. 2010;35:152–161.

Steele S, Nielsen K, Klein S. *Ambulatory Anesthesia and Perioperative Anesthesia*. 1st ed. New York, NY: McGraw-Hill Companies, Inc.; 2005.

21. ANSWER: B

Fractures of long bones can release fat into the systemic circulation, leading to ***fat embolism syndrome***. There is a typically a latent period of 12 to 72 hours after injury before clinical symptoms become apparent. Clinical symptoms of fat embolism syndrome include neurologic, pulmonary, and skin manifestations. Neurologic symptoms can range from confusion to coma. Pulmonary symptoms are often similar to those seen in acute respiratory distress syndrome, including hypoxemia, dyspnea, and diffuse injury on chest x-ray. Skin symptoms are a petechial rash that is usually seen over the upper chest, neck, and face. Other symptoms include fat emboli in the retinal vessels on funduscopic exam, thrombocytopenia, and anemia. Rarely patients can decompensate and develop acute right heart failure.

There are two features that distinguish fat embolism from pulmonary or air embolism: the petechial rash and the presence of a recent long bone fracture. A CO_2 embolism will occur only if CO_2 is directly instilled into the vasculature. This scenario is limited to laparoscopic surgery in which the Veress needle or trocar has been inadvertently placed into the vasculature.

ADDITIONAL READING

Hall J, Schmidt G, Wood L, eds. *Principles of Critical Care*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2005.

22. ANSWER: A

Fat embolism syndrome is the result of fat emboli in the microvasculature of the lung. This results in a diffuse lung injury that is best managed with the same lung-protective ventilator settings that are used in acute respiratory distress syndrome. Under the lung-protective ventilator setting guidelines, the goal of oxygenation is 88% to 90%. A low TV of 4 to 6 mL/kg is used to prevent ventilator-induced lung injury. Using this low TV, a permissive hypercapnia may be required, as the respiratory rate will not provide adequate compensation to maintain minute ventilation.

High-frequency ventilation is a type of mechanical ventilation with very high respiratory rates (>150 breaths per minute) and very small TVs. High-frequency ventilation is used to reduce ventilator-associated lung injury (VALI), especially in the context of acute respiratory distress syndrome and acute lung injury. It would not be appropriate as an initial treatment approach in the setting described above.

ADDITIONAL READING

Hall J, Schmidt G, Wood L, eds. *Principles of Critical Care*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2005.

23. ANSWER: A

Transfusion-related acute lung injury (TRALI) is the leading cause of transfusion-related morbidity and mortality. The diagnosis is often difficult to establish early as it is a clinical diagnosis and can be difficult to distinguish from transfusion-associated circulatory overload (TACO). Diagnostic criteria for TRALI include acute onset of acute lung injury, hypoxemia (Pao_2/FiO_2 < 300), bilateral infiltrates on chest x-ray, no evidence of left atrial hypertension (fluid overload), no preexisting acute lung injury prior to transfusion, onset

within 6 hours of transfusion, and no temporal relationship to an alternative risk factor for acute lung injury.

ADDITIONAL READING

Triulzi D. Transfusion-related acute lung injury: current concepts for the clinician. *Anesth Analg.* 2009;108:770–776.

24. ANSWER: D

Treatment for transfusion-related acute lung injury (TRALI) is supportive and can be as little as supplemental oxygen or as invasive as endotracheal intubation, with aggressive ventilatory support. Aggressive ventilatory support includes using low tidal volumes (4 to 6 mL/kg), high respiratory rates, and the judicious use of positive end-expiratory pressure. TRALI usually resolves relatively quickly, with infiltrate resolution within 96 hours of transfusion. Administration of diuretics can actually worsen the clinical condition of patients with TRALI because it may cause hypovolemia. The position of the ETT is not the cause of the patient's respiratory distress and thus is not going to change the patient's status. Antibiotics are not indicated in TRALI because the lung injury is not microbial in nature.

ADDITIONAL READING

Triulzi D. Transfusion-related acute lung injury: current concepts for the linician. *Anesth Analg.* 2009;108:770–776.

25. ANSWER: E

All of the changes can occur when a tourniquet used during the operative procedure is deflated. These are all usually transient and do not produce a clinically significant change in an otherwise healthy patient. However, prolonged cuff inflation or simultaneous deflation of two or more cuffs can produce a clinically significant change. Therefore, patients should be closely monitored when a tourniquet is deflated.

ADDITIONAL READING

Morgan G, Mikhail M, Murray M, eds. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill Companies, Inc.; 2006.

26. ANSWER: E

Anytime a patient has a reported allergy to contrast dye, the benefits of the procedure must be weighed against the risk of the allergy. In this patient a repair is necessary given both the size of the aneurysm and the recent increase in size. If endovascular repair is possible, it provides many advantages over an open repair. Given this patient's extensive cardiac history, the preferred method of repair would be endovascular, with proper pretreatment to minimize the risk of a contrast allergy.

To make endovascular repair and the needed dye administration safe, the patient should be pretreated for the contrast allergy.

The American College of Radiology has provided recommended ***treatment protocols for patients at increased risk for reaction to IV contrast dye***. There are two protocols, one for corticosteroid therapy alone and one that combines an antihistamine with the corticosteroid. In the corticosteroid-only regimen, methylprednisolone 32 mg PO is given 12 and 2 hours prior to the procedure. In the **corticosteroid/antihistamine regimen**, prednisone 50 mg PO is given 13 hours, 7 hours, and 1 hour prior to the procedure. Diphenhydramine 25 to 50 mg IV/IM/PO is given 1 hour prior to the procedure. Nonionic, low-osmolality contrast medium may be used.

ADDITIONAL READING

Nayak K, White A, Cavendish J, et al. Anaphylactoid reactions to radiocontrast agents: prevention and treatment in the cardiac catheterization laboratory. *J Invasive Cardiol*. 2009;21:548–551.

27. ANSWER: D

There has been much debate about the best protocol for the ***prevention of contrast-induced nephropathy*** in patients at risk. Although most clinicians would agree that sodium bicarbonate is better at preventing contrast-induced nephropathy, recent evidence shows there is no benefit of sodium bicarbonate over half-normal saline. There is also mixed evidence surrounding the use of N-acetylcysteine: some randomized controlled trials have shown significant reduction with the use of N-acetylcysteine, but others have shown no statistical difference.

The following guidelines were established by the Canadian Association of Radiologists:

1. For inpatients, hydration with 1 mL/kg/hr of 0.9% NaCl for 12 hours before and after the procedure
2. For same-day procedures, hydration with 1 to 2 mL/kg/hr of 0.9% NaCl or $NaHCO_3$ for 3 to 6 hours prior to the procedure and 6 hours after the procedure
3. A shorter $NaHCO_3$ regimen that can be used is 150 mEq of $NaHCO_3$ in 1 L of D5W at 3 mL/kg/hr for 1 hour before the procedure and then at 1 mL/kg/hr for 6 hours after the procedure

4. Metformin should be discontinued at the time of the procedure and held for 48 hours or until the patient's baseline kidney function has returned.
5. The use of N-acetylcysteine can be neither recommended or refuted due to the lack of consistent evidence regarding prevention of contrast induced-nephropathy.

ADDITIONAL READING

Benko A, Fraser-Hill M, Magner P, et al. Canadian Association of Radiologists: Consensus Guidelines for the Prevention of Contrast-Induced Nephropathy. *Can Assoc Radiol J.* 2007;2:79–87.

28. ANSWER: E

All of the answer choices listed can contribute to hypothermia. Propofol inhibits vasoconstriction and shivering, which are typical methods for increasing body temperature. Morphine can impair the thermoregulation center, contributing to hypothermia. All the inhaled anesthetics (volatile agents and nitrous oxide) inhibit the thermoregulatory response, leading to peripheral vasodilation and decreased core temperature. This is characterized by a 1-degree C drop in body temperature in the first 30 to 60 minutes after induction. The body temperature will continue to drop under inhaled anesthetics for the first 2 to 3 hours of surgery, when it reaches a plateau with the return of vasoconstriction. Finally, regional anesthesia results in the inability of vasoconstriction and shivering below the level of the block. In addition to the factors listed, the exposure of the abdomen also results in significant heat loss. Given the high vascularity of the bowel combined with an inability to vasoconstrict, significant heat is lost as the blood passes through the bowel exposed to the cold operating room environment.

ADDITIONAL READINGS

Sieber F, ed. *Geriatric Anesthesia*. 1st ed. New York, NY: McGraw-Hill Companies, Inc.; 2007

Yao F, Fontes M, Malhotra VA, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

29. ANSWER: A

Postoperative renal failure is a common complication of aortic aneurysm repair. Six percent of patients undergoing aneurysm repair require dialysis postoperatively. With some techniques, the cross-clamp location and time are extremely important for renal protection. However, the main predictor of postoperative renal failure is preoperative renal failure. Strategies to optimize renal perfusion include maintaining adequate intravascular volume as well as minimizing nephrotoxins and optimizing renal blood flow. Fenoldopam, a selective dopamine-1 agonist, has shown some promising results as a renal protectant.

ADDITIONAL READINGS

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Fleisher LA. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia, PA: Saunders; 2009:226–235.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2013–2014.

30. ANSWER: A

In an otherwise healthy patient who is narcotic-naïve, the combination of 4 mg of midazolam and 4 mg of hydromorphone is likely the cause of her respiratory depression. Of the choices listed, the opioid antagonist naloxone would, by reversing the opioid effect, lead to a restoration of adequate respiration. Although this would likely result in decreased pain control, it would identify narcotic overdose as the cause of her respiratory depression, more likely than a benzodiazepine overdose, which would be diagnosed by giving the benzodiazepine antagonist flumazenil to reverse the midazolam effect.

Naloxone should be used with caution as it has a short half-life and short duration (30 to 60 minutes) and the patient can become "renarcotized." Therefore, the patient should be continuously monitored for respiratory depression in the following hours after using naloxone for the reversal of long-acting opioids. Should respiratory depression occur again, the patient may need additional doses of naloxone.

Giving additional midazolam will only worsen the problem if the patient is suffering from respiratory depression from opioid overdose, as there is a synergistic respiratory depression effect when used with narcotics.

The remaining three drugs, dezocine, meptazinol, and nalbuphine, are agonist-antagonist compounds and will not produce the necessary reversal to determine whether the patient has delayed emergence due to opioid overdose.

ADDITIONAL READING

Miller R, Eriksson L, Fleisher L, Wiener-Kronish J, Young, W, eds. *Miller's Anesthesia*. 7th ed. New York, NY: Churchill Livingstone; 2009.

31. ANSWER: B

EMLA cream is a eutectic mixture of 2.5% lidocaine and 2.5% prilocaine. When applied for 45 to 60 minutes under a bandage, it provides analgesia for IV placement or other procedures. Prilocaine use carries the increased risk of ***methemoglobinemia*** at the dose of approximately 2.5 mg/kg in healthy children and 5 mg/kg in healthy adults. As an amide local anesthetic, it undergoes metabolism in the liver and becomes O-toluidine. This metabolite causes the oxidation of hemoglobin to methemoglobin. Conventional pulse oximeters measure wavelengths for oxyhemoglobin and deoxyhemoglobin forms only. This leads to artificially low readings with methemoglobin, and cooximetry with four-wavelength measurement is required to distinguish these forms. High levels of methemoglobin may be treated with IV methylene blue. A shortened PR interval may be seen in Wolff-Parkinson-White syndrome. Bright-red mucous membranes may be seen in carbon monoxide poisoning. Masseter spasm has been described in children receiving succinylcholine and/or halothane. Seizures are late symptoms of local anesthetic toxicity with high plasma levels, unlikely to occur with the use of topical lidocaine or prilocaine.

ADDITIONAL READINGS

Guay J. Methemoglobinemia related to local anesthetics: a summary of 242 episodes. *Anesth Analg.* 2009;108:837–845.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:929–935.

Schwartz L, Rockoff MA, Koka BV. Masseter spasm with anesthesia: incidence and implications. *Anesthesiology*. 1984;61:72–775.

32. ANSWER: A

Uptake of injected local anesthetics into the blood is related to the degree of vascularity and/or hyperdynamic circulation in the surrounding area. This phenomenon is independent of the type of local anesthetic used; however, it is thought that more lipid-soluble agents may have less uptake owing to increased absorption into local tissues. Absorption rates, from highest to lowest, are as follows: Intercostal > Caudal > Epidural > Brachial Plexus (Interscalene/Supraclavicular/Infraclavicular) > Sciatic/Femoral > Spinal. Highly vascular areas such as the scalp, pleura, and bronchial mucosa show peak blood levels similar to direct intravascular injection.

KEY FACTS: LOCAL ANESTHETIC TOXICITY BY SITE

Intercostal > Caudal > Epidural > Brachial Plexus > Sciatic > Spinal

ADDITIONAL READINGS

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Covino BG. Pharmacology of local anesthetic agents. *Br J Anaesth.* 1986;58:701–716.

Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: A mutifactorial concept. *Reg Anesth Pain Med.* 2004;29:564–575.

33. ANSWER: D

Neuraxial opioids provide analgesia via action at the dorsal horn opioid receptors. In the subarachnoid space, hydrophilic opioids such as morphine are slowly cleared from the cerebrospinal fluid and provide prolonged spinal analgesia. Lipophilic opioids (such as fentanyl) are more quickly cleared and less likely to be associated with late respiratory depression. Respiratory depression after neuraxial morphine is biphasic. Early risk at 30 to 90 minutes is associated with initial systemic absorption. Late risk at 6 to 18 hours is due to rostral spread of morphine through the cerebrospinal fluid to respiratory centers in the brainstem.

ADDITIONAL READINGS

Hadzic A, ed. *Textbook of Regional Anesthesia and Acute Pain Management*. New York: McGraw-Hill; 2007:134, 204.

Carvalho B. Respiratory depression after neuraxial opioids in the obstetric setting. *Anesth Analg.* 2008;107:936–941.

34. ANSWER: H

Cyanide poisoning may occur with use of sodium nitroprusside (SNP) for vasodilation. SNP is constructed from five cyanide molecules, one nitric group, and a ferrous iron moiety. The cyanide is released following reaction between the SNP radical with the ferrous iron in red blood cells. In the liver rhodanase system, the cyanide is metabolized to thiocyanate, which has a half-life of 4 days and is eliminated in the urine. Thiocyanate may be toxic also at high levels, resulting in central nervous system symptoms. Cyanide inhibits cellular metabolism by binding cytochrome oxidase in the mitochondrial electron transport chain. Indicators of cyanide poisoning include metabolic acidosis, elevated mixed venous O_2, and tachyphylaxis to SNP.

The treatment of cyanide poisoning is based on a **two-step strategy**. The ***first step*** is the administration of **amyl nitrate** or **sodium nitrite**. These nitrites convert oxyhemoglobin to methemoglobin by oxidizing the iron group of hemoglobin from Fe^{2+} (ferrous state) to Fe^{3+} (ferric state). Methemoglobin treats cyanide poisoning by diffusing the cyanide from cytochrome A3 (of the respiratory chain) to bind to methemoglobin by forming a methemoglobin–CN

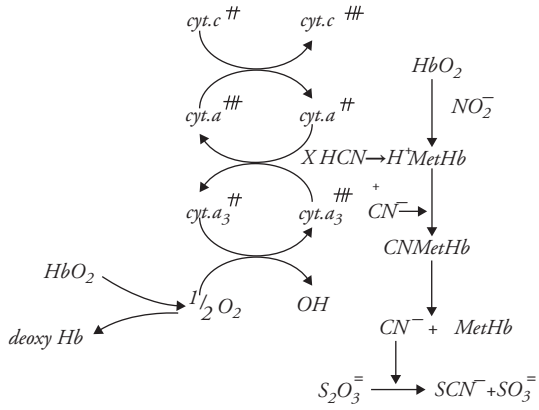

Figure 16.1 Cyanide poisoning.

SOURCE: Beasley DMG, Glass WI. Cyanide poisoning: pathophysiology and treatment recommendations. *Occup Med*. 1998;48(7):427–431.

complex, or cyanomethemoglobin. This cyanomethemoglobin complex is relatively nontoxic. The ***second step*** is adding a sulfur atom compound, usually **thiosulfate** (S_2O_3), to convert cyanide from methemoglobin to a less toxic compound, **thiocyanate**, which is excreted in the urine (Fig. 16.1).

Cyanide also binds tightly to cobalt ions, and **hydroxocobalamin** (a form of vitamin B12) has recently been approved by the U.S. Food & Drug Administration as a cyanide antidote (Cyanokit; King Pharmaceuticals, Bristol, TN). It has the advantages of rapid onset of action and low toxicity at antidotal doses.

Methylene blue has oxidizing properties and is used for the treatment of methemoglobinemia. Methylene blue is reduced to leucomethylene blue, which then acts to reduce the heme group from methemoglobin back to hemoglobin. At high doses, however, methylene blue actually induces methemoglobinemia, reversing this pathway. Methylene blue also blocks accumulation of cyclic guanosine monophosphate (cGMP) by inhibiting the enzyme guanylate cyclase: this action results in reduced responsiveness of vessels to cGMP-dependent vasodilators such as nitric oxide and carbon monoxide. Because its reduction potential is similar to that of oxygen and can be reduced by components of the electron transport chain, large doses of methylene blue are sometimes used as an antidote to cyanide poisoning. Methylene blue was also used in the mid-twentieth century in the treatment of carbon monoxide poisoning.

Ethylenediaminetetraacetic acid (EDTA) is a chelating agent used to treat acute and chronic lead poisoning by removing toxins (including heavy metals such as lead, cadmium, and mercury) from the blood. The word "chelate" comes from the Greek root *chele*, which means "to claw." EDTA has a clawlike molecular structure that binds to heavy metals and other toxins. EDTA chelation therapy is approved by the U.S. Food & Drug Administration as a treatment for lead and heavy metal poisoning. It is also used as an emergency treatment for hypercalcemia and the control of ventricular arrhythmias associated with digitalis toxicity. ***Dicobalt EDTA*** may also be used for cyanide toxicity because it directly binds cyanide, obviating the need to cause methemoglobinemia.

Pralidoxime is an antidote used for organophosphate poisoning by causing acetylcholinesterase inhibition. It removes the organophosphate from cholinesterase, allowing it to work normally again. This is known as "regenerating" or "reactivating" acetylcholinesterase, allowing the breakdown of acetylcholine at the synapse. After some time, though, some inhibitors can develop a permanent bond with cholinesterase, known as aging, where oximes such as pralidoxime cannot reverse the bond. Pralidoxime is often used with atropine (a muscarinic antagonist) to help reduce the parasympathetic effects of organophosphate poisoning. Pralidoxime is not recommended for cyanide poisoning.

ADDITIONAL READINGS

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Beasley DMG, Glass WI. Cyanide poisoning: pathophysiology and treatment recommendations. *Occup. Med*. 1998:48(7):427–431.
Faust RJ, ed. *Anesthesiology Review*. 3rd ed. Philadelphia, PA: Churchill Livingstone; 2002:156–157.
Pincus MR, Abraham Jr NZ. Toxicology and therapeutic drug monitoring. Henry's Clinical Diagnosis and Management by Laboratory Methods, 22nd ed, Philadelphia PA: Elsevier Sanders;2011:329.
Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2116.

35. ANSWER: C

Cyanide poisoning may occur with use of sodium nitroprusside for vasodilation. Metabolic acidosis and elevated mixed venous O_2 levels are laboratory values consistent with cyanide poisoning. Cyanide binds to the mitochondrial cytochrome oxidase, preventing the oxidative phosphorylation pathway for forming ATP. As a result, cells are only able to produce ATP through the anaerobic pathway, leading to an excess of lactate and a metabolic acidosis. The elevated mixed venous O_2 levels are due to the inability to use oxygen at the cellular level because of the blocked oxidative phosphorylation.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:331.
Faust RJ, ed. *Anesthesiology Review*. 3rd ed. Philadelphia, PA: Churchill Livingstone; 2002:156–157.
Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone, 2010:2116.

36. ANSWER: E

Differential diagnosis of ***postpartum headache*** includes tension headache, migraine, caffeine withdrawal, hypertensive headache, infectious (sinusitis, meningitis, encephalitis), thrombotic (cortical vein thrombosis), hemorrhagic (subarachnoid hemorrhage, subdural hemorrhage), increased intracranial pressure, pneumocephalus, or PDPH. The major complaint with PDPH is a positional headache that improves with recumbency. Patients may also report dizziness or vomiting. Other symptoms may include photophobia, tinnitus, visual disturbance, and nuchal rigidity. These cranial nerve symptoms are thought to be related to mechanical traction due to the low cerebrospinal fluid volume. One theory of the mechanism of the headache is that venous dilation occurs in response to the drop in intracranial cerebrospinal fluid pressure, leading to a vascular headache. Careful history and examination must be performed when working up a postpartum headache due to the broad differential diagnosis.

ADDITIONAL READINGS

Bleeker CP, Hendriks IM, Booij LH. Postpartum post-dural puncture headache: is your differential diagnosis complete? *Br J Anaesth*. 2004;93:461–464.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002:414–415.

37. ANSWER: D

Several strategies have been investigated to prevent ***PDPH***. Bed rest and recumbency have not been shown to decrease the risk. Increased hydration has not been found to decrease the risk and does not augment cerebrospinal fluid production. Caffeine is a treatment of PDPH but is not efficacious to prevent the headache. Prophylactic blood patch has been investigated with mixed results. A 2010 Cochrane review did not show enough evidence to recommend prophylactic epidural blood patch.

ADDITIONAL READINGS

Boonmak P, Boonmak S. Epidural blood patching for preventing and treating post-dural puncture headache. *Cochrane Database Syst Rev* 2010; 20:CD001791.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2002:415–417.

38. ANSWER: A

Traction on intracranial structures and venodilation are thought to cause the pain of a PDPH, and are believed to be related to low cerebrospinal fluid volume. This can lead to headache, nuchal stiffness, vomiting, diplopia, tinnitus, and venous hemorrhage. Fever may be associated with sinusitis or meningitis as an etiology for headache.

ADDITIONAL READINGS

Bleeker CP, Hendriks IM, Booij LH. Postpartum post-dural puncture headache: is your differential diagnosis complete? *Br J Anaesth*. 2004;93:461–464.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002:414–415.

39. ANSWER: A

Several needle characteristics are critical determinants in development of PDPH. Larger-gauge needles create a larger hole and therefore increase the risk of PDPH. The incidence of PDPH with the standard 20- or 22-gauge Quincke cutting beveled needle commonly can be as high as 40%. This can be reduced to 5% by using a 24- to 27-gauge needle. Dural wounds from an 18-gauge Tuohy carry a risk greater than 75% for PDPH. An important factor to reduce the risk of PDPH is the shape of the tip of the spinal needle. Blunt-tipped spinal needles separate dural fibers and allow recoil with minimal tearing, which has been shown to reduce cerebrospinal fluid leak and PDPH. Atraumatic needles, such as pencil-point or noncutting needles, result in smaller holes in the dura that tend not to remain open and have three times less cerebrospinal fluid leakage than Quincke needles. Several atraumatic spinal needles have been introduced, the Sprotte and Whitacre being most commonly used. Thomas et al. showed that PDPH incidence could be reduced from 54% to 29% if a 20-gauge atraumatic needle was used rather than a Quincke cutting beveled needle. The incidence could be further reduced to 4% when 22-gauge atraumatic spinal needles are used. Disadvantages of the atraumatic needles include increased cost, different "feel" and lack of "pop" that is often felt upon piercing the dura, occasional failure to obtain cerebrospinal fluid, and difficulty penetrating the skin due to the dull tip (Fig. 16.2).

ADDITIONAL READINGS

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Hadzic A, ed. *Textbook of Regional Anesthesia and Acute Pain Management*. New York: McGraw-Hill; 2007:210–212.

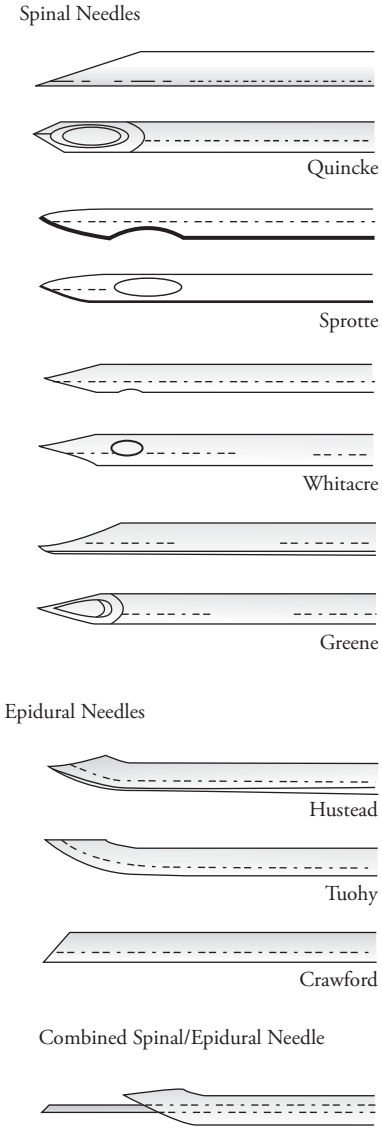

Figure 16.2 Some of the commercially available needles for spinal and epidural anesthesia. Needles are distinguished by the design of their tips.

SOURCE: Barash, *Clinical Anesthesia*, Figure 25–6.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002:414–415.

40. ANSWER: C

Risk factors for pulmonary aspiration of gastric contents include increased gastric contents ("full stomach") as seen with emergent surgeries, as well as with decreased gastric emptying (pregnancy, diabetes, obstruction, pain), increased intragastric pressure (obesity, lithotomy position), gastroesophageal reflux disease, and decreased airway protective reflexes (light anesthetic, low Glasgow Coma Scale score).

ADDITIONAL READINGS

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

41. ANSWER: B

Three main categories of gastric matter may be aspirated:

1. Acidic (pH < 2.5) fluid, which causes chemical pneumonitis (Mendelsson syndrome)
2. Particulate matter
3. Bacterially contaminated matter (e.g., feculent emesis)

The impact of each of these must be considered in the management of an aspiration event. Acidic irritation leads to bronchospasm, bronchiolitis, and pulmonary edema. Solid particles may cause obstructive or ball-valve phenomena. When aspiration is witnessed, the oropharynx should be rapidly suctioned and the patient repositioned to a lateral decubitus or Trendelenburg position. The trachea should be intubated and suctioned, and positive-pressure ventilation with 100% FiO_2 should be instituted. Bronchoscopy may be required to remove any obstructing particles. Prophylactic use of saline lavage, steroids, or antibiotics has not been shown to decrease mortality in pulmonary aspiration.

ADDITIONAL READINGS

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42. ANSWER: D

It is now known that patients demonstrate a transient decrease in performance on cognitive testing after surgery and anesthesia. These deficits have been found to reverse after approximately 3 months. Studies investigating POCD have multiple limitations, including definition/diagnosis of cognitive decline and unknown preoperative trajectory of decline. Although conclusive evidence is still uncertain, randomized controlled trials thus far have suggested that POCD is not associated with the inhalational agent used, fentanyl dosage, anesthetic depth, surgical procedure time, or intraoperative hypotension. Independent predictors of POCD have been

identified as advanced age, low educational level, preoperative cognitive deficit, depression, history of cerebrovascular accident without deficit, and type of surgical procedure (especially cardiac and orthopedic surgery).

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Monk TG, et al. Predictors of cognitive dysfunction after major noncardiac surgery. *Anesthesiology*. 2008;108:18–30.

43. ANSWER: B

Postoperative delirium is defined as an acute alteration of consciousness and cognition that is not due to preexisting dementia or another medical condition. It is theorized to be related to a lack of "brain reserve" in this vulnerable organ. Risk factors include advanced age, male gender, functional/immobility or sensory impairment, polypharmacy, pain, sleep deprivation, intensive care unit admission, decreased oral intake, high-risk or orthopedic surgery, and a history of cognitive impairment or depression.

ADDITIONAL READINGS

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 2000.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2266–2268.

44. ANSWER: D

One unit of cold blood or 1 L of room-temperature (20 degrees C) crystalloid or one unit of packed red cells at 4 degrees C has been found to decrease mean body temperature by approximately 0.25 degrees C. It takes 16 kcal to warm these fluids to body temperature. In a 70-kg person with a specific heat of 0.83 kcal/kg/degree C, the thermal shift is 70 kg × 0.83 kcal/kg/degree C = 58 kcal/degree C. Decrease in body temperature will be 16 kcal/58 kcal/degree C, or 0.28 degree C.

ADDITIONAL READINGS

Forstot RM. The etiology and management of inadvertent perioperative hypothermia. *J Clin Anesth*. 1995;7:657–674.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1546.

45. ANSWER: A

Intraoperative heat loss occurs in four main manners: radiation, convection, conduction, and evaporation. Of these, radiation and convection are the first and second major causes of intraoperative hypothermia. Although volatile agent-associated vasodilation is balanced by decreased metabolic rate, the initial phase of hypothermia is thought to be related to redistribution of core body heat to the periphery related to this vasodilation.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1537–1547.

46. ANSWER: D

Hypothermia has been found to be protective against cerebral ischemia and hypoxia, as well as for out-of-hospital arrest outcomes. However, perioperative complications of hypothermia can include coagulopathy/platelet dysfunction, increased intraoperative blood loss, wound infections, and subjective patient discomfort. Although hypothermia may lead to shivering, which greatly increases oxygen consumption and is associated with myocardial ischemia, as well as increased intracranial and intraocular pressure.

If hypothermia is correctly applied (early, long and cool enough) in the optimal group of traumatic brain injury patients (young with elevated intracranial pressure), there seems to be no doubt that hypothermia is effective in improving both survival and neurologic outcome.

ADDITIONAL READINGS

Davies AR. Hypothermia improves outcome from traumatic brain injury. *Crit Care Resusc*. 2005;7(3):238–243.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1537–1547.

47. ANSWER: E

Postoperative vision loss has the highest incidence after prone spinal surgery. Risk factors for ***ischemic optic neuropathy*** (ION) may include long duration of prone surgery, prolonged hypotension, large blood loss and crystalloid use, anemia, and increased venous pressure from prone positioning. Eye perfusion pressure equals mean arterial pressure minus intraocular pressure. In turn, intraocular pressure depends on central venous pressure, as this is transmitted

to the episcleral veins and ultimately to the optic nerve. The majority of ION cases are bilateral. Staging may decrease duration of surgery and thus the risk for development of ION. Colloids may be used in place of some crystalloid. Anemia and hemodilution can be monitored. The patient's head should be positioned neutrally to avoid increased venous or intraocular pressure and eyes should be checked every 15 to 30 minutes to ensure that there is no direct pressure on the globe.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:993–994.

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:419–423.

48. ANSWER: B

According to the ASA closed claims database, the ulnar nerve is the most commonly damaged nerve in the perioperative setting. The injury is usually multifactorial in etiology. Studies have shown that risk factors include male gender, extreme thinness/obesity, and prolonged hospital stay. Studies of nonsurgical patients also suggest risk with elbow flexion, which is thought to increase the pressure within the cubital tunnel. Supination of the forearm is believed to minimize pressure over the ulnar groove and increase the distance between an armboard/bed and the ulnar nerve. Prevention of perioperative peripheral neuropathies was summarized by a 2000 ASA task force, which, based on expert opinion, recommends decreasing pressure on the ulnar groove and maintaining the forearms in either supination or a neutral position on padded armboards.

ADDITIONAL READINGS

Fleisher LA. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia, PA: Saunders; 2009:210–212.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone, 2010:1165–1166.

49. ANSWER: D

Central nervous system injury after cardiac surgery and bypass is thought to occur at a rate of approximately 6% overall and 4% for isolated CABG. Off-pump CABG appears to carry a lower rate of stroke, at 2%. Imaging-related studies have shown that the majority of postoperative cerebrovascular accidents are embolic in etiology. These emboli may originate from plaque, clot, or fat and may be arterial or paradoxical across a patent foramen ovale. Less likely causes include, in order, unknown, multifactorial, hypoperfusion, lacunar, thrombotic, and hemorrhagic. Suspicious symptoms in a postoperative patient should prompt neurology consultation, imaging, and support of hemodynamics and oxygen delivery. Perioperative anticoagulation may be instituted or held depending on the clinical picture.

ADDITIONAL READINGS

Fleisher LA. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia, PA: Saunders; 2009:33–39.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1958–1959.

50. ANSWER: D

Malignant hyperthermia (MH) is associated with several diseases and clinical phenomena. Central core disease is a myopathy associated with MH. Other rare disorders seen among the pediatric population include King-Denborough syndrome. These patients typically receive nontriggering anesthetics without succinylcholine or volatile inhalational anesthetics. Schwartz-Jampel syndrome and osteogenesis imperfecta may lead to intraoperative fever due to underlying hypermetabolic states. Masseter muscle spasm has been classically described in pediatric patients anesthetized with halothane and succinylcholine. Caffeine-halothane contracture testing has been positive in 25% of these cases.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:530–532.

51. ANSWER: C

MH is linked to mutations in the skeletal muscle ryanodine receptor, which regulates release of calcium ions from the sarcoplasmic reticulum. Dantrolene is a muscle relaxant that diminishes calcium release from the skeletal muscle sarcoplasmic reticulum. During dantrolene treatment of an MH episode, supportive measures are instituted such as 100% oxygen hyperventilation, cooling, treatment of hyperkalemia, acidosis, or arrhythmia, and measurement of laboratory indices and urine output.

ADDITIONAL READING

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:539.

52. ANSWER: E

Arytenoid dislocation is a rare complication of endotracheal intubation. Although traumatic and blind airway manipulation may be associated with arytenoid dislocation or subluxation, this complication may also occur after uneventful laryngoscopy and intubation. The patient's airway and respiratory status must be assessed due to possible laryngeal edema. Differential diagnosis also includes mechanical trauma to vocal cords or recurrent laryngeal nerve palsy due to a malpositioned endotracheal tube cuff. Early diagnosis is critical due to an increased risk of arytenoid fibrosis after 48 hours postdislocation, and the associated morbidity.

ADDITIONAL READING

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:99.

53. ANSWER: C

A history of dental disease or prior trauma should be elicited during preoperative evaluation. The teeth should be grossly inspected during airway examination. The upper front teeth, known as the maxillary central incisors, are the most frequently injured during anesthesia. Approximately half of dental injuries occur during laryngoscopy, 25% with extubation, 10% with emergence, and 5% during regional anesthesia.

ADDITIONAL READING

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:98.

54. ANSWER: C

The cuff of the laryngeal mask airway may induce palsy of the hypoglossal or lingual nerves. With hypoglossal nerve injury, the extended tongue deviates toward the ipsilateral side. Thorough neurologic evaluation (including imaging) is indicated to rule out other structural or infectious neurologic pathology.

ADDITIONAL READINGS

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:100.
Boban M, et al. Isolated hypoglossal nerve palsy: a diagnostic challenge. *Eur Neurol*. 2007;58:177–181.

55. ANSWER: D

Delayed emergence may be caused by many factors. Complications related to the surgical procedure or residual anesthetic drugs may occur. Acid–base balance, hypoxia, or electrolyte derangements are also possible. Neurologic etiologies such as stroke or seizure must be considered. Cerebral perfusion is dependent on arterial perfusion, intracranial pressure, and venous return. Neck flexion is possible in the beach-chair position, which impedes venous return. Jugular lines may also impede venous return.

ADDITIONAL READING

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:357–362.

56. ANSWER: B

End-tidal CO_2 may be seen with increased production (i.e., hypermetabolic state) or decreased removal (i.e., hypoventilation or rebreathing). The expiratory valve is a basic component of the circle breathing system. An expiratory valve stuck in the closed position may cause breath stacking. When stuck in the open position, a malfunctioning expiratory valve can result in rebreathing. Unlike rebreathing associated with exhausted adsorbent, end-tidal CO_2 does not improve with increased flows. A malfunctioning inspiratory valve may result in a characteristic sloped capnograph at early inspiration and the baseline CO_2 will be "normal" at zero if the delivered volume exceeds the volume of the inspiratory tubing (Fig. 16.3).

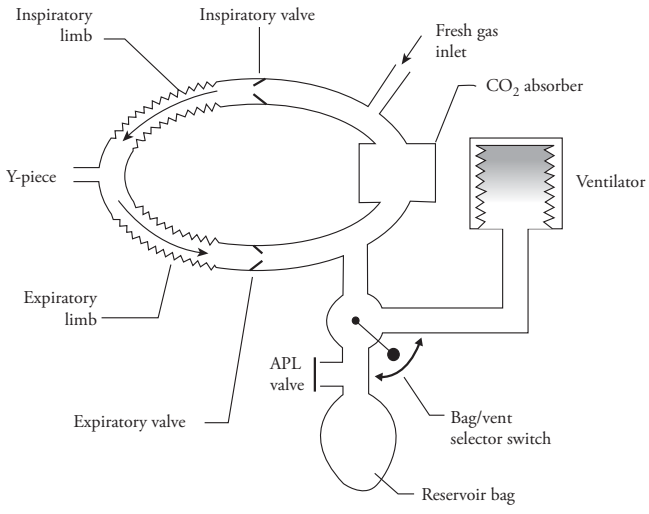

Figure 16.3 Components of the circle system. APL, adjustable pressure-limiting; B, reservoir bag; V, ventilator. (Reproduced with permission from Brockwell RC. Delivery systems for inhaled anesthesia. In Barash PG, ed. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:562.)

ADDITIONAL READINGS

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:813–814.
Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:694–696.

57. ANSWER: D

Leaks within the vaporizer most commonly occur at the O-ring where the vaporizer connects to the circuit. This O-ring can become dried and cracked or break, causing a leak. Unless the vaporizer is turned on, no flow goes to the vaporizer when a positive-pressure leak test is performed. Thus, a faulty O-ring or other vaporizer leak would not routinely be identified during a high-pressure leak test.

ADDITIONAL READINGS

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:813.
Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:670–680.

58. ANSWER: A

IOP is affected by mechanical forces, venous drainage, and aqueous humour circulation. Prone positioning places the orbit in a dependent position and could impede venous drainage. Direct compression may occur on the orbit; thus, frequent eye checks are necessary during a prone anesthetic. Succinylcholine, hypercapnia, and hypoxemia are known to increase IOP. Ketamine has also been suspected to increase IOP. IOP is decreased with hypothermia, barbiturates, etomidate, and inhalational agents.

ADDITIONAL READING

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:410, 423.

59. ANSWER: C

Among available case reports describing postoperative ION, many patients had comorbid diabetes, hypertension, coronary artery disease, and cerebrovascular disease. Intraoperatively, case reports describe high estimated blood losses and prolonged procedural times. Intraoperative hypotension and anemia have also been described, but not definitively linked to ION. Specific goals for intraoperative blood pressure and hemoglobin remain controversial. Patients should be maintained with the neck in neutral position to facilitate normal venous drainage, and external pressure to the orbits should be avoided. A discussion of postoperative visual loss should be considered when reviewing informed consent with high-risk patients undergoing spine and cardiac procedures.

ADDITIONAL READINGS

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:418–419.
Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2826–2835.

60. ANSWER: B

The thoracic duct drains into the central circulation at the junction of the left internal jugular vein and left subclavian vein. The risk of thoracic duct trauma may be minimized by avoiding low approaches to the internal jugular vein on the left side.

ADDITIONAL READING

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:736.

61. ANSWER: B

Anaphylaxis is a type I hypersensitivity reaction involving antigen binding to IgE and subsequent degranulation of mast cells and basophils. Patients are at risk after a primary exposure and development of antibodies to a rubber tree protein. Release of histamine, interstitial migration of intravascular fluid, and smooth muscle contraction can occur during the subsequent mediator cascade. Signs and symptoms include hives, hypotension, tachycardia, bronchospasm, and angioedema. Latex allergy has been associated with chronic exposure, such as in healthcare workers or patients with a history of spina bifida or urologic reconstruction. Proteins in some fruits and nuts are known to cross-react via a similar epitope. Approximately 10% of patients with allergy to kiwi, melon, cherry, peach, banana, or pear will also display allergy to latex. Avocado and chestnut have also been implicated in cross-allergic phenomena.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006: 1309–1310.

Hepner DL, Castells MC. Latex allergy: an update. *Anesth Analg.* 2003;96:1219–1229.

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:707–708.

62. ANSWER: C

0.5% of transfused patients may develop limited urticaria, due to anaphylactoid release of histamine. This is caused directly by donor plasma proteins, without antibody intermediaries. An antihistamine such as diphenhydramine is appropriate. Plasma protein levels can be lowered by selecting "washed" packed red blood cells. Epinephrine and dexamethasone are reserved for anaphylactic reactions. These patients present with hypotension, bronchospasm, edema, and shortness of breath due to IgE-mediated degranulation of mast cells and basophils. Previously transfused patients with IgA deficiency are at risk for anaphylaxis, due to formation of anti-IgA antibodies.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:211–212.

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia: Lippincott Williams & Wilkins; 2008:512.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1754.

63. ANSWER: B

According to the ***American Society of Anesthesiologists practice guideline for preoperative fasting***, patients of all ages should abstain from clear liquids for 2 hours, breast milk for 4 hours, and full liquids or solids for 6 hours. The activity of chewing and swallowing stimulates orogastric secretions. In children, 30 minutes of preoperative gum chewing was found to significantly increase gastric fluid volume and increase gastric fluid pH compared to children who followed the normal guidelines. Results of studies in adults have been mixed, but most practitioners adhere to the 2-hour NPO guideline.

ADDITIONAL READINGS

American Society of Anesthesiologist Task Force on Preoperative Fasting. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. *Anesthesiology*. 1999;90:896–905.

Dubin SA, Jense HG, McCranie JM, Zubar V. Sugarless gum chewing before surgery does not increase gastric fluid volume or acidity. *Can J Anaesth*. 1994;41:603–606.

Schoenfelder RC, et al. Residual gastric fluid volume and chewing gum before surgery. *Anesth Analg*. 2006;102:415–417.

Søreide E, Holst-Larsen H, Veel T, Steen PA. The effects of chewing gum on gastric content prior to induction of general anesthesia. *Anesth Analg*. 1995;80:985–989.

17.

PHARMACOLOGY

Thomas H. Ottens, MD, MSc and Markus Klimek, MD, PhD

1. A 39-year old man presents to the emergency room with hemiplegia, epistaxis, hematuria, nausea, vomiting, and abdominal pain 4 days after taking an overdose of a substance intending to commit suicide. The substance most likely ingested is

A. Rodenticide
B. Flunitrazepam
C. Fluoxetine
D. Cocaine, in combination with alcohol
E. Chlorine bleach

2. Hydrolysis by plasma cholinesterase is the primary elimination route of all the following drugs EXCEPT

A. Succinylcholine
B. Mivacurium
C. Remifentanil
D. Procaine
E. Chloroprocaine

3. Which statement about neuromuscular blocking agents (NMBAs) is INCORRECT?

A. Hypothermia prolongs the duration of action of rocuronium and vecuronium, but not of atracurium and cis-atracurium.
B. The onset time of nondepolarizing NMBAs can be expedited by fast intravenous injection.
C. The difference in onset times of vecuronium and mivacurium in different muscle groups is based on regional perfusion differences between these muscle groups.
D. Neuromuscular blockade onset time is generally shorter in children compared to adults.
E. The duration of action of rocuronium and cis-atracurium is increased during the intravenous administration of magnesium.

4. Which NDMR should be especially avoided in patients with chronic renal failure?

A. Rocuronium
B. Mivacurium
C. Vecuronium
D. Pancuronium
E. Cis-atracurium

5. Which of these statements about liver failure is INCORRECT?

A. Induction of cytochrome P450 occurs in early alcoholic liver failure.
B. Hoffmann elimination is not affected by liver failure.
C. Patients with liver failure need higher doses of NMBA to achieve a certain block level compared to those with normal liver function.
D. Aminosteroid NMBA doses should be reduced in end-stage liver failure.
E. The elimination half-life of atracurium, but not cis-atracurium, is significantly slower in patients with moderate liver failure.

6. Which of the following electrolyte imbalances does NOT enhance neuromuscular block?

A. Hypokalemia
B. Hypercalcemia
C. Hypermagnesemia
D. Hypocalcemia
E. Hypernatremia

7. A patient survived a motorcycle accident 4 days ago but is left paraplegic. In the intensive care unit he develops respiratory failure, requiring urgent intubation. Still sleepy, you forget about the contraindications and decide on rapid-sequence intubation with succinylcholine.

Shortly after administration, the patients develops asystole. Blood gas analysis shows a serum potassium of 8.5 mmol/L. You start cardiopulmonary resuscitation and get help. What treatment would NOT be appropriate at this time?

A. IV calcium chloride (1000 mg = 10 mL of 10% solution)
B. IV insulin and glucose (15 units rapid-acting insulin in 50 mL 50% dextrose)
C. IV sodium bicarbonate (50 mmol)
D. Polystyrene sulfonate
E. Hemodialysis

8. Of the following neuromuscular blocking drugs, the correct order of histamine release potential at equipotent doses, from biggest to smallest potential, is

A. Succinylcholine, rapacuronium, mivacurium, cis-atracurium
B. Cis-atracurium, mivacurium, rapacuronium, succinylcholine
C. Rapacuronium, succinylcholine, cis-atracurium, mivacurium
D. Succinylcholine, rocuronium, mivacurium, cis-atracurium
E. Succinylcholine, mivacurium, rapacuronium, cis-atracurium

9. A burn victim can safely be given succinylcholine when

A. The burn was acquired less than 2 days ago
B. Precurarization with low-dose rocuronium is used
C. The patient's age is less than 6 months
D. Total body surface area (TBSA) burned is less than 40%
E. Never; succinylcholine is always contraindicated in burn victims

10. Side effects of neuromuscular blockade reversal with neostigmine and glycopyrrolate include all of the following symptoms EXCEPT

A. Bronchoconstriction
B. Drowsiness
C. Bradycardia
D. Abdominal cramps
E. Urinary retention

11. Which of the following statements about succinylcholine is correct?

A. Succinylcholine does not effectively bind to presynaptic acetylcholine receptors.
B. Succinylcholine is very short-acting, because it is metabolized at the neuromuscular junction.
C. Succinylcholine is metabolized to the inactive component succinylmonocholine.
D. Succinylcholine is an antagonist of both muscarinic and nicotinic acetylcholine receptors.
E. Succinylcholine is very short-acting, because it binds to the acetylcholine receptor only once before being metabolized.

12. Which of these conditions is NOT a relative contraindication to succinylcholine?

A. Subarachnoid hemorrhage
B. Transplanted heart
C. Sepsis
D. Dibucaine number of 20
E. Strabismus surgery

13. Which statement about the effects of succinylcholine in healthy patients is correct?

A. A phase I block is commonly associated with a fade of train-of-four (TOF).
B. A phase I block can be antagonized with acetylcholinesterase inhibitors.
C. A phase II block is defined as TOF ratio of less than 10%.
D. A phase II block is observed at a cumulative succinylcholine dose of more than 7.5 mg/kg.
E. A phase II block cannot be antagonized with acetylcholinesterase inhibitors.

14. Which of the following statements about dantrolene is correct?

A. It must be reconstituted with sodium bicarbonate solution.
B. It has an elimination half-life of 12 hours.
C. It has a pH of 4.5 after reconstitution.
D. It is a potent diuretic.
E. It must be warmed before administration.

15. Which of the following agents does NOT have parasympathicolytic properties?

A. Pilocarpine
B. Ipratropium bromide
C. Atropine
D. Scopolamine
E. Pancuronium

16. A 6-year-old boy is brought to the emergency department with symptoms of agitation, blurred vision, and flushed, red skin. The boy's mother says the child stayed

at his grandmother's place, where he might have taken something from the drug cabinet. She has no idea what was stored in this cabinet. Upon examination, you see a confused and agitated schoolchild, with bright red, dry skin, wide pupils, and tachycardia. His temperature is 100.22 fahrenheit. What agent is most likely to have been ingested by the child?

A. Pyridostigmine
B. Amiodarone
C. St. John's wort (*Hypericum perforatum*)
D. Atropine
E. Metoclopramide

17. Which of these statements about opioid receptors is INCORRECT?

A. Agonism at the μ_2 receptor produces respiratory depression.
B. Naloxone reverses opioid effects at all opioid receptors.
C. Opioids with a more specific selectivity for the σ receptor could eliminate unwanted neurobehavioral effects.
D. The analgesia produced by agonism at the κ receptor occurs primarily at the spinal level.
E. Bradycardia may result from agonism at the μ_1 receptor.

18. Which of the following statements is INCORRECT?

A. Morphine-6-glucuronide is more potent than morphine.
B. Plasma concentrations after subcutaneous and intramuscular morphine administration peak equally quickly.
C. Morphine is extensively metabolized in the cerebrospinal fluid.
D. An appropriate epidural dose of morphine is 3 to 5 mg.
E. Morphine's duration of action is significantly prolonged in patients with congestive heart failure.

19. Which of the following statements about opioids is correct?

A. The lipid solubility of sufentanil is similar to that of fentanyl.
B. At equianalgesic doses, fentanyl produces similar respiratory depression compared to morphine.
C. Context-sensitive half-times of opioids correspond to their respective elimination half-lives.
D. Intravenous opioid administration produces hypnosis.
E. Pruritus following opioid administration is caused by histamine release.

20. What is the correct order of the following opioids in regards to lipophilic properties, from most to least lipophilic?

A. Morphine—Remifentanil—Alfentanil—Sufentanil
B. Sufentanil—Fentanyl—Alfentanil—Morphine
C. Remifentanil—Alfentanil—Fentanyl—Sufentanil
D. Sufentanil—Remifentanil—Alfentanil—Fentanyl
E. Sufentanil—Morphine—Fentanyl—Remifentanil

21. Which of the following statements about remifentanil is INCORRECT?

A. Remifentanil and fentanyl are approximately equipotent.
B. Remifentanil has minimal affinity for κ- and δ-opioid receptors.
C. Remifentanil has a context-sensitive half-time that is independent of kidney and liver function.
D. Remifentanil passes the placenta.
E. Patients with abnormal plasma cholinesterase activity experience an extended duration of action of remifentanil.

22. Which of the following phenomena is NOT an effect of opioid administration at clinical doses?

A. Negative inotropy
B. Histamine release
C. Biliary colic
D. Vasodilation
E. Delayed gastric emptying

23. Naloxone is not an appropriate choice to antagonize which opioid effect?

A. Respiratory depression
B. Skeletal muscle rigidity
C. Pruritus
D. Postoperative nausea and vomiting
E. Sedation

24. Which statement about meperidine is correct?

A. Meperidine is not likely to cause respiratory depression in neonates.
B. Meperidine is the opioid of choice when spasm of the spincter of Oddi or increased biliary pressure is to be avoided.
C. Naloxone effectively reverses symptoms of neurotoxicity caused by normeperidine accumulation.

D. Active metabolite accumulation after repeated doses of meperidine is unlikely in patients with normal kidney function.
E. Meperidine does not cause miosis.

25. Tolerance is NOT effectively developed for which opioid side effect?

A. Euphoria
B. Miosis and constipation
C. Nausea and vomiting
D. Sedation
E. Tolerance develops to all opioid effects.

26. A 55-year-old man is seen in the preoperative anesthesiology clinic in preparation for a Commando procedure for gingival carcinoma. Not to your surprise, you find out the patient consumes four vodka drinks and takes two or three oxazepam tablets every day. Select the most appropriate statement about the planning of this patient's perioperative care.

A. You plan to give this patient fewer opioids than you would without suspected alcohol dependence in an effort not to encourage a new addiction.
B. You tell the patient to stop drinking any alcoholic beverages from 48 hours before the procedure to avoid any interference with anesthesia drugs.
C. The perioperative hospital stay is an excellent opportunity for this patient to break the habit to treat his addiction.
D. You advise the ENT surgeons to use long-acting local anesthetic infiltration, premedicate with diazepam instead of midazolam, and organize postoperative observation for withdrawal.
E. You prescribe buprenorphine and consult the psychiatrist to prevent delirium.

27. Which of the following opioids causes the LEAST increase in biliary pressure?

A. Morphine
B. Fentanyl
C. Meperidine
D. Pentazocine
E. Buprenorphine

28. Which statement applies to patients with end-stage renal dysfunction?

A. Accumulated morphine-3-glucuronide may compromise analgesia due to antagonism at the μ-opioid receptor.
B. The accumulation of morphine is a particular hazard for the patient with end-stage renal dysfunction.
C. In an adult male patient, neurotoxicity after meperidine administration is not likely to occur when the dose is limited to 600 mg/day.
D. The duration of action of a single dose of alfentanil is likely to be increased.
E. The duration of action of remifentanil is usually not significantly changed, because the offset of its effect depends largely on rapid intercompartmental redistribution.

29. Which receptor is NOT a target of the currently marketed antiemetic drugs?

A. Opioid receptor (μ)
B. Dopamine receptor (D_2)
C. Neurokinin receptor (NK_1)
D. Muscarinic acetylcholine receptor (mAChR)
E. 5-hydroxytriptamine receptor ($5\text{-}HT_3$)

30. A 58-year-old patient is scheduled to undergo a right upper lobectomy for severe sarcoidosis. As far as she can remember, she has never had any other surgeries. Which of the questions below would help you best estimate her risk of postoperative nausea and vomiting (PONV)?

A. Have you ever been nauseated, or have you vomited, after a surgical procedure?
B. Do you get nauseated when you travel as a car passenger?
C. What is your height and weight?
D. Did any of your parents, brothers, or sisters ever experience nausea after anesthesia?
E. Do you experience dizziness or lightheadedness when you stand up quickly?

31. A 7-year-old boy is scheduled to undergo general anesthesia for laparoscopic abdominal surgery. You inform his mother about your plan to use a $5\text{-}HT_3$ antagonist to prevent PONV. The mother has never heard of these drugs and asks for more information before she consents to the procedure. Which information would be INCORRECT to give to the mother?

A. "I plan to use ondansetron, as its safety and efficacy has been evaluated for use in children."
B. "After granisetron administration, your son may experience some dizziness."
C. "Your son is likely to benefit from palonosetron for 12 to 24 hours."
D. "The $5\text{-}HT_3$A antagonists are a group of agents that work on only one specific receptor, found in the brain and gut. They are therefore less likely to cause major adverse effects compared to metoclopramide or droperidol."

E. "The risk of postoperative nausea and vomiting will be significantly reduced when he is given ondansetron during the procedure."

32. Droperidol is contraindicated in

A. Patients with Parkinson's disease
B. Children
C. Patients with kidney failure
D. Patients at very high risk of PONV
E. Patients with hepatitis C

33. Which statement about neurokinin-1 receptor antagonists and PONVis INCORRECT?

A. Oral aprepitant is equally effective compared to ondansetron when used as single-drug prophylaxis strategy for PONV.
B. NK-1 receptor antagonists do not significantly increase the QT interval.
C. The serum half-life of aprepitant is only 4 hours, so it is not likely to be effective beyond 20 hours after administration (±5 times serum half-life).
D. Aprepitant, like other antiemetic strategies, does not prevent PONV in 100% of patients, due to the complex, multireceptor etiology of PONV.
E. Aprepitant may reduce the effectiveness of oral contraceptives, and women receiving aprepitant should be counseled to use additional contraceptive measures to prevent unwanted pregnancy.

34. Which of the following statements about propofol is INCORRECT?

A. Propofol affects the baroreceptor reflex setpoint.
B. Propofol decreases cerebral metabolic rate of oxygen ($CMRO_2$).
C. Propofol sensitizes the heart to catecholamines.
D. Propofol accumulates in adipose tissue during continuous infusion.
E. Propofol effectively relieves pruritus associated with neuraxial opioid administration at subanesthetic doses.

35. Which statement about total intravenous anesthesia (TIVA) with propofol, combined with remifentanil, is INCORRECT?

A. This combination is safe when jet ventilation is used during laryngeal laser surgery.
B. This combination is ideal for eye surgery, as it lowers intraocular pressure (IOP).
C. This strategy is ideal when a member of the operating room staff is pregnant.
D. This combination is contraindicated in patients with acute intermittent porphyria.
E. This strategy results in lower incidences of PONV compared to balanced anesthesia with volatiles.

36. A 6-year-old boy is diagnosed with laryngotracheobronchitis (croup) and requires mechanical ventilation in the pediatric intensive care unit. He is being sedated with a continuous infusion of propofol, combined with remifentanil. On day 3 of admission, he develops bradycardia, right bundle branch block, metabolic acidosis, and hyperlipidemia. Despite maximum supportive therapy, a fatal cardiac arrest follows, 18 hours after the first episode of bradycardia. What is the most likely cause of death?

A. Delayed-type hypersensitivity reaction to propofol
B. Propofol-induced refeeding syndrome
C. Decompensated Wolff-Parkinson-White syndrome
D. Propofol-related infusion syndrome
E. Septic shock

37. After a single intravenous dose of midazolam, which effect is most likely to persist the longest?

A. Respiratory depression
B. Amnesia
C. Hypotension
D. Sedation
E. Inhibition of cytochrome P450, subtype 3A4

38. Select the correct statement about benzodiazepines.

A. Benzodiazepines reduce the ventilatory response to carbon dioxide.
B. Benzodiazepines selectively block the $GABA_A$ receptor.
C. Benzodiazepines inhibit opioid analgesic effects.
D. Benzodiazepines induce sleep characterized by overrepresentation of rapid eye movement (REM) cycles.
E. Benzodiazepines cause anterograde but not retrograde amnesia.

39. Which statement about midazolam is INCORRECT?

A. Midazolam molecules are lipid-soluble.
B. Midazolam is water-soluble.
C. Midazolam's active metabolites have weak benzodiazepine activity.
D. Midazolam is a cytochrome P450 inhibitor.
E. Midazolam is a cytochrome P450 substrate.

40. Which of these effects is commonly seen after oral clonidine but not after oral midazolam premedication in children?

A. Amnesia
B. Synergism with general anesthetics (reduced MAC)
C. Anxiolysis
D. Reduced incidence of PONV
E. Behavioral disturbance

41. A 52-year-old stockbroker, with a smoking history of over 20 pack-years, is admitted to the intensive care unit with exacerbated chronic obstructive pulmonary disease after a night fishing trip with friends from work. He is otherwise healthy and not overweight. He requires light sedation with IV lorazepam (first 3 hours 2.5 mg/hr, then 12 hours 0.75 mg/hr, then 0.5 mg/hr until discontinuation) to tolerate the ventilatory support. After three days, his lung condition has improved significantly, and the lorazepam infusion is discontinued. Assuming no other agents have been used, how long it would take for this patient to emerge from the sedation?

A. 1.5 hours
B. 6 hours
C. 13 hours
D. 19 hours
E. 32 hours

42. Which of these properties does NOT belong to the steady state of an anesthetic drug in the human body?

A. Saturation of peripheral compartments with the agent
B. Constant plasma concentration of the agent
C. Equal concentration of agent in both plasma and peripheral compartments
D. Net transport between central and peripheral compartments equals zero.
E. Infusion rate of the agent equals the elimination rate of the agent from the central compartment.

43. You are taking care of a 47-year-old woman with a refractory generalized convulsive (grand mal) epilepsy attack. While injecting a rapid bolus of sodium thiopental through the 18G cannula (on the distal forearm), you notice blanching of the hand. Unfortunately, you find the cannula was inserted arterially. Which of these measures is NOT appropriate at this time?

A. Immediate removal of the cannula
B. Intra-arterial heparin administration
C. Sympathetic blockade
D. Propofol administration (through a new IV cannula)
E. Elevation of the arm

44. Which of the following statements about barbiturate coma is INCORRECT?

A. It is associated with a high risk of hypotension.
B. It is associated with decreased intracranial pressure.
C. It is not an effective treatment for refractory intracranial hypertension associated with traumatic brain injury.
D. It is the management strategy of first choice for complex partial status epilepticus in adults that does not respond to IV benzodiazepines.
E. It is associated with an inferior outcome when compared to propofol-induced burst suppression in the treatment of refractory generalized convulsive status epilepticus.

45. A 34-year-old man is brought to the emergency room after his motorcycle was hit by a car. His clinical condition demands immediate airway control and mechanical ventilation. Assuming he is hypovolemic due to significant blood loss, which induction anesthetic would be most appropriate for this patient?

A. Etomidate
B. Midazolam
C. Methohexital
D. Propofol
E. Thiopental

46. Which receptor is NOT involved in ketamine's clinical effects?

A. NMDA receptor
B. Opioid receptor
C. Muscarinic acetylcholine receptor
D. Beta-adrenergic receptor
E. $GABA_A$ receptor

47. Which of the following statements about the effect of ketamine on the brain is INCORRECT?

A. Ketamine increases intracranial pressure by increasing cerebral blood flow.
B. Ketamine increases intracranial pressure by increasing cerebrospinal fluid production.
C. Ketamine increases intracranial pressure, but this can be attenuated by maintaining normocapnia under mechanical ventilation.
D. Ketamine increases cerebral blood flow by increasing p_aCO_2.
E. Ketamine increases intracranial pressure by increasing mean arterial pressure.

48. Which patient has the LOWEST risk of adverse effects of ketamine, if this agent is used during their general anesthetic?

A. A 47-year-old woman undergoing a brain tumor resection under general anesthesia
B. A 21-year-old, confused man requiring analgesia and sedation for reduction of a wrist fracture, sustained while trying to fight off a police officer
C. A 32-year-old woman who is 12 weeks pregnant
D. A 55-year-old man with porphyria
E. A 64-year-old man who presents to the emergency room with a unilateral red eye, nausea, vomiting, and visual acuity loss

49. A 32-year-old, 55-kg woman is developing a grand mal seizure followed by cardiac arrest after an attempted epidural injection of 12 mL bupivacaine 0.5%. What would be the most appropriate next step of action?

A. Administer a propofol bolus until an intravenous lipid emulsion becomes available.
B. Administer 1 mg of epinephrine intravenously.
C. Initiate cardiopulmonary resuscitation.
D. Start assisted ventilation, because toxicity from local anesthetics is self-limiting within a very short time.
E. Perform immediate cardioversion, because the bupivacaine injected most likely resulted in ventricular fibrillation.

50. An 62-year-old woman is emerging from anesthesia for myocardial revascularization surgery in the recovery room. Her medical history denotes chronic obstructive pulmonary disease and myocardial infarction. In the postanesthesia care unit she appears agitated and starts to shiver. What would have been the best way to prevent her current clinical condition?

A. Benzodiazepine administration before the end of the procedure
B. Clonidine administration before the end of the procedure
C. Haloperidol administration before the procedure
D. Maintenance of anesthesia with potent volatile anesthetics, not propofol
E. This problem does not require prevention, as shivering is transient and harmless.

51. Choose the correct description of the mechanism of action of methylene blue in the treatment of methemoglobinemia.

A. Methylene blue increases the expression of methemoglobin reductase.
B. Methylene blue increases reduction of methemoglobin to hemoglobin via the NADH-dependent reductase pathway.
C. Methylene blue increases the expression of cytochrome B_5, the enzyme that keeps hemoglobin in its reduced state.
D. Methylene blue increases renal excretion of nitrites, thus reducing the oxidative stress on hemoglobin.
E. Methylene blue protects hemoglobin from oxidization to methemoglobin.

52. Which of the following statements about the effects of mannitol is INCORRECT?

A. Mannitol does not cross the intact blood–brain barrier.
B. Mannitol is more effective than normal saline in protecting the kidney from radiocontrast-induced kidney dysfunction.
C. Mannitol scavenges oxygen free radicals.
D. Mannitol may increase brain swelling after traumatic brain injury.
E. Mannitol-induced diuresis often results in hypokalemia.

53. A 56-year-old man who was in a motorcycle accident requires immediate airway management but appears hemodynamically stable. Increased intracranial pressure is suspected. Which treatment would NOT be appropriate at this time?

A. Administration of fentanyl
B. Induction of anesthesia with etomidate
C. Administration of dexamethasone IV 1 mg/kg to reduce brain edema
D. Administration of hypertonic saline/hydroxyethyl starch (HES) solution
E. Administration of mannitol

54. A 59-year-old man has been treated with furosemide for congestive heart failure for the past 12 years. Which ion is LEAST likely to be found in lower-than-normal concentrations in his blood?

A. Sodium
B. Potassium
C. Bicarbonate
D. Magnesium
E. Chloride

55. Which statement about insulin and glucagon is correct?

A. Insulin and glucagon both have significant effects on muscle glycogen stores.
B. Glucagon increases plasma ketoacid levels.

C. Insulin increases the release of free fatty acids by adipose cells.
D. Glucagon is produced by beta cells in the pancreatic islets.
E. Glucagon increases the plasma concentration of amino acids.

56. Which agent does NOT decrease phenytoin plasma levels?

A. Carbamazepine
B. Alcohol
C. Saquinavir
D. Valproic acid
E. Phenobarbital

57. A 28-year-old man presents to the emergency room with the complaint of a sore throat. He reports that he has had flulike symptoms for the past week, for which he has taken acetaminophen with codeine. He has a history of depression and is treated with venlafaxine. Upon physical examination, he is agitated and sweating and has dilated pupils. He notably startles when a nurse suddenly comes into the room. He has a temperature of 40.6 degrees C (105 degrees F), a heart rate of 140 beats per minute, blood pressure of 200/105 mm Hg, and respiratory rate of 24 breaths per minute. His pupils are dilated. A distinct alcohol breath is noted. What is the most likely diagnosis?

A. Alcohol intoxication
B. Serotonin syndrome
C. Ketamine intoxication
D. Central anticholinergic syndrome
E. Opioid intoxication

58. A 19-year-old girl was found unconscious on the bathroom floor by a friend, who called 911. The paramedics found her tachycardic, hypertensive, and sweating, with a Glasgow Coma Scale score of 10. Her temperature is 38.6 degrees C (101.5 degrees F), and her pupils are dilated. Her friend reports that she uses cocaine and heroin daily. The administration of which agent would be appropriate at this time?

A. Diazepam
B. Naloxone
C. Flumazenil
D. Propranolol
E. Sodium bicarbonate

59. A 45-year-old woman is visiting the preoperative clinic in preparation for coronary artery bypass graft (CABG) surgery. As requested, she brought all her medicines with her. These include garlic tablets, her favorite herbal remedy. Which instruction should be given to this patient?

A. Garlic has detrimental effects on the cardiovascular system; she must discontinue its use immediately.
B. Garlic has beneficial effects on the cardiovascular system; she should continue its use perioperatively.
C. Garlic inhibits platelet aggregation and should be discontinued at least 7 days prior to surgery.
D. Garlic, ubiquitous in food, is ineffective but perfectly safe, and she should use her own best judgment about continuing or stopping it perioperatively.
E. Garlic beneficially affects plasma lipid and cholesterol levels; she should double the dose perioperatively, starting 36 hours prior to surgery.

60. A 45-year-old man uses acenocoumarol. Which of these herbal medicines will NOT affect his coagulation status?

A. Garlic
B. Ginkgo
C. Ginseng
D. St. John's wort
E. Kava

61. The effect of tirofiban on coagulation can be reversed most effectively by

A. Fresh frozen plasma
B. Tranexamic acid
C. Aprotinine
D. Four-factor concentrate (factors II, VII, IX, X)
E. Platelet transfusion

62. A 76-year-old woman broke her left hip when she slipped on the snow. Other than metoprolol and hydrochlorothiazide for hypertension, she takes no medication and is generally in good health. Preoperatively, thromboprophylaxis (once-daily enoxaparin SC) is started. You decide to perform a neuraxial block using an indwelling catheter. When would be the best time to perform the block to decrease the risk of neuraxial bleeding?

A. Patients on low-molecular-weight heparins should not receive neuraxial blocks.
B. 20 to 24 hours after the last dose
C. 10 to 12 hours after the last dose
D. Approximately 4 hours after the last dose
E. Any time is fine; the risk of neuraxial hemorrhage is minimal with once-daily low-molecular-weight heparin regimens.

63. Which is NOT an effect of dexmedetomidine?

A. Bradycardia
B. Sedation
C. Hypotension
D. Decreased gut motility
E. Hypertension

64. Which of the following statements about ketorolac is correct?

A. Ketorolac-induced renal failure is irreversible.
B. Platelet aggregation inhibition induced by ketorolac is irreversible.
C. Ketorolac use is associated with increased risk of gastrointestinal bleeding after prolonged use but not short-term use.
D. An advantage of ketorolac over aspirin is that it does not induce asthmatic reactions.
E. Perioperative use of ketorolac is not commonly associated with increased surgical blood loss.

65. Which statement about the hepatotoxic effect of acetaminophen is INCORRECT?

A. Hepatotoxicity occurs rarely with therapeutic doses.
B. Hepatotoxicity is treated with n-acetylcysteine.
C. Approximately 10% of a dose of acetaminophen is metabolized to the toxic NAPQI metabolite.
D. Hepatotoxicity is seen at normal doses in patients with chronic liver disease.
E. Hepatotoxicity is caused by the glutathione reaction products of acetaminophen's toxic metabolites.

66. Select the correct statement about the differences between nitroglycerin and nitroprusside.

A. Nitroglycerin predominantly produces venodilation; nitroprusside produces venous and arteriolar dilation.
B. Unlike nitroprusside, nitroglycerin does not cause methemoglobinemia.
C. Nitroprusside causes cyanide toxicity, which leads to methemoglobinemia.
D. Nitroglycerin and nitroprusside cause similar degrees of hypotension in equipotent doses when administered to patients with congestive heart failure.
E. Nitroprusside affects capacitance vessels, nitroglycerin resistance vessels.

67. Select the correct order of receptor affinity of dopamine from highest to lowest affinity (α = alpha, β = beta, D = dopamine):

A. $\alpha > D > \beta$
B. $\alpha = \beta = D$
C. $\beta > \alpha > D$
D. $D > \alpha > \beta$
E. $D > \beta > \alpha$

68. Select the correct statement: At lower doses, dobutamine produces (1), and at higher doses it produces (2).

A. 1: bradycardia, 2: tachycardia
B. 1: increased right ventricular preload, 2: decreased right ventricular preload
C. 1: increased pulmonary vascular resistance, 2: decreased pulmonary vascular resistance
D. 1: vasodilation, 2: vasoconstriction
E. 1: increased myocardial oxygen consumption, 2: decreased myocardial oxygen consumption

69. A 45-year-old man is admitted to the intensive care unit with severe sepsis. He is significantly hypotensive despite aggressive volume therapy and requires pharmacologic hemodynamic support to keep up his blood pressure. Which agent will, in this acute situation, produce the LEAST improvement in his hemodynamic profile?

A. Norepinephrine
B. Dobutamine
C. Dopamine
D. Ephedrine
E. Phenylephrine

70. Epinephrine can be used to prolong the duration of local anesthetic blocks. What is the recommended maximum total dose of epinephrine when admixed with a local anesthetic?

A. 50 mL of a solution with epinephrine 1:200,000
B. 40 mL of a solution with epinephrine 1:200,000
C. 30 mL of a solution with epinephrine 1:100,000
D. 20 mL of a solution with epinephrine 1:10,000
E. 10 mL of a solution with epinephrine 1:10,000

71. Which statement about norepinephrine is INCORRECT?

A. Norepinephrine does not have a clinically significant β_2-agonist effect.
B. Norepinephrine has substantially more arrhythmogenic potential compared to epinephrine.
C. Norepinephrine produces less tachycardia than epinephrine.
D. Norepinephrine may decrease renal blood flow.
E. Norepinephrine may increase renal blood flow.

72. Intravenous esmolol shares certain characteristics with remifentanil. Which of the following is NOT a property of esmolol?

A. Rapid onset
B. Short duration of action
C. High relative potency compared to other agents in its pharmacologic group
D. Esterase degradation
E. High receptor selectivity

73. Which class of agents strongly potentiates the effects of directly as opposed to indirectly acting sympathicomimetics?

A. Tricyclic antidepressants
B. Selective serotonin reuptake inhibitors
C. Lithium
D. Monoamine oxidase inhibitors
E. All of the above

74. The effects of digoxin at therapeutic drug concentrations in a patient with heart failure are

A. Negative inotropy, positive chronotropy, vasoconstriction
B. Positive inotropy, negative chronotropy, positive dromotropy
C. Vasodilatation, diuresis, negative inotropy
D. Positive inotropy, negative chronotropy, reduced systemic vascular resistance
E. Vasodilation, positive inotropy, positive chronotropy

75. Which of the following statements about perioperative administration of antibiotics is INCORRECT?

A. The anesthesiologist is responsible for the administration of antibiotics, even if they have been ordered by another physician.
B. Neostigmine is very effective at reversing nondepolarizing neuromuscular blockade augmented by clindamycin.
C. Ototoxicity may develop rapidly.
D. Nephrotoxicity from antibiotics does not often occur when therapy lasts less than 1 day.
E. Penicillins and aminoglycosides must not be administered via the same intravenous tubing.

76. Which of the following statements about buprenorphine use within the therapeutic dose range is INCORRECT?

A. A ceiling effect occurs in respiratory depression.
B. It behaves like a partial μ-opioid agonist.
C. A ceiling effect occurs in analgesic potency.
D. A lower risk of nausea is seen than with morphine.
E. There is a ceiling effect to the strength of reward experienced.

77. A 32-year-old pregnant woman plans to give birth to her second child via cesarean section. When you discuss the neuraxial anesthetic with her, she tells you she had significant itching after receiving intrathecal morphine for her first cesarean. Which drug would you recommend to reduce risk of pruritus?

A. Fentanyl
B. Remifentanil
C. Sufentanil
D. Tramadol
E. Nalbuphine

78. A 69-year-old man is admitted to the intensive care unit for postoperative care after brain tumor resection. He must remain sedated and mechanically ventilated because he is suffering from postoperative status epilepticus. On the second ICU day, he develops intolerance to his enteral feeds and appears to have developed a paralytic ileus. Select the correct statement.

A. Metoclopramide is indicated because of the paralytic ileus.
B. Metoclopramide is contraindicated in patients with epilepsy.
C. Metoclopramide is contraindicated because its sedative effect may interfere with neurologic examination.
D. Metoclopramide will facilitate feeding tube insertion.
E. Metoclopramide will reduce the risk of pneumonia and mortality in this patient.

79. You are taking care of a firefighter who collapsed and suffered convulsions after a rescue operation in a burning plastics factory. A police officer informs you that cyanide inhalation is a possibility, and you decide to initiate cyanide toxicity treatment. Which treatment option is contraindicated until reliable carboxyhemoglobin levels are known?

A. Hydroxocobalamin
B. Sodium nitrite
C. Amyl nitrate inhalation
D. Sodium thiosulfate
E. Sodium bicarbonate

80. Which volatile agent is capable of increasing the toxic potential of methotrexate, potentially leading to severe bone marrow suppression?

A. Nitrous oxide
B. Sevoflurane
C. Isoflurane
D. Desflurane
E. Halothane

81. Which of the following is NOT described by the term "pharmacokinetics"?

A. Elimination
B. Absorption
C. Distribution
D. Receptor binding profile
E. Metabolism

82. A 52-year-old woman weighing 80 kg requires an intravenous loading dose of the fictional drug rapturamine, which has an effective plasma concentration of 10 mg/L. The volume of distribution of IV rapturamine is 0.75 L/kg. Calculate the loading dose.

A. 60 mg
B. 7.5 mg
C. 80 mg/kg
D. 600 mg
E. 75 μg/kg

83. The degree to which a drug is able to produce a defined, desired response is termed

A. Potency
B. Effective dose (ED_{50})
C. Bioavailability
D. Lethal dose (LD_{50})
E. Efficacy

CHAPTER 17 ANSWERS

1. ANSWER: A

The American Association of Poison Control Centers (AAPCC) registered over 14,000 cases of ***rodenticide exposure*** in the United States in 2008. In more than 11,000 cases, the rodenticide involved contained long-acting anticoagulants, commonly referred to as "superwarfarins."

Most rodenticides sold in the Western world are of this superwarfarin type. Once a sufficient amount is ingested by the rat (or any other species), these agents cause lethal bleeding within a few days.

As with ordinary warfarin, these agents have structural similarities to vitamin K. They competitively inhibit enzymatic reduction of vitamin K to its active hydroquinone form. Ultimately, this leads to decreased plasma levels of the vitamin K-dependent clotting factors II, VII, IX, and X. The anticoagulant effect takes some time to develop, as the circulating factors themselves are not affected. Factor VII's half-life is 6 hours. The half-lives of factors IX, X, and II are 24, 40, and 60 hours, respectively. Proteins C and S are also affected.

The bioavailability of warfarin and the superwarfarins is close to 100%. Superwarfarins are more potent than ordinary warfarin and have much longer half-lives. Some of the superwarfarins have been reported to cause significant anticoagulation for several weeks or even months after ingestion.

The patient in this case must have ingested the rodenticide at least a few days before his severe bleeding symptoms occurred. Once laboratory tests show elevated PT/INR values, vitamin K treatment is indicated. In some patients, this may be necessary for several weeks or months. Patients with severe bleeding might also need transfusion of fresh frozen plasma (FFP). An evidence-based guideline for the treatment of rodenticide poisoning is available from the AAPCC.

Flunitrazepam is a benzodiazepine and would not result in bleeding. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) and could result in sedation, or rarely, the serotonin syndrome. Cocaine overdose could result in hypertension and myocardial ischemia, and chlorine bleach ingestion could cause pulmonary edema, nausea, vomiting, and circulatory collapse.

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2. ANSWER: C

Plasma cholinesterase (PChE), also known as pseudocholinesterase, butyrylcholinesterase, or serum cholinesterase, is a serine hydrolase from the family of human cholinesterases. Other pharmacologically relevant members of this family are the acetylcholinesterases. The enzyme is found in blood and several tissues, including the liver. Although PChE transforms a number of drugs and toxic esters, its physiologic function is uncertain. Anesthetic drugs metabolized by PChE include succinylcholine, mivacurium, and all ester local anesthetics (e.g., cocaine, procaine, and chloroprocaine). PChE metabolizes succinylcholine particularly efficiently, at a rate of 90% of an initial dose per minute. Both PChE and erythrocyte acetylcholinesterase hydrolyze heroin. The final step of heroin's transformation into morphine is the hydrolysis of 6-monoacetylmorphine, which is exclusively performed by erythrocyte acetylcholinesterase.

PChE is produced in the liver, and its plasma half-life is approximately 8 to 12 days. PChE is inhibited by the acetylcholinesterase inhibitors neostigmine, edrophonium, and ecothiopate (eyedrops). Liver failure, plasmapheresis, and cardiopulmonary bypass may reduce plasma levels of PChE. Advanced age, pregnancy, and chronic kidney failure may lead to decreased PChE activity. The activity of PChE in children under 6 months of age is approximately 50% of that in adults. An adult activity level is reached at puberty.

A reduction in PChE activity is found in 5% to 10% of patients and is compatible with normal health. However, clinically relevant activity reduction is rare. The PChE gene is located on chromosome 3, and several genetic variants are known. Normal PChE is inhibited by dibucaine. Genetic variants less inhibited by dibucaine are called "atypical." The activity of these variants is expressed as the dibucaine number (DN), representing the percentage of PChE inhibition by dibucaine. Patients with a homozygote normal PChE gene will have a dibucaine number of 70 or more. Heterozygote atypical individuals' DN typically range between 30 and 70, and that of homozygote atypical individuals are typically below 30. Other PChE variants are normally inhibited by dibucaine but show resistance to inhibition by fluoride. Their activity is expressed as the fluoride number (FN). These and other PChE variants are summarized in Table 17.1.

Should a prolonged succinylcholine effect occur, prolonging sedation and mechanical ventilation is the safest strategy. Fresh frozen plasma infusion may be used to increase PChE levels, if necessary.

Table 17.1 PSEUDOCHOLINESTERASE DEFICIENCY VARIANTS

VARIANT	PCHE ACTIVITY REDUCTION	SUCCINYLCHOLINE PARALYSIS DURATION	FREQUENCY	REMARKS
Heterozygote atypical	Moderate, DN 30–70	Increased by 50–100%	1/25	Rarely clinically relevant
Homozygote atypical	Severe, DN <30	Markedly increased, 2–3 h	1/2,500	Rare in Asians and African Blacks
Fluoride resistant	Variable	Moderately increased	1/150,000	Higher frequency in some Punjabi Indians
Silent	(near) complete	Strongly increased 3–24h	1/10,000	Higher frequency in Alaskan Eskimos
J	66%	Mildly prolonged	1/150,000	Normal catalytic activity, reduced plasma levels
K	33%	Mildly prolonged	1/65	
H	90%	Prolonged several hours	Four families	

DN, Dibucaine Number; PChE, plasma cholinesterase.

KEY FACTS: PLASMACHOLINESTERASE DEFICIENCY

- Plasma cholinesterase (PChE) is found in blood and many tissues and transforms succinylcholine, mivacurium, cocaine, and ester-type local anesthetics.
- PChE is produced in the liver and has a T½β of 8 to 12 days.
- Advanced age, pregnancy, chronic kidney failure, or specific gene variations may result in reduced PChE activity.

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3. ANSWER: A

The inspiration for the development of today's NMBAs was found on the banks of the Orinoco River, where native South American people dipped their arrows in curare to create a deadly hunting weapon that paralyzed its prey. In 1942, d-tubocurarine was first used during anesthesia.

Nondepolarizing muscle relaxants (NDMRs) are competitive antagonists of the nicotinic acetylcholine (ACh) receptor at the neuromuscular junction. To completely block neuromuscular signal transmission, at least 95% of postsynaptic ACh receptors must be blocked.

The absorption kinetics of NDMRs are predictable only after intravenous administration. Intramuscular administration must be reserved for urgent muscle relaxation in absence of venous access. NDMRs can't easily cross the placenta, blood–brain barrier, or cell membranes because they are positive charged and thus have poor lipid solubility.

Once injected, NDMRs are distributed in the "central compartment," the extracellular fluid (V_d). After the rapid distribution phase into the central compartment, NDMRs are distributed to less perfused tissues (peripheral compartment), resulting in block recovery. Repeated injection or continuous infusion will saturate the peripheral compartment. Elimination, rather than redistribution, of the agent then becomes a rate-limiting step in block recovery.

Onset time is determined by an NDMR's potency and the perfusion of muscle groups, which affects agent delivery to the neuromuscular junction. NDMRs with a lower receptor affinity require higher initial doses to initiate a complete block. A larger bolus dose means a steeper concentration gradient between the central compartment and the biophase (neuromuscular junction) and thus faster onset. Similarly, faster injection of an agent may result in faster onset due to a steeper concentration gradient. Onset and recovery of block at the diaphragm occurs faster than at the laryngeal, orbicularis oculi, and adductor pollicis muscles due to differences in perfusion between these muscle groups. Onset in the larynx musculature correlates closely to onset in the orbicularis oculi muscles. Some pharmacokinetic properties of NDMRs are summarized in Table 17.2. Factors and conditions influencing the neuromuscular blockade are discussed in detail in the following chapters.

Hypothermia prolongs the duration of action of atracurium and cis-atracurium. Magnesium enhances the effect of neuromuscular blockade.

Table 17.2 OVERVIEW OF NEUROMUSCULAR BLOCKING AGENTS

DRUG	ED_{95} (MG/KG)	ONSET (MIN)	DUR_{25} (MIN)	RECOVERY TO TOF ≥ 0.9 (MIN)	PRIMARY ELIMINATION PATHWAY	T½β ADULTS (MIN)	T½β CHILDREN (MIN)	HISTAMINE RELEASE	REMARKS
Leptocurares									
Succinylcholine		<1		5–10	Plasma cholinesterase			++	Depolarizing muscle relaxant Plasma $[K^+]$ ↑
Aminosteroids									
Rocuronium	0.3–0.4	1.5–2.5	35–50	55–80	Hepatic/renal	70–106	38–56	–	
Vecuronium	0.05–0.06	2–3	30–40	30–40	Renal/hepatic	50–90	28–123	–	
Pancuronium	0.06–0.07	3.5–6	70–120	130–220	Renal/hepatic	115–155	103	–	T½ extensively prolonged in kidney failure
Pipecuronium	0.04–0.05				Renal/hepatic				FDA status: discontinued
Benzylisoquinolines									
Mivacurium	0.07–0.08	2.5–4.5	15–20	25–40	Plasma cholinesterase	1–3		+	↑ histaminergic side effects with rapid injection
Atracurium	0.25	2–3	35–50	55–80	Hoffman elimination + esterase	17–23	14–20	+	↑ histaminergic side effects with rapid injection
Cis-atracurium	0.05	3–6	40–55	60–90	Hoffmann elimination	19–25		-	↓ histamine release compared to atracurium
Tubocurarine	0.5	>5		60–120	Renal/hepatic			++	FDA status: discontinued
Other classes									
Gallamine	3	1–2	60–120	Long	Renal			-	FDA status: discontinued. Marked cardiovascular side effects.

Table 2. Pharmacokinetics of neuromuscular blocking agents (NMBA). ED_{95}: effective dose to suppress 95% of twitch response. Dur_{25}: clinical duration of action, interval between injection and recovery to 25% of baseline twitch response. T½β: elimination half-life.

KEY FACTS: NONDEPOLARIZING MUSCLE RELAXANTS (NDMRS)

- Onset time after NDMR administration depends on the agent's potency and the perfusion of muscle groups.
- Agents with lower receptor affinity require high induction doses but have faster onset.
- Block recovery after a single bolus dose of NDMR is the result of redistribution rather than agent metabolism.

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4. ANSWER: D

Kidney failure causes decreased glomerular filtration, changes in plasma volume, and electrolyte and acid–base imbalances. Edema, ascites, and pleural effusion may be present. Dialysis further subjects the body to fluid shifts and rapid changes in electrolyte and acid–base balance. The pharmacokinetics of neuromuscular blocking agents (NMBAs) is affected to different extents.

Increases in plasma volume affect the NMBA's distribution volume (V_d). Relatively lower plasma concentrations cause delayed block onset.

Redistribution determines block recovery time of single doses of NDMRs. The effect of kidney failure thus becomes apparent after continuous infusion or repeated dosing, when elimination, not redistribution, becomes rate-limiting for the time to recovery.

All NDMRs are excreted by the kidneys to some extent. Rocuronium and vecuronium are mainly eliminated via the liver, but up to 30% of a dose is excreted in the urine. Reduced kidney function will prolong their duration of action and elimination half-life ($T_{½\beta}$). Moreover, interindividual variability increases, which reduces the predictability of these agents' recovery time. For pancuronium, excretion in the urine is the primary elimination route (65%). Severe kidney failure can dangerously prolong pancuronium's $T_{½\beta}$ to several hours, causing an unpredictable duration of action and an increased risk of residual paralysis.

Kidney failure and dialysis affect plasma cholinesterase function, causing an increased $T_{½\beta}$ of mivacurium and succinylcholine. However, the clinical relevance of a few minutes' delay in recovery time of these agents is debatable. Hoffmann elimination of cis-atracurium is unaffected by kidney failure. Laudanosine, the neurostimulant metabolite of atracurium, is cleared more slowly in patients with kidney failure. Still, the plasma concentrations reached with clinical dosages are insufficient to cause central nervous system excitement, even during continuous infusion. Cis-atracurium metabolism produces less laudanosine than atracurium.

If conditions allow, succinylcholine should be avoided in patients with plasma potassium levels of 5.5 mmol/L or more. A rare complication of succinylcholine use is myoglobinemia, which may cause acute kidney failure in patients with chronic renal insufficiency.

KEY FACTS: NEUROMUSCULAR BLOCKING AGENTS AND KIDNEY DISEASE

- Kidney failure may result in a slower onset and a longer duration of action of most neuromuscular blocking agents (NMBAs).
- Kidney failure has little influence on the effects of cis-atracurium.
- Avoid pancuronium in patients with kidney failure.
- High plasma potassium levels (>5.5 mmol/L) are a contraindication for succinylcholine use.

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5. ANSWER: E

In patients with liver disease, changes occur in plasma volume, electrolyte and acid–base balance, metabolism and biliary clearance of drugs, and production of proteins and enzymes.

PLASMA VOLUME

NMBAs are water-soluble, and their distribution volume (V_d) is the total body water content. Liver failure may result in increased central compartment (plasma) volume. Ascites and pleural effusion increase the volume of the peripheral compartment. The speed on onset of a neuromuscular block depends on the concentration gradient between the central

compartment and the receptor sites, and changes in plasma volume may result in delayed block onset and higher dose requirement.

METABOLISM

After a single dose of a NDMR, recovery speed primarily depends on redistribution, not (hepatic) elimination. Reduced elimination due to liver failure becomes significant with repeated dosing or continuous infusion, when elimination speed determines block recovery time. Aminosteroid NDMRs are predominantly metabolized by the liver. Rocuronium undergoes only minimal metabolism and is mainly excreted unchanged. In early (alcoholic) liver failure, cytochrome P450 is induced, leading to faster metabolism of aminosteroid NDMRs. When liver dysfunction progresses, the metabolism of NDMRs is slowed down. Severe liver failure also affects plasma cholinesterase function, which may result in slower recovery from mivacurium- and succinylcholine-induced blocks. Recovery time from mivacurium-induced block may be increased up to 2.5 times.

Hoffmann elimination depends on pH and temperature but is largely independent of liver and kidney function. The elimination half-life of cis-atracurium will not be significantly changed in patients with liver failure, but electrolyte and acid–base imbalances and increased V_d may still affect the onset and recovery of neuromuscular block.

KEY FACTS: NEUROMUSCULAR BLOCKING AGENTS AND LIVER DISEASE

- Increased plasma volume may result in slower neuromuscular block onset and increased dose requirement.
- The recovery speed of single-dose NMBAs depends on redistribution, not elimination.
- Liver failure has little influence on the effects of cis-atracurium.
- Aminosteroid NMBA metabolism speed is increased in early liver failure and decreased in severe liver failure.

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6. ANSWER: D

Many diseases, physiologic states, and drugs can either potentiate or weaken the effect of NMBAs. Table 17.3 shows where some conditions and drugs exert their influence. Important diseases affecting neuromuscular transmission itself, such as myasthenia gravis and liver and kidney disease, are discussed elsewhere.

Because NMBAs compete with acetylcholine for the ACh receptor, decreased levels of ACh in the neuromuscular junction will potentiate a neuromuscular block. An important example of this is the use of IV magnesium for eclampsia. Magnesium reduces ACh release by inhibiting the presynaptic calcium channel. Blocking of ACh receptors (or their ion channels) on the postsynaptic membrane will also disrupt the signal transmission and potentiate block. In contrast, upregulation of ACh receptors causes decreased sensitivity to nondepolarizing NMBAs. This can be induced by burns, prolonged immobilization (>48 hours), sepsis, and denervation and results in resistance to nondepolarizing NMBAs. In these conditions, ACh receptors appear outside the neuromuscular junction and fetal-type ACh receptors are re-expressed, to which succinylcholine binds more efficiently. The resulting larger potassium efflux through the ACh receptor channel may cause potentially lethal plasma potassium levels in these patients.

When muscle contractility itself is reduced, NMBAs will have a more profound effect. Dantrolene decreases muscle contractility by inhibiting calcium release and reuptake at the sarcoplasmic reticulum. Electrolyte imbalances are also associated with changes in muscle contractility, the most dramatic example being the severe muscle spasms seen in patients with hypocalcemia. The influences of some common electrolyte imbalances are shown in Table 17.3.

Although succinylcholine elimination and mivacurium elimination are largely independent of liver and kidney function, their duration of action is prolonged when plasma cholinesterase is inhibited. The only known conditions affecting the Hoffmann elimination of (cis)atracurium are hypothermia and acidosis.

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Table 17.3 CONDITIONS AND DRUGS AFFECTING NEUROMUSCULAR BLOCK

DRUGS/CONDITIONS	MECHANISM	EFFECT
Volatile anesthetics, magnesium (hypermagnesemia)	Presynaptic calcium channel blockade	Potentiation of nondepolarizing NMBA-induced block
Phenytoin, lithium	Decreased ACh release	
Volatile anesthetics, ketamine, midazolam, barbiturates, antibiotics*, tricyclic antidepressants, lidocaine, procaine, procainamide, quinidine	Postsynaptic ACh receptor blockade	
Dantrolene, hypokalemia, hypercalcemia	Direct effect on muscle	
Organophosphates, ecothiopate, metoclopramide, neostigmine, etomidate	Inhibition of plasma cholinesterase	Depends on type of NMBA
Hypothermia, acidosis	Inhibition of Hoffmann elimination	Potentiation of (cis)atracurium-induced block
Immobilization, denervation/motor neuron lesions, burns, sepsis, prolonged NMBA use	ACh receptor upregulation, expression of fetal-type ACh	Resistance to nondepolarizing NMBA-induced block/hyperkalemia after succinylcholine

NMBA, neuromuscular blocking agent; ACh, acetylcholine. *See Question 75.

7. ANSWER: D

When succinylcholine is administered in patients with upregulation of nicotinic acetylcholine receptors (see Table 17.3), life-threatening hyperkalemia may rapidly develop. The mechanism behind this phenomenon is described elsewhere (Question 6).

Urgent treatment must be initiated when plasma K^+ is 6.5 mmol/L or more and/or when electrocardiogram (ECG) changes occur. These typically include small, broad, or absent P waves, peaked T waves, widened QRS complexes, a sinusoidal pattern, ventricular fibrillation/tachycardia, and asystole.

Treatment should focus on decreasing plasma K^+ levels and preventing heart rhythm abnormalities. ECG and plasma K^+ levels must be checked repeatedly (Table 17.4).

Calcium increases the heart's excitation threshold without lowering the plasma K^+ level. Solutions of calcium chloride contain three times more calcium ions per unit than calcium gluconate. The effect is short-lived, and doses may have to be repeated. Insulin drives K^+ into the cell and must be coadministered with glucose to prevent hypoglycemia. After insulin administration, plasma K^+ levels may decrease by 1 mmol/L in 15 minutes. Acidosis increases plasma K^+ levels and should be treated. A 10 mmHg (1.33 kPa) reduction in CO_2 may lower plasma K^+ levels by 0.5 mmol/L. The administration of bicarbonate leads to a decrease in plasma K^+ levels by 0.5 mmol/L for every 0.1 pH increase.

Table 17.4 TREATMENT OF HYPERKALEMIA

Potassium ≥ 6.5 mmol/L and/or ECG changes with hyperkalemia	
No life-threatening arrhythmia	**Life-threatening arrhythmia (VF/VT/Asystole)**
Calcium chloride 10%, 10 mL (1,000 mg), slow IV over 5 min	Calcium chloride 10%, 10 mL (1,000 mg) IV rapid bolus
15 units of short-acting insulin, in 50 mL of 50% dextrose	Acidosis/renal failure: 50–100 mmol sodium bicarbonate, IV rapid bolus (ensure adequate ventilation to eliminate excess CO_2 produced by this treatment)
If respiratory acidosis: adjust ventilation If metabolic acidosis: 50–100 mmol sodium bicarbonate, slow IV	15 units of short-acting insulin, in 50 mL of 50% dextrose, IV rapid bolus
Salbutamol, 5 mg nebulized	If all this is unsuccessful, reconsider differential diagnosis, consider hemodialysis.
Potassium chelation agent (polystyrene sulfonate)	
If all this is unsuccessful, consider differential diagnosis, commence hemodialysis.	

Other measures, such as chelation therapy (with sodium or calcium polystyrene sulfonate), or salbutamol, are much slower and are not appropriate when life-threatening arrhythmias exist.

Dialysis is a final resort for treatment of acute hyperkalemia.

Polystyrene sulfonates (Kayexalate®, Kionex®, Resonium-A®, SPS®) are cation-exchanging resins based on polystyrene. They can be administered orally or rectally, and are used to reduce the total amount of potassium in the body. As side effects, intestinal disturbances are common, including loss of appetite, nausea, vomiting, and constipation. In rare cases it has been associated with colonic necrosis. Polystyrene sulfonates are useful for chronic or subacute hyperkalemia but is not indicated as an emergency treatment for hyperkalemia leading to a cardiac arrest.

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8. ANSWER: A

Histamine release following administration of NMBAs is most apparent after succinylcholine. The other NMBAs that cause histamine release are tubocurarine, mivacurium, and atracurium. Rapacuronium was withdrawn from the market because of its histamine-releasing effect on mucosal mast cells, which may cause bronchospasm.

Mivacurium and atracurium liberate histamine mainly from serosal mast cells and may cause erythema, tachycardia, hypotension, or bronchospasm.

The aminosteroids do not release histamine from mast cells but can still elicit anaphylactic reactions. Despite differences in histamine liberation potential, today's commonly used nondepolarizing NMBAs have comparable anaphylactic potential. Succinylcholine is about three times more likely to cause anaphylaxis compared to the nondepolarizing NMBAs. Actual anaphylactic reactions to NMBAs are rare. Patients at risk of allergic reaction may be given prophylactic H_1 and H_2 receptor antagonists to decrease the severity of the reaction.

KEY FACTS: NEUROMUSCULAR BLOCKING AGENTS AND HISTAMINE RELEASE

- Succinylcholine, mivacurium, and atracurium cause histamine release.
- Aminosteroid muscle relaxants do not cause histamine release.
- Despite differences in histamine liberation potential, all NDMRs carry a comparable risk of anaphylactic reactions.
- Actual anaphylactic reactions to NDMRs are rare.

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9. ANSWER: A

Burn injuries induce systemic changes that influence the pharmacokinetics of NMBAs. As soon as 48 hours after the burn accident, upregulation of acetylcholine receptors (AChRs) is seen, both inside and outside the neuromuscular junction. Concomitantly, fetal-type AChRs are re-expressed. These changes occur in muscle tissue underneath burn areas, as well as in distant sites. It takes 4 to 10 days before the upregulation becomes clinically relevant, and may be present until as long as 18 months after the burns have healed.

AChR upregulation results in increased sensitivity to succinylcholine and decreased sensitivity to NDMRs. Increased numbers of AChRs and the more efficient binding of succinylcholine to fetal-type AChRs result in exaggerated potassium release through the AChR channels, leading to potentially lethal hyperkalemia. This has been reported in patients with as little as 9% total body surface area (TBSA) burns. Precurarization with NDMRs does not prevent this effect.

In patients with major burns (>20% to 30% TBSA), the onset of NDMRs (except mivacurium) is delayed and the duration of action is reduced. Dose escalation or the administration of a priming dose can improve onset time. Rocuronium can be used for modified rapid-sequence induction. The use of a priming dose (0.06 mg/kg, 3 min before intubation dose) improves onset speed but causes difficult breathing in up to 10% of patients. A single bolus of 1.2 to 1.5 mg/kg (four to five times ED_{95}) significantly improves the onset time and the chance of excellent intubation conditions. An advantage of rocuronium is its reversibility by sugammadex.

The onset of mivacurium (0.15 to 0.20 mg/kg, 2 to 2.5 times ED_{95}) is faster in burn patients, while recovery is approximately 10 minutes slower, due to reduced plasma cholinesterase function. One study reports onset times as fast as 1.3 minutes in patients with major burns, making mivacurium a possible choice for modified rapid-sequence induction.

When cis-atracurium or pancuronium is used, doses must be increased by approximately 50%. An advantage of cis-atracurium is that its elimination (Hoffmann) is unaffected by burns, kidney function, or liver function. When using NDMRs in patients with burns, other factors influencing the pharmacokinetics of NDMRs must be carefully considered, including prolonged immobilization, malnourishment, trauma, sepsis, and kidney failure.

KEY FACTS: SUCCINYLCHOLINE IN BURN VICTIMS

- From 4 days after a major burn injury is sustained until 18 months after healing of the injury, clinically relevant upregulation of acetylcholine receptors may be present.
- Succinylcholine may induce potentially lethal hyperkalemia in this situation.
- Higher induction doses of muscle relaxants may be required, and duration of action may be increased in burn victims.
- Burn victims may also suffer from other trauma, sepsis, malnourishment, and liver and kidney failure, which all influence the neuromuscular blockade.

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10. ANSWER: E

Residual neuromuscular block is associated with anxiety, hypoventilation, atelectasis, aspiration of gastric content, pneumonia, and death. Strategies to prevent these sequelae include monitoring of neuromuscular block and, if necessary, reversal.

NDMRs competitively bind to the acetylcholine receptor (AChR). Acetylcholinesterase inhibitors (AChIs) cause accumulation of acetylcholine at the neuromuscular junction, leading to competitive block reversal. Clinically used agents are neostigmine, pyridostigmine, and edrophonium. For dosing, see Table 17.5. Doses of AChIs must be tailored to the depth of block and the type of NMDR used.

AChIs are water-soluble and are eliminated via the kidneys. In patients with kidney failure, the elimination half-life of these agents is increased two to three times. They also block acetylcholinesterase at muscarinic receptors of the autonomic ganglia. This causes parasympathicomimetic effects, including bradycardia, hypotension, bronchoconstriction, hypersalivation, nausea and vomiting, increased bowel motility, abdominal cramps, miosis, and increased urinary frequency but not retention. Neurologic symptoms associated with neostigmine include dizziness, convulsions, loss of consciousness, drowsiness, headache, dysarthria, miosis, and visual changes. Glycopyrrolate (200 μg per mg neostigmine) or atropine (600 to 1,200 μg) is commonly used to reduce parasympathicomimetic effects. Glycopyrrolate does not cross the blood–brain barrier. However, the theoretical advantage of fewer central anticholinergic side effects

Table 17.5 NONSELECTIVE MUSCLE RELAXANT ANTAGONISTS AND THEIR ADJUNCTS

AGENT	DOSE ADULT (μG/KG)	DOSE CHILDREN (MG/KG)	T½β (MIN)	T½β IN KIDNEY FAILURE (MIN)	REMARKS
Neostigmine	30–70	50	77	181	Usually 2 mg will suffice.
Pyridostigmine	250	100–250	113	379	
Edrophonium	500–1000		110	304	Duration of action very short
Atropine	5–15	10–20	120–180		Different formulations available
Glycopyrrolate	10–20	10	30–75		May cause very dry mouth

T½β, elimination half-life.

(amnesia, confusion, delirium) is not supported by evidence. According to some studies, glycopyrrolate causes less arrhythmia and tachycardia than atropine and is a superior antisialogogue in equipotent doses.

It is advisable to wait for spontaneous recovery of muscle function before attempting reversal with AChI. Not only do the higher doses of AChI required to reverse deep blocks potentially cause severe side effects, they may also simply not produce adequate reversal. If reversal of long-acting NDMRs is attempted, higher doses of AChI are required. The effect of neostigmine peaks at 10 minutes after injection, and repeated dosing may be necessary to avoid recurarization.

AChIs inhibit plasma cholinesterase, which may interfere with reversal of mivacurium-induced block.

KEY FACTS: REVERSAL OF NEUROMUSCULAR BLOCKADE

- Acetylcholinesterase inhibitors (AChIs), such as neostigmine, cause acetylcholine accumulation in the neuromuscular junction, leading to competitive neuromuscular block reversal.
- Glycopyrrolate or atropine are used to counteract the parasympathicomimetic adverse effects of AChIs.
- Ideally, AChI reversal should be first attempted when the neuromuscular blockade has recovered spontaneously for more than 70%.
- Repeated doses of AChIs may be required when reversing blocks of long-acting agents.

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11. ANSWER: A

Succinylcholine is the only clinically used depolarizing muscle relaxant. Chemically, it consists of two acetylcholine molecules linked by the acetyl groups. Despite its side-effect profile, it is still commonly used because of its rapid onset and ultra-short duration of action. A 2008 Cochrane review concluded that succinylcholine creates superior intubation conditions compared to rocuronium when used for rapid sequence induction.

Unlike the NDMRs, succinylcholine is a partial agonist of the AChR. When succinylcholine binds the α subunit of the AChR, the ion channel opens, leading to depolarization of the postsynaptic cell membrane. Unlike acetylcholine, succinylcholine is not metabolized by acetylcholinesterase at the neuromuscular junction. It can thus bind to the AChR repetitively, sustaining the depolarized state of the cell membrane. The clinical result is muscle paralysis, preceded by fasciculations.

Succinylcholine binds to both nicotinic and muscarinic AChRs, the latter explaining many of its adverse effects. Unlike the NDMRs, succinylcholine has a low affinity for presynaptic AChR subtypes. The significance of this is discussed elsewhere in this book.

The ED_{95} of succinylcholine is 0.3 to 0.6 mg/kg. When rapid block onset is required, twice the ED_{95} is given. Fasciculations are usually observed in the first minute, followed by paralysis. Recovery is rapid, usually within 5 to 10 minutes. Plasma cholinesterase (PChE), which is present in the bloodstream and other tissues, metabolizes succinylcholine to choline, and the active metabolite succinylmonocholine. Deficiencies in PChE cause prolonged block; this is discussed in detail elsewhere (Question 2). Neonates have less active PChE, and recovery is slower from succinylcholine-induced neuromuscular block. Neuromuscular blocks induced by succinylcholine cannot be reversed with acetylcholinesterase inhibitors, except when phase II block has developed. This phenomenon is described elsewhere (Question 13).

KEY FACTS: SUCCINYLCHOLINE

- Succinylcholine is a partial agonist at acetylcholine receptors (AChRs).
- Succinylcholine produces depolarization of the postsynaptic cell, resulting in fasciculations before block onset.
- Succinylcholine is characterized by its rapid onset (<1 minute) and offset (5 to 10 minutes).
- It is rapidly metabolized by plasma cholinesterase (PChE).

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12. ANSWER: B

The adverse effects of succinylcholine can be grouped into four categories: antimuscarinic action, potassium release-related, allergic, and nonspecific adverse effects. The phenomenon of second phase block is discussed elsewhere (Question 13).

ANTIMUSCARINIC ACTION

Succinylcholine is nonselective and binds to both nicotinic (nAChRs) and muscarinic acetylcholine receptors (mAChRs). Muscarinic AChRs are found in the brain (where they are safe from the polar succinylcholine molecule), the ganglia of the peripheral nervous system, and the synapses between the vagus nerve (cranial nerve X) and the heart. Succinylcholine can excite these vagal mAChRs and cause bradycardia, idioventricular rhythm, or ventricular arrhythmia. This effect is potentiated when other parasympathetically innervated structures are manipulated, such as the cervix and eyeballs. Direct laryngoscopy is also a potential vagal stimulus. A high vagal tone is often seen in children, which makes them vulnerable to the cardiac adverse effects of succinylcholine. Atropine can be given to reduce bradyarrhythmias, but not ventricular dysrhythmias.

POTASSIUM RELEASE

When succinylcholine binds to the nAChRs, its ion channel opens, releasing cations. In healthy individuals, the plasma K^+ level will increase by approximately 0.5 mmol/L and will return to normal within 10 to 15 minutes. However, this effect poses a relative contraindication for individuals with hyperkalemia (>5.5 mmol/L). In certain patients (e.g., those with burns or immobilization), the increase in plasma K^+ is much higher and potentially fatal.

ALLERGIC REACTION

Succinylcholine is about three times more likely to cause allergic reactions than other muscle relaxants. The reaction is IgE-mediated. Anaphylaxis after administration is rare. Cross-reactivity with other muscle relaxants does exist, but is rare.

NONSPECIFIC EFFECTS

Fasciculations could explain postoperative myalgia and the transient increases in ocular pressure seen with succinylcholine use. Although controversial, succinylcholine is thought to increase intracranial pressure, possibly through activation of proprioceptive cortical neurons by the fasciculations, leading to increased cerebral blood flow. Others suggest an increase in abdominal pressure due to fasciculations leading to decreased cerebral venous drainage as the cause of this intracranial pressure increase. Succinylcholine may also increase intraocular pressure, and its use should be avoided in ophthalmic surgery.

Fasciculations can be reduced by precurarization with low-dose NDMRs. This is contraindicated in patients with preexisting muscle weaknesses, such as myasthenia gravis. Succinylcholine must not be administered to patients with a history of malignant hyperthermia (MH), as it is a potent trigger of MH (discussed separately elsewhere (Question 14]). The adverse effects of succinylcholine are summarized in Table 17.6.

Table 17.6 ADVERSE EFFECTS OF SUCCINYLCHOLINE

MECHANISM	ADVERSE EFFECT	MANAGEMENT
Antimuscarinic effects	Bradycardia	Atropine
	Idioventricular arrhythmia, ventricular arrhythmia including ventricular fibrillation	Cardiopulmonary resuscitation
Potassium release	Dangerous hyperkalemia	None, contraindicated when patient at risk (see Question 7)
Hypersensitivity	Allergic reaction/ Anaphylaxis	Discontinue use, treat anaphylaxis, muscle relaxant allergy tests
Aspecific (fasciculations?)	Myalgia	Self-limiting
	Increased intraocular pressure	Deepen anesthesia, precurarization, sublingual nifedipine. Relative contraindication: ocular trauma, open anterior chamber
	Increased intracranial pressure	Precurarization, hyperventilation, thiopenthal, lidocaine
	Malignant hyperthermia	Get help, discontinue anesthesia, give dantrolene (see Question 14)

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13. ANSWER: D

When an intubation dose (1 to 1.5 mg/kg) of succinylcholine is administered to a patient with normal plasma cholinesterase (PChE) function, the agent binds to the α-subunit of the postsynaptic acetylcholine receptor (AChR). The receptor's cation channel opens and the cell membrane depolarizes. Fasciculations occur from the initial stimulation, followed by flaccid paralysis, as the channel cannot close and allow the cell to repolarize while succinylcholine is bound to the AChR. This unique kind of neuromuscular block is referred to as "phase I depolarizing block."

A phase I depolarizing block can be distinguished from nondepolarizing block by the absence of TOF fade and absence of posttetanic potentiation on mechanomyography monitors. During phase I block, a generalized reduction in all four TOF twitches can be observed, with little or no fade, a generalized reduction in all four twitches can be observed with little or no fade. During onset and recovery of the block, TOF fade can be observed, although to a much lesser extent than with nondepolarizing block. Phase I block cannot be reversed with acetylcholinesterase inhibitors (AChIs).

When higher or repeated doses are administered, the neuromuscular block will progress to a state called phase II block, characterized by TOF fade and posttetanic potentiation similar to nondepolarizing block.

The exact mechanism behind phase II block is unclear. Phase II block is usually defined as a TOF ratio of less than 50%. At a total dose of less than 8.0 mg/kg, phase II block is unlikely. However, it may develop at lower doses, and in some patients it will not develop before very high doses (>15 mg/kg) are administered. Volatile anesthetics may reduce the dose threshold (3 to 5 mg/kg). Once phase II block has developed, recovery time becomes unpredictable. It may be unchanged, but also may be significantly prolonged.

In some patients, the twitch response suppression of each subsequent dose is reduced, an example of tachyphylaxis.

Once spontaneous recovery from phase II block begins, block reversal may be attempted with edrophonium or neostigmine. Discussion exists about potential block enhancement caused by AChI administration in attempts to reverse phase II block, but this risk seems to be small. Monitoring of succinylcholine-induced block is recommended to detect phase II block and the effectiveness of subsequent doses and reversal attempts.

KEY FACTS: PHASE I AND II BLOCK WITH SUCCINYLCHOLINE

- A single dose of succinylcholine produces a phase I depolarizing block, which cannot be reversed with acetylcholinesterase inhibitors (AChIs).
- Progression to phase II block occurs with high doses (>3 to 5 mg/g with volatile anesthetics and >8 mg/kg with total intravenous anesthesia). It resembles nondepolarizing block and is characterized by TOF fade and posttetanic potentiation.
- Phase II block recovery time is unpredictable, but reversal with AChIs may be effective once spontaneous recovery has begun.

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14. ANSWER: B

Dantrolene was developed as a peripheral muscle relaxant for the treatment of chronic spasticity. In anesthesia, the compound is the cornerstone of treatment of malignant hyperthermia (MH). Dantrolene blocks muscle spasm, and thus heat production, by preventing calcium release from the sarcoplasmic reticulum.

Each vial contains 20 mg of lyophilized dantrolene and is to be reconstituted with 60 mL of sterile water. Warm water (maximum 39 degrees C [102 degrees F]) speeds up reconstitution, but no time must be wasted if this is not readily available. The solution pH is high (>9), and it is ideally infused via central venous catheter because it may cause thrombophlebitis. However, initiation of treatment

should not be delayed to insert a central venous catheter. Reconstituted vials contain 3 g of mannitol. Brisk diuresis is likely to occur.

Dantrolene is metabolized in the liver and excreted via bile and urine. Its elimination half-life after IV injection is 12 hours.

When MH is diagnosed, the surgical team must be informed and volatile agents and other triggering agents must be discontinued. Hyperventilate the patient with 100% oxygen, and call for help. As soon as possible, an initial dose of 2.5 mg/kg should be rapidly administered via rapid IV bolus. For an 80-kg patient, this is 200 mg, or 10 vials of 20 mg. When the initial dose fails, it should be repeated. The median total dose in a recent evaluation of 157 cases was 6 mg/kg. However, some patients may need up to 20 mg/kg (for an 80-kg patient, 80 vials of 20 mg).

Once the patient is stabilized, dantrolene infusion should be continued for at least 24 hours in the intensive care unit to prevent recrudescence, using a dose of 1 mg/kg every 4 to 6 hours, or a continuous infusion of 0.25 mg/kg/h (protect solution from light and use within 6 hours).

Acute hepatic dysfunction may follow dantrolene use. Avoid skin contact with reconstituted dantrolene. In case of contact, rinse with plenty of water.

KEY FACTS: DANTROLENE

- Dantrolene blocks muscle spasm and heat production by inhibiting calcium release from the muscle's sarcoplasmic reticulum.
- In case of malignant hyperthermia, initiate dantrolene therapy immediately.
- The initial dose is 2.5 mg/kg given by rapid IV bolus. One vial contains 20 mg. An average patient with malignant hyperthermia will require ±6 mg/kg.
- Dantrolene is metabolized in the liver; its T½β is ±12 hours after IV injection.
- Continue the infusion for at least 24 hours in the intensive care unit.

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15. ANSWER: A

G-protein–coupled "muscarinic acetylcholine receptors" (mAChRs) are found in the brain, the ganglia of the peripheral nervous system, the heart, smooth muscle, and exocrine glands. In the brain, they inhibit dopamine-mediated motor effects. Outside the brain, they are responsible for parasympathetic stimulation, commonly remembered as "rest and relax."

Atropine and glycopyrrolate compete with acetylcholine at the mAChR and are used for treatment and prevention of bradycardia, induced by vagal (parasympathetic) stimulation. Furthermore, they counteract the parasympathetic effects of succinylcholine and the cholinesterase inhibitors. Furthermore, they reduce salivation and bronchial secretion and dry out mucous membranes. Both agents may cause paradoxical bradycardia in very small doses, probably due to their effect on presynaptic mAChRs. Atropine and glycopyrrolate are less effective in the elderly due to reduced mAChR density. Some beneficial and adverse effects are shown in Figure 17.1.

PILOCARPINE

Pilocarpine is one of the only parasympathicomimetics still in clinical use. This mAChR agonist is used to stimulate saliva production in patients with Sjögren's disease.

IPRATROPIUM BROMIDE

Ipratropium bromide is a quaternary ammonium anticholinergic compound chemically related to atropine. Ipratropium bromide induces bronchodilation through a selective parasympathetic blockade of the bronchial muscarinic receptors. Because cholinergic tone substantially contributes to airway narrowing in patients with chronic obstructive pulmonary disease (COPD), ipratropium bromide is a mainstay in the management of those patients.

ATROPINE

Atropine is commonly injected IV but can also be administered IM or via the trachea. Usual doses for adults are 0.25 to 0.5 mg IV or IM. IM absorption is slow (T_{max} 30 minutes). After injection, atropine is metabolized to inactive metabolites in the liver (50% to 70%) and partially excreted unchanged via the kidneys (30% to 50%). Its elimination half-life (T½β) is 2 to 5 hours. Clinical duration of action after a single 20-μg/kg IV dose is 3 hours. The administration of more than 3 mg of atropine during cardiopulmonary resuscitation is not useful and should be avoided.

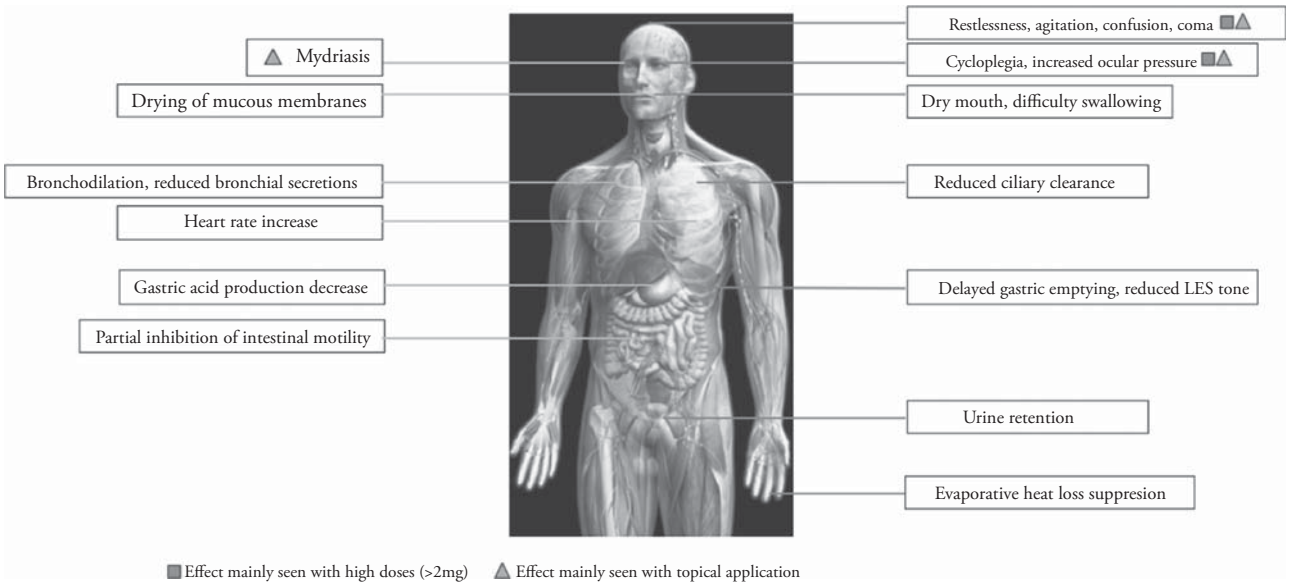

Figure 17.1 Atropine: beneficial and adverse effects. Courtesy of Zygote Media http://3D-science.com.

In febrile children, atropine may cause dangerous hyperthermia due to suppression of evaporative heat loss.

KEY FACTS: ATROPINE

- Atropine and glycopyrrolate compete with acetylcholine at the muscarinic acetylcholine receptor and have parasympathicolytic effects.
- Atropine sulfate crosses the blood–brain barrier; glycopyrrolate and methylatropine do not.
- The antisialogogue effect of glycopyrrolate lasts up to 8 hours, although its circulatory effect lasts only ±1.5 hours, half as long as that of atropine.

GLYCOPYRROLATE

Glycopyrrolate is poorly absorbed from the gastrointestinal tract and mucous membranes. It has a quaternary ammonium structure. The usual IV dose ranges from 2.5 to 20 μg/kg. Glycopyrrolate is eliminated via the kidneys. In health, T½β is 48 to 72 minutes. Its duration of action is prolonged in patients with kidney failure. Glycopyrrolate is highly polar and, unlike atropine, does not cross the blood–brain barrier or the placenta. Cardiovascular effects of glycopyrrolate last only half as long as those of atropine, but its antisialogogue effect is stronger and lasts up to 8 hours. Patients may find the long-lasting mouth dryness highly unpleasant. Some studies report less cardiac arrhythmia with glycopyrrolate compared to atropine.

SCOPOLAMINE

Scopolamine is an anticholinergic alkaloid obtained from the leaves and seeds of several solanaceous plants. It is a central nervous system depressant. It is prescribed for prevention of motion sickness and as an antiemetic, sedative, cycloplegic, and mydriatic.

PANCURONIUM

Pancuronium has parasympathicolytic properties and causes a moderate increase in heart rate and, to a lesser extent, in cardiac output, with little or no change in systemic vascular resistance. Pancuronium-induced tachycardia has been attributed to vagolytic action, probably secondary to inhibition of M2 receptors, and sympathetic stimulation that involves both direct (blockade of neuronal uptake of norepinephrine) and indirect (release of norepinephrine from adrenergic nerve endings) mechanisms.

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16. ANSWER: D

When the antimuscarinergic agent atropine is administered intravenously at single doses of up to 1.5 to 2.0 mg, the agent

does not usually cause significant central (adverse) effects. When higher or repeated doses (5 to 10 mg) are injected, significant amounts penetrate the central nervous system. Central muscarinic acetylcholine receptor (mAChR) blockade leads to anticholinergic symptoms, and in fact to the central anticholinergic syndrome. Intoxication may also follow the installation of eye drops and accidental or intentional oral ingestion of atropine tablets, eye drops, and plants and plant products containing atropine or similar alkaloids. The latter occurs more often in children and adolescents.

Medications with anticholinergic effects are omnipresent. Some examples are displayed in Table 17.7.

Symptoms include mydriasis; blurred vision; dry mucous membranes; difficulty swallowing; dry, red, and warm skin; urine retention; hyperthermia; tachycardia; ataxia; agitation; hallucinations; delirium; hypoventilation; and coma. After anesthesia, mydriasis is less likely to occur because opioids cause profound miosis. Motionlessness may be more prominent.

The differential diagnosis of anticholinergic syndrome includes malignant hyperthermia, neuroleptic malignant syndrome, and drug-induced hyperthermia. It may be very difficult to distinguish between these because mental status changes in these conditions overlap. Distinguishing features of atropine and anticholinergic intoxication are dry skin and mucous membranes. The symptoms can be treated with acetylcholinesterase inhibitors. Physostigmine, in doses of up to 4 mg for adults, is very effective, but doses may have to be repeated, as the half-life of anticholinergic medicines is often longer than that of physostigmine.

After IV administration, the side effects of amiodarone may be confused with anticholinergic toxicity because flushed skin, reflex tachycardia, and extrapyramidal changes may occur. It may also cause vivid dreams, but not mental status change. Furthermore, it causes sweating rather than dry skin.

St. John's wort and metoclopramide are substances that may induce the neuroleptic malignant syndrome.

Table 17.7 **AGENTS WITH ANTICHOLINERGIC EFFECTS**

Antihistamines	**Chlorpheniramine, cyproheptadine, doxylamine, hydroxyzine, diphenhydramine, meclizine, promethazine**
Neuroleptics	**Chlorpromazine, clozapine, mesoridazine, olanzapine, quetiapine, thioridazine**
Tricyclic antidepressants	**Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline**
Antiparkinsonian drugs	**Trihexyphenidyl, benztropine**
Ophthalmic drugs	**Atropine, cyclopentolate**
Antispasmodics	**Clidinium, dicyclomine, hyoscyamine, oxybutynin, propantheline, scopolamine**

KEY FACTS: ANTICHOLINERGIC SYNDROME

- Atropine may induce toxicity due to penetration into the central nervous system. Atropine eye drops and plants containing atropine-like alkaloids are also possible culprits.
- Atropine intoxication induces central anticholinergic syndrome. The differential diagnosis includes neuroleptic malignant syndrome and malignant hyperthermia.
- Physostigmine is used as an antidote, but its half-life is shorter than most drugs inducing anticholinergic symptoms, including atropine.

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17. ANSWER: C

The opioid receptors are a set of G-protein–coupled receptors involved in the modulation of pain experience and arousal. Their natural ligands are endogenous opioids. Subtypes of opioid and opioid-like receptors are summarized in Table 17.8. Opioid receptors located in the brain and spinal cord mediate the analgesic and sedative effect of opioids. Some (adverse) effects are also mediated by peripheral opioid receptors. Opioid effects on all opioid receptors are antagonized by naloxone and naltrexone.

SUPRASPINAL LOCI

Several regions of the brain express opioid receptors. The locus ceruleus, rostral ventral medulla, and periaqueductal gray are key loci of opioid receptors. Other loci are found in the amygdala, hypothalamus, insular cortex, ventral tegmental area, and globus pallidus. The main effect of opioid receptor activation in the brain is inhibition of presynaptic GABA release, although precise mechanisms are very diverse and not very clear. Effects of opioids in the forebrain are responsible for the changes in pain behavior seen after administration.

SPINAL LOCI

Activation of opioid receptors inhibits calcium influx at the presynaptic nerve terminals of primary afferent nociceptive

Table 17.8 OPIOID RECEPTOR SUBTYPES

SUBTYPE	EFFECT AFTER ACTIVATION	LOCATION
μ_1	Supraspinal analgesia, bradycardia, sedation and pruritus, dependence	Brainstem, thalamus, dorsal horn
μ_2	Respiratory depression, euphoria, reduced gastrointestinal motility, dependence, miosis	Brainstem, thalamus, dorsal horn
κ	Spinal analgesia, respiratory depression, sedation, miosis, dysphoria, inhibition of antidiuretic hormone release	Limbic system, diencephalon, brainstem, dorsal horn
Δ	Spinal and supraspinal analgesia, respiratory depression, euphoria, reduced gastrointestinal motility	Brain, dorsal horn, periphery
σ*	Hypertension, tachycardia, dysphoria, delirium, mydriasis	Brain
ORL_1*	Central pain modulation	Brain

* The sigma and opioid receptor-like (ORL_1) receptors are not actual opioid receptors because they also have nonopioid ligands. σ is not a G-protein–coupled receptor.

neurons in the spinal cord, inhibiting the release of excitatory neurotransmitters. At the postsynaptic cell, opioid receptor activation causes potassium release, making the neurons less responsive to nociceptive signals.

Most opioids used in anesthesia are μ agonists with low affinity for the other subtypes. The μ receptors generate effects at the spinal, supraspinal, and peripheral level, whereas κ receptors mediate analgesia primarily at the spinal level. δ receptors act both spinally and supraspinally.

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18. ANSWER: C

Morphine, the classic opioid, is a μ-opioid receptor agonist. When injected intravenously, most of its effect is mediated through opioid receptors in the brain. It is not as lipophilic as its phenylpiperidine cousins. Morphine diffuses in and out of the brain slowly, hence its slow onset and long duration of action.

The liver transforms morphine into morphine-3-glucuronide (M3G, 45% to 55%) and morphine-6-glucuronide (M6G, 10% to 15%). M3G is not analgesic and can produce central nervous system stimulation. M6G is more potent than morphine and may accumulate with repeated dosing or in patients with kidney failure. Liver failure and conditions reducing liver blood flow (such as heart failure) affect the clearance of morphine. In health, the elimination half-life ($T_{½\beta}$) of morphine is 1.3 to 3.4 hours.

IV, IM, AND SC ADMINISTRATION

IV morphine has a broad indication spectrum. Dose is titrated to effect, and normal doses for the opioid-naïve patient are 2.5 to 10 mg, every 3 to 4 hours. Chronic opioid users will need higher doses. Absorption after IM or SC injection is rapid and complete. Peak concentrations are reached after 10 to 20 minutes. SC morphine may be appropriate for chronic use, although more patient-friendly routes are available.

NEURAXIAL ADMINISTRATION

The onset of effect of neuraxial morphine is slow because of its low lipid solubility. When injected epidurally, morphine penetrates through the dura, into the cerebrospinal fluid. Its effect is thus produced on both the spinal and supraspinal level. Minimal metabolism occurs in the cerebrospinal fluid, and the duration of action is very long. In the lumbar epidural space, 3 to 5 mg can be used. The maximum 24-hour dose is 10 mg. Spinally, one-tenth of the epidural dose may suffice. Its duration of action ranges from 12 to 24 hours. Liposomal morphine preparations have a longer duration of action. The cerebrospinal fluid circulation moves morphine slowly toward the brain, where it can cause delayed respiratory depression 6 to 10 hours after injection. Neuraxial opioids often cause pruritus, which can be treated with naloxone or ondansetron. For the spinal and epidural routes, preservative-free preparations of morphine must be used!

ORAL ADMINISTRATION

Morphine is poorly absorbed from the oral mucosa. Gastroenteral absorption is rapid, but subject to extensive first-pass metabolism. Compared to IV administration, more M6G is formed after oral administration. This may explain why efficacy increases with repeated

oral doses. The equianalgesic oral morphine dose is three to four times the IV dose. Peak plasma concentration is reached after 30 to 90 minutes. Faster-acting opioids may be more appropriate for treatment of acute breakthrough pain. Immediate-release preparations must be repeated every 3 to 4 hours, controlled-release preparations every 12 hours.

KEY FACTS: MORPHINE

- Morphine is a μ opioid with intermediate onset and duration of action. Extensive clinical experience makes morphine a valuable first-line opioid.
- Active metabolites include morphine-3-glucuronide (toxic, nonanalgesic) and morphine-6-glucuronide (potent analgesic).
- Neuraxially administered morphine has a duration of action of 12 to 24 hours.
- The equianalgesic oral morphine dose is three to four times the IV dose.

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19. ANSWER: B

20. ANSWER: B

The opioid class of the phenylpiperidines consists of fentanyl, sufentanil, alfentanil, and remifentanil. The latter is discussed in detail elsewhere (Question 21). These μ-opioid receptor agonists share many characteristics with morphine in terms of clinical and adverse effects. However, they act more quickly and have a shorter duration of action. As with all opioids, except remifentanil, duration of action is determined by elimination half-time, lipid solubility, and pKa. The basic pharmacokinetic variables of the synthetic opioids are compared to the characteristics of morphine in Table 17.9. Note that elimination half-life does not correspond well to context-sensitive half-time.

FENTANYL

After IV injection, the highly lipid-soluble fentanyl rapidly enters the brain, with peak concentrations occurring after 2 to 3 minutes. As with sufentanil, rapid redistribution occurs, but fentanyl is metabolized slower. With repeated dosing or continuous infusion, fentanyl accumulates more than sufentanil and alfentanil. After the first hour of infusion, its context-sensitive half-time climbs steeply, to up to 2 hours.

Fentanyl is available as an injectable solution, transdermal system, orobuccal lozenge, sublingual tablet, and nasal spray. The mucosal administration forms can provide rapid relief from breakthrough pain.

SUFENTANIL

Sufentanil has the highest lipid solubility of its class. It easily penetrates the brain and has a quick onset. Rapid redistribution to peripheral tissues accounts for its short duration of action. Sufentanil is rapidly metabolized in the liver and is therefore less likely to accumulate during continuous infusion than fentanyl. Its context-sensitive half-time is therefore short, making sufentanil an appropriate choice for longer operations. It is ±9 times more potent than fentanyl.

ALFENTANIL

Alfentanil is not as lipid-soluble as fentanyl and sufentanil. Therefore, its distribution volume (V_d) is smaller. Furthermore, it has a relatively acidic pKa, which means that, at physiologic blood pH levels, 90% of its molecules are un-ionized and can cross the blood–brain barrier. These characteristics contribute to its fast onset. If only short-lasting peak opioid effects are desirable, alfentanil may be an appropriate choice.

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21. ANSWER: E

The clinical effects of ***remifentanil*** are similar to those of the other fentanyl congeners. However, remifentanil distinguishes itself with a unique, ultra-rapid elimination route. Remifentanil is approximately equipotent to fentanyl.

Table 17.9 OPIOIDS—COMPARATIVE PHARMACOLOGY

DRUG	μ	κ	Δ	PRIMARY ELIMINATION PATHWAY	T½β IN ADULTS	REMARKS
Pure agonists						
Remifentanil	+++	+	+	Erythrocyte acetylcholinesterase	10 min	Ultrashort-acting opoid, beware postoperative pain
Alfentanil	+++	+	+	Hepatic (CYP450), renal excretion	90 min	Low lipid solubility, rapid onset
Morphine	+++	+	+	Hepatic glucuronidation, renal excretion	120 min	Active metabolite morphine-6-glucuronide
Sufentanil	+++	–	+	Hepatic dealkylation, renal excretion	150 min	Most lipid-soluble
Hydromorphone	+++	–	+	Hepatic glucuronidation, renal excretion	150 min	Similar to morphine, but faster onset due to higher lipid solubility. Also less active metabolites.
Codeine	+++	+	+	Hepatic glucuronidation, renal excretion	180 min	Antitussive, less euphoria and abuse potential than morphine. Weak analgesic.
Meperidine (Pethidine)	++	+	+	Hepatic (CYP450), renal excretion	200 min	Anticholinergic side effects. Interacts with MAOIs. Less accumulation in neonate, useful in labor. Less bradycardia.
Fentanyl	+++	–	+	Hepatic (CYP450), renal excretion	220 min	Available as injectable, transdermal patch, orobuccal applicators, and sublingual tablet.
Propoxyphene	+++	+	+	Hepatic (CYP450), renal excretion	8 hr	Inhibits CYP 3A4. Unfavorable risk–benefit balance.
Levorphanol	+++	+	+	Hepatic (CYP450), renal excretion	15 hr	Isomer of propoxyphene.
Methadone	+++	–	–	Hepatic (CYP450), renal excretion	>24 hr	Long half-life, reduced withdrawal. Many drug interactions, especially CYP3A4 inhibitors.
Partial mixed agonists						
Pentazocine	*	++	+		4	Active metabolite with T½β > 24 hr. Use reserved for opioid-naïve patient. Binds to σ-receptor, psychomimetic effects.
Buprenorphine	(+++)	**	–	Hepatic (glucuronidation + CYP450), renal excretion	12 hr (oral), 2–3 hr (IV)	Useful in chronic pain, pronounced respiratory depression. Available as sublingual tablet, transdermal patch, injectable.
Antagonists						
Naloxone	***	**	*		75	
Naltrexone	***	***	*			
Alvimopan						Peripheral μ-receptor antagonist

PHARMACOKINETICS

Remifentanil has a relatively low pKa, leaving most molecules un-ionized at physiologic pH. This facilitates easy passage across the blood–brain barrier. Onset of analgesic effect occurs in 30 to 60 seconds, and peak effect is reached after ±2.5 minutes. Remifentanil is rapidly metabolized by esterases in blood and tissue, but not plasma cholinesterase. Its context-sensitive half-time is ±3.5 minutes and is independent of the duration of infusion, liver and kidney function, age, and weight. Terminal elimination half-life is ±10 minutes.

The rapid offset of analgesic effect necessitates additional analgesics for patients expected to have postoperative pain. Rapid offset of sedation provides an advantage for postoperative neurologic examination. Hypothermia may decelerate the clearance of remifentanil. Bolus doses of remifentanil may cause dose-dependent bradycardia, hypotension, and

respiratory depression. It is therefore usually administered as a continuous infusion, although bolus doses can be safe in experienced hands.

TARGET-CONTROLLED INFUSION (TCI)

Remifentanil is often coadministered with propofol by computer-controlled infusion pumps. These pumps use pharmacokinetic models and automatically titrate the infusion rate to the desired effect target concentration. This optimizes the effect stability of these agents. Remifentanil plasma concentrations of 6 ng/mL reduce the required propofol dose by 25%.

REMIFENTANIL DURING LABOR

Parturients may need systemic opioids when neuraxial blockade fails or is undesired or contraindicated. During labor, remifentanil can be an alternative to meperidine and is administered by patient-controlled analgesia (PCA) systems. Remifentanil may not be as effective as neuraxial blockade but is usually well tolerated. Remifentanil crosses the placenta but is not likely to cause respiratory depression because it is rapidly metabolized by the fetus. Remifentanil is less likely to cause nonreassuring fetal heart rate readings than meperidine.

A 2009 review by Hinova et al. suggests a 40-μg bolus with a 2-minute lockout as a PCA regimen. A bolus dose should be administered at the beginning of a contraction. This dose will then provide analgesia for the next contraction. A continuous-infusion regimen, titrated to effect (and adverse effects), may also be beneficial, but experience with this method is limited.

The potential adverse effects of IV opioid use during labor demand close monitoring of the parturient by an experienced midwife or obstetric nurse.

KEY FACTS: REMIFENTANIL

- Remifentanil is a synthetic μ agonist, approximately equipotent with fentanyl.
- It is rapidly metabolized by blood and tissue esterases and has a constant context-sensitive half-time of ±3.5 min, independent of age, weight, organ function, and duration of infusion.
- Bolus-dose administration carries the risk of acute bradycardia, hypotension, and respiratory depression and should be applied only by experienced providers.
- Remifentanil PCA can be used during labor when neuraxial blockade is not an option, under experienced supervision.

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22. ANSWER: A

The μ-opioid agonists morphine, fentanyl, remifentanil, sufentanil, and alfentanil share most of their adverse effects.

RESPIRATORY DEPRESSION

Respiratory depression is an effect of all opioids, mediated mainly by the μ_2-opioid receptor. The overall incidence of opioid-induced respiratory depression is less than 1%. With PCA devices with morphine, this is less than 0.5%. Delayed respiratory depression after neuraxial opioids occurs in ±0.36% of patients.

Opioids suppress respiratory drive by reducing central CO_2 sensitivity. This adverse effect is most dangerous for patients retaining carbon dioxide—for example, those with chronic obstructive pulmonary disease. Other patients at increased risk include the obese, premature infants, the elderly, and patients with sleep apnea or neuromuscular diseases. Furthermore, recall that hypercarbia may lead to increased intracranial pressure.

The κ-selective opioid pentazocine causes less respiratory depression, but its μ antagonism may cause withdrawal in μ-opioid–dependent patients. Respiratory depression responds to naloxone.

BRADYCARDIA AND VASODILATION

Bradycardia is caused by stimulation of the central vagal nuclei, and vasodilation by depression of the vasomotor centers in the medulla. These effects are dose-dependent and seen at clinical doses. Combinations with other anesthetic agents may aggravate bradycardia and vasodilation. Opioids do not sensitize the heart to arrhythmia and are not negative inotropes at clinical doses. In fact, opioid-based anesthetics are commonly considered cardiovascularly stable.

NAUSEA AND VOMITING

Nausea and vomiting are very common and are caused by an effect at the chemoreceptor trigger zone in the medulla. They usually disappear with repeated opioid administration. 5-HT_3-antagonists, dexamethasone, and antipsychotics are effective treatments.

CONSTIPATION

Agonism at the μ-opioid receptors in the myenteric plexus leads to slower bowel movement. This may contribute to postoperative ileus. Antagonists of peripheral μ-opioid receptors are available orally (alvimopan) and parenterally (methylnaltrexone). Methylnaltrexone has a quaternary structure, preventing easy penetration of the blood–brain barrier. These agents are useful when opioid-induced postoperative ileus develops. Almost no tolerance is developed to constipation, and it must be anticipated with chronic opioid use.

SMOOTH MUSCLE SPASM

Because opioid receptors are found practically everywhere in the body, this effect is observed in the entire gastrointestinal system and the urinary tract. Potential effects include delayed gastric emptying, increased intrabiliary pressure and biliary colic, and urinary retention. The latter is more common in men, especially those receiving neuraxial opioids.

SKELETAL MUSCLE RIGIDITY

The generalized hypertonus of skeletal muscle is seen with the phenylpiperidines, especially after rapid bolus injection. Naloxone reverses the rigidity. During anesthesia induction, muscle relaxants will terminate the rigidity. Some degree of certainty about adequate mask ventilation should exist before inducing paralysis.

HISTAMINE RELEASE

The effect of histamine release is unrelated to opioid receptors. Effects include urticaria and bronchoconstriction; therefore, opioids must be used with caution in asthma patients. Histamine release may contribute to hypotension. Fentanyl, sufentanil, remifentanil, and alfentanil do not cause histamine release.

PRURITUS

This opioid-induced dysesthesia, occurring particularly often with neuraxial opioid administration, can make opioid therapy unacceptable for patients. It is not caused by histamine release, because it is also seen with use of the phenylpiperidines. It responds well to naloxone or very small doses of IV propofol.

KEY FACTS: OPIOID ADVERSE EFFECTS

- The μ opioids share most of their adverse effects.
- Conditions associated with increased risk of harm from respiratory depression are prematurity, obesity, chronic obstructive pulmonary disease, neuromuscular disease, sleep apnea, advanced age, and increased intracranial pressure.
- Other common effects are bradycardia, vasodilation, nausea and vomiting, constipation, smooth muscle spasm, and pruritus.

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23. ANSWER: D

NALOXONE

Naloxone and naltrexone are potent antagonists at μ-, δ-, and κ-opioid receptors and can reverse most opioid effects, including analgesia.

Naloxone is not suitable for oral administration due to its almost complete first-pass effect. After IV administration, reversal of opioid effects occurs rapidly. Naloxone is metabolized by the liver and has a half-life of ±75 minutes. Most opioid analgesics work longer, so repeated doses may be necessary. However, when reversal of full opioid agonists is attempted after anesthesia, plasma concentrations will usually be just above the respiratory depression threshold, and single bolus doses of naloxone may suffice. When titrated to effect, naloxone may reverse respiratory depression before antagonizing analgesia. It is seldom necessary to reverse the effects of remifentanil, as its effects are extremely short-lived.

Reversal of buprenorphine effects, a partial opioid receptor agonist, with naloxone is complex, as the dose–response curve of buprenorphine is nonlinear. After a certain threshold dose (2 to 3 mg), reversal becomes less adequate with higher doses.

When naloxone is administered as rapid bolus injections to patients previously experiencing severe stress or pain, hypotension, or hypovolemia, massive amounts of catecholamine may be released. This may lead to arrhythmia, vasoconstriction, convulsions, and pulmonary edema. These adverse effects are less likely when naloxone is titrated to effect.

OTHER OPIOID RECEPTOR ANTAGONISTS

Naltrexone works much longer than naloxone and has a half-life of ±10 hours. Methylnaltrexone is similar but has a quaternary structure, preventing it from crossing the blood–brain barrier, where it would antagonize analgesia. It is used to treat opioid-induced constipation and ileus. It is administered subcutaneously.

Alvimopan is an orally administered, selective μ-opioid receptor antagonist that is poorly absorbed and thus does not antagonize systemic opioid effects. It can be used to treat opioid-induced constipation and ileus.

It must be stressed once again that opioid adverse effect reversal with systemic antagonists will often result in reversal of beneficial opioid effects as well. Administration of opioid antagonists may precipitate withdrawal symptoms in chronic opioid users.

KEY FACTS: NALOXONE

- The effect of naloxone is shorter than that of most opioids.
- Dose titration of naloxone may result in reversal of adverse effects before reversal of analgesia.
- Rapid administration of naloxone to opioid-dependent patients or patients in extreme pain may lead to dangerous catecholamine release.
- Selective treatment of opioid effects on the intestines can be achieved with alvimopan (oral) or methylnaltrexone (subcutaneous).

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24. ANSWER: E

Meperidine has some unique properties compared to morphine and the other phenylpiperidines.

PHARMACOLOGY

Meperidine is administered orally or parenterally. Its half-life ($T_{½\beta}$) is ±3.5 hours in health. Hepatic extraction is comparable to that of morphine. Oral bioavailability is ±50%, due to first-pass effect. The liver converts meperidine to normeperidine by N-demethylation and to the inactive meperidinic acid via hydrolysis. This is further conjugated and excreted renally. Normeperidine is a convulsant and quickly accumulates in patients with kidney dysfunction when dosed repeatedly. Normeperidine has a $T_{½\beta}$ of 12 to 24 hours. Hepatic cirrhosis decreases meperidine's first-pass effect, resulting in increased bioavailability. In patients with cirrhosis, the $T_{½\beta}$ of meperidine is approximately doubled. Dose reduction is not necessary with single parenteral doses, but oral doses must be reduced because of the increased bioavailability. Repeated dosing is not advisable in patients with liver failure. Symptoms of normeperidine toxicity mimic the serotonin syndrome. Neurotoxicity caused by meperidine or normeperidine is a nonopioid effect and does not respond to naloxone.

SPECIFIC PROPERTIES OF MEPERIDINE

Meperidine has antimuscarinergic effects, leading to dry mouth and blurred vision. Meperidine produces profound euphoria, and some patients experience arousal rather than sedation. Contrary to common belief, meperidine does cause respiratory depression in the neonate. Its $T_{½\beta}$ in neonates may be shorter than that of morphine, as meperidine metabolism does not depend on hepatic conjugation, which is deficient in the neonate.

The belief that meperidine has spasmolytic effects is now considered a myth: meperidine does increase biliary pressure, although not as profoundly as morphine. Like all other opioids, meperidine also causes constipation.

Single IV doses of 30 to 50 mg meperidine can be effective against postoperative shivering.

SPECIFIC DISADVANTAGES

Research suggests that meperidine is not as effective as morphine in controlling postoperative pain occurring with movement. Meperidine also produces less anxiolysis compared to morphine. Meperidine is not recommended for use in PCA systems, or chronic pain management, because of potential metabolite accumulation and lack of superiority to other opioids without this hazard. Meperidine is a weak serotonin reuptake inhibitor, and coadministration of monoamine oxidase inhibitors (MAO-I) may infrequently precipitate the serotonin syndrome. Fatal cases have been described. The profound euphoria caused by meperidine,

its short half-life, and the absence of pupillary constriction make it a popular drug of abuse.

KEY FACTS: MEPERIDINE

- Meperidine is a phenylpiperidine opioid with additional antimuscarinergic and serotonin reuptake-inhibiting effects.
- Meperidine may produce intense euphoria, but not always sedation or anxiolysis. Its analgesic effect is not superior to that of morphine.
- Meperidine has a shorter T½β in neonates than morphine because its metabolic pathway is already available in the neonate.
- Meperidine should not be coadministered with MAO inhibitors.

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25. ANSWER: B

TOLERANCE

Tolerance, or the decreased effect achieved by repeated drug doses, is a phenomenon characteristic of central nervous system (CNS) depressant drugs, and less so of psychostimulant drugs. The responsible mechanism is complex: a key role is played by the ventral tegmental area (VTA) dopaminergic neurons and its connections to the amygdala, nucleus accumbens, and other parts of the limbic system. Chronic exposure to CNS depressants also induces changes in NMDA receptor sensitivity, both at the spinal and the supraspinal level. These changes contribute to tolerance, but also to psychological effects such as craving and drug-seeking behavior.

With opioid use, tolerance develops rapidly and affects analgesia, sedation, and most other opioid effects. Tolerance is not built up against miosis and constipation, and chronic opioid users will continuously experience these effects. Tolerance also makes the endogenous opioid system less effective, resulting in a lower pain threshold or even hyperalgesia. Cross-tolerance occurs between opioids acting at the same receptors. Still, patients' responses to different opioids may vary considerably.

PHYSICAL DEPENDENCE

Abrupt discontinuation, or rapid antagonism, of opioid therapy may precipitate a physical abstinence syndrome characterized by fever, sweating, piloerection, nausea, diarrhea, and insomnia. This may be accompanied by weight loss, shivering, aggressive behavior, or muscle cramps. Simply put, these are all opposites of usual opioid effects. Withdrawal symptoms usually subside within 8 to 10 days, but aggression and irritability may persist for weeks. Treatment of withdrawal is discussed elsewhere (Question 26).

PSYCHOLOGICAL DEPENDENCE

Also called addiction, this phenomenon is as complex as opioid analgesia itself. It is characterized by strong memories of the effects (especially euphoria), called "addiction memory." Other effects are craving and drug seeking. Research data show that addiction and drug-seeking behavior are rare when opioids are used for appropriate indications. Detoxification should be attempted, as addicted persons may sustain great harm to themselves and families to satisfy their addiction. Detoxification should aim to switch patients to long-acting opioids (such as buprenorphine or methadone), treating adverse effects and withdrawal symptoms. Clonidine and lofexine may also be of value, but results with long-acting opioids have been proven superior. Inadequate substitution will induce withdrawal symptoms, which promotes craving and drug seeking, leading to detoxification failure.

KEY FACTS: OPIOID TOLERANCE

- Tolerance means a decreased response to a repeat dose of the same drug.
- Tolerance develops to most opioid effects, but not to constipation and miosis.
- Chronic exposure to opioids reduces the pain threshold.
- Abrupt discontinuation of opioids in chronic users precipitates withdrawal, characterized by fever, sweating, nausea, diarrhea, insomnia, and aggression.
- Addiction is characterized by craving and drug-seeking behavior. Strong memories of pleasant effects (euphoria) of opioids play a central role.

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26. ANSWER: D

Substance abuse, addiction, and dependence all refer to a cluster of "mental and behavioral disorders due to psychoactive substance abuse" (ICD-10: F10–19). Many of our patients are addicted to alcohol, benzodiazepines, opioids, barbiturates, psychostimulants, or some perilous mix of these. Patients addicted to one substance have a sevenfold increased risk of adding a second substance. Some considerations for perioperative management of the substance-dependent patient are discussed below.

TOLERANCE

Tolerance and physical dependence develop mostly in patients using psychodepressant drugs, as opposed to psychostimulant drugs. Tolerance is built up to both desired and adverse effects, such as respiratory depression. Alcohol-dependent patients will show cross-tolerance to barbiturates and benzodiazepines, but not to opioids. However, chronic alcohol consumption induces changes in NMDA-receptor regulation and subsequently lowers the pain threshold and increases the opioid requirement.

WITHDRAWAL

Chronic substance abuse is associated with hyperalgesia and poor ability to cope with the psychological and physical stress encountered perioperatively. If adequate substitution therapy is withheld, physical withdrawal symptoms and resultant high amounts of stress may even precipitate delirium. Withdrawal induces craving and drug-seeking behavior. This is dangerous for the patient, but also for hospital staff and other patients, and interferes with the patient's healing and recovery.

PREOPERATIVE CONSIDERATIONS: WITHDRAWAL THERAPY

When substance dependence is detected preoperatively, consider consulting specialized colleagues. For alcohol, benzodiazepine, or barbiturate dependency, long-acting benzodiazepine substitution is used. Opioid-dependent patients are treated with buprenorphine or methadone. To both therapies, clonidine or naltrexone can be added. The long-acting nonselective opioid antagonist naltrexone will abolish opioid analgesia and should therefore be discontinued ±48 hours before surgery.

PREOPERATIVE CONSIDERATIONS: ALCOHOL WITHDRAWAL

Alcohol withdrawal appears soon after the last drink (12 to 48 hours). Symptoms include seizures, tremulousness, sweating, nausea and vomiting, anxiety, and agitation, often followed by an altered mental state known as "delirium tremens." The profound autonomic hyperactivity associated with this condition can be lethal. Prevention is key: screening for alcoholism should be part of the routine preoperative evaluation. Substitution therapy for alcohol consists of diazepam (2.5 to 10 mg qid) or lorazepam (0.5 to 2 mg qid). Alternatively, allowing the patient small amounts of alcohol is also effective. This is contraindicated in patients with congestive heart failure or infections. Should prevention fail, and withdrawal or delirium occur, consider intensive care unit admission. Titrate diazepam or lorazepam to effect, and add clonidine (for autonomic instability) or haloperidol (for hallucinations). Alcohol-dependent patients are almost invariably thiamine-deficient. Thiamine substitution (IV bolus of 100 mg) may rapidly improve mental status and alcohol-induced cardiomyopathy.

PREOPERATIVE CONSIDERATIONS: COMORBIDITY

Substance abuse is seldom part of a healthy lifestyle. Common accompanying comorbidities are listed in Table 17.10. Beyond screening and treatment of somatic comorbidity, psychiatric support can be of great value, especially for patients with preexisting psychiatric illness.

ANESTHETIC MANAGEMENT OF THE SUBSTANCE-DEPENDENT PATIENT

Regional anesthesia combined with nonopioid analgesia is the preferred strategy. When general anesthesia is required, consider adding a neuraxial or regional block. Intraoperatively, high drug doses may be required, and these should not be withheld for fear of reinforcement of "bad habits," as anesthetized patients do not experience reward. Clonidine and ketamine can be used to ameliorate autonomic dysfunction and reduce the opioid requirement. Ketamine may also prevent hyperalgesia. Flumazenil, naloxone, and remifentanil should be avoided, as they may induce acute, severe withdrawal and hyperalgesia. Avoid succinylcholine, as it may cause rhabdomyolysis. Intraoperative tachycardia, hypertension, and sweating in substance-dependent patients may indicate withdrawal syndrome: consider giving clonidine.

Table 17.10 COMMON COMORBIDITIES OF THE SUBSTANCE-DEPENDENT PATIENT

ORGAN SYSTEM	COMORBIDITY
Heart	Cardiomyopathy, valve dysfunction, endocarditis, coronary disease, arrhythmia Cocaine: myocardial ischemia/infarction
Blood vessels	Thrombophlebitis, vascular sclerosis (difficult to cannulate!), septic emboli, peripheral artery disease, hypertension
Lungs	Chronic obstructive pulmonary disease, infection Opioids: embolism due to foreign body injection Cocaine: pneumothorax
Nervous system	Polyneuropathy, encephalopathy, myelitis, Parkinson's disease, Wernicke-Korsakoff disease Cocaine: intracerebral hematoma
Liver	Hepatitis, cirrhosis, coagulopathy Cocaine: plasma cholinesterase deficiency
Kidneys	Nephropathy, glomerulonephritis
Pancreas	Chronic recurrent pancreatitis
Bone marrow	Alcohol: anemia Cocaine: thrombocytopathy
Muscle	Myopathy Opioids, cocaine: rhabdomyolysis
Spine	Osteomyelitis
Immune system	Infection, abcess, endocarditis, pneumonia, tuberculosis, HIV, hepatitis
Digestive tract	Chronic malnourishment, constipation
Skin	Scarring, burns
Genitals	Sexually transmitted disease
Mind	A broad spectrum of psychiatric illness. Commonly depression, psychosis, delirium.

SOURCE: Jage J, Heid F. Anästhesie und Analgesie bei Suchtpatienten. Grundlagen zur Erstellung einer "Standard Operating Procedure." *Der Anaesthesist*. 2006;55:611–628.

Substance-dependent patients in our care need support rather than moral judgment. Withholding treatment for withdrawal symptoms for the "pedagogical value" of it is not only ethically incorrect but also highly counterproductive.

KEY FACTS: SUBSTANCE ABUSE: PERIOPERATIVE MANAGEMENT

- Many patients are addicted to substances, and rarely to only one.
- Substance abuse is often accompanied by comorbidities.
- Cross-tolerance develops between alcohol and benzodiazepines, but not between alcohol and opioids.
- Chronic substance abusers suffer from hyperalgesia and poor coping ability.
- Remifentanil, flumazenil, and naloxone should be avoided.
- Clonidine and ketamine can be used to spare opioids, ameliorate autonomic instability, and prevent hyperalgesia.

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27. ANSWER: E

Spasm of the sphincter of Oddi (through which bile and pancreatic juice pass into the duodenum) is an adverse effect of opioid administration. Sphincter spasm interferes with cholangiography and may produce images indistinguishable from those produced by an impacted stone, also known as pseudocalculus sign. This potentially leads to unnecessary surgical intervention on the biliary tree. Also, the spasm can be problematic for patients with pancreatic disease. None of the pure μ opioids lacks spasmogenic effect on the sphincter of Oddi. Apart from opioids, bile duct instrumentation, surgical manipulation, and the administration of cholinergic drugs may also cause spasm.

INCIDENCE

Studies about biliary tract surgery with fentanyl-supported anesthesia report a spasm of the sphincter of Oddi attributable to fentanyl in ±3% of patients.

TREATMENT

Sphincter of Oddi spasm has been successfully treated with IV naloxone, but this potentially reverses analgesia. Other studies report success with IV glucagon (2 mg IV).

PREVENTION

Biliary pressure increases significantly after the administration of morphine, the fentanyl congeners, and meperidine.

Pentazocine seems to cause a smaller pressure increase. The partial opioid agonists tramadol and buprenorphine do not seem to affect the sphincter of Oddi. Meperidine should not be considered the ideal drug for pancreatitis pain, as its short duration of action and worrisome adverse effect profile do not outweigh the small reduction in risk of sphincter spasm when compared to the other μ agonists. Tramadol and buprenorphine may be more appropriate. It must be stressed that sphincter spasm is not very common, and can also be reliably reversed with glucagon or naloxone.

KEY FACTS: OPIOIDS AND BILIARY SPHINCTER SPASM

- All opioids may induce spasm of the sphincter of Oddi, which potentially produces the cholangiographic image of an impacted stone.
- Spasm can also be induced by duct manipulation or by cholinergic drugs.
- Actual spasm solely attributable to opioids seems to be rare, but can be treated with naloxone or glucagon.
- Tramadol and buprenorphine seem the least likely to induce sphincter spasm.

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28. ANSWER: A

LIVER DISEASE

Most opioids are metabolized by the liver. The metabolites are excreted in the bile or the urine. An exception is remifentanil, which is hydrolyzed by aspecific esterases. Liver failure generally leads to a prolonged elimination half-life (T½β), increased oral bioavailability, and reduced metabolite formation of opioids. When plasma protein levels fall in severe liver failure, increased free fractions of agents with high protein binding (sufentanil, alfentanil, buprenorphine) will result. Opioids administered orally (buprenorphine, fentanyl, morphine, meperidine) may undergo substantially less first-pass effect in patients with liver failure, resulting in higher oral bioavailability.

In general, alfentanil, meperidine, and tramadol are best avoided in patients with liver failure because their kinetics become unreliable and the duration of their effects may be unpredictably prolonged.

KIDNEY DISEASE

Kidney failure mostly affects opioids with active metabolites that depend on renal excretion for elimination (morphine, meperidine). The metabolite accumulation may lead to prolonged opioid effect, but also nonopioid CNS toxicity.

In general, meperidine is best avoided in patients with kidney disease because the accumulation of its metabolite normeperidine may induce neuroexcitatory adverse effects, even within the clinical dosing range.

The dose of morphine should be reduced. Not morphine itself, but its glucuronide metabolites accumulate in patients with kidney failure. Morphine-6-glucuronide has potent opioid (analgesic) activity, Morphine-3-glucuronide is possibly an opioid antagonist and may be neurotoxic.

Remember that with single bolus doses of most opioids, redistribution accounts for the duration of action, not metabolism. This is not true for remifentanil and alfentanil: their duration of action depends largely on the rate of metabolism. With repeated dosing or continuous infusion, metabolism of the agent determines the duration of action and its context-sensitive half-time.

Opioids should be titrated to effect, especially in patients with organ disease. Careful monitoring is necessary to detect changes in opioid pharmacokinetics due to organ disease.

KEY FACTS: OPIOIDS AND ORGAN FAILURE

- Liver failure may result in increased T½β, increased bioavailability, increased free fractions, and reduced metabolite formation of opioids.
- The kinetics of alfentanil, meperidine, and tramadol are unpredictably prolonged in patients with severe liver failure.
- The metabolites of meperidine and morphine may accumulate in patients with kidney failure.
- The kinetics of remifentanil is largely unaffected by liver or kidney disease.

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29. ANSWER: A

30. ANSWER: B

PATHOPHYSIOLOGY

The pathophysiology of postoperative nausea and vomiting (PONV) is only partly understood. Involved centers in the brain include the area postrema, nucleus vestibularis, nucleus of tractus solitarius, and the vomiting center. Receptors located in these areas are pharmacologic targets in PONV therapy. The most important receptors (and their ligands) are the D_2 (dopamine), 5-HT_3 (serotonin, 5-hydroxytriptamine), H_1 (histamine), muscarinic (acetylcholine), and NK_1 (neurokinin, substance P) receptors. These are all found outside the brain too, where they could influence PONV pathophysiology as well.

IMPORTANCE AND RISK

PONV tops the list of postoperative outcomes patients are most eager to avoid, and patients' willingness to pay to avoid it is as much as $75 to $100. In patient-centered anesthesia, routine assessment of PONV risk and adequate prophylaxis and treatment are key. Easy tools, such as the simplified Apfel score, can reliably predict PONV risk. Risk factors for PONV are listed in Table 17.11. The risk of vomiting in children can be predicted with Table 17.12. Patients undergoing regional anesthesia have a lower risk of PONV than those receiving general anesthesia. The baseline risk of PONV in patients undergoing general anesthesia is ±10%, whereas the risk of those with four or more risk factors on the Apfel score is around 80%.

Table 17.11 **RISK FACTORS FOR POSTOPERATIVE NAUSEA AND VOMITING (PONV) IN ADULTS (AMERICAN SOCIETY OF ANESTHESIOLOGISTS)**

Female sex*
Nonsmoking status*
History of PONV or motion sickness*
Postoperative opioids required*
Inhalation anesthesia
Nitrous oxide
Duration of anesthesia
Young age
High-dose neostigmine antagonization

* = factors in the simplified Apfel Score

EFFECTIVE PHARMACOLOGIC INTERVENTIONS

DEXAMETHASONE

Dexamethasone is effective when given early, either just before or with induction of anesthesia. 4 mg of dexamethasone is equally effective compared to 4 mg of ondansetron or 1.25 mg of droperidol. Adverse effects are not likely after single doses.

5-HT_3 ANTAGONISTS

Ondansetron, granisetron, and dolasetron are equally effective in PONV prophylaxis and treatment. Palonosetron seems to have the longest-lasting effect. These agents are all very safe, and headache (3%) and constipation (4%) are their most common adverse effects. The risk of QT-interval prolongation is present (not in palonosetron) but small.

DROPERIDOL AND HALOPERIDOL

Both are effective in very low doses (droperidol 0.625 mg IV), but their potential adverse effects and contraindications limit their range of use. QT-interval prolongation has been reported within clinical dose ranges but is very rare and is probably not more likely to occur than with the 5-HT_3 antagonists. These agents are not very suitable for use in children.

SCOPOLAMINE

Transdermal scopolamine can be useful for patients who cannot take tablets. The duration of action of one patch

Table 17.12 **RISK FACTORS FOR POSTOPERATIVE NAUSEA AND VOMITING (PONV) IN CHILDREN**

RISK FACTOR	POINTS
Duration of procedure > 30 minutes	1
Age > 3 years old	1
Strabismus surgery	1
History of PONV/ 1st-degree family member with history of PONV	1
Risk prognosis of postoperative vomiting	
0 points	9%
1 points	10%
2 points	30%
3 points	55%
4 points	70%

is up to 3 days. The onset of antiemetic effect after applying a patch is too slow for the treatment of acute PONV, however. The risk of central anticholinergic adverse effects limits its use, especially in the ambulatory setting (working, driving). As with all patches, plasma concentrations decrease slowly after removal of the patch, due to ongoing absorption from the skin. Physostigmine can be used to treat adverse effects if needed. The patches cannot be used for children.

TOTAL INTRAVENOUS ANESTHESIA

Total intravenous anesthesia (TIVA) results in less PONV than balanced anesthesia, especially when nitrous oxide is avoided. Using propofol for induction or maintenance of anesthesia, combined with not using nitrous oxide, reduces the PONV risk by ±30%.

CHOICE OF PROPHYLAXIS STRATEGY

The decision to use antiemetic interventions should be based on a patient's individual risk and preference (Table 17.13). Each of the aforementioned interventions reduces the risk of PONV by ±30%. Patients in the lowest-risk segment (10%) are least likely to benefit from prophylaxis: a single intervention will reduce their risk to 7%. It follows that only 3 out of 100 patients (3%) will benefit from prophylaxis, and thus ±38 patients must be treated for 1 patient to benefit (number needed to treat [NNT] = 38). In this patient group, a "wait and see" approach is acceptable. For patients with two risk factors (risk ±40%), prophylaxis with dexamethasone is recommended. Patients with three or four risk factors require combinations of three or four interventions. In this group, choosing propofol TIVA and dexamethasone to be part of the combination seems wise because these interventions are less useful postoperatively. Thus, rescue options are reserved to treat patients who will still develop PONV despite the combined strategy (±20%). The effectivity of metoclopramide for this indication is debated.

POSTOPERATIVE PONV THERAPY

Despite multimodal strategies, some patients will still experience PONV. They need early intervention to prevent the complications and discomfort associated with PONV. Transdermal scopolamine, and dexamethasone are too slow in this situation. The 5-HT_3 antagonists have the most extensive evidence base. The dose required is the same as for prophylaxis. If PONV occurs during the therapeutic window of one agent, an agent from a different class should be used. There is no evidence that oxygen is effective in the treatment of PONV.

KEY FACTS: ANTIEMETICS

- Each antiemetic intervention reduces the PONV risk by ±30%.
- Patients with multiple risk factors benefit from multiple antiemetic interventions.
- If PONV occurs despite adequate prophylaxis, 5-HT_3 inhibitors seem most suitable.

Table 17.13 **RECOMMENDED DOSES OF DRUGS USED FOR PROPHYLAXIS AND TREATMENT OF POSTOPERATIVE NAUSEA AND VOMITING (PONV)**

CLASS	AGENT	ADULT DOSE	PEDIATRIC DOSE*	REMARKS
Corticosteroids	Dexamethasone	4 mg	0.15 mg/kg	Use for prophylaxis, not treatment/
5-HT_3 antagonist	Ondansetron	4 mg	0.1 mg/kg	Longest experience of its class
	Granisetron	1 mg	20 μg/kg	Only used for patients > 4 yrs old
	Dolasetron	12.5 mg	0.35 μg/kg	Prodrug, takes ±30 min to convert
	Palonosetron	0.075 mg	-	No data on pediatric use available
NK-1 antagonists	(Fos)aprepitant	40 mg (PO)	-	Prodrug fosaprepitant is used IV.
Butyrophenones	Droperidol	0.625–1.25 mg	50 μg/kg	Consider adverse effects, interactions. and contraindications/
	Haloperidol	1–2 mg	-	Not used in children for this indication
Anticholinergics	Scopolamine	1 mg/24 h (transdermal)	-	Should be applied before symptoms occur

* Pediatric doses not to exceed the adult dose shown.

SOURCE: Apfel CC, Greim CA, Haubitz I, Goepfert C, Usadel J, Sefrin P, Roewer N. A risk score to predict the probability of postoperative vomiting in adults. *Acta Anaesthesiol Scand.* 1998;42(5):495–501.

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Table 17.14 PHARMACOLOGY OF CURRENTLY AVAILABLE 5-HT_3 RECEPTOR ANTAGONISTS

AGENT	ADULT IV DOSE	PEDIATRIC DOSE (MG/KG)*	T½β
Ondansetron	4–8 mg	IV 0.05–0.15 mg/kg PO 0.15 mg/kg	3–4 hours
Granisetron	1–3 mg	IV 20–40 μg/kg	9 hours
Dolasetron	12.5 mg	IV 0.35 mg/kg PO 1.2 mg/kg	8 hours
Palonosetron	0.075 mg	-	40 hours

T½β: elimination half-life.

31. ANSWER: C

The 5-hydroxytriptamine-3 receptor antagonists (5-HT_3RAs) are used to prevent and treat PONV. Their effectiveness has been extensively studied. They selectively bind to 5-HT_3 receptors in the CNS, located in the area postrema (or chemoreceptor trigger zone), nucleus of tractus solitarius, cerebral cortex and hippocampus, and peripherally in the gut mucosa, nerve endings, and primary afferent nerve fibers. 5-HT_3 receptors are ligand-gated cation-selective ion channels, and binding of 5-HT_3 results in cell depolarization. Clinically, binding is associated with emesis, delayed gastric emptying, and increased gut transit time.

Currently available 5-HT_3RAs available in the United States are ondansetron, granisetron, dolasetron, and palonosetron. They differ mainly in their half-lives. Dolasetron is a prodrug, which converts to the active hydrodolasetron in ±30 minutes. Palonosetron receptor binding is strong and probably more complex than that of the other drugs in this class. Its use in children has not yet been evaluated. All 5-HT_3RAs are metabolized by the liver and partly excreted in the bile and urine.

The 5-HT_3RAs are safe for most patients and mostly cause mild adverse effects such as dizziness, headache (3%), and constipation (4%). A minor increase in the QT interval is possible, which may cause arrhythmia in susceptible patients. Palonosetron does not appear to increase the QT interval. Patients with increased cytochrome P450, subtype 2D6, have been described to be "rapid metabolizers" and are not likely to benefit from 5-HT_3RAs. Pharmacokinetic properties of the 5-HT_3RAs are shown in Table 17.14.

KEY FACTS: 5-HT_3 RECEPTOR ANTAGONISTS

- 5-HT_3 receptor antagonists (5-HT_3RAs) are generally safe, well tolerated, highly effective interventions for PONV.
- The 5-HT_3 receptor antagonists differ mostly in their duration of action. Ondansetron has the shortest and palonosetron the longest T½β.
- A rapid metabolizing genetic variation exists in humans, which significantly reduces 5-HT_3RA effectiveness.

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32. ANSWER: A

Droperidol, also known as dehydrobenzperidol, is a dopamine antagonist neuroleptic agent with antipsychotic and antiemetic action. Droperidol and many other agents of its class are capable of reducing PONV very effectively and at low doses. However, its use is limited by its risk of adverse effects at therapeutic doses.

Droperidol is used to prevent PONV in both adults and children and is given at the time of anesthesia induction or before the end of the procedure. Usual doses are 0.625 to 1.25 mg IV for adults and 0.075 mg/kg for children. Droperidol is not effective in relieving vomiting induced by labyrinthine stimulation.

The duration of action of droperidol does not correspond well to its elimination half-life (±100 min), probably because its dissociation from the dopamine receptor site in the brain is slow. Droperidol is eliminated by the liver, so its clearance is mainly limited by liver blood flow.

Droperidol may cause sedation, potentially delaying awakening and recovery from anesthesia. Other adverse effects are extrapyramidal symptoms, such as restlessness, anxiety, and muscle spasms such as trismus and torticollis. Pseudoparkinsonism (rigidity, tremor) can also be seen. This is no surprise, as many symptoms of Parkinson's disease are caused by loss of dopaminergic neurons in the substantia nigra. Blocking of the dopamine receptors has a similar

effect. Therefore, droperidol is relatively contraindicated in patients with Parkinson's disease. Droperidol also has a peripheral α-blocking effect, which may result in hypotension with higher doses.

The FDA has issued a ***black box warning*** due to the ***QT-interval prolongation*** effects of droperidol. However, QT prolongation is not commonly seen with low doses in short duration of therapy. As with all the neuroleptics, droperidol may induce dysphoria, tardive dyskinesia, or, rarely, the malignant neuroleptic syndrome.

For children, the use of antiemetics with less severe potential side effects may be more prudent.

KEY FACTS: DROPERIDOL

- Droperidol is a highly effective antiemetic drug, but its use is limited by its risk of adverse effects, such as sedation, dysphoria, and extrapyramidal symptoms.
- Droperidol has a clinical duration of action that exceeds its T½β.
- Droperidol is relatively contraindicated in patients with Parkinson's disease because their symptoms may worsen.
- There is a black box warning by the FDA due to the QT-prolonging effect of droperidol.

ADDITIONAL READING

Evers AS, Maze M. *Anesthetic Pharmacology: Physiologic Principles and Clinical Practice: A Companion to Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2004.

33. ANSWER: C

The neurokinin receptors are a group of G-protein–coupled receptors. Their ligands are substance P and the neurokinins A and B. They are found in large numbers in the centers involved in PONV, such as the area postrema and the nucleus of tractus solitarius. Binding of substance P to neurokinin-1 (NK-1) receptors is associated with nausea and vomiting. This pathway is thus part of the complex, multireceptor etiology of PONV. Whereas 5-hydroxytriptamine (5-HT) is more likely to be involved in acute PONV, substance P probably plays a bigger role in delayed PONV.

Recently, the first ***NK-1 antagonist, aprepitant,*** has been approved for prevention and treatment of PONV. The oral tablet has 60% to 65% bioavailability and a serum half-life of ±4 hours. The prodrug fosaprepitant is used for IV administration and is transformed into aprepitant in ±30 minutes. Despite the rather short half-life, aprepitant's clinical duration of action may be as long as 24 to 48 hours. Clinical studies show that oral aprepitant achieves slightly superior PONV prophylaxis compared to the 5-HT_3 receptor antagonists (5-HT_3RA), and its effect seems to last longer. The adverse effects of aprepitant resemble those of the 5-HT_3RAs: headache and constipation are most commonly seen.

The availability of a new class of safe, effective antiemetics is a major advantage: a safe, effective agent such as aprepitant can now be reserved for patients who fail to respond to PONV prophylaxis and need rescue therapy. When rescue antiemetics are required, switching agents is most effective. Furthermore, aprepitant has added value in antiemetic combination strategies and may contribute to better PONV prophylaxis for very high-risk patients or those failing to respond to single-intervention approaches. In contrast to the 5-HT_3RAs, aprepitant does not affect the QT interval.

A drawback is the metabolism of aprepitant by cytochrome P450, subtype 3A4. Many other drugs share this pathway, and aprepitant administration may interfere with their duration of action. This is of special interest to patients using coumarin derivates and oral contraceptives. For oral PONV prophylaxis, 40 mg of aprepitant is given ±3 hours before anesthesia.

KEY FACTS: NEUROKININ-1 RECEPTOR ANTAGONISTS

- The neurokinin-1 receptor antagonists are a new class of antiemetics, currently represented by (fos)aprepitant.
- Aprepitant's clinical duration of action is 24 to 48 hours, much longer than its T½β of ±4 hours.
- Oral aprepitant is given ±3 hours prior to anesthesia. The IV formulation transforms into the active component within ±30 minutes after administration.
- Aprepitant is a substrate of CYP 3A4.

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34. ANSWER: C

Propofol (di-iso-propylphenol) was first used in 1983. Its mechanism of effect is not entirely clear, but modulation of the gamma-hydroxy-butyric-acid receptor, type A ($GABA_A$) seems responsible for most of its effect. Propofol also seems to affect the glycine receptor.

Propofol is formulated as an aqueous emulsion containing egg phosphatide and soybean oil, with a neutral pH. Formulations with equal concentrations of medium-chain and long-chain triglycerides (MCT/LCT) are also available, and these cause less pain on injection.

In plasma, propofol molecules are bound to plasma proteins. It is highly lipid-soluble due to its un-ionized state (pKa 11.0) and quickly crosses the blood–brain barrier. Propofol has a very large distribution volume (1,000 to 3,940 L) and is cleared at 25 mL/min/kg. The liver rapidly converts propofol to inactive glucuronides, which are excreted by the kidneys. Propofol is probably also metabolized outside the liver. After discontinuation of administration, propofol concentrations in the central compartment (blood) decrease rapidly, resulting in rapid offset of effect: initial half-life is ±2 minutes. Propofol dissolves slowly into fatty tissues, from where it is slowly mobilized, explaining the long terminal elimination half-life ($T\frac{1}{2}\beta$) of 4.8 hours after a single dose.

The time to onset of effect of a bolus dose of propofol differs greatly between patients and depends mostly on age, weight, cardiac output, and liver blood flow. For general anesthesia, the recommended induction dose is 1.5 to 2.5 mg/kg for adults. Children need 2 to 3 mg/kg, infants 4 to 4.5 mg/kg. Propofol should be titrated to effect: 20 to 40 mg should be injected every 10 seconds, or an infusion pump can be used. Anesthesia occurs at blood concentrations of 4 to 6 mg/L. Recovery can be expected when the blood concentration drops below 1 mg/L.

After a single bolus dose, the effect of propofol is rapidly terminated by intercompartmental redistribution. Metabolism speed becomes rate-limiting in terms of the duration of effect when repeated doses are given or a continuous infusion is administered. Propofol's context-sensitive half-time increases slowly over time. This makes propofol highly useful for both short and long procedures.

CARDIOVASCULAR AND RESPIRATORY EFFECTS

As with all general anesthetics (except ketamine), propofol reduces blood pressure and decreases myocardial contractility and systemic vascular resistance. Propofol resets the baroreceptor reflex setpoint, resulting in slower heart rates for a given blood pressure compared to control. Hemodynamic effects are more pronounced in older patients, and dose reduction may be appropriate. Hypovolemic patients may experience hypotension with relative bradycardia.

Propofol does not sensitize the heart to catecholamines and is not generally arrhythmogenic.

Induction doses of propofol are usually followed by apnea periods of 30 to 60 seconds. Propofol reduces the ventilatory response to carbon dioxide and to isocapnic hypoxia. Propofol causes some bronchodilation.

CEREBRAL EFFECTS

Propofol reduces cerebral blood flow (CBF), cerebral metabolic rate for oxygen ($CMRO_2$), and intracranial pressure (ICP) while preserving autoregulation. Propofol has a dose-dependent effect on consciousness. Electroencephalogram changes range from increased β activity (sedation) at low doses to increased δ activity (unconsciousness) and burst suppression at higher doses. Although seizures have been described in susceptible patients, most uncontrolled movements seen after propofol administration are due to spontaneous excitation, caused by subcortical inhibition.

ANTIEMETIC AND ANTIPRURITIC EFFECT

PONV is less likely to occur with propofol use than with volatiles and other general anesthetics. This may be due to antagonist activity at $5\text{-}HT_3$. PONV is effectively treated with subanesthetic doses of 10 to 20 mg IV. This low dose also relieves pruritus caused by neuraxial opioid administration.

FOSPROPOFOL

This newly registered, phosphorylated prodrug of propofol is water-soluble and registered for use in monitored anesthesia care (MAC). Alkaline phosphatases at the endothelial cell surface quickly hydrolyze fospropofol to propofol, formaldehyde, and phosphate. Its use has been studied only in short procedures: bronchoscopies and colonoscopies. The recommended dose to achieve sedation for these procedures is 6.5 mg/kg. Continuous infusion of fospropofol has not yet been studied, but smaller bolus doses may be given to maintain sedation. Most characteristics of fospropofol resemble those of propofol, but fospropofol does not seem to cause pain on injection. Fospropofol also seems to cause less apnea compared to propofol, when doses less than 15 mg/kg are used. A remarkable yet unexplained adverse effect often seen is transient genital and anal pruritus. More studies are required to determine the safety and usefulness of fospropofol. Until then, the FDA requires fospropofol to be administered only by trained anesthesia providers under continuous monitoring in an area where airway and resuscitation equipment is immediately available

KEY FACTS: PROPOFOL

- Modulation of the GABA receptor seems to account for most of the anesthetic effect of propofol.
- Propofol has a fast onset and recovery. It is quickly metabolized, mainly in the liver, leading to a slowly increasing context-sensitive half-time.

- Propofol reduces blood pressure, heart rate, myocardial contractility, systemic vascular resistance, and respiratory drive. The effects are more pronounced in the elderly.
- Propofol also has antiemetic and antipruritic effects at subanesthetic doses.
- A water-soluble prodrug, fospropofol, is now available for use in monitored anesthesia care.

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35. ANSWER: D

PROPOFOL INTERACTIONS

Propofol is mainly metabolized in the liver. However, its clearance rate exceeds liver blood flow, which suggest extrahepatic metabolism. Proposed sites are the lungs and the kidneys.

In the liver, propofol is first hydroxylated, mainly by cytochrome P450 (CYP450) subtypes 2B6 and 2C9. Propofol effectively inhibits many CYP450 subtypes and may thus affect the metabolism of many drugs. Propofol also slows renal clearance by inhibiting specific enzymes as well as by reducing cardiac output. Propofol also decreases hepatic blood flow, affecting the half-life of most drugs that undergo hepatic extraction. At clinical doses, this effect is usually small. Not many evident drug interactions between propofol and other drugs have so far been described.

PROPOFOL SYNERGISM

Combinations of propofol with benzodiazepines, opioids, and other anesthetic drugs (such as dexmedetomidine) result in clinical effects greater than additive effects. Optimal synergism occurs when effect site concentrations peak at the same time. Combining an opioid, a benzodiazepine, and propofol allows dose reductions of all three agents. Propofol does not potentiate the effect of neuromuscular blocking agents.

Synergism is also seen for adverse effects. Other vagotonic drugs, for example opioids, will cause exaggerated hemodynamic effects, which may be a hazard to elderly patients or those with an unstable circulatory system.

PROPOFOL ALLERGY AND INTOLERANCE

Most propofol formulations contain egg phosphatide and soybean oil, and propofol use is contraindicated in patients allergic to these foods. Patients allergic to birch pollen may show cross-sensitivity to soy. Intolerance to propofol is very unlikely: the estimated incidence lies between 1/80,000 and 1/100,000 administrations. Patients with disorders of fat metabolism should not be given the lipid-rich propofol formulation.

PROPOFOL: PAIN ON INJECTION

This is a common adverse effect, with a reported incidence of 30% to 70%. Propofol formulations with MCT/LCT composition are less likely to cause pain on injection. Methods used to reduce pain on injection include admixture of lidocaine to the propofol induction dose, or the infusion of 40 mg of lidocaine with a tourniquet 30 to 120 seconds before administering propofol via the same cannula. However, none of these methods is 100% reliable.

INFECTION RISK OF PROPOFOL

Although formulations with EDTA or bisulphite are available, propofol is not usually formulated with preservatives and supports bacterial growth. Manifold literature reports of infection outbreaks due to contaminated propofol remind us that sterile handling of propofol is essential. Never dispense propofol from multidose vials to different patients. Once drawn up, use propofol immediately on a single patient and discard the remainder. Do not leave uncapped vials to stand at room temperature.

PROPOFOL: PORPHYRIA AND SUSCEPTIBILITY TO MALIGNANT HYPERTHERMIA

Propofol does not trigger malignant hyperthermia. Propofol has been safely used in patients with acute intermittent porphyria.

KEY FACTS: PROPOFOL

- Propofol is a CYP450 substrate but has few significant metabolic interactions.

- Synergistic effects occur between propofol and benzodiazepines, opioids, and other general anesthetics, but not neuromuscular blocking agents.
- Propofol is not suitable for patients with egg or soy intolerance.
- MCT/LCT formulations of propofol seem to cause less pain on injection.
- The propofol formulation is a great bacterial culture medium.

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36. ANSWER: D

The pharmacokinetic properties of propofol make it an excellent agent for continuous infusion for sedation in the intensive care unit (ICU), for procedural sedation, and for maintaining general anesthesia.

TOTAL INTRAVENOUS ANESTHESIA (TIVA) WITH PROPOFOL AND OPIOIDS

TIVA is defined as induction and maintenance of general anesthesia with solely intravenous agents. Benefits of TIVA with propofol combined with opioids compared to balanced anesthesia with volatiles are as follows:

- **Not likely to increase intracranial pressure (ICP)**
- **Reduced intraocular pressure (IOP)**
- **No influence on hypoxic vasoconstriction during single-lung ventilation**
- **Reduced incidence of PONV**
- **Safe for patients susceptible to malignant hyperthermia**
- **Safe for most patients with porphyria**
- **Ideal in situations with open ventilation, such as jet ventilation**
- **Useful for ICU patients on complex ventilator settings (no need to switch to the anesthetic machine during surgery)**
- **No potentially toxic gases in the operating room, safer for pregnant staff and patients**
- **Easier to transport and use outside the operating room complex**
- **Useful in the out-of-hospital setting**

Target-controlled infusion (TCI) strategies are discussed elsewhere (Question 42).

CONTINUOUS PROPOFOL INFUSION IN THE ICU PATIENT

Propofol is widely used in the ICU setting because of its rapid kinetics, even after long-term use. However, accumulation must be taken into account when planning sedation with propofol. Propofol's duration of action is unaffected by liver or kidney disease. The formulation provides 1.1 kcal/mL, and nutritional regimens must be modified accordingly to prevent overfeeding, hypertriglyceridemia, and associated pancreatitis.

PROPOFOL-RELATED INFUSION SYNDROME (PRIS)

This complicated syndrome is characterized by acute, refractory bradycardia together with metabolic acidosis, rhabdomyolysis, hyperlipidemia, enlarged or fatty liver, heart failure, and circulatory collapse, associated with propofol infusion. Right bundle branch block, with convex-curved ST elevation in V1 to V3 on the electrocardiogram, may herald the syndrome. PRIS is seen mostly with high doses of propofol (>4 mg/kg/h) for more than 48 hours. Risk factors include young age, severe critical illness, catecholamine or glucocorticoid administration, low carbohydrate intake, and subclinical mitochondrial disease. The etiology of PRIS possibly involves an effect of propofol (or a component of its formulation) on the mitochondrial respiratory chain or fatty acid metabolism. Once PRIS is suspected, discontinue propofol infusion immediately. No standard treatment is available, but case reports suggest hemodynamic support and hemodialysis.

KEY FACTS: PROPOFOL FOR TIVA

- Propofol–opioid TIVA does not increase intracranial or intraocular pressure, involves no gases, and is generally safe for those susceptible to malignant hyperthermia or porphyria.
- Liver disease and kidney disease have minimal effect on propofol's duration of action.
- Despite propofol's rapid kinetics, some accumulation will occur during long-term use. Its caloric value of 1.1 kcal/mL is also to be taken into account.
- The extremely rare but disastrous propofol-related infusion syndrome occurs mostly in young, critically ill patients or those with mitochondrial disease.
- Long-term infusion of propofol should not exceed 4 mg/kg/h.

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37. ANSWER: B

38. ANSWER: C

The ***benzodiazepines*** most frequently used in anesthesia are midazolam, diazepam, and lorazepam. These agents are lipid-soluble (midazolam> diazepam > lorazepam) and have a high degree of plasma protein binding (>95%). Midazolam is two times, and lorazepam five to six times, more potent than diazepam. Benzodiazepines are selective for the specific benzodiazepine domain in the gamma-amino-butyric-acid receptor type A ($GABA_A$), and binding increases the receptor's affinity to GABA.

Intravenous benzodiazepines induce amnesia, sedation, hypnosis, and muscle relaxation. Benzodiazepines are effective anticonvulsants. Amnesia typically outlasts the other effects, and anterograde amnesia may persist for over 24 hours after discontinuation of administration. Oral forms of the agents mentioned can be used for anesthetic premedication. Midazolam and diazepam are also used to treat epilepsy in children and adults. Diazepam can be administered rectally (also by nonmedically trained persons) for this indication, as well as intravenously. The IV formulation of midazolam is also well absorbed from the nasal and orobuccal mucosa. Both tolerance and dependence to benzodiazepines occur with long-term use.

CARDIOVASCULAR AND RESPIRATORY EFFECTS

Benzodiazepines have minimal cardiovascular effects and do not successfully blunt the stress of endotracheal intubation. Usually, opioids are coadministered to achieve adequate intubation conditions. Benzodiazepines reduce hypoxic drive. This poses a risk to the elderly and patients with chronic obstructive pulmonary disease, who depend on hypoxic drive for control of respiration. Respiratory depression is amplified by coadministration of other anesthetics and opioids. Benzodiazepines do not commonly cause respiratory depression when administered alone to healthy persons.

CEREBRAL EFFECTS

Benzodiazepines suppress cerebral activity in a dose-dependent matter, but sedation and sleep are mediated by different $GABA_A$ receptor subtypes. Benzodiazepines suppress rapid eye movement (REM) sleep. They also reduce the cerebral metabolic rate of oxygen ($CMRO_2$) and cerebral blood flow (CBF). The cerebral effects of benzodiazepines are synergistic with the other general anesthetics. In children and elderly patients, benzodiazepines (particularly in small doses) can produce a paradoxical reaction, with agitation and behavioral disturbance. This effect can last up to several days after administration.

ANTAGONIST: FLUMAZENIL

Flumazenil competitively antagonizes all benzodiazepine effects. It has rapid onset (1 to 2 minutes) and its effect lasts ±45 to 90 minutes. The dose is titrated to effect in steps of 0.2 mg, with a maximum of 3 mg per hour. Use a continuous infusion (0.1 to 0.4 mg/hr) when the expected benzodiazepine effect outlasts that of flumazenil. Flumazenil may elicit seizures in patients on chronic benzodiazepines (e.g., for seizure control) and in epilepsy patients in general. When 5 mg of flumazenil has been administered without response, one is probably not looking at a benzodiazepine effect. Beware of patients with multiple concurrent intoxications: antagonizing the benzodiazepine effect may result in emergence of effects of psychostimulants, and possibly lead to seizures or altered mental status.

BENZODIAZEPINE INTERACTION WITH OPIOIDS

Benzodiazepines reduce the opioid requirement on induction of general anesthesia. They also potentiate opioid-induced respiratory depression. Interestingly, benzodiazepines inhibit the analgesic effect of opioids.

KEY FACTS: BENZODIAZEPINES

- IV benzodiazepines induce anterograde amnesia and potentially also retrograde amnesia.
- Benzodiazepines induce sedation, hypnosis, and muscle relaxation.

- Amnesia is the longest-lasting effect.
- The risk of respiratory depression is higher in the elderly, in those with chronic obstructive pulmonary disease, and during coadministration of opioids and general anesthetics.
- Benzodiazepines may produce paradoxical effects in children.
- Flumazenil is titrated in steps of 0.2 mg, with a maximum of 3 mg/hr.
- Benzodiazepines inhibit the analgesic effects of opioids.

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39. ANSWER: C

STRUCTURE AND FORMULATION OF MIDAZOLAM

Midazolam has a unique chemical structure. The molecule's central ring structure is open at pH values below 4, and it is water-soluble. At higher pH (e.g., in blood), the ring closes to form the active, lipid-soluble agent, which rapidly crosses the blood–brain barrier. Midazolam is thus formulated in an aqueous solution that does not contain the irritant emulgators and additives present in diazepam or lorazepam formulations.

Table 17.15 MIDAZOLAM DOSES FOR PROCEDURAL SEDATION

AGE	MIDAZOLAM IV DOSE	MAX. MIDAZOLAM IV DOSE
Neonates, infants	Concerns raised about effectiveness and safety	
>6 months–5 years	0.05–0.1 mg/kg	6 mg
6–12 years	0.025–0.05 mg/kg	10 mg
12–16 years	0.5–2 mg	10 mg
>16 years (adults)	0.5–5 mg	
The elderly	Reduce adult dose by 25–50%.	

PHARMACOKINETICS AND PHARMACODYNAMICS

Midazolam undergoes hepatic oxidative hydroxylation to the active 1- and 4-hydroxymidazolam (1/4-HML) and inactive metabolites, which are excreted by the kidneys. The liver further conjugates 1-HML to 1-HML glucuronide, which has potent benzodiazepine properties, and may accumulate in patients with kidney failure. Its effect is synergistic with that of the parent compound.

The elimination half-life ($T_{½\beta}$) of midazolam is 1.5 to 3.5 hours. Elimination is delayed in the elderly (due to reduced hepatic metabolic capacity) and the obese (due to larger volume of distribution). Clearance of midazolam is slower in patients with liver disease, and active metabolites may accumulate in patients with kidney disease.

The onset of sedation and hypnosis after a single intravenous bolus dose of 1 to 2 mg of midazolam is longer than 1 minute, which is slower than the typical onset of thiopental or propofol. The sedative effect of a single intravenous dose lasts 15 to 80 minutes. Redistribution and rapid clearance from the central compartment account for the short duration of action of a single bolus. Repeated administration and continuous infusion are associated with increasing duration of action, due to the slow mobilization of midazolam accumulated in fatty tissues. Midazolam has a more favorable context-sensitive half-time profile than diazepam and lorazepam, making it useful in the sedation of patients in the ICU. The short duration of action of single midazolam doses makes it useful in procedural sedation for adults and children.

INTERACTIONS

Midazolam is a substrate of cytochrome P450 (CYP450). Many drugs inhibit or induce the CYP450 system, and

Table 17.16 ADULT DOSES OF BENZODIAZEPINES USED IN ANESTHESIA

AGENT	RELATIVE POTENCY (DIAZEPAM = 1)	IV SEDATION	GENERAL ANESTHESIA INDUCTION	PREMEDICATION FOR GENERAL ANESTHESIA
Diazepam	1	10 mg	0.3–0.5 mg/kg	IV 2–10 mg PO 20–30 mg
Midazolam	2	0.5–5 mg	0.2–0.35 mg/kg	IV 0.5–5 mg PO 5–7.5 mg
Lorazepam	5–6	1–4 mg	0.1 mg/kg*	IV 0.5–2mg**

* Not recommended for this indication.

** 20 to 30 min prior to surgery.

Reduce doses by 25% to 50% in the elderly, titrate to effect, and carefully monitor cardiovascular and respiratory function.

so influence the T½β of midazolam. Midazolam itself is a weak inhibitor of CYP3A4.

KEY FACTS: MIDAZOLAM

- Midazolam is water-soluble at low pH but becomes lipid-soluble at blood pH.
- The hepatic midazolam metabolite 1-hydroxymidazolam glucuronide has potent benzodiazepine properties and may accumulate in patients with kidney failure.
- The sedative effect of a single midazolam dose may last up to 80 minutes.
- Midazolam is a CYP450 substrate and also a weak CYP450 inhibitor.

ADDITIONAL READINGS

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Ng E, Taddio A, Ohlsson A. Intravenous midazolam infusion for sedation of infants in the neonatal intensive care unit. *Cochrane Database Systematic Rev*. 2003. Updated 2010.

Table 17.17 **COMPARISON OF PROPERTIES BETWEEN MIDAZOLAM AND CLONIDINE PREMEDICATION FOR ANESTHESIA**

Desirable effects likely to be achieved with:	Midazolam	Clonidine
Sedation and anxiolysis	✓	✓
Amnesia (may also be undesirable)	✓	X
Analgesia	X	✓
Synergism with general anesthetics	✓	✓
Reduce postop nausea and vomiting	X	✓
Oral and rectal administration	✓	✓
Fast onset	✓	X
Long duration of action	X	✓
Relatively low cost	✓	✓
Adverse effects associated with:	**Midazolam**	**Clonidine**
Respiratory depression (opioid potentiation)	✓	X
Hypotension, bradycardia	X	✓
Behavioral disturbance	✓	X
Amnesia (may also be desirable)	✓	X

✓ likely, X not likely.

40. ANSWER: D

Surgery and anesthesia are a major life event for a child. Anesthesiologists should act accordingly and support patients and parents through careful preoperative evaluation and information consults and postoperative visits, and should supply adequate premedication to reduce adverse outcomes associated with anxiety.

The ideal agent for premedication for pediatric general anesthesia should provide anxiolysis and sedation, reduce required doses of general anesthetics and opioids, be easy to administer (orally or rectally), and have a fast onset and a relatively long duration of action, to cover the dynamics and time changes on the surgical list. It should also be relatively inexpensive and not associated with frequent adverse effects such as oversedation, behavioral disturbance, cardiorespiratory depression, or delay of recovery after anesthesia.

In both adults and children, benzodiazepine premedication for general anesthesia is standard practice in most hospitals. Worldwide, midazolam is the most commonly used agent. It has most of the properties of an ideal premedication agent but is associated with increased postoperative oxygen requirement and anterograde and retrograde amnesia. Recent studies on premedication have pointed out that clonidine may be superior to midazolam in children because it does not cause amnesia and may be associated with reduced postoperative pain, PONV, and agitation. Clonidine is not associated with respiratory depression or potentiation of opioid-induced respiratory depression. Bradycardia and hypoglycemia are potential adverse effects, but their incidence is low in children when doses of less than 10 μg/kg are used. The onset of clonidine's effect is slower, but clonidine's sedative effect lasts much longer than that of midazolam. Both agents can be given orally or rectally.

Doses of oral clonidine for premedication described in the literature range between 3 and 5 μg/kg. The oral midazolam dose ranges between 0.1 and 0.5 mg/kg.

KEY FACTS: PREMEDICATION FOR CHILDREN

- Premedication goals for children are adequate anxiolysis and sedation to avoid the adverse outcomes associated with anxiety and agitation.
- Midazolam is used most commonly worldwide, but clonidine may be a suitable alternative because of its lack of respiratory effects, reduced risk of PONV, and superior pain control.
- Potential adverse effects of clonidine are hypotension and bradycardia.

ADDITIONAL READING

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41. ANSWER: E

DIAZEPAM

Diazepam is available in aqueous and emulsified solutions. The aqueous solution contains benzyl alcohol and benzoic acid. The emulsified formulation causes less irritation and thrombophlebitis compared to the aqueous formulation. The latter is not very suitable for induction of general anesthesia because the high doses required can be given only through a central venous catheter.

The use of diazepam in anesthesia is limited by its unfavorable pharmacokinetic profile. The elimination half-life (T½β) of diazepam ranges between 20 and 50 hours. As with the other IV benzodiazepines, T½β increases in the elderly and the obese. Hepatic biotransformation of diazepam results in the active metabolites oxazepam and desmethyldiazepam (DMD). DMD is metabolized very slowly and easily accumulates. DMD also inhibits the metabolism of diazepam itself. Oxazepam does not readily accumulate. Diazepam is a substrate of cytochrome P450 (CYP450), subtypes 3A4 and 2C19. As with midazolam, inducers or inhibitors of these enzymes will affect diazepam plasma levels.

After IV administration, diazepam has a relatively fast onset (±40 seconds) but a very long duration of action. With repeated dosing, peripheral tissues become saturated with diazepam, and its duration of action then becomes dependent on the speed of its metabolic clearance. This makes diazepam an unattractive agent both perioperatively as well as in the ICU. Diazepam should be used with care in patients with liver disease: cirrhosis may increase its T½β up to fivefold. Diazepam undergoes enterohepatic circulation.

LORAZEPAM

Lorazepam is conjugated in the liver to an inactive compound that is excreted mainly by the kidneys. CYP450 enzymes do not play a significant role in its biotransformation. Some enterohepatic circulation exists. Lorazepam's T½β ranges between 10 and 20 hours. Compared to midazolam and diazepam, lorazepam clearance is less dependent on age, liver function, and enzyme inhibition and induction. As with the other IV benzodiazepines, obesity increases lorazepam's T½β by increasing its volume of distribution.

The slow onset of action of lorazepam, typically 1 to 2 minutes after a single IV bolus dose, makes it less useful for induction of general anesthesia.

Continuous infusion does increase lorazepam's T½β, but the increase is less pronounced compared to diazepam. This, combined with the absence of active metabolites, makes lorazepam more suitable for use in ICU patients compared to diazepam. However, the time to emergence after 3 days of sedation with lorazepam may be as long as 32 hours. Lorazepam's amnesic potency is four times higher than midazolam.

KEY FACTS: DIAZEPAM AND LORAZEPAM

- IV diazepam has a fast onset and a long duration of action. Its T½β is 20 to 50 hours.
- The T½β of diazepam increases dramatically in patients with liver cirrhosis.
- Unlike diazepam, lorazepam is not a CYP450 substrate and has no active metabolites. Its clearance also depends less on age and organ function.
- IV lorazepam has relatively slow onset (1 to 2 minutes).

ADDITIONAL READINGS

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42. ANSWER: C

To understand ***target-controlled infusion (TCI)***, a basic level of knowledge of the principles of the models used by TCI infusion pumps is key.

THREE-COMPARTMENT MODELS

Most general anesthetics have high distribution volumes (V_d) due to their lipid solubility. To get an understanding of the kinetics of such agents, one must theoretically divide the body up into three compartments. Each agent has a different V_d- and equilibration speed between each compartment. During infusion of an agent A, steady state is reached when the peripheral compartments have become saturated with A, and the concentration in the central compartment (plasma) becomes constant. Note that this doesn't

necessarily mean the concentrations in the peripheral and the central compartments are identical, because their saturation levels may differ. In steady state, the net transport of A between all compartments will equal zero, when the elimination rate of A from the central compartment is completely compensated by a constant infusion rate of A.

TCI models take the rate at which A is distributed from the central to the peripheral compartments, the redistribution rate to the central compartment, and the elimination rate into account to calculate the required infusion rate to reach a set target-site concentration and keep this concentration upright. This is why TCI is useful only with agents that generate quick changes in clinical effect (depth of anesthesia) with changes in the effect-site concentration (pharmacodynamics), rapidly distribute between the different compartments, and have rapid elimination rates (pharmacokinetics). Today, propofol, remifentanil, alfentanil, and sufentanil are most commonly used in TCI systems.

ADVANTAGES OF TCI

The TCI system calculates the infusion rate required to reach and maintain the preset effect-site concentration. This saves anesthesia providers from performing complex calculations and timing of dose changes. TCI systems can also predict at which speed the plasma concentration of the agent will decrease. Thus, it becomes easier to time the end of anesthetic agent infusion, and thus plan awakening more precisely compared to an ordinary continuous infusion. TCI may help to reduce consumption of anesthetic drugs.

LIMITATIONS OF TCI

TCI models use pharmacokinetic parameters derived from population studies. The TCI system obviously does not measure the effect-site concentration; it merely estimates it and bases its infusion rates and bolus doses upon it. Anesthesia providers must always observe "clinical" indicators of anesthetic depth. The concentration predicted by the TCI system has an error rate of ±10% to 25%. Different pumps use different models. Some models correct only for body weight (Marsh); others also control for sex, length, lean body mass, and age (Schnider). These parameters all account for most of the interpatient pharmacokinetic variability.

DOSING

When TCI is used in conscious sedation, target propofol concentrations between 0.8 and 0.9 μg/mL will usually suffice. Careful titration is required: some patients will require less than 0.8 μg/mL to achieve adequate sedation and some will require more. For general anesthesia doses, see Table 17.18. Make sure to check whether the TCI device that you use works with effect-site concentrations or plasma concentrations before you program and start the infusion.

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43. ANSWER: A

BARBITURATES: SPECIFIC WARNINGS

NONCOMPATIBILITY

Many commonly used anesthetic drugs cannot be coadministered or admixed with reconstituted barbiturate solutions. Precipitation will occur when, to name a few, pancuronium,

Table 17.18 **PROPOFOL FOR TCI**

GOAL	PROPOFOL TARGET CONCENTRATION		
	NO PREMEDICATION	PREMEDICATED PATIENT/ OPIOID BEFORE INDUCTION	ELDERLY PATIENTS
Induction general anesthesia	4–5 μg/mL	3–5 μg/mL	2–3 μg/mL
	Propofol target concentration when combined with		
	Remifentanil	Alfentanil/Sufentanil	Fentanyl
Maintenance general anesthesia	2.5–2.8 μg/mL	3.2–4.5 μg/mL	3.4–5.4 μg/mL

Please note: These are not effect-site concentrations.

vecuronium, rocuronium, lidocaine, fentanyl, succinylcholine, morphine, and other drugs are coadministered. Some combinations will completely obstruct catheters or veins.

VASCULAR IRRITATION

The highly irritant nature of reconstituted barbiturate solutions may cause thrombophlebitis. It may take several days for this effect to develop.

INJECTION ACCIDENTS: EXTRAVASATION AND ARTERIAL INJECTION

Barbiturates are highly alkaline after reconstitution. Accidental injection into the surrounding tissue of a vein (extravasation) and intra-arterial injection lead to severe reactions varying from nerve damage to ischemic contracture and tissue necrosis. This effect is not commonly seen after such accidents with methohexital.

When arterial injection occurs, the cannula should be left in place and flushed with normal saline and heparin. A sympathetic blockade may reduce the necrotic effect by inducing vasodilation. Elevation of the extremity may be useful as well to prevent reperfusion edema.

BARBITURATES AND CRITICALLY ILL PATIENTS

The cardiorespiratory effects of barbiturates (venodilation, reduced cardiac output and arterial blood pressure, decreased contractility) can be deleterious to patients with marked hypovolemia, anemia, kidney dysfunction (reduced glomerular filtration), ischemic heart disease, and malignant hypertension. Patients using beta blockers cannot compensate for venodilation with tachycardia and may experience steep blood pressure drops due to barbiturates.

PORPHYRIA

Barbiturates are absolutely contraindicated in any patient with (suspicion of) hepatic porphyria.

KEY FACTS: BARBITURATES

- Many drugs are chemically incompatible with reconstituted IV barbiturates.
- IV barbiturate formulations are highly alkaline; thrombophlebitis may occur.
- Extravasation or arterial injection of barbiturates leads to severe tissue damage.
- Patients with hypovolemia, anemia, kidney failure, or ischemic heart disease may not tolerate the circulatory depressant effects of IV barbiturates.
- Barbiturates are contraindicated in patients with porphyria.

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44. ANSWER: D

Barbiturate coma is defined as burst suppression on the electroencephalogram (EEG), induced by barbiturates. Barbiturate coma reduces cerebral blood flow (CBF) and cerebral metabolism by ±55% and leads to a significant decrease in intracranial pressure (ICP). By enhancing $GABA_A$ receptor function, barbiturates can be effective in terminating seizure activity.

REFRACTORY STATUS EPILEPTICUS

Induction of general anesthesia to burst suppression level is a last-resort option for the management of generalized convulsive seizure, or status epilepticus (SE) that does not respond to IV benzodiazepines. This can be done with propofol, thiopental, or pentobarbital; superiority of neither is proven. Burst suppression should be maintained for at least 24 hours. Limited evidence from case series supports the use of ketamine to treat advanced SE unresponsive to general anesthesia.

INTRACRANIAL HYPERTENSION ASSOCIATED WITH TRAUMATIC HEAD INJURY

Despite the clear correlation between raised ICP and adverse neurologic outcome, a 2000 Cochrane Systematic Review did not find evidence to support the theory that barbiturate coma improves the outcome of patients with severe head injury. Barbiturates did significantly increase the risk of hypothermia and hypotension (relative risk 1.80, 95% confidence interval 1.19 to 2.70). The latter endangers the cerebral perfusion pressure, which is also associated with adverse outcome. The Cochrane authors concluded that larger trials are required to arrive at a definitive stand on the use of barbiturates in the management of severe head injury.

ADVERSE EFFECTS OF CONTINUOUS BARBITURATE ADMINISTRATION

Continuous infusion of high doses of barbiturates may be complicated by toxicity from its carrier, propylene glycol, characterized by lactic acidosis. Other potential adverse effects are immunosuppression, severe electrolyte imbalance, and prolonged coma after discontinuation of infusion. Combined with their tendency to cause hemodynamic instability, strong caution must be advised before barbiturate coma is used. Phenobarbital infusions must not be discontinued abruptly, as to avoid severe withdrawal epilepsy.

KEY FACTS: BARBITURATE COMA

- Induction of burst suppression with general anesthetics is a last-resort therapy for benzodiazepine-resistant generalized convulsive status epilepticus.
- Benzodiazepine-resistant complex partial status epilepticus can be managed with valproate, phenobarbital, or levetiracetam before general anesthetics.
- Barbiturate coma does not appear to improve the outcome of patients with severe traumatic head injury, despite effectively lowering intracranial pressure.
- Barbiturate formulations contain propylene glycol, which may cause lactic acidosis during continuous infusion.

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45. ANSWER: A

Etomidate is a carboxylated imidazole, introduced in 1972. It is a popular agent for rapid-sequence induction (RSI). It induces dose-dependent hypnosis by potentiating γ-aminobutyric acid receptors, type A ($GABA_A$). It has no analgesic effect. In some countries, an emulsified formulation is available.

PHARMACOLOGY

Etomidate is a carboxylated imidazole that is insoluble in water. The commercial formulation contains the S-enantiomer, dissolved in 33% propylene glycol solution with a pH of 8.1. It is almost completely (99%) un-ionized at physiologic pH and quickly crosses the blood–brain barrier. As with propofol, etomidate has a rapid onset and a very short duration of action after a single dose. This is due to rapid redistribution to peripheral compartments. Etomidate undergoes esterase metabolism in both liver and plasma. It has no active metabolites. Etomidate's terminal half-life is relatively long (compared to propofol) due to its larger distribution volume, and its clearance rate is similar to that of propofol. Liver and kidney dysfunction minimally affect etomidate's pharmacokinetics. The induction dose for adults is 0.3 mg/kg.

SPECIFIC ADVANTAGES

Etomidate does not induce histamine release, and allergic reactions are rare. Etomidate produces minimal hemodynamic changes and relatively mild respiratory depression while preserving pulmonary hypoxic vasoconstriction. These properties are advantageous when there is no time to optimize a patient's volume status or cardiac reserve. Etomidate has neuroprotective properties because it reduces the cerebral metabolic rate of oxygen ($CMRO_2$, ↓45%) and cerebral blood flow (CBF, ↓35%), which results in reduced intracranial pressure (ICP). In contrast with thiopental, etomidate causes minimal changes in arterial blood pressure (CBP), so cerebral perfusion pressure (CPP) is preserved.

SPECIFIC DISADVANTAGES

With the commercially available formulation, there is a high risk of thrombophlebitis. Etomidate causes pain on injection, especially in small veins. It is ideally injected into a quickly flowing carrier infusion.

Etomidate commonly causes excitatory movement and myoclonus, does not inhibit induced seizure activity (in electroconvulsive therapy), and may induce seizure activity in epilepsy patients. This is probably due to subcortical extrapyramidal pathway disinhibition.

Etomidate anesthesia is associated with high rates of nausea, vomiting, and restlessness in recovery. Etomidate inhibits plasma cholinesterase and may prolong the duration of action of succinylcholine and mivacurium in susceptible patients.

Dose-dependent, transient inhibition of steroid 11-β hydroxylase, a critical enzyme in cortisol biosynthesis, significantly limits the use of etomidate for maintenance of general anesthesia or sedation in the ICU. This effect lasts for 6 to 8 hours after a single dose. Some authors suggest the need for additional corticosteroids when etomidate is used in patients under physical stress (e.g., trauma or sepsis). The use of etomidate in trauma patients is hotly debated in the literature. Some authors favor etomidate for its

hemodynamic stability, but others advise against its use in trauma and sepsis patients because of the adrenal suppression and possible adverse outcome.

There are no large, prospective, randomized trials available that show increased mortality with etomidate use in patients with trauma or sepsis. However, many questions remain about etomidate's safety in critical care.

KEY FACTS: ETOMIDATE

- Etomidate has a rapid onset due to its un-ionized state and high lipid solubility.
- Etomidate produces minimal hemodynamic changes, preserves pulmonary hypoxic vasoconstriction, and reduces ICP while maintaining CPP.
- PONV and thrombophlebitis are common adverse effects of etomidate.
- Etomidate causes transient adrenal suppression, limiting its use in trauma and sepsis patients.

ADDITIONAL READINGS

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Walls RM, Murphy MF. Continue to use etomidate for intubation of patients with septic shock. *Ann Emerg Med*. 2008;52(1):14–16.

46. ANSWER: E

KETAMINE PHARMACOLOGY

PHARMACOKINETICS

Ketamine is a phencyclidine derivate that is both water-soluble (many routes of administration) as well as lipid-soluble (crosses the blood–brain barrier). The formulation available in the United States is ketamine racemate, with equal proportions of the (R)- and (S)-isomers. The anesthetic potency of the (S)-isomer is three to four times greater than that of the (R)-isomer. It can be administered via different routes (Table 17.19).

Plasma protein binding of ketamine is 12%. When given orally, the extensive first-pass effect produces high plasma levels of the active metabolite norketamine. The therapeutic range of ketamine is very wide: its LD_{50} is ±100 times a normal IV dose. The dose–response correlation of ketamine is not as mathematical as that of the other general anesthetics.

Ketamine undergoes biotransformation in the liver and is a substrate of cytochrome P450 (CYP450), subtype 3A4; therefore, its elimination is influenced by inhibition or induction of this enzyme. The first metabolite, norketamine, is six times less potent than ketamine. The final conjugates are excreted in the urine. The elimination half-life is 2.5 to 3 hours, and plasma clearance is 15 to 20 mL/kg in adults. Liver failure and kidney failure have little effect on ketamine's elimination.

Table 17.19 KINETIC PROPERTIES OF DIFFERENT ADMINISTRATION ROUTES OF A SINGLE KETAMINE DOSE

ROUTE	BIOAVAILABILITY	ONSET	DURATION OF ACTION
IV	100%	Seconds	30–40 min
IM	93%	5 min	30–40 min
Intranasal	25–50%	5–10 min	45–60 min
Oral	17%	15–20 min	1–2 hours

RECEPTOR PHARMACODYNAMICS

Ketamine acts on many receptors, but its main target is the NMDA receptor, the key excitatory glutamate receptor in the brain. Ketamine blocks the channel and reduces the mean opening time. Because the NMDA receptor is also involved in the wind-up phenomenon and long-term potentiation, ketamine's clinical effects extend beyond analgesia and anesthesia. Ketamine is a pharmacologically promiscuous agent (Table 17.20), which also binds to opioid receptors

Table 17.20 CLINICAL EFFECTS OF KETAMINE AND THEIR RESPONSIBLE RECEPTORS

EFFECT	NMDA	ACHR	NA+	$CA^{2}+$	OPIOID
Hypnosis	•				
Amnesia	•	•			
Sympathetic activation*		•			
Negative inotropy*				•	
Positive chronotropy		•		•	
Vasodilation				•	
Bronchodilation		•		•	
Analgesia	•				•
Local anesthesia			•		
Hypersalivation		•			
Mydriasis		•			

* These effects counterbalance each other.

($\mu > \kappa > \delta$); however, this effect is irreversible by naloxone, and ketamine does not affect bowel transit time. Furthermore, ketamine inhibits the M1 muscarinic acetylcholine receptor, which contributes to its memory and consciousness effects as well as sympathetic activation, hypersalivation, and bronchodilation. Ketamine's minimal binding to nicotinic acetylcholine receptors may account for its enhancing effect on the neuromuscular blockade. Ketamine reduces sodium permeability and thus has local anesthetic effects. Ketamine has no net effect on GABA receptors.

CLINICAL EFFECTS

Ketamine is believed to affect the thalamocortical system. It produces a unique type of anesthesia termed "dissociative anesthesia." This has been described as a feeling that one's body is detached from one's brain. When ketamine is used as a single agent, patients may keep their eyes open, and nystagmus may be present. (Table 17.21)

Ketamine anesthesia is characterized by increased blood pressure and heart rate (sympathetic activation) and preserved respiration (Table 17.22). This makes ketamine an excellent anesthetic agent for patients with reduced hemodynamic (trauma, sepsis) and/or pulmonary reserve. It is also useful in the prehospital setting. However, the increased work of the heart also increases myocardial oxygen consumption, which makes it less suitable for patients with coronary heart disease. Furthermore, its cerebral effects limit its use in patients with brain injury. Unpleasant psychomimetic effects in awake patients are easily prevented, or blunted, by small doses of benzodiazepines or propofol.

KEY FACTS: KETAMINE

- Ketamine produces dissociative anesthesia, mainly by binding to NMDA receptors. It also binds opioid and mACh receptors and Na^+ and Ca^{2+} channels.
- Liver failure and kidney failure have little effect on ketamine's T½β of 2.5 to 3 hours.
- Ketamine increases blood pressure and heart rate and preserves respiration.
- The psychomimetic effects of ketamine can be prevented with benzodiazepines or propofol.

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Table 17.21 **RELATIONSHIP BETWEEN PLASMA KETAMINE CONCENTRATION AND CLINICAL EFFECT**

PLASMA CONCENTRATION	CLINICAL EFFECT	REQUIRED IV DOSE
50–200 ng/mL	Perceptual disturbance, amnesia	
>100 ng/mL	Analgesia	0.25–0.5 mg/kg
500–1,000 ng/mL	Hypnosis	0.4–1 mg/kg/h (sedation)
2,000–3,000 ng/mL	Surgical anesthesia	1–2 mg/kg (induction) 1–6 mg/kg/h (maintenance)

Table 17.22 **COMPARISON OF CLINICAL EFFECTS OF SOME INTRAVENOUS HYPNOTIC AGENTS**

FUNCTION	PROPOFOL	ETOMIDATE	MIDAZOLAM	KETAMINE	THIOPENTAL
Heart rate	–/↓	–	–/↑	↑↑	↑
Systemic vascular resistance	↓↓	–	↓	–/↑	–/↓
Cardiac contractility	↓	–	–	↑	–/↓
Mean arterial pressure	↓↓	–	–/↓	↑	↓↓
Respiratory rate	↓↓	–/↓	↓	–/↓[1]	↓↓
Cerebral blood flow	↓	↓	↓	↑	↓
Cerebral metabolic rate of oxygen Consumption	↓	↓	↓	↑	↓
Intracranial pressure	↓	↓	–	–/↑	↓
CNS excitation	+	++	–	++	–/+
Histamine release	–/+	–	–	–	+
Injection pain	++	+++	–	–	–[2]
Postoperative nausea and vomiting	–	++	–	++	+

1: induction apnea rare. 2: highly irritant to peripheral veins.

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47. ANSWER: B

Apart from inducing analgesia, amnesia, and hypnosis, ***ketamine*** is known to have other effects on the brain that are of interest for anesthesiologists.

NEUROMONITORING

Ketamine produces high-amplitude θ activity and increased β activity on the EEG, which may be due to thalamic and limbic activation. Ketamine has been reported to cause seizures in patients with epilepsy. Ketamine may increase bispectral index (BIS) values and increase state entropy (SE) and response entropy (RE). The seemingly paradoxical increase in anesthetic depth and increase in BIS or entropy values may confound anesthesiologists and lead to overdoses of other anesthetic agents. However, a dose of less than 0.2 mg/kg may leave the BIS reading unaffected.

Ketamine transiently increases somatosensory evoked potentials (SSEP).

ANTIHYPERALGESIC EFFECT

Chronic opioid use leads to increased dose requirements and may induce hyperalgesia. These effects seem to be mediated by the NMDA receptor. Ketamine blocks the NMDA receptor and has been shown to reduce hyperalgesia, spinal wind-up, and opioid tolerance at subanesthetic doses. Low doses of ketamine also reduce the postoperative opioid requirement. Ketamine should be considered when multimodal acute analgesia is required. The use of ketamine as treatment for chronic pain may reduce hyperalgesia, but it does not always effectively control pain. Studies report various but relatively high rates of nonresponders.

INTRACRANIAL PRESSURE

Ketamine is commonly thought to increase intracranial pressure (ICP) via increased arterial blood pressure and cerebral vasodilatation (due to increased p_aCO_2). Neurotrauma patients should therefore receive ketamine only during mechanical ventilation, so that normocapnia can be maintained to attenuate the increase in ICP. Coadministration of nitrous oxide must be avoided when ICP is of concern because the combination increases cerebral blood flow. Ketamine may increase intraocular pressure as well, and it causes nystagmus.

PSYCHOMIMETIC EFFECTS

Ketamine may induce anxiety, agitation, flashbacks, delirium, dystonia, psychosis, dizziness, and paranoia. It is obvious that these effects are unwanted in patients with preexistent psychiatric illness, children, and the elderly. Low doses of benzodiazepines (e.g., midazolam) can prevent these symptoms. It is recommended that patients who are emerging from ketamine anesthesia be protected from noise and bright light, as adverse psychomimetic effects are most common with declining ketamine plasma levels. However, a quiet environment should obviously be a standard for every recovering patient. When ketamine is used to treat chronic pain, agitation may be avoided by coadministering a low-dose benzodiazepine.

KEY FACTS: KETAMINE AND THE BRAIN

- Ketamine increases BIS, entropy, and SSEP readings.
- Ketamine may reduce opioid-induced hyperalgesia.
- The combination of nitrous oxide and ketamine increases ICP.
- Ketamine may have neuroprotective properties.
- Ketamine may induce anxiety, agitation, delirium, and psychosis. Benzodiazepines can be used to prevent or blunt these effects.

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48. ANSWER: A

Table 17.23 lists contraindications to ketamine use.

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Table 17.23 KETAMINE CONTRAINDICATIONS

CONDITION	MECHANISM
RELATIVE CONTRAINDICATIONS	
Coronary insufficiency	Increased cardiac work and myocardial oxygen consumption (MVO_2)
Epilepsy	Cerebral excitation and potential seizure induction
Severe sepsis	Depleted catecholamine stores can no longer counterbalance ketamine's direct myocardial depressant effect, resulting in hypotension
Preexistent psychiatric illness, high delirium risk	Potent psychomimetic effects (blunted by small benzodiazepine doses)
Increased intracranial pressure (ICP), or those at risk of increased ICP	Cerebral vasodilatation, increased cerebral blood flow and ICP
Increased intraocular pressure (IOP), glaucoma, ophthalmic surgery	Ketamine raises IOP.
Pregnancy	Ketamine is labeled category D; positive evidence of potential fetal harm
Hypertension	Risk of further blood pressure increase
Thyrotoxicosis	Risk of deleterious tachycardia and hypertension
Patient at risk of substance abuse	Ketamine has a relatively high abuse potential.
ABSOLUTE CONTRAINDICATIONS	
Porphyria	May elicit porphyric crisis
Active delirium or psychosis	May aggravate these conditions
First-trimester pregnancy	May induce contractions or harm the embryo
Preeclampsia	May further increase hypertension and tachycardia

49. ANSWER: C

The use of local anesthetics carries the risk of CNS toxicity and cardiotoxicity. Local anesthetic toxicity can be seen as a continuum, and symptoms vary with agent plasma levels. CNS toxicity is related to the local anesthetic's potency, as its membrane-stabilizing effect underlies the toxicity. Minor CNS excitation symptoms are seen first and include tinnitus, altered sound perception, lightheadedness, circumoral numbness, a metallic taste sensation, and paresthesias. Severe excitation, seen with higher concentrations, produces agitation, confusion, tremors, and seizures. Further plasma concentration increases will produce CNS depression and cardiorespiratory depression, characterized by arrhythmia, hypotension, and cardiac arrest. This type of cardiac arrest is typically very difficult to resuscitate.

Local anesthetic toxicity does not occur only with inadvertent intravascular injection but is also seen with "normal" peripheral tissue injection (especially if the recommended dose limits are ignored) and the intrathecal injection of doses intended for the epidural space.

INTRA-ARTERIAL INJECTION

This is most likely to occur during regional block techniques, most commonly with neck area blocks (interscalene, cervical plexus, stellate ganglion). Rapid transport of the agent to the brain via the artery causes symptoms, including seizures at small doses. The effects fade quickly because the agent quickly "passes through" the brain.

INTRAVENOUS INJECTION

This type of inadvertent injection is most common with neuraxial techniques, especially caudal blocks. Toxic effects last longer after IV injection than intra-arterial injection.

PERIPHERAL TISSUE INJECTION

This produces the slowest type of local anesthetic toxicity. The onset of symptoms may be delayed up to 20 minutes after the injection. One particularly notorious technique is tumescent liposuction. The addition of epinephrine allows higher doses of local anesthetics because this delays resorption.

RELATIVE TOXICITY

Racemic bupivacaine is the most potent local anesthetic and is consequently ±4 times more toxic than mepivacaine, ropivacaine, and lidocaine. Bupivacaine's enantiomer, levobupivacaine, appears to be associated with less cardiotoxicity.

MANAGEMENT OF TOXICITY

The management of patients with signs of local anesthetic toxicity should focus on airway management. Small doses of benzodiazepines can be given if symptoms do not disappear spontaneously. In case of cardiac arrest, ACLS guidelines should be followed. An intravenous lipid emulsion (IVLE) should be administered. IVLE injected into the bloodstream behaves like chylomicrons and is cleared similarly. Exactly how IVLE antagonizes the toxic effects of local anesthetics is unknown. One theory is that IVLE creates a large lipid phase in blood, into which the local agent dissolves. Fatty acids may also activate calcium and potassium channels.

The optimal dose of Intralipid is also unknown. Recommended doses for 20% Intralipid include a 1.5-mL/kg bolus, which can be repeated one or two times for persistent asystole, followed by an infusion at 0.25 mL/kg/min for 30 to 60 minutes. The infusion rate may be increased up to 0.50 mL/kg/min for refractory hypotension.

The website www.lipidrescue.org provides a guideline, along with the ability to share knowledge about successful applications of lipid rescue. The authors of this website (Guy Weinberg et al.) advise against the use of propofol, vasopressin, calcium channel blockers, and other local anesthetics (lidocaine) during the resuscitation of patients with local anesthetic toxicity.

KEY FACTS: LOCAL ANESTHETIC TOXICITY

- Local anesthetic toxicity represents a continuum of CNS and cardiac adverse effects.
- Neck area and caudal neuraxial blocks carry the highest risk of vascular injection.
- Cardiac arrests due to local anesthetic toxicity do not respond well to cardiopulmonary resuscitation.
- Intravenous lipid emulsion should be administered parallel to standard resuscitation measures, in case of severe toxicity.

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www.lipidrescue.org. Accessed March 17, 2010.

50. ANSWER: B

Clonidine is an α_2-adrenoreceptor agonist. Although still in use as a centrally acting antihypertensive, it is also commonly used as an anesthetic adjuvant.

PHARMACOLOGY

Clonidine can be given orally and intravenously. Absorption from the gut is almost complete. After oral administration, the peak effect is seen between 60 and 90 minutes. Clonidine is moderately lipid-soluble and can cross the blood–brain barrier. It is metabolized in the liver, and 40% to 60% is excreted unchanged in the urine. The terminal elimination half-life of clonidine is 12 to 24 hours, and this is increased in patients with renal failure.

CLINICAL EFFECTS

After injection, a transient hypertensive phase may be observed, caused by activation of peripheral α adrenoreceptors, followed by a reduction in blood pressure due to the central effect.

Binding of clonidine to α_2 receptors in the brain induces sedation by depressing the locus ceruleus. Clonidine does not induce hypnosis, because it also (if only minimally) binds to α_1 receptors, which antagonizes the sedative α_2 effect. Clonidine's sedative effect makes it a good premedication agent (young adults 2 to 4 μg/kg, elderly patients 1 to 2 μg/kg), reducing induction and maintenance anesthetic requirements by 25% to 40%. Clonidine centrally decreases sympathetic activation, thus blunting the response to intubation and surgical stimuli. It also reduces the hyperdynamic hemodynamic state and agitation, sometimes seen after volatile anesthesia. Clonidine lacks a significant respiratory depressant effect.

Clonidine produces analgesia mainly by stimulating α_2 receptors in the dorsal horn of the spinal cord, an effect that mimics activation of descending inhibitory pathways. A special application of clonidine is intra-articular injection, which produces local analgesia, probably by inhibition of norepinephrine release. Clonidine also potentiates the effect of local anesthetics by depressing nerve fiber

Table 17.24 **BENEFITS OF PERIOPERATIVE CLONIDINE ADMINISTRATION**

INDICATION	MECHANISM
Patients dependent on drugs/alcohol	Reduces sympathetic hyperactivity, reduces withdrawal symptoms
Patients with chronic pain (cancer/noncancer)	Reduction of perioperative opioid requirement and associated adverse effects
Patients with hypertension	Blunting of sympathetic response reduces blood pressure swings.
Patients undergoing cardiovascular surgery	Reduced risk of perioperative myocardial ischemia due to reduced sympathetic activity
Patients undergoing orthopedic/ear surgery	Induction of mild to moderate hypotension without administering more anesthetic agents
Patients undergoing ophthalmic surgery/with glaucoma	Reduction of intraocular pressure (IOP) with premedication with clonidine
Patients at risk of/with postoperative ileus	Reduction of ileus duration by stimulation of α_2 adrenoreceptors in the gut
Patients receiving regional anesthetic techniques	Improved block duration and quality
Patients receiving neuraxial anesthetic techniques	Prolonged duration of spinal block (caveat hypotension and bradycardia with >150 μg) Increased toxicity threshold for bupivacaine Prevention of shivering

action potentials, and it is often used as an adjuvant to Bier's block (1 μg/kg). The local vasoconstrictive effect reduces local anesthetic absorption, and clonidine is therefore often added to caudal block mixtures for children.

Clonidine (1 to 1.5 μg/kg) decreases the shivering threshold through a direct effect on the hypothalamus (Table 17.24).

ADVERSE EFFECTS

Clonidine decreases sympathetic activation by depressing adrenergic cardiovascular neurons in the vasomotor center of the brainstem. This potentially leads to hypotension and bradycardia. When used as an adjuvant to spinal blocks, the total clonidine dose should not exceed 1 μg/kg to prevent exaggerated hypotension and bradycardia. This is especially important in parturients. Clonidine seems safe during labor, but it does pass the placenta and may cause bradycardia of the neonate.

After intravenous injection of clonidine, peripheral α agonism causes a transient rise in blood pressure. Another effect of clonidine is xerostomia. Chronic clonidine users may experience rebound hypertension or even myocardial ischemia when clonidine is suddenly withheld.

KEY FACTS: CLONIDINE

- Clonidine is a centrally acting α_2-receptor agonist, producing sedation and attenuation of responses to intubation and surgical stimuli.
- Clonidine does not cause respiratory depression but may produce hypotension and bradycardia.
- In many situations, clonidine may be a useful anesthetic adjuvant.

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51. ANSWER: B

Methemoglobinemia is the condition where the ferrous iron (Fe^{2+}) in hemoglobin is oxidized to the non–oxygen-binding ferric iron (Fe^{3+}) form. This occurs when oxidative stress exceeds the reducing capacity of the body. The enzyme responsible for most of this reduction is cytochrome B_5. This enzyme is regenerated by methemoglobin (metHb) reductase. MetHb cannot carry oxygen.

Genetic abnormalities resulting in dysfunctional variants of these enzymes have been described, and individuals with these abnormal enzymes are at increased risk of developing methemoglobinemia. However, methemoglobinemia induced by medications or toxins is far more common. Table 17.25 lists agents that may induce methemoglobinemia. Oxidative agents, such as chlorate, which is found in toothpaste and cleaning agents, donate oxygen directly to hemoglobin. Nitrites induce metHb formation by coupled oxidation. The reaction between the nitrite and hemoglobin results in the formation of a nitrate and metHb (Fe^{3+} instead of Fe^{2+}). Nitrites are found in some types of bottled mineral water and can also be formed by reduction of nitrates in the human gut. A good example of a high-nitrate food is spinach. Therefore, spinach and the mineral waters mentioned should not be given to infants because their reducing capacity is higher than that of adults. Other typical

examples are the commonly used nitroglycerin, prilocaine, and amyl nitrite (a drug of abuse). Very high concentrations of nitrites may result in complex formation between the nitrite and hemoglobin.

Aromatic agents are indirect methemoglobinemia inducers. The exact mechanism is complex. Because aromatic amino- and nitrocompounds can continuously contribute to metHb formation, a long-lasting methemoglobinemia may be seen.

Methylene blue (tetramethylthionin) and thionin are colorants with redox properties that may actually induce methemoglobinemia, but this reaction stops when a percentage of 8% metHb has formed. At higher concentrations of metHb, these agents will promote reduction of metHb via NADH-dependent reductase by donating hydrogen to this enzyme.

SYMPTOMS OF METHEMOGLOBINEMIA

MetHb is brown instead of red. This, combined with reduced oxyhemoglobin, will give patients with methemoglobinemia a distinct pallor. The lips show a bluish color. Microscopic examination of blood may reveal Heinz bodies, intracellular inclusions of denaturated hemoglobin. Symptoms are first seen when approximately 10% to 20% of hemoglobin has been transformed to metHb. The blood turns positively brown at concentrations of 30%. At a concentration of 60% to 80% metHb, death by asphyxia occurs. Lower concentrations may be lethal in the presence of reduced cardiorespiratory reserve and anemia.

When all metHb-forming agents are removed from the body, a reduction in metHb concentration of 10% per hour can be expected.

Many metHb-forming agents also cause hemolysis. Patients with glucose-6-phosphatase dehydrogenase (G6PD) deficiency are especially at risk of hemolytic crises induced by the aforementioned agents. Consequently, the administration of methylene blue to a G6PD-deficient patient may also induce a hemolytic crisis.

TREATMENT

IV methylene blue (1 to 2 mg/kg) is used to treat methemoglobinemia. This potent blue colorant turns the urine vividly blue; this will startle the uninformed patient. Be careful not to spill methylene blue on skin (including your own) or clothes, as this will produce reluctant stains. Pulse oximetry becomes unreliable after IV administration of methylene blue, so blood gas analysis should be used instead.

KEY FACTS: METHEMOGOBINEMIA

- In methemoglobinemia, the iron ion is oxidized from the ferrous to the ferric form.
- MetHb cannot carry oxygen and turns the blood brown.
- At a concentration of 60% to 80% metHb, death by asphyxia occurs.
- IV methylene blue (1 to 2 mg/kg) is used to treat methemoglobinemia.
- Table 17.25 lists chemicals that induce methemoglobinemia.

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Table 17.25 **OVERVIEW OF CHEMICALS THAT MAY INDUCE METHEMOGLOBINEMIA IN HUMANS**

OXIDATIVE AGENTS	NITRITES	AROMATIC AGENTS	REDOX COLORANTS	LOCAL ANESTHETICS
Chlorate	Sodium nitrite	Anilin	Methylene blue	Benzocaine[2]
Perchlorate	Potassium nitrite	Phenylhydrazine	Thionin	Prilocaine[3]
	Nitrate	Nitrobenzol		Articaine
	Nitric oxide (NO)[1]	Nitrotoluole		
	Nitrogen dioxide (NO_2)[1]	Phenacetin		
	Amyl nitrite	Acetanilid		
	Nitroglycol	Sulfonamide		
	Nitroglycerin			

1: not to be confused with N_2O, nitrous oxide. 2: sometimes found in personal lubricants and condoms. 3: A compound of EMLA.

SOURCE: adapted from Hemmings Jr, H, Hopkins PM. *Foundations of Anesthesia: Basic Sciences for Clinical Practice.* 2nd ed. Philadelphia, PA: Mosby Elsevier; 2006.

52. ANSWER: B

53. ANSWER: C

Mannitol is a nonmetabolizable, cell-impermeable sugar alcohol with the formula $C_6H_8(OH)_6$. When administered intravenously, it increases the tonicity of the extracellular volume and thus extracts water from the cells into the extracellular volume.

In the proximal tubule and thin descending part of the loop of Henle in the nephron, the presence of a nonreabsorbable osmotic solute will result in water retention in the tubular fluid and reabsorption of sodium from the tubular fluid. Effectively, this increases the urinary flow rate while only modestly increasing natriuresis. Clinically, the visible effect is a profoundly dilute diuresis that may require volume replacement. Hypokalemia is often seen. This has a cascade of effects, including increases in afferent arteriolar vasodilatation, renal blood flow, intratubular pressure, and glomerular filtration rate (GFR). The increased flow of tubular fluid is thought to be capable of flushing cellular debris from the tubules, which reduces tubular obstruction.

Other effects of mannitol are the scavenging of oxygen free radicals and a reduction of tubular energy demand, both hypothesized to contribute to its kidney protective effect.

Despite a lack of solid evidence, mannitol is often used to protect the kidney from ischemia during vascular, cardiac, and transplant surgery, as well as to protect the kidney from nephrotoxic injury. The dose used for kidney protection is 25 to 100 g IV. Patients at risk of renal dysfunction from radiocontrast are not likely to benefit from mannitol, and normal saline or sodium bicarbonate may achieve better kidney protection in this situation.

The extraction of intracellular fluid reduces cellular swelling. Mannitol can reduce brain swelling, resulting in reduced intracranial pressure. A single dose of mannitol produces reduced intracranial pressure for up to 4 hours. However, hypertonic saline/hyroxyethyl starch (HES) solutions may have a comparable or even superior effect on intracranial pressure. Caution must be taken when using mannitol, as evidence of its efficacy is contradictory. When the blood–brain barrier is compromised, for example in severe cerebral ischemia or in brain injury patients more than 24 to 48 hours after the primary injury, mannitol may penetrate into the cerebral tissue and may increase rather than decrease tissue volume.

The dose used for the reduction of brain swelling is 0.25 to 2 g/kg and may be repeated every 6 to 8 hours. To reach a maximum effect, this dose should be given within 15 minutes.

Due to redistribution, mannitol may also cause pulmonary edema, which can be detrimental to patients with poor left ventricular function and congestive heart failure.

As per current recommendation, corticosteroids are not recommended for traumatic brain injuries because they do not improve the outcome of patients.

KEY FACTS: MANNITOL

- Mannitol increases extracellular tonicity, extracting water out of cells into the circulation. This may reduce intracranial pressure but does not necessarily improve outcome.
- Despite a lack of evidence, mannitol is often used to protect the kidney.
- Mannitol produces brisk osmotic diuresis, often requiring volume replacement.
- Mannitol may penetrate a damaged blood–brain barrier, resulting in increased brain swelling, particularly 24 to 48 hours after the injury.

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54. ANSWER: C

The loop diuretic ***furosemide*** is excreted in the tubular lumen. As it travels along the medullary thick ascending part of the loop of Henle, it inhibits the $Na^+/K^+/2Cl^-$ co-transporter. This transporter normally allows the reabsorption of sodium, potassium, and chloride ions into the countercurrent plasma stream. When the transporter is inhibited, the plasma countercurrent stream has lower osmolality and thus less capacity to concentrate the urine and reabsorb water from the collecting duct.

Furthermore, furosemide weakly inhibits carbonic anhydrase and weakly inhibits the thiazide-sensitive Na^+/Cl^- co-transporter system in the distal tubule. Furosemide also inhibits tubuloglomerular feedback. On the vascular level, furosemide causes renal vasodilatation by affecting the prostaglandin levels. This effect is therefore not seen in the presence of nonsteroidal anti-inflammatory drugs (NSAIDs).

All of this results in a forceful diuresis, with loss of sodium, potassium, calcium, and magnesium in the urine.

PHARMACOLOGY

Furosemide can be administered either orally or intravenously. Oral bioavailability is approximately 50%. Furosemide in plasma is highly bound to albumin. After administration, furosemide is partly excreted unchanged, and partly metabolized to an inactive glucuronide in the proximal tubule. One-third of a dose is excreted with the feces. The elimination half-life ($T_{½\beta}$) is 0.5 to 1 hour. In neonates, elimination is far slower, and $T_{½\beta}$ may be as long as 7.5 hours.

CONSIDERATIONS FOR ANESTHESIA

Furosemide use is very common in surgical patients. Chronic furosemide use may lead to dehydration and deficiencies in plasma sodium, potassium, magnesium, and calcium. Metabolic alkalosis due to hypochloremia may accompany these deficiencies. A preoperative electrolyte check may be indicated.

IV furosemide administered intraoperatively may, even in low doses, produce brisk diuresis followed by dehydration and hypotension. This may elicit prerenal kidney failure. Caution is therefore advised when using furosemide in patients with preexisting kidney failure.

However, in patients with acute left ventricular failure, furosemide significantly reduces pulmonary edema and produces vasodilatation, which results in reduced preload.

WARNINGS

The $Na^+/K^+/2Cl^-$ co-transporter is also found in the inner ear, where it plays a role in the composition of endolymph. High doses or very rapid administration of furosemide may therefore induce ototoxicity, particularly in patients with preexisting renal failure. Peak plasma concentrations appear to be the actual culprits, not total dose. A maximum infusion rate of 4 mg/min (240 mg/hour) is advised for patients without preexisting renal failure, and a maximum of 2.5 mg/min (150 mg/hour) for patients with preexisting renal disease. However, ototoxicity has been reported with infusion rates as low as 1.3 mg/min (80 mg/hour) in patients with acute renal failure. Patients concurrently treated with aminoglycoside antibiotics are at increased risk.

KEY FACTS: FUROSEMIDE

- Furosemide inhibits the $Na^+/K^+/2Cl^-$ co-transporter in the loop of Henle, resulting in diuresis with loss of Na^+, K^+, Ca^{2+}, and Mg^{2+}.
- IV furosemide may elicit prerenal kidney failure in patients with preexisting kidney disease.
- Chronic use carries a risk of dehydration and deficits of the aforementioned ions.
- Ototoxicity is seen at high doses or with rapid administration, especially when combined with aminoglycosides or in patients with kidney failure.

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55. ANSWER: B

Glucagon is a peptide hormone produced in the alpha cells of the pancreas. Together with insulin, this hormone regulates energy homeostasis. Glucagon is secreted in response to lowering plasma levels of glucose. Glucagon secretion is inhibited by increases in blood glucose, insulin, and free fatty acids; this is a closed, negative feedback loop.

Normally, glucagon secretion is seen with fasting and exercise. Glucagon secretion also occurs under stressful circumstances, such as surgery and major infections. This is thought to be mediated by sympathetic nervous system stimulation of the alpha cells.

Glucagon is extracted by the liver, where it activates glycogen phosphorylase and inhibits glycogen synthase. This results in net glucose release from the glycogen stores in the liver. Secondly, glycogen stimulates gluconeogenesis from amino acids through upregulation of gluconeogenic enzymes. Thirdly, glucagon suppresses the synthesis of malonyl CoA, an enzyme that normally prevents free fatty acids from being converted to ketoacids in the mitochondria. High levels of glucagon will thus result in net ketoacid production in the liver. The fourth important effect of glucagon is the stimulation of lipolysis in adipose tissue, resulting in increased free fatty acids.

In short, the actions of glucagon are the opposite of the actions of insulin. However, unlike insulin, glucagon does not have an important effect on muscle. Glucagon exerts its effect by increasing intracellular cAMP.

Glucagon also increases cAMP levels in cardiomyocytes, producing positive inotropy and increased heart rate. It can therefore be used as an adjuvant to treatment of beta-blocker overdose. Furthermore, glucagon reduces gastrointestinal tonus and motility. This is sometimes put to use for endoscopic and radiology studies of the gastrointestinal tract as well as for surgical anastomoses of the bowel.

The normal glucagon response is sometimes absent in patients with type 1 diabetes, putting them at risk for

hypoglycemia when missing meals or injecting too much insulin. Glucagon can then be administered to restore normal plasma glucose levels. Glucagon is also an important mediator in the pathogenesis of diabetic ketoacidosis. Insulin administration will help restore normal ketoacid levels and pH.

Recombinant glucagon is available commercially, formulated as hydrochloride salt for injection. For hypoglycemia, 1 mg IV is used. Higher doses (5 to 10 mg) and continuous infusion may be required in the treatment of beta-blocker overdose. Onset of effect after IV injection is seen in approximately 10 minutes. The elimination half-life is approximately 5 minutes.

Glucagon injection will not effectively increase plasma glucose levels in patients with depleted hepatic glycogen stores.

KEY FACTS: GLUCAGON

- Glucagon is produced in the pancreatic alpha cells, excreted during fasting and exercise. Essentially, its effects are the opposite of those of insulin.
- Glucagon activates hepatic glucose release, gluconeogenesis, increased free fatty acids, and the production of ketoacids
- Glucagon also produces positive inotropy and increased heart rate.
- Glucagon can be used to treat hypoglycemia (1 mg IV) or beta-blocker overdose (5 to 10 mg). It has a short T½β of ±5 min.

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56. ANSWER: D

Phenytoin is an antiepileptic for the treatment of generalized and complex partial types of epilepsy. It is also used to treat status epilepticus and to prevent neurosurgery-associated epilepsy. Although structurally related to barbiturates, phenytoin is minimally sedative at therapeutic plasma concentrations. Phenytoin binds to voltage-dependent sodium channels, preferentially in their inactive state (after a depolarization) and prevents the channel from returning to its resting state, from where it could contribute to another action potential. This way, phenytoin "discriminates" between normal, low-frequency firing (inherent to normal brain function) and high-frequency firing (characteristic of epilepsy). This mechanism of action is referred to as use-dependent block. Furthermore, phenytoin also affects calcium channels, posttetanic potentiation, and intracellular mechanisms involved in membrane excitability.

Phenytoin may be very effective, yet it also has significant trade-offs: it has a small therapeutic range (40 to 100 μmol/L), complex pharmacokinetics, serious potential acute adverse effects, and bothersome long-term complications. Phenytoin is not effective in myoclonic or absence seizures, and may even worsen them.

PHARMACOLOGY

Phenytoin can be administered orally (bioavailability 80% to 90%) and parenterally (IM or IV). In plasma, it is highly bound to albumin. Phenytoin is metabolized in the liver. Among others, cytochrome P450 (CYP) subtypes 2C9 and 2C19 are involved. Its kinetics are therefore vulnerable to induction or inhibition by agents affecting these enzymes. Phenytoin induces CYP 2B6, 2C9, 2C19, and 3A4. This pattern of enzyme induction affects the kinetics of many drugs, including phenytoin itself.

The pharmacokinetics of phenytoin is best described by a saturation model: its elimination rate does not increase proportionally to its plasma concentration. Increasing the dose thus results in increased elimination half-life but may also lead to disproportional (and often unpredictable) increases in plasma levels. Therapeutic drug monitoring is mandatory. Initial elimination half-life is 22 hours.

ACUTE ADMINISTRATION FOR STATUS EPILEPTICUS

The initial loading dose is 15 to 20 mg/kg, IV, at a maximum infusion rate of 50 mg/minute. Another 10 mg/kg can be given if there is no response after 20 minutes. After 12 hours, start maintenance therapy. Remember to monitor therapeutic drug levels (TDL). Therapeutic plasma concentrations are 10 to 20 μg/ml (total) and 1 to 2 μg/ml (free), although higher concentrations may be necessary to control status epilepticus. Measure the first TDL 2 to 4 hours after the IV loading dose.

ADVERSE EFFECTS

At plasma concentrations of 100 to 150 μmol/L, vertigo, ataxia, headache, and nystagmus may appear. At higher concentrations, acute (reversible) confusion occurs. Rapid administration (>50 mg/min) is associated with reduced consciousness, arrhythmias, and hypotension. Phenytoin is potentially teratogenic because it reduces folate levels. Long-term adverse effects include gingival hyperplasia,

hirsutism, and coarsening of features. Phenytoin may induce impaired glucose tolerance because it inhibits insulin secretion. Hypocalcemia and osteomalacia may also occur. 5% of patients develop a rash.

INTERACTIONS

Phenytoin interacts with other drugs at three different levels. Firstly, it can displace other drugs (valproic acid, phenylbutazone, salicylates, tolbutamide) from plasma proteins, and thus increase their free fractions. Secondly, certain drugs compete for its metabolic pathway through CYP450 enzymes (chloramphenicol, disulfiram, isoniazid, cimetidine, sulfonamides, valproic acid, phenylbutazone, theophylline), leading to increased phenytoin plasma levels. Thirdly, phenytoin induces hepatic enzymes and speeds up the metabolism of other drugs (corticosteroids, oral contraceptives, theophylline, benzodiazepines, protease inhibitors). Certain agents (including alcohol, protease inhibitors, phenobarbital, and carbamazepine) are inducers of hepatic enzymes themselves and will reduce phenytoin plasma levels. Interactions with other agents should be checked before phenytoin is administered.

KEY FACTS: PHENYTOIN

- Phenytoin is an antiepileptic with minimal sedative potential.
- Although very effective, its therapeutic range is small (40 to 100 μmol/L). Adverse effects include vertigo, ataxia, headache, nystagmus, confusion, and arrhythmia.
- The infusion rate should not exceed 50 mg/min.
- Phenytoin has many interactions because it induces hepatic enzymes as a CYP450 substrate.

ADDITIONAL READINGS

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57. ANSWER: B

The ***serotonin syndrome*** is a potentially life-threatening condition associated with increased serotonergic agonism on both central nervous system (CNS) and peripheral serotonin receptors. It can result from drug therapy at normal doses, drug overdoses, drug–drug interactions, and interactions between drugs and substances of abuse. Many prescription and over-the-counter medicines, drugs of abuse, and herbal remedies have been associated with the serotonin syndrome (Table 17 in Boyer and Shannon, 2005).

CLINICAL MANIFESTATIONS AND DIAGNOSIS

The syndrome may occur at any age, and symptoms range from mild to life-threatening in severity. In contrast to the neuroleptic malignant syndrome, which develops over days to weeks, the serotonin syndrome develops within 24 hours. Symptoms encompass mental status changes, autonomic hyperactivity, and neuromuscular abnormalities, and severity is related to the serotonin concentration. Patients with mild disease may be afebrile, whereas hyperthermia marks more serious disease. Severe cases are characterized by severe hypertension, tachycardia, hyperthermia, agitation, delirium, and muscle rigidity. There is no specific test for the syndrome, but it can be distinguished from related conditions by thorough history and physical examination.

MANAGEMENT

To determine the presence and severity of complications, complete blood count, basic metabolic panel, creatine phosphokinase (CPK), liver panel, coagulation studies, blood cultures, and urinalysis may be required.

All serotonergic medications should be discontinued, and benzodiazepines should be given to control agitation. Supportive therapy should aim for rigorous control of normal vital parameters, including body temperature. Short-acting agents are preferred because drug responses may be exaggerated during autonomic instability. Patients with a temperature above 41.1 degrees C (106 degrees F) should be considered critically ill and require intubation, mechanical ventilation, and muscle paralysis. Avoid the use of succinylcholine, which may induce life-threatening hyperkalemia in patients with this syndrome, possibly due to rhabdomyolysis.

Cyproheptadine, a serotonin antagonist, can be used to treat the syndrome. An initial dose of 12 mg PO (for adults) is advised, followed by 2 mg every 2 hours if symptoms persist. This may induce significant, but not undesired, sedation. Consider IM chlorpromazine (50 to 100 mg) if oral (or nasogastric) administration is impossible.

Clinicians should be aware that patients may deteriorate rapidly and that aggressive treatment is appropriate. There is no place for dantrolene in the management of serotonin syndrome. Remember that the syndrome may have been caused by MAO inhibitors, and consider their interactions with anesthetic and resuscitation agents.

KEY FACTS: SEROTONIN SYNDROME

- Serotonin syndrome develops within 24 hours after administration of the precipitating agent.
- The severity of mental status changes, autonomic hyperactivity, and neuromuscular abnormalities ranges from mild to life-threatening.
- Serotonergic medication should be discontinued and benzodiazepines given to control agitation. Rigorous control of normal vital parameters is required.
- Cyproheptadine (12-mg bolus, then 2 mg every 2 hours) may be effective.

ADDITIONAL READING

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58. ANSWER: A

Cocaine is extracted from leaves of the coca plant (*Erythroxylum coca*). Despite being a former Coca-Cola® ingredient, it is now an illegal substance, and medical use is limited to local anesthesia of mucosa. Cocaine intoxication is the second most common cause of acute drug-related emergency room visits, after alcohol. Besides patients who deliberately ingest cocaine, intoxication may also be an accident, for example in "body packers," or in children, who may find and ingest cocaine belonging to adults. Patients may experience iatrogenic toxicity due to systemic resorption of topically applied cocaine. It is noteworthy that street cocaine is often "stretched" (mixed with other substances, such as atropine analogs), which may produce complex intoxication syndromes.

PHARMACOLOGY

Cocaine exists as a hydrochloride (HCl) salt and as a free base. Cocaine HCl is water-soluble and can be administered IV or applied to mucosa ("snorted"). The melting point of cocaine HCl is too high for it to be smoked (195 degrees C [383 degrees F]). Cocaine freebase ("freebase," "crack") melts at 98 degrees C (208 degrees F) and is smoked. It is insoluble and cannot be injected. Cocaine has excellent oral/mucosal bioavailability (80% to 90%). The effect duration is 15 to 30 minutes after IV injection and smoking, ±1 hour after snorting, and up to 3 hours after oral ingestion. Cocaine is approximately 90% protein-bound and passes the blood–brain barrier. Active metabolites result from spontaneous hydrolysis (50%; benzoylecgonine, a potent vasoconstrictor with a half-life of 5 to 8 hours), plasma cholinesterase metabolism (30% to 50%; ecgonine methylester, half-life of 3.5 to 6 hours), and hepatic metabolism (5%; norcocaine). Cocaine reacts with alcohol to form benzoylmethylecgonine. It is as toxic as cocaine but has a longer duration of action. This combination dramatically increases the risk of cardiac death. When cocaine is heated during smoking, methylecgonine is formed, which contributes to bronchoconstriction.

PHARMACODYNAMICS

Cocaine's sympathicomimetic and vasoconstrictive properties are caused by presynaptic reuptake blockade of serotonin and catecholamines, and peripheral α-adrenergic agonistic activity. Cocaine is also a sodium channel blocker (it was the first local anesthetic), which in severe overdoses may lead to QRS-complex prolongation and negative inotropy. Euphoria is linked to inhibition of serotonin reuptake, and addiction is related to its dopaminergic effect. Cocaine also binds to opioid receptors.

CLINICAL MANIFESTATIONS

Table 17.26 lists potential effects of acute and chronic cocaine exposure by organ system.

MANAGEMENT OF ACUTE COCAINE TOXICITY

Most cases can be managed with supportive care and oxygen. Investigate the possibility of concurrent use of other substances and prescription drugs: alcohol, opioids, and gamma-hydroxybutyrate (GHB) are often used together with cocaine. Avoid the use of flumazenil or naloxone, as the acute withdrawal and CNS excitation that may occur with these agents may aggravate autonomic instability. Naloxone may induce life-threatening arrhythmias in patients with cocaine intoxication. Obtain blood glucose, urine and plasma toxicology screens, and a blood alcohol level. Monitor ECG and vital signs continuously. Remove visible traces of cocaine from the nostrils or mouth. Patients who have ingested cocaine may benefit from activated charcoal administration and whole-bowel irrigation with polyethylene glycol-electrolyte lavage solution.

Myocardial ischemia (on ECG) or chest pain should be treated with sublingual nitroglycerin. If there is no response, immediate coronary angiography must be obtained and aspirin should be given. Beta blockers are contraindicated, as they cause unopposed alpha agonism with worsening of coronary vasoconstriction and arterial hypertension.

Benzodiazepines (i.e., diazepam) can be used to treat agitation, autonomic hyperactivity, and hyperthermia. Treat benzodiazepine-resistant hypertension with 1 to 2.5 mg IV phentolamine (alpha antagonist) every 5 to 15 minutes, to reduce (coronary) vasoconstriction. Severe hypertension

Table 17.26 **POTENTIAL EFFECTS OF ACUTE AND CHRONIC COCAINE EXPOSURE BY ORGAN SYSTEM**

ORGAN SYSTEM	ACUTE TOXICITY
Cardiovascular (acute)	(coronary) vasoconstriction, tachycardia, arrhythmia, hypertension, diaphoresis, increased myocardial oxygen demand, myocardial ischemia, myocardial infarction, negative inotropy, congestive heart failure, increased thrombogenesis, organ infarction, atherogenesis[1], left ventricular hyperthrophy[1]
CNS	Euphoria, alertness, appetite suppression, insomnia, headache, fear, panic, delusions, hallucinations, psychomotor agitation, focal neurologic symptoms, seizures, coma, intracranial hemorrhage, hyperthermia, dependence[1], behavioral disturbance[1]
Pulmonary/airway	Dyspnea, chest pain, exacerbation of asthma/COPD, bronchospasm, angioedema[2], airway burns[2], pneumothorax[2], pneumomediastinum[2], pneumopericardium[2], "crack lung"[2], nasal septum perforation[1]
Gastrointestinal	Gastric/duodenal ulcer (perforation), ischemic colitis, intestinal infarction, metabolic acidosis
Musculoskeletal	Muscle pain, rhabdomyolysis, compartment syndrome, hyperkalemia, hypocalcemia, lactic acidosis, kidney failure
Ophthalmologic	Mydriasis, acute angle-closure glaucoma, vision loss, corneal epithelial damage
Pregnancy	Abruptio placentae, fetal growth retardation, prematurity, fetal death, prematurity

1: with chronic use, 2: with smoking.

may require IV sodium nitroprusside or nitroglycerin. Hyperthermia should be treated aggressively and rapidly.

Avoid the use of succinylcholine in patients requiring intubation because it competes for plasma cholinesterase metabolism.

KEY FACTS: COCAINE

- Cocaine is a highly potent sympathicomimetic and vasoconstrictor.
- Combinations of alcohol and cocaine produce exaggerated toxicity.
- Naloxone, succinylcholine, and beta blockers are contraindicated during cocaine intoxication.
- Supportive care, oxygen, benzodiazepines, and phentolamine are cornerstones of therapy.

ADDITIONAL READINGS

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59. ANSWER: C

60. ANSWER: E

HERBAL MEDICINES AND PERIOPERATIVE CARE

Surveys show that up to 22% to 32% of adults and 6% of children presenting for anesthesia are current users of herbal medicines. Women use herbal medicines more often than men. Most patients will not disclose this information to the anesthesiologist if it is not specifically asked for. The most popular remedies are garlic, ginseng, ginkgo, St John's wort, arnica, and echinacea. Other commonly used remedies are ephedra, kava, and valerian. One out of five patients do not know what kind of remedy they use. Patients should be asked specifically if they use herbal medicines and should be given advice about their use in the perioperative period (Table 17.27).

Although the American Society of Anesthesiologists recommends discontinuing all herbal medicines at least 2 weeks prior to anesthesia, some authors give more specific recommendations based on pharmacologic data. The websites of HerbMed (http://www.herbmed.org) and of the National Center for Complementary and Alternative Medicine (http://www.nccam.nih.gov) are useful and reliable resources about herbal medicines.

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61. ANSWER: E

Oral ***antiplatelet drugs*** are widely used for the primary and secondary prevention of acute coronary syndrome, ischemic stroke, and stent thrombosis. Parenteral antiplatelet drugs are used to prevent myocardial infarction and stent thrombosis and to improve the rate of stent and coronary

Table 17.27 **POPULAR HERBAL MEDICINES AND THEIR POTENTIAL PERIOPERATIVE CONSEQUENCES**

HERB	COMMON USE	PHARMACOLOGIC EFFECTS	POTENTIAL PERIOPERATIVE COMPLICATIONS	DISCONTINUE
Echinacea	Prophylaxis and treatment of viral, bacterial, and fungal infections	Stimulation of the immune system. Long-term use possibly Immunosuppressive.	↓ effectiveness of immunosuppressants. Possible ↑ wound infection risk with long-term use. Hepatotoxicity, especially when used with other hepatotoxic drugs.	ASAP
Ephedra (*ma huang*)	Weight loss, respiratory disease, fatigue	Indirectly and directly acting sympathomimetic	Hemodynamic instability, vasoconstriction, tachyphylaxis with ephedrine, ↑ risk of myocardial infarction, stroke	>24 hours
Garlic (*ajo*)	Modify cardiovascular disease risk (antihypertensive, lipid-lowering, anticoagulant)	Partially irreversible inhibition of platelet aggregation, ↓ serum lipid, cholesterol	Possible potentiation of other platelet inhibitors, ↑ risk of bleeding	>7 days
Ginkgo (maidenhair)	Alzheimer's disease, peripheral vascular disease, impotence (circulatory stimulant)	Inhibits platelet activating factor. Antioxidant. Modulates neurotransmitter activity.	Possible potentiation of other platelet inhibitors. ↑ risk of bleeding.	>36 hours
Ginseng	Stress protection	? Possibly similar to steroids. Partly irreversible inhibition of platelet aggregation, ↑aPTT.	↑ risk of bleeding, ↑ risk of hypoglycemia	>7 days
Kava (ava pepper)	Anxiolysis	Possible potentiation of GABA transmission	Potentiates sedative effects of anesthetic agents. Possible withdrawal syndrome after sudden abstinence. Possible hepatotoxicity	>24 hours
St. John's wort (goatweed, amber)	Depression, anxiety	Central inhibition monoamines. Induction of CYP 3A4 and 2C9.	Decreased effectiveness of cyclosporine, alfentanil, midazolam, lignocaine, calcium channel blockers, and digoxin	>5 days
Valerian (all heal)	Anxiolysis, insomnia	Potentiation of GABA neurotransmission	Potentiates sedative effects of anesthetic agents. Withdrawal-type syndrome with sudden abstinence.	Taper dose slowly or continue use

SOURCE: adapted from Ang-Lee MK, Moss J, Yuan CS. Herbal medicines and perioperative care. *JAMA.* 2001;286(2):208–216.

1. The American Society for Anesthesiologists (ASA) recommends discontinuation of all herbal medicines 2 weeks prior to surgery.

patency after percutaneous coronary angioplasty and stenting (Table 17.28).

ASPIRIN

Long years of experience have accrued with this cyclooxygenase inhibitor. In platelets, aspirin's main mechanism of action is irreversible inhibition of the production of thromboxane A_2 (TxA_2), which is an important factor involved in platelet aggregation and activation. Platelet aggregation is the process that occurs during the formation of a platelet plug, which is an important step in bleeding control. Despite the short half-life of aspirin and its metabolites, its effect on the platelet lasts for the entire 7- to 10-day lifespan of the affected platelet. Clinically, the effect fades in 4 to 6 days. Routine laboratory tests of coagulation (except measuring bleeding time) cannot detect aspirin's effect on coagulation.

DIPYRIDAMOLE

This agent is often combined with aspirin in the secondary prevention after transient ischemic attack (TIA) or ischemic stroke. Dipyridamole can also extend the lifespan of platelets in patients with prosthetic cardiac valves, in combination with oral anticoagulants. It inhibits platelet adenosine uptake. This ultimately leads to inhibition of calcium, serotonin, and ADP release from the platelet, resulting in decreased

Table 17.28 ANTIPLATELET DRUGS, MECHANISM OF ACTION, AND CLINICAL DURATION OF EFFECT

AGENT (BRAND NAME)	MAIN INDICATION	MECHANISM OF ACTION	DURATION OF EFFECT
Oral			
Aspirin (Ascal®)	(Secondary) prevention of ACS, stroke	Thromboxane A_2 inhibitor	1 platelet lifetime
Dipyridamole (Persantine®)	Secondary prevention of stroke. Prevention of perioperative thrombosis, prosthetic valve thrombosis.	Adenosine breakdown and reuptake inhibitor	±24 hours
Clopidogrel (Plavix®)	Secondary prevention of ACS, stroke. Prevention of stent thrombosis.	ADPr antagonist	1 platelet lifetime
Prasugrel (Effient®)	Secondary prevention of ACS, stroke. Prevention of stent thrombosis.	ADPr antagonist	1 platelet lifetime
Ticagrelor (Brilinta®)	Secondary prevention of ACS, stroke. Prevention of stent thrombosis.	ADPr antagonist	± 5 days
Dabigatran (Pradax®)	Prevention of VTE, PE	Thrombin inhibitor	± 24 hours
Parenteral			
Argatroban (Acova®)	Heparin-induced thrombocytopenia	Thrombin inhibitor	
Abciximab (Reopro®)	Prevention of MI after PCI, stenting	GP IIb/IIIa receptor antagonist (antibody)	12–48 hours[1]
Eptifibatide (Integrilin®)	Prevention of MI after PCI, stenting	GP IIb/IIIa receptor antagonist	4–6 hours[1]
Tirofiban (Aggrastat®)	Prevention of MI after PCI, stenting	GP IIb/IIIa receptor antagonist	4–8 hours[1]

One platelet lifetime: 7–10 days. ACS, acute coronary syndrome; ADPr, platelet ADP receptor; GP, glycoprotein; MI, myocardial infarction; PCI, percutaneous coronary intervention; PE, pulmonary embolism; VTE, venous thromboembolism. [1]: after discontinuation of infusion.

platelet adhesion. The effect on platelet aggregation is minimal. Dipyridamole is also a vasodilator and potentiates the effects of NO. This vasodilator effect may result in coronary steal in patients with poor cardiac function.

CLOPIDOGREL, PRASUGREL, AND TICAGRELOR

Clopidogrel, a thienopyridine prodrug, is transformed in the liver by CYP450 enzymes into its active metabolites. These selectively and irreversibly modify ADP receptors on the platelet surface, thus disrupting the activation, aggregation, and degranulation cascade that normally follows binding of ADP to these receptors. ADP-dependent binding of fibrinogen to platelet GP IIb/IIIa receptors is also inhibited. Prasugrel and ticagrelor have a similar mechanism of action, but the effect of ticagrelor is reversible and has a faster onset and offset than clopidogrel. Drugs from this group should be discontinued at least 7 days prior to surgery.

ABCIXIMAB, EPTIFIBATIDE, AND TIROFIBAN

Abciximab, eptifibatide, and tirofiban are a chimeric human–murine monoclonal antibody, a peptide, and a nonpeptide *glycoprotein IIb/IIIa (GPIIb/IIIa) receptor antagonist*, respectively. GPIIb/IIIa is a platelet surface receptor that binds fibrinogen and von Willebrand factor, leading to platelet activation and aggregation. The potent IV antiplatelet agents from this group are usually combined with heparin to prevent embolic events around percutaneous coronary interventions. Their effects last for a shorter time than those of the oral antiplatelet drugs.

ADDITIONAL READING

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62. ANSWER: C

HEPARIN

Heparin, a large glycosaminoglycan molecule present in human mast cells, was first isolated in 1922. Commercial formulations are derived from bovine or porcine sources. The low-molecular-weight fraction forms a complex with antithrombin III (ATIII), which inhibits factor Xa. The

high-molecular-weight fraction of heparin catalyzes binding of ATIII to thrombin (factor IIa), thus inhibiting thrombin. Heparin also inhibits the release of tissue factor, inhibits (but may also activate) platelets, and initiates fibrinolysis.

The onset of anticoagulation is established immediately after IV administration and is somewhat slower after subcutaneous injection. Heparin is eliminated via the kidneys (50%) and via hepatic metabolism. In health, its half-life is ±1 to 2 hours, but this is significantly increased in patients with liver or kidney disease, or when the heparin dose exceeds 100 U/kg. The required loading dose depends on the indication and usually varies between 50 and 400 U/kg. Monitoring of activated partial thromboplastin time (aPTT) and/or activated clotting time (ACT) is vital in maintaining adequate levels of anticoagulation because these vary considerably. For high-dose heparin therapy, automated protamine titration is now rarely used. Thromboelastography with heparinase is also suitable to monitor high-dose heparin therapy.

Heparin may induce thrombocytopenia (HIT), an immune-mediated adverse effect seen mostly after repeated administration.

PROTAMINE

When immediate reversal of heparin-induced anticoagulation is required, protamine can be given. Protamine rapidly binds to heparin molecules to form a stable, inactive salt. One mg of protamine neutralizes ±80 to 100 units of heparin (Table 17.29). The efficacy of reversal should be checked with coagulation studies (aPTT, thrombin time, ACT, automated protamine titration).

Protamine has some potentially serious adverse effects, including noncardiogenic pulmonary edema, pulmonary vasoconstriction, right heart decompensation, and cardiovascular collapse. Because it is derived from salmon sperm, it may induce potentially serious hypersensitivity reactions. Extra caution is advised in patients who have received protamine before (e.g., as slow-release protamine–insulin), patients with fish allergies, and vasectomized men. The use of antihistamines and corticosteroids should be considered when such patients require protamine reversal. Protamine also causes direct histamine release and should be administered slowly.

Table 17.29 **PROTAMINE DOSING**

HEPARIN ROUTE	PROTAMINE DOSE
Subcutaneous	1–1.5 mg/100 U heparin
IV, bolus	1–1.5 mg/100 U heparin
IV, 30–60 min after last bolus	0.5–0.75 mg/100 U heparin
IV, 2 hours after last bolus	0.25–0.375 mg/100 U heparin
IV, continuous	1 mg/100 U heparin over the last 4 hours

Use a test dose to check for intolerance. Administer slowly (±5 mg/min).

LOW-MOLECULAR-WEIGHT HEPARINS

In the early 1990s, the first low-molecular-weight heparins (LMWHs) were registered. This group now consists of enoxaparin, dalteparin, tinzaparin, and fondaparinux. The latter is not a heparin but has similar anti-Xa activity. These agents have little effect on coagulation laboratory studies. Anti-Xa level tests exist but do not predict the risk of bleeding and are not recommended for routine use. Protamine can be used to reverse the effects of enoxaparin, dalteparin, and tinzaparin but not fondaparinux. However, protamine does not completely antagonize the anti-Xa activity of agents, and reversal will be incomplete.

CONSIDERATIONS FOR REGIONAL AND NEURAXIAL ANESTHESIA

Combinations of antiplatelet drugs and LMWH increase the risk of epidural and spinal bleeding after neuraxial techniques. After traumatic attempts, the first LMWH dose should be delayed for 24 hours postoperatively. Attempts to place a neuraxial blockade or to remove an indwelling neuraxial catheter in patients on once-daily LMWH thromboprophylaxis should be timed 10 to 12 hours after the last dose.

KEY FACTS: HEPARIN

- IV heparin has an immediate onset. Its T½β of 1 to 2 hours is prolonged in patients with liver or kidney dysfunction, or with doses exceeding 100 U/kg.
- aPTT and ACT are used to monitor the effect of heparin but not of the LMWHs.
- 1 mg of protamine inactivates 80 to 100 units of heparin.
- Antiplatelet drugs and heparins increase the risk of bleeding from neuraxial techniques. Guidelines are available for timing and doses.

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63. ANSWER: D

Dexmedetomidine is an α_2-adrenergic agonist. It is the s-enantiomer of medetomidine, which is used in veterinary practice. Similar to clonidine, it has analgesic, sedative, and anxiolytic effects, but has an eight times higher affinity for the α_2 receptor. Such receptors are found on blood vessels, where binding induces vasoconstriction (leading to elevated blood pressure), and on sympathetic terminals, where binding inhibits norepinephrine release. Central α_2-receptor binding induces sedation, reduced sympathetic activity (leading to lower blood pressure), and increased vagal stimulation of the heart. The α_2 receptors in the dorsal horn of the spinal cord mediate the analgesic and opioid-potentiating properties of α agonists.

Dexmedetomidine can be used as an adjunct in general anesthesia, or as a single agent in procedural analgosedation, or for sedation in the intensive care unit.

PHARMACOKINETICS

Dexmedetomidine HCl is water-soluble. It is metabolized in the liver via glucuronidation, to inactive metabolites, and via cytochrome P450, subtype 2A6, to 3-OH-dexmedetomidine and 3-carboxy-dexmedetomidine. The metabolites are excreted via the kidneys. The elimination half-life ($T\frac{1}{2}\beta$) is ±2 hours, and clearance is 39 L/hour. Dexmedetomidine is 94% protein-bound. The free fraction of dexmedetomidine is increased in patients with liver and kidney failure, and a dose reduction may be appropriate. Hepatic metabolism in patients with severe liver failure is reduced by ±50%. When dexmedetomidine is abruptly discontinued after infusions of more than 24 hours, withdrawal symptoms may occur, including agitation and hypertension. A transient phase of hypertension after the loading dose may be induced by binding of dexmedetomidine to vascular α_2 receptors (also seen with clonidine), and seldom requires action.

SPECIFIC ADVANTAGES AND TRADE-OFFS

Dexmedetomidine can be administered via many routes, including IM, IV, oral, and mucosal (as a nasal spray). Its use is associated with reduced opioid and hypnotic agent requirements around anesthesia, without producing significant respiratory depression. Patients sedated with dexmedetomidine can be roused easily. Added benefits are its relatively short duration of action, lack of effect on gut motility, and the absence of active metabolites, which makes dexmedetomidine useful in procedural sedation and fast-track surgery.

During cardiac surgery, dexmedetomidine can be used to blunt the postoperative catecholamine surge, and this may lead to reduced myocardial oxygen consumption and reduced mortality. Dexmedetomidine may also have a renoprotective effect. Its effects on the brain require further research, but studies have shown reduced duration of postoperative delirium after cardiac surgery in patients treated with dexmedetomidine.

Dexmedetomidine may induce significant hypotension and bradycardia, which can be treated with atropine or glycopyrrolate. This effect is pronounced in patients with hypovolemia, or patients with low cardiac output due to valvular or myocardial disease.

DOSING

For sedation the IV loading dose is 1 μg/kg, in 10 minutes; the maintenance dose is 0.2 to 0.7 μg/kg/hr, titrated to effect. Children may need higher doses—loading doses as high as 2 μg/kg in 10 minutes, repeated until the desired effect is reached, and a maintenance dose of 1 μg/kg/hr have been reported in the literature.

KEY FACTS: DEXMEDETOMIDINE

- Dexmedetomidine is an α_2 agonist with sedative and anxiolytic effects.
- It is metabolized by the liver, with a $T\frac{1}{2}\beta$ of ±2 hours in healthy persons.
- Patients sedated with dexmedetomidine can be woken up easily.
- Hypotension and bradycardia are common, but dexmedetomidine does not cause respiratory depression or inhibition of gut motility.

ADDITIONAL READINGS

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64. ANSWER: E

Ketorolac is an unselective cyclooxygenase (COX) inhibitor with anti-inflammatory, antipyrectic, and analgesic properties. In the United States, ketorolac is the only nonsteroidal anti-inflammatory drug (NSAID) available for parenteral administration. NSAIDs are effective postoperative analgesics and can be combined with opioids to improve pain relief and reduce opioid requirement. However, its significant

adverse effect profile has led to registration withdrawal of ketorolac in Germany and France.

PHARMACOLOGY

Ketorolac is mainly metabolized in the liver, but less than 50% of the drug is actually metabolized. More than 90% is excreted by the kidneys. Its elimination half-life is ±5.3 hours.

ADVERSE EFFECTS

Gastrointestinal irritation, ulceration, and bleeding are seen with long-term use but may also occur acutely with short-term use. The risk is dose-dependent, and increased in the elderly. The ketorolac dose should be reduced in this group of patients, and agents for gastric protection should be considered.

In contrast to aspirin, which irreversibly modifies COX in platelets, the effect of ketorolac on COX in platelets is reversible. Ketorolac is not normally associated with increased surgical blood loss. However, the perioperative combination of anticoagulants or antiplatelet drugs and NSAIDs does pose a risk of bleeding.

Although NSAIDs are known to impair renal function, this is not usually a significant problem in patients with good kidney function. However, attention must be paid when other insults to kidney function are anticipated (e.g., gentamicin use or hypovolemia).

Patients with asthma and chronic rhinitis are at increased risk of developing bronchospasm when given NSAIDs, particularly aspirin. Ketorolac should be withheld from patients with a history of NSAID-induced bronchospasm.

In short, patients should always receive the smallest possible ketorolac dose, for the shortest possible duration. The longest advised duration of therapy is 5 days. Patients with a history of hypersensitivity to other NSAIDs should not be given ketorolac.

Clinicians should familiarize themselves with ketorolac's boxed warnings before administering the agent.

KEY FACTS: KETOROLAC

- Ketorolac is an unselective COX inhibitor with a T½β of ±5.3 hours.
- The risk of gastrointestinal ulceration and bleeding is increased in the elderly.
- NSAIDs impair kidney function, but healthy patients are usually not affected.
- Asthma and chronic rhinitis predispose to ketorolac-induced bronchospasm.
- Ketorolac should always be used in the smallest possible dose and for not more than 5 days.

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65. ANSWER: E

Acetaminophen, known as paracetamol in some countries, is one of the most widely used medicines worldwide. It is safe and well tolerated, has virtually no important interactions with other medications, and is extraordinarily inexpensive.

MECHANISM OF ACTION

Acetaminophen has analgesic and antipyretic effects but has only minimal anti-inflammatory action. Its exact mechanism of action is unclear. Acetaminophen inhibits COX subtypes 1, 2, and 3, but with negligible gastrointestinal and platelet effect. The effect is thought to originate mainly in the central nervous system. Not only COX inhibition but also effects on serotonergic and cannabinoid systems seem to be involved. A metabolite of acetaminophen that is formed in the brain and spinal cord, N-arachidonylphenolamine (AM404), inhibits cellular uptake of an endocannabinoid (anandamide) agonist of the TRPV1 vanilloid receptor, which is involved in nociception. Paracetamol's serotonergic effects could possibly explain why $5HT_3$ antagonists partially abolish its analgesic effect.

PHARMACOLOGY

Acetaminophen is available in oral, rectal, and IV formulations. The oral bioavailability is ±63% to 89% in adults. Caffeine and prokinetic drugs increase absorption speed, but co-ingestion of food or morphine administration decreases absorption speed. Rectal bioavailability is less predictable, and absorption is slower. In plasma, acetaminophen is minimally protein-bound and non-ionized. It thus crosses the placenta and blood–brain barrier. Peak plasma concentration is reached ±45 minutes after oral administration and is slower after rectal administration. The liver metabolizes 90% of the acetaminophen dose to nontoxic glucuronides and sulphites, which are eliminated by the kidneys. The other 10% is transformed into the highly toxic N-acetyl-p-benzoquinoneimine (NAPQI) by cytochrome P450. Reaction of NAPQI with glutathione results in conjugates that can be eliminated by the kidneys. When large amounts of paracetamol (>6 to 8 g) are ingested, glutathione becomes depleted and NAPQI accumulates, leading

to hepatic necrosis, which may be fulminant in very high doses.

In adults, the elimination half-life (T½β) of acetaminophen is 2 to 4 hours. In newborns, this is 4 to 5 hours; it may be increased to 11 hours in premature infants.

The analgesic and antipyretic effect of acetaminophen is seen at plasma concentrations between 10 and 20 μg/mL. Hepatotoxicity does not usually occur below 150 μg/mL.

HEPATOTOXICITY

At therapeutic doses, hepatotoxicity is extremely rare. Normal doses do not exacerbate stable chronic liver disease. In severe liver disease, the T½β is increased, and the maximum dose should not exceed 3000 mg per day.

The treatment of an overdose of paracetamol should be initiated early, ideally within 8 hours after administration. IV n-acetylcysteine can be given (150 mg/kg IV over 60 minutes, then 50 mg/kg over 4 hours, then 6.25 mg/kg per hour for 16 hours). Gastrointestinal decontamination with activated charcoal is also beneficial.

PERIOPERATIVE USE

Acetaminophen effectively reduces the opioid and NSAID requirement perioperatively. If therapeutic concentrations are desired quickly, for example in ambulatory surgery or in the emergency department, IV paracetamol provides therapeutic plasma levels more quickly. This route of administration is also quicker and more reliable compared to rectal administration and can be used in patients with restricted oral intake.

DOSING

Adults: 4 doses per day, 1 g

Chronic use: maximum 2.5 g/day

Chronic alcohol-abusing patient: maximum 2 g/day

Severe liver disease: maximum 3 g/day

Severe kidney disease: minimum dose interval 6 hours

Children >12 yrs: >50 kg 4 doses per day 1 g, <50 kg 4 doses per day 15 mg/kg (maximum 3 g/day, minimum dose interval 4 hours)

Children <12 yrs: 10 mg/kg (minimum dose interval 4 hours)

KEY FACTS: ACETAMINOPHEN

- Acetaminophen is an effective, safe, well-tolerated, and inexpensive first-line analgesic.
- Its mechanism of action is complex and poorly understood.
- Acetaminophen has virtually no antiplatelet or gastrointestinal effects.
- At normal doses, hepatotoxicity is extremely rare. Fulminant hepatotoxicity is seen with large overdoses. N-acetylcysteine can be given to limit these effects.

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66. ANSWER: A

Nitrovasodilators can be used in the acute management of systemic or pulmonary hypertension. These agents donate nitric oxide (NO) to smooth muscle cells in the vascular wall. NO stimulates guanylyl cyclase, leading to increased cGMP levels. This in turn decreases intracellular Ca^{2+}, which leads to arterial and venous vasodilation. Typically, tolerance to nitrovasodilators is developed over time. All nitrovasodilators, including inspired NO, may cause methemoglobinemia, via a mechanism described elsewhere (Question 51).

NITROGLYCERIN

The effect of nitroglycerin is dose-dependent: at 30 to 40 μg/min, it causes venodilation and dilation of large coronary arteries. At much higher doses (±250 μg/min), it also causes arteriolar dilation. In other words, it predominantly dilates capacitance vessels rather than resistance vessels. Sublingual tablets or sprays with nitroglycerin offer acute relief of angina pectoris due to its effect on coronary arteries and also due to preload reduction, leading to reduced myocardial wall stress. Nitroglycerin reduces pulmonary vascular resistance (PVR), which relieves the right heart and improves cardiac output in patients with pulmonary hypertension and heart failure. Higher doses of intravenous nitroglycerin can be used to manage acute systemic hypertension. The venodilation induced by nitroglycerin leads to reduced left ventricular preload and reduced cardiac output in patients with only slightly increased PVR. Nitroglycerin has a rapid onset of action, and an elimination half-life (T½β) of 1 to 4 minutes. It is metabolized in the liver and eliminated via the kidneys. IV nitroglycerin doses range between 0.1 and 4 μg/kg/min.

NITROPRUSSIDE

Nitroprusside is an unstable molecule and rapidly degrades to NO and other metabolites. Unlike nitroglycerin, nitroprusside produces equivalent arterial and venous vasodilation. It is mostly used to treat hypertensive crises but can also be used to treat pulmonary hypertension. Normal doses range between 0.1 and 0.8 μg/kg/min IV. It also has rapid onset and offset. Nitroprusside eliminates hypoxic pulmonary vasoconstriction, which can cause hypoxemia in patients with lung disease with poor ventilation/perfusion match. It also reduces right coronary artery perfusion. Nitroprusside administration may induce profound systemic hypotension. Its toxic metabolite cyanide is converted to thiocyanide in the liver and kidney. Cyanide that is not converted to thiocyanide inhibits cellular aerobic respiration and is thus highly toxic. Risk factors for toxicity are high dose (>250 μg/min), long duration of therapy (>48 hours), liver failure, or poor cardiac output. Toxicity manifests as tachyphylaxis for vasodilators, elevated mixed venous oxygen tension, and metabolic acidosis. If toxicity occurs, nitroprusside administration should be discontinued. 100% oxygen and an IV bolus of 150 mg/kg thiosulphate should be given.

INSPIRED NO

NO itself can be administered as an inhalational gas. It produces selective pulmonary vasodilation, and bronchodilation, but not systemic hypotension, because it is bound to hemoglobin if not used locally. Inspired NO is used to treat acute respiratory distress syndrome (ARDS) and pulmonary hypertension in adults, and hypoxemic respiratory failure in persistent pulmonary hypertension, meconium aspiration, and diaphragmatic hernia in neonates. It improves gas exchange by increasing blood flow to "working" alveoli, thus reducing shunt and improving the ventilation/perfusion match. This is an advantage over systemic nitrovasodilators, as they also improve blood flow to poorly ventilated alveoli. However, oxygenation may also be compromised because inspired NO inactivates hypoxic pulmonary vasoconstriction. Doses range between 1 and 40 ppm. Inspired NO must not be suddenly discontinued because severe rebound hypoxemia and pulmonary hypertension may occur.

KEY FACTS: NITROGLYCERIN

- Nitroglycerin predominantly dilates veins and large coronary arteries and reduces pulmonary vascular resistance.
- Nitroprusside produces equivalent venous and arterial vasodilation.
- Therapy for more than 48 hours or at high doses (>250 μg/min) with nitroprusside carries a risk of cyanide toxicity.
- Inspired NO produces selective pulmonary vasodilation and bronchodilation.
- All nitrovasodilators can induce methemoglobinemia.

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67. ANSWER: E

Dopamine is an endogenous precursor of norepinephrine, with dose-dependent cardiovascular effects (Table 17.30). Dopamine was once the most widely used vasoactive agent, but concerns about its effectiveness and adverse effects have damaged its reputation. Dopamine is used to treat hypotension secondary to heart failure, sepsis, and anaphylaxis. Although dopamine may increase urinary output, it does not prevent kidney failure. Historical beliefs about improvement of splanchnic perfusion have also been proven to be false. Dopamine has been shown to adversely affect gastrointestinal motility in critically ill patients.

Although dopamine can be used for short-term hemodynamic support in patients with primary volume loss, fluid resuscitation must be the definitive treatment, and dopamine support should be continued for the shortest possible duration.

25% of the dose is metabolized to epinephrine in adrenergic nerve endings. The other 75% is metabolized in blood, and in the liver, to inactive metabolites. The elimination half-life is 1 to 5 minutes.

Table 17.30 **DOPAMINE: DOSE-DEPENDENT HEMODYNAMIC EFFECTS**

DOSE	RECEPTOR	EFFECT
<2 mcg/kg/min	D_1 (coronary, splanchnic, renal)	Vasodilation, natriuresis
2–5 mcg/kg/min	β_1	Positive inotropy, ↑ systolic blood pressure
5–20 mcg/kg/min	α_1	Generalized vasoconstriction, ↑ systolic blood pressure
>20 mcg/kg/min	$>>\alpha_1$	↑ systolic blood pressure, ↓ splanchnic/renal vasodilation

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68. ANSWER: D

Dobutamine is a synthetic catecholamine with β_1- and β_2-agonistic properties. Dobutamine is composed of two stereo-isomers that have opposing agonist and antagonist effects on α receptors. At doses of less than 5 μg/kg/min, it has no α-adrenergic effects. Stimulation of β-adrenergic receptors leads to increased intracellular calcium concentration, via upregulation of adenylyl cyclase. β_1 receptors are found on cardiac myocytes. Stimulation results in increased myocardial contractility but may also increase heart rate. Dobutamine improves perfusion and oxygen delivery in patients with poor cardiac output, which may also lead to decreases in heart rate. β_2 receptors are found on vascular smooth muscle. Stimulation results in modest peripheral vasodilation. The combination of vasodilation and increased myocardial contractility reduces preload and afterload and improves left ventricular/arterial coupling. At high doses, the α_1-agonistic effect of (-)-dobutamine prevents further vasodilation and eventually results in vasoconstriction. Dobutamine has no effect on dopamine receptors.

The inotropic and chronotropic effect of dobutamine increases cardiac oxygen consumption. This may lead to ischemia in patients with coronary artery disease. This mechanism is used to identify ischemic areas of the heart in dobutamine stress ultrasonography.

Dobutamine may increase the incidence of arrhythmia.

The starting dose of IV dobutamine is 0.5 to 1 μg/kg/min, and can be increased to a maximum of 40 μg/kg/min. Dobutamine has a very short half-life. It has direct onset, and the duration of effect is minutes.

KEY FACTS: DOBUTAMINE

- Dobutamine is a synthetic β_1 and β_2 agonist, producing positive inotropy and modest peripheral vasodilation.
- Dobutamine increases cardiac oxygen consumption.
- At doses above 5 μg/kg/min, an α_1-agonistic effect occurs, preventing further vasodilation.

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69. ANSWER: D

EPHEDRINE

Ephedrine is used perioperatively to treat hypotension with concurrent bradycardia, such as often happens around anesthesia induction. It is a natural product, found in the ephedra plant. It has direct and indirect effects on adrenoreceptors. Ephedrine is transported into adrenergic presynaptic nerve terminals, where it displaces norepinephrine from intracellular binding sites. The excess free norepinephrine is subsequently released and stimulates postsynaptic adrenergic receptors. Ephedrine binds directly to β_2 receptors, which limits the increase in arterial pressure.

The effect of ephedrine is thus similar to that of norepinephrine: increased cardiac output, arterial blood pressure, and systemic vascular resistance. However, its effects depend on endogenous reserves of norepinephrine in nerve terminals. Ephedrine is thus not very effective in patients with depleted catecholamine stores, and tachyphylaxis will develop quickly.

Normal doses of ephedrine are 5 to 25 mg IV, repeated until the desired effect is observed, with a maximum of 150 mg/24 hours. Ephedrine is excreted mostly unchanged by the kidneys.

PHENYLEPHRINE

This agent is commonly used perioperatively as well. It is a pure α_1 agonist. It is a less potent α agonist than epinephrine and norepinephrine. It is particularly suitable for the treatment of hypotension with tachycardia, because reflex bradycardia is seen concomitantly with blood pressure increase. The vasoconstrictive effect of phenylephrine produces increased preload, which may lead to increased cardiac output, but also increases afterload, which increases cardiac work.

KEY FACTS: EPHEDRINE AND PHENYLEPHRINE

- Ephedrine has direct and indirect effects on adrenoreceptors.

- Ephedrine's effects are similar to those of norepinephrine.
- Phenylephrine is a pure α_1 agonist. Reflex bradycardia accompanies the blood pressure increase.

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70. ANSWER: B

71. ANSWER: B

EPINEPHRINE

Epinephrine is an endogenous agonist of α_1, β_1, and β_2 adrenoreceptors. It is produced and stored in the chromaffin cells in the adrenal medulla. It is used during cardiac resuscitation, to treat anaphylaxis and acute asthma, and to manage hypotension in the intensive care unit.

The effect of parenterally administered epinephrine is increased systolic blood pressure. Diastolic blood pressure is less affected. β_1 receptors are expressed on cardiac myocytes, where stimulation produces positive inotropy, and on sinoatrial node cells, where stimulation produces positive chronotropy. Myocardial relaxation is also improved, which enhances diastolic function. Epinephrine enhances the conduction velocity of electric impulses in the heart (positive dromotropy), which may induce arrhythmias.

The α_1-agonistic effect produces profound arteriolar vasoconstriction, mainly in the cutaneous, splanchnic, and renal vasculature. Perfusion through skeletal muscle may be improved, due to agonism at the β_2 receptor. The affinity of epinephrine for the β_2 receptor is greater than for the α_1 receptor. Effectively, this means that at lower doses, the β_2 effect predominates, and that the α_1 effect is first seen with higher doses. Very high doses of epinephrine may thus result in such severe vasoconstriction that the resultant increase in afterload adversely affects cardiac output. The addition of a nitrovasodilator may be required to improve cardiac output when very high epinephrine doses are used.

The positive inotropic and chronotropic effect, combined with increased afterload, increases myocardial oxygen consumption and requires sufficient coronary blood flow. However, epinephrine may compromise coronary vasodilation due to its α and β agonism. In the presence of beta blockade, epinephrine behaves like an unopposed α agonist and may produce severe vasoconstriction without positive inotropic and chronotropic effect.

The addition of epinephrine to local anesthetics produces local vasoconstriction and prevents rapid systemic uptake of the local anesthetic. This allows for higher doses of local anesthetic and prolongs the duration of block effect. The total injected dose of epinephrine should not exceed 200 μg (= 40 mL of 1:200,000 solution).

Epinephrine is formulated in different concentrations, mostly 1:1,000, 1:10,000, and 1:200,000 (Table 17.31). Ideally, catecholamines should be administered via central venous lines to prevent damage to peripheral veins. Doses required for the management of hypotension start at 0.1 to 0.5 μg/kg IV, followed by continuous infusion titrated to effect. Epinephrine may also be used to treat anaphylactic/anaphylactoid reactions; normal doses range between 100 and 500 μg IM and SC, and may have to be repeated. For epinephrine doses in Advanced Cardiac Life Support (ACLS), please refer to the most recent tables for up-to-date recommendations.

NOREPINEPHRINE

This endogenous catecholamine is released from adrenergic nerve terminals in response to sympathetic input. Norepinephrine stimulates α_1 and β_1 adrenoreceptors and produces significant vasoconstriction, positive inotropy, and increased arterial blood pressure. Venous capacitance is reduced, which increases venous return and improves stroke volume. It has a less profound effect on heart rate because the normal baroreceptor reflex response to vasoconstriction counteracts β_1-induced chronotropic effects. It does not have significant effects on β_2 adrenoreceptors (Table 17.32).

The profound α_1-agonist effect of norepinephrine may reduce the perfusion of renal and splanchnic beds. This

Table 17.31 **CONVERSION TABLE: CONCENTRATIONS AND PERCENTAGES**

1,000 mg/mL (1 g/mL = 1 kg/L)	**100%**	**1:1**
100 mg/mL	**10%**	**1:10**
10 mg/mL (1 g/dL)	**1%**	**1:100**
1 mg/mL	**0.1%**	**1:1,000**
0.1 mg/mL (100 μg/mL)	**0.01%**	**1:10,000**
0.01 mg/mL (10 μg/mL)	**0.001%**	**1:100,000**
0.005 mg/mL (5 μg/mL)	**0.0005%**	**1:200,000**

As a rule, × % = 10 × mg/mL.

Table 17.32 **RECEPTOR PROFILE OF SOME VASOPRESSOR AGENTS**

AGENT	α_1	β_1	β_2	D_1
Dopamine	•	•		•
Dobutamine	•	•	•	
Ephedrine	•	•	•	
Epinephrine	•	•	•	
Norepinephrine	•	•		
Phenylephrine	•			

limits its use for long duration or in high doses. However, norepinephrine may improve kidney perfusion in patients with deep hypotension, with concurrent poor kidney perfusion and oliguria.

Norepinephrine is often combined with dobutamine in the management of septic shock. When norepinephrine (with or without dobutamine) is used, normotension should be the treatment goal because higher blood pressures are associated with deleterious levels of vasoconstriction.

The arrhythmogenic potential of norepinephrine is substantially less than that of epinephrine.

Both epinephrine and norepinephrine have a very short duration of action, and accidental discontinuation of the infusion or accidental boli (kinked tubing, line and syringe pump manipulation, patient manipulation and transport) may lead to very steep blood pressure changes.

KEY FACTS: EPINEPHRINE AND NOREPINEPHRINE

- Epinephrine is an endogenous α_1, β_1, and β_2 agonist, producing positive inotropy, positive chronotropy, positive dromotropy, increased systolic blood pressure, and peripheral vasoconstriction.
- The total epinephrine dose added to local anesthetic should not exceed 200 μg.
- Norepinephrine is an endogenous α_1 and β_1 agonist, producing positive inotropy, vasoconstriction, and increased arterial blood pressure.
- Norepinephrine has less arrhythmogenic potential than epinephrine.

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72. ANSWER: C

Intravenous beta blockers are used to treat hypertension and tachyarrhythmias. They differ mostly in receptor selectivity and duration of action.

PROPRANOLOL

Propranolol is nonselective. Its β_1-antagonist effect reduces heart rate and cardiac output, whereas its β_2-antagonist effect produces peripheral vasoconstriction and bronchoconstriction. Concomitant administration of catecholamines may result in profound vasoconstriction. Concomitant administration of opioids may produce severe bradyarrhythmias. Propranolol may induce bronchospasm, especially in patients with preexistent asthma.

Propranolol is metabolized in the liver. Cytochrome P450, subtype 2D6, is involved in its biotransformation, and active metabolites exist. Its half-life ($T½\beta$) is ±4 hours.

LABETALOL

Labetalol is not only a beta blocker but also an alpha blocker. Metabolism takes place in the liver. When given intravenously, the α:β potency ratio is 1:7. It is approximately three times less potent than propranolol and metoprolol. The $T½\beta$ of labetalol is approximately 4 hours.

ESMOLOL

Esmolol is the remifentanil of the beta blockers: it is rapidly degraded by aspecific and red blood cell esterases. Its metabolism is thus independent of liver and kidney function. It also has rapid onset and a very short duration of action. Its $T½\beta$ is only 9 to 10 minutes. The analogy with remifentanil ends here, though, because esmolol is not very potent at all: it is approximately 50 times less potent than propranolol and metoprolol. It is a relatively selective β_1 blocker and produces β_2 blockade only with high doses. It therefore has only minimal effect on bronchial and vascular tone. These properties make esmolol useful perioperatively, especially for the management of transient sympathetic stimulation and induced hypotension.

KEY FACTS: BETA BLOCKERS

- Propranolol is a nonselective beta blocker, its $T½\beta$ is ±4 hours.

- Labetalol is an alpha and beta blocker, and it is about three times more potent than propranolol.
- Esmolol is a relatively selective β_1 blocker and minimally affects bronchial and vascular tone.
- Esmolol is rapidly degraded by aspecific esterases, with a T½β of ±10 minutes.

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73. ANSWER: A

Perioperative discontinuation of psychoactive medication is not always an option. Careless discontinuation of lithium or antidepressants may lead to relapse of symptoms, increase the risk of suicidal behavior, and induce withdrawal syndromes. However, many of these agents have significant interactions with anesthesia drugs.

SELECTIVE SEROTONIN/ NORADRENALIN REUPTAKE INHIBITORS (SSRIs/SNRIs)

These agents may precipitate the serotonin syndrome (described in detail elsewhere [Question 57]), when other agents inhibiting their metabolism (proton pump inhibitors, cimetidine) or agents affecting serotonin turnover (tramadol, meperidine) are coadministered. Conversely, SSRIs and SNRIs are inhibitors and substrates of CYP450 enzymes (at varying potencies). Particularly affected is the clearance of drugs metabolized via CYP 2D6, such as metoprolol, haloperidol, and flecainide.

SSRIs and SNRIs inhibit platelet aggregation and may increase perioperative blood loss when combined with other agents that increase bleeding time (e.g., NSAIDs).

When discontinuation of these agents is required, consider their sometimes very long elimination half-lives.

TRICYCLIC ANTIDEPRESSANTS (TCAs)

The elimination speed of TCAs is very sensitive to induction or inhibition of CYP450 enzymes. Interaction with anesthetic drugs is therefore likely. TCAs increase central and peripheral adrenergic tone by inhibiting reuptake of noradrenalin, serotonin, and dopamine into presynaptic nerve endings. The blood pressure response to directly acting sympathicomimetics (norepinephrine, epinephrine, and phenylephrine) is strongly increased: perilous increases in blood pressure may be seen. Remember that epinephrine may be admixed with local anesthetics administered by surgeons. The sedative effect of barbiturates is potentiated by TCAs.

Consider carefully if the manifold interactions and contraindications of TCAs and anesthetics drugs outweigh the risk of symptomatic relapse. Slowly taper the TCA dose, and discontinue at least 2 weeks prior to anesthesia.

LITHIUM

The risk of relapse mania or depression is very high when lithium is suddenly withdrawn. Lithium has a narrow therapeutic index (0.5 to 1.2 mmol/L), and toxicity frequently occurs. It is cleared via the kidneys, dependent on glomerular filtration rate (GFR). Drugs and hemodynamic changes that reduce GFR may elicit lithium toxicity. Of special concern are NSAIDs, diuretics, tetracyclines, phenytoin, and cyclosporine. Lithium may potentiate the neuromuscular blockade.

Toxicity is characterized by dose-dependent neuropsychiatric deterioration ranging from tremor, fasciculations, choreoatheotic movements, hyperreflexia, and clonus to seizures, coma, and cardiovascular collapse. Dysrhythmia and complete heart block may occur, especially in patients with preexistent heart disease. Volume resuscitation and dialysis are the most important methods of lithium intoxication treatment.

MONOAMINE OXIDASE INHIBITORS (MAOIs)

MAOIs irreversibly inhibit the enzyme monoamine oxidase (MAO), an intraneuronal enzyme that deaminates serotonin, norepinephrine, and dopamine. Indirectly acting sympathicomimetic agents administered to patients treated with MAOIs may precipitate hypertensive crisis. The response to directly acting sympathicomimetics is less severe because these can also be metabolized by catechol-O-methyltransferase (COMT). MAOIs potentiate the effect of barbiturates and opioids. Meperidine must not be combined with MAOIs, as the combination precipitates either severe CNS stimulation or CNS depression. Phenelzine lowers plasma cholinesterase activity and may increase the duration of action of succinylcholine and other substrates of this enzyme (see Question 2). Combinations of MAOIs with other agents affecting serotonin turnover may precipitate the serotonin syndrome.

Ideally, MAOIs should be discontinued 2 to 3 weeks prior to anesthesia. Get specialist psychiatric advice when withdrawing this class of medication.

KEY FACTS: ANTIDEPRESSANTS AND ANESTHESIA

- Rapid discontinuation of antidepressants may cause relapse and withdrawal.
- SSRIs and SNRIs are substrates and inhibitors of CYP450, mainly subtype 2D6.
- With TCAs, profound blood pressure increases may follow administration of direct-acting catecholamines.
- Drugs and hemodynamics may reduce the glomerular filtration rate and induce lithium toxicity.
- MAOIs should be discontinued 2 to 3 weeks prior to anesthesia.

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74. ANSWER: D

Digoxin is a cardiac glycoside used to control heart rate in atrial fibrillation (AF), and, as an addition to beta blockers and angiotensin-converting enzyme (ACE) inhibitors, in the treatment of heart failure.

Digoxin reversibly inhibits Na^+/K^+-ATPase in the cardiac myocyte. This ion pump generates the extracellular sodium gradient that drives the Na^+/Ca^{++} exchanger, which normally removes Ca^{++} from the cell. Without the sodium gradient, more calcium accumulates in the myocyte, resulting in a more forceful contraction of the heart muscle (positive inotropy). Digoxin also inhibits Na^+/K^+-ATPase in the renal tubuli. This causes reduced sodium reabsorption and increased diuresis.

Furthermore, digoxin increases the baroreceptor sensitivity, leading to decreased sympathetic drive and mild negative chronotropy. Via other mechanisms, digoxin increases parasympathetic tone. In patients with heart failure, digoxin reduces venous tone and systemic vascular resistance. In patients without heart failure, it is a direct vasoconstrictor. This is most likely explained by the effect of digoxin on the increased sympathetic tone seen in heart failure. Already at low doses, digoxin reduces plasma renin, aldosterone, and norepinephrine.

The effect of digoxin on cardiac electrophysiology is dose-dependent. At plasma concentrations between 1 and 2 ng/mL, automaticity and atrioventricular nodal velocity are reduced and the effective refractory period is increased. At higher doses, digoxin toxicity can occur, which is characterized by decreased atrioventricular conduction, leading to AV block and ventricular dysrhythmias (VT/VF). Other signs of toxicity are anorexia, nausea, vomiting, headache, drowsiness, and altered serum electrolytes. In patients with toxicity, electrolyte imbalances should be corrected. Bradycardia and AV block can be managed with atropine or a pacemaker. When VT occurs, lidocaine can be administered. Severe toxicity leads to increased serum potassium and potentially asystole. In such cases, digitalis antibodies can be given.

The small therapeutic range of digoxin is one of its major trade-offs. Digoxin is not more effective at the high end of its safe plasma concentration scale, and target levels should ideally remain below 1 ng/mL. Plasma concentrations should be measured 8 to 12 hours after the previous dose. Clinically stable patients do not normally require therapeutic drug monitoring, but regular kidney function, sodium, potassium, and magnesium measurements are recommended. Hypomagnesemia, often seen in patients taking diuretics, predisposes to digoxin toxicity. Hypokalemia predisposes to toxicity by reducing renal excretion of digoxin and increasing its uptake in the myocyte. Hypercalcemia may also induce toxicity.

Digoxin is renally cleared, and other factors influencing the glomerular filtration rate will also influence digoxin levels. Digoxin interacts with diuretics, amiodarone, calcium channel blockers, and macrolide antibiotics. In patients with Wolff-Parkinson-White syndrome, digoxin may induce VF.

In patients with end-stage renal disease, the loading dose should be reduced by 50%. The maintenance dose should be decreased depending on creatinine clearance and dose intervals increased.

One tablet of 0.125 mg digoxin is equal to 0.1 mg of the parenteral formulation.

KEY FACTS: DIGOXIN

- Digoxin is used to control heart rate in AF, and together with beta blockers and ACE inhibitors in the treatment of heart failure.
- At therapeutic concentrations (1 to 2 ng/mL), it has positive inotropic, negative dromotropic, and negative chronotropic effects.
- At higher levels, toxicity (AV block, VT, VF, nausea, vomiting, electrolyte imbalance) occurs.
- Electrolyte imbalance and reduced glomerular filtration rate predispose to digoxin toxicity.

ADDITIONAL READINGS

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75. ANSWER: B

Antibiotics are administered by anesthesiologists on a routine basis. Although their interactions with perioperative drugs may most times be of little importance, anesthesiologists should familiarize themselves with the interactions and adverse effects of all agents they administer, because those who administer a drug are also responsible for its effects, even if the drug is ordered by another doctor.

NEUROMUSCULAR BLOCKADE

Although interaction between antibiotics and nondepolarizing muscle relaxants (NDMRs) is well recognized, it is not often clinically relevant. A potentiating effect of aminoglycosides, tetracyclines, polymyxins, clindamycin, lincomycin, and bacitracin should be considered when recovery from neuromuscular blockade is delayed, or when unexpected recurarization occurs. Neostigmine may not adequately reverse such augmented blocks. Calcium administration has been proposed as an alternative. Patients with neuromuscular diseases, such as myasthenia gravis, are at increased risk of exaggerated neuromuscular blockade when these antibiotics are combined with NDMRs.

INTERACTIONS BETWEEN DIFFERENT ANTIBIOTICS

Aminoglycosides are inactivated by contact with penicillins and cephalosporins and should not be admixed or administered via the same tubing. The effect of penicillins and cephalosporins themselves can be antagonized by bacteriostatic agents, such as tetracycline. Clindamycin, erythromycin, and chloramphenicol compete for a binding site on the bacterial ribosome and may inhibit each other's effects. The risk of nephrotoxicity is increased with combinations of cephalosporins and aminoglycosides.

HYPNOTICS

The effects of thiopental are increased by sulfonamides. Erythromycin reduces the hepatic clearance of midazolam.

ORAL ANTICOAGULANTS

The effect of oral anticoagulants may be increased when cephalosporins, metronidazole, sulfonamides, or tetracyclines are administered.

DIURETICS

The risk of ototoxicity and nephrotoxicity from aminoglycosides is increased in the presence of furosemide and bumetanide. Ototoxicity is mainly seen with higher peak plasma levels, due to rapid IV administration of these agents. Nephrotoxicity from cephalosporins is also more likely with diuretic therapy, especially after a few days of therapy.

KEY FACTS: PERIOPERATIVE ANTIBIOTICS

- Aminoglycosides, tetracyclines, polymyxins, clindamycin, lincomycin, and bacitracin may potentiate neuromuscular blockade.
- Aminoglycosides are inactivated by contact with penicillins and cephalosporins.
- Oral anticoagulant effects are increased by cephalosporins, metronidazole, sulfonamides, and tetracyclines.
- Diuretic therapy, together with rapid administration of aminoglycosides or cephalosporins, increases the risk of nephrotoxicity and ototoxicity.

ADDITIONAL READING

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76. ANSWER: C

BUPRENORPHINE

CLINICAL CHARACTERISTICS

Buprenorphine is a thebaine derivative opioid that is 25 to 100 times more potent than morphine. It slowly binds and dissociates from the opioid receptors, resulting in a slow onset but a long duration of action. Together with its lipophilicity, these characteristics make it suitable for administration via transdermal patches. These are advantageous for patients with chronic opioid requirements and provide stable plasma levels, which results in better pain control and fewer adverse effects compared to frequent oral dosing.

Buprenorphine has a complex receptor profile, which is still incompletely understood. It seems to be a partial μ-opioid receptor agonist and a κ-opioid receptor antagonist. It also interacts with the opioid-receptor–like (ORL-1) receptor.

Contrary to popular belief, buprenorphine does not have a "ceiling effect" in humans within the therapeutic dose range. Within the normal dose range, buprenorphine behaves like a μ agonist and does not antagonize the effect of the pure μ agonists. It was also believed that buprenorphine could not be administered together with pure μ agonists, but clinical studies have contradicted this. Additive or even synergistic effects can be expected. The order of use is not important in switching between buprenorphine and other opioids.

The risk of clinically significant respiratory depression is low with buprenorphine, and a ceiling effect is reached within the therapeutic dose range. However, when buprenorphine is combined with other respiratory depressants, the ceiling effect disappears. Buprenorphine has milder withdrawal symptoms, a lower risk of development of dependence and tolerance, a lower risk of nausea, vomiting, and constipation, and a lower abuse potential than the pure μ opioids due to its partial antagonist profile and effects at the ORL-1 receptor. When reversal with naloxone is required, the long duration of action of buprenorphine must be taken into account.

PHARMACOLOGY

Parenterally administered buprenorphine reaches peak plasma levels after 2 to 5 minutes. The elimination half-life (T½β) is 2 to 3 hours. Peak plasma levels after sublingual administration are reached after 2 hours. The oral bioavailability is ±55%. A rapid elimination phase (6 hours) is followed by a slow elimination phase (24 hours). When administered via the transdermal route, peak plasma concentrations are reached after several hours (13 to 30 hours). Buprenorphine is 96% protein-bound, but not primarily to albumin. Two-thirds of the dose is excreted unchanged; the other third is metabolized in the gut wall and in the liver, via glucuronidation and cytochrome P450 3A4 (CYP3A4). The glucuronide metabolite is excreted in the bile, and enterohepatic recirculation occurs. In patients with liver disease, buprenorphine doses should be carefully titrated because clearance may be slowed. Buprenorphine and its metabolites are inhibitors of CYP3A4 and CYP2D6. Kidney failure does not significantly affect buprenorphine kinetics.

The use of buprenorphine in opioid-dependent patients is discussed elsewhere (Question 26).

KEY FACTS: BUPRENORPHINE

- Buprenorphine is a highly lipophilic, highly potent opioid with partial μ-agonist and κ-antagonist characteristics, and also binds the ORL-1 receptor.
- It is available for transdermal, sublingual, and parenteral administration and has a slow onset but a long duration of action.
- At therapeutic doses, it behaves like a pure μ agonist and has no analgesic ceiling effect. Respiratory depression is rare with buprenorphine.

ADDITIONAL READINGS

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Lutfy K, Cowan A. Buprenorphine: a unique drug with complex pharmacology. *Curr Neuropharmacol*. 2004;2(4):395–402.

77. ANSWER: E

Nalbuphine is a synthetic opioid for parenteral administration that is approximately equipotent to morphine. It is a partial agonist/antagonist at the μ-opioid receptor and an agonist at the κ-opioid receptor. Nalbuphine is used for analgesia in the prehospital setting and during childbirth because its use carries a lower risk of respiratory depression compared with pure μ agonists. Similar to buprenorphine, respiratory depression does occur with nalbuphine, but there seems to be a ceiling effect, meaning that above a certain dose threshold, the degree of respiratory depression shows no further increase. Another specific advantage is its antipruritic effect. A 4-mg dose of IV nalbuphine reduces the severity of pruritus induced by postpartum intrathecal opioids. Nalbuphine itself can also be used intrathecally for cesarean section when added to local anesthetic. It provides a faster onset but a shorter duration of analgesia and less pruritus, nausea, and vomiting than morphine.

Nalbuphine's antagonistic properties at the μ-opioid receptor induce withdrawal when administered to patients who chronically use other opioids.

Nalbuphine is metabolized in the liver and excreted via the kidneys. The elimination half-life (T½β) after parenteral administration is approximately 2.5 hours.

KEY FACTS: NALBUPHINE

- Nalbuphine is a partial μ-agonist and a κ-agonist synthetic opioid.
- Similar to buprenorphine, respiratory depression occurs but has a ceiling effect.
- A specific advantage is its reduced risk of pruritus when used peripartum.

ADDITIONAL READINGS

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Culebras X, Gaggero G, Zatloukal J, Kern C, Marti RA. Advantages of intrathecal nalbuphine, compared with intrathecal morphine, after cesarean delivery: an evaluation of postoperative analgesia and adverse effects. *Anesth Analg*. 2000;91(3):601–605.
Lo MW, Lee FH, Schary WL, Whitney CC. The pharmacokinetics of intravenous, intramuscular, and subcutaneous nalbuphine in healthy subjects. *Eur J Clin Pharmacol*. 1987;33:297–301.

78. ANSWER: B

Diminished gastric motility and emptying (gastrointestinal dysmotility) occurs in approximately half of mechanically ventilated patients. Gastrointestinal dysmotility interferes with enteral feeding and oral drug administration and increases the risk of gastroesophageal reflux, pulmonary aspiration, bacterial translocation, and sepsis. It therefore often requires treatment. Several promotility drugs are discussed here.

METOCLOPRAMIDE

Metoclopramide antagonizes the inhibitory effect of dopamine in the gut and sensitizes it to acetylcholine. It also increases motility by binding to enteric 5-HT receptors. Metoclopramide increases lower esophageal sphincter tone. This leads to improved gastrointestinal motility and improved feeding tolerance. However, metoclopramide is not effective in facilitating feeding tube placement, and there is no evidence that metoclopramide administration actually reduces the incidence of pneumonia or mortality in critically ill patients. Metoclopramide is not effective in paralytic ileus. Metoclopramide can be administered via nasogastric tube or IV, in doses of 10 to 20 mg. The elimination half-life is 4 to 6 hours, but this is approximately doubled in patients with significant kidney failure. Metoclopramide has many (central) adverse effects, including sedation, extrapyramidal symptoms, and tardive dyskinesia. Use the smallest effective dose for the shortest possible time. The prokinetic effect of metoclopramide causes reduces uptake of agents primarily absorbed in the stomach and increases the uptake speed of agents primarily absorbed in the small bowel. Metoclopramide antagonizes the effect of levodopa. Metoclopramide is relatively contraindicated in patients with epilepsy because it has been reported to elicit seizures. In patients with pheochromocytoma, metoclopramide may induce severe hypertension.

ERYTHROMYCIN

This macrolide antibiotic triggers the migrating myoelectric complex by activating motilin receptors on enteric nerves and smooth muscle cells. This leads to increased gastric motility and improved feeding tolerance. Erythromycin (200 mg IV) may facilitate feeding tube placement. Prolonged use of erythromycin should be avoided in the absence of an infection with an erythromycin-sensitive microorganism because resistance may be induced.

CISAPRIDE

Although an effective prokinetic agent, cisapride was withdrawn from the U.S. market due to its cardiac adverse effects.

KEY FACTS: PROMOTILITY AGENTS

- Use of a prokinetic agent may improve enteral feeding tolerance and facilitate feeding tube placement in patients with gastrointestinal dysmotility.
- Erythromycin may induce microbial resistance.
- Metoclopramide has significant adverse effects, including sedation, extrapyramidal symptoms, and tardive dyskinesia.
- Metoclopramide is contraindicated in patients using levodopa, and patients with epilepsy or pheochromocytoma. It is ineffective in patients with ileus.

ADDITIONAL READINGS

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79. ANSWER: B

Cyanides contain the CN^- ion, which consists of one carbon and one nitrogen ion, held together by a triple bond. The cyanides most commonly encountered are hydrogen cyanide gas (HCN) and the solid inorganic cyanide salts, including potassium cyanide (KCN). Compounds that release cyanide when metabolized in the body are termed "cyanogens."

SOURCES

SMOKE INHALATION

Many industrial and household plastics and solvents, but also the natural substances wool and silk, contain cyanogens (such as nitriles) that release HCN when burned.

INDUSTRIAL EXPOSURE

Cyanides and cyanogens (mostly nitriles) are used in the plastics and metal industry and as a fumigant. Toxicity may occur after skin contact, ingestion, and inhalation.

INTENTIONAL EXPOSURE

Cyanide ingestion is a rare but highly effective method of suicide and homicide. Healthcare and laboratory workers are at increased risk.

IATROGENIC

Long-term (more than 48 hours) or high-dose administration of nitroprusside may produce cyanide toxicity. This is described in detail elsewhere (Question 66).

PATHOPHYSIOLOGY

The CN^- ion binds to the ferric ion in the a-a_3-complex of cytochrome oxidase in the mitochondria. This blocks cellular respiration, and therefore cells must switch to anaerobic metabolism, resulting in lactate production. The brain and the heart depend on aerobic metabolism and are affected severely. Chronic exposure to cyanide may result in ataxia and optic neuropathy.

SYMPTOMS AND SIGNS

Symptoms occur rapidly after exposure to gaseous cyanides, and more slowly after ingestion of cyanide salts or exposure to cyanogens. Cyanide toxicity symptoms can be very nonspecific. Flushing, tachypnea, tachycardia, headache, and dizziness are rapidly followed by combativeness, CNS depression, apnea, convulsions, and death. The skin may appear either blue or cherry-red (which resembles CO poisoning). The anaerobic cellular metabolism results in severe lactic acidosis with high anion gap, and reduced oxygen use results in increased venous oxygen saturation. The ECG may show ST-segment elevation or depression. The ST segment may be shortened, and the T wave may fuse with the QRS complex. AV block, supraventricular rhythm, ventricular fibrillation, and asystole may follow.

DIFFERENTIAL DIAGNOSIS

Altered mental status and anion-gap metabolic acidosis has a differential diagnosis, summarized by the MUDPILES acronym. This stands for methanol, uremia, diabetic ketoacidosis, paraldehyde/phenformin, iron/isoniazid, lactate, ethylene glycol, and salicylates. Patients rescued from fires should be suspected of having inhaled carbon monoxide, and blood gas analysis should be performed without delay. Cyanide toxicity may mimic hydrogen sulfide toxicity.

MANAGEMENT OF CYANIDE INTOXICATION

- Safety first: protect yourself and coworkers from exposure.
- Do not delay treatment while running additional diagnostic tests.
- Remove the patient from the exposure sources. Remove contaminated clothes.
- Administer 100% oxygen, establish a secure airway, and anticipate respiratory deterioration. Before IV access, amyl nitrate inhalation may be useful.
- Treat acidosis with sodium bicarbonate. Treat hypotension.
- Administer the Cyanokit (hydroxyocobalamin, vitamin B12), which reacts with cyanide to form cyanocobalamin, which is renally cleared. Coadministration of sodium thiosulfate (through a separate line) may have a synergistic effect.
- Alternatively, administer the Cyanide Antidote Kit, which contains amyl nitrate for inhalation, and sodium nitrite and sodium thiosulfate for injection. Follow the instructions in the package insert. **Do not administer sodium nitrite to smoke inhalation victims, as profound methemoglobinemia in combination with the presence of carbon monoxide (CO-Hb) will dramatically reduce oxygen carrying capacity.**
- When cyanides have been ingested, administer activated charcoal (Table 17.33).

ADDITIONAL READINGS

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80. ANSWER: A

ANTICANCER CHEMOTHERAPY AND ANESTHESIA

GENERAL CONSIDERATIONS

Patients undergoing anticancer therapy may have suffered significant weight loss and subsequent plasma protein and electrolyte imbalances. Their therapies commonly induce immune

Table 17.33 CYANIDE TOXICITY TREATMENT

AGENT	ADULTS	CHILDREN	REMARKS
Hydroxocobalamin (Cyanokit)	5 g IV over 15 min (may repeat once, slow infusion over 15 min–2 h)	70 mg/kg IV over 15 min	Administer faster during cardiac arrest. Induces reddish-brown skin and urine discoloration. Interferes with many lab readings.
Sodium nitrite	10 mL of 3% solution (300 mg) slow IV push (2–5 min)	10 mg/kg (0.33 mL/kg) immediately, repeat 5 mg/kg (0.165 mL/kg) in 30 min to a maximum of 300 mg (10 mL), reduce dose when Hb <12 g/100 mL	Induces methemoglobin formation; avoid in smoke inhalation victims with CO-Hb >10%
Sodium thiosulfate	12.5 g (50 mL) IV at 3–5 mL/min, may repeat half dose once after 1 h	412.5 mg/kg IV (1.65 mL/kg) at 3–5 mL/min	Adjunct to sodium nitrite or hydroxocobalamin, slow mechanism of action
Amyl nitrate inhalation	Inhalation, 1 ampoule q30 sec	–	Emergency treatment before IV access is established

suppression and anemia. Although patients may appear to do well when resting, their exercise capacity (such as required during anesthesia and surgery) may be significantly affected. The effects of some anticancer agents are discussed here.

CYCLOPHOSPHAMIDE

Cyclophosphamide is an alkylating agent used to treat chronic lymphatic leukemia, lymphoma, and certain solid cancers. Animal studies have shown increased toxicity from cyclophosphamide when coadministered with halothane. Halothane also seems to slow the clearance of cyclophosphamide. Furthermore, cyclophosphamide inhibits plasma cholinesterase (PChE) for up to 4 weeks after discontinuation, prolonging the duration of action of agents such as succinylcholine and mivacurium.

DOXORUBICIN

This anthracycline and cytotoxic antibiotic is used to treat acute leukemia, lymphoma, and certain solid cancers. High doses are associated with cardiomyopathy, especially after myocardial irradiation, in elderly patients, and those with cardiac disease. Patients treated with anthracyclines such as doxorubicin may have a normal resting cardiac function but decreased capacity with exercise. This may become apparent perioperatively.

Previous treatment with anthracyclines increases the risk of anesthesia-induced QT-interval prolongation.

METHOTREXATE

This agent is used for many indications in oncology and rheumatology. NSAIDs are capable of reducing the clearance of methotrexate. When methotrexate is administered after nitrous oxide-based anesthesia, severe bone marrow suppression and mucositis may occur. Nitrous oxide seems to increase the toxic potential of methotrexate, and the two agents should not be combined.

BLEOMYCIN

This cytotoxic antibiotic is widely used and may cause a dose-related progressive pulmonary fibrosis. The risk of bleomycin-induced lung injury seems to increase with higher inspired oxygen concentrations. Therefore, aim for the lowest acceptable FiO_2 to reduce the risk of lung injury.

ADDITIONAL READING

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81. ANSWER: D

82. ANSWER: D

Pharmacokinetics is the study of how a drug molecule reaches its target and then disappears from the system. This encompasses drug absorption, distribution, metabolism, and elimination and depends upon which (organ) systems are capable of metabolizing and excreting a drug. More simply put, pharmacokinetics is about what the body does with the drug, whereas pharmacodynamics describes what the drug does within the body.

DRUG ABSORPTION AND PKA

Many factors influence drug absorption into the body. Molecular weight, ionization state, lipid and water solubility, and the drug's vehicle (tablet, solution) are key factors. The patient contributes factors such as gastric pH, contents of the intestines, and the perfusion of the area that is to absorb the agent (e.g., skin, bowel). Many anesthetic agents

must cross the blood–brain barrier and dissolve into the lipid-rich brain tissue. Only un-ionized molecules are capable of this. Lipid-soluble agents can often also penetrate the placenta. The pH of the surrounding solute influences the agent's ionization state and thus how well it is absorbed in a particular tissue. The pH at which 50% of the agent's molecules are ionized is termed the pKa.

DRUG DISTRIBUTION

The absorption of a drug into a particular tissue is influenced not only by that drug's lipid solubility, but also by the perfusion of that tissue. An induction dose of thiopental will rapidly induce hypnosis due to its high lipid solubility and the brain's excellent perfusion. Once poorly perfused or watery tissues start absorbing thiopental molecules, the effect-site concentration falls again and the effect disappears, although none of the agent's molecules have been eliminated yet. This phenomenon is termed redistribution. When a continuous infusion of lipid-soluble agents is discontinued, tissues that have become saturated with the agent but are poorly perfused, such as adipose tissue, slowly release the agent back into the circulation, leading to prolonged drug effects.

The volume of distribution (V_d), expressed as L/kg, is defined as the theoretical volume that would have to be available for a drug to disperse in, if the concentration everywhere in the body were the same as that in plasma or serum. A small V_d indicates that the agent is mainly distributed in plasma; a large V_d indicates that the agent is also distributed into other tissues. The loading dose of a particular drug can be calculated by multiplying the V_d with the target plasma concentration (C_p) of that drug.

Drug distribution also depends on protein binding. Agents that are bound to proteins, such as albumin, are not available to bind receptors or cross membranes. Agents sometimes compete for binding sites on plasma proteins and may increase each other's plasma free fraction. When plasma levels of albumin are decreased, many agents' plasma free fraction (and thus effects and toxicity) will increase.

BIOAVAILABILITY

Drugs administered orally, subcutaneously, and intramuscularly require transport to the bloodstream to reach their target site. However, some part of the dose may never be absorbed due to local enzymatic breakdown, autodegradation, or loss with the feces. The proportion of the agent's dose that ultimately reaches the circulation is termed bioavailability. The hepatic first-pass effect is a major determinant of the bioavailability of orally administered drugs. In patients with severe liver failure, or inhibited liver enzymes, oral drugs may escape the first-pass effect, resulting in increased bioavailability.

83. ANSWER: E

EFFICACY

This is defined as the degree to which a drug is able to produce the desired response. Drugs differ in the degree to which they can produce the largest response that their target tissue is capable of giving. In general, full agonists of a particular receptor in sufficient doses will eventually produce the maximum response, whereas partial agonists can produce only a submaximal response, even when they occupy all available target receptors.

POTENCY

An agent's potency is expressed as the amount of agent required to produce 50% of the maximal response that this particular agent is capable of producing. This number can be used to compare different agents from the same class. When comparing agents, their dose–response relation plays an important role. This relation is often nonlinear.

EFFECTIVE DOSE (ED_{50}) AND LETHAL DOSE (LD_{50})

Another way of expressing an agent's potency is the effective dose that produces a specified effect in 50% of subjects (of a given organism): the ED_{50}. In sufficiently high doses, most, if not all, agents will produce toxicity and ultimately death. The dose at which 50% of subjects (of a given organism) die is termed LD_{50}. The therapeutic window lies somewhere between the ED_{50} and LD_{50}. The therapeutic window is also bordered by adverse effects, usually seen at doses well below the LD_{50}. One example is ketamine. Ketamine is lethal at several times the ED_{50}, although adverse effects that will limit its clinical usefulness do occur well before the LD_{50} is reached. For some agents, the window between the effective and the harmful concentration is very small, such as with lithium. Plasma levels of these agents have to be monitored to avoid systemic toxicity. In some agents, the effective dose window overlaps the harmful dose window. For example, chemotherapeutics will induce toxicity at their effective concentrations, but this toxicity is part of the actual purpose of the agent and therefore accepted.

The safety of drugs can be compared with the therapeutic index (TI). TI is calculated by dividing LD_{50} by ED_{50}.

18.

STATISTICS AND ETHICS

D. John Doyle, MD, PhD

1. A researcher obtains the following weights (in kilograms) in five consecutive study subjects: 67, 88, 75, 87, 78. The mean and median values for the study subjects are

A. Mean 67, median 88
B. Mean 88, median 67
C. Mean 87, median 75
D. Mean 79, median 78
E. Mean 79, median 79

2. The range in weights for the study subjects is

A. 16
B. 19
C. 20
D. 21
E. 25

3. A researcher obtains the following heights (in meters) in six consecutive study subjects: 1.49, 1.58, 1.58, 1.62, 1.75, 1.78. The mode for the study subjects is

A. 1.49
B. 1.58
C. 1.62
D. 1.75
E. 1.78

4. If the mean of a normally distributed data set is 100 with a standard deviation of 15, what percentage of data lies between 85 and 115?

A. 10%
B. 33%
C. 52%
D. 68%
E. 95%

5. Figure 18.1 plots two physiologic variables against each other. Identify the INCORRECT statement regarding the figure.

A. The figure is a scatter plot.
B. An equation for the linear correlation between the two variables can be determined by linear regression methods.
C. The two variables are positively correlated.
D. These data imply that there is a causal link between the two variables.
E. The range of the variable of the *x*-axis is 125.

6. Which of the following is the correct definition of a null hypothesis?

A. It is the hypothesis being tested.
B. It is the hypothesis being rejected.
C. It is the hypothesis that equals a zero result.
D. It is the hypothesis that is rejected when it is true.
E. It is the hypothesis that is accepted when it is false.

7. Which of the following statements about the *t* test is INCORRECT?

A. The *t* test tests whether the means of two groups are statistically different from each other.

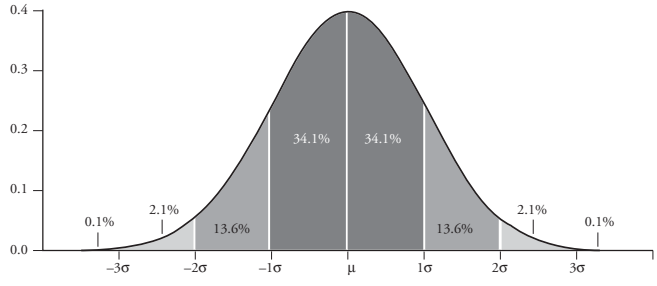


Figure 18.1

B. The *t* test is a statistical procedure for hypothesis testing.
C. By convention, if there is a less than 5% chance of getting the observed difference in group means by chance, we say that a statistically significant difference between the two means exists.
D. The null hypothesis associated with a *t* test is that the means of two variables studied are statistically different from each other.
E. The *t* test is a commonly used statistical test and is widely used in biomedical research.

8. Which of the statements about confidence intervals is INCORRECT?

A. The larger the sample size, the smaller the confidence interval.
B. A 95% confidence interval means that 95% of all observed values fall within that interval.
C. A confidence interval is an interval estimate of a population parameter.
D. Confidence intervals can be used to indicate the reliability of an estimate.
E. The calculation of a confidence interval requires that the data be randomly distributed

9. A study is proposed to compare the effects of a new therapy against standard therapy. The hypothesis of the investigators, given their initial observations, is that the new therapy will show a 20% improvement in their primary outcome compared to the standard. The study is powered to 0.8. Which of the following statements is INCORRECT regarding this study?

A. There is a 20% chance that the study will accept the null hypothesis when the null hypothesis is false.
B. Increasing the power means decreasing the chance of type II error.
C. Increasing the sample size will increase the power of the study.
D. Changing the effect size from 20% to 22% will decrease the power of the study.
E. The power of the study is related to the sensitivity.

10. Which of the following statements about statistical errors is correct?

A. A type I error involves accepting the null hypothesis when you shouldn't have.
B. The power of a statistical test is the probability that it will not make a type I error.
C. A type II error involves rejecting the null hypothesis when you shouldn't have.
D. A type I error is a "false positive."
E. Increasing the sample size will increase both type I and type II errors.

11. Which of the following statements about crossover studies is INCORRECT?

A. A crossover study is one in which two or more interventions (treatments) are applied sequentially to the same experimental subject.
B. In a crossover study each subject then acts as his or her own control.
C. Crossover studies generally require more subjects than do noncrossover designs.
D. Carryover effects, when a treatment effect carries over to the next treatment period, may make a crossover study unreliable.
E. Crossover studies may require a "washout" period between the treatments studied to minimize the effect of interactions between treatments.

12. Randomization of study subjects

A. Increases the power of a study
B. Introduces bias
C. Balances confounders
D. Reduces the number of subjects necessary to make a result significant
E. Controls for placebo effects

13. Which of the following statements about the Likert scale is INCORRECT?

A. The Likert scale is an ordered, one-dimensional scale from which respondents choose the one option that best aligns with their opinion on some manner.
B. The method ascribes quantitative values to qualitative data.
C. All Likert scales have a neutral point in the middle.
D. The response options for a 5-point scale are often similar to "strongly agree," "agree," "neither agree nor disagree," "disagree," and "strongly disagree."
E. A possible item in a Likert questionnaire could be "Anesthesiologists should be well trained in statistical analysis."

14. Which of the following variables is NOT dichotomous?

A. Yes/no
B. Agree/disagree
C. Correct/incorrect
D. Disagree strongly/disagree/neutral/agree/agree strongly
E. Helpful/not helpful

15. A random selection of 500 adults participate in a study of the effects of a newly released drug. They are followed prospectively for 3 years to see if there is an association between the incidence of cardiac arrhythmias and the use of the drug. This type of study is a

A. Crossover study
B. Cross-sectional study
C. Case–control study
D. Cohort study
E. Randomized controlled clinical trial

16. A researcher plans to compare the frequency of postoperative apneic events in children who undergo surgery for tonsillectomy against similar children undergoing strabismus surgery. This type of study is a

A. Crossover study
B. Cross-sectional study
C. Case–control study
D. Cohort study
E. Randomized controlled clinical trial

17. If a test was very difficult, although a few students still obtained very high scores, then the distribution of scores would be

A. Positively skewed
B. Negatively skewed
C. Normally distributed
D. Not skewed
E. Symmetric

18. Which of the following statements about causation and correlation is correct?

A. Correlation implies causation.
B. Correlation depends upon the study sample size.
C. Causation is determined by the statistical test chosen.
D. Causation must be decided by the research team.
E. Causation is determined by the power of the statistical tests used.

19. Which of the following measures of central tendency is most likely influenced by an extreme score?

A. Mean
B. Mode
C. Median
D. Standard deviation
E. Variance

20. A type I error is also known as

A. False positive
B. False negative
C. Sampling error
D. Estimation error
E. Randomization error

21. A type II error is also known as

A. False positive
B. False negative
C. Sampling error
D. Estimation error
E. Randomization error

22. A researcher finds a strong positive association between the number of drownings and ice cream sales. This is an example of an association likely caused by

A. A cause-and-effect relationship
B. A common cause
C. Sampling error
D. A mere coincidence
E. None of the above

23. A researcher develops a regression equation relating two variables: $y = 2.1 + 3.9x$. Which of the following statements is correct?

A. The equation crosses the y-axis at $x = 3.9$.
B. The dependent variable is x.
C. The independent variable is y.
D. y increases by 2.1 for each unit increase in x.
E. y increases by 3.9 for each unit increase in x.

24. An incoming group of anesthesia residents is tested for handedness, with the results shown in the table below. Identify the INCORRECT statement.

	RIGHT-HANDED	LEFT-HANDED	TOTALS
Men	53	11	64
Women	47	6	53
TOTALS	100	17	117

A. Overall, about 14.5% of the residents are left-handed.
B. This is an example of a contingency table.
C. Contingency tables apply where the outcome is a categorical variable such as male versus female, left-handed versus right-handed, disease versus no disease, pass versus fail, open artery versus obstructed artery.

D. To test that the proportion of men who are right-handed is about the same as the proportion of women who are right-handed, one could appropriately use Pearson's chi-square test.
E. None of the above

25. A researcher wishes to compare two unpaired groups whose data are not normally distributed. Which test would be most appropriate in this setting?

A. Paired *t* test
B. Mann-Whitney test
C. Kruskal-Wallis test
D. Kolmogorov-Smirnov test
E. One-way ANOVA

26. A researcher wishes to compare the means for two unpaired groups. The researcher is certain that the mean for the experimental group will be larger than the mean for the control group. Which statistical test would be most appropriate?

A. One-sided paired *t*-test
B. Two-sided paired *t*-test
C. One-sided unpaired *t*-test
D. Two-sided unpaired *t*-test
E. Kolmogorov-Smirnov test

27. Which of following variables is an example of a nominal (categorical) variable?

A. Height
B. Weight
C. Gender
D. Serum sodium concentration
E. Class rank

28. A new treatment for malignant melanoma significantly extends the lifespan of the patient but does not prevent the disease or lead to its cure. Given this scenario, which of the following statements about malignant melanoma is correct?

A. Its incidence will decrease.
B. Its prevalence will decrease.
C. Its incidence will increase.
D. Its prevalence will increase.
E. There will be no change in either incidence or prevalence.

29. Which of the following statements about analysis of variance (ANOVA) is INCORRECT?

A. ANOVA can provide a statistical test of whether the means of several groups are all equal.
B. It can be seen as a generalization of a *t* test to more than two groups.
C. It is an alternative to performing multiple *t* tests (thereby avoiding an increased chance of a type I error).
D. It makes no assumptions about whether the data follow a normal (Gaussian) distribution.
E. ANOVA can be used to test for significant differences among several means without increasing the type I error rate from performing multiple *t* tests.

30. Which of the following is NOT one of the four guiding principles of the "Georgetown School" of bioethics (also known as "principalism")?

A. Autonomy
B. Compassion
C. Beneficence
D. Distributive justice
E. Nonmalfeasance

31. Which of the following statements does NOT stem from the principle of "respect for patient autonomy"?

A. The principle acknowledges the right of a competent adult to have full control over his or her own life, including end-of-life decisions.
B. The principle acknowledges the right of a competent adult patient to refuse a clinically necessary blood transfusion.
C. The principle acknowledges the right of a competent adult patient to be provided with all treatments, even when futile.
D. Competent adult patients should be able to refuse life-saving interventions even when such refusals are perceived as being "unreasonable" by caregivers.
E. The principle acknowledges the right of a competent adult patient to be fully informed about treatment options.

32. A palliative care physician administers morphine to a patient dying in agony. This is done at the patient's request with a view to reducing the patient's suffering, and the physician does this even though it may hasten the patient's demise. Which of the following ethical principles or doctrines is LEAST supportive of this practice?

A. The doctrine of "double effect"
B. The principle of distributive justice
C. Compassion for patients in pain
D. Respect for patient dignity
E. Respect for patient autonomy

33. You are taking care of David, a 49-year-old homosexual man with terminal AIDS. He is intubated and

ventilated with yet another bout of pneumocystis pneumonia and is not doing well despite appropriate therapy. David is unconscious. His longtime partner, Michael, has a signed durable power of attorney (DPOA). You decide that ongoing ventilation is futile. The patient's elderly parents arrive from Texas and threaten to "sue everyone" if ventilation is discontinued. Who should be the legal decision maker in this case?

A. The patient's parents should make any legal decisions because they are his next of kin.
B. Michael should make any legal decisions.
C. This matter should be decided via a court hearing.
D. Any legal decisions should be made by the clinical team.
E. Any legal decisions should be made by the hospital ethics team.

34. A 32-year-old woman is admitted to your intensive care unit with a fever, headache, and nuchal rigidity. Although she is irritable, she is clearly mentally competent. A lumbar puncture study reveals cryptococcal meningitis. Because this is an infection commonly associated with HIV infection, a workup for HIV is recommended. However, she refuses to be tested for HIV. What would be the appropriate action?

A. The patient's wishes should be respected.
B. The patient should be declared incompetent, because her refusal is clearly unreasonable.
C. Matters should be decided via a court hearing.
D. Matters should be decided by the hospital ethics team.
E. The test should be done anyway, because all suspected cases of HIV are reportable.

35. A competent adult Jehovah's Witness patient refuses a clinically necessary blood transfusion. In this situation the principle of beneficence comes into conflict with which of the following principles?

A. Justice
B. Compassion
C. Respect for dignity
D. Autonomy
E. Distributive justice

36. Which of the following intravenous products will orthodox Jehovah's Witnesses accept?

A. Albumin
B. Packed red blood cells
C. Fresh frozen plasma
D. Platelets
E. Whole blood

37. The determination that blood transfusions were a violation of God's law in the Jehovah's Witness faith was made

A. Based on concerns about disease transmission
B. Based on biblical passages
C. Based on a distrust of the medical profession
D. Based on concerns about possible blood incompatibility
E. All of the above

38. Obtaining informed consent entails ensuring that the patient

A. Understands the various clinical choices available
B. Understands the benefits associated with each choice
C. Understands the risks associated with each choice
D. Is not being dictated to or controlled by other parties
E. All of the above

39. Under which of the following circumstances can the acquisition of informed consent be problematic?

A. Sedated patient
B. Parturient in full labor
C. Severe organic brain disease
D. Limited knowledge of English
E. All of the above

40. Which of the following is an unacceptable option for patients who want very detailed risk information as part of the consent process?

A. Answer every question asked in as much detail as possible.
B. Refer patients to the peer-reviewed medical literature.
C. Allow the patient access to the files of patients who have had similar procedures.
D. Refer patients to patient advocacy Web sites such as the American Cancer Society.
E. All of the above

41. Some clinicians maintain that the process of informed consent has potential health risks in and of itself. Under which circumstance would this apply?

A. Illiterate patient
B. Language barrier
C. Minor age

D. Refuses an intervention involving a very small risk even though it would eliminate another, much larger, clinical risk
E. All of the above

42. Which of the following is an approach to medical ethics?

A. Ethical egoism
B. Ethical altruism
C. Deontologic approach
D. Consequentialist approach
E. All of the above

43. Which of the following statements about the deontologic approach to ethics is INCORRECT?

A. It determines moral responsibility by weighing the consequences of one's actions.
B. It stems from the Greek word *deon*, or duty.
C. It is a nonconsequentialist approach to ethics.
D. Deontologic obligations are held to be necessary regardless of any good or bad consequences that might result.
E. It is based on specific obligations or duties.

44. The landmark legal case of *Roe v. Wade*

A. Established a woman's right to obtain a therapeutic abortion in the early stages of pregnancy
B. Established that the principle of medical confidentiality can be trumped by concerns for the safety of third-party individuals
C. Established the notion of informed consent and of the right of a competent adult patient to choose or refuse medical treatment
D. Established the right of a impoverished patients to obtain free emergency medical treatment
E. None of the above

45. Which of the following is NOT an essential element for medical malpractice to have taken place?

A. Preexisting duty of care
B. Breach of duty
C. Injury to the patient
D. Proximate cause
E. Payment for services

46. Which of the following is permitted in the original Hippocratic Oath?

A. Disclosure of confidential information without permission
B. Bladder stone surgery
C. Euthanasia
D. Abortion
E. None of the above

CHAPTER 18 ANSWERS

1. ANSWER: D

The ***mean*** of a series of variables is the arithmetic average of those numbers. It is determined by summing the numbers, then dividing that sum by the number of variables (count) included in that sum. The average or mean of the example above is (67 + 88 + 75 + 87 + 78)/5 = 395/5 = 79 kg.

The ***median*** is the middle value of the given sample of data in their ascending order. It is the average value of two middle elements when the size of the distribution is even. The median can be used as a measure when a distribution is skewed, when end-values are not known, or when reduced importance should be attached to outliers (e.g., because they may be measurement errors). In this example, the median is 78, the middle element when the weights are arranged in order: 67, 75, 78, 87, 88.

2. ANSWER: D

The ***range*** of variables is the difference or interval between the smallest and largest values in a frequency distribution. It is simply the maximum value minus the minimum value, or in this example 88 − 67 = 21 kg.

3. ANSWER: B

The ***mode*** is a value of a dataset or population that occurs most frequently. In this case that number is 1.58, because it occurs twice.

4. ANSWER: D

Within normal distribution, 68.2% of the data lie within one standard deviation of the mean and 95.4% of the data lie within two standard deviations of the mean. In this particular case, 68.2% of the data will lie in the region of ±15 on either side of the mean, for a range of 85 to 115. 95.4% of the data lies within two standard deviations of the mean and 99.6% of the data lies within three standard deviations of the mean (Fig. 18.2).

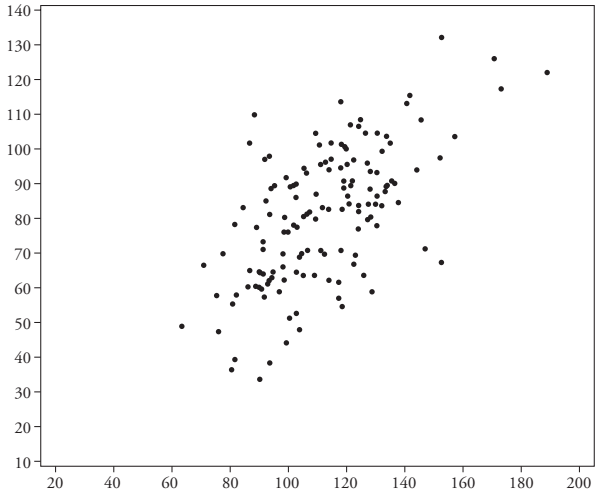


Figure 18.2 Normal (Gaussian) distribution.

5. ANSWER: D

Scatter plots can be helpful to visually illustrate the relationship between two or more variables. Linear correlations between two variables may be **positively correlated** (rising from left to right), **negatively correlated** (falling from left to right), or **uncorrelated**. An equation for the linear correlation between the two variables can be determined by linear regression methods. Remember that correlation between two variables is not proof that there exists a causal relationship between the two. The range of the horizontally plotted variable (*x*-axis) is 190 (maximum value) − 65 (minimum value) = 125.

6. ANSWER: A

The ***null hypothesis (H0)*** is the hypothesis or claim that is being tested. If there is not sufficient evidence to disprove the null hypothesis, then the null hypothesis is accepted. If the null hypothesis is rejected (not true), then the ***alternative hypothesis (H1)*** is accepted. A ***type I error*** occurs when the null hypothesis is rejected but it is actually true. A ***type II error*** occurs when the null hypothesis is accepted but it is actually false.

KEY FACTS: TYPE I AND II ERRORS

Type I error	**Alpha error** **False positive** **Wrongly rejecting the null hypothesis**
Type II error	**Beta error** **False negative** **Failing to reject a false null hypothesis**

7. ANSWER: D

The ***Student* t *test*** is one of the most commonly used techniques for testing a hypothesis on the basis of a difference between sample means. It is most commonly applied when the dataset follows a normal distribution. The null hypothesis associated with a *t* test is that the means of two variables studied are NOT different from each other.

8. ANSWER: E

A ***confidence interval (CI)*** is one kind of interval estimate of a population parameter, such as the mean. Instead of

estimating that parameter by a single number, an interval likely to include that parameter is given. Thus, confidence intervals can be used to indicate the reliability of a parameter estimate. Interval estimates like CIs stand in contrast with single-value-point estimates, such as the mean. The calculation of a CI generally requires assumptions about the nature of the data, such as the assumption that it is normally distributed.

9. ANSWER: D

The ***power of a statistical test*** is the probability that the test will correctly reject the false null hypothesis when the alternative hypothesis is true. In other words, the power of a statistical test is the opposite of a type II error. The chance of creating a type II error decreases with an increase in statistical power. In this case, the alternative hypothesis is the one proposed by the investigators, so they have designed the study to have a sensitivity of 80% to determine a significant difference between the therapies. The power of a study is primarily determined by three variables: the significance level, the sample size, and the effect size. A power of 0.95 may have allowed the investigators to make a more confident assertion about their data by decreasing their chance of type I error, but this comes at the expense of sample size and effect size. In general, increasing the sample size or the effect size will increase the power of the study.

10. ANSWER: D

A ***type I error*** (false positive) involves rejecting the null hypothesis when it is actually correct. A ***type II error*** (false negative) involves failing to reject the null hypothesis when it is incorrect. The power of a statistical test is the probability that it will not make a type II error. Increasing the sample size can be a way to reduce both types of errors.

11. ANSWER: C

Crossover studies or crossover trials are longitudinal studies in which subjects receive a sequence of different treatments or exposures. Although crossover studies can be observational studies, many important crossover studies are controlled experiments. Crossover studies generally require fewer subjects than do noncrossover designs, since each subject is used twice.

12. ANSWER: C

Randomization serves to balance potential confounding factors between treatment groups, not to control for placebo effects. It has no effect on the power of the study or on the number of study subjects that are necessary. Although randomization may decrease certain biases in a study, only appropriate study design can decrease the types of bias in a study.

13. ANSWER: C

A ***Likert scale*** is an ordered, one-dimensional scale from which respondents choose the one option that best aligns with their opinion on some manner. Only odd-point Likert scales have a neutral point in the middle; even-point Likert scales do not. For instance, a 4-point Likert scale such as "strongly agree," "agree," "disagree," and "strongly disagree" forces someone to agree or disagree—a neutral or middle-ground choice is not offered.

14. ANSWER: D

All items are dichotomous (two answers) except for answer D, which has polytomous (multiple) choices.

15. ANSWER: D

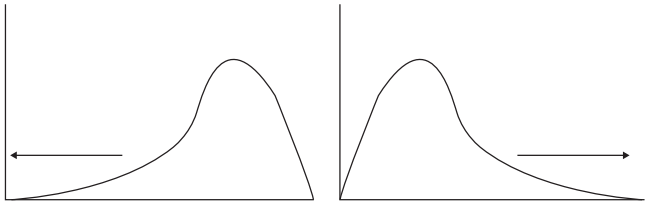
A ***cohort*** is a group of individuals who share a characteristic within a particular time period (e.g., are inoculated with a vaccine, are given a drug, quit smoking). A group of people born in 1980 would be said to form a birth cohort. Cohort studies are sometimes undertaken to determine the frequency of new diseases arising in the cohort. Perhaps the best-known example of a cohort study is the Framingham Heart Study (www.framinghamheartstudy.org), which began in 1948 with 5,209 adult subjects and is now on its third generation of participants.

16. ANSWER: C

Case–control studies are used to identify factors that may contribute to a medical condition (such as postoperative apnea) by comparing a group of patients of interest with a set of control patients.

17. ANSWER: A

Skewness is a measure of the asymmetry of the probability distribution of a real-valued random variable. The skewness value can be positive or negative, or even undefined. Qualitatively, a negative skew indicates that the tail on the left side of the probability density function is longer than the right side and the bulk of the values (possibly including the median) lie to the right of the mean. A positive skew indicates that the tail on the right side is longer than the left side and the bulk of the values lie to the left of the mean. A zero value indicates that the values are relatively evenly distributed on both sides of the mean, typically but not necessarily implying a symmetric distribution (Fig. 18.3).



Negative Skew

Elongated tail at the **left**
More data in the left tail than would be expected in a normal distribution

Positive Skew

Elongated tail at the **right**
More data in the right tail than would be expected in a normal distribution

Figure 18.3

ADDITIONAL READING

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18. ANSWER: D

Causation implies that an action or occurrence is caused by another (such as smoking causing lung cancer). Causation must be decided by the research team and cannot be determined by a statistical test. In ***correlation***, two occurrences are associated with each other but may not be caused by one another. For example, smoking is correlated with alcoholism but is not caused by alcoholism. Just because two things occur together does not mean that one causes the other.

19. ANSWER: A

Although the standard deviation and variance may be influenced by extremes in the data, neither is a measure of central tendency.

20. ANSWER: A

A type I error rejects the null hypothesis when it is in fact true.

21. ANSWER: B

A type II error accepts the null hypothesis when it is in fact false.

22. ANSWER: B

In this case the common cause would likely be beautiful, sunny weather, which encourages people to go swimming as well as to enjoy ice cream.

23. ANSWER: E

In this problem, y is the dependent variable and x is the independent variable. The independent variable is the one being changed, whereas the dependent variable is the observed result of that change. y increases by $2.1 + 3.9x$, as the equation states.

24. ANSWER: E

A ***contingency table*** is a type of table in a matrix format that displays the (multivariate) frequency distribution of the variables. It is often used to record and analyze the relation between two or more categorical variables. An appropriate test to compare proportions of categorical variables would be the Pearson chi-square test.

25. ANSWER: B

The ***Mann-Whitney test*** allows a comparison of unpaired groups for differences in mean when the variables do not follow a normal (Gaussian) distribution. It can also be used for ranked data. Where the data are known to follow a normal (Gaussian) distribution, a simple unpaired t test can be used.

26. ANSWER: C

A ***two-sided or two-tailed test***, using a significance level of 0.05, allots half of alpha to testing the statistical significance

Table 18.1 STATISTICAL TESTS

GOAL	TYPE OF DATA			
	MEASUREMENT (FROM GAUSSIAN POPULATION)	RANK, SCORE, OR MEASUREMENT (FROM NON-GAUSSIAN POPULATION)	BINOMIAL (TWO POSSIBLE OUTCOMES)	SURVIVAL TIME
Describe one group	Mean, SD	Median, interquartile range	Proportion	Kaplan Meier survival curve
Compare one group to a hypothetical value	One-sample *t* test	Wilcoxon test	Chi-square or Binomial test	
Compare two unpaired groups	Unpaired *t* test	Mann-Whitney test	Fisher test (chi-square for large samples)	Log-rank test or Mantel-Haenszel
Compare two paired groups	Paired *t* test	Wilcoxon test	McNemar test	Conditional proportional hazards regression
Compare three or more unmatched groups	One-way ANOVA	Kruskal-Wallis test	Chi-square test	Cox proportional hazard regression
Compare three or more matched groups	Repeated-measures ANOVA	Friedman test	Cochrane Q	Conditional proportional hazards regression
Quantify association between two variables	Pearson correlation	Spearman correlation	Contingency coefficients	
Predict value from another measured variable	Simple linear regression or Nonlinear regression	Nonparametric regression	Simple logistic regression	Cox proportional hazard regression
Predict value from several measured or binomial variables	Multiple linear regression or Multiple nonlinear regression		Multiple logistic regression	Cox proportional hazard regression

SOURCE: Table 37.1. *Intuitive Biostatistics* (ISBN 0–19–508607–4) by Harvey Motulsky. Copyright © 1995 by Oxford University Press Inc.

in one direction and half of alpha to testing statistical significance in the other direction. This means that 0.025 is in each tail of the distribution of the test statistic. When using a two-tailed test, regardless of the direction of the relationship, one tests for the possibility of the relationship in both directions. If one cannot indicate the direction of any group mean difference in advance, then a two-sided *t* test is more appropriate. If in doubt, a two-sided *t* test should be used.

A ***one-sided or one-tailed test***, using a significance level of 0.05, allots all of alpha to testing the statistical significance in the one direction of interest. This means that 0.05 is in one tail of the distribution of the test statistic. When using a one-tailed test, one tests for the possibility of the relationship in one direction and completely disregards the possibility of a relationship in the other direction. The one-tailed test provides more power to detect an effect in one direction by not testing the effect in the other direction. A one-sided *t* test is appropriate when one is certain that there either will be no difference between the two group means or that the difference will go in a direction you can specify in advance. If you consider the consequences of missing an effect in the untested direction and conclude that they are negligible and in no way irresponsible or unethical, then you can proceed with a one-tailed test. Choosing a one-tailed test for the sole purpose of attaining significance is not appropriate. Choosing a one-tailed test after running a two-tailed test that failed to reject the null hypothesis is not appropriate, no matter how "close" to significant the two-tailed test was.

Because the groups in the example above are unpaired, an unpaired *t* test is most appropriate.

The Kolmogorov-Smirnov test does not test for differences in mean.

27. ANSWER: C

A ***nominal variable*** (sometimes called a categorical variable) is one that has two or more categories with no intrinsic ordering. For example, gender is a nominal variable having two categories (male and female). Class rank is not a nominal variable because it has intrinsic ordering;

it is, in fact, an **ordinal** variable. All the other variables are ***quantitative (numerical) variables*** because they are naturally measured as numbers. The statistical methods used in a study must be appropriate for the measurement types used. For instance, taking the average of a nominal variable makes no sense; it makes no sense to compute an average eye color.

28. ANSWER: D

Prevalence and incidence are very different epidemiologic measures. The ***prevalence*** of a condition is the number of people who currently have the condition; the ***incidence*** refers to the number of people per year who acquire the condition. A chronic disease like diabetes can have a low annual incidence but a high prevalence. By contrast, a short-duration condition such as the common cold may have a high incidence but low prevalence.

29. ANSWER: D

The ***analysis of variance (ANOVA)*** is a statistical test that generalizes a *t* test to more than two groups, whether or not the means of several groups are all equal. Doing multiple two-sample *t* tests would result in an increased chance of committing a type I error. For this reason, ANOVAs are useful in comparing two, three, or more means. The mathematics behind ANOVA assumes that the data derives from a normal (Gaussian) distribution. The Kruskal-Wallis test can be used where this assumption is not supportable.

30. ANSWER: B

One commonly used approach to tackling bioethical problems in the Western world is to invoke the guiding principles of the ***"Georgetown School" of bioethics***, a popular and profoundly influential philosophical school so named because of its origins at Georgetown University. In the bioethical literature the "Georgetown School" of bioethics is often referred to as "principalism." The four ethical principles of the Georgetown School are

1. ***Autonomy:*** the right to actively participate in medical decisions concerning oneself without being dictated to or controlled by other parties
2. ***Beneficence:*** the requirement that caregivers, all else being equal, should do what they can to improve the patient's situation
3. ***Distributive justice:*** requiring the fair and impartial treatment of all persons, especially in the context of resource allocation
4. ***Nonmalfeasance:*** the requirement to avoid bringing harm to the patient.

Compassion, while an important trait in physicians, is not one of the guiding principles of principalism.

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Gillon R. Ethics needs principles—four can encompass the rest—and respect for autonomy should be "first among equals." *J Med Ethics*. 2003;29(5):307–312. PMCID: PMC1733972.

31. ANSWER: C

Autonomy implies the right to actively participate in medical decisions concerning oneself without being dictated to or controlled by other parties. Central to the concept of autonomy in this setting is the requirement that a patient understand the various clinical choices available and the risks and benefits associated with those choices. In other words, informed consent is a necessary condition for patient autonomy. This notion of autonomy implies that individuals should be given adequate means to make their own decisions—decisions made based on their personal value system. This also implies that patients must be provided with appropriate information to make possible informed decision making. The information that should be supplied to establish clinical informed consent usually focuses on the nature, risks, and benefits of the proposed intervention with a discussion of the alternatives to the planned intervention, including their associated risks, benefits, and uncertainties. The above notwithstanding, respect for patient autonomy does not automatically grant entitlement to clinical services. Thus, the principle of autonomy does not imply that patients are entitled to futile treatments.

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32. ANSWER: B

Respect for patient dignity implies that patients have an innate right to have their suffering reduced where clinically possible. Respect for patient autonomy has been discussed in some detail earlier. This principle is applicable in this case because the patient requested analgesia.

The doctrine of double effect makes a moral distinction between acting with the intention to harm someone or bring about their death versus performing an act where harm or death is foreseeable but is an unintended consequence. Thus, performing an act such as the administration of a clinically appropriate dose of morphine to reduce suffering is morally right because of its good consequences, even though the good consequences may sometimes be achievable only by putting the patient at risk of a harmful side effect like respiratory depression.

The principle of distributive justice implies that expensive or scarce treatment should not ordinarily be given if it deprives other patients of an even greater benefit. This is a matter concerning the allocation of scarce resources, but it is not appropriate as an ethical principle in this setting, because almost always morphine is freely available for appropriate clinical use.

33. ANSWER: B

The central issue in this scenario concerns who is the legal decision maker. Because Michael has a signed DPOA, unless there has been some legal misadventure in the preparation of that document, Michael is the legal decision maker in this case. An advance directive is a declaration by the patient regarding the type of care the patient wishes to receive should he or she be unable to make independent decisions. Examples of advance directives include DNR orders, living wills, and DPOA documents. There are important differences between these forms of advance directive. For example, a living will doesn't let the patient select someone to make decisions for him or her, whereas a DPOA documents the individual the patient has chosen to make healthcare decisions for him or her should he or she become unable to do so.

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Messinger-Rapport BJ, Baum EE, Smith ML. Advance care planning: Beyond the living will. *Cleve Clin J Med*. 2009;76(5):276–285.

34. ANSWER: A

The patient is within her legal rights to request that she not be tested for HIV. The underlying ethical principle in this case is respect for patient autonomy. Although the patient's refusal may be seen as unreasonable by the clinical team, this is hardly a basis for declaring the patient to be incompetent. An argument could be made that the ethical principle of concern for patient beneficence is being ignored by failing to provide a clinically necessary HIV test. This is an example of a conflict between ethical principles. In this case, however, the principle of patient autonomy is taken as more important than the principle of beneficence, at least in Western society.

A patient who refuses an HIV test is no different from a patient with chest pain who refuses an electrocardiogram or a morbidly obese patient who refuses testing for diabetes. Although most patients consent to such testing if informed of the potential benefits, patients may have personal reasons for refusing. However, as implied above, this situation can also create a moral dilemma for the clinician, because one's moral duty to treat a patient does not include the duty to practice second-rate medicine at the patient's request.

In such a setting it is essential to document the patient's refusal of testing and establish that the patient was fully informed of the reasons for the test. If the physician believes that the patient's HIV status is essential clinical information, he or she may ethically demand that the patient either agree to the test or (in nonemergency settings) find another physician.

35. ANSWER: D

36. ANSWER: A

37. ANSWER: B

The ***Jehovah's Witnesses*** are a fundamentalist Christian religion whose followers believe the Bible to be the true and literal word of God. Today there are about 6 million Jehovah's Witnesses worldwide. The faith began in the late 1870s as a Bible study group led by the American Charles T. Russell. Russell's teachings were subsequently spread through the group's official doctrinal journal, now known as the *Watch Tow*er, which he started in 1879. In 1881 the Watch Tower Bible and Tract Society was formed as the central organization for the Jehovah's Witness faith.

Orthodox Jehovah's Witnesses will not accept homologous or autologous whole blood, packed red blood cells, plasma, platelets, and white blood cells, even when "clinically necessary." This can result in a challenging dilemma for physicians because a routine, safe, and potentially life-saving medical intervention is unacceptable to the patient. Anesthesiologists are particularly affected because they are almost always responsible for intraoperative transfusion management.

Jehovah's Witnesses base their religious beliefs on a strict literal interpretation of the Bible and hold that eternal life may be forfeited if they do not exactingly adhere to biblical commands. The determination that blood transfusions were a violation of God's law was made in 1945 and is primarily based on the following three biblical passages:

- "Every moving animal that is alive may serve as food for you. As in the case of green vegetation, I do give it all to you. Only flesh with its soul—its blood—you must not eat." (Genesis 9:3, 4)
- "As for any man of the house of Israel or some alien resident who is residing as an alien in their midst who eats any sort of blood, I shall certainly set my face against the soul that is eating the blood and I shall indeed cut him off from his people." (Leviticus 17:10–16)
- "The Holy Spirit and we ourselves have favored adding no further burden to you, except these necessary things, to keep abstaining from things sacrificed to idols and from blood and from things strangled and from fornication. If you keep yourselves from these things you will prosper." (Acts 15:28, 29)

Thus Jehovah's Witnesses believe that the biblical injunctions concerning blood include both animal and human blood, and that the transfusion of blood is tantamount to "eating" blood. Even the use of autologous blood predonated in preparation for surgery is prohibited, as are any of the "primary" blood components (red cells, white cells, platelets, and plasma), regardless of their source.

From a legal viewpoint, a patient's legal right to refuse or consent to treatment is generally based on common law and, as such, is in a state of continuous evolution is new cases are decided. In the United States the landmark case that established a competent adult's right to refuse treatment occurred in 1914 in *Schloendorff vs. Society of New York Hospital* (105 N.E. 92 [1914]). A woman agreed to an examination under anesthesia but refused consent for surgery. Despite this, surgery was performed, and serious unexpected complications followed. The presiding judge stated that "Every human being of adult years and sound mind has a right to determine what shall be done with his own body," but despite this ruling the patient lost her case because the hospital was a charitable institution and was consequently immune from liability! Still, the case established the notion of informed consent and of a competent adult patient's right to choose or refuse treatment.

38. ANSWER: E

39. ANSWER: E

40. ANSWER: C

41. ANSWER: D

Respect for patient autonomy implies that individuals should be given adequate means to make their own decisions—decisions made based on their personal value system. This also implies that patients must be provided with appropriate information to make informed decision making possible. The information that should be supplied to establish clinical informed consent usually focuses on the nature, risks, and benefits of the proposed intervention with a discussion of the alternatives to the planned intervention, including their associated risks, benefits, and uncertainties.

Obtaining informed consent also entails ensuring that an adequate degree of patient understanding exists. Thus the clinician must also establish that the patient has sufficient decision-making competence for informed consent to be possible. This is usually accomplished informally by considering whether the patient appears to comprehend the information presented and establishing that the patient can discuss the issues with caregivers in a reasonable and logical manner. In some cases, however, formal psychological consultation is requested.

Although a number of approaches to the issue of providing informed consent have been described, in recent years many states have adopted the "reasonable patient" standard as their legal model. The reasonable patient standard asks, "What would an average patient need to know in order to be an informed participant in the decision?"

Further complicating the issue of informed consent is the recognition that there are a number of circumstances where ensuring that the requirements for full informed consent can be problematic. Such situations include the premedicated patient, the parturient in labor, the "psychologically fragile" patient under enormous emotional stress, the patient with known mental illness, the patient with organic brain disease, the immature adult patient, the patient with a limited understanding of English, and the hostile and distrustful patient who is angry at the world and places absolutely no trust in authority figures.

ADDITIONAL READINGS

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Ivashkov Y, Van Norman GA. Informed consent and the ethical management of the older patient. *Anesthesiol Clin*. 2009;27(3): 569–580.

42. ANSWER: E

43. ANSWER: A

Moral or ethical theory can be approached from many viewpoints. The ***deontologic approach*** to morality (from the Greek word *deon*, or duty) is based on specific obligations or duties. These can be either positive (such as to care for our family) or negative (such as not to steal). This approach is also sometimes called "nonconsequentialist" because these principles are held to be obligatory regardless of any good or bad consequences that might result. For example, it is wrong to kill even if it results in great benefit.

In contrast to the various deontologic approaches to morality, the ***consequentialist*** approach determines moral responsibility by weighing the consequences of one's actions. According to the consequentialist view, correct moral actions are determined by a cost–benefit analysis concerning the consequences of an action. Several subtypes of consequentialism have been proposed:

1. The view that an action is morally correct if its consequences are more positive or favorable than negative to the person performing the action (ethical egoism)
2. The view that an action is morally correct if the consequences of that action are more positive than negative to everyone *except* the person doing the action (ethical altruism)
3. The view that an action is morally correct if the action's consequences are more positive than negative to everyone (utilitarianism)

ADDITIONAL READING

Beauchamp TL, Childress JF. *Principles of Biomedical Ethics*. 5th ed. New York, NY: Oxford University Press; 2001.

44. ANSWER: A

Roe v. Wade was a U.S. Supreme Court decision that established a woman's right to obtain a therapeutic abortion up until the point at which the fetus becomes "viable." The Court defined viability as the potential "to live outside the mother's womb, albeit with artificial aid." The case was decided in 1973.

45. ANSWER: E

All four of the following elements must be proven for medical malpractice to be established:

1. Duty of care resulting from a relationship between the patient and the caregiver. Associated with this is a minimal "standard of care" (duty of care). The question here is, "Did the caregiver agree to treat the patient?" If the answer is yes, then an appropriate degree of skill and competence is required (the minimal standard of care).
2. Breach of that standard of care by caregiver (breach of duty). This is usually established by expert court testimony that defines what the acceptable standard of care is and that explains how the caregiver did not provide that care. Of course, expert witnesses for the other side will usually argue the exact opposite.
3. Injury to the patient. This is often easy to establish, when the patient has had the wrong kidney removed, say, but it can be more difficult to establish, for instance, when the injury is psychological.
4. Proof that the injury was caused by the breach of care (proximate cause). Proximate cause can be determined by asking if the patient would have been harmed in the absence of the caregiver's actions. For example, would a patient undergoing an appendectomy have been harmed if the surgeon had not left a sponge in the patient's abdomen? If the answer is no, then the surgeon's actions are deemed to have caused harm to the patient and thus fit the causation requirements.

A person accused of malpractice can mount a defense by showing that one of the above four elements is missing. For instance, he or she may argue that the injury to the patient was preexisting and not caused by the caregiver. Examples of malpractice claims are failure to diagnose, failure to treat, wrongful death, wrongful life, improper intubation, and improper positioning.

Common theories (types of claims) of malpractice include:

1. Lack of appropriate care, often referred to as "standard of care" as determined by physicians of a similar specialty in a given community
2. Lack of informed consent
3. Negligent supervision
4. Patient abandonment

46. ANSWER: E

The original Hippocratic Oath (translation below) forbids a number of activities, such as abortions, bladder and kidney stone surgery, euthanasia, disclosure of confidential information without the patient's permission, and sex with patients (and their slaves!). Although some of these rules are timeless, some of them have changed over time and are no

longer appropriate to contemporary medical practice. Most urologists would agree.

As a consequence of issues such as these, although the popular perception, especially on television or in the cinema, is that physicians take the Hippocratic Oath on entry into clinical practice, the reality is rather different. In fact, although graduating physicians very often take a professional oath, it is almost always different from the original Hippocratic Oath in a number of important respects.

The Hippocratic Oath for Physicians

I SWEAR by Apollo the physician, and Aesculapius, and Health, and All-heal, and all the gods and goddesses, that, according to my ability and judgment, I will keep this Oath and this stipulation—to reckon him who taught me this Art equally dear to me as my parents, to share my substance with him, and relieve his necessities if required; to look upon his offspring in the same footing as my own brothers, and to teach them this art, if they shall wish to learn it, without fee or stipulation; and that by precept, lecture, and every other mode of instruction, I will impart a knowledge of the Art to my own sons, and those of my teachers, and to disciples bound by a stipulation and oath according to the law of medicine, but to none others. I will follow that system of regimen which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to any one if asked, nor suggest any such counsel; and in like manner I will not give to a woman a pessary to produce abortion. With purity and with holiness I will pass my life and practice my Art. I will not cut persons laboring under the stone, but will leave this to be done by men who are practitioners of this work. Into whatever houses I enter, I will go into them for the benefit of the sick, and will abstain from every voluntary act of mischief and corruption; and, further from the seduction of females or males, of freemen and slaves. Whatever, in connection with my professional practice or not in connection with it, I see or hear, in the life of men, which ought not to be spoken of abroad, I will not divulge, as reckoning that all such should be kept secret. While I continue to keep this Oath unviolated, may it be granted to me to enjoy life and the practice of the art, respected by all men, in all times! But should I trespass and violate this Oath, may the reverse be my lot!

Source: MIT tech classics collection at http://classics.mit.edu/Hippocrates/hippooath.html

19.

TRANSPLANT ANESTHESIA

Douglas Dohl, MD and Charlene Walton, MD

1. A 46-year-old woman with hypertension, diabetes, and end-stage renal disease is undergoing a renal transplant. After the administration of antithymocyte globulin, the patient has profound hypotension. Potential side effects of antithymocyte globulin include all of the following EXCEPT

A. Serum sickness syndrome
B. Fever
C. Thrombocytopenia
D. Leukocytosis
E. Anaphylactic reaction

2. A 56-year-old man with end-stage liver disease secondary to primary biliary cirrhosis presents with suspected hepatopulmonary syndrome (HPS). Which of the following is characteristic of HPS?

A. Increased oxygenation with intrapulmonary vascular dilation
B. Orthodeoxia
C. Lack of pulmonary shunting
D. No resolution after liver transplantation
E. Sildenafil is an alternative preoperative treatment for HPS.

3. During liver transplantation on a 38-year-old woman with sclerosing cholangitis, the thromboelastograph (TEG) tracing showed fibrinolysis. The parameter of the TEG measuring clot strength is

A. R value
B. Maximum amplitude (MA)
C. Alpha angle
D. K value
E. None of the above

4. A 52-year-old woman underwent cardiac transplantation 5 years ago and now presents for laparoscopic-assisted vaginal hysterectomy for uterine fibroids. Which of the following statements is true about patients who have undergone cardiac transplantation?

A. The transplanted heart responds to ephedrine but not to peripheral attempts to induce hemodynamic changes (e.g., carotid massage, Valsalva maneuver).
B. Absence of reflex increases in heart rate can make patients sensitive to rapid vasodilation, which can occur with regional anesthetics.
C. The electrocardiogram of the transplanted heart contains only donor P waves.
D. Absence of vagal tone does not affect resting heart rate.
E. Epinephrine is the drug of choice for chronotropic therapy in the heart-transplant patient.

5. A 15-year-old female with type I diabetes and end-stage renal disease on dialysis is receiving a donor kidney from her identical twin sister. Patients with end-stage renal disease may exhibit which of the following?

A. Normochromic, macrocytic anemia due to decreased erythropoiesis and retained toxins secondary to kidney failure
B. A quantitative defect in platelet function secondary to uremia
C. Central nervous system disturbances secondary to uremia
D. Decreased sensitivity to drugs that depend on the kidney for elimination
E. None of the above

6. A 46-year-old man with postnecrotic cirrhosis due to hepatitis B is experiencing jaundice, poorly controlled ascites, markedly decreased serum albumin levels, mental status changes, and hyperreflexia. Medical management of these complications of end-stage liver disease has failed and he is now a candidate for liver transplantation. Major anesthetic considerations include which of the following?

A. Paracentesis for patients with minimal ascites to avoid circulatory collapse
B. Respiratory acidosis
C. Decreased levels of circulating catecholamines
D. Increased renal perfusion
E. Correction of precipitating causes of encephalopathy preoperatively

7. A 60-year-old woman had a kidney transplant 3 years ago. Recently she has been experiencing an increase in anginal symptoms, pain in her legs when she walks, and worsening hypertension. Which immunosuppressive agent is the most likely cause of her symptoms?

A. Azathioprine
B. Prednisolone
C. Cyclosporine
D. OKT4A
E. Rapamycin

8. A 51-year-old man with coronary artery disease and associated ischemic cardiomyopathy underwent uneventful heart transplantation. In the intensive care unit, 48 hours after transplantation, the patient developed systemic hypotension, low cardiac output, and elevated central venous and pulmonary artery pressures. Transesophageal echocardiography (TEE) showed right atrial and ventricular enlargement with decreased right ventricular systolic function. Acute right ventricular failure was diagnosed. Management of right ventricular failure in the heart transplant patient includes all of the following EXCEPT

A. Maintain coronary perfusion
B. Avoid hypercapnia and hypothermia
C. Consider inotropic and chronotropic support
D. Avoid mechanical support devices
E. Pharmacologically lower pulmonary vascular resistance

9. An 18-year-old woman underwent liver transplantation 1 year ago due to fulminant hepatic failure secondary to an acetaminophen overdose. In recent weeks, her skin has developed a yellowish discoloration and laboratory results show a marked decline in renal function. Rejection of the transplanted liver is best diagnosed by

A. Partial thromboplastin time
B. Serum bilirubin
C. Aminotransferase activity
D. Liver biopsy
E. None of the above

10. A 35-year-old man with hepatitis C is undergoing liver transplantation. During the anhepatic phase, the patient starts to hemorrhage, urine output is markedly decreased, and he is acidotic and hypothermic. Despite venovenous bypass, the patient is hemodynamically unstable and severe coagulopathy is suspected. What single test would provide immediate relevant information to manage this patient's coagulation status?

A. Prothrombin time
B. Platelet count
C. Fibrinogen
D. Thromboelastography
E. Fibrin split products

11. A 58-year-old woman is undergoing liver transplantation for end-stage liver disease. Prior to unclamping of the portal vein, hepatic artery, and vena cava, metabolic acidosis was treated with bicarbonate, ionized Ca^{2+} was normalized, and potassium was less than 5 mEq/L. When the vessels were unclamped, the patient developed a junctional heart rhythm, blood pressure decreased to 70/40 mm Hg, and pulmonary artery catheter measurements showed markedly decreased systemic vascular resistance (SVR) and increased right ventricular filling pressure. Although there was no change in cardiac output, the electrocardiogram now shows peaked T waves. What is the most probable cause of this patient's acute deterioration?

A. Reperfusion of donor liver
B. Transfusion reaction
C. Manipulation of the donor liver
D. Pulmonary or air embolism
E. None of the above

12. A 20-year-old woman with cystic fibrosis suffers from polycythemia, diabetes, and marked pulmonary hypertension and is severely cyanotic. Due to her terminal illness, she is a candidate for heart–lung transplantation. Cardiopulmonary bypass (CPB) was uneventful, but postoperatively the patient experiences postbypass bleeding secondary to anticoagulant use prior to surgery, depressed synthetic liver function, and CPB trauma. Given the risk of bleeding secondary to CPB trauma, what are the indications for CPB for transplant surgery?

A. *En bloc* double lung transplant
B. Heart transplant

C. Heart–lung transplant
D. Single lung transplant refractory to one-lung ventilation
E. All of the above

13. Following induction of a 45-year-old woman undergoing renal transplantation for polycystic kidney disease, antithymocyte globulin is administered by infusion as per protocol to help prevent reperfusion injury at the time of unclamping. Soon after initiation of the infusion, the patient develops hypotension. Assuming no other etiology for the hypotension exists, each of the following could have helped in preventing this reaction EXCEPT

A. Corticosteroid
B. Diphenhydramine
C. Slow infusion (over 4 to 6 hours)
D. Central administration
E. Acetaminophen

14. A 53-year-old woman with end-stage renal disease presents for kidney transplantation. The patient is hemodialysis-dependent and was last dialyzed the day before surgery. Her preoperative serum potassium level is 5.2 mEq/L. The patient has been anuric for the past 1.5 years. Additional past medical history reveals severe gastroesophageal reflux disease secondary to a large hiatal hernia, prompting the decision for rapid-sequence induction of anesthesia. Concerning the use of succinylcholine in this patient, which of the following is true?

A. Cisatracurium is a better choice for use in this patient due to its non–renal-dependent mode of elimination.
B. Succinylcholine should not be used due to the increased risk of a hyperkalemic response.
C. Rocuronium in a standard intubating dose (0.6–1.2 mg/kg) may be administered as a suitable alternative to succinylcholine.
D. Succinylcholine's duration of action is expected to be prolonged in this patient secondary to decreased activity of plasma cholinesterase.
E. Succinylcholine may be safely administered in this patient.

15. Renal transplantation in a 51-year-old woman with end-stage renal disease is completed. At the time of emergence the patient remains deeply sedated despite complete elimination of the end-tidal desflurane that was used as the maintenance anesthetic during the case. Respiratory rate is 7 breaths per minute. The decision is made to keep the patient intubated to complete emergence in the postanesthesia care unit. Assuming no overdosing, which of the following agents most likely accounts for the symptoms seen in this patient?

A. Fentanyl
B. Hydromorphone
C. Morphine
D. Meperidine
E. Sufentanil

16. During liver transplantation, a patient requires massive transfusion of packed red blood cells (PRBCs) for significant surgical hemorrhage. Continued microvascular bleeding is noted in the surgical field following this transfusion. Deficiency of which of the following factors is the LEAST likely etiology of the coagulopathy?

A. Platelets
B. Factor VII
C. Factor V
D. Fibrinogen
E. Factor VIII

17. A 20-year-old man suffered severe blunt hepatic trauma in a motor vehicle accident. Hemorrhage has been refractory to all other management, and liver transplantation has been determined the most appropriate option in this patient. Vascular control during the hepatectomy phase is accomplished using a continuous Pringle maneuver (clamping of the hepatic pedicle). Which of the following statements is INCORRECT regarding this surgical technique?

A. Risk of venous air embolism
B. Decreased venous return
C. Clamping of hepatic artery
D. Clamping of portal vein
E. Decreased systemic vascular resistance

18. A patient who has had a heart transplant 3 years ago presents for open reduction and internal fixation of the left femur following a mechanical fall. All of the following are true of the management of this patient EXCEPT

A. Cardiac output is preload-dependent.
B. Anticipated resting heart rate is 100 to 120 beats per minute.
C. Coadministration of glycopyrrolate with neostigmine is unnecessary.
D. Phenylephrine will be more effective than ephedrine.
E. Two P waves may be seen on the electrocardiogram.

19. The preoperative laboratory workup of a patient scheduled to undergo liver transplantation reveals thrombocytopenia with a platelet count of $12{,}000 \times 10^9$/L. The anesthesiologist determines that prophylactic platelet transfusion is appropriate. Two pheresis units (each pheresis unit being equivalent to six regular donor units) are transfused. What is the expected posttransfusion platelet count?

A. 24,000 × 10^9/L
B. 52,000 × 10^9/L
C. 78,000 × 10^9/L
D. 132,000 × 10^9/L
E. 289,000 × 10^9/L

20. A 57-year-old woman undergoing liver transplantation for end-stage liver disease secondary to alcoholic cirrhosis has required massive transfusion with 36 units of packed red blood cells (PRBCs). The surgeons note continued microvascular bleeding. Her preoperative laboratory workup revealed thrombocytopenia with a platelet count of 71,000 × 10^9/L, and platelets have been transfused without improvement in bleeding despite repeat platelet counts of more than 100,000 × 10^9/L. Prothrombin time (PT) and partial thromboplastin time (PTT) were within normal limits preoperatively, with intraoperative repeat testing results pending. What is the most appropriate next step?

A. Induced hypotension
B. Cryoprecipitate transfusion
C. Repeat platelet transfusion
D. Fresh frozen plasma transfusion
E. Factor V concentrate administration

21. An isolated small bowel transplantation operation is nearing the period of vascular unclamping and reperfusion of the graft. Which of the following prostaglandin subtypes can be administered via continuous infusion to enhance graft perfusion?

A. PGE_1
B. PGF_{2alpha}
C. PGI_2
D. PGE_2
E. PGD_2

22. A prostaglandin E_1 infusion is given during a small bowel transplantation at the time of reperfusion in an attempt to improve organ perfusion. It can have all of the following systemic effects EXCEPT

A. Hypotension
B. Flushing
C. Fever
D. Hyperkalemia
E. Seizure

23. A 26-year-old woman with end-stage renal disease secondary to IgA nephropathy is undergoing renal transplantation. Her preoperative Hct is 22 secondary to chronic anemia of renal disease. Two units of packed red blood cells are transfused at the start of the case. Signs of acute hemolytic transfusion reaction under general anesthesia would include all of the following EXCEPT

A. Tachycardia
B. Hypertension
C. Hemoglobinuria
D. Diffuse oozing of blood in the surgical field
E. Elevated temperature

24. A patient is emergently given 16 units of packed red blood cells during management of an acute hemorrhage from ruptured esophageal varices secondary to end-stage liver disease. The emergent situation necessitated administration of type O-negative units because there was inadequate time for a type and screen. While stabilizing the patient, a type and screen was sent, and screened type A-negative units are now available in the blood bank. What is the most appropriate next step in managing this patient, assuming the patient remains hypotensive and tachycardic and the hematocrit is 17?

A. Await full type and cross before transfusing further.
B. Continue to administer type O-negative units.
C. Begin transfusing the patient's type-specific units.
D. Switch to 5% albumin.
E. No transfusion is indicated at this time.

25. A 46-year-old patient is undergoing liver transplantation for end-stage liver disease secondary to nonalcoholic steatohepatitis (NASH). The procedure is nearing the reperfusion phase of the transplantation. All of the following physiologic and laboratory perturbations must be anticipated by the anesthesiologist EXCEPT

A. Hyperkalemia
B. Hypercalcemia
C. Hypotension
D. Metabolic acidosis
E. Coagulopathy

26. A liver transplantation has reached the anhepatic phase of the procedure. Which of the following laboratory results is most consistent with those expected at the end of this phase?

A. pH 7.27, pCO_2 40, bicarbonate 15, ionized calcium 0.8 mmol/L
B. pH 7.27, pCO_2 40, bicarbonate 15, ionized calcium 1.5 mmol/L
C. pH 7.4, pCO_2 40, bicarbonate 24, ionized calcium 1.1 mmol/L
D. pH 7.53, pCO_2 40, bicarbonate 33, ionized calcium 0.8 mmol/L
E. pH 7.53, pCO_2 40, bicarbonate 33, ionized calcium 1.5 mmol/L

CHAPTER 19 ANSWERS

1. ANSWER: D

Immunosuppressive agents are a necessary part of transplant therapy designed to create recipient tolerance to the grafted organ. However, drugs powerful enough to suppress the immune system inevitably have significant side effects. Chronic immune suppression is associated with severe, life-threatening infections as well as increased risks of progressive vascular disease and malignancy. ***Antithymocyte globulin*** is a polyclonal antibody immunosuppressive agent used to deplete T cells from the circulation. Its side effects include leukopenia, thrombocytopenia, fever, anaphylactic reaction, serum sickness syndrome, and increased incidences of both cytomegalovirus and Epstein-Barr virus infections.

ADDITIONAL READING

Transplant Anesthesia. In: Barash PG, Cullen BF, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:1398–1400.

2. ANSWER: B

Hepatopulmonary syndrome (HPS) is characterized as severe hypoxemia in the patient with end-stage liver disease and was once a contraindication to liver transplantation. The primary finding in this syndrome is decreased oxygenation (Pa_{O_2} < 70 mm Hg or P_{AO_2}–Pa_{O_2} gradient > 20 mm Hg on room air) associated with intrapulmonary shunting. Considered a hallmark for the presence of HPS, orthodeoxia is defined as a decrease in oxygen saturation when going from the supine to standing position. HPS frequently (but not always) resolves spontaneously months after liver transplantation, especially if transplants are performed before anatomic changes of the lungs are fixed. Sildenafil (Viagra), a vasodilator, is sometimes used in the treatment of portopulmonary hypertension. HPS results in intrapulmonary arteriovenous dilatations and, therefore, Sildenafil would not be appropriate.

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3. ANSWER: B

Viscoelastic measures of coagulation were developed in the 1940s, and this type of monitoring focuses on measuring the spectrum of clot formation to fibrinolysis. The ***thromboelastograph (TEG)*** uses a small blood sample in a cuvette on a spindle to detect abnormalities in clot formation and fibrin connections over time. The R value (reaction time), which measures the time to initial clot formation, is considered comparable to whole blood clotting time. Normal R values are 7.5 to 15 minutes. The R value can be prolonged by decreased clotting factors. The maximum amplitude (MA) measures clot strength and may be decreased by platelet dysfunction or fibrinogen concentration. Normal MA is 50 to 60 mm. The alpha angle measures the rate of clot formation, and the K value (BiKoatugulierung or coagulation) measures coagulation time; both values may be prolonged by decreased coagulation factors or heparin administration.

ADDITIONAL READING

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4. ANSWER: B

The ***transplanted heart*** is a denervated organ, i.e. the sympathetic and parasympathetic nerves which ordinarily regulate heart rate are severed, and cannot respond to indirect-acting agents such as ephedrine or dopamine. Isoproterenol is the drug of choice to increase heart rate in these patients. The Valsalva maneuver and carotid massage are also not effective in producing hemodynamic changes in the denervated heart. The electrocardiogram of the transplant patient can contain donor P waves as well as native P waves because the recipient's own sinoatrial (SA) node is left intact. The absence of vagal tone causes a relatively high resting heart rate of 100 to 120 beats per minute.

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Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006: 483–484.

5. ANSWER: C

Patients with ***end-stage renal disease***, presenting for renal transplantation, may exhibit a myriad of conditions affecting multiple organ systems. They usually have a normochromic, normocytic anemia and a qualitative defect in platelet function that is attributed to their uremic state. The defect results from accumulation of the compound guanidinosuccinic acid in uremic blood; this substance inhibits ADP-induced platelet aggregation. Common central

nervous system disturbances secondary to uremia include drowsiness, stupor, coma, or seizure. Drugs that depend on renal excretion have a prolonged duration of action, leading to increased sensitivity in patients with end-stage renal disease.

ADDITIONAL READING

Baker J, Yost CS, Niemann CU. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:2239–2241.

6. ANSWER: E

A progressive disease that can lead to hepatic failure, cirrhosis of the liver can result from alcohol abuse, postnecrotic cirrhosis (chronic active hepatitis), primary biliary cirrhosis, sclerosing cholangitis, cardiac cirrhosis (chronic right-sided congestive heart failure), hemochromatosis, Wilson's disease, and alpha$_1$-antitypsin deficiency.

There are three major complications associated with ***liver cirrhosis***: portal hypertension, ascites and hepatorenal syndrome, and hepatic encephalopathy.

Paracentesis should be considered in patients with massive ascites and pulmonary compromise. Too much fluid removal at one time can cause circulatory collapse. Problems with pulmonary gas exchange can lead to primary respiratory alkalosis secondary to hyperventilation. Patients with ascites have increased levels of circulating catecholamines, possibly due to increased sympathetic outflow. Decreased renal perfusion is present in patients with cirrhosis and ascites because of fluid and electrolyte derangements. Therefore, perioperative fluid management in cirrhotic patients is critical to preserve renal function. Encephalopathic patients benefit from correcting underlying causes, oral lactulose (an osmotic laxative), and neomycin, which inhibits the production of ammonia by intestinal bacteria.

ADDITIONAL READINGS

Anesthesia for Organ Transplantation. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1364.

Morgan GE, Mikhail MS, Murray MJ, *Clinical Anesthesiology*, 4th ed. New York, NY: McGraw-Hill, 2006:792–796.

7. ANSWER: C

Suppression of immune responses to transplanted organs, aiding in recipient tolerance to those organs, is the primary goal of immunosuppressive therapy. Indeed, an undertreated immunosuppressed transplant patient can and will reject the donor organ. Despite the long-term survival of solid organ transplant patients on these agents, the modification of the immune system by immunosuppressive drugs does increase the risk of infection and malignancy as well as the side effects particular to each individual agent. Azathioprine can cause pancytopenia, cardiac arrest, and airway edema. Prednisolone, like all steroids, can lead to diabetes, hypertension, and weight gain. Cyclosporine causes increased risk of coronary artery disease, hypertension, ischemic vascular disease, and nephrotoxicity. OKT4A can result in fatigue/weakness, fever, chills, and hypotension. Rapamycin can lead to increased infection risk, myelosuppression, and hyperlipidemia.

ADDITIONAL READINGS

Anesthesia for Organ Transplantation. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1361.

Organ Transplantation. In: Baker J, Yost CS, Niemann CU. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:2272.

8. ANSWER: D

Right ventricular function is of particular concern after ***heart transplantation*** and is of major importance to cardiac output, hemodynamic stability, and end-organ perfusion. A normal donor heart even without significant ischemia can become dysfunctional if acutely challenged by increased right ventricular afterload (e.g., elevated pulmonary vascular resistance [PVR]). Management includes optimizing preload by avoiding right ventricular distention and underfilling, as well as supplying inotropic and chronotropic support with isoproterenol or dobutamine. Care must be taken to maintain coronary perfusion with vasopressors. Vasopressin is commonly used to maintain systemic vascular resistance in these patients because it has little effect on PVR. Lowering PVR can be accomplished by increasing FiO_2, thus minimizing hypoxic pulmonary vasoconstriction; avoiding hypercapnia and hypothermia; and pharmacologically lowering PVR with nitrates, PGE1, milrinone, and/or inhaled nitric oxide. In cases of refractory right ventricular failure, mechanical support with a right ventricular assist device may restore hemodynamics.

ADDITIONAL READING

Organ Transplantation. In: Baker J, Yost CS, Niemann CU. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:2260.

9. ANSWER: D

The major limitation of the current immunosuppressive drugs used in transplant medicine is that no currently available therapy is entirely effective in preventing rejection. Although ***graft function*** is usually monitored by the prothrombin time, serum bilirubin, aminotransferase activity, and lactate measurements, diagnosis of rejection requires a liver biopsy.

ADDITIONAL READING

Anesthesia for Organ Transplantation. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1373.

10. ANSWER: D

During liver transplantation, patients are prone to a variety of problems with coagulopathy, including decreased coagulation factors and platelets, as well as fibrinolysis. Patients are particularly vulnerable during the anhepatic phase of transplantation. Tests such as platelet count, fibrinogen/fibrin split products, and prothrombin time/partial thromboplastin time (PT/PTT) provide needed information, but the time to perform the tests and getting results back in a timely fashion is critical. ***Thromboelastography (TEG)*** tends to reflect the true coagulability of blood and not specific factors by measuring the viscoelastic properties of blood as clot formation progresses. A small drop of whole blood is inserted between a spindle and a rotating cuvette, and the resulting characteristic patterns formed over time as the blood clots are indicative of various coagulopathies. Many agree that TEG evaluation leads to more rational transfusion therapy.

ADDITIONAL READINGS

Jaffe RA, Samuels SI, eds. *Anesthesiologist's Manual of Surgical Procedures*. New York, NY: Raven Press; 1994:444.

11. ANSWER: A

The ***reperfusion syndrome*** occurs during the neohepatic phase of liver transplantation when the portal vein, hepatic artery, and vena cava are unclamped. At this point, the donor liver is reperfused, and this can result in severe hemodynamic instability, including dysrhythmias, conduction defects, bradycardia, hypotension secondary to decreased SVR, and increased pressure exposure of the right ventricle. Cardiac arrest can occur if a rapid increase in potassium (characterized by peaked T waves) is present. The exact mechanism of the syndrome is unknown, but several factors alone or in combination are suspected, such as high potassium, donor demographics, surgical technique, decreased SVR, hypothermia, metabolic acidosis, vasoactive peptides from the intestines, and sudden atrial stretching in response to unclamping. Treatment centers on correcting hypotension, acidosis, hyperkalemia, any coagulopathy, hypothermia, and fluid overload with associated pulmonary edema.

ADDITIONAL READINGS

Jaffe RA, Samuels SI, eds. *Anesthesiologist's Manual of Surgical Procedures*. New York, NY: Raven Press; 1994:442.

Organ Transplantation. In: Baker J, Yost CS, Niemann CU. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:2252.

12. ANSWER: E

Indications for CPB for transplant include cardiac transplantation (e.g., heart and heart–lung) and *en bloc* double lung transplants. Single and sequential double lung transplants can be performed without CPB; however, CPB is often used, especially for patients with pulmonary hypertension. Indeed, CPB is indicated during single lung transplantation if at any time oxygenation cannot be maintained despite ventilatory and pharmacologic maneuvers or pulmonary artery clamping by the surgeons.

ADDITIONAL READING

Anesthesia for Organ Transplantation. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:1367–1372.

13. ANSWER: D

Antithymocyte globulin is a polyclonal antibody directed at surface antigens on T lymphocytes, the binding of which activates both complement and cell-mediated cellular lysis, resulting in depletion of circulating lymphocytes. It is one of the immunosuppressants used to prevent acute graft rejection. These antibodies are known to elicit side effects upon administration, the most important of which is hypotension. The magnitude of hypotension can be reduced by pretreatment with corticosteroids, diphenhydramine, and acetaminophen. Slow infusion also helps alleviate this side effect. Antithymocyte globulin can be administered either centrally or peripherally.

ADDITIONAL READING

Krensky AM, Vicenti F, Bennett WM, Chapter 52. Immunosuppressants, tolerogens and immunostimulants. In: Brunton LL, Lazo JS, Parker KL, eds. *Goodman & Gilman's The Pharmacologic Basis of Therapeutics*. New York, NY: McGraw-Hill, 2006:1416–1417.

14. ANSWER: E

Succinylcholine administration causes an increase in serum potassium levels of approximately 0.5 to 0.6 mEq/L regardless of renal function. Therefore, its use in patients with chronic renal failure undergoing kidney transplantation is considered safe provided that preadministration potassium levels are no greater than 5.5 mEq/L. Low levels of plasma cholinesterase activity can be seen in patients with end-stage renal disease; however, this depression in activity is rarely sufficient to cause prolongation of succinylcholine's duration. Although cisatracurium is eliminated via Hoffman elimination, independent of renal function, its slow onset of action obviates its use in the rapid securing of the airway in this patient. Rocuronium can be used in rapid-sequence induction as a succinylcholine alternative, but this speed of onset is seen only with higher doses (0.9 to 1.2 mg/kg).

ADDITIONAL READINGS

Baker J, Yost CS, Niemann CU. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:2241.

Morgan GE, Mikhail MS. *Clinical Anesthesiology*. 5th ed. pgs 221, 224, 746.

Yao FF, Fontes ML, Malhotra V, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2008:840.

15. ANSWER: C

In this patient, the most likely explanation for the observed symptoms of central nervous system and respiratory depression is accumulation of morphine metabolites, particularly morphine-6-glucuronide, secondary to insufficient renal clearance. Meperidine administration in the setting of renal failure also results in the accumulation of a metabolite, normeperidine. Normeperidine, however, has been implicated in central nervous system excitatory effects and seizures, not the symptoms seen in this patient. No clinically significant accumulation of other opioid parent compounds or metabolites occurs in the setting of renal failure.

ADDITIONAL READINGS

Baker J, Yost CS, Niemann CU. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:2241.

Sharpe MD, Gelb AW. *Anesthesia and Transplantation*. Boston, MA: Butterworth Heinemann; 1999:261–262.

Yao FF, Fontes ML, Malhotra V, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2008:843–844.

16. ANSWER: B

Transfusion of volumes of PRBCs greater than 1 blood volume (massive transfusion) will predictably lead to dilution of both platelets and clotting factors, resulting in coagulopathy. PRBCs contain little plasma and thus small amounts of clotting factors. Platelet number and function are also significantly reduced, with platelet activity only 10% of normal after storage for 24 hours at 4 degrees C. The labile coagulation factors, V and VIII, are most significantly affected. Dilution appears to occur first in fibrinogen, followed by the coagulation factors II, V, and VIII, followed by platelets. Replacement therapy of fibrinogen, fresh frozen plasma, or platelets, however, should be conducted based on clinical findings rather than laboratory numbers only.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:213–214.

Miller RD. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:1807–1809.

17. ANSWER: E

The ***Pringle maneuver*** is a surgical technique in which the hepatic pedicle (containing the hepatic artery and portal vein) is clamped sufficiently so as to halt hepatic artery flow. This method of hepatic vascular control causes several physiologic changes, including a 10% decrease in cardiac index (CI) secondary to venous pooling in the occluded hepatic segment and subsequent decrease in venous return. This reduction in CI is offset by a sympathetic-mediated reflex resulting in 40% increases seen in both systemic vascular resistance (SVR) and mean arterial pressure (MAP). Of primary concern to the anesthesiologist is the risk of venous air embolism (VAE) resulting from leaving the major hepatic veins open during this inflow occlusion. The risk of VAE can be minimized by placing the patient in Trendelenburg position.

ADDITIONAL READING

Smyrniotis V, et al. Vascular control during hepatectomy: review of methods and results. *World J Surg*. 2005;29:1384–1396.

18. ANSWER: C

The ***transplanted heart*** is denervated, which results in abolition of direct autonomic input. This results in a preload-dependent cardiac output secondary to a relatively fixed heart rate. The lack of vagal nerve influence results in an expected resting heart rate of 100 to 120 beats per minute. Direct sympathetic nerve fibers are also disrupted; however, sympathetic stimulation does occur secondary to circulating catecholamines. Sympathetic denervation results in loss of catecholamine stores necessary in the indirect vasopressors' mechanisms of action (e.g., ephedrine). Two P waves are often present on the electrocardiogram tracing as a result of the presence of both donor and recipient sinoatrial (SA) nodes. Glycopyrrolate should still be coadministered with neostigmine neuromuscular blockade reversal despite lack of parasympathetic activity at the heart because the noncardiac effects of muscarinic activation will still occur.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:483–484.

19. ANSWER: D

The average platelet count response to transfusion of a single donor unit is $10{,}000 \times 10^9$/L (although references vary from 5,000 to 20,000). In this patient, the equivalent of 12 single donor units has been transfused, and at an expected increase of $10{,}000 \times 10^9$/L per unit, the resulting platelet count will be closest to $132{,}000 \times 10^9$/L.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:221.
Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:699–700.

20. ANSWER: D

Massive transfusion is defined as transfusion of whole blood/PRBCs of greater than 1 blood volume. Use of PRBCs during such transfusions often results in posttransfusion coagulopathy, secondary to dilution of platelets and coagulation factors following administration of blood depleted of platelets and coagulation factors. All coagulation factors are dilutionally depleted in this setting. Fresh frozen plasma effectively repletes all coagulation factors, whereas specific factor concentrations (e.g., factor V concentrate) would fail to treat coagulopathy in this setting. Cryoprecipitate administration is appropriate to correct hypofibrinogenemia, which results from a similar dilutional effect, but is not recommended prior to fresh frozen plasma in this setting. Dilutional thrombocytopenia is seen following massive transfusion; however, the repeat platelet count after transfusion in this case was more than $100{,}000 \times 10^9$/L, and so repeat platelet transfusion is not indicated.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Handbook of Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:103–104.
Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:216–217.

21. ANSWER: A

Prostaglandin E_1 (alprostadil) is currently administered in the setting of small bowel transplant graft reperfusion. Continuous infusion (0.1 to 0.6 mcg/kg/hr or 0.6 to 0.8 mg/kg/day) given at the time of vascular clamp release and continued postoperatively enhances graft perfusion through potent vasodilation by direct effects on vascular smooth muscle. Hypotension is commonly seen with intravenous administration. In the operating room this effect can be countered by intravenous volume repletion, reducing volatile anesthetic concentration, and giving infusions of dopamine or epinephrine in more severe cases. Other adverse effects seen with administration include flushing, fever, seizure, and hypokalemia.

ADDITIONAL READINGS

Beebe DS, Belani KG. Chapter 58. Anesthesia for kidney, pancreas, or other organ transplantation. In: Longnecker DE, Brown DL, Newman MF, Zapol WM, eds. *Anesthesiology*. New York, NY: McGraw-Hill; 2008:1414.
Sharpe MD, Gelb AW. *Anesthesia and Transplantation*. Boston, MA: Butterworth Heinemann; 1999:210.
Kutt JA, Asfar S, Ghent C, et al. Small bowel transplantation. In: Sharpe MD, Gelb AW, eds. *Anesthesia and Transplantation*. Boston, MA: Butterworth-Heinemann; 1999:210.

22. ANSWER: D

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with intravenous administration. In the operating room this effect can be countered by intravenous volume repletion, reducing volatile anesthetic concentration, and giving infusions of dopamine or epinephrine in more severe cases. Other adverse effects seen with administration include flushing, fever, seizure, and *hypo*kalemia.

ADDITIONAL READINGS

Beebe DS, Belani KG. Chapter 58. Anesthesia for kidney, pancreas, or other organ transplantation. In: Longnecker DE, Brown DL, Newman MF, Zapol WM, eds. *Anesthesiology*. New York, NY: McGraw-Hill; 2008:1414.

Sharpe MD, Gelb AW. *Anesthesia and Transplantation*. Boston, MA: Butterworth Heinemann; 1999:210.

Kutt JA, Asfar S, Ghent C, et al. Small bowel transplantation. In: Sharpe MD, Gelb AW, eds. *Anesthesia and Transplantation*. Boston, MA: Butterworth-Heinemann, 1999:210.

23. ANSWER: B

Acute hemolytic transfusion reactions occur in approximately 1 in 38,000 red blood cell transfusions. In these cases, transfused red blood cells trigger a recipient antibody-mediated hemolytic reaction. Symptoms of a reaction in the awake patient include chills, nausea, pain in the flank and chest, and fever. Recognition of a reaction under general anesthesia requires a high index of suspicion because only the nonspecific signs of tachycardia, *hypo*tension, elevation of temperature, diffuse oozing, and hemoglobinuria serve as clues to its occurrence. Recognizing such a reaction early and implementing treatment are important in avoiding such major consequences as acute renal failure, disseminated intravascular coagulation, and even death. Steps in the management of a suspected reaction include stopping the transfusion, rechecking the unit for compatibility with the recipient, sending a repeat type and crossmatch, placing a Foley catheter (if not already done) to evaluate for hemoglobinuria, and initiating osmotic diuresis.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:700–701.

24. ANSWER: B

Once the total volume of red cell transfusion exceeds 1 patient blood volume or approximately 10 to 12 units, non–group-O patients should continue to be transfused with type O blood. Type O blood contains anti-A and anti-B antibodies, which, after massive transfusion, may be present in quantities sufficient to react with transfused non-O units. Type-specific units may be transfused if anti-A and anti-B antibody titers are sufficiently low. This patient continues to remain anemic requiring transfusion; thus, awaiting crossmatching is also unreasonable.

ADDITIONAL READING

Miller RD. *Miller's Anesthesia*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2004:1804.

25. ANSWER: B

Reperfusion of the donor liver occurs with unclamping of the major vessels and is accompanied by subsequent release of acidemic blood, remaining preservative solution, air, clot, and debris into the patient's circulation. Physiologic and laboratory implications of this reperfusion are often significant, making this phase the period of greatest instability in the case. Hypotension can be significant and is likely multifactorial in etiology. *Hypo*calcemia likely results in cardiac depression. Return of this acidemic, hypothermic, hyperkalemic blood also likely results in decreased systemic vascular resistance and an increase in pulmonary vascular resistance, resulting in right ventricular overload and subsequent reduction in left ventricular preload. Volume status and hemodynamics must be optimized, with pressors if necessary, prior to this phase. Electrolyte abnormalities should also be corrected before reperfusion, with particular attention paid to hypocalcemia and acidemia, which are treated respectively with calcium chloride and sodium bicarbonate administration as necessary.

ADDITIONAL READINGS

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Sharpe MD, Gelb AW. *Anesthesia and Transplantation*. Boston, MA: Butterworth Heinemann; 1999:192–193.

26. ANSWER: A

During the ***anhepatic phase of liver transplantation***, once the recipient's liver is removed (which marks the

beginning of the second or anhepatic phase of liver transplantation), citrate from transfused blood products is no longer metabolized. As citrate levels rise, calcium is bound in the serum, resulting in hypocalcemia. Calcium levels during this phase must be monitored and optimized to avoid associated reductions in cardiac contractility. Acidic metabolites in venous blood from the bowel and lower body are also not cleared, resulting in metabolic acidosis.

ADDITIONAL READING

Morgan GE, Mikhail MS, Murray MJ. *Clinical Anesthesiology*. 4th ed. New York, NY: McGraw-Hill; 2006:797–801.

20.

INTENSIVE CARE

Chad E. Wagner, MD, Nathan Ashby, MD, and Jason D. Kennedy, MD

1. Acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) can be caused by

A. Severe sepsis
B. Pneumonia
C. Aspiration
D. Trauma
E. All of the above

2. The most common cause of ARDS and ALI is

A. Severe sepsis
B. Pneumonia
C. Aspiration
D. Trauma
E. Transfusion of blood products

3. ARDS presents with all of the following clinical findings EXCEPT:

A. Acute onset
B. P_{O2}-to-FiO_2 (P/F) ratio < 200 mm Hg
C. Bilateral pulmonary infiltrates on chest x-ray
D. Cardiogenic etiology
E. Mortality < 50%

4. Lung protection strategies for patients with ARDS involve all of the following EXCEPT

A. Smaller ventilatory tidal volumes of 6 cc/kg or less
B. Limitation of distending pressures on the ventilator to <30 cm/H_2O
C. Sufficient positive end-expiratory pressures (PEEP) to avoid alveolar collapse
D. Permissive hypocapnia
E. pH correction with $NaHCO_3$

5. In a patient with ARDS, management with a pulmonary artery (PA) catheter compared to central venous pressure (CVP) alone is most likely to result in all the following EXCEPT

A. No difference in mortality
B. No change in intensive care unit length of stay
C. More accurate volume repletion with the PA catheter
D. Fewer complications with CVP monitoring
E. Increased incidence of arrhythmia with PA catheter management

6. Delirium in the intensive care unit can be characterized by all of the following EXCEPT

A. Acute onset of mental status change or fluctuating course
B. Inattention
C. Increased morbidity but not mortality
D. Altered level of consciousness
E. Inability to give consent

7. Evidence-based medicine supports which of the following as an acute treatment for ARDS?

A. Partial liquid ventilation
B. Nitric oxide
C. Prone positioning
D. High-dose methylprednisone
E. None of the above

8. Noninvasive ventilator support is relatively contraindicated in all the following patients EXCEPT

A. Chronic obstructive pulmonary disease (COPD) exacerbation
B. Small bowel obstruction with respiratory distress

C. Altered mental status
D. Self-extubated septic shock patient on 80% FiO_2
E. Trauma patient with head injury

9. Recommended treatments for severe asthma include all the following EXCEPT

A. Inhaled beta agonists
B. Intravenous methylprednisolone
C. Oxygen supplementation
D. Theophylline
E. Inhaled corticosteroids

10. Important clinical features of life-threatening asthma include all the following EXCEPT

A. Severe expiratory wheezing
B. Silent chest to auscultation
C. Cyanosis
D. Bradycardia
E. Confusion and coma

11. ARDS is characterized by all of the following EXCEPT

A. Alveolar capillary injury
B. Abnormal surfactant
C. Capillary thrombi
D. Permeability edema
E. Absence of hyaline membranes

12. With pulmonary contusions, all the following are correct EXCEPT

A. Common after chest trauma
B. Require chest tube placement for curative therapy
C. Cause loss of alveolar and capillary membranes
D. Can display an interstitial infiltrate on chest x-ray
E. Display hypoxia

13. All of the following are true about tension pneumothorax EXCEPT

A. Caused by air entering the pleural space
B. Collapse of affected lung
C. Impaired venous return
D. Impaired ventilation of unaffected lung
E. Associated with pneumomediastinum in more than 20% of cases

14. Physical signs and symptoms of a tension pneumothorax include all the following EXCEPT

A. Early cyanosis
B. Distended neck veins
C. Tracheal deviation
D. Respiratory distress
E. Unilateral absence of breath sounds

15. Beck's triad for cardiac tamponade includes all the following EXCEPT

A. Hypotension
B. Distended neck veins
C. Muffled heart sounds
D. Elevated central venous pressure
E. Diagnosis made by clinical symptoms

16. In central venous pressure tracing, a transient increase in atrial pressure produced by isovolumic ventricular contraction is indicated by the _____ wave.

A. A
B. C
C. V
D. X
E. Y

17. Which statement is correct concerning positive pressure and PEEP?

A. Measured cardiac output can be increased by increasing left ventricular preload with positive-pressure ventilation.
B. The transmural left ventricular pressure is decreased by PEEP application.
C. Positive intrathoracic pressure can cause a decrease in left ventricular afterload, thereby enhancing cardiac performance.
D. Application of PEEP can decrease coronary artery oxygenation in patients with poor heart function.
E. All of the above

18. Select the most likely etiology of shock given this hemodynamic profile: systolic blood pressure 80/46 mm Hg, central venous pressure 10 mm Hg, pulmonary capillary wedge pressure 14 mm Hg, cardiac index 4.7 l/min/m^2.

A. Severe hemorrhage
B. Pneumococcal sepsis
C. Anterolateral myocardial infarction
D. Cardiac tamponade
E. Right ventricular myocardial infarction

19. A diagnostic criterion for diabetic ketoacidosis (DKA) is

A. Hyperglycemia due to insulin resistance
B. Increased anion gap

C. Respiratory alkalosis as a compensation for metabolic alkalosis
D. Absence of ketonemia
E. Hyperosmolarity

20. Treatment of DKA includes which one of the following?

A. Stopping insulin when the serum glucose returns to normal
B. Avoidance of intravenous fluids containing dextrose
C. Awareness of hypophosphatemia
D. Limitation of potassium replacement
E. All of the above

21. Concerns about using sodium bicarbonate therapy for metabolic acidosis include which one of the following?

A. Decreased cerebrospinal fluid pH
B. A resultant shift in the oxygen dissociation curve
C. A resultant sodium overload
D. Causing venous hypercapnia with increased mixed venous carbon dioxide
E. All the above

22. Which statement about the difference between hyperglycemic hyperosmolar state (HHS) and diabetic DKA is correct?

A. No ketonuria with HHS
B. Higher serum glucose in DKA
C. More dehydration with DKA
D. Higher osmolality with DKA (>320 mosm)
E. Acidosis with HHS

23. A 59-year-old man presents to the intensive care unit in early septic shock. He requires central venous access for vasopressor administration. He has a history of right total pneumonectomy for lung cancer, diabetes mellitus, and chronic renal failure. He is dialyzed on a Monday/Wednesday/Friday schedule through a right forearm arteriovenous fistula. Which of the following locations would be most appropriate for central line placement in this individual?

A. Left internal jugular vein
B. Right subclavian vein
C. Left femoral vein
D. Right internal jugular vein
E. Left subclavian vein

24. A 24-year-old woman presents after being an unrestrained driver in a motor vehicle accident. Shortly after intubation her ventilator begins alarming high peak pressures. She is noted to have left tracheal deviation, diminished breath sounds on the right, and an acute drop in blood pressure. Which of the following would be the appropriate immediate intervention?

A. Needle decompression inserted between the xiphoid and left costal margin, passed at 30 to 45 degrees, and angled toward the left shoulder
B. Needle decompression inserted in the left second intercostal space in the midclavicular line
C. Needle decompression inserted in the right second intercostal space in the midclavicular line
D. Tube thoracostomy decompression placed in the right fifth intercostal space at the midaxillary line
E. Change ventilator settings to a pressure-control mode and continue fluid resuscitation

25. A 35-year-old woman presents with complaints of fatigue, poor appetite, weight loss, and nausea. On examination, she appears tanned, although she denies any sun exposure. She is moderately hypotensive. Laboratory studies show that she is mildly hyperkalemic and hyponatremic. Which endocrine disorder is she exhibiting?

A. Cushing's syndrome
B. Addison's disease
C. Conn's syndrome
D. Hypothyroidism
E. Secondary adrenal insufficiency

26. A 36-year-old man with Down syndrome and a history of complete atrioventricular canal repair presents for a repeat abdominal washout procedure. Intraoperative hypotension occurs and is unresponsive to intravenous fluids and vasopressors. What was most likely the induction agent chosen for this patient?

A. Propofol
B. Etomidate
C. Thiopental
D. Ketamine
E. High-dose midazolam

27. A 24-year-old man presents in acute hypovolemic shock following a motor vehicle accident. He has sustained a major pelvic fracture. Which of the following would be the most appropriate access for volume resuscitation in this patient?

A. Two large bore peripheral IV lines in the upper extremities
B. 7F 20-cm triple-lumen central line in the right internal jugular vein
C. 7F 20-cm triple-lumen central line in the left subclavian vein

D. 9F 10-cm single-lumen central line in the right femoral vein
E. 9F 10-cm single-lumen central line in the right internal jugular vein with a pulmonary artery catheter passed though the introducer port

28. A 24-year-old man suffered severe burns after a cigarette set his mattress ablaze. He suffered burns to his face and neck, circumferentially to both arms, and to the front of his trunk. What is the approximate body surface area (BSA) for his burn?

A. 9%
B. 18%
C. 27%
D. 36%
E. 45%

29. Using the Parkland formula, estimate the volume of fluid that the patient in the previous question will need in the first 24 hours for resuscitation, assuming he weighs 70 kg.

A. 4.5 L over 24 hours
B. 6.5 L over 24 hours
C. 8.5 L over 24 hours
D. 10.5 L over 24 hours
E. 12.5 L over 24 hours

30. The patient presents awake and alert. He is on supplemental oxygen with saturations in the high 90s on 100% nonrebreather mask. Burns frequently require intubation due to the injury to the airways. Which of the following signs or symptoms would NOT necessarily indicate a need for intubation in this patient?

A. Singing of the facial hair
B. Soot in the upper airways
C. Hoarseness and stridor
D. Altered mental status
E. Hypoxemia

31. The patient's wife was asleep in the room but did not suffer any burns. She has no signs of thermal inhalational injury. Which of the following would NOT be seen if she is suffering from mild carbon monoxide poisoning?

A. Normal oxygen saturation by pulse oximetry
B. Cherry-red coloration
C. Metabolic acidosis
D. Headache
E. Dizziness

32. A patient receives a dose of ampicillin and a few minutes later becomes profoundly hypotensive and tachycardic, develops difficulty breathing, and begins to show signs of rash. Which of the following is NOT a standard pharmacologic component of therapy?

A. Epinephrine
B. Albuterol
C. Dobutamine
D. Famotidine
E. Diphenhydramine

33. Given the reaction above, which of the following changes in laboratory findings might be expected?

A. Rise in hematocrit
B. Fall in hematocrit
C. Hyperchloremia
D. Hyponatremia
E. Hypernatremia

34. A 59-year-old man has been oliguric overnight, with urine output of less than 0.5 mL/kg/hr over the past 14 hours. His serum creatinine has gone from 1.1 yesterday to 2.3 today. According to the RIFLE criteria for diagnosis of acute renal failure, what category of acute renal failure is this patient exhibiting?

A. Risk
B. Injury
C. Failure
D. Loss
E. End-stage renal disease

35. This patient is being considered for renal replacement therapy. On examination he is resting comfortably with no respiratory distress on room air. He is clear mentally. His laboratory results are N 140, K 6.2, Cl 102, Bicarb 20, BUN 65, Cr 2.5, and Gluc 110. His electrocardiogram shows peaking of the T waves. An arterial blood gas analysis shows normal oxygenation and a mild metabolic acidosis with a compensatory respiratory alkalosis. Which of the following reasons is most compelling for the initiation of renal replacement therapy?

A. Fluid overload
B. Elevated BUN
C. Hyperkalemia
D. Acidosis
E. Low urine output

36. Which of the following interventions for hyperkalemia does NOT directly affect potassium concentrations in the serum?

A. Calcium chloride administration
B. Insulin and glucose administration

C. Albuterol administration
D. Sodium polystyrene sulfonate resin
E. Furosemide administration

37. Which of the following is NOT a commonly noted electrocardiographic (ECG) change in the progression of hyperkalemia?

A. Peaked T waves
B. Flattening and loss of the P wave
C. PR prolongation
D. Widening of the QRS complex
E. Development of a prominent U wave

38. A 73-year-old, 134-pound woman with a history of type 2 diabetes, peripheral vascular disease, and hypertension is in the intensive care unit after an emergent open abdominal infrarenal aortic aneurysm repair. Her baseline creatinine was 0.7 mg/dL. On postoperative day 1 it is 1.4 mg/dL, with a BUN of 36. Her urine output has been consistently 10 to 20 cc/hour during and since surgery. Which of the following is NOT a risk factor for perioperative renal failure?

A. Vascular clamping of the aorta
B. Preoperative hypertension
C. Urine output of 10 to 20 cc/hour intraoperatively
D. Age
E. Diabetes

39. How would you classify this patient's renal dysfunction using RIFLE criteria?

A. Stage 1 (Risk)
B. Stage 2 (Injury)
C. Stage 3 (Failure)
D. Stage 4 (Loss)
E. Unable to classify with the given information

40. What change in serum creatinine represents the largest decrease in creatinine clearance?

A. 0.8 mg/dL to 1.3 mg/dL
B. 1.3 mg/dL to 1.9 mg/dL
C. 2.0 mg/dL to 3 mg/dL
D. 3 mg/dL to 4 mg/dL
E. 4 mg/dL to 5 mg/dL

41. A patient in the intensive care unit is receiving intravascular catheter-directed thrombolysis with tPA for occlusion of the popliteal artery. During the evening the patient develops a large amount of bright red blood per rectum and becomes hypotensive. Other than volume resuscitation with packed red blood cells and IV fluids, what is the most effective method for reversing the effect of tPA?

A. Fresh frozen plasma
B. Activated factor VII
C. Cryoprecipitate
D. Platelets
E. Vitamin K

42. Via what mechanism does transfusion of packed red blood cells increase systemic blood pressure?

A. Increase in preload
B. Shifting the cardiac output curve via the Starling mechanism
C. Increase in viscosity of blood
D. Decrease in inducible nitric oxide in the periphery via sequestration by free hemoglobin, thereby increasing systemic vascular resistance
E. All of the above

43. What blood product is most likely to induce citrate toxicity?

A. Cryoprecipitate
B. Packed red blood cells
C. Fresh frozen plasma
D. Platelets
E. Whole blood

44. What is a consistent finding in ARDS patients treated with a lung protective ventilator strategy?

A. Increased respiratory rate
B. Decreased Pao_2-to-FiO_2 (P/F) ratio
C. Improved survival
D. Increased arterial CO_2 concentration
E. All of the above

45. Which of the following is an absolute contraindication to the administration of Xigris (recombinant activated protein C)?

A. APACHE score of 30
B. Hemorrhagic stroke 10 weeks prior
C. Upper gastrointestinal hemorrhage 6 months prior
D. Platelet count of 25,000 transfused to a level of 100,000
E. Severe head trauma 4 months prior

46. An elderly patient is admitted to the intensive care unit for abdominal sepsis following laparotomy. Which findings would NOT be consistent with the diagnosis of sepsis, as measured by a pulmonary artery catheter?

A. Cardiac index 2.7 $L/min/m^2$
B. Systemic vascular resistance (SVR) 1,800 $dyn/sec/cm^{-5}$
C. Central venous pressure (CVP) 6 mm Hg

D. SvO_2 85%
E. Pulmonary artery pressure (PAP) 27/14 mm Hg

47. Noninvasive positive-pressure ventilation with either CPAP or BiPAP has shown a benefit in which group of patients?

A. Acute chronic obstructive pulmonary disease exacerbation
B. Acute systolic heart failure with pulmonary edema
C. Immunosuppressed patients with hospital- or community-acquired pneumonia
D. Near-drowning pulmonary edema
E. All of the above

48. Which of the following is a known side effect of the administration of inhaled nitric oxide?

A. Anemia
B. Elevation in carboxyhemoglobin levels
C. Hypoxemia
D. Inhibition of platelet aggregation
E. Hypercoagulopathy

49. What is the acute effect of the transfusion of packed red blood cells on the oxyhemoglobin dissociation curve in critically ill patients?

A. Shifted to the right
B. Shifted to the left
C. No change
D. Shifted up and to the right
E. Shifted up and to the left

50. In the management of acute aortic dissection in a hemodynamically stable patient, what would be the ideal order to administer medications to best care for the patient?

A. Esmolol, sodium nitroprusside, morphine
B. Sodium nitroprusside, esmolol, morphine
C. Esmolol, morphine, sodium nitroprusside
D. Morphine, esmolol, sodium nitroprusside
E. Morphine, sodium nitroprusside, esmolol

51. What is usually the first indication of cyanide toxicity in patients receiving IV nitroprusside?

A. Elevated lactate levels
B. Tachyphylaxis
C. Hypoxemia
D. Hypercarbia
E. Tachycardia

52. In what clinical situation will mean pulmonary artery wedge pressure (PAWP) overestimate left ventricular end-diastolic pressure?

A. Tachycardia
B. After cardiac surgery
C. Aortic regurgitation
D. Aortic stenosis
E. After pneumonectomy

53. Which of the following is NOT decreased following transfusion of leukocyte-reduced red blood cells versus non–leukocyte-reduced red blood cells?

A. Recurrence rate of cancer
B. Alloimmunization to platelets
C. Febrile reactions
D. Sepsis
E. Transfusion-related acute lung injury (TRALI)

54. What factor would NOT be normally found in cryoprecipitate?

A. Factor VIII
B. Factor IX
C. Factor XIII
D. von Willebrand factor
E. Fibronectin

CHAPTER 20 ANSWERS

1. ANSWER: E

2. ANSWER: A

3. ANSWER: D

Acute lung injury (ALI) and ***acute respiratory distress syndrome (ARDS)*** are diagnosed by the presence of acute hypoxemic respiratory failure with bilateral pulmonary infiltrates without evidence of left atrial hypertension, which can be defined as a pulmonary capillary wedge pressure (PCWP) less than 18 (to exclude cardiogenic etiology). ALI is defined as a P/F ratio of less than 300 mm Hg and ARDS is defined as a P/F ratio less than 200 mm Hg. Less than 100 mm Hg is considered severe ARDS. The incidence of ARDS varies but is commonly reported as 58 cases per 100,000. The mortality for ARDS is around 40%. In a prospective cohort, Rubenfeld et al. reported that sepsis is the most common cause of ARDS. Other common factors associated with ALI/ARDS are severe trauma, pneumonia, witnessed aspiration, pancreatitis, and drug overdose.

KEY FACTS: ALI/ARDS

ACUTE LUNG INJURY (ALI)	ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)
P/F ratio < 300 mm Hg	P/F ratio < 200 mm Hg

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

Rubenfeld G. Incidence and outcomes of acute lung injury. *N Engl J Med*. 2005;353:1685–1693.

4. ANSWER: D

There are two types of ***ARDS***, primary and secondary. Etiologies of primary ARDS include aspiration, pneumonia, and TRALI. Examples of secondary ARDS are sepsis, pancreatitis, and hypotension. Both primary and secondary ARDS are associated with elevated levels of inflammatory mediators such as IL-6, IL-1, and IFN-gamma.

The ***Acute Respiratory Distress Syndrome Network***, a landmark multicenter randomized trial, compared ventilator strategies of 12 cc/kg tidal volumes to 6 cc/kg tidal volumes and plateau pressures limited to less than 30 cm/H_2O. The trial was stopped after 861 patients because of a lower mortality of 31% to 39% ($p = 0.008$) in the 6-cc/kg tidal-volume group. Lower IL-6 levels in the low-tidal-volume group plus other studies have led to the speculation that less barotrauma from lower driving pressures leads to less of an inflammatory response. The mainstay of treatment for ARDS is supportive ventilator management with 6 cc/kg tidal volume, plateau pressure less than 30 cm/H_2O, sufficient PEEP (5–24 cm H_2O) and FiO_2 to maintain the SaO_2 at greater than 88%. Sacrificing a higher PCO_2 and therefore lower arterial pH for oxygenation is known as permissive hypercapnia. $NaHCO_3$ infusions can be used to maintain pH greater than 7.2 if desired while allowing for elevated PCO_2.

ADDITIONAL READINGS

NIH ARDS Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and ARDS. *N Engl J Med*. 2000;342:1301–1308.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*, 3rd ed. Casa Editrice: Mosby; 2008.

5. ANSWER: C

The *2006* ***ARDS Network*** study compared PA catheter management to CVP management in patients with ARDS. More than 100 patients were enrolled in this multicenter randomized trial. The 50-day mortality was the same in both groups, with no change in the number of ventilator-free days, no improvement in outcomes for patients in shock with ARDS, and no difference with regard to kidney dysfunction or vasopressor use. Fluid balance and diuretic usage were the same in both groups. Overall, there was no benefit to the use of a PA catheter in managing ARDS patients. The PA catheter group had twice the complication rate of the CVP group, most commonly arrhythmias.

ADDITIONAL READING

National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wheeler AP, Bernard GR, Thompson BT, Schoenfeld D, Wiedemann HP, deBoisblanc B, Connors AF Jr, Hite RD, Harabin AL. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med*. 2006;354(21):2213–2224.

6. ANSWER: C

Delirium occurs in up to 60% of older hospitalized patients and is the most common hospital complication in this group. Delirium is associated with increased morbidity and

mortality, prolonged hospital stay, and functional decline. Risk factors include multisystem illness, comorbidities, psychoactive medications, and advanced age. Delirium is characterized by a disturbance of consciousness that is acute in onset, and a fluctuating course of impaired cognitive functioning so that a patient's ability to receive, process, and store information is impaired.

ADDITIONAL READINGS

Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, Speroff T, Gautam S, Bernard GR, Inouye SK. Evaluation of delirium in critically ill patients: Validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001;29:1370–1379.

Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, Truman B, Speroff T, Gautam S, Margolin R, Hart RP, Dittus R. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA*. 2001;286:2703–2710.

7. ANSWER: E

Multiple therapies have been studied to reduce the mortality in ARDS. Most are in an attempt to attenuate the inflammatory response. The therapies of no clinical benefit include high-dose corticosteroids, prostaglandin E_1, nonsteroidal anti-inflammatories, anti-endotoxin, anticytokine therapy, surfactant therapy, prone positioning, and partial liquid ventilation. Only low tidal volumes of 6 cc/kg or less with plateau pressures of less than 30 cm/H_2O have been shown to be of survival benefit.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

8. ANSWER: A

Noninvasive ventilation including continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP) has long been used as a therapy for chronic respiratory diseases such as sleep apnea and COPD. Its use has increased for acute respiratory failure caused by trauma, asthma, COPD exacerbation, congestive heart failure exacerbation, and pneumonia. Patients must be cooperative enough to tolerate the mask and also control their airway. They must be at a low risk for aspiration and lack facial trauma. The mask can be full face or nasal.

ADDITIONAL READINGS

AARC Conference Summarizer. Noninvasive ventilation in acute care: controversies and emerging concepts. *Resp Care*. 2009;54(Issue 1 and 2).

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

9. ANSWER: D

Asthma is the most common chronic lung disease. Acute asthma, also known as life-threatening asthma or status asthmaticus, can be split into two types: sudden progression and slow progression. In sudden progression, the patient's clinical status steadily worsens in less than 6 hours. This occurs in 10% to 20% of patients who present with life-threatening asthma, and it is likely to be triggered by respiratory allergens, exercise, or stress. In slow progression, patients decline over greater than 6 hours. This occurs in 80% to 90% of patients with life-threatening asthma. Slow progression is likely to be triggered by an upper respiratory infection causing an airway inflammatory response. The most specific indicator of an increased risk of dying from asthma is a history of repeated admissions, especially if they required intubation.

Hypoxemia with severe asthma is secondary to V/Q mismatch and is usually fully corrected with modest supplemental oxygen. The cornerstone of therapy is inhaled beta agonists, with intravenous formulations reserved for refractory cases. Simultaneous use of anticholinergics, theophylline, Heliox, and magnesium infusions can be considered, but efficacy is debatable in the literature. Systemic corticosteroids should be used in all cases of severe asthma, but it may take 6 to 24 hours to see the effect. Inhaled corticosteroids should be given and can show effect within 3 hours.

For intubated patients, lung hyperinflation should be minimized by prolonging expiratory time and minimizing inspiratory time. Patients will have auto-PEEP and therefore do not need additional extrinsic PEEP set on the ventilator; They will need auto-PEEP measured on the ventilator to asses the amount of auto-PEEP(also known as dynamic hyperinflation). Hypoventilation, with resultant hypercarbia may be required to avoid auto PEEP in patients with severe obstruction.

ADDITIONAL READINGS

Lugog N, MacIntyre NR. Life-threatening asthma, principles and management. *Resp Care*. 2008;53:726.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

10. ANSWER: A

Physical findings consistent with severe asthma include general ill appearance, use of accessory muscles, respiratory rate greater than 30 breaths per minute, heart rate greater than 120 beats per minute, and paradoxical pulse greater than 25 mm Hg. In life-threatening asthma attacks, no breath sounds can be heard, indicating severely impaired ventilation (silent chest); in less severe conditions, expiratory wheezing can be heard. Signs of impending arrest can include bradycardia, hypotension, cyanosis, lactic acidosis, confusion and coma, pneumothorax, and pneumomediastinum. The decision to intubate these patients is a clinical decision and should not be made based on arterial blood gas findings. Peak flow meter values cannot grade severity but can show progress with treatment.

ADDITIONAL READINGS

Lugog N, MacIntyre NR. Life-threatening asthma, principles and management. *Resp Care*. 2008;53:726.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

11. ANSWER: E

In ARDS there is damage to the capillary endothelial and alveolar epithelial cells. Cellular injury results in a permeability defect that floods the alveoli with protein-rich fluid and inflammatory cells. This results in alteration in pulmonary mechanics, physiology, and gas exchange. Damage to type 2 pneumocytes results in alteration in surfactant production as well as dilution of surfactant by proteinaceous fluid. Histologic features of injury include microthrombi in capillaries, denudation of alveolar epithelial cells, interstitial and alveolar infiltration by polymorphonuclear leukocytes, and hyaline membrane formation from within the alveoli. All of these lead to impaired lung compliance and oxygenation.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

12. ANSWER B

Pulmonary contusions are common in victims of blunt chest trauma. Early after trauma alveolar hemorrhage, atelectasis, and consolidation occur, all leading to increased capillary permeability, plasma protein/red blood cell infiltration of the lung, and interstitial edema. Clinical signs include respiratory distress and hypoxia. Contusions can be unilateral or bilateral, with a chest x-ray displaying a miliary pattern or patchy shadows in the affected region. CT is more sensitive in diagnosis, but clinical correlation with the type of trauma will be most helpful. If significant injury has occurred, ALI and ARDS can develop. Treatment is supportive, and if not contraindicated noninvasive ventilation can be used. ATLS guidelines recommend intubating patients with a pulmonary contusion if the PO_2 is 65 mm Hg or less on room air.

ADDITIONAL READING

Vidhani K, et al. Should we follow ATLS guidelines for the management of traumatic pulmonary contusion. *Resuscitation*. 2002;52(3): 265–268.

13. ANSWER: E

14. ANSWER: A

Tension pneumothorax can cause life-threatening cardiovascular collapse. Increased unilateral pressure can impede venous filling and ventilation in the unaffected lung. Radiographic signs include striking collapse of the lung, contralateral shift of the heart and mediastinum, and inversion of the hemidiaphragm. Physical signs and symptoms include distended neck veins, agitation, progressive hypoxia, hypotension, and Crepitus in the neck, face, chest, or axilla. Tension pneumothorax can occur without these signs and symptoms and can be more subtle initially. Cyanosis may not be an early finding and may occur only late, right before arrest. The diagnosis should be made clinically, not radiographically, by auscultation of the chest, with clinical findings of respiratory distress with unilateral absence of breath sounds. Chest tube is curative therapy.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

15. ANSWER: D

Cardiac tamponade is a condition in which pressure in the pericardial space is increased, resulting in hemodynamic changes reflected as compression of the chambers of the heart. Increased pressure is the result of accumulated fluid in the pericardial space. The amount of fluid in the pericardial space is not as important as the rapidity of fluid collection

and the compliance of the pericardium. Thus, the amount of pericardial fluid cannot define tamponade, only hemodynamics. Fluid accumulation around the heart decreases and eliminates the transmural distending pressure that promotes cardiac filling. As it worsens, diastolic pressures equalize in the atria and ventricles. Common causes include pericarditis, neoplasm, uremia, hemorrhage, aortic dissection, hypocoagulation, trauma, and cardiac surgery. Diagnosis is made by clinical history in conjunction with physical signs such as hypotension and pulsus paradoxus. Pulsus paradoxus is the variation in systolic blood pressure greater than 10 mm Hg. Classical cardiac tamponade presents with three signs, known as ***Beck's triad***. **Hypotension** occurs because of decreased stroke volume, **jugular venous distention** is due to impaired venous return to the heart, and **muffled heart sounds** are due to fluid inside the pericardium. The chest x-ray may show an enlarged pericardium. Echocardiography can be diagnostic, with direct imaging of fluid in the pericardial space and the ability to assess respiratory variation in tricuspid and mitral inflow velocities. Treatment is drainage by either percutaneous pericardiocentesis or open pericardial window. The central venous pressure may be elevated, but this is not part of Beck's triad.

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*, 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

16. ANSWER: B

The A wave indicates atrial contraction. The C wave is the transient increase in atrial pressure produced by isovolumic ventricular contraction. The X descent is the systolic collapse in atrial pressure. The V wave is venous filling of the atrium during late systole while the tricuspid valve remains closed. The Y descent is when the tricuspid valve opens and blood flows from the atrium to the ventricle.

ADDITIONAL READING

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

17. ANSWER: C

Positive-pressure ventilation and PEEP can decrease cardiac output by decreasing venous return and alteration of left ventricular distensibility. In some patients with left ventricular (LV) dysfunction, increased transmural LV pressure from PEEP can result in improved cardiac output by decreasing end-diastolic volume in a patient who is already volume overloaded, therefore moving the patient to a better position on the Starling curve. This ultimately leads to increased coronary artery oxygenation and decreased LV afterload. There is evidence that even with normal compliance of the heart, PEEP of 10 mm Hg or greater can make central venous pressure and pulmonary capillary wedge pressure measurements unreliable.

ADDITIONAL READINGS:

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

18. ANSWER: B

Differentiating types of shock is an essential skill for the anesthesiologist and intensivist. Septic shock is a state of shock with low to normal filling pressures, low arterial blood pressure, high cardiac index, and low systemic vascular resistance (Table 20.1).

Table 20.1 EXAMPLES OF HEMODYNAMIC PROFILES

	BLOOD PRESSURE (MM HG)	CENTRAL VENOUS PRESSURE (MM HG)	PULMONARY CAPILLARY WEDGE PRESSURE (MM HG)	CARDIAC INDEX (L/MIN/M^2)
Anterolateral myocardial infarction	**90/68**	**18**	**22**	**1.8**
Right ventricular myocardial infarction	**88/40**	**20**	**5**	**2.2**
Hemorrhage	**84/60**	**3**	**5**	**1.8**
Tamponade*	**90/68**	**18**	**17**	**1.8**

*Tamponade by pulmonary artery catheter will be diagnosed with equalization of diastolic filling pressures. Central venous pressure = right ventricle = pulmonary artery.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

19. ANSWER: B

Diabetic ketoacidosis (DKA) occurs predominantly in type 1 diabetics but can also occur in type 2. It develops as a consequence of relative insulin deficiency in combination with an excess of glucagon, catecholamines, and cortisol. It usually occurs in poorly controlled diabetics or those with infection, myocardial infarction, or some other acute illness. DKA is defined by hyperglycemia, acidosis (anion gap), and ketonemia. The patients look clinically ill and show evidence of dehydration because of the glucosuria.

20. ANSWER: C

Treatment of DKA includes fluid resuscitation with a balanced salt solution and insulin drip. Once the serum glucose falls below 250 g/dL the intravenous fluids should be changed to a dextrose solution. Basic metabolic panels should be drawn every 4 hours, with attention to the anion gap. Therapeutic endpoints for DKA are not euglycemia, because a serum bicarbonate level less than 20 mEq/L in the presence of normal glucose concentrations is an indicator of the continued need for intracellular glucose and insulin for reversal of lipolysis. DKA results in a profound total body deficit of potassium and phosphorus, even though the levels may be elevated on the initial laboratory assessment. If acidosis persists at extremes of pH (less than 7.1) despite fluids and insulin, a sodium bicarbonate drip can be used.

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.
Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

21. ANSWER: E

Use of ***sodium bicarbonate*** as a therapy for metabolic acidosis is controversial. There is little evidence to support its use in lactic acidosis. In patients with metabolic acidosis from renal tubular acidosis, diarrhea, and uremia, there is some literature support for bicarbonate therapy. However, it is of no benefit in acidosis from cardiac arrest, shock, and sepsis. There is still an argument that if pH is less than 7.2, vasopressors may be less effective and correction may be helpful in normalizing hemodynamics, but there is not much evidence to support this view. Negative effects include venous hypercapnia, decreased cerebrospinal fluid pH, tissue hypoxia, hypernatremia, hyperosmolality of the cerebrospinal fluid, and a shift in the O_2 dissociation curve.

ADDITIONAL READINGS

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Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

22. ANSWER: A

Hyperglycemic hyperosmolar state (HHS) occurs more commonly in type 2 diabetics or older type 1 diabetics. HHS is associated with higher serum glucose levels than DKA, usually greater than 600 g/dL. HHS patients usually have a pH greater than 7.3, higher serum bicarbonate, osmolality greater than 320, no serum or urine ketones, and more dehydration from glucosuria. Treatment includes hydration, insulin, and repletion of profound potassium deficits.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

23. ANSWER: D

Placement of central venous catheters is common in critically ill patients. Central line placement is associated with a number of risks, including bleeding, infection, and damage to surrounding structures. Careful site selection based on the patient's history helps to mitigate some of the risk involved. In this patient, his prior right pneumonectomy makes the left subclavian vein a dangerous target, as any pneumothorax will be a life-threatening issue. The left internal jugular would be risky for this reason as well, especially given that the apex of the lung tends to be somewhat higher on this side. Although ultrasound guidance and good technique would limit the risk, other sites would be preferred. The right subclavian vein would appear to be a better option because there is no risk of pneumothorax with this site. The presence of a right upper extremity dialysis access, however, means any interference with outflow from the arm may compromise the patient's dialysis access. The femoral veins

carry a higher risk of thrombosis and infection according to most authors and should be used only when no better options are available. The right internal jugular would be the best choice in this patient.

ADDITIONAL READINGS

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Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008.

24. ANSWER: C

This patient is showing signs of right-sided tension pneumothorax. Mechanism of injury, high peak pressures, acute hypotension, and shifting of the mediastinum should all be red flags for tension pneumothorax in this patient. Without immediate intervention, cardiovascular collapse and death are likely. Changing the ventilator settings and giving fluid will not address the root cause. Tube thoracostomy would be appropriate but should follow needle decompression. Answer A describes the technique for pericardial drainage and would not be appropriate in this situation. Although needle decompression will only temporize the situation, it directly addresses the root cause of the problem and is quickly accomplished while tube thoracostomy is prepared. Decompression should be performed with a large-bore angiocath (14 gauge is generally used) to allow for rapid decompression of the pressure.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:88–90, 271, 955–959.

25. ANSWER: B

The patient is exhibiting symptoms of ***Addison's disease (primary adrenal insufficiency)***. Addison's is due to a lack of both glucocorticoid and mineralocorticoid activity secondary to adrenal insufficiency. Addison's is characterized by weight loss, weakness and lethargy, hypotension, gastrointestinal symptoms, hyperpigmentation, hyperkalemia, hyponatremia, and hypercalcemia. Autoimmune causes are the most common cause of Addison's today. Secondary adrenal insufficiency is due to failure of the pituitary and lack of ACTH. Secondary adrenal insufficiency does not show the hyperpigmentation of Addison's. This hyperpigmentation is due to an excess of ACTH and beta-lipotropin triggering melanocyte activity. Mineralocorticoid activity is also generally maintained in secondary adrenal insufficiency. Cushing's syndrome occurs due to glucocorticoid excess and is typified by "moon facies," central obesity, striae, thin skin, easy bruising, and proximal muscle wasting. Glucose intolerance, osteopenia, and hypertension are common as well. The most common cause of Cushing's syndrome is exogenous glucocorticoid administration. Conn's syndrome is characterized by hypokalemia, hypernatremia, tetany, polyuria, and alkalosis. Because most exogenous steroids have both glucocorticoid and lesser mineralocorticoid activity, a mixture of the signs is common. Hypothyroidism is characterized by reduced mental acuity, dry skin, depressed reflexes, joint pain, cold intolerance, bradycardia, and in extreme cases heart failure and coma.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2006:1133–1134, 1137–1142.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1078–1083, 1087–1089.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1269–1278.

26. ANSWER: B

Based on his history of complete atrioventricular canal repair, this patient may have received ***etomidate*** as an induction agent for several anesthetics within a short time period. Etomidate inhibits adrenal steroidogenesis by interaction with the 11β-hydroxylase enzyme. This can result in reduced cortisol production in response to ACTH, as demonstrated by failure to increase serum cortisol when cosyntropin is administered. Loss of adrenal responsiveness in times of stress can lead to increased resuscitation needs and poor response to pressor agents in the face of hypotension. The effects were thought to last for 8 to 12 hours after dosing, but newer studies are showing that effects may linger for longer periods, perhaps up to 48 hours. Although propofol can produce a temporary drop in cortisol levels, it does not suppress adrenal responsiveness.

ADDITIONAL READINGS

Evers AS, Maze M. *Anesthetic Pharmacology: Physiologic Principles and Clinical Practice*. Philadelphia, PA: Churchill Livingstone; 2004:403–404.

Hildreth AN, Meija VA, et al. Adrenal suppression following a single dose of etomidate for rapid sequence induction: a prospective randomized study. *J Trauma*. 2008;65:573–579.
Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1275.
Vinclair M, Broux C, Faure P, et al. Duration of adrenal inhibition following a single dose of etomidate in critically ill patients. *Intensive Care Med*. 2008;34:714–719.

27. ANSWER: A

Rapid fluid resuscitation requires appropriate intravascular access. Central access does not always mean better access for resuscitation. Flow through a rigid tube (i.e., catheter) is generally governed by the Hagen–Poiseuille equation, $Q = DP \times (P\ r^4/8mL)$, where Q = rate of flow, DP = the change in pressure through the tube, $P\ r^4$ = size of the tube, m = viscosity of the fluid, and L = length of the tube. Although the diameter of the tube has a magnified effect on flow rates through the tube, length can also adversely affect flow. Given that the length of central venous catheters far exceeds the diameter, catheter length plays a very important role. The length of a 7F catheter prevents it from allowing rapid fluid flow despite having several channels to push fluid through. Larger single-lumen introducer catheters are better choices due to their decreased length and much larger diameter. However, placing a pulmonary artery catheter through them removes this advantage because it impedes flow through the catheter or forces the flow through the much longer pulmonary artery catheter infusion ports. Placing a femoral catheter in a patient with active bleeding from a pelvic fracture would be a poor choice. As is frequently the case, several short large-bore peripheral IV lines are better for resuscitation than central lines.

ADDITIONAL READING

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:12–13.

28. ANSWER: E

There are a number of methods for calculating the ***body surface area (BSA) of a burn***. A rough estimate can be obtained, however, using the "***rule of nines***." This estimates the burn in divisions of nine based on the parts of the body. The head is estimated at 9% of the BSA, each arm is 9%, the trunk is 18% per side, and each leg is 18%. In this case, the head, both arms, and one side of the trunk are involved: 9 + 9 + 9 + 18 = 45% as a rough estimate of the burned area. More precise methods exist for area estimation, but the rule of nines allows a quick quantification of the burn without requiring a complex formula.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2006:1279.
Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1428–1429.

29. ANSWER: E

The ***Parkland formula*** calls for 4 mL of crystalloid fluid per kg per %TBSA burned. In this patient, that equates to 4 mL × 70 kg × 45% TBSA = 12,600 mL, or 12.6 L. Half of the total fluid is given in the first 8 hours and the remainder is given over the remaining 16 hours. The Parkland formula estimates the amount of fluid that will be needed to account for losses through the damaged epidermal layer plus usual fluid loss. There are other equations that are used to estimate this volume, including the modified Brooke equation, which uses 2 mL per kg per %TBSA. The endpoints of fluid resuscitation are the same: adequate urine output (0.5–1 mL/kg/hr minimum), appropriate heart rate, mean arterial pressure greater than 60 mm Hg, appropriate filling pressures, and normalization of lactate and base deficit. Volumes needed may be adjusted up or down based on these parameters.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2006:1281–1282.
Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1733–1734.
Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1431–1433.

30. ANSWER: A

Burn victims often arrive to the hospital awake and talking but ultimately need intubation to deal with the injuries caused by direct thermal damage to the airways and inhalational injuries to the lungs from the many chemical substances produced by fires. The hard part of dealing with these patients is deciding who needs to be intubated electively early on. Failing to use the early window for intubation in a patient may lead to difficult or impossible intubation

after fluid resuscitation occurs and the natural edema of the burn process appears. Significant and rapid facial and airway swelling may occur in patients who have been burned. Singing of external facial hair or even minor burns to the face are not a definitive indication for intubation. They do not necessarily indicate an inhalational injury but should be taken into account with other indications. The presence of carbonaceous material in the throat is more concerning for a need for elective intubation because it indicates inhalation of smoke and toxic gases. The presence of this material in the airways themselves is a definite cause for intubation according to most authors. Hoarseness and difficulty swallowing are also more concerning because they indicate the possibility of direct thermal injury from inhaled gases. Stridor indicates a more urgent need for intubation because the vocal cords have been affected. Altered mental status may be due to hypoxemia or to inhalation of the toxic byproducts of combustion. Low oxygen saturations in a burn patient with supplemental oxygen in place should be a strong indicator for intubation.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2006:1279–1280.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1427–1428.

31. ANSWER: B

Patients suffering from ***carbon monoxide poisoning*** can be difficult to detect unless the diagnosis is suspected. CO has a higher affinity for hemoglobin than oxygen does. This displaces oxygen and diminishes the hemoglobin carrying capacity. Standard pulse oximetry does not differentiate between oxyhemoglobin and carboxyhemoglobin, so pulse oximetry readings are not helpful. Poor oxygen delivery leads to metabolic acidosis as oxidative phosphorylation is uncoupled. Headache and dizziness are common signs of mild CO poisoning. The classically described "cherry-red pigmentation" does not appear until high concentrations of CO are present and thus should not be relied upon for diagnosis, particularly in this case, where the patient is suffering from mild CO poisoning.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2006:1280–1281.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1427.

32. ANSWER: C

The patient has suffered an ***anaphylactic reaction*** to a penicillin-class antibiotic. Anaphylactic reactions are characterized by IgE-mediated release of a host of bioactive compounds from mast cells and basophils. These compounds include histamine, leukotrienes, eosinophil chemotactic factor of anaphylaxis, neutrophil chemotactic factor, platelet activating factor, prostaglandins, and others. This release triggers the symptoms of anaphylactic reactions, including capillary permeability leading to loss of circulating volume, hypotension, and tachycardia. Wheezing occurs secondary to bronchoconstriction. Skin manifestations and gastrointestinal complaints may accompany the hemodynamic and pulmonary complications. Standard therapy includes epinephrine, which inhibits mediator release by increasing levels of cAMP. Epinephrine also affects symptoms by relaxing bronchoconstriction and improving hemodynamics. H1 blockers such as diphenhydramine and H2 blockers such as famotidine help to blunt the response to histamine, including capillary permeability and cardiac dysfunction. Corticosteroids increase tissue response to epinephrine and inhibit histamine synthesis. They also help to block late-phase reactions. Albuterol may be added to help with the pulmonary complications of anaphylaxis. Fluid resuscitation and airway management are also important. There is no recognized role for dobutamine in these patients.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:545–555.

33. ANSWER: A

As the vasculature becomes permeable in anaphylactic shock, intravascular fluid moves into the tissue, triggering acute tissue edema. This movement of fluid out of the vessels leads to a drop in intravascular volume and acute hemoconcentration. A rise in hematocrit may be seen in patients suffering an anaphylactic reaction.

ADDITIONAL READING

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:545–555.

34. ANSWER: B

The ***RIFLE criteria*** were established to better stratify levels of acute renal injury. The RIFLE criteria encompass three levels of dysfunction and two levels of loss that help to define the type and level of renal function loss in critically ill patients. Morbidity and mortality increase as the higher classes of the RIFLE criteria are met. The RIFLE criteria are assigned based on urine output and changes in creatinine/glomerular filtration rate (GFR). **Risk** is characterized by an increase in serum creatinine by 1.5 times (or a decrease in GFR of >25%) and/or urine output of less than 0.5 mL/kg/hr for 6 hours. **Injury** is characterized by an increase in serum creatinine of 2 times (or a decrease in GFR of >50%) and/or urine output of less than 0.5 mL/kg/hr for 12 hours. **Failure** is characterized by an increase in serum creatinine of 3 times (or a decrease in GFR of >75%) or an absolute serum creatinine of greater than 4 mg/dL and/or urine output of less than 0.3 mL/kg/hr for 24 hours of total anuria. **Loss** is characterized by complete loss of kidney function for greater than 4 weeks. **End-stage renal disease** is defined as loss of kidney function for greater than 3 months.

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2861.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1165–1166.

35. ANSWER: C

Institution of ***renal replacement therapy*** may be indicated for a number of reasons. Chief among these are hyperkalemia, fluid overload, profound acid–base disturbances, and uremia with clinical effects (altered mental status or platelet dysfunction). This patient has significant hyperkalemia with electrocardiogram changes. Although other forms of potassium control might be tried, this is the most pressing indication for renal replacement therapy in this patient. He does not have signs of clinical fluid overload, as indicated by a lack of oxygen requirement. Although his BUN is elevated, he does not show indications of clinically significant uremia such as altered mental status or platelet dysfunction. He is currently compensating for his acidosis without significant difficulty. Low urine output is not an indication for renal replacement therapy. Institution of hemodialysis in the face of urine production may lead to more significant renal dysfunction if blood flow is compromised to the kidneys during dialysis (secondary to hypotension).

ADDITIONAL READINGS

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:2861.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1177–1182.

36. ANSWER: A

A number of interventions can be employed in ***hyperkalemia***. Some temporarily move potassium out of the serum and into the intracellular space. Albuterol will trigger this move for 1 to 2 hours. Insulin and glucose or alkalization will also trigger this intracellular move. Furosemide will trigger potassium loss in the urine, although frequently acute renal failure is the cause of hyperkalemia. Ultimately, dialysis and the use of potassium exchange resins such as sodium polystyrene sulfonate (via the gastrointestinal tract) are the only other ways to remove excess potassium in patients with renal failure. Calcium helps in the treatment of hyperkalemia by an entirely different means: it helps to change the threshold potential of the myocardium conducting cells, blunting the ability of hyperkalemia to trigger myocardial arrhythmias.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2006:196–198.

Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1177–1178, 1217–1218.

37. ANSWER: E

As hyperkalemia progresses, it produces a very distinctive pattern of ECG changes. T waves initially get taller and more peaked. The PR interval lengthens and the P wave flattens out. The QRS then begins to widen and the ECG eventually assumes a "sine-wave pattern" before developing asystole. Development of a prominent U wave is characteristic of hypokalemia and is generally accompanied by flattening of the T waves and ST depression.

ADDITIONAL READINGS

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 2006: 196–197.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:1362.
Parrillo JE, Dellinger PR. *Critical Care Medicine: Principles of Diagnosis and Management in the Adult*. 3rd ed. Casa Editrice: Mosby; 2008:1177.

38. ANSWER: C

Intraoperative urine output has not been shown to be a predictor of postoperative renal dysfunction, as demonstrated by multiple studies dating back to the mid-1980s up until the current era, including very large cohorts of patients. Most recently, in 2007, Kheterpal et al. published in *Anesthesiology* a large retrospective cohort study showing that intraoperative urine output was not a predictor of perioperative renal failure. All of the other listed factors have been associated with an increase in perioperative renal failure, including suprarenal aortic cross-clamping. Another important observation is that patients with pulse pressures of greater than 80 mm Hg had a significantly greater incidence of postoperative renal failure. This may reflect more severe degrees of hypertension or peripheral vascular disease.

ADDITIONAL READINGS

Alpert RA, Roizen MF, Hamilton WK, et al. Intraoperative urinary output does not predict postoperative renal function in patients undergoing abdominal aortic revascularization. *Surgery*. 1984;95:707–711.
Kheterpal S, Tremper KK, Englesbe MJ, O' Reilly M, Shanks AM, Fetterman DM, et al. Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. *Anesthesiology*. 2007;107:892–902.
Knos GB, Berry AJ, Isaacson IJ, Weitz FI. Intraoperative urinary output and postoperative blood urea nitrogen and creatinine levels in patients undergoing aortic reconstructive surgery. *J Clin Anesth*. 1989;1:181–185.
Novis BK, Roizen MF, Aronson A, et al. Association of preoperative risk factors with postoperative ARF. *Anesth Analg*. 1994;78:143–149.

39. ANSWER: B

The term ***acute renal failure*** is a nonspecific description of an acute, sustained decrease in renal function. There is a wide spectrum of severity of acute renal injury, ranging from mild reversible impairment to severe dysfunction necessitating renal replacement therapy. An international interdisciplinary collaborative group, the Acute Dialysis Quality Initiative (ADQI), has recently formulated a standard grading system for acute renal dysfunction. The term **acute renal dysfunction** encompasses the full range of abnormalities of renal function. The acronym **RIFLE** defines three grades of increasing severity of acute renal dysfunction (R, risk; I, injury; F, failure) and two outcome variables (L, loss; E, end-stage) based on the change in serum creatinine or urine output. The RIFLE criteria have undergone evaluation in cardiac surgical patients and in intensive care unit patients and have been shown to appropriately define acute renal dysfunction. The term **acute kidney injury** (AKI) has been recently proposed to define the full spectrum of severity of acute renal dysfunction (Fig. 20.1).

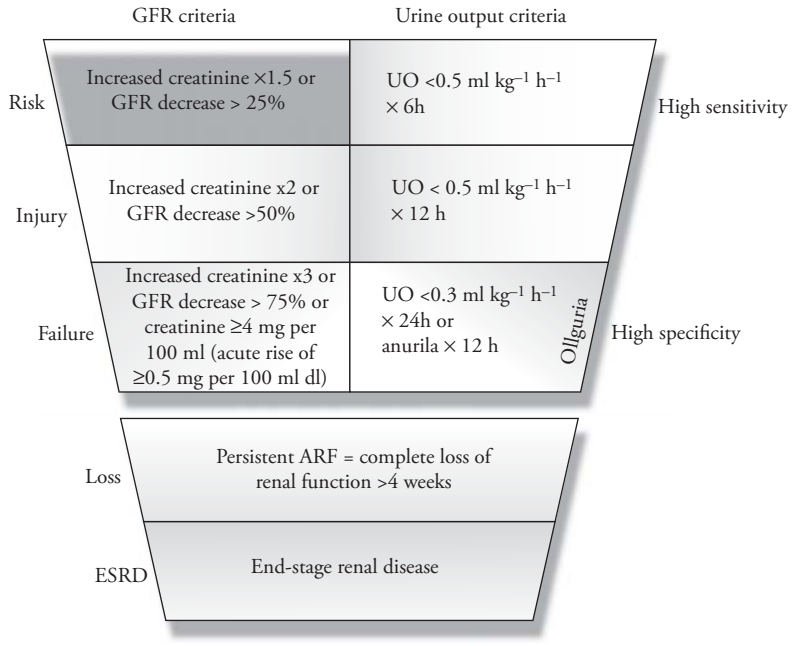


Figure 20.1 Acute renal dysfuction and RIFLE criteria.

ADDITIONAL READING

Webb ST and Allen JSD. Perioperative renal protection. *Contin Educ Anaesth Crit Care Pain*. 2008;8(5):176–180. First published online August 22, 2008. doi:10.1093/bjaceaccp/mkn032

40. ANSWER: A

The normal kidneys have a significant ability to increase creatinine excretion via tubular excretion in order to compensate for decrease in GFR. Therefore, the initial increase in serum creatinine from 0.8 to 1.3 mg/dL is the most concerning because it reflects approximately a 50% decrease in GFR (from 96.5 mL/min to 50 mL/min). At this point there may still be a window of opportunity to reverse possible injury and prevent further worsening of renal function. This change represents stage 1 (Risk) in the RIFLE scheme of classification of acute renal injury. The likelihood of recovery is high, but there is still an almost doubling of perioperative mortality in some patient cohorts. The increase in creatinine from 1.3 to 1.9 mg/dL indicates a drop in GFR from 51 mL/min to 36 mL/min, a 30% drop. This more than doubling of the serum creatinine would meet RIFLE criteria for kidney injury. The jump from 2 mg/dL to 3 mg/dL in the creatinine represents a drop of less than 30% in creatinine clearance.

ADDITIONAL READING

Chapter 65, Anesthesia and the Renal and Genitourinary Systems. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010.

41. ANSWER: C

Cryoprecipitate or fibrinogen concentrates (which have only recently become available in the United States) replace fibrinogen and represent the accepted method for treating acute life-threatening bleeding after the administration of fibrinolytics. Randomized controlled clinical trials of cryoprecipitate versus placebo for treatment of tPA-related bleeding are not available. However, various guidelines, as well as articles in peer-reviewed journals, suggest using cryoprecipitate as the first-line reversal agent for tPA.

ADDITIONAL READING

Levine MN, Goldhaber SZ, Gore JM, et al. Hemorrhagic complications of thrombolytic therapy in the treatment of myocardial infarction and venous thromboembolism. *Chest*. 1995;108(4 suppl):291S-301S.

42. ANSWER: E

All of these mechanisms are true for the transfusion of red blood cells. Probably the most important would be the increase in preload, but the other points cannot be forgotten, especially since an increase in inducible nitric oxide and the resulting vasodilatation are normal compensatory mechanism for anemia. Inhibiting this mechanism may account for some of the potential detrimental effects of transfusion of red blood cells.

ADDITIONAL READING

Ho J, Sibbald WJ, Chin-Yee IH. Effects of storage on efficacy of red cell transfusion: when is it not safe? *Crit Care Med*. 2003;31:S687.

43. ANSWER: C

Blood products with high levels of clotting factors have higher levels of citrate to prevent clotting. Fresh frozen plasma has the highest level of clotting factors and a larger volume. This is important because rapid administration of fresh frozen plasma can lead to hypotension and prevent normal clotting. This is also described in patients undergoing plasma exchange in the intensive care unit and other settings. Cryoprecipitate also has a high level of citrate but is a very small volume compared to fresh frozen plasma.

44. ANSWER: E

The ARDS Network trial demonstrated a decrease in mortality from about 40% to 31% with the use of low tidal volume and controlling plateau pressures to less than 30 cm H_2O. This improved survival was actually accompanied by an increase in the respiratory rate, increased arterial CO_2, and a decrease in oxygenation.

ADDITIONAL READING

NIH ARDS Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and ARDS. *N Engl J Med*. 2000;342:1301–1308.

45. ANSWER: B

The use of ***Xigris*** should be limited to patients with severe sepsis and a high risk of death, such as an APACHE score of greater than 25 (Table 20.2).

Table 20.2 CONTRAINDICATIONS TO THE USE OF XIGRIS

Absolute Contraindications

- Active internal bleeding
- Recent (within 3 months) hemorrhagic stroke
- Recent (within 2 months) intracranial or intraspinal surgery, or severe head trauma
- Trauma with an increased risk of life-threatening bleeding
- Presence of an epidural catheter
- Intracranial neoplasm or mass lesion or evidence of cerebral herniation

Relative Contraindications

- Concurrent therapeutic dosing of heparin to treat an active thrombotic or embolic event
- Platelet count $<30{,}000 \times 10^6$/L, even if the platelet count is increased after transfusions
- Prothrombin time-INR > 3.0
- Recent (within 6 weeks) gastrointestinal bleeding
- Recent administration (within 3 days) of thrombolytic therapy
- Recent administration (within 7 days) of oral anticoagulants or glycoprotein IIb/IIIa inhibitors
- Recent administration (within 7 days) of aspirin >650 mg/day or other platelet inhibitors
- Recent (within 3 months) ischemic stroke (see Absolute Contraindications)
- Intracranial arteriovenous malformation or aneurysm
- Known bleeding diathesis
- Chronic severe hepatic disease
- Any other condition in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location

ADDITIONAL READINGS

Package insert, Xigris.

Abraham E, Laterre P-F, Garg R, Levy H, Talwar D, Trzaskoma BL, et al. Drotrecogin alfa (activated) for adults with severe sepsis and a low risk of death. *N Engl J Med.* 2005;353:1332–1341.

46. ANSWER: B

The SVR of 1,800 dyn/sec/cm^{-5} is higher than the normal of 1,200 to 1,500 dyn/sec/cm^{-5}. An SVR of 2,000 dyn/sec/cm^{-5} is consistent with a high afterload/SVR state. ***Sepsis*** is characterized by a low vascular resistance. The CVP is consistent with a patient who is septic and would suggest the administration of additional IV fluids. The SvO_2 is consistent with a picture of sepsis and low peripheral oxygen extraction, as can be found in severe sepsis. The cardiac index is lower than expected in a hyperdynamic shock picture such as sepsis but is not an uncommon finding in the setting of hypervolemia and can also be seen with the depressed ventricular function that occurs with sepsis. Cardiovascular dysfunction is pronounced and characterized by elements of hypovolemic, cytotoxic, and distributive shock. In addition, significant myocardial depression is commonly observed. This septic cardiomyopathy is characterized by biventricular impairment of intrinsic myocardial contractility, with a subsequent reduction in left ventricular ejection fraction and left ventricular stroke work index.

ADDITIONAL READINGS

Huner JD et al. Sepsis and the heart. *Br J Anaesth.* 2010;104(1):3–11.

47. ANSWER: E

Noninvasive positive-pressure ventilation (NIPPV) with either BiPAP or CPAP has become a common mode of supporting patients with acute respiratory failure. NIPPV has been shown to improve outcomes, decrease the rate of intubation (and accompanying ventilator-associated pneumonia) in chronic obstructive pulmonary disease exacerbations, in acute heart failure exacerbations, and in immunosuppressed patients with pneumonia. Usually this is a temporizing measure pending further treatments to alleviate the underlying problem. It requires a cooperative patient and can be very dangerous in a patient with moderate to severe hypoxemic respiratory failure; it has been shown in several studies to increase mortality in these patients. A trial of NIPPV may be worthwhile in most patients who do not require emergent intubation and who have a disease known to respond to NIPPV, assuming that they lack contraindications. This is especially true for patients who have features that predict success using NIPPV. Despite evidence of efficacy, NIPPV may be underused among patients with cardiogenic pulmonary edema or hypercapnic chronic obstructive pulmonary disease exacerbations.

The need for emergent intubation is an absolute contraindication to NIPPV. There are numerous relative contraindications to NIPPV: cardiac or respiratory arrest; inability to cooperate, protect the airway, or clear secretions; severely impaired consciousness; nonrespiratory organ failure; facial surgery, trauma, or deformity; high aspiration risk; prolonged duration of mechanical ventilation anticipated; and recent esophageal anastomosis

ADDITIONAL READING

International Consensus Conferences in Intensive Care Medicine. Noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med.* 2001;163:283.

48. ANSWER: D

Nitric oxide is a potent pulmonary vasodilator that has many clinical uses. Among its known important side effects is platelet dysfunction. Methemoglobinemia, not carboxyhemoglobinemia, is also a concern. One of the benefits of nitric oxide is improvement in oxygenation. Anemia is not a known side effect of nitric oxide administration.

ADDITIONAL READING

Chapter 31, Inhaled Nitric Oxide and Pulmonary vasodilators. In Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

49. ANSWER: B

As ***packed red blood cells*** are being stored, there is a gradual decrease in 2,3-DPG, thereby shifting the oxyhemoglobin curve to the left. This will increase the total oxygen carried, but it may not be available for offloading into the tissues.

ADDITIONAL READING

Riggs TE, Shafer AW, Guenter CA, et al. Acute changes in oxyhemoglobin affinity: effects on oxygen transport and utilization. *J Clin Invest.* 1973;52:2660–2663.

50. ANSWER: D

In the management of ***acute aortic dissection***, there is a medical and possibly surgical component. In type A dissections the medical management should be taking place at the same time that preparations for the patient to go to the operating room are being carried out, because a type A dissection is a surgical emergency that has an hourly increase in mortality of between 1% and 3%. In the patient who is not hemodynamically compromised, morphine or some other narcotic analgesic should be administered if there are no contraindications. Frequently, control of the patient's pain will help with control of the blood pressure. The patient should also be started on a beta blocker to help decrease dP/dT, or the shear stress on the aorta. This can be accomplished with many agents, including esmolol, metoprolol, and labetalol. Esmolol has the advantage of being rapidly titratable due to its short half-life. The goal would be to get the heart rate to between 55 and 65 beats per minute. Once a beta blocker is on board and as heart rate and dP/dT are controlled, a vasodilator can be added to achieve a systolic blood pressure of between 90 and 110 mm Hg, as long as end-organ perfusion is maintained. A potent vasodilator such as sodium nitroprusside should NOT be started without a beta blocker on board because this may cause an increase in wall stress and increase the risks of rupture or further dissection. This is in contrast to a patient with a pheochromocytoma, who should have either a vasodilator started first or a combined alpha and beta blocker given.

51. ANSWER: B

The first signs of ***cyanide toxicity*** in patients treated with sodium nitroprusside are behavioral changes, decreased oxygen extraction, and tachyphylaxis. Lactic acidosis, coma, and seizures are late findings.

ADDITIONAL READINGS

Marino PL. *The ICU Book*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:308.

52. ANSWER: A

Tachycardia decreases the duration of diastole. There is insufficient time for pressure to equalize at both the mitral and pulmonary vascular levels, and pressure gradients develop as diastole progressively shortens. Consequently, pulmonary artery diastolic pressure overestimates mean PAWP, which in turn overestimates left ventricular end-diastolic pressure. The remainder of the conditions tend to underestimate left ventricular end-diastolic pressure.

ADDITIONAL READING

Chapter 40, Monitoring the Cardiovascular System. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

53. ANSWER: E

In terms of preventing ***transfusion-related acute lung injury (TRALI)***, leukocyte reduction probably has no role. It is usually the antibody from the donor, not the leukocytes themselves, that is implicated in the TRALI reaction. There is much debate about the relative benefits of leukoreduction on red blood cells. Accepted indications for leukocyte reduction include reduction in HLA alloimmunization, avoidance of febrile nonhemolytic transfusion reactions, and prevention of the platelet refractory state. Leukocyte-reduced blood products can also be used as an alternative to cytomegalovirus-seronegative blood products. Other possible but less accepted indications include reducing perioperative infections and reducing tumor recurrence rates after surgery.

ADDITIONAL READINGS

Looney MR, Gropper MA, Matthay MA Transfusion-related acute lung injury: a review. *Chest*. 2004;126:249–258.

Sharma AD, Sreeram G, Erb T, et al. Leukocyte-reduced blood transfusions: perioperative/ indications, adverse effects, and cost analysis. *Anesth Analg*. 2000;90:1315–1323.

54. ANSWER: B

Knowledge of the components of blood products is crucial to their rational and appropriate use. Cryoprecipitate contains on average 250 mg fibrinogen per 10- to 12-cc pack, fibronectin, factor XIII, factor VIII, and von Willebrand factor. There are not appreciable amounts of factor IX in cryoprecipitate.

ADDITIONAL READING

Chapter 55, Transfusion Therapy. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Churchill Livingstone; 2009.

21.

HIGH-YIELD BOARD REVIEW TOPICS

Kaveh Aslani, MD, Richard Han, MD, MPH, and Dominic Monterosso, DO

The following 60 topics were frequently missed by examinees sitting for the board certification examination in anesthesiology over the past 4 years. Use this list of testable concepts and their related explanations to help reinforce your studying.

Testable Concept #1: Knowledge of estimated blood volumes (EBV) in pediatric patients and the calculation of maximum allowable blood loss

To calculate allowable blood loss, one must be aware of EBV ranges. For instance, the EBV of a premature neonate is 90 to 100 cc/kg. Term neonates have an EBV between 80 and 90 cc/kg. Infants (<1 year old) have an EBV ranging from 75 to 80 cc/kg. Older children have an EBV between 70 and 75 cc/kg.

$$MABL = (EBV \times (\text{pt hct} - \text{minimum tolerated hct}))/\text{Pt hct}$$

where MABL = maximum allowable blood loss, EBV = estimated blood volume, HCT = hematocrit.

Testable Concept #2: A patient's history of ventricular tachycardia does not preclude the use of albuterol during an episode of acute bronchospasm.

Albuterol is a relatively selective $beta_2$-adrenergic bronchodilator. The primary action of beta-adrenergic drugs, including albuterol, is to stimulate adenyl cyclase, the enzyme that catalyzes the formation of cyclic-3′,5′-adenosine monophosphate (cyclic AMP) from adenosine triphosphate (ATP) in beta-adrenergic cells. The cyclic AMP thus formed mediates the cellular responses. Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells. Albuterol is contraindicated in patients with a history of hypersensitivity to albuterol, but it may be used with caution in patients with cardiovascular disorders.

Testable Concept #3: Pain caused by cancer of the pancreas is unlikely to be treated effectively by a spinal cord stimulator.

Spinal cord stimulation is used for pain control. A spinal cord stimulation system produces an electrical field over the spinal cord, which blocks some, but not all, types of pain. Spinal cord stimulators are used to control pain that comes from damage to the nervous system or that is caused by abnormal processes such as complex regional pain syndrome. Other common causes of neuropathic pain include phantom limb and postherpetic neuralgia. Other indications include interstitial cystitis, pancreatitis, motility disorders, and urinary urgency and frequency.

Testable Concept #4: The maximum acceptable dose of lidocaine is 35–55 mg/kg when given during liposuction using the tumescent technique.

Tumescent liposuction is a technique that uses large volumes of dilute lidocaine with epinephrine to facilitate anesthesia and hemostasis during the procedure. Although the acceptable lidocaine dose ranges from 35 to 55 mg/kg, there is marked controversy regarding this issue. When dealing with these patients, it is best to have them discontinue any medications that interfere with cytochrome P450 3A4 (i.e., antifungals, selective serotonin reuptake inhibitors [SSRIs], erythromycin). It is also advisable to confirm normal hepatic function.

Testable Concept #5: Heart rate changes in the sinoatrial (SA) node are determined by the rate of diastolic depolarization (phase 4).

During diastolic depolarization, or phase 4, the resting membrane potential gradually depolarizes toward a threshold potential. When reached, an action potential is triggered and a heartbeat occurs. Cardiac tissue with the more rapid rate of rise of diastolic depolarization is the pacemaker and thus determines heart rate. This cardiac tissue is most often found in the SA node.

Testable Concept #6: There is an association between neuraxial morphine and reactivation of herpes simplex virus.

Neuraxial morphine is a widely accepted technique to control postoperative pain after cesarean section. Although effective, this practice is also associated with side effects including pruritus, nausea, vomiting, urinary retention, and potentially catastrophic delayed respiratory depression. There is also evidence supporting an association between both epidural and intrathecal morphine use and reactivation of herpes simplex labialis.

Testable Concept #7: There is a reciprocal relationship between hepatic artery and portal vein blood flow.

The hepatic arterial buffer response is the phenomenon by which decreases in portal blood flow are associated with increased hepatic arterial blood flow. This reciprocal relationship between the hepatic artery and the portal vein tends to maintain the constancy of the hepatic oxygen supply (which is essential for hepatocyte function) and the total hepatic blood flow (which is essential for clearance of exogenous and endogenous substances). Thus, when portal venous flow decreases, hepatic arterial resistance decreases and hepatic arterial blood flow increases, and vice versa.

Testable Concept #8: Logistic regression is the statistical test of choice (rather than analysis of variance [ANOVA]) when assessing the effects of a combination of several categorical and numerical factors upon the likelihood of a particular outcome.

A logistic regression model is a statistical test that uses independent variables to predict a dependent categorical (usually dichotomous) outcome. The independent variables can be dichotomous, discrete, continuous, or any combination. This model enables the statistician to determine the impact of individual independent variables on the dependent one, rank the importance of independent variables compared to one another, and assess the presence of interactions between independent variables. On the other hand, an analysis of variance (ANOVA) is conducted to assess for significant differences between the means of multiple groups (two or more). If only two means are being compared, the ANOVA will yield the same results as the *t* test. Similar to the *t* test, when using the ANOVA, one must assume that the sampled populations have a normal distribution.

Testable Concept #9: Lidocaine's peak plasma concentration occurs more than 6 hours after injection when given for tumescent liposuction procedures.

The tumescent technique uses a relatively large amount of volume infiltrated into the area to be treated. The solution is a mixture of saline, local anesthetic, and epinephrine. The peak serum lidocaine levels occur 12 to 14 hours after injection and subsequently decrease. Doses of up to 55 mg/kg of lidocaine have been used safely with this technique.

Testable Concept #10: The Bainbridge reflex is characterized by an elevated heart rate as intravascular volume increases.

The Bainbridge reflex, also called the arterial reflex, is characterized by an increase in heart rate due to an increase in central venous pressure. Increases in blood volume are detected by stretch receptors located in the right atrium and the venoatrial junctions. This increase in volume on the venous side (not to be confused with increases in arterial blood pressure) is what triggers the stretch receptors and the Bainbridge reflex. The Bainbridge reflex and the baroreceptor reflex work antagonistically. When right atrial pressure is high (central venous pressure), the Bainbridge reflex is dominant. When the carotid artery baroreceptors detect low arterial blood pressure, the baroreceptor reflex becomes dominant, causing an increase in heart rate.

Testable Concept #11: During positive-pressure ventilation and a state of hypovolemia, pulse pressure will decrease during expiration, not inspiration.

Pulse pressure respiratory variation has been described as being much more accurate for detecting fluid responsiveness than cardiac filling pressures. Positive-pressure ventilation promotes cyclic changes in stroke volume and is coupled with arterial pulse pressure changes. Stroke volume and arterial pulse pressure rise during inspiration; conversely, stroke volume and arterial pulse pressure drop during expiration. The systolic and pulse pressure reduction seen during expiration reflects the expiratory reduction in stroke volume. During positive-pressure ventilation, the intrathoracic pressure is minimal during expiration, the aortic compliance increases, and arterial systolic pressure drops along with pulse pressure.

Testable Concept #12: Guillain-Barré syndrome (GBS) typically causes pain.

GBS is an autoimmune disorder. The cause is unknown, although it may follow an episode of infection such a lung

or gastrointestinal infection. It is most common between the ages 30 and 50. It causes a polyneuropathy that results in muscle paralysis. In most cases the weakness starts in the legs and ascends to the trunk and arms. The muscles of respiration may be affected, requiring mechanical ventilation. Pain may be one of the presenting symptoms in GBS and is present in more than 75% of patients. In many patients it precedes weakness. Pain may last throughout the course of the disease and it may be severe, but pain severity does not correlate with neurologic disability. The major painful symptoms seen in GBS are back and leg pain, extremity pain, and myalgia.

Testable Concept #13: Hypernatremia is the most common electrolyte abnormality in organ donors who are brain dead.

Brain death rapidly affects the hypothalamic–pituitary axis, leading to a marked decrease in vasopressin release. This leads to diabetes insipidus and ensuing polyuria and hypernatremia.

Testable Concept #14: The rule of three can be used to calculate the risk of a rare event.

The rule of three states that if none of *n* patients showed the event about which we are concerned, we can be 95% confident that the chance of this event is at most 3 in *n*. This rule is useful in situations where adverse events are rare.

Testable Concept #15: Positive end-expiratory pressure (PEEP) will not decrease extravascular lung water.

PEEP is often used to improve oxygenation in patients with respiratory failure. It works by increasing alveolar recruitment and increasing functional residual capacity, thereby reducing intrapulmonary shunting. PEEP redistributes extravascular lung water from interstitial spaces between alveoli toward peribronchial regions but does not decrease total extravascular lung water.

Testable Concept #16: Neuraxial anesthesia can prolong the second stage of labor.

Labor is divided into three continuous stages. The first stage consists of two phases, the latent phase and the active phase. They encompass the time from the onset of labor until full cervical dilation. The second stage of labor is defined as the time from full cervical dilation until delivery of the infant. Continued administration of epidural anesthesia during the second stage of labor prolongs the duration of the second stage. A prolonged second stage does not directly result in maternal or fetal complications. ACOG has defined a prolonged second stage of labor as lasting longer than 2 hours in women without regional anesthesia and longer than 3 hours in women with regional anesthesia. This may be due to decreased maternal expulsive forces. There is no difference in cesarean section rates in women with or without epidural analgesia for labor.

Testable Concept #17: Enteral feedings are unacceptable in patients with ileus, but acceptable in patients with pancreatitis.

Patients with undernutrition to a degree that may impair immunity, wound healing, muscle strength, and psychological drive have greater morbidity and longer hospital stays. To date, there is substantial scientific proof that enteral feeding is superior to total parenteral nutrition (TPN). The beneficial effects of enteral feeding on mucosal integrity and the prevention of bacterial overgrowth may well explain the superiority of enteral feeding over TPN. Enteral feeding significantly reduces the risk of infections, lowers the need for surgical interventions, and reduces the length of hospital stay. Enteral nutrition has a beneficial influence on the outcome of acute pancreatitis and should be initiated as early as possible (within 48 hours). Ileus is a decrease in the normal propulsive ability of the gastrointestinal tract. It represents decreased motor activity of the gastrointestinal tract due to nonmechanical causes. In patients with ileus, a nasogastric tube should be placed and parenteral nutrition started until motility is restored. Enteral feedings in such cases risk perforation of the bowel.

Testable Concept #18: Verapamil is contraindicated in a patient exhibiting signs of malignant hyperthermia (MH).

MH is a life-threatening hypermetabolic condition that results from exposure to volatile anesthetics and succinylcholine. The proper management of an MH crisis involves the following:

- Get help. Get dantrolene. Notify the surgeon.
- Administer dantrolene sodium for injection 2.5 mg/kg rapidly IV through a large-bore IV, if possible.
- Give bicarbonate for metabolic acidosis.
- Cool the patient.
- Dysrhythmias usually respond to treatment of acidosis and hyperkalemia.
- Follow $ETCO_2$, electrolytes, blood gasses, creatine kinase, serum myoglobin, core temperature, urine output and color, and coagulation studies.
- Verapamil is *not* a useful therapy during an MH crisis. It neither prevents nor reverses episodes of MH. Furthermore, IV treatment with diltiazem and verapamil calcium channel blockers in conjunction with dantrolene can result in dysrhythmias, myocardial depression, hyperkalemia, and cardiovascular collapse.

Testable Concept #19: The vaporizer dial setting of isoflurane, when administered at an altitude of 7,000 feet, should achieve a similar depth of anesthesia as when administered at sea level because the increased

concentration of isoflurane delivered is offset by a reduction in potency.

The definition of MAC is the concentration of the vapor (measured as a percentage at 1 atmosphere [i.e., the partial pressure]) that prevents the reaction to a standard surgical stimulus in 50% of subjects. Because most of us work nearly at sea level, 1 atmosphere, we can think in terms of % concentration, but what is physiologically important is the partial pressure in mm Hg, not the concentration (760 mm Hg × 1.1% = 8.4 mm Hg is partial pressure of isoflurane at sea level).

At a higher altitude, where the barometric pressure is half that at sea level, the amount of isoflurane vapor output is increased due to the lower barometric pressure; the concentration of anesthetic vapor, as a fraction of ambient atmosphere, rises with increasing atmosphere. Therefore, the settings that delivered 1.1% isoflurane now deliver 2.2% isoflurane. However, according to Dalton's law, the partial pressure of isoflurane delivered would be approximately the same at both altitudes because 1.1% isoflurane at 760 mm Hg (8.4 mm Hg) is the same as 2.2% isoflurane at 380 mm Hg (8.4 mm Hg). In summary, you need the same partial pressure of anesthetic to produce a particular drug effect at altitude as that at sea level. To achieve this partial pressure at altitude, you need a higher percent of the ambient atmosphere, because the air is thinner.

Testable Concept #20: Failure of a pneumatically powered ventilator due to failure of the wall oxygen supply should prompt one to begin manual ventilation.

Mechanical ventilation requires energy to drive inspiratory gas flow and run the systems that regulate the respiratory cycle. Pneumatic-powered ventilators use pneumatic energy (compressed air/gas) to provide these functions. The pneumatic systems of modern ventilators are powered by a pressurized gas source providing oxygen and medical air. The pneumatic system delivers breaths to the patient via flexible tubing connected to the endotracheal tube. Upon failure of the pressurized gas source, the wall oxygen supply, this system fails and the patient must be manually ventilated from an alternate oxygen source.

Testable Concept #21: The most notable difference between primary polycythemia and secondary polycythemia is the association of primary polycythemia with an elevated platelet count.

Primary polycythemia is a neoplastic problem with bone marrow stem cells that results in increased red blood cell production. Thrombocytosis and leukocytosis can also accompany the increased hematocrit (Hct) value, which is often greater than 55%. Patients with primary polycythemia often complain of cognitive dysfunction and headaches. They can also experience weight loss, fever, and excessive sweating. Hepatomegaly and splenomegaly are associated physical examination findings. Secondary polycythemia results from an increase in the production of the hormone erythropoietin. There are several situations in which secondary polycythemia occurs as an appropriate physiologic adaptation. These include adjustment to high altitudes, genetic predisposition, iatrogenic (specifically phlebotomy), and diseases that result in hypoxemia (cardiopulmonary disease, obstructive sleep apnea, obesity-hypoventilation syndrome). Hct values for patients with secondary polycythemia are often less than 55%.

Testable Concept #22: Epidural analgesia in the first stage of labor has a higher likelihood of causing fever than prolonging a parturient's labor.

Epidural analgesia is the most effective means of controlling pain in the laboring obstetric patient. However, its use does have several drawbacks, including a slight prolongation in the second stage of labor, an increase in the incidence of instrument-assisted vaginal deliveries, and also a higher incidence of maternal fever (Table 21.1).

Testable Concept #23: The Wilcoxon rank-sum test should be used to assess ordinal data, not chi-square or *t* test.

The Wilcoxon rank-sum test is a nonparametric alternative to the two-sample *t* test that is based solely on the order in which the observations from the two samples fall. It can be used as an alternative to the paired Student *t*-test when the population cannot be assumed to be normally distributed or the data are on the ordinal scale. When assessing ordinal data, the Wilcoxon rank-sum test is a better test of choice than a chi-square or *t* test.

Testable Concept #24: In the setting of severe systemic hypotension, it is not recommended to administer milrinone alone.

Milrinone lactate is an inodilator: a positive inotrope and a vasodilator. Significant hypotension due to peripheral vasodilation is common during its administration. In the presence of hypotension, the isolated use of milrinone is not recommended. The vasodilatory effects of milrinone are generally treated with noradrenaline (norepinephrine).

Testable Concept #25: In a patient's blood, hemoglobin has a greater buffering capacity than bicarbonate.

A buffer is a substance that resists changes in pH (acid concentration) by undergoing a reversible reaction, limiting changes in the hydrogen ion concentration. Hemoglobin

Table 21.1 EFFECTS OF EPIDURAL ANALGESIA ON LABOR AND MATERNAL AND INFANT OUTCOMES

LABOR FACTORS	OUTCOME*	*P* VALUE
	EFFECTS ON LABOR	
Duration of first stage	Increased by 26 minutes	NS†
Duration of second stage	Increased by 15 minutes	<0.05
Pain score (100-mm VAS)		
First stage	40 mm lower	<0.0001
Second stage	29 mm lower	<0.001
Use of oxytocin (Pitocin) after analgesia	Increased (OR, 2.8; 95% CI, 1.89– 4.16)	<0.05
Third- or fourth-degree perineal laceration	Increased (OR, 1.7–2.7)	N/A
Instrument-assisted delivery	Increased (OR, 2.1; 95% CI, 1.48–2.93)	<0.05
Cesarean delivery	OR, 1.0; 95% CI, 0.77–1.28	NS‡
	MATERNAL OUTCOMES	
Fever >38 C (100.4 F)	Increased (OR, 5.6; 95% CI, 4.0–7.8)	<0.001
Low backache		
At 3 months	OR, 1.0; 95% CI, 0.6–1.6	NS
At 12 months	OR, 1.4; 95% CI, 0.9–2.3	NS
Urinary incontinence	No increase	NS§
Breastfeeding success at 6 weeks	No difference	NS§
	INFANT OUTCOMES	
5-minute Apgar score <7	No difference	NS
Low umbilical cord pH	No difference	NS
Neonatal sepsis evaluation	Increased	N/A
Neonatal antibiotic treatment	Increased	N/A

NS = not significant; VAS = visual analog scale; OR = odds ratio; CI = confidence interval; N/A = not applicable.

Leeman et al. The nature and management of labor pain: Part II. Pharmacologic pain relief. *Am Fam Physician*. 2003;68(6):1115–1120.

plays a central role in the transport of CO_2 by acting as a buffer for the hydrogen ions generated by the hydration of CO_2 in the red blood cell. The buffering actions of hemoglobin are attributed to imidazole groups that are found on the 38 histidine residues in the molecule. These imidazole groups have a dissociation constant with a pK of 7.0, so they will act as effective buffers in the pH range between 6 to 8 (buffers are effective within one pH unit on either side of the pK). In contrast, the carbonic acid–bicarbonate buffer system has a pK of 6.1, so this buffer system will be effective in the pH range from 5.1 to 7.1. Comparing the buffer ranges of hemoglobin and bicarbonate shows that hemoglobin is a more effective buffer than bicarbonate in the pH range encountered clinically (pH 7 to 8).

Testable Concept #26: The electroencephalographic (EEG) endpoint for determining the adequacy of unconsciousness during a barbiturate-induced coma is burst suppression.

A barbiturate-induced coma is used for neuroprotection during brain surgery and also as a last-line treatment in the management of status epilepticus. The most commonly used barbiturates for this purpose are pentobarbital and sodium thiopental. These drugs decrease the cerebral metabolic rate and cerebral blood flow, and therefore reduce intracranial pressure. Furthermore, barbiturates reduce electrical activity in the brain, which has the theoretic advantage of decreasing oxygen and metabolic requirements. The EEG endpoint for determining the adequacy of unconsciousness during a barbiturate-induced coma is 30- to 60-second burst suppression.

Testable Concept #27: Elevation in $EtCO_2$ during laparoscopic hernia repair is more likely due to absorption of insufflated CO_2 than malignant hyperthermia.

Malignant hyperthermia is a rare life-threatening condition usually triggered by exposure to certain drugs used for general anesthesia. The earliest signs are a rise in $EtCO_2$ (despite increased minute ventilation), tachycardia, and muscle rigidity. Most laparoscopic procedures are performed with the insufflation of CO_2. CO_2 gas is used because it is inexpensive, easy to handle, and noncombustible and dissolves quickly in the plasma. As CO_2 diffuses through the peritoneum into the bloodstream, a "pseudo-ventilatory" acidosis occurs, which is detected by a rising $EtCO_2$. The rise in CO_2 is not as significant as that seen in malignant hyperthermia and returns toward normal with increased minute ventilation. Due to the hypermetabolic state of malignant hyperthermia, the rapid rise in CO_2 is not affected by increased minute ventilation.

Testable Concept #28: During laryngeal tumor laser excision, jet ventilation reduces the risk of an airway fire.

Airway fires can have life-threatening consequences for the patient. Airway fires, like all fires, require three components (fire triad): an oxidizer, an ignition source, and fuel. In the operating room oxygen and nitrous oxide are the oxidizing agents and will contribute to the extent of the fire. The most common ignition sources in the operating room are electrocautery devices and lasers. Fuels for fire can include endotracheal tubes, sponges, and drapes, among others. Laser fires are especially concerning because they are used commonly in the airway. Several methods are used to decrease the risk of airway fires, including decreasing oxygen and nitrous oxide concentrations in the environment. Fuel sources should also be kept as far from the ignition source as possible. When using lasers in the airway, the endotracheal tube is the main fuel for the fire. Removal of the fuel by use of a jet ventilator reduces the risk. The use of metal endotracheal tubes does not provide absolute protection from fire. YAG lasers have been reported to ignite Laser Flex tubes. Risks of jet ventilation include barotraumas, pneumothorax, and crepitus.

Testable Concept #29: Eligibility for treatment of pain caused by prostate cancer using a neurolytic subarachnoid block can be determined using an epidural.

Relief of pain due to cancer can be accomplished with different techniques. A neurolytic block involves the destruction of the nerve root by using alcohol or phenol. The destruction of selected nerve roots interrupts nociceptive pathways and can create excellent analgesia in a relatively selective body area. Prior to performing a neurolytic block a more temporary "trial" using an epidural block should be done to ascertain whether the patient will benefit from the neurolytic block.

Testable Concept #30: To determine agreement of two measurement techniques, a Bland-Altman plot provides a better assessment than a Pearson's correlation.

Pearson's correlation is used as a measure of dependence between two quantities. If the variables are independent, the Pearson's correlation coefficient is 0. The Bland-Altman, or difference plot, is a graphical method comparing two measurement techniques. The differences between the two techniques are plotted against the averages of the two techniques.

Testable Concept #31: When comparing data from two small groups of patients, one should use a Fisher exact test.

The Fisher exact test is a statistical test used to determine whether there are nonrandom associations between two categorical variables. The test is most commonly applied to 2×2 matrices. When there are larger sample sizes or more than two categorical variables, the chi-square test should be used.

Testable Concept #32: Neck *flexion* is more likely to induce atlantoaxial subluxation than neck *extension* in patients with rheumatoid arthritis.

C1 (atlas) and C2 (axis) articulation is synovial in nature, which accounts for its frequent involvement in patients with rheumatoid arthritis (RA). Atlantoaxial subluxation can occur in up to 70% of patients with RA. Approximately 11% of RA patients will develop cord compression from atlantoaxial subluxation. Pannus formation occurs at synovial joints between the dens, C1, and transverse ligament, which results in destruction of the transverse ligament, dens, or both. Stretching and destruction of these structures allow the atlas vertebra to move forward relative to the axis. During cervical spine flexion, the atlas moves forward relative to the axis. This anterior subluxation that occurs most often in RA patients causes cord compression between the posterior arch of the atlas and the odontoid peg during flexion.

Testable Concept #33: Bladder temperature usually rises before rectal temperature during rewarming after cardiopulmonary bypass.

Hypothermia is used to provide neuroprotection during cardiopulmonary bypass (CPB). Although moderate hypothermia is associated with a reduction in the rate of stroke, it has the disadvantage of potentially increasing myocardial damage and perioperative mortality (unrelated to stroke).

There is also evidence supporting the link between deep hypothermia and cerebral protection in cases of circulatory arrest. On the other hand, hyperthermia can have a detrimental impact on neuronal injury during cerebral ischemia. Given these issues, an accurate means of measuring core temperature during these cases is crucial. Temperature measurements from the nasopharyx and tympanic membrane are both accurate reflections of brain temperature but often lag behind the actual brain temperature. A bladder temperature probe can also be used to measure core temperature, but this is less reliable when urine output decreases or renal blood flow is compromised. Esophageal temperature is not an accurate reflection of core temperature in CPB cases because it is a mediastinal structure and therefore is markedly influenced by blood returning from the bypass machine. Rectal temperature is not a measure of core temperature and is consequently the weakest surrogate of brain temperature.

Testable Concept #34: Dexamethasone does not possess any mineralocorticoid activity.

Corticosteroids can be divided into two primary groups: glucocorticoids and mineralocorticoids. Glucocorticoids not only possess anti-inflammatory and immunosuppressive effects, but are also important for homeostatic, metabolic, and cardiovascular functions. Cortisol (hydrocortisone) is the most important endogenous glucocorticoid. On the other hand, mineralocorticoids are involved in fluid and electrolyte homeostasis. Aldosterone is the primary mineralocorticoid in humans. Its effects include sodium retention, potassium/hydrogen ion excretion, and intravascular volume expansion. Remember that as the potency and duration of action of glucocorticoids increase, there is a concomitant decrease in their mineralocorticoid activity (Table 21.2).

Testable Concept #35: In bipolar patients taking lithium, celecoxib (Celebrex) raises the lithium levels.

Lithium is used to treat bipolar disorder. It is effective in decreasing episodes of mania in people with this disease. Lithium's narrow therapeutic index requires regular monitoring of serum levels. Several drugs interact with lithium. These may increase lithium levels and precipitate lithium toxicity. The most common drugs associated with increased lithium levels include nonsteroidal anti-inflammatories, angiotensin-converting enzyme (ACE) inhibitors, and diuretics. Signs and symptoms of acute lithium toxicity include nausea, vomiting, hyperreflexia, and ataxia. The most common electrocardiogram finding is flattened T waves. Chronic toxicity can lead to mental status changes, seizures, and coma.

Testable Concept #36: Standard deviation can be calculated from the standard error and sample size.

Standard deviation is a measure of variability and indicates how much dispersion there is from the average. A low standard deviation means that all of the data points are near the mean. A high standard deviation means that the data points are more spread out. Standard error is calculated by dividing the standard deviation by the square root of the sample size. Standard error is a representation of how well the sample mean approximates the population mean. The smaller the standard error, the larger the sample size, the closer the sample mean approximates the population mean. In other words, standard deviation refers to how spread out "things" are in a given population. It is useful in describing the population itself. It shows how much variation or dispersion there is from the average (mean, or expected value). The standard error is the standard deviation of the sampling distribution

Table 21.2 APPROXIMATE RELATIVE POTENCY AND HALF-LIVES OF CORTICOSTEROIDS

CORTICOSTEROID	RELATIVE ANTI-INFLAMMATORY ACTIVITY	RELATIVE MINERALOCORTICOID ACTIVITY	EQUIVALENT DOSE (MG)	PLASMA HALF-LIFE (MIN)
Cortisone	0.8	0.8	25	30
Hydrocortisone	1.0	1.0	20	90
Prednisone	4.0	0.8	5	60
Prednisolone	4.0	0.8	5	200
Triamcinolone	5.0	0.0	4.0	300
Methylprednisolone	5.0	0.0	4.0	180
Betamethasone	25.0	0.0	0.75	100–300
Dexamethasone	25–30	0.0	0.75	100–300
Fludrocortisone	10	125	—	200

SOURCE: Asare K. Diagnosis and treatment of adrenal insufficiency in the critically ill patient. *Pharmacotherapy.* 2007;27(11):1512–1528.

of a statistic, or how spread out the sample mean will be around the true population mean.

$$SD = SE \times \sqrt{n}$$

where SD = standard deviation, SE = standard error, and n = sample size (number of observations).

Testable Concept #37: In myxedema coma, respiratory compromise is due to reduced hypoxic ventilatory drive.

Myxedema is caused by severe hypothyroidism. It manifests as lethargy progressing to coma. Patients may have respiratory failure and hypothermia. This may be significantly worsened by drugs that depress respiration and other central nervous system functions. Most patients have other signs and symptoms of hypothyroidism. Respiratory failure in these patients is due to suppressed hypoxic ventilatory drive. This is significantly improved with thyroid replacement therapy.

Testable Concept #38: Plateau pressure should be used when calculating respiratory system static compliance, not peak inspiratory pressure.

Pulmonary compliance (lung compliance) can refer to either dynamic or static lung compliance. Static compliance is the pressure it takes to overcome the elastic resistance to ventilation with no gas flow (i.e., end inspiration). Plateau pressure is the overall pressure it takes to overcome the elastic resistance to inflation of the lungs during the static phase (no gas flow) of inspiration. Peak inspiratory pressure is the overall pressure it takes to overcome all the forces resisting inflation of the lungs during the dynamic phase of inspiration (which includes airway resistance). To determine the compliance of the lungs in the static phase, one would take peak plateau pressure (static phase of ventilation) and subtract baseline pressure at end expiration or positive end-expiratory pressure (PEEP). This is defined as the pressure it takes to overcome the elastic forces opposing lung inflation or static lung compliance.

Testable Concept #39: Routine antibiotic prophylaxis against infective endocarditis is no longer recommended for gastrointestinal or genitourinary procedures.

The American Heart Association revised its guidelines for the prophylaxis of infective endocarditis (IE) in 2007 for the following reasons (Table 21.3):

1. IE is much more likely to result from frequent exposure to random bacteremias associated with daily activities than from bacteremia caused by a dental, gastrointestinal tract, or genitourinary tract procedure.
2. Prophylaxis may prevent an exceedingly small number of cases of IE, if any, in individuals who undergo a dental, gastrointestinal tract, or genitourinary tract procedure.
3. The risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotic therapy.
4. Maintenance of optimal oral health and hygiene may reduce the incidence of bacteremia from daily activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE.

(Source: Wilson, W, et al. Prevention of Infective Endocarditis: Guidelines From the American Heart Association: A Guideline From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki

Table 21.3 INDICATIONS FOR PROPHYLAXIS AGAINST INFECTIVE ENDOCARDITIS IN PATIENTS UNDERGOING DENTAL PROCEDURES

PROPHYLAXIS INDICATED	PROPHYLAXIS NOT INDICATED
Prosthetic cardiac valves	Atrial septal defects
Previous infective endocarditis	Ventricular septal defects
Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits	Patent ductus arteriosus
Completely repaired congenital heart defect with prosthetic material or device, during the first 6 months after the procedure	Mitral valve prolapse
Repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)	Previous Kawasaki disease
Cardiac transplant recipients with cardiac valvulopathy	Hypertrophic cardiomyopathy
Rheumatic heart disease if prosthetic valves or prosthetic material used in valve repair	Previous coronary artery bypass graft surgery
	Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators
	Bicuspid aortic valves
	Coarctation of the aorta
	Calcified aortic stenosis
	Pulmonic stenosis

Allen UD; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Infective endocarditis: Updated guidelines. *Paediatr Child Health.* 2010;15(4):205–208.

Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116:1736–1754.)

Dental procedures requiring prophylaxis (for patients in the high-risk category) include those that involve the manipulation of gingival tissue, the periapical region of teeth, or the perforation of the oral mucosa. Respiratory tract procedures that require prophylaxis are invasive and involve either biopsy or incision into the respiratory mucosa. Routine prophylaxis is no longer recommended for gastrointestinal or genitourinary tract procedures. The exceptions are patients in the high-risk category who have a current gastrointestinal or genitourinary tract infection, or those receiving antibiotics to prevent sepsis and wound infection associated with a gastrointestinal or genitourinary tract procedure (Table 21.4).

Testable Concept #40: Preoperative exposure to low ambient temperatures may increase the early reduction in a patient's temperature after induction of general anesthesia.

Maintaining normal body temperature for patients under general anesthesia is an important role of the anesthesiologist. Hypothermia has several negative perioperative consequences, including

1. Increased blood loss from coagulopathy and platelet dysfunction
2. Postoperative shivering and increased oxygen consumption
3. Cardiac events such as dysrhythmias and myocardial ischemia
4. Delayed wound healing and increased rates of surgical site infection
5. Longer postanesthesia care unit stays due to altered drug metabolism

The initial temperature drop during the first hour of general anesthesia is attributable to the redistribution of heat from the core to the periphery. A study by Matsukawa et al. found that core temperature decreased 1.6 ± 0.3 degrees C during the first hour under general anesthesia. Another study, by Camus et al., found that patients with 1 hour of preoperative skin surface warming (with a forced-air warming blanket) were significant less likely to develop core hypothermia during the first hour of general anesthesia. This illustrates the importance of maintaining euthermia during the preoperative phase, and that doing so may reduce the early drop in temperature after induction of anesthesia.

Testable Concept #41: The masseter muscle is innervated by the trigeminal nerve.

The trigeminal nerve (cranial nerve V) has three branches: the ophthalmic, maxillary, and mandibular nerves. Fibers of the mandibular branch carry motor fibers to the muscles of mastication. The remainder of the trigeminal nerve branches are only sensory.

Testable Concept #42: Inhaled nitric oxide does not affect a patient's systemic blood pressure due to its hemoglobin binding.

Nitric oxide (NO) activates soluble guanylyl cyclase to elevate cGMP levels in vascular smooth muscle. Increased cGMP levels result in endovascular smooth muscle relaxation. Inhalation of NO leads to increased blood flow to the

Table 21.4 ANTIBIOTIC REGIMENS FOR DENTAL PROCEDURES (SINGLE DOSE ADMINISTERED 30–60 MINUTES BEFORE THE PROCEDURE)

SITUATION	AGENT	ADULTS	CHILDREN
Able to take oral medication	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin	2 g IM or IV	50 mg/kg IM or IV
	Cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillin or ampicillin	Cephalexin	2g	50 mg/kg
	Clindamycin	600 mg	20 mg/kg
	Azithromycin or clarithromycin	500 mg	15 mg/kg
Allergic to penicillin or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
	Clindamycin	600 mg IM or IV	20 mg/kg IM or IV

Allen UD; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Infective endocarditis: Updated guidelines. *Paediatr Child Health.* 2010;15(4):205–208.

parts of the lung exposed to NO and decreased pulmonary vascular resistance. It is commonly used to treat pulmonary hypertension and hypoxic respiratory failure. NO rapidly binds to hemoglobin, thus limiting its effect on the systemic vasculature. The vasodilatory effect of inhaled NO is limited to the lung. NO is rapidly metabolized to nitrate with the formation of methemoglobin. Methemoglobin is reduced back to ferrous hemoglobin in the red blood cell.

Testable Concept #43: Sensory innervation of the tongue comes from the mandibular nerve (cranial nerve V3).

Two nerves control the sensory innervation of the anterior two-thirds of the tongue. The lingual nerve, a branch of the mandibular nerve (cranial nerve V3), provides general sensation for the anterior two-thirds of the tongue. Taste (for the anterior two-thirds of the tongue) is controlled by the chorda tympani, a branch of the facial nerve (cranial nerve VII). The glossopharyngeal nerve (cranial nerve IX) is responsible for both taste and general sensation for the posterior third of the tongue. Motor innervation of the intrinsic and extrinsic tongue muscles is by the hypoglossal nerve (cranial nerve XII). The only exception is the palatoglossus muscle, which is controlled by cranial nerve X.

Testable Concept #44: Stroke volume and stroke index are different measurements.

In cardiovascular physiology, stroke volume (SV) is the volume of blood pumped from one ventricle of the heart with each beat. SV is calculated using measurements of ventricle volumes from an echocardiogram and subtracting the volume of the blood in the ventricle at the end of a beat (called end-systolic volume) from the volume of blood just prior to the beat (called end-diastolic volume). SV can apply to each of the two ventricles of the heart, although it usually refers to the left ventricle. SV is generally the same for each ventricle, both being approximately 70 mL in a healthy 70-kg man. SV is an important determinant of cardiac output, which is the product of SV and heart rate, and is also used to calculate ejection fraction, which is SV divided by end-diastolic volume. Because SV decreases in certain conditions and disease states, it correlates with cardiac function.

Stroke index (SI) correlates the SV with the patient's body surface area (i.e., left ventricular SI = SV/body surface area times 1,000). The normal range of stroke volume index (SVI) is 33 to 47 mL/m^2 per beat.

Testable Concept #45: Nitrous oxide acts as an NMDA receptor antagonist.

NMDA (*N*-methyl-d-aspartate) receptors are postsynaptic receptors for the excitatory neurotransmitter glutamate. NMDA receptor antagonists include nitrous oxide, xenon, cyclopropane, and ketamine. These agents are inactive at the GABA receptor.

Testable Concept #46: Understanding the relationship between right atrial pressure and venous return when this relationship is depicted graphically.

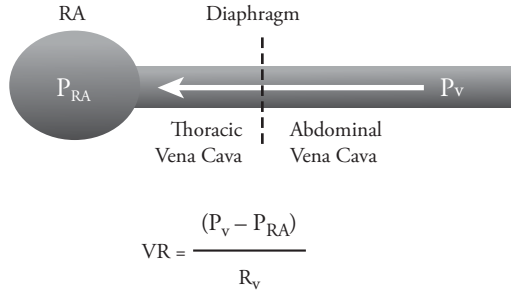
Venous return to the heart is dependent on a number of factors. Muscle contraction, decreased peripheral venous compliance, and the inspiratory phase of respiration all increase venous return to the heart. On the other hand, vena cava compression and gravity (standing vs. supine) both decrease venous return (Fig. 21.1).

Testable Concept #47: To determine the fraction of expired gases, infrared absorption spectrophotometry is the means most often used.

Infrared absorption spectrophotometry (IRAS) is the most commonly used method for the clinical analysis of expired gases in the operating room. IRAS is based on the principle that gases (asymmetric and polyatomic molecules) absorb infrared light at specific wavelengths. Therefore, the operating room spectrophotometer effectively measures the energy absorbed by specific gases when exposed to an infrared beam. The sampling of gas occurs from both the inspiratory and expiratory limb of the anesthetic breathing circuit.

Testable Concept #48: Airway resistance is increased by hyperventilation.

The effect of hyperventilation was studied in healthy and asthmatic patients. Patients were subjected to both hypoventilation (hypercapnia) and hyperventilation (hypocapnia). The authors demonstrated that hypercapnia decreases airway resistance in both healthy and asthmatic individuals. Hypocapnia increased airway resistance in the asthmatic patients but not in the healthy subjects.



Hemodynamic factors determining venous return (VR) from peripheral veins to the right atrium (RA). Pv,venous pressure; P_{RA}, right atrial perssure,R_V, venous resistance.

Figure 21.1 Klabunde RE. Cardiovascular Physiology Concepts. 2nd ed. Philadelphia, Lippincott Williams & Wilkins; 2011.

Testable Concept #49: Interpretation of a posttetanic twitch count

The posttetanic twitch count can help quantify the degree of neuromuscular blockade when there is a lack of response to a single twitch. The prejunctional effect of sustained tetany is to increase both recruitment and production of acetylcholine. Therefore, an increased amount of acetylcholine will be released upon nerve stimulation. This phenomenon is called posttetanic facilitation. To elicit an accurate posttetanic twitch count, one should administer 50-Hz sustained tetany for 5 seconds, followed by single twitch stimulation at 1 Hz after 3 seconds. The posttetanic twitch count is the number of single 1-Hz twitches that can be elicited after sustained tetany. This number has an inverse relationship with the length of time until spontaneous recovery (i.e., a higher number of posttetanic twitches indicates a shortened time until recovery).

Testable Concept #50: In patients undergoing general anesthesia, sufentanil administration leads to a decrease in frequency and a bilateral increase in the amplitude of the electroencephalogram (EEG) tracing.

Inhalational anesthetics change EEG activity from low-voltage fast waves (beta) to high-voltage slow waves (delta). Increasing levels of volatile anesthetics will eventually lead to burst suppression. However, increasing levels of opioids (sufentanil) will not lead to burst suppression. The most common manifestations of EEG ischemia during carotid endarterectomy are ipsilateral attenuation, ipsilateral slowing with attenuation, and ipsilateral slowing without attenuation.

Testable Concept #51: Factor VIII mediates the anticoagulant effect of Hetastarch.

Hydroxyethyl starch (HES) can be used for plasma volume expansion. Volume expansion produced by Hetastarch injection approximates that of 5% albumin. HES solutions have been demonstrated to decrease plasma concentrations of factor VIII and von Willebrand factor by up to 80%. This effect is observed in healthy volunteers at recommended doses. Hetastarch has also been shown to interfere with platelet function and clot formation. It should not be used in patients with coagulopathy.

Testable Concept #52: Calculate the volume of oxygen (L) remaining in an E cylinder when given the tank pressure.

A full E cylinder of oxygen contains 660 L of oxygen (at atmospheric pressure and a temperature of 20 degrees C) and has a pressure of 2,000 psig. The pressure in the cylinder is directly proportional to the number of liters of oxygen remaining in the tank. This allows one to calculate the approximate number of liters of oxygen remaining when given the pressure in the E cylinder. For instance, a pressure of 1,000 psig indicates that an E cylinder is half-full (approximately 330 L). In this situation, if a patient is being treated with 3 L/min of oxygen via nasal cannula, the tank will be empty in 110 minutes.

Testable Concept #53: Hepatic function does not affect the clearance of remifentanil.

Remifentanil is a short-acting synthetic opioid metabolized rapidly by blood and tissue esterases. Unlike other synthetic opioids, which are hepatically metabolized, remifentanil has an ester linkage that undergoes rapid hydrolysis by nonspecific tissue and plasma esterases.

Testable Concept #54: After performing a retrobulbar block, if proptosis (eye dislocation) occurs, one can attempt to apply gentle ocular pressure prior to initiating surgical exploration.

Retrobulbar hemorrhage is one of several complications that can occur after performing a retrobulbar block as the primary anesthetic for ocular procedures. Most retrobulbar hemorrhages are venous and the bleeding is slow. The less common but more serious arterial hemorrhage becomes evident quickly after the block is performed. Symptoms include proptosis and tight eyelids, ecchymosis, chemosis, blood staining of periorbital tissues, lid swelling, and a dramatic increase in intraocular pressure. Timely, effective treatment for retrobulbar hemorrhage can prevent permanent impairment of vision. Most retrobulbar hemorrhages can be successfully treated conservatively. Immediate ocular compression helps limit the extent and severity of the hemorrhage. The goal of treatment is to reduce compartment pressure, thereby reducing intraocular pressure, which in turns reduces negative outcomes on retinal circulation and the need for surgical intervention.

Testable Concept #55: The most common cause of a normal anion gap in the setting of lactic acidosis is hypoalbuminemia.

The anion gap = $[Na+] - [Cl^-] - [HCO^{3-}]$. Common causes of elevated anion gap are lactic acidosis, ketoacidosis, and uremia. Several toxins can also cause an increased anion gap acidosis, including methanol. Albumin is a negatively charged protein. To correct the anion gap for hypoalbuminemia, add to the calculated anion gap twice the difference between normal serum albumin and actual serum albumin.

Testable Concept #56: The chi-square statistic is a better statistical test than the *t* -test to compare the number

of patients who experience a specific outcome in a study comparing two drugs.

The chi-square test is useful for assessing a difference between distributions of categorical data. In this example, the categorical data would be the specific outcomes experienced by the patients in each drug group. Chi-square testing can be done only on actual number counts, and not on percentages, means, or other measures of central tendency. The *t*-test (or Student *t*-test) is a statistical test used to determine whether two populations are the same regarding the variable of interest. This test assumes that continuous, numerical data are being used. A second requirement is that the data are derived from a normally distributed population.

Testable Concept #57: Distinguish between additive, synergistic, and antagonistic reactions on an isobologram.

There are three basic types of reactions that occur between two drugs: additive, synergistic, and antagonistic (Fig. 21.2). An additive reaction occurs when the total effect of two drugs is equal to the sum of their individual effects. A synergistic reaction is characterized by a combined effect that is greater than the sum of their individual effects. An antagonistic reaction occurs when the total effect of taking two drugs is less than the sum of their independent effects.

Testable Concept #58: Altitude changes affect volatile anesthetic delivery.

Anesthetic potency or effect is dependent on the partial pressure of the gas, not the concentration of the agent.

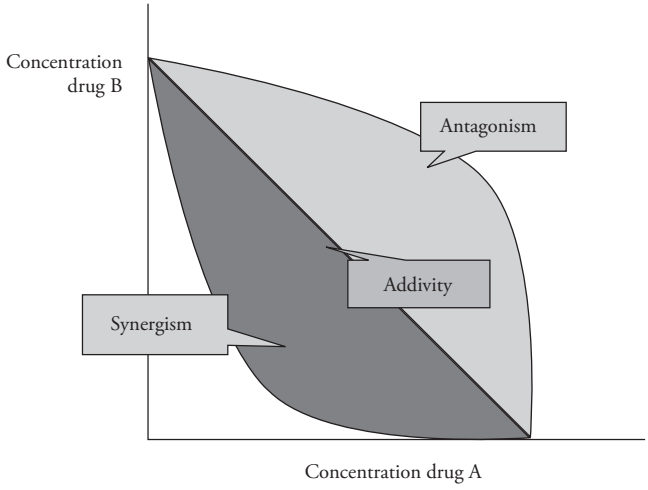


Figure 21.2 CXR Biosciences Scotland 2007.

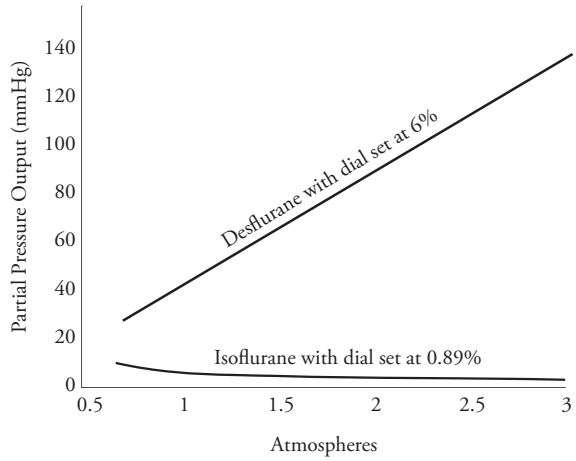


Figure 21.3 Image courtesy J. Ehrenfeld.

Current isoflurane and sevoflurane variable bypass vaporizers automatically compensate for this change in altitude. For practical purposes, the effect of barometric pressure can generally be ignored when using these vaporizers. However, the Tec 6 desflurane vaporizer delivers a constant concentration of agent, not a constant partial pressure. At high altitudes the partial pressure of desflurane will be decreased in proportion to the atmospheric pressure (Fig. 21.3).

Testable Concept #59: Vocal cord paralysis may result from prolonged overinflation of an endotracheal tube cuff.

Vocal cord paralysis may follow endotracheal intubation. The recurrent laryngeal nerve may be compressed from an overinflated cuff. This damage can cause a peripheral nerve injury of the recurrent laryngeal nerve and vocal cord paralysis. This is usually temporary, and most patients recover. The pressure in the endotracheal tube cuff should be checked when prolonged intubation is expected. The use of nitrous oxide may increase the risk of overinflation of the cuff.

Testable Concept #60: Allergic reactions to hyperosmolar contrast dye.

Modern radiocontrast dyes are safe but have the potential to cause adverse effects such as anaphylactoid reactions and contrast-induced nephropathy. Anaphylactoid reactions are clinically indistinguishable from anaphylactic reactions, but the former are not IgE-mediated.

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