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# SECRETS

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**JAMES DUKE MD**

**ANESTHESIA**

**SECRETS**

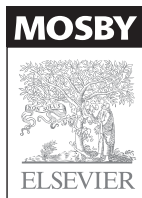
# ANESTHESIA

# SECRETS

Fourth Edition

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ANESTHESIA SECRETS

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# DEDICATION

Dedicated to Renee, my wife and constant companion, and to Desi, Audrey, Sailor, and Famous.

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# PREFACE

In this fourth edition of *Anesthesia Secrets*, the goal continues to be concise presentation of a wide range of topics important to anyone interested in anesthesiology. My goal has always been to not merely offer a few words suitable for the sake of familiarity, but to provide suitable depth to allow readers to integrate the concerns of this field into their wider knowledge of medicine in general.

I am humbled by the reception *Anesthesia Secrets* has received since the first edition was published in 1996. I take it as an affirmation that my contributors and I have a good idea of the important concepts in the field, as much as they can be described in a text of this size. I thank my contributors for this edition and all previous editions. Over the years my contributors have gone on to successful careers across the country, yet their imprint remains throughout. Although they may no longer be listed as authors, they nonetheless have my thanks.

And to you, the reader, thank you for making *Anesthesia Secrets* a part of your educational program.

James Duke, MD, MBA

# TOP 100 SECRETS

These secrets are 100 of the top board alerts. They summarize the concepts, principles, and most salient details of anesthesiology.

1. Patients should take prescribed  $\beta$ -blockers on the day of surgery and continue them perioperatively. Because the receptors are up-regulated, withdrawal may precipitate hypertension, tachycardia, and myocardial ischemia. Clonidine should also be continued perioperatively because of concerns for rebound hypertension.
2. Under most circumstances peri-induction hypotension responds best to administration of intravenous fluids and the use of direct-acting sympathomimetics such as phenylephrine.
3. To determine the etiology of hypoxemia, calculate the A-a gradient to narrow the differential diagnosis.
4. Calculating the anion gap ( $\text{Na}^+ - [\text{HCO}_3^- + \text{Cl}^-]$ ) in the presence of a metabolic acidosis helps narrow the differential diagnosis.
5. Estimating volume status requires gathering as much clinical information as possible because any single variable may mislead. Always look for supporting information.
6. Rapid correction of electrolyte disturbances may be as dangerous as the underlying electrolyte disturbance.
7. When other causes have been ruled out, persistent and refractory hypotension in trauma or other critically ill patients may be caused by hypocalcemia or hypomagnesemia.
8. There is no set hemoglobin/hematocrit level at which transfusion is required. The decision should be individualized to the clinical situation, taking into consideration the patient's health status.
9. An outpatient with a bleeding diathesis can usually be identified through history (including medications) and physical examination. Preoperative coagulation studies in asymptomatic patients are of little value.
10. Thorough airway examination and identification of the patient with a potentially difficult airway are of paramount importance. The "difficult-to-ventilate, difficult-to-intubate" scenario must be avoided if possible. An organized approach, as reflected in the American Society of Anesthesiologists' Difficult Airway Algorithm, is necessary and facilitates high-quality care for patients with airway management difficulties.
11. No single pulmonary function test result absolutely contraindicates surgery. Factors such as physical examination, arterial blood gases, and coexisting medical problems also must be considered in determining suitability for surgery.
12. Speed of onset of volatile anesthetics is increased by increasing the delivered concentration of anesthetic, increasing the fresh gas flow, increasing alveolar ventilation, and using nonlipid-soluble anesthetics.

13. Opioids depress the carbon dioxide–associated drive to breathe, resulting in hypoventilation. Because of the active metabolites, patients with renal failure may experience an exaggerated reaction to morphine.
14. Appropriate dosing of intravenous anesthetics requires considering intravascular volume status, comorbidities, age, and medications.
15. Termination of effect of intravenous anesthetics is by redistribution, not biotransformation and breakdown.
16. Although succinylcholine is the usual relaxant used for rapid sequence induction, agents that chelate nondepolarizing relaxant molecule may alter this paradigm in the future.
17. Leave clinically weak patients intubated and support respirations until the patient can demonstrate return of strength.
18. Lipid solubility,  $pK_a$ , and protein binding of the local anesthetics determine their potency, onset, and duration of action, respectively.
19. Local anesthetic-induced central nervous system toxicity manifests as excitation, followed by seizures, and then loss of consciousness. Hypotension, conduction blockade, and cardiac arrest are signs of local anesthetic cardiovascular toxicity.
20. There is sound scientific evidence that low-dose dopamine is ineffective for prevention and treatment of acute renal injury and protection of the gut.
21. A preoperative visit by an informative and reassuring anesthesiologist provides useful psychologic preparation and calms the patient's fears and anxiety before administration of anesthesia.
22. The risk of clinically significant aspiration pneumonitis in healthy patients having elective surgery is very low. Routine use of pharmacologic agents to alter the volume or pH of gastric contents is unnecessary.
23. The most important information obtained in a preanesthetic evaluation comes from a thorough, accurate, and focused history and physical examination.
24. When compressed, some gases condense into a liquid ( $N_2O$  and  $CO_2$ ) and some do not ( $O_2$  and  $N_2$ ). These properties define the relationship between tank volume and pressure.
25. The semiclosed circuit using a circle system is the most commonly used anesthesia circuit. Components include an inspiratory limb, expiratory limb, unidirectional valves, a  $CO_2$  absorber, a gas reservoir bag, and a pop-off valve on the expiratory limb.
26. Every patient ventilated with an ascending bellows anesthesia ventilator receives approximately 2.5 to 3 cm  $H_2O$  of positive end-expiratory pressure (PEEP) because of the weight of the bellows.
27. The output of traditional vaporizers depends on the proportion of fresh gas that bypasses the vaporizing chamber compared with the proportion that passes through the vaporizing chamber.
28. A conscientious approach to positioning is required to facilitate the surgical procedure, prevent physiologic embarrassment, and prevent neuropathy and injury to other aspects of the patient's anatomy.

29. The first step in the care of the hypoxic patient fighting the ventilator is to ventilate the patient manually with 100% oxygen.
30. Risk factors for auto-PEEP include high minute ventilation, small endotracheal tube, chronic obstructive pulmonary disease, and asthma.
31. When determining whether an abnormal electrocardiogram (ECG) signal may be an artifact, look to see if the native rhythm is superimposed on (*marching through*) the abnormal tracing.
32. A patient with new ST-segment depression or T-wave inversion may have suffered a non-ST-elevation myocardial infarction.
33. Pulse oximetry measures arterial oxygenation using different wavelengths of light shone through a pulsatile vascular bed. Pulse oximetry can detect hypoxemia earlier, providing an early warning sign of potential organ damage.
34. Below a hemoglobin saturation of 90%, a small decrease in saturation corresponds to a large drop in PaO<sub>2</sub>.
35. Except for visualization with bronchoscopy, CO<sub>2</sub> detection is the best method of verifying endotracheal tube location.
36. Analysis of the capnographic waveform provides supportive evidence for numerous clinical conditions, including decreasing cardiac output; altered metabolic activity; acute and chronic pulmonary disease; and ventilator, circuit, and endotracheal tube malfunction.
37. Trends in central venous pressures are more valuable than isolated values and should always be evaluated in the context of the patient's scenario.
38. Pulmonary catheterization has not been shown to improve outcome in all patient subsets.
39. The risks of central venous catheterization and pulmonary artery (PA) insertion are many and serious, and the benefits should be identified before initiation of these procedures to justify their use.
40. To improve accuracy in interpretation of PA catheter data, always consider the timing of the waveforms with the ECG cycle.
41. Ipsilateral ulnar arterial catheterization should not be attempted after multiple failed attempts at radial artery catheterization.
42. With the exception of antagonists of the renin-angiotensin system and possibly diuretics, antihypertensive therapy should be given up to and including the day of surgery.
43. Symptoms of awareness may be very nonspecific, especially when muscle relaxants are used.
44. When a patient with structural heart disease develops a wide-complex tachycardia, assume that the rhythm is ventricular tachycardia until proven otherwise. When a patient develops tachycardia and becomes hemodynamically unstable, prepare for cardioversion (unless the rhythm is clearly sinus!).
45. When a patient develops transient slowing of the sinoatrial node along with transient atrioventricular block, consider increased vagal tone, a medication effect, or both.

46. Even mild hypothermia has a negative influence on patient outcome, increasing rates of wound infection, delaying healing, increasing blood loss, and increasing cardiac morbidity threefold.
47. If a patient's exercise capacity is excellent, even in the presence of ischemic heart disease, the chances are good that the patient will be able to tolerate the stresses of surgery. The ability to climb two or three flights of stairs without significant symptoms (e.g., angina, dyspnea, syncope) is usually an indication of adequate cardiac reserve.
48. Patients with decreased myocardial reserve are more sensitive to the cardiovascular depressant effects caused by anesthetic agents, but careful administration with close monitoring of hemodynamic responses can be accomplished with most agents.
49. For elective procedures, the most current fasting guidelines are as follows:
- |   |         |
|---|---------|
| Clear liquids (water, clear juices)           | 2 hours |
| Nonclear liquids (Jello, breast milk)         | 4 hours |
| Light meal or snack (crackers, toast, liquid) | 6 hours |
| Full meal (fat containing, meat)              | 8 hours |
50. "All that wheezes is not asthma." Also consider mechanical airway obstruction, congestive failure, allergic reaction, pulmonary embolus, pneumothorax, aspiration, and endobronchial intubation.
51. Patients with significant reactive airway disease require thorough preoperative preparation, including inhaled  $\beta$ -agonist therapy and possibly steroids, methylxanthines, or other agents.
52. The necessary criteria for acute lung injury/acute respiratory distress syndrome (ALI/ARDS) include:
- (1) Acute onset
  - (2)  $\text{PaO}_2/\text{FiO}_2$  ratio of 300 for ALI
  - (3)  $\text{PaO}_2/\text{FiO}_2$  ratio of 200 for ARDS
  - (4) Chest radiograph with diffuse infiltrates
  - (5) Pulmonary capillary wedge pressure of 18 mm Hg
53. Mechanical ventilation settings for patients with ARDS or ALI include tidal volume of at 6 to 8 ml/kg of ideal body weight while limiting plateau pressures to  $<30$  cm  $\text{H}_2\text{O}$ . PEEP should be adjusted to prevent end-expiratory collapse.  $\text{FiO}_2$  should be adjusted to maintain oxygen saturations between 88% and 92%.
54. Acute intraoperative increases in PA pressure may respond to optimizing oxygenation and ventilation, correcting acid-base status, establishing normothermia, decreasing the autonomic stress response by deepening the anesthetic, and administering vasodilator therapy.
55. The best way to maintain renal function during surgery is to ensure an adequate intravascular volume, maintain cardiac output, and avoid drugs known to decrease renal perfusion.
56. Measures to acutely decrease intracranial pressure (ICP) include elevation of the head of the bed; hyperventilation ( $\text{PaCO}_2$  25 to 30 mm Hg); diuresis (mannitol and/or furosemide); and minimized intravenous fluid. In the setting of elevated ICP, avoid ketamine and nitrous oxide.

57. Airway comes first in every algorithm; thus succinylcholine is the agent of choice for a rapid-sequence induction for the full-stomach, head-injured patient, despite the transient rise in ICP seen with succinylcholine. Succinylcholine must be avoided in children with muscular dystrophy and should be avoided except in airway emergencies in young males.
58. Malignant hyperthermia (MH) is an inherited disorder that presents in the perioperative period after exposure to inhalational agents and/or succinylcholine. The disease may be fatal if the diagnosis is delayed and dantrolene is not administered. The sine qua non of MH is an unexplained rise in end-tidal carbon dioxide with a simultaneous increase in minute ventilation in the setting of an unexplained tachycardia.
59. Patients with Alzheimer's disease may become more confused and disoriented with preoperative sedation.
60. In patients with multiple sclerosis spinal anesthesia should be used with caution and only in situations in which the benefits of spinal anesthesia over general anesthesia are clear.
61. Patients with diabetes have a high incidence of coronary artery disease with an atypical or silent presentation. Maintaining perfusion pressure, controlling heart rate, continuous ECG observation, and a high index of suspicion during periods of refractory hypotension are key considerations.
62. The inability to touch the palmar aspects of the index fingers when palms touch (the prayer sign) can indicate a difficult oral intubation in patients with diabetes.
63. Thyroid storm may mimic MH. It is confirmed by an increased serum tetraiodothyronine ( $T_4$ ) level and is treated initially with  $\beta$ -blockade followed by antithyroid therapy.
64. Perioperative glucocorticoid supplementation should be considered for patients receiving exogenous steroids.
65. Obese patients may be difficult to ventilate and difficult to intubate. Backup strategies should always be considered and readily available before airway management begins.
66. A patient with a Glasgow Coma Scale of 8 is sufficiently depressed that endotracheal intubation is indicated.
67. The initial goal of burn resuscitation is to correct hypovolemia. Burns cause a generalized increase in capillary permeability with loss of significant fluid and protein into interstitial tissue.
68. From about 24 hours after injury until the burn has healed, succinylcholine may cause hyperkalemia because of proliferation of extrajunctional neuromuscular receptors. Burned patients tend to be resistant to the effects of nondepolarizing muscle relaxants and may need two to five times the normal dose.
69. Abrupt oxygen desaturation while transporting an intubated pediatric patient is probably the result of main stem intubation.
70. Because children have stiff ventricles and rely on heart rate for cardiac output, maintain heart rate at all costs by avoiding hypoxemia and administering anticholinergic agents when appropriate.

71. Infants may be difficult to intubate because they have a more anterior larynx, relatively large tongues, and a floppy epiglottis. The narrowest part of the larynx is below the vocal cords at the cricoid cartilage.
72. Hyperventilation with 100% oxygen is the best first step in treating a pulmonary hypertensive event.
73. If a child with tetralogy of Fallot has a hypercyanotic spell during induction of anesthesia, gentle external compression of the abdominal aorta can reverse the right-to-left shunt while pharmacologic treatments are being prepared.
74. The patient with a ventricular obstructive cardiac lesion is at high risk for perioperative cardiac failure or arrest because of ventricular hypertrophy, ischemia, and loss of contractile tissue.
75. Pregnant patients can pose airway management problems because of airway edema, large breasts that make laryngoscopy difficult, full stomachs rendering them prone to aspiration, and rapid oxygen desaturation caused by decreased functional residual capacity.
76. In preeclampsia hypertension should be treated, but blood pressure should not be *normalized*. Spinal anesthesia may be preferable to general anesthesia when the preeclamptic patient does not have an existing epidural catheter or there is insufficient time because of nonreassuring fetal heart rate tracing.
77. Intrauterine fetal resuscitation and maternal airway management are of overriding importance in patients with eclamptic seizures.
78. Basal function of most organ systems is relatively unchanged by the aging process per se, but the functional reserve and ability to compensate for physiologic stress are reduced.
79. In general, anesthetic requirements are decreased in geriatric patients. There is an increased potential for a wide variety of postoperative complications in the elderly, and postoperative cognitive dysfunction is arguably the most common.
80. Anesthesiologists increasingly are asked to administer anesthesia in nontraditional settings. Regardless of where an anesthetic is administered, the same standards apply for safety, monitors, equipment, and personnel.
81. O-negative blood is the *universal donor* for packed red blood cells; for plasma it is AB positive.
82. If a patient is pacemaker dependent, the interference by electrocautery may be interpreted by the device as intrinsic cardiac activity, leading to profound inhibition of pacing and possible asystole. Devices should be programmed to the asynchronous mode before surgery.
83. Pacemaker-mediated tachycardia is an endless-loop tachycardia caused by retrograde atrial activation up the conduction system, with subsequent tracking of this atrial signal and then pacing in the ventricle. It can be terminated by application of a magnet that prevents tracking.
84. Loss of afferent sensory and motor stimulation renders a patient sensitive to sedative medications secondary to deafferentiation. For the same reason neuraxial anesthesia decreases the minimum alveolar concentration of volatile anesthetics.



85. Patients with sympathectomies from regional anesthesia require aggressive resuscitation, perhaps with unusually large doses of pressors, to reestablish myocardial perfusion after cardiac arrest.
86. Although patients with end-stage liver disease have a hyperdynamic circulation characterized by increased cardiac index and decreased systemic vascular resistance, impaired myocardial function, coronary artery disease, and pulmonary hypertension are common.
87. Patients with liver disease commonly have an increased volume of distribution, necessitating an increase in initial dose requirements. However, because the drug metabolism may be reduced, smaller doses are subsequently administered at longer intervals.
88. There is no *best* anesthetic technique during cardiopulmonary bypass. Patients with decreased ejection fraction will not tolerate propofol infusions or volatile anesthesia as well as patients with preserved stroke volume and will probably require an opioid-based technique.
89. Always reassess optimal positioning of any lung-isolation device after repositioning the patient. A malpositioned tube is suggested by acute increases in ventilatory pressures and decreases in oxygen saturation.
90. Methods to improve oxygenation during one-lung ventilation include increasing  $FI_{O_2}$ , adding PEEP to the dependent lung, adding continuous positive airway pressure to the nondependent lung, adjusting tidal volumes, and clamping the blood supply to the nonventilated lung.
91. To decrease airway pressures, always use the largest double-lumen endotracheal tube available.
92. If ICP is high, as evidenced by profound changes in mental status or radiologic evidence of cerebral swelling, avoid volatile anesthetics and opt instead for a total intravenous anesthetic technique.
93. If  $PaCO_2$  significantly increases after 30 minutes of pneumoperitoneum, search for another cause of hypercapnia such as capnotherax, subcutaneous  $PaCO_2$ ,  $CO_2$  embolism, or endobronchial intubation.
94. Pulmonary arterial occlusion pressure is an unreliable indicator of cardiac filling pressures during pneumoperitoneum.
95. Postoperative nausea and vomiting are common after laparoscopic surgery; they should be anticipated and treated prophylactically.
96. Methohexital should be considered the drug of choice for the induction of anesthesia for electroconvulsive therapy (ECT). ECT causes pronounced sympathetic activity, which may result in myocardial ischemia or even infarction in patients with coronary artery disease.
97. To perform ECT safely it is necessary to complete a preoperative history and physical examination, use standard monitors, have readily available equipment and medications appropriate for full cardiopulmonary resuscitation, use an induction agent (e.g., methohexital) and muscle relaxant (e.g., succinylcholine), and have a  $\beta$ -blocker readily available (e.g., esmolol).

98. Doses of morphine differ by a factor of 10 between intravenous, epidural, and intrathecal routes.
99. Chronic pain is best treated by using multiple therapeutic modalities, including physical therapy, psychologic support, pharmacologic management, and rational use of more invasive procedures such as nerve blocks and implantable technologies.
100. Neuropathic pain is usually less responsive to opioids than pain originating from nociceptors.

# AUTONOMIC NERVOUS SYSTEM

James Duke, MD, MBA

## 1. Describe the autonomic nervous system.

The autonomic nervous system (ANS) is a network of nerves and ganglia that controls involuntary physiologic actions and maintains internal homeostasis and stress responses. The ANS innervates structures within the cardiovascular, pulmonary, endocrine, exocrine, gastrointestinal, genitourinary, and central nervous systems (CNS) and influences metabolism and thermal regulation. The ANS is divided into two parts: the sympathetic (SNS) and parasympathetic (PNS) nervous system. When stimulated, the effects of the SNS are widespread across the body. In contrast, PNS stimulation tends to produce localized, discrete effects. The SNS and PNS generally have opposing effects on end-organs, with either the SNS or the PNS exhibiting a dominant tone at rest and without exogenous stimulating events (Table 1-1). In general the function of the PNS is homeostatic, whereas stimulation of the SNS prepares the organism for some stressful event (this is often called the fight-or-flight response).

TABLE 1-1. AUTONOMIC DOMINANCE PATTERNS AT EFFECTOR SITES

Sympathetic Nervous System	Parasympathetic Nervous System
Arterioles	Sinoatrial node
Veins	Gastrointestinal tract
Sweat glands	Uterus
	Urinary bladder
	Salivary glands
	Iris
	Ciliary muscle

## KEY POINTS: AUTONOMIC NERVOUS SYSTEM

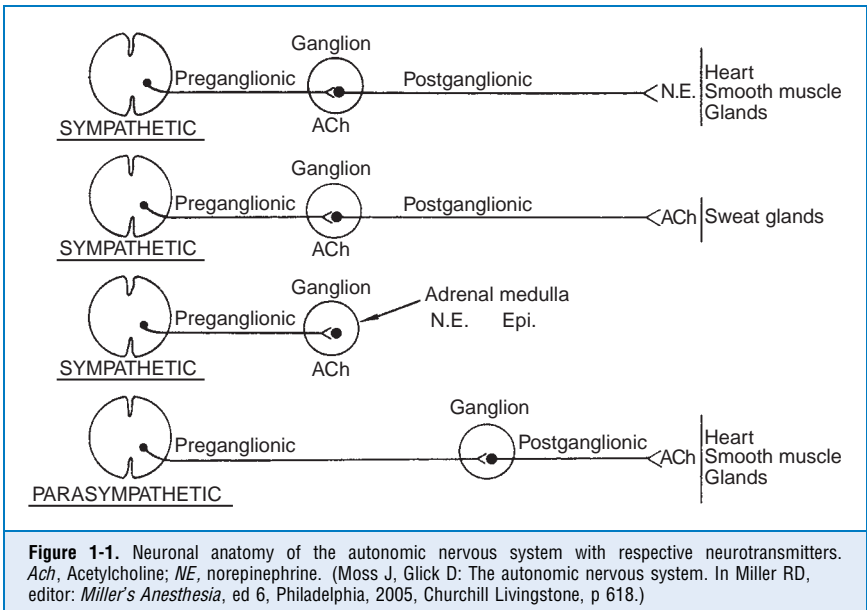


1. Patients should take  $\beta$ -blockers on the day of surgery and continue them perioperatively. Because the receptors are up-regulated, withdrawal may precipitate hypertension, tachycardia, and myocardial ischemia.
2. Clonidine should also be continued perioperatively because of concerns for rebound hypertension.
3. Indirect-acting sympathomimetics (e.g., ephedrine) depend on norepinephrine release to be effective. Norepinephrine-depleted states will not respond to ephedrine administration.

- Under most circumstances peri-induction hypotension responds best to intravenous fluid administration and the use of direct-acting sympathomimetics such as phenylephrine.
- Orthostatic hypotension is common after surgery and may be caused by the use of any or all anesthetic agents and lying supine for extended periods. It is necessary to be cognizant of this potential problem when elevating a patient's head after surgery or even when moving the patient from the operating room table to a chair (e.g., procedures requiring only sedation and monitoring).

## 2. Review the anatomy of the sympathetic nervous system.

Preganglionic sympathetic neurons originate from the intermediolateral columns of the thoracolumbar spinal cord. These myelinated fibers exit via the ventral root of the spinal nerve and synapse with postganglionic fibers in paravertebral sympathetic ganglia, unpaired prevertebral ganglia, or a terminal ganglion. Preganglionic neurons may ascend or descend the sympathetic chain before synapsing. Preganglionic neurons stimulate nicotinic cholinergic postganglionic neurons by releasing acetylcholine. Postganglionic adrenergic neurons synapse at targeted end-organs and release norepinephrine (Figure 1-1).



## 3. Elaborate on the location and names of the sympathetic ganglia. Practically speaking, what is the importance of knowing the name and location of these ganglia?

Easily identifiable paravertebral ganglia are found in the cervical region (including the stellate ganglion) and along thoracic, lumbar, and pelvic sympathetic trunks. Prevertebral ganglia are named in relation to major branches of the aorta and include the celiac, superior and inferior mesenteric, and renal ganglia. Terminal ganglia are located close to the organs that they serve. The practical significance of knowing the location of some of these ganglia is that local anesthetics can be injected in the region of these structures to ameliorate sympathetically mediated pain.

#### 4. Describe the postganglionic adrenergic receptors of the sympathetic nervous system and the effects of stimulating these receptors.

There are  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ , and  $\beta_2$  adrenergic receptors. The A1, A2, and B2 receptors are postsynaptic and are stimulated by the neurotransmitter norepinephrine. The A2 receptors are presynaptic, and stimulation inhibits release of norepinephrine, reducing overall the autonomic response. Molecular pharmacologists have further subdivided these receptors, but this is beyond the scope of this discussion. Dopamine stimulates postganglionic dopaminergic receptors, classified as DA1 and DA2. The response to receptor activation in different sites is described in [Table 1-2](#).

Receptor	Organ	Response
$\beta_1$	Heart	Increases heart rate, contractility, and conduction velocity
	Fat cells	Lipolysis
$\beta_2$	Blood vessels	Dilation
	Bronchioles	Dilation
	Uterus	Relaxation
	Kidneys	Renin secretion
	Liver	Gluconeogenesis, glycogenolysis
	Pancreas	Insulin secretion
$\alpha_1$	Blood vessels	Constriction
	Pancreas	Inhibits insulin release
	Intestine, bladder	Relaxation but constriction of sphincters
$\alpha_2$	Presynaptic nerve endings	Inhibits norepinephrine release
Dopamine-1	Blood vessels	Dilates renal, coronary, and splanchnic vessels
Dopamine-2	Presynaptic endings	Inhibits norepinephrine release
	Central nervous system	Psychic disturbances

#### 5. Review the anatomy and function of the parasympathetic nervous system.

Preganglionic parasympathetic neurons originate from cranial nerves III, VII, IX, and X and sacral segments 2-4. Preganglionic parasympathetic neurons synapse with postganglionic neurons close to the targeted end-organ, creating a more discrete physiologic effect. Both preganglionic and postganglionic parasympathetic neurons release acetylcholine; these cholinergic receptors are subclassified as either nicotinic or muscarinic. The response to cholinergic stimulation is summarized in [Table 1-3](#).

#### 6. What are catecholamines? Which catecholamines occur naturally? Which are synthetic?

Catecholamines are hydroxy-substituted phenylethylamines and stimulate adrenergic nerve endings. Norepinephrine, epinephrine, and dopamine are naturally occurring catecholamines, whereas dobutamine and isoproterenol are synthetic catecholamines.

#### 7. Review the synthesis of dopamine, norepinephrine, and epinephrine.

The amino acid tyrosine is actively transported into the adrenergic presynaptic nerve terminal cytoplasm, where it is converted to dopamine by two enzymatic reactions: hydroxylation of tyrosine by tyrosine hydroxylase to dopamine and decarboxylation of dopamine by aromatic

TABLE 1-3. END-ORGAN EFFECTS OF CHOLINERGIC RECEPTOR STIMULATION

Receptor	Organ	Response
Muscarinic	Heart	Decreased heart rate, contractility, conduction velocity
	Bronchioles	Constriction
	Salivary glands	Stimulates secretion
	Intestine	Contraction and relaxation of sphincters, stimulates secretions
	Bladder	Contraction and relaxation of sphincters
Nicotinic	Neuromuscular junction	Skeletal muscle contraction
	Autonomic ganglia	SNS stimulation

*SNS*, Sympathetic nervous system.

L-amino acid decarboxylase. Dopamine is transported into storage vesicles, where it is hydroxylated by dopamine  $\beta$ -hydroxylase to norepinephrine. Epinephrine is synthesized in the adrenal medulla from norepinephrine through methylation by phenylethanolamine *N*-methyltransferase (Figure 1-2).

### 8. How is norepinephrine metabolized?

Norepinephrine is removed from the synaptic junction by reuptake into the presynaptic nerve terminal and metabolic breakdown. Reuptake is the most important mechanism and allows reuse of the neurotransmitter. The enzyme monoamine oxidase (MAO) metabolizes norepinephrine within the neuronal cytoplasm; both MAO and catecholamine *O*-methyltransferase (COMT) metabolize the neurotransmitter at extraneuronal sites. The important metabolites are 3-methoxy-4-hydroxymandelic acid, metanephrine, and normetanephrine.

### 9. Describe the synthesis and degradation of acetylcholine.

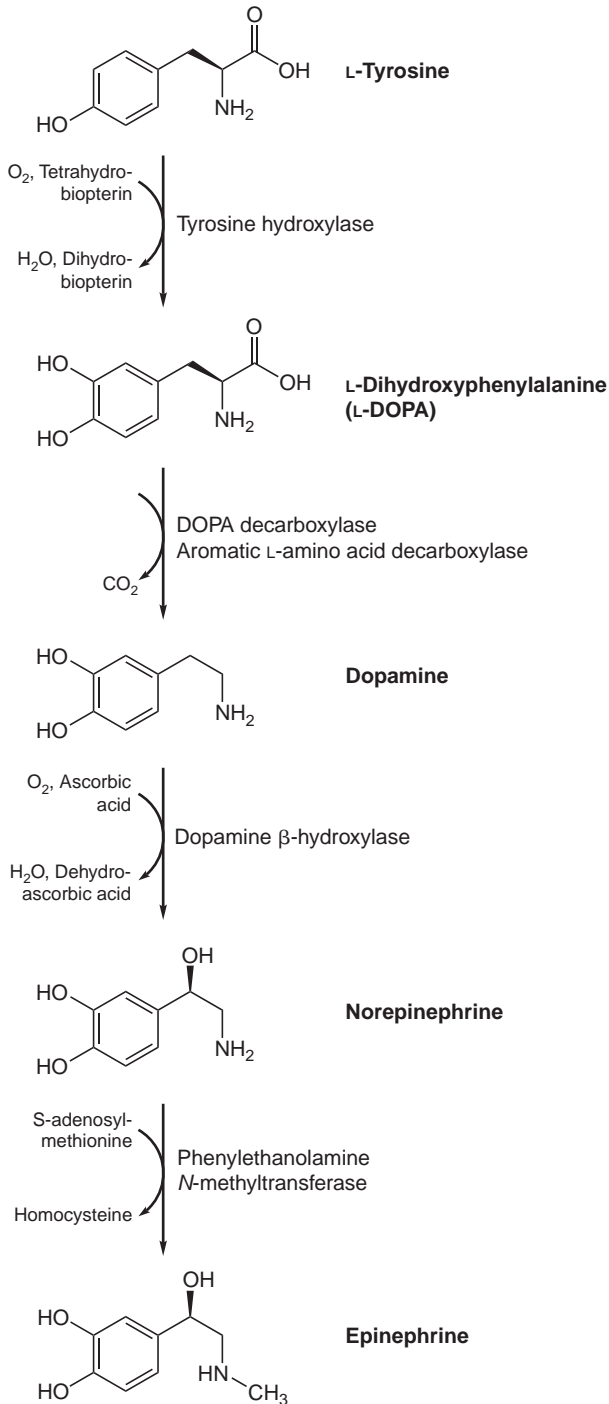
The cholinergic neurotransmitter acetylcholine (ACh) is synthesized within presynaptic neuronal mitochondria by esterification of acetyl coenzyme A and choline by the enzyme choline acetyltransferase; it is stored in synaptic vesicles until release. After release, ACh is principally metabolized by acetylcholinesterase, a membrane-bound enzyme located in the synaptic junction. Acetylcholinesterase is also located in other nonneuronal tissues such as erythrocytes.

### 10. What are sympathomimetics?

Sympathomimetics are synthetic drugs with vasopressor and chronotropic effects similar to those of catecholamines. They are commonly used in the operating room to reverse the circulatory depressant effects of anesthetic agents by increasing blood pressure and heart rate; they also temporize the effects of hypovolemia while fluids are administered. They are effective during both general and regional anesthesia.

### 11. Review the sympathomimetics commonly used in the perioperative environment.

Direct-acting sympathomimetics are agonists at the targeted receptor, whereas indirect-acting sympathomimetics stimulate release of norepinephrine. Sympathomimetics may be mixed in their actions, having both direct and indirect effects. Practically speaking, phenylephrine (direct acting) and ephedrine (mostly indirect acting) are the sympathomimetics commonly used



**Figure 1-2.** The catecholamine synthetic pathway. (From <http://www.answers.com/topic/epinephrine>.)

perioperatively. Also, epinephrine, dopamine, and norepinephrine may be used perioperatively and most often by infusion since their effects on blood pressure, heart rate, and myocardial oxygen consumption can be profound. Dopamine is discussed in Chapter 15.

**12. Discuss the effects of phenylephrine and review common doses of this medication.**

Phenylephrine stimulates primarily A1 receptors, resulting in increased systemic vascular resistance and blood pressure. Larger doses stimulate A2 receptors. Reflex bradycardia may be a response to increasing systemic vascular resistance. Usual intravenous doses of phenylephrine range between 50 and 200 mcg. Phenylephrine may also be administered by infusion at 10 to 20 mcg/min.

**13. Discuss the effects of ephedrine and review common doses of this medication. Give some examples of medications that contraindicate the use of ephedrine and why.**

Ephedrine produces norepinephrine release, stimulating mostly A1 and B1 receptors; the effects resemble those of epinephrine although they are less intense. Increases in systolic blood pressure, diastolic blood pressure, heart rate, and cardiac output are noted. Usual intravenous doses of ephedrine are between 5 and 25 mg. Repeated doses demonstrate diminishing response known as *tachyphylaxis*, possibly because of exhaustion of norepinephrine supplies or receptor blockade. Similarly, an inadequate response to ephedrine may be the result of already depleted norepinephrine stores. Ephedrine should not be used when the patient is taking drugs that prevent reuptake of norepinephrine because of the risk of severe hypertension. Examples include tricyclic antidepressants, monoamine oxidase inhibitors, and acute cocaine intoxication. Chronic cocaine users may be catecholamine depleted and may not respond to ephedrine.

**14. What are the indications for using  $\beta$ -adrenergic antagonists?**

$\beta$ -Adrenergic antagonists, commonly called  *$\beta$ -blockers*, are antagonists at  $\beta_1$ - and  $\beta_2$ - receptors.  $\beta$ -blockers are mainstays in antihypertensive, antianginal, and antiarrhythmic therapy. Perioperative  $\beta$ -blockade is essential in patients with coronary artery disease, and atenolol has been shown to reduce death after myocardial infarction.

**15. Review the mechanism of action for  $\beta_1$ -antagonists and side effects.**

$\beta_1$ -Blockade produces negative inotropic and chronotropic effects, decreasing cardiac output and myocardial oxygen requirements.  $\beta_1$ -Blockers also inhibit renin secretion and lipolysis. Since volatile anesthetics also depress contractility, intraoperative hypotension is a risk.  $\beta$ -Blockers can produce atrioventricular block. Abrupt withdrawal of these medications is not recommended because of up-regulation of the receptors; myocardial ischemia and hypertension may occur.  $\beta$ -Blockade decreases the signs of hypoglycemia; thus it must be used with caution in insulin-dependent patients with diabetes.  $\beta$ -Blockers may be cardioselective, with relatively selective B1 antagonist properties, or noncardioselective. Some  $\beta$ -Blockers have membrane-stabilizing (antiarrhythmic effects); some have sympathomimetic effects and are the drugs of choice in patients with left ventricular failure or bradycardia.  $\beta$ -Blockers interfere with the transmembrane movement of potassium; thus potassium should be infused with caution. Because of their benefits in ischemic heart disease and the risk of rebound,  $\beta$ -blockers should be taken on the day of surgery.

**16. Review the effects of  $\beta_2$ -antagonism.**

$\beta_2$ -Blockade produces bronchoconstriction and peripheral vasoconstriction and inhibits insulin release and glycogenolysis. Selective  $\beta_1$ -blockers should be used in patients with chronic or reactive airway disease and peripheral vascular disease because of respective concerns for bronchial or vascular constriction.



**17. How might complications of  $\beta$ -blockade be treated intraoperatively?**

Bradycardia and heart block may respond to atropine; refractory cases may require the  $\beta_2$ -agonism of dobutamine or isoproterenol. Interestingly, calcium chloride may also be effective, although the mechanism is not understood. In all cases expect to use larger than normal doses.

**18. Describe the pharmacology of  $\alpha$ -adrenergic antagonists.**

$\alpha_1$ -Blockade results in vasodilation; therefore  $\alpha$ -blockers are used in the treatment of hypertension. However, nonselective  $\alpha$ -blockers may be associated with reflex tachycardia. Thus, selective  $\alpha_1$ -blockers are primarily used as antihypertensives. Prazosin is the prototypical selective  $\alpha_1$ -blocker, whereas phentolamine and phenoxybenzamine are examples of nonselective  $\alpha$ -blockers. Interestingly, labetalol, a nonselective  $\beta$ -blocker, also has selective  $\alpha_1$ -blocking properties and is a potent antihypertensive.

**19. Review  $\alpha_2$ -agonists and their role in anesthesia.**

When stimulated,  $\alpha_2$ -receptors within the CNS decrease sympathetic output. Subsequently, cardiac output, systemic vascular resistance, and blood pressure decrease. Clonidine is an  $\alpha_2$ -agonist used in the management of hypertension. It also has significant sedative qualities. It decreases the anesthetic requirements of inhaled and intravenous anesthetics. It has also been used intrathecally in the hopes of decreasing postprocedural pain, but unacceptable hypotension is common after intrathecal administration, limiting its usefulness. Clonidine should be continued perioperatively because of concerns for rebound hypertension.

**20. Discuss muscarinic antagonists and their properties.**

Muscarinic antagonists, also known as *anticholinergics*, block muscarinic cholinergic receptors, producing mydriasis and bronchodilation, increasing heart rate, and inhibiting secretions. Centrally acting muscarinic antagonists (all nonionized, tertiary amines with the ability to cross the blood-brain barrier) may produce delirium. Commonly used muscarinic antagonists include atropine, scopolamine, glycopyrrolate, and ipratropium bromide. Administering muscarinic antagonists is a must when the effect of muscle relaxants is antagonized by acetylcholinesterase inhibitors, lest profound bradycardia, heart block, and asystole ensue. Glycopyrrolate is a quaternary ammonium compound, cannot cross the blood-brain barrier, and therefore lacks CNS activity. When inhaled, ipratropium bromide produces bronchodilation.

**21. What is the significance of autonomic dysfunction? How might you tell if a patient has autonomic dysfunction?**

Patients with autonomic dysfunction tend to have severe hypotension intraoperatively. Evaluation of changes in orthostatic blood pressure and heart rate is a quick and effective way of assessing autonomic dysfunction. If the autonomic nervous system is intact, an increase in heart rate of 15 beats/min and an increase of 10 mm Hg in diastolic blood pressure are expected when changing position from supine to sitting. Autonomic dysfunction is suggested whenever there is a loss of heart rate variability, whatever the circumstances. Autonomic dysfunction includes vasomotor, bladder, bowel, and sexual dysfunction. Other signs include blurred vision, reduced or excessive sweating, dry or excessively moist eyes and mouth, cold or discolored extremities, incontinence or incomplete voiding, diarrhea or constipation, and impotence. Although there are many causes, it should be noted that people with diabetes and chronic alcoholics are patient groups well known to demonstrate autonomic dysfunction.

**22. What is a pheochromocytoma, and what are its associated symptoms? How is pheochromocytoma diagnosed?**

Pheochromocytoma is a catecholamine-secreting tumor of chromaffin tissue, producing either norepinephrine or epinephrine. Most are intra-adrenal, but some are extra-adrenal (within the bladder wall is common), and about 10% are malignant. Signs and symptoms include paroxysms of

hypertension, syncope, headache, palpitations, flushing, and sweating. Pheochromocytoma is confirmed by detecting elevated levels of plasma and urinary catecholamines and their metabolites, including vanillylmandelic acid, normetanephrine, and metanephrine.

### 23. Review the preanesthetic and intraoperative management of pheochromocytoma patients.

These patients are markedly volume depleted and at risk for severe hypertensive crises. It is absolutely essential that before surgery,  $\alpha$ -blockade and rehydration should first be instituted. The  $\alpha_1$ -antagonist phenoxybenzamine is commonly administered orally.  $\beta$ -Blockers are often administered once  $\alpha$ -blockade is achieved and should never be given first because unopposed  $\alpha_1$ -vasoconstriction results in severe, refractory hypertension. Labetalol may be the  $\beta$ -blocker of choice since it also has  $\alpha$ -blocking properties.

Intraoperatively intra-arterial monitoring is required since fluctuations in blood pressure may be extreme. Manipulation of the tumor may result in hypertension. Intraoperative hypertension is managed by infusing the  $\alpha$ -blocker phentolamine or vasodilator nitroprusside. Once the tumor is removed, hypotension is a risk, and fluid administration and administration of the  $\alpha$ -agonist phenylephrine may be necessary. Central venous pressure monitoring will assist with volume management.

## SUGGESTED READING

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1. Neukirchen M, Kienbaum P: Sympathetic nervous system. Evaluation and importance for clinical general anesthesia, *Anesthesiology* 109:1113–1131, 2008.

# RESPIRATORY AND PULMONARY PHYSIOLOGY

*Matthew D. Coleman, MD*

## 1. What is the functional residual capacity? What factors affect it?

The functional residual capacity (FRC) is the volume in the lungs at the end of passive expiration. It is determined by opposing forces of the expanding chest wall and the elastic recoil of the lung. A normal FRC = 1.7 to 3.5 L. FRC is increased by:

- Body size (FRC increases with height)
- Age (FRC increases slightly with age)
- Certain lung diseases, including asthma and chronic obstructive pulmonary disease (COPD).

FRC is decreased by:

- Sex (women have a 10% decrease in FRC when compared to men)
- Diaphragmatic muscle tone (individuals with paralyzed diaphragms have less FRC when compared to normal individuals)
- Posture (FRC greatest standing > sitting > prone > lateral > supine)
- Certain lung diseases in which elastic recoil is diminished (e.g., interstitial lung disease, thoracic burns, and kyphoscoliosis)
- Increased abdominal pressure (e.g., obesity, ascites)

## 2. What is closing capacity? What factors affect the closing capacity? What is the relationship between closing capacity and functional residual capacity?

Closing capacity is the point during expiration when small airways begin to close. In young individuals with average body mass index, closing capacity is approximately half the FRC when upright and approximately two thirds of the FRC when supine.

Closing capacity increases with age and is equal to FRC in the supine individual at approximately 44 years and in the upright individual at approximately 66 years. The FRC depends on position; the closing capacity is independent of position. Closing capacity increases with increasing intraabdominal pressure, age, decreased pulmonary blood flow, and pulmonary parenchymal disease, which decreases compliance.

## 3. What muscles are responsible for inspiration and expiration?

The respiratory muscles include the diaphragm, internal and external intercostals, abdominal musculature, cervical strap muscles, sternocleidomastoid muscle, and large back and intervertebral muscles of the shoulder girdle. During normal breathing inspiration requires work, whereas expiration is passive. The diaphragm, scalene muscles, and external intercostal muscles provide most of the work during normal breathing. However, as the work of breathing increases, abdominal musculature and internal intercostal muscles become active during expiration, and the scalene and sternocleidomastoid muscles become increasingly important for inspiration.

## 4. What is the physiologic work of breathing?

The physiologic work of breathing involves the work of overcoming the elastic recoil of the lung (compliance and tissue resistance work) and the resistance to gas flow. The elastic recoil is altered in certain pathologic states, including pulmonary edema, pulmonary fibrosis, thoracic burns, and COPD. The resistance to gas flow is increased dramatically during labored breathing. In addition to the physiologic work of breathing, a patient on a ventilator must also overcome the resistance of the endotracheal tube.

**5. Discuss the factors that affect the resistance to gas flow. What is laminar and turbulent gas flow?**

The resistance to flow can be separated into the properties of the tube and the properties of the gas. At low flow, or laminar flow (nonobstructed breathing), the viscosity is the major property of the gas that affects flow. Clearly the major determining factor is the radius of the tube. This can be shown by the Hagen-Poiseuille relationship:

$$R = (8 \times L \times \mu) / (\pi \times r^4)$$

where R is resistance, L is the length of the tube,  $\mu$  is the viscosity, and r is the radius of the tube. At higher flow rate (in obstructed airways and heavy breathing), the flow is turbulent. At these flows the major determinants of resistance to flow are the density of the gas ( $\rho$ ) and the radius of the tube, r.

$$R \propto \rho / r^5$$

**6. Suppose a patient has an indwelling 7-mm endotracheal tube and cannot be weaned because of the increased work of breathing. What would be of greater benefit, cutting off 4 cm of endotracheal tube or replacing the tube with one of greater internal diameter?**

According to the Hagen-Poiseuille relationship discussed previously, if the radius is halved, the resistance within the tube increases to sixteenfold; but if the length of the tube is doubled, the resistance is only doubled. Cutting the length of the tube minimally affects resistance, but increasing the tube diameter dramatically decreases resistance. Therefore, to reduce the work of breathing the endotracheal tube should be changed to a larger size.

**7. Why might helium be of benefit to a stridorous patient?**

When flow is turbulent, as is the case in a stridorous patient, driving pressure is mostly related to gas density. Use of low-density gas mixtures containing helium and oxygen lowers the driving pressure needed to move gas in and out of the area, decreasing the work of breathing.

**8. Discuss dynamic and static compliance.**

Compliance describes the elastic properties of the lung. It is a measure of the change in volume of the lung when pressure is applied. The lung is an elastic body that exhibits elastic hysteresis. When the lung is rapidly inflated and held at a given volume, the pressure peaks and then exponentially falls to a plateau pressure. The volume change of the lung per the initial peak pressure change is the dynamic compliance. The volume change per the plateau pressure represents the static compliance of the lung.

**9. How does surface tension affect the forces in the small airways and alveoli?**

Laplace's law describes the relationship between pressure (P), tension (T), and the radius (R) of a bubble and can be applied to the alveoli.

$$P = 2T/R$$

As the radius decreases, the pressure increases. In a lung without surfactant present, as the alveoli decrease in size, the pressure is higher in small alveoli, causing gas to move from the small to larger airways, collapsing in the process. Surfactant, a phospholipid substance produced in the lung by type II alveolar epithelium, reduces the surface tension of the small airways, thus decreasing the pressure as the airways decrease in size. This important substance helps keep the small airways open during expiration.

## 10. Review the different zones (of West) in the lung with regard to perfusion and ventilation.

West described three areas of perfusion in an upright lung, and a fourth was later added. Beginning at the apices, they are:

- Zone 1: Alveolar pressure ( $P_{Alv}$ ) exceeds pulmonary artery pressure ( $P_{pa}$ ) and pulmonary venous pressure ( $P_{pv}$ ), leading to ventilation without perfusion (alveolar dead space) ( $P_{Alv} > P_{pa} > P_{pv}$ ).
- Zone 2: Pulmonary arterial pressure exceeds alveolar pressure, but alveolar pressure still exceeds venous pressure ( $P_{pa} > P_{Alv} > P_{pv}$ ). Blood flow in zone 2 is determined by arterial-alveolar pressure difference.
- Zone 3: Pulmonary venous pressure exceeds alveolar pressure, and flow is determined by the arterial-venous pressure difference ( $P_{pa} > P_{pv} > P_{Alv}$ ).
- Zone 4: Interstitial pressure ( $P_{interstitium}$ ) is greater than venous and alveolar pressures; thus flow is determined by the arterial-interstitial pressure difference ( $P_{pa} > P_{interstitium} > P_{pv} > P_{Alv}$ ). Zone 4 should be minimal in a healthy patient.

A change from upright to supine position increases pulmonary blood volume by 25% to 30%, thus increasing the size of larger-numbered West zones.

## 11. What are the alveolar gas equation and the normal alveolar pressure at sea level on room air?

The alveolar gas equation is used to calculate the alveolar oxygen partial pressure:

$$P_AO_2 = FiO_2 (P_B - P_{H_2O}) - P_aCO_2/RQ$$

where  $P_AO_2$  is the alveolar oxygen partial pressure,  $FiO_2$  is the fraction of inspired oxygen,  $P_B$  is the barometric pressure,  $P_{H_2O}$  is the partial pressure of water (47 mm Hg),  $P_aCO_2$  is the partial pressure of carbon dioxide, and RQ is the respiratory quotient, dependent on metabolic activity and diet and is considered to be about 0.825. At sea level the alveolar partial pressure ( $P_AO_2$ ) is:

$$P_AO_2 = 0.21(760 - 47) - 40/0.8 = 99.7$$

Knowing the  $P_AO_2$  allows us to calculate the alveolar-arterial  $O_2$  gradient (A-a gradient). Furthermore, by understanding the alveolar gas equation we can see how hypoventilation (resulting in hypercapnia) lowers  $P_aO_2$ , and therefore  $P_AO_2$ .

## 12. What is the A-a gradient and what is a normal value for this gradient?

The alveolar-arterial  $O_2$  gradient is known as the A-a gradient. It is the difference in partial pressure of  $O_2$  in the alveolus ( $P_AO_2$ ), calculated by the alveolar gas equation, and the partial pressure of  $O_2$  measured in the blood ( $P_aO_2$ ):

$$\text{A-a gradient} = P_AO_2 - P_aO_2$$

A normal A-a gradient is estimated as follows:

$$\text{A-a gradient} = (\text{age}/4) + 4.$$

## 13. What is the practical significance of estimating A-a gradient?

The A-a gradient, together with the  $P_aO_2$  and  $P_aCO_2$ , allows systematic evaluation of hypoxemia, leading to a concise differential diagnosis. As previously stated, the ABG provides an initial assessment of oxygenation by measuring the  $P_aO_2$ . The A-a gradient is an extension of this, for by calculating the difference between the  $P_AO_2$  and the  $P_aO_2$  we are assessing the efficiency of gas exchange at the alveolar-capillary membrane.

## 14. What are the causes of hypoxemia?

- **Low inspired oxygen concentration ( $FiO_2$ ):** To prevent delivery of hypoxic gas mixtures during an anesthetic, oxygen alarms are present on the anesthesia machine.

- **Hypoventilation:** Patients under general anesthesia may be incapable of maintaining an adequate minute ventilation because of muscle relaxants or the ventilatory depressant effects of anesthetic agents. Hypoventilation is a common problem after surgery.
- **Shunt:** Sepsis, liver failure, arteriovenous malformations, pulmonary emboli, and right-to-left cardiac shunts may create sufficient shunting to result in hypoxemia. Since shunted blood is not exposed to alveoli, hypoxemia caused by a shunt cannot be overcome by increasing  $\text{FiO}_2$ .
- **Ventilation-perfusion (V/Q) mismatch:** Ventilation and perfusion of the alveoli in the lung ideally have close to a one-to-one relationship, promoting efficient oxygen exchange between alveoli and blood. When alveolar ventilation and perfusion to the lungs are unequal (V/Q mismatching), hypoxemia results. Causes of V/Q mismatching include atelectasis, lateral decubitus positioning, bronchial intubation, bronchospasm, pneumonia, mucous plugging, pulmonary contusion, and adult respiratory distress syndrome. Hypoxemia caused by V/Q mismatching can usually be overcome by increasing  $\text{FiO}_2$ .
- **Diffusion defects:** Efficient  $\text{O}_2$  exchange depends on a healthy interface between the alveoli and the bloodstream. Advanced pulmonary disease and pulmonary edema may have associated diffusion impairment.

## KEY POINTS: CAUSES OF HYPOXEMIA



1. Low inspired oxygen tension
2. Alveolar hypoventilation
3. Right-Left shunting
4. V/Q mismatch
5. Diffusion abnormality

### 15. What are the A-a gradients for the different causes of hypoxemia:

- Low fractional concentration of inspired  $\text{O}_2$ : normal A-a gradient
- Alveolar hypoventilation: normal A-a gradient
- Right-to-left shunting: elevated A-a gradient
- Ventilation/perfusion mismatch: elevated A-a gradient
- Diffusion abnormality: elevated A-a gradient

### 16. Discuss V/Q mismatch. How can general anesthesia worsen V/Q mismatch?

V/Q mismatch ranges from shunt at one end of the spectrum to dead space at the other end. In the normal individual alveolar ventilation (V) and perfusion (Q) vary throughout the lung anatomy. In the ideal situation V and Q are equal, and  $V/Q = 1$ . In shunted lung the perfusion is greater than the ventilation, creating areas of lung where blood flow is high but little gas exchange occurs. In dead-space lung, ventilation is far greater than perfusion, creating areas of lung where gas is delivered but little blood flow and gas exchange occur. Both situations can cause hypoxemia. In the case of dead space, increasing the  $\text{FiO}_2$  will potentially increase the hemoglobin oxygen saturation, whereas in cases of shunt it will not. In many pathologic situations both extremes coexist within the lung.

Under general anesthesia FRC is reduced by approximately 400 ml in an adult. The supine position decreases FRC another 800 ml. A large enough decrease in FRC may bring end-expiratory volumes or even the entire tidal volume to levels below the closing volume (the volume at which small airways close). When small airways begin to close, atelectasis and low V/Q areas develop.

**17. Define anatomic, alveolar, and physiologic dead space.**

Physiologic dead space ( $V_D$ ) is the sum of anatomic and alveolar dead space. Anatomic dead space is the volume of lung that does not exchange gas. This includes the nose, pharynx, trachea, and bronchi. This is about 2 ml/kg in the spontaneously breathing individual and is the majority of physiologic dead space. Endotracheal intubation will decrease the total anatomic dead space. Alveolar dead space is the volume of gas that reaches the alveoli but does not take part in gas exchange because the alveoli are not perfused. In healthy patients alveolar dead space is negligible.

**18. How is  $V_D/V_T$  calculated?**

$V_D/V_T$  is the ratio of the physiologic dead space to the tidal volume ( $V_T$ ), is usually about 33%, and is determined by the following formula:

$$V_D/V_T = [(alveolar\ PCO_2 - expired\ PCO_2)]/alveolar\ PCO_2$$

Alveolar  $PCO_2$  is calculated using the alveolar gas equation, and expired  $PCO_2$  is the average  $PCO_2$  in an expired gas sample (not the same as end-tidal  $PCO_2$ ).

**19. Define absolute shunt. How is the shunt fraction calculated?**

Absolute shunt is defined as blood that reaches the arterial system without passing through ventilated regions of the lung. The fraction of cardiac output that passes through a shunt is determined by the following equation:

$$Q_s/Q_t = (CiO_2 - CaO_2)/(CiO_2 - CvO_2)$$

where  $Q_s$  is the physiologic shunt blood flow per minute,  $Q_t$  is the cardiac output per minute,  $CiO_2$  is the ideal arterial oxygen concentration when  $V/Q = 1$ ,  $CaO_2$  is arterial oxygen content, and  $CvO_2$  is mixed venous oxygen content. It is estimated that 2% to 5% of cardiac output is normally shunted through postpulmonary shunts, thus accounting for the normal alveolar-arterial oxygen gradient (A-a gradient). Postpulmonary shunts include the thebesian, bronchial, mediastinal, and pleural veins.

**20. What is hypoxic pulmonary vasoconstriction?**

Hypoxic pulmonary vasoconstriction (HPV) is a local response of pulmonary arterial smooth muscle that decreases blood flow in the presence of low alveolar oxygen pressure, helping to maintain normal  $V/Q$  relationships by diverting blood from under ventilated areas. HPV is inhibited by volatile anesthetics and vasodilators but is not affected by intravenous anesthesia.

**21. Calculate arterial and venous oxygen content ( $CaO_2$  and  $CvO_2$ ).**

Oxygen content (milliliters of  $O_2$ /dl) is calculated by summing the oxygen bound to hemoglobin (Hgb) and the dissolved oxygen of blood:

$$\text{Oxygen content} = 1.34 \times [\text{Hgb}] \times \text{SaO}_2 + (\text{PaO}_2 \times 0.003)$$

where 1.34 is the  $O_2$  content per gram hemoglobin,  $\text{SaO}_2$  is the hemoglobin saturation,  $[\text{Hgb}]$  is the hemoglobin concentration, and  $\text{PaO}_2$  is the arterial oxygen concentration.

If  $[\text{Hgb}] = 15$  g/dl, arterial saturation = 96%, and  $\text{PaO}_2 = 90$  mm Hg, mixed venous saturation = 75%, and  $\text{PvO}_2 = 40$  mm Hg, then:

$$CaO_2 = (1.34\text{ ml } O_2/\text{g Hgb} \times 15\text{ g Hgb/dl} \times 0.96) + (90 \times 0.003) = 19.6\text{ ml } O_2/\text{dl}$$

and

$$CvO_2 = (1.34\text{ ml } O_2/\text{g Hgb} \times 15\text{ g Hgb/dl} \times 0.75) + (40 \times 0.003) = 15.2\text{ ml } O_2/\text{dl}$$

**22. How is  $CO_2$  transported in the blood?**

$CO_2$  exists in three forms in blood: dissolved  $CO_2$  (7%), bicarbonate ions ( $HCO_3^-$ ) (70%), and combined with hemoglobin (23%).

**23. How is  $PCO_2$  related to alveolar ventilation?**

The partial pressure of  $CO_2$  ( $PCO_2$ ) is inversely related to the alveolar ventilation and is described by the equation:

$$PCO_2 = (V_{CO_2}/V_{\text{alveolar}})$$

where  $V_{CO_2}$  is total  $CO_2$  production and  $V_{\text{alveolar}}$  is the alveolar ventilation (minute ventilation less the dead space ventilation). In general, minute ventilation and  $PCO_2$  are inversely related.

**KEY POINTS: USEFUL PULMONARY EQUATIONS**

1. Alveolar gas partial pressure:  $P_{AO_2} = FiO_2 (P_B - P_{H_2O}) - P_aCO_2/Q$
2. Oxygen content of blood:  $C_aO_2 = 1.34 \times [Hgb] \times SaO_2 + (PaO_2 \times 0.003)$
3. Resistance of laminar flow through a tube:  $R = (8 \times L \times \mu)/(\pi \times r^4)$
4. Resistance of turbulent flow through a tube:  $R \propto \rho/r^5$
5. Calculation of shunt fraction:  $Q_s/Q_t = (CiO_2 - CaO_2)/(CiO_2 - CvO_2)$

**24. What factors alter oxygen consumption?**

Factors increasing oxygen consumption include hyperthermia (including malignant hyperthermia), hypothermia with shivering, hyperthyroidism, pregnancy, sepsis, burns, pain, and pheochromocytoma. Factors decreasing oxygen consumption include hypothermia without shivering, hypothyroidism, neuromuscular blockade, and general anesthesia.

**25. Where is the respiration center located in the brain?**

The respiratory center is located bilaterally in the medulla and pons. Three major centers contribute to respiratory regulation. The dorsal respiratory center is mainly responsible for inspiration, the ventral respiratory center is responsible for both expiration and inspiration, and the pneumotaxic center helps control the breathing rate and pattern. The dorsal respiratory center is the most important. It is located within the nucleus solitarius where vagal and glossopharyngeal nerve fibers terminate and carry signals from peripheral chemoreceptors and baroreceptors (including the carotid and aortic bodies) and several lung receptors. A chemosensitive area also exists in the brainstem just beneath the ventral respiratory center. This area responds to changes in cerebrospinal fluid (CSF) pH, sending corresponding signals to the respiratory centers. Anesthetics cause repression of the respiratory centers of the brainstem.

**26. How do carbon dioxide and oxygen act to stimulate and repress breathing?**

Carbon dioxide (indirectly) or hydrogen ions (directly) work on the chemosensitive area in the brainstem. Oxygen interacts with the peripheral chemoreceptors located in the carotid and aortic bodies. During hypercapnic and hypoxic states the brainstem is stimulated to increase minute ventilation, whereas the opposite is true for hypocapnia and normoxia. Carbon dioxide is by far more influential in regulating respiration than is oxygen.

**27. What are the causes of hypercarbia?**

- **Hypoventilation:** Decreasing the minute ventilation ultimately decreases alveolar ventilation, increasing  $PCO_2$ . Some common causes of hypoventilation include muscle paralysis, inadequate mechanical ventilation, inhalational anesthetics, and opiates.
- **Increased  $CO_2$  production:** Although  $CO_2$  production is assumed to be constant, there are certain situations in which metabolism and  $CO_2$  production are increased.



Malignant hyperthermia, fever, thyrotoxicosis, and other hypercatabolic states are some examples.

- **Iatrogenic:** The anesthesiologist can administer certain drugs to increase  $\text{CO}_2$ . The most common is sodium bicarbonate, which is metabolized by the enzyme carbonic anhydrase to form  $\text{CO}_2$ .  $\text{CO}_2$  is absorbed into the bloodstream during laparoscopic procedures. Rarely  $\text{CO}_2$ -enriched gases can be administered. Carbon dioxide insufflation for laparoscopy is a cause. Exhaustion of the  $\text{CO}_2$  absorbent in the anesthesia breathing circuit can result in rebreathing of exhaled gases and may also result in hypercarbia.

## 28. What are the signs and symptoms of hypercarbia?

Hypercarbia acts as a direct vasodilator in the systemic circulation and as a direct vasoconstrictor in the pulmonary circulation. It is also a direct cardiac depressant. Cerebral blood flow increases in proportion to arterial  $\text{CO}_2$ . An increase in catecholamines is responsible for most of the clinical signs and symptoms of hypercarbia. Hypercarbia causes an increase in heart rate, myocardial contractility, and respiratory rate along with a decrease in systemic vascular resistance. Higher systolic blood pressure, wider pulse pressure, tachycardia, greater cardiac output, higher pulmonary pressures, and tachypnea are common clinical findings. In awake patients symptoms include headache, anxiety/restlessness, and even hallucinations. Extreme hypercapnia produces hypoxemia as  $\text{CO}_2$  displaces  $\text{O}_2$  in alveoli.

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# BLOOD GAS AND ACID-BASE ANALYSIS

Matthew D. Coleman, MD, and Steven T. Morozowich, DO, FASE

## 1. What are the normal arterial blood gas values in a healthy patient breathing room air at sea level?

See Table 3-1.

TABLE 3-1. ARTERIAL BLOOD GAS VALUES AT SEA LEVEL

pH	7.36–7.44
PaCO <sub>2</sub>	33–44 mm Hg
PaO <sub>2</sub>	75–105 mm Hg
HCO <sub>3</sub>	20–26 mmol/L
Base deficit	+3 to –3 mmol/L
SaO <sub>2</sub>	95%–97%

## 2. What information does arterial blood gas provide about the patient?

Arterial blood gas (ABG) provides an assessment of the following:

- **Oxygenation** (PaO<sub>2</sub>). The PaO<sub>2</sub> is the amount of oxygen dissolved in the blood and therefore provides initial information on the efficiency of oxygenation.
- **Ventilation** (PaCO<sub>2</sub>). The adequacy of ventilation is inversely proportional to the PaCO<sub>2</sub> so that, when ventilation increases, PaCO<sub>2</sub> decreases, and when ventilation decreases, PaCO<sub>2</sub> increases.
- **Acid-base status** (pH, HCO<sub>3</sub><sup>-</sup>, and base deficit [BD]). A plasma pH of >7.4 indicates alkalemia, and a pH of <7.35 indicates acidemia. Despite a normal pH, an underlying acidosis or alkalosis may still be present.

Oxygenation and ventilation were discussed in Chapter 2 and acid-base status will be the area of focus for this chapter.

## 3. How is the regulation of acid-base balance traditionally described?

Acid-base balance is traditionally explained using the Henderson-Hasselbalch equation, which states that changes in HCO<sub>3</sub><sup>-</sup> and PaCO<sub>2</sub> determine pH as follows:

$$\text{pH} = \text{pK} + \log\left[\frac{\text{HCO}_3^-}{(0.03 \times \text{PaCO}_2)}\right]$$

To prevent a change in pH, any increase or decrease in the PaCO<sub>2</sub> should be accompanied by a compensatory increase or decrease in the HCO<sub>3</sub><sup>-</sup>. The importance of other physiologic nonbicarbonate buffers was later recognized and partly integrated into the BD and the corrected anion gap, both of which aid in interpreting complex acid-base disorders.

## KEY POINTS: MAJOR CAUSES OF AN ANION GAP METABOLIC ACIDOSIS



Elevated anion gap metabolic acidosis is caused by accumulation of unmeasured anions:

- Lactic acid
- Ketones
- Toxins (ethanol, methanol, salicylates, ethylene glycol, propylene glycol)
- Uremia

#### 4. What is the physiochemical approach (Stewart model) for the analysis of acid-base balance?

In 1981 Stewart proposed a conceptually different model for analyzing acid-base disorders. His method used two important principles of solution chemistry: the conservation of mass, and electroneutrality. He described three independent variables that determine the pH in the extracellular fluid. These variables are the strong ion difference (SID), the  $\text{PaCO}_2$ , and the concentration of weak acids ( $A_{\text{TOT}}$ ). The SID is calculated as follows with the normal value given:

$$\text{SID} = ([\text{Na}^+] + [\text{K}^+] + [\text{Ca}^{2+}] + [\text{Mg}^{2+}]) - ([\text{Cl}^-] + [\text{other anions}]) = 40 - 42 \text{ mEq/L}$$

The concentration of other anions consists of proteins and weak acids. The primary weak acids in the plasma are proteins (primarily albumin), phosphate, and sulfate. In pathologic states other weak acids might include lactate, ketones, or toxins. As anions accumulate, the SID decreases, resulting in an acidosis. If the balance shifts to a predominance of cations, an alkalosis develops. Stewart developed several equations to show that these parameters were independent variables and showed that  $\text{HCO}_3^-$  and pH were dependent on the three independent variables, contrary to the Henderson-Hasselbalch and standard base excess approaches. This model has been most useful in interpreting complex acid-base disorders in patients with mixed acid-base disorders and disorders that were not observable with conventional acid-base analysis such as hypoalbuminemia and hyperchloremic metabolic acidosis.

#### 5. What are the common acid-base disorders and their compensation?

See Table 3-2.

TABLE 3-2. MAJOR ACID-BASE DISORDERS AND COMPENSATORY MECHANISMS\*

Primary Disorder	Primary Disturbance	Primary Compensation
Respiratory acidosis	↑ $\text{PaCO}_2$	↑ $\text{HCO}_3^-$
Respiratory alkalosis	↓ $\text{PaCO}_2$	↓ $\text{HCO}_3^-$
Metabolic acidosis	↓ $\text{HCO}_3^-$	↓ $\text{PaCO}_2$
Metabolic alkalosis	↑ $\text{HCO}_3^-$	↑ $\text{PaCO}_2$

\*Primary compensation for metabolic disorders is achieved rapidly through respiratory control of  $\text{CO}_2$ , whereas primary compensation for respiratory disorders is achieved more slowly as the kidneys excrete or absorb acid and bicarbonate. Mixed acid-base disorders are common.

## 6. How do you calculate the degree of compensation?

See Table 3-3.

TABLE 3-3. CALCULATING THE DEGREE OF COMPENSATION\*

Primary Disorder	Rule
Respiratory acidosis (acute)	$\text{HCO}_3^-$ increases $0.1 \times (\text{PaCO}_2 - 40)$ pH decreases $0.008 \times (\text{PaCO}_2 - 40)$
Respiratory acidosis (chronic)	$\text{HCO}_3^-$ increases $0.4 \times (\text{PaCO}_2 - 40)$
Respiratory alkalosis (acute)	$\text{HCO}_3^-$ decreases $0.2 \times (40 - \text{PaCO}_2)$ pH increases $0.008 \times (40 - \text{PaCO}_2)$
Respiratory alkalosis (chronic)	$\text{HCO}_3^-$ decreases $0.4 \times (40 - \text{PaCO}_2)$
Metabolic acidosis	$\text{PaCO}_2$ decreases 1 to $1.5 \times (24 - \text{HCO}_3^-)$
Metabolic alkalosis	$\text{PaCO}_2$ increases $0.25$ to $1 \times (\text{HCO}_3^- - 24)$

\*Compensatory mechanisms never overcorrect for an acid-base disturbance; when ABG analysis reveals apparent overcorrection, the presence of a mixed disorder should be suspected. Data from Schrier RW: *Renal and electrolyte disorders*, ed 3, Boston, 1986, Little, Brown.

## 7. What are the common causes of respiratory acid-base disorders?

- **Respiratory alkalosis:** Sepsis, hypoxemia, anxiety, pain, and central nervous system lesions
- **Respiratory acidosis:** Drugs (residual anesthetics, residual neuromuscular blockade, benzodiazepines, opioids), asthma, emphysema, obesity-hypoventilation syndromes, central nervous system lesions (infection, stroke), and neuromuscular disorders

## 8. What are the major buffering systems of the body?

Bicarbonate, albumin, intracellular proteins, and phosphate are the major buffering systems. The extracellular bicarbonate system is the fastest to respond to pH change but has less total capacity than the intracellular systems, which account for 60% to 70% of the chemical buffering of the body. Hydrogen ions are in dynamic equilibrium with all buffering systems of the body.  $\text{CO}_2$  molecules also readily cross cell membranes and keep both intracellular and extracellular buffering systems in dynamic equilibrium. In addition,  $\text{CO}_2$  has the advantage of excretion through ventilation.

## 9. What organs play a major role in acid-base balance?

- The lungs are the primary organ involved in rapid acid-base regulation. Carbon dioxide produced in the periphery is transported to the lung, where the low carbon dioxide tension promotes conversion of bicarbonate to carbon dioxide, which is then eliminated. The respiratory regulatory system can increase and decrease minute ventilation to compensate for metabolic acid-base disturbances.
- The kidneys act to control acid-base balance by eliminating fixed acids and to control the elimination of electrolytes, bicarbonate, ammonia, and water.

- The liver is involved in multiple reactions that result in the production or metabolism of acids.
- The gastrointestinal tract secretes acidic solutions in the stomach, and absorbs water and other electrolytes in the small and large intestines. This can have a profound effect in acid-base balance.

#### 10. What is meant by pH?

pH is the negative logarithm of the hydrogen ion concentration ( $[H^+]$ ). pH is a convenient descriptor for *power of hydrogen*. Normally the  $[H^+]$  in extracellular fluid is 40 nmol/L, a very small number. By taking the negative log of this value we obtain a pH of 7.4, a much simpler way to describe  $[H^+]$ . The pH of a solution is determined by a pH electrode that measures the  $[H^+]$ .

#### 11. Why is pH important?

pH is important because hydrogen ions react highly with cellular proteins, altering their function. Avoiding acidemia and alkalemia by tightly regulating hydrogen ions is essential for normal cellular function. Deviations from normal pH suggest that normal physiologic processes are in disorder and the causes should be determined and treated.

#### 12. List the major consequences of acidemia.

Severe acidemia is defined as blood pH  $<7.20$  and is associated with the following major effects:

- Impairment of cardiac contractility, cardiac output, and the response to catecholamines
- Susceptibility to recurrent arrhythmias and lowering the threshold for ventricular fibrillation
- Arteriolar vasodilation resulting in hypotension
- Vasoconstriction of the pulmonary vasculature, leading to increased pulmonary vascular resistance
- Hyperventilation (a compensatory response)
- Confusion, obtundation, and coma
- Insulin resistance
- Inhibition of glycolysis and adenosine triphosphate synthesis
- Hyperkalemia as potassium ions are shifted extracellularly

#### 13. List the major consequences of alkalemia.

Severe alkalemia is defined as blood pH  $>7.60$  and is associated with the following major effects:

- Increased cardiac contractility until pH  $>7.7$ , when a decrease is seen
- Refractory ventricular arrhythmias
- Coronary artery spasm/vasoconstriction
- Vasodilation of the pulmonary vasculature, leading to decreased pulmonary vascular resistance
- Hypoventilation (which can frustrate efforts to wean patients from mechanical ventilation)
- Cerebral vasoconstriction

- Neurologic manifestations such as headache, lethargy, delirium, stupor, tetany, and seizures
- Hypokalemia, hypocalcemia, hypomagnesemia, and hypophosphatemia
- Stimulation of anaerobic glycolysis and lactate production

**14. Is the  $\text{HCO}_3^-$  value on the arterial blood gas the same as the  $\text{CO}_2$  value on the chemistry panel?**

No. The  $\text{HCO}_3^-$  is a calculated value, whereas the  $\text{CO}_2$  is a measured value. Because the  $\text{CO}_2$  is measured, it is thought to be a more accurate determination of  $\text{HCO}_3^-$ . The ABG  $\text{HCO}_3^-$  is calculated using the Henderson-Hasselbalch equation and the measured values of pH and  $\text{PaCO}_2$ . In contrast, a chemistry panel reports a measured serum carbon dioxide content ( $\text{CO}_2$ ), which is the sum of the measured bicarbonate ( $\text{HCO}_3^-$ ) and carbonic acid ( $\text{H}_2\text{CO}_3$ ). The  $\text{CO}_2$  is viewed as an accurate determination of  $\text{HCO}_3^-$  because the  $\text{HCO}_3^-$  concentration in blood is about 20 times greater than the  $\text{H}_2\text{CO}_3$  concentration; thus  $\text{H}_2\text{CO}_3$  is only a minor contributor to the total measured  $\text{CO}_2$ .

**15. What is the base deficit? How is it determined?**

The BD (or base excess) is the amount of base (or acid) needed to titrate a serum pH back to normal at  $37^\circ\text{C}$  while the  $\text{PaCO}_2$  is held constant at 40 mm Hg. The BD represents only the metabolic component of an acid-base disorder. The ABG analyzer derives the BD from a nomogram based on the measurements of pH,  $\text{HCO}_3^-$ , and the nonbicarbonate buffer hemoglobin. Although the BD is determined in part by the nonbicarbonate buffer hemoglobin, it is criticized because it is derived from a nomogram and assumes normal values for other important nonbicarbonate buffers such as albumin. Thus in a hypoalbuminemic patient the BD should be used with caution since it may conceal an underlying metabolic acidosis.

**16. What is the anion gap?**

The anion gap (AG) estimates the presence of unmeasured anions. Excess inorganic and organic anions that are not readily measured by standard assays are termed *unmeasured anions*. The AG is a tool used to further classify a metabolic acidosis as an AG metabolic acidosis (elevated AG) or a non-AG metabolic acidosis (normal AG). This distinction narrows the differential diagnosis. The AG is the difference between the major serum cations and anions that are routinely measured:

$$\text{AG} = \text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$$

A normal value is  $12 \text{ mEq/L} \pm 4 \text{ mEq/L}$ . When unmeasured acid anions are present, they are buffered by  $\text{HCO}_3^-$ , thereby decreasing the  $\text{HCO}_3^-$  concentration. According to the previous equation, this decrease in  $\text{HCO}_3^-$  will increase the AG. Keep in mind that hypoalbuminemia has an alkalinizing effect that lowers the AG, which may mask an underlying metabolic acidosis caused by unmeasured anions. This pitfall can be avoided by correcting the AG when evaluating a metabolic acidosis in a hypoalbuminemic patient:

$$\text{Corrected AG} = \text{observed AG} + 2.5 \times (\text{normal albumin} - \text{observed albumin})$$

**KEY POINTS: MAJOR CAUSES OF A NONANION GAP METABOLIC ACIDOSIS**

Nonanion gap metabolic acidosis results from loss of  $\text{Na}^+$  and  $\text{K}^+$  or accumulation of  $\text{Cl}^-$ . The result of these processes is a decrease in  $\text{HCO}_3^-$ :

- Iatrogenic administration of hyperchloremic solutions (hyperchloremic metabolic acidosis)
- Alkaline gastrointestinal losses
- Renal tubular acidosis
- Ureteric diversion through ileal conduit
- Endocrine abnormalities

**17. List the common causes of a metabolic alkalosis.**

Metabolic alkalosis is commonly caused by vomiting, volume contraction (diuretics, dehydration), alkali administration, and endocrine disorders.

**18. List the common causes of elevated and nonelevated anion gap metabolic acidosis.**

- Nonelevated AG metabolic acidosis is caused by iatrogenic administration of hyperchloremic solutions (hyperchloremic metabolic acidosis), alkaline gastrointestinal losses, renal tubular acidosis (RTA), or ureteric diversion through ileal conduit. Excess administration of normal saline is a cause of hyperchloremic metabolic acidosis.
- Elevated AG metabolic acidosis is caused by accumulation of lactic acid or ketones, poisoning from toxins (e.g., ethanol, methanol, salicylates, ethylene glycol, propylene glycol) or uremia.

**19. Describe a stepwise approach to acid-base interpretation.**

- Check the pH to determine acidemia or alkalemia.
- If the patient is breathing spontaneously, use the following rules:
  - If the  $\text{PCO}_2$  is increased and the pH is  $<7.35$ , the primary disorder is most likely a respiratory acidosis.
  - If the  $\text{PCO}_2$  is decreased and the pH  $>7.40$ , the primary disorder is most likely a respiratory alkalosis.
  - If the primary disorder is respiratory, determine if it is acute or chronic.
  - If the  $\text{PCO}_2$  is increased and the pH is  $>7.40$ , the primary disorder is most likely a metabolic alkalosis with respiratory compensation.
  - If the  $\text{PCO}_2$  is decreased and the pH  $<7.35$ , the primary disorder is most likely a metabolic acidosis with respiratory compensation.
- Metabolic disorders can also be observed by analyzing the base excess or BD.
  - If there is a metabolic acidosis, calculate the AG and determine if the acidosis is a non-AG or AG acidosis, remembering to correct for hypoalbuminemia.
  - If the patient is mechanically ventilated or if the acid-base disorder doesn't seem to make sense, check electrolytes, albumin, and consider calculating the SID. Also consider the clinical context of the acid-base disorder (e.g., iatrogenic fluid administration, massive blood resuscitation, renal failure, liver failure, diarrhea, vomiting, gastric suctioning, toxin ingestion). This may require further testing, including measuring urine electrolytes, serum, and urine osmolality, and identifying ingested toxins.

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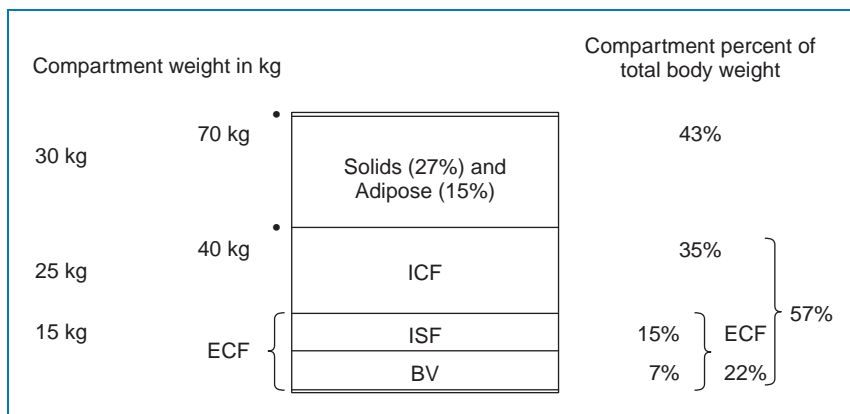
# FLUIDS, VOLUME REGULATION, AND VOLUME DISTURBANCES

James Duke, MD, MBA

## 1. Describe the functionally distinct compartments of body water, using a 70-kg patient for illustration.

Accurate estimations are difficult because ordinarily ideal body weight (IBW) is used as a basis for calculation. Obesity is rampant in our society, making accurate estimations difficult.

Figure 4-1 estimates body water compartments in a patient with an IBW of 70 kg.



**Figure 4-1.** Body water compartments in a patient with an ideal body weight of 70 kg. *BV*, Blood volume; *ECF*, extracellular fluid; *ICF*, intracellular fluid; *ISF*, interstitial fluid.

## 2. Describe the dynamics of fluid distribution between the intravascular and interstitial compartments.

The intravascular and interstitial fluid spaces compose the extracellular fluid and are in dynamic equilibrium, governed by hydrostatic and oncotic forces. Under normal circumstances the capillary hydrostatic pressure produces an outward movement of fluid, whereas the capillary oncotic pressure results in resorption. The sum of the forces leads to an egress of fluids from arterioles; about 90% of the fluid returns into the venules. The remainder of the fluid is subsequently returned to the circulation via the lymphatic system.

## 3. How are body water and tonicity regulated?

Antidiuretic hormone (ADH) is a primary mechanism; it circulates unbound in plasma, has a half-life of roughly 20 minutes, and increases production of cyclic adenosine monophosphate in the distal collecting tubules of the kidney. Tubular permeability to water increases, resulting in conservation of water and sodium and production of concentrated urine. Stimuli for the release of ADH include the following:

- Hypothalamic osmoreceptors have an osmotic threshold of about 289 mOsm/kg. Above this level ADH release is stimulated.

- Hypothalamic thirst center neurons regulate conscious desire for water and are activated by an increase in plasma sodium of 2 mEq/L, an increase in plasma osmolality of 4 mOsm/L, and loss of potassium from thirst center neurons and angiotensin II.
- Aortic baroreceptors and left atrial stretch receptors respond to volume depletion and stimulate hypothalamic neurons.

#### 4. Discuss the synthesis of antidiuretic hormone.

ADH, or vasopressin, is synthesized in the supraoptic and paraventricular nuclei of the hypothalamus. It is transported attached to carrier proteins down the pituitary stalk in secretory granules into the posterior pituitary gland (neurohypophysis). There it is stored and released into the capillaries of the neurohypophysis in response to stimuli from the hypothalamus. ADH-producing neurons receive efferent innervation from osmoreceptors and baroreceptors.

#### 5. List conditions that stimulate and inhibit release of antidiuretic hormone.

See Table 4-1.

**TABLE 4-1. CONDITIONS THAT STIMULATE AND INHIBIT RELEASE OF ADRENOCORTICOTROPIC HORMONE**

	<b>Stimulates Adrenocorticotrop Hormone Release</b>	<b>Inhibits Adrenocorticotrop Hormone Release</b>
Normal physiologic states	Hyperosmolality Hypovolemia Upright position $\beta$ -Adrenergic stimulation Pain and emotional stress Cholinergic stimulation	Hypo-osmolality Hypervolemia Supine position $\alpha$ -Adrenergic stimulation
Abnormal physiologic states	Hemorrhagic shock Hyperthermia Increased intracranial pressure Positive airway pressure	Excess water intake Hypothermia
Medications	Morphine Nicotine Barbiturates Tricyclic antidepressants Chlorpropamide	Ethanol Atropine Phenytoin Glucocorticoids Chlorpromazine
Results	Oliguria, concentrated urine	Polyuria, dilute urine

#### 6. What is diabetes insipidus?

Diabetes insipidus (DI) is caused by a deficiency of ADH synthesis, impaired release of ADH from the neurohypophysis (neurogenic DI), or renal resistance to ADH (nephrogenic DI). The result is excretion of large volumes of dilute urine, which, if untreated, leads to dehydration, hypernatremia, and serum hyperosmolality. The usual test for DI is cautious fluid

restriction. The inability to decrease and concentrate urine suggests the diagnosis, which may be confirmed by plasma ADH measurements. Administration of aqueous vasopressin tests the response of the renal tubule. If the osmolality of plasma exceeds that of urine after mild fluid restriction, the diagnosis of DI is suggested.

### 7. List causes of diabetes insipidus.

See Table 4-2.

Vasopressin Deficiency (Neurogenic Diabetes Insipidus)	Vasopressin Insensitivity (Nephrogenic Diabetes Insipidus)
Familial (autosomal-dominant)	Familial (X-linked recessive)
Acquired	Acquired
Idiopathic	Pyelonephritis
Craniofacial, basilar skull fractures	Postrenal obstruction
Craniopharyngioma, lymphoma, metastasis	Sickle cell disease and trait
Granuloma (sarcoidosis, histiocytosis)	Amyloidosis
Central nervous system infections	Hypokalemia, hypercalcemia
Sheehan's syndrome, cerebral aneurysm, cardiopulmonary bypass	Sarcoidosis
Hypoxic brain injury, brain death	Lithium

### 8. Discuss alternative treatments for diabetes insipidus.

Available preparations of ADH include pitressin tannate in oil, administered every 24 to 48 hours; aqueous pitressin, 5 to 10 units intravenously or intramuscularly every 4 to 6 hours; desmopressin (DDAVP), 10 to 20 units intranasally every 12 to 24 hours; or aqueous vasopressin, 100 to 200 mU/hr. Incomplete DI may respond to thiazide diuretics or chlorpropamide (which potentiates endogenous ADH).

Because the patient is losing water, administration of isotonic solutions may cause hypernatremia; in addition, excessive vasopressin causes water intoxication. Measurement of plasma osmolality, urine output, and osmolality is indicated when vasopressin is infused.

## KEY POINTS: FLUIDS AND VOLUME REGULATION



1. Estimating volume status requires gathering as much clinical information as possible because any single variable may be misleading. Always look for supporting information.
2. Replace intraoperative fluid losses with isotonic fluids.
3. Normal saline, when administered in large quantities, produces a hyperchloremic metabolic acidosis; the associated base deficit may lead the provider to conclude incorrectly that the patient continues to be hypovolemic.
4. Hypotension is a late finding in acute hypovolemia because sympathetic tone will increase vascular tone to maintain cardiac output.

**9. Define the syndrome of inappropriate antidiuretic hormone release. What is the primary therapy?**

Hypotonicity caused by the nonosmotic release of ADH, which inhibits renal excretion of water, typifies the syndrome of inappropriate antidiuretic hormone (SIADH) release. Three criteria must be met to establish the diagnosis of SIADH:

- The patient must be euvolemic or hypervolemic.
- The urine must be inappropriately concentrated (plasma osmolality  $<280$  mOsm/kg, urine osmolality  $>100$  mOsm/kg).
- Renal, cardiac, hepatic, adrenal, and thyroid function must be normal.

The primary therapy for SIADH is water restriction. Postoperative SIADH is usually a temporary phenomenon and resolves spontaneously. Chronic SIADH may require the addition of demeclocycline, which blocks the ADH-mediated water resorption in the collecting ducts of the kidney.

**10. What disorders are associated with SIADH?**

Central nervous system events are frequent causes, including acute intracranial hypertension, trauma, tumors, meningitis, and subarachnoid hemorrhage. Pulmonary causes are also common, including tuberculosis, pneumonia, asthma, bronchiectasis, hypoxemia, hypercarbia, and positive-pressure ventilation. Malignancies may produce ADH-like compounds. Adrenal insufficiency and hypothyroidism also have been associated with SIADH.

**11. What is aldosterone? What stimulates its release? What are its actions?**

Aldosterone, a mineralocorticoid, is responsible for the precise control of sodium excretion. A decrease in systemic or renal arterial blood pressure, hypovolemia, or hyponatremia leads to release of renin from the juxtaglomerular cells of the kidney. Angiotensinogen, produced in the liver, is converted by renin to angiotensin I. In the bloodstream angiotensin I is converted to angiotensin II, and the zona glomerulosa of the adrenal cortex is then stimulated to release aldosterone. An additional effect of angiotensin II is vasoconstriction. Aldosterone acts on the distal renal tubules and cortical collecting ducts, promoting sodium retention. In addition to hyponatremia and hypovolemia, stimuli for aldosterone release include hyperkalemia, increased levels of adrenocorticotropic hormone, and surgical stimulation.

**12. Discuss issues associated with estimating volume status in outpatients.**

For most outpatients the period of fasting would provide a rough estimate of volume deficit. A patient's hourly metabolic requirement is roughly 4 ml/kg for the first 10 kg, 2 ml/kg for the second 10 kg, and 1 ml/kg for the remainder of his or her weight. The actual deficit may be less than calculated because of renal conservation of fluids. Factors that may result in volume depletion include chronic hypertension, diuretic use, diabetes mellitus, alcohol ingestion, and bowel preparations (2 to 4 L may be lost).

**13. Discuss estimating volume status in acutely ill patients.**

Acutely ill patients are often hypovolemic as a result of conditions such as bleeding, peritonitis, pancreatitis, sepsis, gastrointestinal losses, traumatic injury, and inadequate fluid replacement.

Physical findings suggesting inadequate intravascular fluid include dry mucous membranes, loss of skin turgor, capillary refill greater than 2 seconds, postural hypotension, tachycardia, and oliguria (less than 0.5 ml/hr in adults, less than 1 ml/hr in children). If present, central venous or (rarely) pulmonary artery catheters may assist in the diagnosis of hypovolemia.

Useful laboratory values in the assessment of volume status include hemoglobin, hematocrit, electrolytes, blood urea nitrogen (BUN), creatinine, proteins, urine osmolality, specific gravity, and sodium concentration.

**14. Are there distinct advantages to using colloids to resuscitate a patient?**

Colloid advocates claim that, because these solutions have an intravascular space half-life of 3 to 6 hours (much greater than crystalloids), they are superior resuscitation fluids. When

compared to crystalloids in a controlled fashion, they have not been shown to improve outcomes. Further, in cases in which capillary permeability increases (e.g., burns, sepsis, trauma), colloids accumulate extracellularly, pulling other fluids along because of the osmotic gradient, resulting in extracellular edema. Finally, colloid solutions are more expensive.

Although only a third to a fourth of a liter of crystalloid remains in the intravascular space, if given in sufficient quantities (replacing losses in a ratio of 3-4 to 1), crystalloids are excellent resuscitation fluids. It should be noted that dehydrated patients suffer from fluid losses in both intracellular and extracellular compartments and crystalloids will replete both compartments.

#### 15. Review the composition of crystalloid solutions.

Fluid resuscitation in the operating room is accomplished with isotonic fluids since intraoperative losses include both salts and water. Thus only relatively isotonic fluids are listed. Patients requiring replacement of maintenance fluids are usually treated with hypotonic fluids because their losses are predominantly free water, but this is uncommon intraoperatively. Although normal saline is the preferred crystalloid to dilute packed red blood cells, administering large quantities results in hyperchloremic metabolic acidosis caused by dilution of bicarbonate (Table 4-3).

**TABLE 4-3. MOST COMMON INTRAOPERATIVE BALANCED CRYSTALLOID SOLUTIONS**

	Osmolality*	Na	Cl <sup>-</sup>	K	Ca <sup>2+</sup>	Mg <sup>2+</sup>	Lactate	Acetate	Gluconate
NS	308	154	154						
LR	273	120	109	4	3		28		
Plasma-Lyte	294	140	98	5		3		27	23

*LR*, Lactated Ringer's solution; *NS*, normal saline.  
\*Osmolality is measured in mOsm/L; other substances are measured in mEq/L.

#### 16. Review the colloidal solutions that are available.

There are two albumin preparations, 5% and 25%. Preparation methods eliminate the possibility of infection. The 5% solution has a colloid osmotic pressure of about 20 mm Hg, which is the approximate colloid osmotic pressure under normal circumstances. The 25% solution (also called *salt-poor* albumin) obviously has a colloid osmotic pressure of about five times the normal situation. If intravascular volume is depleted yet extracellular volume is greatly expanded, this excess colloid osmotic pressure will draw fluid from the interstitium into the vascular space.

Hydroxyethyl starch in a 6% solution (dissolved in either normal saline or lactated Ringer's solution) is another colloid preparation. The heterogeneous preparation contains polymerized molecules with molecular weights of between 20,000 and 100,000 daltons. Metabolized by amylase, it accumulates in the reticuloendothelial system and is renally excreted. Partial thromboplastin time is increased. It has dilutional effects on clotting factors, and the hetastarch molecules can move into organizing fibrin clot. Thus coagulation can be impaired. It is recommended that not more than 20 ml/kg be administered. The preparation dissolved in lactated Ringer's is thought to have lesser effects on coagulation, perhaps because it is less heterogeneous in molecular weight dispersion. There are no effects on crossmatching of blood.

Dextrans are water-soluble, polymerized glucose molecules. Two preparations are available (dextran 40 and 70), and the molecular weights of the respective solutions are 40 and 70 kilodaltons. Anaphylactic and anaphylactoid reactions and inhibition of platelet adhesiveness have been noted. Crossmatching of blood may be difficult (Table 4-4).

TABLE 4-4. COMMONLY ADMINISTERED COLLOIDS

Colloid	Benefits and Risks
Albumin (5% or 25%)	Expensive; allergic reactions; question its use where there is a loss of capillary integrity
Hetastarch	Currently constituted in either NS or RL; administer less than 20 ml/kg to avoid antiplatelet effects; renally excreted; increases serum amylase
Dextran (40 or 70)	Anaphylactic reactions; interferes with platelet function and crossmatching; increases hepatic transaminases

*LR*, Lactated Ringer's solution; *NS*, normal saline.

### 17. What is the normal range for serum osmolality?

Different sources quote different ranges, but in general normal serum osmolality ranges between 285 and 305 mOsm/L. A quick rough estimate is to double the sodium concentration. A more accurate estimate of osmolality can be obtained using the following equation:

$$2 \times [\text{Na}] + [\text{Glucose}]/18 + \text{BUN}/2.8$$

where the values in the brackets are the concentrations of the substances (sodium in mEq/L, glucose and BUN in g/L).

### 18. What situations might be appropriate for the use of hypertonic saline?

Hypertonic saline (usually 3%) has been used successfully during aortic reconstructions and extensive cancer resections; for hypovolemic shock, slow correction of symptomatic chronic hyponatremia, transurethral resection of the prostate syndrome, and increased intracranial pressure; and to reduce peripheral edema after major fluid resuscitations. It has been used in far forward combat situations and in trauma patients with prolonged transportation times (rural areas), but its use is still not extremely common.

### 19. How do you estimate fluid loss during a surgical procedure?

This is an inexact process. Gather as much information as you can. Estimating the volume found in suction canisters and subtracting whatever volume has been used for irrigation can assess blood loss. Surgical sponges can be weighed; a large laparotomy sponge can hold more than 100 ml of blood. Blood loss can also be occult, soaking into surgical drapes or running down onto the floor. Measure gastric aspirate. Significant peritoneal fluid collections may require replacement. Insensible losses are associated with intra-abdominal procedures in which the abdominal viscera are exposed, but estimating these can be problematic, and cookbook methods are not evidence based. For example, be smart when replacing urine output; if the patient has been given 5 L too much fluid, expect a vigorous urine output and do not replace this.

### 20. What is meant by third-space losses? What are the effects of such losses?

In certain clinical conditions such as major intra-abdominal operations, hemorrhagic shock, burns, and sepsis, patients develop fluid requirements that are not explained by externally measurable losses. Losses are internal, a temporary sequestration of intravascular fluid into a functionless *third space*, which may not readily participate in the dynamic fluid exchanges at the microcirculatory level. The volume of this internal loss is proportional to the degree of injury, and

its composition is similar to plasma or interstitial fluid. The creation of the third space necessitates further fluid infusions to maintain intravascular volume, adequate cardiac output, and perfusion, and third-space fluids will persist until the patient's primary problem has resolved.

### 21. How much fluid is appropriate to administer during a surgical procedure?

As has been previously mentioned, many *cookbook recipes* exist for administering intravenous fluids during surgical procedures. Many of these traditional recommendations have little evidence to support them. Clearly some fluid is better than none. For instance, nausea and vomiting and postural hypotension are reduced in patients having outpatient surgical procedures if the patient receives a liter or two of intravenous fluid perioperatively. But how much and for what procedure continue to be investigated. Every patient is different because each has differing periods of fasting, severity of illness, volume contraction, and coexisting disease.

There is good evidence that fluid restriction is beneficial in patients having thoracotomy and lung resections because of concern for postoperative pulmonary edema. Similarly, elective neurosurgical procedures and hepatic resections require judicious fluid administration. The viability of myocutaneous flaps is impaired in the setting of excess edema.

Recent investigations have compared liberal (consider this 12 to 15 ml/kg/hr or greater) to restrictive (consider this 4 to 8 ml/kg/hr) fluid administration protocols in patients having bowel resections. In the fluid-restricted group decreases in blood pressure of 20% of baseline or urine output of less than 0.5 ml/kg/hr were treated with repeated boluses of Ringer's lactate, 250 ml. The restricted group had shorter hospitalizations, more rapid return of bowel function, and fewer surgical complications.

### 22. Is blood pressure a good sign of hypovolemia?

Blood pressure is not significantly affected until approximately 30% of blood volume is lost. Early compensatory mechanisms, including peripheral vasoconstriction and tachycardia, may mask significant volume loss.

### 23. What clinical findings support a diagnosis of hypervolemia?

The patient may have rales on lung auscultation, frothy secretions in the endotracheal tube, edematous mucous membranes and conjunctiva (although edematous conjunctiva by itself is not enough to make the diagnosis, especially when the patient has been in the prone position), polyuria, and peripheral edema. Like hypovolemia, hypervolemia is best diagnosed when a constellation of findings, and not just a single finding, is present.

## WEBSITE



<http://www.fluidtherapy.net>

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3. Nisanevich V, Felsenstein I, Almogy G, et al: Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology* 103:25–32, 2005.

# ELECTROLYTES

James Duke, MD, MBA

## 1. What is a normal sodium concentration? What degree of hyponatremia is acceptable to continue with a planned elective procedure?

A normal sodium level is between 135 and 145 mEq/L. Generally a sodium level of 130 mEq/L will not result in cancellation of a planned procedure as long as the patient is not symptomatic and hyponatremia is not an expected result of the procedure. It is important to note that recognizing hyponatremia should prompt an investigation as to the cause. Whether the investigation should take priority over the surgery depends on the urgency of the procedure and an overall assessment of the patient's condition.

## 2. How is hyponatremia classified?

Hyponatremia may occur in the presence of hypotonicity, normal tonicity, or hypertonicity; thus it is important to measure serum osmolality to determine the cause of hyponatremia. Assessment of volume status is also important in determining the cause. An excess of total body water is more common than a loss of sodium in excess of water. [Table 5-1](#) summarizes causes and treatment of hyponatremia.

TABLE 5-1. CAUSES OF HYPONATREMIA

Total Sodium Content	Causes	Treatment (Always Treat Underlying Disorder)
Decreased	Diuretics (including osmotic diuretics); renal tubular acidosis; hypoaldosteronism; salt-wasting nephropathies, vomiting; diarrhea	Restore fluid and sodium deficits with isotonic saline
Normal	SIADH; hypothyroidism; cortisol deficiency	Water restriction
Increased	Congestive heart failure; cirrhosis; nephrotic syndrome	Water restriction, loop diuretics

*SIADH*, Syndrome of inappropriate antidiuretic hormone.

## 3. How should acute hyponatremia be treated?

The rate at which hyponatremia develops and the presence of symptoms determine the aggressiveness of treatment. If hyponatremia has developed quickly, the patient may develop nausea, vomiting, visual disturbances, muscle cramps, weakness, hypertension, bradycardia, confusion, apprehension, agitation, obtundation, or seizures; usually the sodium content is found to be less than 125 mEq/L. The aggressiveness of treatment depends on the extent of symptoms.



In the simplest cases fluid restriction may be sufficient. Administration of loop diuretics may also be indicated. Severe neurologic symptoms require careful administration of hypertonic (3%) saline. The dose of 3% saline (513 mEq Na/L) is determined as follows:

$$\text{Dose (mEq)} = (\text{Weight in kg}) \times (140 - \text{measured sodium concentration in mEq/L}) \times 0.6$$

Correction should occur slowly, with serial sodium concentrations measured. Below 125 mEq/L, correct at a rate of about 1 mEq/L/hr. Once a concentration of 125 mEq/L has been achieved, the likelihood of continued severe neurologic symptoms has diminished. It should be noted that aggressive correction may result in central pontine myelinolysis.

Seizures require securing a protected airway, oxygenation, ventilation, and perhaps administration of anticonvulsants, although seizures are usually self-limited.

#### 4. Is there a subset of patients who may tend to have residual neurologic sequelae from a hyponatremic episode?

Females of reproductive age, and especially during menstruation, have been noted to be at greatest risk for residual sequelae. There may be an estrogen-related impairment of the adaptive ability of the brain in the setting of hyponatremia.

#### 5. What may cause acute hyponatremia in the operating room?

Administration of hypotonic fluids or absorption of sodium-poor irrigants may result in hyponatremia. Such irrigants are used to facilitate transurethral resection of the prostate or distend the uterus during hysteroscopies. However, isotonic fluids are used increasingly in these settings when bipolar electrical cautery is used for the surgical procedure. Thus hyponatremia as a consequence of these procedures has been observed with decreasing frequency. However, some surgeons may still prefer monopolar cautery because the resection is more rapid. In this instance a hypotonic irrigation fluid is used to prevent dispersal of the electrical current, and in such a scenario hyponatremia is a risk. The most common cause of postoperative hyponatremia is syndrome of inappropriate antidiuretic hormone secretion and subsequent water retention.

#### 6. Discuss hypernatremia and its causes.

Hypernatremia is less common than hyponatremia and is always associated with hypertonicity. Hypernatremia can be associated with either low, normal, or high total body sodium content. Frequently hypernatremia is the result of decreased access to free water, as in elderly or debilitated patients with impaired thirst and decreased oral intake. Other causes include a lack of antidiuretic hormone (diabetes insipidus) and an excess sodium intake (either parenterally or intravenously such as with administration of sodium bicarbonate or 3% sodium chloride). Table 5-2 lists causes and treatment for each category.

#### 7. What problems does hypernatremia pose for the anesthesiologist?

Most often hypernatremia is associated with fluid deficits, and the hypovolemia poses the greater challenge to the anesthesiologist. Complicating this, fluid deficits must be corrected slowly lest cellular edema ensue. Generally elective surgery should be delayed if serum sodium levels exceed 150 mEq/L. Hypernatremia increases minimal alveolar concentration.

#### 8. Review hypokalemia and its causes.

A serum level of less than 3.5 mEq/L defines hypokalemia. Hypokalemia may be the result of total body loss of potassium (gastrointestinal and renal), transcellular shifts in potassium, or inadequate intake. Diuretics frequently cause hypokalemia, as do gastrointestinal losses and renal tubular acidosis.  $\beta$ -Adrenergic agonists, insulin, and alkalosis (respiratory and metabolic) shift potassium to the intracellular space. Hypokalemia is not uncommon in pregnant women receiving tocolytic therapy or in patients requiring inotropic support because  $\beta$ -agonists are used in both instances.

TABLE 5-2. CAUSES OF HYPERNATREMIA

Total Sodium Content	Causes	Treatment (Always Treat Underlying Disorder)
Decreased	Osmotic diuresis; increased insensible losses	First restore intravascular volume with isotonic fluids; then correct Na with hypotonic fluids
Normal	Diabetes insipidus (neurogenic nephrogenic); diuretics; renal failure	Correct water loss with hypotonic fluids
Increased	Excessive Na administration (NaHCO <sub>3</sub> ; 3% NaCl); hyperaldosteronism	Slowly correct fluid deficits with D <sub>5</sub> W, loop diuretics

### 9. What are the risks of hypokalemia?

Hypokalemia produces electrocardiogram abnormalities (ST segment and T wave depression and onset of U waves) and cardiac arrhythmias (often premature ventricular contractions and atrial fibrillation). It also impairs cardiac contractility. These cardiac abnormalities are usually not seen until serum K decreases to 3 mEq/L. Hypokalemia is especially worrisome in patients taking digitalis or with ischemic heart disease or preexisting arrhythmias. Hypokalemia renders muscles weak and sensitive to muscle relaxants. But no definitive data suggest that patients having surgery with potassium levels as low as 2.6 mEq/L have adverse outcomes.

### 10. A patient takes diuretics and is found to have a potassium level of 3 mEq/L. Why not give the patient enough potassium to restore the serum level to normal?

The total body deficit of potassium, primarily an intracellular cation, is not reflected by serum concentrations. A patient with a serum potassium of 3 mEq/L may have a total body potassium deficit of 100 to 200 mEq. Rapid attempts to correct hypokalemia poorly address the problem and have resulted in cardiac arrest. Hypokalemic patients without the risk factors previously discussed who are not undergoing major thoracic, vascular, or cardiac procedures can tolerate modest hypokalemia (certainly 3 and possibly as low as 2.8 mEq/L).

### 11. If potassium is administered, how much should be administered and how fast should it be administered?

Potassium should be administered at a rate no greater than 0.5 to 1 mEq/L. As a safety measure, no more than 20 mEq of potassium, diluted in a carrier and run through a controlled infusion pump, should be connected into a patient's intravenous lines at any one time.

### 12. Define hyperkalemia and review its symptoms.

Hyperkalemia is defined as serum concentration greater than 5.5 mEq/L. Hyperkalemia may produce profound weakness. Cardiac conduction manifestations include enhanced automaticity and repolarization. T waves become peaked, and there is PR interval and QRS prolongation and an increased risk for severe ventricular arrhythmias.

### 13. What are some causes of hyperkalemia?

Hyperkalemia may be either acute or chronic in etiology and secondary to increased intake, decreased excretion, or intracellular shifts related to acid-base status. Hyperkalemia may be iatrogenic (e.g., potassium supplementation, potassium-containing medications) and

associated with massive transfusion, metabolic acidosis, and renal failure (acute and chronic); it may also occur after massive tissue trauma or rhabdomyolysis. Medications that may cause hyperkalemia include angiotensin antagonists and receptor blockers, potassium-sparing diuretics (spironolactone and triamterene), and succinylcholine.

**14. Describe the patterns of hyperkalemia observed after the administration of succinylcholine.**

Mild hyperkalemia (an increase of approximately 0.5 mEq/L) occurs after routine administration of succinylcholine, but susceptible patients may experience life-threatening hyperkalemia. Examples of such patients include those with chronic spinal cord or denervation injuries, head injuries, and unhealed significant burns, and patients who have been immobile (e.g., patients in intensive care). I am aware of an otherwise healthy patient who experienced hyperkalemic cardiac arrest after administration of succinylcholine. His only risk factor was that he was a hospitalized prisoner chained to the bed day after day.

**15. A patient with chronic renal failure requires an arteriovenous fistula for hemodialysis. Potassium is measured as 7 mEq/L. What are the risks of general anesthesia?**

Hyperkalemia  $>6$  mEq/L should be corrected before elective procedures. Usually dialysis is the treatment. Always consider hyperkalemia when a patient with renal failure suffers cardiac arrest.

**16. How is hyperkalemia treated?**

Emergent treatment of hyperkalemia is threefold. Treat cardiotoxicity with intravenous calcium chloride. Potassium can be quickly shifted intracellularly by hyperventilation,  $\beta$ -adrenergic stimulation (e.g.,  $\beta$ -agonist nebulizer), sodium bicarbonate, and insulin (if insulin is given, one should consider glucose supplementation). Bodily excretion of potassium is more time-consuming but is accomplished using diuretics, Kayexalate, and dialysis.

**17. What are the major causes and manifestations of hypocalcemia?**

The major causes of hypocalcemia are hypoparathyroidism, hyperphosphatemia, vitamin D deficiency, malabsorption, rapid blood transfusion (chelated by citrate), pancreatitis, rhabdomyolysis, and fat embolism. Hypocalcemia is a concern after thyroidectomy if no parathyroid tissue is left, and the patient may develop laryngeal spasms and stridor. This must be differentiated from other causes of postoperative stridor, including wound hematoma and injury to the recurrent laryngeal nerves. Hypocalcemia also impairs cardiac contractility, resulting in hypotension, a not uncommon event during massive transfusion. Patients may also be confused.

## KEY POINTS: ELECTROLYTES



1. Rapid correction of electrolyte disturbances may be as dangerous as the underlying electrolyte disturbance.
2. Electrolyte disturbances cannot be corrected without treating the underlying cause.
3. Acute hyperkalemia is life threatening and associated with ventricular tachycardia and fibrillation. It should always be suspected when cardiac collapse follows succinylcholine administration or in any patient with chronic renal disease.
4. When other causes have been ruled out, persistent and refractory hypotension in trauma or other critically ill patients may be caused by hypocalcemia or hypomagnesemia.

**18. How is hypocalcemia treated?**

Treatment of acute hypocalcemia is straightforward: administer calcium chloride. Volume to volume this provides more calcium than the gluconate preparation. Always remember to address the primary disturbance.

**19. Does hypomagnesemia pose a problem for the anesthesiologist?**

Hypomagnesemia is increasingly recognized in critically ill patients, often in association with hypokalemia and hypophosphatemia. It is common in alcoholic patients. Hypokalemia cannot be corrected unless hypomagnesemia is also treated. Hypomagnesemic patients have increased susceptibility to muscle relaxants and may be weak after surgery, including having respiratory insufficiency. They may have impaired cardiac contractility and dysrhythmias.

Trauma patients having massive blood resuscitations may also become hypomagnesemic, and such patients should be administered magnesium chloride, 1 to 2 g, if dysrhythmias develop or refractory hypotension ensues.

**20. Hyperchloremia has been increasingly recognized after administration of what standard resuscitation fluid?**

Hyperchloremia is associated with massive resuscitation with normal saline and with metabolic acidosis caused by dilution of sodium bicarbonate, and it should be part of the differential diagnosis of metabolic acidosis in this setting. Besides after trauma, it has been noted during aortic, gynecologic, and cardiopulmonary bypass surgeries and during the management of sepsis.

**SUGGESTED READING**

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# TRANSFUSION THERAPY

James Duke, MD, MBA

## 1. How would knowledge of oxygen delivery impact the decision to transfuse?

A transfusion would be indicated when oxygen delivery falls to a critical level ( $DO_{2crit}$ ) and oxygen consumption ( $VO_2$ ) needs are not met. Recall that  $DO_2$  is a function of cardiac output (CO) and the arterial oxygen content ( $CaO_2$ ). Arterial oxygen content is a function of arterial oxygen saturation, the oxygen-carrying capacity of hemoglobin, the hemoglobin concentration, and, for the amount of oxygen dissolved in blood (unbound to hemoglobin), the partial pressure of oxygen.

Ordinarily  $DO_2$  exceeds  $VO_2$  by a factor of four (800 to 1200 ml/min vs. 200 to 300 ml/min). Thus the extraction ratio ( $O_{2ER} = VO_2/DO_2$ ) is 20% to 30%. As long as  $DO_2$  exceeds  $VO_2$ ,  $VO_2$  is “supply independent.” However, below  $DO_{2crit}$   $VO_2$  becomes “supply dependent,” and  $VO_2$  decreases as  $DO_2$  decreases, creating a situation in which end-organs are at risk for ischemia. It is at this point that a transfusion is clearly indicated.

## 2. At what point is $DO_{2crit}$ reached? What are our surrogate measures for $DO_{2crit}$ ?

As long as the patient is euvolemic,  $DO_{2crit}$  is not reached until hemoglobin decreases to about 3.5 g/dl. This also requires that pulmonary function is intact since it requires full hemoglobin oxygen saturation and oxygen dissolved in blood (not bound to hemoglobin). It should be noted that at this hemoglobin level the oxygen dissolved in blood becomes a major contributor (almost 75%) to the oxygen delivered. It should also be mentioned that the  $DO_{2crit}$  is modified by the patient’s oxygen requirements above baseline (e.g., catabolic states such as sepsis, burns) and the presence of end-organ disease such as coronary artery disease.

Given that in the course of normal operating room conditions,  $DO_{2crit}$  is unavailable, other variables are used to determine whether the patient is transfused. These include hypotension, tachycardia, urine output, the presence of lactic acidosis, signs of myocardial ischemia (new ST-segment depression  $>0.1$  mV, new ST-segment elevation  $>0.2$  mV, regional wall motion abnormalities by echocardiography), and low mixed venous oxygen saturation ( $<50\%$ , requires pulmonary artery catheterization to determine).

## 3. What are the physiologic adaptations to acute normovolemic anemia?

During surgery acute blood loss is usually replaced with crystalloid solutions and, if in sufficient volume, results in acute normovolemic hemodilution. Compensatory changes include sympathetic stimulation, resulting in tachycardia and increased cardiac output. Decreased viscosity reduces afterload, increases preload, and improves flow at the capillary level. Since capillary flow is not maximal under resting conditions, capillary recruitment is an adaptive mechanism as well. In addition, there is redistribution of blood to the tissues that are oxygen supply dependent (e.g., heart and brain) and oxygen extraction is increased.

It is important to note that myocardial oxygen extraction is high under normal circumstances; thus the reserve is less. The brain has greater extraction reserve than the heart. Thus the heart is more dependent on increasing blood flow to increase oxygen delivery; the significance of this becomes clear in coronary artery disease. A failure for acute normovolemic anemia to deliver oxygen in excess of consumption is another argument in favor of blood transfusion.

**4. Historically, a hemoglobin level of 10 g/dl (hematocrit of 30) was used as a transfusion trigger. Why is this no longer an accepted practice?**

In patients with coronary artery disease having signs of myocardial ischemia, this level of hemoglobin might be appropriate. Otherwise it has come to be viewed as a liberal transfusion trigger. Recall that in an otherwise normal situation,  $DO_{2crit}$  has not been reached until hemoglobin decreases to 3.5 g/dl. Although no clinician probably pushes a patient to this extreme (unless the patient requests no transfusion based on religious reasons and the like), the less likely a transfusion is really indicated, the more the risks of transfusion negatively impact the risk/benefit ratio.

It is also interesting to note that men and women tend to be treated equally when the decision to transfuse is made, despite the fact that normal women are anemic relative to men. Using the same transfusion triggers hardly seems rational. Finally there is a concern that a transfusion might not substantially increase oxygen delivery (see discussion of blood storage lesions in question 8). These are strong arguments for closely scrutinizing the consideration to transfuse.

**5. What are the risks of transfusion?**

The risks include contracting an infectious disease through transfusion, transfusion reactions, and the immunomodulatory effects of transfusion.

**6. What infectious diseases can be contracted from a transfusion and how significant is that risk?**

At this point in time, the blood supply is as safe as it has ever been, with risks of contracting hepatitis or human immunodeficiency virus (HIV) in a developed nation estimated at 1 in 2.4 million units transfused. Donated blood is tested for hepatitis B (hepatitis B core antigen), hepatitis C (hepatitis C antibody), syphilis, HIV, human T cell lymphotropic virus, West Nile virus, and cytomegalovirus. Because of improvements in testing, the window between donation and seroconversion is becoming increasingly narrow.

However, there are new infectious risks, including contracting prion-mediated diseases (variant Creutzfeldt-Jakob disease (vCJD), parasitic disease (Chagas disease, malaria), and avian flu. There are concerns that severe acute respiratory syndrome will eventually be spread through the blood supply. The risks of these diseases vary with the geographic locality. For instance, malaria is a greater risk in undeveloped countries (as is HIV); the only known cases of contraction of vCJD through transfusion are in the United Kingdom.

Because platelets are stored at a higher temperature (20 to 22° C) than red blood cells (4° C) or other blood products, platelets are the blood component at greatest risk for bacterial infection. However, testing for sepsis in platelet units is improving, and the risk will likely decrease over time.

**7. Review the major transfusion-related reactions.**

- **Hemolytic transfusion reactions** caused by ABO incompatibility are most commonly caused by clerical errors and transfusion of the wrong unit. Mistransfusion is thought to occur with a frequency between 1:14,000 and 1:18,000. Most reactions occur during or shortly after a transfusion. Clinical manifestations include fever; chills; chest, flank, and back pain; hypotension; nausea; flushing; diffuse bleeding; oliguria or anuria; and hemoglobinuria. General anesthesia may mask some of the clinical manifestations, and hypotension, hemoglobinuria, and diffuse bleeding may be the only signs. It should be noted that the signs of a severe hemolytic reaction might be missed while the patient is under general anesthesia or attributed to another cause.
- **Anaphylactic reactions** are caused by binding of IgE; present with bronchospasm, edema, redness, and hypotension; and require urgent treatment with epinephrine, fluid infusions, corticosteroids and antihistamines, and other therapies as indicated by severity and progression of symptoms.

- **Febrile reactions** may be an early sign of hemolytic transfusion reaction (but other symptoms should be present) or bacterial contamination of the blood product. Febrile nonhemolytic transfusion reactions usually occur in patients who have had prior transfusions; headache, nausea, and malaise are associated symptoms. The reaction is caused by leukocyte antibodies, and leukocyte-depleted red blood cells may be indicated for these patients. Antipyretics may decrease the symptoms if given before the transfusion; meperidine may decrease the severity of chills.
- **Transfusion-related acute lung injury (TRALI)** is in the top three of transfusion-related deaths, having a mortality of 50%. A form of noncardiogenic pulmonary edema, TRALI is also immune related and is usually noted within 6 to 12 hours after transfusion. Symptoms include hypoxia, dyspnea, fever, and pulmonary edema; treatment is supportive.
- **Urticarial reactions** secondary to mast cell degranulation do not require that the transfusion be stopped; antihistamines may be given.
- These transfusion reactions are compared in [Table 6-1](#).

**TABLE 6-1. DIFFERENTIAL DIAGNOSIS OF TRANSFUSION-RELATED ACUTE LUNG INJURY\***

Diagnostic Entity	Onset	Major Signs and Symptoms	Differentiating Features
Transfusion-related acute lung injury	Minutes to hours	Dyspnea, respiratory distress, hypoxemia, cyanosis, pulmonary edema, fever, tachycardia	Noncardiogenic pulmonary edema, frequent fever
Anaphylactic or anaphylactoid reaction	Minutes to hours	Bronchospasm, respiratory distress, hypotension, cyanosis, generalized erythema and urticaria, mucous membrane edema	Rash, urticaria, and edema present; hypotension and bronchospasm prominent
Bacterial contamination of blood products	Minutes	Fever, rigors, hypotension, and vascular collapse	Fever, rigors, and vascular collapse predominant; most common with platelets
Hemolytic transfusion reaction	Minutes	Fever, rigors, hypotension, hemoglobinuria, disseminated intravascular coagulation	Usually with red blood cell transfusion, hemolysis

\*Symptoms may be missed while under general anesthesia, and differential diagnosis should be expanded to include common intraoperative problems. (Permission from Boskkov LK: Transfusion-related acute lung injury and the ICU, *Crit Care Clin* 21:479-495, 2005.)

### 8. What are the current standards for the length of storage of blood? What is a blood storage lesion?

Federal regulation requires that at least 70% of transfused red blood cells survive 24 hours after CPDA-1 and for 42 days when AS-1 (Adsol) or AS-3 (Nutrice) is added.

Changes in stored blood that reduce post-transfusion viability are known as *storage lesions*. They include reduction in red cell deformability; altered red cell adhesiveness; depletion of adenosine triphosphate stores; and reduction in 2,3-diphosphoglycerate (2,3-DPG) which decreases the ability of the hemoglobin dissociation curve to shift to the right, which enhances peripheral oxygen release. Proinflammatory cytokines accumulate and, even after 2 weeks, are capable of significantly priming neutrophils for an exacerbated inflammatory response.

### 9. Is there convincing evidence that the effect of a transfusion on immune function is harmful?

Much of the evidence for immune modulation and infection related to transfusion is retrospective in nature and as such suffers from a failure to control for confounding variables. There are insufficient numbers of randomized, controlled studies of sufficient power, and the studies that do exist have been conducted on critically ill patients, not in the perioperative setting (perhaps with the exception of patients having coronary bypass). As such, definitive recommendations await. However, a few points are worthy of discussion.

The Transfusion Requirements in Critical Care trial was sufficiently powered to evaluate the impact of transfusion on outcome. The groups under study were divided into a restrictive transfusion (hemoglobin trigger of 7 g/dl, targeting a hemoglobin level between 7 and 9 g/dl) and a liberal transfusion group (hemoglobin transfusion trigger of 10 g/dl, targeting a hemoglobin level of 10 to 12 g/dl). Thirty-day mortality was lower in the restrictive transfusion group, although a statistical significance of  $p < 0.05$  was not met. However, if the patients were subdivided by acuity of illness, fewer acutely ill patients in the restrictive transfusion group had lower 30-day mortality.

Other prospective studies are less convincing in their findings, but there are overlapping transfusion triggers, and the patient populations differ. Some but not all observational studies have found that the number of transfused units is an independent risk factor for mortality and increased length of stay. Overall it must be said that the final word on the impact of transfusion on mortality has yet to be written. It should be noted that many countries now routinely perform leukoreduction on donated blood out of concern for the impact of transfusion on the recipient's immune function.

### 10. Review the features of transfusion-related acute lung injury.

Recently TRALI has been identified as the leading cause of transfusion-related deaths in the United States. It is estimated that 1 in 5000 transfusions will result in TRALI. All blood components have resulted in TRALI, including packed erythrocytes, random donor platelets, single donor (apheresis) platelets, fresh frozen plasma, and cryoprecipitate. However, the cellular components have a greater association with TRALI. Even autologous blood has resulted in TRALI, suggesting that there may be some storage lesion contributing to its etiology.

Although donor antibodies have been shown to be present in many TRALI series, their presence is neither necessary nor sufficient to result in TRALI. It is now believed that TRALI is multifactorial and a two-event subtype of acute lung injury. Because of some associated conditions, the recipient has a high level of inflammatory mediators (e.g., cytokines), primed white blood cells, and pulmonary endothelium. The administered blood product provides the second event, through classic antibody-antigen coupling or the lipid products or other cytokines generated during storage of the blood products. The primed white blood cells are activated to release substances such as superoxides that damage the pulmonary endothelium.



### 11. What conditions may predispose a patient to transfusion-related acute lung injury?

Some conditions that have been associated with TRALI include sepsis, organ ischemia, massive transfusion, extracorporeal circulation, malignancies, recent surgical procedures, aspiration of gastric contents, near-drowning, pneumonia, long-bone fractures, burns, pulmonary contusion, and disseminated intravascular coagulation. Obviously the patient must be ill enough to require a transfusion.

### 12. Discuss the criteria for diagnosis of transfusion-related acute lung injury.

- Acute onset: often occurring in less than 2 hours after a transfusion, but usually less than 6 hours
- Pulmonary arterial occlusion pressure  $\leq 18$  mm Hg or lack of clinical evidence of left atrial overload (i.e., the problem is noncardiogenic pulmonary edema)
- Bilateral infiltrates observed on chest radiograph
- Hypoxemia with a ratio of  $\text{PaO}_2/\text{FiO}_2 \leq 300$  mm Hg regardless of the level of positive end-expiratory pressure, or oxygen saturation  $\leq 90\%$  on room air
- No acute lung injury existed prior to transfusion

### 13. What treatments are available for transfusion-related acute lung injury?

If the patient experiences deterioration in oxygenation during transfusion, the transfusion should be discontinued, and the remainder of the transfused blood returned to the laboratory for analysis. Of course, some other form of transfusion injury besides TRALI may be taking place.

Therapy is supportive, continuing to treat the patient's other medical problems (which may have been the priming event for TRALI) and aggressive pulmonary support. If further transfusions are needed, it is wise to use blood products that have a reduced likelihood of having inflammatory mediators, including leukoreduced packed erythrocytes, packed units less than 14 days old, washed erythrocytes, or, in the case of platelets, apheresis units less than 3 days old.

### 14. Review the ABO and Rh blood genotypes and the associated antibody patterns.

Blood type is determined by two alleles of three types: O, A, and B. A and B refer to antigens on the red blood cell surface. An individual can have either A or B, both A and B, or neither (blood type O). If an individual does not have the type A antigen, over time anti-A antibodies (also known as *agglutinins*) form. A patient with type AB blood has both antigens and will form no agglutinins. Individuals with type O blood have no antigen and develop both A and B antibodies (Table 6-2). The antibodies are primarily immunoglobulin (Ig)M or IgG. Acute hemolytic reactions are caused by complement activation and release of proteolytic enzymes that digest the red cell membrane.

TABLE 6-2. BLOOD TYPES AND THEIR CONSTITUENT ANTIGENS AND ANTIBODIES

Blood Genotypes	Blood Type	Antigens (Agglutinogens)	Antibodies (Agglutinins)
OO	O	None*	Anti-A and Anti-B
OA or AA	A	A	Anti-B
OB or BB	B	B	Anti-A
AB	AB	A and B	None†

\*The absence of agglutinogens makes the O-packed cells the universal packed cells donor.

†The absence of agglutinins makes AB plasma the universal plasma donor.

People with type O blood have neither A nor B antigens (agglutinogens) on their cell surface. These cells cannot be agglutinated by antibodies (agglutinins) that may be present in a transfusion recipient's blood. Thus type O blood is known as the *universal donor* for red blood cells. Patients with type AB blood have both classes of antigens (agglutinogens) and therefore do not form A or B antibodies (agglutinins). Because there are no antibodies in the plasma, type AB patients are universal donors for plasma.

There are six common antigens in the Rh system; the presence of the *D* antigen is what is most commonly referred to as *Rh positive*. The Rh blood type system is slightly different because Rh agglutinins rarely form spontaneously. Usually massive exposure, as from a prior transfusion, is necessary to stimulate their formation. An Rh-negative patient can receive Rh-positive blood in an emergency situation, although antibodies will form in some patients, and there may be a delayed, usually mild, hemolytic transfusion reaction. But now the patient is Rh sensitized and can have a more significant transfusion reaction if exposed to Rh-positive blood at a later date.

### 15. What is the difference between a type and screen and a crossmatch?

The patient's blood is typed for ABO and Rh group by placing his or her red cells with commercially available anti-A and anti-B reagents and reverse typing the patient's serum against A and B reagent cells. A screen for antibodies involves placing the patient's serum with specially selected red cells containing all relevant blood group antigens. In a crossmatch the patient's serum is also incubated with a small quantity of red cells from the proposed donor unit to verify *in vitro* compatibility. A crossmatch also detects more unique antibodies (Table 6-3).

TABLE 6-3. CROSSMATCH AND COMPATIBILITY

Degree of Crossmatch	Chance of Compatible Transfusion
ABO-Rh type only	99.8%
ABO-Rh type + antibody screen	99.94%
ABO-Rh type + antibody screen crossmatch	99.95%

### 16. What type of blood should be used in an emergency situation?

Transfusions in emergency situations do not allow time for a complete crossmatch. Under these circumstances the fastest choice is to use type O, Rh-negative (or Rh positive in males), uncrossmatched blood. If more than two units of type O blood are given to patients who are type A or B, because of the anti-A and anti-B antibodies in type O blood, type O blood should continue to be administered until complete testing of the patient's blood has ensured that hemolysis of his or her native cells will not take place. Type-specific, uncrossmatched blood would be the next choice, followed by type-specific, partially crossmatched blood and finally fully crossmatched blood.

### 17. What are some of the complications of massive blood transfusion?

Massive transfusion is defined as the administration of more than one blood volume within several hours. Complications include:

- Coagulopathy secondary to dilutional thrombocytopenia, lack of labile coagulation factors V and VIII, and disseminated intravascular coagulation
- Metabolic disturbances associated with banked blood, including hyperkalemia, hypocalcemia (citrate toxicity), acidosis, and impaired oxygen delivery caused by reduced 2,3-DPG

- Hypothermia. Interestingly, a meta-analysis (Rajagopalan et al, 2008) found that mild hypothermia (34° to 36° C) increases blood loss by 16% and increases the relative risk for transfusion by 22%. Hypothermia impairs platelet function and proteins of the coagulation cascade.

#### 18. If suspected, how should a major transfusion reaction be managed?

- Stop the transfusion immediately and remove the blood tubing.
- Alert the blood bank and send a recipient and donor blood specimen for compatibility testing.
- Treat hypotension aggressively with intravenous fluids and pressor agents.
- Maintain urine output with intravenous hydration. Mannitol and loop diuretics are used on occasion.
- Massive hemolysis can result in hyperkalemia. Follow serum potassium levels and continuously monitor the electrocardiogram for electrocardiographic signs of hyperkalemia.
- Disseminated intravascular coagulation may occur. The best treatment is identifying and treating the underlying cause. Follow prothrombin, partial thromboplastin, fibrinogen, and D-dimer levels.
- Check urine and plasma hemoglobin levels and verify hemolysis with direct antiglobulin (Coombs') test, bilirubin, and plasma haptoglobin levels.
- The availability of thromboelastography is increasing and is very useful for assessing coagulation disturbances.

#### 19. What alternatives are there to transfusion of donor blood?

- Autologous transfusion (the collection and reinfusion of the patient's own blood). It should be noted that only about 55% of predonated units are returned to the patient. The patient scheduled to autologous transfusion still runs the risk of clerical errors and bacterial infection. There is also a report of a patient who received an autologous transfusion developing TRALI.
- Preoperative use of erythropoietin to stimulate erythrocyte production. Erythropoietin stimulates erythrocyte production in 5 to 7 days and has been shown to reduce use of allogeneic blood in patients with renal insufficiency and anemia of chronic disease and when transfusion is refused.
- Intraoperative collection and reinfusion of blood lost during surgery
- Intraoperative isovolemic hemodilution (the reduction of hematocrit or hemoglobin by withdrawal of blood and simultaneous intravascular replacement with crystalloid)
- Use of hemoglobin solutions

#### 20. What are the limitations, advantages, and disadvantages of alternative hemoglobin solutions?

The benefits of alternatives to erythrocyte transfusion include a lack of antigenicity, possible unlimited availability, no disease transmission risk, long storage life, and better rheologic properties. Two types of oxygen-carrying solutions have been developed:

- Perfluorocarbon emulsions that have a high gas-dissolving capacity for oxygen
- Hemoglobin-based oxygen carriers.

This discussion focuses on the latter. Such compounds are manufactured from human recombinant hemoglobin, outdated human blood, or bovine blood. The stromal components of erythrocytes are removed, and the hemoglobin molecule polymerized or liposome encapsulated to prevent rapid renal excretion and nephrotoxicity. Cell-free hemoglobin solutions have two major problems. First, they have low concentrations of 2,3-DPG. The lack of 2,3-DPG shifts the oxyhemoglobin dissociation curve to the left, the affinity of hemoglobin for oxygen increases, and oxygen cannot be off-loaded at the tissue level. Second, they are nitric oxide scavengers and produce excessive vasoconstriction. Pulmonary hypertension and myocardial ischemia are risks; in fact, reports of death from myocardial infarction have delayed release of these solutions for general use. These solutions also result in platelet activation; release of proinflammatory mediators; methemoglobinemia; and, because of their color, interference with laboratory tests.

**KEY POINTS: TRANSFUSION THERAPY**

1. There is no set hemoglobin/hematocrit level at which transfusion is required. The decision should be individualized to the clinical situation, taking into consideration the patient's health status.
2. If blood is needed in an emergency, type O–packed cells and/or type-specific blood may be used.
3. There are numerous transfusion-related reactions, and vigilance while administering under anesthesia is a must because many of the classic signs and symptoms might be missed in a draped patient under general anesthesia.

**WEBSITE**

American Society of Anesthesiologists  
<http://www.asahq.org>

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# COAGULATION

Jason P. Krutsch, MD

## 1. How can you identify a patient at risk for bleeding?

Preoperative evaluation includes history, physical examination, and performance of appropriate laboratory tests. Questions about bleeding disorders and problems (e.g., tendency to form large hematomas after minor trauma, severe bleeding while brushing teeth) and bleeding after previous surgical procedures (e.g., dental extractions, tonsillectomy) are important. Prior surgery without transfusion suggests the absence of an inherited coagulation disorder. Review of medications is necessary to identify medications with anticoagulant potential (e.g., nonsteroidal antiinflammatory drugs [NSAIDs], antiplatelet drugs, and anticoagulants). Coagulation studies may confirm a clinical suspicion that the patient has a bleeding disorder. No evidence supports the value of preoperative coagulation studies in asymptomatic patients.

## 2. What processes form the normal hemostatic mechanism?

Three intertwined processes ensure that blood remains in a liquid state until vascular injury occurs: primary hemostasis, secondary hemostasis, and fibrinolysis.

## 3. Describe primary hemostasis.

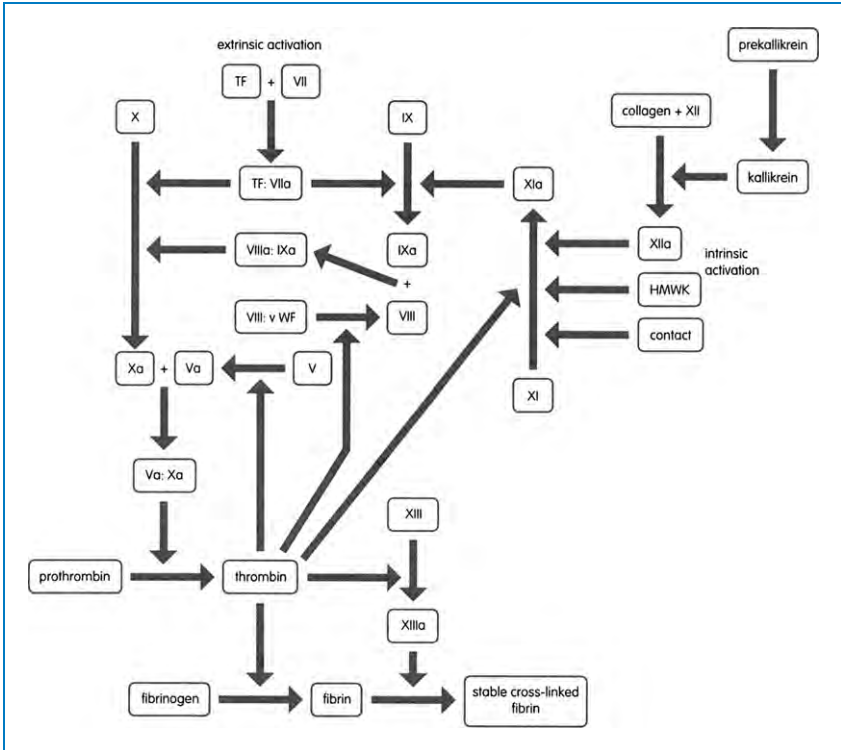
Within seconds of vascular injury, platelets become activated and adhere to the subendothelial collagen layer of the denuded vessel via glycoprotein receptors; this interaction is stabilized by von Willebrand's factor (vWF). Collagen and epinephrine activate phospholipases A and C in the platelet plasma membrane, resulting in formation of thromboxane A<sub>2</sub> (TXA<sub>2</sub>) and degranulation, respectively. TXA<sub>2</sub> is a potent vasoconstrictor that promotes platelet aggregation. Platelet granules contain adenosine diphosphate (ADP), TXA<sub>2</sub>, vWF, factor V, fibrinogen, and fibronectin. ADP alters the membrane glycoprotein IIb/IIIa, facilitating the binding of fibrinogen to activated platelets. Thus a platelet plug is constructed and reinforced.

## 4. Review secondary hemostasis.

Secondary hemostasis involves the formation of a fibrin clot. The fibrin network binds and strengthens the platelet plug. Fibrin can be formed via two pathways (intrinsic and extrinsic) and involves activation of circulating coagulation precursors. Regardless of which pathway is triggered, the coagulation cascade results in the conversion of fibrinogen to fibrin.

## 5. What are the intrinsic and extrinsic coagulation pathways?

Traditionally these two pathways have been viewed as separate mechanisms that merge after the formation of activated factor X (Figure 7-1). This rigid division has lost absolute validity because of the crossover of many factors. For instance, factor VIIa can activate factor IX; but factors IXa, Xa, thrombin, and XIIa can activate factor VII. However the classic two-pathway model is still useful for the interpretation of in vitro coagulation studies.



**Figure 7-1.** The clotting cascade, including intrinsic and extrinsic pathways. The roman numerals indicate the different clotting factors. The letter "a" indicates the activated form. *HMWK*, high-molecular-weight heparin; *TF*, tissue factor; *vWF*, von Willebrand's factor. (From Griffin J, Arif S, Mufti A: *Crash course: immunology and hematology*, ed 2, St. Louis, 2004, Mosby.)

The intrinsic pathway occurs within the blood vessel and is triggered by the interaction between subendothelial collagen with circulating factor XII, high-molecular-weight kininogen, and prekallikrein. Platelet phospholipid (PF3) serves as a catalyst to this pathway. The extrinsic pathway begins with the release of tissue thromboplastin (factor III) from the membranes of injured cells.

## 6. Explain fibrinolysis.

The fibrinolytic system is activated simultaneously with the coagulation cascade and functions to maintain the fluidity of blood during coagulation. It also serves in clot lysis once tissue repair begins. When a clot is formed, plasminogen is incorporated and then converted to plasmin by tissue plasminogen activator (tPA) and fragments of factor XII. Endothelial cells release tPA in response to thrombin. Plasmin degrades fibrin and fibrinogen into small fragments. These fibrin degradation products possess anticoagulant properties because they compete with fibrinogen for thrombin; they are normally cleared by the monocyte-macrophage system.

## 7. Why doesn't blood coagulate in normal tissues?

Coagulation is limited to injured tissue by localization of platelets to the site of injury and maintenance of normal blood flow in noninjured areas. The monocyte-macrophage system

scavenges activated coagulation factors in regions of normal blood flow. Normal vascular endothelium produces prostacyclin (prostaglandin  $I_2$ ); it is a potent vasodilator that inhibits platelet activation and helps confine primary hemostasis to the injured area. In addition, antithrombin III, proteins C and S, and tissue factor pathway inhibitor are coagulation inhibitors that are normally present in plasma. Antithrombin III complexes with and deactivates circulating coagulation factors (except factor VIIIa). Protein C inactivates factors Va and VIIIa; protein S augments the activity of protein C. Finally tissue factor pathway inhibitor antagonizes factor VIIa.

### 8. What is an acceptable preoperative platelet count?

A normal platelet count is 150,000 to 440,000/mm<sup>3</sup>. Thrombocytopenia is defined as a count of <150,000/mm<sup>3</sup>. Intraoperative bleeding can be severe with counts of 40,000– to 70,000/mm<sup>3</sup>, and spontaneous bleeding usually occurs at counts <20,000/mm<sup>3</sup>. The minimal recommended platelet count before surgery is 75,000/mm<sup>3</sup>. However, qualitative differences in platelet function make it unwise to rely solely on platelet count.

Thrombocytopenic patients with accelerated destruction but active production of platelets have relatively less bleeding than patients with hypoplastic disorders at a given platelet count.

Assessment of preoperative platelet function is further complicated by lack of correlation between bleeding time or any other test of platelet function and a tendency for increased intraoperative bleeding. However, normal bleeding times range from 4 to 9 minutes, and a bleeding time >1.5 times normal (>15 minutes) is considered significantly abnormal.

### 9. List the causes of platelet abnormalities.

#### Thrombocytopenia

- Dilution after massive blood transfusion
- Decreased platelet production caused by malignant infiltration (e.g., aplastic anemia, multiple myeloma), drugs (e.g., chemotherapy, cytotoxic drugs, ethanol, hydrochlorothiazide), radiation exposure, or bone-marrow depression after viral infection
- Increased peripheral destruction caused by hypersplenism, disseminated intravascular coagulation (DIC), extensive tissue and vascular damage after extensive burns, or immune mechanisms (e.g., idiopathic thrombocytopenic purpura, drugs such as heparin, autoimmune diseases)

#### Qualitative platelet disorders

- Inherited (e.g., von Willebrand's disease)
- Acquired (uremia, cirrhosis, medications [e.g., aspirin, NSAIDs])

### 10. How does aspirin act as an anticoagulant?

Primary hemostasis is controlled by the balance between the opposing actions of two prostaglandins, TXA<sub>2</sub> and prostacyclin. Depending on the dose, salicylates produce a differential effect on prostaglandin synthesis in platelets and vascular endothelial cells. Lower doses preferentially inhibit platelet cyclooxygenase, impeding production of TXA<sub>2</sub> and inhibiting platelet aggregation. The effect begins within 2 hours of ingestion. Because platelets lack a cell nucleus and cannot produce protein, the effect lasts for the entire life of the platelet (7 to 10 days). NSAIDs have a similar but more transient effect than aspirin, lasting for only 1 to 3 days after cessation of use.

### 11. Review the properties of factor VIII.

Factor VIII is a large protein complex of two noncovalently bound factors, vWF (factor VIII: vWF) and factor VIII antigen. Factor VIII:vWF is necessary for both platelet adhesion and formation of the hemostatic plug through regulation and release of factor VIII antigen. In von Willebrand's disease there is a decrease of both factor VIII antigen and factor VIII:vWF.

## KEY POINTS: COAGULATION



1. An outpatient with a bleeding diathesis can usually be identified through history (including medications) and physical examination. Preoperative coagulation studies in asymptomatic patients are of little value.
2. In vivo, coagulation is initiated primarily by contact of factor VII with extravascular tissue.
3. The most common intraoperative bleeding diathesis is dilutional thrombocytopenia.
4. The primary treatment for DIC is to treat the underlying medical condition.
5. Thromboelastography is a dynamic test of clotting and can be as useful as all other clotting tests combined.

### 12. How does vitamin K deficiency affect coagulation?

Four clotting factors (II, VII, IX, and X) are synthesized by the liver. Each factor undergoes vitamin K-dependent carboxylation to bind to the phospholipid surface. Without vitamin K the factors are produced but are not functional. The extrinsic pathway is affected first by vitamin K deficiency because the factor with the shortest half-life is factor VII, found only in the extrinsic pathway. With further deficiency both extrinsic and intrinsic pathways are affected.

The warfarin-like drugs compete with vitamin K for binding sites on the hepatocyte. Administration of subcutaneous vitamin K reverses the functional deficiency in 6 to 24 hours. With active bleeding or in emergency surgery, fresh frozen plasma (FFP) can be administered for immediate hemostasis.

### 13. How does heparin act as an anticoagulant?

Heparin is a polyanionic mucopolysaccharide that accelerates the interaction between antithrombin III and the activated forms of factors II, X, XI, XII, and XIII, effectively neutralizing each. The half-life of heparin's anticoagulant effect is about 90 minutes in a normothermic patient. Patients with reduced levels of antithrombin III are resistant to the effect of heparin. Heparin may also affect platelet function and number through an immunologically mediated mechanism.

### 14. Give a general description of the different coagulation tests.

The basic difference between the intrinsic and extrinsic pathways is the phospholipid surface on which the clotting factors interact before merging at the common pathway. Either platelet phospholipid (intrinsic pathway) or tissue thromboplastin (extrinsic pathway) can be added to the patient's plasma, and the time taken for clot formation is measured. Less than 30% of normal factor activity is required for the tests to be affected. The tests are also prolonged in the setting of decreased fibrinogen concentration (<100 mg/dl) and dysfibrinogenemias. The partial thromboplastin time (PTT), activated partial thromboplastin time (aPTT), and activated clotting time (ACT) measure intrinsic and common pathways.

### 15. What does the partial thromboplastin time measure?

PTT measures the clotting ability of all factors in the intrinsic and common pathways except factor XIII. Partial thromboplastin is substituted for platelet phospholipid and eliminates platelet variability. Normal PTT is about 40 to 100 seconds; >120 seconds is abnormal.

### 16. Describe the activated partial thromboplastin time.

Maximal activation of the contact factors (XII and XI) eliminates the lengthy natural contact activation phase and results in more consistent and reproducible results. An activator is added to the test tube before addition of partial thromboplastin. Normal aPTT is 25 to 35 seconds.



**17. How is the activated clotting time measured?**

Fresh whole blood (providing platelet phospholipid) is added to a test tube already containing an activator. The automated ACT is widely used to monitor heparin therapy in the operating room. The normal range is 90 to 120 seconds.

**18. What is the prothrombin time?**

Prothrombin time (PT) measures the extrinsic and common pathways. Tissue thromboplastin is added to the patient's plasma. The test varies in sensitivity and response to oral anticoagulant therapy whether measured as PT in seconds or simple PT ratio ( $PT_{\text{patient}}/PT_{\text{normal}}$ ), where "normal" is the mean normal PT value of the laboratory test system. Normal PT is 10 to 12 seconds.

**19. Explain the international normalized ratio.**

The international normalized ratio (INR) was introduced to improve the consistency of oral anticoagulant therapy. INR is calculated as  $(PT_{\text{patient}}/PT_{\text{normal-ISI}})$ , where ISI is the international sensitivity index assigned to the test system. The recommended therapeutic ranges for standard oral anticoagulant therapy and high-dose therapy, respectively, are INR values of 2 to 3 and 2.5 to 3.5.

**20. What are the indications for administering fresh frozen plasma?**

When microvascular bleeding is noted and PT or PTT exceeds 1.5 the control value, FFP should be considered. The usual dose is 10 to 15 ml/kg. FFP will also reverse the anticoagulant effects of warfarin (5 to 8 ml/kg). (Administration of vitamin K will have the same result but will take 6 to 12 hours to become effective.) Volume expansion is not an indication for FFP.

**21. What is cryoprecipitate? When should it be administered?**

Cryoprecipitate is the cold-insoluble white precipitate formed when FFP is thawed. It is removed by centrifugation, refrozen, and thawed immediately before use. Cryoprecipitate contains factor VIII, vWF, fibrinogen, and factor XIII. It is used to replace fibrinogen, factor VIII deficiencies, and factor XIII deficiencies. It has been used to treat von Willebrand's disease (unresponsive to desmopressin) and hemophilia. There is now a purified factor VIII concentrate more appropriate for use in these selected problems. One unit of cryoprecipitate per 10 kg of body weight will increase fibrinogen levels by 50 mg/dl. Since cryoprecipitate lacks factor V, for the treatment of disseminated intravascular coagulation, FFP is also necessary.

**22. What is disseminated intravascular coagulation?**

DIC is usually seen in clinical situations in which clotting pathways are activated by circulating phospholipid, leading to thrombin generation, but the usual mechanisms preventing unbalanced thrombus formation are impaired. The fibrinolytic system is activated, and plasmin begins to cleave fibrinogen and fibrin into fibrin degradation products (FDPs). DIC is not a disease entity but rather a clinical complication of other problems:

- Obstetric conditions (e.g., amniotic fluid embolism, placental abruption, retained fetus syndrome, eclampsia, saline-induced abortion)
- Septicemia and viremia (e.g., bacterial infections, cytomegalovirus, hepatitis, varicella, human immunodeficiency virus)
- Disseminated malignancy and leukemia
- Transfusion reactions, crush injury, tissue necrosis, and burns
- Liver disease (e.g., obstructive jaundice, acute hepatic failure)

**23. What tests are used for the diagnosis of disseminated intravascular coagulation?**

There is no one diagnostic test. More often than not, both PT and PTT are elevated, and platelet count is reduced. Hypofibrinogenemia is common. In 85% to 100% of patients FDPs are elevated. One measured form of FDP is the D-dimer. D-dimer is a neoantigen formed by the action of thrombin in converting fibrinogen to cross-linked fibrin. It is specific for FDPs formed from the digestion of cross-linked fibrin by plasmin.

**24. Describe the treatment of disseminated intravascular coagulation**

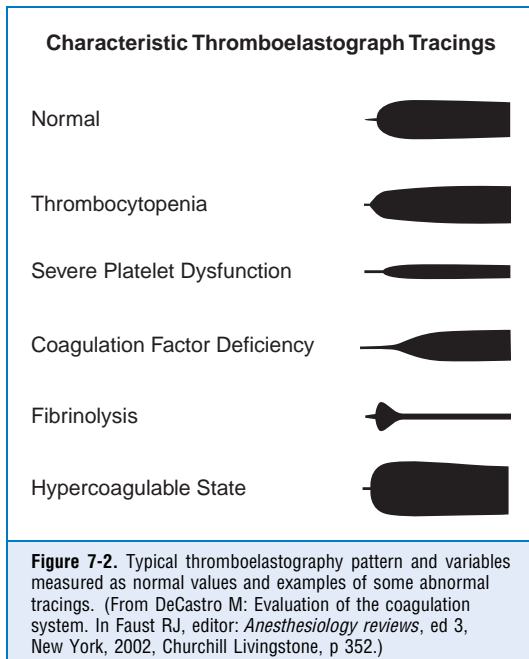
The most important measure is to treat the underlying disease process. Often specific blood components are depleted and require repletion based on tests of coagulation. Occasionally, if bleeding persists despite conventional treatment, antifibrinolytic therapy with  $\epsilon$ -aminocaproic acid should be considered, but only if the intravascular coagulation process is under control and residual fibrinolysis continues.

**25. What is recombinant factor VIIa (NovoSeven)?**

Factor VIIa complexes with tissue factor to activate factors IX and X. Factor Xa subsequently aids in the conversion of prothrombin to thrombin, which leads to the activation of fibrinogen to fibrin. The beneficial effects of recombinant factor VIIa have been demonstrated in the settings of hemophilia, liver transplantation, major trauma, intracerebral hemorrhage, gastrointestinal bleeding, cardiac surgery, and warfarin-induced bleeding when traditional approaches to the bleeding patient have proved to be marginally effective or noneffective.

**26. Discuss the basic principles of thrombelastography.**

The thromboelastography (TEG) measures the viscoelastic properties of blood as it is induced to clot in a low shear environment resembling venous flow, providing some measure of clot strength and stability, including the time to initial clot formation, the acceleration phase, strengthening, retraction, and clot lysis. A sample of celite-activated whole blood is placed into a prewarmed cuvette. A suspended piston is then lowered into the cuvette that rotates back and forth. The forming clot transmits its movement on to the suspended piston. A weak clot stretches and delays the arc movement of the piston and is graphically expressed as a narrow TEG. Conversely, a strong clot will move the piston simultaneously in proportion to the movements of the cuvette, creating a thick TEG.



**27. Discuss the parameters measured by thromboelastography.**

There are five parameters of the TEG tracing: R, k, alpha angle, MA, and MA60 (Figure 7-2).

- R: Period of time from the initiation of the test to initial fibrin formation
- k: Time from the beginning of clot formation until the amplitude of TEG reaches 20 mm, representing the dynamics of clot formation
- Alpha angle: Angle between the line in the middle of the TEG tracing and the line tangential to the developing body of the tracing, representing the kinetics of fibrin cross-linking
- MA (maximum amplitude): Reflects the strength of the clot, which depends on the number and function of platelets and their interaction with fibrin
- MA60: Measures the rate of amplitude reduction 60 minutes after MA, representing the stability of the clot (Figure 7-2)

**WEBSITE**

<http://www.ispub.com>

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# AIRWAY MANAGEMENT

*James Duke, MD, MBA*

## 1. List several indications for endotracheal intubation.

- General anesthesia but there are alternatives to endotracheal intubation
- Positive-pressure ventilation
- Protecting the respiratory tract from aspiration of gastric contents
- Surgical procedures in which the anesthesiologist cannot easily control the airway (e.g., prone, sitting, or lateral decubitus procedures)
- Situations in which neuromuscular paralysis has been instituted
- Surgical procedures within the chest, abdomen, or cranium
- When intracranial hypertension must be treated
- Protecting a healthy lung from a diseased lung to ensure its continued performance (e.g., hemoptysis, empyema, pulmonary abscess)
- Severe pulmonary and multisystem injury associated with respiratory failure (e.g., severe sepsis, airway obstruction, hypoxemia, and hypercarbia of various etiologies)

## 2. Review objective measures suggesting the need to perform endotracheal intubation.

These objective measures are often used for patients in critical-care settings, not necessarily perioperatively. But they also are useful in determining which patients should not be extubated after surgery.

- Respiratory rate  $>35$  breaths/min
- Vital capacity  $<5$  ml/kg in adults and 10 ml/kg in children
- Inability to generate a negative inspiratory force of 20 mm Hg
- Arterial partial pressure of oxygen ( $\text{PaO}_2$ )  $<70$  mm Hg on 40% oxygen
- Alveolar-arterial (A-a) gradient  $>350$  mm Hg on 100%  $\text{O}_2$
- Arterial partial pressure of carbon dioxide ( $\text{PaCO}_2$ )  $>55$  mm Hg (except in chronic retainers)
- Dead space ( $V_D/V_T$ )  $>0.6$

## 3. What historical information might be useful in assessing a patient's airway?

Patients should be questioned about adverse events related to previous airway management episodes. For instance, have they ever been informed by an anesthesiologist that they had an airway management problem (e.g., “difficult to ventilate, difficult to intubate”)? Have they had a tracheostomy or other surgery or radiation about the face and neck? Have they sustained significant burns to these areas? Do they have obstructive sleep apnea, snoring, or temporomandibular joint (TMJ) dysfunction? Review of prior anesthetic records is always helpful.

## 4. Describe the physical examination of the oral cavity.

Examine the mouth and oral cavity, noting the extent and symmetry of opening (three fingerbreadths is optimal), the health of the teeth (loose, missing, or cracked teeth should be documented), and the presence of dental appliances. Prominent buck teeth may interfere with the use of a laryngoscope. The size of the tongue should be noted (large tongues rarely make airway management impossible, only more difficult), as should the arch of the palate (high-arched palates have been associated with difficulty in visualizing the larynx).

## 5. Review the Mallampati classification.

The appearance of the posterior pharynx may predict difficulty in laryngoscopy and visualization of the larynx. It has been noted through meta-analysis that, when used alone, the Mallampati test has limited accuracy for predicting the difficult airway and thus it is clear that a comprehensive airway examination, not just a Mallampati classification, is necessary to identify patients who may be difficult to intubate. This classification also does not address the issue of ease of mask ventilation.

Mallampati has organized patients into classes I to IV based on the visualized structures (Figure 8-1). Visualization of fewer anatomic structures (particularly classes III and IV) is associated with difficult laryngeal exposure. With the patient *sitting upright*, mouth fully open, and tongue protruding, classification is based on visualization of the following structures:

- Class I: Pharyngeal pillars, entire palate, and uvula are visible.
- Class II: Pharyngeal pillars and soft palate are visible, with visualization of the uvula obstructed by the tongue.
- Class III: Soft palate is visible, but pharyngeal pillars and uvula are not visualized.
- Class IV: Only the hard palate is visible; the soft palate, pillars, and uvula are not visualized.

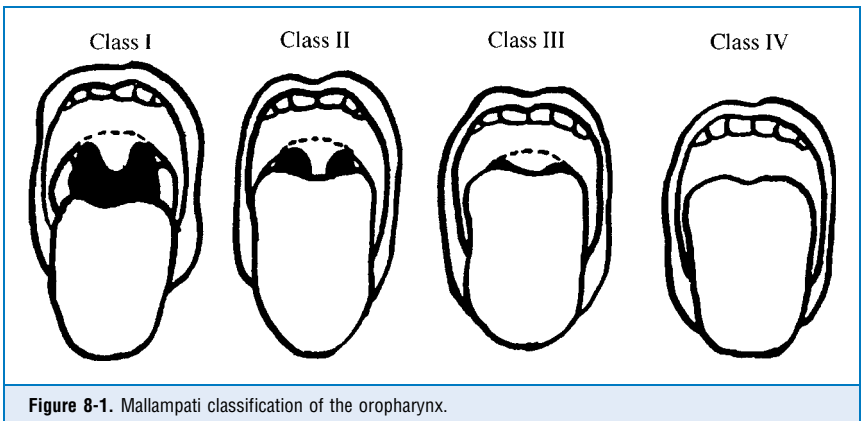


Figure 8-1. Mallampati classification of the oropharynx.

## 6. What is the next step after examination of the oral cavity?

After examination of the oral cavity is completed, attention is directed at the size of the mandible and quality of TMJ function. A short mandible (shorter than three fingerbreadths) as measured from the mental process to the prominence of the thyroid cartilage (thyromental distance) suggests difficulty in visualizing the larynx. Patients with TMJ dysfunction may have asymmetry or limitations in opening the mouth and popping or clicking. Manipulation of the jaw in preparation for laryngoscopy may worsen symptoms after surgery. Curiously some patients with TMJ dysfunction have greater difficulty opening the mouth after anesthetic induction and neuromuscular paralysis than when they are awake and cooperative.

## 7. Describe the examination of the neck.

Evidence of prior surgeries (especially tracheostomy) or significant burns is noted. Does the patient have abnormal masses (e.g., hematoma, abscess, cellulitis or edema, lymphadenopathy, goiter, tumor, soft-tissue swelling) or tracheal deviation? A short or thick neck may prove problematic. A neck circumference of greater than 18 inches has been reported to be associated with difficult airways. Large breasts (e.g., a parturient) may make using the laryngoscope itself difficult, and short-handled laryngoscope handles have been developed with this in mind.

It is also important to have the patient demonstrate the range of motion of the head and neck. Preparation for laryngoscopy requires extension of the neck to facilitate visualization. Elderly patients and patients with cervical fusions may have limited motion. Furthermore, patients with cervical spine disease (disk disease or cervical instability, as in rheumatoid arthritis) may develop neurologic symptoms with motion of the neck. Radiologic views of the neck in flexion and extension may reveal cervical instability in such patients.

It is my experience that the preoperative assessment of range of motion in patients with prior cervical spine surgery does not equate well with their mobility after anesthetized and paralyzed, suggesting that in this patient group wariness is the best policy and advanced airway techniques, as will be described, should be considered.

Particularly in patients with pathology of the head and neck such as laryngeal cancer, it is valuable to know the results of nasolaryngoscopy performed by otolaryngologists. (This is always the case in ear, nose, and throat surgery—never assume anything. Always work closely and preemptively with the surgeon to determine how the airway should be managed.) Finally, if history suggests dynamic airway obstruction (as in intrathoracic or extrathoracic masses), pulmonary function tests, including flow-volume loops, may alert the clinician to the potential for loss of airway once paralytic agents are administered.

#### 8. Discuss the anatomy of the larynx.

The larynx, located in adults at cervical levels 4 to 6, protects the entrance of the respiratory tract and allows phonation. It is composed of three unpaired cartilages (thyroid, cricoid, and epiglottis) and three paired cartilages (arytenoid, corniculate, and cuneiform). The thyroid cartilage is the largest and most prominent, forming the anterior and lateral walls. The cricoid cartilage is shaped like a signet ring, faces posteriorly, and is the only complete cartilaginous ring of the laryngotracheal tree. The cricothyroid membrane connects these structures anteriorly. The epiglottis extends superiorly into the hypopharynx and covers the entrance of the larynx during swallowing. The corniculate and cuneiform pairs of cartilages are relatively small and do not figure prominently in the laryngoscopic appearance of the larynx or in its function. The arytenoid cartilages articulate on the posterior aspect of the larynx and are the posterior attachments of the vocal ligaments (or vocal cords). Identification of the arytenoid cartilages may be important during laryngoscopy. In a patient with an *anterior* airway the arytenoids may be the only visible structures. Finally the vocal cords attach anteriorly to the thyroid cartilage.

#### 9. Describe the innervation and blood supply to the larynx.

The superior and recurrent laryngeal nerves, both branches of the vagus nerve, innervate the larynx. The superior laryngeal nerves decussate into internal and external branches. The internal branches provide sensory innervation of the larynx above the vocal cords, whereas the external branches provide motor innervation to the cricothyroid muscle, a tensor of the vocal cords. The recurrent laryngeal nerves provide sensory innervation below the level of the cords and motor innervation of the posterior cricoarytenoid muscles, the only abductors of the vocal cords. The glossopharyngeal or ninth cranial nerve provides sensory innervation to the vallecula (the space anterior to the epiglottis) and the base of the tongue.

Arteries that supply the larynx include the superior laryngeal (a branch of the superior thyroid artery) and inferior laryngeal (a branch of the inferior thyroid artery). Venous drainage follows the same pattern as the arteries; there is also ample lymphatic drainage.

#### 10. Summarize the various instruments available to facilitate oxygenation.

Oxygen supplementation is always a priority when patients are sedated or anesthetized. Devices range from nasal cannulas, face tents, and simple masks to masks with reservoirs and masks that can be used to deliver positive-pressure ventilation. Their limitation is the oxygen concentration that can be delivered effectively.

### 11. What are the benefits of oral and nasal airways?

Oral airways are usually constructed of hard plastic; they are available in numerous sizes and shaped to curve behind the tongue, lifting it off the posterior pharynx. The importance of these simple devices cannot be overstated because the tongue is the most frequent cause of airway obstruction, particularly in obtunded patients. Nasal airways (*trumpets*) can be gently inserted down the nasal passages into the nasopharynx and are better tolerated than oral airways in awake or lightly anesthetized patients. However, epistaxis is a risk.

### 12. How are laryngoscopes used?

Laryngoscopes are usually left-handed tools designed to facilitate visualization of the larynx. Short handles work best for obese patients or those with thick chests or large breasts. Laryngoscope blades come in various styles and sizes. The most commonly used blades include the curved Macintosh and the straight Miller blades. The curved blades are inserted into the vallecula, immediately anterior to the epiglottis, which is literally flipped out of the visual axis to expose the laryngeal opening. The Miller blade is inserted past the epiglottis, which is simply lifted out of the way of laryngeal viewing.

### 13. What structures must be aligned to accomplish visualization of the larynx?

To directly visualize the larynx it is necessary to align the oral, pharyngeal, and laryngeal axes. To facilitate this process, elevating the head on a small pillow and extending the head at the atlanto-occipital axes are necessary (Figure 8-2).

### 14. What is a GlideScope?

Different laryngoscope blades have been discussed, and it should be no surprise that various arrangements of laryngoscope handles and blades have been developed. The GlideScope Video Laryngoscope (Verathon, Inc., Bothell, WA) has a one-piece rigid plastic handle and curved blade; at the tip of the blade is not only the light but a camera eye. The image is transmitted to a screen at bedside. By using the GlideScope, it has not been necessary to align the three axes as discussed in the prior question. Thus the patient might easily be intubated with the neck in a neutral position. In addition, in patients in whom, on conventional laryngoscopy, the laryngeal aperture is anterior to the visual axis, the GlideScope facilitates visualization of the larynx and endotracheal intubation. The GlideScope has proven to be an outstanding addition to the airway management armamentarium.

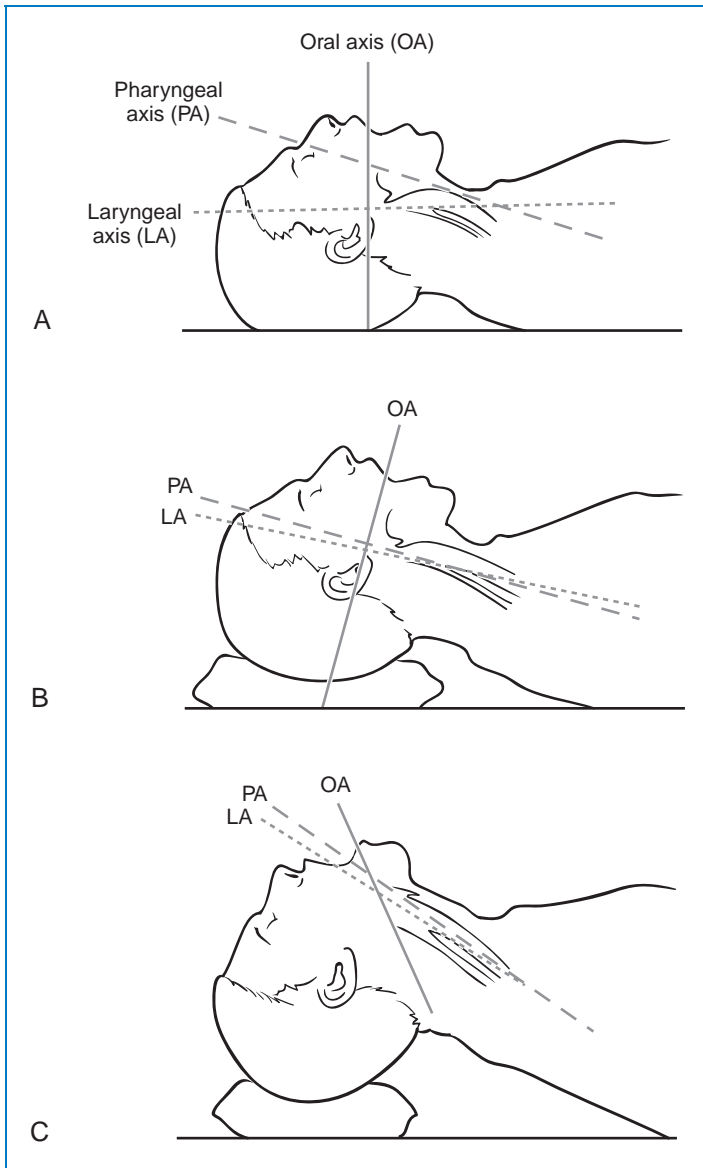
## KEY POINTS: AIRWAY MANAGEMENT



1. A thorough airway examination and identification of the patient with a potentially difficult airway are of paramount importance.
2. The *difficult-to-ventilate, difficult-to-intubate* scenario must be avoided if possible.
3. An organized approach, as reflected in the American Society of Anesthesiologists' Difficult Airway Algorithm, is necessary and facilitates high-quality care for patients with airway management difficulties.

### 15. What endotracheal tubes are available?

Endotracheal tubes come in a multitude of sizes and shapes. They are commonly manufactured from polyvinyl chloride, with a radiopaque line from top to bottom; standard-size connectors for anesthesia circuits or resuscitation bags; a high-volume, low-pressure cuff and pilot balloon; and a hole in the beveled, distal end (the Murphy eye). Internal diameter



**Figure 8-2.** Schematic diagram demonstrating the head position for endotracheal intubation. **A**, Successful direct laryngoscopy for exposure of the glottic opening requires alignment of the oral, pharyngeal, and laryngeal axes. **B**, Elevation of the head about 10 cm with pads below the occiput and with the shoulders remaining on the table aligns the laryngeal and pharyngeal axes. **C**, Subsequent head extension at the atlanto-occipital joint creates the shortest distance and most nearly straight line from the incisor teeth to glottic opening. (From Gal TJ: Airway management. In Miller RD: *Miller's anesthesia*, ed 6, Philadelphia, 2005, Churchill Livingstone, p 1622.)



ranges from 2 to 10 mm in half-millimeter increments. Endotracheal tubes may be reinforced with wire, designed with laser applications in mind, or unusually shaped so they are directed away from the surgical site (oral or nasal RAE tubes).

#### 16. What are laryngeal mask airways?

Laryngeal mask airways (LMAs) maintain a patent airway during anesthesia when endotracheal intubation is neither required nor desired (e.g., asthmatic patients, the lead soprano in the local opera company). Increasingly LMAs are being substituted for endotracheal tubes. They are an important part of the management of difficult airways and patients can be intubated through a well-placed LMA.

#### 17. What other airway management devices are available?

Light wands may be useful for blind intubation of the trachea. The technique is termed *blind* because the laryngeal opening is not seen directly. When light is well transilluminated through the neck (the jack-o'-lantern effect), the end of the endotracheal tube is at the entrance of the larynx, and the tube can be threaded off the wand and into the trachea in a blind fashion. Gum elastic bougies are flexible, somewhat malleable stylets with an anteriorly directed, bent tip that may be useful for intubating a tracheal opening anterior to the visual axis. Fiberoptic endoscopy is commonly used to facilitate difficult intubations and allows endotracheal tube insertion under direct visualization. Finally the trachea may be intubated using a retrograde technique. In simplistic terms a long Seldinger-type wire is introduced through a catheter that punctures the cricothyroid membrane. The wire is directed superiorly and brought out through the nose or mouth, and an endotracheal tube is threaded over the wire and lowered into the trachea.

#### 18. Describe the indications for an awake intubation.

If the physical examination leaves in question the ability to ventilate and intubate once the patient is anesthetized and paralyzed, consideration should be given to awake intubation. Patients with a previous history of difficult intubation, acute processes that compromise the airway (e.g., soft-tissue infections of the head and neck, hematomas, mandibular fractures, or other significant facial deformities), morbid obesity, or cancer involving the larynx are reasonable candidates for awake intubation.

#### 19. How is the patient prepared for awake intubation?

A frank discussion with the patient is necessary because patient safety is the priority. The anticipated difficulty of airway management and the risks of proceeding with anesthesia without previously securing a competent airway are conveyed in clear terms. Despite our best efforts to provide topical anesthesia and sedation, sometimes the procedure is uncomfortable for the patient, and this should be discussed as well.

#### 20. How is awake intubation performed?

In preparing the patient, administration of glycopyrrolate, 0.2 to 0.4 mg 30 minutes before the procedure, is useful to reduce secretions. Many clinicians also administer nebulized lidocaine to provide topical anesthesia of the entire airway, although many techniques are available to provide airway anesthesia. Once the patient arrives in the operating suite, standard anesthetic monitors are applied, and supplemental oxygen is administered. The patient is sedated with appropriate agents (e.g., opioid, benzodiazepine, propofol). The level of sedation is titrated so the patient is not rendered obtunded, apneic, or unable to protect the airway (Table 8-1).

The route of intubation may be oral or nasal, depending on surgical needs and patient factors. If nasal intubation is planned, nasal and nasopharyngeal mucosa must be anesthetized; vasoconstrictor substances are applied to prevent epistaxis. Often nasal trumpets with lidocaine ointment are gently inserted to dilate the nasal passages. A transtracheal injection of lidocaine is often performed via needle puncture of the cricothyroid membrane. Nerve blocks are also useful to provide topical anesthesia (see the following question).

TABLE 8-1. USEFUL MEDICATIONS FOR AWAKE INTUBATIONS

Medication	Purpose	Dose	Route
Glycopyrrolate	Antisialagogue	0.2–0.4 mg	IV or IM
Midazolam	Sedation/amnesia	1–4 mg	IV
Fentanyl	Analgesic	50–250 mcg	IV
Cocaine	Topical anesthesia and vasoconstriction	40–160 mg	Intranasal
1% Phenylephrine	Vasoconstriction	Spray	Intranasal
2% Viscous lidocaine	Topical anesthesia	5–20 ml	Orally
Cetacaine spray	Topical anesthesia	2–4 sprays	Orally
Lidocaine 1%–4%	Airway anesthesia	2–3 ml	Transtracheal or nerve block

*IM*, Intramuscular; *IV*, intravenous.

Once an adequate level of sedation and topical anesthesia is achieved, the endotracheal tube is loaded on the fiberoptic endoscope. The endoscope is gently inserted into the chosen passage, directed past the epiglottis, through the larynx, into the trachea, visualizing tracheal rings and carina. The endotracheal tube is passed into the trachea, and the endoscope is removed. Breath sounds and end-tidal carbon dioxide are confirmed, and general anesthesia is begun.

### 21. What nerve blocks are useful when awake intubation is planned?

The glossopharyngeal nerve, which provides sensory innervation to the base of the tongue and the vallecula, may be blocked by transmucosal local anesthetic injection at the base of the tonsillar pillars. The superior laryngeal nerve provides sensory innervation of the larynx above the vocal cords and may be blocked by injection just below the greater cornu of the hyoid. Care must be taken to aspirate before injection because this is carotid artery territory. Many clinicians are reluctant to block the superior laryngeal nerves and perform a transtracheal block in patients with a full stomach because all protective airway reflexes are lost. Such patients are unable to protect themselves from aspiration if gastric contents are regurgitated.

### 22. What are predictors of difficult mask ventilation? Why is this important?

There is much focus on intubation and predictors of difficult intubation. It should be recognized that the ability to mask-ventilate a patient is equally and perhaps more important. For instance, if it is determined at the time of intubation that perhaps a patient is impossible to intubate by conventional laryngoscopy, if the patient's oxygen saturations can be maintained through mask ventilation, the situation remains under a degree of control while help and additional airway management tools are summoned. However, if you have a patient who is difficult to intubate and ventilate, the situation is not under control, and the patient is at risk for hypoxic injury.

Between 1% and 2% of patients will be difficult to ventilate. Predictors of difficult mask ventilation include limitations in mandibular protrusion; a thyromental distance less than 6 cm; advanced age (older than 57 years in one study); abnormal neck anatomy; sleep apnea, snoring; body mass index of 30 kg/m<sup>2</sup> or greater; and the presence of a beard. A beard may in of itself make mask ventilation difficult, but it may also hide a small thyromental distance. Some men may choose to wear a beard because they don't care for their weak chin facies, which is another way of saying that they have a small thyromental distance.

**23. The patient has been anesthetized and paralyzed, but the airway is difficult to intubate. Is there an organized approach to handling this problem?**

The patient who is difficult to ventilate and intubate is quite possibly the most serious problem faced by anesthesiologists because hypoxic brain injuries and cardiac arrest are real possibilities in this scenario. It has been established that persistent failed intubation attempts are associated with death. Although a thorough history and physical examination are likely to identify the majority of patients with difficult airways, unanticipated problems occasionally present. Only through preplanning and practiced algorithms are such situations managed optimally. The American Society of Anesthesiologists has prepared a difficult airway algorithm (Figure 8-3) to assist the clinician. The relative merits of different management options (surgical vs. nonsurgical airway, awake vs. postinduction intubation, spontaneous vs. assisted ventilation) are weighed. Once these decisions have been made, primary and alternative strategies are laid out to assist in stepwise management. This algorithm deserves close and repeated inspection before the anesthesiologist attempts to manage such problems. This is no time for heroism; if intubation or ventilation is difficult, call for help.

It is always wise to consider the merits of regional anesthesia to avoid a known or suspected difficult airway. However, in patients with a difficult airway, the use of regional anesthesia does not relieve the anesthesiologist of some planning for airway difficulties.

Death and central nervous system injuries remain the leading cause of adverse outcomes in the perioperative setting. However, it has been noted through analysis of closed medicolegal claims that the incidence of these injuries has decreased since these algorithms and advanced airway techniques have been introduced.

**24. Describe the technique of transtracheal ventilation and its limitations.**

Transtracheal ventilation is a temporizing measure if mask ventilation becomes inadequate. A catheter (12- or 14-G) is inserted through the cricothyroid membrane and then connected to a jet-type (Sanders) ventilator capable of delivering oxygen under pressure. The gas is delivered intermittently by a handheld actuator. The duration of ventilation is best assessed by watching the rise and fall of the chest; an inspiratory to expiratory ratio of 1:4 seconds is recommended. Usually oxygenation improves rapidly; however, patients frequently cannot expire fully, perhaps because of airway obstruction, and can develop increased intrathoracic pressures, putting them at risk for barotrauma or decreased cardiac output. Carbon dioxide retention limits the duration of the usefulness of the technique.

**25. What are criteria for extubation?**

The patient should be awake and responsive with stable vital signs. Adequate reversal of neuromuscular blockade must be established as demonstrated by sustained head lift. In equivocal situations negative inspiratory force should exceed 20 mm Hg (see Question 2).

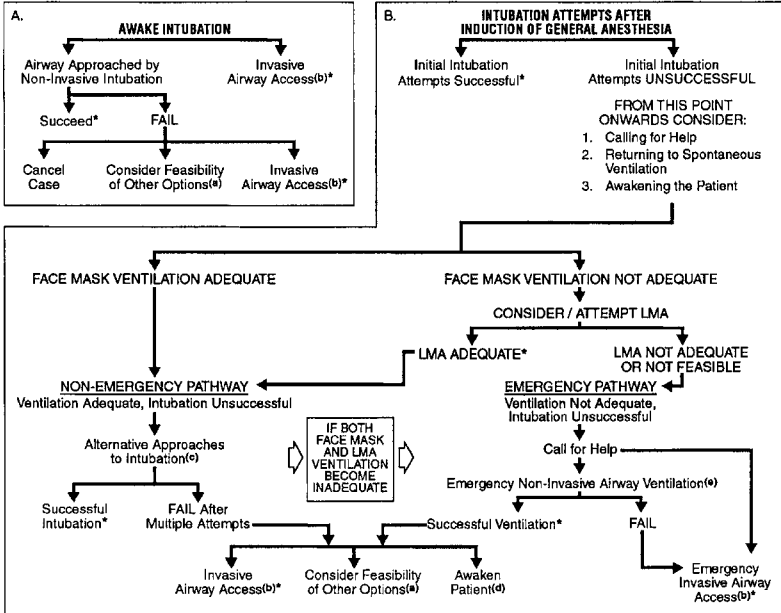
**26. What is rapid-sequence induction? Which patients are best managed in this fashion?**

It is easiest to appreciate the distinctions of rapid-sequence induction (RSI) if an induction under nonrapid-sequence conditions is understood. Ordinarily the patient has fasted for at least 6 to 8 hours and is not at risk for pulmonary aspiration of gastric contents. The patient is preoxygenated, and an anesthetic induction agent is administered. Once it is established that the patient can be mask-ventilated satisfactorily, a muscle relaxant is given. The patient is then mask-ventilated until complete paralysis is ensured by nerve stimulation. Laryngoscopy and endotracheal intubation are undertaken, and the case proceeds.

In contrast, RSI is undertaken in patients who are thought to be at risk for pulmonary aspiration of gastric contents. Patients with full stomachs are at risk; other risk factors include pregnancy, diabetes, pain, opioid analgesics, recent traumatic injury, intoxication, and pathologic involvement of the gastrointestinal tract such as small bowel obstruction.

- Assess the likelihood and clinical impact of basic management problems:
  - Difficult Ventilation
  - Difficult Intubation
  - Difficulty with Patient Cooperation or Consent
  - Difficult Tracheostomy
- Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management
- Consider the relative merits and feasibility of basic management choices:
  - Awake Intubation vs. Intubation Attempts After Induction of General Anesthesia
  - Non-Invasive Technique for Initial Approach to Intubation vs. Invasive Technique for Initial Approach to Intubation
  - Preservation of Spontaneous Ventilation vs. Ablation of Spontaneous Ventilation

4. Develop primary and alternative strategies:



\* Confirm ventilation, tracheal intubation, or LMA placement with exhaled CO<sub>2</sub>

a. Other options include (but are not limited to): surgery utilizing face mask or LMA anesthesia, local anesthesia infiltration or regional nerve blockade. Pursuit of these options usually implies that mask ventilation will not be problematic. Therefore, these options may be of limited value if this step in the algorithm has been reached via the Emergency Pathway.

b. Invasive airway access includes surgical or percutaneous tracheostomy or cricothyrotomy.

c. Alternative non-invasive approaches to difficult intubation include (but are not limited to): use of different laryngoscope blades, LMA as an intubation conduit (with or without fiberoptic guidance), fiberoptic intubation, intubating stylet or tube changer, light wand, retrograde intubation, and blind oral or nasal intubation.

d. Consider re-preparation of the patient for awake intubation or canceling surgery.

e. Options for emergency non-invasive airway ventilation include (but are not limited to): rigid bronchoscope, esophageal-tracheal combi-tube ventilation, or transtracheal jet ventilation.

Figure 8-3. Management of the difficult airway. LMA, Laryngeal mask airway. (From the American Society of Anesthesiologists.)

Patients with full stomachs should be premedicated with agents that reduce the acidity and volume of gastric contents such as histamine-2 receptor blockers (ranitidine, cimetidine), nonparticulate antacids (Bicitra or Alka-Seltzer), and gastrokinetics (metoclopramide).

## 27. How is RSI performed?

The goal of RSI is to secure and control the airway rapidly. The patient is preoxygenated. An induction agent is administered, followed quickly by a rapid-acting relaxant, either succinylcholine or larger doses of rocuronium. Simultaneously an assistant applies pressure

to the cricoid cartilage (the only complete cartilaginous ring of the respiratory tract), which closes off the esophagus and prevents entry of regurgitated gastric contents into the trachea and lungs. Known as the Sellick maneuver, such pressure is maintained until the airway is protected by tracheal intubation.

**28. What is the purpose of preoxygenation before the induction of anesthesia?**

Preoxygenation is an important part of any general anesthetic. Inspired room air contains approximately 21% O<sub>2</sub>, with the remainder being mostly nitrogen (N<sub>2</sub>). Not many people can go more than a few minutes without ventilation before desaturation occurs. If patients breathe 100% oxygen for several minutes, they may not desaturate for up to 3 to 5 minutes because the functional residual capacity (FRC) of the lung has been completely washed of N<sub>2</sub> and filled with O<sub>2</sub>.

**29. Anesthesiologists routinely deliver 100% oxygen for a few minutes before extubation. What is the logic behind this action and why might an FiO<sub>2</sub> of 80% be better?**

Patients emerging from general anesthesia may develop airway obstruction or disorganized breathing patterns. A 5-minute period of inspiring 100% oxygenation is sufficient to fill the patient's FRC with 100% oxygen, establishing a depot of oxygen should airway obstruction or other respiratory difficulties accompany extubation. Unfortunately 100% oxygen promotes atelectasis, reducing the surface area available for gas exchange and causing intrapulmonary shunting. Although an FiO<sub>2</sub> of 0.8 appears to prevent atelectasis, it is not clear whether the small increase in atelectasis associated with breathing 100% oxygen is of clinical importance. Until this is demonstrated, the best practice is to administer 100% oxygen before extubation.

## WEBSITE



<http://www.asahq.org>

## SUGGESTED READINGS

1. American Society of Anesthesiologists. Practice guidelines for management of the difficult airway: an updated report by the ASA Task Force on management of the difficult airway. *Anesthesiology* 98:1269–1277, 2003.
2. Kheterpal S, Han R, Tremper KK, et al: Incidence and predictors of difficult and impossible mask ventilation. *Anesthesiology* 105:885–891, 2006.
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# PULMONARY FUNCTION TESTING

James Duke, MD, MBA

## 1. What are pulmonary function tests and how are they used?

The term *pulmonary function test (PFT)* refers to a standardized measurement of a patient's airflow (spirometry), lung volumes, and diffusing capacity for inspired carbon monoxide (DLCO). These values are always reported as a percentage of a predicted normal value, which is calculated on the basis of the age and height of the patient. Used in combination with the history, physical examination, blood gas analysis, and chest radiograph, PFTs facilitate the classification of respiratory disease into obstructive, restrictive, or mixed disorders.

## 2. What is the benefit of obtaining pulmonary function tests?

The primary goal of preoperative pulmonary function testing, also called *spirometry*, is to recognize patients at high or prohibitive risk for postoperative pulmonary complications. Abnormal PFTs identify patients who will benefit from aggressive perioperative pulmonary therapy and in whom surgery should be avoided entirely. However, no single test or combination of tests will definitely predict which patients will develop postoperative pulmonary complications.

## 3. Besides abnormal pulmonary function tests, what are recognized risk factors for postoperative pulmonary complications?

Risk factors for pulmonary complications include:

- Age >70 years
- Obesity
- Upper abdominal or thoracic surgery
- History of lung disease
- Greater than 20-pack/year history of smoking
- Resection of an anterior mediastinal mass

## 4. What factors should be taken into consideration when interpreting pulmonary function tests?

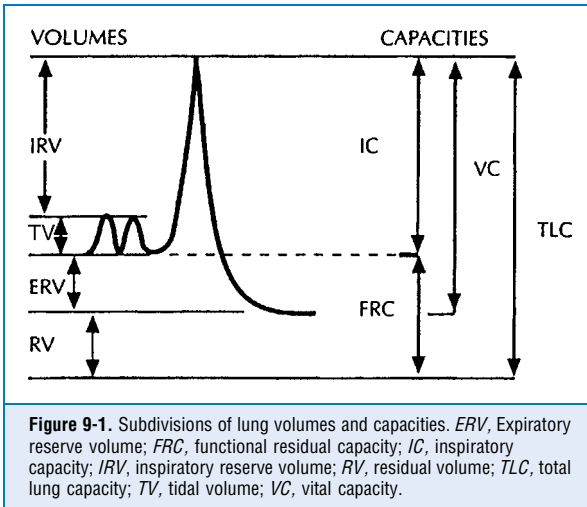
The predicted PFT values are based on test results from healthy individuals and vary according to age, height, gender, and ethnicity. For example, vital capacity and total lung capacity are 13% to 15% lower in blacks than in whites. Reliable testing requires patient cooperation and a skilled technician.

## 5. Describe standard lung volumes.

The tidal volume (TV) is the volume of air inhaled and exhaled with each normal breath. Inspiratory reserve volume (IRV) is the volume of air that can be maximally inhaled beyond a normal TV. Expiratory reserve volume (ERV) is the maximal volume of air that can be exhaled beyond a normal TV. Residual volume (RV) is the volume of air that remains in the lung after maximal expiration (Figure 9-1).

## 6. What are the lung capacities?

Lung capacities are composed of two or more lung volumes. Total lung capacity (TLC) is the sum of IRV, tidal volume (TV), ERV, and RV. Vital capacity (VC) is the sum of IRV, TV, and ERV. Inspiratory capacity (IC) is the sum of IRV and TV. Functional residual capacity (FRC) is the volume of air in the lung at the end of a normal expiration and is the sum of RV and ERV (see Figure 9-1).



### 7. What techniques are used to determine functional residual capacity?

Measuring FRC is the cornerstone for determining the remainder of the lung volumes. The FRC can be measured by three different techniques:

- Helium equilibration/dilution
- Nitrogen washout
- Body plethysmography

Plethysmography is most accurate for determining FRC in patients with obstructive airway disease and applies Boyle's law, which states that the volume of gas in a closed space varies inversely with the pressure to which it is subjected. All measurements of FRC, if performed correctly, are independent of patient effort.

### 8. What information is obtained from spirometry?

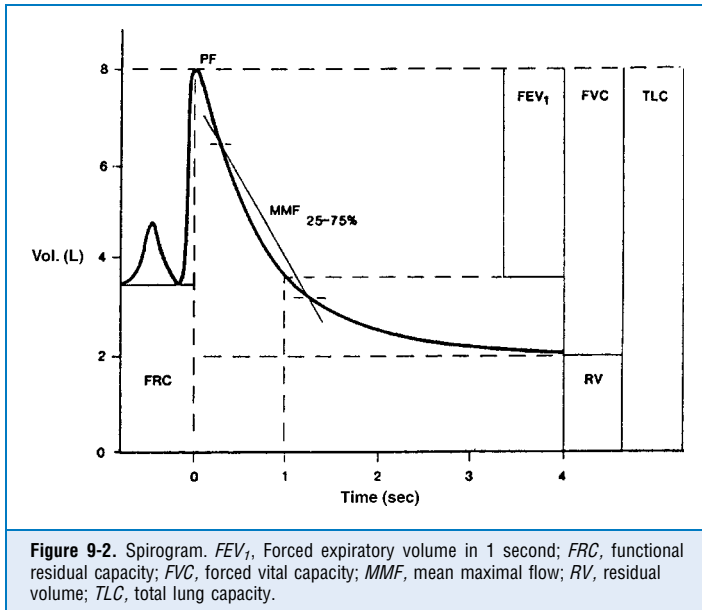
Spirometry is the foundation of pulmonary function testing and provides timed measurements of expired lung volumes (Figure 9-2). With automated equipment it is possible to interpret more than 15 different measurements from spirometry alone. Forced vital capacity (FVC), forced expiratory volume in 1 second ( $FEV_1$ ),  $FEV_1/FVC$  ratio, and flow between 25% and 75% of the FVC (mean maximal flow [ $MMF$ ]<sub>25-75</sub>) are the most clinically helpful indices obtained from spirometry. Although spirometry demonstrates airflow limitations, it does not determine the cause (e.g., airway obstruction vs. decreased alveolar elastic recoil vs. decreased muscle strength). It is also effort dependent and requires a motivated patient.

### 9. What is the diffusing capacity for the single-breath diffusion capacity (DLCO)?

The DLCO measures the rate of uptake of the nonphysiologic gas carbon monoxide (CO). CO is used because of its affinity for hemoglobin and because it reflects the diffusing capacity of the physiologic gases oxygen and carbon dioxide. DLCO is dependent on membrane-diffusing capacity and the pulmonary vasculature and thus is a measure of functioning alveolar capillary units. This test has been used as an indicator of suitability for pulmonary resection and a predictor of postoperative pulmonary morbidity.

### 10. What disease states cause a decrease in DLCO?

Any disease process that compromises the alveolar capillary unit may cause a decrease in DLCO. Three major types of pulmonary disorders cause a decrease in DLCO:



- Obstructive airway disease
- Interstitial lung disease
- Pulmonary vascular disease

### 11. What disease states cause an increase in DLCO?

In general, conditions that cause a relative increase in the hemoglobin concentration result in an increased DLCO. Congestive heart failure, asthma, and diffuse pulmonary hemorrhage are the most common causes of an increased DLCO. A perforated tympanic membrane may cause an artifactually high DLCO by permitting an escape of CO by a nonpulmonary route.

### 12. Review obstructive airway diseases and their pulmonary function test abnormalities.

Obstructive airway diseases, including asthma, chronic bronchitis, emphysema, cystic fibrosis, and bronchiolitis, exhibit diminished expiratory airflow and involve airways distal to the carina. The  $FEV_1$ ,  $FEV_1/FVC$  ratio, and the forced expiratory flow at 25% to 75% of FVC ( $FEF_{25-75}$ ) are below predicted values. A decreased  $FEF_{25-75}$  reflects collapse of the small airways and is a sensitive indicator of early airway obstruction. The FVC may be normal or decreased as a result of respiratory muscle weakness or dynamic airway collapse with subsequent air trapping. Table 9-1 compares the alterations in measures of lung function in various obstructive lung diseases. Table 9-2 grades the severity of obstruction based on the  $FEV_1/FVC$  ratio.

### 13. Review restrictive lung disorders and their associated pulmonary function test abnormalities.

Disorders that result in decreased lung volumes include abnormal chest cage configuration, respiratory muscle weakness, loss of alveolar air space (e.g., pulmonary fibrosis, pneumonia), and encroachment of the lung space by disorders of the pleural cavity (e.g., effusion, tumor). The characteristic restrictive pattern is a reduction in lung volumes, particularly TLC and VC. Airflow rates can be normal or increased.



TABLE 9-1. ALTERATIONS IN MEASURES OF LUNG FUNCTION IN OBSTRUCTIVE LUNG DISEASE

Measure	Asthma	Bronchitis	Emphysema
TLC	Increased	Normal or increased	Increased
VC	Normal or decreased	Normal or decreased	Normal or decreased
RV	Increased	Increased	Increased
FRC	Increased	Increased	Increased
DLCO	No change or increased	No change or decreased	Decreased
FEV <sub>1</sub>	Decreased	Decreased	Decreased

Adapted from Taylor AE et al: *Clinical respiratory physiology*, Philadelphia, 1989, Saunders.  
 DLCO, Diffusing capacity for inspired carbon monoxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity; VC, vital capacity.

TABLE 9-2. SEVERITY OF OBSTRUCTIVE AND RESTRICTIVE AIRWAY DISEASES AS MEASURED BY FEV<sub>1</sub>/FVC AND TLC\*

	Normal	Mild	Moderate	Severe
FEV <sub>1</sub> /FVC	>73%	61%–73%	51%–60%	<50%
TLC	>81%	66%–80%	51%–65%	<50%

FEV<sub>1</sub>, Forced expiratory volume in 1 second; FVC, forced vital capacity; TLC, total lung capacity.  
 \*Percentages are of predicted values.

#### 14. What is a flow-volume loop and what information does it provide?

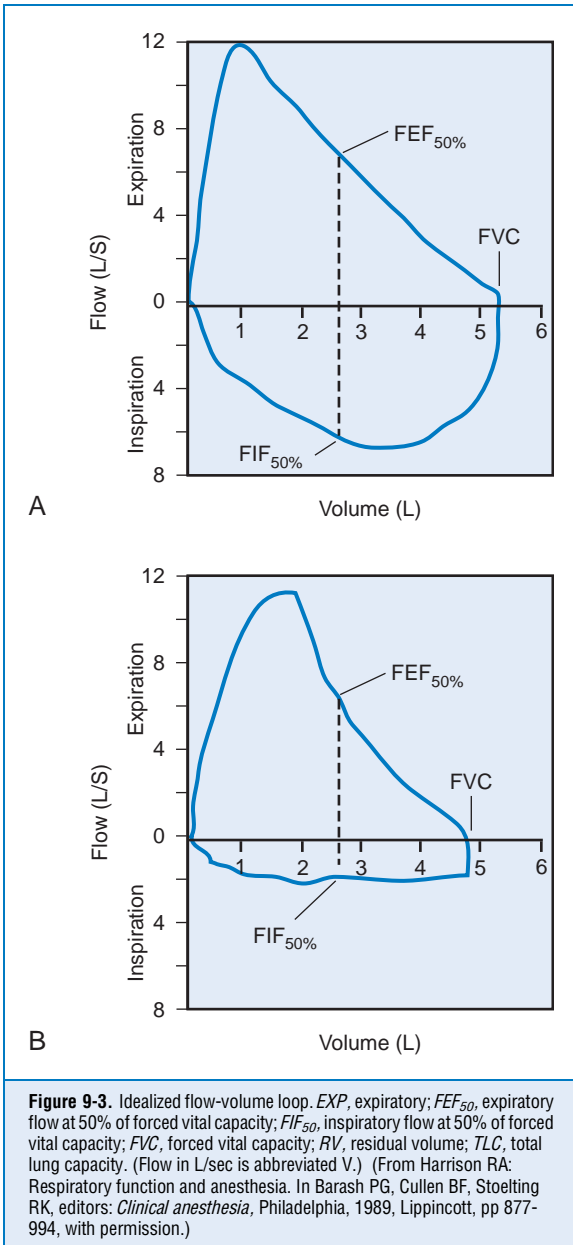
Using routine spirometric values, flow-volume loops assist in identifying the anatomic location of airway obstruction. Forced expiratory and inspiratory flow at 50% of FVC (FEF<sub>50</sub> and FIF<sub>50</sub>) are shown in Figure 9-3. Note that expiratory flow is represented above the x-axis, whereas inspiratory flow is represented below the axis. In a normal flow-volume loop the FEF<sub>50</sub>/FIF<sub>50</sub> ratio is 1.

#### 15. What are the characteristic patterns of the flow-volume loop in a fixed airway obstruction, variable extrathoracic obstruction, and intrathoracic obstruction?

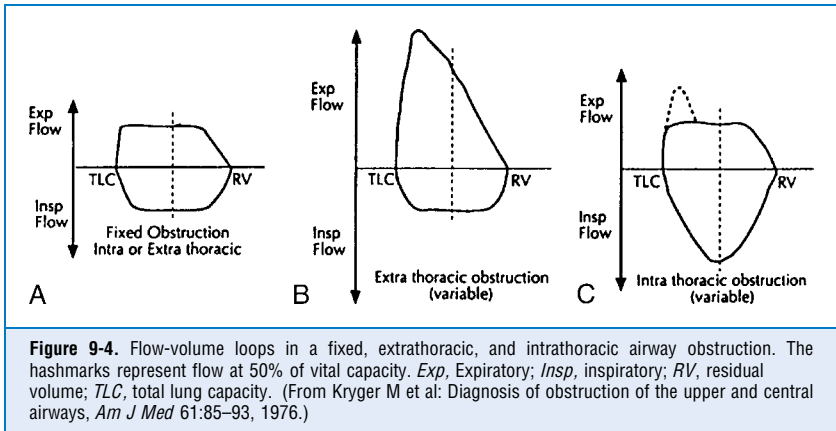
Upper airway lesions (e.g., tracheal stenosis) are fixed when there is a plateau during both inspiration and expiration. The FEF<sub>50</sub>/FIF<sub>50</sub> ratio remains unchanged. An extrathoracic obstruction occurs when the lesion (e.g., tumor) is located above the sternal notch and is characterized by a flattening of the flow-volume loop during inspiration. The flattening of the loop represents no further increase in airflow because the mass causes airway collapse. The FEF<sub>50</sub>/FIF<sub>50</sub> ratio is >1. An intrathoracic obstruction is characterized by a flattening of the expiratory loop of a flow-volume loop, and the FEF<sub>50</sub>/FIF<sub>50</sub> ratio is <1. The lesion causes airway collapse during expiration (Figure 9-4).

#### 16. What is the value of measuring flow-volume loops in a patient with an anterior mediastinal mass?

Injudicious anesthetic induction and paralysis in patients with an anterior mediastinal mass (e.g., lymphoma, thymoma, thyroid mass) may result in an inability to ventilate the patient and



cardiovascular collapse caused by compression of the tracheobronchial tree, vena cava, pulmonary vessels, or heart. The change from spontaneous negative-pressure respirations to assisted positive-pressure ventilation is a significant factor in this collapse. The preoperative evaluation of flow-volume loops in sitting and supine positions helps to assess potentially obstructive lesions of the airway and identify patients in whom alternative management may be indicated.



### 17. What are the effects of surgery and anesthesia on pulmonary function?

All patients undergoing general anesthesia and surgical procedures (particularly in the thorax and upper abdomen) exhibit changes in pulmonary function that promote postoperative pulmonary complications. For instance, VC is reduced to approximately 40% of preoperative values and remains depressed for at least 10 to 14 days after open cholecystectomy. Upper abdominal procedures result in a decrease in FRC within 10 to 16 hours; FRC gradually returns to normal by 7 to 10 days. The normal pattern of ventilation is also altered, with decreased sigh breaths and decreased clearance of secretions.

### 18. What pulmonary function test values predict increased perioperative pulmonary complications after abdominal or thoracic surgery?

See Table 9-3.

**TABLE 9-3. PULMONARY FUNCTION CRITERIA SUGGESTING INCREASED RISK FOR ABDOMINAL AND THORACIC SURGERY**

	Abdominal	Thoracic
FVC	<70% predicted	<70% predicted or <1.7 L
FEV <sub>1</sub>	<70% predicted	<2 L, * <1 L, † <0.6 L‡
FEV <sub>1</sub> /FVC	<65%	<35%
MVV	<50% predicted	<50% predicted or <28 L/min
RV		<47% predicted
DLCO		<50%
VO <sub>2</sub>		<15 ml/kg/min

Data from Gass GD, Olsen GN: Preoperative pulmonary function testing to predict postoperative morbidity and mortality, *Chest* 89:127–135, 1986.

DLCO, Diffusing capacity for inspired carbon monoxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; MVV, maximal voluntary ventilation; RV, residual volume; VO<sub>2</sub>, oxygen consumption.

\*Pneumectomy.

†Lobectomy.

‡Segmentectomy.

**19. Are there absolute values of specific pulmonary function tests below which the risk of surgery is prohibitive?**

No single PFT result absolutely contraindicates surgery. Factors such as physical examination, arterial blood gases, and coexisting medical problems also must be considered in determining suitability for surgery. Ultimately the decision to operate weighs all risks and benefits and is a collaborative decision between the surgeon, the anesthesiologist, and the patient.

**KEY POINTS: PULMONARY FUNCTION TESTING**

1. Abnormal PFTs identify patients who will benefit from aggressive perioperative pulmonary therapy and in whom surgery should be avoided entirely. This is especially the case when pulmonary resections are planned.
2. FVC, FEV<sub>1</sub>, the FEV<sub>1</sub>/FVC ratio, and the flow between 25% and 75% of the FVC (MMF<sub>25-75</sub>) are the most clinically helpful indices obtained from spirometry.
3. No single PFT result absolutely contraindicates surgery. Factors such as physical examination, arterial blood gases, and coexisting medical problems also must be considered in determining suitability for surgery.

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## VOLATILE ANESTHETICS

Michelle Dianne Herren, MD

## 1. What are the properties of an ideal anesthetic gas?

An ideal anesthetic gas would be predictable in onset and emergence; provide muscle relaxation, cardiostability, and bronchodilation; not trigger malignant hyperthermia or other significant side effects (such as nausea and vomiting); be inflammable; undergo no transformation within the body; and allow easy estimation of concentration at the site of action.

## 2. What are the chemical structures of the more common anesthetic gases? Why do we no longer use the older ones?

Isoflurane, desflurane, and sevoflurane are the most commonly used volatile anesthetics. As the accompanying molecular structures demonstrate, they are substituted halogenated ethers, except halothane, a halogenated substituted alkane. Many older anesthetic agents had unfortunate properties and side effects such as flammability (cyclopropane and fluroxene), slow induction (methoxyflurane), hepatotoxicity (chloroform and fluroxene), nephrotoxicity (methoxyflurane), and the theoretic risk of seizures (enflurane) (Figure 10-1).

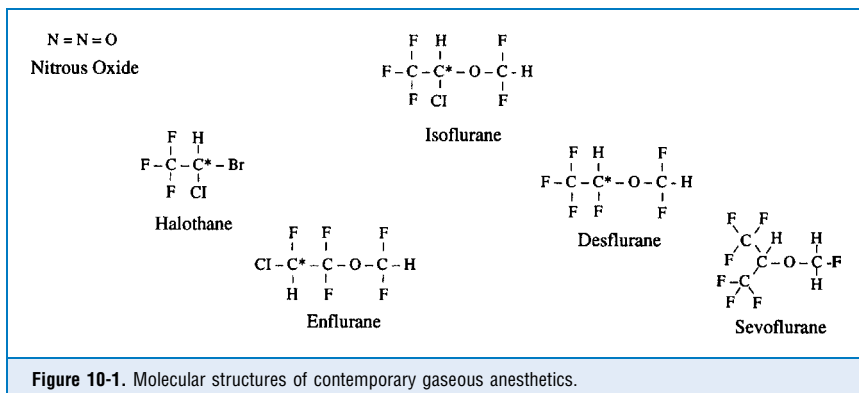


Figure 10-1. Molecular structures of contemporary gaseous anesthetics.

## 3. How are the potencies of anesthetic gases compared?

The potency of anesthetic gases is compared using minimal alveolar concentration (MAC), which is the concentration at one atmosphere that abolishes motor response to a painful stimulus (i.e., surgical incision) in 50% of patients. Of note, 1.3 MAC is required to abolish this response in 99% of patients. Other definitions of MAC include the MAC-BAR, which is the concentration required to block autonomic reflexes to nociceptive stimuli (1.7 to 2 MAC), and the MAC-awake, the concentration required to block appropriate voluntary reflexes and measure perceptive awareness (0.3 to 0.5 MAC). MAC appears to be consistent across species lines. The measurement of MAC assumes that alveolar concentration directly reflects the partial pressure of the anesthetic at its site of action and equilibration between the sites.

#### 4. What factors may influence MAC?

The highest MACs are found in infants at 6 to 12 months of age and decrease with both increasing age and prematurity. For every Celsius degree drop in body temperature, MAC decreases approximately 2% to 5%. Hyponatremia, opioids, barbiturates,  $\alpha_2$ -blockers, calcium channel blockers, acute alcohol intoxication, and pregnancy decrease MAC. Hyperthermia, chronic alcoholism, and central nervous system (CNS) stimulants (cocaine) increase MAC. Factors that do not affect MAC include hypocarbia, hypercarbia, gender, thyroid function, and hyperkalemia. MAC is additive. For example, nitrous oxide potentiates the effects of volatile anesthetics.

#### 5. Define partition coefficient. Which partition coefficients are important?

A partition coefficient describes the distribution of a given agent at equilibrium between two substances at the same temperature, pressure, and volume. Thus the blood-to-gas coefficient describes the distribution of anesthetic between blood and gas at the same partial pressure. A higher blood-to-gas coefficient correlates with a greater concentration of anesthetic in blood (i.e., a higher solubility). Therefore a greater amount of anesthetic is taken into the blood, which acts as a reservoir for the agent, reducing the alveolar concentration and thus slowing the rate of induction. Equilibration is relatively quick between alveolar and brain anesthetic partial pressure. Thus alveolar concentration ultimately is the principal factor in determining onset of action.

Other important partition coefficients include brain to blood, fat to blood, liver to blood, and muscle to blood. Except for fat to blood, these coefficients are close to 1 (equally distributed). Fat has partition coefficients for different volatile agents of 30 to 60 (i.e., anesthetics continue to be taken into fat for quite some time after equilibration with other tissues) (Table 10-1).

TABLE 10-1. PHYSICAL PROPERTIES OF CONTEMPORARY ANESTHETIC GASES

	Isoflurane	Desflurane	Halothane	Nitrous Oxide	Sevoflurane
Molecular weight	184.5	168	197.5	44	200
Boiling point (°C)	48.5	23.5	50.2	-88	58.5
Vapor pressure (mm Hg)	238.0	664	241	39,000	160
<b>Partition coefficients at 37° C</b>					
Blood to gas	1.4	0.42	2.3	0.47	0.69
Brain to blood	2.6	1.2	2.9	1.7	1.7
Fat to blood	45	27	60	2.3	48
Oil to gas	90.8	18.7	224	1.4	47.2
MAC (% of 1 ATM)	1.15	6	0.77	104	1.7
<i>MAC, Minimum alveolar concentration.</i>					

#### 6. Review the evolution in hypothesis as to how volatile anesthetics work.

- At the turn of the century Meyer and Overton independently observed that an increasing oil-to-gas partition coefficient correlated with anesthetic potency. The Meyer-Overton lipid solubility theory dominated for nearly half a century before it was modified.

- Franks and Lieb found that an amphophilic solvent (octanol) correlated better with potency than lipophilicity and concluded that the anesthetic site must contain both polar and nonpolar sites.
- Modifications of Meyer and Overton's membrane expansion theories include the excessive volume theory, in which anesthesia is created when a polar cell membrane components and amphophilic anesthetics synergistically create a larger cell volume than the sum of the two volumes together.
- In the critical volume hypothesis, anesthesia results when the cell volume at the anesthetic site reaches a critical size. These theories rely on the effects of membrane expansion on and at ion channels.
- The previous theories oversimplify the mechanism of anesthetic action and have been abandoned for the following reasons: volatile anesthetics lead to only mild perturbations in lipids, and the same changes can be reproduced by changes in temperature without leading to behavioral changes; also, variations in size, rigidity, and location of the anesthetic in the lipid bilayer are similar to those in compounds that do not have anesthetic activity, which implies that specific receptors are involved.
- Newer accepted theories propose distinct molecular targets and anatomic sites of action rather than nonspecific actions on cell volume or wall. Volatile anesthetics are thought to enhance inhibitory receptors, including  $\gamma$ -aminobutyric acid (GABA) type A and glycine receptors.
- There is also evidence supporting an inhibitory effect on excitatory channels such as neuronal nicotinic and glutamate receptors.
- Most likely the actions of immobilization and amnesia are caused by separate mechanisms at different anatomic sites. At the spinal cord level anesthetics lead to suppression of nociceptive motor responses and are responsible for immobilization of skeletal muscle. Supraspinal effects on the brain are responsible for amnesia and hypnosis. The thalamus and midbrain reticular formation are more depressed than other regions of the brain.

## 7. What factors influence speed of induction?

Factors that increase alveolar anesthetic concentration speed onset of volatile induction:

- Increasing the delivered concentrations of anesthetic
- High flow within the breathing circuit
- Increasing minute ventilation

Factors that decrease alveolar concentration slow onset of volatile induction:

- Increase in cardiac output
- Decreased minute ventilation
- High anesthetic lipid solubility
- Low flow within the breathing circuit

## 8. What is the second gas effect? Explain diffusion hypoxia.

In theory this phenomenon should speed the onset of anesthetic induction. Because nitrous oxide is insoluble in blood, its rapid absorption from alveoli results in an abrupt rise in the alveolar concentration of the accompanying volatile anesthetic. However, even at high concentrations (70%) of nitrous oxide, this effect accounts for only a small increase in concentration of volatile anesthetic. Recent studies have had conflicting results as to whether this phenomenon is valid. When nitrous oxide is discontinued abruptly, its rapid diffusion from the blood to the alveolus decreases the oxygen tension in the lung, leading to a brief period of decreased oxygen concentration known as *diffusion hypoxia*. Administering 100% oxygen at the end of a case can mitigate this.

## KEY POINTS: VOLATILE ANESTHETICS



1. Speed of onset of volatile anesthetics is increased by increasing the delivered concentration of anesthetic, increasing the fresh gas flow, increasing alveolar ventilation, and using nonlipid-soluble anesthetics.
2. Volatile anesthetics lead to a decrease in tidal volume and an increase in respiratory rate, resulting in a rapid, shallow breathing pattern.
3. MAC is decreased by old age or prematurity, hyponatremia, hypothermia, opioids, barbiturates,  $\alpha_2$ -blockers, calcium channel blockers, acute alcohol intoxication, and pregnancy.
4. MAC is increased by hyperthermia, chronic alcoholism, and CNS stimulants (e.g., cocaine).
5. The physiologic response to hypoxia and hypercarbia is blunted by volatile anesthetics in a dose-dependent fashion.
6. Because of its insolubility in blood and rapid egress into air-filled spaces, nitrous oxide should not be used in the setting of pneumothorax, bowel obstruction, or pneumocephalus or during middle ear surgery.
7. Degradation of desflurane and sevoflurane by desiccated absorbents may lead to CO production and poisoning.
8. Nitrous oxide toxicity is a rare but real threat in abusers, patients with vitamin B<sub>12</sub> deficiencies, and possibly unborn fetuses because of impaired methionine synthesis and results in neurologic sequelae.

**9. Should nitrous oxide be administered to patients with pneumothorax? Are there other conditions in which nitrous oxide should be avoided?**

Although nitrous oxide has a low blood-to-gas partition coefficient, it is 20 times more soluble than nitrogen (which comprises 79% of atmospheric gases). Thus nitrous oxide can diffuse 20 times faster into closed spaces than it can be removed, resulting in expansion of pneumothorax, bowel gas, or air embolism or in an increase in pressure within noncompliant cavities such as the cranium or middle ear (Figure 10-2).

**10. Describe the ventilatory effects of the volatile anesthetics.**

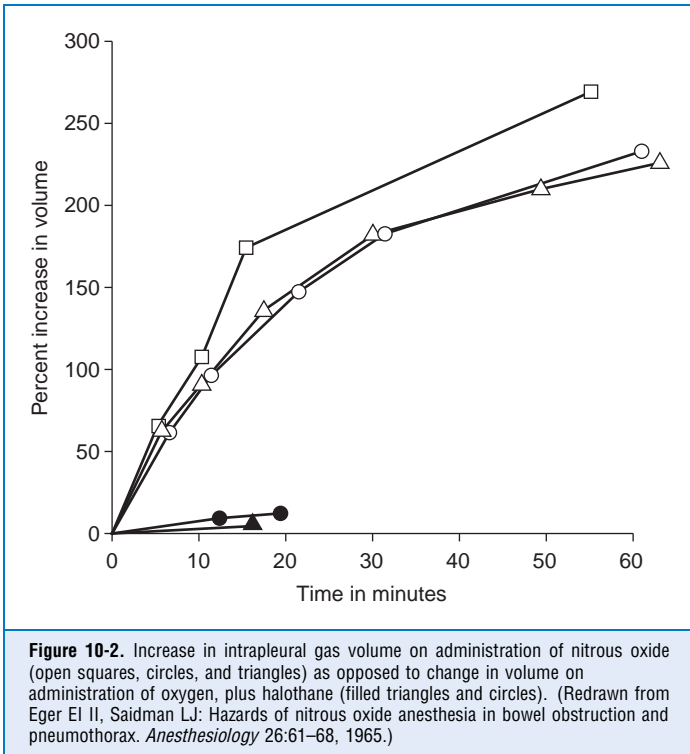
Delivery of anesthetic gases results in dose-dependent depression of ventilation mediated directly through medullary centers and indirectly through effects on intercostal muscle function. Minute volume decreases secondary to reductions in tidal volume, although rate appears generally to increase in a dose-dependent fashion. Ventilatory drive in response to hypoxia can be easily abolished at one MAC and attenuated at lower concentrations. The ventilatory response to hypercarbia is also attenuated by increasing the delivered anesthetic concentration.

**11. What effects do volatile anesthetics have on hypoxic pulmonary vasoconstriction, airway caliber, and mucociliary function?**

Hypoxic pulmonary vasoconstriction (HPV) is a locally mediated response of the pulmonary vasculature to decreased alveolar oxygen tension and serves to match ventilation to perfusion. Inhalational agents decrease this response.

All volatile anesthetics appear to decrease airway resistance by a direct relaxing effect on bronchial smooth muscle and by decreasing the bronchoconstricting effect of hypocapnia.





The bronchoconstricting effects of histamine release also appear to be decreased when an inhalational anesthetic is administered.

Mucociliary clearance appears to be diminished by volatile anesthetics, principally through interference with ciliary beat frequency. The effects of dry inhaled gases, positive-pressure ventilation, and high inspired oxygen content also contribute to ciliary impairment.

## 12. What effects do volatile anesthetics have on circulation?

See Table 10-2.

## 13. Which anesthetic agent is most associated with cardiac dysrhythmias?

Halothane has been shown to increase the sensitivity of the myocardium to epinephrine, resulting in premature ventricular contractions and tachydysrhythmias. The mechanism may be related to the prolongation of conduction through the His-Purkinje system, which facilitates the reentrant phenomenon and  $\beta_1$ -adrenergic receptor stimulation within the heart. Compared with adults, children undergoing halothane anesthesia appear to be relatively resistant to this sensitizing effect, although halothane has been shown to have a cholinergic, vagally induced bradycardic effect in children.

## 14. Discuss the biotransformation of volatile anesthetics and the toxicity of metabolic products.

For the most part oxidative metabolism occurs within the liver via the cytochrome P-450 system and to a lesser extent within the kidneys, lungs, and gastrointestinal tract. Desflurane and isoflurane are metabolized less than 1%, whereas halothane is metabolized more than 20% by the liver. Under hypoxic conditions halothane may undergo reductive metabolism,

TABLE 10-2. CIRCULATORY EFFECTS OF CONTEMPORARY ANESTHETIC GASES

	Isoflurane/Desflurane	Sevoflurane	Halothane	Nitrous Oxide
Cardiac output	0	0	—*	+
Heart rate	++/0	0	0	+
Blood pressure	—*	—*	—*	0
Stroke volume	—*	—*	—*	—
Contractility	—*	—*	—*	—*
Systemic vascular resistance	—	—	0	0
Pulmonary vascular resistance	0	0	0	+
Coronary blood flow	+	+	0	0
Cerebral blood flow	+	+	++	0
Muscle blood flow	+	+	—	0
Catecholamine levels	0	0	0	0

\*. Dose-dependent; +, increase; ++, large increase; 0, no change; —, decrease; —, large decrease.

producing metabolites that may cause hepatic necrosis. Halothane hepatitis is secondary to an autoimmune hypersensitivity reaction.

Fluoride is another potentially toxic product of anesthetic metabolism. Fluoride-associated renal dysfunction has been linked to the use of methoxyflurane and greatly contributed to the withdrawal of methoxyflurane from the market. The fluoride produced by sevoflurane has not been implicated in renal dysfunction, perhaps because sevoflurane is not as lipid soluble as methoxyflurane and the time of exposure (fluoride burden) is much less.

Soda lime can also degrade sevoflurane. One of the metabolic by-products is a vinyl ether known as *Compound A*. Compound A has been shown to be nephrotoxic to rats, but no organ dysfunction in association with clinical use in humans has been noted. Compound A may accumulate during longer cases, low-flow anesthesia, and dry absorbent and with high sevoflurane concentrations.

#### 15. Review the effects of CO<sub>2</sub> absorbants on volatile anesthetic by-products.

Desflurane, much more than any other volatile anesthetic, has been associated with the production of carbon monoxide (CO). There are a number of key conditions. The volatile compound must contain a difluoromethoxy group (desflurane, enflurane, and isoflurane). This group interacts with the strongly alkaline and desiccated CO<sub>2</sub> absorbent. A base-catalyzed proton abstraction forms a carbanion that can either be reprotonated by water to regenerate the original anesthetic or form CO when the absorbent is dry. Because of the greater opportunity to dry the absorbent out, the incidence of CO exposure is highest, the first case of the day, when machines have not been used for some time, or when fresh gas flow has been left on for a protracted period of time. The prior conditions are often found to be most significant on Monday morning if the machine has not been used during the weekend. Absorbants should be changed routinely despite lack of apparent color change, and moisture levels monitored.

Potassium hydroxide (KOH)-containing absorbents are the stronger alkalis and result in greater CO production. From greatest to least, KOH-containing absorbents are Baralyme (4.6%) > classic soda lime (2.6%) > new soda lime (0%) > calcium hydroxide lime (Amsorb) (0%). Choice of volatile anesthetic also determines the amount of CO produced, and at

equiMAC concentrations desflurane > enflurane > isoflurane. Sevoflurane, once thought to be innocent, has recently been implicated as well when exposed to dry absorbant (especially KOH-containing). This leads to CO production and a rapid increase in absorbant temperature, generation of formic acid leading to severe airway irritation, and a lower effective circuit concentration of delivered sevoflurane compared to that of vaporizer dial concentration.

**16. Which anesthetic agent has been shown to be teratogenic in animals? Is nitrous oxide toxic to humans?**

Nitrous oxide administered to pregnant rats in concentrations greater than 50% for over 24 hours has been shown to increase skeletal abnormalities. The mechanism is probably related to the inhibition of methionine synthesis, which is necessary for synthesis; the mechanism may also be secondary to the physiologic effects of impaired uterine blood flow by nitrous oxide. Although ethically this is not possible to study in humans, it may be prudent to limit the use of nitrous oxide in pregnant women.

Several surveys have attempted to quantify the relative risk of operating room personal exposure to nonscavenged anesthetic gases. Pregnant women were found to have a 30% increased risk of spontaneous abortion and a 20% increased risk for congenital abnormalities. However, in these investigations responder bias and failure to control for other exposure hazards may account for some of these findings.

Nitrous oxide can be toxic to humans because of its ability to prevent cobalamin (vitamin B<sub>12</sub>) to act as a coenzyme for methionine synthase. Generally toxic effects are seen in persons abusing nitrous oxide for long periods of time (e.g., myelinopathies, spinal cord degeneration, altered mental status, paresthesias, ataxia, weakness, spasticity). Other patients may be disposed to toxicity during routine nitrous-based anesthetics, including pernicious anemia and Vitamin B12 deficiency. Patients having surgery where 70% nitrous oxide was used for over 2 hours have been shown to have more postoperative complications, including atelectasis, fever, pneumonia, and wound infections. It seems prudent then to limit the use of nitrous oxide in longer procedures.

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# OPIOIDS

Christopher L. Ciarallo, MD

## 1. What is an opiate? An opioid? A narcotic?

- Opiates are analgesic and sedative drugs that contain opium or an opium derivative from the poppy plant (*Papaver somniferum*). Opiates include opium, morphine, and codeine.
- An opioid is any substance with morphinelike activity that acts as an agonist or antagonist at an opioid receptor. Opioids may be exogenous or endogenous (such as the endorphins) and may be natural, derived, or completely synthetic.
- The term *narcotic* is not specific for opioids and refers to any substance with addictive potential that induces analgesia, euphoria, or altered sensorium.

## 2. What are endogenous opioids?

The endorphins, enkephalins, and dynorphins are the three classes of endogenous peptides that are derived from prohormones and are functionally active at opioid receptors. Although their physiologic roles are not completely understood, they appear to modulate nociception. Endorphins are not limited to the central nervous system and may even be expressed by activated leukocytes. A fourth class, the nociceptins, is currently being investigated.

## 3. Differentiate opioid tolerance, dependence, and abuse.

Tolerance is a diminution in the physiologic effects of a substance resulting from repeated administration. Dependence may be physical or psychological and refers to the repeated use of a substance to avoid withdrawal symptoms. Tolerance may be necessary to establish the diagnosis of dependence. Abuse refers to the habitual use of a substance despite adverse consequences, including social and interpersonal problems.

## 4. Name the opioids commonly used in the perioperative setting, their trade names, equivalent morphine doses, half-lives, and chemical classes.

See Table 11-1.

## 5. Describe the various opioid receptors and their effects.

See Table 11-2.

## 6. What is an opioid agonist-antagonist?

Drugs such as pentazocine, butorphanol, buprenorphine, and nalbuphine were initially thought to be  $\mu$ - and  $\kappa$ -receptor agonists. However, they are now classified as  $\mu$ - and  $\kappa$ -receptor partial agonists. These drugs provide analgesia but with less euphoria and risk of dependence compared with pure agonists. Agonist-antagonists in general cause less respiratory depression than agonists and may reverse the respiratory depression and pruritus caused by pure agonists.

## 7. Explain the mechanism of action, duration, and side effects of the opioid antagonist naloxone.

Naloxone is a  $\mu$ -,  $\kappa$ -, and  $\delta$ -receptor antagonist that will reverse the effects of agonist drugs. The peak effect occurs within 1 to 2 minutes of intravenous administration. The duration of

TABLE 11-1. COMPARISON OF COMMONLY USED OPIOIDS

Generic Name	Trade Name	Equipotent IV/IM (mg)	Equipotent PO (mg)	Plasma	Chemical Class
				Half-Life (hr)	
Morphine	Morphine sulfate	10	30	2	Phenanthrene
Morphine CR	Ms Contin	—	30	15	Phenanthrene
Diacetylmorphine	Heroin	5	45–60	0.5	Phenanthrene
Alfentanil	Alfenta	1	—	1.5	Phenylpiperidine
Fentanyl	Sublimaze	0.1	—	3–4	Phenylpiperidine
Sufentanil	Sufenta	0.01–0.02	—	2.5–4	Phenylpiperidine
Remifentanil	Ultiva	0.04	—	9 min	Phenylpiperidine
Hydromorphone	Dilaudid	1.3–2	7.5	2–3	Phenanthrene
Oxymorphone	Opana	1	10	7–9	Phenanthrene
Meperidine	Demerol	75	300	3–4	Phenylpiperidine
Methadone (acute)	Dolophine	10	20	15–40	Diphenylheptane
(chronic)		2–4	2–4		
Codeine	Tylenol No. 3*	130 IM	200	2–4	Phenanthrene
Hydrocodone	Vicodin, Lortab*	—	30	4	Phenanthrene
Oxycodone	Percocet*	—	20	4–5	Phenanthrene
Oxycodone SR	OxyContin	—	20	5–6.5	Phenanthrene
Tramadol	Ultram	100	120–150	5–7	Cyclohexanol

*CR*, Controlled release; *IM*, intramuscular; *IV*, intravenous; *SR*, sustained release.  
\*Opioid compounded with acetaminophen.

action is between 30 and 60 minutes and may be shorter than the duration of the offending opioid agonist. Incremental doses of 0.5 to 1 mcg/kg should be used initially to reverse respiratory depression to minimize the side effects such as acute opioid withdrawal, severe hypertension, ventricular dysrhythmias, or pulmonary edema.

#### 8. Describe the various routes of administration of opioids.

Typical routes of administration include oral, intravenous, intramuscular, epidural, subarachnoid, and rectal. Intranasal, nebulized, and subcutaneous may also be used. Lipophilic opioids such as fentanyl are also available in transdermal, transmucosal, and sublingual formulations.

#### 9. What are the typical side effects of opioids?

Opioid side effects include respiratory depression, nausea and vomiting, pruritus, cough suppression, urinary retention, and biliary tract spasm. Some opioids may induce histamine release and cause hives, bronchospasm, and hypotension. Intravenous opioids may cause abdominal and chest wall rigidity. Most opioids, with the notable exception of meperidine, produce a dose-dependent bradycardia.

TABLE 11-2. OPIOID RECEPTOR SUBTYPES

Opioid Receptor Subtype	Agonists	Agonist Response
Mu-1 ( $\mu$ -1)	Enkephalin	Supraspinal analgesia
	$\beta$ -endorphin	Euphoria
	Phenanthrenes	Miosis
	Phenylpiperidines	Urinary retention
	Methadone	
Mu-2 ( $\mu$ -2)	Enkephalin	Spinal analgesia
	$\beta$ -endorphin	Respiratory depression
	Phenanthrenes	Bradycardia
	Phenylpiperidines	Constipation
	Methadone	Dependence
Kappa ( $\kappa$ )	Dynorphin	Spinal analgesia ( $\kappa$ -1)
	Butorphanol	Supraspinal analgesia ( $\kappa$ -2)
	Levorphanol	Dysphoria
	Nalbuphine	Sedation
	Oxycodone	
Delta ( $\delta$ )	Enkephalin	Spinal analgesia ( $\delta$ -1)
	Deltorphan	Supraspinal analgesia ( $\delta$ -2)
	Sufentanil	Respiratory depression
		Urinary retention
Sigma ( $\sigma$ ) (no longer classified as opioid receptor)	Pentazocine	Dependence
		Dysphoria
		Tachypnea
		Hallucinations

Modified from Stoelting RK, Miller RD: *Basics of Anesthesia*, ed 4, New York, 2000, Churchill Livingstone, p 71.

#### 10. Which opioids are associated with histamine release?

Parenteral doses of meperidine, morphine, and codeine have been associated with histamine release and resultant cutaneous reactions and hypotension. The incidence and severity, at least with morphine, appears to be dose dependent.

#### 11. Describe the mechanism of opioid-induced nausea.

Opioids bind directly to opioid receptors in the chemotactic trigger zone in the area postrema of the medulla and stimulate the vomiting center. They exert a secondary effect by sensitizing the vestibular system. The incidence of nausea and vomiting is similar for all opioids and appears irrespective of the route of administration.

#### 12. What is methylnaltrexone and what potential role does it have in opioid therapy?

Methylnaltrexone is a peripheral opioid receptor antagonist derived from naltrexone. It is a charged, polar molecule that is unable to cross the blood-brain barrier. Methylnaltrexone has

been approved in the United States for palliative care use in the treatment of opioid-induced constipation. A related drug, alvimopan, has been approved in an oral form for the treatment of postoperative ileus after bowel resection.

### 13. Describe the cardiovascular effects of opioids.

As a group opioids have minimal effects on the cardiovascular system. With the exception of meperidine, they cause a dose-dependent bradycardia through vagal nucleus stimulation. Other than the myocardial depressant activity of meperidine, opioids have minimal inotropic effect on the myocardium. Some opioids may induce histamine release and significantly reduce systemic vascular resistance (SVR), but most effect only a moderate reduction of SVR, even at anesthetic doses.

## KEY POINTS: OPIOIDS



1. Common opioid side effects include nausea, pruritus, bradycardia, urinary retention, and respiratory depression.
2. Morphine and meperidine should be used with caution in patients with renal failure because of the risk of prolonged ventilatory depression and seizures, respectively.
3. Neuraxial opioids and local anesthetics act synergistically to provide analgesia with reduced side effects.
4. Naloxone should be titrated in incremental doses for opioid-induced respiratory depression and may require repeated dosing for reversal of long-acting opioid agonists.
5. Opioid equianalgesic conversions are approximations, and they do not account for incomplete opioid cross-tolerance.

### 14. Describe the typical respiratory pattern and ventilatory response to carbon dioxide in the presence of opioids.

Opioids reduce alveolar ventilation in a dose-dependent manner. They slow the respiratory rate and may cause periodic breathing or apnea. Graphically opioids shift the alveolar ventilatory response-to-carbon dioxide curve down and to the right. Accordingly, for a given arterial carbon dioxide level the alveolar ventilation will be reduced in the presence of opioids. Furthermore, an increase in arterial carbon dioxide will not stimulate an appropriate increase in ventilation. Opioids also impair the hypoxic ventilatory drive (Figure 11-1).

### 15. Describe the analgesic onset, peak effect, and duration of intravenous fentanyl, morphine, and hydromorphone.

See Table 11-3.

### 16. Explain how fentanyl can have a shorter duration of action but a longer elimination half-life than morphine.

Elimination half-lives correspond with duration of action in a single-compartment pharmacokinetic model. Lipophilic opioids such as fentanyl are better represented by a multicompartment model since redistribution plays a much larger role than elimination in determining their duration of action.

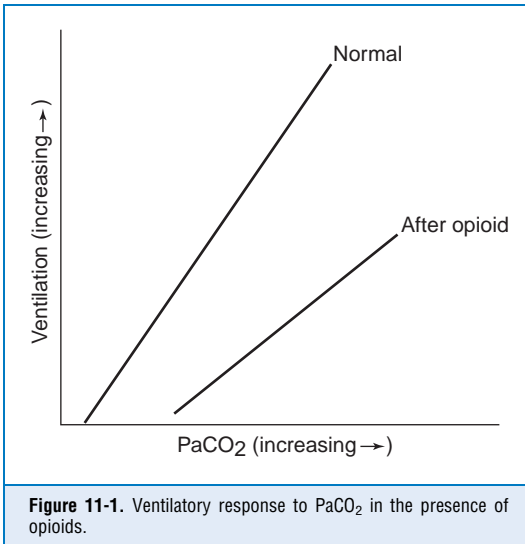


TABLE 11-3. COMPARISON OF COMMONLY USED INTRAVENOUS OPIOIDS

Opioid	Onset (min)	Peak Effect (min)	Duration (hr)
Fentanyl	1–3	3–5	0.5–1
Morphine	5–15	30–90	4–5
Hydromorphone	5	15–30	4–5

**17. Explain the concept of context-sensitive half-time and its relevance to opioids.**

Context-sensitive half-time is the time required for a 50% reduction in the plasma concentration of a drug on termination of a constant infusion. This time is determined by both elimination and redistribution, and it varies considerably as a function of infusion duration for commonly used opioids (Figure 11-2).

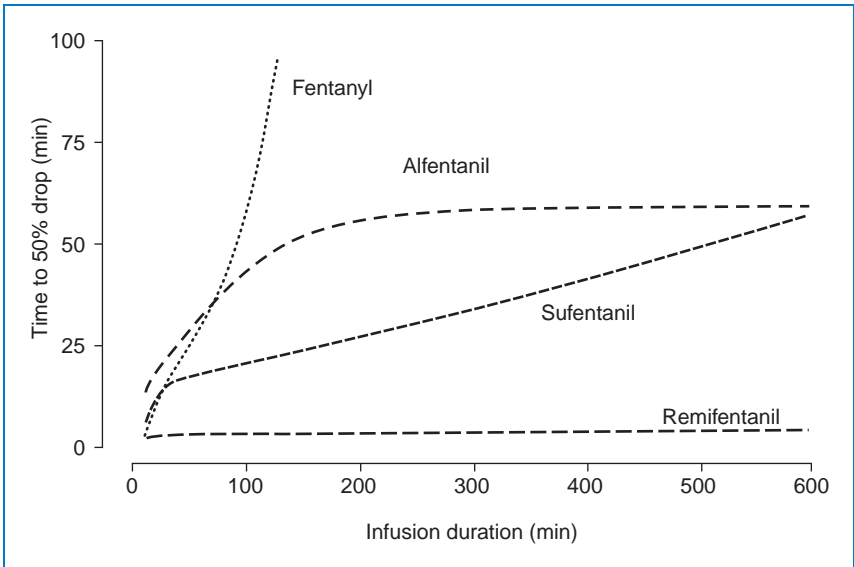
**18. Explain why morphine may cause prolonged ventilatory depression in patients with renal failure.**

A morphine dose of 5% to 10% will be excreted unchanged in the urine. The remainder is primarily conjugated in the liver as morphine-3-glucuronide (50% to 75%) and morphine-6-glucuronide (10%), of which 90% is renally excreted. Morphine-3-glucuronide is inactive, but morphine-6-glucuronide is approximately 100 times more potent than morphine as a  $\mu$ -receptor agonist.

**19. Which opioids may be associated with seizure activity in patients with renal failure?**

Hydromorphone and meperidine are associated with seizure activity in patients with renal failure. Rarely the metabolites hydromorphone-3-glucuronide and normeperidine can accumulate in renal failure and promote myoclonus and seizures.





**Figure 11-2.** Context-sensitive half-times of commonly used opioids as a function of infusion duration. (Adapted from Egan TD et al: The pharmacokinetics of the new short-acting opioid remifentanil (Gl87084B) in healthy adult male volunteers, *Anesthesiology* 79:881, 1993.)

## 20. What is remifentanil and how does it differ from other opioids?

Remifentanil is an ultrashort-acting opioid with a duration of 5 to 10 minutes and a context-sensitive half-time of 3 minutes. It contains an ester moiety and is metabolized by nonspecific plasma esterases. Although remifentanil is most commonly administered as a continuous infusion, it has been used as an intravenous bolus to facilitate intubation but with a significant incidence of bradycardia and chest-wall rigidity. Remifentanil has been shown to induce hyperalgesia and acute opioid tolerance, and its use should be questioned in patients with chronic pain syndromes.

## 21. Describe the metabolism of codeine.

Codeine is metabolized by cytochrome P-450 2D6 (CYP2D6) and undergoes demethylation to morphine. Genetic polymorphisms in the CYP2D6 gene lead to patient stratification into poor metabolizers, extensive metabolizers, and ultrafast metabolizers. Poor metabolizers may obtain marginal analgesia from codeine, whereas ultrafast metabolizers may have up to 50% higher plasma concentrations of morphine and morphine-6-glucuronide than the extensive metabolizers. Ultrafast metabolizers may be at significant risk of opioid intoxication and apnea with typical perioperative doses of codeine.

## 22. What are some particular concerns with methadone dosing?

As methadone has a particularly long and variable half-life, repeated dosing may lead to excessive plasma levels, particularly on days 2 to 4 after initiating therapy. Methadone acts both as an agonist at  $\mu$ -opioid receptors and as an antagonist at the *N*-methyl-D-aspartate (NMDA) receptor. NMDA-receptor antagonism may potentiate the  $\mu$ -receptor effects and prevent opioid tolerance. Finally, methadone may prolong the electrocardiographic QT interval and increase the risk of torsades de pointes. Expert panel recommendations include a baseline electrocardiogram (ECG) and a follow-up ECG at 30 days and annually while continuing methadone.

**23. What is tramadol?**

Tramadol is a codeine analog that acts as a  $\mu$ -,  $\delta$ -, and  $\kappa$ -receptor agonist and a reuptake inhibitor of norepinephrine and serotonin. It is a moderately effective analgesic with a lower incidence of respiratory depression, constipation, and dependence than other  $\mu$ -receptor agonists. Rarely tramadol may induce seizures, and it is contraindicated in patients with a preexisting seizure disorder.

**24. What are some of the unique characteristics of meperidine?**

Unlike other opioids, meperidine has some weak local anesthetic properties, particularly when administered neuraxially. Meperidine does not cause bradycardia and may induce tachycardia, perhaps related to its atropine-like structure. As a  $\kappa$ -receptor agonist, meperidine may be used to suppress postoperative shivering. Notably meperidine is contraindicated for use in patients taking monoamine oxidase inhibitors because the combination may lead to serotonin toxicity, hyperthermia, and death.

**25. Describe the site and mechanism of action of neuraxial opioids.**

Neuraxial opioids bind to receptors in Rexed lamina II (substantia gelatinosa) in the dorsal horn of the spinal cord. Activation of  $\mu$ -receptors appears to reduce visceral and somatic pain via  $\gamma$ -aminobutyric acid-mediated descending pain pathways. Activation of  $\kappa$ -receptors appears to reduce visceral pain via inhibition of substance P. The effect of  $\delta$ -receptors is not entirely elucidated but appears minimal in some animal models.

**26. Discuss the effect of lipid solubility on neuraxial opioid action.**

Lipophilic opioids diffuse across spinal membranes more rapidly than hydrophilic opioids. As a result, they have a more rapid onset of analgesia. However, they also diffuse across vascular membranes more readily, typically resulting in increased serum concentrations and a shorter duration of action. Hydrophilic opioids achieve greater cephalo-caudal spread when administered into the epidural or subarachnoid space. They attain broader analgesic coverage than lipophilic opioids but may result in delayed respiratory depression following cephalad spread to the brainstem.

**27. Are opioid receptors exclusively in the central nervous system?**

No. Peripheral opioid receptors exist on primary afferent neurons, but they are functionally inactive under normal conditions. Tissue inflammation may induce opioid receptor up-regulation and signaling efficiency.

**28. Describe the advantages of combining local anesthetics and opioids in neuraxial analgesia.**

Despite their analgesic benefits, epidural local anesthetics have troublesome side effects such as motor blockade and systemic hypotension. Epidural opioids are burdened with causing pruritus and nausea. Combined, opioids and local anesthetics function in a synergistic manner to provide analgesia with attenuated side effects.

**29. What is DepoDur and how is it different from other neuraxial opioids?**

DepoDur is an opioid agonist that consists of lipid-based particles with internal morphine vesicles (DepoFoam). It is approved only for single-dose epidural use and may provide up to 48 hours of analgesia. Except for the epidural test dose, DepoDur may not be coadministered with local anesthetics because of the risk of accelerated morphine release. No other medication may be dosed within the epidural space for 48 hours after DepoDur administration.

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# INTRAVENOUS ANESTHETICS AND BENZODIAZEPINES

Theresa C. Michel, MD

## 1. What qualities would the ideal intravenous induction agent possess?

The ideal agent would have a rapid onset, producing amnesia, analgesia, and hypnosis with hemodynamic stability. It would have few enduring side effects, few interactions with other medications, and allow for rapid recovery after surgery.

## 2. List the commonly used induction agents and their properties. Compare their cardiovascular effects.

- Sodium thiopental (STP) is a direct myocardial depressant, produces peripheral vasodilation resulting in decreased mean arterial pressure (MAP), and produces a reflex tachycardia.
- Etomidate is an imidazole derivative the induction properties of which result from Gamma-amino butyric acid (GABA) receptor modulation. It is noted for its hemodynamic stability. Cardiac output (CO) and contractility are preserved, and only a mildly decreased MAP is noted. Side effects include pain on injection, nausea and vomiting, hiccups, myoclonus, seizures, thrombophlebitis, and most important, adrenal suppression.
- Propofol: Myocardial depression and peripheral vasodilation are more profound than with thiopental and may result in a more significant decrease in MAP. There are minimal effects on heart rate (HR).
- Ketamine: The sympathomimetic effects result in increased CO, MAP, and HR. It is a myocardial depressant, but usually its sympathomimetic properties dominate.
- Midazolam is the principal benzodiazepine used perioperatively. Benzodiazepines provide anxiolysis, sedation, amnesia, and in high doses unconsciousness. Midazolam has minimal myocardial depression. There is no effect on MAP or CO; HR may increase slightly.
- Opioids: High doses of most opioids have a vagolytic effect, producing bradycardia. The exception is meperidine, which has sympathomimetic effects that produce tachycardia. A decreased MAP may be noted secondary to bradycardia, vasodilatation, blockade of sympathetic response, and histamine release (especially evident with morphine and meperidine).

These effects are noted when these medications are individually administered. When given in concert (e.g., midazolam followed by an opioid followed by pentothal), the effects are synergistic, and hemodynamic instability is not guaranteed (Tables 12-1 and 12-2).

## 3. Instead of injecting pentothal intravenously, you have inadvertently administered it into the patient's intra-arterial line. What is the impact on the patient and how should potential problems be addressed?

Intra-arterial STP is likely to cause significant discomfort, vasospasm, and possibly thrombus formation. Leave the catheter in place and inject dilute papaverine, procaine, or lidocaine through the catheter to inhibit smooth muscle vasospasm. If this does not re-establish perfusion, consider brachial plexus block or  $\alpha$ -blockade. Also administer heparin to prevent thrombus formation.

## 4. What are contraindications to STP use?

- **Thiopental allergy:** STP contains a sulfur molecule that results in an increased risk of histamine release. Patients allergic to sulfates should not receive STP.

TABLE 12-1. DOSING GUIDELINES FOR ANESTHETIC INDUCTION AND SEDATION \*

Agent	Class	Dose for Anesthetic Induction	Dose for Sedation
Sodium thiopental	Barbiturate	3–6 mg/kg IV	0.5–1.5 mg/kg IV
Ketamine	Phencyclidine derivative	1–2 mg/kg IV 2–4 mg/kg IM	0.2–0.5 mg/kg IV
Etomidate	Imidazole derivative	0.2–0.5 mg/kg IV	Inappropriate use
Propofol	Substituted phenol	1–2.5 mg/kg IV bolus 50–200 mcg/kg/min infusion	25–100 mcg/kg/min IV
Midazolam	Benzodiazepine	0.1–0.4 mg/kg IV	0.01–0.1 mg/kg IV

*IM*, Intramuscular; *IV*, intravenous.  
\*Doses of medications should be adjusted for intravascular volume status, comorbidities, and other medications.

TABLE 12-2. CARDIOVASCULAR EFFECTS OF INDUCTION AGENTS

Agent	MAP	HR	SVR	CO	Contractility	Venodilation
Thiopental	–	+	0 to +	–	–	+
Ketamine	++	++	+	+	+ or –*	0
Midazolam	0 to –	0 to +	0 to –	0 to –	0 to –	+
Propofol	–	+	–	0	–	+
Etomidate	0	0	0	0	0	0

*CO*, Cardiac output; *HR*, heart rate; *MAP*, mean arterial pressure; *SVR*, systemic vascular resistance; +, increases; 0, no effect; –, decreases.  
\*The effect of ketamine depends on patient's catecholamine levels.

- **Porphyria:** Barbiturates increase porphyrin synthesis and may precipitate an acute porphyria attack with symptoms such as abdominal pain, weakness, autonomic dysfunction, and gastrointestinal and sleep disturbances.
- Use with caution in patients with hypovolemia and poor systolic function because of its cardiovascular depressant effects. STP may be a poor choice in this scenario.
- Advanced age, hepatic dysfunction, and obesity may result in slower redistribution and prolonged effects.

### 5. How do induction agents affect respiratory drive?

All intravenous induction agents with the exception of ketamine produce dose-dependent respiratory depression manifested by decreased tidal volume, decreased minute ventilation, decreased response to hypoxia, and a rightward shift in the carbon dioxide response curve, culminating in hypoventilation or apnea.

**6. How does ketamine differ from other induction agents?**

Ketamine is an *N*-methyl-D-aspartate receptor antagonist with profound analgesic properties. Chemically related to phencyclidine, it causes a dose-dependent dissociative state and unconsciousness and may cause hallucinations or disturbing dreams in the emotionally susceptible. Its amnestic ability is weak. Concurrent administration of a benzodiazepine may decrease the incidence of adverse sensory effects.

The sympathomimetic effects of ketamine result in tachycardia, increased CO, and MAP. It is an ideal induction agent in patients with such conditions as shock, significant hypovolemia, and cardiac tamponade.

As previously mentioned, ketamine has direct myocardial depressant effects that tend not to be manifested because of overriding sympathetic stimulation. However, in catecholamine-depleted states the myocardial depressant effects may become manifest.

Other desirable side effects include bronchodilation and preserved respiratory drive. Undesirable side effects include increased cerebral blood flow, which would be problematic when there is increased intracranial pressure. It increases oral secretions remarkably, is emetogenic, and can cause nystagmus.

**7. Discuss the concerns for the use of etomidate in the critically ill patient.**

Etomidate decreases serum cortisol levels by blocking two enzymes in the cortisol pathway: 11- $\beta$ -hydroxylase and 17- $\alpha$ -hydroxylase. Clinically significant adrenal suppression and increased morbidity and mortality have been documented in critically ill patients and those with septic shock after receiving even a single dose of etomidate. Annane and associates reported that 68 of the 72 patients (94%) who received etomidate for the induction of anesthesia did not respond to a high-dose cosyntropin stimulation test. This is consistent with other reports of adrenal insufficiency 12 to 24 hours after the administration of etomidate. The results seem to indicate a significant mortality for etomidate anesthetic induction in septic patients. However, the stable hemodynamic properties of etomidate make it a desirable induction agent for patients with shock. As the debate continues and further data are collected, some authors are advocating the use of etomidate in conjunction with exogenous corticosteroid replacement therapy (e.g., 100 mg of hydrocortisone every 8 hours) while measuring stress cortisol levels.

**KEY POINTS: INTRAVENOUS ANESTHETICS AND BENZODIAZEPINES**

1. Appropriate dosing of intravenous anesthetics requires considering intravascular volume status, comorbidities, age, and chronic medications.
2. Benzodiazepines and opioids have synergistic effects with intravenous induction agents, requiring adjustment in dosing.
3. Ketamine is the best induction agent for hypovolemic trauma patients as long as there is no risk for increased intracranial pressure. It is also a good agent for patients with active bronchospastic disease.
4. Propofol is the least likely of all induction agents to result in nausea and vomiting.
5. Termination of the effects of intravenous anesthetics is by redistribution, not biotransformation and breakdown.

**8. Describe propofol infusion syndrome.**

First reported in the pediatric population in 1992, this syndrome has now been noted in adults as well. Actual incidence is unknown but is estimated to be approximately 1 in 270 patients. The population at risk is critically ill patients receiving high-dose propofol infusions over long

periods of time (higher than 4 mg/kg/hr for longer than 48 hours). Critically ill children are at the highest risk. Risk is increased with the administration of exogenous steroids and catecholamines and inadequate carbohydrate intake. Manifestations include cardiac failure, rhabdomyolysis, severe metabolic acidosis, hyperlipidemia, renal failure, and sometimes death. Currently propofol is not approved for use for pediatric intensive care unit sedation. Although the morbidity and mortality are currently very high for those with recognized propofol infusion syndrome and treatment options are limited, best outcomes have been achieved with supportive care such as hemodialysis and cardiorespiratory support.

### 9. What are some contraindications to the use of propofol?

Propofol contains soy oil and egg lecithin; thus patients with allergies to eggs and soy products should not receive this medication. Propofol crosses the placenta and may be associated with neonatal depression. It has cardiodepressant effects; thus patients with cardiomyopathies and hypovolemia may not be ideal candidates. Finally consider the advisability of its use in patients with disorders of lipid metabolism such as primary hyperlipoproteinemia, diabetic hyperlipemia, and pancreatitis.

### 10. What would be an appropriate induction agent for a 47-year-old healthy male with a parietal lobe tumor scheduled for craniotomy and tumor excision?

Sodium thiopental has the most cerebral protective profile since it decreases cerebral oxygen consumption (CRMO<sub>2</sub>) and preserves cerebral perfusion pressure. Ketamine should be avoided because it increases cerebral blood flow and intracranial pressure.

### 11. Describe the mechanism of action of benzodiazepines.

Benzodiazepine receptors, which are found on postsynaptic nerve endings in the central nervous system (CNS), are part of the GABA receptor complex. GABA is the primary inhibitory neurotransmitter of the CNS. The GABA receptor complex is composed of two  $\alpha$ -subunits and two  $\beta$ -subunits. The  $\alpha$ -subunits are the binding sites for benzodiazepines. The  $\beta$ -subunits are the binding sites for GABA. A chloride ion channel is located in the center of the GABA receptor complex.

Benzodiazepines produce their effects by enhancing the binding of GABA to its receptor. GABA activates the chloride ion channel, allowing chloride ions to enter the neuron. The flow of chloride ions into the neuron hyperpolarizes and inhibits the neuron.

Benzodiazepines are metabolized in the liver by microsomal oxidation and glucuronidation. They should be used with caution in those with liver disease and the elderly. The potency, onset, and duration of action of benzodiazepines depend on their lipid solubility. Onset of action is achieved by rapid distribution to the vessel-rich brain. Termination of effect occurs as the drug is redistributed to other parts of the body.

### 12. What benzodiazepines are commonly administered intravenously?

- **Midazolam** is lipid soluble and therefore has the most rapid onset and shortest duration of action. Unlike other benzodiazepines, midazolam is both lipid soluble and water soluble and therefore can be manufactured without the pain-inducing solvent propylene glycol. It has a single metabolite with minimal activity. It is by far the most common benzodiazepine used perioperatively.
- **Diazepam** is slightly slower in onset. It has a long elimination half-life and two active metabolites that may prolong sedation.
- **Lorazepam** is the least lipid soluble and therefore slowest in onset and longest in duration of action. It also has a long elimination half-life.

### 13. How should oversedation induced by benzodiazepines be managed?

As a first principle, always provide supportive care. Open the airway and mask-ventilate if needed. Assess the adequacy of the circulation. Second, administer the benzodiazepine antagonist flumazenil. Flumazenil works by competitive inhibition, reversing sedation and

respiratory depression in a dose-dependent fashion. Onset is rapid and peaks within 1 to 3 minutes. It should be titrated to effect by administering doses of 0.2 mg intravenously for a maximum dose of 3 mg. It should be used with caution if at all in patients with a history of seizure disorder.

**14. What do you tell the nurses who will monitor this patient about possible side effects of flumazenil?**

The elimination half-life of midazolam is 2 to 3 hours, whereas the elimination half-life of flumazenil is 1 hour. Resedation is a risk. Flumazenil may be repeated. It may be administered as an infusion at 0.5 to 1 mcg/kg/min.

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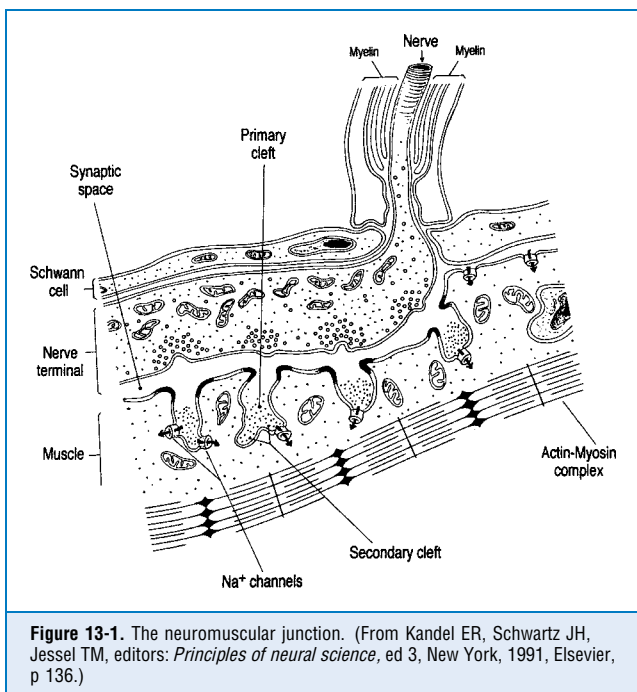


# MUSCLE RELAXANTS AND MONITORING OF RELAXANT ACTIVITY

James Duke, MD, MBA

## 1. Describe the anatomy of the neuromuscular junction.

A motor nerve branches near its terminus to contact many muscle cells, losing myelin to branch further and come into closer contact with the junctional area of the muscle surface. Within the most distal aspect of the motor neuron, vesicles containing the neurotransmitter acetylcholine (ACh) can be found. The terminal neuron and muscle surface are loosely approximated with protein filaments, and this intervening space is known as the junctional cleft. Also contained within the cleft is extracellular fluid and acetylcholinesterase, the enzyme responsible for metabolizing ACh. The postjunctional motor membrane is highly specialized and invaginated, and the shoulders of these folds are rich in ACh receptors (Figure 13-1).



## 2. What is the structure of the acetylcholine receptor?

The ACh receptor is contained within the motor cell membrane and consists of five glycoprotein subunits: two alpha and one each of  $\beta$ ,  $\delta$ , and  $\epsilon$ . These are arranged in a cylindrical fashion; the center of the cylinder is an ion channel. ACh binds to the  $\alpha$ -subunits.

### 3. With regard to neuromuscular transmission, list all locations for acetylcholine receptors.

ACh receptors are found in several areas:

- About 5 million ACh receptors per neuromuscular junction (NMJ) are located on the postjunctional motor membrane.
- Prejunctional receptors are present and influence the release of ACh. The prejunctional and postjunctional receptors have different affinities for ACh.
- Extrajunctional receptors are located throughout the skeletal muscle in relatively low numbers owing to suppression of their synthesis by normal neural activity. In cases of traumatized skeletal muscle or denervation injuries, these receptors proliferate.

### 4. Review the steps involved in normal neuromuscular transmission.

- A nerve action potential is transmitted, and the nerve terminal is depolarized.
- ACh is released from storage vesicles at the nerve terminal. Enough ACh is released to bind 500,000 receptors.
- ACh molecules bind to the  $\alpha$ -subunits of the ACh receptor on the postjunctional membrane, generating a conformational change and opening receptor channels. Receptors do not open unless both  $\alpha$ -receptors are occupied by ACh (a basis for the competitive antagonism of nondepolarizing relaxants).
- Sodium and calcium flow through the open receptor channel generating an end-plate potential.
- When between 5% and 20% of the receptor channels are open and a threshold potential is reached, a muscle action potential (MAP) is generated.
- Propagation of the MAP along the muscle membrane leads to muscle contraction.
- The rapid hydrolysis of ACh by acetylcholinesterase (true cholinesterase) within the synaptic cleft and return of normal ionic gradients return the NMJ to a nondepolarized, resting state, and the ACh receptors are closed.

### 5. What are the benefits and risks of using muscle relaxants?

By interfering with normal neuromuscular transmission, these drugs paralyze skeletal muscle and can be used to facilitate endotracheal intubation, assist with mechanical ventilation, and optimize surgical conditions. Occasionally they may be used to reduce the metabolic demands of breathing and facilitate the treatment of raised intracranial pressure (ICP). Because they paralyze all respiratory muscles, they are dangerous drugs to use in the unintubated patient unless the caregiver is trained in airway management.

### 6. How are muscle relaxants classified?

- Depolarizing relaxants: Succinylcholine (SCH) is two molecules of ACh bound together, an agonist at the NMJ, and the only depolarizing relaxant available clinically. As such, SCH binds to the  $\alpha$ -subunits of the ACh receptor. After binding, SCH can open the ion channel and depolarize the end plate. Although SCH, like ACh, binds only briefly to the receptor, it is not hydrolyzed in the synaptic cleft by acetylcholinesterase. In fact, SCH molecules may unbind and rebind receptors repeatedly. SCH must diffuse away and be broken down in the plasma by enzymes called plasma- or pseudocholinesterase, and time for clearance from the body is an accurate measure of its duration of effect.
- Nondepolarizing relaxants: These drugs are competitive antagonists to ACh at the postsynaptic membrane. They need only bind to one of the two  $\alpha$ -subunits to prevent opening of the ionic pore.

### 7. What are the indications for using succinylcholine?

SCH provides the most rapid onset and termination of effect of any neuromuscular blocker (NMB) currently available. Its onset is 60 to 90 seconds, and the duration of effect is only 5 to 10 minutes. When the patient has a full stomach and is at risk for pulmonary aspiration of

gastric contents, rapid paralysis and airway control are priorities, and SCH is often the drug indicated. (Rocuronium when given in large doses also has a SCH-like onset of action, although a prolonged duration of effect would contraindicate its use in patients likely to be difficult to ventilate or intubate.) Patients at risk for full stomachs include those with diabetes mellitus, hiatal hernia, obesity, pregnancy, severe pain, bowel obstructions, and trauma.

#### 8. If succinylcholine works so rapidly and predictably, why not use it all the time?

SCH has numerous side effects:

- SCH stimulates both nicotinic and muscarinic cholinergic receptors. Stimulation of muscarinic receptors within the sinus node results in numerous bradyarrhythmias, including sinus bradycardia, junctional rhythms, ventricular escape and asystole.
- SCH is a trigger for malignant hyperthermia.
- Prolonged exposure of the receptors to SCH results in persistent open receptor channel and ionic fluxes through the ion pore, known as *phase II* or *desensitization blockade*. Normal depolarization/repolarization is not possible until SCH is metabolized.
- In patients ambulatory soon after surgery, random generalized muscle contractions (fasciculations) have been associated with painful myalgias. Whether pretreating with a subparalyzing dose of a nondepolarizing relaxant before SCH is effective in reducing myalgias continues to be a matter of debate.
- SCH increases ICP. The etiology is not completely understood, but it is known that a subparalyzing dose of a nondepolarizing relaxant before SCH administration reduces the increase in ICP; thus perhaps fasciculations are the cause of the increase in ICP.
- In the presence of immature extrajunctional receptors, administration of SCH may result in severe hyperkalemia and malignant ventricular arrhythmias. Extrajunctional receptors are normally suppressed by activity. Any condition that decreases motor-nerve activity results in a proliferation of these receptors. Examples include spinal cord and other denervation injuries, upper and lower motor neuron disease, closed head injuries, burns, neuromuscular diseases, and even prolonged immobility.
- SCH increases intraocular pressure (IOP). There is a theoretic risk for the use of SCH in patients with open eye injury (i.e., extrusion of extraocular contents). However, the increases in IOP are modest, and from a clinical perspective extrusion of ocular contents has not been observed. Certainly if a nondepolarizing agent is administered instead of SCH and the patient is intubated before optimal intubating conditions, coughing on the endotracheal tube (called "bucking") increases IOP significantly and puts the patient at risk for extruding ocular contents.

#### 9. How do mature and immature acetylcholine receptors differ?

Mature ACh receptors are also known as *innervated* or  *$\epsilon$ -containing* receptors (because of the  $\epsilon$ -subunit within the ACh receptor). They are tightly clustered at the NMJ and are responsible for normal neuromuscular activation. Immature receptors, also known as *fetal*, *extrajunctional*, or  *$\gamma$ -receptors*, differ from the mature receptors in that they are present during fetal development and suppressed by normal activity, are dispersed across the muscular membrane rather than localized at the NMJ, and have a  $\gamma$ , not an  $\epsilon$ -subunit as part of the receptor. The half-life of mature receptors is about 2 weeks, whereas the half-life of immature receptors is less than 24 hours. The immature receptors depolarize more easily in the presence of ACh or SCH and thus are more prone to release potassium. Also, once depolarized, immature receptors tend to stay open longer. Immature receptors are up-regulated in the presence of denervation injuries, burns, and the like. This also exaggerates the potential for hyperkalemia when SCH is administered.

#### 10. Differentiate between qualitative and quantitative deficiencies in pseudocholinesterase.

Pseudocholinesterase is produced in the liver and circulates in the plasma. Quantitative deficiencies of pseudocholinesterase are observed in liver disease, pregnancy, malignancies,

malnutrition, collagen vascular disease, and hypothyroidism; they slightly prolong the duration of blockade with SCH. However, from a practical standpoint the increase in duration of SCH is probably not clinically important.

There may also be qualitative deficiencies in pseudocholinesterase (i.e., the activity of the enzyme is impaired). These are genetic diseases and as such can be present in heterozygotic or homozygotic forms. The most common form is called dibucaine-resistant cholinesterase deficiency and refers to the laboratory test that characterizes it. When added to the serum under study, dibucaine inhibits normal plasma cholinesterase by 80%, whereas the atypical plasma cholinesterase is inhibited by only 20%. Therefore a patient with normal pseudocholinesterase is assigned a dibucaine number of 80. If a patient has a dibucaine number of 40 to 60, that patient is heterozygous for this atypical pseudocholinesterase and will have a moderately prolonged and usually clinically insignificant block with SCH. If a patient has a dibucaine number of 20, he or she is homozygous for atypical plasma cholinesterase and will have an extremely prolonged block with SCH.

### 11. Review the properties of nondepolarizing muscle relaxants.

Nondepolarizing relaxants are competitive antagonists at the NMJ and are classified by their duration of action (short-, intermediate-, and long-acting). The doses, onset, and duration of effect are described in Table 13-1.

TABLE 13-1. PROPERTIES OF NONDEPOLARIZING MUSCLE RELAXANTS

Relaxant	ED <sub>95</sub> * (mg/kg)	Intubating Dose (mg/kg)	Onset After Intubating Dose (minutes)	Duration† (minutes)
<b>Short-acting</b>				
Mivacurium	0.08	0.2	1–1.5	15–20
Rocuronium	0.3	0.6	2–3	30
<b>Intermediate-acting</b>				
Rocuronium‡	0.3	1.2	1	60
Vecuronium	0.05	0.15–0.2	1.5	60
Atracurium	0.23	0.75	1–1.5	45–60
Cisatracurium	0.05	0.2	2	60–90
<b>Long-acting</b>				
Pancuronium	0.07	0.08–0.12	4–5	90
Pipecuronium	0.05	0.07–0.85	3–5	80–90
Doxacurium	0.025	0.05–0.08	3–5	90–120

\*ED<sub>95</sub>, Dose expected to reduce single twitch height by 95%.  
†Duration measured as return of twitch to 25% of control.  
‡Rocuronium, when administered in a dose of 1.2 mg/kg, has an onset similar to succinylcholine, although the duration is significantly longer.

### 12. Review the metabolism of nondepolarizing neuromuscular blockers.

■ Aminosteroid relaxants (e.g., pancuronium, vecuronium, pipecuronium, and rocuronium) are diacetylated in the liver, and their action may be prolonged in the presence of hepatic dysfunction. Vecuronium and rocuronium also have significant biliary excretion, and their action may be prolonged with extrahepatic biliary obstruction.

- Relaxants with significant renal excretion include tubocurarine, metocurine, doxacurium, pancuronium, and pipecuronium.
- Atracurium is unique in that it undergoes spontaneous breakdown at physiologic temperatures and pH (Hoffmann elimination) as well as ester hydrolysis, and thus it is ideal for use in patients with compromised hepatic or renal function.
- Mivacurium, like SCH, is metabolized by pseudocholinesterase.

### 13. Describe common side effects of nondepolarizing neuromuscular blockers.

Histamine release is most significant with *d*-tubocurarine but is also noted with mivacurium, atracurium, and doxacurium. The amount of histamine released is frequently dose related. Cisatracurium does not seem to cause significant histamine release. Tachycardia is usually a side effect of pancuronium because of ganglionic stimulation and vagolysis.

### 14. Review medications that potentiate the actions of muscle relaxants.

- Volatile anesthetics potentiate relaxants for a number of reasons, including central nervous system depression, increasing blood flow (and relaxant molecules) to muscle, and desensitization of the postjunctional membrane.
- Local anesthetics affect the prejunctional, postjunctional, and motor membranes, depressing normal functions at all these sites.
- Calcium channel and  $\beta$ -adrenergic blockers impair ion transport, but the clinical significance at the NMJ is probably not important.
- Antibiotics, and most notably aminoglycosides, appear to have negative prejunctional and postjunctional effects. Penicillin and cephalosporins do not affect relaxant activity.
- Magnesium inhibits the release and the depolarizing effect of ACh and decreases muscle fiber excitability. Lithium also potentiates neuromuscular blockade.
- Long-term use of steroids results in a myopathy and also has some effect on the NMJ, particularly when muscle relaxants have been used for a prolonged period.
- Dantrolene depresses skeletal muscle directly and impairs excitation-contraction.

### 15. What clinical conditions potentiate the actions of neuromuscular blockers?

Respiratory acidosis, metabolic alkalosis, hypothermia, hypokalemia, hypercalcemia, and hypermagnesemia potentiate blockade. Hepatic or renal dysfunction also increases the duration of action of relaxants.

### 16. Discuss important characteristics of a nerve stimulator.

A nerve stimulator should be capable of delivering single-twitch stimulation at 0.1 Hz (1 stimulus every 10 seconds), train of four (TOF) at 2 Hz (2 per second), and tetanic stimulation at 50 Hz (50 per second). The black electrode of the stimulator is negatively charged, and the red electrode is positively charged. The black electrode depolarizes the membrane, and the red electrode hyperpolarizes the membrane. Although stimulation is possible however the electrodes are placed, maximal twitch height occurs when the negative electrode is placed in closest proximity to the nerve.

### 17. List the different patterns of stimulation.

- Single stimulus
- TOF stimulation
- Tetanic stimulation
- Posttetanic facilitation and posttetanic count
- Double-burst (DB) stimulation

### 18. Which is the simplest mode of stimulation?

Single stimulus is the simplest mode of stimulation. It consists of the delivery of single impulses separated by at least 10 seconds but is of limited clinical use.

### 19. Which mode is most commonly used to assess degree of blockade? How is it done?

TOF stimulation is the most common modality used to assess degree of blockade. Four stimuli are delivered at a frequency of 2 Hz (2 per second), and the ratio of the amplitude of the fourth to the first response in a train (T4:T1) ratio estimates the degree of block. The four twitches of the TOF disappear in reverse order as the degree of blockade deepens. The fourth twitch of the TOF disappears when 75% to 80% of the receptors are occupied, the third twitch disappears at 85% occupancy, the second twitch disappears at 85% to 90% occupancy, and the first twitch disappears at 90% to 95% occupancy. However, there is accumulating evidence that visual or tactile evaluation of the TOF response is inadequate for evaluating neuromuscular function because it has been demonstrated repeatedly that, even with experienced practitioners, subjective TOF estimations correlate poorly with true TOF fade. Recently there has been a call for more objective measures of return of motor function such as acceleromyography, strain-gauge monitoring, and electromyography.

## KEY POINTS: MUSCLE RELAXANTS



1. Metabolism of relaxants is more important than pharmacologic reversal for termination of relaxant effect.
2. Train-of-four assessment is highly subjective and has been repeatedly demonstrated to underestimate residual neuromuscular blockade.
3. It may be a best practice to administer reversal agents to all patients receiving nondepolarizing relaxants.
4. Leave clinically weak patients intubated and support respirations until the patient can demonstrate return of strength.

### 20. What is tetanic stimulation?

Tetanic stimulation consists of repetitive, high-frequency stimulation at frequencies of 50 Hz or greater. Loss of contraction during tetanic stimulation, known as *tetanic fade*, is a sensitive indicator of residual neuromuscular blockade. Tetanus stimulates the release of ACh from the presynaptic membrane, decreasing the validity of further nerve stimulation for upward of 30 minutes, leading to overestimating the return of neuromuscular function. A tetanic stimulus is painful.

### 21. Explain posttetanic facilitation and posttetanic count.

This mode of stimulation is useful during periods of intense neuromuscular blockade (when there is no response to TOF stimulation) and extends our range of monitoring. It provides an indication as to when recovery of a single twitch is anticipated and thus when reversal of neuromuscular blockade is possible. An application of a 50-Hz stimulus for 5 seconds is followed in 3 seconds by repetitive single twitches at 1 Hz. The number of twitches observed is inversely related to the degree of blockade.

### 22. What is double-burst stimulation?

DB stimulation appears to be more sensitive than TOF stimulation for detecting small degrees of residual neuromuscular blockade. DB involves the application of an initial burst of three 0.2-ms impulses at 50 Hz followed by an identical stimulation in 750 ms. The magnitude of the responses to double burst is approximately three times greater than that of TOF stimulation, thus making it easier to assess degree of fade present.

**23. What is acceleromyography?**

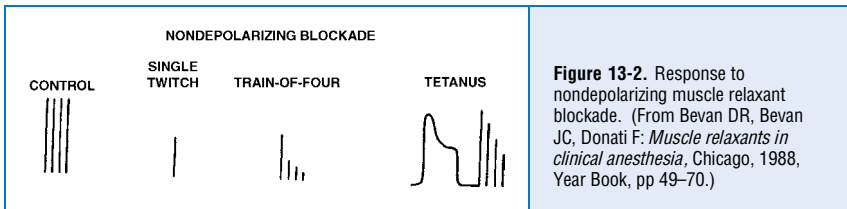
There is concern that the visual and tactile qualities of conventional TOF stimulation and assessments of strength such as 5-second head lift are not sufficiently quantitative to detect all instances of residual neuromuscular blockade. The operating concept is, as force is proportional to acceleration, acceleration is measured during TOF stimulation. Acceleromyography is thought to provide comparatively more quantitative information about TOF stimulation, and there is growing evidence that acceleromyography should be routinely used to reduce the incidence of residual weakness.

**24. Which nerves can be chosen for stimulation?**

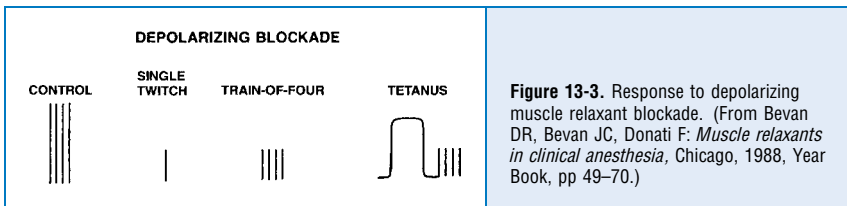
Any easily accessible nerve may be used, but the most common nerve stimulated is the ulnar nerve. Contraction of the adductor pollicis muscle of the thumb is observed. The ophthalmic branch of the facial nerve may also be stimulated, monitoring the contraction of the orbicularis oculi muscle. Stimulating the peroneal nerve near the fibular head results in dorsiflexion of the ankle. Stimulating the posterior tibial nerve and ankle results in plantar flexion of the big toe.

**25. What are the characteristic responses to the various patterns of stimulation produced by nondepolarizing agents?**

- Repetitive stimulation (TOF or tetanus) is associated with fade in the muscle response.
- Following a tetanic stimulus, response to subsequent stimulations is increased (posttetanic facilitation). This may be caused by increased ACh release or increased sensitivity at the end plate (Figure 13-2).

**26. Summarize the characteristic responses to the various patterns of stimulation produced by depolarizing relaxants (succinylcholine).**

The single-twitch, TOF, and tetanus amplitudes are uniformly decreased at any level of blockade. There is lack of fade in response to TOF and tetanus and lack of posttetanic facilitation. A desensitization or phase II blockade may develop with prolonged exposure to SCH. Phase II blockade has the same twitch characteristics as nondepolarizing blockade (Figure 13-3).

**27. For surgical purposes, based on nerve stimulation, what is adequate muscular relaxation?**

Adequate relaxation is generally present when one to two twitches of the TOF response are present, correlating with 80% depression of single-twitch height. However, volatile anesthetics, other medications, and the patient's underlying health also affect strength, and under these conditions lighter levels of blockade may be satisfactory.

**28. How might relaxant activity be terminated?**

There may be competitive agonism at the NMJ, as when acetylcholinesterase inhibitors are administered to prevent metabolism of ACh, increasing the concentration of ACh at the NMJ. Alternatively the relaxant might migrate away from its site of action, suggesting that there is a concentration gradient favoring this. Commonly such a concentration gradient is created through metabolism of the relaxant. However, selective binding of relaxant molecules is a pharmacologic alternative that is emerging in clinical practice. The first of this class of drugs likely to become commonly available is sugammadex.

**29. Review the properties of sugammadex.**

Sugammadex is a modified cyclodextrin that forms extremely tight water-soluble complexes with relaxants having steroidal nuclei (rocuronium > vecuronium >> pancuronium). The cyclodextrin molecule is rather doughnut shaped; the relaxant is bound within the doughnut hole, roughly speaking; and the dissociation rate is very low. Binding of the relaxant molecule to sugammadex creates a concentration gradient away from the NMJ. Its efficacy does not depend on renal excretion of the cyclodextrin-relaxant complex. Sugammadex appears to be relatively free of side effects. Sugammadex has no effect on acetylcholinesterase or any other cholinergic receptors.

**30. How might sugammadex alter anesthetic practice?**

The role of SCH for rapidly securing the airway has been discussed, as have the numerous side effects of SCH. Pharmacologic innovation in development of muscle relaxants per se has not resulted in a nondepolarizing relaxant with quick-onset, short duration of action and freedom from worrisome side effects. However, sugammadex may provide a useful alternative if it allows the caregiver to administer rocuronium in rapid paralysis doses ( $\approx 1.2$  mg/kg) and have an avenue for pharmacologic antagonism soon after dosing of the relaxant through tight binding of circulating relaxant molecules. In fact, the use of sugammadex after rocuronium dosing may provide faster onset-offset profile than SCH given at 1 mg/kg and eliminate the need to ever administer anticholinesterase medications. Finally, it should be mentioned that elimination of residual neuromuscular blockade in the postoperative period would be of definite clinical benefit.

**31. Discuss the appropriate time to reverse neuromuscular blockade based on nerve stimulation.**

The best method of terminating the relaxant effect is to dose sparingly and allow the relaxant to be metabolized. Recall that only one of the  $\alpha$ -subunits of the postjunctional receptor need be occupied by a relaxant molecule to inhibit function, whereas two molecules of ACh are necessary to stimulate the receptor; thus, even though the nondepolarizing relaxants are competitive antagonists, the receptor dynamics favor the relaxants. With these caveats, neuromuscular blockade can be reversed when there is at least one twitch with TOF stimulation. However, this still reflects a very deep level of blockade, and the clinician should monitor the patient closely for clinical signs of inadequate return of strength. The greater the TOF when reversed, the better. It is also important to remember that recent tetanic stimuli will result in overestimating the TOF.

**32. Review the acetylcholinesterase inhibitors commonly used to antagonize nondepolarizing blockade.**

Acetylcholinesterase inhibitors prevent the breakdown of acetylcholinesterase, increasing the amount of ACh available at the NMJ. Neostigmine, 25 to 70 mcg/kg, and edrophonium, 0.5 to 1 mg/kg, are commonly used for this purpose perioperatively. Edrophonium also stimulates the prejunctional membrane, increasing release of ACh. These medications contain positively charged quaternary ammonium groups, are water soluble, and are renally excreted.

**33. Review important side effects of acetylcholinesterase administration.**

Increasing the available ACh at the NMJ (a nicotinic receptor) also stimulates muscarinic cholinergic receptors. Of particular concern is the effect on cardiac conduction. Unopposed



muscarinic effects impair sinus-node conduction, resulting in sinus bradycardia, junctional rhythms, and in the extreme asystole. To prevent this, anticholinergics are administered in concert with the acetylcholinesterase. Glycopyrrolate, 7 to 15 mcg/kg, is coadministered with neostigmine and atropine, 7 to 10 mcg/kg, with edrophonium so the onset of anticholinergic activity is appropriately timed with the onset of acetylcholinesterase inhibition.

#### 34. Should all patients who receive nondepolarizing relaxants be reversed?

There is mounting evidence that residual neuromuscular blockade and clinical weakness occur with disturbing frequency, even when the patient has received only one dose of an intermediate-duration nondepolarizing relaxant. These residual effects have been noted even 2 hours after a single dose. Part of the problem appears to be subjective misinterpretations of full return of TOF as discussed earlier. It appears that routine reversal of all patients might be a prudent practice. How sugammadex changes anesthetic practice remains to be determined.

#### 35. Review the clinical signs associated with return of adequate strength.

See [Table 13-2](#).

**TABLE 13-2. TESTS OF RETURN OF NEUROMUSCULAR FUNCTION**

Test	Results	Percentage of Receptors Occupied
Tidal volume	>5 ml/kg	80
Single twitch	Return to baseline	75–80
Train of four	No fade	70–75
Sustained tetanus (50 Hz, 5 seconds)	No fade	70
Vital capacity	>20 ml/kg	70
Double-burst stimulation	No fade	60–70
Sustained tetanus (100 Hz, 5 seconds)	No fade	50
Inspiratory force	>–40 cm H <sub>2</sub> O	50
Head lift	Sustained 5 seconds	50
Hand grip	Return to baseline	50
Sustained bite	Sustained clenching of a tongue depressor	50

#### 36. A patient appears weak after pharmacologic reversal of neuromuscular blockade. What factors should be considered?

- Has enough time elapsed to observe peak reversal effect?
- Was blockade so intense that reversal is not possible?
- Is your twitch monitor functioning and are leads well placed?
- Are body temperature, acid-base status, and electrolyte status normal?
- Hypothermia potentiates neuromuscular blockade, as does acidosis, hypokalemia, hypocalcemia and hypermagnesemia. Is the patient receiving medications that potentiate neuromuscular blockade?
- What is the patient's renal and hepatic function?
- Importantly, if the patient is weak, do not extubate. Time usually cures all that ails.

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# LOCAL ANESTHETICS

Sunil Kumar, MD, FFARCS

## 1. What role do local anesthetics play in the practice of anesthesiology?

As local anesthetics reversibly block nerve conduction, they are used to provide regional anesthesia for surgery and postoperative analgesia for painful surgical procedures. Local anesthetics given intravenously attenuate the pressor response to tracheal intubation, decrease coughing during intubation and extubation, and are antiarrhythmic.

## 2. How are local anesthetics classified?

- **Aminoesters:** Esters are local anesthetics the intermediate chain of which forms an ester link between the aromatic and amine groups. Commonly used ester local anesthetics include procaine, chlorprocaine, cocaine, and tetracaine (Figure 14-1).
- **Aminoamides:** Amides are local anesthetics with an amide link between the aromatic and amine groups. Commonly used amide anesthetics include lidocaine, prilocaine, mepivacaine, bupivacaine, levobupivacaine, ropivacaine, and etidocaine.

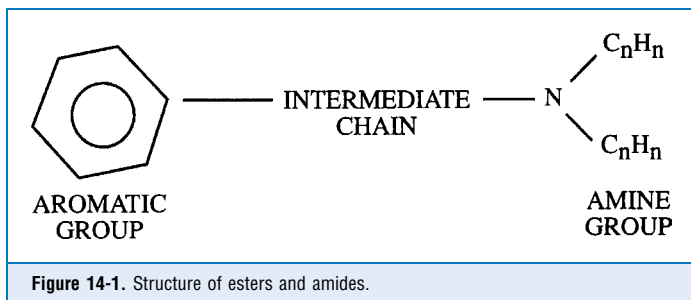


Figure 14-1. Structure of esters and amides.

## 3. How are local anesthetics metabolized?

Esters undergo hydrolysis by pseudocholinesterases found principally in plasma. Amides undergo enzymatic biotransformation primarily in the liver. The lungs may also extract lidocaine, bupivacaine, and prilocaine from circulation. Chlorprocaine is least likely to produce sustained elevation in blood levels because of very rapid hydrolysis in the blood. Risk of toxicity to esters is increased in patients with atypical pseudocholinesterase and severe liver disease and in neonates. Liver disease or decreases in liver blood flow as may occur in patients with congestive heart failure or during general anesthesia can decrease the metabolism of aminoamides.

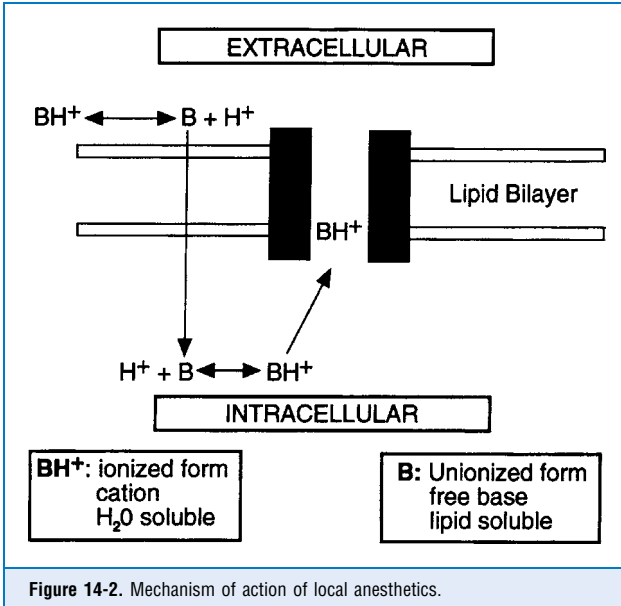
## 4. How are impulses conducted in nerve cells?

Transmission of impulses depends on the electrical gradient across the nerve membrane, which in turn depends on the movement of sodium ( $\text{Na}^+$ ) and potassium ( $\text{K}^+$ ) ions. Application of a stimulus of sufficient intensity leads to a change in membrane potential (from  $-90$  mV to  $-60$  mV), subsequent depolarization of the nerve, and propagation of the impulse. Depolarization is caused by inflow of  $\text{Na}^+$  ions from the extracellular to the intracellular space. Repolarization is caused by outflow of  $\text{K}^+$  ions from the intracellular to the extracellular space. The  $\text{Na}^+\text{-K}^+$  pump restores equilibrium in the nerve membrane after completion of the action potential.

### 5. What is the mechanism of action of local anesthetics?

The cascade of events (Figure 14-2) follows:

- Diffusion of the unionized (base) form across the nerve sheath and membrane
- Reequilibration between the base and cationic forms in the axoplasm
- Binding of the cation to a receptor site inside of the Na channel, resulting in its blockade and consequent inhibition of Na conductance



### 6. Your patient states that he was told he is allergic to Novocain, which he received for a tooth extraction. Should you avoid using local anesthetics in this patient?

Probably not. Allergy to local anesthetics is rare despite frequent use of local anesthetics. Less than 1% of adverse reaction to local anesthetics is true allergy. Most reactions labelled as allergy are probably one of the following: vasovagal response, systemic toxicity, or systemic effects of epinephrine. True allergy would be suggested by history of rash, bronchospasm, laryngeal edema, hypotension, elevation of serum tryptase, and positive intradermal testing.

Esters produce metabolites related to *p*-aminobenzoic acid and are more likely to produce allergic reactions than are amide local anesthetics. Allergic reactions following use of local anesthetics may also be caused by methylparaben or other preservatives in commercial preparations of local anesthetics. There is no cross-sensitivity between classes of local anesthetics. Therefore patients known to be allergic to ester local anesthetics could receive amide local anesthetics. Caution is still warranted in case the patient is allergic to the preservative that may be common to both classes of drugs.

### 7. What determines local anesthetic potency?

The higher the solubility, the greater the potency (Table 14-1). This relationship is more clearly seen in isolated nerve than in clinical situations when factors such as vasodilation and tissue redistribution response to various local anesthetics influence the duration of local anesthetic effect. For example, high lipid solubility of etidocaine results in profound nerve blockade in isolated nerve. Yet, in clinical epidural use etidocaine is considerably sequestered in epidural fat, leaving a reduced amount of etidocaine available for neural blockade.

TABLE 14-1. LOCAL ANESTHETIC POTENCY

Agent	Lipid Solubility	Relative Potency	Protein Binding (%)	Duration	pK <sub>a</sub>	Onset Time
Procaine	<1	1	5	Short	8.9	Slow
2-Chloroprocaine	>1	3	—	Short	8.7	Very quick
Mepivacaine	1	1.5	75	Medium	7.7	Quick
Lidocaine	3	2	65	Medium	7.9	Quick
Bupivacaine	28	8	95	Long	8.1	Moderate
Tetracaine	80	8	85	Long	8.5	Slow
Etidocaine	140	8	95	Long	7.9	Quick
Ropivacaine	14	8	94	Long	8.1	Moderate

### 8. What factors influence the duration of action of local anesthetics?

The greater the protein binding, the longer the duration of action. The duration of action is also influenced by peripheral vascular effects of the local anesthetics. For example, lidocaine, prilocaine, and mepivacaine provide anesthesia of similar duration in an isolated nerve. However, lidocaine is a more potent vasodilator, increasing absorption and metabolism of the drug, thus resulting in a shorter clinical blockade than that produced by prilocaine or mepivacaine.

### 9. What determines local anesthetic onset time?

Degree of ionization: the closer the pK<sub>a</sub> of the local anesthetic is to tissue pH, the more rapid the onset time. pK<sub>a</sub> is defined as the pH at which the ionized and unionized forms exist in equal concentrations. Because all local anesthetics are weak bases, those with pK<sub>a</sub> that lies near physiologic pH (7.4) will have more molecules in the unionized, lipid-soluble form. At physiologic pH less than 50% of the drug exists in unionized form. As mentioned, the unionized form must cross the axonal membrane to initiate neural blockade. The latency of a local anesthetic can also be shortened by using a higher concentration and carbonated local anesthetic solutions to adjust the local pH.

### 10. How does the onset of anesthesia proceed in a peripheral nerve block?

Conduction blockade proceeds from the outermost (mantle) to the innermost (core) nerve bundles. Generally speaking, mantle fibers innervate proximal structures, and core fibers innervate distal structures. This accounts for early block of more proximal areas, and muscle weakness may appear before the sensory block if motor fibers are more peripheral.

### 11. What are the maximum safe doses of various local anesthetics?

See Table 14-2.

TABLE 14-2. MAXIMUM SAFE DOSES OF LOCAL ANESTHETICS\*

Drug	Maximum Dose (mg/kg)	Drug	Maximum Dose (mg/kg)
Procaine	7	Mepivacaine	5
Chloroprocaine	8–9	Bupivacaine	2.5
Tetracaine	1.5 (topical)	Etidocaine	5
Lidocaine	5 or 7 (with epinephrine)		

\*These doses are based on subcutaneous administration and apply only to single-shot injections. Continuous infusions of local anesthetic, as might occur over several hours during labor epidural anesthesia, allow a greater total dose of anesthetic before toxic plasma levels are reached. Maximum safe dose is also influenced by vascularity of the tissue bed and whether epinephrine is added to the local anesthetic.

**12. Which regional anesthetic blocks are associated with the greatest degree of systemic vascular absorption of local anesthetic?**

Intercostal nerve block > caudal > epidural > brachial plexus > sciatic-femoral > subcutaneous. Because the intercostal nerves are surrounded by a rich vascular supply, local anesthetics injected into this area are more rapidly absorbed, thus increasing the likelihood of achieving toxic levels.

**13. Why are epinephrine and phenylephrine often added to local anesthetics? What cautions are advisable regarding the use of these drugs?**

These drugs cause local tissue vasoconstriction, limiting uptake of the local anesthetic into the vasculature and thus prolonging its effects and reducing its toxic potential (see Question 14). Epinephrine, usually in 1:200,000 concentration, is also a useful marker of inadvertent intravascular injection. Epinephrine is contraindicated for digital blocks or other areas with poor collateral circulation. Systemic absorption of epinephrine may also cause hypertension and cardiac dysrhythmias, and caution is advised in patients with ischemic heart disease, hypertension, preeclampsia, and other conditions in which such responses may be undesirable.

**14. How does a patient become toxic from local anesthetics? What are the clinical manifestations of local anesthetic toxicity?**

Systemic toxicity is caused by elevated plasma local anesthetic levels, most often a result of inadvertent intravascular injection and less frequently a result of systemic absorption of local anesthetic from the injection site. Toxicity involves the cardiovascular and central nervous systems (CNS). Because the CNS is generally more sensitive to the toxic effects of local anesthetics, it is usually affected first. The manifestations are presented below in chronologic order:

- CNS toxicity
  - Light-headedness, tinnitus, perioral numbness, confusion
  - Muscle twitching, auditory and visual hallucinations
  - Tonic-clonic seizure, unconsciousness, respiratory arrest
- Cardiotoxicity
  - Less common, but can be fatal
  - Hypertension, tachycardia
  - Decreased contractility and cardiac output, hypotension
  - Sinus bradycardia, ventricular dysrhythmias, circulatory arrest

**15. Is the risk of cardiotoxicity the same with various local anesthetics?**

There have been multiple case reports of cardiac arrest and electrical standstill after bupivacaine administration, many associated with difficult resuscitation. The cardiotoxicity of more potent drugs such as bupivacaine and etidocaine differs from that of lidocaine in the following manner:

- The ratio of the dosage required for irreversible cardiovascular collapse and the dosage that produces CNS toxicity is much lower for bupivacaine and etidocaine than for lidocaine.
- Pregnancy, acidosis, and hypoxia increase the risk of cardiotoxicity with bupivacaine.
- Cardiac resuscitation is more difficult following bupivacaine-induced cardiovascular collapse. It may be related to the lipid solubility of bupivacaine, which results in slow dissociation of this drug from cardiac sodium channels (fast-in, slow-out). By contrast, recovery from less lipid-soluble lidocaine is rapid (fast-in, fast-out).

In an effort to minimize the risk of cardiac toxicity in the event of an accidental intravascular injection, the use of bupivacaine in concentrations greater than 0.5% should be avoided, especially in obstetric epidural anesthesia. For postoperative analgesia bupivacaine concentrations of 0.25% generally provide excellent effect.

**KEY POINTS: LOCAL ANESTHETICS**

1. Local anesthetic agents are either aminoesters or aminoamides. The two classes of agents differ in their allergic potential and method of biotransformation.
2. Lipid solubility,  $pK_a$ , and protein binding of the local anesthetics determine their potency, onset, and duration of action, respectively.
3. Local anesthetic-induced CNS toxicity manifests with excitation, followed by seizures, then loss of consciousness, whereas hypotension, conduction blockade, and cardiac arrest are signs of local anesthetic cardiovascular toxicity.
4. Bupivacaine has the highest risk of producing severe cardiac dysrhythmias and irreversible cardiovascular collapse. Use of more than 0.5% concentration should be avoided, especially in obstetric epidurals.

**16. How will you prevent and treat systemic toxicity?**

- Most reactions can be prevented by careful selection of dose and concentration, use of test dose with epinephrine, incremental injection with frequent aspiration, monitoring patient for signs of intravascular injection, and judicious use of benzodiazepine to raise the seizure threshold.
- Seizures can quickly lead to hypoxia and acidosis, and acidosis worsens the toxic effects. A patent airway and adequate ventilation with 100% oxygen should be ensured.
- If seizures develop, small doses of intravenous diazepam (0.1 mg/kg) or thiopental (1 to 2 mg/kg) may terminate the seizure. Short-acting muscle relaxants may be indicated for ongoing muscle activity or to facilitate intubation if necessary.
- Cardiovascular collapse with refractory ventricular fibrillation following local anesthetics, particularly bupivacaine, can be extremely difficult to resuscitate. Treatment includes sustained cardiopulmonary resuscitation, repeated cardioversion, high doses of epinephrine, and use of bretylium to treat ventricular dysrhythmias. Intravenous intralipid has been used successfully in cases in which conventional resuscitation measures were unsuccessful. Suggested dose is initial bolus of 1.5 ml/kg of 20% intralipid solution, which can be repeated every 3 to 5 minutes up to a total maximum dose of 8 ml/kg.

**17. What is the risk of neurotoxicity with local anesthetics?**

The overall risk of permanent neurologic injury from regional anesthesia is extremely small. However, in recent years the following two complications have been described after spinal and epidural anesthesia:

- Transient neurologic symptoms manifest in the form of moderate-to-severe pain in the lower back, buttocks, and posterior thighs. These symptoms appear within 24 hours of spinal anesthesia and generally resolve within 7 days. The delayed onset may reflect an inflammatory etiology for these symptoms. They are seen most commonly with lidocaine spinal anesthesia and are rare with bupivacaine. Patients having surgery in the lithotomy position appear to be at increased risk of neurologic symptoms following either spinal or epidural anesthesia.
- Cauda equina syndrome: A few cases of diffuse injury to the lumbosacral plexus were initially reported in patients receiving continuous spinal anesthesia with 5% lidocaine dosed via microcatheters. The mechanism of neural injury is thought to be that nonhomogeneous distribution of spinally injected local anesthetic may expose sacral nerve roots to a high concentration of local anesthetic with consequent toxicity. Rare cases in the absence of microcatheters have also been described. Avoid injecting large amounts of local anesthetic in the subarachnoid space, especially if less than an anticipated response is obtained with the initial dose.

**18. Which local anesthetic is associated with the risk of methemoglobinemia?**

Prilocaine and benzocaine are the two local anesthetics responsible for most cases of local anesthetic–related methemoglobinemia, although in rare instances other agents have been implicated. Prilocaine is metabolized in the liver to O-toluidine, which is capable of oxidizing hemoglobin to methemoglobin. Prilocaine in a dose greater than 600 mg can produce clinical methemoglobinemia, making the patient appear cyanotic. Benzocaine, used as a spray for topical anesthesia of mouth and throat, can result in methemoglobinemia if excessive amounts are used in the form of multiple sprays or spraying the area for a longer duration than recommended. Methemoglobin is reduced through methemoglobin reductase, and this process is accelerated by intravenous methylene blue (1 to 2 mg/kg).

**19. Describe the role of lipid infusion in the treatment of local anesthetic toxicity.**

Systemic local anesthetic toxicity is rare but can be fatal because of relative resistance of local anesthetic–induced cardiac arrest to standard resuscitative measures. Cardiotoxicity from bupivacaine has almost always been fatal, often requiring placement of the patient on cardiopulmonary bypass while the drug slowly clears from the cardiac muscle tissue. Animal studies demonstrated that lipid infusion increases resistance to local anesthetic toxicity and improves success of resuscitation from local anesthetic overdose. In the past few years there have been several case reports of successful use of lipid emulsion in treatment of local anesthetic toxicity in humans. The mechanism of beneficial effect is thought to be a reduction in tissue binding of local anesthetic and a beneficial energetic-metabolic effect. The protocol for intralipid administration is as follows:

- Initially administer intralipid 20% at a dose of 1.5 ml/kg over 1 minute.
- Follow immediately with an infusion at a rate of 0.25 ml/kg/minute.
- Continue chest compressions (lipid must circulate).
- Repeat bolus every 3 to 5 minutes up to 3 ml/kg total dosage until circulation is restored.
- Continue infusion until hemodynamic stability is restored.
- Increase the rate to 0.5 ml/kg/min if blood pressure declines.
- A maximum total dose of 8 ml/kg is recommended.

**20. What are some of the newer local anesthetics and what are their potential applications?**

Ropivacaine is a new amide local anesthetic that is structurally and behaviorally similar to bupivacaine. Like bupivacaine, it is highly protein bound and has a long duration of action. When compared to bupivacaine, it is less cardiotoxic and produces less motor block, thus allowing analgesia with less motor compromise (differential blockade). However, some of these benefits may be related to somewhat lower potency of ropivacaine and may not exist when equipotent doses are compared. Levobupivacaine is an S(–) isomer of the racemic bupivacaine and has a safer cardiac and CNS toxicity profile compared to bupivacaine. Local anesthetic effects are similar to those of bupivacaine. Because of their superior toxicity profile, both ropivacaine and levobupivacaine are suitable for situations requiring relatively large doses of local anesthetics.

**WEBSITE**

Lipid rescue, resuscitation for cardiac toxicity  
[www.lipidrescue.org](http://www.lipidrescue.org)



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# INOTROPES AND VASODILATOR DRUGS

*Nathanael Weitzel, MD*

Editors note: chapter 1 complements this discussion.

## 1. What are the benefits of cardiovascular drugs?

All of the components of organ perfusion, including preload (end-diastolic volume), afterload, inotropy, heart rate, and myocardial oxygen supply and demand can be pharmacologically modified. An underlying concept is the Frank-Starling principle, which states that increased myocardial fiber length (i.e., end-diastolic volume) improves contractility up to a point of optimal contractile state, further stretching results in declining performance.

## 2. Discuss the limitations of drugs that alter vascular tone.

Preload can be altered with intravascular volume shifts and with drugs that change vascular tone, most notably the venous capacitance vessels. In addition, arterial vasodilators may shift failing myocardium to a more effective contractile state as a result of afterload reduction and decreased impedance to ventricular ejection. However, the intrinsic contractile state is not improved by vasodilators, in contrast to the effect of positive inotropic agents.

## 3. What are the general goals of inotropic support and the characteristics of the ideal inotrope?

The goal is increasing cardiac output by improving myocardial contractility to optimize end-organ perfusion. In addition, for enlarged hearts a decrease in ventricular diameter, wall tension, and myocardial oxygen demand is also desirable and should enhance the contractile state and myocardial perfusion. Some inotropic agents also decrease pulmonary vascular resistance, improving right heart output and forward flow.

## 4. Discuss the hemodynamic profile of the phosphodiesterase III inhibitors amrinone and milrinone.

Amrinone and milrinone are approximately equipotent to dopamine and dobutamine in increasing cardiac output through increased inotropy and improved lusitropy (myocardial relaxation). In addition to direct myocardial effects, vasodilation typically occurs, making it difficult to separate the relative contributions of these effects on enhanced cardiac output. Right ventricular function can be favorably impacted as these agents decrease pulmonary vascular resistance (comparable to 20 ppm of nitric oxide in cardiac surgery patients), thus improving forward flow. Coronary vessels and arterial bypass grafts (internal mammary and gastroepiploic arteries and radial artery grafts) become dilated; furthermore, in the presence of these drugs they are less subject to the vasoconstrictive effects of concomitantly administered  $\alpha$ -adrenergic agonists.

## 5. What untoward effects can result from use of phosphodiesterase inhibitors? How are these minimized?

Because the vasodilator effects may be profound, concurrent use of vasoconstrictors (e.g., epinephrine, norepinephrine, and phenylephrine) is often necessary, particularly after cardiopulmonary bypass. Prolonged infusion of amrinone, but not milrinone, may cause significant thrombocytopenia through nonimmune-mediated peripheral platelet destruction.

## 6. What are other advantages of the phosphodiesterase inhibitors?

In addition to positive inotropy, lusitropy, vasodilation, and a relative lack of significant tachyarrhythmias, these inhibitors may transiently restore  $\beta$ -adrenergic function by decreasing cyclic adenosine monophosphate (cAMP) breakdown and potentiating the action of administered  $\beta$ -adrenergic agonists. These drugs dilate coronary arteries and grafts, improving collateral coronary circulation and attenuating thromboxane activity; in certain clinical situations they may help decrease myocardial oxygen consumption.

## 7. What intracellular intermediary is involved in the actions of phosphodiesterase III inhibitors and sympathomimetic amines?

Both drug classes increase intracellular cAMP concentrations. Sympathomimetic  $\beta$ -adrenergic stimulation activates sarcolemmal adenylyl cyclase, resulting in the generation of increased cAMP from adenosine triphosphate (ATP). Phosphodiesterase (PDE) III inhibitors decrease the breakdown of cAMP. A synergistic effect is noted when  $\beta$ -adrenergic agonists are infused along with PDE III inhibitors.

## 8. How does increased intracellular cAMP affect the cardiac myocyte? What are the corresponding effects on myocardial function?

Increased intracellular cAMP activates protein kinases, which phosphorylate proteins in the sarcolemma, sarcoplasmic reticulum (SR), and tropomyosin complex. This causes elevated calcium ( $\text{Ca}^{2+}$ ) influx via  $\text{Ca}^{2+}$  channels, amplifying the effects of  $\text{Ca}^{2+}$  on contractile elements. In addition, increased protein phosphorylation in the SR and tropomyosin complex improves lusitropy by stimulating reuptake of  $\text{Ca}^{2+}$  into the SR. The end result is a restoration of the myofilaments to their resting state.

## 9. Describe the hemodynamic profiles of epinephrine, norepinephrine, and dopamine.

The effects of a low-dose infusion of epinephrine ( $<0.04$  mcg/kg/min) are primarily limited to stimulation of  $\beta_1$ - and  $\alpha_2$ -adrenergic receptors in the heart and peripheral vasculature, resulting in positive chronotropy, dromotropy (conduction velocity), inotropy, increased automaticity, and vasodilation. Moderate-dose infusion (0.04 to 0.12 mcg/kg/min) generates greater  $\alpha$ -adrenergic effects and vasoconstriction, and high-dose infusion results in such prominent vasoconstriction that many of the  $\beta$ -adrenergic effects are blocked.

Hemodynamic dose-response relationship of epinephrine:

- $<0.04$  mcg/kg/min      Primarily  $\beta$ -stimulation
- 0.04 to 0.12 mcg/kg/min      Mixed alpha and  $\beta$ -stimulation
- $>0.12$  mcg/kg/min      Primarily  $\alpha$ -stimulation

The potency of norepinephrine in stimulating  $\beta$ -adrenergic receptors is similar to that of epinephrine, but it results in significant  $\alpha$ -adrenergic stimulation at much lower doses. Typical dosage ranges are 0.02 to 0.25 mcg/kg/min.

Dopamine stimulates specific postjunctional dopaminergic receptors in renal, mesenteric, and coronary arterial beds to produce vasodilation. These dopaminergic effects occur at lower doses (0.5 to 1.0 mcg/kg/min), becoming maximal at 2 to 3 mcg/kg/min. At intermediate doses (2 to 6 mcg/kg/min)  $\beta_1$ -adrenergic stimulation is evident. Beginning at doses of about 10 mcg/kg/min (but as low as 5 mcg/kg/min),  $\alpha$ -adrenergic stimulation is seen, which at higher doses overcomes dopaminergic effects, producing vasoconstriction.

## 10. Describe the hemodynamic profiles of isoproterenol and dobutamine.

Isoproterenol is an extremely potent  $\beta_1$ - and  $\beta_2$ -agonist that possesses no  $\alpha$ -stimulating properties. Therefore isoproterenol increases heart rate, automaticity, and contractility and dilates both venous capacitance and arterial vessels. It may be a good choice for

heart-rate maintenance in a denervated nonpaced transplanted heart. Dobutamine acts principally on  $\beta$ -adrenergic receptors, impacting  $\beta_1$ -receptors in a relatively selective fashion. In addition, it has a mild indirect  $\beta_1$ -stimulating effect that is secondary to prevention of norepinephrine reuptake but is offset by slightly more potent  $\beta_2$ -stimulation. Generally at clinical doses minimal increases in heart rate, positive inotropy, increased cardiac output, and minimal or modest decreases in systemic and pulmonary vascular resistance occur. Because of the indirect  $\beta_1$ -stimulating effect, patients concurrently receiving  $\beta$ -blockers can exhibit marked increases in systemic vascular resistance without improvement in cardiac output. In addition, an occasional patient will display dose-related increases in heart rate.

**11. Which characteristics of  $\beta$ -adrenergic agonists limit their effectiveness?**

- Positive chronotropic and arrhythmogenic effects (dose-dependent effect with epinephrine, isoproterenol, and dobutamine) result in increased myocardial oxygen consumption.
- Vasoconstriction secondary to  $\alpha_1$ -activation (with norepinephrine, high-dose epinephrine, and high-dose dopamine) results in increased afterload and subsequent increased myocardial wall tension.
- Isoproterenol and dobutamine to a lesser extent produce vasodilation caused by stimulation of vascular  $\beta_2$ -receptors. Excessive vasodilation may decrease coronary perfusion.

**12. How may the side effects and limitations of  $\beta$ -adrenergic agonists be minimized?**

Side effects may be decreased by appropriate dosage adjustments and use of combinations of agents. Currently PDE III inhibitors have a prominent role in this regard. However, both vasopressin and nifedipine at low doses may prove beneficial in these circumstances.

**13. Is digitalis useful as an inotrope intraoperatively?**

Because of its narrow therapeutic ratio and adverse interactions with fluid and electrolyte shifts, digitalis is rarely used intraoperatively as an inotrope.

**14. What are the mechanism and sites of action of nitrovasodilators?**

Nitrates such as nitroglycerin and sodium nitroprusside are pro-drugs that penetrate the vascular endothelium and become reduced to nitric oxide (NO). Nitroglycerin requires intact endothelial enzymatic activity, which is not present in the smallest or damaged vessels, whereas nitroprusside nonenzymatically degrades into NO and cyanide (a compound highly toxic to the mitochondrial respiratory chain). NO then stimulates production of cyclic guanosine monophosphate (cGMP), resulting in decreased cellular calcium levels and thus vascular smooth muscle relaxation.

Sodium nitroprusside acts primarily on the arterial vasculature whereas nitroglycerin has its most prominent effect on venous capacitance vessels (although this is less true with higher doses). NO can also be delivered directly to the pulmonary circulation by inhalation, thereby reaching the pulmonary vascular smooth muscle by diffusion across the alveolar-capillary membrane. Direct delivery to the pulmonary circulation reduces potentially undesirable systemic hypotension and causes specific pulmonary vasodilation.

**15. Describe the antianginal effects of nitrates.**

Beneficial effects of nitroglycerin and other nitrates in anginal therapy result from improved coronary perfusion, a reduction in myocardial oxygen consumption ( $MVO_2$ ), and antiplatelet effects. Coronary artery spasm is ameliorated, and dilation of epicardial coronary arteries, coronary collaterals, and atherosclerotic stenotic coronary segments occurs. Venodilation reduces venous return, ventricular filling pressures, wall tension, and  $MVO_2$  and improves subendocardial and collateral blood flow. Platelet aggregation is inhibited by release of NO and increased formation of cGMP.

**KEY POINTS: INOTROPES AND VASODILATOR DRUGS**

1. Congestive heart failure with preserved left ventricular systolic function (EF >35%) in the absence of ischemia and valvular pathology suggests diastolic heart failure.
2. Vasopressin has a role in blood pressure maintenance in septic shock, cardiogenic shock, and other shock states.
3. Beneficial effects of nitroglycerin and other nitrates in anginal therapy result from a reduction in  $MVO_2$ , improved coronary perfusion, and platelet effects.
4. Nicardipine and clevidipine are fast-acting CCB agents with a nearly ideal hemodynamic profile for many cardiac patients with hypertension. They act by reducing afterload, increasing coronary blood flow, and improving myocardial oxygen balance.
5. Low-dose dopamine is ineffective for prevention and treatment of acute renal failure and protection of the gut, and dopamine in general is not an effective treatment for septic shock.
6. Levosimendan is a newer agent that shows promise in the treatment of heart failure and cardiogenic shock following cardiac surgery.

**16. Describe the etiology of tachyphylaxis with nitrovasodilators.**

Therapy with nitroglycerin is often confounded by tachyphylaxis, especially with long-term use, because of changes in the enzymatic machinery responsible for its transformation into NO. Tachyphylaxis may also be caused by adaptive changes in the vascular system itself. Nitrates may also be of limited clinical effect in the presence of a preload insensitive system and fixed pulmonary hypertension.

The presence of tachyphylaxis with administration of sodium nitroprusside suggests a therapeutic ceiling and ensuing cyanide toxicity and is usually associated with prolonged infusions of more than 2 mcg/kg/min or when sulfur donors and methemoglobin stores are exhausted.

**17. Discuss the types and mechanisms of action of selective vasodilating agents available for clinical use.**

Hydralazine directly relaxes smooth muscle, dilating arterioles to a much greater extent than veins and decreasing diastolic more than systolic blood pressure. The response is slow, with onset of 15 to 20 minutes, and somewhat unpredictable, often causing prolonged hypotension. Reflex tachycardia may also be an undesired side effect.

Nicardipine is a short-acting selective calcium channel blocker (CCB) that acts on the arteriolar beds, providing easier titration and controlled reduction in systemic blood pressure. Nicardipine is becoming the arterial vasodilator of choice for cardiac surgery patients with hypertension since it has more selective coronary vasodilation than systemic vasodilation. The end result is a reduction in afterload; increased stroke volume; and increased coronary blood flow, which results in a favorable effect on myocardial oxygen balance. Onset is 5 to 15 minutes, and duration of action is 4 to 6 hours.

Clevidipine is a new third-generation CCB that is considered an ultrashort-acting arteriolar vasodilator. Metabolized by plasma esterases, the half-life of clevidipine is approximately 2 minutes, with a context-sensitive half-life of 2 to 5 minutes regardless of duration of infusion. It acts much like nicardipine in that it selectively dilates the arteriolar bed, reducing afterload without affecting cardiac filling pressures. It comes in an emulsion much like propofol.

Fenoldopam is a unique parenteral vasodilator that acts via peripheral dopamine-1 receptors. This has a vasodilatory effect that is selective for renal and splanchnic vasculature and causes mild renal diuresis. Onset is 5 minutes, and half-life is roughly 5 minutes with a

duration of action of 30 to 60 minutes with infusion. Fenoldopam was thought to provide some degree of renal protection against acute kidney injury (at least in patients having abdominal aortic surgery), but trials in intensive care unit patients and the operative setting have not shown clear benefit. Fenoldopam can cause significant hypotension; thus, if it is used as a renal protective agent, close monitoring of the blood pressure is needed to ensure adequate renal perfusion.

**18. Describe the mechanism of action of vasopressin.**

Arginine vasopressin (AVP) has action at three subtypes of receptors (V1, V2, and V3). The V1 receptor stimulates vascular smooth muscle contraction, resulting in the vasopressor response of AVP. The V2 receptors primarily act in the kidney to produce water retention (antidiuretic hormone), and the V3 receptors act in the central nervous system, and modulate corticotropin secretion. The vasopressin system makes up one of the three vasopressor systems in the body along with the sympathetic system and the renin-angiotensin system. The plasma half-life of AVP is 4 to 20 minutes; thus it must be delivered by infusion for prolonged effects.

**19. How may vasopressin aid in the management of cardiogenic or septic shock?**

Vasopressin is becoming a mainstay in the treatment of shock states in combination with adrenergic inotropic agents. In the presence of a systemic inflammatory response it has been noted that septic shock patients tend to have low plasma vasopressin concentrations. The use of vasopressin has been shown to improve hemodynamics and reduce requirements of adrenergic agents. The dosage range is still debated, with many studies show doses of 0.01 to 0.04 units/min to be effective. There are published data supporting use of vasopressin following cardiopulmonary bypass, with doses as high as 0.1 unit/min. Bolus doses in situations of cardiac arrest are 20 to 40 units per ACLS guidelines. Higher doses of vasopressin carry higher risk of intense vasoconstriction, bringing up concerns for splanchnic hypoperfusion; however, studies have not clearly defined the extent of this risk.

**20. How may  $\beta$ -type natriuretic peptide aid in the management of end-stage congestive heart failure?**

Although large, prospective randomized trials have not been conducted to date with nesiritide ( $\beta$ -type natriuretic peptide), some initial data seem to indicate that it may be beneficial for the management of precardiac transplant patients with increased pulmonary vascular resistance and renal failure. Indeed,  $\beta$ -type natriuretic peptide improves the hemodynamic profile, increases renal sodium excretion, and suppresses the renin-angiotensin-aldosterone system, improving clinical symptomatology.

**21. What is diastolic heart failure and what management options are available?**

Congestive heart failure in the presence of preserved left ventricular systolic function (ejection fraction [EF] >35%) and the absence of ischemia and valvular pathology suggests diastolic heart failure. Chronic management with angiotensin-converting enzyme inhibitors is being evaluated in several large clinical trials, with the premise that decreased aldosterone and angiotensin levels ameliorate deleterious collagen remodeling of the cardiac structure. Acute management is directed at alleviating diastolic dysfunction by the following:

- Reduction in heart rate with  $\beta$ -blockade may benefit preload-sensitive diastolic dysfunction.
- Low-dose PDE inhibitors and L-type CCBs (dihydropyridines) may improve cellular myocardial relaxation.
- Nitrates may improve symptomatology in certain volume-overloaded cases of diastolic dysfunction.

**22. What are the clinical indications and current evidence for using dopamine?**

There is now scientific evidence that low-dose dopamine is ineffective for prevention and treatment of acute renal failure and protection of the gut. It may be apparent that low-dose

dopamine, in addition to not achieving the preset goal of organ protection, may also be deleterious because it can induce renal failure in normovolemic and hypovolemic patients. Dopamine also suppresses the secretion and function of anterior pituitary hormones, thereby aggravating catabolism and cellular immune dysfunction and inducing central hypothyroidism. In addition, it blunts the ventilatory drive, increasing the risk of respiratory failure in patients who are being weaned from mechanical ventilation. There have also been recent observational trials that seem to indicate an increased mortality in septic patients treated with dopamine, whereas similar patients treated with norepinephrine did not demonstrate this mortality risk. Based on current metaanalysis (which is lacking good, prospective randomized data), dopamine is now considered a fourth-line agent for cardiogenic, septic, or vasodilatory shock.

**23. Describe the new inotropic agent levosimendan, including mechanism of action and place in clinical therapy.**

Levosimendan is a pyridazinone-dinitrite and a member of a new class of pharmacologic agents, the “calcium sensitizers.” This drug acts to increase contractility without elevating intramyocardial calcium levels. This is achieved by stabilizing troponin C in an active form, thus providing inotropic support in similar fashion to other agents but with much lower intracellular calcium requirements. It increases systolic force while maintaining coronary perfusion via coronary artery vasodilation, along with mild systemic and pulmonary vasodilation. It can be used synergistically with  $\beta$ -adrenergic agents and seems to have a low arrhythmogenic potential.

Levosimendan performs as well if not better in congestive heart failure when compared to dobutamine. In cardiac surgery patients the combination of dobutamine and levosimendan resulted in better maintenance of stroke volume following bypass than dobutamine and milrinone combined. Based on current evidence, recommended dosing is to start with a  $<36$  mcg/kg bolus followed by a 0.4 mcg/kg/min infusion. There are numerous trials demonstrating success with this agent, but more randomized trials are needed. Infusion durations in current studies only reach 24 hours, limiting long-term use recommendations.

**24. What mechanism of action accounts for the inotropic effect of thyroid hormone?**

Thyroid hormone affects chronic changes in protein synthesis such as alterations of nuclear synthetic machinery, structural changes of the myosin isozyme, and increased expression of  $\beta$ -adrenergic receptors. In addition, more immediate augmentation of contractility results secondary to an increase in mitochondrial respiration and ATP production, enhanced function of sarcolemmal Ca-ATPase, and augmented sodium entry into myocytes. Elevated intracellular sodium levels increase intracellular calcium concentration and activity.

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# PREOPERATIVE MEDICATION

*Sunil Kumar, MD, FFARCS*

## 1. List the major goals of premedication.

Premedication needs to be tailored to the needs of individual patient. Important goals include:

- Sedation and anxiolysis
- Analgesia and amnesia
- Antisialagogue effect
- To maintain hemodynamic stability, including decrease in autonomic response
- To prevent and/or minimize the impact of aspiration
- To decrease postoperative nausea and vomiting
- Prophylaxis against allergic reaction

## 2. List the most commonly used preoperative medications with the appropriate dose.

See [Table 16-1](#).

## 3. What factors should be considered in selecting premedication for a patient?

- Patient age and weight
- Physical status
- Levels of anxiety and pain
- Previous history of drug use or abuse
- History of postoperative nausea, vomiting or motion sickness
- Drug allergies
- Elective or emergency surgery
- Inpatient or outpatient status

## 4. What factors limit the ability to give depressant medications preoperatively?

- Extremes of age
- Head injuries or altered mental status
- Limited cardiac or pulmonary reserve
- Hypovolemia
- Full stomach

## 5. What is meant by psychologic premedication?

Most patients are very anxious before surgery. An informative and comforting visit by an anesthesiologist may replace many milligrams of depressant medication and acts as psychologic premedication. During this visit a full description of the planned anesthetic events to anticipate in the perioperative period should be provided to the patient and family members, and all questions the patient or family may have should be answered. However, psychologic preparation cannot accomplish everything and will not relieve all anxiety.

## 6. Discuss the role of benzodiazepines in premedication.

Benzodiazepines are the most popular drugs used for premedication. They act on receptors for the inhibitory neurotransmitter,  $\gamma$ -aminobutyric acid, producing anxiolysis, amnesia, and sedation at doses that do not produce significant cardiovascular or ventilatory depression.



TABLE 16-1. COMMON PREOPERATIVE MEDICATIONS, DOSAGE, AND ROUTE\*

Medication	Route of Administration	Dose (mg)	Purposes
Diazepam	Oral, IV	5–10	Sedation
Midazolam	IV	1–2	Sedation
Morphine	IV	2–10	Analgesia
Meperidine	IM	25–100	Analgesia
Ranitidine	Oral, IV	150 mg and 50 mg, respectively	Decrease gastric pH
Metoclopramide	Oral, IV	5–20	Gastrokinetic
Omeprazole	Oral	20	Proton pump inhibitor
Pantoprazole	IV	40	Proton pump inhibitor
Glycopyrrolate	IV	0.1–0.3	Weak sedative, antisialagogue
Scopolamine	IM, IV	0.3–0.6	Sedative, antisialagogue
Promethazine <sup>†</sup>	IM	25–50	Antiemetic
Ketamine	IM, oral	1–2 mg/kg and 6 mg/kg, respectively	Sedation

*IM*, Intramuscular; *IV*, intravenous.  
 \*Potent medications should always be titrated to effect.  
<sup>†</sup>FDA black box warning against use in children younger than 2 years old.

These drugs are not analgesic and are not associated with nausea and vomiting. Side effects of benzodiazepines include excessive and prolonged sedation in occasional patients, especially with lorazepam. Sometimes paradoxical agitation rather than anxiolysis may follow these drugs. The most commonly used benzodiazepine in current practice is midazolam, administered intravenously in small incremental doses in the immediate preoperative period. Diazepam is associated with pain on intramuscular or intravenous injection and increased risk of phlebitis.

#### 7. List the most common side effects when opioids are used as a premedication.

Pruritus	Histamine release
Nausea and vomiting	Delayed gastric emptying
Respiratory depression	Stiff chest syndrome
Orthostatic hypotension	Sphincter of Oddi spasm

#### 8. Describe the reasons to include an anticholinergic agent in premedication.

The main indications for these drugs include the following:

- Drying of airway secretions. They are particularly useful for intraoral or airway surgery, before applying topical anesthesia to the airway, and general anesthesia with endotracheal intubation.

- Prevention of reflex bradycardia when vagal overactivity is anticipated, particularly during pediatric anesthetic induction and airway manipulation. Atropine or glycopyrrolate can best be given intravenously just before anticipated vagal stimulation.
- Sedative and amnesic effect: Being tertiary amines, scopolamine and atropine can cross the blood-brain barrier and produce sedation and amnesia. In this regard scopolamine is about 8 to 10 times as potent as atropine. Glycopyrrolate is a quaternary amine, does not cross the blood-brain barrier, and therefore is devoid of appreciable sedative effect.

### 9. Summarize the effects of commonly used anticholinergic agents.

See Table 16-2.

TABLE 16-2. EFFECTS OF COMMONLY USED ANTICHOLINERGIC AGENTS			
	Atropine	Scopolamine	Glycopyrrolate
Tachycardia	++	+	++
Antisialagogue effect	+	+++	++
Sedation, amnesia	+	+++	0
Central nervous system toxicity	+	++	0
Lower esophageal sphincter relaxation	++	++	++
Mydriasis and cycloplegia	+	+++	0

0, None; +, mild; ++, moderate; +++, marked.

### 10. List the common side effects of anticholinergic medications.

- Drying and thickening of airway secretions
- Decrease in lower esophageal sphincter tone
- Mydriasis and cycloplegia
- Central nervous system toxicity
- Prevention of sweating
- Hyperthermia

### 11. A patient in the preoperative holding area is delirious after receiving only 0.4 mg of scopolamine as a premedication. What is the cause of the delirium? How is it managed?

The most likely cause of the delirium is central anticholinergic syndrome produced by scopolamine. Central toxicity can follow the administration of tertiary amine scopolamine (and less frequently following atropine), which crosses the blood-brain barrier. The toxic symptoms are infrequent following the usual premedication dose. However, elderly patients are more prone to this side effect. Physostigmine is the only acetylcholinesterase inhibitor that crosses the blood-brain barrier and can be used to treat the central anticholinergic syndrome in a dose of 15 to 60 mcg/kg intravenously, administered slowly to prevent seizures.

### 12. How does the concern for aspiration pneumonitis influence the choice of premedication?

Aspiration is discussed more fully in Chapter 39. The actual incidence of clinically significant aspiration pneumonitis is extremely rare in healthy patients having elective surgery. In the past many anesthesiologists routinely administered pharmacologic agents such as H<sub>2</sub> antagonists, antacids, and gastrokinetics in an attempt to reduce the volume and increase the

pH of the gastric contents of their patients in the preoperative period. In view of the extremely low incidence of clinically significant aspiration pneumonitis in healthy patients having elective surgery, *routine and indiscriminate* use of antacids, gastric acid secretion blockers, antiemetics, anticholinergics, and gastrokinetic medications is not warranted.

## KEY POINTS: PREOPERATIVE MEDICATION



1. A preoperative visit by an informative and reassuring anesthesiologist provides useful psychologic preparation and calms the patient's fears and anxiety before anesthesia.
2. The choice of premedication depends on the physical and mental status of the patient, whether the patient is an inpatient or outpatient, whether the surgery is elective or emergent, and whether the patient has a history of postoperative nausea and vomiting.
3. The risk of clinically significant aspiration pneumonitis in healthy patients having elective surgery is very low. Routine use of pharmacologic agents to alter the volume or pH of gastric contents is unnecessary.
4. In the patients considered to be at increased risk of pulmonary aspiration, a 15- to 30-ml oral dose of nonparticulate acid given 15 to 30 minutes before induction of anesthesia is the most effective way to raise gastric pH above 2.5.
5. Many patients require little or no premedication.
6. Pediatric patients are especially prone to bradycardia during anesthesia and benefit from anticholinergic premedication.

### 13. Is it safe to allow patients to drink some water to swallow preoperative medications?

Yes, it is acceptable to allow patients to take preoperative medications, including the patient's usual medications, with up to 150 ml of water in the hour preceding induction of anesthesia.

### 14. What are the differences between premedication of pediatric vs. adult patients?

Pediatric patients have the following special needs:

- They are more difficult to prepare psychologically for surgery and anesthesia.
- There is greater emphasis on the oral route of administration because most children fear needles.
- Vagolytics are used more frequently because of a greater incidence of bradycardia on induction.

### 15. How does the age of pediatric patients influence premedication?

Children up to 6 months of age do not appear to suffer anxiety when separated from parents. However, preschool children older than 6 months are at greatest risk of separation anxiety and may suffer long-term psychologic trauma from a negative hospital experience. It is difficult to reassure and explain the expected events to this group. It is easier to communicate with patients older than 5 years, who can be reassured. Parental behavior is also important in the psychologic preparation of pediatric patients. The needs of each patient must be assessed individually. Most children older than 1 year benefit from some sedative premedication. Oral midazolam (0.5 mg/kg dissolved in flavored syrup, to a maximum dosage of 20 mg) is commonly used. Atropine may be given intravenously once venous access has been obtained, just before airway manipulation, which can provoke vagal reflexes.

**16. Describe the preoperative management of a morbidly obese patient with a difficult airway. Assume that the patient is otherwise healthy.**

A morbidly obese patient is considered at increased risk of pulmonary aspiration during induction of anesthesia because of delayed gastric emptying and the possibility of difficult airway management. Therefore H<sub>2</sub> blockers given the evening before (if possible) and the morning of surgery, preoperative metoclopramide, and oral nonparticulate antacids are in order. Glycopyrrolate is useful for planned fiberoptic intubation. It improves visualization by drying secretions, increases the effectiveness of the topical anesthesia, and decreases airway responsiveness. Opioids and benzodiazepines should be judiciously titrated, using supplemental oxygen and close observation to ensure an awake, appropriately responding patient who can protect his or her own airway.

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# PREOPERATIVE EVALUATION

*Mark H. Chandler, MD*

## 1. What are the goals of the preoperative evaluation?

The preoperative evaluation consists of gathering information about the patient and formulating an anesthetic plan. The overall objective is reduction of perioperative morbidity and mortality. Ideally the preoperative evaluation is performed by the person who will administer the anesthetic.

## 2. Discuss the important features of the preoperative evaluation.

The anesthesiologist should review the surgical diagnosis, organ systems involved, and planned procedure. Important features include personal interview, physical examination, and review of medical records. Important questions involve medications, drug allergies, substance abuse (e.g., cigarettes, alcohol, illicit drugs), review of systems, and prior anesthetic experience (i.e., history of difficult intubation, delayed emergence, malignant hyperthermia, prolonged neuromuscular blockade, or postoperative nausea and vomiting). From this evaluation the anesthesiologist decides if any preoperative tests or consultations are indicated and then formulates an anesthetic care plan.

## 3. How often does the preoperative evaluation alter care plans?

It has been found that care plans were altered in 20% of all patients (including 15% of American Society of Anesthesiologists [ASA] class 1 and 2 patients) because of conditions identified at the preoperative evaluation. The most common conditions resulting in changes were gastric reflux, insulin-dependent diabetes mellitus, asthma, and suspected difficult airway. These findings indicate that, whenever possible, it is preferable in all patients to do the preoperative evaluation before the day of surgery.

## 4. What are the features of informed consent?

Informed consent involves the communication of the anesthetic plan in terms the patient understands and covers everything from premedication and preoperative procedures to intraoperative management and postprocedural care (e.g., management of pain, nausea, and vomiting). The alternatives, potential complications, and risks vs. benefits are discussed, and the patient's questions are answered. Preoperative evaluation and informed consent establish a trusting doctor-patient relationship that significantly diminishes patient anxiety and measurably influences postoperative recovery and outcome.

## 5. What is the physical status classification of the ASA?

The ASA classification was created in 1940 for the purposes of statistical studies and hospital records. It is useful both for outcome comparisons and as a convenient means of communicating the physical status of a patient. Unfortunately it is imprecise, and a patient often may be placed in different classes by different anesthesiologists. In addition, the higher ASA class only roughly predicts anesthetic risk. The six classes are:

- Class 1: A normal healthy patient.
- Class 2: A patient with mild systemic disease.
- Class 3: A patient with severe systemic disease.

- Class 4: A patient with severe systemic disease that is a constant threat to life.
- Class 5: A moribund patient who is not expected to survive without the operation.
- Class 6: A declared brain-dead patient whose organs are being removed for donor purposes.

An “E” is added to the status number to designate an emergency operation.

### 6. How long should a patient fast before surgery?

In 1999 the American Society of Anesthesiologists task force on preoperative fasting reviewed a series of studies and compiled guidelines for practitioners (Table 17-1).

These guidelines should be modified according to the patient’s disease state and airway difficulty. Current fasting guidelines for pediatric patients are as follows: clear liquids up to 2 hours before surgery; breast milk up to 4 hours before surgery; and solid foods, including nonhuman milk and formula, up to 6 hours before surgery.

**TABLE 17-1. PREOPERATIVE FASTING RECOMMENDATIONS**

Ingested Material	Minimum Fasting Period (Hours)
Clear liquids (examples include water, fruit juices without pulp, carbonated beverages, clear tea and black coffee; clear liquids should not include alcohol)	2 hours
Breast milk	4 hours
Infant formula	6 hours
Nonhuman milk	6 hours
Light meal (a light meal typically consists of toast and clear liquids)	6 hours
Full, heavy, fatty meal	8 hours

### 7. What are the appropriate preoperative laboratory tests? Which patients should have an electrocardiogram? Chest radiography?

No evidence supports the use of routine laboratory testing. Rather, there is support for the use of selected laboratory analysis based on the patient’s preoperative history, physical examination, and proposed surgical procedure (Table 17-2). Unless there has been an intervening change in status, electrocardiogram and chest radiograph obtained within 6 months of the procedure need not be repeated. Likewise, chemistries and hemoglobin/hematocrit values obtained within 1 month are acceptable in the stable situations. Coagulation studies should be no more than 1 week old.

### 8. What is the generally accepted minimum hematocrit for elective surgery?

There is no specific minimum; it depends on the clinical setting. Screening baseline hemoglobins for surgeries without significant blood loss do not add any value to estimations of perioperative risk or adverse outcomes. The potential blood loss and oxygen demands associated with the proposed surgical procedure must be considered, as well as patients’ medical conditions that may place them at increased risk for ischemia, including coronary atherosclerosis, cerebral insufficiency, or renovascular disease. Patients with advanced pulmonary disease also tolerate anemia poorly. Elderly patients with anemia often have a poorer functional status, longer hospitalizations, and higher mortality at 1 year.

**TABLE 17-2. APPROPRIATE PREOPERATIVE LABORATORY TESTS BASED ON PATIENT HISTORY AND PHYSICAL EXAMINATION\***

Test	Indications
Electrocardiogram	Cardiac and circulatory disease, respiratory disease, advanced age
Chest radiograph	Chronic lung disease, history of congestive heart disease
Pulmonary function tests	Reactive airway disease, chronic lung disease, restrictive lung disease
Hemoglobin/hematocrit	Advanced age, anemia, bleeding disorders, other hematologic disorders
Coagulation studies	Bleeding disorders, liver dysfunction, anticoagulants
Serum chemistries	Endocrine disorders, medications, renal dysfunction
Pregnancy test	Uncertain pregnancy history, history suggestive of current pregnancy

\*At least 50% of the task force experts agreed that the listed tests were beneficial when used selectively. Because of a lack of solid evidence in the literature, these indications are somewhat broad and vague and limit the clinical use of the guidelines. The definition of advanced age is vague and should be considered in the context of that patient's overall health.

### 9. Are there ways of predicting which patients will have pulmonary complications?

Among the most common risk factors for postoperative pulmonary complications (PPCs) is chronic obstructive pulmonary disease and advanced age; a more complete list of risk factors is in [Table 17-3](#). Fortunately the more commonly seen PPCs rarely result in postoperative mortality; thus most surgeries may be performed even when these risk factors are present.

Indications for pulmonary function testing are addressed in Chapter 9.

**TABLE 17-3. RISK FACTORS FOR POSTOPERATIVE PULMONARY COMPLICATIONS**

Preoperative Risk Factors	Intraoperative Risk Factors
COPD	Site of surgery
Age	General anesthesia
Inhaled tobacco use	Pancuronium use
NYHA class II pulmonary hypertension	Duration of surgery
OSA	Emergency surgery
Nutrition status	

From the New York Heart Association (NYHA).  
*COPD*, Chronic obstructive pulmonary disease; *OSA*, obstructive sleep apnea.

### 10. When are preoperative consultations with other specialists indicated?

Preoperative consultations fall into two general categories:

- Those cases that need more information or expertise to establish or quantify a diagnosis that has implications for anesthetic management. An example is asking a cardiologist to evaluate a 50-year-old man with recent onset of exertional chest pain.

- Patients in whom the diagnosis is known, but further evaluation and treatment are needed to optimize their medical condition before surgery. Referring patients with poorly controlled diabetes, hypertension, or asthma to an internist are examples.

## KEY POINTS: PREOPERATIVE EVALUATION



1. Preoperative laboratory testing should be selective and individualized.
2. The American College of Cardiology/American Heart Association guidelines for cardiac testing for noncardiac procedures is the current gold standard for preoperative cardiac assessment.
3. The most important information obtained in a preanesthetic evaluation comes from a thorough, accurate, and focused history and physical examination.
4. A patient's baseline hemoglobin tends to predict the need for transfusion when large blood loss occurs.
5. The four active cardiac conditions that will likely result in surgical cancellation to allow further cardiac evaluation and treatment are unstable coronary syndrome, decompensated heart failure, significant cardiac arrhythmias, and severe valvular disease.
6. Before halting a patient's anticoagulation, one must consider the type and urgency of surgery, the possibility and consequences of intraoperative hemorrhage, and, perhaps most important, the reason the patient is anticoagulated.

### 11. What benefits and risks are associated with preoperative cigarette cessation?

All health care providers should take advantage of *any* opportunity to encourage patients to quit smoking. In years past various arguments were made to suggest that smoking cessation immediately before surgery increased certain perioperative risks such as increased airway irritability, diminished wound healing with nicotine replacement therapy, and increased patient anxiety associated with nicotine withdrawal. Most of these arguments have since been disproven and nonetheless pale in comparison to the overall health benefit of smoking cessation.

### 12. How long before surgery must a patient quit smoking to realize any health benefits?

All patients who smoke should understand that smoking cessation even immediately before surgery has profound, measurable health benefits. Nicotine is a stimulant and has a half-life of only 1 to 2 hours; its adverse effects on systolic blood pressure and heart rate can be seen after only 12 hours of smoking cessation. Carbon monoxide (CO), which diminishes oxygen-carrying capacity, has a half-life of only 4 hours. Diminished levels of nicotine and CO were likely behind the outcome of a study looking at episodes of ST depression in patients who smoked and underwent vascular surgery. This study showed that patients who smoked immediately before surgery had increased episodes of ST segment depression when compared to nonsmokers, prior smokers, and chronic smokers who did not smoke before surgery.

The longer a patient can abstain from smoking before surgery, the greater the perioperative health benefit: Bronchociliary function improves within 2 to 3 days of cessation, and sputum volume decreases to normal levels within about 2 weeks. A study of 120 orthopedic surgery patients randomized to receive an intervention to help them stop smoking 6 to 8 weeks before surgery saw a dramatic decrease in the overall complication rate in the smoking cessation group, mainly from diminished wound infections.



### 13. What are current guidelines for perioperative cardiac evaluation of patients scheduled for noncardiac surgery?

The American College of Cardiologists and the American Heart Association (ACC/AHA) have established an algorithmic approach to considering a patient's cardiac risks before surgery, taking into account the urgency of surgery, the presence of *active cardiac conditions* (see Question 14), the invasiveness of the planned surgery, the patient's functional status, and the presence of *clinical risk factors* for ischemic heart disease (see Question 15). Taken together, this algorithm underscores the importance of a history focused on cardiac issues for all surgical patients.

### 14. What are active cardiac conditions?

Active cardiac conditions are serious cardiac conditions that warrant immediate evaluation and treatment before undergoing surgery. There are four active cardiac conditions:

1. Unstable coronary syndromes, which include unstable or severe angina and recent myocardial infarction
2. Decompensated heart failure
3. Significant arrhythmias such as symptomatic ventricular arrhythmias, high-grade atrioventricular block, and symptomatic bradycardia
4. Severe valvular disease such as symptomatic mitral stenosis or severe aortic stenosis

### 15. What are the clinical risk factors for a major perioperative cardiac event?

The Revised Cardiac Risk Index (Table 17-4) has six components: history of ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, preoperative treatment with insulin, surgical risk, and elevated preoperative serum creatinine. The patient is assigned one point for each of these risk factors, which are then translated into percentage risks of perioperative major cardiac events such as myocardial infarction, pulmonary edema, ventricular fibrillation, primary cardiac arrest, and complete heart block.

### 16. What constitutes the basic laboratory evaluation of coagulation status?

Chapter 7 reviews physical and historical information that might suggest disruption in coagulation. The basic laboratory evaluation includes platelet count, bleeding time, prothrombin time (PT), partial thromboplastin time (PTT), and thrombin time. The minimal number of normally functioning platelets to prevent surgical bleeding is  $50,000/\text{mm}^3$ . It is important to note that both the PT and PTT require about a 60% to 80% loss of coagulation activity before becoming abnormal, but patients with smaller decreases in function can still have significant surgical bleeding. Therefore the history is still very important. Thromboelastography measures the combined function of platelets and coagulation factors.

### 17. Are there special anesthetic considerations for surgical patients on warfarin?

Warfarin is a vitamin K antagonist and is used to prevent thrombosis and emboli. A patient on warfarin is at high risk for intraoperative bleeding. Before stopping a patient's warfarin, it is important to know the indication for anticoagulation, the type and urgency of the surgery, and the consequences of intraoperative bleeding. Some patients are considered low risk for thromboembolism such as those with lone atrial fibrillation, and others are very high risk such as those with prosthetic heart valves. Patients who are at very high risk of thromboembolism but nonetheless need to discontinue their anticoagulant in the perioperative setting are often *bridged* with heparin, another much shorter-acting anticoagulant. Because warfarin has such a long half-life (about 2.5 days) and heparin has such a short half-life (about 1.5 hours), a patient may be instructed to stop warfarin 4 days before surgery and then, often as an inpatient, undergo regular heparin injections up until a few hours before surgery. Once the surgery is completed (and depending on the postoperative bleeding risk), the warfarin can be restarted.

TABLE 17-4. REVISED CARDIAC RISK INDEX

Each of the following six risk factors is assigned one point.

**1. High-risk surgical procedures**

- Intraoperative
- Intrathoracic
- Suprainguinal vascular

**2. History of ischemic heart disease**

- History of myocardial infarction
- History of positive exercise test
- Current complaint of chest pain considered secondary to myocardial ischemia
- Use of nitrate therapy
- Electrocardiogram with pathologic Q waves

**3. History of congestive heart failure**

- History of congestive heart failure
- Pulmonary edema
- Paroxysmal nocturnal dyspnea
- Bilateral rales or S3 gallop
- Chest radiograph showing pulmonary vascular redistribution

**4. History of cerebrovascular disease**

- History of transient ischemic attack or stroke

**5. Preoperative treatment with insulin**

**6. Preoperative serum creatinine >2 mg/dl**

**Risk of Major Cardiac Event**

Points	Class	Risk
0	I	0.4%
1	II	0.9%
2	III	6.6%
3 or more	IV	11%

Major cardiac events include myocardial infarction, pulmonary edema, ventricular fibrillation, primary cardiac arrest, and complete heart block.

**18. What are considerations for patients with coronary stents?**

Coronary stents, which are small metal mesh tubes that hold stenosed coronary arteries open, fall into two broad categories: bare metal stents and drug-eluting stents. The latter slowly release a chemical that helps prevent endothelialization. An ongoing debate among cardiologists is how long after stent placement a patient should remain anticoagulated. This is discussed further in Chapter 33. This anticoagulation issue adds considerably to the complexity of recommending cardiac workups for patients undergoing surgery.

**19. A 3-year-old child presents for an elective tonsillectomy. His mother reports that for the past 3 days he has had a runny nose and postnasal drip. Should you postpone surgery?**

Viral upper respiratory infection (URI) alters the quality and quantity of airway secretions and increases airway reflexes to mechanical, chemical, or irritant stimulation. Some clinical studies

have shown associated intraoperative and postoperative bronchospasm, laryngospasm, and hypoxia. There is evidence that the risk of pulmonary complications may remain high for at least 2 weeks and possibly 6 to 7 weeks after a URI. Infants have a greater risk than older children, and intubation probably confers additional risk.

Young children can average five to eight URIs per year, mostly from fall through spring. If a 4- to 7-week delay for elective surgery were rigorously followed, then elective surgery might be postponed indefinitely. Therefore most anesthesiologists distinguish uncomplicated URI with chronic nasal discharge from nasal discharge associated with more severe URI with or without lower respiratory infection (LRI). Chronic nasal discharge is usually noninfectious in origin and caused by allergy or vasomotor rhinitis. An uncomplicated URI is characterized by sore or scratchy throat, laryngitis, sneezing, rhinorrhea, congestion, malaise, nonproductive cough, and temperature  $<38^{\circ}$  C. More severe URI or LRI may include severe nasopharyngitis, purulent sputum, high fever, deep cough, and associated auscultatory findings of wheezes or rales.

It is generally agreed that chronic nasal discharge poses no significant anesthesia risk. In contrast, elective surgery is almost always postponed in children with severe URI or LRI. Most anesthesiologists will proceed to surgery with a child with a resolving uncomplicated URI unless the child has a history of asthma or other significant pulmonary disease.

## WEBSITE



ACC/AHA Guideline for perioperative cardiovascular evaluation and care for noncardiac surgery  
<http://circ.ahajournals.org/cgi/reprint/116/17/e418>

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# THE ANESTHESIA MACHINE AND VAPORIZERS

James Duke, MD, MBA

## 1. What is an anesthesia machine?

A more modern and correct name for an anesthesia machine is an anesthesia delivery system. The job of the first anesthesia machines was to supply a mixture of anesthetizing and life-sustaining gases to the patient. A modern anesthesia delivery system performs these functions and also ventilates the patient and provides a number of monitoring functions. The most important purpose is to help the anesthesiologist keep the patient alive, safe, and adequately anesthetized. Anesthesia machines have become rather standardized. Currently there are two major manufacturers in the United States: Drager and Datex-Ohmeda.

## 2. Describe the plumbing of an anesthesia machine to create an overview of its essential interconnections.

Leaving out the safety features and monitors, the anesthesia machine is divided into three sections:

- A gas delivery system that supplies at its outlet a defined mixture of gases chosen by the anesthesiologist
- The patient breathing system, which includes the patient breathing circuit, absorber head, ventilator, and often gas pressure and flow monitors
- A scavenger system that collects excess gas and expels the gas outside the hospital, reducing the exposure of operating room personnel to anesthetic gases

## 3. What gases are ordinarily available on all anesthesia machines and what are their sources?

Oxygen ( $O_2$ ) and nitrous oxide ( $N_2O$ ) are available on almost every anesthesia machine. Most commonly the third gas is air, but it can also be helium (He), heliox (a mixture of He and  $O_2$ ), carbon dioxide ( $CO_2$ ), or nitrogen ( $N_2$ ). If the third gas does not contain  $O_2$  (as do air and heliox), it is possible to deliver a (dangerous) hypoxic mixture to the patient.

Usually the gas source for anesthesia machines in hospitals is from a centralized wall or pipeline supply. An emergency backup supply of gases is stored in tanks called E-cylinders attached to the rear of the anesthesia machine. These tanks should be checked daily to ensure that they contain an adequate backup supply in case of pipeline failure.

## 4. Since the flow rates of $N_2O$ and $O_2$ are controlled independently, can the machine be set to deliver a hypoxic mixture to the patient?

Different machine manufacturers have different ways of protecting the patient from hypoxic mixtures. The Drager's ORMC (oxygen ratio monitor and controller) senses the oxygen flow rate and controls  $N_2O$  flow pneumatically. Datex-Ohmeda's Link-25 system mechanically links the  $O_2$  and  $N_2O$  flow knobs to ensure that the proportion of  $N_2O$  to  $O_2$  remains in a safe range as the  $N_2O$  flow is increased.

## 5. What is a regulator? How does it control the flow of gas?

Oxygen and air in the E-cylinders is pressurized up to approximately 2200 psig, but the anesthesia machine needs to work with gas at an initial pressure of about 50 psig, slightly less than the pressure of the gas from the wall supply. A regulator performs this function. Each gas

is regulated separately. Gas from both the cylinder and the wall supply encounters a check valve that selects the gas source with the highest pressure for use by the machine. Under normal circumstances the wall supply is used preferentially, and the tank supply is spared for use if the wall supply fails.

**6. How does the hospital piped gas supply compare to the use of tank gas?**

For practical purposes, wall gases are continuous in volume availability, as long as the central oxygen supply is refilled. Wall gas pressures are typically about 55 psig. Tank pressure is generally regulated by the first-stage regulator to 45 psig. The anesthesia machine preferentially chooses the source with the highest pressure. As long as everything is working correctly, the wall supply is used rather than the tank supply. Use of the wall supply oxygen is preferable because it is available in greater volume, is cheaper, and preserves the tank supply for use only in emergency situations.

**7. The hospital supply of oxygen is lost. The gauge on the O<sub>2</sub> tank reads 1000 psi. How long will you be able to deliver oxygen before the tanks are empty?**

Contemporary anesthesia machines have two sources of gases: the wall outlet and E-cylinders attached to the machine itself. The cylinders are color coded and usually left shut off, being saved for use in an emergency, but a normally functioning anesthesia machine and normal wall outlet oxygen pressures will use the wall outlet preferentially.

A full green E-cylinder of O<sub>2</sub> has a pressure of 2000 psi and contains about 625 L of O<sub>2</sub>. Since the O<sub>2</sub> is a compressed gas, the volume in the tank correlates linearly with the pressure on the gauge. Therefore a pressure of 1000 psi means that the O<sub>2</sub> tank has about 312 L of gas left.

Besides delivering oxygen flow directly to the patient, oxygen also powers the ventilator bellows, and the patient's minute ventilation approximates the driving flow of the bellows. Thus, if a patient is receiving an oxygen flow of 2 L/min and a minute ventilation of 8 L/min, 10 L of oxygen will be drained from the oxygen tank every minute. A tank with 312 L remaining will last for 31 minutes at this rate. To reduce consumption of the tank oxygen, decrease the oxygen flow rate and hand-ventilate; also request that additional oxygen tanks be brought to the room.

**8. A new tank of N<sub>2</sub>O is installed, and the pressure gauge reads only about 750 psig. Why is the pressure in the N<sub>2</sub>O tank different from the pressures of other gases?**

Air and O<sub>2</sub> are compressed gases and cannot be compressed to liquids in a room temperature environment because the critical temperature (the temperature at which a gas can be compressed into a liquid) is exceeded. However, at room temperature N<sub>2</sub>O condenses into a liquid at 747 psi. E-cylinders of N<sub>2</sub>O contain the equivalent of about 1600 L of gas when full, whereas E-cylinders of O<sub>2</sub> and air hold only about 600 L. The pressure in the N<sub>2</sub>O tank remains constant until the N<sub>2</sub>O has been vaporized. About only a quarter of the initial volume of N<sub>2</sub>O remains when the cylinder pressure drops, although accurate estimation would require weighing the cylinder, knowing the empty (tare) weight of the cylinder, and determining the moles of N<sub>2</sub>O remaining.

In contrast, being a compressed gas, the volume of gas remaining in an oxygen or air cylinder is directly proportional to the pressure. The pressure of a filled cylinder is 2200 psig. A pressure reading of 1100 would suggest that the tank is half full or has about 300 L remaining.

**9. List the uses of O<sub>2</sub> in an anesthesia machine.**

- Contributes to the fresh gas flow
- Provides gas for the O<sub>2</sub> flush
- Powers the low O<sub>2</sub> alarm
- Controls the flow of nitrous oxide
- Powers the *fail-safe* valves
- Is the driving gas for the ventilator

**10. Describe the safety systems used to prevent incorrect gas connections at the wall and cylinders.**

- All wall-supply gas connectors are keyed so only the O<sub>2</sub> supply hose can be plugged into the O<sub>2</sub> connector on the wall, the N<sub>2</sub>O hose into the N<sub>2</sub>O outlet, and so on. This is known as a Diameter-Index-Safety-System (DISS).
- The gas cylinders are keyed using a Pin-Index-Safety-System (PISS—no kidding) so that only the correct tank can be attached to the corresponding yolk on the anesthesia machine, *assuming that the pins have not been sheared off!*
- These safety systems should be backed up by a monitor that measures the delivered concentration of oxygen in a mixed gas. It is this monitor that is most critical in preventing delivery of a hypoxic gas mixture.

**11. In addition to the distinctions described previously, what other ways are gases distinguished to help prevent human error?**

- First, the O<sub>2</sub> flow knob is distinctively fluted. Knobs for other gases are knurled.
- Second, a color code exists such that each gas knob, flowmeter, tank, and wall attachment bears the corresponding color for its associated gas. In the United States O<sub>2</sub> is green, air is yellow, and N<sub>2</sub>O is blue. International standards differ.

**12. There are two flowmeters for each gas on an anesthesia machine. Couldn't you safely get away with only one?**

Two flowmeters are used to increase the range of flows over which an accurate measurement can be obtained. The flow tubes in anesthesia machines are always placed in series so all the gas flows sequentially through both tubes. To measure flows accurately in the ranges used for low flow or even closed-circuit anesthesia (200 to 1000 ml/min), two flow tubes are essential. Flowmeters, also known as *Thorpe tubes*, are also specific to the gas for which they have been designed and are not interchangeable with other gases.

**13. Why are the flowmeters for air, O<sub>2</sub>, and N<sub>2</sub>O arranged in a specific order?**

Reasons include U.S. (NIOSH) government standards, manufacturer's conventions, and safety. Requiring the O<sub>2</sub> knob to be in the same relative position on all anesthesia machines decreases the risk of the anesthesiologist turning the wrong knob. In the United States the O<sub>2</sub> flowmeter must always be on the right, closest to the point of egress into the common gas manifold, just proximal to the anesthesia vaporizers. With the O<sub>2</sub> flowmeter in that position, most leaks will tend to selectively lose gases other than O<sub>2</sub>. This configuration is least likely to deliver a hypoxic gas mixture. Again, the best way to detect a hypoxic gas mixture is through use of an oxygen analyzer.

**14. What is meant by a fail-safe valve?**

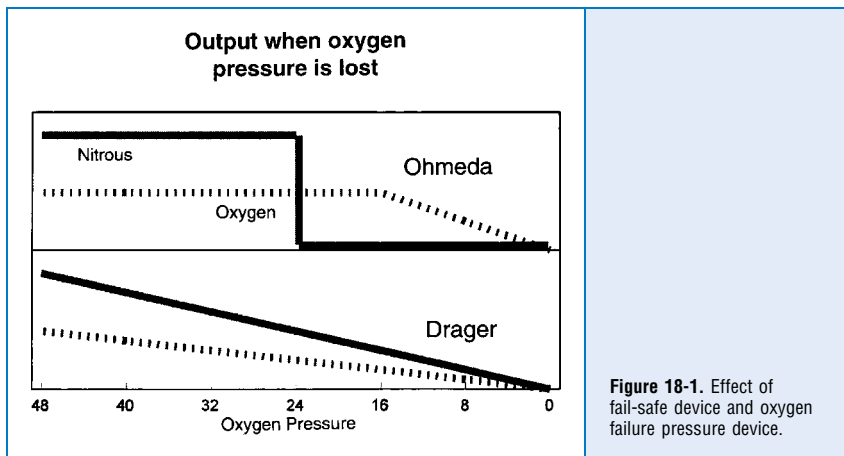
The fail-safe valve device is designed to cut off the flow of all gases except O<sub>2</sub> when the O<sub>2</sub> pressure falls below a set value, usually about 25 psig (Figure 18-1).

**15. Would it be safer to leave the tank O<sub>2</sub> supply on your machine turned on so, if the pipeline O<sub>2</sub> failed, the machine would automatically switch immediately to the backup tank supply?**

No. First, when all equipment is functioning properly, the disadvantage of leaving the tank on is that, if a failure in wall O<sub>2</sub> should occur, your machine will use gas from the tank, unknown to you. You may not recognize the problem until the machine (and tank) is totally out of O<sub>2</sub> and the low O<sub>2</sub> pressure alarm begins to sound. At this point you must scramble to find O<sub>2</sub> quickly.

The second reason allows for equipment failure, and there are two parts to the explanation:

1. When no gas is flowing, it is possible for pressure to be maintained in the gauge despite a leak where the tank is connected to the yolk. Thus it is possible to have a full indication on the pressure gauge and an empty tank. The pressure in the tank should be checked after the wall supply is disconnected and the system pressure bled down, and then the tank should be turned off.



2. If wall  $O_2$  pressure drops too low, the tank could be drained, supplying the anesthesia machine rather than saving tank  $O_2$  for emergencies. A second check valve prevents the tank  $O_2$  from entering the wall supply plumbing should the wall supply fail. If this valve fails, the tank could, for the short period until the tank empties, backfill the hospital system, helping to supply  $O_2$  to ward patients.

#### 16. How long can you continue to deliver $O_2$ when the wall supply fails?

The E-cylinders that supply  $O_2$  to most anesthesia machines hold 600 L when full. If the ventilator is not in use (remember that  $O_2$  powers the ventilator), the  $O_2$  flowmeter indicates how much  $O_2$  is being used. With a flow of  $O_2$  of 2 L/min, there is approximately 300 minutes (or 5 hours) of  $O_2$  available. If the ventilator is in use, the additional gas required for this purpose is roughly equal to the ventilator minute volume, and the length of time the tank supply will last will be significantly decreased below the previously estimated 5 hours for a full tank. It should be noted that manually ventilating the patient in this instance would preserve the oxygen supply. Reducing the oxygen flow would also extend the life of the tank.

#### 17. What physical principles are involved in the process of vaporization?

The saturated vapor pressure of the volatile anesthetic, which varies with temperature, determines the concentration of vapor molecules above the liquid anesthetic. The heat of vaporization is the energy required to release molecules of a liquid into the gaseous phase. The liquid phase draws external heat during vaporization, or it will become cooler as molecules leave and enter the gaseous phase. To address this problem, vaporizers are constructed of metals with high thermal conductivity. High thermal conductivity ensures that there is a conduit of heat so the heat required for vaporization is constantly restored from the environment and the rate of vaporization of the volatile anesthetic is independent of changes in the temperature of the vaporizer.

#### 18. What does it mean when it is said that a vaporizer has variable bypass? What is the effect of having such a vaporizer turned on its side?

The vaporizers are located downstream from the flowmeters. Fresh gas from the flowmeters enters the vaporizer and is divided into two streams. Most of the gas enters the bypass chamber and is not exposed to the volatile agent. The remaining gas enters the vaporizing chamber and becomes saturated with anesthetic. The concentration dial determines

the proportion of gas flow that enters each of the two streams. These then reunite near the vaporizer outlet. The fresh gas leaving the vaporizer contains a concentration of vapor specified by the concentration dial.

Should a variable bypass vaporizer be turned on its side, liquid anesthetic may spill from the vaporizing chamber to the bypass chamber, effectively creating two vaporizing chambers and increasing vaporizer output. This could create toxic levels of volatile anesthetic being delivered to the patient. However, most but not all modern vaporizers have mechanisms minimizing this effect.

#### 19. What does temperature compensation mean?

During vaporization the liquid anesthetic will cool, drawing heat from the metal of the vaporizer, which draws heat from the operating room. As liquid anesthetic cools, the saturated vapor pressure decreases, as does vaporizer output. Temperature compensation means the vaporizer has mechanisms for adjusting the output to compensate for temperature.

#### 20. What is the pumping effect?

Positive pressure can be transmitted back into the vaporizer during ventilation of the patient. The positive pressure can briefly cause gas to reverse flow within the vaporizer, allowing gas to periodically reenter the vaporizing chamber. The result of the pumping effect is increased vaporizer output beyond that indicated on the concentration dial. Modern vaporizers have mechanisms to reduce but not eliminate the pumping effect.

#### 21. How does altitude affect modern vaporizers?

The effect of the change in barometric pressure on volume percent output can be calculated as follows:  $x' = x (p/p')$ , where  $x'$  is the output in volume percent at the new altitude ( $p'$ ), and  $x$  is the concentration output in volume percent for the altitude ( $p$ ), when the vaporizer is calibrated. Consider the following example: A vaporizer is calibrated at sea level ( $p = 760$  mm Hg), taken to Denver ( $p' = 630$  mm Hg), and set to deliver 1% isoflurane vapor ( $x$ ). The actual output ( $x'$ ) is  $1\% (760/630) = 1.2\%$ . Remember that partial pressure of the vapor, and not the concentration in volume percent, is the important factor in depth of anesthesia. Note that 1% at sea level (760 mm Hg) is 7.6 mm Hg and that 1.2% at Denver (630 mm Hg) is 7.6 mm Hg; thus, regardless of altitude, the clinical effect is unchanged.

#### 22. What happens if you put the wrong agent in a vaporizer calibrated for another agent?

The incorrect agent in an agent-specific vaporizer typically delivers either an overdose or underdose. The most important factor in determining the direction of error is the vapor pressure or the agent. If an agent with a high vapor pressure is put into a vaporizer meant for a less volatile agent, the output will be excessive. If an agent with a vapor pressure lower than the agent intended for the vaporizer is accidentally used, the anesthetic output will be lower than anticipated. Increasingly, vaporizers and bottles of volatile anesthetics are keyed to prevent incorrect addition of volatile anesthetics into vaporizers.

#### 23. What is different about the desflurane vaporizer?

Desflurane has a vapor pressure of 664 mm Hg at 20° C. In other words the boiling point of this agent is approximately at room temperature. Desflurane is also less potent than other common agents (minimum alveolar concentration [MAC] = 6%), and up to 18% volume percent may be delivered. Passively vaporizing this volume of agent will result in large temperature variations that require compensation. The desflurane vaporizer actively heats the liquid agent to 39° C. At this temperature the vapor pressure of the agent is approximately two atmospheres. This has proven a practical means of accurately delivering an anesthetic with such a high vapor pressure.



**24. What prevents turning on two vaporizers simultaneously?**

Modern anesthesia machines have an interlock system or an interlocking manifold that allows only one vaporizer to be turned on at a time. However, in anesthesia machines that allow for three vaporizers, the center spot must be occupied, or the interlocking manifold will not be operational.

**25. At an altitude of 7000 feet, you have to set the vaporizer to deliver more desflurane than you would expect given the published minimum alveolar concentration of that agent. Explain why this does not happen with vaporizers for other anesthetic agents.**

Conventional vaporizers (for halothane, isoflurane, and sevoflurane) are altitude compensated. The altitude compensation occurs because the diverting valve is functionally located at the outlet of the vaporizer, a variation in design that minimizes the pumping and pressurizing effects. The output of these vaporizers is a constant partial pressure of agent, not a constant volume percent. The desflurane vaporizer does not divert a portion of the fresh gas flow through a vaporizing chamber but rather adds vapor to the gas flow to produce a true volume percent output. Because it is the number of molecules of agent (the partial pressure) that anesthetizes the patient, conventional vaporizers provide the same anesthetizing power at any altitude. The desflurane vaporizer delivers the set volume percent regardless of altitude, which represents a partial pressure (anesthetizing power) that is 24% less than the same concentration at sea level. Thus a correspondingly higher percentage of desflurane must be delivered to achieve MAC at 7000 feet.

**26. A patient with malignant hyperthermia needs to be anesthetized. Should the vaporizers be removed from the anesthesia machine?**

Datex-Ohmeda vaporizers are easily removed simply by releasing a latch and lifting the vaporizer from the machine. On the Drager anesthesia machines it is necessary to remove two Allen screws to release the vaporizers. Then unless the vaporizer is being replaced by a second one, it is necessary to install a bypass block to the empty vaporizer slot. These tasks are easily accomplished by anyone capable of manipulating an Allen wrench, but Drager recommends that their vaporizers be changed only by authorized service personnel. However, flushing the machine with oxygen for several minutes should remove all agent (except from rubber parts in the absorber and circle). The anesthesia provider should ensure that the user of the machine cannot accidentally turn on a vaporizer.

**KEY POINTS: THE ANESTHESIA MACHINE AND VAPORIZERS**

1. Anesthesia machines are an integrated system that not only delivers anesthetic gases but also monitors both itself and the patient.
2. When compressed, some gases condense into a liquid ( $N_2O$  and  $CO_2$ ), and some do not ( $O_2$  and  $N_2$ ). These properties define the relationship between tank volume and pressure.
3. Anesthesia machines must have a backup supply of oxygen in case the wall oxygen fails.
4. Flowmeters accurately measure only the gas for which they were explicitly calibrated.
5. The output of traditional vaporizers depends on the proportion of fresh gas that bypasses the vaporizing chamber compared with the proportion that passes through the vaporizing chamber.
6. The desflurane vaporizer actively injects vapor into the fresh gas stream, whereas all traditional vaporizers use a passive variable bypass system.

### 27. What is a scavenger?

Except in a close-circuit situation, gas is always entering and leaving the anesthesia breathing circuit. The exhaust gas is a mixture of expired gas from the patient and excess fresh gas that exceeded the patient's needs but contains anesthetic agent. To reduce exposure of operating room personnel to trace amounts of anesthetic agents, it is considered appropriate to capture and expel this anesthetic-laden gas from the operating room environment. The device used to transfer this gas safely from the breathing circuit into the hospital vacuum system is called a *scavenger*. Because of the periodicity of breathing, gas exits the breathing circuit in puffs. The scavenger provides a reservoir for the exhaust gas until the exhaust or vacuum system, which works at a constant flow rate, can dispose of the gas. The scavenger must also prevent excess suction or an occlusion from affecting the patient breathing circuit. It does this by providing both positive and negative relief valves. Thus, if the vacuum system fails or is adjusted to too low a rate, back pressure exits through a positive-pressure relief valve. (Granted it contaminates the operating room, but that problem is minimal compared to blowing the patient's lungs up like a balloon.) If the vacuum is adjusted too high, a negative-pressure relief valve allows room air to mix with the exhaust gas, preventing buildup of more than a 2.5 mm Hg suction at the breathing circuit.

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1. Brockwell RC, Andrews JJ: Inhaled anesthetic delivery systems. In Miller RD, editor: *Miller's anesthesia*, ed 6, Philadelphia, Elsevier Churchill Livingstone, 2005, pp 273–316.
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# ANESTHESIA CIRCUITS AND VENTILATORS

James Duke, MD, MBA

## 1. What are the different types of anesthesia breathing circuits?

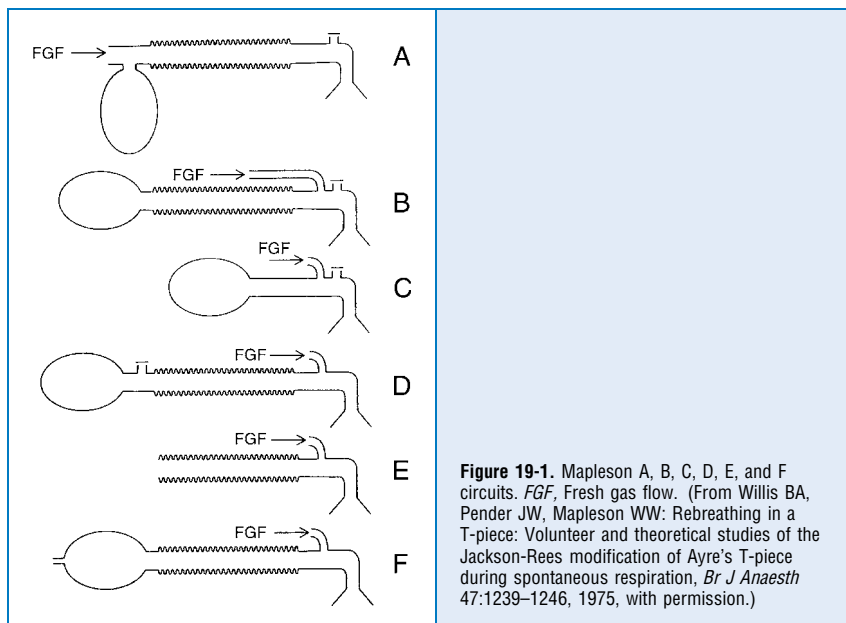
Breathing circuits are usually classified as open, semiopen, semiclosed, or closed. They include various components configured to allow the patient to breathe (or be ventilated) with a gas mixture that differs from room air.

## 2. Give an example of an open circuit.

An open circuit is the method by which the first true anesthetics were given 160 years ago. A bit of cloth saturated with ether or chloroform was held over the patient's face. The patient breathed the vapors and became anesthetized. The depth of anesthesia was controlled by the amount of liquid anesthetic on the cloth; thus it took a great deal of trial and error to become good at the technique.

## 3. Give an example of a semiopen circuit.

The various semiopen circuits were fully described by Mapleson and are commonly known as the Mapleson A, B, C, D, E, and F circuits (Figure 19-1). All have in common a source of fresh gas, corrugated tubing (more resistant to kinking), and a pop-off or adjustable pressure-limiting valve. Differences among the circuits include the locations of the pop-off valve, fresh gas input, and whether or not a gas reservoir bag is present. Advantages of the Mapleson

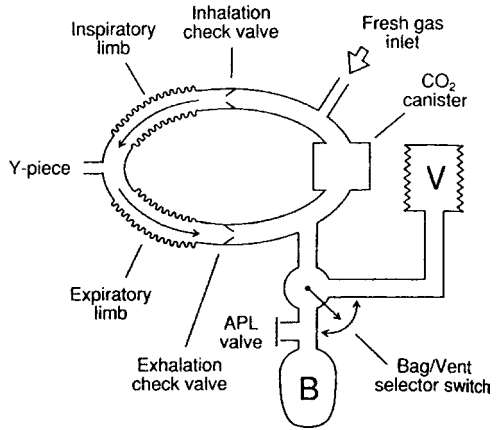


**Figure 19-1.** Mapleson A, B, C, D, E, and F circuits. FGF, Fresh gas flow. (From Willis BA, Pender JW, Mapleson WW: Rebreathing in a T-piece: Volunteer and theoretical studies of the Jackson-Rees modification of Ayre's T-piece during spontaneous respiration, *Br J Anaesth* 47:1239–1246, 1975, with permission.)

series are simplicity of design, ability to change the depth of anesthesia rapidly, portability, and lack of rebreathing of exhaled gases (provided the fresh gas flow is adequate). Disadvantages include lack of conservation of heat and moisture, limited ability to scavenge waste gases, and high requirements for fresh gas flow. These are rarely used today except for patient transport.

#### 4. Give an example of a semiclosed circuit.

The prototypical semiclosed circuit is the circle system, which is found in most operating rooms in the United States (Figure 19-2). Every semiclosed system contains an inspiratory limb, expiratory limb, unidirectional valves, carbon dioxide (CO<sub>2</sub>) absorber, gas reservoir bag, and a pop-off valve on the expiratory limb. Advantages of a circle system include conservation of heat and moisture, the ability to use low flows of fresh gas (thereby conserving volatile anesthetic and the ozone layer), and the ability to scavenge waste gases. A disadvantage is its complex design; it has approximately 10 connections, each of which has the potential for disconnection.



**Figure 19-2.** Circle system. (From Andrews JJ: Inhaled anesthetic delivery system. In Miller RD, editor: *Anesthesia*, ed 4, New York, 1994, Churchill Livingstone, pp 185–228.)

#### 5. Give an example of a closed circuit.

Like the semiclosed circuit, the closed circuit is a circle system adjusted so the inflow of fresh gas just matches the patient's oxygen (O<sub>2</sub>) consumption and anesthetic agent uptake. The CO<sub>2</sub> is eliminated by the absorber.

#### 6. Rank the Mapleson circuits in order of efficiency for controlled and spontaneous ventilation.

- Controlled: D > B > C > A (Pneumonic: *Dog Bites Can Ache*)
- Spontaneous: A > D > C > B (Pneumonic: *All Dogs Can Bite*)

#### 7. What circuit is most commonly used in anesthesia delivery systems today?

Almost every anesthesia manufacturer supplies a circle system with its equipment. When compared with other available circuits, the circle system provides the most advantages.

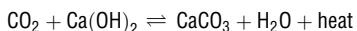
#### 8. How is a breathing circuit disconnection detected during delivery of an anesthetic?

Breath sounds are no longer detected with an esophageal or precordial stethoscope, and, if the parameters are properly set, the airway pressure monitor and tidal volume–minute volume monitor alarm will sound. The capnograph no longer detects CO<sub>2</sub>, and soon thereafter the

O<sub>2</sub> saturation begins to decline. Exhaled CO<sub>2</sub> is probably the best monitor to detect disconnections; a decrease or absence of CO<sub>2</sub> is sensitive although not specific for disconnection.

#### 9. How is CO<sub>2</sub> eliminated from a circle system?

The exhaled gases pass through a canister containing a CO<sub>2</sub> absorbent such as soda lime or Baralyme. Soda lime consists of calcium hydroxide (Ca[OH]<sub>2</sub>) with lesser quantities of sodium hydroxide (NaOH) and potassium hydroxide (KOH). Baralyme substitutes barium for calcium. Both soda lime and Baralyme react with CO<sub>2</sub> to form heat, water, and the corresponding carbonate. The soda lime reaction is as follows:



#### 10. How much CO<sub>2</sub> can the absorbent neutralize? What factors affect its efficiency?

Soda lime is the most common absorber, and at most can absorb 23 L of CO<sub>2</sub> per 100 g of absorbent. However, the average absorber eliminates 10 to 15 L of CO<sub>2</sub> per 100 g absorbent in a single-chamber system and 18 to 20 L of CO<sub>2</sub> in a dual-chamber system. Factors affecting efficiency include the size of the absorber canister (the patient's tidal volume should be accommodated entirely within the void space of the canister), the size of the absorbent granule (optimal size is 2.5 mm or between 4 and 8 mesh), and the presence or absence of channeling (loose packing allowing exhaled gases to bypass absorber granules in the canister).

#### 11. How do you know when the absorbent has been exhausted? What adverse reactions can occur between volatile anesthetic and CO<sub>2</sub> absorbents?

A pH-sensitive dye added to the granules changes color in the presence of carbonic acid, an intermediary in the CO<sub>2</sub> absorption chemical reaction. The most common dye in the United States is ethyl violet, which is white when fresh and turns violet when the absorbent is exhausted. Adverse reactions between volatile anesthetics and absorbents are discussed in Chapter 10.

#### 12. How can you check the competency of a circle system?

You should close the pop-off valve, occlude the Y-piece, and press the O<sub>2</sub> flush valve until the pressure is 30 cm H<sub>2</sub>O. The pressure will not decline if there are no leaks. Then you should open the pop-off valve to ensure that it is in working order. In addition, you should check the function of the unidirectional valves by breathing down each limb individually, making sure that you cannot inhale from the expiratory limb or exhale down the inspiratory limb.

#### 13. How do anesthesia ventilators differ from intensive care unit ventilators?

Intensive care unit (ICU) ventilators usually are more powerful (allowing greater inspiratory pressures and tidal volumes, which is important in patients with decreased pulmonary compliance) and support more modes of ventilation. However, new generations of anesthesia machines continue to offer more ventilatory modes. See Chapter 21.

#### 14. What gas is used to drive the bellows in an anesthesia ventilator?

O<sub>2</sub> is usually used for this purpose because it is cheap and always available. On modern ascending bellows ventilators the pressure inside the bellows is always slightly higher than in the chamber outside the bellows because of the weight of the bellows itself and amounts to 1 to 2 cm H<sub>2</sub>O. Where there is a bellows leak, any net gas flow would be out of (not into) the bellows and would not change the composition of the breathing mixture. When the bellows reaches the top of its ascent, an additional 1 to 2 cm H<sub>2</sub>O pressure causes the exhaust valve to open.

**15. What is the status of the scavenger system when the bellows is below the top of its excursion?**

When the ventilator is engaged and the bellows is below the top of its excursion, the breathing circuit is completely closed. Excess gas can escape from the breathing circuit only when a special pneumatic valve is activated by the bellows as it reaches the top of its range.

**16. What is the effect of the extra pressure required to open the exhaust valve on the patient?**

A patient being ventilated with an ascending bellows ventilator is usually subjected to 2.5 to 3 cm H<sub>2</sub>O of positive end-expiratory pressure (PEEP). Most experts agree that this addition of PEEP is actually more physiologic than ventilating the patient with no PEEP.

**17. What parameters can be adjusted on an anesthesia ventilator?**

Most anesthesia ventilators allow adjustment of:

- Tidal volume (or minute volume)
- Respiratory rate
- Inspiratory-to-expiratory (I:E) ratio
- Sometimes inspiratory pause
- PEEP

Some newer anesthesia ventilators allow other adjustments, including the selection of different ventilation modes such as pressure support and synchronized intermittent mandatory ventilation.

## KEY POINTS: ANESTHESIA CIRCUITS AND VENTILATORS



1. Except for anesthesia machines in which there are flow compensators, fresh gas flow contributes to tidal volume.
2. Although the capabilities of anesthesia ventilators have improved greatly in recent years, they still are not as powerful as typical ICU ventilators.
3. Every patient ventilated with an ascending bellows anesthesia ventilator receives approximately 2.5 to 3 cm H<sub>2</sub>O of PEEP because of the weight of the bellows.
4. The semiclosed circuit using a circle system is the most commonly used anesthesia circuit.
5. Advantages of a circle system include conservation of heat and moisture, the ability to use low flows of fresh gas, and the ability to scavenge waste gases. Disadvantages include multiple sites for disconnection and high compliance.

**18. Why have descending bellows been abandoned in favor of ascending bellows?**

Bellows are classified according to their movement during expiration (i.e., their position when the ventilator is not ventilating the patient). Hanging or descending bellows are considered unsafe for two reasons. First, if a circuit disconnection occurs, the bellows will fill with room air; and, although its movement may appear normal, the ventilator will be ventilating the room rather than the patient. Second, since the weight of the bellows creates a slight negative pressure in the circuit, this can cause negative end-expiratory pressure and can suck room air backward through the scavenger, interfering with the anesthesiologist's control of gas concentrations breathed by the patient.

**19. What would be the cause when the bellows fails to rise completely between each breath?**

The most obvious reason for this is that a leak exists in the breathing circuit, a disconnect has occurred, or the patient has become extubated. If the fresh gas flow is too low, it is possible for the patient to use O<sub>2</sub> from the circuit faster than it is replenished.

**20. How does fresh gas flow rate contribute to tidal volume?**

The flow during the inspiration phase of the ventilatory cycle adds to the tidal volume. Let us assume that the respiratory rate is set at 10 breaths/min with an I:E ratio of 1:2 and a tidal volume of 1000 ml. Each breath cycle is then 6 seconds long, 2 seconds for inspiration and 4 seconds for expiration. If the fresh gas flow is 6 L/min,  $2/60 \times 6000 = 200$  ml of fresh gas is added to each inspiration. Most modern anesthesia ventilators automatically compensate for this addition to tidal volume.

**21. How and where is tidal volume measured? Why are different measures frequently not equal?**

Tidal volume is measured using several techniques and at several sites in the breathing circuit. Common measures include the setting on the ventilator control panel, bellows excursion, and flow through the inspiratory or expiratory limbs of the circuit. These measures frequently differ because they may or may not include the contribution of the inspiratory flow, are measured at different pressures, and compensate differently for flow rates. Since each measure can in theory be an accurate measure of a different parameter, it is more important to record a consistent measure of tidal volume than to debate which measure is correct.

**22. When using very low flows of fresh gas, why is there sometimes a discrepancy between inspired oxygen concentration and fresh gas concentration?**

At low fresh gas flows concentrations in the circuit are slow to change. However, this question refers to the fact that the patient will take up different gases (removing them from the circuit) at rates different from the rates at which the gases are added to the circuit. In the case of  $O_2$ , an average adult patient consumes (permanently removing from the circuit) approximately 200 to 300 ml/min of  $O_2$ . If nitrogen or nitrous oxide is supplied along with the  $O_2$ , the patient continues to consume  $O_2$  while the nitrogen or nitrous oxide builds up in the circuit. It is possible for a hypoxic mixture to develop in the circuit, even though the fresh gas contains 50% or more  $O_2$ .

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2. Dorsch JA, Dorsch SE: Understanding anesthesia equipment, ed 5 Philadelphia, Lippincott Williams & Wilkins, 2008.

# PATIENT POSITIONING

*James Duke, MD, MBA*

## 1. What is the goal of positioning a patient for surgery?

The goal of surgical positioning is to facilitate the surgeon's technical approach while balancing the risk to the patient. The anesthetized patient cannot make the clinician aware of compromised positions; therefore the positioning of a patient for surgery is critical for a safe outcome. Proper positioning requires that the patient be securely placed on the operating table; all potential pressure areas padded; the eyes protected; no muscles, tendons, or neurovascular bundles stretched; intravenous lines and catheters free flowing and accessible; the endotracheal tube in the proper position; ventilation and circulation uninterrupted; and general patient comfort and safety maintained for the duration of the surgery. It is always advisable to question a patient or ascertain if there is impaired mobility at any joint; never attempt to position patients beyond their limitations.

Throughout the surgical procedure it is also important to reassess the positioning, readjust as needed, and document any positioning actions and reassessments.

## 2. Review the most common positions used in the operating room.

See [Figure 20-1](#).

## 3. What physiologic effects are related to change in body position?

An important consideration is the gravitational effects on the cardiovascular and respiratory systems. A change from an erect to a supine position increases cardiac output secondary to improved venous return to the heart, but there is minimal change in blood pressure secondary to reflex decreases in heart rate and contractility. Conditions that increase intra-abdominal pressure in the supine position, including abdominal tumors, ascites, obesity, pregnancy, or carbon dioxide insufflation for laparoscopy, decrease venous return and cardiac output.

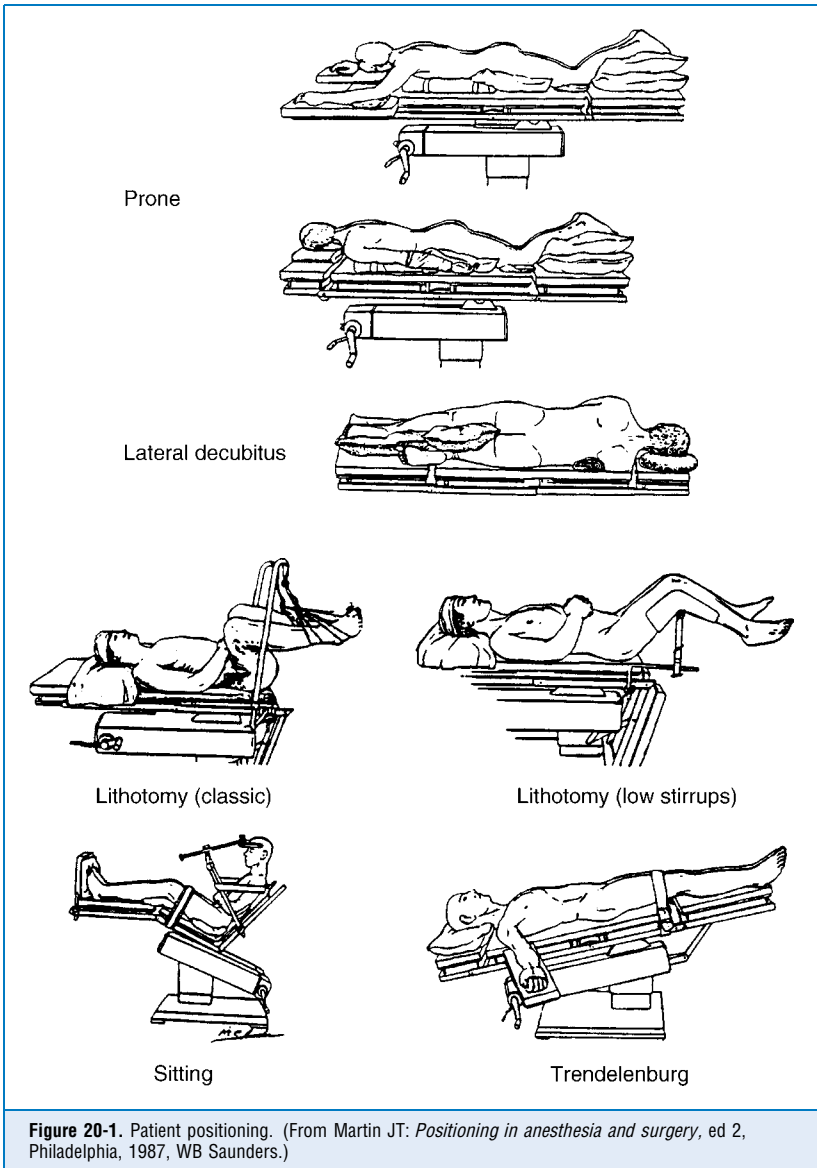
The supine position results in decreased functional residual capacity and total lung capacity secondary to the abdominal contents impinging on the diaphragm. Anesthesia and muscular relaxation further diminish these lung volumes. Trendelenburg and lithotomy positions result in further compression of the lung bases, with a subsequent decrease in pulmonary compliance. Although some improvement is achieved with positive-pressure ventilation, the diaphragm is not restored to the awake position. In the supine position spontaneous ventilation to the dependent lung areas increases. Matching of ventilation to perfusion improves because blood flow also increases to dependent areas.

## 4. Describe the lithotomy position and its common complications.

The patient's hips and knees are flexed, and the patient's feet are placed in stirrups to gain ready access to the genitalia and perineum. The range of flexion may be modest (low lithotomy) or extreme (high lithotomy). The feet may be suspended on vertical structures known as candy canes or in boots, or the knees may be supported with crutches. With elevation of the legs, pressure is taken off the lower back, and blood is translocated from the lower extremities to the central compartments.

Compression to lower extremity peripheral nerves is the most common injury, occurring in about 1% to 2% of patients placed in the lithotomy position. Neuropathies may be unilateral or bilateral and are a function of the time in this position (especially longer than 2 hours).





They are noted soon after surgery, may present with paresthesias and/or motor weakness, and usually resolve completely, although this may require a few months. Before these injuries are attributed to lithotomy positioning, consider if use of neuraxial needles, lower extremity tourniquets, or surgical trauma (e.g., use of retractors) may have contributed.

To prevent dislocation of the hips, at case conclusion both feet should be released from the lithotomy stirrups and lowered simultaneously. When the leg section of the operating table is elevated, ensure that the fingers are clear to avoid crush or amputation injuries.

### 5. What nerves may be affected from lithotomy positioning?

- Femoral nerve: A reasonable practice is to avoid hip flexion  $>90$  degrees, although it remains a matter of debate whether extreme flexion predisposed the patient to a femoral neuropathy. The femoral nerve is also at risk from pelvic retractors.
- Common peroneal nerve: May be injured when the head of the fibula is insufficiently padded and compressed against the stirrup canes.
- Sciatic nerve: Avoid stretching the hamstring muscle group by avoiding hip flexion  $>90$  degrees.
- Saphenous nerve: May become injured if the medial tibial condyle is compressed.
- Obturator nerve: May be stretched as it exits the obturator foramen during thigh flexion.
- Lateral femoral cutaneous nerve: Would always present with only sensory findings.

### 6. What are the special concerns for a patient positioned in the lateral decubitus position?

All patients in the lateral position should have an axillary roll positioned to distribute weight to the patient's rib cage and prevent compression of the neurovascular bundle of the dependent arm. Loss of pulse to the dependent arm suggests excessive compression, but the presence of a pulse does not ensure that the brachial plexus is protected. The arms are usually supported and padded in a position perpendicular to the shoulders. The dependent leg is usually flexed at the hip and knee, with padding between the legs and under the inferior fibular head to reduce pressure on the peroneal nerve. The head position should be in line with the vertebral column to prevent stretching of the brachial plexus of the nondependent arm. Horner's syndrome has been reported when the head was not supported in a neutral position. Facial structures, breasts, and genitalia should also be protected.

Ventilation-perfusion mismatching is a risk in the lateral position. The dependent lung is underventilated and relatively overperfused. In contrast, the nondependent lung is overventilated because of the increase in compliance. Usually there is some physiologic compensation, and changes in ventilation and perfusion are usually well tolerated, although in a compromised patient they may prove problematic.

### 7. What are the physiologic effects and risks associated with the Trendelenburg position?

Head down, or Trendelenburg position, further increases translocation of blood to the central compartment. Intracranial and intraocular pressure increase in the Trendelenburg position secondary to decreased cerebral venous drainage. Adverse outcomes in healthy patients have not been noted, although the Trendelenburg position is clearly contraindicated in patients with increased intracranial pressure. Lengthy procedures may result in significant facial and upper airway edema. The likelihood of postextubation airway obstruction should be considered, and the ability of the patient to breathe around the endotracheal tube with the cuff deflated is reassuring, although it does not completely ensure that postextubation airway obstruction will not occur. After prolonged surgery in the Trendelenburg position, particularly when there has been substantial intravenous fluid administration, it may be prudent to leave the patient intubated with the upper torso elevated, allowing time for fluid redistribution to take place. Decreases in pulmonary compliance and functional residual and vital capacity also occur in the Trendelenburg position. Peak airway pressures during mechanical ventilation are also noted. Shoulder braces used to keep the patient from sliding off the surgical table have been associated with brachial plexus injuries.

### 8. What specific concerns are associated with the prone position?

The prone position results in a cephalad displacement of the diaphragm. Chest rolls are used to decrease abdominal compression, improving diaphragmatic excursion while limiting compression on the aorta and inferior vena cava. Proper padding of all pressure points,

including the face, eyes, ears, arms, knees, hips, ankles, breasts, and genitalia, is necessary in this position. The arms should be placed in a neutral position to avoid traction on the brachial plexus, although modest abduction  $>90$  degrees is acceptable. Electrocardiogram electrodes should not be placed so the patient is lying on them.

#### 9. What is the *beach chair* position?

This position is used to improve access and mobility of the shoulder for surgery. When finally positioned, the anesthesiologist does not have easy access to the head or endotracheal tube; thus these structures must be well secured and in a neutral position before initiation of the surgery. Perfusion pressure must be closely monitored since the head is well above the level of the heart. Special care should also be taken to protect the eyes because the surgeon is working very close to the face and instruments and the like could place pressure on the eyes. Protective plastic eye shields are often used in this instance.

#### 10. When is a sitting position used?

The sitting position is used to gain access to the posterior fossa of the cranium and perform cervical laminectomy. However, these procedures are now often performed with the patient in a prone position, and the use of the sitting position is decreasing.

#### 11. What are the advantages of the sitting position?

- Optimal positioning for surgical exposure with significantly less blood loss, improved surgical field, and perhaps improved resection of the lesion
- Decreased facial swelling
- Relatively easy access to the endotracheal tube
- Less cranial nerve damage

#### 12. List the disadvantages of the sitting position.

- Hypotension. Because of decreased venous return, cardiac output may be reduced by as much as 20% but improves with fluid administration and pressors. Consider lower extremity compression hose to improve venous return. Intra-arterial monitoring is essential. Level the transducer at the level of the external auditory meatus to monitor cerebral perfusion pressure.
- Brainstem manipulations resulting in hemodynamic changes.
- Risks of severe neck flexion include spinal cord ischemia and airway obstruction (caused by severe swelling of the tongue or kinking of the endotracheal tube). Two fingerbreadths of space should be allowed between the chin and sternum.
- Venous air embolism (VAE).

#### 13. How does venous air embolism occur? What are the sequelae?

Because the surgical site is above the level of the heart, air entrainment into the venous circulation is a risk. VAE may result in pulmonary air embolism, hypotension, and paradoxical air embolism if an intracardiac shunt is present. Unless massive, VAE usually responds to fluid challenge and pressor therapy. The surgical site must also be flooded with fluid to prevent continued air entrainment.

#### 14. Review the sensitivity and limitations of monitors for detecting venous air embolism.

There are numerous monitors for detection of VAE. No single technique is totally reliable; thus the more monitors used, the greater the likelihood for detecting VAE. In decreasing order of sensitivity the monitors are transesophageal echocardiography and Doppler ultrasound  $>$  increases in end-tidal nitrogen fraction  $>$  decreases in end-tidal carbon dioxide  $>$  increases in right atrial pressure  $>$  esophageal stethoscope.

A right atrial catheter has the advantage of being able to aspirate intracardiac air. Therefore, of all modalities mentioned it is the only one capable of diagnosis and treatment. Multiorifice catheters are clearly preferable and should be placed high in the right atrium.

**15. What are the concerns for positioning a pregnant patient?**

The pregnant patient is susceptible to aortocaval compression secondary to the gravid uterus exerting pressure on these vascular structures, potentially decreasing the uteroplacental blood flow and venous return to the heart. Left uterine displacement decreases intra-abdominal pressure and is achieved by placing a pillow or wedge under the right hip.

**16. What peripheral neuropathies are associated with cardiac surgery?**

The brachial plexus may be injured. Anatomic features of the plexus, including its superficial location, tethering between the intervertebral foramina and investing fascia, and the limited space in its course between the first rib and clavicle, render it vulnerable to injury. Sternal retraction and first rib fractures predispose to this injury. There does not appear to be a significant difference in brachial neuropathy when the arms are tucked against the body vs. when the arms are abducted 90 degrees with elbows elevated and palms up. The best recommendations are to maintain the head in a neutral position, place the sternal retractor as far caudally as possible, and use asymmetric retractors cautiously.

**17. What is the most common perianesthetic neuropathy?**

The ulnar nerve is the most frequently injured peripheral nerve, although its incidence is still relatively infrequent. There is a distinct predilection for men older than 50 years of age, and it is not uncommon for there to be a few days' delay in presentation. Occasionally the neuropathy is bilateral. Of interest, the American Society of Anesthesiologists' (ASA) Closed Claims Analysis found that 15% of ulnar neuropathies occurred in patients who were sedated and received spinal or epidural anesthesia or monitored anesthesia care. One would presume that, being awake, the patient would readjust their arms if they felt numbness or paresthesias developing during the procedure. Ulnar neuropathies tend to be mild, mostly sensory in nature, and self-limited. Return of function within 6 weeks is reasonable advice for patients so affected, although deficits have been reported to last up to 2 years. There are numerous cases of ulnar neuropathy in which padding to protect the ulnar nerve was undertaken; thus perioperative ulnar neuropathies are clearly multifactorial in nature. Some patients may have a subclinical ulnar neuropathy before recognition after surgery.

**18. Review the incidence of brachial plexus injuries.**

Closed Claims Analysis found that brachial plexus injuries account for 20% of all anesthesia-related nerve injuries. Risk factors include use of shoulder braces in head-down positions, malposition of the arms, and sustained neck extension. Although not a matter of positioning, upper-extremity regional anesthetic techniques may also cause brachial plexus injuries. Of interest, eliciting paresthesias during needle placement or injection of local anesthetics was not a common finding.

**19. How might upper extremity neuropathies be prevented through careful positioning?**

Arm abduction should be limited to 90 degrees in supine patients. Protective padding is essential to avoid upper extremity neuropathies but does not guarantee against them. The ulnar groove should be padded, and pronation avoided since this places the ulnar nerve in its most vulnerable position. When arms are tucked at the side, a neutral position is preferable. Flexion at the elbow may increase the risk of ulnar neuropathy. Pressure on the spiral groove of the humerus may result in radial neuropathy. Range limitation is not uncommon at the elbow, and overextension may place the median nerve at risk. Properly functioning automated blood pressure cuffs do not alter the risk of upper extremity neuropathy.

**KEY POINTS: PATIENT POSITIONING**

1. A conscientious attitude toward positioning is required to facilitate the surgical procedure, prevent physiologic embarrassment, and prevent injury to the patient.
2. Postoperative blindness is increasing in frequency, but it is unclear exactly which patients are at risk. Although not a guarantee to prevent this complication, during lengthy spine procedures in the prone position maintain intravascular volume, hematocrit, and perfusion pressure.
3. The most common postoperative nerve injury is ulnar neuropathy. It is most commonly found in men older than 50 years, is delayed in presentation, is not invariably prevented by padding, and is multifactorial in origin.
4. In order of decreasing sensitivity, monitors for detection of VAE are transesophageal echocardiography and Doppler ultrasound > increases in end-tidal nitrogen fraction > decreases in end-tidal carbon dioxide > increases in right atrial pressure > esophageal stethoscope. It should be noted that, of all these monitors, only the right atrial catheter can treat a recognized air embolism.

**20. What injuries may occur to the eye?**

The most common injury is corneal abrasion, but patients may also develop conjunctivitis, chemical injury, direct trauma, blurred vision, and ischemic optic neuropathy. Symptoms range from discomfort to pain to blindness. The relatively minor injuries are caused by direct pressure on the eye from face masks, surgical drapes, chemicals that touch the eye, and failure to administer ocular protection. Positions other than supine are more commonly associated with eye injuries. Although in the past it was recommended that a corneal abrasion be treated with an eye patch, this appears to delay healing; use of nonsteroidal anti-inflammatory ophthalmic ointments is now recommended by some. Repetitive use of local anesthetic or steroid drops is not recommended.

**21. Review the procedures that have been associated with postoperative visual loss.**

The incidence of blindness after cardiac surgery has been estimated at about 4%. The mechanisms are thought to be embolic, thrombotic, oncotic, and ischemic and related to the surgical procedures themselves. These patients may develop central retinal artery occlusion or ischemic optic neuropathy (ION).

Other surgical procedures that have been associated with postoperative visual loss (POVL) include neck dissections (including when there is ligation of the internal jugular veins), thyroidectomy, major vascular surgery, and craniotomy. It is of concern that the incidence of POVL associated with prone spine surgery seems to be on the increase.

**22. What factors may predispose a patient having spine surgery to postoperative visual loss?**

The causative factors associated with POVL after spine surgery are not fully understood. The incidence appears to be about 0.2%. The ASA has developed a visual loss registry in an effort to identify predisposing factors and make recommendations to reduce the incidence of this tragic complication. It is thought that there is a subset of patients at high risk for this complication, although it is not always possible to identify before surgery which patients are at high risk. These patients may have a history of hypertension, diabetes mellitus, smoking, other vasculopathies, and morbid obesity.

Longer spine surgeries (longer than 6 hours) with significant blood loss (1 to 2 L or more) are common features in patients who have sustained POVL. It does not appear to be a pressure effect on the globe since many of these patients were placed in Mayfield pins. Deliberate hypotensive anesthetic techniques do not appear to be a factor, although it may be argued that sustained

hypotension in the setting of anemia requires therapy. It is interesting that, in this day when transfusion triggers are being pushed downward (to lower hematocrits), long spine cases may not be a subset in which profound anemia is acceptable. It may be that, in spine cases that require both anterior and posterior stabilization, staging the procedure might be advisable. Although the complication is devastating, its incidence remains small, and the patients at risk, the factors that contribute to POVL, and recommendations for preventing POVL remain speculative.

**23. What patterns of blindness are noted?**

ION is noted in about 90% of cases, and central retinal artery occlusion is noted in the remainder. Posterior ION is more common than anterior ION, and ION is more likely to be bilateral (approximately two thirds of the time), suggesting that the etiologies are different. Substantive recovery of vision is not frequent.

**24. How does the head position affect the position of the endotracheal tube with respect to the carina?**

Flexion of the head may move the endotracheal tube toward the carina; extension moves it away from the carina. A general rule is that the tip of the endotracheal tube follows the direction of the tip of the patient's nose. The change in tube position is probably more problematic in a child than in an adult. Sudden increases in airway pressure or oxygen desaturation may be caused by mainstem bronchial intubation.

## WEBSITE



<http://www.asahq.org>

## SUGGESTED READINGS

1. ASA Task Force Perioperative Blindness: Practice advisory for perioperative visual loss associated with spine surgery. *Anesthesiology* 104:1319–1328, 2006.
2. Lee LA, Roth S, Posner KL, et al: The American Society of Anesthesiologists postoperative visual loss registry: analysis of 93 spine surgery cases with postoperative visual loss. *Anesthesiology* 105:652–659, 2006.

# MECHANICAL VENTILATION IN CRITICAL ILLNESS

James B. Haenel, RRT, and Jeffrey L. Johnson, MD

## 1. Why might a patient require mechanical ventilation?

There are three conditions for which mechanical ventilation (MV) may be required:

1. Inadequate respiratory drive
2. Inability to maintain adequate alveolar ventilation
3. Hypoxia

The decision to provide MV should be based on clinical examination and assessment of gas exchange by arterial blood gas analysis. This decision must be individualized because arbitrary cutoff values for  $PO_2$ ,  $PCO_2$ , or pH as indicators of respiratory failure may not be germane to all patients. Physiologic derangements necessitating the need for MV include primary parenchymal disorders such as pneumonia, pulmonary edema, or pulmonary contusion or systemic disease that indirectly compromises pulmonary function such as sepsis or central nervous system dysfunction. The principal goal of MV in the setting of respiratory failure is to minimize the potential for ventilator-induced injury and support gas exchange while the underlying disease process is reversed.

## 2. Which is the most common mode of ventilation, volume or pressure control?

From a classification standpoint neither is a true mode of ventilation. To be precise, conventional modes of MV control either volume or pressure. The mode of ventilation is a function of the types of breaths delivered (e.g., either mandatory and/or spontaneous breaths) and how the timing of each breath is determined. Volume control provides breaths that are volume constant and pressure variable. Pressure control provides breaths that are pressure constant and volume variable. It is the response of the ventilator to the patient's effort that determines the mode.

## 3. What are the most commonly used modes of positive-pressure ventilation?

Currently there are nine modes that are based on using either volume or pressure as the control variable:

- VC-CMV, volume control–continuous mandatory ventilation
- VC-A-C, volume control–assist control (ventilation)
- VC-IMV or VC-SIMV, volume-control intermittent or synchronized intermittent mandatory ventilation
- PC-CMV, pressure control–continuous mandatory ventilation
- PC-A-C, pressure control–assist control (ventilation)
- PC-IMV or PC-SIMV, pressure control–intermittent mandatory ventilation or pressure control–synchronized intermittent ventilation
- PSV, pressure support ventilation

## 4. Does PC-CMV permit the patient to interact with the ventilator?

Use of a term such as PC-CMV frequently leads to confusion to the uninitiated. The term *controlled* MV implies that the patient is receiving a neuromuscular blocking agent and is prevented or locked out from triggering the ventilator. Therefore, when speaking of volume control or pressure control, more descriptive terms such as *volume-targeted* or *pressure-targeted ventilation* may minimize any misunderstanding.

### 5. How does VC-A-C mode work?

The VC-A-C mode delivers a set minimum number of mandatory breaths and also allows the patient to trigger (or assist) additional breaths. Each breath (mandatory or assisted) is associated with a preset flow rate to deliver a preset tidal volume ( $V_T$ ). AC-A-C may cause respiratory alkalosis more often and may promote auto-positive end-expiratory pressure (PEEP) because the patient receives a full set  $V_T$  with every breath, even when tachypneic.

### 6. Do VC-A-C and VC-SIMV differ?

Both modes deliver mandatory breaths at a preset frequency, a preset  $V_T$ , and a preset inspiratory gas flow rate. Between machine-initiated breaths in the VC-A-C mode, the patient can trigger the ventilator and receive an assisted breath at the set  $V_T$ . In the VC-SIMV mode the ventilator generates a timing window based on the set frequency of the mandatory breaths, and attempts to *synchronize* the delivery of the breath in concert with the patient's spontaneous effort. In between the mandatory breaths, while in the SIMV mode, the patient is free to initiate a totally spontaneous effort and generate a  $V_T$  compatible with the patient's inspiratory muscular effort. Flow rates of gas will vary during these spontaneous breaths and will be based on the patient's efforts and demands.

### 7. When initiating mechanical ventilation, how do you decide on VC-A-C over VC-SIMV?

If the intent of MV is to provide full ventilator support, provision of a sufficient level of alveolar ventilation is obligatory. The preference of VC-A-C over VC-SIMV, assuming that minute ventilation demands (set frequency and set  $V_T$ ) are being met, is really a point of style or preference. However, once the patient has achieved cardiopulmonary stability and the goal is now to initiate partial ventilator support, the options for VC-A-C vs. VC-SIMV are very different. A patient on a set respiratory frequency of 4 breaths/min in the VC-A-C mode with a total respiratory rate of 18 breaths/min is still receiving full ventilator support. In contrast, in the VC-SIMV mode a patient with the same set frequency is considered to be in a partial mode of support and must be capable of supporting the bulk of his or her own gas exchange demands.

### 8. What other variables are associated with conventional modes of MV?

Simplistically ventilators are classified as either a pressure, volume, or flow controller. Current intensive care unit (ICU) ventilators can mix pressure control with flow control, all within a single breath. Next there are the phase variables, events that take place during a ventilator cycle. These phase variables control how the breath is

- *Triggered* (i.e., patient or machine)
- *Limited* (i.e., pressure or volume)
- *Cycled* from inspiration to exhalation (i.e., pressure, volume, flow, or time)

### 9. What is pressure support ventilation?

PSV augments a patient's spontaneous inspiratory effort with a clinician-selected level of positive airway pressure. Inspiration is completed when the patient's spontaneously generated peak flow rate decreases below a minimum level or a percentage of the initial inspiratory flow, typically less than 25%. Therefore PSV is a purely patient-triggered, pressure-limited, and flow-cycled mode of ventilation. PSV allows patients to establish their own respiratory rate (RR), vary their peak flow rate based on breath-to-breath demands, and enhance delivered  $V_T$ . Taken together the RR, peak flow, and  $V_T$  determine the inspiratory to expiratory (I:E) ratio. It is much more physiologic and comfortable for the patient to control the I:E ratio than to impose a fixed I:E ratio that will not respond favorably to increased patient demands.

### 10. How does pressure control ventilation differ from pressure support ventilation?

PCV, unlike PSV, is a pressure-limited, time-cycled mode of ventilation. The  $V_T$  generated results from the clinician-determined inspiratory time and the applied airway pressure and are



predominantly influenced by flow resistance and respiratory system compliance. Practically speaking, PCV is used as a mode of ventilation when full ventilatory support is necessary, whereas PSV is optimal for providing partial ventilatory support.

### 11. What are trigger variables?

All modern ICU ventilators constantly measure one or more of the phase variables (i.e., pressure, volume, flow, or time) (Table 21-1). Inspiration occurs when one of these variables reaches a preset value. Clinically this is referred to as *triggering* the ventilator. The following conditions are necessary to initiate a breath under each individual variable:

- Pressure triggering: requires patient-initiated effort to decrease circuit pressure below a preset value (e.g.,  $-2$  cm H<sub>2</sub>O below baseline end-expiratory pressure is common).
- Flow or volume triggering: again requires patient effort that results in a drop in the flow rate or volume of gas that is continually present within the circuit.
- Time triggering: does not require patient effort but occurs when the set respiratory rate on the ventilator becomes due.

Two potentially hazardous forms of triggering have also been identified:

- Auto-triggering: occurs when the ventilator is rapidly cycling without apparent patient effort. If the triggering system is overly sensitive (e.g., the pressure is set for  $-1$  cm H<sub>2</sub>O) and excessive condensation is present within the circuit, water motion can result in a drop in circuit pressure, causing auto-cycling.
- Ineffective triggering: occurs when the ventilator doesn't recognize a patient's inspiratory effort. This is commonly seen during pressure triggering in the presence of auto-PEEP that may prevent the patient from achieving the necessary drop in circuit pressure.

TABLE 21-1. BREATH TYPES FOR VOLUME AND PRESSURE MODES OF VENTILATOR OPERATION

Mode (Common Names)	Mandatory			Assisted		
	Trigger	Limit	Cycle	Trigger	Limit	Cycle
VC-CMV	Time	Flow	Volume or Time	—	—	—
VC-A-C	Time	Flow	Volume or Time	Patient	Flow	Volume or Time
VC-SIMV	Time	Flow	Volume or Time	—	—	—
PC-CMV	Time	Pressure	Time	—	—	—
PC-A-C	Time	Pressure	Time	Patient	Pressure	Time
PC-SIMV	Time	Pressure	Time	—	—	—

### 12. What are the goals of mechanical ventilation in patients with acute respiratory failure?

Most patients with acute respiratory failure require full ventilatory support. The goals are to preserve or optimize lung mechanics and gas exchange and promote patient comfort while preventing ventilator-induced lung injury. Complications may arise from elevated alveolar pressures or persistently high inspired concentrations of oxygen (FiO<sub>2</sub>).

**13. What are the initial ventilator settings in acute respiratory failure?**

Commonly one begins with the VC-A-C mode, which ensures delivery of a preset  $V_T$ . Pressure-cycled modes are acceptable but probably offer only theoretic advantage. The  $FiO_2$  begins at 1 and is titrated downward as tolerated. High  $FiO_2$  in the face of acute lung injury results in worsening of intrapulmonary shunting, probably as a result of absorption atelectasis.  $V_T$  is based on ideal body weight (IBW) and the pathophysiology of lung injury. Volumes of 6 to 10 ml/kg/IBW are acceptable as long as the plateau pressure is  $<30$  cm  $H_2O$ . However, acute respiratory distress syndrome (ARDS) decreases the volume of the lung available for ventilation. Because large pressures or volumes may exacerbate the underlying lung injury, smaller volumes in the range of 6 to 8 ml/kg/IBW are chosen. A respiratory rate (f) is chosen, usually in the range of 10 to 20 breaths/min. Patients with high minute volume requirements or a low  $V_T$  (lung protective strategy) may require an f of 32 breaths/min. Carbon dioxide elimination does not improve significantly with rates  $>25$ /min, and rates  $>30$ /min predispose to gas trapping secondary to abbreviated expiratory times.

**14. What is the role of positive end-expiratory pressure?**

PEEP has been a cornerstone in the management of respiratory failure for over 40 years. Specifically it is applied to the exhalation circuit of the mechanical ventilator. The main goals of PEEP are to:

- Increase functional residual capacity by preventing alveolar collapse and recruiting atelectatic alveoli.
- Decrease intrapulmonary shunting.
- Reduce the work of breathing.

PEEP adjustments should be considered in response to periods of desaturations (after common causes for hypoxemia have been ruled out) such as mucous plugging and barotrauma) to assess recruitment potential.

**15. How is optimal positive end-expiratory pressure identified?**

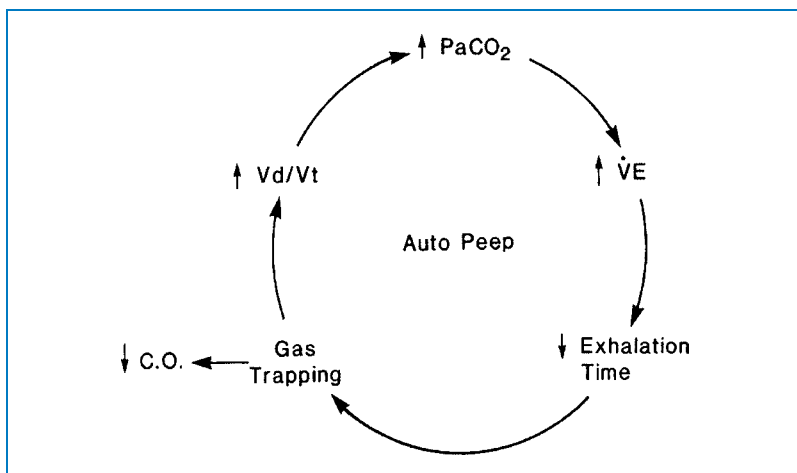
Although various methods for lung recruitment have been suggested, we use the following approach to identify the optimal PEEP:

Patients experiencing an acute desaturation event are placed in the pressure control mode, with respiratory rate set at 10 breaths/min, I:E ratio at 1:1, and peak pressure at 20 cm  $H_2O$ . The PEEP is increased to 25 to 40 cm  $H_2O$  for 2 minutes. The patient is continuously monitored for adverse effects. The PEEP is then returned to the baseline value. If the patient again desaturates, the trial is repeated, but the baseline PEEP is set 5 cm  $H_2O$  higher. This process is continued until the patient no longer desaturates. To enhance safety, identification of intravascular fluid deficits and optimization of the hemodynamic status should be addressed before application of high PEEP levels.

**16. What is intrinsic or auto-positive end-expiratory pressure?**

Intrinsic PEEP (PEEPi) is unrecognized positive alveolar pressure at end exhalation during MV. Patients with high minute ventilation requirements or patients with chronic obstructive pulmonary disease (COPD) or asthma are at risk for PEEPi. In healthy lungs during MV, if the respiratory rate is too rapid or the expiratory time too short, there is insufficient time for full exhalation, resulting in stacking of breaths and generation of positive airway pressure at end exhalation. Small-diameter endotracheal tubes may also limit exhalation and contribute to PEEPi. Patients with increased airway resistance and decreased pulmonary compliance are at high risk for PEEPi. Such patients have difficulty exhaling gas because of small airway obstruction/collapse and are prone to development of PEEPi during spontaneous ventilation and MV. PEEPi has the same side effects as PEEPe, but detecting it requires more vigilance.

Failure to recognize the presence of auto-PEEP can lead to inappropriate ventilator changes (Figure 21-1). The only way to detect and measure PEEPi is to occlude the expiratory port at end expiration while monitoring airway pressure. Decreasing rate or increasing inspiratory flow (to increase I:E ratio) may allow time for full exhalation. Administering a bronchodilator therapy in the setting of bronchospasm is usually beneficial.



**Figure 21-1.** Failure to appreciate auto-PEEP can lead to a vicious cycle in which an increased minute ventilation ( $\dot{V}_E$ ) in response to a rise in  $\text{PaCO}_2$  decreases exhalation time, augments gas trapping, increases dead space ventilation ( $V_D/V_T$ ), and paradoxically decreases  $\text{CO}_2$  elimination. A further increase in  $\dot{V}_E$  repeats the cycle, allowing pleural pressure to increase so that the adverse effects of PEEP (e.g., decreased cardiac output) emerge.

### 17. What are the side effects of PEEP and PEEPi?

- Barotrauma may result from overdistention of alveoli.
- Cardiac output may be decreased because of increased intrathoracic pressure, producing an increase in transmural right atrial pressure and a decrease in venous return. PEEP also increases pulmonary artery pressure, potentially decreasing right ventricular output. Dilation of the right ventricle may cause bowing of the interventricular septum into the left ventricle, thus impairing filling of the left ventricle, decreasing cardiac output, especially if the patient is hypovolemic.
- Incorrect interpretation of cardiac filling pressures. Pressure transmitted from the alveolus to the pulmonary vasculature may falsely elevate the readings.
- Overdistention of alveoli from excessive PEEP decreases blood flow to these areas, increasing dead space ( $V_D/V_T$ ).
- Work of breathing may be increased with PEEP because the patient is required to generate a larger negative pressure to trigger flow from the ventilator.
- Increase in intracranial pressure (ICP) and fluid retention.

### 18. What is a ventilator bundle?

The ventilator bundle is a series of interventions related to ventilator care that have been identified to significantly reduce the incidence of ventilator-associated pneumonia. The key components of the ventilator bundle are:

- Elevation of the head of the bed
- Daily *sedation vacations* and assessment for the readiness to extubate
- Stress ulcer prophylaxis
- Deep venous thrombosis

Additional interventions likely complementary to the ventilator bundle are implementation of a hand hygiene campaign and an oral care protocol.

### 19. What is controlled hypoventilation with permissive hypercapnia?

Controlled hypoventilation (or permissive hypercapnia) is a pressure- or volume-limiting, lung-protective strategy whereby  $\text{PCO}_2$  is allowed to rise, placing more importance on

protecting the lung than on maintaining eucapnia. The set  $V_T$  is lowered to a range of approximately 4 to 6 ml/kg/IBW in an attempt to keep the Peak airway pressure ( $P_{aw}$ ) below 35 to 40 cm H<sub>2</sub>O and the static plateau pressure below 30 cm H<sub>2</sub>O. Several studies in ARDS and status asthmaticus have shown a decrease in barotrauma, intensive care days, and mortality. The  $PCO_2$  is allowed to rise slowly to a level of up to 80 to 100 mm Hg. If pH falls below 7.20, it may be treated with a buffer. Alternatively one may wait for the normal kidney to retain bicarbonate in response to the hypercapnia. Permissive hypercapnia is usually well tolerated. Potential adverse effects include cerebral vasodilation leading to increased ICP, and intracranial hypertension is the only absolute contraindication to permissive hypercapnia. Increased sympathetic activity, pulmonary vasoconstriction, and cardiac arrhythmias may occur but are rarely significant. Depression of cardiac contractility may be a problem in patients with underlying ventricular dysfunction.

#### 20. What is compliance? How is it determined?

Compliance is a measure of distensibility and is expressed as the change in volume for a given change in pressure. Determination of compliance involves the interrelationship among pressure, volume, and resistance to airflow. The two relevant pressures that must be monitored during MV are peak and static pressures.

#### 21. How is peak pressure measured?

Peak pressure is measured during the delivery of airflow at the end of inspiration. It is influenced by the inflation volume, airway resistance, and elastic recoil of the lungs and chest wall and reflects the dynamic compliance of the total respiratory system.

#### 22. How is static pressure measured?

Static or plateau pressure is measured during an end-inspiratory pause, during a no-flow condition, and reflects the static compliance of the respiratory system, including the lung parenchyma, chest wall, and abdomen.

#### 23. How is compliance calculated?

Both dynamic and static compliance should be calculated. Dynamic compliance is calculated as  $V_T/(P_{aw} - \text{total PEEP})$ , and plateau or static compliance is  $V_T/(\text{plateau pressure} - \text{total PEEP})$ . Normal values for both dynamic and static compliance are 60 to 100 ml/cm H<sub>2</sub>O. A decrease in dynamic compliance without a change in the static compliance suggests an acute increase in airway resistance and can be assessed further by comparing peak pressure and plateau pressure. The normal gradient is approximately 10 cm H<sub>2</sub>O. A gradient >10 cm H<sub>2</sub>O may be secondary to endotracheal tube obstruction, mucous plugging, or bronchospasm. If volume is constant, acute changes in both dynamic and static compliance suggest a decrease in respiratory system compliance that may be caused by worsening pneumonia, ARDS, atelectasis, or increasing abdominal pressures.

Compliance is a global value and does not describe what is happening regionally in the lungs with ARDS, in which diseased regions are interspersed with relatively healthy regions. Compliance values of 20 to 40 cm H<sub>2</sub>O are common in advanced ARDS. Decreased lung compliance reflects the compliance of the lung that is participating in gas exchange, not the collapsed or fluid-filled alveoli.

#### 24. Is ventilation in the prone position an option for patients who are difficult to oxygenate?

Absolutely! Studies have shown that the  $PaO_2$  improves significantly in approximately two thirds of patients with ARDS when they are placed prone. The mechanisms include:

- Recruitment of collapsed dorsal lung fields by redistribution of lung edema to ventral regions.
- Increased diaphragm motion enhancing ventilation.

- Elimination of the compressive effects of the heart on the inferior lower lung fields, thus improving regional ventilation.
- Maintenance of dorsal lung perfusion in the face of improved dorsal ventilation, which leads to improved V/Q matching.

### 25. What are the indications for prone ventilation?

Indications for prone ventilation are not clearly established. We initiate a prone trial in any patient who remains hypoxemic or requires high  $\text{FiO}_2$  concentrations after the performance of recruitment/PEEP maneuvers. The best predictor of improved outcome during prone ventilation may be a decrease in the  $\text{PaCO}_2$  and not improved oxygenation.

### 26. How is the patient who is fighting the ventilator approached?

Initially the potential causes are separated into ventilator (machine, circuit, and airway) problems and patient-related problems. Patient-related causes include hypoxemia, secretions or mucous plugging, pneumothorax, bronchospasm, infection (pneumonia or sepsis), pulmonary embolus, myocardial ischemia, gastrointestinal bleeding, worsening PEEP<sub>i</sub>, and anxiety. The ventilator-related issues include system leak or disconnection; inadequate ventilator support or delivered  $\text{FiO}_2$ ; airway-related problems such as extubation, obstructed endotracheal tube, cuff herniation, or rupture; and improper triggering sensitivity or flows. Until the problem is sorted out, the patient should be ventilated manually with 100% oxygen. Breath sounds and vital signs should be checked immediately. Arterial blood gas analysis and a portable chest radiograph are valuable, but, if a tension pneumothorax is suspected, immediate decompression precedes the chest radiograph.

## KEY POINTS: MECHANICAL VENTILATION IN CRITICAL ILLNESS



1. Three indications for MV are: inadequate respiratory drive, inability to maintain alveolar ventilation, and hypoxia.
2. Two indications for noninvasive positive-pressure ventilation: hypercapnic respiratory failure and comfort in terminally ill patients.
3. Risk factors for auto-PEEP: high minute ventilation, small endotracheal tube, COPD, and asthma.
4. The normal airway gradient between peak and static pressure is approximately 10 cm  $\text{H}_2\text{O}$ .
5. The first step in the care of the hypoxic patient fighting the ventilator is to ventilate the patient manually with 100% oxygen.

### 27. Should neuromuscular blockade be used to facilitate mechanical ventilation?

Neuromuscular blocking agents (NMBAs) are commonly used to facilitate MV during ARDS; but, despite wide acceptance, there are few data and as yet no consensus available for when these agents should be used. Gannier and associates (2004) were the first to report the effects of a 48-hour NMBA infusion on gas exchange in patients with early ARDS. All patients were ventilated according to the ARDSNet protocol. Significant improvements in oxygenation and ability to lower PEEP occurred in the NMBA group and were sustained beyond the 48-hour infusion period. Although it remains to be elucidated why muscle paralysis improves oxygenation, NMBAs are thought to decrease oxygen consumption, promote patient-ventilator interface, and increase chest wall compliance.

Muscle paralysis may also be of benefit in specific situations such as intracranial hypertension or unconventional modes of ventilation (e.g., inverse ratio ventilation or

extracorporeal techniques). Drawbacks to the use of these drugs include loss of neurologic examination, abolished cough, potential for an awake paralyzed patient, numerous medication and electrolyte interactions, potential for prolonged paralysis, and death associated with inadvertent ventilator disconnects. Use of NMBAs must not be taken lightly. Adequate sedation should be attempted first; if deemed absolutely necessary, use of NMBAs should be limited to 24 to 48 hours to prevent potential complications.

### 28. Is split-lung ventilation ever useful?

Split-lung ventilation (SLV) refers to ventilation of each lung independently, usually via a double-lumen endotracheal tube and two ventilators. Patients with severe unilateral lung disease may be candidates for SLV. SLV has been shown to improve oxygenation in patients with unilateral pneumonia, pulmonary edema, and contusion. Isolation of the lungs can save the life of patients with massive hemoptysis or lung abscess by protecting the good lung from spillage. Patients with a bronchopleural fistula also may benefit from SLV. Different modes of ventilation may be applied to each lung individually. The two ventilators need not be synchronized, and, in fact, hemodynamic stability is better maintained by using the two ventilators asynchronously.

## WEBSITE



Institute for Healthcare Improvement: Implement the ventilator bundle  
[www.IHI.org](http://www.IHI.org)

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# ELECTROCARDIOGRAPHY

William A. Baker, MD, and Christopher M. Lowery, MD

## 1. Are all abnormal ECGs indicative of heart disease?

No. Just as some individuals are very tall, some individuals without real cardiac pathology have electrocardiogram (ECG) findings that deviate enough from the population mean to raise the question of heart disease. Careful history and physical examination may help identify individuals who truly have cardiac pathology. Noninvasive techniques such as echocardiography and cardiac magnetic resonance imaging may aid in separating patients with true structural heart disease from those with unusual variations who are abnormal only in a statistical sense.

Other findings such as right bundle-branch block (RBBB), are present in patients with heart disease but also occur frequently in patients who have no evidence of heart disease by history, physical examination, or echocardiography.

## 2. What is the differential diagnosis for low voltage?

Chronic obstructive pulmonary disease, hypothyroidism, pericardial effusion, anasarca, amyloidosis, ischemic cardiomyopathy, and obesity are included in the differential diagnosis.

## 3. Is electrocardiography sensitive or insensitive for detecting chamber enlargement and hypertrophy?

It is insensitive. When echocardiography or autopsy is used as the gold standard, ECG misses many patients with real chamber enlargement or hypertrophy. This is particularly true with patients who have less severe (yet still potentially meaningful) degrees of these findings. Although useful because of low cost and ease of application, electrocardiography certainly has its limitations.

## 4. Which clues suggest that a patient may have left ventricular hypertrophy?

High QRS voltage is the hallmark of left ventricular hypertrophy (LVH), although many young patients have high QRS voltage without real LVH. Other associated hints (albeit nonspecific) are left axis deviation, left atrial enlargement, widening of the QRS, and *strain* (associated ST-T abnormalities).

Patients with left bundle-branch block (LBBB) cannot be diagnosed with LVH from the ECG, but it is important to remember that many patients with LBBB actually have LVH by echocardiography. There are a number of *scoring systems* to decide whether a patient meets ECG criteria for LVH, and all of them are insensitive.

## 5. An adult has a large R wave in V1. What is the differential diagnosis?

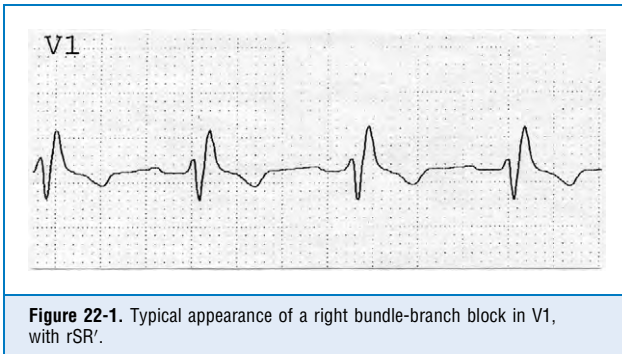
- Right ventricular hypertrophy (look for associated right axis deviation, right atrial enlargement, and right ventricular (RV) strain with ST-T abnormalities)
- Posterior myocardial infarction
- Wolff-Parkinson-White (WPW) syndrome
- Muscular dystrophy
- Normal early transition

**6. What leads are most helpful when looking for a bundle-branch block?**

- V1, V6, I, and to some extent II
- The QRS duration should be more than 120 ms to identify a bundle-branch block. Not every wide QRS is a bundle-branch block; the differential diagnosis also includes a ventricular beat, intraventricular conduction delay, hyperkalemia, drug effect, and WPW with conduction through an accessory pathway.

**7. What are the characteristics of a right bundle-branch block?**

Patients with RBBB typically have an rSR' pattern in V1 and a broad terminal S wave in I and V6 (Figure 22-1).



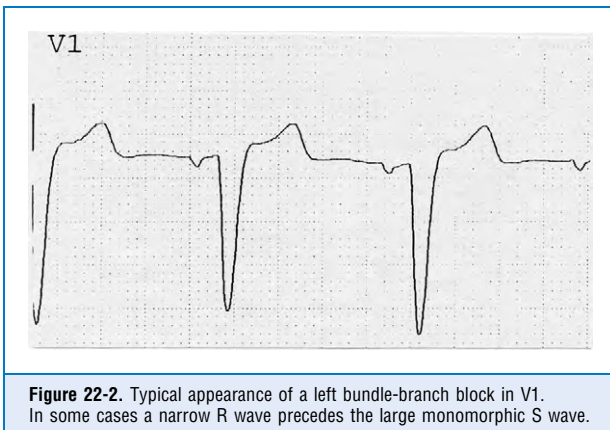
**Figure 22-1.** Typical appearance of a right bundle-branch block in V1, with rSR'.

**8. What is an intraventricular conduction delay? When is it seen?**

An intraventricular conduction delay is a wide QRS that arises from supraventricular conduction that is neither a typical RBBB nor a typical LBBB. It is often noted in patients with a cardiomyopathy.

**9. What are the characteristics of a left bundle-branch block?**

In V1 there is a broad, deep S wave (or QS wave), with ST segment elevation, that may be preceded by a very narrow R wave (Figure 22-2). In lead I there is a broad R wave (sometimes notched) without a Q or S wave.



**Figure 22-2.** Typical appearance of a left bundle-branch block in V1. In some cases a narrow R wave precedes the large monomorphic S wave.



**10. What is a hemiblock?**

The left bundle bifurcates into two *fascicles* (anterior and posterior), and either one may be blocked. With a hemiblock the QRS duration is generally less than 120 milliseconds unless there is an associated RBBB (commonly termed a *bifascicular block*).

**11. You are attempting to pass a Swan-Ganz catheter into the pulmonary artery in a patient with LBBB. When the hemodynamic tracing suggests that the catheter tip is in the right ventricle, the patient suddenly becomes bradycardic, with a heart rate of 25. What happened?**

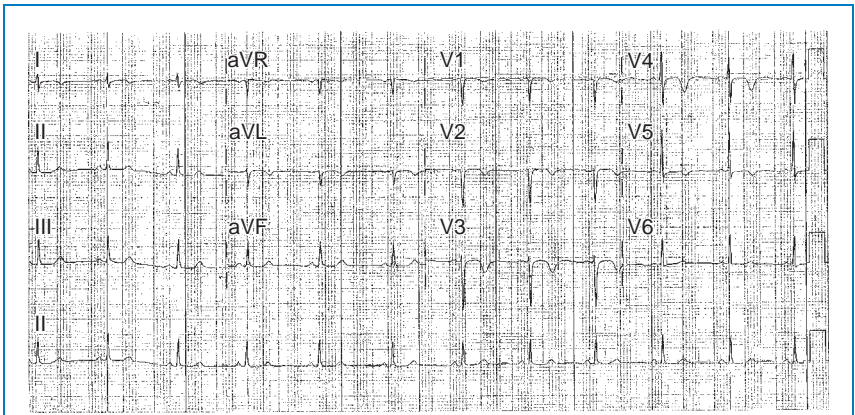
The patient is probably in complete heart block as a result of a catheter-induced RBBB (together with a preexisting LBBB). Fortunately the injury to the right bundle branch is often brief, but temporary pacing may be required.

For patients with LBBB, consider the value of a pulmonary artery catheter carefully before proceeding. In addition, you should have emergency pacing equipment readily available to respond properly if this complication develops. Transient stunning of the right bundle may occur in as many as 5% to 10% of cases.

**12. Does a normal ECG exclude the possibility of severe coronary artery disease?**

No, although an ECG done during ischemic chest pain is usually abnormal. It is common for patients with severe coronary artery disease (CAD) to have an ECG with only nonspecific abnormalities.

For an example of ECG findings noted in a patient with exertional angina, see [Figure 22-3](#).



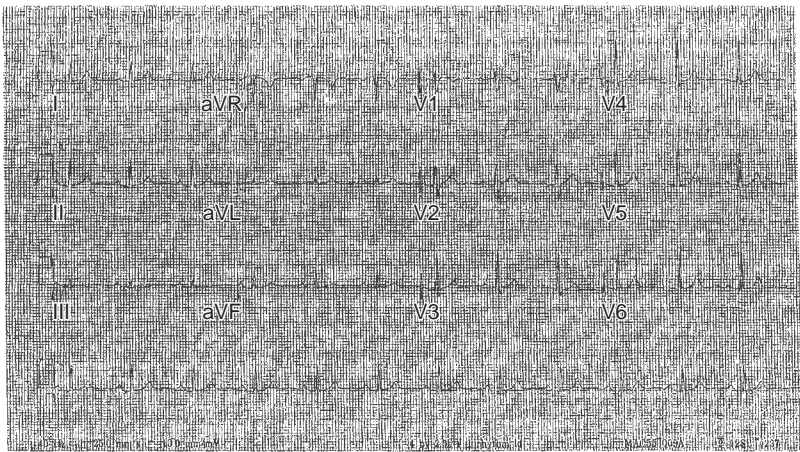
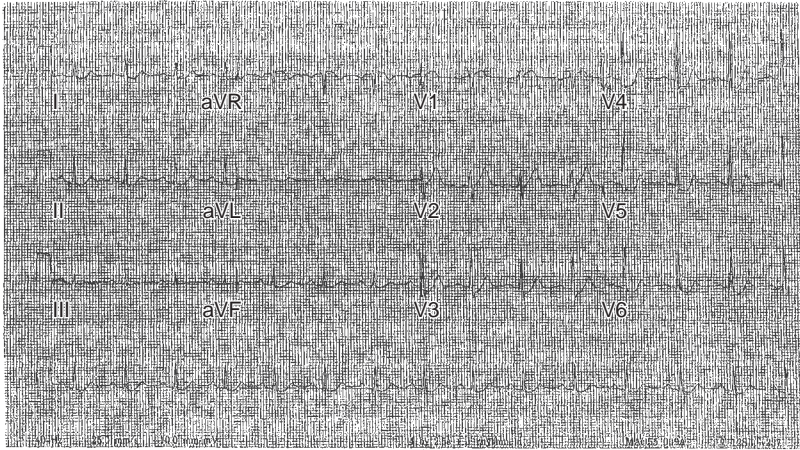
**Figure 22-3.** This 12-lead ECG shows deep relatively symmetric T wave inversions, meeting ECG criteria for ischemia. Coronary insufficiency is generally the most common life-threatening cause of this pattern. Not uncommonly patients with chest pain at rest from coronary insufficiency (an acute coronary syndrome) may present with an ECG like this. They might also present with ST segment depression, nonspecific ST-T abnormalities, or even a normal ECG. Although deep symmetric T inversions should generally provoke a clinical evaluation for coronary disease, other causes should be considered, including pulmonary embolus, acute central nervous system pathology (classically a subarachnoid bleed), a cardiomyopathy, abnormal repolarization from ventricular hypertrophy, or significant electrolyte disturbances. This patient was a 42-year-old woman with history of smoking who presented with progressive angina, occurring with only minimal exertion. Catheterization showed severe multivessel disease for which she underwent coronary artery bypass surgery.

**13. How are patients with myocardial infarction subdivided on the basis of ECG changes during infarction?**

Myocardial infarctions (MIs) are often divided into two types: ST segment elevation MI and non-ST segment elevation MI. Patients with ST segment elevation should be considered for immediate percutaneous coronary intervention (PCI), or thrombolytic therapy if PCI is unavailable. Q waves usually develop over time in the leads where there is elevation. Q waves

may diminish in size or go away over time. Patients with acute MI without ST elevation often have ST-segment depression (which may be dynamic) and/or T-wave inversions. Patients with non-ST-elevation MI can usually be made pain-free with medical therapy, and cardiac catheterization is often performed within several days. However, ongoing symptoms and ECG changes refractory to medical therapy can prompt emergent invasive evaluation.

For an example of ECG changes associated with a non-ST segment elevation MI, see [Figures 22-4 and 22-5](#).



**Figures 22-4 and 22-5.** These ECGs are from the same patient, a vigorous 78-year-old with new chest pain that began after moderate exertion. [Figure 22-4](#) was obtained while the patient was in an emergency room with persistent chest pain. The main finding is significant ST segment depression in the anterolateral precordial leads. The chest pain and ST segment changes resolved over the next 30 minutes (see [Figure 22-5](#)). Troponin I serum levels were mildly elevated. Because the pain was provoked by minimal exertion, with significant ECG abnormalities and abnormal troponin I, coronary angiography was performed instead of stress testing. Significant left main and multivessel coronary artery disease (CAD) was found, and the patient underwent successful coronary artery bypass surgery. In this example the suspicion of CAD was very strong, based on the ECG changes and clinical characteristics. However, more modest degrees of ST depression are less specific for coronary insufficiency, particularly when differences are subtle and when there is a potential alternative explanation (electrolyte imbalance, digoxin effect, or repolarization abnormality from left ventricular hypertrophy).

#### 14. Does ST-segment elevation always indicate a myocardial infarction?

No. Other causes of ST-segment elevation are listed in [Table 22-1](#).

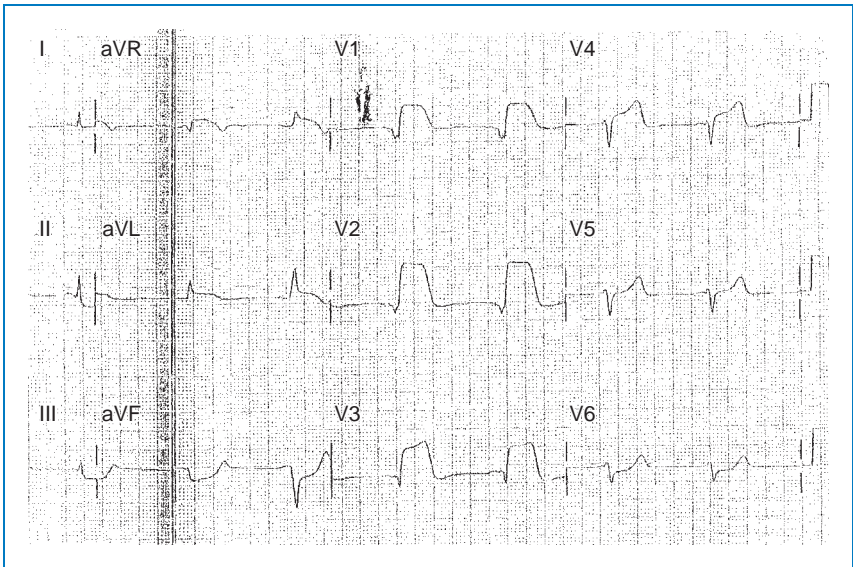
TABLE 22-1. CAUSES OF ST-SEGMENT ELEVATION

Acute subepicardial injury (i.e., acute ST-segment elevation myocardial infarction)	Hypercalcemia
Early repolarization pattern	Left ventricular hypertrophy
Pericarditis	Left bundle-branch block
Hyperkalemia	Brugada syndrome
	Normal variant

#### 15. For patients with ST-segment elevation myocardial infarction, how is the location identified?

- Patients with inferior MI generally have ST elevation in II, III, and aVF
- Patients with lateral MI have ST elevation in I, aVL, V5, and V6
- Patients with anterolateral MI have ST elevation in I, aVL, and V3-V6
- Patients with septal MI have ST elevation in V1-V2
- Patients with anteroseptal MI have ST elevation in V1-V4
- Patients with anterior MI have ST elevation in V3-V4

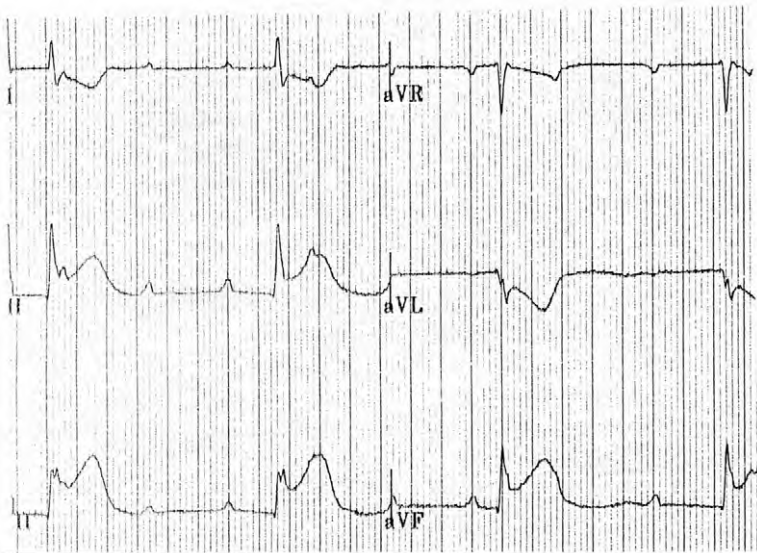
For an example of an ST segment elevation MI, see [Figure 22-6](#).



**Figure 22-6.** This 12-lead ECG was obtained from a 60-year-old woman with chest pain. Massive ST segment elevation (*subepicardial injury*) accompanied by Q waves in V1-3 and reciprocal inferior ST depression, is noted in this florid example of an anterior ST elevation myocardial infarction, or STEMI. The prominent rectangular-shaped ST elevation is sometimes referred to as a *tombstone*. The infarct vessel was the left anterior descending (LAD) coronary artery. Patients with a STEMI should receive some form of emergent reperfusion therapy (percutaneous coronary intervention, if readily available, or thrombolytic therapy when not contraindicated).

**16. A patient has evidence on ECG of an acute inferior myocardial infarction. What associated findings should you look for?**

- Evidence of right ventricular involvement. Since V1 is really a right-sided lead, ST elevation in V1 accompanying an inferior MI suggests right ventricular involvement. Alternatively you may check right-sided leads over the right precordium. ST elevation of 1 mm in right-sided V4 or V5 indicates RV infarction.
- Evidence of lateral wall involvement, usually suggested by ST elevation in V5-V6.
- Evidence of posterior wall involvement, as suggested by an R wave in V1 that is broad and/or tall, particularly in comparison with prior ECGs. Patients with posterior MI often have ST depression in V1-V2.
- Evidence of bradycardia caused by sinoatrial (SA) or atrioventricular (AV) nodal block. Patients with inferior MI may require atropine and/or temporary pacing (Figure 22-7).



**Figure 22-7.** Limb leads from a patient with inferior myocardial infarction and complete heart block (see Chapter 30). The patient has ST segment elevation in II, III, and aVF, along with ST segment depression in I and aVL (reciprocal change). Complete heart block is indicated by atrioventricular dissociation with the atrial rate ( $\approx 110$ ) greater than the ventricular rate ( $\approx 40/\text{min}$ ) with a regular RR interval.

**17. What is reciprocal change? Why is it important?**

Reciprocal change is ST-segment depression that occurs in patients with an ST-elevation MI. For example, a patient with an inferior MI may have ST elevation in II, III, and aVF, with ST depression (reciprocal change) in I and aVL. Not all patients with ST-elevation MI have reciprocal change, but when it is seen, it generally confirms the diagnosis of acute MI (see Figure 22-7).

**18. What ECG findings suggest hypothyroidism?**

Low QRS voltage, bradycardia, and QT interval prolongation. There may also be associated T-wave abnormalities and AV block.

19. An elderly patient presents with fatigue, confusion, and atrial fibrillation with a slow ventricular response (heart rate = 40). The ECG demonstrates ST depression that is concave upward. The family states that the patient is on an unknown medication that is locked in his apartment. What laboratory test should you order to confirm your suspicion?

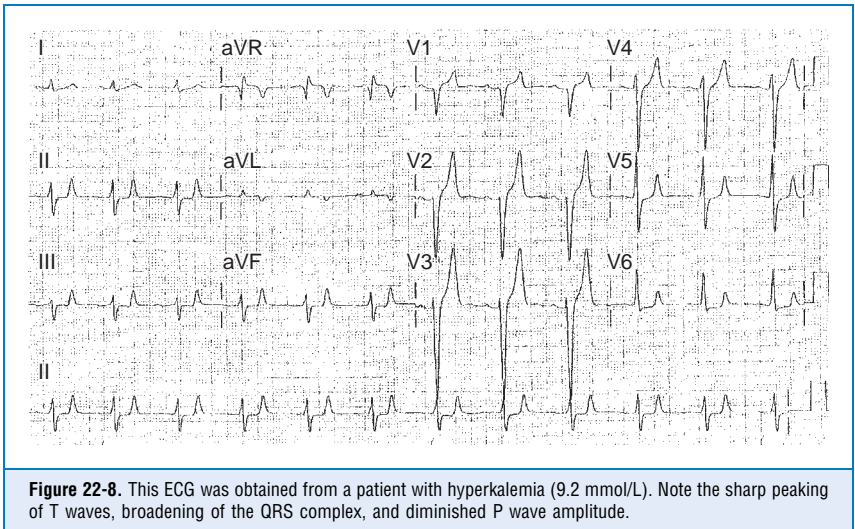
Serum digoxin level.

20. An ECG recorded when the operating room nurse is scrubbing the patient's chest demonstrates wide complex electrical activity. The patient is asymptomatic. What do you suspect? How can you prove that you are correct when you analyze the ECG tracing?

Artifact is common in this scenario, and in other situations in which there is *to-and-fro* activity such as tooth brushing. With artifact the heart rate is generally about the same before and immediately after the wide complex signal. With calipers, QRS complexes *marching through* the artifact at the baseline heart rate can often be seen. If simultaneous pulse oximetry waveforms are available, it is possible to confirm that the heart rate is relatively constant throughout the "*arrhythmia*."

21. What ECG findings suggest hyperkalemia?

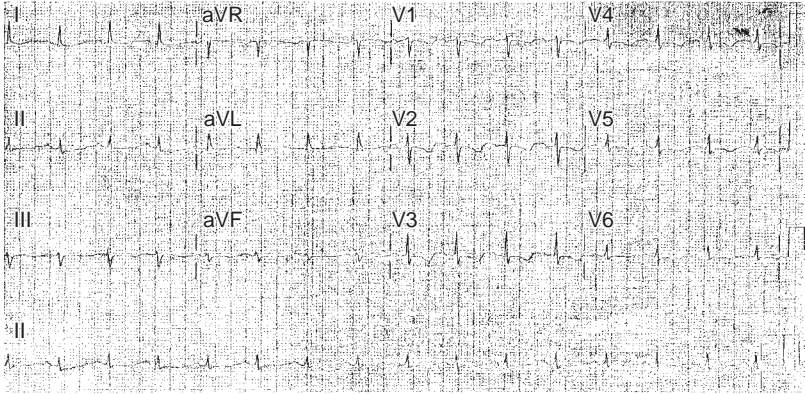
QRS widening and/or peaked T waves (Figure 22-8). In the worst cases the ECG looks like a sine wave.



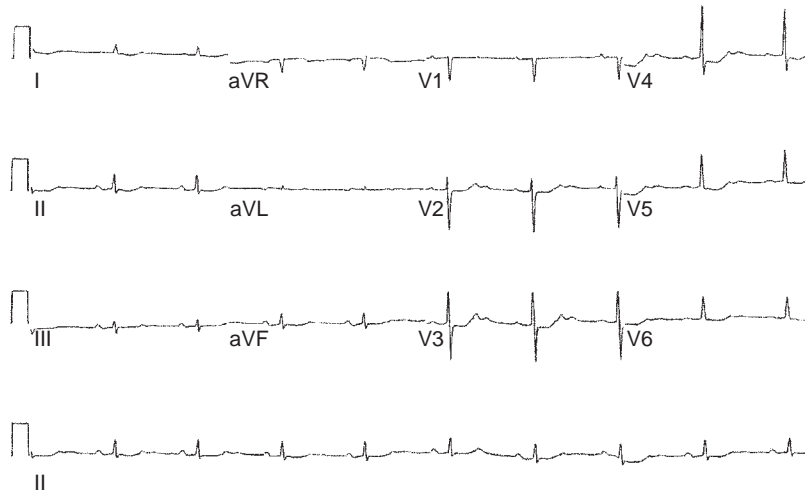
**Figure 22-8.** This ECG was obtained from a patient with hyperkalemia (9.2 mmol/L). Note the sharp peaking of T waves, broadening of the QRS complex, and diminished P wave amplitude.

22. What ECG findings suggest hypokalemia?

U waves (which occur after the T wave) are prominent and may merge with the T wave, creating a broad T wave and a prolonged QT interval. In addition, the P wave may be amplified, and ST depression may occur (Figures 22-9 and 22-10).



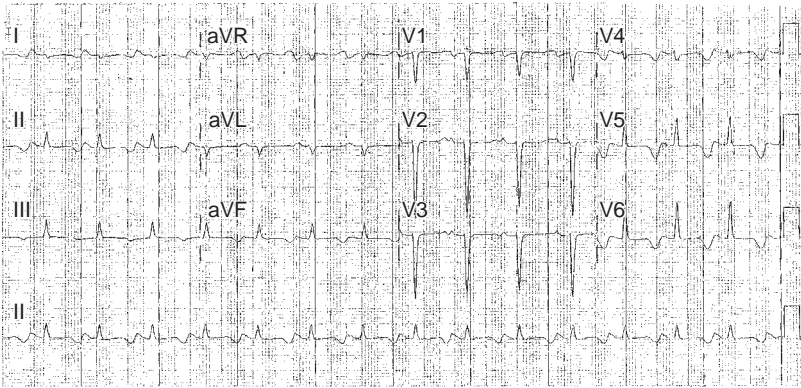
**Figure 22-9.** This ECG was obtained from a patient with hypokalemia (2.1 mmol/L). ST-T wave abnormalities in the anterior leads raised concern for myocardial ischemia, but abnormalities were substantially improved after repletion of potassium.



**Figure 22-10.** This ECG was obtained from a patient with hypokalemia (3.2 mmol/L). Note the prominent U wave after the T wave in the precordial leads V2-6. There is often TU fusion with hypokalemia, creating a broad T wave and an increase in the measured QT interval. Polymorphic ventricular tachycardia may result from hypokalemia.

### 23. What ECG findings suggest hypocalcemia?

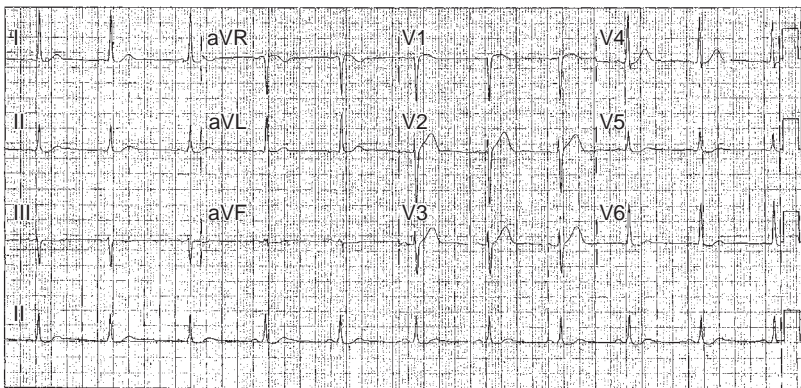
The QT interval is prolonged without broadening of the T wave (in contrast to the situation with hypokalemia). The T wave appears to be *pushed away* from the QRS complex. See Figure 22-11.



**Figure 22-11.** This ECG was obtained from a 34-year-old man with pseudohypoparathyroidism and a dilated cardiomyopathy. Serum calcium was 5.9 mg/dl, with ionized calcium 0.74 mmol/L. The QT was measured at 484 msec, with QTc 586. The QT is *pushed away* from the QRS complex, merging with the P wave in some leads. This patient's dilated cardiomyopathy gradually resolved after treatment with calcium.

### 24. What ECG changes suggest hypercalcemia?

Shortening of the QT interval, with or without ST segment elevation (Figure 22-12).



**Figure 22-12.** This ECG was obtained from a patient with hypercalcemia (serum calcium 12.5 mg/dl). The ST-T complex is *pushed up*, and the QT is shortened. Hypercalcemia may be a result of malignancy (especially with bone metastasis), hyperparathyroidism, sarcoid, or other conditions.

## KEY POINTS: ELECTROCARDIOGRAPHY



Differential diagnosis of large R wave in V1:

1. Right ventricular hypertrophy
2. Posterior wall myocardial infarction
3. Normal variant (*early transition*)
4. WPW syndrome
5. Muscular dystrophy

### 25. What are some of the common causes of a prolonged QT interval?

- Abnormal electrolytes, especially hypokalemia, hypocalcemia, and hypomagnesemia, can contribute to lengthening of the QT.
- Many medications may contribute to QT prolongation, and certain categories are more *notorious* than others. Psychoactive medications, particularly phenothiazines, tricyclic antidepressants, methadone, and butyrophenones, can prolong the QT.
- Many antiarrhythmics (especially sotalol, amiodarone, and type Ia antiarrhythmics such as procainamide) prolong the QT.
- In other cases introduction of medications (cimetidine, verapamil, ketoconazole, erythromycin) or cirrhosis may interfere with hepatic metabolism of agents that prolong the QT.
- Structural heart disease from a cardiomyopathy or myocardial ischemia may prolong the QT.
- Patients with bradycardia or QRS prolongation (e.g., from a bundle-branch block) may have QT prolongation.
- Systemic illnesses such as hypothyroidism may result in QT prolongation.
- Some patients have a hereditary predisposition to QT prolongation (a congenital long QT syndrome resulting from abnormal ion channels), which can become more evident during pregnancy.

Many patients have QT prolongation from a combination of the above factors. For example, a patient with congenital long QT syndrome may have more extreme prolongation with the addition of a new drug or electrolyte abnormality. In some cases these multifactorial processes can result in life-threatening ventricular arrhythmias such as torsades de pointes (see Chapter 30).

### 26. A patient has a right bundle-branch block that is new compared to the ECG from 2 years ago. How should I proceed?

Although a RBBB can be caused by CAD (e.g., with a large anterior infarct destroying some of the conduction system in the interventricular septum), this is only true in a minority of RBBB patients. Such patients typically have a qR in V1 instead of an rSR' prime because the initial r wave is lost as a consequence of the MI.

Occasionally an RBBB may be caused by congenital heart disease (such as tetralogy of Fallot), prior cardiac surgery, a cardiomyopathy, or pulmonary hypertension. History and physical examination can supplement the ECG in these cases; and, if clinical signs of structural heart disease are noted, echocardiography may be useful.

In a minority of cases RBBB may be present in patients with significant conduction system disease. For example, some patients with coexisting hemiblock, first-degree AV block, and RBBB may be at risk for complete heart block. However, in the absence of symptoms of complete heart block (e.g., syncope or near syncope) or some ECG evidence of higher degree AV block, prophylactic pacing is not indicated.



Patients who have had (at different times) *both* an RBBB and an LBBB are at significant risk of complete heart block; permanent pacing is generally indicated.

For most patients with RBBB, the prognosis is excellent, and the likelihood of serious underlying heart disease is low. If the history and physical examination do not reveal any evidence of such disease, no further testing or consultation is necessary.

**27. A patient has a left bundle-branch block that is new compared to the ECG from 2 years ago. How should I proceed?**

In a patient with signs and symptoms of acute myocardial ischemia (e.g. chest pain, new congestive heart failure (CHF), hemodynamic instability), a new LBBB may be a sign of a new, large acute anterior MI. However, in the vast majority of cases a new LBBB is not caused by an acute MI. Sometimes a 12-lead ECG may indicate superimposed subepicardial injury in acute MI cases, but the diagnosis is more difficult than the diagnosis of an ST elevation MI without a bundle-branch block.

Even in the absence of an acute MI, an LBBB may indicate underlying structural heart disease such as a dilated cardiomyopathy or left ventricular hypertrophy. History and physical examination looking for signs and symptoms of angina, heart failure, syncope, hypertension, and valvular heart disease, are important. For elective situations echocardiography is reasonable to look for structural heart disease. Some practitioners obtain stress imaging (such as with adenosine or persantine nuclear perfusion scintigraphy) to exclude chronic ischemic heart disease as a cause of LBBB.

Overall LBBB is a less favorable prognostic sign than RBBB, even in the absence of abnormalities noted on history, physical examination, and noninvasive testing. However, the timing and necessity of any noninvasive testing depends on the patient's clinical situation and the acuity of the surgical need. For an urgent surgical indication in a patient without other signs and symptoms of CHF or acute myocardial ischemia, it is reasonable to proceed with surgery.

## WEBSITE



ECG Library  
<http://www.ecglibrary.com/ecghome.html>

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# PULSE OXIMETRY

*Lyle E. Kirson, DDS, and Renee Koltjes-Edwards, MD*

## 1. What is pulse oximetry?

Pulse oximetry is a noninvasive method by which arterial oxygenation can be approximated. It is based on the Beer-Lambert law and spectrophotometric analysis. When applied to pulse oximetry, the Beer-Lambert law essentially states that the intensity of transmitted light passing through a vascular bed decreases exponentially as a function of the concentration of the absorbing substances in that bed and the distance from the source of the light to the detector.

## 2. How important is pulse oximetry?

Physiologic monitors provide the anesthesiologist information that must be integrated into the overall clinical picture. Every anesthesiologist should know the limits of the various physiologic monitors, and every monitor that is used in the operating room will, under the right conditions, give false readings. Pulse oximeters are no exception, and the clinician should have a good idea as to when the readings may be spurious.

## 3. What are *transmission pulse oximetry* and *reflection pulse oximetry*?

As the names suggest, in transmission pulse oximetry light-emitting diodes (LEDs) transmit light through a vascular bed to a photodetector. In reflection pulse oximetry LEDs transmit light that is reflected back to a photodetector on the same side of the vascular bed as the LEDs. Transmission pulse oximetry is the most common form of pulse oximetry used in the operating room, although reflective pulse oximetry is becoming more popular because of the improved accuracy and ease of placement over various vascular beds. Transmission pulse oximetry is the subject of this chapter unless otherwise noted.

## 4. How does a pulse oximeter work?

A sensor is placed on either side of a pulsatile vascular bed such as the fingertip or earlobe. The LEDs on one side of the sensor send out two wavelengths of light, one red (600 to 750 nm wavelength) and one infrared (850 to 1000 nm wavelength). Most pulse oximeters use wavelengths of 660 nm (red) and 940 nm (infrared). The two wavelengths of light pass through the vascular bed to the other side of the sensor where a photodetector measures the amount of red and infrared light received.

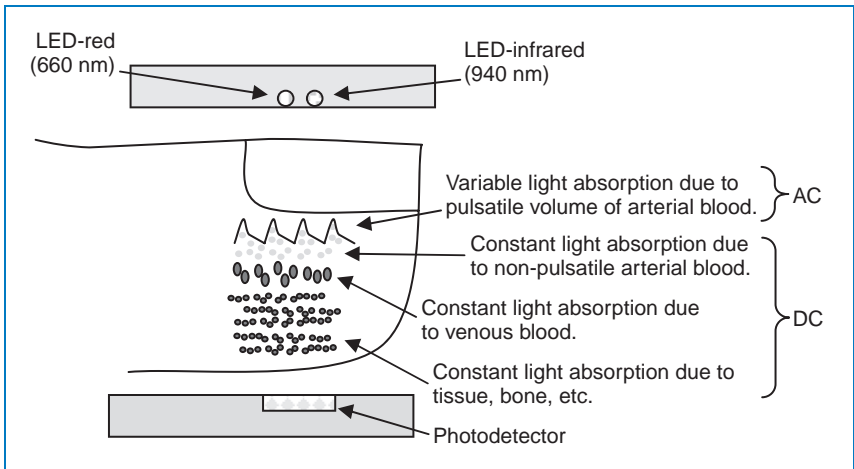
## 5. How is oxygen saturation determined from the amount of red and infrared light received and absorbed?

A certain amount of the red and infrared light is absorbed by the tissues (including blood) that are situated between the emitters and detector. Therefore not all the light emitted by the LEDs makes it to the detector. Reduced hemoglobin absorbs much more of the red light (660 nm) than does oxyhemoglobin. Oxyhemoglobin absorbs more infrared light (940 nm) than does reduced hemoglobin. The detector measures the amount of light not absorbed at each wavelength, which in turn allows the microprocessor to determine a very specific number for the amount of hemoglobin and oxyhemoglobin present.

## 6. How does the pulse oximeter determine the degree of arterial hemoglobin saturation?

In the vascular bed being monitored, the amount of blood is constantly changing because of the pulsation caused by each heart beat. Thus the light beams pass not only through a relatively stable volume of bone, soft tissue, and venous blood, but also through arterial blood, which is made up of a nonpulsatile portion and a variable, pulsatile portion. By measuring transmitted light several hundred times per second, the pulse oximeter is able to distinguish the changing, pulsatile component (AC) of the arterial blood from the unchanging, static component of the signal (DC) made up of the soft tissue, venous blood, and nonpulsatile arterial blood. The pulsatile component (AC), generally comprising 1% to 5% of the total signal, can then be isolated by canceling out the static components (DC) at each wavelength (Figure 23-1).

The photodetector relays this information to the microprocessor. The microprocessor knows how much red and infrared light was emitted, how much red and infrared light has been detected, how much signal is static, and how much signal varies with pulsation. It then sets up what is known as the red/infrared (R/IR) ratio for the pulsatile (AC) portion of the blood. The R and IR of this ratio is the total of the absorbed light at each wavelength, respectively, for only the AC portion.



**Figure 23-1.** Transmitted light passes through pulsatile arterial blood (AC) and other tissues (DC). The pulse oximeter can distinguish the AC from the DC portion by measuring transmitted light several hundred times per second.

## 7. What is the normalization procedure?

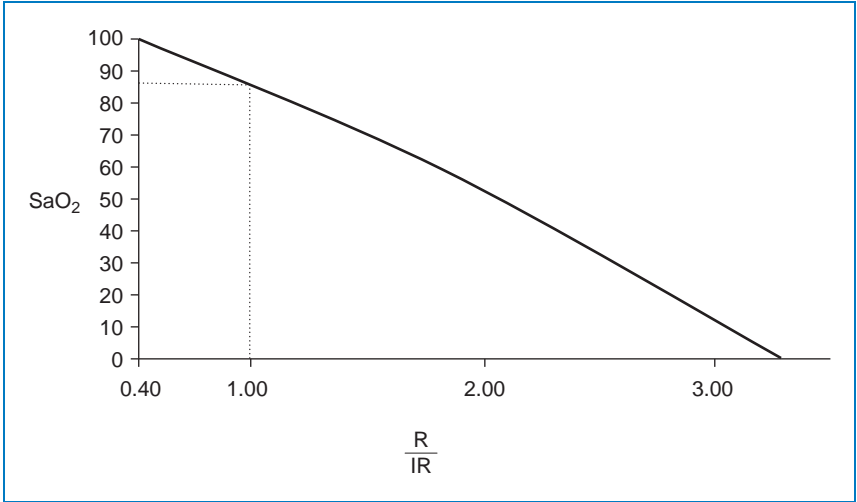
Because the transmitted light intensities depend on the sensitivity of the detector and the individual intensities of the light sources and because tissue absorption can vary a great deal between individuals, a normalization procedure is commonly used. The normalization involves dividing the pulsatile (AC) component of the red and infrared photoplethysmogram by the corresponding nonpulsatile (DC) component of the photoplethysmogram. This scaling process results in a normalized R/IR ratio, which is virtually independent of the incident light intensity.

$$R/IR \text{ ratio} = (AC_{\text{red}}/DC_{\text{red}})/(AC_{\text{ir}}/DC_{\text{ir}})$$

## 8. How does the R/IR ratio relate to the oxygen saturation?

The normalized R/IR ratio is compared to a preset algorithm that gives the microprocessor the percentage of oxygenated hemoglobin in the arterial blood (the oxygen saturation percentage),

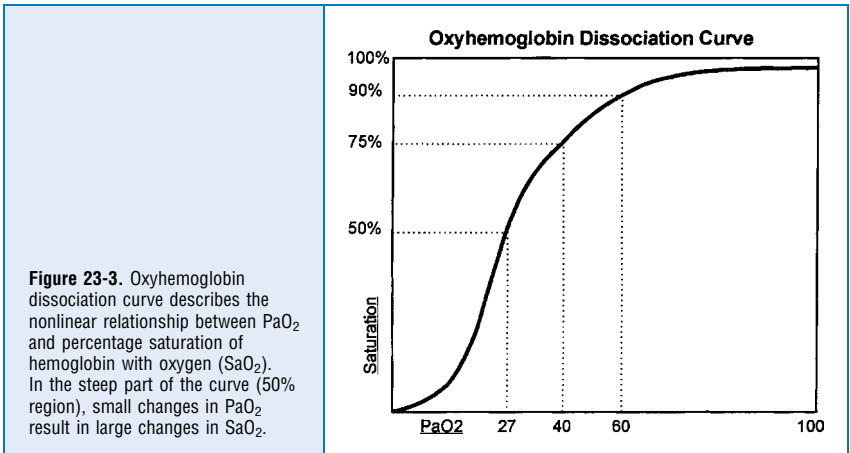
and this percentage is displayed. This algorithm is derived from volunteers, usually healthy individuals who have been desaturated to a level of 75% to 80%; their arterial blood gas is drawn, and saturation measured in a standard laboratory format. Manufacturers keep their algorithms secret, but in general an R/IR ratio of 0.4 corresponds to a saturation of 100%, an R/IR ratio of 1.0 corresponds to a saturation of about 87%, and an R/IR ratio of 3.4 corresponds to a saturation of 0% (Figure 23-2).



**Figure 23-2.** The ratio of absorbed red to infrared light corresponds to the appropriate percentage of oxygenated hemoglobin.

### 9. What is the oxyhemoglobin dissociation curve?

It is a curve that describes the relationship between oxygen tension and binding (percentage oxygen saturation of hemoglobin) (Figure 23-3). Efficient oxygen transport relies on the ability of hemoglobin to reversibly load and unload oxygen. The sigmoid shape of the curve



**Figure 23-3.** Oxyhemoglobin dissociation curve describes the nonlinear relationship between PaO<sub>2</sub> and percentage saturation of hemoglobin with oxygen (SaO<sub>2</sub>). In the steep part of the curve (50% region), small changes in PaO<sub>2</sub> result in large changes in SaO<sub>2</sub>.

facilitates unloading of oxygen in the peripheral tissues, where the  $\text{PaO}_2$  is low. At the capillary level a large amount of oxygen is released from the hemoglobin, resulting in a relatively small drop in tension. This allows an adequate gradient for diffusion of oxygen into the cells and limits the degree of hemoglobin desaturation. The curve may be shifted to the left or right by many variables (Table 23-1).

**TABLE 23-1. LEFT AND RIGHT SHIFTS OF THE OXYHEMOGLOBIN DISSOCIATION CURVE**

Right Shift	Left Shift
<p><b>Effects:</b> Decreased affinity of Hb for <math>\text{O}_2</math> (facilitates unloading of <math>\text{O}_2</math> to tissues)</p> <p><b>Causes:</b> Increased <math>\text{PCO}_2</math> Hyperthermia Acidosis Increased altitude Increased 2, 3-DPG Sickle cell anemia</p>	<p><b>Effects:</b> Increased affinity of Hb for <math>\text{O}_2</math> (decreases unloading of <math>\text{O}_2</math> from Hb)</p> <p><b>Causes:</b> Decreased <math>\text{PCO}_2</math> Hypothermia Alkalosis Fetal hemoglobin Decreased 2, 3-DPG Carboxyhemoglobin Methemoglobin</p>
<p>Hb = hemoglobin, 2, 3-DPG = 2, 3-diphosphoglycerate.</p>	

#### 10. Why might the pulse oximeter give a false reading? Part 1—not R/IR related

- The algorithm that the pulse oximeter uses to determine the saturation loses significant accuracy as saturation drops below 80% because, as mentioned, healthy volunteers have historically been used to establish these algorithms, and it would be unethical to desaturate someone below 80%. Therefore the percentage saturation below 75% to 80% is extrapolated from these data. As the saturation lowers, it becomes less accurate.
- Saturation is averaged over a time period of anywhere from 5 to 20 seconds. As a patient is desaturating, the reading on the monitor screen will be higher than the actual saturation. This becomes critical as the patient enters the steep part of the oxyhemoglobin desaturation curve because the degree of desaturation increases dramatically and may exceed the ability of the monitor to change rapidly enough to show the true level of oxygen saturation. Likewise, as a person's saturation increases, the displayed reading on the screen will be lower than the actual saturation.
- Dark pigmentation of the skin may cause overestimates of oxygen saturation.
- Response time to changes in saturation is related to probe location. Response time is less with ear probes and greater with finger probes and may increase with hypoxia and vasoconstriction.
- If the monitor is not able to detect a good pulse during a period of desaturation, it may display an artificially high saturation reading. This is so because when the pulse oximeter cannot find a good pulsation, the prior saturation reading may freeze on the screen while the monitor continues to search for a pulse. Once that patient enters the steep part of the oxyhemoglobin dissociation curve, the difference in the displayed reading and the true saturation can be significant.

- Venous congestion, particularly when caused by tricuspid regurgitation, may produce venous pulsations that are interpreted as a signal. This will result in an artificially low reading as venous blood is interpreted to be arterial blood.
- Anemia, hypotension; poor perfusion at the site of measurement; and nail polish, especially blue or black polish, also lead to false readings.

### 11. Why might the pulse oximeter give a false reading? Part 2—R/IR related.

As previously mentioned, the R/IR ratio determines the displayed saturation. Any circumstance that erroneously drives the R/IR number toward 1.0 will result in a saturation reading approaching 87%. The overwhelming majority of times, these circumstances develop in well-oxygenated patients and results in a falsely low displayed saturation. Of greater consequence, however, is when these circumstances occur in dangerous situations when the patient's oxygenation is critically low and a *falsely elevated saturation reading* results. What can affect the R/IR number?

- Optical shunting takes place when some of the light from the LED does not pass through the vascular bed before reaching the detector and is a result of poor, incomplete probe placement. The R/IR number trends toward 1.0 (87%) and results in a falsely low measurement for a patient who is actually better saturated. However, if it occurs in a patient who is difficult to ventilate and is desaturating, falsely high measurement will be displayed regardless of how hypoxic the patient becomes.
- The penumbra effect, similar to optical shunting, occurs when the probe is not positioned appropriately and the path length between each of the LEDs and the photodetector are not equal, causing a relative distortion in the absorption reading. The R/IR ratio is driven toward 1.0.
- Motion artifact causes a low signal-to-noise ratio, alters the absorption detection of both the red and infrared light by the photodetector, drives the R/IR ratio toward 1.0, and results in false saturation readings.
- If the probe does not fit well on the finger or ear, fluorescent lighting and operating room lights, because of their phased light production (which is too fast for the human eye to detect) can cause false R/IR readings. When ambient light from either of the above sources is not eliminated, it is detected in both the red and infrared range and fools the microprocessor. As this occurs, the R/IR number is driven toward 1.0 (87% saturation). To minimize false readings from outside lights, pulse oximeters work in three phases, hundreds of times per second. During the first phase a wavelength of 660 nm is emitted, during the second phase a wavelength of 940 nm is emitted, and during the third phase no wavelength is emitted. This third phase allows the photodetector to measure ambient light contamination. The microprocessor then discards the ambient light contamination from its measurements. However, this solution to the ambient light problem is not totally effective; this is why manufacturers recommend placing opaque material over the oximeter probe.
- Dyshemoglobinemias carboxyhemoglobin (COHb) and methemoglobin (MetHb) pose a problem for accurate oxygen saturation measurement. At 660 nm, COHb absorbs light, much like oxygenated hemoglobin, causing an overestimation of true saturation. The influence of methemoglobinemia on SpO<sub>2</sub> readings is more complicated. MetHb looks much like reduced Hb at 660 nm. However, more important, at 940 nm the absorbance of MetHb is markedly greater than that of either reduced or oxygenated Hb. Therefore the monitor reads it as absorption of both species, driving the R/IR number toward 1.0 and the saturation toward 87%. Therefore at a high SaO<sub>2</sub> level the probe underestimates the true value; at a low SaO<sub>2</sub> the value is falsely elevated.

### 12. The saturation plummets after injection of methylene blue. Is the patient desaturating?

Because of changes in light absorption (and alterations in the R/IR ratio), methylene blue fools the pulse oximeter into thinking that more reduced hemoglobin is present. The apparent, but false, SpO<sub>2</sub> reading returns to normal within a few minutes.

**13. Explain the difference between *functional hemoglobin* and *fractional hemoglobin saturation*.**

Functional hemoglobin saturation is the ratio of oxyhemoglobin to all the hemoglobin capable of carrying oxygen. Fractional hemoglobin saturation is the ratio of oxyhemoglobin to all hemoglobin, including dyshemoglobins (Hb + MetHb + COHb).

$$\text{Functional SaO}_2 = (\text{O}_2\text{Hb}/[\text{O}_2\text{Hb} + \text{Hb}]) \times 100\%$$

$$\text{Fractional SaO}_2 = (\text{O}_2\text{Hb}/[\text{O}_2\text{Hb} + \text{Hb} + \text{COHB} + \text{MetHb}]) \times 100\%$$

**14. Do pulse oximeters measure functional hemoglobin saturation or fractional hemoglobin saturation?**

In the past pulse oximeters measured functional hemoglobin only because there was no method for detecting the dyshemoglobinemias with operating room oximeters. This is no longer true. There are now pulse oximeters that will provide readings for COHB, MetHb, and the normal hemoglobin species. Accomplishing this requires use of four LEDs and corresponding photodetectors.

**15. Since the patient is oxygenated before anesthetic induction, if the pulse oximeter reaches 100%, does this indicate complete denitrogenation?**

Replacing all alveolar nitrogen with oxygen provides a depot of oxygen that might be necessary if mask ventilation or intubation proves difficult. Hemoglobin may be completely saturated with oxygen before total pulmonary washout of nitrogen. Thus a reading of 100% in and of itself is not an accurate indication of denitrogenation.

**16. Is the pulse oximeter a good indicator of ventilation?**

A pulse oximeter gives no indication of ventilation, only of oxygenation. For instance, in the postanesthetic care unit a patient can have an oxygen mask delivering 50% or more oxygen and an SpO<sub>2</sub> reading in the 90s, yet be hypoventilating and hypercapnic. In this situation the pulse oximeter gives a false sense of security. A better approach would be to administer less oxygen; and, as the pulse oximeter values decrease below 90, it would alert the nurse to tend to the patient. Arousing the patient from sleep, encouraging him or her to breathe deeply, and elevating the head of their bed are better strategies than just increasing the delivered oxygen concentration. Of course these interventions may not improve the situation considerably, but then the caregiver knows to pursue other reasons why the patient is not oxygenating. Always treat the cause, not the symptom; treat the patient, not the numbers.

**17. Are there complications associated with the use of pulse oximetry probes?**

Pressure necrosis of the skin has been reported in both neonates and adults when the probe has been left on the same digit for prolonged periods of time. Digital burns from the LEDs have been reported in patients undergoing photodynamic therapy.

## KEY POINTS: PULSE OXIMETRY



1. Use of pulse oximetry has allowed the anesthesiologist to rapidly detect and treat acute decreases in oxygen saturation.
2. As with all monitors, understanding its methods of operation and its limitations is critical to the delivery of safe care. Pulse oximeters can give falsely high and low numbers; understand the reasons why that is so.
3. Treat the patient, not the symptom! Oxygenation and ventilation are separate processes, and pulse oximetry does not assess adequacy of ventilation.

**WEBSITE**

<http://www.asa-abstracts.com>

**SUGGESTED READINGS**

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1. Barker S: Motion-resistant pulse oximetry: a comparison of new and old models. *Anesth Analg* 95:967–972, 2002.
2. Moyle J: *Pulse oximetry*. ed 2, London, BMJ Publishing Group, 2002.
3. Pedersen T, Moller A, Pedersen B: Pulse oximetry for perioperative monitoring: systematic review of randomized, controlled trials. *Anesth Analg* 96:426–431, 2003.



# CAPNOGRAPHY

James Duke, MD, MBA

## 1. What is the difference between capnometry and capnography? Which is better?

Capnometry is defined as the numeric measurement and display of the level of  $\text{CO}_2$ . It is not nearly as valuable as capnography, in which the expired  $\text{CO}_2$  level is graphically displayed as a function of time and concentration.

## 2. Describe the most common method of gas sampling and the associated problems.

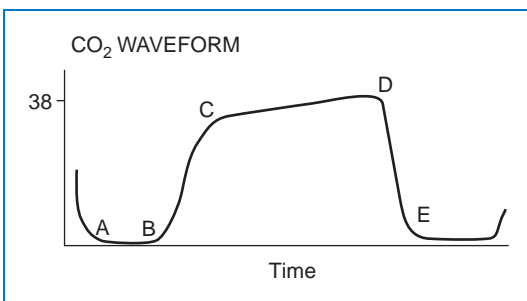
Sidestream devices aspirate gas (typically 50 to 250 ml/min), usually from the Y-piece of the circuit, and transport the gas via small-bore tubing to the analyzer. Sampling can also be performed by nasal cannulas; but, because of room air entrainment and dilution of the  $\text{CO}_2$  concentration, the Y-piece provides qualitatively and quantitatively a better sample than nasal cannulas. Problems with sidestream measurement include a finite delay until the results of the gas sample are displayed and possible clogging of the tubing with condensed water vapor or mucus. Infrared absorption is the most common method of  $\text{CO}_2$  analysis.

## 3. What is the importance of measuring $\text{CO}_2$ ?

End-tidal carbon dioxide ( $\text{ETCO}_2$ ) monitoring has been an important factor in reducing anesthesia-related mortality and morbidity. Short of bronchoscopy, carbon dioxide monitoring is considered the best method of verifying correct endotracheal tube (ETT) placement. In addition to its value as a safety monitor, evaluation of expiratory  $\text{CO}_2$  provides valuable information about important physiologic factors, including ventilation, cardiac output, and metabolic activity, and proper ventilator functioning.  $\text{ETCO}_2$  levels have also been used to predict outcome of resuscitation. A prospective observation study of 150 out-of-hospital cardiac arrests found that an  $\text{ETCO}_2$  level less than 10 mm Hg after 20 minutes of standard advanced cardiac life support was 100% predictive of failure to resuscitate.

## 4. Describe the capnographic waveform.

The important features include baseline level, the extent and rate of rise of  $\text{CO}_2$ , and the contour of the capnograph. Capnograms may be evaluated breath by breath, or trends may be assessed as valuable clues to a patient's physiologic status. There are four distinct phases to a capnogram (Figure 24-1). The first phase (A–B) is the initial stage of exhalation, in which the gas sampled is dead space gas,



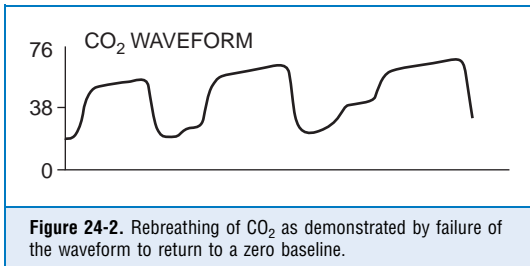
**Figure 24-1.** The capnographic waveform. A–B: Exhalation of  $\text{CO}_2$  free gas from dead space; B–C: combination of dead space and alveolar gas; C–D: exhalation of mostly alveolar gas; D: *end-tidal* point (alveolar plateau); D–E: inhalation of  $\text{CO}_2$  free gas.

free of  $\text{CO}_2$ . At point B, there is mixing of alveolar gas with dead space gas, and the  $\text{CO}_2$  level abruptly rises. The expiratory or alveolar plateau is represented by phase C–D, and the gas sampled is essentially alveolar. Point D is the maximal  $\text{CO}_2$  level, the best reflection of alveolar  $\text{CO}_2$ , and is known as  $\text{ETCO}_2$ . Fresh gas is entrained as the patient inspires (phase D–E), and the trace returns to the baseline level of  $\text{CO}_2$ , approximately zero.

### 5. What may cause elevation of the baseline of the capnogram?

The baseline of the capnogram may not return to zero at high respiratory rates. However, if the baseline is elevated more than approximately 2 mm Hg  $\text{CO}_2$ , the patient is receiving  $\text{CO}_2$  during inspiration, and this is often termed *rebreathing* (Figure 24-2). Possible causes of rebreathing include the following:

- An exhausted  $\text{CO}_2$  absorber
- Channeling of the gas within the  $\text{CO}_2$  absorber
- An incompetent unidirectional inspiratory or expiratory valve
- Accidental administration of  $\text{CO}_2$  (perhaps from a  $\text{CO}_2$  tank used for laparoscopy)
- Inadequate fresh gas flow



**Figure 24-2.** Rebreathing of  $\text{CO}_2$  as demonstrated by failure of the waveform to return to a zero baseline.

### 6. Does $\text{ETCO}_2$ correlate with $\text{PaCO}_2$ ?

$\text{CO}_2$  is easily diffusible across the endothelial-alveolar membrane; thus  $\text{ETCO}_2$  should provide an estimate of alveolar  $\text{CO}_2$  partial pressures and arterial carbon dioxide partial pressures ( $\text{PaCO}_2$ ). Alveolar carbon dioxide partial pressures and  $\text{PaCO}_2$  normally differ by about 5 mm Hg, the small difference caused mostly by alveolar dead space (nonperfused areas of the lung that are ventilated.)

As maldistribution between ventilation and perfusion increases, the correlation between  $\text{ETCO}_2$  and  $\text{PaCO}_2$  decreases, with  $\text{ETCO}_2$  being lower. Increased dead space results in an increased gradient and may be associated with shock, air embolism or thromboembolism, cardiac arrest, chronic lung disease, reactive airway disease, or lateral decubitus positioning. Conversely, increases in cardiac output and pulmonary blood flow will decrease the gradient.

When increases in dead space ventilation are suspected, the gradient between  $\text{ETCO}_2$  and  $\text{PaCO}_2$  can be determined by arterial blood gas analysis. With the gradient factored in, tracking of  $\text{ETCO}_2$  is still a useful, indirect measure of arterial  $\text{CO}_2$  content. Of note, shunt has minimal effect on arterial-alveolar  $\text{CO}_2$  gradients.

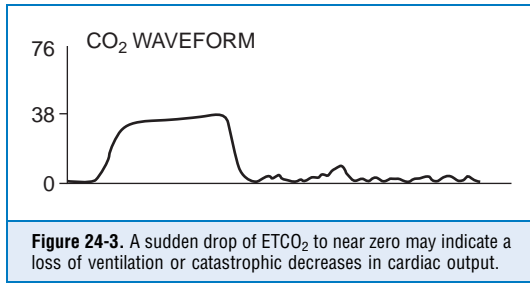
### 7. Is it possible to see exhaled $\text{CO}_2$ after accidental intubation of the esophagus?

Carbonated beverages or medications (e.g., Alka-Seltzer) return  $\text{CO}_2$  after esophageal intubation. However, the usual  $\text{CO}_2$  values and waveform would not be expected, and the  $\text{CO}_2$  would likely exhaust quickly. Some  $\text{CO}_2$  can also reach the stomach if mask ventilation is suboptimal.

### 8. What might result in sudden loss of capnographic waveform?

A sudden loss of capnographic waveform (Figure 24-3) may be caused by the following:

- Esophageal intubation
- Ventilator disconnection or malfunction
- Capnographic disconnection or malfunction
- Obstructed ETT
- Catastrophic physiologic disturbance such as cardiac arrest or massive pulmonary embolus



## KEY POINTS: CAPNOGRAPHY



1. Short of visualizing with bronchoscopy,  $\text{CO}_2$  detection is the best method of verifying ETT location.
2. In the absence of ventilation-perfusion abnormalities,  $\text{ETCO}_2$  roughly approximates  $\text{PaCO}_2$ .
3. Analysis of the capnographic waveform provides supportive evidence for numerous clinical conditions, including decreasing cardiac output; altered metabolic activity; acute and chronic pulmonary disease; and ventilator, circuit, and endotracheal tube malfunction.

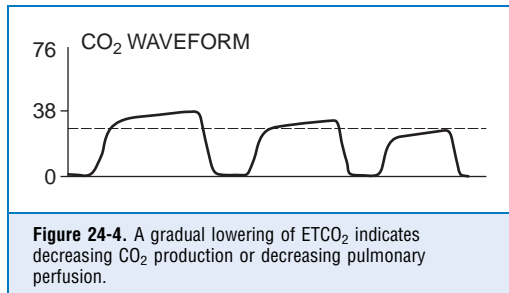
### 9. What process might lead to decreases in $\text{ETCO}_2$ ?

Rapid decreases in  $\text{CO}_2$  waveforms may be associated with the following:

- Hypotension
- Hypovolemia
- Decreased cardiac output
- Lesser degrees of pulmonary embolism
- Dislodgement of a correctly placed ETT

Other, and usually less dramatic, decreases in  $\text{ETCO}_2$  may be caused by the following:

- Incomplete exhaled gas sampling
- Airway leaks (including endotracheal cuff leaks)
- Partial circuit disconnections
- Partial airway obstruction
- Hyperventilation
- Hypothermia
- Increasing dead space
- Decreased metabolic activity (e.g., after neuromuscular blockade) (Figure 24-4)



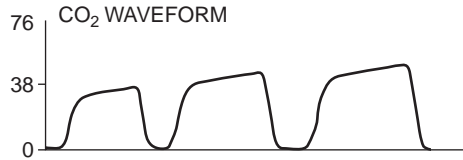
### 10. What processes may increase $\text{ETCO}_2$ ?

$\text{ETCO}_2$  values may rise gradually secondary to the following (Figure 24-5):

- Hypoventilation
- Increasing body temperature
- Increased metabolic activity (e.g., fever, sepsis, malignant hyperthermia)

- Partial airway obstruction
- Bronchial intubation
- Rebreathing
- Exogenous CO<sub>2</sub> absorption (such as during laparoscopy) and venous CO<sub>2</sub> embolism
- Exhausted CO<sub>2</sub> absorber
- Inadequate fresh gas flow
- Faulty ventilator or anesthesia circuit valves
- Transient increases in

ETCO<sub>2</sub> (may be noted after intravenous bicarbonate administration, release of extremity tourniquets, or removal of vascular cross-clamps)



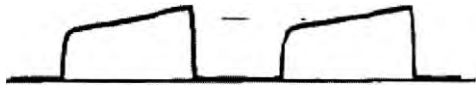
**Figure 24-5.** A rising ETCO<sub>2</sub> is associated with hypoventilation, increasing CO<sub>2</sub> production, and absorption of CO<sub>2</sub> from an exogenous source such as CO<sub>2</sub> laparoscopy.

### 11. What processes can change the usual configuration of the waveform?

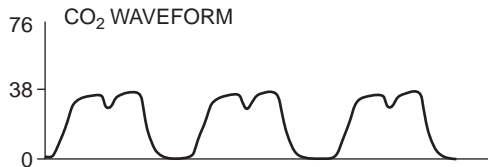
Asthma and chronic obstructive pulmonary diseases cause a delayed upslope and steep alveolar plateau (Figure 24-6).

A commonly seen abnormal capnogram results when the patient makes spontaneous respiratory efforts and inhales before the next mechanical inspiration. This characteristic *cleft* in the alveolar plateau is a useful clinical sign indicating that the patient has started to breathe (Figure 24-7). Finally, a cuff leak may result in variable early decreases in the normal waveform configuration (Figure 24-8). Waveforms that are irregular and unlike neighboring waveforms may be caused by manipulation against the diaphragm by the surgeons, pressure of a surgeon against the chest wall, percussing against an abdomen distended by CO<sub>2</sub>, or spontaneous breathing out of phase with mechanical ventilation.

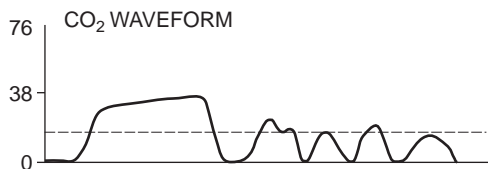
**Figure 24-6.** A steep slope suggests obstructive lung disease.



**Figure 24-7.** A cleft in the alveolar plateau usually indicates partial recovery from neuromuscular blockade. Surgical manipulation against the inferior surface of the diaphragm or weight on the chest may produce similar though usually other irregular waveforms as seen in Figure 24-8.



**Figure 24-8.** A sudden drop of ETCO<sub>2</sub> to a low but nonzero value is seen with incomplete sampling of patient exhalation, system leaks, or partial airway obstruction.



## WEBSITE



Capnography

[www.capnography.com](http://www.capnography.com) (Excellent and interactive)

## SUGGESTED READING

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1. Moon RE, Camporesi EM: Respiratory monitoring. In Miller RD, editor: *Miller's anesthesia*, ed 6, Philadelphia, Elsevier Churchill Livingstone, 2005, pp 1437–1482.

# CENTRAL VENOUS CATHETERIZATION AND PRESSURE MONITORING

Lyle E. Kirson, DDS, and Jacob Friedman, MD

## 1. Define central venous catheterization.

Central venous catheterization involves inserting a catheter into the venous circulation and advancing it so its distal orifice is positioned immediately adjacent to or within the right atrium of the heart (Figure 25-1).

## 2. What are the perioperative indications for placement of a central venous catheter?

- Guiding fluid replacement
- Evaluating cardiac function
- Providing access for the following:
  - Aspiration of air emboli that can occur during neurosurgical procedures
  - Drug infusion
  - Blood and fluid infusion
  - Introducing a pulmonary artery catheter or transvenous pacemaker
  - Blood sampling

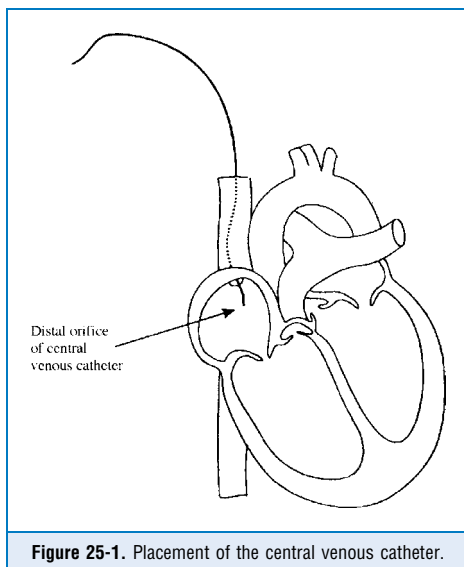


Figure 25-1. Placement of the central venous catheter.

## 3. What are the nonoperative indications for placement of a central venous catheter?

- Hyperlimentation
- Temporary hemodialysis
- Long-term chemotherapy
- Frequent therapeutic plasmapheresis

## 4. What is the best approach to central venous cannulation?

Numerous access points are available for introduction of a catheter into the venous circulation. All approaches carry risks, and none will work successfully for every patient. Therefore it is important to become familiar with several approaches: subclavian vein, internal jugular vein, antecubital external jugular vein, and femoral vein. It is also of interest that peripheral venous pressure when measured at the antecubital vein closely mirrors the central venous pressure (CVP).

## 5. Describe the subclavian vein approach.

The subclavian approach is commonly used because of the ease of access to the vessel. The subclavian vein is best cannulated from the subclavicular approach with the patient in the

Trendelenburg position. The skin puncture is made just lateral to, and one fingerbreadth below, the costoclavicular ligament, which can be identified by a notch two thirds of the length down the clavicle. The needle is directed along the posterior border of the clavicle in the direction of the sternal notch until venous blood is aspirated.

#### 6. Describe the internal jugular vein approach.

There are several approaches to the internal jugular vein, three of which are briefly described here. The patient is put in the Trendelenburg position.

- **Low anterior:** Locate the point at which the sternal and clavicular heads of the sternocleidomastoid muscle join. Introduce the needle at this point and direct it at a 30-degree angle to the skin. Advance the needle toward the ipsilateral nipple until venous blood is aspirated.
- **High anterior:** Palpate the carotid artery at the level of the cricothyroid membrane. Introduce the needle just lateral to the carotid pulsation and advance it toward the ipsilateral nipple at a 30-degree angle until venous blood is aspirated. This approach frequently requires penetration of the sternocleidomastoid muscle by the introducer needle.
- **Posterior:** Locate the junction of the posterior border of the sternocleidomastoid muscle and the external jugular vein. Introduce the needle just posterior to this point and advance it along the deep surface of the muscle toward the ipsilateral corner of the sternal notch until venous blood is aspirated.

#### 7. Describe the external jugular vein approach.

When the patient is in a Trendelenburg position, the external jugular vein frequently can be visualized where it crosses the sternocleidomastoid muscle. The needle is advanced in a direction paralleling the vessel and is introduced into the vein approximately two finger widths below the inferior border of the mandible. Difficulty may arise in advancing the catheter or guidewire into the central circulation from the external jugular vein approach because the patient's anatomy frequently directs the catheter into the subclavian rather than the innominate vein. It is also frequently difficult to pass the guidewire or catheter past the clavicle.

#### 8. When is the femoral vein approach used?

The femoral vein is not a preferred approach because of the high risk of infection. Femoral venous cannulation may be undertaken when subclavian or internal jugular catheterization is unsuccessful. Femoral lines should be removed as soon as it is practical.

#### 9. Review the different types of central venous catheters.

Single-lumen catheters may have single distal port or multiport tips. Triple-lumen catheters have three channels and lumens at slightly different positions on the distal cannula, providing ports for simultaneous drug infusion, blood drawing, and CVP monitoring. They are available in 7.5- and 9-Fr sizes. A percutaneous introducer sheath is designed for insertion of a pulmonary artery catheter into the central circulation. It is a large-bore catheter (9 Fr) and has a side port that can be used for CVP monitoring or for fluid infusion. Some catheters are heparin coated.

#### 10. How is a catheter introduced into the central venous circulation?

Before cannulation is attempted, Trendelenburg positioning will increase venous pressure at the target vessel. As the needle is advanced toward a vessel, slight and constant aspiration is required. Occasionally during needle advancement the vessel walls will collapse on themselves so the needle passes through the entire vessel and blood can be aspirated by slowly withdrawing the needle, all the while gently aspirating. Finally, thorough knowledge of adjacent vital structures is important to avoid unwarranted complications.

Although a catheter can be inserted through a large-bore needle, the most common technique involves passing it over a guidewire, commonly referred to as the Seldinger technique. An 18- or 20-G needle is introduced into the vessel, and a guidewire is threaded through the needle and into

the vein. The needle is removed, leaving the guidewire in place. The catheter is then passed over the guidewire and into the vessel. Finally the guidewire is removed. The obvious benefit of the Seldinger technique rests in the use of a smaller-gauge introducer needle.

**11. In attempting a central venous puncture, dark blood returns. Does this satisfy you that you are indeed within a vein?**

Arterial blood may be dark because the patient is cyanotic, cardiac output is inadequate, or the patient may have methemoglobinemia, for example. The flow of blood also may be nonpulsatile in cardiac failure. The best way to determine whether you are indeed in a vein is to thread a short, small-gauge catheter (e.g., 18- or 20-G) over the wire, remove the wire, and transduce the small catheter.

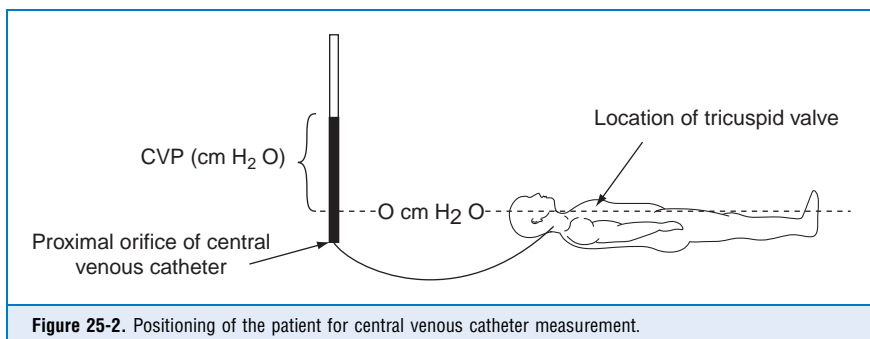
**12. How is central venous pressure measured?**

The central venous catheter is attached to a fluid-filled manometer or electronic pressure transducer. The pressure at the distal orifice is transmitted through the fluid path within the catheter and, if a manometer is used, supports the fluid column within the manometer. If the base of the fluid column is placed at the level of the right atrium, the height of the fluid column represents the pressure (in centimeters of  $H_2O$ ) at the distal orifice of the catheter, the CVP. More commonly the catheter is attached to a pressure transducer that converts the pressure transmitted via the catheter into an electrical signal that is displayed (in millimeters of mercury) on a real-time display screen ( $1 \text{ mm Hg} = 1.3 \text{ cm of } H_2O$ ). When measuring CVP, it is crucial to place the pressure transducer or base of the manometer at the same (atrial) level each time because a variance of only a few centimeters from that level will result in a significant measurement error since the range of CVP is only 0 to 13 cm of  $H_2O$ . In contrast, variation in the transducer position during arterial pressure measurement will result in a much smaller error since the range of arterial pressures is 0 to 200 mm Hg, and an error in transducer positioning for pulmonary artery pressure measurement would fall somewhere in between.

**13. At what point on the body should central venous pressure be measured?**

The ideal point at which to measure CVP is at the level of the tricuspid valve. It is at this point that in the healthy heart hydrostatic pressures caused by changes in body position are almost zero. This phenomenon exists because, as the pressure at the tricuspid valve changes (e.g., if it increases from position change), the right ventricle will fill to a greater degree, right ventricular output will transiently increase, and the change in pressure at the tricuspid valve will be brought back toward zero. The opposite will occur if pressure at the tricuspid valve decreases.

An external landmark for the tricuspid is a point 2 inches behind the sternum, roughly the anterior axillary line, at the fourth intercostal space. Ongoing adjustment is necessary to ensure that the transducer or manometer is consistently at this level whenever the patient's position or bed height is changed (Figure 25-2).



**Figure 25-2.** Positioning of the patient for central venous catheter measurement.



#### 14. Where should the distal orifice of the catheter be positioned?

When pressure measurements guide fluid management, the tip of the catheter can be positioned within either the atrium or the vena cava near the caval-atrial junction.

For monitoring the waveform of the CVP tracing, position the catheter within the atrium. By so positioning, the waveform will not be damped and will accurately reflect the pressure changes within the right atrium.

Placement of the catheter for aspiration of air emboli during neurosurgical cases requires positioning of the catheter (preferably multiport) tip in the right atrium near the superior vena cava-atrial junction. Embolized air flows past this point and accumulates in the superior aspect of the atrium. Positioning the catheter tip at the superior vena cava-atrial junction allows for optimal aspiration.

#### 15. How can you judge the correct positioning of the distal orifice of the catheter?

- Before insertion, measure the distance from the point of insertion to the right atrium (external landmark—immediately to the right of the third costal cartilage), giving a rough estimate of the length of inserted catheter necessary.
- Advancing the catheter under fluoroscopy is the most accurate method for positioning the catheter tip but is time consuming and cumbersome.
- With a specialized central venous catheter, the tip can be used as an electrocardiogram (ECG) electrode. After insertion the catheter is filled with electrolyte solution (normal saline or 8.4%  $\text{NaHCO}_3$ ), and the V lead of the ECG is attached to a proximal connection. The catheter is advanced toward the right atrium. The P-wave axis and voltage on the V lead tracing indicates the catheter tip position. As the catheter tip passes the area of the sinoatrial node, the P wave becomes equal in height to the R wave of the ECG. The catheter tip passing the mid-atrial position is demonstrated by a decreasing or biphasic P wave. Low atrial positioning is indicated by an inverted P wave or absence of the P wave.

#### 16. Describe the normal central venous pressure waveform and relate its pattern to the cardiac cycle.

The normal CVP waveform shows a pattern of three upstrokes and two descents that correspond to certain events in the cardiac cycle (Figure 25-3).

- The a wave represents the increase in atrial pressure that occurs during atrial contraction.
- The x' descent is the decrease in atrial pressure as the atrium begins to relax.
- Before total relaxation is completed, the c wave occurs, which is caused by the bulging of the tricuspid valve into the atrium during the early phases of right ventricular contraction.

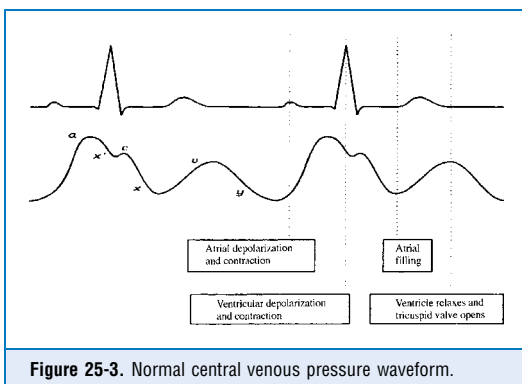


Figure 25-3. Normal central venous pressure waveform.

- The x descent follows the c wave and is a continuation of the x' descent. The x descent is caused by a drop in pressure brought about by a downward movement of the ventricle and tricuspid valve during the later stages of ventricular contraction.
- The v wave represents the increase in atrial pressure that occurs while the atrium fills against a closed tricuspid valve.
- The y descent represents a drop in pressure as the ventricle relaxes, the tricuspid valve opens (because atrial pressure is higher than ventricular pressure at this point in time), and blood passively enters the ventricle.

#### 17. What influences central venous pressure?

CVP is directly related to returning blood volume, venomotor tone, and intrathoracic pressure and inversely related to cardiac function. The following perioperative events may change these variables:

- Anesthetic-induced vasodilation and cardiac depression
- Hypovolemia, hemorrhage, and rapid fluid replacement
- Positive-pressure ventilation and positive end-expiratory pressure
- Increased abdominal pressure (pneumoperitoneum)
- Sympathetic activation caused by agonist drugs and surgical stress
- Intraoperative ischemia may cause diastolic dysfunction or heart failure

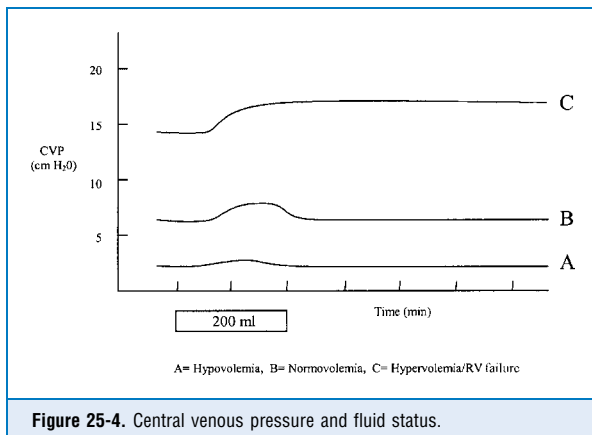
#### 18. Is central venous pressure an indicator of cardiac output?

Cardiac output is primarily a function of venous return (in the absence of frank heart failure), along with modulation by heart rate, cardiac contractility, and peripheral vascular resistance. Since CVP does not solely reflect intravascular volume, it must be considered within the clinical context to be valuable. For instance, although a rising CVP suggests an increased intravascular volume and improved venous return to the thorax, CVP will also increase in conditions such as right heart failure, cardiac tamponade, tension pneumothorax, pulmonary embolism, and increasing intra-abdominal pressure. These events are associated with decreasing cardiac output.

#### 19. How does central venous pressure relate to right ventricular preload?

CVP has long been thought to reflect right ventricular preload or more specifically right ventricular end-diastolic volume. End-diastolic volume is a key parameter in the Frank-Starling *law of the heart*. Recently it has been shown that CVP does not necessarily correlate with ventricular volume, cardiac performance, or the response of the heart to volume infusions in both normal and compromised patients. The likely reason for this is a large spread and nonlinearity in diastolic ventricular compliances among individuals and incomplete knowledge of *transmural* pressures.

Despite the previous findings, it is widely held that CVP measurement is useful to the clinician as a guide to intravenous fluid replacement, especially at the upper and lower range of CVP. Thus a low (0 to 2 mm Hg) or decreasing CVP may indicate a need for fluid administration, whereas an increasing or elevated CVP (above 12 mm Hg) may indicate overresuscitation or a patient with impaired cardiac performance. The response of CVP to a fluid bolus has also been shown to be useful in assessing fluid status. In [Figure 25-4](#) it can be seen that a 200-ml fluid bolus in the hypovolemic patient will result in a small but transient increase in CVP, whereas the same bolus in the normovolemic patient will result in a larger but still transient increase. However, in the hypervolemic patient with right ventricular failure, the same bolus results in a sustained increase in CVP. The CVP is best used to monitor a trend; an isolated determination is of limited value.



**Figure 25-4.** Central venous pressure and fluid status.

## KEY POINTS: CENTRAL VENOUS CATHETERIZATION AND PRESSURE MONITORING



1. Trends in CVPs are more valuable than isolated values and should always be evaluated in the context of the patient's scenario.
2. At best, CVP gives an estimate of cardiac preload, and there are many variables that influence its numeric value and interpretation.
3. Since complications of central venous catheterization are serious and include pneumothorax, arterial injury, hemothorax, thoracic duct laceration, catheter and air embolus, thromboembolism, and infection and since information obtained is supportive rather than definitive, this procedure should not be performed casually.
4. The CVP provides limited information about left heart function.

### 20. Does central venous pressure relate to left ventricular preload?

CVP possibly reflects right ventricular preload only. In patients whose left and right ventricles are functioning normally, CVP often parallels the left atrial pressure, which may reflect the *preload* of the left ventricle. However, in patients with pulmonary hypertension, lung disease, or right or left ventricular function abnormality, a pulmonary artery catheter provides better information with regard to the left side of the heart than does a central venous catheter.

### 21. Is there a single normal central venous pressure reading?

No single CVP is normal for all patients. Resting CVP may range from 0 to 10 mm Hg in different individuals and varies little over time. The reason for this spread is not clear, although it is not necessarily related to blood volume. In the operating room there are frequent perturbations that can impact the CVP, and the correct interpretation of a changing CVP is often not obvious. Because of this it becomes important to use all available clinical signs, including fluid resuscitation, urine output, blood pressure, and effects of anesthetic agents to determine an appropriate range of CVP for that patient.

## 22. Are there noninvasive alternatives to central venous pressure that better indicate volume status?

In recent years as it has become clear that CVP does not reliably correlate with preload and may be a useful indicator of the hemodynamic state only at the extremes, the more dynamic concept of *fluid responsiveness* has emerged for optimizing fluid therapy. Various techniques have been used to measure fluid responsiveness. For example, respiratory variation in systolic pressure during positive-pressure ventilation will decrease as volume is infused in a hypovolemic patient, or an esophageal Doppler can be used to measure increased descending aortic flow velocity (which mirrors cardiac output) as fluid is infused.

## 23. How can an abnormal central venous pressure waveform be used to diagnose abnormal cardiac events?

It may be used to assist in diagnosis of pathophysiologic events affecting right heart function. For example, atrial fibrillation is characterized by absence of the normal a wave component. Tricuspid regurgitation results in a *giant V wave* that replaces the normal c, x, and v waves. Other events that can change the normal shape of the CVP waveform include junctional rhythm with *cannon A waves*, atrioventricular dissociation, asynchronous atrial contraction during ventricular pacing, tricuspid stenosis, cardiac tamponade, increased ventricular afterload (from pulmonary hypertension or pulmonary embolus), and right ventricular ischemia and failure.

## 24. Can you use the central venous catheter for blood transfusions?

It depends on catheter size. For instance, 7-Fr triple-lumen catheters have narrow lumens, long lengths, and high resistance to flow, restricting the rate of blood administration and creating increased shear force on blood cells that can damage them. Nine French triple-lumen catheters have larger lumens and shorter lengths and are satisfactory for blood administration. Percutaneous introducer sheath used for pulmonary artery catheterization are short and have 9-Fr lumens and are excellent for blood administration. Always warm blood administered through central access to prevent hypothermia and arrhythmias.

## 25. Describe complications associated with placement of the central venous catheter.

- Considering the proximity of the carotid artery to the internal jugular vein, it is not surprising that carotid artery puncture is one of the more common complications associated with all internal jugular vein approaches.
- Pneumothorax may occur and is more commonly associated with a subclavian, low anterior (internal jugular), or junctional approach (junction of the internal jugular vein and subclavian vein).
- Hemothorax is associated primarily with the subclavian vein approach and occurs secondary to subclavian artery puncture or laceration.
- The thoracic duct, as it wraps around the left internal jugular vein, can reach as high as 3 or 4 cm above the sternal end of the clavicle. This places the duct in a vulnerable position for puncture or laceration when a left internal jugular venipuncture is attempted.
- Shearing and embolization of a catheter tip may occur when a catheter is withdrawn through a needle. Likewise a Seldinger guidewire can be sheared and embolized if attempts are made to withdraw it through an introducer needle. Therefore, if a catheter or wire cannot be advanced through an introducer needle, remove the parts in unison.
- Air embolism is a risk, and to avoid this problem the patient should be positioned head down (if entry is at a point superior to the heart) until the catheter is inserted and the hub of the catheter is occluded.
- Late complications include infection, vascular damage, hematoma formation, clot formation, dysrhythmia, and extravascular catheter migration.

**26. Are any special precautions needed when removing a central venous catheter?**

Before a subclavian or internal jugular catheter is removed, the patient should be placed in a head-down position to increase venous pressure at the point of removal and thereby prevent air aspiration into the vein. Following removal of the catheter, external pressure should be maintained on the area from which the catheter is withdrawn until clot formation has sealed the vessel.

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# PULMONARY ARTERY CATHETERIZATION

James Duke, MD, MBA

## 1. What pressures are measured by pulmonary artery catheters?

Pulmonary artery (PA) catheters are balloon-tipped catheters with multiple orifices. After the catheter is attached to a transducer system and the balloon is inflated, the flow-directed catheter tip passes through the right-sided chambers of the heart into the pulmonary artery. The PA catheter continuously measures right atrial pressure (or central venous pressure [CVP]) and pulmonary artery pressures. Although in the pulmonary artery, this balloon can be intermittently inflated and wedged into a segment of the pulmonary artery; and the pulmonary artery occlusion pressure (PAOP), commonly referred to as the *wedge* pressure, is measured.

## 2. What are normal values for central venous, pulmonary artery, and pulmonary artery occlusion pressures?

Normal values are listed below. Slight discrepancies are found among different references.

■ CVP	2 to 6 mm Hg
■ PA systolic	20 to 30 mm Hg
■ PA diastolic	5 to 15 mm Hg
■ PAOP	8 to 12 mm Hg

## 3. What other hemodynamic variables can be measured or calculated from the pulmonary artery catheter? What are their normal values?

Most PA catheters can also measure cardiac output and mixed venous oxygen saturation (SvO<sub>2</sub>). Other variables such as heart rate, systemic blood pressure, and body mass index may be needed to derive additional hemodynamic indices such as those in the following list:

■ SvO <sub>2</sub>	60% to 75%
■ Cardiac output	4 to 8 L/min
■ Cardiac index	2.5 to 4 L/min/m <sup>2</sup>
■ Stroke volume	50 to 100 ml
■ Stroke index	25 to 45 ml/m <sup>2</sup>
■ Systemic vascular resistance	900 to 1300 dyn/sec cm <sup>-5</sup>
■ Pulmonary vascular resistance	100 to 300 dyn/sec cm <sup>-5</sup>

## 4. In what surgical procedures are pulmonary artery catheters most likely to be placed? What medical problems might influence a clinician's likelihood to insert a pulmonary artery catheter before surgery?

PA catheters are useful in patients undergoing cardiac surgery (valves, coronary arteries, heart and lung transplantation), liver transplantation, and vascular surgery and in high-risk patients having extensive operative procedures with high likelihood of substantial blood loss and fluid shifts. High-risk patients include those with valvular or ischemic heart disease, compromised ventricular function or pulmonary hypertension, or significant deterioration in

other organ function (e.g., liver and kidney). In addition, patients who are hemodynamically unstable (e.g., shock or sepsis) or who have extreme ventilatory requirements (e.g., acute lung injury) are often catheterized to guide therapy.

### 5. Do pulmonary artery catheters improve patient outcomes?

PA catheters entered regular clinical use in the 1970s and still enjoy widespread use (estimated at more than 1.2 million insertions per year). However, only in the past decade have clinicians investigated in a rigorous fashion their clinical efficacy. The strength of evidence demonstrating a benefit has not been substantial overall, and there was some evidence demonstrating that PA catheters were in fact detrimental. At this time well-designed studies do not demonstrate a benefit in all groups. Certainly the issue continues to be examined and debated. Trials are ongoing in many patient subsets such as sepsis, acute lung injury, and congestive heart failure; such well-designed studies will continue to refine our knowledge of the risks and benefits of PA catheters. Finally it is important to note that the data obtained from PA catheterization must guide therapies of proven benefit.

### 6. What complications are associated with pulmonary artery catheterization?

There are the standard risks associated with central line placement, including infection, pneumothorax, hemothorax, carotid or subclavian artery injury, and nerve injury. Concerning the PA catheter itself, patients with complete left bundle-branch block may develop right bundle-branch block as the catheter passes through the right ventricle, resulting in complete heart block. This may be a transient event or require pacing. Other noted arrhythmias include both supraventricular and ventricular tachyarrhythmias and atrial fibrillation. Other complications include knotting, pulmonary hemorrhage and infarction, thromboembolism and air embolism, bacteremia, endocarditis, and sepsis. Air embolism is especially problematic if the patient has a right-to-left intracardiac shunt. To avoid balloon rupture, slowly inflate the balloon using the minimum pressure necessary to acquire the PAOP waveform and allowing the balloon to passively deflate. Finally and not inconsiderably, a complication of PA catheterization is misinterpreting the data.

### 7. Summarize the usual presentation, major risk factors, and management of pulmonary artery rupture.

Pulmonary artery rupture usually manifests as rapid hypotension with hemoptysis. Major risk factors for pulmonary artery rupture include pulmonary hypertension; cardiopulmonary bypass; hypothermia; and aggressive or excessively prolonged balloon inflation, tip migration, and catheter manipulation. Management includes fluid resuscitation, leaving the PA catheter in place, placing a double-lumen endotracheal tube to isolate the affected lung, reversing anticoagulation if any, and preparing the patient for thoracotomy and possible lobectomy or pneumonectomy. Positive end-expiratory pressure (PEEP) has also been found to be useful to control hemorrhage.

Strategies to decrease the risk of pulmonary hemorrhage include not advancing the PA catheter beyond 55 cm and reviewing a chest radiograph after catheter placement—the catheter should not be noted beyond the lateral mediastinal border. Of course, the balloon should only be inflated during measurements of occlusion pressure and then deflated. Some centers withdraw the catheter slightly between occlusion pressure measurements.

### 8. How might kinking of the pulmonary artery catheter be avoided?

Pay close attention to the depth of catheter insertion. The distance from the access site to the right ventricle (RV) is 35 cm when either the right internal jugular or subclavian veins are accessed and 45 cm if the left internal jugular or subclavian veins are accessed. The PA tracing should be noted within 15 cm of the RV tracing. PA catheters may be difficult to float when pulmonary hypertension, right ventricular distention, or tricuspid regurgitation is present.

## KEY POINTS: PULMONARY ARTERY CATHETERIZATION



1. Pulmonary catheterization has not been shown to improve outcome in all patient subsets. Identifying patients that benefit from such treatment continues to be investigated in rigorous scientific fashion.
2. Evaluate the following issues when considering PA catheterization:
  - The risks of central venous catheterization and PA insertion are many and serious, and the benefits should be identified before these procedures to justify their use.
  - What are the indications for PA catheter insertion? Consider their use early rather than late and remove them when their usefulness in directing therapy diminishes.
  - Ensure that the data obtained from the PA catheter are accurate and interpreted correctly.
  - Based on the data, what are the therapeutic goals and how will they be achieved?
3. To improve accuracy in interpretation, always consider the timing of the waveforms with the ECG cycle.

### 9. What is the phlebostatic axis?

Reliable and reproducible measurements of intravascular pressures require a fixed reference point. The level of the right heart, located 5 cm below the angle of Lewis (the sternomanubrial angle), is the commonly accepted reference point and is called the *phlebostatic axis*.

### 10. Describe the features of the central venous waveform.

See Chapter 25, Question 16 (CVP).

### 11. Describe the features of the right ventricle waveform.

The right ventricle waveform has a rapid upstroke to peak systole, a rapid downstroke, and a small terminal rise at the end of diastole. The peak systolic pressure is found after the QRS complex but before the peak of the T wave. End diastole is found near the end of the QRS complex (Figure 26-1).

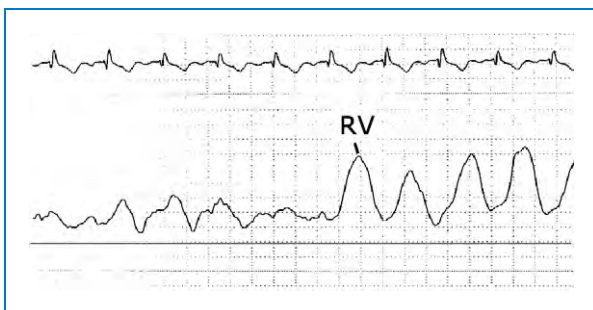
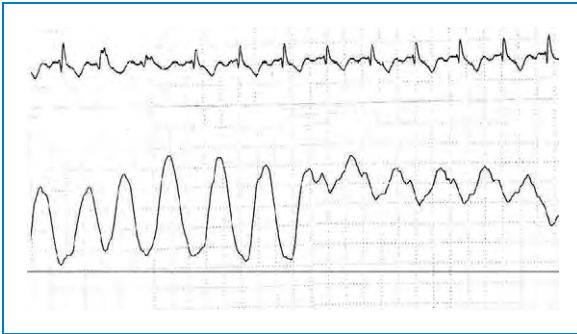


Figure 26-1. Right ventricle (RV) waveform.

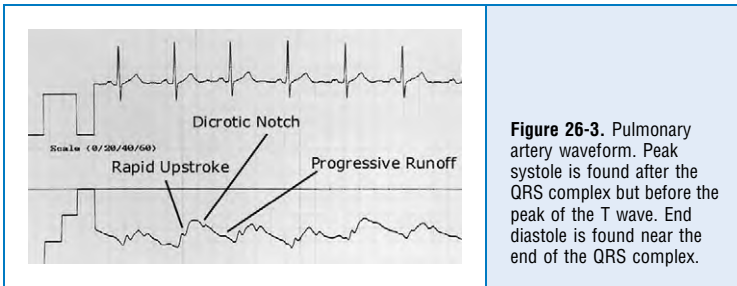
### 12. Describe the pulmonary artery waveform.

Perhaps the most noticeable change as the catheter tip enters the PA is the upstroke in diastolic pressure (Figure 26-2). Other features include a rapid upstroke, a progressive diastolic runoff, and a dicrotic notch secondary to pulmonic valve closure (Figure 26-3). Peak systole is found after the QRS complex but before the peak of the T wave. End diastole is found near the end of the QRS complex.





**Figure 26-2.** Diastolic pressure increases as the pulmonary artery (PA) catheter tip crosses from the right ventricle to the PA.



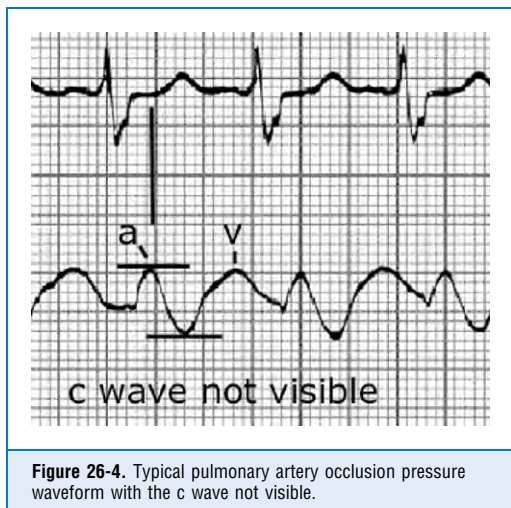
**Figure 26-3.** Pulmonary artery waveform. Peak systole is found after the QRS complex but before the peak of the T wave. End diastole is found near the end of the QRS complex.

### 13. Review the pulmonary artery occlusion pressure waveform.

Like the CVP waveform, the PAOP has three positive waves (a, c, and v). Typically the a wave is most prominent, and the c wave is nonvisible. The a wave occurs with left atrial contraction, the c wave with mitral valve closure, and the v wave with left atrial filling. Note that the v wave occurs after the T wave of the electrocardiogram (ECG). The a wave is averaged to determine the PAOP (Figure 26-4).

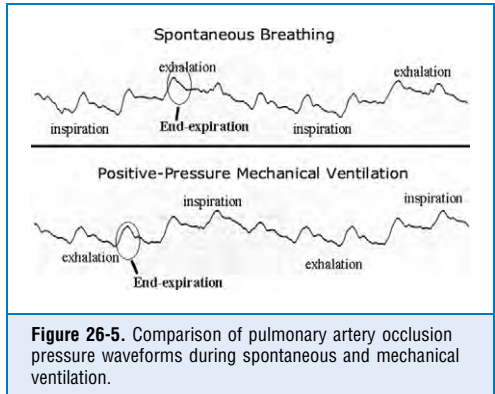
### 14. Contrast spontaneous breathing and positive-pressure mechanical ventilation and their effect on pulmonary artery occlusion pressure waveforms.

The measurement desired is a transmural pressure (i.e., the difference between the chamber undergoing measurement and pleural pressure). As pleural



**Figure 26-4.** Typical pulmonary artery occlusion pressure waveform with the c wave not visible.

pressures are not measured in clinical practice, the next best thing is to measure the pressure when intrathoracic pressure is least. Intrathoracic pressures are least at end-expiration while breathing spontaneously (Figure 26-5). PEEP and active expiration confound interpretation of the PAOP.

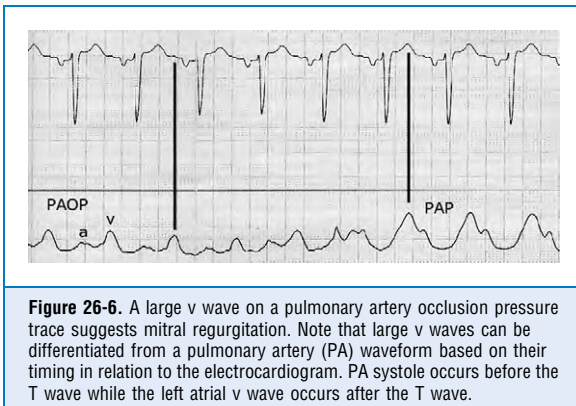


**Figure 26-5.** Comparison of pulmonary artery occlusion pressure waveforms during spontaneous and mechanical ventilation.

**15. Pulmonary artery catheter pressures are surrogate measures for what important physiologic variables? What**

**assumptions are made about the variables obtained through pulmonary artery catheterization?**

Numerous assumptions are made to try to estimate the most important information, left ventricular end-diastolic volume (LVEDV). First, we are using pressures to estimate volume. Second, although we can measure pulmonary artery systolic, diastolic, and occlusion pressures, we are using these measures to estimate left atrial pressure (LAP) and left ventricular end-diastolic pressure (LVEDP). PA diastolic pressure in the healthy heart is a reliable estimate of PAOP, LAP, and LVEDP. However, clearly these relationships fall apart in the presence of cardiac and lung disease. LVEDP is dependent not only on volume but also on ventricular compliance, which can be decreased by ischemia, ventricular hypertrophy and dilation, septal shifts, aortic stenosis, pericardial effusions, use of inotropic agents, and hypertension; in these situations LAP poorly estimates LVEDP. In this instance estimating LVEDP by measuring the wave of the PAOP is best. LAP may be higher than LVEDP in the presence of mitral regurgitation, as evidenced by a large v wave on the PAOP waveform (Figure 26-6). Increased pulmonary vascular resistance, present in chronic obstructive pulmonary disease, pulmonary embolic disease, acute respiratory failure, hypoxia, and hypercarbia, also decreases the correlation between PA diastolic and occlusion pressures.



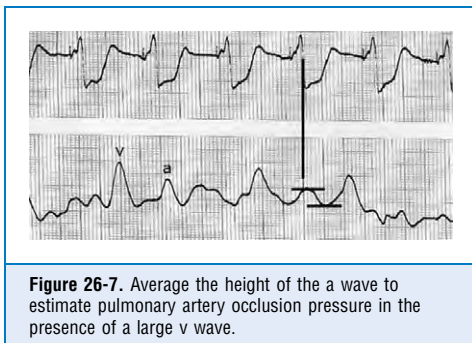
**Figure 26-6.** A large v wave on a pulmonary artery occlusion pressure trace suggests mitral regurgitation. Note that large v waves can be differentiated from a pulmonary artery (PA) waveform based on their timing in relation to the electrocardiogram. PA systole occurs before the T wave while the left atrial v wave occurs after the T wave.

**16. In the presence of a large pulmonary artery occlusion pressure v wave, how should pulmonary artery occlusion pressure be estimated?**

The best way to estimate PAOP is to average the a wave (Figure 26-7).

**17. How might catheter position within the lung lead to errors in interpreting left atrial pressure catheter data?**

The zones of West, as described in Chapter 2, describe the pressure relationship between pulmonary arterial, pulmonary venous, and alveolar pressure in different anatomic areas of the lung. The zones can change as a patient's position and intravascular volume status changes. Mechanical ventilation and PEEP also change the zones. Usually a PA catheter will float into zone 3 and in fact must do so to accurately reflect left atrial pressure because only in zone 3 is there a constant fluid column between the pulmonary artery and left atrium. However, it should be noted that, once the catheter is inserted, the patient's volume and ventilatory status may change remarkably, and the catheter tip may no longer be in a suitable position for correct interpretation (the catheter didn't wander—the patient's physiology wandered!).



**Figure 26-7.** Average the height of the a wave to estimate pulmonary artery occlusion pressure in the presence of a large v wave.

## ACKNOWLEDGMENT

The author gratefully acknowledges Dr. Robert Taylor for contributing the figures used in this chapter.

## WEBSITE



Pulmonary Artery Catheter Education Project—an excellent, interactive website  
<http://www.pacep.org>

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# ARTERIAL CATHETERIZATION AND PRESSURE MONITORING

*James Duke, MD, MBA*

## 1. Why is arterial blood pressure monitored?

Blood pressure monitoring is fundamental in determining the effects of anesthesia on the cardiovascular system. Because decisions about patient care may be based on blood pressure data, it is important to understand how the data are obtained. Arterial pressure is monitored either noninvasively with a blood pressure cuff or invasively with arterial cannulation and a pressure transducer.

## 2. How do noninvasive blood pressure devices work?

Blood pressure is usually measured either manually (auscultatory method) or with an automated device (oscillometric method). With the auscultatory method, a pneumatic cuff is inflated to occlude arterial blood flow. As the cuff is deflated, audible frequencies called Korotkoff sounds are created by turbulent blood flow in the artery. The pressure at which the sounds are first audible is taken as the systolic pressure, and the pressure at which the sounds become muffled or disappear is taken as the diastolic pressure. Errors in measurement may be caused by:

- Long stethoscope tubing
- Poor hearing in the observer
- Calibration errors in the sphygmomanometer
- Decreased blood flow in the extremities caused by either hypovolemia or the use of vasopressors
- Severe atherosclerosis that prevents occlusion of the artery at suprasystolic pressures
- Inappropriate cuff size
- Too rapid of a deflation rate

With the oscillometric method, a pneumatic cuff is also inflated to occlude the arterial blood flow. As the cuff is deflated, the arterial pulsations cause pressure changes in the cuff that are analyzed by a computer. The systolic pressure is taken as the point of rapidly increasing oscillations, the mean arterial pressure as the point of maximal oscillation, and the diastolic pressure as the point of rapidly decreasing oscillations. Errors in measurement may occur from inappropriate cuff size or factors that prevent detection of cuff pressure variations, such as patient shivering. Prolonged use of the stat mode, in which the cuff reinflates immediately after each measurement is obtained, may lead to complications such as ulnar nerve paresthesia, thrombophlebitis, or compartment syndrome.

## 3. What are the indications for intra-arterial blood pressure monitoring?

Intra-arterial blood pressure monitoring is indicated when:

- Blood pressure changes may be rapid.
- Moderate blood pressure changes may cause end-organ damage.
- Frequent arterial blood gases may be needed.
- Noninvasive blood pressure monitoring is inaccurate.

Clinical examples include anticipated cardiovascular instability (e.g., massive fluid shifts, intracranial surgery, significant cardiovascular disease, valvular heart disease, diabetes), direct manipulation of the cardiovascular system (e.g., cardiac surgery, major vascular surgery, deliberate hypotension), frequent sampling of blood gases for pulmonary disease acid-base status or single-lung ventilation, or morbid obesity, which prevents accurate noninvasive measurements.

#### 4. What are the complications of invasive arterial monitoring?

Complications include distal ischemia, arterial thrombosis, hematoma formation, catheter site infection, systemic infection, necrosis of the overlying skin, and potential blood loss caused by disconnection. The incidence of infection increases with duration of catheterization. The incidence of arterial thrombosis increases with:

- Duration of catheterization.
- Increased catheter size.
- Catheter type (Teflon catheters cause more thrombosis than catheters made of polypropylene).
- Proximal emboli.
- Prolonged shock.
- Preexisting peripheral vascular disease.

#### 5. How is radial artery catheterization performed?

The wrist is dorsiflexed and immobilized, the skin is cleaned with an antiseptic solution, the course of the radial artery is determined by palpation, and local anesthetic is infiltrated into the skin overlying the artery (if the patient is awake). A 20-G over-the-needle catheter apparatus is inserted at a 30- to 45-degree angle to the skin along the course of the radial artery. After arterial blood return, the angle is decreased, and the catheter is advanced slightly to ensure that both the catheter tip and the needle have advanced into the arterial lumen. The catheter is then threaded into the artery. Alternatively the radial artery may be transfixated. After arterial blood return, the apparatus is advanced until both the catheter and the needle pass completely through the front and back walls of the artery. The needle is withdrawn into the catheter, and the catheter is pulled back slowly. When pulsatile blood flow is seen in the catheter, it is advanced into the lumen. If the catheter will not advance into the arterial lumen and blood return is good, a sterile guidewire may be placed into the lumen through the catheter, and the catheter advanced over the wire.

Some arterial cannulation kits have a combined needle-guidewire-cannula system, in which the guidewire is advanced into the lumen after good blood flow is obtained and the catheter is then advanced over the guidewire. After cannulation low-compliance pressure tubing is fastened to the catheter, a sterile dressing is applied, and the catheter is fastened securely in place. Care must be taken to ensure that the pressure tubing is free from bubbles before connection. After the procedure it is advisable to remove any devices that have dorsiflexed the wrist because of concerns for median nerve palsy.

#### 6. Describe the normal blood supply to the hand.

The hand is supplied by the ulnar and radial arteries. These arteries anastomose via four arches in the hand and wrist (the superficial and deep palmar arches, the anterior and posterior carpal arches) and between their metacarpal and digital branches. Because of the dual arterial blood supply, the hand usually has collateral flow, and the digits can be supplied by either artery if the other is occluded. Both ulnar and radial arteries have been removed and used successfully as coronary artery bypass grafts without ischemic sequelae to the hand.

#### 7. Describe Allen's test. Explain its purpose.

Allen's test is performed before radial artery cannulation to determine whether ulnar collateral circulation to the hand is adequate in case of radial artery thrombosis. The hand is exsanguinated by having the patient make a tight fist. The radial and ulnar arteries are occluded by manual compression, the patient relaxes the hand, and the pressure over the ulnar artery is released. Collateral flow is assessed by measuring the time required for return of normal coloration. Return of color in less than 5 seconds indicates adequate collateral flow, return in

5 to 10 seconds suggests an equivocal test, and return in more than 10 seconds indicates inadequate collateral circulation. In 25% of the population the collateral circulation to the hand is inadequate.

### 8. Is Allen's test an adequate predictor of ischemic sequelae?

Although some clinicians advocate use of Allen's test, others have demonstrated that Allen's test of radial artery patency has no relationship to distal blood flow as assessed by fluorescein dye injection. There are many reports of ischemic sequelae in patients with normal Allen's tests; conversely, patients with abnormal Allen's tests may have no ischemic sequelae. Apparently Allen's test alone does not reliably predict adverse outcome.

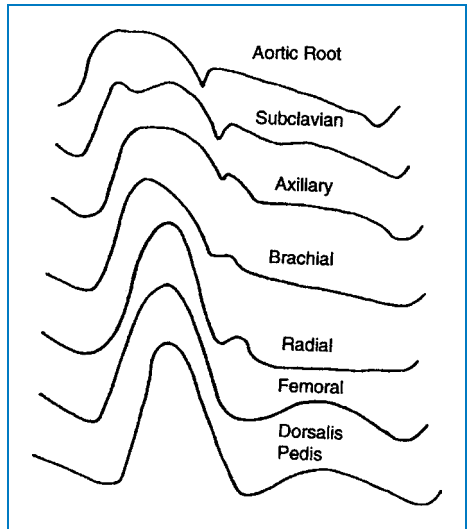
Furthermore, it appears that arterial thrombosis is not uncommon after decannulation. Rates of thrombosis of 25% and greater have been noted without evidence of ischemia. Arterial thrombosis also seems to be a self-limited event.

### 9. What alternative cannulation sites are available?

The ulnar, brachial, axillary, femoral, dorsalis pedis, and posterior tibial arteries are all acceptable cannulation sites. The ulnar artery may be cannulated if the radial artery provides adequate collateral flow. The brachial artery does not have the benefit of collateral flow, but many studies have demonstrated the relative safety of its cannulation. Cannulation of the axillary artery is also relatively safe, but the left side is preferred because of a lower incidence of embolization to the carotid artery. The femoral artery is an excellent site for cannulation because of the large size, the technical ease of cannulation, and the low risk of ischemic sequelae. Although some studies have indicated a slightly higher incidence of infection with a femoral catheter, other studies have not demonstrated this increase. The small size of the dorsalis pedis and posterior tibial arteries makes cannulation difficult and poses an increased risk for ischemic complications; cannulation of these arteries is relatively contraindicated for patients with peripheral vascular disease and diabetes mellitus. The ulnar site should not be attempted after the radial artery on the same side has been punctured on previous attempts.

### 10. How does a central waveform differ from a peripheral waveform?

As the arterial pressure is transmitted from the central aorta to the peripheral arteries, the waveform is distorted (Figure 27-1). Transmission is delayed, high-frequency components such as the dicrotic notch are lost, the systolic peak increases, and the diastolic trough is decreased. The changes in systolic and diastolic pressures result from a decrease in the arterial wall compliance and from resonance (the addition of reflected waves to the arterial waveform as it travels distally in the arterial tree). The systolic blood pressure in the radial artery may be as much as 20 to 50 mm Hg higher than the pressure in the central aorta.



**Figure 27-1.** Configuration of the arterial waveform at various sites in the arterial tree. (From Blitt CD, Hines RL: *Monitoring in anesthesia and critical care medicine*, ed 3, New York, 1995, Churchill Livingstone, with permission.)

**11. What information can be obtained from an arterial waveform?**

The arterial waveform provides valuable information about the patient's hemodynamic status:

- The waveform determines the heart rate during electrocardiographic electrocautery interference and whether the electrical spikes from a pacemaker result in ventricular contractions.
- The slope of the upstroke may be used to evaluate myocardial contractility.
- Large respiratory variations suggest hypovolemia.
- The waveform provides a visual estimate of the hemodynamic consequences of various arrhythmias.

## KEY POINTS: ARTERIAL CATHETERIZATION AND PRESSURE MONITORING



1. Prolonged use of automated blood pressure cuffs in the “stat” mode, in which the cuff reinflates immediately after each measurement is obtained, may lead to complications such as ulnar nerve paresthesia, thrombophlebitis, or compartment syndrome.
2. In 25% of the population the collateral circulation to the hand is inadequate.
3. Ipsilateral ulnar arterial catheterization should not be attempted after multiple failed attempts at radial catheterization on the same side.
4. Peripherally measured arterial waveforms seem amplified and demonstrate higher systolic pressures, wider pulse pressures, and somewhat lower diastolic pressures. The mean arterial pressure is reduced only slightly.
5. The systolic blood pressure in the radial artery may be as much as 20 to 50 mm Hg higher than the pressure in the central aorta.

**12. How is the arterial waveform reproduced?**

Reproduction of the arterial waveform requires the following equipment:

- Intravascular catheter
- Fluid-filled pressure tubing and a stopcock
- Electromechanical transducer
- Electronic analyzer and display system

The mechanical energy at the catheter tip is transmitted to the transducer by the fluid-filled tubing and then converted to an electrical signal. The electrical signal is then converted to a waveform by the analyzer and displayed.

**13. Define damping coefficient and natural frequency.**

Natural frequency, a property of the catheter-stopcock-transducer apparatus, is the frequency at which the monitoring system resonates and amplifies the signals it receives. The natural frequency is directly proportional to the diameter of the catheter lumen and an inverse function of the length of the tubing, the system compliance, and the density of the fluid contained in the system. Because the natural frequency of most monitoring systems is in the same range as the frequencies used to recreate the arterial waveform, significant amplification and distortion of the waveform may occur.

The damping coefficient reflects the rate of dissipation of the energy of a pressure wave. This property may be adjusted to counterbalance the erroneous amplification that results when the natural frequency of the monitoring system overlaps with the frequencies used to recreate the waveform.

#### 14. What are the characteristics of overdamped and underdamped monitoring systems?

The damping coefficient is estimated by evaluating the time for the system to settle to zero after a high-pressure flush (Figure 27-2). An underdamped system continues to oscillate for three or four cycles; it overestimates the systolic and underestimates the diastolic blood pressure. An overdamped system settles to baseline slowly without oscillating; it underestimates the systolic and overestimates the diastolic blood pressure. However, in both cases the mean blood pressure is relatively accurate.

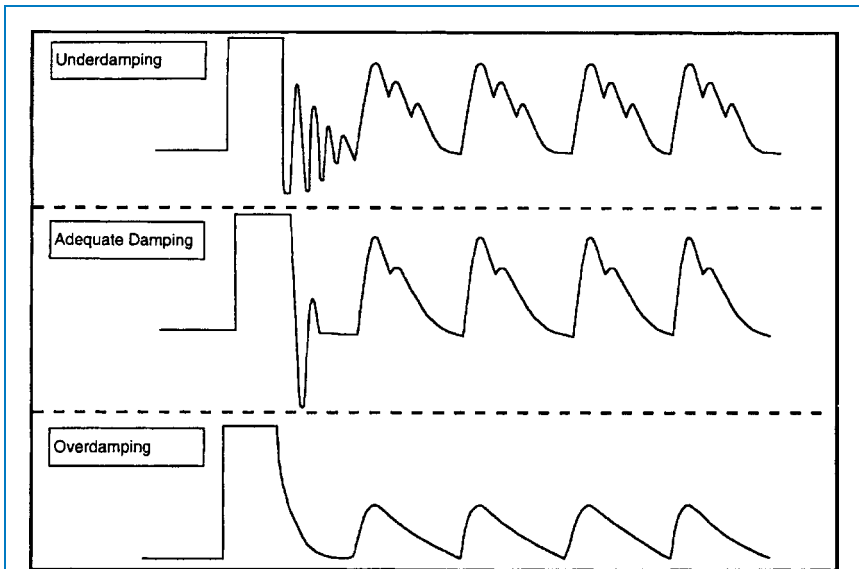


Figure 27-2. Underdamped, adequately damped, and overdamped arterial pressure tracings after a high-pressure flush.

#### 15. How can the incidence of artifacts in arterial monitoring systems be reduced?

The incidence of artifacts can be reduced by meticulous care of the monitoring system:

- The connecting tubing should be rigid with an internal diameter of 1.5 to 3 mm and a maximal length of 120 cm.
- The lines should be kept free of kinks, clots, and bubbles, which cause overdamping of the system.
- Only one stopcock per line should be used to minimize possible introduction of air.
- The mechanical coupling system should be flushed with saline to maintain the patency of the arterial line and minimize the risk of distal embolization and nosocomial infection.
- The transducer should be placed at the level of the right atrium, the midaxillary line in the supine position.
- The transducer should be electrically balanced or rezeroed periodically because the zero point may drift if the room temperature changes.

#### 16. What is distal pulse amplification?

The shape of the arterial pressure wave changes as it travels from the low-resistance ascending aorta to the high-resistance arteriolar bed. This dramatic change in resistance causes the pressure wave to be reflected back toward the ascending aorta, influencing the



shape of the pressure wave. Although the changes in shape do vary with age, sympathetic tone, and vascular impedance, generally peripherally measured arterial waveforms seem amplified and demonstrate higher systolic pressures, wider pulse pressures, and somewhat lower diastolic pressures. The mean arterial pressure is only slightly reduced.

**17. What are the risks and benefits of having heparin in the fluid of a transduction system?**

Heparinized infusions have been used for over 25 years for the purposes of reducing the incidence of arterial catheter thrombosis. However, a recent comparison of use of heparinized vs. nonheparinized solutions for arterial transducer systems found no increase in catheter thrombosis when a nonheparinized solution was used. The benefit of not using heparinized solutions would be decreased exposure to heparin and the possibility of leading to heparin-induced thrombocytopenia.

**18. Are any risks associated with flushing the catheter system?**

On occasion arterial catheter systems are flushed to improve the quality of the arterial waveform. Retrograde embolization of air or thrombus into the cerebral vasculature is a risk. Flush rates of greater than 1 ml/min have been observed to result in retrograde flow. It should be noted that adverse neurologic events associated with arterial cannulation are extremely rare events and remain anecdotal at this time.

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# BLOOD PRESSURE DISTURBANCES

James Duke, MD, MBA

## 1. What is the significance of hypertension to the general patient population?

The prevalence of hypertension (HTN) is about 20% to 25% of the general population, making it a common preoperative comorbidity. It is a leading cause of death and disability in most Western societies. Long-standing HTN leads to atherosclerosis and chronic organ failure. It is a major risk factor for cardiac, vascular, cerebral, and renal disease.

## 2. What blood pressure value is considered hypertensive?

The numbers are somewhat arbitrary. Blood pressure (BP) changes throughout the day and can be affected by posture, exercise, medications, smoking, caffeine ingestion, and mood. HTN cannot be diagnosed on the basis of one abnormal BP reading but requires sustained elevations over multiple measurements on different days. Systemic hypertension is usually considered sustained elevations of diastolic BP greater than 90 to 95 mm Hg or a systolic BP greater than 140 to 160 mm Hg. Borderline HTN is defined as diastolic BP between 85 and 89 mm Hg or a systolic BP between 140 and 159 mm Hg. Diastolic pressures between 110 and 115 mm Hg define severe HTN, and malignant HTN is defined by BPs greater than 200/140 mm Hg. Malignant HTN is a medical emergency.

## 3. What causes hypertension?

- Essential (or idiopathic) HTN: Unknown cause; >90% of all cases fall into this category.
- Endocrine: Cushing's syndrome, hyperaldosteronism, pheochromocytoma, thyrotoxicosis, acromegaly, estrogen therapy
- Renal: Chronic pyelonephritis, renovascular stenosis, glomerulonephritis, polycystic kidney disease
- Neurogenic: Increased intracranial pressure, autonomic hyperreflexia
- Miscellaneous: Obesity, hypercalcemia, preeclampsia, acute intermittent porphyria

## 4. What are some of the physiologic processes that occur as a patient becomes hypertensive?

Often cardiac output temporarily increases, followed by sustained increases in systemic vascular resistance. Vascular smooth muscular hypertrophy is observed, and there is increased arteriolar tone. Extracellular fluid volume and renin activity have no consistent pattern, but usually intracellular sodium and calcium concentrations increase. Sustained HTN leads to concentric hypertrophy of the left ventricle and impaired ventricular relaxation, known as *diastolic dysfunction*. Diastolic dysfunction leads to increased end-diastolic pressures.

## 5. Identify current drug therapies for hypertensive patients.

Single-agent therapy is usually initiated; if this is ineffective, multiple agents may be prescribed. Multiple factors determine which agents are used, including race, gender, age, and comorbidities. For instance, black patients respond better to calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and  $\beta$ -blockers.  $\beta$ -Blockers are relatively contraindicated in patients with reactive airway disease, and patients with renal artery stenosis should not receive ACE inhibitors. Diuretics produce hypokalemia and hyperglycemia.  $\beta$ -Blockers are not particularly effective in elderly patients. [Table 28-1](#) reviews commonly prescribed antihypertensive medications.

TABLE 28-1. COMMONLY PRESCRIBED ANTIHYPERTENSIVE MEDICATIONS

Class	Examples	Side Effects
Thiazide diuretics	Hydrochlorothiazide	Hypokalemia, hyponatremia, hyperglycemia, hypomagnesemia, hypocalcemia
Loop diuretics	Furosemide	Hypokalemia, hypocalcemia, hyperglycemia, hypomagnesemia, metabolic alkalosis
$\beta$ -Blockers	Propranolol, metoprolol, atenolol	Bradycardia, bronchospasm, conduction blockade, myocardial depression, fatigue
$\alpha$ -Blockers	Terazosin, prazosin	Postural hypotension, tachycardia, fluid retention
$\alpha_2$ -Agonists	Clonidine	Postural hypotension, sedation, rebound hypertension, decreases MAC
Calcium channel blockers	Verapamil, diltiazem, nifedipine	Cardiac depression, conduction blockade, bradycardia
ACE inhibitors	Captopril, enalapril, lisinopril, ramipril	Cough, angioedema, fluid retention, reflex tachycardia, renal dysfunction, hyperkalemia
Angiotensin receptor antagonists	Losartan, irbesartan, candesartan	Hypotension, renal failure, hyperkalemia
Vascular smooth muscle relaxants	Hydralazine, minoxidil	Reflex tachycardia, fluid retention

Adapted from Morgan GE, Mikhail MS, Murray MJ: *Clinical anesthesiology*, ed 4, New York, 2005, McGraw-Hill, Chapter 20.  
 ACE, Angiotensin-converting enzyme; MAC, minimal alveolar concentration.

## 6. What are the consequences of sustained hypertension?

Untreated hypertensive patients develop end-organ disease, including left ventricular hypertrophy, coronary artery disease, congestive heart failure, cardiomyopathy, renal failure, and cerebrovascular accidents. Hypertensive patients also demonstrate labile BPs intraoperatively.

## 7. Why should antihypertensives be taken up until the time of surgery?

A well-controlled hypertensive patient has less intraoperative lability in BP. Acute withdrawal of antihypertensives may precipitate rebound HTN or myocardial ischemia. In particular,  $\beta$ -blockers and  $\alpha_2$ -agonists are associated with rebound hypertension. In general antihypertensive therapy should be maintained until the time of surgery and restarted as soon as possible after surgery.

**8. Which antihypertensives should be held the day of surgery?**

Although there is no universal agreement, many believe ACE inhibitors and angiotensin receptor antagonists should be held the day of surgery (see Question 15). Diuretics may be withheld when depletion of intravascular volume is a concern.

**9. Is regional anesthesia a viable option for hypertensive patients?**

Yes, but a high level of sympathetic blockade in hypertensive patients may produce excessive reductions in BP because decreased intravascular fluid volume exacerbates vasodilation. These patients should have intravascular fluids given before the regional anesthetic.

**10. Provide a differential diagnosis for intraoperative hypertension.**

See [Table 28-2](#).

**TABLE 28-2. DIFFERENTIAL DIAGNOSIS OF INTRAOPERATIVE HYPERTENSION**

Related to preexisting disease	Chronic hypertension, increased intracranial pressure, autonomic hyperreflexia, aortic dissection, early acute myocardial infarction
Related to surgery	Prolonged tourniquet time, postcardiopulmonary bypass, aortic cross-clamping, postcarotid endarterectomy
Related to anesthetic	Pain, inadequate depth of anesthesia, catecholamine release, malignant hyperthermia, shivering, hypoxia, hypercarbia, hypothermia, hypervolemia, improperly sized (too small) blood pressure cuff, intra-arterial transducer positioned too low
Related to medication	Rebound hypertension (from discontinuation of clonidine, $\beta$ -blockers, or methyldopa), systemic absorption of vasoconstrictors, intravenous dye (e.g., indigo carmine)
Other	Bladder distention, hypoglycemia

**11. How should intraoperative and postoperative hypertension be managed?**

Pain is the most common cause of postoperative hypertension, but other causes should always be considered. Intraoperatively consider increasing the delivered concentration of volatile anesthetic or administering additional opioids. Consider the usual hourly doses of common opioids and determine whether the maximum limit has been reached. The usual guidelines for opioid administration may not apply to patients receiving opioids chronically. If administration of volatile agents and opioids does not address HTN sufficiently, consider primary antihypertensive agents.

After surgery opioid therapy should be titrated to respiratory rate and the patient's interpretation of the severity of pain. Nerve blocks and analgesic adjuvants such as ketorolac should be considered. Frequently used antihypertensive agents in the perioperative period are discussed in [Table 28-3](#).

TABLE 28-3. ANTIHYPERTENSIVE AGENTS USED PERIOPERATIVELY

Drug	Dose	Onset
Labetalol	5-20 mg	1-2 minutes
Esmolol bolus	0.5 mg/kg over 1 minute	1-2 minutes
Esmolol infusion	50-300 mg/kg/min	1-2 minutes
Propranolol	1-3 mg	1-2 minutes
Hydralazine	5-20 mg	5-10 minutes
Sodium nitroprusside infusion	0.5-10 mg/kg/min	1 minute
Nitroglycerin	0.5-10 mg/kg/min	1 minute

### 12. Are hypertensive patients undergoing general anesthesia at increased risk for perioperative cardiac morbidity?

Although numerous studies have demonstrated that increased preoperative systolic BP is a significant predictor of postoperative morbidity, there are no data that establish definitively whether the preoperative treatment of hypertension reduces perioperative risk. However, poorly treated hypertensive patients have increased intraoperative BP lability, and hemodynamic fluctuations do have some relationship to postoperative complications. In addition, some patients with hypertension will have end-organ damage. It seems reasonable that for nonemergent surgical procedures hypertension should be treated before surgery.

### 13. Broadly categorize the causes of perioperative hypotension.

- **Hypovolemia:** Dehydration, inadequate oral intake or preoperative intravenous fluid administration, bowel cathartics ("preps"), fever, diarrhea, vomiting
- **Functional hypovolemia** (shock states):
  - Sepsis: decreased systemic vascular resistance, increased venous capacitance
  - Cardiac failure: ischemic heart disease, cardiomyopathy, pulmonary embolus, valvular disease, dysrhythmia
  - Hemorrhage: trauma, surgical blood loss, "third-spacing"
  - Neurogenic: loss of systemic vascular resistance from spinal cord injury
  - Anaphylaxis: Acute loss of systemic vascular resistance
  - **Drugs:** Including anesthetic induction agents, volatile anesthetics, histamine-releasing medications, butyrophenones, medications used to induce hypotension (e.g., ganglionic blockers, vasodilators,  $\alpha$ - and  $\beta$ -adrenergic blockers), regional anesthetics
  - **Positive-pressure ventilation**
  - **Cardiac tamponade, tension pneumothorax**
  - **Autonomic neuropathy:** Diabetes mellitus, spinal cord injuries, Guillain-Barré syndrome, familial dysautonomia, Shy-Drager syndrome, human immunodeficiency virus, or acquired immunodeficiency syndrome. Orthostatic hypotension is discussed in Chapter 1.
  - **Medical and surgical disease:** Hematemesis, melena, diabetic ketoacidosis, diabetes insipidus, high-output renal failure, bowel disease, burns

### 14. What is joint cement and how does it cause hypotension?

Methylmethacrylate, a cement used in joint replacement, undergoes an exothermic reaction that causes it to adhere to imperfections in the bony surface. Hypotension usually occurs 30 to 60 seconds after placement of the cement but can occur up to 10 minutes later. Postulated mechanisms include tissue damage from the reaction, release of vasoactive substances when it is hydrolyzed to methacrylate acid, embolization, and vasodilation caused by absorption of the volatile monomer.

**KEY POINTS: BLOOD PRESSURE DISTURBANCES**

1. Although numerous studies have demonstrated that increased preoperative systolic BP is a significant predictor of postoperative morbidity, no data have established definitively whether the preoperative treatment of hypertension reduces perioperative risk.
2. It seems rational that for nonemergent surgical procedures hypertension should be treated before surgery.
3. With the exception of antagonists of the renin-angiotensin system and possibly diuretics, antihypertensive therapy should be taken up to and including the day of surgery.

**15. Why does administration of renin-angiotensin system antagonists result in hypotension in the peri-induction period? How might the hypotension be treated?**

The mechanism is believed to be loss of sympathetic tone superimposed on renin-angiotensin system (RAS) blockade. The vasopressin system is the only intact system left to maintain BP, and vasopressin release is not a fast-response system compared to the sympathetic nervous system. Administration of intravenous fluids is a proper first response. The usual pressor agents used in the operating room (phenylephrine and ephedrine) may prove insufficient if administered because of the blockade of the RAS system and the loss of sympathetic tone associated with anesthetic induction. Preparations of vasopressin have been used to correct refractory hypotension.

**16. How does regional anesthesia create hypotension?**

Both spinal and epidural anesthesia produce hypotension through sympathetic blockade and vasodilation, although the effects of spinal anesthesia may be more precipitous. Blocks lower than the fifth thoracic dermatome have less hypotension because of compensatory vasoconstriction of the upper extremities. Blocks higher than the fourth thoracic dermatome may affect cardioaccelerator nerves, resulting in bradycardia and diminished cardiac output (see Chapters 65 and 66).

**17. How is intraoperative hypotension evaluated and treated?**

Precipitous hypotension understandably requires quick treatment before all facts are at hand. Administration of adrenergic agonists and fluids is recommended. Decrease volatile or intravenous anesthetic levels. If hypotension is gradual and progressive, more facts can be taken into consideration as to the cause, but hypovolemia is the likely candidate. The effects of surgery, anesthesia, and coexisting disease are dynamic; and any single piece of information may be misleading. Thus always take into consideration as many variables as can be obtained. In addition, heart rate, BP, urine output, hematocrit, base deficit, serum lactate concentration, and response to fluid administration are valuable estimators of the cause of hypotension. Refractory hypotension requires invasive monitoring to obtain additional information about cardiac filling pressures and function.

**18. Review the standard adrenergic agonists used to manage hypotension during anesthesia.**

The most common agents are phenylephrine and ephedrine. Their use is described in Chapter 1. Other inotropes and chronotropes are discussed in Chapter 15.

**19. How should hypotension caused by cardiac ischemia be treated?**

Considerations include the following:

- Reducing ischemia by increasing delivered oxygen, decreasing heart rate, and coronary vasodilation with nitroglycerin

- Reducing cardiac afterload (sodium nitroprusside is an arterial dilator)
- Increasing contractility, using inotropes such as dopamine, dobutamine, and amrinone
- Should these fail, perhaps thrombolytic therapy should be considered in concert with a cardiology consultation

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# AWARENESS DURING ANESTHESIA

Aaron Murray, MD

## 1. Review the classifications of memory and awareness.

The current classifications of memory include both implicit, or unconscious memory, and explicit, or conscious memory. Explicit memory refers to the conscious recollection of specific intraoperative events that took place during general anesthesia, also called *anesthetic awareness*. Recall can only be determined after surgery. These memories can occur with or without pain and can range from vivid recollections to vague memories. It was reported in 2008 that subjective auditory perceptions represented 50% of intraoperative awareness experiences. By contrast, implicit memory reflects changes in behavior or performance secondary to an anesthetic experience without the ability to specifically recall the event. The 2006 American Society of Anesthesiologists' (ASA) practice advisory regarding intraoperative awareness excludes dreaming as anesthetic awareness.

## 2. What is the incidence of awareness?

Estimates of awareness during anesthesia in nonobstetric and noncardiac surgeries are approximately 0.1% to 0.2%. Whenever lighter anesthesia is provided, the incidence increases. During cardiac surgery the incidence ranges from 1.1% to 1.5%. A higher incidence is also seen in obstetric (0.4%) and trauma cases (11% to 43%). Interestingly, although the use of anesthetic techniques associated with increased awareness (e.g., nitrous-narcotic) has decreased, the claims against anesthesiologists for awareness are increasing, recently accounting for 2% of all claims. This claim rate rivals other common complications such as aspiration pneumonia and myocardial infarction.

## 3. Are certain techniques and clinical situations more likely to result in awareness?

Recognized risk factors for awareness include the following:

- Light levels of anesthesia, which are common in hypovolemic, injured, and obstetric patients
- Prior history of intraoperative awareness
- Patients undergoing cardiac surgery with cardiopulmonary bypass; a higher incidence of postoperative recall (about 1%) occurs because of the reliance on narcotic-based anesthesia, which minimizes myocardial depression but produces unreliable amnesia
- The use of muscle relaxants
- Machine malfunction such as empty vaporizers, intravenous anesthetic pump malfunction or disconnection, and syringe swaps
- Other patient risks implicated in awareness include: the very young, chronic substance-abusing patients, chronic pain patients, and patients with hypernatremia.

## 4. Describe clinical signs and symptoms of light anesthesia.

Both motor signs and sympathetic activation can indicate lighter levels of anesthesia. Motor signs in response to light anesthesia frequently precede hemodynamic changes or sympathetic activation. Specific motor signs include eyelid or eye motion, swallowing, coughing, grimacing, and movement of the extremities or head. Increased respiratory effort is caused by activity of intercostal and abdominal muscles, which are suppressed at deeper levels of anesthesia. With the use of neuromuscular blockade, motor signs do not provide information



about anesthetic depth. Consequently sympathetic activation represents an additional method for assessing light anesthesia. Sympathetic effects associated with light anesthesia include hypertension, tachycardia, mydriasis, tearing, sweating, and salivation. Such findings are nonspecific and are modified by anesthetic agents; thus their presence or absence is also an unreliable indicator of awareness. Other perioperative medications such as  $\beta$ -blockers and sympathetic blockade render these findings unreliable. In fact, signs of *light* anesthesia (e.g., tachycardia, hypertension) were found in only a minority of patients claiming awareness.

## KEY POINTS: AWARENESS DURING ANESTHESIA



1. Awareness most likely occurs in cases in which minimal anesthetic is administered such as cardiopulmonary bypass, trauma, and obstetric patients.
2. Symptoms of awareness may be very nonspecific, especially when muscle relaxants are used.
3. The small risk of awareness should be discussed during informed consent, especially if patients are at higher risk for recall.

### 5. What are the ramifications of awareness?

Intraoperative awareness has a powerful association with patient dissatisfaction. Untreated pain is one such disturbing possibility. Other possibilities include the ability to hear operating personnel, sensations of weakness or paralysis, anxiety, helplessness, and fear of death. Subsequent effects can range from sleep disturbances, anxiety, and depression to posttraumatic stress disorder (PTSD). One study indicated late psychological symptoms occurred in 33% of patients with awareness. Symptoms of PTSD can include flashbacks, nightmares, avoidance, emotional numbing, hyperarousal, and preoccupation with death.

### 6. How should a patient who may have been aware during a recent anesthetic be approached?

First, it is not necessary to ask all patients if they have any recollections because recall is not a common problem. They may volunteer information or may seem angry or sad without a clear reason, as if something is *just not right*. In instances in which for some reason you have concerns, begin with a structured interview, asking general, open-ended questions. An example would be, "What is the last thing you remember?"

Once a case is identified, a detailed note in the chart is appropriate. Listen to the patient's story and explain the circumstances surrounding the situation (cardiovascular instability, trauma). What trauma patients may remember is their time in the emergency room or intensive care, not necessarily intraoperative events. Reassure the patient, apologize, offer psychologic support, and continue to stay in touch with the patient, even after discharge. Notify the surgeons, nursing staff, and hospital legal counsel. The ASA Task Force on Intraoperative Awareness disagrees if all patients should be advised of intraoperative awareness during informed consent but agrees that those at increased risk should be informed before surgery.

### 7. What are methods to avoid awareness?

- Premedication with amnesic drugs such as benzodiazepines or scopolamine is a standard method of potentially reducing the likelihood of intraoperative awareness, especially in higher-risk patients, surgeries, or anesthetic techniques.

- Administer appropriate doses of induction agents and supplement them if airway management is difficult and the opportunity to administer volatile anesthetics is truncated.
- Avoid muscle relaxants unless necessary.
- Supplement nitrous-narcotic techniques with volatile anesthetics.
- Attempt to use 0.8 to 1 minimum alveolar concentration of anesthetic or more if feasible.
- Maintain anesthetic machines appropriately, ensure proper intravenous pump function with pressure/volume alarms, and administer anesthetic agents via a dedicated and functioning intravenous line.
- Consider using neurophysiologic monitoring to assess depth of anesthesia.

### 8. Are monitors available to assess the depth of anesthesia?

Brain electrical activity monitoring can be used to assess depth of anesthesia and includes two categories: processed electroencephalogram (pEEG) and evoked responses (e.g., auditory). No single monitor can provide a fail-safe answer to the question of depth of anesthesia. pEEG waveform technology of differing formats can be used and has entered the market to a greater extent than evoked responses. The most familiar technology is known as the bispectral index (BIS). The purpose of any of these forms of EEG analysis is to estimate the degree of hypnosis that the patient is experiencing. Raw data, collected by electrodes placed on the forehead and temporal area, are processed by the computer module to create a dimensionless numeric representation of the degree of sedation. Lower numbers correspond to a greater depth, whereas higher numbers are found in awake or lightly sedated patients. The incidence of awareness in high-risk cases was reduced by approximately 82% (0.91% to 0.17%) when BIS-guided anesthesia was provided with a BIS goal of 40 to 60 during anesthesia. Using BIS during general anesthesia with concurrent muscle relaxation resulted in a similar reduction of 77% (0.18% to 0.04%) in the incidence of awareness. In addition to the Food and Drug Administration–approved use of the BIS monitor for depth of anesthesia, using the BIS may help the anesthetist to better titrate the anesthesia to the individual. A deeper anesthetic has been associated with higher 1-year mortality in older adults, leading investigators to the conclusion that titrating BIS values may improve outcomes other than awareness. Although a BIS score less than 60 may reduce probability of awareness, the risk is not eliminated. A case report highlighted a patient with chronic pain and intraoperative hemodynamic lability who had vivid and painful explicit recall of surgery despite an average BIS score of 44. The ASA Task Force suggests that brain electrical activity monitoring is not routinely indicated but the use of brain monitoring should be considered on a case-by-case basis for selected patients (high-risk patients, light general anesthesia).

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# CARDIAC DYSRHYTHMIAS

William A. Baker, MD, and Christopher M. Lowery, MD

## 1. Name some of the causes of sinus bradycardia.

Causes include high vagal tone, medications, hypoxia, hypothyroidism, intrinsic sinus node dysfunction, electrolyte abnormalities, and hypothermia.

## 2. A postoperative patient develops light-headedness with sinus bradycardia and a heart rate of 36. Systolic blood pressure is 83 mm Hg. What treatment should be undertaken?

Atropine, 0.5 mg intravenously, may be effective in increasing heart rate. In addition, search for clues to the etiology of the bradycardia such as those listed in Question 1.

## 3. How is first-degree atrioventricular block identified?

The PR interval is abnormally prolonged ( $>0.20$  second), but all of the P waves conduct (i.e., they are followed by a QRS complex).

## 4. Describe the types of second-degree atrioventricular block.

- **Mobitz type I (Wenckebach):** Involves progressive lengthening of the PR interval followed by a nonconducted P wave, followed by a conducted P wave with a shorter PR interval. When lengthening of the PR is difficult to identify, comparing the PR duration before and after the blocked P wave may confirm Wenckebach. The level of block is usually in the atrioventricular (AV) node with Mobitz I.
- **Mobitz type II:** Far less common than Wenckebach. With Mobitz II block there is no progressive prolongation of the PR interval, which for the first conducted beat is the same as the PR interval before the nonconducted beat. The level of the AV block is generally below the AV node with Mobitz II, as suggested by a wide QRS complex. Permanent pacing is usually indicated in patients with Mobitz II block.
- **2:1 AV block:** A rhythm in which every other P wave is conducted. Because there is no opportunity to evaluate successive conducted beats, 2:1 AV block is neither Mobitz I nor Mobitz II.

## 5. What is third-degree atrioventricular block?

This is also known as complete heart block, with no P waves conducted to the ventricles. The RR interval is regular unless there are premature ventricular complexes. The level of the block may be either at the AV node (usually with a narrow QRS) or below the node (with a wide QRS and a particularly slow heart rate).

Complete heart block is one form, but not the only form, of AV dissociation. Not infrequently a patient will have a rhythm in which only occasional P waves conduct, as indicated by a transient shortening of the RR interval. Officially this does not constitute complete heart block since a P wave does *get through* the AV node to the ventricles. This *incomplete* AV dissociation is commonly referred to as high-degree AV block.

## KEY POINTS: COMMON CAUSES OF BRADYCARDIA



1. Medications
2. High vagal tone
3. Electrolyte or thyroid abnormalities
4. Age-related degeneration of the sinus node, atrioventricular node, or conduction system
5. Structural disease of the conduction system related to coronary artery disease or ventricular hypertrophy

### 6. In addition to complete heart block, what are some other causes of atrioventricular dissociation?

Other causes include accelerated junctional rhythm and ventricular tachycardia (VT).

### 7. What are some of the causes of atrioventricular block?

As with sinus node dysfunction, causes of AV block may be intrinsic (associated with structural heart disease) or extrinsic (related to external factors).

- Extrinsic causes: include medications, electrolyte abnormalities, hypothyroidism, hypoxia, and increased vagal tone
- Intrinsic conduction abnormalities: may arise in a patient with coronary artery disease (sometimes as a complication of acute myocardial infarction), ventricular hypertrophy, myocarditis, sarcoidosis, recent cardiac surgery (especially valve surgery), or calcific degeneration of the conduction system

### 8. Your patient exhibits transient evidence of both sinoatrial node and atrioventricular node dysfunction with simultaneous slowing of the sinus rate and second-degree atrioventricular block, type I. What is going on?

Simultaneous sinoatrial and AV nodal blockade is commonly seen with increased vagal tone, often in a sleeping patient or a patient with vagally mediated syncope. Another consideration is a pharmacologic effect such as that seen with  $\beta$ -blockers or adenosine.

### 9. Which antihypertensive agents are to be avoided in patients with significant bradycardia or heart block?

$\beta$ -Blockers such as metoprolol and esmolol, nondihydropyridine calcium blockers (verapamil and diltiazem), and central sympatholytics such as clonidine should be avoided. In addition, lithium and some anticonvulsants may cause bradycardia.

### 10. Name some of the arrhythmias seen with digoxin toxicity.

Sinus bradycardia, AV block, atrial tachycardia with 2:1 block, accelerated junctional rhythm, and VT are seen with digoxin toxicity.

### 11. Is it always appropriate to treat sinus tachycardia with $\beta$ -blockers?

Not always. Sinus tachycardia may be a response to many insults, and the best approach is to identify why the patient is tachycardic and treat the underlying cause. In some cases such as myocardial ischemia from hypertension,  $\beta$ -blockers may be a useful adjunct. In other cases (e.g., acute bronchospasm, pulmonary edema, tamponade, and hypovolemia)  $\beta$ -blockers can be harmful. Pain, fever, volume shifts, and anemia are all important causes of tachycardia to consider in a postoperative patient.

**12. What is meant by the term paroxysmal supraventricular tachycardia?**

Paroxysmal supraventricular tachycardia (PSVT) is a regular tachycardia with sudden onset and offset that usually has a narrow complex. It may be aborted with vagal maneuvers such as carotid sinus massage or Valsalva. Generally PSVT is responsive to agents such as adenosine,  $\beta$ -blockers, or verapamil if the rhythm is AV nodal dependent. PSVT is actually a *family* of specific rhythms that fit these characteristics, including AV nodal reentrant tachycardia (AVNRT), AV reentrant tachycardia (AVRT), and some types of atrial tachycardia. Other causes of narrow-complex tachycardia are listed in Table 30-1.

**TABLE 30-1. DIFFERENTIAL DIAGNOSIS FOR A NARROW-COMPLEX TACHYCARDIA**

Sinus tachycardia	Atrial tachycardia
Atrial flutter	Atrioventricular nodal reentrant tachycardia (AVNRT)
Atrial fibrillation	Atrioventricular reentrant tachycardia (AVRT)
Multifocal atrial tachycardia	Junctional tachycardia

**13. What is multifocal atrial tachycardia? When is it seen?**

Multifocal atrial tachycardia (MAT) is a supraventricular rhythm (SVT) rhythm with heart rate greater than 100 when there are at least three different P wave morphologies. MAT is commonly seen in patients with significant lung disease or high catecholamine states.

**14. What is the main contraindication to adenosine?**

Bronchospasm. Despite its short half-life, adenosine can provoke severe exacerbations of bronchospasm, and it should be used with caution in patients with a history of asthma or reactive chronic obstructive pulmonary disease.

**15. A patient suddenly develops an irregular rhythm with heart rate of 170. A 12-lead electrocardiogram shows no P waves. What is the likely rhythm? How should it be managed?**

The patient has probably developed atrial fibrillation with rapid ventricular response. If the patient is unstable, electrical cardioversion would be appropriate. If symptoms are mild, hemodynamics may improve with reduction in heart rate (*rate control*) with agents such as diltiazem or  $\beta$ -blockers. Of note, rate control via initiation of moderate doses of  $\beta$ -blockers is contraindicated in patients with significant left ventricular dysfunction who are not already on  $\beta$ -blockers. Some patients are candidates for *chemical cardioversion* with agents such as amiodarone, procainamide, or ibutilide. This may be followed by electrical cardioversion if the antiarrhythmic agent does not convert the rhythm on its own.

Patients with intractable rapid atrial fibrillation who require a pressor should receive an agent that does not increase tachycardia further. In most of these cases phenylephrine is generally preferable to dopamine if a pressor must be used.

**16. Is adenosine useful for the treatment of atrial fibrillation?**

No. Adenosine does not convert atrial fibrillation, and the half-life is so short (seconds) that reduction of the heart rate is quite brief. For atrial flutter adenosine may occasionally make the diagnosis more clear if it is not already evident from the baseline tracing. Adenosine causes transient slowing of the RR interval, which makes flutter waves easier to identify.

**17. What should be done to reduce the risk of stroke in a patient with chronic or paroxysmal atrial fibrillation?**

Anticoagulation should generally be undertaken in cases of atrial fibrillation when it is not contraindicated. For a patient who recently underwent an invasive procedure, the surgeon should be involved in the decision regarding the risk of bleeding posed by anticoagulation.

Stable patients who have been in atrial fibrillation for more than 48 hours should not undergo cardioversion unless they have been anticoagulated for 3 weeks or have had a transesophageal echocardiogram to exclude atrial clot.

**18. What is a wide-complex tachycardia? What is in the differential diagnosis?**

A wide-complex tachycardia is a fast (>100 beats/min) rhythm in which the QRS duration is greater than 120 milliseconds. The differential diagnosis includes VT, SVT with aberrant conduction, and conduction from the atria to the ventricles via an accessory pathway (Wolff-Parkinson-White [WPW] syndrome).

## KEY POINTS: DIFFERENTIAL DIAGNOSIS FOR A WIDE COMPLEX TACHYCARDIA



1. Ventricular tachycardia
2. SVT with aberrant conduction such as with a bundle-branch block
3. Tachycardia with activation of the ventricles via an accessory pathway (WPW syndrome)

**19. A 60-year-old man with a history of prior anterior myocardial infarction develops a monomorphic wide complex tachycardia after noncardiac surgery. What is the most likely diagnosis, and which treatments would be appropriate or inappropriate?**

In the setting of structural heart disease, a wide-complex tachycardia should be assumed to be VT until proven otherwise. In unstable patients electrical cardioversion is appropriate.

- For stable patients a 12-lead electrocardiogram (ECG) should be obtained to aid definitive diagnosis. Amiodarone, procainamide, and lidocaine are reasonable therapeutic choices for monomorphic VT.
- Tragic outcomes may occur when VT is unrecognized and mistakenly treated as SVT. Diltiazem and verapamil (which depress contractility and lower blood pressure) may be life threatening in these patients.

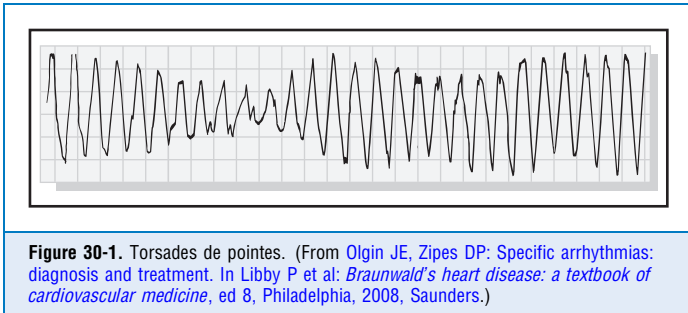
**20. What characteristics of a wide-complex tachycardia suggest ventricular tachycardia rather than supraventricular tachycardia with aberrancy?**

- AV dissociation, if present, confirms the diagnosis of VT.
- The ability of a P wave to conduct to the ventricle and capture the rhythm with a narrow QRS complex is diagnostic for VT.
- Concordance (QRS entirely above the baseline in all precordial leads or below the baseline in all precordial leads) is seen in a minority of cases of VT. When present, concordance strongly suggests VT. However, the absence of concordance is common with VT and does not imply that a wide-complex tachycardia is SVT with aberrancy.
- When the interval from the beginning of the QRS to the nadir of the S wave is greater than 100 milliseconds in any precordial lead, VT is suggested.
- The QRS in patients with SVT with aberrancy usually looks like a typical right or left bundle-branch block. If it does not look like either one, the rhythm is usually VT.

- A P wave before each wide QRS suggests SVT with aberrancy.
- In some cases a previous 12-lead ECG from the patient shows the same wide QRS morphology without tachycardia, suggesting SVT rather than VT.

### 21. Why is it important to distinguish between polymorphic and monomorphic ventricular tachycardia?

The differential diagnosis and treatment for each are somewhat different. Monomorphic VT is common in patients with structural heart disease (such as a previous Q wave myocardial infarction), but it is generally not caused by acute ischemia. Polymorphic VT may be seen in a variety of settings. Patients may have a long QT interval associated with polymorphic VT, commonly referred to as torsades de pointes. This may arise from medications, electrolyte derangements, a congenital predisposition (long QT syndrome), severe bradycardia, or myocardial ischemia (Figure 30-1).



### 22. How is torsades de pointes treated?

- If the patient is unstable with ongoing VT, electrical cardioversion is warranted.
- If an offending drug (such as procainamide) is suspected as the cause, the drug should be discontinued immediately.
- Magnesium should generally be given even if the patient's serum levels are normal. Look for and correct other electrolyte abnormalities such as hypokalemia.
- Acute myocardial ischemia should be considered and treated if present.
- In certain cases isoproterenol or temporary pacing (to avoid bradycardia) may be life saving. Pacing is the treatment of choice when torsades is the consequence of a severe bradyarrhythmia such as complete heart block.

### 23. How are patients with congenital long QT syndrome and syncope treated?

Syncope in these individuals may be a consequence of torsades de pointes, a type of VT. If not recognized and treated, a fatal recurrence of torsades could develop. Treatment is generally with  $\beta$ -blockers and a pacemaker/ defibrillator. Relatives of the affected individuals should be screened for congenital long QT syndrome.

### 24. Are implantable cardioverter-defibrillators curative for ventricular arrhythmias?

No. They merely treat the episodes with shock or overdrive pacing. A patient with intractable VT must be stabilized before being considered for such a device. Many patients with such a device need adjunctive pharmacologic therapy to minimize VT (and firing of the device).

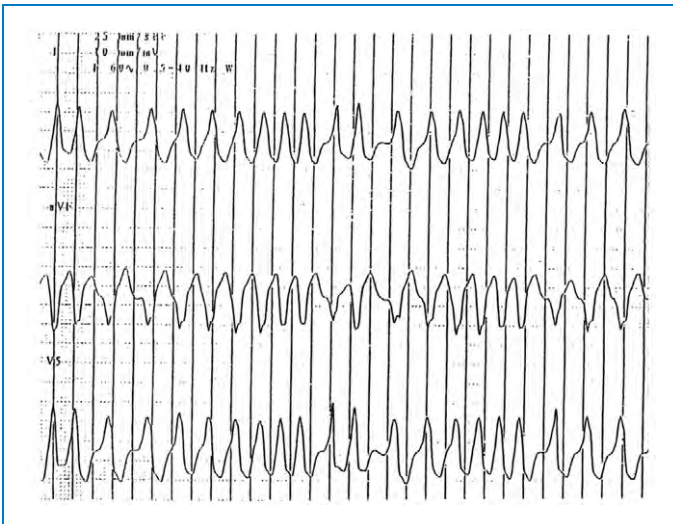
### 25. Do all patients with an accessory pathway have a delta wave (WPW pattern) on their baseline electrocardiogram?

No. Many accessory pathways conduct only in a retrograde fashion (from ventricle to atrium) or have very slow antegrade (atrial to ventricular) conduction.

These patients may or may not have narrow-complex SVT (AVRT). In contrast, some patients have a delta wave on the baseline ECG with no clinical symptoms. In many cases these asymptomatic patients do not need pharmacologic treatment or invasive electrophysiologic testing.

26. **A 25-year-old patient presenting with palpitations is noted to have a wide-complex, irregular tachycardia at a rate of 260. The upstroke of the QRS is slurred. The blood pressure is normal, and the patient appears well. What is the most likely diagnosis? What treatments are indicated? What treatments are potentially harmful?**

This is probably a case of atrial fibrillation with WPW syndrome (Figure 30-2). The wide QRS is a result of conduction down the accessory pathway from the atrium to the ventricular myocardium. In an unstable patient electrical cardioversion is warranted. In a stable patient amiodarone or procainamide would be reasonable. In these patients avoid using digoxin, calcium blockers, adenosine, and  $\beta$ -blockers. Heart rate may actually increase, and ventricular fibrillation has been reported from AV nodal blocking agents. Elective radiofrequency ablation of the pathway is indicated. This is a percutaneous catheter-based approach that is performed by a cardiac electrophysiologist.



**Figure 30-2.** Irregularly irregular wide complex tachycardia in a young patient with Wolff-Parkinson-White syndrome and atrial fibrillation. The QRS complex is wide because the ventricles are activated via an accessory pathway rather than the atrioventricular (AV) node. Drugs that primarily block the AV node such as digoxin, diltiazem, verapamil,  $\beta$ -blockers, and adenosine are contraindicated in this situation because they may precipitate ventricular fibrillation.

27. **Why is it important to save electrocardiogram tracings that document an arrhythmia?**

A cardiologist or cardiac electrophysiologist will be able to give much more meaningful advice if the arrhythmia can be properly diagnosed. The initiation and termination of the event may help to determine the specific type of arrhythmia. General descriptions of the arrhythmia such as bradycardia, or wide complex tachycardia may not be enough to enable specific treatment.



Artifact cannot be diagnosed unless the actual tracing is available for analysis. Finally, third-party payers (such as insurance companies) may be reluctant to reimburse for devices such as pacemakers and defibrillators unless there is proof of an arrhythmia.

## WEBSITE



ECG Library  
<http://www.ecglibrary.com/ecghome.html>

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# TEMPERATURE DISTURBANCES

James Duke, MD, MBA

## 1. Describe the processes that contribute to thermoregulation.

There are three phases of thermoregulation: afferent sensing, central thermoregulatory integration, and efferent response. Distinct receptors are distributed about the body for sensing warmth and cold. Cold impulses travel centrally via myelinated A-delta fibers, warmth is transmitted by unmyelinated C fibers, and most ascending thermal information travels cephalad via the anterior spinothalamic tract. Thermal information is integrated within the spinal cord and centrally in the hypothalamus. Within a narrow range of temperatures (the interthreshold range) no efferent response is triggered by the hypothalamus. Above and below certain thresholds, efferent mechanisms activate in an attempt to decrease or increase body temperature, respectively. Warm responses include active vasodilation and sweating; cold responses include vasoconstriction, nonshivering thermogenesis, and shivering.

## 2. Which patients are at risk for hypothermia?

All patients having either general or neuraxial anesthesia or even just sedation are at risk. Patients especially at risk include the elderly, who have reduced autonomic vascular control, and infants, who have a large surface area-to-mass ratio. Patients with burns, spinal cord injuries that involve autonomic dysfunction, and endocrine abnormalities are also at risk.

## 3. Does hypothermia have an impact on patient outcome?

Mild hypothermia (1° to 3° C) has the following effects:

- Increases incidence of surgical site infections (SSIs). Although this is a multifactorial problem, it has been noted that vasoconstriction secondary to hypothermia decreases blood flow to the wound and bacterial killing by neutrophils.
- Increases the period of hospitalization by increasing the likelihood of SSIs and delayed healing
- Reduces platelet function and impairs activation of the coagulation cascade, increasing blood loss and transfusion requirements (shown by some to also be a cause of increased SSIs)
- Triples the incidence of ventricular tachycardia and morbid cardiac events
- Prolongs the activity of muscle relaxants and anesthetic agents, increasing the likelihood of postoperative weakness and prolonging postoperative recovery.
- The pathophysiologic effects of hypothermia are reviewed in [Table 31-1](#).

## 4. Characterize the different stages of hypothermia.

Hypothermia is a clinical state of subnormal body temperature in which the body is unable to generate enough heat to maintain a normal temperature.

- **Mild hypothermia** (32° to 35° C, 90° to 95° F) is associated with mild central nervous system depression (dysarthria, amnesia, ataxia, and apathy), decreased basal metabolic rate, tachycardia, peripheral vasoconstriction, and shivering.

- **Moderate hypothermia** (27° to 32° C, 80° to 90° F) results in further depression in consciousness, decreased motor activity, mild depression of vital signs, arrhythmias, and cold diuresis.
- In **severe hypothermia** (<27° C, 80° F) the patient may be comatose and areflexic and have significantly depressed vital signs. Left untreated, such profound hypothermia leads to death.

TABLE 31-1. THE EFFECTS OF HYPOTHERMIA ON ORGAN SYSTEMS

System	Effects
Vascular	Increases systemic vascular resistance and peripheral hypoperfusion; plasma volume decreases because of cold diuresis
Cardiac	Decreases heart rate, contractility, and cardiac output and produces arrhythmias
Pulmonary	Increases pulmonary vascular resistance; decreases hypoxic pulmonary vasoconstriction; increases ventilation-perfusion mismatching; depresses ventilatory drive; decreases bronchial muscle tone increasing anatomic dead space; oxyhemoglobin dissociation curve shifts to the left
Renal	Decreases renal blood flow and glomerular filtration rate; impaired sodium resorption and diuresis leading to hypovolemia
Hepatic	Decreases hepatic blood flow, metabolic and excretory functions
Central nervous system	Decreases cerebral blood flow; increases cerebral vascular resistance; oxygen consumption decreases by 7%/°C; evoked potential latencies are increased; MAC is decreased
Hematologic	Decreased platelet aggregation and clotting factor activity; increased blood viscosity, impaired immune response
Metabolic	Basal metabolic rate decreases; hyperglycemia and insulinopenia; decreased oxygen consumption and CO <sub>2</sub> production
Healing	Increased wound infections

*MAC*, Minimum alveolar concentration.

### 5. Which perioperative events predispose a patient to hypothermia?

Heat loss is common in all patients during general anesthesia because of peripheral vasodilation, altered thermoregulation, and the inability to generate heat by shivering. General anesthesia widens the interthreshold range; and, since the thermoregulatory response is markedly less robust, body temperature changes passively with existing temperature gradients. Hypothermia is as common during neuraxial anesthesia as general anesthesia and is a result of sympathetic blockade, muscle relaxation, and a lack of afferent sensory input into central thermoregulatory centers.

## 6. Which physical processes contribute to a patient's heat loss in the operating room?

- **Radiation:** The dissipation of heat to cooler surroundings, which accounts for about 60% of a patient's heat loss, depending on cutaneous blood flow and exposed body surface area.
- **Evaporation:** The energy required to vaporize liquid from any surface, be it skin, serosa, or mucous membranes. It accounts for 20% of heat loss and is a function of the exposed surface area and the relative humidity.
- **Convection:** Is responsible for about 15% of heat loss and depends on the air flow over exposed surfaces.
- **Conduction:** Describes the transfer of heat between adjacent surfaces, accounts for about 5% of the total heat loss, and is a function of the temperature gradient and thermal conductivity.

## 7. As a practical matter, what is done to a patient in the operating room that increases heat loss?

Cool rooms, cold intravenous and sterile preparation solutions, and exposure of the patient to the environment contribute significantly to hypothermia. Cutaneous heat loss is proportional to the exposed surface area and accounts for 90% of heat loss. One unit of refrigerated blood or 1 L of room-temperature crystalloid decreases the body temperature about 0.25° C. The effects of general anesthesia, regional anesthesia, and neuromuscular blockade have been discussed. Less than 10% of heat loss is through the respiratory tract.

## 8. Should all patients receive temperature monitoring within the operating room? What are acceptable sites for temperature monitoring?

The American Society of Anesthesiologists' Standards for Basic Anesthesia Monitoring state: "Every patient receiving anesthesia shall have temperature monitored when *clinically significant changes* in body temperature are intended, anticipated or suspected." Sites for monitoring temperature include skin, rectum, esophagus, external auditory canal, nasopharynx, bladder, or pulmonary artery catheter.

## 9. Review shivering and nonshivering thermogenesis.

Shivering is the spontaneous, asynchronous, random contraction of skeletal muscles in an effort to increase the basal metabolic rate. Shivering is modulated through the hypothalamus and can increase the body's production of heat by up to 300% in young, muscular individuals. It increases oxygen consumption and carbon dioxide production. This effect may be undesirable in the patient with coronary artery disease or pulmonary insufficiency.

Infants younger than 3 months of age cannot shiver and mount a caloric response by nonshivering thermogenesis, which increases metabolic heat production without producing mechanical work. Skeletal muscle and brown fat tissue are the major energy sources for this process.

## 10. Describe the electrocardiographic manifestations of hypothermia.

Mild hypothermia may be associated only with sinus bradycardia. Moderate hypothermia may result in prolonged PR intervals, widened QRS complexes, and a prolonged QT interval. Below 32° C an elevation of the junction of the QRS and ST segments known as the hypothermic hump or Osborne or J wave may be seen. Its size increases with decreasing body temperature; it usually is seen in leads II and V6 and may spread to leads V3 and V4. The J wave is not specific for hypothermia; it also may be seen in hypothalamic lesions and cardiac ischemia. Nodal rhythms are common below 30° C. Below 28° C premature ventricular contractions, atrioventricular blocks, and spontaneous atrial or ventricular fibrillation also occur. Ventricular fibrillation or asystole below 28° C is relatively unresponsive to atropine, countershock, or pacing. Resuscitative efforts should persist until the patient is rewarmed.

## KEY POINTS: TEMPERATURE DISTURBANCES



1. Hypothermia is an extremely common event in the operating room because the environment and the effects of anesthetics increase heat loss. Anesthetics also decrease the ability to generate a response to hypothermia (shivering and vasoconstriction).
2. Even mild hypothermia has a negative influence on patient outcome, increasing wound infection rates, delaying healing, increasing blood loss, and increasing cardiac morbidity.
3. The best method to treat hypothermia is use of forced-air warming blankets. Warm all fluids and blood products. Cover all body surfaces possible, including the head, to further reduce heat loss.

### 11. How does hypothermia affect the actions and metabolism of drugs used in the operative environment?

Drug effects are prolonged by decreased hepatic blood flow and metabolism and decreased renal blood flow and clearance. Protein binding increases as body temperature decreases. The minimum alveolar concentration of inhalational agents is decreased about 5% to 7% per degree centigrade decrease in core temperature. The effects of sedative agents are also decreased. Hypothermia may prolong the duration of neuromuscular blocking agents because of decreased metabolism. Hypothermia delays discharge from the postanesthetic care unit and may prolong the need for mechanical ventilation.

### 12. Discuss methods of rewarming.

- **Passive rewarming** uses the body's ability to generate heat if continued heat loss is minimized by covering exposed areas. Because passive rewarming relies on shivering thermogenesis, hypothalamic mechanisms must be intact, and sufficient glycogen stores available.
- **Active rewarming** is readily performed in the operating room and includes increasing the ambient temperature, administering warmed intravenous fluids, and radiant heat warming. Forced-air warming devices are especially beneficial and superior to circulating water blankets. Airway rewarming is less effective because the heat content of gases is poor. Blood can be drawn from the femoral artery, run through a warming circuit, and returned to the femoral vein; in the extreme, extracorporeal rewarming with cardiopulmonary bypass may be used. A core temperature afterdrop (a secondary decline in core temperature with rewarming) may result from the return of cold blood from the periphery.

### 13. Define hyperthermia.

Hyperthermia is a rise in body temperature of 2° C/hr. Because it is uncommon in the operating room, its cause must be investigated. The usual cause is sepsis or overheating. Hypothalamic lesions and hyperthyroidism are less common. Malignant hyperthermia is a great concern because it is caused by volatile anesthetics or succinylcholine and can be fatal if untreated.

### 14. Describe the manifestations of hyperthermia.

Hyperthermia is a hypermetabolic state associated with increased oxygen consumption, increased minute ventilation, sweating, tachycardia, and vasodilation. An awake patient may experience general malaise, nausea, and light-headedness. With prolonged hyperthermia the patient may develop heat exhaustion or heat stroke. In the anesthetized patient signs and symptoms include tachycardia, hypertension, increased end-tidal carbon dioxide, increased drug metabolism, rhabdomyolysis, oliguria, and hypovolemia. Heart rate increases by 10 beats/min per degree centigrade increase in temperature.

**15. What conditions are associated with hyperthermia?**

- Malignant hyperthermia, as discussed in Chapter 46
- Hypermetabolic states, including sepsis, thyrotoxicosis, and pheochromocytoma
- Hypothalamic lesions secondary to trauma, anoxia, or tumor
- Neuroleptic malignant syndrome
- Transfusion reaction
- Medications

**16. What drugs increase the risk of hyperthermia?**

Sympathomimetic drugs, monoamine oxidase inhibitors, cocaine, amphetamines, and tricyclic antidepressants increase the basal metabolic rate and heat production. Anticholinergics and antihistamines may elevate temperature by suppressing sweating.

**17. What are the pharmacologic effects of hyperthermia?**

Increases in basal metabolic rate and hepatic metabolism decrease the half-life of anesthetic drugs. Anesthetic requirements may be increased.

**18. What is the treatment for the hyperthermic patient in the operating room?**

Expose skin surfaces and use cooling blankets and cool intravenous fluids. Correctable causes of hyperpyrexia should be ruled out. Consider administering antipyretics, although it is always best to treat the cause, not the symptom.

**WEBSITE**

<http://www.asahq.org/publicationsAndServices/standards/>

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# POSTANESTHETIC CARE

*Michael M. Sawyer, MD*

## 1. Which patients should be cared for in the postanesthetic care unit?

Postanesthetic care unit (PACU) care is traditionally divided into phase 1, during which monitoring and staffing ratios are equivalent to an intensive care unit, and phase 2, wherein transition is made from intensive observation to preparation for care on a surgical ward or at home.

Fast-track recovery is emerging because of fast-offset anesthetic agents and adjunctive drugs. Most patients who have had monitoring plus sedation or extremity regional anesthesia should be appropriate for fast track recovery, bypassing phase 1. Typically, however, after inhalation general anesthesia or neuraxis regional anesthesia, a period of phase 1 care is required. Coexisting disease, the surgical procedure, and pharmacologic implications of the anesthetic agents used ultimately determine the most appropriate sequence of postoperative care for each patient.

## 2. Review important considerations as the patient is about to be moved from the operating room to the postanesthetic care unit.

Transport from the operating room (OR) to the PACU can be a dangerous time for patients. Recent PACU designs have been developed to make this trip as short as possible. However, many institutions still are burdened with PACUs remote from the ORs. This has also become an issue with the development of many newer satellite locations where anesthetics are performed (e.g., magnetic resonance imaging). Before transport a patient should be able to maintain a patent airway with spontaneous respirations. The use of supplemental oxygen for transport is recommended. More complicated patients require the use of a transport monitor to facilitate close assessment.

## 3. Describe the process for postanesthetic care unit admission.

A report is given by the anesthesia caregiver to the PACU nurse, reviewing the patient's prior health status, surgical procedure, intraoperative events, agents used, and anesthetic course. The use of muscle relaxants and reversal of neuromuscular blockade, the intraoperative interventions for analgesia, and the intraoperative fluids and blood products received guide in planning PACU care. Initial assessment of the patient by the PACU nurse includes vital signs, baseline responsiveness, adequacy of ventilation, and adequacy of analgesia. Various scoring systems have been used to allow numeric scoring of subjective observations as an indicator of progress toward discharge. The Aldrete scoring system (Table 32-1) tracks five observations: activity, respiratory effort, circulation, consciousness, and oxygenation. Scales for each are 0 to 2, and a total score of 8 to 10 indicates readiness to move to the next phase of care. Regression of motor block in the case of regional anesthesia is also an important determinant of readiness for discharge.

## 4. What monitors should be used routinely in the postanesthetic care unit?

The level of care will depend on the clinical status of the patient. Pulse oximetry and periodic blood pressure monitoring should be used routinely on all patients. Interestingly, routine electrocardiogram (ECG) monitoring has not been found to be of value in patients without risk factors of coronary disease. Finally temperature, urine output, and surgical drainage require monitoring as appropriate.

TABLE 32-1. THE ALDRETE SCORE

Activity	Able to move four extremities	2
	Able to move two extremities	1
	Not able to move extremities voluntarily or on command	0
Respiration	Able to breathe and cough	2
	Dyspnea or limited breathing	1
	Apneic	0
Circulation	BP $\pm$ 20% of preanesthetic level	2
	BP $\pm$ 21%-49% of preanesthetic level	1
	BP $\pm$ 50% of preanesthetic level	0
Consciousness	Fully awake	2
	Arousable on calling	1
	Not responding	0
O <sub>2</sub> saturation	Maintain O <sub>2</sub> saturation >92% in room air	2
	Needs O <sub>2</sub> to maintain O <sub>2</sub> saturation >90%	1
	O <sub>2</sub> saturation <90% with O <sub>2</sub> supplement	0

BP, Blood pressure.

Adapted from Aldrete AJ, Krovlik D: The postanesthetic recovery score, *Anesth Analg* 49:924-933, 1970.

### 5. What problems should be resolved during postanesthetic care?

- **Hypoventilation:** The patient should be breathing easily and able to cough on command and oxygenate to near preanesthetic levels.
- **Hemodynamic stability:** Blood pressure should be within 20% of preanesthetic measurements with stable heart rate and rhythm.
- **Attenuated sensorium:** The patient should be fully awake and voluntarily move all extremities.
- **Postoperative pain:** Pain management should no longer require continuous nursing intervention.
- **Postoperative nausea and vomiting (PONV):** PONV should be treated aggressively since it is associated with prolonged length of stay in the PACU and decreased patient satisfaction with the perioperative experience.

### 6. How is ventilation adversely affected by anesthesia?

Residual neuromuscular blockade, opioid effects, and lingering effects of inhalational anesthesia can result in postoperative hypoventilation (Table 32-2).

### 7. Describe the appearance of residual neuromuscular blockade.

The patient appears *flippy*, with poorly coordinated and ineffective respiratory muscle activity. The patient may complain that breathing is restricted and efforts to deliver supplemental oxygen are suffocating. The patient is unable to sustain a head lift or hand grasp. In the worst case weakness of the pharyngeal muscles results in upper airway collapse and postextubation airway obstruction. Neither a good response to train-of-four testing in the operating room nor spontaneous rhythmic ventilation before extubation rules out residual neuromuscular blockade.



TABLE 32-2. VENTILATION PROBLEMS IN THE POSTANESTHETIC CARE UNIT

Problem	Symptoms	Treatment
Residual neuromuscular blockade	Uncoordinated, ineffectual respiratory effort	Neostigmine, 0.05 mg/kg IV
Opioid narcosis	Slow ventilation, sedated and difficult to arouse	Respiratory support, naloxone 0.04–0.4 mg IV
Residual inhalation anesthesia	Sleepy, shallow breathing	Encourage deep breathing

### 8. How do opioids and residual volatile anesthetics affect breathing?

Slow rhythmic breathing or apneic pauses in a patient who is hard to arouse suggest residual narcosis. In contrast to the patient with residual muscle relaxation, the narcotized patient is often unconcerned about ventilation despite obvious hypoxia. Hypoventilation also slows elimination of volatile anesthetics, potentiating hypoventilation. Surprising degrees of hypercapnia may be found, even with relatively normal pulse oximetry values when supplemental oxygen is delivered.

### 9. How should these causes of hypoventilation be treated?

Hypoventilation resulting from residual neuromuscular blockade should be treated urgently and aggressively. Additional reversal agents may be given in divided doses up to the usual dose limitations. Treatment decisions for residual narcosis may prove to be more problematic. Opioid antagonism for the sake of ventilatory support reverses adequate analgesia. The agonist/antagonist class of analgesic drugs seldom yields a net improvement in ventilation when used for reversal of opioid-induced hypoventilation. Usually the best alternatives are airway support with nasal or oral airways and continuous stimulation until the clinical effects of the opioid on ventilation and responsiveness have resolved. Other supportive measures include increasing inspired oxygen concentrations ( $FiO_2$ ) by switching from nasal cannula to mask (Table 32-3). However, an important caveat—increasing  $FiO_2$  does not reverse hypoventilation, only masks it.

TABLE 32-3. PREDICTED  $FiO_2$  WITH SUPPLEMENTAL OXYGEN DELIVERY

System	Delivery Flow (L/min)	$FiO_2$ Predicted
Nasal cannula	2	0.28
Nasal cannula	4	0.36
Face mask	6	0.50
Partial rebreathing mask	6	0.6
Total rebreathing mask	8	0.8

$FiO_2$ , Fractional inspired oxygen concentration.

**10. The patient has been delivered to the postanesthetic care unit. Oxygen saturations are noted to be in the upper 80s, and chest wall movement is inadequate. How should the patient be managed?**

Establish a patent airway (chin lift, jaw thrust) and administer oxygen. Suction the patient's airway if needed. Is the trachea in midline? Once the airway is patent, observe and auscultate the chest. Is the patient hypoventilating? Perhaps reversal of opioid effect is necessary. Does the abdomen distend and the chest retract with inspiration (paradoxical respirations), suggesting airway obstruction or inadequate reversal of neuromuscular blockade?

Assess the patient's strength by hand grip and sustained head lift. Are there wheezes or rales, requiring inhaled  $\beta$ -agonists or diuresis? Palpate pulses and listen to the heart because circulatory depression causes oxygen desaturation. The patient may require assisted ventilation or reintubation.

Most hypoxia in the PACU is caused by atelectasis, which is treated by sitting the patient upright, asking him or her to breathe deeply and cough, incentive spirometry, and nasal BiPap.

**11. The patient develops stridorous breath sounds. Describe the likely cause and the appropriate management.**

A likely cause of stridorous breath sounds in the early postextubation period is laryngospasm, although other causes of upper airway obstruction (e.g., postextubation croup, expanding hematomas, soft-tissue swelling) should be excluded. Laryngospasm may be precipitated by extubation during light planes of anesthesia or secretions falling on the vocal cords. If laryngospasm is incomplete, the patient will have stridorous breath sounds. If laryngospasm is complete, little air movement is possible, and breath sounds will be absent.

An assessment of airway obstruction is facilitated by observing the chest and abdominal wall. Paradoxical motion, in which the chest contracts as the abdomen expands, suggests that inspiration is being attempted against a closed glottis or some other source of airway obstruction.

**12. How is laryngospasm treated?**

The treatment for laryngospasm is to support ventilation. Call for an assistant, provide a jaw thrust, and assist the patient's inspiratory efforts with positive-pressure ventilation, using 100% oxygen. If this proves unsatisfactory, administer succinylcholine, 0.15 to 0.30 mg/kg (about 10 to 20 mg in adults), to relax the vocal cords. (I have had success with even 5 mg of succinylcholine administered intravenously to an adult—in this setting a little seems to go a long way; another advantage is that the diaphragm and accessory muscles of respiration remain functional.) If the patient continues to experience difficulty with ventilation, reintubation after administering approximately 100 mg of succinylcholine may be necessary. Once intubation is completed and end-tidal  $\text{CO}_2$  has been verified, the patient should receive assisted ventilation. Sedation may be appropriate. When re-extubation is attempted, be prepared for a possible recurrence of laryngospasm. If stridorous breath sounds are caused by laryngeal edema, administration of nebulized racemic epinephrine and intravenous steroids may be indicated.

**13. The laryngospasm resolves. Chest auscultation reveals bilateral rales. What is the most likely cause?**

Although congestive heart failure, fluid overload, adult respiratory distress syndrome, and aspiration of gastric contents need to be considered, negative-pressure pulmonary edema (NPPE) is the likely cause. NPPE results from generation of negative intrapleural pressures when the patient inspires against a closed or obstructed glottis. Whereas intrapleural pressures vary between negative 5 and negative 10 cm  $\text{H}_2\text{O}$  during a normal respiratory cycle, inspiration against a closed glottis may generate between negative 50 and negative 100 cm  $\text{H}_2\text{O}$  pressure. Such increased pressures increase venous return to the thorax and pulmonary vasculature, increasing transcapillary hydrostatic pressure gradients, producing pulmonary edema.

The onset of edema has been noted from 3 to 150 minutes after the inciting event. Some authorities refer to this syndrome as negative-pressure pulmonary injury (NPPI) because pink or frankly bloody pulmonary secretions suggest that some alveolar injury has taken place during attempts to breathe against a closed glottis.

#### 14. How is negative-pressure pulmonary edema treated?

Once the airway obstruction is relieved, treatment is supportive. The pulmonary edema usually resolves between 12 and 24 hours. Continue oxygen therapy; continuous positive airway pressure and mechanical ventilation with positive end-expiratory pressure may occasionally be needed, depending on the severity of gas exchange impairment. Diuretics should be administered only if the patient has intravascular fluid overload or perhaps in the most severe cases.

## KEY POINTS: POSTANESTHETIC CARE AND COMPLICATIONS



1. Postanesthetic care is part of the continuum of perioperative care and the responsibility of the anesthesiologist.
2. Adequate oxygenation, postoperative pain, and PONV are common problems that delay PACU discharge.

#### 15. Describe an approach to the evaluation of postoperative hypertension and tachycardia.

A hyperdynamic postoperative phase is not an uncommon event. Frequently observed and readily treatable causes include pain, hypoventilation, hypercarbia, hypothermia with shivering, bladder distention, and essential hypertension. Also consider hypoxemia, hyperthermia and its causes, anemia, hypoglycemia, tachydysrhythmias, withdrawal (e.g., drug and alcohol), myocardial ischemia, prior medications administered, and coexisting disease. Rarely the hyperdynamic state may reflect hyperthyroidism, pheochromocytoma, or malignant hyperthermia.

#### 16. What might cause hypotension in the postoperative phase?

Prior or ongoing blood loss, third-space sequestration of fluid, and inadequate volume replacement manifest as hypotension. Myocardial ischemia or heart failure may present as hypotension, as can sepsis or anaphylaxis.

#### 17. How should hypotension be treated?

Consider the surgical procedure, intraoperative events, medications, and past medical history. Evaluate blood loss and urine output. Review the ECG rhythm strip and consider a 12-lead ECG. Volume expansion with balanced crystalloid solutions is first-line therapy. Elevation of legs and Trendelenburg positioning may help transiently. Circumstances may require administration of colloid or packed red blood cells. Should volume expansion prove unsatisfactory, vasopressors or inotropes may be necessary, but these suggest the need for further evaluation.

#### 18. Under what circumstances is a patient slow to awaken?

A reasonable initial assumption is that such patients are displaying residual drug effects. Should decreased awareness persist beyond a reasonable period of observation, ventilatory, metabolic, and central nervous system (CNS) etiologies must be considered. Does the patient have a seizure history and is the patient currently postictal? CNS ischemia caused by

decreased perfusion or embolic phenomena should be considered. Has the patient had documented CNS ischemic events or strokes? Laboratory analysis should include arterial blood gases as well as measurements of serum sodium and glucose. Should these be normal, perhaps a computed tomography of the brain is needed.

**19. Discuss the issues surrounding postoperative nausea and vomiting.**

PONV remains a significant, troublesome postanesthetic problem. It results in delayed PACU discharge and occasional unplanned hospital admissions and is a recurring cause of patient dissatisfaction. Both the surgical procedure and anesthetic agents administered may increase PONV risk. Procedural risks include laparoscopic surgery; surgery on genitalia; craniotomies; and shoulder, middle ear, or eye muscle procedures. Patient factors are female sex, nonsmoker, prior PONV or motion sickness history, and school-age children. Anesthetic agents with a high association with PONV include the opioids, volatile inhalation agents, and nitrous oxide. Propofol has the lowest incidence of any of the induction agents and has been used effectively as a rescue medication. Risk assessment should be made on the basis of these factors, and prophylactic treatment or alteration of the anesthetic plan determined by evidence of efficacy. PONV rescue (treatment once PONV has ensued) requires balancing drug benefits with side effects and cost.

**20. Should ambulatory patients be treated differently in the postanesthetic care unit?**

The goal of postanesthetic care of the ambulatory patient is to render the patient *street ready*. Pain should be treated with short-acting agents such as fentanyl. Nonnarcotic analgesia and nerve blocks should be used whenever possible. Oral analgesics should be used in phase 2 recovery as prescribed for postoperative care. After regional anesthesia, extremities should be protected while the patient is mobilized, and ambulation should be assisted if transient segmental paresthesia makes movement unsteady. No ambulatory surgery patient should be discharged after receiving any sedating medication without a companion to ensure safe transportation to a place of residence.

**21. Should patients be required to tolerate oral intake before postanesthetic care unit discharge?**

Taking clear liquids before discharge can increase length of stay in the PACU. It is unclear if the ability to tolerate clear liquids decreases adverse outcomes and at present time is not recommended to be a requirement for PACU discharge. However, it may be helpful in selected patients.

**22. A patient has undergone a general anesthetic for an outpatient procedure. Recovery has been uneventful, yet the patient has no ride home. How should this be handled?**

Patients should be required to have a responsible party accompany them home after anesthesia. It has been shown to decrease adverse events. The responsible party will be able to promptly report any adverse events that may arise. The patient in this case should be kept at the health care facility, possibly under 23-hour observation, or until a responsible party is available.

**23. In designing a postanesthetic care unit for a new outpatient surgical center, the board of directors states that all patients should be kept in the postanesthetic care unit for at least 1 hour for recovery. Is this minimal postanesthetic care unit stay reasonable?**

Although this time may be reasonable, the American Society of Anesthesiologists has no recommendation for the minimal length of stay in the PACU. Length of stay should be determined on a case-by-case basis. A discharge protocol should be designed that allows patients to reach postoperative goals that will direct them toward discharge.

**WEBSITE**

<http://www.asahq.org/>

**SUGGESTED READINGS**

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1. ASA Task Force on Post Anesthesia Care: Practice guidelines for postanesthesia care. *Anesthesiology* 96:742–752, 2002.
2. Feeley TW, Macario A: The postanesthetic care unit. In Miller RD, editor: *Miller's anesthesia*, ed 6, Philadelphia, Elsevier Churchill Livingstone, 2005, pp 2701–2728.
3. Gan TJ, Meyer T, Apfel CC, et al: Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg* 96:62–71, 2003.

# ISCHEMIC HEART DISEASE

Tamas Seres, MD, PhD

## 1. Name the known risk factors for the development of ischemic heart disease.

Age, male gender, and positive family history are risk factors that cannot be modified. Smoking, hypertension, diet, hyperlipidemia, physical inactivity, obesity, and diabetes mellitus are modifiable and should be considered in all adults as risk factors for which interventions are likely to lower ischemic heart disease (IHD) risk.

## 2. Describe the normal coronary blood flow.

The resting coronary blood flow (CBF) averages about 225 ml/min, which is 4% to 5% of the total cardiac output in normal adults. The CBF increases threefold to fourfold to supply the extra nutrients needed by the heart at maximum exercise level. The CBF is determined by the pressure gradient between the aorta and the ventricle. There are phasic changes in CBF during systole and diastole in the left ventricle. The blood flow falls to a low value during systole, especially in the subendocardial area because of compression of the left ventricular muscle around the intramuscular vessels and the small pressure gradient between the aorta and the left ventricle (aortic systolic pressure–left ventricular systolic pressure). During diastole the cardiac muscle relaxes and no longer obstructs the blood flow through the left ventricular capillaries. The pressure gradient is high during diastole (aortic diastolic pressure–left ventricular end-diastolic pressure).

The phasic changes of the CBF are much less in the right ventricle because the force of contraction of the right ventricle is much weaker than that of the left ventricle and the pressure gradient is high between the aorta and the right ventricle during the entire cardiac cycle.

## 3. Describe the coronary anatomy.

The right coronary artery system is dominant in 80% to 90% of people and supplies the sinoatrial node (60%), atrioventricular node (85%), and right ventricle. In 84% of the cases it terminates as the posterior descending artery (PDA). Right-sided coronary artery occlusion can result in bradycardia, heart block, and inferior or right ventricular myocardial infarction (MI).

The left main coronary artery gives rise to the circumflex artery and left anterior descending (LAD) artery, which supplies the majority of the interventricular septum (septal branches) and left ventricular wall (diagonal branches). When the circumflex gives rise to the PDA, the circulation is said to be left dominant, and the left coronary circulation supplies the entire septum and the atrioventricular node. In 40% of patients the circumflex artery supplies the sinoatrial node. Significant stenosis of the left main coronary artery (left main disease) or the proximal circumflex and left anterior descending arteries (left main equivalent) may cause severely depressed myocardial function during ischemia.

## 4. Explain the determinants of myocardial oxygen demand and delivery.

*Myocardial oxygen demand* is determined by wall tension and contractility. Wall tension (T) is the product of intraventricular pressure (P), radius (R) and the wall thickness (h):

$$T = PR/2h$$

Increased ventricular volume (preload) and increased blood pressure (afterload) both increase wall tension and oxygen demand. Increase in contractility in response to sympathetic stimulation or inotropic medications increases oxygen demand also.

Increase in heart rate increases myocardial contractility but decreases the ventricular diameter and the wall tension. Thus the increase in oxygen demand caused by enhanced contractility is in large part offset by the reduction in oxygen demand that accompanies the reduced wall tension. The oxygen demand increases because more contraction is performed per minute.

**Myocardial oxygen delivery** is determined by oxygen content and coronary blood flow. Oxygen content can be calculated by the following equation:

$$\begin{aligned} \text{O}_2 \text{ content} = & [1.39 \text{ ml O}_2/\text{g of hemoglobin} \times \text{hemoglobin (g/dl)} \times \text{saturation (\%)}] \\ & + [0.003 \times \text{PaO}_2] \end{aligned}$$

Coronary blood flow is determined by coronary perfusion pressure, the time available for perfusion, and the patency of coronary arteries. Coronary perfusion pressure is altered by diastolic hypotension, left ventricular hypertrophy, and increased left ventricular end-diastolic pressure. The diastolic time for perfusion decreases with tachycardia.

### 5. What is the clinical manifestation of myocardial ischemia?

The clinical manifestations of myocardial ischemia are varied. Angina pectoris with or without arrhythmias or heart failure is assumed to be the classic manifestation of myocardial ischemia. However, myocardial ischemia may present as ventricular failure or arrhythmias without angina or may remain clinically silent. The dynamic nature of coronary stenosis accounts for the changes in vessel caliber that may produce pain at rest at one time and angina with varying degrees of exercise at other times.

### 6. How is angina graded?

The Canadian Cardiovascular Society introduced a grading system for angina:

Class I	Angina with strenuous or rapid prolonged exertion at work or recreation
Class II	Angina with walking or climbing stairs rapidly, walking uphill, or walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace
Class III	Angina with walking one to two blocks on the level and climbing one flight of stairs at a normal pace
Class IV	Angina may be present at very low level of physical activity or at rest

### 7. Describe the pathogenesis of a perioperative myocardial infarction.

MI is usually caused by platelet aggregation, vasoconstriction, and thrombus formation at the site of an atheromatous plaque in a coronary artery. Sudden increases in myocardial oxygen demand (tachycardia, hypertension) or decreases in oxygen supply (hypotension, hypoxemia, anemia, tachycardia, coronary occlusion) can precipitate MI in patients with IHD. However, recent studies have confirmed that most perioperative ischemic events are unrelated to hemodynamic perturbations, suggesting that intracoronary events may be important in the genesis of perioperative ischemia.

### 8. What clinical factors increase the risk of a perioperative myocardial infarction following noncardiac surgery?

There are active cardiac conditions, clinical risk factors, and minor clinical predictors based on the algorithm for risk stratification and appropriate use of diagnostic testing of cardiac patients undergoing noncardiac surgery by the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Perioperative Evaluation (2007). The guidelines integrate clinical risk factors, exercise capacity, and the surgical procedure in the decision-making process. They are discussed in more detail in Chapter 17.

### 9. What is the definition of recent and prior myocardial infarction?

Based on the decreased risk for perioperative reinfarction, the American College of Cardiology National Database defines recent MI as occurring  $>7$  days but  $\leq 30$  days before the surgery. Prior MI is defined as MI  $>30$  days before the surgery.

### 10. How does the type of surgery influence the risk stratification for perioperative ischemia?

- **High-risk** surgery (risk of perioperative adverse cardiac events  $>5\%$ ) includes aortic and major vascular procedures and peripheral vascular surgeries.
- **Intermediate-risk** procedures (risk of perioperative adverse cardiac events  $<5\%$ ) are: carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic surgery, orthopedic surgery, and prostate surgery.
- **Low-risk** procedures (risk of perioperative adverse cardiac events  $<1\%$ ) are endoscopic procedures, superficial procedures, cataract surgery, and breast surgery.

### 11. How can cardiac function be assessed by history and physical examination?

If a patient's exercise capacity is excellent, even in the presence of IHD, chances are good that the patient will be able to tolerate the stresses of the surgery. Poor exercise tolerance in the absence of pulmonary or other systemic disease indicates an inadequate cardiac reserve. All patients should be questioned about their ability to perform daily activities such as described in the Canadian classification of angina pectoris or the New York Heart Association (NYHA) classification of exercise tolerance. The ability to climb two-to-three flights of stairs without significant symptoms (angina, dyspnea, syncope) is usually an indication of adequate cardiac reserve as defined by  $>4$  metabolic equivalents (METs) exercise capacity (1 MET equals 3.6 ml/kg/min oxygen uptake at rest).

Signs and symptoms of congestive heart failure include dyspnea, orthopnea, paroxysmal nocturnal dyspnea, peripheral edema, jugular venous distention, a third heart sound, rales, and hepatomegaly.

### 12. When would you consider noninvasive stress testing before noncardiac surgery?

The guidelines integrate clinical risk factors, exercise capacity, and the surgical procedure in the decision making process. Noninvasive stress testing should be considered if it will change the management of the patients. Examples include:

- Patients with active cardiac conditions in whom noncardiac surgery is planned should be evaluated and treated per ACC/AHA guidelines before noncardiac elective surgery.
- Patients with three or more clinical risk factors and poor functional capacity who require vascular surgery.
- Patients with at least one or two clinical risk factors and poor functional capacity who require intermediate-risk noncardiac surgery.
- Patients with at least one or two clinical risk factors and good functional capacity who are undergoing vascular surgery.

### 13. What tests performed by medical consultants can help further evaluate patients with known or suspected ischemic heart disease?

- Exercise electrocardiogram (ECG) is a noninvasive test that attempts to produce ischemic changes on ECG (ST depression = 1 mm from baseline) or symptoms by having the patient exercise to maximum capacity. Information obtained relates to the thresholds of heart rate and blood pressure that can be tolerated. Maximal heart rates, blood pressure response, and clinical symptoms guide interpretation of the results.
- Exercise thallium scintigraphy increases the sensitivity and specificity of the exercise ECG. The isotope thallium is almost completely taken up from the coronary circulation by the myocardium and can then be visualized radiographically. Poorly perfused areas that later



refill with contrast delineate areas of myocardium at risk for ischemia. Fixed perfusion defects indicate infarcted myocardium.

- Dipyridamole thallium imaging is useful in patients who are unable to exercise. This testing is frequently required in patients with peripheral vascular disease who are at high risk for IHD and in whom exercise test is limited by claudication. Dipyridamole is a potent coronary vasodilator that causes differential flow between normal and diseased coronary arteries detectable by thallium imaging.
- Echocardiography can be used to evaluate left ventricular and valvular function and measure ejection fraction.
- Stress echocardiography (dobutamine echo) can be used to evaluate new or worsened regional wall motion abnormalities in the pharmacologically stressed heart. Areas of wall motion abnormality are considered at risk for ischemia.
- Coronary angiography is the gold standard for defining the coronary anatomy. Valvular and ventricular function can be evaluated, and hemodynamic indices can be measured. Because angiography is invasive, it is reserved for patients who require further evaluation based on previous tests or who have a high probability of severe coronary disease.

## KEY POINTS: ISCHEMIC HEART DISEASE



1. The clinical predictors, the surgical procedure, and exercise capacity should be integrated in the decision-making process to avoid adverse perioperative cardiac events.
2. Patients with active cardiac conditions (unstable or severe angina, recent MI) should be determined and treated before noncardiac elective surgery.
3. The risk of the surgical procedure should also be considered. Patients for vascular surgery represent very high risk for perioperative ischemic events.

Patients with excellent exercise capacity, even in the presence of ischemic heart disease, will be able to tolerate the stresses of noncardiac surgery. The ability to climb two-to-three flights of stairs without significant symptoms (angina, dyspnea) is usually an indication of adequate cardiac reserve.

The type of acute revascularization should be carefully planned because patients with a drug-eluting stent should be on dual-antiplatelet therapy for at least a year.

### 14. What are the main indications for coronary revascularization before noncardiac surgery?

Consistent with the ACC/AHA 2004 Guideline Update for coronary artery bypass graft surgery, the following patients need coronary revascularization (either coronary artery bypass grafting or percutaneous coronary intervention) before noncardiac surgery:

- Patients with stable angina who have significant left main coronary artery stenosis.
- Patients with stable angina who have three-vessel disease. Survival benefit is greater when left ventricular ejection fraction is less than 50%.
- Patients with stable angina who have two-vessel disease with significant proximal left anterior descending stenosis and either ejection fraction less than 50% or demonstrable ischemia on noninvasive testing.
- Patients with high-risk unstable angina or non-ST-segment elevation MI.
- Patients with acute ST-elevation MI.

### 15. A patient after percutaneous coronary intervention is scheduled for surgery. What is your concern?

After percutaneous coronary intervention (PCI), patients need to be on dual-antiplatelet therapy (aspirin and clopidogrel). Discontinuation of this therapy for surgical procedure creates

high risk for coronary artery thrombosis and myocardial events in the perioperative period. The appropriate timing of surgery is still under investigation, but the following guidelines are acceptable:

- After balloon angioplasty nonurgent surgery can be performed with aspirin after 14 days, but ideally these patients should be on dual-antiplatelet therapy for 4 to 6 weeks.
- After bare-metal or drug-eluting stent placement, nonurgent surgery can be performed with aspirin after 30 to 45 days or >365 days, respectively.

**16. Why do patients with drug-eluting stents need significantly longer time than those with bare metal stents?**

Drug-eluting stents in current clinical use were approved by the Food and Drug Administration after clinical trials showed they were statistically superior to bare-metal stents for treatment of coronary artery occlusions, having lower rates of major adverse cardiac events (usually defined as a composite clinical end point of death + MI + repeat intervention because of restenosis). The eluting drugs (sirolimus, paclitaxel) released from the stent inhibit endothelial surface formation inside the stent, thus requiring longer-duration dual-antiplatelet therapy.

**17. Should all cardiac medications be continued throughout the perioperative period?**

Patients with a history of IHD are usually taking medications intended to decrease myocardial oxygen demand by decreasing the heart rate, preload, afterload or contractile state ( $\beta$ -blockers, calcium channel antagonists, nitrates) and increase the oxygen supply by causing coronary vasodilation (nitrates). Generally these drugs should be administered throughout the perioperative period.

**18. How would you give  $\beta$ -blockers to high-risk patients?**

$\beta$ -Blockers should be given to patients undergoing vascular surgery who are at high cardiac risk owing to the finding of ischemia on preoperative testing. They are probably indicated for patients undergoing vascular or intermediate-risk surgery in which perioperative assessment identifies coronary artery disease or more than one clinical risk factor. Finally, they should be continued in patients undergoing surgery who are already receiving these medications for the treatment of angina, symptomatic arrhythmias, or hypertension.

**19. Would you give prophylactic intraoperative nitroglycerin infusion?**

The usefulness of intraoperative nitroglycerin as a prophylactic agent to prevent myocardial ischemia and cardiac morbidity is unclear for high-risk patients undergoing noncardiac surgery, particularly those who have required nitrate therapy to control angina. The recommendation for prophylactic use of nitroglycerin must take into account the anesthetic plan and patient hemodynamics and must recognize that vasodilation and hypovolemia can readily occur during anesthesia and surgery.

**20. What electrocardiogram findings support the diagnosis of ischemic heart disease?**

The resting 12-lead ECG remains a low-cost, effective screening tool in the detection of IHD. It should be evaluated for the presence of ST-segment depression or elevation, T-wave inversion, old MI as demonstrated by Q waves, disturbances in conduction and rhythm, and left ventricular hypertrophy. Ischemic changes in leads II, III, and aVF suggest right coronary artery disease, leads I, aVL, V<sub>5</sub> and V<sub>6</sub> monitor the circumflex artery distribution, and leads V<sub>1</sub> to V<sub>4</sub> look at the distribution of the left anterior descending artery.

**21. When is a resting 12-lead ECG recommended?**

- Patients with at least one clinical risk factor (history of ischemic heart disease, history of compensated or prior heart failure, history of cerebrovascular disease, diabetes mellitus, and renal insufficiency) who are undergoing vascular surgical procedures.

- Patients with known coronary heart disease, peripheral arterial disease, or cerebrovascular disease who are undergoing intermediate-risk surgical procedures.
- It is reasonable in patients with no clinical risk factors who are undergoing vascular surgical procedures.

**22. How long should a patient with a recent myocardial infarction wait before undergoing elective noncardiac surgery?**

The risk of reinfarction during surgery in a patient with recent MI has traditionally depended on the time interval between the MI and the procedure. The ACC/AHA task force eliminated the arbitrary 6-month time interval and suggested that elective surgery is associated with prohibitive risk only during the initial 4 to 6 weeks. The patient's functional status following rehabilitation from an MI is probably more important than the absolute time interval. Patients with ongoing symptoms are candidates for coronary revascularization before their noncardiac procedure.

**23. Outline the hemodynamic goals of induction and maintenance of general anesthesia in patients with IHD.**

The anesthesiologist's goal must be to maintain the balance between myocardial oxygen demand and supply throughout the perioperative period. During induction wide swings in heart rate and blood pressure should be avoided. Ketamine should be avoided because of the resultant tachycardia and hypertension. Prolonged laryngoscopy should be avoided, and the anesthesiologist may wish to blunt the stimulation of laryngoscopy and intubation by the addition of opiates,  $\beta$ -blockers, or laryngotracheal or intravenous lidocaine. Maintenance drugs are chosen with knowledge of the patient's ventricular function. In patients with good left ventricular function, the cardiac depressant and vasodilator effects of inhaled anesthetics may reduce myocardial oxygen demand. A narcotic-based technique may be chosen to avoid undue myocardial depression in patients with poor left ventricular function. Muscle relaxants with minimal cardiovascular effects are usually preferred. Blood pressure and heart rate should be maintained near baseline values. This can be accomplished by blunting sympathetic stimulation with adequate analgesia and aggressively treating hypertension (anesthetics, nitroglycerin, nitroprusside,  $\beta$ -blockers), hypotension (fluids, phenylephrine, inotropic drugs), and tachycardia (fluids, anesthetics,  $\beta$ -blockers).

**24. What monitors are useful for detecting ischemia intraoperatively?**

The  $V_5$  precordial lead is the most sensitive single ECG lead for detecting ischemia and should be monitored routinely in patients at risk for IHD. Lead II can detect ischemia of the right coronary artery distribution and is the most useful lead for monitoring P waves and cardiac rhythm.

**25. Would you use transesophageal echocardiography routinely in patients with high cardiac risk undergoing noncardiac surgery?**

Transesophageal echocardiography (TEE) can provide continuous intraoperative monitoring of left ventricular function. In high-risk patients detection of regional wall motion abnormalities with this technique is the most sensitive monitor for myocardial ischemia. However, no study has clearly demonstrated a change in outcome from the routine use of TEE. Therefore the choice of using TEE is best left to the discretion of the anesthesia care team.

**26. Is a pulmonary artery catheter reasonable to use routinely for optimization of high-risk patients? What is its potential benefit?**

The use of pulmonary artery catheters in patients with IHD has not been shown to improve outcome; thus it should be restricted to a very small number of well-selected patients whose presentation is unstable and who have multiple comorbid conditions. When used, the pulmonary artery occlusion (wedge) pressure gives an estimation of the left ventricular end-diastolic pressure, which is a useful guide for optimizing intravascular fluid therapy. Sudden increases in the wedge pressure may indicate acute left ventricular dysfunction caused by ischemia. See Chapter 26.

## SUGGESTED READINGS

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# HEART FAILURE

Tamas Seres, MD, PhD

## 1. What is heart failure?

Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. The cardinal manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary congestion and peripheral edema. Some patients have exercise intolerance but little evidence of fluid retention, whereas others complain primarily of edema and report few symptoms of dyspnea or fatigue. Because not all patients have volume overload at the time of initial or subsequent evaluation, the term *heart failure* is preferred over the older term *congestive heart failure*.

## 2. Name the causes of heart failure.

The most common causes of HF in the United States are coronary artery disease, systemic hypertension, dilated cardiomyopathy, and valvular heart disease (Table 34-1).

TABLE 34-1. CAUSES OF HEART FAILURE CONDITIONS

### Mechanical abnormalities

Pressure overload

Aortic stenosis, systemic hypertension, pulmonary hypertension

Volume overload

Valvular regurgitation, anemia, thyrotoxicosis, circulatory shunts

Restriction of ventricular filling

Mitral stenosis, constrictive pericarditis, left ventricular hypertrophy

### Myocardial disease

Primary

Hypertrophic, restrictive, or dilated cardiomyopathies

Secondary

Coronary artery disease and ischemic cardiomyopathy

Alcoholism, thyroid disorders, pheochromocytoma, uremic cardiomyopathy

Bacterial, viral, parasitic, and mycotic myocarditis

Drugs: doxorubicin, heroin, and cocaine

Metals: iron overload, lead or cobalt poisoning

Connective tissue diseases: rheumatoid disease, lupus erythematosus, scleroderma

Neurologic diseases: muscular or myotonic dystrophy

Inherited diseases: glycogen storage diseases, mucopolysaccharidoses

Other diseases: amyloidosis, leukemia, postradiation therapy

### 3. Describe the classification of heart failure.

- **Stage A:** Patients with coronary artery disease, hypertension, or diabetes mellitus who do not yet demonstrate impaired left ventricular (LV) function, LV hypertrophy, or geometric chamber distortion
- **Stage B:** Patients who are asymptomatic but demonstrate LV hypertrophy, geometric chamber distortion, and/or impaired LV systolic or diastolic function
- **Stage C:** Patients with current or past symptoms of HF associated with underlying structural heart disease
- **Stage D:** Patients with HF refractory to medical therapy that might be eligible for specialized advanced treatment strategies such as mechanical circulatory support, procedures to facilitate fluid removal, continuous inotropic infusions, cardiac transplantation, or end-of-life care.

This classification system recognizes that there are established risk factors and structural prerequisites for the development of HF (stages A and B) and that therapeutic interventions introduced even before the appearance of LV dysfunction or symptoms can reduce the morbidity and mortality of HF.

### 4. How is the severity of heart failure classified?

Typically the status of patients with heart failure can be classified on the basis of symptoms, impairment of lifestyle, or severity of cardiac dysfunction. The New York Heart Association (NYHA) classification is used to assess symptomatic limitations of heart failure and response to therapy:

- **Class I:** Ordinary physical activity does not cause symptoms. Dyspnea occurs with strenuous or prolonged exertion at work or with recreation.
- **Class II:** Ordinary physical activity results in symptoms. Dyspnea is occurring while walking or climbing stairs rapidly or walking uphill. Walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace results in symptoms.
- **Class III:** Less than ordinary activity results in symptoms. Dyspnea occurs with walking one to two blocks on the level or climbing one flight of stairs at a normal pace.
- **Class IV:** Dyspnea occurs at low level of physical activity or at rest.

The NYHA classification describes the functional status of patients with stages C or D heart failure. The severity of symptoms characteristically fluctuates even in the absence of changes in medications, and changes in medications can have either favorable or adverse effects on functional capacity in the absence of measurable changes in ventricular function. Some patients may demonstrate remarkable recovery associated with improvement in structural and functional abnormalities. Usually sustained improvement is associated with drug therapy, and that therapy should be continued indefinitely.

### 5. What major alterations in the heart occur in patients with heart failure?

LV dysfunction begins with some injury to, or stress on, the myocardium and is generally a progressive process. The principal manifestation of such progression is a change in the geometry and structure of the left ventricle such that the chamber dilates and/or hypertrophies and becomes more spherical—a process referred to as cardiac remodeling. Specific patterns of ventricular remodeling occur in response to the imposed augmentation in workload. With pressure overload, the increased wall tension during systole initiates parallel addition of new myofibrils, causing wall thickening and concentric hypertrophy. With volume overload the wall tension increases during diastole, initiating series addition of new sarcomeres, resulting in chamber enlargement and eccentric hypertrophy. Ventricular dilation allows the chamber to eject an adequate stroke volume with less muscle shortening, but wall stress is increased as described by the Laplace relationship:

$$\text{Wall tension} = P \times R/2h$$

where  $P$  = intracavity pressure,  $R$  = the radius of the chamber, and  $h$  = the thickness of the chamber wall.

Increasing wall tension requires higher oxygen demand for the same performance. Myocardial hypertrophy with increasing wall thickness allows the heart to overcome pressure overload with decreased wall tension.

#### 6. What is the Frank-Starling law?

The Frank-Starling law states that the force or tension developed in a muscle fiber depends on the extent to which the fiber is stretched. In a clinical situation, when increased quantities of blood flow into the heart (increasing preload), the walls of the heart stretch. The cardiac muscle then contracts with increased force and, within limits, empties the expanded chambers with increasing stroke volume. There is an optimal sarcomere length and thus an optimal fiber length from which the most forceful contraction occurs. The left ventricle normally operates at an LV end-diastolic volume with less than optimal fiber lengths. The clinical implication of this is that stroke volume increases with increasing preload until the optimal fiber length of the myocardium is reached. Increasing the preload further causes a decrease in stroke volume.

#### 7. How is cardiac output calculated? What is a normal cardiac output and index?

Cardiac output (CO) is the amount of blood that the heart can pump during 1 minute. The main determinants of CO:

$$CO = SV \times HR$$

where CO = arterial pressure/ total peripheral resistance, SV = stroke volume and HR = heart rate.

CO varies widely with the level of activity of the body. The average value for resting adults is about 5 L/min. For women this value is 10% to 20% less. CO increases in proportion to the surface area of the body. To compare the CO of different-size people to each other, the term of *cardiac index* (CI) was introduced, which is the CO per square meter of body surface area. The normal average CI for adults is about 3 L/min/m<sup>2</sup>. There are definite limits to the amount of blood the heart can pump. The normal heart, functioning without any excess nervous stimulation, can pump an amount of venous return up to about 2.5 times the normal venous return, which is about 13 L/min CO. Nervous stimulation increases HR and contractility. These two effects can raise the CO up to 25 L/min.

#### 8. What is the connection between exercise and cardiac output?

Oxygen delivery is the product of CO and arterial blood oxygen content. Exercise increases the oxygen consumption of the body. This increased oxygen demand is covered by increasing CO. Heart failure results in a mismatch between tissue oxygen consumption and tissue perfusion based on the generated CO at a certain exercise level. The mismatch creates tissue hypoxemia, acidosis, and the inability to hold the exercise at the level at which the mismatch occurs.

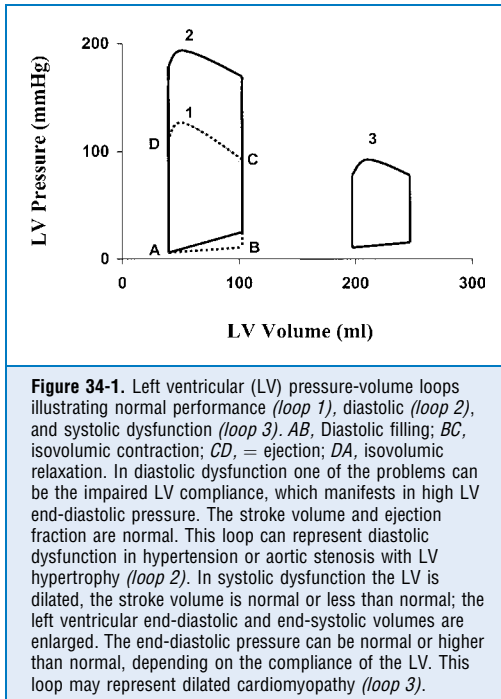
#### 9. What is systolic dysfunction?

The symptoms and signs of heart failure can be caused by either an abnormality in systolic function that leads to diminished ejection fraction (EF) or an abnormality in diastolic function that leads to altered ventricular filling.

Systolic dysfunction leads to decreased ejection of blood from the left ventricle. The EF is diminished, the end-systolic and end-diastolic volume are enlarged, and the left ventricle is dilated. The stroke volume can be normal, but it is generated by a dilated ventricle with higher wall tension and oxygen consumption. In this pathologic condition the left ventricle has less reserve capacity to overcome pressure or volume load, which manifests in decreased exercise capacity (Figure 34-1, Loop 3).

#### 10. What is diastolic dysfunction?

Diastolic dysfunction can occur with normal LV EF in many patients. Impaired LV relaxation or compliance or both are the major characteristic features of LV diastolic dysfunction. Early diastolic filling depends on the rapidity of ventricular relaxation, characterized by an



energy-dependent reuptake of calcium from the cytosol into the sarcoplasmic reticulum of the myocytes. Late diastolic filling (atrial contraction) depends on LV compliance, which is the ratio of change in ventricular volume to change in ventricular diastolic pressure. In diastolic dysfunction the size of the LV cavity can be normal but is ischemia, myocardial hypertrophy, pericardial constriction, fibrosis, or myocardial diseases alter the diastolic filling process. Systolic dysfunction with dilated left ventricle and high LV end-diastolic pressure accompanies significant diastolic dysfunction because of decreased LV relaxation and compliance (see [Figure 34-1](#), Loop 2).

#### 11. Do the neurohumoral responses in heart failure have therapeutic significance?

Although several factors can accelerate the process of LV remodeling, there is substantial evidence that the activation of endogenous neurohumoral systems plays an important role in cardiac remodeling and thereby in the progression of HF. Patients with HF have elevated circulating or tissue levels of norepinephrine, angiotensin II, aldosterone, endothelin, vasopressin, and cytokines, which can adversely affect the structure and function of the heart. These neurohumoral factors not only increase the hemodynamic stresses on the ventricle by causing sodium retention and peripheral vasoconstriction but may also exert direct toxic effects on cardiac cells and stimulate myocardial fibrosis, which can further alter the architecture and impair the performance of the failing heart.

$\beta$ -Blockers and angiotensin-converting enzyme inhibitors (ACEIs) are cornerstones in the management of heart failure because they attenuate the deleterious effects of the neurohumoral mediators on the performance of the heart.



**12. What are the presenting symptoms of heart failure?**

Exertional dyspnea and fatigue are most often the primary complaints. Paroxysmal nocturnal dyspnea, nocturia, coughing, wheezing, right upper quadrant pain, anorexia, and nausea and vomiting also may be complaints. Although HF is generally regarded as a hemodynamic disorder, many studies have indicated that there is a poor relation between measures of cardiac performance and the symptoms produced by the disease. Patients with a very low EF may be asymptomatic (stage B), whereas patients with preserved LVEF may have severe disability (stage C). The apparent discordance between EF and the degree of functional impairment is not well understood but may be explained in part by alterations in ventricular distensibility, valvular regurgitation, pericardial restraint, cardiac rhythm, conduction abnormalities, and right ventricular function. In addition, in ambulatory patients many noncardiac factors may contribute substantially to exercise intolerance. These factors include but are not limited to changes in peripheral vascular function, skeletal muscle physiology, pulmonary dynamics, neurohumoral and reflex autonomic activity, and renal sodium handling.

**13. What physical signs suggest heart failure?**

Cardiac palpation may reveal an expanded impulse area (ventricular dilation) or a forceful sustained impulse with LV hypertrophy. Auscultation reveals a gallop rhythm with  $S_3$  or  $S_4$  secondary to impaired LV filling or forceful atrial contraction, respectively. Murmurs of valvular diseases should be looked for. Severe failure may result in cyanosis.

Pulmonary examination often reveals rales located most prominently over the lung bases. Decreased breath sounds secondary to pleural effusions occur more often in patients with chronic heart failure.

Jugular venous distention  $>4$  cm above the sternal angle with the patient recumbent at a 45-degree angle is considered abnormal.

**KEY POINTS: HEART FAILURE**

1. The symptoms and signs of heart failure can be caused by either an abnormality in systolic function that leads to a diminished ejection fraction or an abnormality in diastolic function that leads to a defect in ventricular filling.
2. Patients in decompensated heart failure are not candidates for elective procedures and require a few days to optimize cardiac performance.
3. In emergent circumstances invasive monitoring (arterial line, pulmonary artery catheter, and transesophageal echocardiography) is indicated to guide fluid therapy and assess response to anesthetic agents and inotropic or vasodilator therapy.
4. Patients with decreased myocardial reserve are more sensitive to the cardiovascular depressant effects caused by anesthetic agents, but careful administration with close monitoring of hemodynamic responses can be accomplished with most agents.

**14. What laboratory studies are useful in evaluating the patient with heart failure?**

The posteroanterior and lateral chest radiograph may detect cardiomegaly or evidence of pulmonary vascular congestion, including perihilar engorgement of the pulmonary veins, cephalization of the pulmonary vascular markings, or pleural effusions.

The electrocardiogram is often nonspecific, but ventricular or supraventricular dysrhythmias; conduction abnormalities; and signs of myocardial hypertrophy, ischemia, or infarction are present frequently.

Echocardiography characterizes chamber size, wall motion, valvular function, and LV wall thickness. Stroke volume can be measured using Doppler methods. EF can be calculated by

measuring the end-diastolic and end-systolic volumes. Diastolic function can be evaluated by studying the flow pattern through the mitral valve and the left upper pulmonary vein using Doppler technique. Radionuclide angiography provides a fairly reproducible and accurate assessment of left and right ventricular ejection fraction.

Serum electrolytes, arterial blood gases, liver-function tests (LFTs), and blood cell counts are frequently evaluated. Many patients with heart failure are hyponatremic from activation of the vasopressin system or from the treatment with ACEI. Treatment with diuretics may lead to hypokalemia and hypomagnesemia. Some degree of prerenal azotemia, hypocalcemia, and hypophosphatemia is often present. Hepatic congestion may result in elevated bilirubin levels and elevated LFTs. Elevated brain natriuretic peptide levels may help in suspected diagnosis of HF or trigger consideration of HF when the diagnosis is unknown but should not be used in isolation to confirm or exclude the presence of HF.

## 15. What treatment strategies are used in the different stages of heart failure?

### ■ Stage A: Patients at high risk for developing HF

In patients at high risk for developing HF, systolic and diastolic hypertension, lipid disorders, thyroid disorders, and diabetes mellitus should be controlled. Patients should be counseled to avoid smoking, excessive alcohol consumption, and illicit drug use that may increase the risk of HF. Patients who have known atherosclerotic vascular disease should be followed for secondary prevention. ACEIs or angiotensin II receptor blockers can be useful to prevent HF in patients who have a history of atherosclerotic vascular disease, diabetes mellitus, or hypertension.

### ■ Stage B: Patients with cardiac structural abnormalities or remodeling who have not developed HF symptoms

All recommendations for stage A should apply to patients with cardiac structural abnormalities who have not developed symptoms.  $\beta$ -Blockers and ACEIs should be used in all patients with a recent or remote history of myocardial infarction (MI) regardless of EF or presence of HF.  $\beta$ -Blockers and ACEIs are indicated in all patients without a history of MI who have a reduced LVEF with no HF symptoms.

### ■ Stage C: Patients with current or prior symptoms of HF

#### *Patients with Reduced LVEF:*

Measures listed as recommendations for patients in stages A and B are also appropriate for patients in stage C. Diuretics and salt restriction are indicated in patients with current or prior symptoms of HF and reduced LVEF who have evidence of fluid retention. ACEIs and/or  $\beta$ -blockers (using one of the three proven to reduce mortality [i.e., bisoprolol, carvediol, and sustained release metoprolol succinate]) are recommended for all patients with current or prior symptoms of HF and reduced LVEF unless contraindicated. Addition of an aldosterone antagonist is reasonable in selected patients with moderately severe-to-severe symptoms of HF and reduced LVEF. Implantable cardioverter-defibrillator therapy and cardiac resynchronization therapy can be instituted in high-risk patients.

#### ■ *Patients with Normal LVEF:*

Systolic and diastolic hypertension should be controlled in patients with HF and normal LVEF. Ventricular rate should be controlled in patients with atrial fibrillation. Diuretics should be used to control pulmonary congestion and peripheral edema. Coronary revascularization is reasonable in patients with coronary artery disease in whom symptomatic or demonstrable myocardial ischemia is judged to be having an adverse effect on cardiac function.

### ■ Stage D: Patients with refractory end-stage heart failure

Such patients characteristically have symptoms at rest or on minimal exertion. They cannot perform most activities of daily living, frequently have evidence of cardiac cachexia, and typically require repeated and/or prolonged hospitalizations for intensive management. A critical step in the successful management is the recognition and meticulous control of fluid retention. These individuals represent the most advanced stage of HF and should

be considered for specialized treatment strategies such as mechanical circulatory support, continuous intravenous positive inotropic therapy, referral for cardiac transplantation, or hospice care.

**16. What should be considered in preparing to conduct an anesthetic on patients with heart failure?**

- Patients with stages A or B heart failure have good functional status; thus they can go for surgery after routine preoperative evaluation.
- In stage C heart failure the NYHA functional status should be evaluated, and signs of decompensated HF should be checked. Patients with dyspnea, worsening dyspnea, or other change in clinical status are reasonable candidates to undergo preoperative noninvasive evaluation of LV function and postpone elective surgery until compensation.
- Stage D heart failure represents patients in NYHA class IV who are refractory to standard medical therapy. They can be on intravenous inotropic medications or assist device therapy and need special anesthetic management for noncardiac surgery.

**17. How would you manage a patient with decompensated heart failure?**

In general patients in decompensated HF are not candidates for elective procedures. Waiting a few days to optimize cardiac performance is indicated. In emergent circumstances invasive monitoring (arterial line, pulmonary artery catheter) is indicated to guide fluid therapy and assess response to anesthetic agents and inotropic or vasodilator therapy. Transesophageal echocardiography is extremely helpful to evaluate the effect of the fluid therapy on the heart, measure stroke volume and CO, and evaluate systolic and diastolic function.

**18. Which anesthetic agents can be used in decompensated heart failure?**

Avoiding myocardial depression still remains the goal of anesthetic management. The barbiturates and propofol generally produce the most profound depression of cardiac function and blood pressure when used for induction of general anesthesia. Etomidate produces few aberrations in cardiovascular status, although hypotension may occur in the setting of hypovolemia. Ketamine administration may result in elevated CO and blood pressure secondary to increased sympathetic activity. However, in patients with increased sympathetic activation from decompensated HF, ketamine acts as a negative inotropic agent and can cause severe hypotension and cardiac failure. Cardiovascular side effects (decreasing blood pressure) are mild when benzodiazepines are given in sedative doses but become moderate when induction doses are given or when administered in combination with opioids. All of the potent volatile anesthetic agents are myocardial depressants, but low doses are usually well tolerated. For the patient with severely compromised myocardial function, narcotic-based anesthesia with or without low-dose volatile agent is useful. Remifentanyl, a short-acting opioid, can be well suited especially to short surgical procedures.

**19. Is regional anesthesia contraindicated in patients with heart failure?**

No. Regional anesthesia, when prudently administered, is an acceptable anesthetic technique. In fact, modest afterload reduction may enhance CO. Continuous regional techniques (spinal or epidural) are preferable because they are associated with gradual loss of sympathetic tone, which may be treated with titration of fluids and vasoactive drugs. Invasive monitoring is necessary during regional anesthesia. An arterial line is important to keep the blood pressure in an appropriate range, and pulmonary artery catheter can be helpful in selected cases.

**20. How would you support the heart in decompensated heart failure during anesthesia?**

Patients with HF often require circulatory support intraoperatively and after surgery. After optimization of preload and afterload, inotropic drugs such as dopamine or dobutamine have been shown to be effective in low output states and produce modest changes in systemic

vascular resistance at lower doses. In severe failure more potent drugs such as epinephrine may be required. Phosphodiesterase III inhibitors such as milrinone, with inotropic and vasodilating properties, may improve hemodynamic performance. Stroke volume is inversely related to afterload in the failing ventricle, and the reduction of LV afterload with vasodilating drugs such as nitroprusside and nesiritide is also effective to increase CO.

## WEBSITE



Systolic and diastolic dysfunction

<http://www.uptodate.com>

## SUGGESTED READINGS

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# VALVULAR HEART DISEASE

*Tamas Seres, MD, PhD*

## 1. Discuss the basic pathophysiology of valvular heart diseases.

Valvular heart diseases cause chronic volume or pressure overload, and each evokes a characteristic ventricular response called ventricular hypertrophy. Ventricular hypertrophy is defined as increased left ventricular (LV) mass. Pressure overload produces concentric ventricular hypertrophy with an increase in ventricular wall thickness with a cardiac chamber of normal size. Volume overload leads to eccentric hypertrophy with normal wall thickness and dilated cardiac chamber.

## 2. Describe common findings of the history and physical examination in patients with valvular heart disease.

Most systolic heart murmurs do not signify cardiac disease, and many are related to physiologic increases in blood flow velocity. Diastolic murmurs virtually always represent pathologic conditions and require further cardiac evaluation, as do most continuous murmurs.

A history of rheumatic fever, intravenous drug abuse, embolization in different organs, genetic diseases such as Marfan syndrome, heart surgery in childhood, or heart murmur should alert the examiner to the possibility of valvular heart disease. Exercise tolerance is frequently decreased; patients may exhibit signs and symptoms of heart failure, including dyspnea, orthopnea, fatigue, pulmonary rales, jugular venous congestion, hepatic congestion, and dependent edema. Angina may occur in patients with a hypertrophied left ventricle, and atrial fibrillation frequently accompanies enlargement of the atria.

## 3. Which tests are useful in the evaluation of valvular heart disease?

Echocardiography with Doppler technology is a fundamental diagnostic method in evaluation of valvular heart diseases. The size and function of heart chambers and the pressure gradients at the valves and the valve areas can be measured, and the severity of the diseases can be determined.

Echocardiography is recommended for:

- Asymptomatic patients with diastolic murmurs, continuous murmurs, holosystolic murmurs, grade 3 or louder mid-peaking systolic murmurs, late systolic murmurs, murmurs associated with ejection clicks, or murmurs that radiate to the neck or back.
- Patients with heart murmurs and symptoms or signs of heart failure, myocardial ischemia/infarction, syncope, thromboembolism, infective endocarditis, or other clinical evidence of structural heart disease.

An electrocardiogram should be examined for evidence of ischemia, arrhythmias, atrial enlargement, and ventricular hypertrophy. Chest radiograph may show enlargement of cardiac chambers, suggest pulmonary hypertension, or reveal pulmonary edema and pleural effusions. Cardiac catheterization is used in the evaluation of such patients before surgery, mostly for diagnosing coronary artery disease. This method allows measurement of pressures in various heart chambers and pressure gradients across different valves.

## 4. How is echocardiography helpful in anesthesia management?

Transesophageal echocardiography can be used in the operating room during the surgical management of valvular diseases. The severity of the valvular disease and accompanying

structural or functional changes can be reevaluated. Evaluation of valve repair or function of artificial valves is an important part of the patient management. Systolic and diastolic function of the left and right ventricle before and after cardiopulmonary bypass can be assessed, and appropriate management can be planned and followed.

### 5. Which other monitors aid the anesthesiologist in the perioperative period?

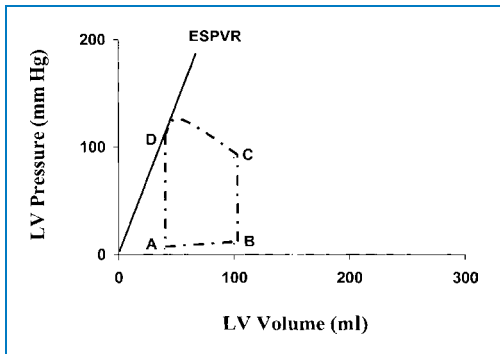
Besides standard American Society of Anesthesiologists (ASA) monitors, an arterial catheter provides beat-to-beat blood pressure measurement and continuous access to the bloodstream for sampling. Pulmonary artery catheters enable the anesthetist to measure cardiac output (CO), mixed venous saturation, central venous and pulmonary artery pressures, and pulmonary capillary wedge pressure, which are important indexes of right and LV function and filling and are useful for guiding intravenous fluid and inotropic therapy.

### 6. What is a pressure-volume loop?

A pressure-volume loop plots LV pressure against volume through one complete cardiac cycle. Each valvular lesion has a unique profile that suggests compensatory physiologic changes by the left ventricle.

### 7. How does a normal pressure-volume loop appear?

The AB segment is ventricular filling, BC is isovolumic contraction, CD is ejection, and DA is isovolumic relaxation. D point represents the aortic valve closing, A the mitral valve (MV) opening, B the MV closing, and C the aortic valve opening. Stroke volume through the aortic valve is the distance between C and D points. End-systolic volume can be measured at the D point, and end-diastolic volume can be measured at the B point. The end-systolic pressure-volume relationship slope is a measure of contractility. A horizontal-clockwise shift of the slope represents a decrease in contractility (Figure 35-1).



**Figure 35-1.** Pressure-volume loop in normal heart performance. *AB*, Diastolic filling; *BC*, isovolumic contraction; *CD*, ejection; *DA*, isovolumic relaxation. *A*, Mitral valve opening; *B*, mitral valve closing; *C*, aortic valve opening; *D*, aortic valve closing. The end-systolic pressure volume relationship curve (*ESPVR*) is a load-independent index of myocardial contractility. If the contractility is increasing, the *ESPVR* curve is moving counterclockwise. The pressure-volume loop is an excellent tool to characterize the performance of the heart in different pathologic conditions. *LV*, Left ventricular.

### 8. Discuss the pathophysiology of aortic stenosis.

Aortic stenosis (AS) is classified as valvular, subvalvular, or supra-valvular obstruction of the LV outflow tract. Concentric hypertrophy (thickened ventricular wall with normal chamber size) develops in response to the increased intraventricular systolic pressure and wall tension necessary to maintain forward flow. Ventricular relaxation decreases, causing diastolic dysfunction. Decreasing LV compliance accompanies elevated LV end-diastolic pressure. Contractility and ejection fraction are usually maintained until late in the disease process. Atrial contraction may account for up to 40% of ventricular filling (normally 20%). In developing countries rheumatic valve disease is still the most common cause of AS. In North America and Europe AS is primarily caused by calcification of a native trileaflet or a congenital bicuspid valve. Patients often present with angina, syncope, or congestive heart failure. Angina with

exertion can occur in the absence of coronary artery disease because the thickened myocardium is susceptible to ischemia and the elevated LV end-diastolic pressure reduces coronary perfusion pressure. Life expectancy with symptoms of angina is about 5 years. Once syncope appears, the average life expectancy is 3 to 4 years. Once congestive heart failure occurs, the average life expectancy is 1 to 2 years.

### 9. How can the severity of aortic stenosis be characterized by echocardiography?

AS severity is graded on the basis of a variety of hemodynamic and natural history data using definitions of valve area, mean pressure gradient, and aortic jet velocity (Table 35-1).

TABLE 35-1. SEVERITY OF AORTIC STENOSIS		
	Mild	Severe
Aortic valve area (cm <sup>2</sup> )	>1.5	<1
Mean aortic valve pressure gradient (mm Hg)	<25	>40
Aortic jet velocity (m/s)	<3	>4

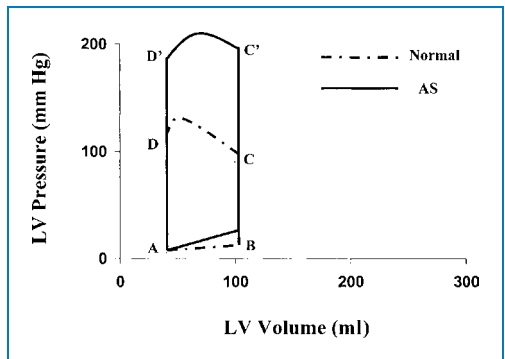
### 10. What is the indication for aortic valve replacement in aortic stenosis?

Based on the 2006 guidelines from the American College of Cardiology/American Heart Association (ACC/AHA), aortic valve replacement is indicated in the following patients:

- Symptomatic patients with severe AS
- Patients with severe AS undergoing coronary artery bypass graft surgery (CABG)
- Patients with severe AS undergoing surgery on the aorta or other heart valves
- Patients with severe AS and LV systolic dysfunction (ejection fraction less than 50%)
- It is reasonable for patients with moderate AS undergoing CABG or surgery on the aorta or other heart valves.

### 11. How are the compensatory changes in the left ventricle represented by a pressure-volume loop?

Because of the AS, the left ventricle is working with higher intraventricular pressures to generate a normal stroke volume. The higher systolic wall tension initiates myocardial thickening and LV hypertrophy (LVH). The hypertrophied left ventricle has increased contractility to accomplish the pressure work (Figure 35-2). LVH decreases the wall tension during systole, improving the relationship of systolic work to oxygen demand. As the AS increases, LV systolic pressure increases to the level at which LVH cannot normalize the wall tension. At this point the heart starts dilating, resulting in systolic dysfunction and decreasing CO.



**Figure 35-2.** Pressure-volume loop in aortic stenosis (AS) compared to the normal loop. To generate normal stroke volume the intraventricular pressure is high because of the pressure gradient at the aortic valve level. The end-diastolic pressure is higher than normal in cases when left ventricular (LV) hypertrophy alters LV compliance. Myocardial contractility is higher than normal.

## 12. What are the hemodynamic goals in the anesthetic management of patients with aortic stenosis?

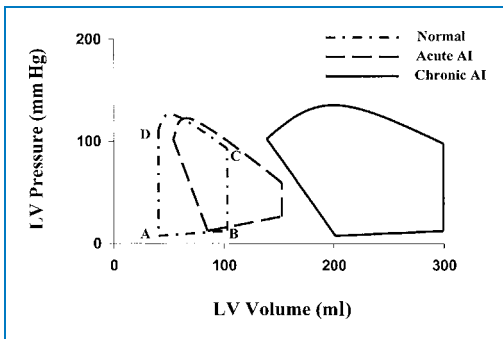
Patients must have adequate intravascular volume to fill the noncompliant ventricle. Contractility should be maintained to overcome the high pressure gradient across the aortic valve. Reductions in blood pressure or peripheral resistance do not decrease LV afterload because of the fixed valvular resistance, but they do decrease coronary perfusion, with a great risk for development of subendocardial ischemia and sudden death. Extremes of heart rate should be avoided. Bradycardia leads to a decrease in CO in patients with relatively fixed stroke volume. Tachycardia may produce ischemia with a limited diastolic time for coronary perfusion. Maintenance of sinus rhythm is imperative because of the importance of atrial contraction in LV filling.

## 13. Discuss the management of the patients with aortic stenosis after aortic valve replacement.

After surgery, LV end-diastolic pressure decreases and stroke volume increases, but the hypertrophied LV still may require an elevated preload to function adequately. Depressed myocardial function may suggest inadequate myocardial protection during the surgery due to the difficulty perfusing the hypertrophied left ventricle. Inotropic agents (dopamine, dobutamine, and epinephrine) can improve the LV performance in this situation.

## 14. Discuss the pathophysiology of aortic insufficiency.

In chronic aortic insufficiency (AI) there is an LV diastolic volume overload because part of the stroke volume regurgitates across the incompetent aortic valve during diastole. Patients have large end-diastolic and stroke volumes. The volume load generates high wall tension in diastole, initiating eccentric hypertrophy (dilated left ventricle with normal or thickened wall). Increasing regurgitant orifice area, slow heart rate (relatively more time spent in diastole) and increased systemic vascular resistance increase the amount of regurgitant flow. Compliance and stroke volume may be markedly increased in chronic AI, whereas contractility gradually diminishes (Figure 35-3). AI can be caused by diseased valve leaflets or enlargement of the



**Figure 35-3.** Pressure-volume loops in aortic regurgitation compared to the normal loop. In acute aortic insufficiency (AI) the end-diastolic and end-systolic volume is increasing. The stroke volume can be increased, normal or decreased, depending on the severity of AI. The left ventricular (LV) volume is increasing during the isovolumic relaxation period (DA segment). The end diastolic pressure (AB segment, B point) is high. Contractility is decreased because the myocardium is overstretched. In chronic AI the end-diastolic, end-systolic, and stroke volumes are enlarged. Cardiac output is normal, and the contractility is decreased. The LV volume is increasing during the isovolumic relaxation period also (DA segment), but the end diastolic pressure (AB segment, B point) is normal; thus the heart has diastolic reserve to accommodate to limited volume or pressure load. LV, Left ventricular.



aortic root. In the developing world the most common cause of AI is rheumatic heart disease. In developed countries AI is most often caused by aortic root dilation, congenital bicuspid aortic valve, or infective endocarditis. Causes of acute AI are infective endocarditis, aortic dissection (Marfan syndrome), and AI after aortic balloon valvotomy or a failed surgical valve repair.

Ideally patients with chronic AI should have valve replacement surgery before the onset of irreversible myocardial damage. In acute AI the left ventricle is subjected to rapid, massive volume overload with elevated end-diastolic pressure. Hypotension and pulmonary edema may necessitate emergent valvular replacement (see [Figure 35-3](#)).

### 15. What parameters can be used in echocardiography to characterize the severity of aortic insufficiency?

See [Table 35-2](#).

	Mild	Severe
Color Doppler jet width (% of LVOT diameter)	<25	>65
Color Doppler vena contracta (cm)	<0.3	>0.6
Regurgitant volume (ml)	<30	≥60
Regurgitant fraction (%)	<30	≥50
Regurgitant orifice area (cm <sup>2</sup> )	<0.1	≥0.3
Left ventricle size	Normal	Increased

*LVOT*, Left ventricular outflow tract.

### 16. What is the indication for aortic valve replacement in aortic stenosis?

Based on the ACC/AHA 2006 guidelines, aortic valve replacement is indicated in the following patients:

- Symptomatic patients with severe AI irrespective of LV systolic function
- Asymptomatic patients with chronic severe AI and LV systolic dysfunction (ejection fraction 50% or less) at rest
- Asymptomatic patients with chronic severe AI while undergoing CABG or surgery on the aorta or other heart valves
- It is reasonable for asymptomatic patients with severe AI with normal LV systolic function (ejection fraction greater than 50%) but with severe LV dilation (end-diastolic dimension greater than 75 mm or end-systolic dimension greater than 55 mm).

### 17. What does the pressure-volume loop look like in acute and chronic aortic insufficiency?

In acute AI the end-diastolic and end-systolic volume is increasing. The stroke volume can be increased, normal, or decreased, depending on the severity of AI. The LV volume is increasing during the isovolumic relaxation period. The end-diastolic pressure is high. End-diastolic pressure >25 to 30 mm Hg manifests as pulmonary edema. Contractility is decreased because the myocardium is overstretched. There is no diastolic reserve, thus the heart cannot increase the stroke volume with increasing preload or afterload (see [Figure 35-3](#)).

In chronic AI the end-diastolic, end-systolic and stroke volumes are enlarged. Cardiac output is normal, although the contractility is decreased. Despite the enlarged LV end-diastolic volume, the end-diastolic pressure is normal; thus the heart has diastolic reserve to increase the stroke volume with increasing preload or afterload (see [Figure 35-3](#)).

**18. What are the hemodynamic goals in the anesthetic management of patients with aortic insufficiency?**

In acute AI the goal is to achieve the lowest tolerable systemic blood pressure to increase the stroke volume and CO. Appropriate preload is necessary for maintenance of forward flow. Modest tachycardia reduces ventricular volumes and limits the time available for regurgitation. Contractility must be maintained;  $\beta$ -adrenergic agonists may be used if necessary. Dobutamine can be ideal because it does not increase the afterload. Afterload reduction augments forward flow, but additional intravascular volume may be necessary to maintain preload. Increases in afterload result in increasing LV end-diastolic pressure and pulmonary hypertension.

**19. Discuss the hemodynamic changes in patients with aortic insufficiency after aortic valve replacement.**

After surgery LV end-diastolic volume and pressure decrease. Preload should be increased by volume administration to maintain filling of the dilated left ventricle. The decreased myocardial contractility may necessitate inotropic or intra-aortic balloon pump support.

**20. What is the pathophysiology of mitral stenosis?**

As the orifice of the MV narrows, the left atrium experiences pressure overload. In contrast to other valvular lesions, the left ventricle shows relative volume underload because of the obstruction of forward blood flow from the atrium. The elevated atrial pressure may be transmitted to the pulmonary circuit and thus lead to pulmonary hypertension and right heart failure. The overdistended atrium is susceptible to fibrillation with resultant loss of atrial systole, leading to reduced ventricular filling and CO. Symptoms (fatigue, dyspnea on exertion, hemoptysis) may be worsened when increased CO is needed (e.g., with pregnancy, illness, anemia, and exercise). Blood stasis in the left atrium is a risk for thrombus formation and systemic embolization. MS is usually secondary to rheumatic disease (80% to 90%), infective endocarditis (3.3%), and mitral annular calcification (2.7%). Critical stenosis of the valve occurs 10 to 20 years after the initial rheumatic disease.

**21. What parameters can be used in echocardiography to characterize the severity of mitral stenosis?**

See Table 35-3.

TABLE 35-3. SEVERITY OF MITRAL STENOSIS		
	Mild	Severe
Mean mitral valve pressure gradient (mm Hg)	<5	>10
Valve area (cm <sup>2</sup> )	>1.5	<1
Pulmonary artery systolic pressure (mm Hg)	<30	>50

**22. What is the indication for mitral valve replacement in mitral stenosis?**

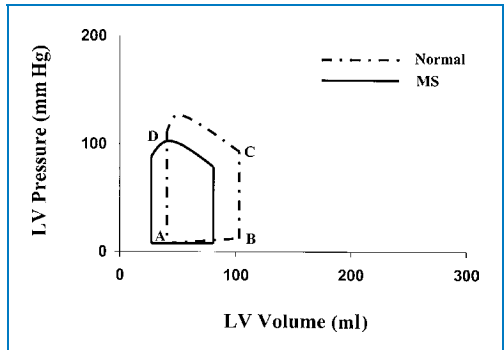
Based on the ACC/AHA 2006 guidelines, MV surgery is indicated in the following patients:

- MV surgery (repair if possible) is indicated in patients with symptomatic moderate or severe MS (NYHA functional class III–IV) when:
  - Percutaneous mitral balloon valvotomy is unavailable.
  - Percutaneous mitral balloon valvotomy is contraindicated because of left atrial thrombus despite anticoagulation or because concomitant moderate-to-severe mitral regurgitation (MR) is present.

- The valve morphology is not favorable for percutaneous mitral balloon valvotomy in a patient with acceptable operative risk.
- Symptomatic patients with moderate-to-severe MS who also have moderate-to-severe MR should receive MV replacement unless valve repair is possible at the time of surgery.
- MV replacement is reasonable for patients with severe MS and severe pulmonary hypertension (pulmonary artery systolic pressure greater than 60 mm Hg) with NYHA functional class I–II symptoms who are not considered candidates for percutaneous mitral balloon valvotomy or surgical MV repair.

**23. How is the pressure-volume loop changed from normal in mitral stenosis?**

The end-diastolic, end-systolic, and stroke volume are small because of the limited flow into the LV. The LV generates low blood pressure. The contractility is decreased because of chronic underfilling of the left ventricle (Figure 35-4).



**Figure 35-4.** Pressure-volume loop in mitral stenosis compared to the normal loop. In mitral stenosis (*MS*) the end-diastolic, end-systolic, and stroke volume is small. The left ventricle (*LV*) generates low blood pressure. The contractility is decreasing due to the chronic underfilling of the LV.

**24. What are the anesthetic considerations in mitral stenosis?**

The intravascular volume must be adequate to maintain flow across the stenotic valve. A slower heart rate allows more time for the blood to flow across the valve, increasing ventricular filling. Sinus rhythm should be maintained because atrial contraction contributes about 30% of the stroke volume. Afterload should be kept in the normal range. Chronic underfilling of the left ventricle leads to depressed ventricular contractility even after the restoration of normal filling. Negative inotropic agents should be avoided. Increases in pulmonary vascular resistance may exacerbate right ventricular failure; thus hypoxemia, hypercarbia, and acidosis should be avoided. For this reason the respiratory depressant effects of preoperative medications may be particularly deleterious.

**25. Discuss the postoperative management of patients with mitral stenosis after mitral valve replacement.**

Decreases in left atrial pressure result in declines in pulmonary artery resistance and pulmonary artery pressure and increased CO. However, the LV performance can be depressed because of the chronic underfilling of the left ventricle, especially after cardiopulmonary bypass. Preload augmentation and afterload reduction should be applied to improve forward blood flow. Inotropic or intraaortic balloon pump support may be necessary to improve the systolic performance of the left ventricle.

**26. Describe the pathophysiology of mitral regurgitation.**

The causes of primary valve disease and chronic mitral regurgitation (MR) include MV prolapse, infective endocarditis, trauma, rheumatic heart disease, drugs (ergotamine, pergolide), and congenital valve cleft. The secondary causes of MR include ischemic heart disease, LV systolic dysfunction, and hypertrophic cardiomyopathy.

In chronic mitral regurgitation the left ventricle and atrium show volume overload, leading to increased LV end-diastolic volume with normal end-diastolic pressure. Left ventricular end-systolic volume is normal; thus the stroke volume is high, but part of the stroke volume escapes through the incompetent valve into the left atrium. Ejection fraction is usually high because of the low resistance against the regurgitation. An ejection fraction of 50% may indicate significant LV dysfunction. A large distensible left atrium can maintain near-normal left atrial pressure despite large regurgitant volumes. Regurgitant flow depends on regurgitant orifice size, time available for regurgitant flow (bradycardia), and transvalvular pressure gradient.

In acute MR end-diastolic volume and pressure increase; and the pulmonary circuit and right heart are subjected to sudden increases in pressure and volume, which may precipitate acute pulmonary hypertension, pulmonary edema, and right heart failure. Acute MR may occur in the setting of flailed leaflet caused by MV prolapse, infective endocarditis, or trauma. Chordae tendineae may rupture spontaneously or from trauma, infective endocarditis, or rheumatic fever. Papillary muscles may rupture because of acute myocardial infarction or trauma.

## 27. What parameters can be used in echocardiography to characterize the severity of mitral regurgitation?

See Table 35-4.

	Mild	Severe
Color Doppler jet area (cm <sup>2</sup> )	<4	>8.0
Color Doppler jet area (% of left atrium)	<20	>40
Color Doppler vena contracta (cm)	<0.3	>0.7
Regurgitant volume (ml)	<30	≥60
Regurgitant fraction (%)	<30	≥50
Regurgitant orifice area (cm <sup>2</sup> )	<0.1	≥0.3
Left atrial end ventricular size	Normal	Enlarged

## 28. What is the indication for mitral valve replacement in mitral regurgitation?

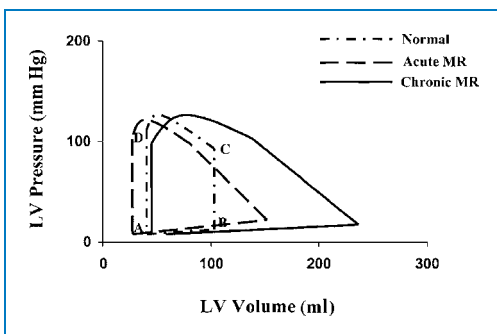
Based on the ACC/AHA 2006 guidelines, MV surgery is indicated in the following patients:

- Symptomatic patients with acute severe MR
- Symptomatic patients (NYHA functional classes II, III, or IV) with chronic severe MR
- Asymptomatic patients with chronic severe MR and mild-to-moderate LV dysfunction (ejection fraction 30% to 60%, and/or end-systolic dimension ≥40 mm but ≤55 mm)
- MV repair is recommended over MV replacement in the majority of patients with severe chronic MR who require surgery

## 29. How is the pressure-volume loop in mitral regurgitation changed from normal?

In acute MR the end-diastolic volume increases with high end-diastolic pressure. End-systolic volume is normal or decreased, stroke volume is increased, but the ejected volume into the aorta is relatively small, depending on the regurgitant volume (Figure 35-5).

In chronic MR the end-diastolic volume is increased with normal end-diastolic pressure resulting from the chronic myocardial remodeling process. The end-systolic volume is normal. The markedly increased stroke volume preserves the forward CO despite the significant regurgitation. The contractility is decreased (see Figure 35-5).



**Figure 35-5.** Pressure-volume loop in mitral regurgitation compared to the normal loop. In acute mitral regurgitation (MR) the end-diastolic volume is increasing with higher end-diastolic pressure. The end-systolic volume is either normal or less than normal because part of the stroke volume is flowing back the low-pressure left atrium during the isovolumic contraction period (*BC segment*). In chronic MR the end-diastolic volume is high with normal or slightly elevated end-diastolic pressure. The end-systolic volume is normal or bigger than normal, depending on the severity of the MR and the systolic function of the left ventricle (LV). The ejected stroke volume is sufficient to maintain adequate cardiac output. The contractility is decreased.

## KEY POINTS: VALVULAR HEART DISEASE



1. Hemodynamic goals in AS include maintaining intravascular volume, contractility, peripheral vascular resistance, and sinus rhythm while avoiding extremes in heart rate. Arrhythmias associated with hypotension require emergent cardioversion.
2. Hemodynamic goals in the patient with AI include augmenting preload, maintaining contractility, normal or elevated heart rate, and reduction of afterload.
3. Hemodynamic goals in the patient with MS include maintaining intravascular volume, afterload, sinus rhythm, and a slower heart rate. Avoid hypoxemia, hypercarbia, and acidosis because they may increase pulmonary vascular resistance. Sedative medications should be given with great care.
4. Hemodynamic goals in the patient with MR include maintaining intravascular volume, contractility, and elevated heart rate while reducing afterload. As in MS, avoid situations that will increase pulmonary vascular resistance.

### 30. What are the hemodynamic goals in anesthetic management of mitral regurgitation?

The intravascular volume should remain full to supply the dilated left ventricle. The best level of preload augmentation for a patient must be based on the clinical response to a fluid load. Bradycardia increases the regurgitant volume, decreasing the ejected volume into the aorta. Normal or slightly elevated heart rate helps to decrease the regurgitant flow volume. Dobutamine or milrinone can be administered to enhance contractility while reducing afterload. Afterload reduction augments forward flow and decreases regurgitation. As in MS, drugs and maneuvers that increase pulmonary vascular resistance must be avoided.

**31. Discuss the hemodynamic management after mitral valve repair or replacement in patient with mitral regurgitation.**

Once the valve is in place, the LV has to eject the full stroke volume into the aorta. This immediate pressure load increases LV tension and may compromise the ejection fraction. Therefore inotropic or intraaortic balloon pump support can be necessary until the left ventricle can adjust to the new hemodynamic condition. Preload should be augmented to fill up the dilated left ventricle.

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# AORTO-OCCLUSIVE DISEASE

Luke Osborne, MD

## 1. Define aortic vascular disease.

Aorto-occlusive disease is characterized by atherosclerotic changes within the aorta (usually abdominal) that extend into the iliac and femoral arteries and result in hypoperfusion of vital organs and the lower extremities. Involvement at iliac bifurcation and renal arteries is common; aneurismal changes may be found as well. Seventy percent of aortic aneurysms are infrarenal, and 30% include the renal arteries.

## 2. What risk factors and coexisting diseases are common in these patients?

Risk factors include smoking, family history, obesity, atherosclerotic disease elsewhere, advanced age and male sex. Common diseases include hypertension, ischemic heart disease, heart failure (HF), chronic obstructive pulmonary disease (COPD), diabetes mellitus, chronic renal disease, and carotid artery disease.

## 3. What is the natural progression of aortic vascular disease?

The natural history of aneurismal disease is one of continuing enlargement. Operative or endovascular repair should be undertaken when the aneurysm is 6 cm or larger. The incidence of rupture increases with size (9.4% chance of rupture within 1 year for aneurysms 5.5 to 5.9 cm, increasing to 32.5% for aneurysms 7 cm and larger).

National mortality from elective open abdominal aneurysm repair is <5%. For repair of an acutely ruptured aneurysm, perioperative mortality remains high, about 50%. Mortality with open thoracic aneurysm repair ranges from 5% to 14%. Endovascular repair has decreased mortality. The survival rate is 92% at 1 year and 67% at 5 years.

Aorto-occlusive disease results in hypoperfusion distal to the occlusion. Unlike surgery for aneurismal disease, surgery for occlusive disease should be undertaken when the patient becomes symptomatic and fails medical therapy.

## 4. Describe preoperative preparation of such patients in the presence of concurrent disease.

The goal of preoperative evaluation is to optimize any significant organ dysfunction.

- **Coronary artery disease:** This is the major cause of perioperative mortality and morbidity. Myocardial infarction occurs in 4% to 15% of patients, and HF is noted in 30% of postoperative aneurysm repairs. If the patient has an acute coronary syndrome, decompensated heart failure, severe valvular disease, or significant arrhythmias, he or she should undergo preoperative cardiac testing, including echocardiography, stress testing, and coronary angiography. Similarly coronary artery evaluation may be strongly indicated in the presence of renal insufficiency, history of HF or cerebrovascular disease, or if the patient has diabetes mellitus or cannot achieve a metabolic equivalent (MET) level of four.
- **Pulmonary:** It has been mentioned that COPD is common. Physical examination, pulmonary function testing, arterial blood gas analysis, and chest radiography may suggest the need for preoperative incentive spirometry and bronchodilator and antibiotic therapy.
- **Renal:** The incidence of postoperative renal dysfunction in elective infrarenal aorta repair is 3% and up to 30% in thoracic aorta repair. The primary cause of postoperative

renal failure is preexisting kidney disease. The degree of renal dysfunction should be characterized, and the patient adequately hydrated. Poorly controlled hypertension should be optimized. If the patient requires a contrast study before surgery, he or she should be well hydrated before dye administration and exposed to a minimum amount of contrast; repeated studies should be avoided.

- **Cerebrovascular disease:** Signs and symptoms of cerebrovascular insufficiency should be elucidated. Cerebral hypoperfusion during surgery could result in stroke. If carotid stenosis is found, endarterectomy may need to precede aortic repair. Chronically hypertensive patients also have shifts in cerebral autoregulation, and this is a second justification for preoperative management of hypertension.
- **Diabetes mellitus:** This should be well controlled.

#### 5. List the appropriate intraoperative monitors for aortic surgery.

- Standard monitors include pulse oximetry and noninvasive blood pressure and temperature monitoring. Continuous cardiac rhythm monitoring for rhythm (lead II) and ischemia (lead V<sub>5</sub>) is essential.
- Also essential are the usual anesthesia machine monitors, including capnography and delivered oxygen concentration.
- Intra-arterial monitoring rapidly detects swings in blood pressure and facilitates laboratory analysis.
- Monitoring of urine output with a Foley catheter and urimeter is essential.
- Use of central venous pressures, pulmonary artery catheters, and/or transesophageal echocardiography is appropriate when myocardial dysfunction and valvular disease are present.
- Somatosensory and motor-evoked potential can be useful if spinal cord ischemia is considered a risk.

#### 6. Discuss the physiologic implications of aortic clamping and unclamping.

Aortic cross-clamping increases left ventricular afterload. Preparation for this cross-clamping includes increasing depth of anesthesia, vasodilator therapy with nitroglycerin or sodium nitroprusside, and possibly administration of  $\alpha$ -blockers or calcium channel blockers. A decrease in renal blood flow occurs in about 90% of patients having thoracic aortic cross-clamping and in about 40% of patients having infrarenal cross-clamping. There is redistribution of renal blood flow to the cortex and a decrease in glomerular filtration. These changes persist to some degree even after cross-clamp removal. The potential for a clinically profound decrease in anterior spinal artery blood flow is more likely in thoracic aortic repair, making spinal cord ischemia a risk; and in certain cases lumbar drainage of spinal fluid has been instituted to mitigate decreases in spinal cord perfusion pressure.

Hypotension and a decrease in systemic vascular resistance are noted after unclamping. Ischemic metabolites, lactic acid, and potassium returning to the central circulation depress contractility and potentiate the hypotension.

#### 7. Review the anesthetic goals for these surgical patients.

- Provide anesthesia, analgesia, amnesia, and muscle relaxation.
- Maintain cardiac output and coronary perfusion and limit myocardial workload by controlling heart rate and afterload, especially during aortic cross-clamping.
- Aggressively replace blood loss with crystalloids, colloids, and blood and blood products when necessary. Massive blood loss will likely result in a coagulopathy that will require correction.
- Maintain oxygenation and ventilation, guided by blood gas analysis. Excessive ventilatory pressures may compromise preload.
- The best way to preserve renal function is to maintain normal intravascular volume, cardiac output, and oxygenation.



- Especially in patients with diabetes, blood glucose should be monitored and controlled. Insulin therapy not only controls hyperglycemia but prevents ketoacidosis and may improve wound healing and long-term outcome.
- Hypoperfusion of the anterior spinal artery during aortic cross-clamping or extended hypoperfusion places the patient at risk for paraplegia, especially during thoracic aorta surgery.
- Before unclamping, an intravenous bolus of fluid is wise. It may be necessary to reclamp the aorta or provide some minor degree of occlusion to allow the patient time to equilibrate and stabilize.

### 8. What can be done intraoperatively to preserve renal function?

The incidence of acute kidney injury after elective repair of infrarenal aneurysms is about 3%. But of these patients the mortality is 40%, and this incidence has not changed in decades.

The biggest predictor of postoperative renal dysfunction is preexisting renal disease. The adequacy of renal perfusion cannot be assumed by the amount of urine output since it does not correlate with postoperative renal function. That fact that urine output can be stimulated with diuretics (furosemide and mannitol) and dopamine does not ensure that renal function will be preserved into the postoperative period.

Major factors that impact postoperative renal function include preoperative renal function, the degree of aortic disease, and the duration of cross-clamping. Therefore optimizing renal function before surgery, maintaining euolemia and renal perfusion, and minimizing cross-clamp time are paramount. Nephrotoxic medications (e.g., gentamycin) or medications that decrease renal blood flow (nonsteroidal antiinflammatory drugs) should be eliminated from the perioperative period as well.

Dopamine, furosemide, mannitol, and fenoldopam (a selective dopamine type 1 receptor agonist) have all been used to prevent renal failure, but evidence is either lacking or controversial as to the efficacy of these treatments. The evidence that low-dose dopamine (2 mcg/kg/min) has a positive effect is equivocal at best. In addition, dopamine has the harmful property of inducing tachycardia and increased cardiac workload in patients predisposed to myocardial disease. Furosemide may cause renal hypoperfusion in hypovolemic states and induce electrolyte imbalances. Evidence of renal protection with mannitol is inconclusive, but it is still widely used to encourage preclamping diuresis. Many clinicians believe that this osmotic diuretic benefits the kidneys by increasing cortical blood flow and reducing endothelial edema and vascular congestion. Fenoldopam is an antihypertensive agent that dilates renal and splanchnic vessels. This increase in renal blood flow may be advantageous, but more prospective studies are required.

### 9. What are the potential advantages to postoperative epidural analgesia?

Epidural anesthesia may suppress sympathetic tone and the stress response while providing excellent analgesia. This limits myocardial work by attenuating tachycardia and hypertensive swings in a patients predisposed to cardiac ischemia. It also provides titratable postoperative pain relief without excessive sedation. However, a concern with neuraxial analgesia is hematoma formation in the setting of anticoagulation. It is considered safe practice to use these techniques as long as there is a least 1 hour from epidural placement to heparinization of the patient.

### 10. What specific concerns exist for endovascular repair of the aorta?

Endovascular repair of the aorta is a relatively new technique using stents passed through an artery (usually femoral) and guided to the aorta via fluoroscopy. The patient must be motionless during the procedure; but general, neuraxial, or local anesthesia is appropriate. Local anesthesia has the advantage of requiring less fluid and vasopressor support, although the same degree of pulmonary and cardiac complications occur when compared to general anesthesia. Usually only an arterial line and standard monitors are necessary, but conversion

to an open procedure is possible, and aggressive intravenous access is justified. Overall endovascular techniques require less fluid and hemodynamic support, and the 30-day mortality for abdominal aortic aneurysms is less than that for open repairs (3% vs. 4%). The cardiac, pulmonary, renal, and bleeding complications are fewer as well.

#### 11. Describe the primary aspects of management when a patient presents with an acute abdominal aortic rupture.

The primary determinants of morbidity and mortality are extent, size, and location. Rupture of the intimal and medial aortic layers is less ominous in the short term as a pseudoaneurysm forms. Although hemorrhage is minimal, proximal increases in afterload and distal ischemia are risks. A larger aortic tear results in rapid and significant blood loss. A retroperitoneal rupture may be temporarily more stable than the almost always fatal intraabdominal rupture.

Resuscitation should be done in the operating room since rapid surgical intervention is necessary to prevent death. Rapid airway control must be obtained to optimize ventilation and oxygenation. The initial goal is to maintain perfusion and oxygenation to the heart and brain. Efforts are directed toward intravascular volume restoration. Multiple large bore intravenous lines are necessary, as is intra-arterial monitoring and probably central venous pressure monitoring as well. Transesophageal echocardiography or pulmonary artery catheterization may be valuable when preexisting myocardial dysfunction is present, but vigorous intravascular restoration and treatment of the inevitable coagulopathy should take precedence. The patient should have 10 units of blood available, universal donor blood if necessary, and the laboratory should be made aware that this case will probably require massive transfusion, with requirements for fresh frozen plasma, platelets, and cryoprecipitate. Disturbances in coagulation are best followed with thromboelastography. Blood pressure may require inotropic or chronotropic support, although volume resuscitation is the mainstay of treatment. A systolic blood pressure of 80 to 100 mm Hg is an ideal goal, although communication about hemodynamic goals should involve the surgeons.

### KEY POINTS: AORTO-OCCLUSIVE DISEASE



1. Coexisting diseases are extremely common and include coronary artery disease, hypertension, COPD, chronic renal disease, and diabetes mellitus. These comorbidities have a very important impact on outcome.
2. Preoperative assessment as guided by the 2007 ACC/AHA Guidelines determines the need for testing and evaluation.
3. The most common cause of perioperative mortality is cardiac disease. Postoperative renal failure also has an important impact on outcome.
4. Goals of anesthesia are to maintain intravascular volume and attenuate the acute and severe hemodynamic changes that occur with vascular cross- and uncross-clamping.

#### 12. Discuss the important elements of postoperative care.

- Intensive care unit admission is absolutely essential.
- **Cardiac:** Patients should be monitored for ischemia and hypotension. The incidence of myocardial ischemia is greatest about the third postoperative day.
- **Pulmonary:** Many patients remain intubated after surgery if poor baseline pulmonary function exists, if they have left ventricular dysfunction, or if massive fluid shifts have occurred. Epidural analgesia may be of benefit in weaning the patient from mechanical ventilation.

- **Renal:** Monitoring electrolytes, renal markers, and urine output is important for assessing kidney failure and fluid status.
- Other complications include bleeding, graft dysfunction, bowel ischemia, stroke, embolic events, and extremity hypoperfusion.

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# INTRACRANIAL AND CEREBROVASCULAR DISEASE

Gurdev S. Rai, MD, and Luke Osborne, MD

## 1. What is cerebrovascular insufficiency?

Cerebrovascular insufficiency results from an inadequate supply of blood flow, oxygen, and/or glucose to the brain. Cerebral ischemia develops, and neurologic damage will ensue if the underlying process is not corrected within 3 to 8 minutes.

## 2. Compare global ischemia with focal ischemia.

Global ischemia refers to global hypoxia (respiratory failure, asphyxia) or circulatory arrest wherein the brain is not perfused. Focal ischemia can result from vasospasm, traumatic, hemorrhagic, embolic, or atherosclerotic events. If the underlying cause is reversed rapidly and perfusion and oxygenation are restored, neurologic damage can be avoided.

## 3. How does cerebrovascular insufficiency manifest itself?

Manifestations include transient ischemic attacks (TIAs) and cerebrovascular accidents (CVAs).

- TIAs are acute in onset, involve neurologic dysfunction for minutes to hours (<24 hours), resolve spontaneously, and are associated with a normal computed tomography (CT) scan.
- CVAs may develop acutely or chronically progress over time (minutes to days). Strokes can be classified as minor, with an eventual full recovery, or major, with severe and permanent disability or death. In addition to cerebrovascular abnormalities, CVAs are associated with other comorbidities, including hypertension, diabetes, coagulopathies, atrial fibrillation, mitral valve disease, endocarditis, and substance abuse.
- A third group of patients experience neurologic dysfunction for longer than 24 hours, with spontaneous and complete recovery within 1 to 2 weeks. This phenomenon is termed *reversible ischemic neurologic deficit* and should be pathophysiologically grouped with TIAs.

## 4. What is the etiology of cerebrovascular accidents and transient ischemic attacks?

Atherosclerosis at the bifurcation of the common carotid artery is the source of most cerebral ischemic events. The thrombus itself or more likely embolic plaques and debris can dislodge to the brain, resulting in neurologic injury. Resolution of TIAs within 24 hours is the result of the inherent mechanisms of the body for breaking down such emboli. Ischemia of the brainstem and the temporal and occipital lobes is thought to be caused by a transient decrease in blood flow or blood pressure in the vertebrobasilar system. Hypoperfusion to the brain secondary to the atherosclerotic stenosis itself accounts for less than 10% of ischemic events.

## 5. Are other factors involved in neurologic outcome following an episode of cerebrovascular insufficiency?

The type and size of plaque or embolus, the site of ischemia, the extent of collateral circulation, the duration of inadequate perfusion, and the inherent response of the brain to the insult all contribute to the neurologic sequelae.

### 6. List the risk factors for cerebral ischemic events.

Hypertension and cigarette smoking are the strongest risk factors. Cardiac diseases (e.g., left ventricular hypertrophy, atrial fibrillation, cardiomyopathy, endocarditis, valvular disease, coronary artery disease) are major risk factors. Other risk factors include age, diabetes, hyperlipidemia, coagulopathies, vascular disease elsewhere, and a maternal history of stroke. The 5-year risk of stroke in a patient who has had a TIA is nearly 35%.

### 7. Who is a candidate for carotid endarterectomy?

Asymptomatic bruits are heard in 5% to 10% of the adult population. A 1989 prospective study of 566 patients with asymptomatic carotid bruits revealed a 1-year stroke or TIA rate of 2.5% compared with a rate of 0.7% in patients without carotid bruits. The European Carotid Surgery Trial (ECST) demonstrated that carotid endarterectomy (CEA) is not indicated for most patients with moderate (30% to 69%) stenoses, even if they are symptomatic. However, the rate of stroke or TIA increases dramatically with increasing stenosis, reaching a 1-year stroke or TIA rate of 46% for stenoses greater than 80%. It is well accepted that symptomatic patients and asymptomatic patients with a stenosis >70% are candidates for CEA.

Carotid stenting is now available for patients who fit these criteria but are high-risk surgical candidates. Stenting is an alternative to CEA in this select patient population and involves only local anesthesia and a small femoral incision.

### 8. Define cerebral autoregulation. How is it affected in cerebrovascular disease and what are the anesthetic implications?

Cerebral autoregulation is the ability of the brain to maintain cerebral blood flow relatively constant (40 to 60 ml/100 g/min) over a wide range (50 to 150 mm Hg) of arterial pressures. Stenosis or obstruction in the internal carotid artery causes a pressure drop beyond the obstruction. In an effort to maintain cerebral blood flow, the cerebral vasculature dilates. As the degree of carotid obstruction progresses, the cerebral vasculature distal to the obstruction maximally dilates. At this point the cerebral vasculature loses its autoregulatory ability. Cerebral blood flow becomes passive and depends on systemic blood pressure. It thus becomes critically important to maintain the blood pressure of patients with carotid stenosis because they have minimal or no autoregulatory reserve to counter anesthetic-induced reductions in blood pressure.

### 9. How are the cerebral responses to hypercapnia and hypocapnia altered in cerebrovascular disease? What are the anesthetic implications?

Normal cerebral vessels are highly sensitive to arterial carbon dioxide partial pressure ( $\text{PaCO}_2$ ), dilating in response to hypercapnia and constricting in response to hypocapnia. However, in ischemic and already maximally vasodilated areas of the brain, this relationship breaks down, and responses to hypercapnia and hypocapnia may be paradoxical. Because cerebral vessels in an area of ischemia are already maximally dilated, hypercapnia may result in dilation of only normally responsive vessels outside the area of ischemia. This phenomenon, termed *steal*, may divert blood flow away from the ischemic area, further compromising perfusion. On the other hand, hypocapnia may cause vessels in normal areas to undergo constriction, diverting blood to marginally perfused areas. This phenomenon is termed the *Robin Hood* or *inverse steal* effect. Therefore it is generally recommended that normocapnia be maintained in patients undergoing endarterectomy.

### 10. What is normal cerebral blood flow? At what level is cerebral blood flow considered ischemic?

Normal cerebral blood flow in humans is 40 to 60 ml/100 g/min (15% of cardiac output). The cerebral metabolic rate for oxygen in adults is 3 to 4 ml/100 g/min (20% of whole-body oxygen consumption). The cerebral blood flow at which ischemia becomes apparent on electroencephalogram (EEG), termed the *critical regional cerebral blood flow*, is 18 to 20 ml/100 g/min.

**11. How do inhalational anesthetics affect cerebral perfusion and cerebral metabolic rate?**

In the normal brain cerebral blood flow varies directly with the cerebral metabolic rate for oxygen. Inhalational agents are said to *uncouple* this relationship. They decrease the cerebral metabolic rate for oxygen but concurrently cause dilation of cerebral blood vessels, thus increasing cerebral blood flow.

**12. How should patients having carotid endarterectomy be monitored?**

In addition to standard monitoring, intra-arterial blood pressure monitoring is indicated to continuously monitor blood pressure. Carotid surgery does not involve large fluid shifts, and monitoring central venous or pulmonary artery pressures is rarely necessary. Since the potential for uncontrolled carotid arterial bleeding always exists, large-bore intravenous access is recommended. Additional intravenous lines dedicated for the use of vasoactive and anesthetic agents is also recommended.

**13. Is regional or general anesthesia preferred for the endarterectomy patient?**

No controlled, randomized, prospective study exists that demonstrates a long-term benefit of one technique over the other. Ultimately the choice between regional and general anesthesia is based on patient suitability and preference, surgeon and anesthesiologist experience and expertise, and the availability of cerebral perfusion monitoring.

**14. What are the advantages of regional anesthesia for carotid endarterectomy?**

The main advantage of regional anesthesia is the ability to perform continuous neurologic assessment of the awake, cooperative patient and thus evaluate the adequacy of cerebral perfusion. However, this can become a disadvantage if the patient develops cerebral ischemia. Cerebral ischemia in this setting may lead to disorientation, inadequate ventilation and oxygenation, and a disrupted surgical field. Providing maximal cerebral protection often requires conversion to a general anesthetic, but endotracheal intubation in this setting may prove difficult. Sedation may impair the value of the awake neurologic assessment and must be titrated carefully. There is some evidence that 30-day mortality and postoperative hemorrhage are reduced with regional anesthesia.

**15. What are the advantages and disadvantages of general anesthesia for patients undergoing carotid endarterectomy?**

Advantages of general anesthesia include control of the airway, a quiet operative field, and the ability to maximize cerebral perfusion if ischemia develops. The main disadvantage of general anesthesia is loss of the continuous neurologic evaluation that is possible in the awake patient.

**16. What methods of monitoring cerebral perfusion during general anesthesia are available?**

Available techniques include stump pressure monitoring, intraoperative EEG, monitoring of somatosensory-evoked potentials, monitoring of jugular venous or transconjunctival oxygen saturation, transcranial Doppler, and tracer wash-out techniques. Newer methods include transcutaneous cerebral oximetry. None of the methods has been demonstrated to improve outcome, and none has gained widespread acceptance as the monitor of choice.

**17. Do stump pressures provide reliable cerebral perfusion information?**

No. The stump pressure is the pressure in the portion of the internal carotid artery immediately cephalad to the carotid cross-clamp. This pressure is presumed to represent pressure transmitted from the contralateral carotid and vertebral arteries via the circle of Willis. Stump pressures have no correlation with flow. Some patients with stump pressures less than 50 mm Hg are adequately perfused, whereas some patients with "adequate" stump pressures have suffered ischemic injury.

### 18. Does intraoperative electroencephalogram provide clinically useful information during carotid endarterectomy?

No data show that EEG during CEA results in improved patient outcomes. Although the EEG is a highly sensitive and an early indicator of global cortical ischemia, it is not highly specific and results in many false-positive (though few false-negative) warnings. Other concerns include the time of ischemia needed before detecting EEG changes. The issue is that, once EEG changes occur, irreversible damage might have already taken place.

### 19. What are the common postoperative complications of carotid endarterectomy?

- **Hypotension:** A common complication that is believed to be caused by an intact carotid sinus responding to higher arterial pressures after removal of the atheromatous plaque. Such hypotension responds well to fluid administration and vasopressors.
- **Hypertension:** Also common but less understood. Obviously the high incidence of preoperative hypertension, particularly when it is poorly controlled, may result in labile postoperative hypertension. It may also be the result of denervation or trauma to the carotid sinus. Given the high association of postoperative hypertension with onset of new neurologic deficit, postoperative hypertension must be monitored and treated with some consideration given to the patient's baseline blood pressures.
- **Cerebral hyperperfusion:** After correction of the stenosis, blood flow may increase by as much as 200%. Poorly controlled hypertension contributes to this complication. Symptoms and side effects of hyperperfusion are headache, face and eye pain, cerebral edema, nausea and vomiting, seizure, and intracerebral hemorrhage. The blood pressure of such patients should be very carefully controlled, preferably without the use of cerebral vasodilators.
- **Airway obstruction:** This could result from hematomas and tissue edema. Treatment involves reestablishing an airway, possibly requiring intubation, opening the incision, and draining the hematoma. Respiratory problems also may result from vocal cord paralysis caused by damage to recurrent laryngeal nerves and from phrenic nerve palsy after cervical plexus block. The chemoreceptor function of the carotid bodies is predictably lost in most patients after CEA, as evidenced by a complete loss of the respiratory response to hypoxia and an average increase in the resting  $\text{PaCO}_2$  of 6 mm Hg.
- Most **strokes** associated with CEA occur after surgery as a result of surgical factors involving carotid thrombosis and emboli from the surgical site. Immediate and progressive postoperative strokes are a surgical emergency and require prompt exploration.

### 20. What are the major causes and presentations of spontaneous subarachnoid hemorrhage?

Intracranial aneurysm rupture is the most common cause of subarachnoid hemorrhage (SAH) (75% to 80%). Risk factors are smoking and systemic hypertension. Rupture depends on the size, with a 6% chance per year if the aneurysm is 25 mm or larger. Arteriovenous malformation (AVM,  $\approx 5\%$ ), idiopathic ( $\approx 14\%$ ), hemorrhagic tumors, and vasculitides are other causes. SAH often presents as a severe frontal or occipital headache, often with associated neurologic deficits, photophobia, stiff neck, and nausea/vomiting. SAH may also manifest as temporary loss of consciousness or even death. Changes in the electrocardiogram (T wave and ST segment changes) and signs of pulmonary edema within 2 days of the bleed are the result of catecholamine release. Establishing the diagnosis and quick intervention decreases the patient's morbidity and mortality.

### 21. List the Hunt-Hess classification of neurologic status following spontaneous subarachnoid hemorrhage.

- **Grade I:** Asymptomatic, minimal headache and/or nuchal rigidity
- **Grade II:** Moderate-to-severe headache/nuchal rigidity; cranial nerve palsy (often cranial nerve III)

- **Grade III:** Confusion, drowsiness, or mild focal deficit
- **Grade IV:** Stupor, hemiparesis, early decerebrate rigidity, vegetative disturbances
- **Grade V:** Moribund, deep coma, decerebrate rigidity

**22. Describe the management of intracranial aneurysms following spontaneous subarachnoid hemorrhage.**

Early surgical intervention (aneurysm clipping) within the first 72 hours of the initial bleed improves neurologic outcome, but early treatment may be technically difficult secondary to cerebral edema and unstable concomitant medical conditions. Surgery is often delayed until the risk of maximal vasospasm has decreased. Initial treatment includes close hemodynamic monitoring and stabilization, stool softeners to prevent straining, bed rest, and analgesia. Anticoagulation, if present, should be reversed. If a patient does not have any neurologic deficits, is alert and appropriate, and has appropriate cerebral perfusion pressure (CPP), antihypertensive therapy may be used; but most hypertensive patients are left untreated so as to maintain CPP.

When blood pressure control is necessary, usually nitroprusside or nitroglycerin is avoided because it increases cerebral blood flow; labetalol is an acceptable alternative. The use of fibrinolytics is controversial and discouraged. Glucocorticoids confer neither a benefit nor a risk. If the patient is stuporous, has decerebrate posturing, or is in a coma, interventional radiologic procedures, ventriculostomy, or burr holes may be indicated. Patients chosen for aneurysmal coiling often have a number of uncontrolled comorbidities. Interventional radiologic procedures have become the treatment of choice for selected patient groups after cerebral aneurysm rupture.

**23. Why is early surgical clipping so critical in the management of spontaneous subarachnoid hemorrhage resulting from aneurysm rupture?**

Rebleeding and vasospasm are two devastating early complications of SAH. Rebleeding, the principal cause of death in patients after SAH, can be seen years after the initial bleed. Yet 20% of aneurysms rebleed in the first 2 weeks, with the highest risk posed on postbleed day 1. Surgical intervention prevents rebleeding, thus the reason for early clipping. Vasospasm causes delayed cerebral ischemia following SAH. It can present on a neurologic continuum from drowsiness to stroke. The etiology is believed to be subarachnoid blood around the circle of Willis in the basal cisterns. Such blood can be removed at the time of surgical clipping to decrease the incidence of vasospasm. Signs/symptoms of vasospasm are seen in roughly 30% of patients 4 to 14 days following aneurysm rupture.

**24. How is vasospasm diagnosed? Who is at risk?**

Patients at risk for vasospasm include those with hypertension on admission, age >60, decreased level of consciousness, a large amount of blood in subarachnoid space on CT scan, hydrocephalus, and overall poor health. Intravascular volume depletion, hydrocephalus, sepsis, and electrolyte abnormalities must be considered as alternative causes of acute neurologic deterioration. Vasospasm is most clearly demonstrated by angiography and involves the middle cerebral artery 75% of the time. The pathophysiology of vasospasm is complex and not well understood, but it is thought to be related to products released by the breakdown of erythrocytes in the subarachnoid space. Autoregulation is lost in the vasospastic vessels. Surgery is often delayed if vasospasm is suspected.

**25. Describe the treatment options if vasospasm is suspected following an spontaneous subarachnoid hemorrhage.**

Traditionally vasospasm has been treated with hypertensive, hypervolemic, hemodilution (HHH). Hypervolemia is achieved with colloid administration, with a goal of central venous pressure of 8 to 12 mm Hg or pulmonary artery wedge pressure of 18 to 20 mm Hg.



The desired level is a hematocrit of 27 to 30, thereby reducing viscosity and improving microcirculation. If the aneurysm is clipped, vasopressors (dopamine, phenylephrine) can be used to induce hypertension, with the goal being a mean arterial pressure approximately 20 to 30 mm Hg greater than baseline systolic pressure. Increased perfusion pressure will attenuate any cerebral ischemia and promote blood flow to transitional areas of injury (known as the *penumbra*). Calcium channel blockers (CCBs) are usually started empirically following SAH. CCBs have not been found to be consistent in decreasing the incidence of vasospasm (either angiographically or clinically). The CCB nimodipine has been shown to improve outcomes in SAH and should be used with appropriate monitoring. The overall mechanism of action in this setting is unknown, but decreased platelet aggregation, dilation of small arterioles, and reduction of calcium-mediated excitotoxicity are considered possible etiologies. Angioplasty can be performed, and papaverine infused if segmental vasospasm is present on angiogram.

### KEY POINTS: INTRACRANIAL AND CEREBROVASCULAR DISEASE



1. Atherosclerosis at the bifurcation of the common carotid artery is the source of most cerebral ischemic events.
2. Cerebral autoregulation usually maintains cerebral blood flow relatively constant over a wide range of arterial pressures. It is critically important to maintain the blood pressure of carotid endarterectomy patients because they have minimal or no autoregulatory reserve to counter anesthetic-induced reductions in blood pressure.
3. Normal cerebral vessels are highly sensitive to PaCO<sub>2</sub>, dilating in response to hypercapnia and constricting in response to hypocapnia. However, in ischemic and already maximally vasodilated areas of the brain, this relationship breaks down, and responses to hypercapnia and hypocapnia may be paradoxical.
4. In the normal brain cerebral blood flow varies directly with the cerebral metabolic rate. Inhalational agents are said to *uncouple* this relationship in that they decrease the cerebral metabolic rate while concurrently dilating cerebral blood vessels and increasing cerebral blood flow.
5. No particular anesthetic technique for CEA has been shown to improve outcome.
6. None of the methods of monitoring cerebral blood flow during CEA has been demonstrated to improve outcome, and none has gained widespread acceptance as the monitor of choice.
7. The key to SAH management is early diagnosis and surgical treatment within 72 hours. Vasospasm should be treated with HHH therapy.

### 26. How can surgical exposure be improved and the brain be protected during aneurysm surgery?

Hypocapnia can be used to relax the brain, but cerebral ischemia to marginally perfused regions is a concern and usually is best avoided. Mannitol is usually given after the dura is opened to facilitate exposure and relax the brain. Lumbar cerebrospinal fluid (CSF) drains can be placed, and CSF can be drained off after the dura has been opened. Glucose must be maintained between 80 and 120 mg/dl to prevent further neurologic insult. Neurosurgeons commonly place temporary occlusion clips on the parent artery that feeds the aneurysm before clipping it. Most studies have shown that this is tolerated for 10 to 14 minutes. The risk of

ischemic injury increases up until 31 minutes of temporary clipping, at which time the chance of ischemic insult is nearly 100%. Induced hypertension, mild hypothermia, and burst suppression with high-dose barbiturates should be considered during temporary occlusion to protect against cerebral ischemia. EEG should be used to monitor the effects of occlusion and/or burst suppression. Overall maintaining CPP and minimizing the time of vessel occlusion best protect the brain.

**27. What is a cerebral arteriovenous malformation?**

AVMs are congenital vascular abnormalities that usually arise during the fetal stage of development as capillary beds are formed. The development of capillary beds is arrested, and direct communications between arteries and veins are formed. As the brain develops, the AVM acquires increased arterial blood flow and becomes a shunt system of high flow and low resistance. AVMs increase in size as they acquire further blood supply.

**28. How do arteriovenous malformations typically present?**

Most AVMs are symptomatic by the age of 40, usually with the presentation of hemorrhage (nearly 50%), seizure (17% to 50%), or headache (7% to 45%). Less commonly focal neurologic deficits, increased intracranial pressure, and high-output heart failure are the presenting features. Hemorrhage, epilepsy, and neurologic deficits are the traditional indications for surgery, but newer techniques (endovascular and microsurgical/radiation) have allowed for more aggressive surgical intervention in nonruptured aneurysms. Age is also an important factor in the decision to operate.

**29. What are the common treatment modalities for arteriovenous malformations?**

Conservative treatment is reserved for inoperable AVMs. Inoperable AVMs (e.g., because of size, location) can now be treated with radiosurgery or endovascular embolization. Radiosurgery directs radiation to the AVM to induce fibrosis and obliteration of the communicating vessels. Embolization is often used to decrease the size of an AVM before surgery, decreasing the risks of intraoperative bleeding and postoperative hyperemia. Surgical resection remains the definitive treatment for AVMs, virtually eliminating the risk of hemorrhage following excision.

**30. Describe the anesthetic management for surgical excision of an arteriovenous malformation.**

Most important, acute hypertensive episodes must be avoided. Intra-arterial blood pressure monitoring and large-bore intravenous access are imperative because of the potential for rapid and massive blood loss. Such blood loss can be decreased by preoperative embolization. Some surgeons still advocate high-dose barbiturates, hypocapnia, hypothermia, and deliberate hypotension for cerebral protection.

**31. What is normal perfusion pressure breakthrough?**

This phenomenon of cerebral edema is also called *autoregulation breakthrough*. It is commonly seen following AVM resection or embolization. With large AVMs the high-flow, low-resistance shunt can lead to underperfusion of adjacent brain tissue so the vessels supplying the underperfused region of brain lose the ability to autoregulate. Once the shunt is excised, all of the blood flow is diverted to the previously marginally perfused tissues, and the maximally dilated vessels are unable to vasoconstrict. This leads to the potential of cerebral edema, hyperperfusion, and hemorrhage into surrounding areas. The precise mechanism of how and why this occurs is not clear. Neurologic dysfunction following such episodes is a major cause of morbidity and mortality following AVM surgery. Treatment modalities of hyperperfusion include hyperventilation, osmotic diuresis (mannitol), head-up positioning, cautious use of deliberate hypotension, barbiturate coma, and moderate hypothermia.

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# REACTIVE AIRWAY DISEASE

Malcolm Packer, MD

## 1. Define reactive airway disease, in particular, asthma.

The term *reactive airway disease (RAD)* is used to describe a family of diseases that shares an airway sensitivity to physical, chemical, or pharmacologic stimuli. This sensitivity results in a bronchoconstrictor response and is seen in patients with asthma, chronic obstructive pulmonary disease (COPD), emphysema, viral upper respiratory illness, and other disorders.

Asthma is defined by the American Thoracic Society as “a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli manifested by a widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy.” Asthma is manifested by episodes of dyspnea, cough, and wheezing. These symptoms are related to the increased resistance to airflow in the patient’s airways.

## 2. What are the different types of asthma?

Although the common denominator lies in airway hyperreactivity, patients may fit into two subgroups: allergic (extrinsic) and idiosyncratic (intrinsic). Many believe that the terms *extrinsic* and *intrinsic* should be discarded. Underlying all types of asthma are airway hyperreactivity, inflammation, and an interaction between allergic and nonallergic stimuli.

Allergic asthma is thought to result from an immunoglobulin E–mediated response to antigens such as dust and pollen. Among the mediators released are histamine, leukotrienes, prostaglandins, bradykinin, thromboxane, and eosinophilic chemotactic factor. Their release leads to inflammation, capillary leakage in the airways, increased mucus secretion, and bronchial smooth muscle contraction.

Idiosyncratic asthma is mediated by nonantigenic stimuli, including exercise, cold, pollution, and infection. Bronchospasm is caused by increased parasympathetic (vagal) tone. Although the primary stimulus differs, the same mediators as allergic asthma are released (and some patients with allergic asthma have enhanced vagal tone).

## 3. What diseases mimic asthma?

- Upper and lower airway obstruction from tumor, aspirated foreign bodies, or stenosis
- Left ventricular failure (cardiac asthma) and pulmonary embolism
- Gastroesophageal reflux and aspiration
- Viral respiratory illnesses (e.g., respiratory syncytial virus)
- Allergic reactions and anaphylaxis
- A careful history and physical examination will differentiate these diseases from primary reactive disease

## 4. What are the important historical features of an asthmatic patient?

- Duration of disease
- Frequency, initiating factors, and duration of attacks
- Has the patient ever required inpatient therapy? Did the patient require intensive care admission or intubation?
- What are the patient’s medications, including daily and as-needed usage, over-the-counter medications, and steroids?

### 5. What physical findings are associated with asthma?

The most common physical finding is expiratory wheezing. Wheezing is a sign of obstructed airflow and is often associated with a prolonged expiratory phase. As asthma progressively worsens, patients use accessory respiratory muscles. A significantly symptomatic patient with quiet auscultatory findings may signal impending respiratory failure because not enough air is moving to elicit a wheeze. Patients also may be tachypneic and probably are dehydrated; they prefer an upright posture and demonstrate pursed-lip breathing. Cyanosis is a late and ominous sign.

### 6. What preoperative tests should be ordered?

The patient's history guides the judicious ordering of preoperative tests. A mild asthmatic maintained on as-needed medication who is currently healthy will not benefit from preoperative testing. Symptomatic patients with no recent evaluation deserve closer attention.

The most common test is a pulmonary function test, which allows simple and quick evaluation of the degree of obstruction and its reversibility (see Chapter 9). A comparison of values obtained from the patient with predicted values helps to assess the degree of obstruction. Severe exacerbation correlates with a peak expiratory flow rate (PEFR) or forced expiratory volume in 1 second ( $FEV_1$ ) of less than 30% to 50% of predicted, which for most adults is a PEFR of less than 120 L/min and an  $FEV_1$  of less than 1 L. Tests should be repeated after a trial of bronchodilator therapy to assess reversibility and response to treatment.

Arterial blood gases are usually not helpful. Electrocardiograms, chest radiographs, and blood counts are rarely indicated for evaluation of asthma unless particular features of the patient's presentation suggest alternative diagnoses (e.g., fever and rales suggesting pneumonia).

### 7. Describe the mainstay of therapy in asthma.

The mainstay of therapy remains inhaled  $\beta$ -adrenergic agonists. Selective  $\beta_2$ -agonists such as albuterol, terbutaline, and fenoterol offer greater specificity for  $\beta_2$ -mediated bronchodilation and fewer side effects (e.g.,  $\beta_1$ -associated tachydysrhythmias and tremors). Albuterol can be nebulized or administered orally or by metered-dose inhaler (MDI). Terbutaline is effective via nebulizer, subcutaneously, or as a continuous intravenous infusion (beware of hypokalemia, lactic acidosis, and cardiac tachydysrhythmias with intravenous use). Epinephrine is available for subcutaneous use in severely asthmatic patients. Patients with coronary artery disease have difficulty with tachycardia and need the more  $\beta_2$ -specific agents. Routinely the inhaled route is preferred.

### 8. What other medications and routes of delivery are used in asthma?

- **Corticosteroids:** Reverse airway inflammation, decrease mucus production, and potentiate  $\beta$ -agonist-induced smooth muscle relaxation. Steroids are strongly recommended in patients with moderate-to-severe asthma or patients who have required steroids in the past 6 months. Onset of action is 1 to 2 hours after administration. Methylprednisolone is popular because of its strong antiinflammatory powers but weak mineralocorticoid effect. Side effects include hyperglycemia, hypertension, hypokalemia, and mood alterations, including psychosis. Long-term steroid use or prolonged use with muscle relaxants is associated with myopathy. Steroids may be given orally, via MDI, or intravenously.
- **Anticholinergic agents:** Cause bronchodilation by blocking muscarinic cholinergic receptors in the airways, therefore attenuating bronchoconstriction caused by inhaled irritants and associated with  $\beta$ -blocker therapy. They are particularly valuable in patients with COPD or with severe airway obstruction ( $FEV_1 < 25\%$  predicted). Ipratropium, glycopyrrolate, and atropine may be given via nebulizer; and ipratropium is available in an MDI.

- **Theophylline:** The use in asthma is controversial. Theophylline has some bronchodilatory effects and improves diaphragmatic action. Such benefits must be weighed against a long list of side effects: tremor, nausea and vomiting, palpitations, tachydysrhythmias, and seizures. Until definite proof is available, many investigators suggest that theophylline therapy should be initiated only in patients with acute asthma who do not improve with maximal  $\beta$ -agonist and corticosteroid therapy. Careful monitoring of serum levels is mandatory. Theophylline is the oral preparation; whereas aminophylline, its water-soluble form, is for intravenous use.
- **Cromolyn sodium:** A mast cell stabilizer useful for long-term maintenance therapy. Patients younger than 17 years of age and with moderate-to-severe exercise-induced asthma appear to benefit the most. Side effects include some minimal local irritation on delivery. Cromolyn sodium may be administered via multidose inhaler or as a powder in a turboinhaler. Cromolyn sodium is not effective and in fact is contraindicated in acute asthmatic attacks.
- **Leukotriene modifiers:** Relative newcomers in the treatment of mild-to-moderate asthma. These drugs either selectively compete with LTd4 and LT $\epsilon$ 4 receptors or directly inhibit the lipoygenase pathway of arachidonic acid metabolism. At this time their use is limited to long-term treatment in a select group of patients.
- **Methotrexate or gold salts:** Patients with severe asthma may require one of these medications. Both have undesirable side-effect profiles and are reserved for patients who have major difficulties with corticosteroids (Table 38-1).

TABLE 38-1. USEFUL MEDICATIONS FOR PATIENTS WITH REACTIVE AIRWAY DISEASE

Medication	Dose	Comments
Albuterol	2.5 mg in 3 ml of normal saline for nebulization or 2 puffs by MDI	May need repeat treatments
Terbutaline	0.3-0.4 mg subcutaneously	May repeat as required every 20 minutes for three doses
Epinephrine	0.3 mg subcutaneously	May repeat as required every 20 minutes for three doses
Corticosteroids	Methylprednisolone, 60-125 mg intravenously every 6 hours, or prednisone, 30-50 mg, orally daily	Steroids are usually tapered at the first opportunity
Anticholinergics	Ipratropium, 0.5 mg by nebulization or 4-6 puffs by MDI; atropine, 1-2 mg per nebulization	Useful with severe RAD and COPD
Theophylline	5 mg/kg intravenously over 30 minutes (loading dose in patients not previously taking theophylline)	After the loading dose, start continuous infusion at the appropriate rate according to age and disease state of the patient, being watchful for any drug interactions

*COPD*, Chronic obstructive pulmonary disease; *MDI*, metered-dose inhaler; *RAD*, reactive airway disease,

### 9. What is the best approach to preoperative management of the patient with reactive airway disease?

Patients should be classified according to the urgency of the operation required and their particular history of reactive airways.

- Patients who are scheduled for elective procedures but are actively wheezing are probably best cancelled, administered therapy, and rescheduled.
- Asymptomatic patients on no medications currently and with no recent bouts of asthma and no history of serious illness may require no therapy or, at most, inhaled  $\beta$ -agonists.
- Mild asthmatics ( $FEV_1 >80\%$ ) with ongoing or recent symptoms should definitely have  $\beta$ -adrenergic therapy before surgery.
- Moderate asthmatics ( $FEV_1$  65% to 80%) should continue their  $\beta$ -adrenergic therapy and either double their inhaled steroid dose for a week before surgery or start oral steroids 2 days before surgery. When symptomatic, these patients should start  $\beta$ -adrenergic and oral steroid therapy. Important factors to consider before beginning steroids include the following:
  - Have the patients had intensive care admissions or mechanical ventilation related to their asthma?
  - Have steroids been administered in the past 6 months?
  - Are the patients at risk for adrenal insufficiency?
- Severe asthmatics ( $FEV_1 <65\%$ ) should be on  $\beta$ -adrenergic therapy and be given 2 days of oral steroids before surgery. Patients with  $FEV_1 <70\%$  have improvements in pulmonary function with either inhaled  $\beta$ -adrenergic or oral steroids with only 1 day of therapy. Combining  $\beta$ -adrenergic and oral steroid therapy also significantly decreases postintubation wheezing when compared to  $\beta$ -adrenergic therapy alone. Finally patients having upper abdominal or thoracic surgery and emergency cases are at particular risk and deserve aggressive therapy.

### 10. Review the pros and cons of induction agents in asthmatic patients.

Intravenous induction agents used in asthmatic patients include oxybarbiturates, thiobarbiturates, ketamine, and propofol. Thiobarbiturates constrict airways in laboratory investigations and may have a loose association with clinical bronchospasm. The most common cause of bronchospasm is the stimulus of intubation, and large doses of barbiturates are required to block this effect successfully. Ketamine has well-known bronchodilatory effects secondary to the release of endogenous catecholamines with  $\beta_2$ -agonist effects. Ketamine also has a small, direct relaxant effect on smooth muscles. Propofol decreases both airway resistance and airway reflexes after administration. Intravenous lidocaine is a useful adjunct for blunting the response to laryngoscopy and intubation.

Mask induction with halothane or sevoflurane is an excellent method to block airway reflexes and to relax airway smooth muscles directly. These agents are much more palatable to the airway than isoflurane or desflurane.

Atracurium and mivacurium are commonly used muscle relaxants that have demonstrated histamine release and may cause bronchoconstriction. Vecuronium, rocuronium, pancuronium are not associated with histamine release. Cis-atracurium is associated with less histamine release relative to atracurium.

### 11. What agents may be used for maintenance anesthesia?

Sevoflurane, halothane, and isoflurane are effective in blocking airway reflexes and bronchoconstriction; sevoflurane appears to be the most effective. Inhaled anesthetics have been used in the intensive care unit to provide bronchodilation in intubated patients with severe asthma, improving indices of respiratory resistance (inspiratory and expiratory flows), decreasing hyperinflation, and lowering intrinsic positive end-expiratory pressure (PEEP).

Opioids at higher doses block airway reflexes but do not provide direct bronchodilation. Morphine remains controversial because of its histamine-releasing activity. Anesthetics relying

primarily on opioids may cause problems with respiratory depression at emergence (particularly in patients with COPD with an asthmatic component).

Neuromuscular blocking agents with a benzyloquinolinium nucleus such as *d*-tubocurarine, atracurium, and mivacurium release histamine from mast cells on injection. They also may bind directly to muscarinic receptors on ganglia, nerve endings, and airway smooth muscle. Both mechanisms theoretically may increase airway resistance. Relaxants with an aminosteroid nucleus such as pancuronium and vecuronium continue to be used safely in asthmatic patients. In patients with bronchospasm neuromuscular blocking agents improve chest wall compliance, but smooth muscle airway tone and lung compliance remain the same. Prolonged use of muscle relaxants in ventilated asthmatic patients is associated with increases in creatine kinase and clinically significant myopathy.

## 12. What are the complications of intubation and mechanical ventilation in asthmatic patients?

The stimulus of intubation causes significant increases in airway resistance. Lung hyperinflation occurs when diminished expiratory flow prevents complete emptying of the alveolar and small airway gas. Significant gas trapping may cause hypotension by increasing intrathoracic pressure and reducing venous return. Pneumomediastinum and pneumothorax are also potential causes of acute respiratory decompensation.

Several measurements of ventilator function may give some insight into a patient's improving or worsening status. Plateau pressures (the pressure measured at end inspiration and before expiration starts, averaged over a 0.4-second pause) correlate loosely with complications at pressures greater than 30 cm H<sub>2</sub>O. Auto-PEEP is the measurement of end-expiratory pressure (taken at end expiration while the expiratory port is momentarily occluded) and may correlate with alveolar pressures in the bronchospastic patient. However, auto-PEEP does not specifically correlate with complications. Plateau pressure and auto-PEEP measurements require a relaxed patient.

Patients on prolonged high-dose corticosteroids and muscle relaxation are at risk for a severe myopathy. Pancuronium and vecuronium are the worse offenders, but all muscle relaxants are suspect.

Several strategies for mechanically ventilating bronchospastic patients have been developed:

- Pressure-support ventilation allows for spontaneous ventilation in the sedated patient with less work of breathing and less risk of barotrauma AND IF MANDATORY BREATHS ARE REQUIRED.
- Increase expiratory time by decreasing ventilator rate, increasing inspiratory flow rates to decrease inspiratory time, and directly increasing the inspiratory-to-expiratory ratio.
- Be careful of ventilator-applied PEEP.
- Decrease minute volume, allowing controlled hypoventilation and permissive hypercapnia.

## 13. What are the causes of intraoperative wheezing and the correct responses to asthmatic patients with acute bronchospasm?

Causes include airway secretions, foreign body, pulmonary edema (cardiac asthma), obstructed endotracheal tube, endotracheal tube at the carina or down a main-stem bronchus, allergic or anaphylactic response to drugs, and asthma. A number of medications cause wheezing in asthmatic patients, including  $\beta$ -blockers, muscle relaxants, and aspirin.

After carefully checking the endotracheal tube and listening for bilateral breath sounds, increase the inspired oxygen to 100% and deepen the anesthetic if hemodynamically tolerated by the patient. Provoking factors such as medication infusions, misplaced endotracheal tubes, or other causes of airway stimulation should be corrected. Manipulating the ventilator (see question 14) may help. Administer medications as suggested in Question 7.



## KEY POINTS: REACTIVE AIRWAY DISEASE



1. The patient with reactive airway disease is at increased risk for intraoperative bronchoconstriction as manifested by increased peak airway pressures, difficulty in ventilation, and hypoxemia.
2. Most, if not all, patients with reactive airway disease will benefit from preoperative bronchodilator therapy.
3. Actively wheezing patients scheduled for elective surgery should be delayed until the reactive component of their pulmonary disease and other contributing factors have been treated and have come under satisfactory control.

#### 14. Describe the emergence techniques for asthmatic patients under general endotracheal anesthesia.

Awake and deep extubations are alternatives in patients under general endotracheal anesthesia. The endotracheal tube is a common cause of significant bronchospasm, and its removal under deep-inhaled anesthetic in a spontaneously ventilating patient often leads to a smooth emergence. Deep extubations should be avoided in patients with difficult airways, morbidly obese patients, and patients with full stomachs.

#### 15. What new therapies are available to anesthesiologists treating asthmatic patients in bronchospasm?

- **Magnesium sulfate:** Has been administered to patients in status asthmaticus. Hypothetically magnesium interferes with calcium-mediated smooth muscle contraction and decreases acetylcholine release at the neuromuscular junction. Magnesium reduces histamine- and methacholine-induced bronchospasm in controlled studies, but so far clinical studies have failed to show a significant response.
- **Heliox:** A blend of helium and oxygen that decreases airway resistance, peak airway pressures, and PaCO<sub>2</sub> levels when administered to spontaneously and mechanically ventilated patients. The mixture contains 60% to 80% helium and 20% to 40% oxygen and is less dense than air. The decrease in density allows less turbulent flow and significant declines in resistance to flow. The device for heliox administration in intubated patients is cumbersome unless the anesthesia machine is already equipped.
- **Lita-Tube:** This endotracheal tube allows intraoperative instillation of lidocaine at and below the cords of the intubated patient. This technique decreases airway stimulation from the endotracheal tube and may prevent reflex bronchospasm.
- **Extracorporeal oxygenation:** Using veno-venous oxygenation and CO<sub>2</sub> removal allows for minimal ventilatory support (lung rest) and the removal of dangerously high CO<sub>2</sub> with resulting improvement in pH.

## WEBSITES



American Academy of Allergy, Asthma, and Immunology  
<http://www.aaai.org>

Asthma and Allergy Foundation of America  
<http://www.aafa.org>

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# ASPIRATION

*Malcolm Packer, MD*

## 1. What is aspiration and what differentiates aspiration pneumonitis from aspiration pneumonia?

Aspiration is the passage of material from the pharynx into the trachea. Aspirated material can originate from the stomach, esophagus, mouth, or nose. The materials involved can be particulate such as food or a foreign body or fluid such as blood, saliva, or gastrointestinal contents. Aspiration of gastric contents may occur by vomiting, which is an active propulsion from the stomach up the esophagus, or by regurgitation, which is the passive flow of material along the same path.

Aspiration pneumonitis describes the initial inflammatory response after aspiration, and aspiration pneumonia describes the consolidation along with the inflammation.

## 2. How often does aspiration occur and what is the morbidity and mortality rate?

The results of several different retrospective and prospective surveys of adult anesthetics place the incidence at one to seven cases of significant aspiration per 10,000 anesthetics. Studies of children's anesthetics demonstrate about twice that occurrence. The average hospital stay is 21 days, much of which is in intensive care. Complications range from bronchospasm and pneumonia to acute respiratory distress syndrome, lung abscess, and empyema. The average mortality rate is 5%.

## 3. What are risk factors for aspiration?

- Extremes of age
- Emergency cases
- Type of surgery (most common in cases of esophageal, upper abdominal, or emergency laparotomy surgery)
- Recent meal (Preoperative fasting guidelines for elective surgery are discussed in Chapter 17.)
- Delayed gastric emptying and/or decreased lower esophageal sphincter tone (diabetes, gastric outlet obstruction, hiatal hernia)
- Medications (e.g., narcotics, anticholinergics)
- Trauma
- Pregnancy
- Pain and stress
- Depressed level of consciousness
- Morbid obesity (including after bariatric surgery and the resulting weight loss)
- Difficult airway
- Neuromuscular disease (impaired ability to protect the trachea)
- Esophageal disease (e.g., scleroderma, achalasia, diverticulum, Zenker's diverticulum)

## 4. What precautions before anesthetic induction are required to prevent aspiration or mollify its sequelae?

The main precaution is to recognize which patients are at risk. Patients should have an adequate fasting period to improve the chances of an empty stomach. Gastrokinetic medications such as metoclopramide have been thought to be of benefit because they enhance

gastric emptying, but no good data support this belief. It is helpful to increase gastric pH by either nonparticulate antacids such as sodium citrate or histamine-receptor ( $H_2$ ) antagonists, which decrease acid production. The market now includes several  $H_2$  antagonists, giving anesthesiologists a choice (e.g., cimetidine, ranitidine, and famotidine). Cimetidine was first on the market and is still widely used. Although cimetidine increases gastric pH, it also has a significant side-effect profile, including hypotension, heart block, central nervous dysfunction, decreased hepatic blood flow, and significant retardation of the metabolism of many drugs. Ranitidine, a newer  $H_2$  antagonist, is much less likely to cause side effects; only a few cases of central nervous dysfunction and heart block have been reported. Famotidine is equally as potent as cimetidine and ranitidine and has no significant side effects. To be effective at induction,  $H_2$  blockers must be administered 2 to 3 hours before the procedure, although medications given near the time of induction may have some benefit after extubation. The use of proton pump inhibitors in place of or in concert with  $H_2$  antagonists has not proven to be more efficacious. The use of orogastric or nasogastric drainage preinduction is most effective in patients with intestinal obstruction.

### 5. How might a patient with a difficult airway and at risk for aspiration be managed?

A regional anesthetic is a desirable alternative when appropriate for the surgery and has been shown to definitely be of value in the setting of cesarean section, during which the patient population is definitely at risk for aspiration. A rapid sequence with cricoid pressure is preferred when a general anesthetic is needed and the patients are thought not to have a difficult airway. Discussions on the efficacy and potential hazards of cricoid pressure continue, but to date is usually recommended for rapid sequence intubations.

Patients with difficult airways may require placement of an endotracheal tube while awake to allow spontaneous breathing and protect the airway from aspiration. Awake intubations are facilitated by devices such as light wands, fiberoptic bronchoscopes, and retrograde intubation kits. Patient comfort is aided by the judicious use of sedation and topical local anesthetic. Oversedation and a topicalized airway may make the patient unable to protect the airway. Therefore keeping the patient conscious and applying topical local anesthetic only to the airway above the glottis lead to safe intubation. Endotracheal intubation does not guarantee that no aspiration will occur. Material may still slip past a deflated or partly deflated cuff.

### 6. Describe the different clinical pictures caused by the three broad types of aspirate: acidic fluid, nonacidic fluid, and particulate matter.

- **Acidic aspirates** with a pH less than 2.5 and volumes of more than 0.4 ml/kg immediately cause alveolar-capillary breakdown, resulting in interstitial edema, intra-alveolar hemorrhage, atelectasis, and increased airway resistance. Hypoxia is common. Although such changes usually start within minutes of the initiating event, they may worsen over a period of hours. The first phase of the response is direct reaction of the lung to acid; hence the name chemical pneumonitis. The second phase, which occurs hours later, is caused by a leukocyte or inflammatory response to the original damage and may lead to respiratory failure.
- Aspiration of **nonacidic fluid** destroys surfactant, causing alveolar collapse and atelectasis. Hypoxia is common. The destruction of lung architecture and the late inflammatory response are not as great as in acid aspiration.
- Aspiration of **particulate food matter** causes both physical obstruction of the airway and a later inflammatory response related to the presence of a foreign body. Alternating areas of atelectasis and hyperexpansion may occur. Patients show hypoxia and hypercapnia caused by physical obstruction of airflow. If acid is mixed with the particulate matter, damage is often greater, and the clinical picture worse.

**7. Review the clinical signs and symptoms after aspiration.**

Fever occurs in over 90% of aspiration cases, with tachypnea and rales in at least 70%. Cough, cyanosis, and wheezing occur in 30% to 40% of cases. Aspiration may occur *silently*—without the anesthesiologist's knowledge—during anesthesia. Any of the previous clinical deviations from the expected course may signal an aspiration event. Radiographic changes may take hours to occur and may be negative, especially if performed soon after an event.

**8. When is a patient suspected of aspiration believed to be out of danger?**

The patient who shows none of the previous signs or symptoms and has no increased oxygen requirement at the end of 2 hours should recover completely.

**9. Describe the treatment for aspiration.**

Any patient who is thought to have aspirated should receive a chest radiograph and, at a minimum, many hours of observation. Supportive care remains the mainstay. Immediate suctioning should be instituted. Supplemental oxygen and ventilatory support should be initiated if respiratory failure is a problem. Patients with respiratory failure often demonstrate atelectasis with alveolar collapse and may respond to positive end-expiratory pressure. Patients with particulate aspirate may need bronchoscopy to remove large obstructing pieces. Antibiotics should not be administered unless there is a high likelihood that gram-negative or anaerobic organisms have been aspirated such as with a bowel obstruction. However, a worsening clinical course over the next few days suggests that a broad-spectrum antibiotic may be indicated. Corticosteroids have not been shown to be helpful in human studies. Lavaging the trachea with normal saline or sodium bicarbonate after aspiration has not been shown to be helpful and may actually worsen the patient's status.

More aggressive treatments of severe aspiration usually occur in the critical care setting. Surfactant installation, high-frequency oscillatory ventilation, nitric oxide, and prone positioning have all shown some promise for certain patients with severe aspirations.

**KEY POINTS: ASPIRATION**

1. Numerous patient subgroups are at increased risk of aspiration, including patients presenting for emergency surgery, those having had a recent meal, those with bowel obstruction or delayed gastric emptying, the obese, trauma or pregnant patients, those having pain or being treated with opioids, and those who cannot protect the airway such as patients with a depressed level of consciousness or neuromuscular disease.
2. Such patients may require prophylaxis to decrease the severity of aspiration should it occur, and medications valuable for decreasing the acidity of gastric secretions include nonparticulate antacids, H<sub>2</sub> blockers, and proton pump inhibitors given at an interval before surgery appropriate to their onset of action. Patients with bowel obstruction should receive gastric decompression before anesthetic induction.
3. Regional anesthetics are ideal for patients at risk for aspiration if appropriate. A rapid-sequence induction with cricoid pressure is the technique of choice when general anesthesia is required in patients with manageable airways. Awake intubation may be necessary in patients with difficult airways.
4. Should aspiration occur, the treatment is mostly supportive.

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# CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Howard J. Miller, MD

## 1. Define chronic obstructive pulmonary disease.

Chronic obstructive pulmonary disease (COPD) is a spectrum of diseases that includes emphysema, chronic bronchitis, and asthmatic bronchitis. It is characterized by progressive increased resistance to breathing. Airflow limitation may be caused by loss of elastic recoil or obstruction of small or large (or both) conducting airways. The increased resistance may have some degree of reversibility. Cardinal symptoms are cough, dyspnea, and wheezing.

## 2. What are the features of asthma and asthmatic bronchitis?

### Asthma

- This heterogeneous disorder is characterized by reversible airway obstruction.
- Precipitating factors include exercise, dander, pollen, and intubation.
- Symptoms improve with bronchodilator and immunosuppressive therapy.

### Asthmatic bronchitis

- It consists of airway obstruction, chronic productive cough, and episodic bronchospasm.
- It can result from progression of asthma or chronic bronchitis.
- There is less improvement with bronchodilator therapy; some degree of airway obstruction at all times.

## 3. Describe chronic bronchitis and emphysema.

- **Chronic bronchitis:** Characterized by cough, sputum production, recurrent infection, and airway obstruction for many months to several years. Patients with chronic bronchitis have mucous gland hyperplasia, mucus plugging, inflammation and edema, peribronchiolar fibrosis, airway narrowing, and bronchoconstriction. Decreased airway lumina caused by mucus and inflammation increase resistance to flow of gases.
- **Emphysema:** Characterized by progressive dyspnea and variable cough. Destruction of the elastic and collagen network of alveolar walls without resultant fibrosis leads to abnormal enlargement of air spaces. In addition, the loss of airway support leads to airway narrowing and collapse during expiration (air trapping).

## 4. List contributory factors associated with the development of chronic obstructive pulmonary disease.

- **Smoking:** Smoking impairs ciliary function, depresses alveolar macrophages; leads to increased mucous gland proliferation and mucus production; increases the inflammatory response in the lung; leading to increased proteolytic enzyme release; reduces surfactant integrity; and causes increased airway reactivity.
- **Occupational and environmental exposure:** Animal dander, toluene and other chemicals, various grains, cotton, and sulfur dioxide and nitrogen dioxide in air pollution.
- **Recurrent infection:** Bacterial, atypical organisms (mycoplasma), and viral (including human immunodeficiency virus, which can produce an emphysema-like picture).

- **Familial and genetic factors:** A predisposition to COPD exists and is more common in men than women.  $\alpha_1$ -antitrypsin deficiency is a genetic disorder resulting in autodigestion of pulmonary tissue by proteases and should be suspected in younger patients with basilar bullae on chest x-ray film. Smoking accelerates its presentation and progression.

#### 5. What historical information should be obtained before surgery?

- Smoking history: number of packs per day and duration in years
- Dyspnea, wheezing, productive cough, and exercise tolerance
- Hospitalizations for COPD, including the need for intubation and mechanical ventilation
- Medications, including home oxygen therapy and steroid use, either systemic or inhaled
- Recent pulmonary infections, exacerbations, or change in character of sputum
- Weight loss that may be caused by end-stage pulmonary disease or lung cancer
- Symptoms of right-sided heart failure, including peripheral edema, hepatomegaly, jaundice, and anorexia secondary to liver and splanchnic congestion

#### 6. What features distinguish pink puffers from blue bloaters?

##### **Pink puffers (emphysema)**

Usually older (>60 years)  
Pink in color  
Thin  
Minimal cough

##### **Blue bloaters (chronic bronchitis)**

Relatively young  
Cyanotic  
Heavier in weight  
Chronic productive cough; frequent wheeze

#### 7. List abnormal physical findings in patients with chronic obstructive pulmonary disease.

- Tachypnea and use of accessory muscles
- Distant or focally diminished breath sounds, wheezing, or rhonchi
- Jugular venous distention, hepatojugular reflux, and peripheral edema suggest right heart failure
- Palpation of peripheral pulses is an indirect measure of stroke volume

#### 8. What laboratory examinations are useful?

- White cell count and hematocrit: Elevation suggests infection and chronic hypoxemia, respectively.
- Electrolytes: Bicarbonate levels are elevated to buffer a chronic respiratory acidosis if the patient retains carbon dioxide. Hypokalemia can occur with repeated use of  $\beta$ -adrenergic agonists.
- Chest x-ray film: Look for lung hyperinflation, bullae or blebs, flattened diaphragm, increased retrosternal air space, atelectasis, cardiac enlargement, infiltrate, effusion, masses, or pneumothorax.
- Electrocardiogram: Look for decreased amplitude, signs of right atrial (peaked P waves in leads II and  $V_1$ ) or ventricular enlargement (right axis deviation, R/S ratio in  $V_6 \leq 1$ , increased R wave in  $V_1$  and  $V_2$ , right bundle-branch block), and arrhythmias. Atrial arrhythmias are common, especially multifocal atrial tachycardia and atrial fibrillation.
- Arterial blood gas: Hypoxemia, hypercarbia, and acid-base status, including compensation, can be evaluated.
- Spirometry is discussed in Chapter 9.

#### 9. How does a chronically elevated arterial carbon dioxide partial pressure affect the respiratory drive in a person with chronic obstructive pulmonary disease?

Persons with COPD have a reduced ventilatory drive in response to levels of carbon dioxide ( $\text{CO}_2$ ). Chronically elevated arterial carbon dioxide partial pressure ( $\text{PaCO}_2$ ) produces



increased cerebrospinal fluid bicarbonate concentrations. The respiratory chemoreceptors at the medulla become “reset” to a higher concentration of  $\text{CO}_2$ . Thus diminished ventilatory drive secondary to  $\text{CO}_2$  exists. In these patients ventilatory drive may be more dependent on  $\text{PO}_2$ .

**10. What are the deleterious effects of oxygen administration in these patients?**

Inhalation of 100% oxygen may increase ventilation-perfusion mismatch by inhibiting hypoxic pulmonary vasoconstriction (HPV). HPV is an autoregulatory mechanism in the pulmonary vasculature that decreases blood flow to poorly ventilated areas of the lung, ensuring that more blood flow is available for gas exchange in better ventilated areas of the lung. Inhibition of HPV results in increased perfusion of poorly ventilated areas of lung, contributing to hypoxemia and/or hypercarbia. It is prudent to always administer the minimum oxygen necessary to achieve the desired goal, perhaps a pulse oximetry value between 90% and 95%.

**11. How do general anesthesia and surgery affect pulmonary mechanics?**

Vital capacity is reduced by 25% to 50%, and residual volume increases by 13% following many general anesthetics and surgical procedures. Upper abdominal incisions and thoracotomy affect pulmonary mechanics the greatest, followed by lower abdominal incisions and sternotomy. Expiratory reserve volume decreases by 25% after lower abdominal surgery and 60% after upper abdominal and thoracic surgery. Tidal volume decreases 20%, and pulmonary compliance and functional residual capacity decrease 33%. Atelectasis, hypoventilation, hypoxemia, and pulmonary infection may result. Many of these changes require a minimum of 1 to 2 weeks to resolve.

**12. What factors are associated with an increased perioperative morbidity or mortality?**

Increased morbidity results from hypoxemia, hypoventilation resulting in acute hypercarbia, pulmonary infection, prolonged intubation, and mechanical ventilation. Intensive care days and overall hospitalization are prolonged, and mortality is increased.

Patients presenting for lobectomy or pneumonectomy must have pulmonary function and arterial blood gas values that are superior to the values in [Table 40-1](#). If any of the aforementioned criteria are not satisfied, further preoperative testing is indicated to determine the risk-benefit ratio for lung resection. Further tests include split-lung function, regional perfusion, regional ventilation, regional bronchial balloon occlusion, and pulmonary artery

**TABLE 40-1. PULMONARY FUNCTION VALUES ASSOCIATED WITH INCREASED PERIOPERATIVE MORTALITY/MORBIDITY\***

PFT	Abdominal Surgery	Thoracotomy	Lobectomy/Pneumonectomy
FVC	<70%	<70%	<50% or <2 L
FEV <sub>1</sub>	<70%	<1 L	<1 L
FEV <sub>1</sub> /FVC	<50%	<50%	<50%
FEF <sub>25-75</sub>	<50%	<50%	
RV/TLC			40%
PaCO <sub>2</sub>	>45–55 mm Hg	>45–50 mm Hg	

FEF<sub>25-75</sub>, Forced expiratory flow in the midexpiratory phase; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; PFT, pulmonary function test; RV, residual volume; TLC, total lung capacity.

\*Percentages are of predicted values.

balloon occlusion studies. A forced expiratory volume in 1 second ( $FEV_1$ ) less than 800 ml in a 70-kg person is probably incompatible with life and is an absolute contraindication to lung resection because of the high incidence for extended mechanical ventilation.

### 13. List the common pharmacologic agents used to treat COPD and their mechanisms of action.

See Table 40-2.

Class and Examples	Actions
$\beta$ -Adrenergic agonists: albuterol, metaproterenol, fenoterol, terbutaline, epinephrine	Increases adenylate cyclase, increasing cAMP and decreasing smooth muscle tone (bronchodilation); short-acting $\beta$ -adrenergic agonists (e.g., albuterol, terbutaline, and epinephrine) are the agents of choice for acute exacerbations
Methylxanthines: aminophylline, theophylline	Phosphodiesterase inhibition increases cAMP; potentiates endogenous catecholamines; improves diaphragmatic contractility; central respiratory stimulant
Corticosteroids: methylprednisolone, dexamethasone, prednisone, cortisol	Antiinflammatory and membrane stabilizing; inhibits histamine release; potentiates $\beta$ -agonists
Anticholinergics: atropine, glycopyrrrolate, ipratropium	Blocks acetylcholine at postganglionic receptors, decreasing cGMP, relaxing airway smooth muscle
Cromolyn sodium	Also a membrane stabilizer, preventing mast cell degranulation, but must be given prophylactically
Antileukotrienes: zileuton, montelukast	Inhibition of leukotriene production and/or zafirlukast, leukotriene antagonism; antiinflammatory; used in addition to corticosteroids; however, may be considered first-line antiinflammatory therapy for patients who cannot or will not use corticosteroids

*cAMP*, Cyclic adenosine monophosphate; *cGMP*, cyclic guanosine monophosphate.

### 14. What therapies are available to reduce perioperative pulmonary risk?

- Stop smoking.
  - Cessation for 48 hours before surgery decreases carboxyhemoglobin levels. The oxyhemoglobin dissociation curve shifts to the right, allowing increased tissue oxygen availability.

- Cessation for 4 to 6 weeks before surgery has been shown to decrease the incidence of postoperative pulmonary complications.
- Cessation for 2 to 3 months before surgery results in all of the previous benefits plus improved ciliary function, improved pulmonary mechanics, and reduced sputum production.
- Optimize pharmacologic therapy. Continue medications even on the day of surgery.
- Recognize and treat underlying pulmonary infection.
- Maximize nutritional support, hydration, and chest physiotherapy.
- Institute effective postoperative analgesia, allowing the patient to cough effectively, take large tidal volumes, and ambulate early after surgery.

#### 15. Do advantages exist with regional anesthesia techniques in patients with chronic obstructive pulmonary disease?

Regional anesthesia, including extremity and neuraxial blockade, avoids endotracheal intubation. However, spinal or epidural blockade above the T10 dermatome may reduce effective coughing secondary to abdominal muscle dysfunction, leading to decreased sputum clearance and atelectasis. Concerning brachial plexus anesthesia, pneumothorax or blockade of the phrenic nerve, causing hemidiaphragmatic paralysis, is a risk. Sedation administered during or after these procedures may depress respiratory drive and should be titrated to effect.

Local anesthetics infused through catheters placed into the brachial plexus sheath or the lumbar and thoracic epidural space provide superior postoperative analgesia. Neuraxial techniques improve pulmonary mechanics and opioids can be administered at much lower doses and with less sedation when compared to other parenteral routes.

#### 16. What agents can be used for induction and maintenance of general anesthesia?

The standard induction agents can all be used safely. Ketamine produces bronchodilation secondary to its sympathomimetic effects by direct antagonism of bronchoconstricting mediators, but secretions increase remarkably. Anecdotal evidence exists of bronchodilating properties from propofol. Intravenous lidocaine given before intubation can help blunt airway reflexes.

All volatile anesthetics produce bronchodilation. Desflurane is an airway irritant, although once the patient is intubated this is rarely a problem; it has the advantage of rapid clearance once discontinued.

Nitrous oxide increases the volume and pressure of blebs or bullae, thereby increasing the risk of barotrauma and pneumothorax. In addition, it may increase pulmonary vascular resistance and pulmonary artery pressures. This would be especially deleterious in patients with coexisting pulmonary hypertension or cor pulmonale. Therefore nitrous oxide should be avoided in patients with COPD.

#### 17. Discuss the particular concerns regarding muscle relaxation (and reversal) in patients with chronic obstructive pulmonary disease.

Atracurium and *d*-tubocurarine produce histamine release and might best be avoided. Succinylcholine also produces histamine release, and the benefits and risks of rapid paralysis and endotracheal intubation must be evaluated when considering its use.

Anticholinesterases (neostigmine and edrophonium) reverse the effects of nondepolarizing relaxants. Theoretically they may precipitate bronchospasm and bronchorrhoea secondary to stimulation of postganglionic muscarinic receptors. However, clinically bronchospasm is rarely seen after administration of these agents, possibly because anticholinergic agents (atropine or glycopyrrrolate) are concurrently administered.

#### 18. Discuss the choice of opioids in these patients.

Opioids blunt airway reflexes and deepen anesthesia. Morphine produces histamine release and should be used with caution. Hydromorphone, fentanyl, sufentanil, and remifentanil do not cause histamine release. Always consider the residual respiratory depressant affects of opioids at the end of surgery.

**19. Define auto-PEEP.**

Air trapping is known as auto-PEEP (positive end-expiratory pressure) and results from “stacking” of breaths when full exhalation is not allowed to occur. Auto-PEEP results in impairment of oxygenation and ventilation and hemodynamic compromise by decreasing preload and increasing pulmonary vascular resistance. Increasing expiratory time reduces the likelihood of auto-PEEP. This can be accomplished by increasing the expiratory phase of ventilation and decreasing the respiratory rate.

## KEY POINTS: CHRONIC OBSTRUCTIVE PULMONARY DISEASE



1. Patients with a significant reactive (and reversible) component to their lung disease require thorough preoperative preparation, including inhaled  $\beta$ -agonist therapy and possibly steroids.
2. Consider alternatives to general anesthesia in patients with a significant reactive component. An actively wheezing patient is not a good candidate for an elective surgical procedure.
3. *All that wheezes is not asthma*. Also consider mechanical airway obstruction, congestive failure, allergic reaction, pulmonary embolus, pneumothorax, aspiration, and endobronchial intubation.
4. Patients with chronic bronchitis may require antibiotic therapy, inhaled  $\beta$ -agonists, and measures to mobilize and reduce sputum before surgery to improve outcome. Smoking cessation is very beneficial in the long term.
5. Patients for planned pulmonary resections absolutely require pulmonary function tests to ensure that more lung is not resected than is compatible with life. Injudicious resections may create a ventilator-dependent patient.

**20. Form a differential diagnosis for intraoperative wheezing.**

- Bronchoconstriction (but remember: *all that wheezes is not asthma*)
- Mechanical obstruction of the endotracheal tube by secretions or kinking
- Aspiration of gastric contents or of a foreign body (i.e., a dislodged tooth)
- Endobronchial intubation (most commonly right mainstem intubation)
- Inadequate anesthesia
- Pulmonary edema (cardiogenic and noncardiogenic)
- Pneumothorax
- Pulmonary embolus

**21. How would you treat intraoperative bronchospasm?**

- Administer 100% oxygen and manually ventilate, allowing sufficient expiratory time. Identify and correct the underlying condition as discussed in Question 20.
- Administer therapy:
  - Relieve mechanical obstructions.
  - Increase the volatile anesthetic agents and/or administer intravenous lidocaine, ketamine, or propofol.
  - Administer  $\beta$ -adrenergic agonists: aerosolized via the endotracheal tube (e.g., albuterol), subcutaneously (e.g., terbutaline), or intravenously (e.g., epinephrine or terbutaline).
  - Administer anticholinergic bronchodilators: aerosolized via the endotracheal tube (e.g., ipratropium) or intravenously (e.g., atropine or glycopyrrolate).
  - Intravenous aminophylline and corticosteroids are also suggested therapies.
  - Although controversial, extubation may be beneficial because the endotracheal tube may be a stimulus for bronchoconstriction.

**22. What factors may determine the need for postoperative mechanical ventilation?**

Patients who exhibit a resting  $\text{PaCO}_2 >45$  to 50,  $\text{FEV}_1 <1$  L, forced vital capacity (FVC)  $<50\%$  to 70% of predicted, or  $\text{FEV}_1/\text{FVC} <50\%$  may require postoperative ventilation, especially for upper abdominal and thoracic surgeries. Consider how well the patient was prepared before surgery, the respiratory rate and work of breathing, the tidal volume and negative inspiratory force generated by the patient, arterial blood gas parameters, and body temperature. Is there residual neuromuscular blockade or effects of anesthetic agents? Is analgesia satisfactory?

**23. Should  $\text{H}_2$ -receptor antagonists be avoided in patients with chronic obstructive pulmonary disease?**

$\text{H}_1$ -receptor stimulation results in bronchoconstriction and  $\text{H}_2$ -receptor stimulation results in bronchodilation. Theoretically  $\text{H}_2$ -receptor antagonists would result in unopposed  $\text{H}_1$ -receptor stimulation, causing bronchoconstriction. Many patients with COPD take corticosteroids, have symptoms of gastritis or peptic ulcers, and receive  $\text{H}_2$  antagonists. Use of  $\text{H}_2$ -receptor antagonists should be individualized, and the patients observed for adverse side effects.

**24. At the conclusion of surgery, should a patient with chronic obstructive pulmonary disease be extubated deep or awake?**

Perhaps the better question is: can the surgical procedure be performed under regional anesthesia, avoiding endotracheal anesthesia altogether? If general anesthesia is required, perhaps a mask anesthetic or use of the laryngeal mask airway would limit the stimulation inherent in endotracheal intubation.

In an intubated patient with reactive airway disease, airway reflexes may be blunted through use of lidocaine (intravenous or intratracheal) and aerosolized  $\beta$ -adrenergic agonists. Selected patients may be candidates for deep extubation. Patients at risk for aspiration and those with difficult airways are not candidates for deep extubation. Typically deep extubation is accomplished with the patient breathing spontaneously, deeply anesthetized with a volatile agent, with airway reflexes suppressed. Deep extubation is not a 100% guarantee against bronchospasm as the patient awakens further.

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# ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

James B. Haenel, RRT, and Jeffrey L. Johnson, MD

## 1. What is the difference between acute lung injury and acute respiratory distress syndrome?

In 1992 the North American-European Consensus Committee (NAECC) on acute respiratory distress syndrome (ARDS) convened with the goal of providing a clearer and more uniform definition of acute lung injury (ALI)/ARDS. Two years later ALI was defined as an acute inflammatory condition resulting in increased lung permeability. The clinical presentation of ALI and ARDS in terms of timing, etiologies, chest film appearance, and lack of primary left atrial hypertension is comparable. ALI/ARDS is the same syndrome, but the degree of hypoxemia is worse in ARDS. Of importance, the degree of the hypoxemia is reflective of disease severity only; it does not predict mortality.

## 2. How would you define acute respiratory distress syndrome?

Three clinical definitions are commonly used: the NAECC definition, the Murray Lung Injury Score, and the Delphi definition (Table 41-1). The NAECC definition of ALI/ARDS offers two advantages; first, it provides a method of classifying patients who have less severe or a milder form of lung injury; and second, the definition is simple enough for those with even limited

TABLE 41-1. DEFINITIONS OF ACUTE LUNG INJURY AND ACUTE RESPIRATORY DISTRESS SYNDROME (AMERICAN-EUROPEAN CONSENSUS CONFERENCE)

### Acute Lung Injury Criteria

Timing: acute

Oxygenation:  $\text{PaO}_2/\text{FiO}_2 \leq 300$  mm Hg (regardless of PEEP)

Chest radiograph bilateral infiltrates on anteroposterior film

Pulmonary artery occlusion pressure:  $< 8$  mm Hg or no clinical evidence of left arterial hypertension

ARDS criteria

Same as acute lung injury except

Oxygenation:  $\text{PaO}_2/\text{FiO}_2 \leq 200$  mg Hg regardless of PEEP)

### Murray

#### Lung Injury Score

#### Chest Radiograph Score

No alveolar consolidation	0
Alveolar consolidation: 1 quadrant	1
Alveolar consolidation: 2 quadrants	2
Alveolar consolidation: 3 quadrants	3
Alveolar consolidation: 4 quadrants	4

(continued)

**TABLE 41-1. DEFINITIONS OF ACUTE LUNG INJURY AND ACUTE RESPIRATORY DISTRESS SYNDROME (AMERICAN-EUROPEAN CONSENSUS CONFERENCE)**  
(continued)

**Hypoxemia Score**

$\text{PaO}_2/\text{FiO}_2 \geq 300$	0
$\text{PaO}_2/\text{FiO}_2$ 225–299	1
$\text{PaO}_2/\text{FiO}_2$ 175–224	2
$\text{PaO}_2/\text{FiO}_2$ 100–174	3
$\text{PaO}_2/\text{FiO}_2$ 100	4

**PEEP Score (when ventilated)**

PEEP $\geq$ 5 cm H <sub>2</sub> O	0
PEEP 6–8 cm H <sub>2</sub> O	1
PEEP 9–11 cm H <sub>2</sub> O	2
PEEP 12–14 cm H <sub>2</sub> O	3
PEEP $\geq$ 15 cm H <sub>2</sub> O	4

**Respiratory System Compliance Score**

Compliance $\geq$ 80 ml/cm H <sub>2</sub> O	0
Compliance 60–79 ml/cm H <sub>2</sub> O	1
Compliance 40–59 ml/cm H <sub>2</sub> O	2
Compliance 20–39 ml/cm H <sub>2</sub> O	3
Compliance $\leq$ 19 ml/cm H <sub>2</sub> O	4

The final value is obtained by dividing the aggregate sum by the number of components that were used: no lung injury, 0; mild-to-moderate injury, 1–2.5; severe lung injury (ARDS), 2.5.

**DELPHI Definition of ARDS**

Timing: acute onset

Oxygenation:  $\text{PaO}_2/\text{FiO}_2 \leq 200$  With PEEP  $>$  10

Chest radiograph: bilateral infiltrates

Absence of congestive heart failure *or* presence of recognized risk factors for ARDS

ARDS, Acute respiratory distress syndrome; PEEP, positive end-expiratory pressure.

experience to readily apply. Unlike other definitions the NAECC has no reference to the set positive end-expiratory pressure (PEEP) level. This absence of a minimum level of PEEP and other ventilator settings maintains the simplicity of the NAECC definition but makes it too nonspecific. For example, a patient on 5 cm H<sub>2</sub>O of PEEP could have a  $\text{PaO}_2/\text{FiO}_2$  ratio of  $<$ 200; but, after a recruitment maneuver (RM) using a higher level of PEEP, 5 minutes later that same patient may have a  $\text{PaO}_2/\text{FiO}_2$  level of  $>$ 300.

**3. What are the risk factors for acute respiratory distress syndrome?**

Historically ARDS has been described as being a homogeneous and overwhelming inflammatory reaction of the pulmonary parenchyma to a variety of insults. Currently classification and identification of risk factors for ARDS are based on whether the inciting event is either a direct or indirect insult to the lung parenchyma (Table 41-2).

TABLE 41-2. CLASSIFICATION OF INCITING EVENTS ASSOCIATED WITH ALI/ARDS

Direct Lung Injury	Indirect Lung Injury
Aspiration of gastric contents	Sepsis
Pulmonary contusion	Multisystem trauma associated with shock
Diffuse pulmonary infections	Massive transfusion > 6 units PRBCs in ≤12 hours
<ul style="list-style-type: none"> <li>■ Bacterial</li> <li>■ Fungal</li> <li>■ Viral</li> <li>■ Pneumocystis</li> </ul>	Drug overdose
Inhalational injury	Acute pancreatitis
Near drowning	Cardiopulmonary bypass (rare)
	Fat emboli syndrome

*ALI*, Acute lung injury; *ARDS*, acute respiratory distress syndrome; *PRBC*, packed red blood cells.

Stratification of risk factors based on whether ARDS is caused by a pulmonary or extrapulmonary etiology has important implications beyond establishing its epidemiology and incidence. There are identified important mechanical differences in the lungs and chest wall compliance of patients based on whether there is a pulmonary or extrapulmonary cause for the ARDS. ARDS resulting from direct pulmonary disease is associated predominantly with lung tissue consolidation; therefore the response of a stiff lung to an RM with PEEP may be modest at best and carry the risk of overdistention of normal alveoli. In contrast, the lung suffering from an indirect insult demonstrates increased interstitial edema and diffuse alveolar collapse. Application of an RM with PEEP in this situation often results in a salient improvement in lung compliance and oxygenation.

#### 4. What is the most common cause and mortality rate for acute respiratory distress syndrome?

In the past sepsis syndrome was the most common risk factor for the development of ARDS. In the 1980s three prospective studies evaluated the risk factors for ARDS, and sepsis was identified as a risk in 43% of the cases. The most common diagnosis associated with ARDS, reported in the National Institutes of Health (NIH) Acute Respiratory Distress Syndrome Network (ARDS NET) study, was pneumonia (incidence = approximately 35%); sepsis as an etiology had an incidence of 27%.

The difficulty with interpreting mortality data is that the definition for this syndrome has changed at least three times. Yet three large randomized trials involving over 2000 patients provided consistent mortality data of between 33.9% and 36.3%.

#### 5. Describe the pathogenesis of acute respiratory distress syndrome.

Despite more than 30 years of clinical and basic laboratory work, the genesis for ARDS remains elusive. Common to all inciting risk factors is an intense inflammatory pulmonary reaction initially targeted at the interstitial and alveolar-capillary membrane. As a result of injury to the alveolar epithelial and endothelial membranes, flooding of the alveolar space with proteinaceous exudates containing vast numbers of neutrophils results in severe shunting and



altered gas exchange. Attraction of polymorphonuclear leukocytes (PMNs) to the injured lung has been linked to the presence of proinflammatory cytokines, endotoxins, thrombin, compliment, and vascular endothelial growth factor. Lung injury and other organ dysfunction may be exacerbated and perpetuated by inappropriate mechanical ventilation, suggesting that a combined biochemical and biophysical injury from alveolar overdistention and shear injury related to repeated opening and closing of distal airways exacerbates parenchymal damage.

#### 6. Describe the stages of acute respiratory distress syndrome.

Regardless of the specific etiology, clinical, radiographic, and histopathologic abnormalities generally progress through three overlapping phases, an acute or exudative phase, a proliferative phase, and finally a fibrotic phase also referred to as late ARDS. Identifying each phase in a particular patient is complicated and may be influenced by other confounding variables such as episodes of ventilator-associated pneumonia and the harmful effects of mechanical ventilation.

1. The exudative phase persists for about a week and is characterized clinically by symptoms of respiratory distress (dyspnea and tachypnea), refractory hypoxemia, and patchy bilateral radiographic infiltrates and pathologically by sequestration of neutrophils.
2. The proliferative phase manifests early in the second week. Clinically lung compliance remains low because of edema and replacement of fibrin and cell debris with collagen within the intra-alveolar space. There is persistent hypoxemia and increased alveolar dead space hampering CO<sub>2</sub> elimination. Pulmonary hypertension progressively worsens as the capillary network is destroyed, and intimal proliferation leads to a reduction of the luminal cross-sectional area. Radiographically there are diffuse alveolar infiltrates and air bronchograms on the chest x-ray film. Histologically there are increased amounts of inflammatory exudate consistent with PMNs and the beginning of fibroblast proliferation within the interstitium and alveoli.
3. Some time after 10 days the fibrotic or late phase of ARDS occurs. Clinically lung compliance is markedly decreased with static compliance values as low as 10 to 20 cm H<sub>2</sub>O, resulting in increased work of breathing and ventilator dependence. Radiographically the chest x-ray film reveals linear opacities consistent with fibrosis. The histopathologic correlate is progressive scarring of the lungs caused by dramatic increases in collagen levels. Many investigators have used steroids during this late phase of ARDS to attenuate host inflammatory responses.

#### 7. How do patients who develop acute respiratory distress syndrome typically present?

Within 24 hours of an identified risk factor, 80% of patients present with respiratory dysfunction; and within 72 hours the remaining patients progress to signs of respiratory compromise. Most patients will be receiving mechanical ventilation based on physiologic instability from their injury. The extent of hypoxemia (refractory to supplemental O<sub>2</sub>) cannot be predicted but may be exacerbated by the patient's baseline pulmonary function, intravascular volume status, adequacy of cardiac output, and severity of the inciting risk factor. Concurrent with worsening of intrapulmonary shunting the lung compliance is reduced, as evidenced by rising peak alveolar pressures (static plateau pressure). This reflects that the volume of aerated lung is diminished from persistent edema, atelectasis, and consolidation of the diseased lung. It is important to emphasize that the decreased compliance reflects the poor compliance of the lung tissue that is participating in ventilation and not the fluid-filled, consolidated lung. In the nonsedated patient tachypnea and air hunger with elevated minute ventilation are common. Auscultation of the lungs is surprisingly normal, and as a rule volume of secretions aspirated from the artificial airway is minimal.

**8. Do any pulmonary diseases mimic acute respiratory distress syndrome?**

Based on the NAEC criteria, a number of diffuse noninfectious parenchymal lung diseases fulfill all of the necessary criteria for ALI/ARDS (Table 41-3). Most of the patients who meet these criteria are initially diagnosed with ALI/ARDS secondary to pneumonia. Although pneumonia is one of the most prevalent causes for ARDS, an infectious etiology can be found in about 50% of the cases. Patients who present without an obvious risk factor for pneumonia should undergo a bronchoscopic alveolar lavage and may require an open lung biopsy to fully exclude a noninfectious etiology for their lung disease. The misdiagnosis of a patient having a noninfectious cause for the onset of acute pulmonary dysfunction may exclude them from receiving appropriate therapy with systemic corticosteroids.

**TABLE 41-3. CAUSES OF ACUTE NONINFECTIOUS LUNG DISEASES**

Acute interstitial pneumonia
Acute eosinophilic pneumonia
Acute bronchiolitis obliterans organizing pneumonia
Diffuse alveolar hemorrhage
Acute hypersensitivity pneumonia

**9. Are any drug therapies available to treat acute respiratory distress syndrome?**

Unfortunately, despite the establishment of an NIH network (ARDS NET) of interactive critical-care treatment groups involved in performing prospective, randomized, controlled, multicenter trials, no effective drug therapy has been identified. Thromboxane synthetase inhibitors, nitric oxide (NO), corticosteroids, surfactant, *N*-acetylcysteine, inhaled prostacyclin, liquid ventilation, activated protein C, and other agents have also been trialed but with unconvincing success.

**10. Does that mean that none of these agents has a role in patients with refractory acute respiratory distress syndrome?**

Because no one pharmacologic agent has demonstrated a reduction in mortality rates doesn't mean that an individual patient may not respond favorably to a targeted drug therapy. For example, inhaled NO, once considered a promising therapy because of its ability to provide selective pulmonary vasodilation and improve ventilation-perfusion mismatch, has not demonstrated improved mortality outcomes. However, if a patient is dying from refractory hypoxemia, trials of inhaled NO have consistently resulted in improved oxygenation and pulmonary hemodynamics in 60% of patients. These benefits are short lived, diminishing over a 24- to 48-hour period; but this *bought* time may allow for other therapies such as antibiotics to become effective. Similarly, a recent study from ARDS NET pertaining to the safety and efficacy of corticosteroids in persistent ARDS concluded that the *routine* use of methylprednisolone was not warranted. Nonetheless, to date there have been five trials consisting of 518 patients who have received corticosteroids as part of an ARDS protocol and have demonstrated significant improvements in gas exchange, reduction in markers of inflammation, and decreased duration of mechanical ventilation and intensive care unit (ICU) days. There is nothing *routine* about refractory ARDS; therefore decisions regarding advanced pharmacologic therapies must be evaluated in light of the patient's physiologic status.

**11. Is there an optimal fluid strategy in acute respiratory distress syndrome?**

Recently the ARDS NET demonstrated that a conservative fluid management approach that resulted in a negative fluid balance at day seven ( $-136 \pm 491$  ml) vs. a liberal fluid strategy

(6992 ± 502 ml) resulted in fewer ventilator days, fewer ICU days, and no increase in nonpulmonary-organ failures. An aside, the use of a pulmonary artery catheter when compared to a central venous catheter demonstrated no differences in outcome.

## 12. Can mechanical ventilation exacerbate or delay healing from acute respiratory distress syndrome?

Yes. The syndrome of ALI/ARDS results in a very inhomogeneous pattern of lung consolidation. Early in the course of lung injury these heterogeneous changes in lung morphology may give rise to lung zones that consist of normal lung regions; potentially recruitable lung regions within the mid portion of the lungs; consolidated, gravity-dependent lung; and areas of hyperinflated lung tissue. As a consequence of the ongoing structural changes occurring within the lung parenchyma, a ventilator-associated lung injury (VALI) may result from maldistribution of tidal volumes ( $V_T$ s) and high airway pressures creating overdistention of remaining normal, aerated lung regions. This high-volume induced form of lung injury is known as *volutrauma*. Conversely, parenchymal injury also occurs when the lungs are being ventilated from a low lung volume and with low end-expiratory pressures. Although not completely understood, the formation of this low-volume environment probably occurs as a consequence of the increased shear stress) resulting from repeated opening and closing of occluded bronchioles and alveoli from surfactant deficiency. This low-volume induced region of injury is referred to as atelectrauma. Undoubtedly there needs to be a balance between providing a sufficient inspiratory plateau pressure (peak alveolar pressure) while at the same time avoiding insufficient amounts of end-expiratory pressures.

## 13. How should patients with acute respiratory distress syndrome be ventilated?

As a result of mounting evidence for increased morbidity and mortality associated with ventilator-induced lung injury, clinicians have focused on providing lung protective strategies in patients with ALI/ARDS. Numerous trials have compared the efficacy of a low  $V_T$  approach to more traditional  $V_T$ . The largest trial was the ARDS NET study involving 861 patients that compared a  $V_T$  of 6 ml/kg of predicated body weight to a  $V_T$  of 12 ml/kg. Further reduction in  $V$  as low as 4 ml/kg was permitted in the low group if end-inspiratory plateau pressures remained >30 cm H<sub>2</sub>O, whereas  $V_T$  reduction could not occur in the traditional group unless plateau pressures were >50 cm H<sub>2</sub>O. Mortality was 39.8% in the traditional  $V_T$  group and 31% in the low  $V_T$  patients, resulting in approximately a 20% reduction in mortality. In other words, for every 10 patients ventilated with a lung protective approach, one life will be saved.

## 14. Define lung recruitment maneuver and the different techniques for performing it.

Lung recruitment is defined as the application of a prolonged increase in airway pressure, with the goal being reversal of atelectasis; this is followed by the application of sufficient amounts of PEEP to ensure that the lung stays open. Various techniques are available to accomplish recruitment maneuver (RM) (Table 41-4). Most RMs are performed on an intermittent basis through manipulation of the mechanical ventilator, whereas some other techniques are continuous.

Although RMs are commonly accepted as part of a lung protective strategy for ALI/ARDS, there is still much to be learned about their use: which patients will benefit, direct vs. indirect lung injury, optimal duration for RM, whether RMs should be applied routinely or only during acute hypoxic events, and whether the baseline PEEP makes a difference in terms of response.

## 15. How does prone ventilation improve oxygenation?

The primary pulmonary defect based on computed tomographic scans of supine patients with ARDS is the opacification of the gravity-dependent areas of the lung as a result of atelectasis and consolidation. Clearly alveolar flooding from formation of edema fluid is partially responsible for the atelectasis, but mechanical imbalances caused by cephalic displacement of

TABLE 41-4. TECHNIQUES FOR PERFORMANCE OF RECRUITMENT MANEUVERS

Conventional Ventilation	Unconventional Modes	Positioning
Sustained inflation/CPAP <ul style="list-style-type: none"> <li>■ CPAP of 30–40 cm H<sub>2</sub>O</li> </ul>	High-frequency ventilation <ul style="list-style-type: none"> <li>■ High-frequency oscillation</li> </ul>	Prone ventilation <ul style="list-style-type: none"> <li>■ Use reverse Trendelenburg position; maintain for PEEP 12–24 hours</li> </ul>
PEEP <ol style="list-style-type: none"> <li>1. Incremental increases by 2.5–5 cm H<sub>2</sub>O until increase in P/F ratio</li> <li>2. PCV mode: RR 10/min, I:E 1: PIP 20 cm H<sub>2</sub>O, increase PEEP to 30–40 cm H<sub>2</sub>O for 2 minutes</li> </ol> Addition of sighs Consider spontaneous breathing	Airway pressure release ventilation <ul style="list-style-type: none"> <li>■ Pressure-control inverse ratio ventilation</li> </ul>	Supine position <ul style="list-style-type: none"> <li>■ Maintain head of bed at 30 to 45 degrees with frequent turning</li> </ul>

*CPAP*, Continuous positive airway pressure; *I:E*, inspiratory-to-expiratory ratio; *PCV*, pressure-control ventilation; *PEEP*, positive end-expiratory pressure; *PIP*, peak inspiratory pressure; *RR*, respiratory rate.

the diaphragm with positive-pressure ventilation, decreased thoracic and abdominal compliance, increased pleural pressure in dorsal lung regions, and the weight of the heart causing compression of the lower lung regions all act in concert to worsen atelectasis and promote ventilation-perfusion mismatching. Interestingly, gravity plays only a minor role in perfusion heterogeneity in the lung; therefore the dorsal regions of the lung, regardless of positioning, always receive preferential perfusion. Improvements in oxygenation by using the prone position probably result from:

- Recruitment of collapsed dorsal lung fields by a redistribution of lung edema to ventral regions.
- Increased diaphragm motion enhancing ventilation.
- Elimination of the compressive effects of the heart on the inferior lower lung fields, thus improving regional ventilation.
- Maintenance of dorsal lung perfusion in the face of improved dorsal ventilation leads to improved V/Q matching.

#### 16. Does prone ventilation offer a survival benefit in acute respiratory distress syndrome patients?

Since 2001 there have been over nine randomized prospective trials of prone ventilation in critically ill patients. In 2008 alone there have been four metaanalyses of prone ventilation reporting on approximately 1562 patients. All but two of these trials used some form of lung-protective ventilation strategy. The unwavering findings from all of these reports is that prone ventilation results in a consistent improvement in oxygenation but unfortunately shows no clear impact on mortality.

**KEY POINTS: ADULT RESPIRATORY DISTRESS SYNDROME**

1. Historically sepsis has been identified as the most common risk factor for ARDS.
2. VALI is thought to be caused by two mechanisms:
  - Overdistention of normal aerated lung by using high tidal volumes
  - Lung collapse that occurs as a result of ventilating the lungs with low end-expiratory volumes and pressures
3. Mechanical ventilation settings for patients with ARDS or ALI include tidal volume at 6 to 8 ml/kg of ideal body weight and limiting plateau pressures to <30 cm H<sub>2</sub>O.
4. PEEP should be adjusted to prevent end-expiratory collapse.
5. FiO<sub>2</sub> should be adjusted to maintain oxygen saturations between 88% and 92%.

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# PULMONARY HYPERTENSION

*James Duke, MD, MBA*

## 1. Define pulmonary hypertension.

Although there is no widely accepted range for normal pulmonary blood pressures, pulmonary hypertension (PH) exists when the pulmonary systolic pressure exceeds 25 mm Hg in the presence of normal cardiac output (CO) and pulmonary capillary wedge pressure. During exercise PH is considered a pulmonary artery pressure (PAP) greater than 30 mm Hg.

## 2. List conditions that produce pulmonary hypertension.

PH is said to be idiopathic if it is found in the absence of secondary causes such as pulmonary disease (congenital or parenchymal), cardiac disease (e.g., shunts, mitral stenosis, left ventricular failure), thromboembolic or obliterative pulmonary vascular disease, connective tissue disease (especially the scleroderma family), exogenous vasoconstrictive substances (e.g., the appetite suppressant flufenamine), or portal hypertension. Although rare in the general population, at-risk populations include those with connective tissue disease and human immunodeficiency virus. Idiopathic PH was formally called primary PH, is a diagnosis of exclusion, affects one to two per million populations, sometimes has a familial link, and is found more in women than in men. PAPs tend to be higher in idiopathic PH when compared to secondary causes of PH.

## 3. Discuss the pathophysiology and natural history of pulmonary hypertension.

Endothelial cell injury leads to imbalances between vasodilator and vasopressor molecules. Reductions in the endogenous vasodilators nitric oxide (NO) and prostacyclin (PGI<sub>2</sub>) are noted, whereas the vasoconstrictors thromboxane and endothelin are increased. But vasoconstriction appears to be only part of the answer because thrombosis, inflammation, free radical generation, and smooth muscle hyperplasia are also common features noted in PH. Indeed, vascular remodeling is a prominent feature of PH.

The pulmonary circulation has high flow and low resistance. Changes in CO, airway pressure, and gravity affect the pulmonary circulation more than the systemic circulation. The right ventricle is thin walled and accommodates changes in volume better than changes in pressure. To accommodate increases in flow such as during exercise, unopened vessels are recruited, patent vessels distended, and pulmonary vascular resistance (PVR) may decrease. Such normal adaptive mechanisms can accommodate threefold to fivefold increases in flow without significant increases in PAPs.

Early in the evolution of PH, the pressure overload results in hypertrophy of the right ventricle without significant changes in CO or RV filling pressures either at rest or during exercise. As the disease progresses, the vessel walls thicken and smooth muscle cells hypertrophy and increase in number. Vessels become less distensible, and the actual cross-sectional area of the pulmonary circulation decreases. Initially with exercise CO eventually declines despite modest increases in right ventricular (RV) end-diastolic pressures (RVEDP). Mechanisms for enhancing contractility are few for the right ventricle. In time, RV failure (RV ejection fraction below 45%) ensues, and the patient is symptomatic even at rest. RV myocardial blood flow becomes compromised, and tricuspid regurgitation develops secondary to right ventricle distention, further increasing RVEDP and worsening failure. In addition, left ventricular (LV) diastolic function may deteriorate, and LV filling may be compromised by excessive septal incursion into the left ventricle, with a resultant decrease in CO.

Without treatment PH is universally fatal, with a mean survival of 2.8 years. One-, 3, and 5-year survival rates are 68%, 48%, and 34%, respectively. The mortality rate during pregnancy is 30% to 50%, and most experts recommend early termination of pregnancy in these women should pregnancy occur.

#### 4. What is the blood supply to the right ventricle?

It depends on whether the right or left coronary artery is dominant. Usually the right and left anterior descending coronary arteries supply the septum and portions of the RV free wall. Normally the RV free wall is perfused during systole and diastole. RV performance is directly related to systemic pressure during PH.

#### 5. How is pulmonary vascular resistance calculated and what are normal values?

$$PRV = (\text{mean PAP} - \text{LAP}) / \text{pulmonary blood flow}$$

where LAP is left atrial pressure. CO is often substituted for pulmonary blood flow, although intracardiac and other shunts make these unequal. Normal PVR is 1.1 to 1.4 Woods units or about 90 to 120 dynes/sec/cm<sup>-5</sup>. (A Woods unit is 240 dynes/sec/cm<sup>-5</sup>.) A PVR greater than 300 dynes/sec/cm<sup>-5</sup> is indicative of PH.

#### 6. What are some electrocardiographic and radiologic features of the disease?

The electrocardiogram commonly shows right axis deviation, RV hypertrophy (tall R waves in V<sub>1</sub>-V<sub>3</sub>), RV strain (T-wave inversion in V<sub>1</sub>-V<sub>3</sub>), S wave in V<sub>6</sub>, and enlarged P waves in II, III, and aVF. Although atrial fibrillation is rare, its presence should be viewed with concern because the contribution of *atrial kick* to ventricular filling is unavailable.

Radiologic abnormalities have been observed in over 90% of cases. Abnormalities on chest radiographs suggestive of PH include prominence of the right ventricle and the hilar pulmonary artery trunk, rapid tapering of vascular markings, a hyperlucent lung periphery, and decrease in the retrosternal air space.

#### 7. What signs and symptoms suggest pulmonary hypertension?

##### Symptoms

- Dyspnea, initially on exertion (almost all patients with PH eventually become dyspneic)
- Angina (50% of patients)
- Fatigue (20% of patients)
- Weakness
- Syncope

##### Early signs

- Increase in the pulmonic component of S2
- Narrowly split S2
- Ventricular fourth heart sound
- Early diastolic murmur of tricuspid regurgitation
- RV heave

##### Late signs

- Jugular venous distention (giant systolic V waves)
- Peripheral edema
- Cyanosis
- RV S3 gallop
- Ascites and hepatomegaly

#### 8. Discuss the observed abnormalities on pulmonary function testing.

Pulmonary function tests demonstrate mild restrictive defects secondary to the effects of the noncompliant pulmonary vasculature. Arterial blood gases reveal varying degrees of hypoxemia.

### 9. What additional diagnostic tests are available for evaluating pulmonary hypertension? What results may be expected?

An echocardiogram is an excellent noninvasive method for following progression of the disease. Echocardiographic features of PH include enlarged RV dimension, small LV dimension, thickened interventricular septum, systolic mitral valve prolapse, and abnormal septal motion. Determination of PAPs and PVR by pulsed Doppler echocardiography correlates well with values determined at cardiac catheterization.

Perfusion lung scans are particularly important in patients in whom thromboembolic disease is suspected. Thromboembolic disease is remediable with thromboendarterectomy and anticoagulation, whereas primary PH (PPH) is not. Lung scan demonstrates segmental defects in patients with thromboemboli but not in patients with PPH. Pulmonary angiography is indicated in patients demonstrating segmental perfusion scan defects, but it should be undertaken cautiously in patients with PH. Although they are not contraindications, the associated risks of this procedure, including hypotension, worsening oxygenation, and cardiac arrest, should be weighed carefully against the potential benefit. In particular, patients with RV failure and increased RVEDP tolerate this procedure poorly.

Finally, cardiac catheterization is mandatory for confirming the diagnosis of PH and ruling out intracardiac shunts as a cause. In PH catheterization may prove to be technically demanding and require guidewire assistance. Detection of an elevated wedge pressure is an indication for left-sided heart catheterization to rule out mitral stenosis, congenital heart disease, and left-sided heart failure as causes of PH.

The degree to which PAP and PVR can be decreased acutely by the administration of a vasodilator reflects the extent to which smooth muscle constriction is contributing to the hypertensive state and suggests that vasodilator therapy may be of some benefit.

### 10. Discuss standard therapies for patients suffering from pulmonary hypertension.

Supplemental oxygen therapy is common, the goal being to maintain saturations above at least 90%. Diuretics may be prescribed to patients with RV failure, hepatic congestion, and peripheral edema, although excessive diuresis may decrease RV preload and CO.

Anticoagulation is often instituted (usually oral warfarin, dosed to achieve an international normalized ratio of 1.5 to 2.0), because patients are at great risk for thromboembolic events (which may prove to be terminal). Cardiac glycosides are used when there are signs of RV failure and in patients who have developed atrial arrhythmias (e.g., multifocal atrial tachycardia, atrial fibrillation, or atrial flutter), although serum electrolytes must be closely followed when digoxin is administered to a patient on diuretics. Vasodilator therapy is discussed subsequently. Finally lung or heart-lung transplantation must be considered a contemporary yet expensive option in selected patients with PH.

### 11. What medications are available to treat increased pulmonary artery pressures?

Almost all classes of vasodilators have been investigated, including direct smooth muscle vasodilators,  $\alpha$ -adrenergic antagonists,  $\beta$ -adrenergic agonists, calcium channel blockers, prostaglandins, phosphodiesterase inhibitors, and angiotensin-converting enzyme inhibitors. Intravenous medications available for intraoperative use and intensive care management include nitroglycerin, nitroprusside, prostaglandin E<sub>1</sub> (alprostadil), PGI<sub>2</sub>, phentolamine, and isoproterenol. Calcium channel blockers are the current outpatient therapy of choice. High doses of nifedipine, diltiazem, or amlodipine have produced reductions in PA pressures and PVR and regression of RV hypertrophy. Verapamil is not used because of its negative inotropic effects. The phosphodiesterase III inhibitors milrinone and amrinone have successfully been used to treat postcardiac surgery PH. Adenosine may decrease PVR and has been used in conjunction with calcium channel blockers. However, because of its negative inotropic and chronotropic effects and its effects on sinus and atrioventricular nodal conduction, it should be used with caution in patients with ischemic heart disease. Finally, endothelin receptor antagonists are now available. They include bosentan, sitaxsentan, and ambrisentan.



### 12. A patient with a history of pulmonary hypertension presents for a surgical procedure. How should this patient be monitored intraoperatively?

In addition to the routine monitors, invasive monitoring is standard management for patients with PH. Intra-arterial pressure monitoring allows beat-to-beat assessment of blood pressure and frequent blood gas analysis. Central venous pressure (CVP) monitoring is inaccurate when there is tricuspid regurgitation or when RV compliance is decreased. A PA catheter allows direct monitoring of PAP and right atrial pressure and indirect assessment of LV volume and performance through measuring of pulmonary occlusion pressures. However, it should be recognized that patients with PH having PA catheterization are at increased risk for PA rupture.

Transesophageal echocardiography (TEE) is particularly useful in assessing volume status, LV and RV performance and valvular regurgitation, and early detection of segmental wall motion abnormalities secondary to myocardial ischemia. Because of the concerns for PA rupture, in skilled hands TEE may obviate the need for PA catheterization.

### 13. What intraoperative measures may decrease PH?

- As hypoxemia and hypercarbia increase PAPs, optimize the patient's oxygenation and ventilation. In contrast to systemic vessels, pulmonary vessels constrict with hypoxia. Recruitment maneuvers may improve ventilation-perfusion matching, but avoid overinflation. High levels of positive end-expiratory pressure (PEEP) may narrow vessels to well-ventilated areas of the lung, decreasing  $PO_2$ . Levels of PEEP greater than 15 cm  $H_2O$  should be avoided.
- Assess myocardial performance; increasing PA pressures may be secondary to a failing left ventricle. If ischemia is associated with a decreasing CO, consider infusing nitroglycerin to improve coronary perfusion. Inotropic drugs such as dobutamine or dopamine may enhance contractility and improve CO.
- Assess volume status. Although the right ventricle is less preload responsive than the left ventricle, CVP values less than 10 mm Hg suggest the need for preload augmentation. Before surgery an *endogenous volume loading* test can be performed by raising the patient's legs. *Responders* have an improvement in blood pressure with this maneuver and would be candidates for intraoperative fluid challenge. *Nonresponders* probably have RV failure, and fluid challenges may worsen this.
- Correct acidosis and ensure the patient is not becoming hypothermic. Both acid-base abnormalities and hypothermia may cause increased PA pressure. The effects of acidosis are worse in the presence of hypoxemia. Moderate hyperventilation (a  $PaCO_2$  of about 30 mm Hg) is suggested.
- Deepen the anesthetic. Catecholamine release will increase PA pressure.
- Consider the use of inotropes in the setting of RV failure. The phosphodiesterase III inhibitors milrinone and amrinone prevent the breakdown of cyclic guanosine monophosphate (cGMP) and increase LV contractility while dilating the pulmonary vasculature. Dobutamine is also an option.
- If systemic hypotension and coronary perfusion are problematic, vasoconstrictors may be superior to volume loading and inotropes. Because of the balance between  $\alpha$ - and  $\beta$ -adrenergic effects, norepinephrine is the vasoconstrictor of choice. Norepinephrine should be administered carefully because it can increase PA pressure.
- Consider the use of direct-acting vasodilators. This will be discussed in further detail.

### 14. Discuss the effect of volatile anesthetics and nitrous (not nitric) oxide on the pulmonary circulation.

When used as part of a maintenance anesthetic, isoflurane at 1 to 1.2 minimum alveolar concentration (MAC) levels has been demonstrated to lower PAP and PVR and improve CO in this setting. Its presumed mechanism is direct action on pulmonary vascular smooth muscle. Of the volatile anesthetics, isoflurane probably has the greatest effect on vascular smooth muscle. The suggested MAC levels maintain  $PaO_2$  as well, suggesting that hypoxic pulmonary

vasoconstriction (HPV) is not inhibited at this depth of anesthesia. However, isoflurane and any other volatile anesthetic should be titrated carefully since impaired RV function is a risk.

Nitrous oxide can increase PVR and attenuate HPV; its use in PH is best avoided.

**15. What are the effects of intravenous anesthetics on pulmonary artery pressure and hypoxic pulmonary vasoconstriction?**

Propofol infusions have been shown to decrease PAP and PVR. Simultaneous reductions in mean arterial pressure also occur. Intravenous anesthetics have minimal effect on hypoxic pulmonary vasoconstriction and oxygenation. Opioids do not have a direct vasodilator effect but may attenuate the vasoconstrictor effect of noxious pain stimuli. In children with intracardiac shunts ketamine may prevent reversal of left-to-right shunts because it increases systemic vascular resistance to a greater extent than PVR.

**16. Are regional anesthetics an option?**

Epidural anesthesia has been used safely in patients with PH. Acute changes in systemic vascular resistance (SVR) associated with spinal anesthesia suggest that epidural anesthesia is preferred. Invasive monitoring is still suggested. Loss of cardioaccelerator fibers found from T1-T4 may result in undesirable bradycardia. Before the procedure the patient should be cautiously preload augmented, and medications to treat acute decreases in SVR or heart rate should be at hand.

**17. Discuss the advantages and disadvantages of the intravenous nitrovasodilators.**

Because of their ready availability, titratability, and common use, intravenous nitrovasodilators are popular in the acute management of increased PAPs. Commonly used nitrovasodilators include nitroglycerin and sodium nitroprusside, and their mechanism of effect is release of NO. Nitroglycerin has the advantage of providing coronary vasodilation. Principally a venodilator, nitroglycerin may excessively decrease preload. Nitroglycerin infusion is started at about 1 mcg/kg/min and ordinarily produces a smooth reduction in vascular pressures. Above 3 mcg/kg/min, venodilation may become excessive, decreasing preload and requiring intravenous fluid augmentation.

Sodium nitroprusside (SNP) is an extremely potent, principally arterial vasodilator. Infusions begin about 0.5 to 1 mcg/kg/min and are carefully adjusted upward to effect. SNP is extremely effective at afterload reduction. Despite its potency and potential for creating excessive hypotension, SNP is safe for short-term use. Long-term use is associated with tachyphylaxis and the potential for cyanide toxicity.

Despite their effects of pulmonary vascular resistance, they are nonselective and also decrease systemic blood pressure and threaten myocardial ischemia, especially in the setting of a hypertrophied ventricle. Further, they nonselectively dilate pulmonary blood vessels, increase perfusion of underventilated alveoli, and increase ventilation-perfusion mismatch, resulting in hypoxemia.

**18. Discuss the properties of nitric oxide (NO).**

NO is a small molecule produced by vascular endothelium. Formed from the action of NO synthetase on arginine, NO crosses into vascular smooth muscle and stimulates guanylate cyclase, resulting in formation of 3',5'-cGMP. Subsequently cGMP produces smooth muscle relaxation and vasodilation.

NO is administered by inhalation and crosses the alveolar membrane to the vascular endothelium, producing smooth muscle relaxation. But when it crosses into the circulation, it is rapidly bound to hemoglobin (with an affinity 1500 times greater than carbon monoxide) and deactivated; thus it has no systemic vasodilator effect. In addition, since it is only delivered to perfused alveoli, it may increase blood flow to ventilated alveoli. Dosage ranges can be quite wide, but 20 to 40 parts per million is not an atypical dose.

Deactivation on entering the circulation also limits the effectiveness of NO to the period in which it is administered by inhalation. Because storage in oxygen produces toxic higher oxides of nitrogen, especially nitrogen dioxide (NO<sub>2</sub>), NO is stored in nitrogen and blended with ventilator gases immediately before administration. The potential for increased methemoglobin levels during NO administration should also be recognized. It has proinflammatory and antiinflammatory effects, and the significance of this is not fully understood. It also impairs platelet aggregation and adhesion.

### 19. Discuss the therapeutic usefulness and limitations of nitric oxide in pulmonary hypertension.

During evaluation of a patient diagnosed with PH, inhaled NO (and intravenous epoprostenol or adenosine) is used to assess vasodilator response. A positive response is a decrease in mean PAP of 10 mm Hg to a value of less than 40 mm Hg and a maintained or increased CO. Patients with such a response are candidates for long-term oral calcium channel blocker therapy.

Cardiopulmonary bypass (CPB) induces pulmonary endothelial injury, probably caused by ischemia-reperfusion injury, although other factors are probably involved as well. Levels of the vasoconstrictors thromboxane and endothelin are increased, whereas levels of the vasodilators PGI<sub>2</sub> and endogenous NO are decreased. PH coming off of CPB is a predictor of increased mortality and postoperative myocardial infarction. NO has been tested for the treatment of PH after valve replacement, correction of congenital cardiac defects, and cardiac transplantation; improvements in outcome have not been uniformly beneficial. It has also been used as a bridge to lung transplantation.

There are numerous investigations concerning the efficacy of NO in improving oxygenation and PH in adult respiratory distress syndrome (ARDS). Factors that produce PH in ARDS include parenchymal destruction, microthrombi, airway collapse, pulmonary vasoconstriction, and adverse effects of PEEP. Although oxygenation improves, taking all comers, there are no randomized, controlled studies that show improved outcomes when ARDS is treated with NO.

Numerous neonatal conditions are associated with PH, including congenital diaphragmatic hernias, congenital heart disease, and persistent PH of the neonate. At this time, NO is only approved for use in infants with respiratory distress syndrome.

Portal pulmonary hypertension (PPHTN) is a complication of cirrhosis and portal hypertension and has previously been considered a contraindication to liver transplantation. Epoprostenol has demonstrated some benefit in PPHTN; the benefit of NO has been less convincing.

## KEY POINTS: PULMONARY HYPERTENSION



1. Give fluid infusions.
2. Optimize oxygenation and ventilation.
3. Correct acid-base status.
4. Establish normothermia.
5. Decrease the autonomic stress response by deepening the anesthetic.
6. Administer vasodilator therapy.

### 20. What are prostanoids and their therapeutic counterparts?

Prostanoids are found in vascular endothelium and act via specific prostaglandin receptors to stimulate adenylate cyclase and increase cyclic adenosine monophosphate. Prostaglandins

relax smooth muscle relaxation and platelet inhibition. The production of the naturally occurring PGI<sub>2</sub> is decreased in PH.

When administered by continuous intravenous infusion, eprostenol (PGI<sub>2</sub>) has a half-life of 2 to 3 minutes. Like the nitrovasodilators, intravenous prostanoids lack pulmonary selectivity, and systemic hypotension and decreased RV coronary perfusion are a risk.

Prostanoid analogs are now available that may be delivered by the inhaled route, subcutaneously, or orally. The inhaled route has some limitations because aerosolization is rather inefficient for delivery of the active agent to distal airways.

#### 21. What is the value of adenosine?

Adenosine relaxes smooth muscle cells in the pulmonary circulation. It has a half-life of only 9 seconds; thus, when administered intravenously, its actions are relatively confined to the pulmonary circulation. Although it is a potent vasodilator, ventilation-perfusion mismatch increases.

#### 22. What are phosphodiesterase-5 inhibitors?

PDE<sub>5</sub> is an enzyme that degrades cGMP. The PDE-5 inhibitors are orally administered vasodilators that prevent the degradation of cGMP, potentiating the effect of NO. Currently available PDE<sub>5</sub> inhibitors include zaprinast and sildenafil. They are synergistic when used in conjunction with NO or prostanoids.

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# PERIOPERATIVE HEPATIC DYSFUNCTION

Matthew J. Fiegel, MD

## 1. What is the normal physiologic function of the liver?

The human liver consists of four anatomic lobes (left, right, caudate, quadrate) and eight surgical lobes (I–VIII). The liver receives approximately 20% to 25% of the cardiac output and contains 10% to 15% of the total blood volume. The portal vein supplies 75% of the blood flow of the liver and 50% of its oxygen requirements.

Almost all plasma proteins are synthesized in the liver. These include albumin,  $\alpha_1$ -acid glycoprotein, pseudocholinesterase, and all coagulation factors except factors III, IV, and VIII. The liver is also involved in carbohydrate, lipid, and cholesterol metabolism and bile synthesis. The liver produces 20% of the body's heme. The liver possesses an immune function in that hepatic Kupffer cells filter splanchnic venous blood of bacteria. Last, the liver serves as the main organ of drug metabolism and detoxification. Through three hepatic reactions (phases I, II, and III), drugs are metabolized to a more water-soluble form and excreted in the urine or bile. Phase I reactions use the cytochrome P-450 family of proteins and consist of oxidation, reduction, or hydrolysis. Phase II reactions undergo conjugation with substances such as glucuronic acid and amino acids. In phase III reactions, endogenous hepatic proteins use adenosine triphosphate to excrete various substances. Within the liver, nitrogen-containing compounds are degraded to urea.

## 2. What is the most common cause of acute parenchymal liver disease?

Viral infection is responsible for the majority of cases of acute hepatitis. Traditionally hepatitis B (HBV) was the most common form of acute viral hepatitis. However, with the advent of the HBV vaccine, hepatitis A and C are accounting for a larger percent of cases worldwide. Epstein-Barr virus and cytomegalovirus also cause acute hepatitis. Nonviral causes include drugs and toxins. Drug-induced liver injury (DILI) can mimic acute viral hepatitis and is most commonly caused by alcohol, antibiotics, and nonsteroidal anti-inflammatory drugs. DILI causing an elevation in bilirubin carries a 10% mortality rate.

## 3. What is cirrhosis?

Cirrhosis, the most serious sequelae of chronic hepatitis, is characterized by diffuse death of liver cells, causing fibrous tissue formation and nodular regeneration of hepatic tissue. The consequent distortion of the hepatic circulation further propagates cellular damage and results in a progressive reduction of liver cells, which eventually manifests as impairment of liver function. Hepatic synthetic failure, indicated by a prolonged prothrombin time (PT)/international normalized ratio (INR), decrease in serum albumin levels, and impairment of detoxification mechanisms resulting in encephalopathy, is often termed *end-stage liver disease* (ESLD).

## 4. Describe the neurologic derangements in patients with cirrhosis.

Central nervous system dysfunction presents as hepatic encephalopathy, ranging from confusion to coma, and may be secondary to increased dietary protein consumption or gastrointestinal (GI) bleeding. Increased ammonia levels do not correlate with the degree of encephalopathy. Treatment consists of a low protein diet, lactulose, and rifaximin. Acute fulminating liver failure may present with cerebral edema and increased intracranial pressure.

### 5. What pulmonary changes occur in a patient with cirrhosis?

Arterial hypoxemia with compensatory hyperventilation may be secondary to atelectasis from ascites/hydrothorax or hepatopulmonary syndrome (HPS). HPS is caused by intrapulmonary arteriovenous (AV) shunting. Portal hypertension and neovascularization are responsible for these AV shunts. The clinical features of HPS include platypnea (shortness of breath while standing) and orthodeoxia (decreased saturation when upright). They are indicative of the ventilation/perfusion mismatching.

Portal pulmonary hypertension (PPH), defined as a mean pulmonary artery pressure greater than 25 mm Hg, is seen in 2% to 4% of patients with cirrhosis. Its etiology is unclear. Severe PPH is a contraindication to liver transplantation.

### 6. Describe the changes in the cardiovascular system in patients with cirrhosis.

As liver disease progresses, most patients develop a hyperdynamic circulatory state, characterized by a fall in total peripheral resistance and a compensatory rise in cardiac output. The circulating plasma volume increases in response to vasodilation, and peripheral blood flow is enhanced. Although total body volume is increased, cirrhotic patients possess decreased effective arterial blood volume. The AV oxygen gradient narrows as a result of increased peripheral shunting. Consequently the mixed venous oxygen saturation of blood is higher than normal. The response to vasopressors is decreased with cirrhosis.

### 7. What is hepatorenal syndrome? How does it differ from acute renal failure in patients with end-stage liver disease?

Both types of renal failure occur in patients with cirrhosis and are characterized by oliguria and increases in serum creatinine. The etiology in both cases is renal hypoperfusion. Differentiation is important because treatment and prognosis vary.

Hepatorenal syndrome (HRS) occurs in cirrhotic patients with portal hypertension and ascites. HRS is defined as a plasma creatinine of  $>1.5$  mg/dl and a urine sodium  $<10$  mmol/L in the absence of other renal disease. The etiology is thought to be renal hypoperfusion resulting from a decrease in vasodilating prostaglandins and profound splanchnic sequestration of blood. HRS exists in two forms, types I and II. Type I progresses rapidly and requires immediate dialysis and liver transplantation. Type II HRS is less severe and responsive to conservative treatments, including terlipressin and a Transhepatic Intraportal Portosystemic Shunt procedure.

Acute renal failure (ARF) is caused by decreased blood flow to the kidneys. It may be the result of hemorrhage (e.g., ruptured varices), splanchnic sequestration of blood, ascites formation, or dehydration. Restoring arterial blood volume typically corrects ARF, but it can progress to acute tubular necrosis. In acute tubular necrosis, the ability to retain sodium is lost. Urine analysis will show sodium of 50 to 70 mmol/L and frequent tubular casts.

### 8. Describe volume assessment and fluid management in patients with hepatorenal syndrome.

Optimization of renal blood flow by correction of hypovolemia may prevent further renal injury during surgery in these patients. Volume assessment may be difficult since central venous pressures are often elevated despite relative hypovolemia from increased back pressure in the inferior vena cava from hepatic enlargement or scarring. A trial of volume expansion should be undertaken as the initial treatment of oliguria. Although immediate improvement occurs in more than one third of patients treated, HRS leads to progressive renal failure unless hepatic function improves.

### 9. What are the gastrointestinal and hematologic derangements that occur with cirrhosis?

GI complications result from portal hypertension ( $>10$  mm Hg). Portal hypertension leads to the development of portosystemic venous collaterals, including esophagogastric varices. Ruptured varices with hemorrhage account for one third of the mortality in patients with cirrhosis.

Hematologic disorders include anemia, thrombocytopenia and coagulopathy. Anemia is secondary to GI bleeding, malnutrition, and bone marrow suppression. Thrombocytopenia is caused by splenic sequestration, bone marrow depression, and immune-mediated destruction. Coagulopathy is caused by decreased synthesis of clotting factors, accelerated fibrinolysis, and disseminated intravascular coagulation.

**10. Which liver function tests are used to detect hepatic cell damage?**

The cytosolic enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are released into the blood as a result of increased membrane permeability or cell necrosis. They tend to rise and fall in parallel, although AST is cleared more rapidly from the circulation by the reticuloendothelial system. Their levels are not affected by changes in renal or biliary function. In contrast to ALT, which is mainly confined to hepatocytes, AST is found in heart and skeletal muscle, pancreas, kidney, and red blood cells. Therefore AST lacks specificity as a single diagnostic test. ALT is more specific but less sensitive for detection of hepatic disease.

**11. Describe the laboratory tests used to assess hepatic synthetic function and their limitations.**

All clotting factors are synthesized by the liver. Factor VIII is synthesized by hepatic endothelial sinusoidal cells. PT/INR indirectly determines the amount of clotting factors available and therefore is used to assess hepatic synthetic function. Elevation in PT/INR is not specific for liver disease and is altered, for instance, by the hemophilias and disseminated intravascular coagulation. Vitamin K deficiency resulting from malabsorption in liver disease or GI diseases and anticoagulant therapy can also prolong PT/INR. Once other disease processes have been excluded, PT/INR becomes a sensitive prognostic indicator for acute hepatocellular injury.

Albumin is synthesized in the liver and also reflects hepatic synthetic ability. However, renal and gastrointestinal losses can affect plasma levels, as can changes in vascular permeability in critically ill patients. A reduction in synthesis caused by liver disease may require 20 days to detect because of the long plasma half-life of albumin. Therefore low serum albumin levels are more useful indicators of chronic liver disease.

**12. What laboratory tests are used to diagnosis cholestatic liver disease?**

Alkaline phosphatase (ALP),  $\gamma$ -glutamyltransferase (GGT), and 5'-nucleotidase are commonly used to assess biliary tract function. These enzymes are located in the biliary epithelial cell membranes. ALP occurs in a wide variety of tissues and is elevated in a number of conditions, including bone disease and pregnancy. The hepatic origin of an elevated ALP is often suggested by the clinical context and simultaneous elevations of GGT and 5'-nucleotidase.

**13. How can laboratory results be used to stratify perioperative risk in patients with cirrhosis?**

In acute liver disease, plasma transaminase concentrations often increase to 10 to 100 times normal. The higher plasma concentrations are associated with greater hepatocellular death and increased mortality. Relatively normal plasma levels can also be found in patients in the earliest and latest stages of acute liver disease, signifying massive cellular necrosis, and are associated with a very high mortality. PT/INR is usually grossly prolonged, reflecting decreased synthetic ability. Albumin levels are often normal. The mortality for intra-abdominal surgery in patients with severe acute hepatic disease approaches 100%.

Liver function tests have also been used to predict outcome following surgery in patients with chronic hepatic impairment. Child's scoring system (Table 43-1) was originally used to stratify risk in patients undergoing portosystemic shunting procedures. Using this method, 30-day mortality rates of 10%, 14% to 31%, and 51% to 80% were identified in Child's class A, B, and C patients, respectively, when undergoing noncardiac surgery. More recently the Model for End-Stage Liver Disease (MELD) scoring system was created as a more objective method for assessing mortality in cirrhotic patients (Table 43-2). When compared to the

TABLE 43-1. MODIFIED CHILD-TURCOTTE-PUGH SCORE

Presentation	Points		
	1	2	3
Albumin (g/dl)	>3.5	2.8–3.5	<2.8
International normalized ratio	<1.7	1.7–2.3	>2.3
Bilirubin (mg/dl)	<2	2–3	>3
Ascites	Absent	Moderate	Tense
Encephalopathy	None	Grade I–II	Grade III–IV

Class A = 5–6 points; Class B = 7–9 points; Class C = 10–15 points.

TABLE 43-2. MODEL FOR END-STAGE LIVER DISEASE EQUATION

MELD Score =  $3.8 \times \log(e)$  (bilirubin mg/dl) +  $11.2 \times \log(e)$  (INR) +  $9.6 \log(e)$  (creatinine mg/dl)

MELD <10 = Low perioperative mortality

MELD 10–14 = Moderate perioperative mortality

MELD >14 = Severe perioperative mortality

INR, International normalized ratio; MELD, Model for End-Stage Liver Disease.

Child's scoring system, the MELD is a superior predictor of perioperative risk in patients with cirrhosis. MELD scores of <10, 10 to 14, and >14 correlate well with the Child's A, B, and C classifications.

#### 14. What risk factors for liver disease can be identified by history and physical examination?

Table 43-3 lists risk factors for liver disease easily obtained in a brief medical history. Physical examination may yield stigmata of chronic liver disease, including ascites, hepatosplenomegaly, spider angiomas, caput medusae, and gynecomastia. Patients with these signs or a prior history of jaundice or liver disease should have liver function tests evaluated before surgery.

#### 15. What is jaundice?

Jaundice is a visible yellow or green discoloration, usually first observed in the sclera, caused by elevation of serum bilirubin. Levels of 2 to 2.5 mg/dl (normal 0.5 to 1 mg/dl) result in jaundice. The oxidation of bilirubin to biliverdin gives the green hue often observed.

#### 16. Distinguish between unconjugated and conjugated hyperbilirubinemia.

The distinction is essential to the differential diagnosis of jaundice. Elevations in the serum unconjugated bilirubin fraction are usually related to changes in the turnover of red blood cells and their precursors. Conjugated hyperbilirubinemia always signifies dysfunction of the liver or biliary tract.



TABLE 43-3. RISK FACTORS FOR LIVER DISEASE

Risk Factor	Example
Viral hepatitis	Intravenous drug abuse, transfusion, tattoos, contact with infected person
Drugs	Alcohol, prescription medications (e.g., acetaminophen, haloperidol, tetracycline, isoniazid, hydralazine, captopril, and amiodarone)
Autoimmune disease	Systemic lupus erythematosus, sarcoidosis, mixed connective tissue disorder
Metabolic disease	Hemochromatosis, Wilson's disease, cystic fibrosis, $\alpha_1$ -antitrypsin deficiency, and glycogen storage disease
Inflammatory bowel disease	Crohn's disease and ulcerative colitis/primary sclerosing cholangitis

17. **List the common causes of unconjugated and conjugated hyperbilirubinemia.** Unconjugated hyperbilirubinemia is defined as an elevation of the total serum bilirubin of which the conjugated fraction does not exceed 15%. The causes are listed in [Table 43-4](#).

TABLE 43-4. CAUSES OF UNCONJUGATED BILIRUBIN

Cause	Example
Hemolysis	Incompatible blood transfusion, arterial/venous bypass circuit, congenital or acquired defects (e.g., autoimmune and drug-induced hemolytic anemia, glucose-6-phosphatase deficiency)
Hematoma resorption	Retroperitoneal or pelvic hematoma
Enzymatic deficiencies	Congenital deficiency (Gilbert syndrome) to complete absence (Crigler-Najjar syndrome) of hepatic uridine diphosphoglucuronyl transferase

Elevations of conjugated bilirubin are caused by hepatocyte dysfunction and/or intrahepatic or extrahepatic stasis. A differential diagnosis of biliary stasis is listed in [Table 43-5](#).

18. **What are the main causes of hepatocyte injury?**

See [Table 43-6](#).

19. **How do inhalational anesthetic gases produce hepatic dysfunction?**

Although rare, all inhalational agents can cause inflammation or death of hepatocytes by direct toxicity. Adverse reactions are caused by metabolic products of halogenated inhalational agents. Generally the degree of metabolism of the agents is halothane > sevoflurane > enflurane > isoflurane > desflurane. Halothane, the most extensively metabolized agent, is associated with mild hepatic dysfunction in up to 30% of individuals exposed and manifests as asymptomatic transient elevation of hepatic AST and ALT.

TABLE 43-5. CAUSES OF BILIARY OBSTRUCTION/STASIS

Extrahepatic Obstruction	Intrahepatic Obstruction
Tumor (bile duct, pancreas, and duodenum)	Primary biliary cirrhosis
Cholecystitis	Drugs (estrogens, anabolic steroids, tetracycline, and valproic acid)
Biliary stricture	Total parenteral nutrition
Ascending cholangitis	Pregnancy
Sclerosing cholangitis	

TABLE 43-6. CAUSES OF HEPATOCYTE INJURY

Cause	Example
Infection	Hepatitis A, B, and C; cytomegalovirus; Epstein-Barr virus
Drugs	Acetaminophen, isoniazid, phenytoin, hydralazine, $\alpha$ -methyl dopa, sulfasalazine
Sepsis	Pneumonia
Total parenteral nutrition (TPN)	Abnormal liver function tests in 68%–93% of patients given TPN for longer than 2 weeks
Hypoxemia	Lower arterial oxygen or interference with peripheral use as in cyanide and carbon monoxide poisoning
Ischemia	Increased venous pressure (e.g., congestive heart failure, pulmonary embolus, and positive-pressure ventilation) Decreased arterial pressure (e.g., hypovolemia, vasopressors, and aortic cross-clamp)

Rarely an immunologically mediated idiosyncratic reaction occurs in individuals exposed to volatile anesthetics. The formation of immune complexes is related to the extent of metabolism. As halothane has the greatest degree of metabolism associated with it, hepatitis resulting from halothane exposure is the most common. However, given that halothane use is now rare in the United States, this problem is not likely to be encountered.

## 20. How do inhalational agents alter hepatic blood flow?

All these agents dilate the hepatic artery and preportal blood vessels. This dilation decreases mean hepatic artery pressure and increases venous pooling in the splanchnic vessels. Portal flow decreases. Overall the result is suboptimal perfusion of the liver. However, at levels below 1 minimum alveolar concentration (MAC), isoflurane, sevoflurane, and desflurane only minimally decrease hepatic blood flow. In addition, autoregulation of the hepatic artery is abolished, and blood flow becomes pressure dependent. This is usually tolerated well in patients with normal hepatic function since metabolic demand is also decreased by these drugs. Patients with hepatic disease are more susceptible to injury secondary to preexisting impaired perfusion and therefore should be anesthetized at levels below 1 MAC.

**KEY POINTS: PERIOPERATIVE HEPATIC DYSFUNCTION**

1. Patients with end-stage liver disease have a hyperdynamic circulation with increased cardiac output and decreased systemic vascular resistance.
2. Although the portal vein supplies up to 75% of total hepatic blood flow, only 45% to 55% of the oxygen requirements are provided by this part of the circulation.
3. Because of the large reserve of the liver, significant impairment of physiologic function must occur before clinical signs and symptoms of hepatic failure become evident.
4. Because of potential perioperative complications of GI hemorrhage, sepsis, renal failure, and volume overload, elective surgery should not be performed in Child's class C (MELD >14) cirrhotics.
5. Patients with liver disease can be tenuous perioperatively. Coagulopathies should be corrected before surgery, drug dosing should be judicious intraoperatively, and cirrhotics should go to a monitored setting after surgery.

**21. What are the preoperative management goals in a patient with liver disease?**

The type and severity of liver disease should be determined. Patients with acute hepatitis or Child's type C (MELD >14) cirrhosis should have elective surgeries cancelled. A complete organ system review should be performed, specifically looking for encephalopathy, ascites, portal hypertension, and renal insufficiency. A complete laboratory evaluation should be performed, including transaminases, bilirubin, albumin, basic metabolic profile, complete blood count with platelets, and a coagulation profile. For major surgery, coagulopathy should be corrected to an INR <1.5, platelets corrected to  $>100 \times 10^9$ , and fibrinogen to  $>100$  mg/dl. A thromboelastogram may be useful in guiding component therapy when correcting a preexisting coagulopathy.

**22. What are the intraoperative management goals in a patient with liver disease?**

Preservation of hepatic blood flow and existing hepatic function are key. Hypoxemia, hemorrhage, and hypotension may all reduce hepatic blood flow thus these should be avoided when possible. Drug selection and dosing should be judicious. The operating room should be warmed, and a fluid warming/rapid infusion device should be available. Regional anesthesia is a good option if coagulopathy is not present.

**23. What adjustment in anesthetic medications should be made in a patient with liver disease?**

The induction agents propofol, etomidate, and ketamine possess a high hepatic extraction ratio; and their pharmacokinetic profile is relatively unchanged in mild-to-moderate cirrhosis. With severe hypoalbuminemia, an exaggerated induction response can be seen with thiopental. Although pseudocholinesterase levels are decreased in liver disease, the clinical prolongation of succinylcholine is not significant. Intermediate-acting steroidal nucleus nondepolarizing muscle relaxants such as vecuronium and rocuronium display a prolonged effect in cirrhotics. Their prolonged duration is accentuated with repeated dosing. Benzyl-isoquinoline relaxants such as atracurium and cisatracurium undergo organ-independent elimination, and their duration is not affected by liver disease.

Benzodiazepines metabolized by phase I oxidative reactions such as midazolam and diazepam have a prolonged duration of action. Lorazepam, cleared by phase II glucuronidation, undergoes normal metabolism. All benzodiazepines should be dosed judiciously in patients with liver disease.

All opioids, with the exception of remifentanyl, are metabolized in the liver. Morphine and meperidine have a prolonged half-life in liver disease and can precipitate hepatic encephalopathy. Fentanyl, although completely metabolized by the liver, does not have a prolonged clinical effect in cirrhosis. Therefore fentanyl and remifentanyl are the opioids of choice in liver disease.

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# RENAL FUNCTION AND ANESTHESIA

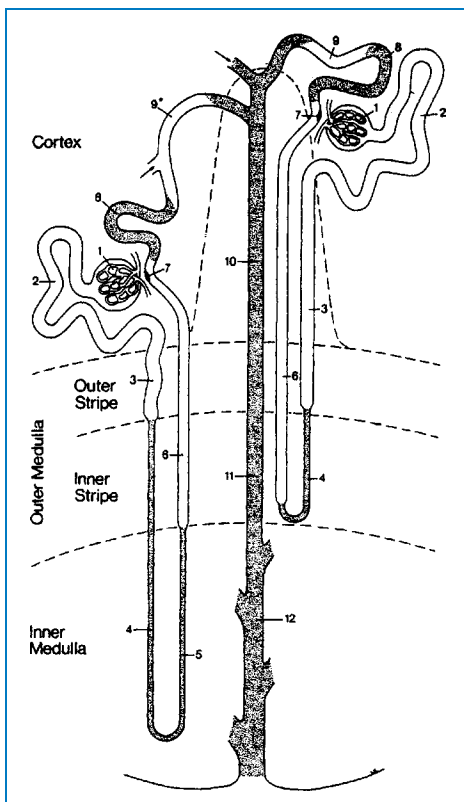
James Duke, MD, MBA

## 1. Describe the anatomy of the kidney.

The kidneys are paired organs lying retroperitoneally against the posterior abdominal wall. Although their combined weight is only 300 g (about 0.5% of total body weight), they receive 20% to 25% of the total cardiac output. The renal arteries are branches of the aorta, originating below the superior mesenteric artery. The renal veins drain into the inferior vena cava. Nerve supply is abundant; sympathetic constrictor fibers are distributed via celiac and renal plexuses. There is no sympathetic dilator or parasympathetic innervation. Pain fibers, mainly from the renal pelvis and upper ureter, enter the spinal cord via splanchnic nerves.

On cross section of the kidney, three zones are apparent: cortex, outer medulla, and inner medulla (Figure 44-1). Eighty percent of renal blood flow is distributed to cortical structures. Each kidney contains about 1 million nephrons. Nephrons are classified as superficial (about 85%) or juxtamedullary, depending on location and length of the tubules. The origin of all nephrons is within the cortex.

The glomerulus and capsule are known collectively as the renal corpuscle. Each Bowman's capsule is connected to a proximal tubule that is convoluted within its cortical extent but becomes straight limbed within the outer cortex; at this point the tubule is known as the *loop of*



**Figure 44-1.** This scheme depicts a short-looped and a long-looped nephron together with the collecting system (not drawn to scale). Within the cortex a medullary ray is delineated by a dashed line. 1, Renal corpuscle, including Bowman's capsule and the glomerulus (glomerular tuft). 2, Proximal convoluted tube. 3, Proximal straight tubule. 4, Descending thin limb. 5, Ascending thin limb. 6, Distal straight tubule (thick ascending limb). 7, Macula densa located within the final portion of the neck of the thick ascending limb. 8, Distal convoluted tube. 9, Connecting tubule of the juxtamedullary nephron that forms an arcade. 10, Cortical collecting tubule. 11, Outer medullary collecting duct. 12, Inner medullary collecting duct. (From Kriz W, Bankir I: A standard nomenclature for structures of the kidney, *Am J Physiol* 254:F1, 1988, with permission.)

*Henle.* The loop of Henle of superficial nephrons descends only to the intermedullary junction, where it makes a hairpin turn, becomes thick limbed, and ascends back into the cortex, where it approaches and touches the glomerulus with a group of cells known as the *juxtaglomerular apparatus*. The superficial nephrons form distal convoluted tubules that merge to form collecting tubules within the cortex. The renal corpuscles of juxtamedullary nephrons are located at juxtamedullary cortical tissue. They have long loops of Henle that descend deep into the medullary tissue; the loops also reascend into cortical tissue, where they form distal convoluted tubules and collecting tubules. These nephrons (15% of the total) are responsible for conservation of water.

About 5000 tubules join to form collecting ducts. Ducts merge at minor calyces, which in turn merge to form major calyces. The major calyces join and form the renal pelvis, the most cephalic aspect of the ureter.

## 2. List the major functions of the kidney.

- Regulation of body fluid volume and composition
- Acid-base balance
- Detoxification and excretion of nonessential materials, including drugs
- Elaboration of renin, which is involved in extrarenal regulatory mechanisms
- Endocrine and metabolic functions such as erythropoietin secretion, vitamin D conversion, and calcium and phosphate homeostasis

## 3. Discuss glomerular and tubular function.

Glomerular filtration results in production of about 180 L of glomerular fluid each day. Filtration does not require the expenditure of metabolic energy; rather it is caused by a balance of hydrostatic and oncotic forces. Glomerular filtration rate (GFR) is the most important index of intrinsic renal function. Normal GFR is 125 ml/min in males, slightly less in females.

Tubular function reduces the 180 L/day of filtered fluid to about 1 L/day of excreted fluid, altering its composition through active and passive transport. Transport is passive when it is the result of physical forces such as electrical or concentration gradients. When transport is undertaken against electrochemical or concentration gradients, metabolic energy is required, and the process is termed active.

Substances may be either resorbed or secreted from tubules and may move bidirectionally, taking advantage of both active and passive transport. The direction of transit for resorbed substances is from tubule to interstitium to blood, whereas the direction for secreted substances is from blood to interstitium to tubule. Secretion is the major route of elimination for drugs and toxins, especially when they are plasma protein bound.

## 4. Review the site of action and significant effects of commonly used diuretics.

See Table 44-1.

## 5. Describe the unique aspects of renal blood flow and control.

Renal blood flow (RBF) of about 1200 ml/min is well maintained (autoregulated) at blood pressures of 80 to 180 mm Hg. The cortex requires about 80% of blood flow to achieve its excretory and regulatory functions, and the outer medulla receives 15%. The inner medulla receives a small percent of blood flow; a higher flow would wash out solutes responsible for the high tonicity (1200 mOsm/kg) of the inner medulla. Without this hypertonicity, urinary concentration would not be possible.

Control of RBF is through extrinsic and intrinsic neural and hormonal influences; a principal goal of blood flow regulation is to maintain GFR. The euvolemic, nonstressed state has little baseline sympathetic tone. Under mild-to-moderate stress RBF decreases slightly; but efferent arterioles constrict, maintaining GFR. During periods of severe stress

TABLE 44-1. DIURETICS\*

Drug (Example)	Site of Action	Action and Side Effects
Carbonic anhydrase inhibitors (acetazolamide)	Proximal convoluted tubule	Inhibits sodium resorption; interferes with H excretion; hyperchloremic, hypokalemic acidosis
Thiazides (hydrochlorothiazide)	Cortical diluting segment (between ascending limb and aldosterone-responsive DCT)	Inhibits sodium resorption; accelerates sodium-potassium exchange (hypokalemia); decreases GFR in volume-contracted states
Potassium-sparing diuretics (spironolactone, triamterene)	Competitive inhibition of aldosterone in DCT	Inhibiting aldosterone prevents sodium resorption and sodium-potassium exchange
Loop diuretics (furosemide, bumetanide, ethacrynic acid)	Inhibit Cl <sup>-</sup> resorption at thick ascending loop of Henle	Potent diuretic; acts on critical urine-concentrating process; renal vasodilator; hypokalemia; can produce hypovolemia
Osmotic diuretics (mannitol, urea)	Filtered at glomerulus but not resorbed; creates osmotic gradient in tubules; excretion of water and some sodium	Hyperosmolality reduces cellular water; limited ability to excrete sodium; renal vasodilator

*DCT*, Distal convoluted tubule; *GFR*, glomerular filtration rate.

\*With the exception of osmotic diuretics, all diuretics interfere with sodium conservation.

(e.g., hemorrhage, hypoxia, major surgical procedures) both RBF and GFR decrease secondary to sympathetic stimulation.

The renin-angiotensin-aldosterone axis also has an effect on RBF. A proteolytic enzyme formed at the macula densa of the juxtaglomerular apparatus, renin acts on angiotensinogen within the circulation to produce angiotensin I. Enzymes within lung and plasma convert angiotensin I to angiotensin II, which is a potent renal vasoconstricting agent (especially of the efferent arteriole) and a factor in the release of aldosterone. During periods of stress levels of angiotensin are elevated and contribute (along with sympathetic stimulation and catecholamines) to decreased RBF.

Prostaglandins (PGs) are also found within the kidney. PGE<sub>2</sub> and PGE<sub>3</sub> are intrinsic mediators of blood flow, producing vasodilation.

## 6. Describe the sequence of events associated with decreased renal blood flow.

The initial response to decreased RBF is to preserve ultrafiltration through redistribution of blood flow to the kidneys, selective afferent arteriolar vasodilation, and efferent arteriolar vasoconstriction. Renal hypoperfusion results in active absorption of sodium and passive absorption of water in the ascending loop of Henle. Oxygen demand is increased in an area

particularly vulnerable to decreased oxygen delivery. Compensatory sympathoadrenal mechanisms redistribute blood flow from the outer cortex to the inner cortex and medulla. If renal hypoperfusion persists or worsens despite early compensatory mechanisms and as sodium is resorbed in the ascending loop, increased sodium is delivered to the macula densa, producing afferent arteriolar vasoconstriction and decreasing glomerular filtration. Because GFR is decreased, less solute is delivered to the ascending loop. Because less solute is delivered, less is resorbed (an energy requiring process); thus less oxygen is needed, and the net effect is that afferent arteriolar vasoconstriction decreases oxygen-consuming processes. The result is oliguria. However, the kidney is attempting to maintain intravascular volume and, to that end, the process described has been denoted *renal success*. In reality oliguria is a poor measure of renal function since more often than not acute renal failure (ARF) is nonoliguric.

#### 7. What preoperative risk factors are associated with postoperative renal failure?

Preoperative renal risk factors (increased blood urea nitrogen [BUN] and creatinine and a history of renal dysfunction), left ventricular dysfunction, advanced age, jaundice, and diabetes mellitus are predictive of postoperative renal dysfunction. Patients undergoing cardiac or aortic surgery are particularly at risk for developing postoperative renal insufficiency.

#### 8. Discuss the major causes of perioperative acute renal failure.

ARF is defined as a significant decrease in GFR over a period of 2 weeks or less. Renal failure, or azotemia, can be categorized into prerenal, renal, and postrenal etiologies. Prerenal azotemia is caused by decreased blood flow to the kidney and accounts for about 60% of all cases of ARF. In the perioperative setting ischemia may be caused by inadequate perfusion from blood and volume losses. Other mechanisms include hypoperfusion secondary to myocardial dysfunction or shunting of blood away from the kidneys, as in sepsis.

Renal causes account for 30% of all cases of ARF. Acute tubular necrosis is the leading cause and may be to the result of either ischemia or toxins. In the setting of preexisting renal disease nephrotoxins include radiocontrast media, aminoglycosides, ACE inhibitors and fluoride associated with volatile anesthetic metabolism. Hemolysis and muscular injury (producing hemoglobinuria and myoglobinuria) are also causes of intrinsic ARF.

Postrenal causes (10% of cases) are caused by obstructive nephropathy and may be observed in men with conditions such as prostatism and ureteral obstruction from pelvic malignancies.

“Acute Kidney Injury” is now increasingly replacing the term “Acute Renal Failure.”

#### 9. What laboratory abnormalities are observed in renal failure?

Patients have uremia (elevation of BUN and creatinine), hyperkalemia, hyperphosphatemia, hypocalcemia, hypoalbuminemia and metabolic acidosis. They are also anemic and have platelet and leukocyte dysfunction, rendering them prone to bleeding and infection.

#### 10. Comment on various laboratory tests and their use in detecting acute renal dysfunction.

Indices of renal function can be roughly divided into measures of glomerular or tubular function. Measures of clearance assess glomerular function, whereas the ability to concentrate urine and retain sodium are indices of tubular function. The majority of renal function tests are neither sensitive nor specific in predicting perioperative renal dysfunction and are affected by many variables common to the perioperative environment.

The ammonia generated from amino acid metabolism in the liver is converted to BUN. Urea is cleared rapidly by glomerular filtration but also resorbed in the tubules. Thus BUN cannot be used as a marker of glomerular filtration, only azotemia. Creatinine is the end product of creatinine phosphate metabolism and is generated from muscle and handled by the kidney in a relatively uniform fashion. Dietary meat is also a source of creatinine. Serum creatinine (Scr) is a function of muscle mass and such factors of activity, diet, and hemodilution alter its serum concentration. Scr can be artifactually increased by barbiturates or cephalosporins.



Additional nonrenal variables may also be responsible for elevation of BUN and creatinine, including increased nitrogen absorption, muscle trauma from burns or injury, hypercatabolism, hepatic disease, diabetic ketoacidosis, hematoma resorption, gastrointestinal bleeding, hyperalbuminemia, and many drugs (e.g., steroids). The usual ratio of BUN to creatinine is 10:1, and a ratio greater than 20:1 implies a prerenal syndrome.

Elevation of Scr is a late sign of renal dysfunction. The relationship between Scr and GFR is inverse and exponential. That is to say, a doubling of Scr reflects halving the GFR. This is of greater clinical significance at lower levels of creatinine; an increase of creatinine from 4 to 8 mg/dl does not represent a large absolute decrease in GFR because GFR is already remarkably diminished at 4 mg/dl.

When renal function is stable, using nomograms, creatinine is a reasonable measure of GFR. However, Scr measurements are inaccurate when GFR is rapidly changing. GFR may be reduced by 50% or more before abnormal elevation is observed. Because creatinine production is proportionate to muscle mass, in situations in which substantial wasting has already occurred (e.g., chronic illness, advanced age) creatinine levels may be *normal* despite markedly reduced GFR.

GFR declines with age. A healthy individual of age 20 has a GFR of about 125 ml/min; an otherwise healthy patient at age 60 has a GFR about 60 ml/min. Scr does not begin to increase until GFR falls to about 50 ml/min. GFR can be estimated using population studies based on the patient's age, Scr, sex, and weight. The method of Cockcroft and Gault uses the following formula for estimating GFR:  $GFR = (140 - \text{age}) \times \text{weight (kg)} / (\text{Scr} \times 72)$ . This is the formula for male, and the result is multiplied by 0.85 to determine the GFR for females. It is obvious that this overestimates GFR in obese patients when total body weight, not ideal body weight, is used. This formula may also overestimate GFR in cachectic patients in whom creatinine production is low.

Creatinine clearance (Ccr) is a sensitive test of renal function. Creatinine is filtered at the glomerulus and not resorbed. There is also some secretion of creatinine with the tubules, and this results in about a 15% overestimation of Ccr. (In actuality, clearance of inulin, a polyfructose sugar, is the gold standard for measurement of GFR because it is filtered at the glomerulus and neither resorbed nor secreted at the tubules.) It has been a long held belief that measurement of Ccr required 12- to 24-hour urine collections. In fact, if Scr is rapidly changing, calculations of Ccr based on 24 hours of urine collection and a single creatinine measurement may be inaccurate. In addition, this method requires meticulous urine collection, and failure to accomplish this is a common source of laboratory error. Two-hour spot tests are thought to be reasonably accurate, and serial 2-hour spot tests may be particularly valuable when renal function is acutely deteriorating. [Table 44-2](#) describes various tests of renal function.

TABLE 44-2. VARIOUS TESTS OF RENAL FUNCTION

Test	Normal Values	Abnormal Values	Comments
Specific gravity	1.010–1.030	Prerenal azotemia >1.030; loss of concentrating ability <1.010	Nonspecific, affected by glucose, mannitol, diuretics, endocrine disease, radiocontrast
Serum BUN	10–20	>50 definitely associated with renal impairment	Nonspecific, influenced by a wide variety of processes

(continued)

TABLE 44-2. VARIOUS TESTS OF RENAL FUNCTION (continued)

Test	Normal Values	Abnormal Values	Comments
Serum creatinine (mg/dl)	0.8-1.3 (men) 0.6-1.0 (women)	A doubling of the creatinine value associated with 50% reduction in GFR	A late indicator of renal failure; normal values reflect decreased function as patient ages and muscle mass decreases
Urine-plasma creatinine ratio (U:PCR)—proportion of water filtered by glomerulus that is resorbed	Between 20 and 40:1	ATN < 20:1; prerenal azotemia >40:1	Neither sensitive nor specific; of value only at extremes
Urinary sodium ( $U_{Na}$ ) (mEq/L)	$U_{Na} \approx 20$	ARF >60-80; prerenal azotemia <20	Changes with composition of resuscitation fluid; affected by aldosterone, ADH, diuretics
Fractional excretion of sodium (FENa)—sodium clearance as a percentage of creatinine clearance	1%-3%	Prerenal azotemia—FENa <1%; ATN—FENa >3%	May not be accurate early in disease process (when most valuable); also nonspecific; affected by diuretics
Creatinine clearance (ml/min)	100-125	Decreased renal reserve 60-100; mild renal impairment 40-60; renal failure <25 ml/min	A good test for measuring GFR; requires 24-hr urine collection but a 2-hour collection may be reasonably accurate

ADH, Antidiuretic hormone; ARF, acute renal failure; ATN, acute tubular necrosis; BUN, blood urea nitrogen; GFR, glomerular filtration rate.

### 11. What are measures of tubular function?

As opposed to the measures of glomerular function previously discussed (creatinine, GFR, Ccr), tests of tubular function describe the ability of the kidney to concentrate urine and handle sodium. Tests of concentrating ability differentiate between prerenal azotemia (dehydration, decreased renal perfusion) and acute tubular necrosis (ATN) and demonstrate abnormalities

24 to 48 hours before increases in BUN and creatinine. Measures of tubular function give no estimate of renal reserve.

With hypovolemia, renal tubules retain salt and water and result in a relatively hyponatremic, concentrated urine. Concentrating ability is lost during ATN and results in increased volumes of dilute urine high in sodium. As mentioned, in ATN loss of concentrating ability may be detected 24 to 48 hours before BUN or creatinine begins to rise. Other tests of tubular function include urine-to-plasma osmolar ratio, free water clearance, urine-to-plasma creatinine ratio, urine sodium ( $U_{Na}$ ), and fractional excretion of sodium (FENa). With hypovolemia or dehydration  $U_{Na}$  is less than 20 mEq/L. In ATN  $U_{Na}$  exceeds 60 mEq/L. However, diuretics may increase  $U_{Na}$  to this level despite hypovolemia.

**12. At what point is renal reserve lost and do patients develop laboratory evidence of renal insufficiency?**

Patients will remain asymptomatic with only 40% of nephrons functioning. Renal insufficiency describes the state in which between 10% and 40% of nephrons remain; and, because there is no renal reserve, these patients are at risk for ARF with any renal insult such as hypovolemia or administration of nephrotoxins. Patients require dialysis when fewer than 10% of nephrons remain. In terms of Ccr, patients with renal insufficiency have Ccr of less than 40 ml/min, with renal failure they have Ccr less than 25 ml/min, and they require dialysis when Ccr is less than 10 ml/min.

**13. Discuss the usefulness of urine output in assessing renal function.**

Urine output is easily measured through insertion of an indwelling Foley catheter and connection to a urometer. A daily output of 400 to 500 ml of urine is required to excrete obligatory nitrogenous wastes. In adults an inadequate urine output (oliguria) is often defined as  $<0.5$  ml/kg/hr. GFR is decreased by the effects of anesthesia, sympathetic activity, hormonal influences, and redistribution of blood away from outer cortical nephrons. Invariably urine output decreases as blood pressure falls; thus perioperative oliguria is not uncommon, is usually prerenal in origin, and is not a reflection of ARF. A normal urine output does not rule out renal failure.

**14. What is the best way to protect the kidneys during surgery?**

There are no *magic bullets* to prevent perioperative ARF. The best way to maintain renal function during surgery is to ensure an adequate intravascular volume, maintain cardiac output, and avoid drugs known to decrease renal perfusion.

**15. Does dopamine have a role in renal preservation?**

There is now considerable evidence that dopamine is not renoprotective (i.e., improves renal perfusion) nor does it improve splanchnic perfusion (see Chapter 15).

**16. Describe the effects of volatile anesthetics on renal function.**

General anesthesia temporarily depresses renal function as measured by urine output, GFR, RBF, and electrolyte excretion. Renal impairment is usually short lived and completely reversible. Maintenance of systemic blood pressure and preoperative hydration decrease the effect on renal function. Spinal and epidural anesthesia also appear to depress renal function but not to the same extent as general anesthesia.

Fluoride-induced nephrotoxicity has been noted with volatile anesthetics used in the past (e.g., methoxyflurane). Sevoflurane, a volatile anesthetic in current use, has fluoride as a metabolic product (about 3.5% of the total fluoride burden appears in the urine as inorganic fluoride; peak concentrations of about 25  $\mu$ mol appear within 2 hours of discontinuing the agent). Extensive experience with sevoflurane confirms its safety. Its remarkable insolubility when compared to methoxyflurane may be explanatory; there is simply less sevoflurane deposited in lipid stores to be later metabolized to fluoride, and the overall fluoride burden is less.

An additional breakdown product of sevoflurane is known as Compound A and is noted mostly during low-flow anesthetic techniques. Although renal failure has been noted in animal models, no such problems have been observed in humans.

### 17. What is the best relaxant for patients with renal insufficiency?

Atracurium undergoes spontaneous degradation under physiologic conditions (Hofmann degradation and ester hydrolysis) and is preferred. Because atracurium is water soluble, patients with altered body water composition may require larger initial doses to produce rapid paralysis but smaller and less frequent doses to maintain paralysis. Succinylcholine may be used in patients with renal insufficiency if the serum potassium concentration is  $<5$  mEq/L (Table 44-3).

TABLE 44-3. MUSCLE RELAXANTS AND RENAL EXCRETION

Gallamine	90%	Doxacurium	30%
Tubocurarine	45%	Vecuronium	15%
Metocurine	43%	Atracurium	10%
Pancuronium	40%	Rocuronium	10%
Pipecuronium	38%	Mivacurium	10%

### 18. How are patients with renal insufficiency managed perioperatively?

Preoperative preparation is of benefit for patients with end-stage renal disease (ESRD), who have up to a 20% mortality for emergent surgical procedures. Primary causes of death include sepsis, dysrhythmias, and cardiac dysfunction. Hemodynamic instability is common. From the standpoint of renal dysfunction, there may be a decreased ability to concentrate urine, decreased ability to regulate extracellular fluid and sodium, impaired handling of acid loads, hyperkalemia, and impaired excretion of medications. Renal impairment is confounded by anemia, uremic platelet dysfunction, arrhythmias, pericardial effusions, myocardial dysfunction, chronic hypertension, neuropathies, malnutrition, and susceptibility to infection. Nephrotoxic agents (e.g., amphotericin, nonsteroidal antiinflammatory drugs, aminoglycosides) should be avoided. If a radiocontrast is contemplated, the real value of the test should be considered. If the contrast study is definitely indicated, the patient should be well hydrated, and the contrast dose limited to the minimum needed.

Medications commonly used perioperatively may have increased effects in patients with chronic renal insufficiency. Because these patients are hypoalbuminemic, medications that are usually protein bound such as barbiturates and benzodiazepines may have increased serum levels. Both morphine and meperidine have metabolites that are excreted by the kidney. Succinylcholine increases extracellular potassium but can be used if serum potassium is normal. Hyperkalemia should be considered in patients with ESRD who develop ventricular arrhythmias or cardiac arrest. Rapid administration of calcium chloride temporizes the cardiac effects of hyperkalemia until further measures (administration of insulin and glucose, hyperventilation, administration of sodium bicarbonate and potassium-binding resins, and dialysis) can be taken to shift potassium intracellularly and decrease total body potassium.

Before surgery patients must be euolemic, normotensive, normonatremic, normokalemic, not acidotic or severely anemic, and without significant platelet dysfunction. Ideally they should have had dialysis the day of or day before surgery. Dialysis usually corrects uremic platelet dysfunction and is best performed within the 24 hours before surgery, although 1-deamino-8-D-arginine vasopressin (DDAVP) may also be administered if bleeding is persistent. Other

indications for acute dialysis include uremic symptoms, pericardial tamponade, bleeding, hypervolemia, congestive heart failure, hyperkalemia, and severe acidosis.

Patients with ESRD who have left ventricular dysfunction or undergo major procedures with significant fluid shifts require invasive monitoring to guide fluid therapy. A sterile technique should be strictly followed when inserting any catheters. In minor procedures fluids should be limited to replacement of urine and insensible losses. Normal saline is the fluid of choice as it is free of potassium. However, if large fluid requirements are necessary, normal saline administration may result in hyperchloremic metabolic acidosis. Clearly cases of this magnitude require invasive monitoring and repeated laboratory analysis.

## KEY POINTS: RENAL FUNCTION AND ANESTHESIA



1. Preoperative renal risk factors (increased creatinine and a history of renal dysfunction), left ventricular dysfunction, advanced age, jaundice, and diabetes mellitus are predictive of postoperative renal dysfunction.
2. Patients undergoing cardiac or aortic surgery are particularly at risk for developing postoperative renal insufficiency.
3. The majority of renal function tests are neither sensitive nor specific in predicting perioperative renal dysfunction and are affected by many variables common to the perioperative environment.
4. Succinylcholine may be used if serum potassium concentration is  $<5$  mEq/L.
5. The best way to maintain renal function during surgery is to ensure an adequate intravascular volume, maintain cardiac output, and avoid drugs known to decrease renal perfusion.

### 19. What is accomplished during hemodialysis?

Blood is drawn from the patient and flows toward a semipermeable membrane, the area of which is about 1 to 1.8 m<sup>2</sup>. Across the membrane is a dialysate with normal electrolyte concentrations. Electrolytes and waste products move down their concentration gradients. In addition, alkali within the dialysate moves into the patient. Negative pressure within the dialysate results in excess fluid removal. The duration of hemodialysis (HD) depends on flow rates and usually lasts from 4 to 6 hours. High flow rates are associated with rapid changes in electrolytes and volume status that are poorly tolerated by the patient. Usually these patients have dialysis three times weekly. The mortality associated with intermittent dialysis is 5% annually.

Critically ill patients in ARF with hypotension and sepsis frequently tolerate HD poorly. In this case, continuous veno-venous HD (CVVHD) or filtration (CVVHF) is used. Only fluid is drawn off during CVVHF, whereas CVVHD also removes waste products, acid metabolites, and potassium.

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# INCREASED INTRACRANIAL PRESSURE AND TRAUMATIC BRAIN INJURY

*Matthew Hall, MD*

## 1. Define elevated intracranial pressure.

Elevated intracranial pressure (ICP) is usually defined as a sustained pressure of greater than 20 mm Hg within the subarachnoid space. The normal ICP is approximately 10 to 18 mm Hg.

## 2. What are the determinants of intracranial pressure?

The space-occupying contents of the skull, the brain (85%), the cerebrospinal fluid (CSF) (10%), and cerebral blood volume (15%), are all contained in the virtually fixed volume of the cranium. Once compensatory mechanisms are exhausted (mostly translocation of CSF), any increase in volume will cause a rise in ICP.

## 3. How is intracranial pressure measured?

Various techniques are available, including ventricular catheters, subdural-subarachnoid bolts, epidural transducers, and intraparenchymal fiber-optic devices. The standard method is a ventriculostomy, in which a plastic catheter is introduced into the anterior aspect of the lateral ventricle via a burr hole in the cranium. The catheter is attached to saline-filled tubing, and the pressure is transduced. In addition, this catheter can be used to drain CSF via a pop-off valve set at 20 cm H<sub>2</sub>O. Another common method is the subarachnoid bolt, which is also placed through a burr hole but does not require insertion through brain tissue or identification of the position of the ventricle. A third technique involves the insertion of a fiber-optic bundle through a small burr hole. The fiber-optic bundle senses changes in the amount of light reflected off a pressure-sensitive diaphragm at its tip. However, the fiber-optic bundle is subject to drift in the measurements over time and cannot be recalibrated in situ. In addition, the intraparenchymal and subdural methods are limited by the inability to withdraw CSF and manage ICP. Newer generations of fiber-optic ICP monitors allow simultaneous measurement of ICP, local cerebral blood flow (CBF) with Doppler, pH, PO<sub>2</sub>, and PCO<sub>2</sub> and avoid the potential infectious problems of a fluid-filled transducing system.

## 4. Summarize the conditions that commonly cause elevated intracranial pressure.

See [Table 45-1](#).

## 5. Describe the symptoms of increased intracranial pressure.

Symptoms associated with increased ICP alone include headache, vomiting, papilledema, drowsiness, loss of consciousness, and behavioral changes. Several other symptoms such as pathologic (decerebrate) posturing, oculomotor nerve palsy, abnormalities of brainstem reflexes, and abnormal respiratory patterns (including apnea), are probably caused by brainstem distortion or ischemia secondary to impending herniation. The Cushing reflex, consisting of hypertension and reflex bradycardia, is likely caused by medullary ischemia and occurs when ICP approaches systemic arterial pressure.

TABLE 45-1. COMMON CAUSES OF ELEVATED INTRACRANIAL PRESSURE

Increased CSF Volume	Increased Blood Volume	Increased Brain Tissue Volume
Communicating hydrocephalus	Intracerebral hemorrhage (aneurysm or AVM)	Neoplasm
Obstructing hydrocephalus	Epidural or subdural hematoma Malignant hypertension	Cerebral edema (CVA, encephalopathic, metabolic, traumatic) Cysts

*AVM, Arteriovenous malformation; CSF, cerebrospinal fluid; CVA, cerebrovascular accident; ICP, intracranial pressure.*

**6. Discuss the possible consequences of increased intracranial pressure.**

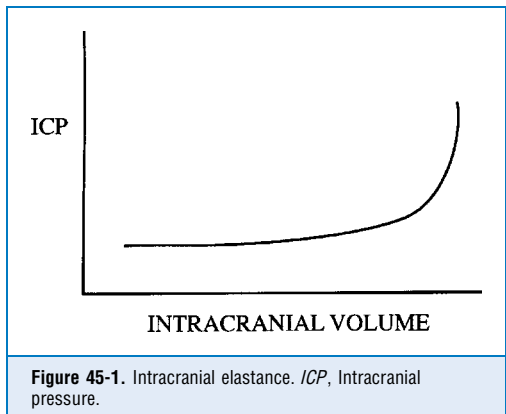
In addition to producing the previously mentioned symptoms, increased ICP can lead to a decrease in cerebral perfusion pressure, which may result in regional or global cerebral ischemia. Further elevations in ICP may result in herniation of brain contents (across the falx cerebri, tentorium, or foramen magnum).

**7. What are the determinants of cerebral perfusion pressure?**

Cerebral perfusion pressure (CPP) is usually defined as the difference between mean arterial pressure (MAP) and ICP or central venous pressure, whichever is higher.

**8. What is intracranial elastance? Why is it clinically significant?**

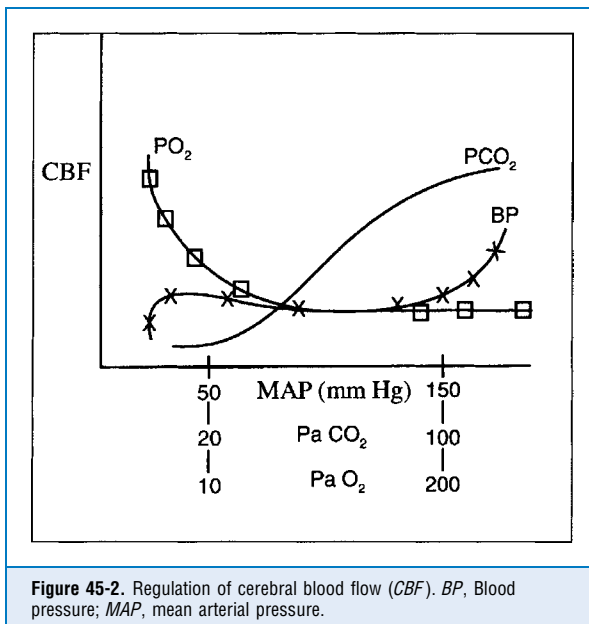
Intracranial elastance, commonly misnamed intracranial compliance, refers to the variation in ICP in accordance with intracranial volume. Because intracranial components can shift their volumes to an extent (e.g., CSF movement from the intracranial compartment to the spinal compartment), ICP remains somewhat constant over a certain range of volume. However, when compensatory mechanisms are exhausted, ICP rises rapidly with further increases in volume (Figure 45-1).



**9. How is cerebral blood flow regulated?**

CBF is coupled to cerebral metabolic rate by an uncharacterized mechanism but may involve potassium, hydrogen, calcium ions, adenosine, nitric oxide, and prostaglandins. In general, increases in the cerebral metabolic rate for oxygen (CMRO<sub>2</sub>) lead to increases in CBF,

although the increase in flow is delayed by 1 to 2 minutes. Several other parameters influence flow. Specifically an increase in the partial pressure of carbon dioxide in arterial blood ( $\text{PaCO}_2$ ) is a powerful cerebral vasodilator, with CBF increasing/decreasing 1 to 2 ml/100g/min with a 1-mm Hg change in  $\text{PaCO}_2$ . Similarly, a decrease in the partial pressure of oxygen ( $\text{PaO}_2$ ) in arterial blood below 50 mm Hg greatly increases flow. Variations in MAP also may result in large increases or decreases in flow, but over a broad range (50 to 150 mm Hg) flow is nearly constant. This constancy of flow over a range of pressures is known as autoregulation. Chronic hypertension shifts the autoregulation curve to the right. Following a brain injury such as stroke, tumor accompanied by edema, or trauma, autoregulation may be disrupted, and flow becomes pressure dependent (Figure 45-2).



#### 10. What is the goal of anesthetic care for patients with elevated intracranial pressure?

Because patients with elevated ICP may be approaching the upslope of the elastance curve, in which a small change in volume leads to a large increase in ICP, the goal of anesthetic care is to use all possible measures to reduce intracranial volume while maintaining cerebral perfusion.

#### 11. Can this goal be aided by preoperative interventions?

Traditionally several techniques have been used to decrease intracranial volume before surgery. Mild fluid restriction (intake of one third to one half of daily maintenance requirements) may decrease ICP over a period of several days. Corticosteroids are particularly effective in decreasing edema associated with tumors.



**12. How is the goal of reduced intracranial volume achieved at induction of anesthesia?**

The measures used at induction of anesthesia are chosen to reduce cerebral blood volume. Thiopental and propofol are the preferred intravenous induction agents because they reduce both CBF and  $CMRO_2$ . Ketamine and etomidate should be avoided because ketamine increases CBF and ICP and the propylene glycol formulation of etomidate may induce neurologic deficits in at-risk tissue. Opioids have a variable effect on CBF but are commonly used to blunt the sympathetic response to laryngoscopy and tracheal intubation. However, administer opioids cautiously in the spontaneously breathing patient since hypoventilation can lead to an increase in  $PaCO_2$  and thus CBF. Common adjuncts used at induction include intravenous lidocaine, a cerebral vasoconstrictor that blunts the response to intubation, and short-acting  $\beta$ -blockers such as esmolol that blunt systemic hypertension caused by laryngoscopy.

**13. How is intracranial pressure moderated during maintenance of anesthesia?**

Most intraoperative maneuvers for controlling ICP rely on reduction of cerebral blood volume or total brain water content. Blood volume is minimized by hyperventilation to lower  $PaCO_2$  (25 to 30 mm Hg), which results in transient cerebral vasoconstriction, and by using anesthetic agents that decrease CBF. Halogenated volatile agents should be limited to less than 1 minimum alveolar concentration. Nitrous oxide should be avoided because it increases both CBF and  $CMRO_2$  and may be neurotoxic. Maintaining the patient in a slightly head-up position promotes venous drainage. Brain water can be decreased acutely with diuretics such as mannitol (0.25 to 1g/kg bolus) and/or furosemide. In addition, intravenous fluids are limited to the minimal amount necessary to maintain cardiac performance. The surgeon may drain CSF directly from the surgical field or use an intraventricular catheter to decrease total intracranial volume. If oxygenation is not problematic, positive end-expiratory pressure (PEEP) should be avoided because it can be transmitted to the intracranial compartment. If PEEP is necessary for ventilation, the head of the bed should be elevated to avoid the increase in ICP caused by decreased venous return.

**14. Is hyperventilation a reasonable strategy for long-term intracranial pressure management?**

Hyperventilation (achieving a  $PaCO_2$  of 0 to 25 mm Hg) decreases ICP as a result of cerebral vasoconstriction, decreasing cerebral blood volume. This effect is mediated by an elevation in cerebral pH. This response occurs and is effective over the course of several hours. However, cerebral pH decreases by a gradual decrease in the bicarbonate concentration in newly formed CSF. Thus hyperventilation becomes ineffective for lowering ICP after 24 to 48 hours. Hyperventilation below a  $PaCO_2$  of 25 mm Hg should be avoided out of concern for focal cerebral ischemia caused by profound decreases in CBF.

**15. Which intravenous fluids are used during surgery to minimize intracranial pressure?**

In general hypotonic crystalloid infusions should be avoided because they may increase brain water content. Normal saline may be superior to lactated Ringer's because of the higher sodium and lower free water content. Some centers resuscitate with small volumes (4 ml/kg) of hypertonic saline to minimize free water in the setting of elevated ICP. Glucose-containing solutions are avoided because of evidence of worsened neurologic outcome if ischemia occurs in the setting of hyperglycemia. Hyperglycemia (serum glucose >180 mg/dl) should be treated with insulin. Colloidal solutions are not superior to crystalloid solutions.

**KEY POINTS: MEASURES TO DECREASE ICP**

1. Elevation of head of bed
2. Analgesia and anxiolysis
3. Osmotherapy (mannitol 1g/kg/24 hours or bolus doses of either mannitol 0.25 to 1 g/kg or 3% hypertonic saline 15 ml/kg)
4. Furosemide
5. Intraventricular drainage
6. Corticosteroids (dexamethasone for tumor-related edema)
7. Avoid hypervolemia
8. Hyperventilation (PaCO<sub>2</sub> 25 to 30 mm Hg)
9. Barbiturate coma (10 mg/kg given over 30 minutes followed by 1 to 2 mg/kg/hr)

**16. What are the effects of volatile anesthetics on cerebral blood flow?**

All of the commonly used inhaled anesthetics have been noted to increase CBF and decrease CMRO<sub>2</sub>. The response of CBF to changes in PaCO<sub>2</sub> is preserved.

**17. How do neuromuscular blocking agents affect intracranial pressure?**

Succinylcholine has been reported to increase ICP, but the clinical significance of this transient increase is probably not of concern. Therefore, in cases of emergent surgery in patients with a full stomach, rapid-sequence induction with succinylcholine is acceptable. Commonly used nondepolarizing agents have no effect on ICP and can be used safely.

**18. Discuss strategies for controlling intracranial pressure at emergence from anesthesia.**

β-Blockers such as esmolol and labetalol can be titrated to attenuate the increased sympathetic tone present at emergence. They are particularly useful in their ability to cause peripheral dilation without cerebral vasodilation, which can increase CBF. Nitroprusside, a direct-acting vasodilator, is also useful in controlling blood pressure when administered by infusion but can worsen ICP through cerebral vasodilation. The head of the bed should be elevated, and hypercarbia should be avoided.

**KEY POINTS: FACTORS AFFECTING CBF**

1. CPP
2. PaO<sub>2</sub>
3. PaCO<sub>2</sub>
4. Metabolism (CMRO<sub>2</sub>)

**19. If the previously mentioned measures fail to control intracranial pressure, what other measures are available?**

Barbiturate coma has been used in patients who are refractory to other methods of ICP control. Typical doses of pentobarbital are 10 mg/kg given over 30 minutes to load, followed by three hourly doses of 5 mg/kg. This regimen usually provides a therapeutic serum level of 30 to 50 mcg/ml. Maintenance is usually achieved by dosing of 1 to 2 mg/kg/h.

**KEY POINTS: AGENTS TO AVOID IN THE SETTING OF ELEVATED ICP**



1. Ketamine
2. Nitrous oxide
3. Hypotonic or glucose-containing intravascular fluid
4. High concentrations of inhalation agents

**20. What are the mechanisms behind traumatic brain injury?**

The damage to the brain after traumatic injury can be divided into two categories:

1. Damage from the primary mechanism of injury
2. Damage from secondary insults (hypotension, hypoxia)

The primary mechanism (e.g., motor vehicle crash, gunshot) can result in focal or global damage to the brain tissue. Focal injuries are primarily caused by penetrating trauma, contusions, or intracranial hemorrhage. On the other hand, global injuries are often the result of diffuse axonal injury in which rapid deceleration and rotation result in shearing between neocortical grey and white matter. The primary insult may not be responsive to therapeutic interventions. In contrast, secondary injuries from hypoperfusion or hypoxia that often occur in the intensive care unit or operating room should be prevented lest there be further deterioration in the patient's status.

**21. What are the anesthetic goals in a patient with traumatic brain injury?**

As previously mentioned, the anesthetic goals for managing a patient with traumatic brain injury (TBI) should be geared to prevent secondary injury. The already damaged brain tissue is extremely susceptible to hypoperfusion and hypoxia. Intubation should be achieved rapidly, with hemodynamic stability ensured and adequate oxygenation maintained. Adequate cerebral perfusion should be closely monitored, and a CPP between 60 to 80 mm Hg maintained. A MAP of  $>90$  is generally accepted and should be achieved with fluid resuscitation and vasopressors. Increases in ICP should also be addressed by measures previously discussed. Of note, cerebral autoregulation is commonly disrupted in TBI; and hypertension can similarly be deleterious by worsening vasogenic edema, resulting in an increased ICP and a subsequent decrease in CPP. In TBI oxygen demand may be increased as a result of a disproportional release of excitatory neurotransmitters, and hypoxia can worsen the ischemic injury.

**22. In a patient with traumatic head injury, how should fluid resuscitation be prioritized and what fluids are beneficial?**

As a general rule, hemodynamic stability takes precedence because cerebral hypoperfusion is clearly detrimental. The choice of resuscitative fluids in TBI is an ongoing debate. Traditionally Ringer's lactate and normal saline (0.9%) have been used. Ringer's lactate

has an osmolarity (273 mOsm/L) less than serum osmolarity, which in large volumes can decrease serum osmolarity and increase cerebral blood volume. In some institutions Ringer's lactate is limited to 2 L to minimize this effect. Normal saline has an osmolarity closer to serum osmolarity and does not result in a decrease in serum osmolarity. Some institutions use hypertonic saline (3% or 7.5%) for fluid resuscitation. Small quantities of hypertonic saline can be used to maintain intravascular volume because they result in movement of water from the intracellular space to the extracellular space. This may improve hemodynamics and decrease ICP. However, hypertonic saline does not reliably improve cerebral oxygen delivery and can result in electrolyte abnormalities. Colloid solutions (Hextend, albumin) can provide acute intravascular volume expansion. However, albumin has been implicated in increases in morbidity and mortality in TBI, and hetastarch has been associated with an elevation of prothrombin and partial thromboplastin times when given in volumes  $>20$  ml/kg. In the event of acute or continued blood loss, packed red blood cells provide excellent volume expansion.

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# MALIGNANT HYPERTHERMIA AND OTHER MOTOR DISEASES

James Duke, MD, MBA

## 1. What is malignant hyperthermia and its underlying defect?

Malignant hyperthermia (MH) is a myopathy characterized by an uncontrolled increase in skeletal muscle metabolism after exposure to a triggering agent. Patients with MH have an uncontrolled release of calcium from the sarcoplasmic reticulum caused by an abnormal ryanodine receptor (RyR1) isoform, a protein crucial for the release of calcium during normal excitation-contraction coupling. RyR1 mutations on chromosome 19 are found in 25% of known MH-susceptible individuals in North America. There are also associations between MH and another protein associated with the calcium channel, the dihydropyridine receptor. The gene for this protein is located on chromosome 7. Other RyR1 mutations are noted in other countries.

## 2. What are the inheritance pattern and triggering agents for malignant hyperthermia?

MH is inherited as an autosomal-dominant disorder with reduced penetrance and variable expressivity. Succinylcholine and the halogenated inhalational agents may precipitate an episode in a susceptible patient. MH is rare in infants and decreases after 50 years of age.

## 3. Describe the cellular events, presentation, and metabolic abnormalities associated with malignant hyperthermia.

Hypermetabolism of skeletal muscle leads to hydrolysis of adenosine triphosphate, glycolysis, glycogenolysis, uncoupled oxidative phosphorylation, increase in oxygen consumption, and heat production. The earliest symptom is often unexplained tachycardia. The sine qua non of MH is an unexplained rise in end-tidal  $\text{CO}_2$ . Patients may demonstrate peculiar rigidity, even after nondepolarizing relaxants have been administered. If untreated, the patient develops numerous metabolic abnormalities, including metabolic acidosis, respiratory acidosis, hypoxemia, hyperthermia, rhabdomyolysis, hyperkalemia, hypercalcemia, hyperphosphatemia, elevations in creatine kinase, myoglobinuria, acute renal failure, cardiac dysrhythmias, and disseminated intravascular coagulation. Death is common if the problem is unrecognized and untreated. Data from the North American Malignant Hyperthermia Registry (NAMHR) have determined a rate of cardiac arrest of 2.7% and of death 1.4%. Interestingly, although the malady is called MH, temperature increase is a relatively late manifestation.

## 4. How is malignant hyperthermia treated?

- Call for assistance because aggressive therapy requires more than one person.
- Turn off all triggering agents and hyperventilate the patient with 100% oxygen.
- Change to a non-triggering anesthetic such as propofol infusion.
- Notify the surgeon and operating-room personnel of the situation at hand and expedite conclusion of the procedure, even if it may require that surgery go unfinished.
- Administer dantrolene, 2 mg/kg; repeat every 5 minutes to a total dosage of 10 mg/kg if needed. Dantrolene sodium inhibits calcium release via RyR1 antagonism.
- Monitor blood gases. Administer bicarbonate, 2 to 4 mEq/kg for a pH < 7.1.
- Cool the patient, using interventions such as iced fluids and cooling blankets, but become less aggressive in reducing body temperature at about 38° C.

- Promote urine output (2 ml/kg/hr), principally with aggressive fluid therapy, although mannitol and furosemide may also be required.
- Treat hyperkalemia with calcium chloride, bicarbonate, and insulin.
- Check for hypoglycemia and administer dextrose, particularly if insulin has been administered.
- Treat dysrhythmias with procainamide and calcium chloride, 2 to 5 mg/kg intravenously (calcium chloride is used to treat the hyperkalemia-associated dysrhythmias).

#### 5. How does dantrolene work? How is dantrolene prepared?

Dantrolene impairs calcium-dependent muscle contraction. This rapidly halts the increases in metabolism and secondarily results in a return to normal levels of catecholamines and potassium. The solution is prepared by mixing 20 mg of dantrolene with 3 g of mannitol in 60 ml of sterile water. Since dantrolene is relatively insoluble, preparation is tedious and time consuming, and its preparation should not be the responsibility of the primary anesthesiologist involved in the patient's management.

#### 6. How is malignant hyperthermia susceptibility assessed in an individual with a positive family history or prior suggestive event?

The diagnosis of MH is immensely difficult. There are clinical grading scales that have been used to help determine how likely a suspected episode is a true MH episode. The gold standard for diagnosis is the caffeine-halothane contracture test (CHCT). The patient's muscle is exposed to incremental doses of halothane and caffeine, and the muscle is evaluated for the degree of contracture. The test is offered at only five centers in the United States and two in Canada. The test is 85% to 90% specific and 99% to 100% sensitive. It is important that patients who have experienced MH episodes undergo further evaluation because some of these patients will be found to be MH negative.

Genetic testing for the abnormal RyR1 isoform is now available in the United States and other selected countries. The role for genetic testing is expanding. It is much cheaper than muscle biopsy and CHCT and can be performed on children too young to have CHCT (less than 10 years of age or less than 40 kg). Genetic testing is especially valuable in homogeneous populations in whom the genetic defect is constant. However, if genetic testing is negative in a susceptible individual, a CHCT must be performed.

#### 7. What are the indications for muscle biopsy and halothane-caffeine contracture testing?

- Definite indications: Suspicious clinical history for MH, family history of MH, prior episode of masseter muscle rigidity
- Possible indications: Unexplained rhabdomyolysis during or after surgery, sudden cardiac arrest caused by hyperkalemia, exercise-induced hyperkalemia, moderate-to-mild masseter muscle rigidity with evidence of rhabdomyolysis
- Probably not indications: Diagnosis of neuroleptic malignant syndrome or sudden unexplained cardiac arrest during anesthesia or early postoperative period not associated with rhabdomyolysis

#### 8. What is masseter muscle rigidity and what is its relation to malignant hypothermia?

Masseter muscle rigidity (MMR) is defined as jaw muscle tightness with limb muscle flaccidity following a dose of succinylcholine. There is a spectrum of masseter response, from a tight jaw to a rigid jaw to severe spasticity, or trismus, otherwise described as *jaws of steel*. Of concern, the mouth cannot be opened sufficiently to intubate the patient. If jaws of steel are present, the incidence of MH susceptibility is increased. There is some controversy as to the management of patients experiencing MMR. Most pediatric anesthesiologists agree that, if trismus occurs, the triggering agent should be halted along with the surgical procedure if

feasible. The patient should be admitted to the hospital for 24 hours of close observation. Creatine kinase levels should be followed every 6 hours. Creatine kinase levels greater than 20,000 have a 95% predictive value that the patient is MH susceptible.

**9. Describe the preparation of an anesthetic machine and anesthetic for a patient with known malignant hypothermia susceptibility.**

Clean the anesthetic machine; remove vaporizers; and replace CO<sub>2</sub> absorbant, bellows, and gas hose. Flush the machine for 20 minutes with 10 L/min of oxygen. Have the MH cart in the operating room. Schedule the patient for the first case of the day and notify the postanesthesia care unit to be prepared with an appropriate number of personnel. A cooling blanket should be placed under the patient. Refrigerated saline should be available. A nontriggering anesthetic technique such as continuous intravenous infusion of propofol should be used. The patient should be monitored for 6 to 8 hours after surgery.

**10. Should malignant hypothermia–susceptible patients be pretreated with dantrolene?**

Dantrolene pretreatment is no longer indicated, providing that a nontriggering agent and appropriate monitoring are used and an adequate supply of dantrolene is available. Dantrolene pretreatment may cause mild weakness in normal patients and significant weakness in patients with muscle disorders. MH-susceptible patients with an uncomplicated intraoperative course should be monitored for at least 4 hours after surgery.

**11. What patients are at risk for redeveloping symptoms of malignant hypothermia after treatment with dantrolene?**

Review of data from the NAMHR suggests that about 20% of patients redevelop symptoms, known as *recrudescence*. It should be mentioned that the accuracy of these data is limited by their retrospective nature. The mean time until symptoms redevelop was 13 hours, with a range of 2.5 to 72 hours. Eighty percent manifested symptoms by 16 hours. Patients at risk were more muscular and thus had greater muscle mass, an MH score of 35 or greater (meaning that MH is very likely to be present), and a temperature increase as much as 38.8° C. There was no strong relationship between use of succinylcholine or a particular volatile anesthetic. Probably the most severely affected are likely to develop recrudescence; these findings suggest that all patients who develop MH require at least 24 hours of posttreatment management in a critical-care setting.

**12. What drugs commonly administered intraoperatively are safe to use in malignant hyperthermia–susceptible patients.**

- Induction agents: barbiturates, propofol, etomidate, ketamine
- Benzodiazepines and opiates
- Amide and ester local anesthetics
- Nitrous oxide
- Nondepolarizing muscle relaxants
- Calcium

**13. Compare neuroleptic malignant syndrome with malignant hypothermia.**

Neuroleptic malignant syndrome (NMS) is characterized by akinesia, muscle rigidity, hyperthermia, tachycardia, cyanosis, autonomic dysfunction, sensorium change, tachypnea, and elevated levels of creatine kinase. It is associated with administration of the psychotropic drugs haloperidol, fluphenazine, perphenazine, and thioridazine, to name a few, and is caused by dopamine receptor blockade in the hypothalamus and basal ganglia. NMS is treated with dantrolene or bromocriptine (a dopamine receptor agonist) and has a mortality rate of 10%. Patients with NMS are not prone to MH.

**14. What are the muscular dystrophies and their underlying defect?**

The muscular dystrophies (MDs) are genetically determined degenerative muscle diseases and are divided further into muscular and myotonic dystrophies. Painless muscle degeneration and atrophy are common features. MD is associated with mutations of the gene that codes for the protein dystrophin. Dystrophin attaches muscle fibers to an extracellular matrix. Inadequately tethered muscle fibers are injured by shearing forces, degenerate, and are replaced by adipose and connective tissue. Dystrophin also seems to have other roles, including clustering of acetylcholine receptors on the postsynaptic motor membrane and modulation of ionic channels.

**15. What are the most common muscular dystrophies and their clinical history?**

Duchenne MD (DMD) is the most common. It is an X chromosome–linked recessive disease with signs and symptoms presenting between 2 and 5 years of age. Death often occurs in late adolescence and is typically caused by heart failure or pneumonia. Degeneration of cardiac muscle, as demonstrated by a progressive decrease in R-wave amplitude on electrocardiogram (ECG), is observed to some degree in 70% of DMD patients and may lead to a decrease in contractility and mitral regurgitation secondary to papillary muscle dysfunction. Thus patients with MD may be sensitive to the myocardial depressant effects of inhaled anesthetics. There is weakness of respiratory muscles, and a restrictive pattern is observed on pulmonary function testing. Smooth muscle may also be affected in patients with MD, manifesting as gastrointestinal tract hypomotility, delayed gastric emptying, and impaired swallowing, which may lead to increased risk of aspiration.

Becker MD has similar, although milder, symptoms and a more protracted course.

**16. Briefly review of forms of muscular dystrophy.**

Other forms include the limb-girdle, oropharyngeal, and fascioscapulohumeral muscular dystrophies. Some of these forms are transmitted as autosomal and/or dominant and thus can be identified in both females and males. Bulbar muscles are usually spared; therefore aspiration is less of a risk, although dysrhythmias, conduction abnormalities, occasional sudden death, and cardiomyopathies are noted. One form, Emery-Dreifuss MD, has posterior nuchal muscle contractures as a feature and may render airway management difficult.

**17. How do patients with muscular dystrophy respond to muscle relaxants and volatile anesthetics?**

Succinylcholine should not be used because of the possibility of severe hyperkalemia and cardiac arrest. Cardiac arrest has been reported in patients with unrecognized MD. Because children with MD may not develop noticeable weakness until they are several years old, many authorities believe succinylcholine should not be used in children except in airway emergencies. Nondepolarizing relaxants are acceptable but may be associated with longer-than-normal recovery times.

There are reports of massive elevations in creatine kinase, severe myoglobinuria, and cardiac arrest after use of volatile anesthetics. Although not all patients with MD are at risk for MH, some are; thus a nontriggering general anesthetic or regional anesthesia is preferred.

**18. Are patients with muscular dystrophy at risk for malignant hyperthermia?**

After succinylcholine administration children with MH and MD may have similar clinical pictures, including hyperkalemia, elevated creatine kinase, and cardiac arrest, although the mechanism of the diseases is different. There are also reports of children with MD exposed to inhalational agents but not succinylcholine that have demonstrated suggestive signs of MH. However, it is not believed that children with MD are at increased risk for MH.



**19. What is myotonic dystrophy?**

Myotonic dystrophy is an autosomal-dominant disease that usually presents in the second or third decade and is the most common inherited myopathy in adults. It is characterized by persistent contraction of skeletal muscle after stimulation. The contractions are not relieved by regional anesthetics, nondepolarizing muscle relaxants, or deep anesthesia. It is a multisystem disease; deterioration of skeletal, cardiac, and smooth muscle function is progressive.

**20. How does myotonic dystrophy affect the cardiopulmonary system?**

Heart failure is rare, but dysrhythmias and atrioventricular block are common. Mitral valve prolapse occurs in 20% of patients. Restrictive lung disease, with mild hypoxia on room air, a weak cough, and inadequate airway protective reflexes, may lead to pneumonia. These patients are also sensitive to medications that depress ventilatory drive.

**21. What are the important muscle relaxant considerations in patients with myotonic dystrophy?**

Succinylcholine produces exaggerated contraction of skeletal muscles, possibly making mask ventilation and tracheal intubation difficult or impossible. The response to nondepolarizing muscle relaxants is normal; nondepolarizing relaxants will not ablate myotonic contractures.

**22. What is myasthenia gravis?**

Myasthenia gravis is an autoimmune disease of the neuromuscular junction. Antibodies to the acetylcholine receptor may reduce the absolute number of functional receptors by direct destruction of the receptor, blockade of the receptor, or complement-mediated destruction.

**23. Describe the clinical presentation of myasthenia gravis.**

Myasthenic patients present with generalized fatigue and weakness that worsens with repetitive muscular use and improves with rest. Very commonly extraocular muscles are the first affected, and the patient complains of diplopia or ptosis. Of particular concern are myasthenic patients who develop weakness of their respiratory muscles or the muscles controlling swallowing and the ability to protect the airway from aspiration. Depending on whether extraocular, airway, or respiratory muscles are affected, myasthenia gravis (MG) may be described as ocular, bulbar, or skeletal, respectively.

**24. How is myasthenia gravis treated? What can lead to an exacerbation of symptoms?**

Cholinesterase inhibitors, corticosteroids, and other immunosuppressants are effective, as is plasmapheresis, although in many thymectomy results in remission. Physiologic stress such as an acute infection, pregnancy, or surgical procedure can lead to exacerbations of MG.

**25. What are some of the principal anesthetic concerns in the management of a myasthenic patient for any operative procedure?**

Principal concerns include the degree of pulmonary impairment, the magnitude of bulbar involvement with attendant difficulty managing oral secretions (risk of pulmonary aspiration), and adrenal suppression from long-term steroid use. Although uncommon, cardiac disease that is MG related should be considered in the preoperative evaluation. Because symptoms are primarily related to arrhythmias, an ECG should be evaluated. Symptoms of congestive heart failure should be sought as well.

**26. Describe the altered responsiveness of myasthenic patients to muscle relaxants.**

Patients are resistant to succinylcholine. However, the degree of resistance does not appear to be of great clinical significance, and increasing the dose of succinylcholine to 2 mg/kg results in satisfactory intubating conditions.

Myasthenic patients are more sensitive than nonmyasthenic persons to nondepolarizing relaxants. Dosing nondepolarizing relaxants should start at about one tenth the usual

recommended doses. Recovery time for these reduced doses varies but may be quite prolonged. Relaxation should be reversed at case conclusion, and the patient carefully evaluated for return of strength.

Often at anesthetic induction no muscle relaxant is necessary to achieve endotracheal intubation. These patients are already weak; if volatile anesthetics are administered, suitable muscle relaxation is achieved. The best course of action for myasthenic patients may be to avoid muscle relaxants altogether.

**27. What is Lambert-Eaton myasthenic syndrome? Describe its symptoms, associations, and treatment.**

This is an immune-mediated disease of the neuromuscular junction that frequently arises in the setting of malignancy, often small-cell carcinoma of the lung. Other associated malignancies include lymphoma, leukemia, prostate, and bladder. Antibodies affect the presynaptic junction and result in decreased acetylcholine release. As opposed to MG, weakness improves with motor activity, although frequently the improvement is transient. Proximal muscles are affected more than distal, and legs more than arms. Cranial nerve involvement is also less frequent when compared to MG. Interestingly, weakness often precedes the cancer diagnosis, although treatment focuses on treatment of the underlying malignancy. Autonomic dysfunction is common and manifests as dry mouth, orthostatic hypotension, and bowel and bladder dysfunction. Corticosteroids, 3,4-diaminopyridine, and other immunosuppressants improve strength.

**28. Review the anesthetic concerns for a patient with Lambert-Eaton syndrome.**

These patients are exquisitely sensitive to both depolarizing and nondepolarizing muscle relaxants, and these medications are best avoided. If given, paralysis can last for days and is not reversible with anticholinesterase medications. Volatile anesthetics are safe and often provide the necessary degree of muscle relaxation to facilitate endotracheal intubation. When applicable, regional techniques are encouraged.

## KEY POINTS: MALIGNANT HYPERTHERMIA AND OTHER MOTOR DISEASES



1. MH is a hypermetabolic disorder that presents in the perioperative period after exposure to inhalational agents or succinylcholine.
2. Early recognition is critical; and treatment is complex and multifaceted, requiring the assistance of other experienced personnel.
3. The sine qua non of MH is an unexplained rise in end-tidal carbon dioxide in a patient with unexplained tachycardia. A temperature rise is a late feature.
4. Patients with a history of MH or who are MH susceptible must receive anesthesia with a nontriggering agent. The anesthesiologist must have a heightened awareness of MH, have prepared the anesthetic machine, and have the MH cart in the room.
5. Succinylcholine must be avoided in children with MD and should be avoided except in airway emergencies in male children.
6. Nondepolarizing muscle relaxants should be used at about one tenth of normal doses (if at all) in patients with myasthenia gravis.
7. Patients with Lambert-Eaton myasthenic syndrome are sensitive to both depolarizing and nondepolarizing muscle relaxants, and these medications are best avoided.
8. Patients with MDs are prone to aspiration and respiratory insufficiency and may have dysrhythmias, conduction blockade, and cardiomyopathy.

## WEBSITES



Myasthenia Gravis Foundation of America

<http://www.myasthenia.org>

Malignant Hyperthermia Association of the United States

<http://www.mhaus.org>

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# DEGENERATIVE NEUROLOGIC DISEASES AND NEUROPATHIES

James Duke, MD, MBA

## 1. What is amyotrophic lateral sclerosis and its anesthetic considerations?

Also known as Lou Gehrig's disease, amyotrophic lateral sclerosis (ALS) is a disease of both upper and lower motor neurons. It usually affects men in the fourth or fifth decade of life. Patients with ALS develop progressive weakness and eventually die (from pneumonia and pulmonary failure), often in a 3- to 5-year period. Although extremities are involved first, eventually bulbar muscles become affected, increasing the risk of aspiration. The pathogenesis is poorly understood but thought to be caused by mutations in the superoxide dismutase-1 gene. Treatment options are limited.

Reports of anesthetic difficulties are anecdotal. There is no evidence that either regional or general anesthesia exacerbates the disease. Succinylcholine-induced hyperkalemia and subsequent cardiac arrest have been reported. Nondepolarizing muscle relaxants have a prolonged duration of action. Aspiration is an increased risk, as is the need for postoperative ventilatory support. These patients are not at risk for malignant hyperthermia.

## 2. Review the clinical manifestations of Guillain-Barré syndrome.

Acute idiopathic polyneuritis (Guillain-Barré syndrome) is currently the most frequent cause of generalized paralysis and usually presents with sudden onset of weakness or paralysis, typically in the legs, that spreads to the trunk, arms, and bulbar muscles over several days. Bulbar involvement may be suggested by facial muscle weakness. Areflexia is also a feature. Respiratory failure requiring mechanical ventilation occurs in 20% to 30% of cases. About half of all cases are preceded by a respiratory or gastrointestinal infection; and the pathogenesis is thought to be autoimmune, possibly related to similarities between bacterial liposaccharides and axonal gangliosides. Recovery may occur within weeks, although some residual weakness remains secondary to axonal degeneration. Mortality (3% to 8%) typically results from sepsis, adult respiratory distress syndrome, pulmonary embolism, or cardiac arrest. Plasmapheresis and immunoglobulin therapy result in some improvement, whereas glucocorticoid supplementation does not.

## 3. How is the autonomic nervous system affected in Guillain-Barré syndrome?

Autonomic dysfunction is a common finding. Patients may experience wide fluctuations in blood pressure, profuse diaphoresis, peripheral vasoconstriction, tachyarrhythmias and bradyarrhythmias, cardiac conduction abnormalities, and orthostatic hypotension. Sudden death has been described.

## 4. What are the major anesthetic considerations for patients with Guillain-Barré syndrome?

Patients may not handle oral secretions well because of pharyngeal muscle weakness and have respiratory insufficiency secondary to intercostal muscle paralysis. Aspiration is a risk. Secondary to autonomic dysfunction, compensatory cardiovascular responses may be absent, and patients may become hypotensive with mild blood loss or positive-pressure ventilation. Alternatively laryngoscopy may produce exaggerated increases in blood pressure. The response to indirect-acting vasoactive drugs may also be exaggerated.

Because of the unpredictable and wide swings in blood pressure, intra-arterial monitoring should be considered. There is no evidence that either general or regional anesthesia worsens the disease.

Since Guillain-Barré syndrome is a lower motor neuron disease, succinylcholine is contraindicated because of the potential for exaggerated potassium release. Pancuronium should also be avoided because of its autonomic effects. Postoperative ventilation may be necessary because of respiratory muscle weakness.

#### 5. Review the pathophysiologic features of Parkinson's disease.

Parkinson's disease, an adult-onset degenerative disease of the extrapyramidal system, is characterized by the loss of dopaminergic neurons in the basal ganglia. With the loss of dopamine, there is diminished inhibition of the extrapyramidal motor system and unopposed action of acetylcholine.

#### 6. Describe the clinical manifestations of Parkinson's disease.

Patients with Parkinson's disease display increased rigidity of the extremities, facial immobility, shuffling gait, rhythmic resting tremor, dementia, depression, diaphragmatic spasms, and oculogyric crisis (a dystonia in which the eyes are deviated in a fixed position).

#### 7. What are the effects of levodopa therapy, particularly on intravascular volume status?

Levodopa, the immediate precursor to dopamine, crosses the blood-brain barrier, where it is converted to dopamine by a decarboxylase enzyme. Treatment with levodopa increases dopamine both in the central nervous system and peripherally. Increased levels of dopamine may increase myocardial contractility and heart rate. Renal blood flow increases, as does glomerular filtration rate and sodium excretion. Intravascular fluid volume decreases, the renin-angiotensin-aldosterone system is depressed, and orthostatic hypotension is a common finding. High concentrations of dopamine may cause negative feedback for norepinephrine production, which also causes orthostatic hypotension.

#### 8. Review the anesthetic considerations for a patient with Parkinson's disease.

- Abrupt withdrawal of levodopa may lead to skeletal muscle rigidity, which interferes with adequate ventilation. Levodopa should be administered on the morning of surgery and restarted after surgery.
- Extremes of blood pressure and cardiac dysrhythmias may occur.
- Phenothiazines (e.g., chlorpromazine, promethazine, fluphenazine, prochlorperazine) and butyrophenones (e.g., droperidol and haloperidol) may antagonize the effects of dopamine in the basal ganglia. Metoclopramide inhibits dopamine receptors in the brain. These medications should be avoided.
- Patients may be intravascularly volume depleted; therefore aggressive administration of crystalloid or colloid solutions may be required in the setting of peri-induction hypotension.

#### 9. What are the clinical signs and symptoms of Alzheimer's disease?

Alzheimer's disease accounts for most of the severe cases of dementia in the United States. The disease follows an insidious onset, with progressive worsening of memory and decreased ability to care for oneself and manage the usual activities of daily life.

#### 10. What is the most significant anesthetic problem associated with Alzheimer's disease?

The inability of some patients to understand their environment or to cooperate with health care providers becomes an important consideration. Sedative drugs may exacerbate confusion and probably should be avoided in the perioperative period. Regional techniques may be used with the understanding that the patient may be frightened or confused by the operating-room

environment. Reductions in the level of volatile anesthetic or opioid administered may be of benefit. A lack of cooperation and unanticipated outbursts during the surgical procedure are arguments for general anesthesia.

#### 11. What are the hallmark features of multiple sclerosis?

The corticospinal tract neurons of the brain and spinal cord show random and multifocal demyelination, which slows nerve conduction, resulting in visual and gait disturbances, limb paresthesias and weaknesses, and urinary incontinence. There is increasing evidence that there is demyelination of peripheral nerves as well. The onset of disease is typically between the ages of 15 and 40 years. The cause appears to be multifactorial, including viral and genetic factors. The course of multiple sclerosis is characterized by symptomatic exacerbations and remissions, although symptoms eventually persist. Female patients often experience remission during pregnancy. Symptoms of multiple sclerosis (MS) usually develop over a few weeks, persist for a few months, and resolve to varying degrees over a few months. The etiology is unknown; however, viral infection leading to immunologically mediated destruction of myelin is one hypothesis.

#### 12. Do steroids have a role in the treatment of multiple sclerosis?

Steroids may shorten the duration and severity of an attack but probably do not influence progression of the disease. Other therapies such as immunosuppressive drugs, interferon, and plasmapheresis are also occasionally of benefit.

#### 13. What factors have been associated with an exacerbation of multiple sclerosis?

Emotional stress, fatigue, infections, hyperthermia, trauma, and surgery may exacerbate symptoms. It is thought that elevated temperature causes complete blocking of conduction in demyelinated neurons.

#### 14. Review some perioperative concerns for patients with multiple sclerosis. Are medications used for most general anesthetics safe?

Surgical stress most likely will exacerbate the symptoms of MS. Even modest increases in body temperature ( $>1^{\circ}\text{C}$ ) must be avoided. There are no known unique interactions between MS and drugs selected for general anesthesia. However, severe disease is often accompanied by varying degrees of dementia. Demented patients will likely have an increased sensitivity to the sedative effects of anesthetic agents, and short-acting agents are recommended. Controlling the known factors associated with MS exacerbation is more important than the choice of medications for general anesthesia.

#### 15. Are local anesthetics especially toxic for patients with multiple sclerosis?

Above threshold concentrations local anesthetics are neurotoxic. This potential may be amplified in the setting of MS because of the loss of the protective effect of the myelin, resulting in the spinal cord and nerves being exposed to higher local anesthetic concentrations.

#### 16. Are epidural and spinal anesthetics safe for patients with multiple sclerosis?

Regional anesthesia may be beneficial in the patient with MS because of a decreased stress response to surgery. Epidural anesthesia is considered safe by most authorities. The safety of peripheral nerve blocks cannot be guaranteed as evidenced by a patient with MS sustaining a severe brachial plexopathy after interscalene block (see Koff 2008). Exacerbation of MS symptoms has been reported after spinal anesthesia. This difference in outcomes may be caused by reduced concentrations of local anesthetic at the spinal cord when epidural is compared to spinal techniques and there is less exposure of unmyelinated nerve roots to local anesthetics. When performing an epidural anesthetic or labor analgesic, recommendations are to use the minimum dose necessary and to use shorter-acting agents. Supplementation with epidural opioids will also reduce the local anesthetic requirement. In summary, spinal anesthetic is a technique best avoided in patients with MS.

**17. Are muscle relaxants safe in patients with multiple sclerosis?**

Since these patients (particularly the patients with severe disease) can have significant motor impairment with associated muscle wasting, succinylcholine might be best avoided because of a potential hyperkalemic response. Lower doses of nondepolarizing relaxants should be used in patients with baseline motor weakness. Shorter-duration nondepolarizing relaxants may be advantageous in this situation.

**18. Describe postpoliomyelitis syndrome.**

Postpolio syndrome is characterized by progressive weakness of the previously affected muscles that begins years after a severe attack of poliomyelitis. Muscles never affected by polio are less often affected. Common signs and symptoms include fatigue, cold intolerance, joint deterioration, muscle pain, atrophy, respiratory insufficiency, dysphagia, and sleep apnea. Patients with postpolio syndrome who complain of dysphagia may have some degree of vocal cord paralysis. Some patients have decreased lung function, and considerable cardiorespiratory deconditioning may also be present.

**19. What are the anesthetic considerations for patients with postpolio syndrome?**

Patients should be informed about the possibility of postoperative mechanical ventilation. If sleep apnea is present, the patient may have coexisting pulmonary hypertension. Dysphagia and vocal cord paralysis may place patients at increased risk for aspiration. If progressive skeletal muscle weakness is present, succinylcholine should be avoided because of the possibility of exaggerated potassium release.

**20. Review critical illness polyneuropathy and the patient subsets prone to developing it.**

As many as 70% of patients with sepsis, multiple organ dysfunction, or systemic inflammatory response syndrome develop generalized weakness associated with sensory loss and other neurologic findings. This syndrome has been termed *critical illness polyneuropathy* (CIP). The longer the duration of the underlying illness, the more severe the weakness. Patients with mild or moderate underlying critical illness are likely to have improvement in strength once their primary condition improves, although death is not infrequent in those severely affected (and usually related to the primary illness). Although the mechanism is unknown, it is thought to be a disturbance of the microvasculature, resulting in neuronal ischemia and increased capillary permeability. Factors that may be associated with CIP include long-term administration of muscle relaxants, steroids, malnutrition, and hyperglycemia.

**21. Describe the clinical features of critical illness polyneuropathy.**

Failure to wean is the most common presentation, but coexistent encephalopathy often clouds the clinical picture. Severe cases may present as areflexic quadriplegia. Other clinical characteristics include predominantly distal limb weakness with muscle wasting, decreased or absent deep tendon reflexes, and variable sensory loss, often in a stocking and glove distribution. Cranial nerves are intact. Creatine kinase levels are normal or slightly elevated. Cerebrospinal fluid is normal. Biopsies of nerves show fiber loss with axonal degeneration, whereas muscle biopsies demonstrate denervation atrophy. Electrophysiologic studies reveal an axonal polyneuropathy.

**22. Review the anesthetic concerns in patients with critical illness polyneuropathy.**

The response to nondepolarizing relaxants cannot be predicted. Succinylcholine should be avoided out of concerns for hyperkalemia. The associated medical problems are probably the greatest risk for the patient.

**NOTE:** Perioperative neuropathies are discussed in Chapter 20.

**KEY POINTS: DEGENERATIVE NEUROLOGIC DISEASES**

1. Patients with neuropathies often are aspiration risks secondary to bulbar muscle weakness.
2. Similarly, orthostatic hypotension is a common finding.
3. Often these patients require postoperative mechanical ventilation.
4. Because of denervation atrophy, succinylcholine may produce severe hyperkalemia, resulting in cardiac arrest. Thus succinylcholine should be avoided.
5. The response to nondepolarizing muscle relaxants is unpredictable, but most of these patients are probably sensitive to them.
6. Spinal anesthesia should be avoided in patients with multiple sclerosis.
7. With the exception of spinal anesthesia in multiple sclerosis, neither general nor regional anesthesia exacerbates the course of disease in the neuropathies described.

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# ALCOHOL AND SUBSTANCE ABUSE

James Duke, MD, MBA

## 1. How is alcohol absorbed and metabolized?

Alcohol is absorbed across the gastrointestinal mucosa, more so in the small intestine than in the stomach. The volume of distribution ( $V_D$ ) of alcohol is that of body water. Alcohol easily crosses the blood-brain barrier. Arterial blood levels of alcohol correlate well with concentrations in lung alveoli, thus the basis of the breathalyzer test used by law-enforcement officers.

Alcohol is metabolized primarily in the liver. Most consumed alcohol is converted to acetaldehyde by the enzyme alcohol dehydrogenase. Alcohol metabolism follows Michaelis–Menten zero-order kinetics. When alcohol dehydrogenase is saturated with ethanol, the rate of metabolism is constant, although alcohol concentration may increase. A 5% to 10% amount of consumed alcohol is excreted unchanged in the breath and urine.

## 2. What are the acute and chronic effects of alcohol on the nervous system?

Acutely alcohol depresses the central nervous system by inhibiting polysynaptic function, which is characterized by generalized blunting and loss of higher motor, sensory, and cognitive function. Although the behavioral effects of alcohol consumption may seem excitatory or stimulating to observers and users, this impression is probably caused by a depressive effect on inhibitory pathways (disinhibition).

Chronic alcohol use is associated with peripheral nerve and neuropsychiatric disorders, many of which (e.g., Wernicke's encephalopathy and Korsakoff's psychosis) may be linked to nutritional deficiencies. Alcohol-related neuropathy usually involves pain and numbness in the lower extremities, often with concomitant weakness of the intrinsic muscles of the feet. Patients may exhibit hypalgesia in a stocking-foot distribution, and the Achilles tendon reflex may be absent. Generalized weakness in the proximal limb musculature may also be noted.

## 3. What are the effects of alcohol on the cardiovascular system?

Moderate acute ingestion of alcohol produces no significant changes in blood pressure or myocardial contractility. Cutaneous vasodilation occurs, and heart rate increases. At toxic levels of acute alcohol ingestion, a decrease in central vasomotor activity causes respiratory and cardiac depression.

The leading cause of death in chronic users of alcohol is cardiac dysfunction. Consumption of 60 oz of ethanol per month (8 pints of whiskey or 55 cans of beer) may lead to alcohol-induced hypertension. An intake  $>90$  oz per month over a 10-year period may result in congestive cardiomyopathy with associated pulmonary hypertension, right-heart failure, and dysrhythmias (usually atrial fibrillation and premature ventricular contractions). Ventricular tachydysrhythmias, ventricular fibrillation, and sudden death are also risks.

## 4. How does alcohol affect the respiratory system?

Acute alcohol intake may cause hyperventilation via disinhibition of central respiratory regulation centers and increases in dead-space ventilation. Despite hyperventilation, alcohol depresses the ventilatory response to carbon dioxide. Aspiration of gastric contents is a risk. Chronic alcohol users are susceptible to pulmonary infections, often by staphylococci or gram-negative organisms. There is also a generalized decrease in all lung capacities (vital, functional residual, and inspiratory capacity).

**5. How does alcohol affect the gastrointestinal and hepatobiliary systems?**

Acute alcohol use may cause esophagitis, gastritis, and pancreatitis. Chronic alcohol use leads to delayed gastric emptying and relaxation of the lower esophageal sphincter, increasing the risk of aspiration. The liver undergoes transient and reversible fatty infiltration during acute alcohol use. Although such changes resolve with abstinence and the cycle can repeat itself many times, prolonged alcohol exposure leads to chronic infiltration of fat, which over time progresses to necrosis and fibrosis of liver tissue. The initial presentation of fatty liver is hepatomegaly. When necrosis, fibrosis, and cirrhosis become apparent, the liver regresses in size. Chronic severe consumption of alcohol leads to irreversible cirrhosis and alcohol-induced hepatitis. Hepatic synthetic function is also impaired. Production of albumin and coagulation factors II, V, VII, X, and XIII is decreased. Reduction of albumin results in lower intravascular oncotic pressure and may lead to tissue edema. A reduction in circulating coagulation factors may predispose to bleeding, which is evidenced by a prolonged prothrombin time.

**6. Which nutritional deficiencies are seen in chronic alcohol users?**

Deficiency of thiamine leads to Wernicke's encephalopathy, polyneuropathy, and cardiac failure characterized by high cardiac output, low systemic vascular resistance, and loss of vasomotor tone. Folic acid deficiency causes bone-marrow depression and thrombocytopenia, leukopenia, and anemia.

**7. What are the effects of alcohol on inhalational anesthetics?**

In acutely intoxicated, nonhabituated patients, the minimal alveolar concentration (MAC) of inhalational agents is reduced. For chronic users of alcohol the MAC for inhalational agents is increased.

Acutely intoxicated patients are more sensitive to the effects of barbiturates, benzodiazepines, and opioids. Cross-tolerance develops to intravenous agents with chronic alcohol exposure.

**8. How does alcohol affect muscle relaxants?**

Patients with liver disease may have decreased levels of circulating plasma cholinesterase, and the effects of succinylcholine may be prolonged. Cirrhotic patients with poor liver function have a greater  $V_D$  for injected drugs and thus require a larger dose of nondepolarizing relaxants. Relaxants that rely on hepatic clearance may have a prolonged duration of action. Muscle relaxants that are metabolized independently of organ function (e.g., cisatracurium) are good choices for patients with liver disease.

**9. Describe special considerations in the perioperative assessment of alcohol-abusing patients.**

Special consideration must be given to the cardiovascular system of chronic alcohol users. Tachycardia, dysrhythmias, or cardiomegaly may indicate alcohol-related cardiac dysfunction; and a 12-lead electrocardiogram (ECG) should be evaluated. Patients with alcohol-induced cardiac disease are less sensitive to endogenous or parenteral catecholamines. Hypokalemia and hypoglycemia are common, as are anemia, thrombocytopenia, and altered coagulation. These patients are often volume depleted and will require fluid resuscitation. Insert a urinary catheter to follow urine output. Intravascular monitoring should be individualized. Instrumentation of the esophagus should be avoided in patients with known liver disease because of the possibility of rupturing esophageal varices.

**10. How should sober chronic alcohol abusers be anesthetized?**

Sober chronic alcohol users can tolerate intravenous and inhalational anesthetics. Isoflurane may be the best inhalational agent for maintaining hepatic blood flow. In general, a balanced anesthetic technique using amnestics, opioids, muscle relaxants, and an inhalational agent will suffice.

**11. What are the signs and symptoms of alcohol withdrawal?**

Alcohol withdrawal presents as anorexia, insomnia, weakness, combativeness, tremors, disorientation, auditory and visual hallucinations, and convulsions. Onset is usually 10 to 30 hours after abstinence, and the symptoms may last for 40 to 50 hours. Prolonged abstinence may lead to delirium tremens or autonomic hyperactivity (tachycardia, diaphoresis, fever, anxiety, and confusion). Alcohol withdrawal syndrome may occur while under anesthesia and manifest as uncontrolled tachycardia, diaphoresis, and hyperthermia. The treatment is administration of benzodiazepines or intravenous infusion of ethanol.

**KEY POINTS: CONCERNS IN CHRONIC ALCOHOLICS**

1. May have cardiomyopathy and dysrhythmias
2. Predisposed to aspiration and have diminished pulmonary function
3. Portal hypertension and varices (avoid orogastric and nasogastric tubes)
4. Impaired synthetic liver function (important screening tests are albumin and prothrombin time)
5. Alcohol withdrawal may cause seizures.

**12. Review the differences between addiction, dependence, pseudoaddiction, and tolerance.**

According to the American Pain Society:

- Dependence implies “a state of adaptation that is manifested by a drug class–specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.”
- Opioid tolerance is “a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug’s effects over time.”
- Addiction “is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.”
- Pseudoaddiction refers to an iatrogenic state in which the patient displays addiction-type behaviors, but the cause is inadequate treatment of a painful condition. Often the setting is an acute pain condition superimposed on a chronic pain state. Patients on prolonged opioid therapy develop physical dependence and potentially tolerance, but they usually do not develop addictive behaviors.

**13. List complications of chronic opioid abuse.**

Cellulitis	Pneumonia
Adrenal suppression	Tetanus
Abscess formation	Subacute bacterial endocarditis
Thrombophlebitis	Hepatitis
Atelectasis	Acute pulmonary edema
Anemia	Systemic and pulmonary emboli
Pulmonary hypertension	Acquired immunodeficiency syndrome
Sepsis	Sclerosing glomerulonephritis
Death from overdose	

**14. Discuss perioperative problems associated with the chronic opioid abuser.**

The perioperative period is not an appropriate time to attempt opioid withdrawal. It is necessary to know the patient's usual opioid requirements to avoid undermedication. Associated behavioral and psychologic problems may make general anesthesia a better option than regional or local anesthesia. These patients may be in acute withdrawal and be uncooperative. Intravenous access may be difficult, and central venous catheterization may be necessary. A substantially increased dose of opioids to achieve the desired effect is the norm. Consultation with a pain-management team may help with development of a realistic postoperative pain-management strategy.

**15. Describe the time frame and stages of opioid withdrawal.**

The onset and duration of withdrawal vary with the drug used. For example, meperidine withdrawal symptoms peak in 8 to 12 hours and last for 4 to 5 days. Heroin withdrawal symptoms usually peak within 36 to 72 hours and may last for 7 to 14 days. Symptoms of withdrawal include restlessness, sweating, nausea, rhinorrhea, nasal congestion, abdominal cramping, lacrimation, and drug craving. Overt withdrawal results in piloerection, emesis, diarrhea, muscle spasms (thus the term *kicking the habit*), fever, chills, tachycardia, and hypertension.

**16. What medications are used to stabilize and detoxify the withdrawing opioid patient?**

Long-acting medications (e.g., methadone and sustained-release morphine) are used because they have a slower onset of action and the *high* experienced with rapid-onset medications is less prominent. Autonomic hyperactivity and other symptoms of acute opiate withdrawal are treated with  $\beta$ -adrenergic antagonists and  $\alpha_2$ -agonists such as clonidine.

**17. To what arrhythmias are methadone-treated patients prone?**

There are multiple reports of these patients having prolonged correct QT intervals, torsades de pointes, and sudden death.

Other important facts about methadone are that it has no effect on seizure disorders, has no active metabolites, is relatively safe in renal failure, and has not been associated with hepatic toxicity.

**18. What are the various forms of cocaine and routes of administration?**

A hydrochloride salt of cocaine is a powdery, white crystalline, water-soluble substance that can be sniffed or injected. A lipid-soluble form, called crack or free-base cocaine, is inexpensively manufactured by mixing the hydrochloride salt with an alkali. Crack is more stable on heating, vaporizes readily, and has high bioavailability when smoked.

**19. How is cocaine metabolized and excreted?**

Peak plasma concentrations occur 15 to 60 minutes after intranasal ingestion; its biologic half-life is about 45 to 90 minutes. Plasma (pseudocholinesterase) and liver esterases hydrolyze cocaine to ecgonine methyl ester (EME) and benzoylecgonine. EME and benzoylecgonine constitute 80% of the metabolites of cocaine and are detected in urine for 14 to 60 hours after cocaine use. Only 1% to 5% is cleared unmetabolized in the urine.

**20. What are the mechanism of action and physiologic effects of cocaine?**

There is inhibition of the norepinephrine, dopamine, and serotonin transporter mechanisms. However, the physiologic effects are caused principally by increases in norepinephrine levels. At adrenergic nerve endings cocaine inhibits the reuptake of norepinephrine into the neuron. Increases in serum norepinephrine levels increase systolic, diastolic, and mean arterial pressure; heart rate; and body temperature.

**21. List the common signs and symptoms of acute cocaine intoxication.**

Nausea and vomiting	Headache
Rapid or irregular heartbeat	High or low blood pressure
Hallucinations	Chest pain
Convulsions and stroke	Mydriasis

**22. What is the most life-threatening toxic side effect and its treatment?**

Cardiac ischemia and subsequent acute myocardial infarction are present in approximately 6% of all hospital admissions for chest pain secondary to cocaine ingestion. Although acute vasoconstriction with or without thrombus formation has been considered the principal cause, it is now believed to be the result of sympathetic stimulation associated with increased norepinephrine levels. Treatment of cocaine-induced chest pain includes the use of selective  $\beta_1$ -adrenergic blockade, nitrates, calcium channel blockers, and  $\alpha$ -adrenergic blockers. Selective  $\beta_2$ -blockade should generally be avoided since it may lead to unopposed  $\alpha_1$ -mediated coronary and peripheral vasoconstriction.

**23. List the signs and symptoms of cocaine withdrawal.**

Agitation	Anxiety and depression
Fatigue	Irritability and disturbed sleep
Tremors	Myalgias

**24. What are the anesthetic concerns in the acutely intoxicated cocaine user?**

Preoperative sedation and a deep level of general anesthesia inhibit adrenal release of catecholamines, potentially reducing the dysrhythmic effects of cocaine. The patient should be well anesthetized before airway instrumentation to avoid severe tachycardia and hypertension. Cocaine sensitizes the cardiovascular system to the effects of endogenous catecholamines. Ketamine and pancuronium potentiate the cardiovascular toxicity of cocaine and should be avoided. The MAC of inhalational anesthetic agents is increased in the setting of acute intoxication. Should hypotension require pressor therapy, direct-acting agents such as phenylephrine may be better since these patients may be catecholamine depleted.

**25. Can the nonacutely intoxicated patient who has used cocaine be safely anesthetized?**

A recent study in a large urban public hospital determined that general anesthesia can be safely administered. However, cocaine is known to prolong the QT interval, predisposing the patient to ventricular arrhythmias, including torsades de pointes. Thus an ECG must be obtained before surgery, and, if the QT interval is less than 500 msec, the patient may be anesthetized.

**KEY POINTS: CONCERNS IN PATIENTS TAKING COCAINE**

1. Myocardial ischemia is not uncommon in cocaine-abusing patients, and selective  $\beta_2$ -blockade should be avoided because it may cause vasoconstriction and worsen the ischemia.
2. Severe hypertension and tachycardia are risks during airway management unless the patient is deeply anesthetized.
3. Cocaine sensitizes the cardiovascular system to the effects of endogenous catecholamines. Ketamine and pancuronium potentiate the cardiovascular toxicity of cocaine and should be avoided.

**26. What is crystal methamphetamine and what are its properties?**

This refers to the synthetic stimulant methamphetamine. Most methamphetamine users are white and young adult. Most users are male, but it is the most common drug of abuse among women. Use of methamphetamine is common among homosexual males, and there is a strong relationship between its use and having the human immunodeficiency virus.

Methamphetamine use produces a rapid pleasurable rush followed by euphoria, heightened attention, and increased energy. These effects are caused by release of norepinephrine, dopamine, and serotonin. It is quite similar to cocaine in its manifestations, and its relatively lower costs may account for its increasing abuse.

Recommendations for anesthetizing a methamphetamine-abusing patient are similar to those for cocaine. Avoid anesthetizing the acutely intoxicated patient for elective procedures. Anesthesia is probably safely started in patients who are chronic users but not acutely intoxicated. There may be an increased incidence of dental trauma because of the common finding of dental decay.

**27. What are the signs of symptoms of methamphetamine intoxication and withdrawal?**

Signs and symptoms of intoxication include anorexia, diaphoresis, hypertension, tachycardia, hyperthermia, agitation, and psychosis. Patients can also have myocardial infarctions, seizures, strokes, rhabdomyolysis, and renal failure. The withdrawing patient will experience fatigue, irritability, insomnia, anxiety, and psychotic reactions. An unusual sign seen in chronic methamphetamine users is dental decay, known as *meth mouth*.

**28. What is ecstasy and what are its mechanism of action and route of administration?**

Ecstasy, or 3,4-methylenedioxymethamphetamine, is a synthetic, psychoactive drug similar to the stimulant methamphetamine and the hallucinogen mescaline. It increases the activity of multiple neurotransmitters, including serotonin, dopamine, and norepinephrine. It is taken orally in capsule or tablet form. Its effects last 3 to 6 hours. Additional doses slow its enzymatic degradation, resulting in increased duration of action and increased risk of toxicity.

**29. What are the cognitive, physical, and psychologic effects of ecstasy?**

Abusers experience a sense of well-being and decreased anxiety. Memory impairment may occur. Physical effects include nausea, chills, involuntary teeth clenching, muscle cramping, and blurred vision. Hypertension, loss of consciousness, and seizures are also frequent. Rarely hyperthermia develops, which may precipitate cardiovascular collapse and multiorgan failure. Withdrawal may involve drug craving, depression, confusion, and severe anxiety. In nonhuman primates as little as a 4-day exposure has been associated with damage to neurons involved in mood, thinking, and judgment.

**30. What is phencyclidine and what is its mechanism of action?**

Phencyclidine (PCP) is a cyclohexylamine that was developed in the 1950s as an anesthetic but was subsequently taken off the market because of its tendency to produce hallucinations. The precise mechanism of action of PCP is unknown, but it is thought to depress cortical and thalamic function while stimulating the limbic system. PCP may block afferent impulses associated with the affective component of pain perception and suppress spinal cord activity. PCP can also inhibit pseudocholinesterase. Of note, the intravenous anesthetic ketamine is produced by chemical modification of PCP.

**31. Discuss the physical and psychologic effects of phencyclidine.**

PCP produces a dissociative state or *out-of-body* experience. It crosses the blood-brain barrier to produce amnesia, delirium, disordered thought processes, paranoia, hostility, and delusions. Dissociation may resemble schizophrenia. Nystagmus, ataxia, and difficulty speaking may

occur. Autonomic stimulation and cerebral vasodilation are also effects. No significant ventilatory depression is observed, and airway reflexes are maintained. Copious oral secretions may be noted. General anesthesia is preferable in these patients because of their frequent dissociative state and unpredictable violent behavior.

### 32. How do you increase clearance of phencyclidine?

Clearance is increased by acidification of the urine and nasogastric suction.

## KEY POINTS: CONCERNS IN PATIENTS TAKING ECSTASY AND PHENCYCLIDINE



1. Hyperthermia and cardiovascular collapse with ecstasy
2. Dissociative state, severe behavior disturbances, and enhanced sympathomimetic effects with phencyclidine

## WEBSITES



American Pain Society

<http://www.ampainsoc.org>

World Health Organization: Management of Substance Abuse

[http://www.who/int/substance\\_abuse](http://www.who/int/substance_abuse)

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# DIABETES MELLITUS

*Robert H. Slover, MD, and Robin Slover, MD*

## 1. Describe the principal types of diabetes mellitus.

- Type 1 diabetes mellitus: An autoimmune disorder in which destruction of the pancreatic islet cells results in the inability to produce insulin. Onset is more common in children and young adults.
- Type 2 diabetes mellitus: A disorder in the body's ability to use insulin. Early in the course of the disease the patient may be able to make sufficient insulin, but cell-receptor impairment results in hyperglycemia despite normal or high insulin levels. Type 2 diabetes is usually a disease of older adults; onset in the sixth decade and beyond is common. As obesity increases in the population type 2 diabetes also increases. Type 2 diabetes is now commonly seen in adolescents and young adults with obesity and a sedentary lifestyle.
- Gestational diabetes: Seen in 2% to 5% of pregnant women, and 40% to 60% of these women will develop type 2 diabetes mellitus later in life.

## 2. What is considered ideal (target) glucose control?

The American Diabetes Association (ADA) 2008 Clinical Practice Recommendations recommend an A<sub>1</sub>C goal for nonpregnant adults in general of <7% (6% or lower is the nondiabetic A<sub>1</sub>C range). Less stringent goals apply to children, patients with a history of severe hypoglycemia, and individuals with comorbid conditions.

## 3. What comorbidities are frequently observed in patients with diabetes mellitus and to what significance?

- Hypertension is seen in 40% of patients with poorly controlled diabetes who undergo surgery. Hypertension is a risk factor for coronary artery disease and cardiac failure. If these patients are treated with potassium-wasting diuretic agents, there is often significant total body loss of potassium.
- Coronary artery disease is common, occurs in younger patients, and may be silent or present atypically.
- Autonomic neuropathy may compromise neuroreflexic control of cardiovascular and gastrointestinal function, manifesting as orthostatic hypotension, gastroparesis (increased risk of aspiration), ileus, and urinary retention. Peripheral neuropathies are common.
- Disturbances in renal function are common, including increased blood urea nitrogen (BUN) and creatinine, protein loss, hypoalbuminemia, acidosis, and electrolyte disturbances.
- Occult infections are present in 17% of patients with diabetes.
- Retinal hemorrhages are seen in up to 80% of patients with diabetes over 15 years' duration and may lead to retinal detachment and vision loss.

## 4. What oral medications are currently used in type 2 diabetes?

There are two categories of drugs used in treating type 2 diabetes: those that enhance the effectiveness of insulin and those that increase the supply of insulin to the cells. These drugs are outlined in [Table 49-1](#).



### 5. What insulins are in current use?

Modern intensive insulin therapy relies on newly designed insulin analogs. Insulin therapy is given using a *basal-bolus* construct: long-acting (24-hour) insulin is used to provide a steady basal platform, and rapid-acting insulin is used to provide boluses for carbohydrate intake in meals and snacks. This necessitates giving at least four injections per day or the use of an insulin pump. The specific insulins are outlined in Table 49-1.

TABLE 49-1. ORAL DRUGS USED IN TYPE 2 DIABETES

Action	Generic Name	Brand Name	Dose	Dosing Interval	Side Effects
<b>Enhance Insulin Effect</b>					
Biguanide	Metformin	Glucophage	1000 mg	bid or tid	Transient gastrointestinal symptoms; Lactic acidosis*
Thiazolidinedione “glitazones”	Rosiglitazone Pioglitazone	Avandia Actos	Up to 600 mg daily Used in combination	Daily or bid	Weight gain, anemia, edema, congestive heart failure,* hepatocellular disease*
$\alpha$ -Glucosidase inhibitors	Acarbose Miglitol	Precose Glyset	50 mg tid (acarbose) 25 mg tid (miglitol)	bid to qid	Flatulence, intestinal disease*
<b>Increase Insulin Supply</b>					
Sulfonylureas	Tobutamide	Orinase	2.5–5 mg (Glyburide)	Daily to tid	Hypoglycemia, weight gain, allergy*
	Chlorpropamide	Diabinese			
	Tolazamide	Tolinase			
	Glipizide	Glucotrol			
	Glyburide	DiaBeta, Micronase, Glynase			
	Glimepiride	Amaryl	2 mg tid	bid to qid	Hypoglycemia
Nonsulfonylureas	Repaglinide	Prandin			

\*Indicates rare but serious side effects.

**6. Is there an advantage to the use of insulins that are in solution as opposed to insulin that is in a suspension?**

Insulins in solution provide exact dosing. For example, 10 units of Humalog will always be exactly 10 units. NPH, the only remaining insulin that is in suspension, does not provide exact or reproducible dosing, but varies by as much as 30% either way. Ten units of NPH could really be 7 to 13 units!

**7. Describe the role of insulin on glucose metabolism and the impact of stress.**

Insulin enhances glucose uptake, glycogen storage, protein synthesis, amino-acid transport, and fat formation. Basal insulin secretion is essential even in the fasting state to maintain glucose homeostasis.

Surgical procedures lead to increased stress and high counterregulatory hormone activity with a decrease in insulin secretion. Counterregulatory hormones, including epinephrine, cortisol, glucagon, and growth hormone, promote glycogenolysis, gluconeogenesis, proteolysis, and lipolysis. Therefore, in diabetic patients without adequate insulin replacement, the combination of insulin deficiency and excessive counterregulatory hormones can result in severe hyperglycemia and diabetic ketoacidosis, which are associated with hyperosmolarity, increases in protein catabolism, fluid loss, and lipolysis.

**8. Is there evidence that tight glucose control is beneficial in critically ill patients?**

It has recently been believed that intensive insulin therapy to maintain glucose at or below 110 mg/dl reduces morbidity and mortality in critically ill patients in a surgical intensive care unit (ICU). However, it has subsequently been determined that extremely tight glucose control in surgical and medical ICUs significantly increases the risk of hypoglycemia and is not associated with significantly reduced hospital mortality. However, tight control does seem to significantly reduce septicemia and improve wound healing.

**9. What are the complications of hyperglycemia in the perioperative setting?**

- Impaired polymorphonuclear cellular phagocytic function, increased risk of infection, and increased length of hospitalization
- Osmotic diuresis, dehydration, and hyperosmolarity
- Ketogenesis and diabetic ketoacidosis
- Proteolysis and decreased amino acid transport, resulting in retarded wound healing
- Hyperviscosity, thrombogenesis, and cerebral edema

**10. What considerations are important during the preoperative evaluation?**

Important considerations include type of diabetes, duration of disease, oral hypoglycemic or insulin therapy, and diabetic complications, including hypertension, renal disease, coronary artery disease (which may be silent or present atypically), and neuropathies (early satiety and reflux suggest gastroparesis). If patients have end-stage renal disease or require dialysis, fluid restrictions may be necessary.

**11. What is the significance of autonomic neuropathy? How can it be assessed?**

Autonomic neuropathy may affect cardiovascular (silent ischemia), gastrointestinal (gastroparesis with increased risk of aspiration), thermoregulatory (decreased ability to alter

blood vessel flow to conserve temperature), and neuroendocrine systems (decreased catecholamine production in response to stimulation). Autonomic neuropathy can be assessed by these tests:

- An intact sympathetic nervous system can be assessed by the following: A normal response in diastolic pressure (from lying to standing) is a change of at least 16 mm Hg; an affected patient has a response of <10 mm Hg. Autonomic neuropathy is also evidenced by a large change in systolic blood pressure when changing from lying to standing posture. A normal decrease is <10 mm Hg; an affected patient has a decrease of at least 30 mm Hg.
- An intact parasympathetic nervous system can be assessed by observing heart rate response to breathing. Normal patients increase heart rate by at least 15 beats/min. Affected patients have an increase of 10 or fewer beats/min. Finally, concurrent with electrocardiogram (ECG) monitoring, the R-R ratio can be measured during a Valsalva maneuver. A normal ratio is >1.2; an abnormal response is <1.1.

Patients with autonomic neuropathy should be considered for preoperative aspiration prophylaxis, which may include an H<sub>2</sub>-blocking agent, a gastric stimulant to decrease gastroparesis, and/or a nonparticulate antacid.

## 12. What preoperative laboratory tests are appropriate for the patient with diabetes?

Evaluate electrolytes, phosphate, and magnesium, BUN and creatinine, blood glucose and ketones, urinalysis, and ECG. Proteinuria is an early manifestation of diabetic nephropathy. A cardiac stress test should be considered in sedentary patients with cardiac risk factors. Measuring hemoglobin A<sub>1c</sub> will provide valuable information about the level of glucose control. Patients with hemoglobin A<sub>1c</sub> >9% are usually noncompliant and have an increased risk of dehydration.

## 13. Are there any signs that oral intubation may be difficult?

Although the remainder of the airway examination may be normal, patients with diabetes may have decreased mobility in the atlanto-occipital joint, which can complicate oral intubation. This can be evaluated radiographically. Patients may also have stiff joint syndrome with anterior fixation of the larynx. Stiff joint syndrome is suggested by the inability to approximate the palmar aspect of the pharyngeal joints of the fingers (also known as the prayer sign, the patient cannot touch the palmar aspects of the fingers together when the palms are together). The palmar print is another way of assessing stiff joints.

## 14. How should the patient with diabetes be prepared before surgery? Should all patients with diabetes receive insulin intraoperatively?

Patients with type 1 diabetes having short or minimally invasive procedures should receive a reduced dose of insulin and have their serum glucose followed. Patients with type 2 diabetes on oral medications should not take these medications the day of surgery. It is ideal to schedule the surgery early in the day.

Patients having longer or more stressful surgeries have increased levels of counterregulatory hormones and are likely to benefit from tighter glucose control. Furthermore, insulin requirements are increased by infection, hepatic disease, obesity, steroids, and cardiovascular procedures and pain. An insulin infusion may be considered to establish tighter glucose control. Before surgery, hyperglycemia, fluid and electrolyte imbalances, and ketosis should be corrected. Ideally in patients with renal failure surgery should occur the day after hemodialysis.

Blood glucose levels under 200 mg/dl in the days preceding surgery are ideal and ensure adequate glycogen stores and insulin sufficiency. On the day before surgery glucose should be monitored at bedside before each meal, at bedtime, and in the early morning. The goal is to have most glucose between 120 and 180 mg/dl.

**15. How do you make an insulin and glucose infusion?**

Ideally the glucose and insulin infusion should be started at least 1 hour before surgery. Glucose and insulin can be mixed together. They can also be given as separate infusions, but the combination infusion is safer because it is hard to have an accidental bolus of one or the other. Add 8 units regular insulin to 500 ml D<sub>5</sub>W. Connect the tubing, shake well, and discard the first 100 ml through the tubing since insulin binds to polyvinyl chloride (PVC) bags and tubing. If a non-PVC bag is used, only 5 units of regular insulin is added to 500 ml of glucose. Again discard the first 100 ml of fluid. The mixture is infused at a rate of 100 ml/hr, and a blood glucose measurement should be obtained 20 minutes after starting the infusion and then hourly. The infusion will usually maintain the blood glucose level, although it may lower the level by 20 to 40 mg/dl.

For longer cases or in more fragile patients, 16 units of regular insulin is added to 1000 ml of D<sub>5</sub>W. Consider adding 20 mEq/L of potassium, unless the patient's potassium is >5.5 mEq/L. If the patient's potassium is <4 mEq/L, 40 mEq/L should be added to the infusion. After mixing and discarding the first 100 ml through the tubing, the infusion is run at 100 ml/hr. Again blood glucose measurements are checked 20 minutes after starting the infusion and then hourly. The infusion may be increased or decreased by 4-unit increments.

**16. How fast can the blood glucose be lowered in a markedly hyperglycemic patient?**

Blood glucose levels should not be lowered more than 100 mg/dl/hr if possible. Since the blood-brain barrier is slower to respond, a rapid drop in blood glucose could lead to cerebral swelling and in rare cases to symptomatic cerebral edema.

**17. Describe the postoperative management of the patient with diabetes.**

In significant procedures with prolonged recovery, it is easier to manage the patient by continuing the insulin and glucose infusion for up to 48 hours, matching increased or decreased insulin needs with changes in rate or concentration of the infusion. Continue bedside monitoring of glucose, electrolytes, and fluids. A blood glucose goal of 120 to 180 mg/dl is reasonable. If total parenteral nutrition is used, the insulin rate may need to increase and should be adjusted based on glucose monitoring.

With the resumption of oral feeding, insulin is given subcutaneously according to the patient's preoperative schedule. If pain or stress is still significant, it will be necessary to increase the dosage by as much as 20%. Monitor glucose at bedside before meals, at bedtime, and early in the morning, adjusting doses as necessary.

**18. How do you manage patients using subcutaneous insulin pumps?**

Insulin pumps are now commonly used and can ensure good glucose control. The pumps use one of the newer analog insulins (Humalog, Novolog, and Apidra) and deliver both basal and bolus insulin doses. Since the basal rate is set to deliver necessary insulin for the fasting state, the pump can be used for insulin delivery during the perioperative and

intraoperative periods, continuing the established basal rates. Check blood sugars at regular intervals, every 1 to 2 hours, to ensure that the patient's blood sugar stays between 80 and 180 mg/dl. If the stress of a long surgery raises glucose levels, the basal infusion rate can be safely raised in increments of 0.1 unit per hour. If glucose levels fall, the rate can be safely reduced in increments of 0.1 unit per hour, or the pump can be suspended until glucose levels rise. When the patient is fully recovered, return to normal routines for pump use. The patients may consume a regular diet, as appropriate, when fully alert, awake, and with good bowel sounds.

### 19. What insulins are preferred for pump use?

The rapid-acting analogs (Novolog, Humalog, Apidra) are used in the insulin pumps. Interestingly, when insulin is given intravenously, there is no advantage to the analogs compared to regular human insulin. For that reason the less expensive regular insulin is usually used for intravenous therapy.

### 20. Describe the management of patients with diabetes requiring urgent surgery.

If at all possible, electrolyte and glucose imbalance should be corrected before surgery. Sufficient rehydration, electrolyte replacement, and insulin treatment can be achieved in 4 to 6 hours, improving hyperglycemia, ketosis, and acidosis. Rehydration is initiated with 10 to 20 ml/kg of normal saline (NS). Infuse insulin at 0.1 unit/kg/hr using 0.45 NS (or D<sub>10</sub> in 0.45 NS if glucose is <150 mg/dl). Patients in ketoacidosis requiring emergency surgery may receive insulin therapy according to the guidelines in [Table 49-2](#).

TABLE 49-2. INSULIN THERAPY GUIDELINES

	Onset of Action	Peak	Duration of Action
<b>Long-Acting (basal)</b>			
Lantus (Glargine)	2–3 hr	None	24 hr
Levemir (Detemir)	2–3 hr	None	24 hr
<b>Intermediate-Acting</b>			
Regular	30–60 min	2–4 hr	6–9 hr
NPH (suspension)	4 hr	4–8 hr	8–13 hr
<b>Rapid-Acting</b>			
Humalog (lispro)	10–30 min	30–90 min	3–4 hr
Novolog (Aspart)	10–30 min	30–90 min	3–4 hr
Apidra (glulisine)	10–30 min	30–90 min	3–4 hr

### 21. Are regional anesthetics helpful in patients with insulin-dependent diabetes? Can epinephrine be added to local anesthetic solutions?

Regional anesthetic techniques decrease the stress response and may help maintain a more stable blood glucose and decrease stress on the cardiovascular system. Epinephrine should not be used in peripheral nerve blocks (e.g., ankle blocks) because of the risk of decreasing blood flow to an area possibly already affected by impaired microcirculation. In blocks with high systemic absorption such as brachial plexus or intercostal blocks, low-dose epinephrine may be used.

## 22. Is it possible to achieve continuous monitoring of glucose levels in the operating room and in the perioperative period?

The technology is commercially available to have continuous glucose monitoring before, during, and after a procedure. Currently there are three continuous glucose monitoring (CGM) systems that have Food and Drug Administration approval. Each of these samples interstitial fluid every 30 seconds to report an interstitial fluid glucose level every 5 minutes. Adjustment to insulin infusions can be made in response to changing glucose levels. Within a few years we expect to see continuous glucose tracings just as we now see continuous oxygen tracings.

### KEY POINTS: DIABETES MELLITUS



1. Careful attention to glucose control before, during, and after surgery is important to reduce risk of infection, promote more rapid healing, avoid metabolic complications, and shorten hospital stay.
2. The goal for insulin management during surgery is to maintain glucose between 120 and 200 mg/dl.
3. Intraoperative glucose control in all but the shortest cases is best achieved by using a glucose-insulin intravenous infusion or a pump.
4. Patients with diabetes have a high incidence of coronary artery disease with an atypical or silent presentation. Maintaining perfusion pressure, controlling heart rate, continuous ECG observation, and a high index of suspicion during periods of refractory hypotension are key considerations.
5. The inability to touch the palmar aspects of index fingers when palms touch (the prayer sign) can indicate a difficult oral intubation in patients with diabetes.

### WEBSITES



American Diabetes Association

<http://www.diabetes.org>

The Children's Diabetes Foundation at Denver

<http://www.childrensdiabetesfdn.org>

Juvenile Diabetes Research Foundation

<http://www.jdrf.org>

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# NONDIABETIC ENDOCRINE DISEASE

Joel E. Wilson, MD

## 1. Describe four steps involved in thyroid hormone synthesis.

- Uptake of iodide:** Iodide from the bloodstream is concentrated in thyroid cells by an active transport mechanism.
- Iodination of thyroglobulin:** Thyroglobulin, a large glycoprotein rich in tyrosine, is enzymatically iodinated and stored in the thyroid follicles.
- Coupling reactions:** The monoiodotyrosine and di-iodotyrosine moieties within the thyroglobulin molecule are coupled to one another to form tri-iodothyronine ( $T_3$ ) and thyroxine ( $T_4$ ).
- Release of hormones:**  $T_3$  and  $T_4$  are enzymatically cleaved from thyroglobulin within the follicular cell and released into the bloodstream.

## 2. How much tri-iodothyronine and thyroxine are produced? What regulates their production?

Approximately 8 mcg of  $T_3$  and 90 mcg of  $T_4$  are produced daily. Additional  $T_3$  is formed from the peripheral conversion of  $T_4$  to  $T_3$ .  $T_3$  is approximately four times more potent than  $T_4$  but has a much shorter half-life; therefore the contribution of each to total thyroid activity is approximately equal. Thyroid-stimulating hormone (TSH) (produced by the anterior pituitary gland) acts on thyroid tissue to increase the rates of all steps involved in thyroid hormone synthesis and release. Thyrotropin-releasing hormone (TRH) (produced by the hypothalamus) in turn regulates the amount of TSH produced by the pituitary.  $T_3$  and  $T_4$  inhibit release of TSH and to a much smaller degree the release of TRH, thus establishing a negative feedback control mechanism.

## 3. List the common thyroid function tests and their use in assessment of thyroid disorders.

Thyroid function tests include total  $T_4$  level, total  $T_3$  level, TSH level, and resin  $T_3$  uptake ( $T_3RU$ ). The  $T_3RU$  is useful in conditions that alter levels of thyroid-binding globulin, which would alter total  $T_4$  results (Table 50-1).

TABLE 50-1. USEFULNESS OF THYROID FUNCTION TESTS IN THE DIAGNOSIS OF HYPOTHYROID OR HYPERTHYROID STATES

Disease	$T_4$	$T_3$	TSH	$T_3RU$
Primary hypothyroidism	–	–	+	–
Secondary hypothyroidism	–	–	–	–
Hyperthyroidism	+	+	0	+
Pregnancy	+	0	0	+

$T_4$ , thyroxine;  $T_3$ , tri-iodothyronine; TSH, thyroid-stimulating hormone;  $T_3RU$ , resin  $T_3$  uptake; +, increased; –, decreased; 0, no change.



#### 4. List common signs, symptoms, and causes of hypothyroidism.

Symptoms	Signs
Fatigue	Bradycardia
Cold intolerance	Hypothermia
Constipation	Deep tendon reflex relaxation phase prolongation
Dry skin	Hoarseness
Hair loss	Periorbital edema
Weight gain	

The most common cause of hypothyroidism is surgical or radioiodine ablation of thyroid tissue in the treatment of hyperthyroidism, most commonly Graves' disease. Other causes of hypothyroidism include chronic thyroiditis (Hashimoto's thyroiditis), drug effects, iodine deficiency, and pituitary or hypothalamic dysfunction.

The signs and symptoms observed in patients with mild hypothyroidism are nonspecific, and clinical detection is extremely difficult. Patients with severe long-term untreated hypothyroidism may progress to myxedema coma, which is frequently fatal. Factors that may lead to myxedema coma in hypothyroid patients include cold exposure, infection, trauma, and administration of central nervous system depressants. Myxedema coma is characterized by hypoventilation, hypothermia, hypotension, hyponatremia, hypoglycemia, obtundation, and adrenal insufficiency.

#### 5. Of the numerous manifestations of hypothyroidism, which are most important in relation to anesthesia?

Hypothyroidism causes depression of myocardial function caused by protein and mucopolysaccharide deposition within the myocardium and depression of intracellular myocardial metabolism. Cardiac output declines as a result of decreased heart rate and stroke volume. Decreased blood volume, baroreceptor reflex dysfunction, and pericardial effusion may also accompany hypothyroidism. All of these effects make the hypothyroid patient sensitive to the hypotensive effects of anesthetics.

Hypoventilation may be a feature of hypothyroidism. The ventilatory responses to both hypoxia and hypercarbia are significantly impaired, making the hypothyroid patient sensitive to drugs that cause respiratory depression. Hypothyroidism also decreases the hepatic and renal clearance of drugs. In addition, patients are prone to hypothermia because of lowered metabolic rate and consequent lowered heat production.

#### 6. How does hypothyroidism affect minimum alveolar concentration of anesthetic agents?

Animal studies show that minimum alveolar concentration (MAC) is not affected by hypothyroidism. Clinically it has been noted that hypothyroid patients have increased sensitivity to anesthetic agents. This is caused not by a decrease in MAC per se but by the patient's metabolically depressed condition.

#### 7. How is hypothyroidism treated?

Treatment consists of supplementation with exogenous thyroid hormones, most frequently levothyroxine ( $T_4$ ), because its long half-life, 6 to 7 days, results in a more constant serum level. Levothyroxine is available for intravenous use with the intravenous dose being one half the oral dose. The principal risk with treatment is in patients with coronary artery disease (CAD). An increase in the basal metabolic rate may result in myocardial ischemia. A suggested thyroid supplementation protocol for hypothyroid patients is summarized below:

- Patients without CAD:  $T_4$  50 mcg/day increasing monthly by 50-mcg/day increments until a euthyroid state is reached.
- Patients with CAD:  $T_4$  25 mcg/day increasing monthly by 25-mcg/day increments until a euthyroid state is achieved.

- In urgent situations thyroid supplementation may be given with caution intravenously. The recommended dose is  $T_4$  300 mcg/m<sup>2</sup> by slow infusion. Hypothyroid patients receiving intravenous supplementation must be monitored closely for signs and symptoms of cardiac ischemia and adrenal insufficiency.
- When treating severe hyperthyroidism, glucocorticoids should also be administered.

### 8. Under what circumstances should elective surgery be delayed for a hypothyroid patient?

Patients with mild to moderate hypothyroidism are not at increased risk when undergoing elective surgical procedures. Some authorities suggest that elective surgery in patients who are symptomatic should be delayed until the patient is rendered euthyroid. Other authorities recommend against delaying surgery if thyroid replacement can begin before surgery (in patients without CAD). In patients with severe hypothyroidism, elective surgery should be delayed until they have been rendered euthyroid. This may require 2 to 4 months of replacement therapy for complete reversal of cardiopulmonary effects. Normalization of the patient's TSH level reflects reversal of hypothyroid-induced changes.

### 9. List common signs, symptoms, and causes of hyperthyroidism.

Signs	Symptoms	Causes
Goiter	Anxiety	Graves' disease
Tachycardia	Tremor	Toxic multinodular goiter
Proptosis	Heat intolerance	
Atrial fibrillation	Fatigue	
Weight loss		
Muscle weakness		

### 10. How is hyperthyroidism treated?

There are three approaches to treatment:

1. **Antithyroid drugs** such as propylthiouracil (PTU) inhibit iodination and coupling reactions in the thyroid gland, thus reducing production of  $T_3$  and  $T_4$ . PTU also inhibits peripheral conversion of  $T_4$  to  $T_3$ . Iodine in large doses not only blocks hormone production, but it also decreases the vascularity and size of the thyroid gland, making iodine useful in preparing hyperthyroid patients for thyroid surgery.
2. **Radioactive iodine**,  $^{131}\text{I}$ , is actively concentrated by the thyroid gland, resulting in destruction of thyroid cells and a decrease in the production of hormone.
3. **Surgical subtotal thyroidectomy**  
All of these approaches may render the patient hypothyroid.

### 11. Which effects of hyperthyroidism are the most important with regard to anesthesia?

In hyperthyroidism the metabolic rate of the body is increased, causing significant changes in the cardiovascular system, the magnitude of which is proportional to the severity of the thyroid dysfunction. Because of the elevated oxygen consumption, the cardiovascular system is hyperdynamic. Tachycardia and elevated cardiac output are present, and tachyarrhythmias, atrial fibrillation, left ventricular hypertrophy, and congestive heart failure may develop. Hyperthyroid patients with proptosis are more susceptible to ocular damage during surgery because of difficulty with taping their eyelids closed.

### 12. How is minimum alveolar concentration affected by hyperthyroidism?

As in hypothyroidism, MAC is not affected by hyperthyroidism, although clinically hyperthyroid patients appear to be resistant to the effects of anesthetic agents. Inhalation

induction is slowed by the increased cardiac output. The rate of drug metabolism is increased, giving the appearance of resistance. Hyperthyroidism-induced hyperthermia may indirectly elevate MAC.

### 13. Define thyrotoxicosis.

Also known as *thyroid storm*, this is an acute exacerbation of hyperthyroidism usually caused by a stress such as surgery or infection. It is characterized by extreme tachycardia, hyperthermia, and possibly severe hypotension. Perioperatively it usually occurs 6 to 18 hours after surgery but can occur intraoperatively and be confused with malignant hyperthermia.

### 14. How is thyrotoxicosis treated?

Intraoperative treatment must be immediate, consisting of careful  $\beta$ -adrenergic blockade, infusion of intravenous fluids, and temperature control if hyperthermia is present. Corticosteroids should be considered for refractory hypotension because hyperthyroid patients may have a relative cortisol deficiency. Antithyroid drugs should be added after surgery.

### 15. What complications may occur after a surgical procedure involving the thyroid gland?

Because of the close proximity of the thyroid gland to the trachea and larynx, many of the complications that occur (such as cervical hematoma) can cause airway obstruction. For example, chronic pressure on the trachea from a goiter can lead to tracheomalacia, rendering the patient prone to tracheal collapse and airway obstruction following extubation.

Inadvertent resection of the parathyroid glands in turn can lead to hypocalcemia, which may produce laryngospasm. Innervation to the vocal cord musculature may be compromised by surgical damage to the recurrent laryngeal nerves (RLNs). Bilateral *partial* RLN injury can result in the vocal cords being passively drawn together during inspiration, leading to severe obstruction that necessitates emergent tracheostomy. Destruction of the bilateral RLNs results in the vocal cords being in a midposition and usually does not result in total airway obstruction.

Unilateral injury results in dysfunction of the ipsilateral vocal cord. Damage to the nerve fibers innervating the vocal cord adductors results in unopposed abduction of the ipsilateral vocal cord, increasing the risk of aspiration. Damage to the innervation of the abductor muscles results in an abnormally adducted vocal cord, which can cause hoarseness. Vocal cord function may be assessed following surgery with direct or fiber-optic laryngoscopy.

### 16. Describe the functions and regulation of the adrenal gland.

The adrenal gland can be functionally divided into the adrenal cortex and the adrenal medulla. The adrenal cortex principally produces the steroid hormones cortisol (the main glucocorticoid) and aldosterone (the main mineralocorticoid). Production of cortisol is regulated by adrenocorticotropic hormone (ACTH) produced by the anterior pituitary. The release of ACTH is promoted by corticotropin-releasing hormone (CRH) derived from the hypothalamus, completing the hypothalamic-pituitary-adrenal (HPA) axis. Cortisol inhibits release of both CRH and ACTH, establishing negative feedback control. Ectopic ACTH can be produced by various neoplasms such as small-cell lung carcinomas. Aldosterone secretion is regulated by the renin-angiotensin system. The adrenal medulla secretes epinephrine and norepinephrine. Their release is governed by the sympathetic nervous system.

### 17. What is a pheochromocytoma?

A pheochromocytoma is a neoplasm arising from the adrenal medulla or paravertebral chromaffin tissue and is discussed in greater detail in Chapter 1.

**18. How much cortisol is produced by the adrenal cortex?**

Normally approximately 20 to 30 mg of cortisol per day is produced. This amount increases dramatically as a response to a stress such as infection or surgery. Under stressful conditions 75 to 150 mg/day may be produced, with the increase in production being generally proportional to the severity of the stress.

**19. What is the most common cause of hypothalamic-pituitary-adrenal axis disruption?**

Exogenous steroids (glucocorticoids) result in HPA axis suppression. Short-term steroid administration—no longer than 7 to 10 days—results in suppression of CRH and ACTH release, which usually returns to normal about 5 days after discontinuation of steroid therapy. Long-term administration of exogenous steroids results in adrenocortical atrophy secondary to a lack of ACTH. This results in prolonged adrenocortical insufficiency, which can last a year or more following steroid discontinuation. Therefore long-term steroid administration should not be terminated abruptly; rather it should be gradually tapered off over a period of 1 to 4 weeks. Other less common causes of HPA axis disruption include CNS mass lesions (tumor or abscess), head injury or subarachnoid hemorrhage, vascular injury, and adrenal causes (etomidate, ketoconazole, hemorrhage, infection [including human immunodeficiency virus], and bilateral adrenal metastases)

**20. What is an Addisonian crisis?**

Also referred to as acute adrenocortical insufficiency, an Addisonian crisis is caused by a relative lack of cortisol or other glucocorticoid in relation to a physiologic stress such as surgery. It is a shock state characterized by refractory hypotension, hypovolemia, and electrolyte disturbances. Causes of adrenocortical insufficiency include the following:

- HPA axis suppression by exogenous corticosteroid administration
- Autoimmune adrenalitis
- Adrenal hemorrhage
- Adrenal tuberculosis
- Septic shock

**21. How is an Addisonian crisis treated?**

Treatment must be immediate and consists of intravenous glucocorticoid, fluid replacement, physiologic monitoring, and correction of electrolyte abnormalities.

**22. How do exogenous steroids compare to cortisol?**

See [Table 50-2](#).

**TABLE 50-2. RELATIVE POTENCY OF CORTISOL AND EXOGENOUS STEROIDS**

<b>Steroid</b>	<b>Glucocorticoid</b>	<b>Mineralocorticoid</b>	<b>Half-Life (hours)</b>
Cortisol	1	1	8–12
Cortisone	0.8	0.8	8–12
Prednisone	4	0.25	12–36
Methylprednisolone	5	0.25	12–36
Triamcinolone	5	0.25	12–36
Dexamethasone	20–30	—	26–54
Fludrocortisone	5	200	12–36

**KEY POINTS: NONDIABETIC ENDOCRINE DISEASE**

1. Perioperatively mild to moderate hypothyroidism is of little concern even for elective surgery. Patients with severe, symptomatic hypothyroidism should be treated before surgery.
2. MAC of volatile anesthetics is unchanged in both hypothyroid and hyperthyroid states.
3. Thyroid storm may mimic malignant hyperthermia. It is detected by an increased serum  $T_4$  level and treated initially with  $\beta$ -blockade followed by antithyroid therapy.
4. Perioperative glucocorticoid supplementation should be considered for patients receiving exogenous steroids.
5. Chronic exogenous glucocorticoid therapy should not be discontinued abruptly. Doing so may precipitate acute adrenocortical insufficiency.

**23. Is perioperative stress steroid supplementation for patients on steroid therapy necessary?**

Few documented cases of acute perioperative adrenal insufficiency (i.e., Addisonian crisis) exist. Studies have shown that patients who have been on long-term steroid therapy undergoing even major surgery rarely become hypotensive because of glucocorticoid deficiency. If observed, hypotension is usually the result of hypovolemia or cardiac dysfunction. The possible side effects of perioperative steroid supplementation include the following:

- Hyperglycemia
- Gastric ulceration
- Fluid retention
- Impaired wound healing
- Aggravation of hypertension
- Immunosuppression

One approach to this issue might be that no supplementation is required unless hypotension refractory to standard treatment occurs. However, although considerable data exist regarding the problems associated with long-term steroid therapy, few data indicate any significant problems related to short-term perioperative steroid supplementation. Despite its rarity, acute adrenal insufficiency is associated with significant morbidity and mortality. Therefore, because perioperative steroid supplementation is associated with few risks in itself and because acute adrenal insufficiency can potentially lead to death, supplemental steroids should be given. Currently this seems to be the view of most authorities.

**24. If supplemental corticosteroids are to be administered perioperatively, how much should be given?**

The optimal dosing, frequency, and duration continue to be debated, but more recent guidelines suggest lower doses and shorter durations than those recommended in the past. The recommended dosage is also highly dependent on the amount of stress that the surgery is likely to cause. Patients receiving 5 mg/day or less of prednisone should receive their normal daily replacement but do not require supplementation. For minor surgery no supplementation or minimal supplementation such as hydrocortisone, 25 mg, may suffice. For moderate surgery give 50 to 75 mg of hydrocortisone on the day of procedure and taper the dose quickly over 1 to 2 days. For major surgery a variety of dosages have been suggested, with none being shown to be superior to the rest. A suggested regimen would be 100 to 150 mg of hydrocortisone on the day of procedure with a quick 1- to 2-day taper. The goal of these regimens is to give the lowest dose that provides sufficient supplementation while avoiding potential side effects.

**25. Review calcium homeostasis.**

Because of the importance of calcium in nearly all cellular functions, its intracellular and extracellular concentrations are tightly controlled through the action of parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D ( $1,25[\text{OH}]_2\text{D}$ ). Changes in the serum calcium concentration are detected by extracellular calcium-sensing receptors expressed on parathyroid cells. When calcium levels decrease, PTH is released (or conversely suppressed with increasing calcium levels). PTH stimulates bone resorption, which delivers calcium and phosphorus into the bloodstream and increases the resorption of calcium in the kidney. PTH also enhances the conversion of 25-hydroxyvitamin D ( $25[\text{OH}]\text{D}$ ) to the active  $1,25[\text{OH}]_2\text{D}$ , which increases the transepithelial transport of calcium and phosphorus in the gastrointestinal tract. It is estimated that one normal parathyroid gland is sufficient for maintaining PTH levels and calcium homeostasis. Magnesium depletion or excess may cause hypocalcemia by inducing functional hypoparathyroidism.

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# OBESITY AND SLEEP APNEA

Gillian E. Johnson, MBBChir, BSc

## 1. Define obesity.

Obesity is defined using the body mass index (BMI) (Table 51-1).

TABLE 51-1. DEFINITION OF OBESITY	
BMI	
18.5–25	Normal range
26–30	Overweight
31–35	Class I obesity
36–40	Class II obesity
41+	Morbid obesity

*BMI*, Body mass index.

$$\text{BMI} = \frac{\text{Weight (Kg)}}{\text{Height squared (m}^2\text{)}}$$

## 2. Discuss the cardiovascular considerations in the obese patient.

Systemic hypertension, pulmonary hypertension, left and right heart failure, and coronary artery disease are all more common in the obese patient. As body mass increases, so does oxygen consumption. Cardiac output, stroke volume, and circulating blood volume increase to meet increased demand. Systemic hypertension in time results in left ventricular hypertrophy. Coronary artery disease, combined with the increased likelihood of diabetes mellitus in the obese, increases the risk for silent myocardial infarction.

## 3. Review some pulmonary and respiratory considerations in the obese patient.

Respiratory concerns include the potential for a difficult airway, increased incidence of asthma, sleep disordered breathing or obstructive sleep apnea, restrictive lung disease, chronic hypoxia with or without polycythemia, and pulmonary hypertension.

Obesity is typically associated with hypoxemia, the mechanisms of which include:

- Increased work of breathing. Because of an increased chest wall mass, decreased chest wall compliance, and abdominal cavity adipose tissue decreasing diaphragmatic excursion, work of breathing is two to four times greater than normal.
- Restrictive lung disease develops, areas of the lung become underventilated, ventilation/perfusion mismatch occurs, and the lungs compensate by selective vasoconstriction of poorly ventilated regions. Ultimately pulmonary hypertension develops, which leads to right heart failure.
- The large tissue mass increases the total oxygen consumption and increases carbon dioxide production.

## 4. What are the gastrointestinal and hepatic changes seen in obese patients?

Obesity increases intra-abdominal and intragastric pressures. Hiatal hernias and gastric reflux are common. Despite an 8-hour fast, 85% to 90% of morbidly obese patients have gastric

volumes >25 ml, thus increasing their risk of pulmonary aspiration. These patients typically have fatty infiltration of the liver and may have hepatic inflammation, focal necrosis, or cirrhosis. At present no causal relationship between fatty infiltration and cirrhotic changes is known. Hepatic enzymes are generally altered, especially after jejunoileal bypass operations. Aminotransferases and  $\gamma$ -glutamyltranspeptidase are increased in this patient population.

##### 5. Discuss the pharmacokinetic changes found in the obese patient.

Obesity causes unpredictable changes in drug metabolism. Worsening obesity increases the duration of effect and degree of biotransformation of lipid-soluble (lipophilic) anesthetics. Lipophilic intravenous agents, including opioids, benzodiazepines, and barbiturates, have an increased volume of distribution and decreased elimination half-life, resulting in lower serum drug concentrations and decreased clearance. However, fentanyl shows similar pharmacokinetics in the obese and nonobese patient. In obese patients hydrophilic, water-soluble drugs generally have volumes of distribution, elimination half-lives, and rates of clearance similar to those in the nonobese patient.

Pseudocholinesterase activity is increased with obesity; thus larger doses of succinylcholine are required. Nondepolarizing muscle relaxants show variability in dosing, duration, and recovery; thus redosing should be guided by peripheral nerve stimulator. There is no evidence to suggest that any one inhalational anesthetic is superior to another when caring for the obese patient.

Loading doses of most intravenous agents are based on volume of distribution; maintenance dosing is based on clearance. In obese patients the volume of distribution is usually increased, but clearance approaches normal or is increased compared to a lean patient (Table 51-2).

TABLE 51-2. LOADING DOSE STRATEGY FOR INTRAVENOUS DRUGS

Drugs	Dosing Strategy
Fentanyl	Loading dose based on TBW; decrease maintenance
Sufentanil	Loading dose based on TBW; decrease maintenance
Remifentanyl	Dose based on IBW
Succinylcholine	Dose based on TBW
Atracurium	Dose using TBW
Vecuronium	Dose using IBW
Rocuronium	Dose using IBW
Propofol	Loading dose and maintenance based on TBW
Thiopental	Reduce loading dose
Midazolam	Loading dose based on TBW; adjust maintenance to IBW

*IBW*, Ideal body weight; *TBW*, total body weight.

##### 6. Discuss the appropriate preoperative assessment of this population.

See Chapters 8 and 17 for important historical information and airway concerns. As far as laboratory testing is concerned:

- An electrocardiogram should be obtained for all obese patients to evaluate for atrial or ventricular enlargement, arrhythmias, and ischemia. Ventricular arrhythmias are common. Further cardiac testing such as exercise stress tests or chemically induced stress testing may be required. Echocardiography can be used to assess cardiac function and presence of pulmonary hypertension.



- Chest radiographs may not be generally useful unless the history suggests additional information may be gleaned.
- Laboratory analysis should include a complete blood count, electrolytes, blood sugar, blood urea nitrogen, and creatinine. Elevated bicarbonate suggests carbon dioxide retention. Hypokalemia may occur with chronic use of diuretics. A room air arterial blood gas analysis will identify hypoxemia, hypercarbia, and metabolic compensation.
- If chronic lung disease is suspected, pulmonary function testing may also be necessary to characterize the extent of disease and amenability to preoperative optimization.

## 7. What are the advantages or disadvantages of offering regional anesthesia to the obese patient?

### Advantages

- Minimal airway intervention, avoiding difficult airway and obstructive sleep apnea (OSA) concerns
- Decreased cardiopulmonary depression
- Good postoperative analgesia with decreased need for narcotics
- Less postoperative nausea and vomiting, shorter postanesthesia care unit stay

### Disadvantages

- Technical difficulties arise in performing the blocks because of body habitus.
- Intraoperative failed block may require intubation under suboptimal conditions.
- The patient may not be able to tolerate positioning for the surgical procedure. For example, the patient may not be able to tolerate prolonged periods in the supine position.

## 8. Review the challenges in monitoring these patients.

ASA standard monitoring devices should be used in all cases. Blood pressure cuffs should span a minimum of 75% of the patient's upper arm circumference. The ankle or wrist may be used as alternate sites for taking blood pressure. Invasive arterial monitoring should be used for severely obese patients and those with significant cardiopulmonary disease or when noninvasive blood pressure monitoring devices are unreliable.

Establishing peripheral intravenous access can be difficult in obese patients. Central venous catheters should be used in cases in which peripheral access may be difficult either intraoperatively or after surgery.

## 9. Discuss positioning the obese patient.

Care should be taken to ensure that an appropriately sized operating room bed, built to accommodate additional body weight and girth, is available. In addition, all pressure points should be adequately padded, as postoperative neuropathies and pressure necrosis are more common in the obese and anesthetized population. There have been reports of rhabdomyolysis of the gluteal muscles, leading to renal failure. Sequential compression devices for the lower extremities are recommended. These are especially useful in the setting of laparoscopic surgery, where increased intra-abdominal pressure is likely to decrease venous return. It is also preferable to have assisted lifting devices to help move the patient from table to bed at the end of the case.

When planning airway management, it should be noted that many of these patients do not tolerate a flat, supine position. Placing the patient head up in a reclining position improves airway mechanics by dropping the panniculus down and unloading the diaphragm, increasing the functional residual volume.

Obese patients have an increased risk of atelectasis, which persists for a greater number of days than in the nonobese patient. In addition, they have increased risk of hypoxia for 4 to 7 days after surgery. Postoperative pulmonary physiotherapy is recommended.

**10. What extubation criteria would you use for the obese patient?**

The patient must be hemodynamically stable. Muscle relaxants should be adequately reversed and verified by peripheral nerve stimulator findings (sustained tetanus and with no post-tetanic facilitation of twitches). The patient should be awake, alert, and able to sustain a head lift for 5 seconds (Table 51-3).

**TABLE 51-3. RESPIRATORY VALUES NEEDED FOR EXTUBATION**

Respiratory rate	<30 Breaths/min
Maximal inspiratory force	–25 to –30 cm H <sub>2</sub> O
Vital capacity	10–15 ml/kg
Tidal volume	5 ml/kg (lean body weight)

**11. Review special concerns for pregnant women and children with obesity.**

Management of the morbidly obese parturient can be hazardous. In addition to the considerations discussed previously, there is also the desire for labor analgesia and potential for emergent cesarean section. The risk of difficult or failed intubation in these women is high. Placement of an epidural catheter early in the laboring process may overcome the need for general anesthesia. However, because of the technical difficulty of catheter placement and maintenance, regular assessment of the block with a low threshold for replacement is advised. Some authors recommend a continuous spinal technique, thus providing predictability and reliability of the block and rapid conversion to appropriate anesthesia for cesarean section should the need arise.

Recent studies suggest that, unlike their adult counterparts, obese children have a relatively small increase in anesthetic risk. A slight increase in minor postoperative complications is seen, predominantly respiratory. A higher rate of oxygen desaturation requiring supplemental oxygen and unplanned hospital admission is seen. This may reflect the lower prevalence of physiologic changes associated with long-standing obesity.

**12. What is obstructive sleep apnea?**

OSA is a syndrome characterized by periodic, partial, or complete obstruction of the upper airway during sleep. The sufferer (or his or her bed partner) reports snoring and periods of apnea. He or she has daytime somnolence and an increased incidence of hypoxia, dysrhythmias, hypertension, myocardial ischemia, and pulmonary hypertension. A number of case reports have documented an increase in the incidence of postoperative complications and deaths among patients suspected of having OSA. These patients have been shown to be particularly sensitive to the respiratory depressant effects of opioids, likely because of an up-regulation of the mu receptors, and postoperative respiratory arrest is reported more frequently in this group. Untreated OSA patients are known to have a higher incidence of difficult intubation, postoperative complications, increased intensive care unit admissions, and greater duration of hospital stay.

**13. Is obstructive sleep apnea common?**

The prevalence of adult sleep apnea is approximately 2% in women and 4% in men. The prevalence of childhood sleep apnea is up to 10%. These children are commonly seen on the otolaryngology surgical schedule for tonsillectomy and adenoidectomy; this is curative in 75% to 100% of cases, even in the obese population. However, it is estimated that nearly 80% of men and 93% of women with moderate to severe sleep apnea are undiagnosed. Undiagnosed OSA may pose a variety of problems for anesthesiologists.

**14. Which techniques can be used to identify patients with obstructive sleep apnea?**

Identifying patients with OSA is the first step in preventing postoperative complications caused by OSA. Questionnaires that have been designed to screen for the presence of OSA include the Berlin questionnaire, the STOP questionnaire, and the American Society of

Anesthesiologists' (ASA) checklist. Each of these has been validated in surgical patients as a screening tool for OSA and has demonstrated a moderately high level of sensitivity. All three of the tests evaluate snoring, daytime tiredness, presence of hypertension, and observed apnea. Because of the easy-to-use format and self-administered testing, the STOP questionnaire might be easier for patients to complete and more suitable in the busy preoperative clinics.

#### 15. What procedures are performed to aid in weight loss?

Bariatric surgery broadly describes several surgical weight loss procedures used in the treatment of morbid obesity. The most common procedures include gastric banding, adjustable gastric banding, and Roux-en-Y gastric bypass. The surgeries cause weight loss by limiting both the volume of food a person can ingest and the absorption of calories, vitamins, and minerals. Bariatric surgery has become increasingly common, and the surgical candidate population is widening.

These procedures are often performed laparoscopically. The increased intraabdominal pressure of morbid obesity combined with a pneumoperitoneum results in venous stasis, reduced intraoperative portal venous blood flow, decreased urinary output, lower respiratory compliance, increased airway pressure, and impairment of cardiac function. In addition, there is less efficient elimination of carbon dioxide and increased PaCO<sub>2</sub> when compared with nonobese patients. As a consequence, pneumoperitoneum is not recommended in morbidly obese patients with severe cardiac, pulmonary, hepatic, or pulmonary dysfunction.

Intraoperative management to minimize the adverse changes include appropriate ventilatory adjustments to avoid hypercapnia and acidosis, the use of sequential compression devices to minimize venous stasis, and optimized intravascular volume to minimize the effects of increased intraabdominal pressure on renal and cardiac function.

#### 16. Is bariatric surgery used in the pediatric population?

Childhood and adolescent obesity is associated with the onset of adult cardiovascular and endocrine problems at earlier ages. Dietary modifications alone have not been successful in slowing the rising incidence of obesity. Bariatric surgery in adolescents may provide the start to long-term improvements in the quality of life, psychosocial status, and physical well-being for these patients. Although obese patients have been traditionally believed to be at very high risk during the perioperative period, recent investigations in adults and children are challenging this view, and bariatric surgery is now seen more commonly in the pediatric population.

### KEY POINTS: OBESITY AND SLEEP APNEA



1. Morbidly obese patients have numerous systemic disorders and physiologic challenges, including restrictive lung disease, obstructive sleep apnea, coronary artery disease, diabetes, hypertension, cardiomegaly, pulmonary hypertension, and delayed gastric emptying. Safe anesthetic practice requires preparation for diagnosis, monitoring, and emergent treatment of any of these conditions.
2. Obese patients may be difficult to ventilate and intubate, and they may desaturate quickly after anesthetic induction. Backup strategies should always be considered and readily available before airway management begins.
3. Pharmacokinetic changes in the obese secondary to large volumes of adipose tissue require some drugs to be dosed for lean body weight and others based on total body weight.
4. Obese patients often have OSA, requiring appropriate diagnosis and care, especially in the postoperative period.

## WEBSITES



The Obesity Society  
<http://www.obesity.org>

Anesthesia Patient Safety Foundation  
<http://www.apsf.org>

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# ALLERGIC REACTIONS

James Duke, MD, MBA

## 1. Review the four types of immune-mediated allergic reactions and their mechanisms.

- **Type I**, or immediate hypersensitivity, is immunoglobulin (Ig) E-mediated hypersensitivity and in its most severe form results in anaphylaxis. Usually there is a previous exposure to the antigen during which IgE is produced and binds to mast cells and basophils. After reexposure the antigen cross-links two IgE receptors, initiating the cascade that ultimately results in release of potent vasodilating mediators. Type I reactions will be discussed in greater detail subsequently.
- **Type II** reactions involve IgG, IgM, and the complement cascade to mediate cytotoxicity; an example is Goodpasture's syndrome.
- **Type III** reactions are the result of immune-complex formation, and their deposition in tissue leads to tissue damage; an example is hypersensitivity pneumonitis.
- **Type IV** reactions, or delayed hypersensitivity, are mediated by T lymphocytes; the best example is contact dermatitis.

## 2. What is meant by anaphylaxis?

Anaphylaxis is an unanticipated and severe allergic reaction with numerous clinical manifestations, including the following:

- Hypotension, tachycardia, and cardiovascular collapse
  - Bronchospasm
  - Cutaneous symptoms, including flushing, urticaria, and angioedema
  - Gastrointestinal symptoms, including abdominal pain, nausea and vomiting, and diarrhea
- Because surgical patients are under drapes, the usual presenting features intraoperatively are hypotension, tachycardia, and bronchospasm. Since these are not uncommon problems encountered by anesthesiologists, a degree of clinical acumen is necessary to arrive at the diagnosis of anaphylaxis and quickly institute therapy.

## 3. What is an anaphylactoid reaction?

Although the symptoms are indistinguishable from anaphylaxis, an anaphylactoid reaction is nonimmune mediated. Release of inflammatory mediators from mast cells and basophils results in activation of the complement cascade.

## 4. What are the common causes of anaphylaxis in the operating room?

- About 80% of all anaphylactic reactions are caused by either muscle relaxants (e.g., succinylcholine, rocuronium, and atracurium) or latex exposure, but there are other causes:
- **Antibiotics**, usually penicillin and other  $\beta$ -lactam antibiotics (cephalosporins) (see Question 6).
  - **Propofol and thiopental**: The incidence of allergic reaction to the most current preparation of propofol is estimated to be 1:60,000 administrations; current evidence also suggests that egg-allergic patients are not at increased risk for allergic reactions. The incidence of anaphylaxis is 1:30,000 administrations and may be caused by the presence of sulfur in the compound. No allergic reactions to methohexital have ever been reported.

- **Colloids:** Dextran and gelatin have an allergic reaction incidence of about 0.3%. Hetastarch is the safest colloid.
- **Morphine and meperidine:** More than likely the reaction seen is to the result of nonimmunologic histamine release.
- **Aprotinin, heparin, and protamine:** Allergic reactions to aprotinin occur in <1% of patients, but reexposure increases the risk. Allergic reactions to unfractionated heparin are rare and to low-molecular-weight heparin are even rarer. The most common reaction to heparin is heparin-induced thrombocytopenia (HIT), which is nonimmunologic in origin. Patients with prior exposure to protamine such as those taking neutral protamine Hagedorn (NPH) insulin have the greatest risk of allergic reaction, about 0.4% to 0.76%.
- **Local anesthetics:** Allergies to local anesthetics with amide linkages (e.g., bupivacaine, lidocaine, mepivacaine, ropivacaine) are extremely rare. True allergic reactions to local anesthetics with ester linkages (e.g., procaine, chlorprocaine, tetracaine, benzocaine) are also rare and may be caused by a para-aminobenzoic acid metabolite. Methylparaben, a preservative in local anesthetics, may cause allergic reactions.

### 5. Review the issues concerning allergic reactions to muscle relaxants.

About 70% of all intraoperative anaphylactic reactions are associated with relaxants. IgE immunoglobulins are sensitive to the tertiary or quaternary ammonium groups found in these compounds. Since such chemical groups are commonly found in foods, cosmetics, and over-the-counter medications, prior exposure to muscle relaxants is often unnecessary. Succinylcholine is more likely to result in anaphylaxis than nondepolarizing relaxants because its smaller, flexible molecular structure can more easily cross-link mast cell IgE receptors. Benzylisoquinolium relaxants are more likely to result in anaphylaxis than aminosteroid relaxants, and benzylisoquinolium relaxants can also cause nonimmunologic histamine release.

### 6. Should a penicillin-allergic patient receive cephalosporins?

Authorities disagree on this issue. Although penicillin is the most common cause of anaphylaxis in the general population, interestingly only about 10% to 20% of patients reporting a penicillin reaction have a well-documented allergy, and numerous complaints such as gastrointestinal symptoms or rashes of nonimmunologic origin are labeled *allergy*. An oft-quoted statistic is that there is an 8% to 10% risk of cross-sensitivity between penicillin and cephalosporins because they share a  $\beta$ -lactam ring, but this is now disputed.

In earlier times this may have been true, possibly because earlier generations of cephalosporins contained trace amounts of penicillin. Some authorities believe cephalosporins are safe to be administered to penicillin-allergic patients as long as these patients have not experienced a prior anaphylactic reaction or have a documented positive skin test for penicillin. However, a 1995 review by Anne et al (1995) found that penicillin-allergic patients were three times as likely to have an anaphylactic reaction to any other drug. Clearly there is a lack of consensus on this issue, and the risks of anaphylaxis must be weighed against the benefits of penicillin therapy. A careful and thorough history of what is meant by *penicillin allergy* is important in this decision process.

### 7. What is latex?

Latex is derived from the sap of the Brazilian rubber tree. There are numerous proteins within this product that may produce allergic reactions. Latex products may differ dramatically in the number of allergens detectable within the product. Unfortunately, with the dramatic increase in need for latex products, quantity has been sacrificed for quality. Chemicals from the manufacturing process of commercial latex products may also result in irritant and allergic contact dermatitis.

### 8. What demographic groups are at risk for latex allergy?

- Historically patients with meningocele, myelomeningocele, and spina bifida were at increased risk for latex allergy because they required chronic bladder catheterization with latex catheters.
- Patients with spinal cord injury and developmental abnormalities of the genitourinary system are also at risk.
- Patients having had multiple operations may develop a latex allergy.
- Atopic individuals (i.e., multiple food allergies, eczema, and asthma) are prone as well.
- Individuals who have problems (rash, itching, edema) with latex products such as condoms, diaphragms, gloves, or dental dams may have severe latex-associated allergic reactions.
- Anyone having had a severe allergic reaction during medical care in the past may have latex hypersensitivity.

### 9. Has the incidence of latex allergy increased?

In the general population the incidence of latex allergy may be decreasing because of improved recognition of at-risk groups, strategies to avoid latex exposure, and a decrease in latex-containing hospital products. However, in the health-care profession, the incidence is increasing. Standard (previously called *universal*) precautions have become an everyday practice for health care workers and latex products are an essential feature. The benefit of such practice is to protect these workers from exposure to viral illnesses such as human immunodeficiency virus, hepatitis B and C, and other communicable diseases. Patients are protected from each other as well.

### 10. How is a latex allergy developed?

There are multiple routes by which individuals can be exposed to allergens, including contact with intact or abraded skin and mucous membranes, inhalation, or exposure to an open vascular tree. Latex gloves are the major source of latex proteins and are the primary factor associated with latex-associated allergic reactions. Powderless gloves reduce latex exposure through the inhalational route.

### 11. How should an operating room be prepared for a latex-allergic patient?

The cases should be scheduled first since the amount of airborne latex particles is least at the beginning of the day. Nonlatex surgical and anesthesia supplies and nonlatex gloves are essential. Increasingly latex-free medical supplies are the standard for all patients, but it is important to be familiar with supplies at hand since a totally latex-free environment for all cases has yet to be achieved. Ordinarily latex-containing supplies are labeled as such.

### 12. How should any allergic reaction be treated?

The typical presentation for a severe reaction is in a patient with prior exposure with symptoms developing soon after repeat exposure, although cross-sensitization with commercial products may permit a severe reaction on initial exposure. Respiratory symptoms include edema, especially of mucous membranes and the larynx, bronchospasm, and pulmonary edema. Cardiovascular symptoms include hypotension and tachycardia. Cutaneous manifestations include flushing and hives. These are the manifestations of the most severe, potentially fatal, IgE-mediated reaction known as anaphylaxis. Should a real or likely anaphylactic reaction be recognized, the following recommendations are made:

- Call for help and remove the offending stimulus.
- Limit the use of anesthetic agents as much as possible.
- Complete the procedure as quickly as possible or arrive at a suitable stopping point.
- Administer 100% oxygen.
- Aggressive volume expansion may require many liters of crystalloid.
- Epinephrine 5 to 10 mcg initial bolus, increasing up to 500 mcg if ineffective. Consider epinephrine infusions beginning at 1 mcg/min.
- Antihistamines (histamine-1 receptor blocker): diphenhydramine 25 to 50 mg.
- Antihistamines (histamine-2 receptor blocker): ranitidine 150 mg or cimetidine 400 mg.
- Corticosteroids: hydrocortisone, 1 to 5 mg/kg or methylprednisolone 1000 mg.
- Nebulized albuterol 0.3% for bronchospasm.
- Norepinephrine if epinephrine is insufficient; start about 0.3 mcg/kg/min and increase based on response.
- Vasopressin has also been shown to be effective in doses of 2 to 5 units.

### 13. Should patients with a prior history of allergic reaction be pretreated with histamine blockers or corticosteroids?

Probably not, because pretreatment may delay recognition of early symptoms until a full-blown reaction manifests, but there is disagreement here.

### 14. What tests are available to diagnose and characterize a prior allergic reaction? Should patients having a prior anaphylactic reaction be tested?

Serum tryptase, a mast cell protease, will be elevated after both immunologic and nonimmunologic mast cell activation, so is probably of little value. In vitro tests such as the radioallergosorbent test (RAST) detect IgE antibodies and can be performed for specific drugs but are insensitive. In vivo testing such as skin prick and intradermal testing is of variable usefulness because many patients in the general population are also cross-sensitized to many drugs. For instance, over 9% of the general population will have a positive skin prick test to muscle relaxants. In regard to latex, there are so many proteins that usual skin testing may not identify the causative allergen. Furthermore, skin testing can induce a systemic reaction severe enough to require therapy! Many authorities believe that the costs, risks, and limited information gained suggest that testing be undertaken only in unusual circumstances. One instance may be the individual suspected of occupation-related allergies.

### 15. What are the implications of occupational latex exposure?

Currently about 70% of all allergic reactions are reported in health care workers, and it is estimated that 3% to 12% of this group have developed some degree of latex sensitivity. The majority of allergic reactions are probably caused by inhalational exposure from latex particles adhering to the powder of powdered gloves. Since signs and symptoms may be very nonspecific (puffy eyes, nasal congestion, sneezing, wheezing, coughing, hoarseness), the connection may not be made to an occupational exposure. Workers who develop hand dermatitis or have an atopic history may be at increased risk. It is important to note that, although sensitization may occur at work, severe allergic manifestations may occur while these workers are receiving medical care. The key to the protection of health care workers is to reduce work-related exposure (*Stop the Sensitization!*). The use of nonpowdered latex or latex-free gloves is probably the most important intervention. Maintaining good skin care is also important, and workers who develop skin rashes might consider visiting an employee health clinic and possible latex sensitivity testing. It is also important not to wear scrub suits home because there are reports of family members developing latex sensitivity by this route.



**KEY POINTS: ALLERGIC REACTIONS**

1. To prevent severe allergic reactions, it is important to identify patients at risk and to take a good history.
2. The major causes of anaphylactic reactions in the operating room are muscle relaxants, followed by latex allergy.
3. Concerning latex allergy, proper preparation of the operating room environment is critical. Schedule patients at risk as first cases. Latex and nonlatex-containing supplies should be clearly identified and the former avoided. Powdered gloves should be avoided.
4. The proper medications needed to adequately treat a reaction should it occur must be at hand. Treat allergic reactions aggressively. Accelerate epinephrine doses if needed.
5. It is important to recognize that health care workers are at increased risk for latex hypersensitivity. Avoid the use of powdered gloves wherever possible and be alert for the development of symptoms that might signify latex allergy.
6. Health care workers with type I latex allergy should have proper allergy identification and always carry an epinephrine Autoinjector device.

**WEBSITE**

American Society of Anesthesiologists.  
<http://www.asahq.org/publicationsAndServices/latexallergy.pdf>

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# HERBAL SUPPLEMENTS

James Duke, MD, MBA

## 1. How does the Federal Food and Drug Administration regulate herbal medications?

In 1994 the Food and Drug Administration (FDA) implemented the Dietary Supplement Health and Education Act, which outlines the regulation of botanicals, called *dietary supplements*. Under this act manufacturers of alternative medications operate under less rigid guidelines than prescription pharmaceutical companies. The lack of rigorous regulation has resulted in a lack of standardization of doses and purity, contamination with undeclared pharmaceuticals and heavy metals, failure to report adverse events, and no requirement to demonstrate safety or efficacy. However, when presented with a supplement with obvious toxicity issues such as the stimulant effects of ephedra, the FDA does intervene to limit its availability; ephedra is no longer available as an over-the-counter product.

## 2. What is the incidence of herbal medicine use in the surgical patient population? What are commonly used herbal medicines?

In 2001 over \$4 billion was spent on herbs and other botanical remedies. Reported use varies widely, but a self-administered questionnaire of preoperative patients found an incidence of about 40%. Often these are taken without input from a physician. The number of individuals using herbal remedies is rising annually. Use in women is higher than in men, and patients with either neoplastic disease or human immunodeficiency virus have also been noted to use supplements with greater frequency. Supplements most commonly used include vitamins (especially vitamins E and C), garlic (*Allium sativum*), fish oil, ginkgo biloba (ginkgo), ginseng, *Zingiber officinale* (ginger), *Hypericum perforatum* (St. John's wort), *Echinacea angustifolia*, valerian, 2-amino-2-deoxyglucose sulfate (glucosamine), chondroitin 4-sulfate, chamomile, kava, and *Tanacetum parthenium* (feverfew). Oriental patients who receive concoctions from Chinese herbalists often receive more potent compounds with many different herbs contained therein.

## 3. How can commonly used herbal medicines adversely affect the surgical patient?

Although these supplements are considered *natural*, they are not free of harmful side effects. They have central nervous and cardiovascular effects (e.g., ephedra) and interact with prescription drugs. For example, St. John's wort induces the cytochrome P-450 enzymes, accelerating the breakdown of cyclosporine, antiretroviral drugs, digoxin, and warfarin, resulting in a fall in drug levels to subtherapeutic concentrations. Nephrotoxic, hepatotoxic, and carcinogenic effects have been associated with products containing kava, comfrey. Of greatest concern in the perioperative period are effects on coagulation. Vitamin E, garlic, fish oil, ginkgo, ginseng, ginger, and feverfew have anticoagulant potential.

## 4. What are the risks involved in consuming ephedra?

Ephedra alkaloids have been marketed as a way to boost energy and lose weight. These compounds are powerful cardiovascular and central nervous system stimulants, and severe hypertension, dysrhythmias, myocardial infarction, acute psychosis, seizures,

cerebrovascular accidents, and death have been associated with their use. It may be particularly toxic when combined with caffeine. Many hundreds of people have been hospitalized after their use and, as mentioned previously, the FDA has prevented its over-the-counter availability.

#### 5. Review the effects of vitamin E.

Vitamin E is consumed for the prevention and treatment of cardiovascular disease, diabetes mellitus, and some forms of cancer. Vitamin E is an antioxidant that prevents the formation of free radicals, but high doses may increase bleeding caused by antagonism of vitamin K–dependent clotting factors and platelet aggregation. Concomitant use of vitamin E and anticoagulant or antiplatelet agents, including aspirin, clopidogrel (Plavix), dalteparin (Fragmin), enoxaparin (Lovenox), heparin, ticlopidine (Ticlid), and warfarin (Coumadin) may potentiate the risk of bleeding.

#### 6. What are the reported benefits and adverse effects of fish oil?

Fish oils are used primarily in the treatment of hyperlipidemia, hypertension, and chronic inflammatory states such as rheumatoid arthritis and autoimmune disease. Fish oils contain two long-chain omega-3 fatty acids that compete with arachidonic acid in the cyclooxygenase and lipoxygenase pathways and have antiinflammatory effects, likely caused by the inhibition of leukotriene synthesis. Fish oils decrease blood viscosity and increase red blood cell deformability. The antithrombotic activity of fish oils results from prostacyclin inhibition, vasodilation, reduction in platelet count and adhesiveness, and prolongation of bleeding time. Concomitant use of fish oils and anticoagulant and antiplatelet drugs previously mentioned may increase the risk of bleeding.

#### 7. What are the beneficial properties and side effects of kava and valerian?

Kava is antiepileptic, anxiolytic, and sedative in its effects and may potentiate prescribed medications with similar properties. Its action is thought to be through stimulation of  $\gamma$ -aminobutyric (GABA) pathways. Valerian is also a sedative, potentiates the actions of barbiturates and other sedatives, and is probably GABA stimulating. These medications may potentiate the effects of anesthetic medications.

#### 8. Review the alleged benefits and risks of ginkgo.

Ginkgo is used for the treatment of dementia, Alzheimer's disease, and conditions associated with cerebral vascular insufficiency, including memory loss, headache, tinnitus, vertigo, difficulty concentrating, mood disturbances, and hearing disorders. Active ingredients of ginkgo leaf and its extracts include flavonoids, terpenoids, and organic acids. Although the mechanism of action is only partially understood, there are several theories about how ginkgo works. Ginkgo may protect tissues from oxidative damage by preventing or reducing cell membrane lipid peroxidation and decreasing oxidative damage to erythrocytes, and it may protect neurons and retinal tissue from oxidative stress. Extracts from the ginkgo leaf competitively inhibit platelet-activating factor, decreasing platelet aggregation, phagocyte chemotaxis, smooth muscle contraction, and free radical production, and prevent neutrophil degranulation. A case of bilateral spontaneous subdural hematomas has been linked to chronic ginkgo ingestion. Use of ginkgo may potentiate anticoagulant or antiplatelet agents.

#### 9. What are the alleged benefits and risks of ginseng?

Ginseng is a general tonic for improving well-being and stamina and may increase resistance to environmental stress. The active constituents of ginseng are ginsenosides; these compounds may raise blood pressure and act as a central nervous system stimulant. Adrenal function and cortisol release may increase. Ginsenosides are reported to interfere with platelet aggregation and coagulation *in vitro*, but this effect has not been demonstrated in humans. Ginseng is also associated with hypoglycemia, interferes with warfarin, and may increase partial thromboplastin time.

**10. Review the alleged benefits and risks of garlic.**

Garlic decreases blood pressure and reduces plasma lipids. It may produce smooth muscle relaxation and vasodilation by activation of endothelium-derived relaxation factor. It has been shown to have antithrombotic properties by increasing thrombolytic activity secondary to plasminogen activation and decreasing platelet aggregation through inhibition of thromboxane B<sub>2</sub> formation. Garlic may potentiate the effects of warfarin, heparin, nonsteroidal antiinflammatory drugs (NSAIDs), and aspirin. A spontaneous spinal epidural hematoma associated with excessive garlic ingestion has been reported. However, garlic taken in normal dietary doses does not impair platelet function.

**11. What about ginger?**

Ginger is used for the treatment of arthritis, for a variety of gastrointestinal complaints, for vertigo and motion sickness, and as an antiemetic. It is effective in controlling nausea and vomiting in hyperemesis gravidarum. Its active component is gingerol, and its mechanism of action is unclear, although gingerols are thought to inhibit prostaglandin and leukotriene synthesis. Ginger is believed to inhibit thromboxane synthetase, decreasing platelet aggregation. Like garlic, it may potentiate the effect of medications having anticoagulant properties.

**12. Review the properties and effects of feverfew.**

Feverfew is used for fever, headache, and prevention of migraine headaches. At least 39 compounds within feverfew have been identified. It is not yet clear how feverfew works in the prevention of migraine. Laboratory evidence suggests that feverfew extracts might inhibit platelet aggregation and serotonin release from platelets and leukocytes. It may inhibit serum proteases and leukotrienes and block prostaglandin synthesis by inhibiting phospholipase, preventing the release of arachidonic acid.

**13. Review the effects of St. John's wort.**

St. John's wort is used for the treatment of mild to moderate depression through impaired reuptake of serotonin, norepinephrine, and dopamine. As such, when taken in conjunction with selective serotonin reuptake inhibitors (SSRIs) prescribed by a physician, serotonin excess may be an undesired effect. Like SSRIs, St. John's wort should also not be administered to patients on monoamine oxidase inhibitors and  $\beta$ -sympathomimetic amines such as pseudoephedrine). It may alter the metabolism of immunosuppressants (e.g., cyclosporin) and cancer chemotherapy by stimulating cytochrome P-450 3A4. Metabolism of such drugs as warfarin, NSAIDs, local anesthetics, alfentanil, and midazolam may be enhanced.

**14. Since these medications appear to impair coagulation, how can their effect be evaluated clinically?**

The best means for detecting a coagulation defect secondary to herbal medications is a properly taken clinical history. Especially important are questions related to the hemostatic response during previous surgeries. Also important are questions regarding bleeding tendencies such as easy bruising, gingival bleeding, or excessive bleeding following procedures such as dental extractions. Positive responses suggest the need for laboratory testing. The most commonly used measures of coagulation include the activated partial thromboplastin time, which evaluates the intrinsic system, the prothrombin time, which evaluates the extrinsic pathway, platelet count, and bleeding time. However, bleeding time, the most commonly used measure of platelet function, is subject to many variables and may not always be reliable. More reliable tests of platelet function are available but are expensive, time-consuming, and not appropriate for routine screening.

## KEY POINTS: HERBAL SUPPLEMENTS



1. Herbal does not necessarily mean safe. Few controlled scientific data exist on the risks and benefits of herbal medications.
2. Always ask patients about herbal/alternative medications that they may be taking. Do not depend on them to volunteer that information.
3. In situations in which excessive bleeding may prove especially problematic or in the patient taking multiple supplements thought to have anticoagulant potential, it may be best to discontinue these medications for 2 to 3 weeks before surgery.
4. Coagulation defects secondary to herbal medicines may not be evident using standard laboratory studies.

### 15. What are current recommendations regarding discontinuing use of herbal medications before surgery?

Most patients will not admit to the use of herbal medications unless directly questioned. The use of herbal medications is not necessarily a contraindication to surgery. But, because the pharmacodynamic and pharmacokinetic features of most of these drugs have yet to be determined, it might be best to discontinue use of these agents and other over-the-counter medications as far in advance of surgery as possible. If regional anesthesia is planned and the patient is on prescribed medications with antiplatelet effects, it may be wise to discontinue the herbal supplements at least a week before surgery. However, it should be noted that the Second American Society of Regional Anesthesia Consensus Conference on Neuraxial Anesthesia and Antithrombotic Therapy has stated, “Herbal drugs, by themselves, appear to represent no added significant risk for the development of spinal hematoma in patients having epidural or spinal anesthesia.”

Finally, it may be of some comfort to clinicians who often do not see patients until just before surgery and do not have an opportunity to make the recommendation to discontinue such supplements before surgery that serious complications associated with use of herbal medications still appear to be distinctly rare events.

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## TRAUMA

*James Duke, MD, MBA***1. Review conditions that predispose trauma patients to increased anesthetic risk.**

A depressed level of consciousness may lead to hypoventilation, loss of protective airway reflexes, inappropriate behavior, and decreased ability to examine and interview the patient. Full stomachs increase the risk of pulmonary aspiration of gastric contents. Because of blood loss, hypothermia, alcohol and drug intoxication, and organ injury, these patients are prone to altered responsiveness to anesthetic agents.

**2. Outline the initial management of an unconscious, hypotensive patient.**

The ABCs (airway, breathing, and circulation) are essential. Unconscious patients require rapid and definitive airway control. The trachea should be intubated in a rapid-sequence fashion. Establish numerous large-gauge sites of intravenous access, using either short 14- or 16-G catheters peripherally or 9 Fr introducers into the central circulation. Quickly bolus the patient with at least 2 L of balanced crystalloid solution. Failure to respond indicates a need for blood. If crossmatched blood is unavailable, transfuse O-negative or type-specific red blood cells. If more than 2 units of O-negative red blood cells is given, continue administering O-negative blood. Establish an arterial catheter for continuous monitoring and blood analysis (arterial blood gases, hematocrit, platelet count, coagulation profiles, and blood chemistries).

**3. What is the significance of Glasgow Coma Scale (GCS) score of 8?**

The GCS is an assessment for patients with head injury. The final score is the sum of scores for best eye opening, best motor and best verbal responses; scores range from 3 to 15. Generally, the GCS for severe head injury is 9 or less; for moderate injury, 9–12; and for minor injury, 12 and higher. A patient with a GCS of 8 is sufficiently depressed that endotracheal intubation is indicated (see [Table 54-1](#)).

TABLE 54-1. GLASGOW COMA SCALE\*

Score	Motor	Verbal	Eye Opening
6	Obeys commands	X	X
5	Localizes stimulus	Oriented	X
4	Withdraws from stimulus	Confused	Spontaneously
3	Flexes arm	Words/phrases	To voice
2	Extends arm	Makes sounds	To pain
1	No response	No response	Remain closed

\*Scores from 3 to 15.

4. Describe the changes in vital signs associated with progressive blood loss. See Table 54-2.

Parameter	<15%	15%–30%	30%–40%	>40%
Heart rate	<100	>120	>120	>140
Systolic blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure*	Normal to increased	Decreased	Decreased	Decreased
Capillary refill	Normal	Delayed	Delayed or absent	Absent
Respiratory rate	14–20	20–30	30–40	>35
Mental status	Anxious	Anxious	Confused	Lethargic

From the American College of Surgeons: *Advanced trauma life support manual*, ed 6, Chicago, 1997, American College of Surgeons.  
\*Pulse pressure is the difference between systolic and diastolic pressures.

5. What is the initial therapy for hypovolemic shock?

Initially replace estimated blood losses with balanced crystalloid solutions. The volume administered is three or four times the estimated blood loss. Continued hemodynamic instability suggests that blood transfusion is necessary, although other causes of hypotension such as head injury, hemothorax, tension pneumothorax, or pericardial tamponade should be considered. Patients who have lost more than 25% or 30% of their blood volume may likely require transfusion with packed red blood cells.

6. Why is rapid-sequence induction preferred for airway management in trauma patients?

Rapid-sequence induction is used because trauma patients are at risk for pulmonary aspiration of gastric contents and it minimizes the time between loss of consciousness and airway protection with a cuffed endotracheal tube (ETT). The usual rapid-sequence induction begins with preoxygenation with 100% oxygen. A cardiostable induction agent (ketamine or etomidate) in reduced doses is chosen in the unstable patient. The moribund patient may require only paralysis. A rapid-acting relaxant, usually succinylcholine (SCh), is chosen. Before induction, pressure is applied firmly over the cricoid ring (Sellick maneuver) to prevent regurgitation of gastric contents. The patient is intubated as soon as adequate muscle relaxation is achieved (usually around 45 to 60 seconds). The presence of end-tidal CO<sub>2</sub> is confirmed, and breath sounds are assessed before release of cricoid pressure.

7. How does an uncleared cervical spine modify the approach to the airway?

Patients requiring emergent surgical procedures do not have time to have their cervical spines evaluated fully. There is no airway management technique that results in no cervical motion. However, there is no documentation of iatrogenic neurologic injury in patients with cervical fractures when cervical spine precautions are used. These precautions include an appropriately sized Philadelphia collar, sand bags placed on each side of the head and neck, and the patient resting on a hard board with the forehead taped and secured to it.

Alternative airway management techniques in the traumatized patient include rapid-sequence induction with in-line stabilization, use of the Bullard laryngoscope, blind nasal intubation, and fiber-optic bronchoscopic-assisted ventilation. A Glidescope is a laryngoscope with a camera

lens on its tip and is very useful when a patient's neck must be maintained in a neutral position. An unstable or uncooperative patient likely would receive a rapid-sequence induction.

When a cervical fracture or cervical spinal cord injury (SCI) is documented, most anesthesiologists choose fiber-optic intubation facilitated by some form of topical anesthesia to the airway and sedation, titrated to effect, keeping in mind the patient's other injuries and hemodynamic status. This allows postintubation assessment of neurologic status before induction of unconsciousness. It would not be advisable to ablate all protective airway reflexes in a patient with a full stomach.

### 8. Which induction agents are best for trauma patients?

Far more important than the particular drug is the dose given because most induction agents produce hypotension through loss of sympathetic tone. Ketamine may be the best agent in the hypovolemic patient because its sympathetic stimulation supports the blood pressure; it should be recognized that on occasion its direct myocardial depressant effects may result in hypotension. It is contraindicated in patients with increased intracranial pressure because it increases cerebral blood flow. Etomidate may be used in some trauma patients because of its minimal effect on hemodynamic variables; however, it will decrease sympathetic tone in patients probably relying on enhanced autonomic tone to maintain cardiac output; thus reductions in usual doses are appropriate. It also depresses adrenal function, although the impact of one dose is unclear.

### 9. Why are trauma patients hypothermic?

Hypothermia results from the same events as in any surgical patient, including loss of hypothalamic regulation, peripheral vasodilation, and exposure within a cold environment. However, trauma patients are often hypothermic on arrival to the hospital because of environmental exposure, are often not well covered during their diagnostic period, and may be receiving unwarmed intravenous fluids and blood. Hypothermia also contributes to coagulopathy. The following strategies are recommended:

- Warm the room before arrival.
- Warm all fluids and blood products.
- Use convective air-warming blankets and cover all nonprepped exposed skin surfaces.
- Warming of gases is not particularly useful because the heat content of gas is negligible.

### 10. What is meant by damage control surgery?

Damage control is the principle of performing the minimum necessary interventions to save life and limb, leaving further reconstructive procedures to a later time, after the patient has obtained hemodynamic stability.

From a historical view, patients would present with life-threatening injuries (e.g., high-grade liver lacerations) and undergo heroic surgical procedures with massive blood loss. As a consequence of the aggressive surgical efforts, the patients would become hypothermic, acidotic, and coagulopathic (the lethal triad) and often succumb to these complications.

In the present day the same patient might be submitted to an abbreviated damage control procedure. For a liver laceration the injured surface of the liver is packed with surgical sponges to temporize bleeding while the anesthesia team concentrates on resuscitation. Once stabilized, the patient's abdominal cavity is covered with a sterile dressing, and the resuscitative efforts continue in the intensive care unit. Perhaps only the next day when the patient has stabilized is he or she returned to the operating room and re-explored and further procedures undertaken as indicated. The damage control philosophy has been embraced by other surgical disciplines as well, particularly orthopedics.

### 11. How have damage control concepts been applied in orthopedic injuries?

Many patients with femur or pelvic fractures have multisystem injuries and are hemodynamically unstable. Pulmonary contusions can be problematic in these patients because reaming of the femoral canal for intramedullary nailing can shower the lungs with fat emboli at a vulnerable period, propagating an inflammatory reaction that may lead to increased



morbidity (e.g., adult respiratory distress syndrome, prolonged intensive care stays and hospitalizations, and increased ventilator days) and mortality. Rather than perform definitive surgery at the time of injury, damage control is practiced by using temporary external fixation as a bridge until the patients are better able to tolerate internal fixation.

#### 12. What is the universal theory of the compartment syndrome?

Increased pressure within any semi-rigid anatomic structure will increase to the point at which perfusion is diminished by the increasing pressure. This can apply to the cranium, thorax, pericardium, abdomen, and extremities. Failure to recognize and rapidly treat any compartment syndrome results in increased morbidity and may result in death.

#### 13. How does cardiac tamponade present? What is Beck's triad? How should anesthesia be managed in a patient with tamponade?

Cardiac tamponade may arise from either blunt or penetrating trauma. When bleeding into the pericardial space increases pericardial pressures, cardiac filling is impaired. Positive-pressure ventilation further decreases venous return and may greatly exacerbate the reduction in cardiac output. Stroke volume decreases, and tachycardia compensates for a time to increase cardiac output. Beck's triad consists of hypotension, distant heart sounds, and distended neck veins, the classic signs associated with cardiac tamponade, although neck vein distention may not be observed because of hypovolemia. Electrical alternans, in which the major electrocardiogram (ECG) axis is constantly changing, may be noted. This is because the heart floats freely in the expanded pericardium.

A patient with tamponade is at risk for cardiovascular collapse with anesthetic induction. Because of this, it may be wise to drain the pericardium using local anesthesia at the operative site (a subxiphoid pericardial window) before general anesthetic induction.

#### 14. What is the significance, clinical presentation, and treatment of a tension pneumothorax?

Patients may sustain a pneumothorax in association with trauma such as rib fractures, stab wounds, and central line placement. If the pleural cavity does not communicate with the ambient environment, air may accumulate between the chest wall and lung and may expand quickly with positive-pressure ventilation. Eventually a tension pneumothorax decreases venous return to the thorax and causes torsion of mediastinal vessels, leading to cardiovascular collapse.

The chest may rise unevenly with inspiration, breath sounds become unequal, the hemithorax is tympanitic to percussion, and the trachea may shift away from the affected side. Neck veins may become distended if the patient is normovolemic. Airway pressures rise.

The immediate treatment is the placement of a large-bore needle through the chest wall in the second intercostal space in the midclavicular line. A rush of air confirms the diagnosis. The needle should be left in place until a tube thoracostomy is performed. Tension pneumothorax is a clinical diagnosis; do not delay treatment for radiologic confirmation of this life-threatening condition. Nitrous oxide should not be used in trauma patients because it quickly diffuses into any air-filled cavity such as a pneumothorax.

#### 15. What is the abdominal compartment syndrome?

A victim of polytrauma experiencing hypotension, oliguria, and respiratory failure manifesting as increasing airway pressures and decreasing oxygenation may have abdominal compartment syndrome (ACS). ACS is often noted after massive fluid and blood resuscitations, and the patient may be coagulopathic. Diagnosis is by clinical suspicion and confirmed by measuring bladder pressure (>25 cm H<sub>2</sub>O is suspicious). Treatment involves fluid resuscitation and abdominal decompression. The increased intra-abdominal pressures also increase intrathoracic pressures, and "normal" central pressures may actually be associated with hypovolemia. Thus it is usually wise to always respond to hypotension with a fluid bolus. However, excessive fluid administration may increase bowel edema, delaying later closure of the abdomen. Refractory intracranial pressure may be caused by ACS and improve with decompression.

### 16. What challenges do spinal cord–injured patients pose?

Airway management has been discussed briefly. The technique of choice depends on the urgency of the situation but might be direct laryngoscopy with in-line stabilization, intubation using a Bullard laryngoscope, or fiberoptic intubation. When moved, patients should be *log-rolled*; that is, rolled and moved with care to maintain the neck in a neutral position.

Some degree of neurogenic shock should be expected with injuries above the T6 level. However, hypotension in cord-injured patients is most likely caused by other injuries. Catecholamine surges may produce pulmonary vascular damage, resulting in neurogenic pulmonary edema. There may be some element of myocardial dysfunction. If moderate fluid resuscitation does not result in hemodynamic improvement, central venous catheterization for monitoring may be required. Spinal cord injuries cephalad to midthoracic levels interrupt sympathetic cardioaccelerator fibers, resulting in bradycardia. If accompanied by hypotension, administration of atropine is indicated. Occasionally infusion of vasopressors such as phenylephrine is needed to support blood pressure. Anesthetic agents should be titrated carefully since drug-associated cardiovascular depression cannot be compensated for by increases in sympathetic tone. Doses of 30% to 50% of normal are likely to be sufficient. SCH may be administered in the first 24-hour period after cord injury but not thereafter to avoid the potential for life-threatening hyperkalemia.

Corticosteroids have been administered to cord-injured patients, although this remains controversial; universal application in this setting is dwindling. Corticosteroids are not without their own risks, including immunosuppression, hyperglycemia, and delayed wound healing.

Sympathetic tone eventually returns after injury, and sympathetic responses to stimuli distal to the injury may be exaggerated. Despite a loss of sensation, any surgical procedure or distention of a hollow viscus below the injury may produce life-threatening hypertension, termed *autonomic hyperreflexia*. Exaggerated reactions manifest as the patient moves into the period of spastic paralysis (4 to 8 weeks after injury) and beyond. The more distal the stimulus, the more exaggerated the reaction. Urologic procedures or fecal disimpaction, common procedures in chronic cord patients, are examples. All procedures on chronic cord-injured patients require some anesthetic to prevent or attenuate autonomic hyperreflexia. Neuraxial and inhalational anesthetics are usually satisfactory, although occasionally vasodilators such as nitroprusside are necessary to control hypertension.

### 17. Should succinylcholine be used in patients with spinal cord injury?

Within 48 to 72 hours after acute SCI, the denervated muscles respond with proliferation of extrajunctional acetylcholine receptors along the muscle cell membrane. When SCH is administered in the presence of extrajunctional receptors, a large release of potassium into the circulation results in ventricular fibrillation and cardiac arrest. Prior administration of a nondepolarizing muscle relaxant does not reliably decrease the potassium release associated with administration of SCH in patients with SCI. Ch should be avoided in patients with SCI.

### 18. Describe the presentation of a myocardial contusion.

Blunt chest trauma may cause cardiac contusion. Associated injuries include sternal fractures, rib fractures, and pulmonary contusion. Dysrhythmias are common, the most common being sinus tachycardia with nonspecific ST segment changes. Conduction blocks and ventricular rhythms may also be observed. Patients may also sustain injury to valves or papillary muscles and sustain thrombosis to coronary arteries, most commonly the right coronary artery (presenting with ischemic changes in inferior ECG leads). The absence of dysrhythmias for 24 hours is reassuring. Pump failure is an ominous finding. Cardiac enzymes add little to the evaluation of a patient suspected of having a contusion. Echocardiography is perhaps the most useful test and in the presence of contusion reveals segmental wall motion defects. Urgent surgery need not be delayed in the presence of contusion, although the threshold for invasive monitoring is lower. Myocardial contusion is predominantly a clinical diagnosis.

## KEY POINTS: TRAUMA



1. The initial management of a trauma patient requires attention to the ABCs: airway, breathing, and circulation. Ensuring numerous large-gauge intravenous sites for resuscitation is a priority.
2. Precipitous cardiovascular collapse may be caused by cardiac tamponade, tension pneumothorax, or air embolism.
3. Unstable, hemorrhaging patients should receive O-negative, type-specific, or crossmatched blood if still unstable after resuscitation with 2 L of balanced crystalloid solution.
4. Transfusions of over 5 units of red blood cells require administration of plasma or platelets to address dilutional coagulopathy. In the setting of massive transfusion, it is the current practice to transfuse 1 unit of plasma with each unit of packed red blood cells. (See Chapter 6.)
5. The triad of hypothermia, acidosis, and coagulopathy is highly lethal; in this scenario damage-control surgical principles should be considered.

**19. Describe the management of a pregnant trauma patient.**

The usual concerns for pregnant women apply. Because of airway edema and large breasts, airway management may be difficult, and these patients are at risk for pulmonary aspiration. The gravid uterus may render the patient hypotensive, especially if there has been blood loss. Patients should be positioned with left uterine displacement. Pregnancy is also a vasodilated state, confounding interpretation of vital signs. Probably because of the effects of progesterone, pregnant women have increased sensitivity to sedatives and local anesthetics. Pregnant women have dilutional anemia, confounding interpretation of the hematocrit. Consult an obstetrician concerning fetal viability. Seat belts may produce uterine rupture. If fetal distress occurs, an emergency cesarean section may be required, depending on fetal age. Aggressive resuscitation of the maternal circulation will improve the fetal circumstances. After surgery the patient may experience premature labor that may be masked by the administration of opioids for surgical pain. Monitoring uterine contractions and fetal heart tones is necessary.

**20. Review concerns for the elderly trauma patient.**

Elderly patients may have significant, life-threatening injuries despite seemingly trivial mechanisms of injury. They have diminished organ reserves and numerous comorbidities. They are on numerous medications that may have led to the injury (e.g., benzodiazepines and other psychotropic medications) or may render them prone to bleeding (e.g., antiplatelet drugs, warfarin). They may easily lose airway protective reflexes, rendering them prone to aspiration, and have blunted cardiovascular reflexes as well. Elderly patients have increased mortality rates when compared to younger cohorts.

**21. How might a bronchial or tracheal tear present? What are alternatives for managing ventilation during operative repair?**

Large airway injuries usually occur within 2.5 cm of the carina and are usually immediately recognizable; distal bronchial injuries are more difficult to identify. Physical features that may be associated with these injuries include respiratory distress, subcutaneous or mediastinal air, hemoptysis, pneumothorax, and persistent large air leak after tube thoracostomy.

Any injury near the carina is likely to require lung isolation and single-lung ventilation. A single-lumen ETT might be inserted into the uninvolved main stem bronchus. Other options include inserting a double-lumen ETT or using a bronchial blocker. A fiber-optic bronchoscope is invaluable for any option chosen.

## 22. How is air embolism diagnosed and managed?

Penetrating lung injuries may result in systemic air entrainment via bronchovenous or alveolocapillary fistulas. Increased airway pressures associated with loss of pulmonary compliance and reduced venous pressure increase the likelihood of air embolism. Frothy, sanguineous secretions emanating from injured lung surfaces should make one wary of systemic air embolization. Air may be observed within coronary arteries. Systemic air embolism should be suspected whenever unexpected signs of central nervous system or myocardial ischemia and precipitous cardiovascular collapse occur in the appropriate clinical context. When treating patients at risk, minimize inspiratory airway pressure, avoid positive end-expiratory pressure, and administer small tidal volumes.

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# THE BURNED PATIENT

*Philip R. Levin, MD, and Alma N. Juels, MD*

## 1. Who gets burned?

Approximately 2 million fires are reported each year, which result in 1.2 million people with burn injuries. Approximately 45,000 people are hospitalized in the United States for thermal injury. There are about 5000 fire and burn deaths per year. The majority of burns are thermal injuries. Electrical burns usually cause tissue destruction by thermal and associated injuries. In chemical burns the degree of injury depends on the particular chemical, its concentration, and duration of exposure. Seventy percent of burn patients are men. Mean age for all cases is 35 years old. Scalds are the most common in those below 5 years of age, whereas fire injuries are more common in older patients.

## 2. What are the three main factors that correlate with increased mortality with burn injury?

Advanced age, burn size, and presence of inhalation injury correlate with increased mortality.

## 3. What are the consequences of skin damage?

The skin is the largest organ of the human body. It has three principal functions, all of which are disrupted by burn injury:

- The skin is an important sensory organ.
- It performs a major role in thermoregulation for the dissipation of metabolic heat.
- The skin acts as a barrier to protect the body against the entrance of microorganisms in the environment. A burn patient may have extensive evaporative heat and water loss, and loss of thermoregulation may lead to hypothermia. Burn patients have a profound risk of infection and sepsis.

## 4. How are burns classified?

The severity of the burn is graded by its depth, which depends on the extent of tissue destruction.

- **Superficial burns** involve the upper layers of the epidermis; the skin is painful and appears red and slightly edematous, much like a sunburn.
- **Superficial partial-thickness burns** occur when tissue damage extends into the superficial layer of the dermis, which is still lined with intact epithelium that proliferates and regenerates new skin. These burns develop blisters and have red or whitish areas that are very painful.
- **Deep partial-thickness burns** extend downward into the deeper layer of the dermis. Edema is marked, and sensation is altered.
- **Full-thickness and subdermal burns** affect every body system and organ. A full-thickness burn extends through the epidermis and dermis and into the subcutaneous tissue layer. A subdermal burn damages muscle, bone, and interstitial tissue. Some centers are now using laser Doppler imaging to better determine burn depth.

## 5. What systems are affected by burns?

All physiologic functions can be affected by burns, including the cardiovascular and respiratory systems; hepatic, renal, and endocrine function; the gastrointestinal tract; hematopoiesis; coagulation; and immunologic response.

## 6. How is the cardiovascular system affected?

A transient decrease in cardiac output, as much as 50% from baseline, is followed by a hyperdynamic response. In the acute phase organ and tissue perfusion decreases because of hypovolemia, depressed myocardial function, increased blood viscosity, and release of vasoactive substances. The acute phase starts immediately after injury; the second phase of burn injury, termed the *metabolic phase*, begins about 48 hours after injury and involves increased blood flow to organs and tissues. Geriatric patients may have a delayed or nonexistent second phase. Hypertension of unknown cause develops and may be quite extensive.

## 7. How is the respiratory system affected?

Pulmonary complications can be divided into three distinct syndromes based on clinical features and temporal relationship to the injury. Early complications, occurring 0 to 24 hours postburn, include carbon monoxide (CO) poisoning and direct inhalation injury and can lead to airway obstruction and pulmonary edema. Delayed injury, occurring 2 to 5 days after injury, includes adult respiratory distress syndrome. Late complications, occurring days to weeks after the injury, include pneumonia, atelectasis, and pulmonary emboli. The two most common complications of burn injury are pneumonia and respiratory failure.

## 8. What is inhalation injury?

Inhalation injury occurs when hot gases, toxic substances, and reactive smoke particles reach the tracheobronchial tree. These substances result in wheezing, bronchospasm, corrosion, and airway edema and should be suspected if the burn was sustained in a closed space. The presence of carbonaceous sputum, perioral soot, burns to the face and neck, stridor, dyspnea, or wheezing are indications for complete respiratory tract evaluation. Inhalation injury can cause damage to the upper airway (i.e., airway compromise, nasal obstruction, and acute laryngitis with varying degrees of laryngeal edema), damage to the conducting airway (i.e., tracheitis and bronchitis), and injury to the lower respiratory tract (i.e., pneumonitis, pulmonary edema, and adult respiratory distress syndrome). Chest radiographs during the initial phase usually underestimate the severity of lung damage because the injury is usually confined to the airways. Fiber-optic bronchoscopy has been quite useful in diagnosis of inhalation injury.

## 9. What is the best way to treat inhalation injury?

Management is generally supportive. Oxygen should be provided as necessary to ensure adequate oxygenation. Bronchospasm usually responds to  $\beta$ -agonists. Patients with smoke inhalation can require greater fluid resuscitation than other patients with burns. Pulmonary toilet may be important if there is excessive carbonaceous material in the lungs. Intubation or tracheotomy may be necessary if there is significant upper airway compromise. Patients with heat and smoke injury plus extensive face and neck burns usually all require intubation. Patients with oral burns but no smoke injury should still be intubated early because these patients have significant edema and secretions and it may be nearly impossible to intubate at a later date. If intubation occurs, make sure to secure the endotracheal tube because it may be extremely difficult to replace it if it becomes dislodged. High-frequency percussive ventilation has also been shown to be effective in clearing secretions.

## 10. What are the features of carbon monoxide poisoning?

CO toxicity is one of the leading causes of death in fires. CO is produced by incomplete combustion associated with fires, exhaust from internal combustion engines, cooking stoves, and charcoal stoves. Its affinity for hemoglobin is 200 times that of oxygen. When CO combines with hemoglobin, forming carboxyhemoglobin (COHb), the pulse oximeter may overestimate hemoglobin saturation. Symptoms are caused by tissue hypoxia, shift in the oxygen-hemoglobin dissociation curve, direct cardiovascular depression, and cytochrome

inhibition. The persistence of a metabolic acidosis in the patient with adequate volume resuscitation and cardiac output suggests the persistent CO impairment of oxygen delivery and use. Treatment is initiated with 100% oxygen, which decreases the serum half-life of COHb. Hyperbaric oxygen (2 to 3 ATM) produces an even more rapid displacement and is most useful in cases of prolonged exposure, when it is more difficult to displace CO from the cytochrome system. The drawback of hyperbaric oxygen use is the inability to *get to the burn patient* during the crucial period of hemodynamic and pulmonary instability. The vast majority of cases can be managed simply by using 100% oxygen.

#### 11. How do burns affect the gastrointestinal tract?

Ileus may occur. Acute ulceration of the stomach or duodenum, referred to as Curling's ulcer, may lead to gastrointestinal bleeding. The small and large intestine may develop acute necrotizing enterocolitis with abdominal distention, hypotension, and bloody diarrhea.

#### 12. How is renal function affected?

Renal blood flow and glomerular filtration diminish immediately, activating the renin-angiotensin-aldosterone system. Antidiuretic hormone is released, resulting in retention of sodium and water and loss of potassium, calcium, and magnesium. The incidence of acute renal failure in burned patients varies from 0.5% to 38%, depending primarily on the severity of the burn. The associated mortality rate is very high (77% to 100%). Hemoglobinuria secondary to hemolysis and myoglobinuria secondary to muscle necrosis can lead to acute tubular necrosis and acute renal failure.

#### 13. How is myoglobinuria treated?

Myoglobinuria is treated by vigorous fluid resuscitation, to the end point of a urine output of 2 ml/kg/hr. Administration of bicarbonate to alkalize the urine may reduce the incidence of pigment-associated renal failure. Osmotic diuretics (i.e., mannitol) can be used in rare circumstances, except that its use obscures urine output as an indicator of circulating volume.

#### 14. How is hepatic function affected?

Acute reduction of cardiac output, increased viscosity blood, and splanchnic vasoconstriction can cause hepatic hypoperfusion, which can result in decreased hepatic function.

#### 15. Are drug responses altered?

Drugs administered acutely by any route other than intravenously have delayed absorption. After 48 hours the plasma albumin concentration is decreased, and albumin-bound drugs such as benzodiazepines and anticonvulsants have an increased free fraction and therefore a prolonged effect. The effect of drugs metabolized in the liver by oxidative metabolism (phase I reaction) is prolonged (e.g., diazepam). However, drugs metabolized in the liver by conjugation (phase II) are not affected (e.g., lorazepam). Opioid requirements are increased, most likely because of habituation and hypercatabolism. Ketamine may cause hypotension secondary to hypovolemia and depleted catecholamine stores, exerting its direct cardiodepressant effect. Propofol, thiopental, and etomidate may cause hypotension secondary to hypovolemia in the acute phase. Inhalational agents are likewise poorly tolerated in hypovolemic patients.

#### 16. What is the endocrine response to a burn?

The endocrine response to a thermal burn involves massive release of catecholamines, glucagon, adrenocorticotropic hormone, antidiuretic hormone, renin, angiotensin, and aldosterone. Glucose levels are elevated, and patients are susceptible to nonketotic hyperosmolar coma. Patients with larger burns are more highly associated with development of adrenal insufficiency.

### 17. What are the hematologic complications that occur with burns?

Anemia is a common finding in severely burned patients. In the immediate postburn period erythrocytes are damaged or destroyed by heat and removed by the spleen in the first 72 hours. This decrease in red cell mass is not immediately apparent because of the loss of plasma fluid and hemoconcentration. With fluid resuscitation the deficit becomes more apparent. In the early postburn period more red cell loss occurs secondary to decreased erythropoiesis. In addition, ongoing infection can result in subacute activation of the coagulation cascade. Consumption of circulating procoagulants results in various degrees of coagulopathy. Platelet function is both qualitatively and quantitatively depressed. Antithrombin deficiency has been noted in severe burn patients, usually found in the first 5 days after injury. The incidence was higher with increasing burn size and the diagnosis of inhalation injury.

### 18. What are the immunologic complications that occur with burns?

Infection in the burn patient is a leading cause of morbidity and mortality and remains one of the most demanding concerns for the burn team. Initially the burn wound is colonized principally with gram-positive organisms. Within a week they usually are replaced by antibiotic-susceptible gram-negative organisms. If wound closure is delayed and the patient becomes infected, requiring treatment with broad-spectrum antibiotics, these flora may be replaced by yeasts, fungi, and antibiotic-resistant bacteria. As burn wound size increases, bloodstream infection increases dramatically secondary to increased exposure to intravascular catheters and burn wound manipulation-induced bacteremia. Systemic antimicrobials are indicated to treat only documented infections such as pneumonia, bacteremia, wound infection, and urinary tract infection. Prophylactic antimicrobial therapy is only recommended if the burn wound must be excised or grafted in the operating room. It should be used only for coverage of the immediate perioperative period. Fifty percent or more of patients with both a major burn and an inhalation injury develop pneumonia. One of the major concerns is the worldwide emergence of antimicrobial resistance among a wide variety of nosocomial bacterial and fungal burn wound pathogens, which seriously limits the available effective treatment of burn wound infections.

### 19. How are patients with burns resuscitated?

The goal of fluid resuscitation is to correct hypovolemia and optimize organ perfusion. Adequate fluid administration is critical to the prevention of burn shock and other complications of thermal injury. Burns cause a generalized increase in capillary permeability, with loss of fluid and protein into interstitial tissue; this loss is greatest in the first 12 hours. A perfect formula for predicting fluid requirements remains elusive despite decades of research and debate. Two general principles most agree on are to give only what is needed and continuously reassess fluid requirements to prevent underresuscitation or overresuscitation. The goal of fluid resuscitation is to maintain a urinary output of 0.5 ml/kg/hr, which is thought to indicate adequate renal perfusion. The most common formula used today is the Parkland formula. The *Parkland formula* involves giving 4 ml of lactated Ringer's (LR) solution per kilogram of body weight per percent of total body surface area (TBSA) burned (4 ml/kg/% TBSA). One half of the calculated amount is given during the first 8 hours, and the remainder is given over the next 16 hours, in addition to daily maintenance fluid. Most burn centers use crystalloid as the primary fluid for burn resuscitation. Another formula that some use is the *modified Brooke formula*: 2 ml/kg/% TBSA LR administered as noted previously. The administration of colloid has been associated with increased risk of lung injury. In the United States most believe that colloid solutions should not be used in the first 24 hours. On the second day after injury capillary integrity is restored, and the amount of required fluid is decreased. Infusion of crystalloid is decreased after the first day, and colloids are administered:

- 0% to 30% TBSA burned: no colloid required
- 30% to 50% TBSA burned: 0.3 ml/kg/%burn/24 hr of colloid required
- 50% to 70% TBSA burned: 0.4 ml/kg/%burn/24 hr of colloid required
- 70% to 100% TBSA burned: 0.5 ml/kg/%burn/24 hr of colloid required



**20. How do you calculate the percent of total body surface burned?**

The severity of a burn injury is based on the amount of surface area covered in deep partial-thickness, full-thickness, and subdermal burns. The *rule of nines* method allows reasonable estimation (Table 55-1). Because of the difference in body habitus (particularly head and neck), the rule of nines must be altered in children (Table 55-2).

**TABLE 55-1. RULE OF NINES FOR ADULTS**

Head and neck	9%
Upper extremities	9% each
Chest (anterior and posterior)	9% each
Abdomen	9%
Lower back	9%
Lower extremities	18%
Perineum	1%

**TABLE 55-2. RULE OF NINES FOR CHILDREN: PERCENT OF BODY SURFACE ACCORDING TO AGE**

	Newborn	3 Years	6 Years
Head	18	15	12
Trunk	40	40	40
Arms	16	16	16
Legs	26	29	32

**21. Early surgical burn wound intervention has recently been shown to be one of the major reasons for the improved outcome in burn patients. What are the four categories of operations that are common for the burn-injured patient?**

- Decompression procedures (escharotomies and fasciotomies)
- Excision and closure operations
- Reconstruction operations
- Supportive general surgical procedures (tracheostomy, gastrostomy, cholecystectomy, bronchoscopy, vascular access procedures)

**22. What is important in the preoperative history?**

It is important to know at what time the burn occurred for fluid replacement. The type of burn is also important to assess airway damage, associated injuries, and the possibility of more extensive tissue damage than initially appreciated (electrical burns). A standard preoperative anesthetic history also must be taken, including past coexisting medical conditions, medications, allergies, and anesthetic history.

**23. What should the anesthesiologist look for on the preoperative physical examination?**

In addition to the conventional concerns of any patient about to undergo surgery, the status of the patient's airway should be the number one priority. A complete airway examination is a must. Excessive sputum, wheezing, and diminished breath sounds may suggest inhalation injury to the lungs. The cardiovascular system should also be evaluated, noting pulse rate and rhythm, blood pressure, cardiac filling pressures (if available), and urine output. Special attention should be given to the neurologic examination. It is important to assess the patient's level of consciousness and orientation.

**24. What preoperative tests are required before induction?**

Special emphasis should be placed on correcting the acid-base and electrolyte imbalance during the acute phase. Therefore an arterial blood gas analysis and a chemistry panel are suggested. In the presence of CO poisoning, the pulse oximeter may overestimate the saturation of hemoglobin; therefore a COHb level, determined by co-oximetry, may be helpful to assess the degree of the CO poisoning and to guide treatment. Coagulation tests are also helpful, because such patients often have bleeding diathesis. A urine myoglobin should be done in patients with a history of electrical injury or pigmented urine.

**25. What monitors are needed to give a safe anesthetic?**

Access for monitoring may be difficult. Needle electrodes or electrocardiogram (ECG) pads sewn on the patient may be required for the ECG monitor and nerve stimulator. A blood pressure cuff may be placed on a burned area, but an arterial catheter may be better and allows frequent blood analysis. Temperature measurement is a must because of exaggerated decreases in body temperature. Invasive monitors are placed as deemed necessary, taking into account the patient's previous baseline medical condition. If the procedure involves a large amount of blood loss, central venous pressure (right atrial pressure) should be monitored through an introducer sheath. If myocardial dysfunction is likely, a pulmonary artery catheter may be necessary, although authorities disagree on this point.

**26. How must the use of muscle relaxants be modified for a burned patient?**

From about 24 hours after injury until the burn has healed, succinylcholine may cause hyperkalemia because of proliferation of extrajunctional neuromuscular receptors. On the other hand, burned patients tend to be resistant to the effects of nondepolarizing muscle relaxants and may need two to five times the normal dose.

**27. What techniques have been used to markedly reduce blood loss in excisional burn surgery?**

Subeschar and subcutaneous epinephrine clisis, extremity exsanguinations, pneumatic tourniquet use, and maintenance of intraoperative euthermia are all simple surgical techniques that have been found to significantly decrease blood loss.

**28. What induction drugs are good for burn patients?**

Various medications have been given successfully to burn patients. In patients who are adequately volume resuscitated and not septic, propofol is an acceptable induction agent. Ketamine offers the advantage of stable hemodynamics and analgesia and has been used extensively for both general anesthesia and analgesia for burn dressing changes. Unfortunately it tends to produce dysphoric reactions. If the patient is hemodynamically unstable, etomidate is a reasonable induction alternative.

**KEY POINTS: THE BURNED PATIENT**

1. The initial goal of resuscitation in burn patients is to correct hypovolemia. Burns cause a generalized increase in capillary permeability with loss of significant fluid and protein into interstitial tissue.
2. There should be a low threshold for elective intubation in patients suspected of having inhalation injury.
3. From about 24 hours after injury until the burn has healed, succinylcholine may cause hyperkalemia, because of proliferation of extrajunctional neuromuscular receptors.
4. Burned patients tend to be resistant to the effects of nondepolarizing muscle relaxants and may need two to five times the normal dose.

**29. Describe specific features of electrical burns.**

Care of electrical burns is similar to care of thermal burns, except that the extent of injury may be misleading. Areas of devitalized tissue may be present under normal-appearing skin. The extent of superficial tissue injury may result in underestimation of initial fluid requirements. Myoglobinuria is common, and urine output must be kept high to avoid renal damage. The development of neurologic complications after electrical burns is common, including peripheral neuropathies or spinal cord deficits. Many believe that regional anesthesia is contraindicated. Cataract formation may be another late sequela of burn injury. Cardiac dysrhythmias and ventricular fibrillation or asystole may occur up to 48 hours after injury. Apnea may result from titanic contraction of respiratory muscles or cerebral medullary injury.

**WEBSITE**

American Burn Association

[www.ameriburn.org](http://www.ameriburn.org)

**SUGGESTED READINGS**

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# NEONATAL ANESTHESIA

Rita Agarwal, MD, and Jennifer F. Brunworth, MD

## 1. Why are neonates and preterm infants at increased anesthetic risk?

- **Pulmonary factors.** Differences in the neonatal airway, including large tongue and occiput, floppy epiglottis, small mouth, and short neck predispose infants to upper airway obstruction. The more premature the infant is, the higher the incidence of airway obstruction. The carbon dioxide response curve is shifted farther to the right in neonates than in adults (i.e., infants have a comparatively decreased ventilatory response to hypercarbia). Newborn vital capacity is about one half of an adult's vital capacity, respiratory rate is twice that of an adult, and oxygen consumption is two to three times greater. Consequently opioids, barbiturates, and volatile agents have a more profound effect on oxygenation and ventilation in neonates than in adults.
- **Cardiac factors.** Newborn infants have relatively stiff ventricles that function at close to maximal contractility. Cardiac output is heart rate dependent, and neonates are highly sensitive to the myocardial depressant effects of many anesthetic agents, especially those that may produce bradycardia. Inhalational agents and barbiturates should be used cautiously.
- **Temperature.** Infants have poor central thermoregulation, thin insulating fat, increased body surface area-to-mass ratio, and high minute ventilation. These factors make them highly susceptible to hypothermia in the operating room. Shivering is an ineffective mechanism for heat production because infants have limited muscle mass. Nonshivering thermogenesis uses brown fat to produce heat, but it is not an efficient method to restore body temperature and increases oxygen consumption significantly. Cold-stressed infants may develop cardiovascular depression and hypoperfusion acidosis.
- **Pharmacologic factors.** Neonates have a larger volume of distribution and less tissue and protein binding of drugs than older children and adults. They also have immature livers and kidneys and a larger distribution of their cardiac output to the vessel-rich tissues. Neonates often require a larger initial dose of medication but are less able to eliminate the medication. Uptake of inhalation agents is more rapid, and minimum alveolar concentration is lower.

## 2. Do neonates have normal renal function?

Glomerular function of the kidneys is immature, and the concentrating ability is impaired. Renal clearance of drugs may be delayed. Extra salt and water are not handled well.

## 3. Why is it important to provide infants with exogenous glucose?

Neonates have low stores of hepatic glucose, and mechanisms for gluconeogenesis are immature. Infants who have fasted may develop hypoglycemia. Symptoms of hypoglycemia include apnea, cyanosis, respiratory difficulties, seizures, high-pitched cry, lethargy, limpness, temperature instability, and sweating.

## 4. What are the differences in the gastrointestinal or hepatic function of neonates?

Gastric emptying is prolonged, and the lower esophageal sphincter is incompetent; thus the incidence of reflux may be increased. Elevated levels of bilirubin are common in neonates. Kernicterus, a complication of elevated levels of bilirubin, may lead to neurologic dysfunction and even death in extreme cases. Commonly used medications such as furosemide and

sulfonamide may displace bilirubin from albumin and increase the risk of kernicterus. Diazepam contains the preservative benzyl alcohol, which also may displace bilirubin. Hepatic metabolism is immature, and hepatic blood flow is less than that in older children or adults. Drug metabolism and effect may be prolonged.

### 5. What is retinopathy of prematurity?

Retinopathy of prematurity is a disorder that occurs in premature and occasionally full-term infants who have been exposed to high inspired concentrations of oxygen. Proliferation of the retinal vessels, retinal hemorrhage, fibroproliferation, scarring, and retinal detachment may occur, with decreased visual acuity and blindness. Premature and full-term infants should have limited exposure to high concentrations of inspired oxygen. Oxygen saturation should be maintained between 92% and 95%, except during times of greater risk for desaturation.

### 6. How is volume status assessed in neonates?

Blood pressure is not a reliable measure of volume in neonates. If the anterior fontanelle is sunken, skin turgor is decreased, and the infant cries without visible tears, the diagnosis is dehydration. Capillary refill after blanching of the big toe should be less than 5 seconds. The extremities should not be significantly cooler than the rest of the body. Finally the skin should look pink and well perfused—not pale, mottled, or cyanotic.

### 7. What problems are common in premature infants?

See Table 56-1.

TABLE 56-1. COMMON PROBLEMS IN PREMATURE INFANTS

Problem	Significance
Respiratory distress syndrome	Surfactant, which is produced by alveolar epithelial cells, coats the inside of the alveolus and reduces surface tension. Surfactant deficiency causes alveolar collapse. BPD occurs in about 20% of cases.
Bronchopulmonary dysplasia (BPD)	Interstitial fibrosis, cysts, and collapsed lung impair ventilatory mechanics and gas exchange.
Apnea and bradycardia (A and B)	This is the most common cause of morbidity in postoperative period. Sensitivity of chemoreceptors to hypercarbia and hypoxia is decreased. Immaturity and poor coordination of upper airway musculature also contribute. If apnea persists >15 sec, bradycardia may result and worsen hypoxia.
Patent ductus arteriosus (PDA)	Incidence of hemodynamically significant PDA varies with degree of prematurity but is high. Left-to-right shunting through the PDA may lead to fluid overload, heart failure, and respiratory distress.
Intraventricular hemorrhage (IVH)	Hydrocephalus usually results from IVH. Avoiding fluctuations in blood pressure and intracranial pressure may reduce the risk of IVH.
Retinopathy of prematurity	See Question 5.
Necrotizing enterocolitis	Infants develop distended abdomen, bloody stools, and vomiting. They may go into shock and require surgery.

**8. What special preparations are needed before anesthetizing a neonate?**

The room should be warmed at least 1 hour before the start of the procedure to minimize radiant heat loss. A warming blanket and warming lights also help to decrease heat loss. Covering the infant with plastic decreases evaporative losses. Forced-air warming blankets have been shown to be very efficient at keeping infants warm. They work equally well if the infant is placed on them or if the blanket is placed on the infant. Temperature should be monitored carefully because it is easy to overheat a small infant.

- Routine monitors in a variety of appropriately small sizes should be available. At least two pulse oximeter probes are helpful in measuring preductal and postductal saturation.
- Listening to heart and breath sounds with a precordial or esophageal stethoscope is invaluable.
- Calculate estimated blood volume, maintenance, and maximal acceptable blood loss.
- Placing 25 to 50 ml of balanced salt solution in a buretrol prevents inadvertent administration of large amounts of fluid.
- Five percent albumin and blood should be readily available.

**9. What intraoperative problems are common in small infants?**

See [Table 56-2](#).

**TABLE 56-2. COMMON INTRAOPERATIVE PROBLEMS IN INFANTS**

Problem	Possible causes	Solution
Hypoxia	<ol style="list-style-type: none"> <li>1. Short distance from cords to carina; ETT is easily dislodged or displaced into bronchus.</li> <li>2. Pressure on abdomen or chest by surgeons may decrease FRC and vital capacity.</li> </ol>	<ol style="list-style-type: none"> <li>1. After intubation, place ETT into right main stem and, carefully listening to breath sounds, pull tube back. Tape ETT 1-2 cm above level of carina.</li> <li>2. Inform surgeons when they are interfering with ventilation. Hand ventilation helps to compensate for changes in peak pressure.</li> </ol>
Bradycardia	<ol style="list-style-type: none"> <li>1. Hypoxia</li> <li>2. Volatile agents</li> <li>3. Succinylcholine</li> </ol>	<ol style="list-style-type: none"> <li>1. Preoxygenate before intubation or extubation; all airway manipulations should be performed expeditiously</li> <li>2. Minimize amount of volatile agent administered, especially halothane.</li> <li>3. Give atropine before administering succinylcholine to blunt vagal effects.</li> </ol>
Hypothermia	See <a href="#">Question 1</a> .	Warm operating room; have warming blanket, warming lights, warm fluids, humidifier; keep infant covered whenever possible.

(continued)

TABLE 56-2. COMMON INTRAOPERATIVE PROBLEMS IN INFANTS (continued)

Problem	Possible causes	Solution
Hypotension	<ol style="list-style-type: none"> <li>1. Bradycardia</li> <li>2. Volume depletion</li> </ol>	<ol style="list-style-type: none"> <li>1. Treat bradycardia with anticholinergics and ensure oxygenation.</li> <li>2. Many neonatal emergencies are associated with major fluid loss. Volume status should be carefully assessed, with replacement as needed</li> </ol>

*ETT*, Endotracheal tube; *FRC*, functional residual capacity.

#### 10. What are the most common neonatal emergencies?

Tracheoesophageal fistula (TEF)	Gastroschisis
Congenital diaphragmatic hernia (CDH)	Patent ductus arteriosus (PDA)
Omphalocele	Intestinal obstruction
Pyloric stenosis	

#### 11. Discuss the incidence and anesthetic implications of congenital diaphragmatic hernia.

- The incidence is 1 to 2:5000 live births.
- The diaphragm fails to close completely, allowing the peritoneal contents to herniate into the thoracic cavity. Abnormal lung development and hypoplasia usually occur on the side of the hernia but may be bilateral.
- The majority of hernias occur through the left-sided foramen of Bochdalek.
- Associated cardiovascular abnormalities present in 23% of patients.
- Patients present with symptoms of pulmonary hypoplasia. The severity of symptoms and prognosis depend on the severity of the underlying hypoplasia.
- Mask ventilation may cause visceral distention and worsen oxygenation. The infant should be intubated while awake. Low pressures must be used for ventilation to prevent barotrauma. Pneumothorax of the contralateral (healthier) lung may occur when high pressures are needed. Some patients may require high-frequency ventilation or extracorporeal membrane oxygenation.
- A nasogastric tube should be used to decompress the stomach.
- A transabdominal approach is used for the repair.
- Good intravenous (IV) access is mandatory. An arterial line may be necessary if the infant has significant lung or cardiac abnormalities.
- Pulmonary hypertension may complicate management by impairing oxygenation and decreasing cardiac output. Most patients need to remain intubated in the postoperative period.
- Opioids and muscle relaxants should be the primary agents used. Inhalational agents may be used to supplement the anesthetic if tolerated by the infant.

#### 12. Which congenital anomalies are associated with tracheoesophageal fistula?

TEFs may occur alone or as part of a syndrome. The two most common syndromes are the VATER and the VACTERL syndromes. Patients with VATER have vertebral anomalies, imperforate anus, tracheoesophageal fistula, and renal or radial abnormalities. Patients with VACTERL have all of the above in addition to cardiac and limb abnormalities.

**13. How should patients with tracheoesophageal fistula be managed?**

- Patients usually present with excessive secretions, inability to pass a nasogastric tube, and regurgitation of feedings. Respiratory symptoms are uncommon.
- Positive-pressure ventilation may cause distention of the stomach. In a spontaneously breathing patient either an awake intubation or inhalational induction may be carried out.
- The endotracheal tube (ETT) should be placed into the right main stem and gradually withdrawn until bilateral breath sounds are heard. The stomach should be auscultated to ensure that it is not overinflated. If the infant has significant respiratory distress because of overinflation of the stomach, it may be necessary to perform a gastrostomy before anesthetizing the patient.
- An arterial line is frequently not necessary in an otherwise healthy infant with no other congenital anomalies. In selected patients it may be helpful to monitor blood gas values.
- Pulse oximetry is invaluable. Probes should be placed at a preductal (right hand or finger) and postductal site (left hand or feet).
- Once the airway has been secured, the infant is placed in the left lateral decubitus position. Placing a precordial stethoscope on the left chest helps to detect displacement of the ETT.
- A right-sided thoracotomy is made, and the fistula is divided. If possible, the esophagus is reanastomosed; if not, a gastrostomy tube is placed.
- It is desirable to extubate the infant as soon as possible to prevent pressure on the suture line.

**14. What are the differences between omphalocele and gastroschisis?**

An omphalocele is a hernia within the umbilical cord caused by failure of the gut to migrate into the abdomen from the yolk sac. The bowel is completely covered with chorioamniotic membranes but otherwise usually normal. Patients with omphalocele frequently have associated cardiac, urologic, and metabolic anomalies.

In gastroschisis the bowel is not covered with chorioamniotic membranes; often there is an inflammatory exudate, and the bowel anatomy may be abnormal. The exact cause of gastroschisis is unknown; it may be to the result of vascular occlusion of blood supply to the abdominal wall or fetal rupture of an omphalocele.

**15. How are patients with omphalocele or gastroschisis managed in the perioperative period?**

- It is important to prevent evaporative and heat loss from exposed viscera. The exposed bowel should be covered with warm, moist saline packs and Saran wrap until the time of surgery. The operating room should be warmed before the arrival of the infant. Warming lights and a warming blanket help to decrease conductive and radiation loss. Covering the head and extremities with plastic prevents evaporative loss.
- Respiratory distress is uncommon; therefore infants usually arrive in the operating room breathing spontaneously. Awake intubation or rapid-sequence induction quickly establishes airway control.
- Ventilation is controlled with muscle relaxants to facilitate return of the bowel into the abdomen.
- After intubation a nasogastric tube should be placed if not already present.
- Patients need good IV access to replace third-space and evaporative losses. An arterial line can be helpful.
- Once the surgeons begin to put the viscera into the abdomen, the ventilatory requirements change. Hand ventilation during this phase allows the anesthesiologist to feel peak airway pressures and changes in airway pressures. If peak airway pressures are greater than 40 cm H<sub>2</sub>O, the surgeons must be notified.



- The abdominal cavity may be too small for the viscera. Venous return from or blood flow to the lower extremity may be compromised. A pulse oximeter on the foot helps to detect such changes. Renal perfusion may decrease and manifest as oliguria.
- If primary closure is not possible, the surgeons choose either to do a fascial (skin) closure or place a synthetic mesh silo over the defect. Both approaches necessitate return trips to the operating room for the final corrective procedure.
- Patients usually remain intubated after surgery.

#### 16. How does pyloric stenosis present?

Pyloric stenosis is a common surgical problem, occurring in 1 out of 300 live births. First-born males are more commonly affected, and it usually presents between 2 and 6 weeks of age. Patients present with persistent vomiting. Dehydration, hypochloremia, and metabolic alkalosis can develop. Continued severe vomiting and dehydration can lead to metabolic acidosis. An olive-like mass can be felt in the epigastrium. Confirmation of the diagnosis by barium swallow roentgenogram has largely been replaced by abdominal ultrasound. Surgeons may choose to repair the pylorus laparoscopically or by an open approach.

#### 17. Discuss the perioperative management of patients with pyloric stenosis.

- Electrolyte and volume imbalances need to be corrected before taking the patient to the operating room.
- A gastric tube should be placed, and continuous suction applied. The patient may have a large gastric volume of oral x-ray film contrast.
- Patients are at risk for aspiration; therefore rapid-sequence intubation or modified rapid-sequence intubation should be performed. Awake intubation in this situation has been associated with greater desaturation and a longer time to intubate.
- Choice of anesthetic agents and muscle relaxants will be guided by the speed of the surgeon (duration of surgery can be 10 to 60 minutes).
- Opioids are usually unnecessary and should be avoided intraoperatively.

#### 18. Are there any benefits to specific ventilator strategies in neonates?

Evidence has begun to emerge that strongly supports the use of lung protective ventilation (8ml/kg) in the management of neonates with respiratory distress syndrome (RDS), meconium aspiration syndrome, or congenital diaphragmatic hernia. Injury that has resulted in heterogeneous lung mechanics may cause a particular susceptibility to overdistention because of small absolute lung volumes and a highly compliant chest wall. Regional overdistention and lung stretch from large tidal volumes and elevated airway pressures may be more significant in neonates than adults because of the difference in chest wall compliance and abdominal compartment pressures. In addition to barotrauma caused by high airway pressure, atelectotrauma, related to repeated alveolar recruitment and derecruitment, have been identified as potentially injurious to the lung in patients at risk for RDS.

#### 19. At what age should the former premature infant be allowed to go home after surgery?

Premature infants are at increased risk for the development of postoperative apnea even after relatively minor surgery. Postoperative apnea has been reported in ex-premature infants up to 60 weeks' postconceptual age (PCA). Côté and associates showed that, in ex-premature infants born at a gestational age of 32 weeks undergoing inguinal herniorrhaphy, the risk of postoperative apnea was not less than 1% until 56 weeks' PCA. Anemia appropriate for gestational age or high-for-gestational age infants and a history of continuing apnea at home increased the risk of postoperative apnea.

## KEY POINTS: NEONATAL ANESTHESIA



1. Neonates are at increased anesthetic risk because they:
  - Desaturate quickly.
  - Are more prone to airway obstruction.
  - Have noncompliant ventricles and depend on adequate heart rate to maintain cardiac output.
  - Can get hypothermic very quickly.
  - Have immature kidney and liver function, which affects the pharmacology of administered medications.
2. Common neonatal emergencies include:
 

TEF	Gastroschisis
CDH	PDA
Omphalocele	Intestinal obstruction
Pyloric stenosis	
3. Careful preparation for anesthetizing neonates includes:
  - Warming the room, having warming lights, blankets, and convection air warming blankets available to maintain body heat.
  - Having multiple sizes available for the standard monitoring devices.
  - Estimating fluid maintenance, deficit, blood volume, and maximal acceptable blood loss before the start of the case.
  - Limiting the amount of volume placed in the IV buretrol to prevent accidental overhydration
4. All pyloric stenosis patients:
  - Should be treated as having full stomachs. Always suction the stomach before induction.
  - Usually present with metabolic alkalosis, but if very dehydrated may present with metabolic acidosis.
  - Volume and electrolyte imbalances need to be corrected before they are brought to the operating room for surgical correction.
  - Opioids are usually unnecessary and should be avoided intraoperatively.

## 20. Does regional anesthesia protect the patient from developing postoperative anesthesia?

Spinal anesthesia without supplemental sedation has been associated with less apnea than general anesthesia. Caudal epidural blockade may also be used. The addition of sedation may increase the incidence of postoperative apnea.

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# PEDIATRIC ANESTHESIA

Rita Agarwal, MD, and Sola Olamikan, MD

## 1. What are the differences between the adult and pediatric airways?

See Table 57-1.

TABLE 57-1. DIFFERENCES BETWEEN THE ADULT AND PEDIATRIC AIRWAYS

Infant Airway	Significance
Obligate nose breathers, narrow nares	Infants can breathe only through their noses, which can become easily obstructed by secretions.
Large tongue	May obstruct airway and make laryngoscopy and intubation difficult.
Large occiput	Sniffing position achieved with roll under shoulder.
Glottis located at C3 in premature babies, C3-C4 in newborns, and C5 in adults	Larynx appears more anterior; cricoid pressure frequently helps with laryngeal visualization.
Larynx and trachea are funnel shaped	Narrowest part of the trachea is at the vocal cords; the patient should have an ETT leak of <30 cm H <sub>2</sub> O to prevent excessive pressure on the tracheal mucosa, barotrauma.
Vocal cords slant anteriorly	Insertion of ETT may be more difficult.

ETT, Endotracheal tube.

## 2. Are there any differences in the adult and pediatric pulmonary systems?

See Table 57-2.

## 3. How does the cardiovascular system differ in a child?

- Newborns are unable to increase cardiac output (CO) by increasing contractility; they can increase CO only by increasing heart rate.
- Babies have an immature baroreceptor reflex and limited ability to compensate for hypotension by increasing heart rate. Therefore they are more susceptible to the cardiac depressant effects of volatile anesthetics.
- Babies and infants have increased vagal tone and are prone to bradycardia. The three major causes of bradycardia are hypoxia (most common cause), vagal stimulation (laryngoscopy), and volatile anesthetics. Bradycardia decreases CO.

TABLE 57-2. DIFFERENCES IN THE PEDIATRIC AND ADULT PULMONARY SYSTEMS

Pediatric Pulmonary System	Significance
Decreased, smaller alveoli	Thirteenfold growth in number of alveoli between birth and 6 years; threefold growth in size of alveoli between 6 years and adulthood
Decreased compliance	Increased likelihood of airway collapse
Increased airway resistance, vulnerability to smaller airways	Increased work of breathing and disease affecting small airways
Horizontal ribs, pliable ribs and cartilage	Inefficient chest wall mechanics
Less type 1, high-oxidative muscle	Babies tire more easily
Decreased total lung capacity, faster respiratory and metabolic rate	Quicker desaturation
Higher closing volumes	Increased dead-space ventilation

#### 4. What are normal vital signs in children?

See Table 57-3.

TABLE 57-3. NORMAL VITAL SIGNS IN CHILDREN

Age (years)	HR	RR	SBP	DPB
<1	120–160	30–60	60–95	35–69
1–3	90–140	24–40	95–105	50–65
3–5	75–110	18–30	95–110	50–65
8–12	75–100	18–30	90–110	57–71
12–16	60–90	12–16	112–130	60–80

*DBP*, Diastolic blood pressure; *HR*, heart rate; *RR*, respiratory rate; *SBP*, systolic blood pressure. A good rule of thumb is normal BP = 80 mm Hg + 2 × age.

#### 5. When should a child be premedicated? Which drugs are commonly used?

Children may have fear and anxiety when they are separated from their parents and during anesthetic induction. Children who are 2 to 6 years old who have had previous surgery or no preoperative tour and education or who fail to interact positively with health care providers in the preoperative area should be premedicated. Children who are anxious during induction may suffer from negative postoperative behavioral changes. Children who receive premedication with midazolam have fewer negative postoperative changes than children who do not.

#### 6. Should parents be allowed to accompany their children to the operating room?

Young children may become anxious and frightened when they are separated from their parents. Allowing parents to accompany children to the operating room (OR) may facilitate

anesthetic induction in some cases. Parents and children should be educated and prepared for what to expect, and parents should be prepared to leave when the anesthesiologist believes it to be appropriate. Anxious, reluctant, or hysterical parents are a hindrance. An anesthesiologist who is not comfortable with parental presence probably should not allow them to be present. An uncooperative, frightened child may not benefit from parental presence. Although allowing parents to be present during induction of anesthesia is beneficial to the parents, premedication with midazolam actually is associated with lower levels of anxiety in the child. The benefit of both premedication and parent presence during anesthesia appears to be additive.

## 7. What medications are available for premedication?

See Table 57-4.

**TABLE 57-4. ROUTES OF ADMINISTRATION FOR PREMEDICATIONS IN CHILDREN**

Drug	Route	Comments	Disadvantages
Midazolam	PO, PR, IN, IV, SL	Quick onset, minimal side effects	Tastes bad when given orally, burns intranasally
Ketamine	PO, PR, IN, IV, SL	Quick onset, good analgesia	May slow emergence, tastes bad, burns intranasally
Fentanyl	OTFC	Tastes good, good analgesic, onset at 45 minutes	Possible hypoxemia, nausea
Diazepam	PO, PR, IM	Cheap, minimal side effects	Long onset time, may prolong emergence

*IM*, Intramuscular; *IV*, intravenous; *IN*, intranasal; *OTFC*, oral transmucosal fentanyl citrate; *PO*, by mouth; *PR*, per rectum; *SL*, sublingual.

## 8. Describe the commonly used induction techniques in children.

- Inhalational induction is the most common induction technique in children younger than 10 years who do not have intravenous (IV) access. The child is asked to breathe 70% nitrous oxide (N<sub>2</sub>O) and 30% oxygen for approximately 1 minute; sevoflurane is then turned on. The sevoflurane concentration can be increased slowly or rapidly.
- Rapid inhalational induction is used in an uncooperative child. The child is held down, and a mask containing 70% N<sub>2</sub>O, 30% oxygen, and 8% sevoflurane is placed on the child's face. This unpleasant technique should be avoided if possible. Once anesthesia has been induced, the concentration of sevoflurane should be decreased.
- Steal induction may be used if the child is already sleeping. Inhalational induction is accomplished by holding the mask near the child's face while gradually increasing the concentration of sevoflurane. The goal is to induce anesthesia without awakening the child.
- IV induction is used in a child who already has an IV line in place and in children >10 years. Typical medications used in children are thiopental, 5 to 7 mg/kg; propofol, 2 to 3 mg/kg; and ketamine, 2 to 5 mg/kg. EMLA cream (eutectic mixture of local anesthesia) applied at least 90 minutes before starting the IV infusion makes this an atraumatic procedure.

### 9. How does the presence of a left-to-right shunt affect inhalational induction and intravenous induction?

A left-to-right intracardiac shunt leads to volume overload of the right heart and pulmonary circulation, resulting in congestive heart failure and decreased lung compliance. Uptake and distribution of inhaled agents are minimally affected; onset time for IV agents is slightly prolonged.

### 10. How about a right-to-left shunt?

Right-to-left shunting causes hypoxemia and left ventricular overload. Patients compensate by increasing blood volume and hematocrit. It is important to maintain a high systemic vascular resistance (SVR) to prevent increased shunting from right to left. Such shunts may slightly delay inhalation induction and shorten the onset time of IV induction agents.

### 11. What other special precautions need to be taken in a child with heart disease?

- The anatomy of the lesion(s) and direction of blood flow should be determined. Pulmonary vascular resistance (PVR) needs to be maintained. If the PVR increases, right-to-left shunting may increase and worsen oxygenation, whereas a patient with a left-to-right shunt may develop a reversal in the direction of blood flow (Eisenmenger's syndrome). If a patient has a left-to-right shunt, decreasing the PVR may increase blood flow to the lungs and lead to pulmonary edema. Decreasing the PVR in patients with a right-to-left shunt may improve hemodynamics. Conditions that can increase shunting are listed in [Table 57-5](#).
- Air bubbles should be meticulously avoided. If there is a communication between the right and left sides of the heart (ventricular septal defect, atrial septal defect), air injected intravenously may travel across the communication and enter the arterial system. This may lead to central nervous system symptoms if the air obstructs the blood supply to the brain or spinal cord (paradoxical air embolus).
- Prophylactic antibiotics should be given to prevent infective endocarditis. Recommendations for medications and doses can be found in the American Heart Association guidelines.
- Avoid bradycardia.
- Recognize and be able to treat a "tet spell." Children with tetralogy of Fallot have right ventricular outflow tract (RVOT) obstruction (pulmonary artery stenosis or atresia), an overriding aorta, ventricular septal defect, and right ventricular hypertrophy. They may or may not have cyanosis at rest. However, many are prone to hypercyanotic spells (tet spells) as they get older. Such episodes are characterized by worsening RVOT obstruction, possibly as a result of hypovolemia, increased contractility, or tachycardia during times of stimulation or stress. Patients are frequently treated with  $\beta$ -blockers, which should be continued perioperatively. Hypovolemia, acidosis, excessive crying or anxiety, and increased airway pressures should be avoided. The SVR should be maintained. If a hypercyanotic spell

**TABLE 57-5. CONDITIONS THAT CAN INCREASE SHUNTING**

Left-to-Right Shunt	Right-to-Left Shunt
Low hematocrit	Decreased SVR
Increased SVR	Increased PVR
Decreased PVR	Hypoxia
Hyperventilation	Hypercarbia
Hypothermia	Acidosis
Isoflurane	Nitrous oxide, ketamine

*PVR*, Pulmonary vascular resistance; *SVR*, systemic vascular resistance.

occurs in the perioperative period, treatment includes maintaining the airway, volume infusion, increasing the depth of anesthesia, or decreasing the surgical stimulation. Phenylephrine is extremely useful in increasing SVR. Additional doses of  $\beta$ -blockers may also be tried. Metabolic acidosis should be corrected.

## 12. How is an endotracheal tube of appropriate size chosen?

An endotracheal tube (ETT) a half size above and a half size below the estimated size in Table 57-6 should be available, the leak around the tube should be  $<30$  cm  $H_2O$ , and the ETT should be placed to a depth of approximately three times its internal diameter.

TABLE 57-6. GUIDELINES FOR ENDOTRACHEAL TUBE SIZE

Age	Size—Internal Diameter (mm)
Newborns	3.0–3.5
Newborn–12 months	3.5–4.0
12–18 months	4.0
2 years	4.5
>2 years	ETT size = $(16 + \text{age})/4$

*ETT*, Endotracheal tube.

## 13. Can cuffed endotracheal tubes be used in children and laryngeal mask airways?

Most of us have been taught for years that cuffed ETTs should not be used in children  $<8$  years old. The reasons are twofold:

1. Avoid trauma to the narrowest part of the pediatric airway—the cricoid.
2. Allow a bigger uncuffed ETT to be passed, which would decrease the work of breathing (WOB). Early studies were all done in cadavers, and indeed in cadaveric models the airway is cone shaped, with the cricoid at its apex. More recent magnetic resonance imaging studies to measure laryngeal and tracheal parameters in anesthetized, nonparalyzed spontaneously breathing children found that, although the airway was cone shaped, the apex and narrowest diameters were at the vocal cords. In addition, they found that the airway was elliptical and not circular.

Many patients who are intubated (in either the operating room or intensive care unit) are mechanically ventilated; thus the WOB is not as much of an issue as it used to be. Newer circuits and anesthesia machines have also helped decrease the problem of WOB.

Tracheal mucosal inflammation and injury are related to a number of factors, including duration of intubation and number of intubation attempts. Several recent studies have found that cuffed ETTs decrease the number of intubation attempts and are associated with decreased air leak (resulting in decreased OR pollution and greater ability to use low fresh gas flows) and provide better protection from aspiration.

Cuffed ETTs can be used in children and neonates. Of course, the cuff takes up space, thus limiting the size of the ETT. Use the cuffed tube one size smaller than the appropriate uncuffed tube. The advantages of cuffed ETTs are that they avoid repeat laryngoscopy and may allow use of lower fresh gas flows.

New Microcuff ETTs are formulated with microthin polyurethane cuff material that is reputed to seal the airway with half the pressure of conventional cuffed ETTs. Their cuff is short and cylindrical and placed near the tube tip. This positions the cuff lower in the airway.

Laryngeal mask airways (LMAs) are also useful in pediatrics. They can help secure a difficult airway, either as the sole technique or as a conduit to endotracheal intubation, and are being used increasingly for routine airway management in minor procedures.

#### 14. How is an appropriate-size laryngeal mask airway chosen?

See Table 57-7.

Size of Child	LMA Size
Neonates up to 5 kg	1
Infants 5–10 kg	1½
Children 10–20 kg	2
Children 20–30 mg	2½
Children/small adults >30 kg	3
Children/adults >70 kg	4
Children/adults >80 kg	5

*LMA*, Laryngeal mask airway.

#### 15. How does the pharmacology of commonly used anesthetic drugs differ in children?

- The minimal alveolar concentration (MAC) of the volatile agents is higher in children than adults. The highest MAC is in infants ages 1 to 6 months. Premature babies and neonates have a lower MAC, but it is still higher than in adults.
- Children have a higher tolerance to the dysrhythmic effects of epinephrine during general anesthesia with volatile agents.
- In general, children have higher drug requirements (mg/kg) because they have a greater volume of distribution (more fat, more body water).
- Opioids should be used carefully in children less than 1 year old who are more sensitive to the respiratory depressant effects.

#### 16. How is perioperative fluid managed in children?

- Maintenance is calculated as follows:
  - Infant <10 kg: 4 ml/kg/hr
  - 10 to 20 kg: 40 ml/hr plus 2 ml/kg/hr for every kg over 10
  - Child >20 kg: 60 ml/hr plus 1 ml/kg/hr for every kg over 20
- Estimated fluid deficit (EFD) should be calculated and replaced as follows:
  - $EFD = \text{maintenance} \times \text{hours since last oral intake}$
  - ½ EFD + maintenance given over the first hour
  - ¼ EFD + maintenance given over the second hour
  - ¼ EFD + maintenance given over the third hour
- All EFDs should be replaced for major cases. For minor cases 10 to 20 ml/kg of a balanced salt solution (BSS) with or without glucose is usually adequate.
- Estimated blood volume (EBV) and acceptable blood loss (ABL) should be calculated for every case.

#### 17. What is the most common replacement fluid used in children? Why?

A BSS such as lactated Ringer's (LR) with glucose (D<sub>5</sub>LR) or without glucose (LR) is recommended. Hypoglycemia may occur in healthy children undergoing minimally invasive



procedures if glucose-containing fluids are not used, but administration of 5% glucose-containing solutions results in hyperglycemia in the majority of children. Perhaps fluid containing 1% or 2.5% glucose is best. Others still use 5% glucose solutions for maintenance but recommend nonglucose-containing BSS for third space or blood loss. In major operations it is prudent to check serial glucose levels and avoid hyperglycemia or hypoglycemia.

### 18. What is the estimated blood volume in children?

See Table 57-8.

**TABLE 57-8. GUIDELINES FOR ESTIMATED BLOOD VOLUME IN CHILDREN**

Age	EBV (ml/kg)
Neonate	90
Infant up to 1 year old	80
Older than 1 year	70

*EBV*, Estimated blood volume.

### 19. How is acceptable blood loss calculated?

$$\text{ABL} = [\text{EBV} \times (\text{pt hct} - \text{lowest acceptable hct})] / \text{average hct}$$

where ABL = acceptable blood loss, EBV = estimated blood volume, pt = patient, and hct = hematocrit. The lowest acceptable hematocrit varies with circumstances. Blood transfusion is usually considered when the hematocrit is <21% to 25%. If problems with vital signs develop, blood transfusion may need to be started earlier. For example, a 4-month-old infant is scheduled for craniofacial reconstruction. He is otherwise healthy, and his last oral intake was 6 hours before arriving in the operating room; weight = 6 kg, preoperative hct = 33%, lowest acceptable hct = 25%.

- Maintenance = weight  $\times$  4 ml/hr = 24 ml/hr
- EFD = maintenance  $\times$  6 hr = 144 ml
- EBV = weight  $\times$  80 ml/kg = 480 ml
- ABL =  $[\text{EBV} \times (\text{pt hct} - \text{lowest acceptable hct})] / \text{average hct} = [480 \times (33 - 25)] / 29 = 132 \text{ ml}$

### 20. How do the manifestations of hypovolemia differ in children?

Healthy children compensate for acute volume loss of 30% to 40% before blood pressure changes. The most reliable early indicators of compensated hypovolemic shock in a child are persistent tachycardia, cutaneous vasoconstriction, and diminution of pulse pressure.

### 21. What are the systemic responses to blood loss?

See Table 57-9.

### 22. What is the most common type of regional anesthesia performed in children? Which local anesthetic is used and what dose is appropriate?

Caudal epidural block is the most common regional technique. It is usually performed in an anesthetized child and provides intraoperative and postoperative analgesia. It is used most commonly for surgery of the lower extremities, perineum, and lower abdomen. Lumbar and thoracic epidural blocks are also used for postoperative pain relief.

TABLE 57-9. SYSTEMIC RESPONSE TO BLOOD LOSS IN CHILDREN

Organ System	<25% Blood Loss	25%–40% Blood Loss	>45% Blood Loss
Cardiac	Weak, rapid, pulse; thready pulse	Tachycardia	Hypotension, tachycardia; bradycardia indicates severe blood loss and impending circulatory collapse
Central nervous system	Lethargic and confused	Obtunded, dulled response to pain	Comatose
Skin	Cool, clammy	Cyanotic, decreased capillary refill, cold extremities	Pale, cold
Kidneys	Oliguria	Minimal UOP	Minimal if any UOP

*UOP*, Urine output.

Bupivacaine (0.125% to 0.25%) is most commonly used. Bupivacaine 0.25% produces intraoperative analgesia and decreases the required volatile anesthetic. However, it may produce postoperative motor blockade that interferes with discharge of outpatients. Bupivacaine 0.125% causes minimal postoperative motor block but may not provide intraoperative analgesia or decrease the anesthetic requirements. Bupivacaine 0.175% produces good intraoperative analgesia and minimal motor block and decreases the required MAC of volatile anesthetics. The toxic dose of bupivacaine in the child is 2.5 mg/kg; in the neonate, 1.5 mg/kg. Commonly used doses are listed in Table 57-10.

TABLE 57-10. COMMONLY USED DOSES OF LOCAL ANESTHETIC FOR CAUDAL BLOCK

Dose (ml/kg)	Level of Block	Site of Operation
0.5	Sacral/lumbar	Penile, lower extremity
1	Lumbar/thoracic	Lower abdominal
1.2	Upper thoracic	Upper abdominal

Data from Gunter JB, et al: Optimum concentration of bupivacaine for combined caudal-general anesthesia in pediatric patients, *Anesth Analg* 66:995–998, 1982.  
*UOP*, Urine output.

### 23. Describe the common postoperative complications.

- Postoperative nausea and vomiting (PONV)** is the most common cause of delayed discharge or unplanned admission. Factors associated with PONV include age >6 years, length of surgery >20 minutes, previous history of PONV, eye surgery, inner ear procedures, history of motion sickness, tonsillectomy/adenoidectomy, preoperative nausea

or anxiety, hypoglycemia, female gender, gynecologic procedures, and use of opioids and  $N_2O$ . The best treatment for PONV is prevention. Prophylactic administration of an antiemetic should be considered for patients at high risk for PONV. Avoiding opioids decreases the incidence of PONV as long as pain relief is adequate (e.g., patient has a caudal block). Management includes administering IV fluid, limiting oral intake, and administering dexamethasone, metoclopramide, or ondansetron.

- **Laryngospasm** and **stridor** are more common in children than in adults. Management for laryngospasm includes oxygen, positive pressure ventilation, jaw thrust, succinylcholine, propofol, and reintubation if necessary. Stridor is usually treated with humidified oxygen, steroids, and racemic epinephrine.
- **Emergence agitation** has increased in incidence with the use of short-acting volatile agents (sevoflurane and desflurane). Pain can worsen, and analgesics improve agitation. Agitation can occur even in patients undergoing nonpainful procedures, although fentanyl, 1 mg/kg, reduces agitation.

## KEY POINTS: PEDIATRIC ANESTHESIA



1. Infants may be difficult to intubate because they have a more anterior larynx, relatively large tongues, and a floppy epiglottis. The narrowest part of the larynx is below the vocal cords at the cricoid cartilage.
2. Children desaturate more rapidly than adults because of increased metabolic rate, increased dead space, inefficient chest wall mechanics, and (in neonates) immature alveoli.
3. Premedication with midazolam has been shown to be superior in decreasing a child's anxiety when compared to a placebo or parental presence at the time of induction.
4. Children who receive premedication have a lower incidence of postoperative negative behavioral changes than those who do not.

### 24. What is the significance of masseter muscle rigidity?

Rigidity of the masseter muscles occurs in 1% of children receiving halothane and succinylcholine. Masseter muscle rigidity (MMR) may be the first symptom of malignant hyperthermia (MH), but it may also occur in patients who are not susceptible to MH. When MMR develops, the major issue is whether to substitute a nontriggering technique or stop the procedure. We usually switch to a nontriggering technique and continue with the operation unless other signs of MH develop or such severe masseter muscle spasm occurs that intubation is impossible.

After surgery patients should be admitted and followed for signs of MH (tachycardia, blood pressure lability, hyperthermia [which is usually a late symptom], urine myoglobin). If creatine phosphokinase (CPK) is  $>20,000$ , the patient should be considered to have MH. If the CPK is  $<20,000$  but still significantly elevated, an MH work-up should be considered, including a muscle biopsy. If CPK is normal or minimally elevated, the patient is probably not at increased risk for MH.

### 25. Should children with upper respiratory infection receive general anesthesia?

The risk of adverse respiratory events is 9 to 11 times greater up to 6 weeks after an upper respiratory infection (URI). Underlying pulmonary derangements include decreased diffusion capacity for oxygen, decreased compliance, increased airway resistance, decreased closing volumes, increased shunting (ventilation-perfusion mismatch), hypoxemia, and increased airway reactivity (desaturation, bronchospasm, laryngospasm). Associated factors predicting

an increased likelihood of perioperative complications include airway instrumentation, fever, productive cough, lower respiratory tract involvement, a history of snoring, passive smoking, induction anesthetic agent, copious secretions, nasal congestion, and anticholinesterase use.

General recommendations for a child with a mild URI include the following:

- Discuss increased risk with parents.
- Try to avoid intubation (LMA or mask use has a lower risk).
- Use anticholinergics to help decrease secretions and airway reactivity.
- Humidification and hydration are thought to decrease airway dryness and maintain ciliary clearance.
- The child who has a fever, rhonchi that do not clear with coughing, an abnormal chest x-ray film, elevated white count, or decreased activity levels should be rescheduled.

The child presenting with symptoms of an uncomplicated URI and who are afebrile with clear secretions and appearing otherwise healthy or those with noninfectious conditions should be able to undergo surgery.

## 26. What are the implications of sleep-disordered breathing in children?

Sleep-disordered breathing (SDB) is a continuum that ranges from normal breathing and oxygenation to chronic intermittent desaturation (CIND) and obstructive sleep apnea (OSA).

Obstructive sleep apnea is known to be associated with decreased CO<sub>2</sub> response curve and a higher incidence of perioperative respiratory problems such as desaturation, obstruction, apnea, and increased opioid sensitivity. It is important to assess the severity and comorbidities present in each particular patient.

In children SDB can be caused by narrowing of the upper airway usually secondary to adenotonsillar hypertrophy, obesity, neuromuscular problems and/or craniofacial abnormalities. Children with SDB can have significant behavioral and performance problems. Tonsillectomy and adenoidectomy have been shown to completely eliminate airway obstruction in 85% to 95% of otherwise healthy patients with OSA and result in significant improvement in clinical symptoms. Recent studies have challenged the myth of adverse effects from preoperative sedation in these children.

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# CONGENITAL HEART DISEASE

Robert H. Friesen, MD

## 1. What is the incidence of congenital heart disease?

Although a variable range can be found in the literature, a reasonable estimate of the incidence is 1 in 250 live births.

## 2. What causes pulmonary hypertension in association with congenital heart disease?

Pulmonary artery hypertension (PAH) is associated with a variety of disease states and can also be idiopathic. When associated with congenital heart disease, PAH is usually the result of high blood flow and pressure in the pulmonary vasculature caused by left-to-right intracardiac shunting at the ventricular level. This situation is typically present with ventricular or atrioventricular septal defects, in which blood flows along a pressure gradient from the high-pressure left ventricle to the lower-pressure right ventricle.

## 3. Describe the pulmonary vascular effects of left-to-right shunts.

Chronic high flow and pressure in the pulmonary vasculature leads to medial hypertrophy and intimal hyperplasia of the pulmonary arteries, resulting in a progressive increase in pulmonary vascular resistance (PVR). This pulmonary vascular obstructive disease eventually becomes irreversible. This irreversible state is rare in patients younger than 1 year of age, except in special situations (e.g., Down syndrome, high altitude, or concurrent existence of cyanotic heart disease).

Several years of progression of pulmonary vascular obstructive disease can result in PVR being greater than systemic vascular resistance (SVR). When this happens, the intracardiac shunt is reversed and flows right to left. This life-threatening situation is called Eisenmenger's syndrome.

## KEY POINTS: CONDITIONS THAT INCREASE PULMONARY VASCULAR RESISTANCE



1. Hypoxia
2. Acidosis
3. Hypercarbia
4. Stress-inducing noxious stimuli

## 4. How do left-to-right shunts affect the heart?

Over time both ventricles suffer from such shunting. The right ventricle must pump a higher than normal volume of blood through a progressively resistant pulmonary vasculature. The left ventricle is overworked because it receives a higher volume load from pulmonary venous return and because maintenance of cardiac output is less efficient when some blood exits the left ventricle through a septal defect rather than the aorta. Biventricular dilation, hypertrophy, and eventually ischemia, fibrosis, and failure are the result.

### 5. What is a pulmonary hypertensive crisis? How is it treated?

In patients with PAH, the pulmonary vasculature is hyperreactive to various stimuli that cause pulmonary vasoconstriction. These stimuli include hypoxia, acidosis, hypercarbia, and stress associated with noxious stimuli such as pain or tracheal suctioning. When PVR suddenly increases as a result of such hyperreactivity to a point at which right ventricular pressure equals or exceeds left ventricular pressure, a pulmonary hypertensive crisis is said to occur. This is a dangerous situation in which death can occur as a result of rapidly progressive right ventricular failure, diminishing pulmonary blood flow and cardiac output, poor coronary artery flow, and hypoxia. Table 58-1 outlines the treatment of pulmonary hypertension.

TABLE 58-1. TREATMENT OF PULMONARY HYPERTENSION

Goal	Method
Increase PO <sub>2</sub>	Increase FiO <sub>2</sub> Treat atelectasis Control ventilation
Alkalosis	Hyperventilation Treat metabolic acidosis
Control stress response	Adequate analgesia
Pulmonary vasodilation	Inhaled nitric oxide Intravenous prostacyclin (PGI <sub>2</sub> )

*FiO<sub>2</sub>*, Fractional concentration of oxygen in inspired gas; *PO<sub>2</sub>*, partial pressure of oxygen.

### 6. How does PAH affect perioperative risk?

PAH is an independent predictor of perioperative morbidity and mortality in both adults and children, and the severity of baseline PAH correlates with the incidence of major complications, including cardiac arrest and pulmonary hypertensive crisis. Children with suprasystemic pulmonary artery pressures were eight times more likely to experience a major perioperative complication than were those with subsystemic pulmonary hypertension. Choosing a balanced anesthetic technique that minimizes hemodynamic changes and using perianesthetic pulmonary vasodilators are important in the care of patients with PAH.

### 7. How are shunts calculated?

Using cardiac catheterization data, relative flows in the pulmonary and systemic circulations can be calculated using the Fick principle (flow is inversely related to oxygen extraction):

$$Q_p/Q_s = \frac{SaO_2 - SvO_2}{SpvO_2 - SpaO_2}$$

where  $Q_p$  = pulmonary blood flow,  $Q_s$  = systemic blood flow,  $SaO_2$  = systemic arterial oxygen saturation,  $SvO_2$  = systemic mixed venous oxygen saturation,  $SpvO_2$  = pulmonary venous oxygen saturation, and  $SpaO_2$  = pulmonary arterial oxygen saturation.

### 8. How are pulmonary vascular resistance and systemic vascular resistance calculated?

Resistance is related to pressure and flow:

$$PVR = (PAP - LAP)/Q_p$$

$$SVR = (MAP - CVP)/Q_s$$

where PAP = pulmonary artery pressure, LAP = left atrial pressure, Qp = pulmonary blood flow, MAP = mean arterial pressure, CVP = central venous pressure, and Qs = systemic blood flow. The results of this equation are expressed in Wood units. Multiply by 80 to express in dyne  $\bullet$  s  $\bullet$  cm<sup>-5</sup>.

### 9. Do anesthetic drugs affect pulmonary vascular resistance?

Most anesthetics do not have undesired effects on the pulmonary vasculature. Inhalational anesthetics are vasodilators and probably have similar effects on both SVR and PVR. Fentanyl does not have direct effects on the pulmonary vasculature, but it can prevent the stress response to noxious stimuli. Ketamine can increase PVR significantly in some patients who have pulmonary hypertension, especially if accompanied by hypoventilation, but this increase can sometimes be attenuated by administering oxygen, ventilatory support, or a pulmonary vasodilator. Propofol may decrease SVR more than PVR. Almost any sedative drug can depress ventilation and cause changes in oxygen saturation or carbon dioxide tension that could increase PVR.

### 10. What causes cyanosis in congenital heart disease?

When at least 5 g/dl of desaturated hemoglobin is present in arterial blood, the lips, nailbeds, and mucous membranes appear blue, or cyanotic. Cyanosis occurs in patients with congenital heart lesions involving a right-to-left shunt and decreased pulmonary blood flow (including tetralogy of Fallot, pulmonary stenosis or atresia with septal defect, and tricuspid atresia), in lesions involving mixing of right- and left-sided blood without decreased pulmonary blood flow (including truncus arteriosus, anomalous pulmonary venous return, single ventricle, and double-outlet right ventricle), and in parallel right and left circulations (transposition of the great arteries).

### 11. Describe the clinical problems associated with cyanotic congenital heart disease.

In response to chronic hypoxemia, these patients develop polycythemia. When hematocrit exceeds about 65%, increased blood viscosity is associated with a greater risk of intravascular thrombosis, stroke, coagulopathy, and poor flow in the microcirculation. The combination of hypoxemia and impaired blood flow can lead to tissue ischemia and organ dysfunction. In the heart ventricular dysfunction occurs as the myocardium is subjected to chronic ischemia and is exacerbated by the hypertrophy associated with ventricular outflow obstruction as in pulmonary stenosis.

In the presence of right-to-left shunting, air bubbles inadvertently injected into a vein can cross to the left side of the heart and enter the systemic arterial circulation, where they may cause stroke or myocardial ischemia.

## KEY POINTS: PATHOPHYSIOLOGIC EFFECTS OF CYANOTIC HEART DISEASE

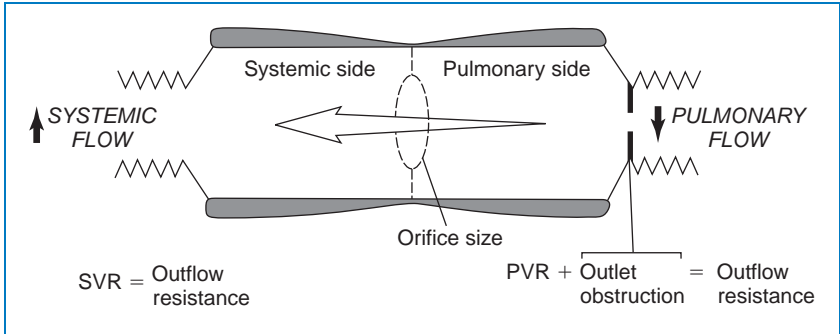


1. Polycythemia
2. Increased blood viscosity
3. Coagulopathy
4. Decreased tissue perfusion
5. End-organ ischemia

### 12. What is tetralogy of Fallot? What are tet spells?

The tetrad of anatomic findings described by Fallot for this congenital heart lesion are pulmonary stenosis, overriding aorta, ventricular septal defect, and right ventricular hypertrophy. The pulmonary stenosis has a dynamic component: the subvalvular right

ventricular outflow tract is muscular and contracts in response to inotropic stimuli (catecholamines). When such contraction occurs—or if SVR decreases significantly—less blood can flow into the pulmonary artery; thus more desaturated blood is shunted right to left across the ventricular septal defect into the left ventricle. An acute hypercyanotic episode, or tet spell, is the result (Figure 58-1).



**Figure 58-1.** In tetralogy of Fallot an acute increase in pulmonary outflow resistance causes an increase in right-to-left shunting of blood across the ventricular septal defect, resulting in a hypercyanotic spell. Treatment goals are to reduce pulmonary vascular resistance (*PVR*) and/or increase systemic vascular resistance (*SVR*). (Reprinted from Hickey PR, Wessel DL: *Anesthesia for treatment of congenital heart disease*. In Kaplan JA [ed]: *Cardiac Anesthesia*, 2nd ed. New York, Grune & Stratton, 1987, p 648, with permission from Elsevier.)

### 13. How are tet spells treated?

Hypercyanotic spells and their treatment illustrate the importance of the balance between SVR and PVR (see Figure 58-1). In the presence of a shunt such as a ventricular septal defect, blood flow will follow the path of least resistance. If SVR is lower than PVR or right ventricular outflow tract resistance, as is the case in a tet spell, blood will shunt right to left. Treatment is aimed toward alteration of the resistance relationships (Table 58-2).

**TABLE 58-2. TREATMENT OF HYPERCYANOTIC SPELLS**

Goal	Method
Relax the right ventricular outflow tract	$\beta$ -blockade with propranolol 0.1 mg/kg or esmolol 0.5–1 mg/kg
Increase SVR	Phenylephrine 5–10 mcg/kg Compress femoral arteries or abdominal aorta
Increase stroke volume	Intravenous fluid bolus
Improve oxygenation	Increase $FiO_2$

*FiO<sub>2</sub>*, Fractional concentration of oxygen in inspired gas; *SVR*, systemic vascular resistance.

### 14. What effects do anesthetic agents have on shunting in patients with cyanotic congenital heart disease?

Anesthetics can affect myocardial contractility, SVR, and PVR, and shunting can be influenced by any of these. Although it has been postulated that halothane or isoflurane may cause



hypercyanotic spells by decreasing SVR, studies have demonstrated that right-to-left shunting usually does not change significantly as long as ventilation and oxygenation are maintained. Nevertheless, as with any patient with cardiovascular disease, it is wise to avoid great changes in hemodynamic parameters by careful dosing, combining anesthetic drugs to achieve a balanced technique, and using muscle relaxants to facilitate lower anesthetic doses.

#### 15. What is the main problem associated with ventricular obstructive lesions?

Obstruction to ventricular outflow such as is observed in aortic stenosis, interrupted aortic arch, coarctation of the aorta, or pulmonary stenosis is associated with progressive deterioration of ventricular performance because of ventricular hypertrophy and myocardial ischemia. The hypertrophy develops because the ventricle must work extra hard to overcome the obstruction and maintain stroke volume. Eventually oxygen demand exceeds supply, and myocardial ischemia occurs. Fibrosis and ventricular failure follow. Neonates with left-sided obstructive lesions commonly present with ventricular failure and acidosis and have a high mortality rate.

### KEY POINTS: MYOCARDIAL EFFECTS OF VENTRICULAR OBSTRUCTION



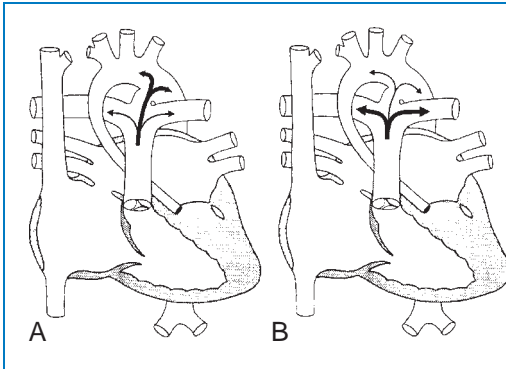
1. Ventricular hypertrophy
2. Subendocardial ischemia
3. Fibrosis and loss of contractile tissue
4. Ventricular failure

#### 16. What is a ductal-dependent lesion?

In some congenital heart defects a patent ductus arteriosus is the only route by which blood can flow into either the pulmonary artery or the systemic aorta. For example, neither tricuspid atresia nor pulmonary atresia allows direct blood flow from the right ventricle into the pulmonary artery. Instead blood must be shunted into the left side of the heart across an atrial or ventricular septal defect, flow into the aorta, and then flow through the ductus arteriosus into the pulmonary artery for gas exchange in the lungs. Similarly, the hypoplastic left heart has no direct blood flow from the heart to the aorta for systemic circulation; blood must flow from the pulmonary artery across the ductus arteriosus into the descending aorta. In these cases maintenance of ductal patency by infusion of prostaglandin  $E_1$  is essential to support life until a palliative or corrective procedure can be performed.

#### 17. Why can oxygen be dangerous in patients with single ventricle physiology?

Maintenance of high PVR is of key importance in providing adequate systemic (and coronary) perfusion in infants with single ventricle physiology such as hypoplastic left heart syndrome. Ventilation with subambient oxygen concentrations ( $FiO_2$  0.16 to 0.18) or hypercarbic mixtures are frequently used for this purpose. If 100% oxygen is inadvertently administered, the acute decrease in PVR can rapidly lead to pulmonary edema from high  $Q_p$  and to systemic hypotension and coronary ischemia from low  $Q_s$  (Figure 58-2).



**Figure 58-2.** Hypoplastic left heart syndrome. In single ventricle physiology, blood flow from the heart follows the path of least resistance. **A.** Maintenance of high pulmonary vascular resistance promotes flow across the ductus arteriosus to the aorta, thus supporting systemic and coronary perfusion. **B.** If a high  $\text{FiO}_2$  is inadvertently administered, most of the cardiac output may flow to the lungs at the expense of the systemic circulation.

**18. What is the best anesthetic technique for patients with congenital heart disease?**

There is no simple recipe for anesthetic management of the patient with congenital heart disease, and many rational approaches can be used. Choices depend on a thorough assessment of the patient's condition, the type of surgical procedure to be performed, and postoperative goals (e.g., mechanical ventilation vs. extubation). Review of cardiac catheterization and echocardiographic data will provide information concerning shunts, valve function, pulmonary hypertension, and ventricular function. It is necessary to understand the anatomy and pathophysiology of the patient's cardiac lesion so shunt balance, ventricular function, and rhythm can be better maintained; maintain good oxygenation and ventilation; and be familiar with the cardiovascular effects of anesthetic drugs and avoid cardiovascular depressants. A balanced technique using more than one anesthetic can often ensure adequate anesthesia while minimizing side effects. Be careful!

**19. How soon does cardiac function return to normal after surgical repair?**

Although restoration of improved cardiac function is a very rewarding aspect of pediatric cardiac surgery, some experts believe that normal function is rarely achieved. Long-term cardiac function following repair of congenital heart disease depends on the duration and severity of cardiac impairment before correction and on the surgical result. Myocardial ischemia and fibrosis associated with obstructive or cyanotic lesions are irreversible changes that can have permanent effects on cardiac function. Residual postoperative valvular stenosis or regurgitation may be associated with progression of cardiac disease. Inadequate myocardial preservation during cardiopulmonary bypass can injure the heart. Even years after straightforward repair of ventricular septal defects, cardiac function has been observed to be abnormal. Therefore, do not assume that cardiac function is normal in a child or adult who has undergone successful surgical repair of congenital heart disease in the past.

**20. What is subacute bacterial endocarditis and how can it be prevented?**

Turbulent or high-velocity blood flow in the heart associated with congenital heart defects can cause damage to the endocardium of the heart or valves. Damaged endocardium is rough and can be a nidus for infection in the presence of bacteremia or septicemia. Bacteremia can occur during dental or surgical procedures in the oral cavity, the alimentary tract, or the genitourinary system. Prophylactic administration of antibiotics during these procedures has been recommended for many years to prevent the development of endocarditis, but current recommendations of the American Heart Association have been revised to limit such prophylaxis to patients with complex cyanotic lesions.

## WEBSITES



American Heart Association  
<http://www.americanheart.org>

Yale University  
<http://www.med.yale.edu/intmed/cardio/chd/>

## SUGGESTED READINGS

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1. Friesen RH, Williams GD: Anesthetic management of children with pulmonary arterial hypertension [review]. *Pediatr Anesth* 18:208–216, 2008.
2. Hickey PR, Wessel DL: Anesthesia for treatment of congenital heart disease. In Kaplan JA [ed]: *Cardiac Anesthesia*, 2nd ed. New York, Grune & Stratton, 1987, p 648.
3. Laussen PC, Wessel DL: Anesthesia for congenital heart disease. In Gregory GA, editor: *Pediatric anesthesia*, ed 4, New York, Churchill Livingstone, 2002, pp 467–539.
4. Wilson W, Taubert KA, Gewitz M, et al: Prevention of infective endocarditis: guidelines from the American Heart Association. *Circulation* 116:1736–1754, 2007.

# FUNDAMENTALS OF OBSTETRIC ANESTHESIA

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## 1. What are the cardiovascular adaptations to pregnancy?

The major cardiovascular adaptations to pregnancy are summarized in [Table 59-1](#). During pregnancy cardiac examination reveals a shift of the apex cephalad and to the left. By the second half of pregnancy the third heart sound can commonly be detected on auscultation, and a fourth heart sound can be heard in up to 16% of patients. A grade I–II systolic murmur can often be heard secondary to increased blood flow. Chest x-ray film usually reveals an enlarged cardiac silhouette.

TABLE 59-1. CARDIOVASCULAR CHANGES DURING PREGNANCY

Oxygen consumption	Increase 30%–40%
Cardiac output	Increase 50% (plateaus by 28 weeks)
During labor	Additional 30%–40% increase
Immediately postpartum	75% increase above prelabor value
48 hours postpartum	At or below prelabor value
2 weeks postpartum	10% above prepregnant value (returns to normal by 12–24 weeks postpartum)
Stroke volume	Increase 25% (between 5 and 8 weeks)
Heart rate	Increase 25% (increases 15% by end of first trimester)
Mean arterial pressure	Decrease 15 mm Hg (normal by second trimester)
Systemic vascular resistance	Decrease 21%
Pulmonary vascular resistance	Decrease 34%
Central venous pressure	No change
Uterine blood flow	10% maternal cardiac output (600–700 ml/min) at term

## 2. What hematologic changes accompany pregnancy?

[Table 59-2](#) summarizes the hematologic changes of pregnancy. Plasma volume increases from 40 to 70 ml/kg near term, and blood volume increases by 1000 to 1500 ml. The relative anemia of pregnancy is caused by a relatively slower rise in red blood cell mass compared to plasma volume. Maternal anemia, usually the result of iron deficiency, occurs when the hemoglobin falls below 10 g or the hematocrit is <30%.

Pregnancy is associated with an increase in platelet activation and consumption and most coagulation factors. Because of this, parturients are hypercoagulable and at risk for thrombotic events (such as deep vein thrombosis and pulmonary embolism). The increase in

TABLE 59-2. HEMATOLOGIC CHANGES OF PREGNANCY

Plasma volume	Increase 15% during first trimester Increase 55% during second trimester
Red blood cell volume	Increase 30% at term
Blood volume	Increase 45%
Hemoglobin	Decrease 15% by midgestation (to $\approx 11.6$ g/dl)
Platelet count	No change or decrease
PT and PTT	Decreased
Fibrinogen	Increased
Fibrinolysis	Increased
Factors VII, VIII, IX, X, XII	Increased

*PTT*, Partial thromboplastin time; *PT*, prothrombin time.

platelet consumption is compensated for by an increase in platelet production; therefore, the platelet count is usually normal. Thrombocytopenia can occur in 0.9% of normal patients, although it is often associated with preeclampsia or hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome. The prothrombin time and partial thromboplastin times are shortened.

### 3. What pulmonary and respiratory changes occur with pregnancy?

Table 59-3 summarizes the respiratory changes of pregnancy. Pregnancy leads to capillary engorgement and edema of the respiratory tract. The mucosa also becomes friable, which may

TABLE 59-3. RESPIRATORY CHANGES AT TERM IN PREGNANCY

Minute ventilation	50% increase (can go up to 140% of pre pregnancy values in first stage of unmedicated labor and up to 200% in the second stage)
Alveolar ventilation	70% increase
Tidal volume	40% increase
Oxygen consumption	20% increase
Respiratory rate	15% increase
Dead space	No change
Lung compliance	No change
Residual volume	29% decrease
Vital capacity	No change
Total lung capacity	5% decrease
Functional residual capacity	15%–20% decrease
FEV <sub>1</sub>	No change

*FEV<sub>1</sub>*, Forced expiratory volume in 1 second.

lead to bleeding with manipulation or trauma. These changes in the airway and the enlarged breasts of the pregnant patient make laryngoscopy difficult. Adding to the problem, the increased oxygen consumption and decreased functional residual capacity (FRC) make the laboring patient more prone to hypoxia and rapid desaturation during apneic periods.

#### 4. What is a normal arterial blood gas in a pregnant patient?

See Table 59-4.

	pH	PaO <sub>2</sub>	PCO <sub>2</sub>	HCO <sub>3</sub>
Pregnant	7.41–7.44	85–103	27–33	21–27
Nonpregnant	7.35–7.45	60–100	35–45	24

#### 5. What gastrointestinal changes occur during pregnancy?

The upward displacement of the stomach by the expanding uterus shifts the gastroesophageal junction. This decreases the tone of the lower esophageal sphincter and predisposes the pregnant patient to reflux. The gravid uterus also increases intragastric pressure. These in combination make the parturient prone to regurgitation and aspiration. Gastric motility and emptying time can be prolonged, and the pregnant patient is always considered to have a full stomach. Standard preoperative aspiration prophylaxis includes metoclopramide, an H<sub>2</sub>-blocker, and a nonparticulate antacid.

#### 6. What renal changes are associated with pregnancy?

Renal plasma flow, glomerular filtration rate, and creatinine clearance increase by the fourth month of gestation. Blood urea nitrogen (BUN) and creatinine are decreased; normal values in pregnancy are 6 to 9 and 0.4 to 0.6 mg/dl, respectively. Glucosuria up to 10 g/dl and proteinuria up to 300 mg/dl are not abnormal. Anatomically the renal calyces, pelves, and ureters dilate beginning around 12 weeks' gestation. Urinary stasis contributes to the frequency of urinary tract infections seen in pregnancy.

#### 7. What changes occur in the central nervous system of pregnant patients?

Progesterone in both the plasma and cerebrospinal fluid increases tenfold to twentyfold in late pregnancy. Progesterone is sedating and potentiates the effects of volatile anesthetics. Pregnant patients are also more sensitive to local anesthetics.

#### 8. What hepatic alterations occur with pregnancy?

Liver size, blood flow, and liver morphology do not change during pregnancy. Lactate dehydrogenase, serum bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase (of placental origin) increase with pregnancy. Gallbladder emptying is slowed during pregnancy, and the bile tends to be concentrated, predisposing the pregnant patient to gallstone formation.

#### 9. What pregnancy-related changes occur to plasma proteins?

Plasma albumin concentrations decrease during pregnancy. Free fractions of protein-bound drugs increase with decreasing albumin levels. Total protein levels also decrease, as does maternal colloid osmotic pressure (by approximately 5 mm Hg). Plasma cholinesterase concentrations decrease by about 25% before delivery and 33% by day 3 after delivery but are probably not clinically significant.

**10. What is the uterine blood flow at term?**

Uterine blood flow is approximately 50 to 190 ml/min before pregnancy and reaches approximately 10% of maternal cardiac output (600 to 700 ml/min) at term. This places the pregnant patient at particular risk for hemorrhage in cases of uterine rupture, uterine atony, placenta previa, or placental abruption.

**11. What is aortocaval compression syndrome? How is it treated?**

Aortocaval compression is caused by the gravid uterus compressing the inferior vena cava and the aorta and manifests principally as hypotension and tachycardia. Aortic compression may lead to decreases in uterine and placental blood flow, resulting in nonreassuring fetal heart rate (FHR) changes. Aortocaval compression is prevented by uterine displacement (lateral position or a wedge under the right hip) to increase venous return. Symptoms may be treated with intravenous fluid administration, supplemental oxygen, and the use of appropriate vasopressor.

**12. What are the most important physiologic changes during labor?**

During active labor cardiac output increases by 40% above prelabor values. Immediately after delivery cardiac output sharply increases, reaching 75% of prelabor values. This is mainly caused by autotransfusion during uterine contractions, particularly after delivery of the placenta. Hyperventilation is common during active labor and may contribute to the preexisting respiratory alkalosis leading to uterine vasoconstriction and decreased placental perfusion, hypoxemia, and fetal distress. Regional anesthesia has been shown to decrease circulating maternal catecholamine levels and may attenuate the hemodynamic changes, hyperventilation, and stress response associated with active labor.

**13. How quickly do the physiologic alterations of pregnancy return to normal after delivery?**

Cardiac output rises immediately after delivery because of autotransfusion of 500 to 750 ml of blood from the uterus. Patients with pulmonary hypertension and stenotic valvular lesions are at a particular risk at this time. Cardiac output returns to slightly above prepregnancy values about 2 to 4 weeks after delivery.

- FRC and residual volume rapidly return to normal. Many of the pulmonary changes caused by mechanical compression by the gravid uterus resolve quickly. Alveolar ventilation returns to baseline by 4 weeks postpartum, and there is a rise in maternal  $PCO_2$  as the progesterone levels decrease.
- The *dilutional* anemia of pregnancy resolves, and the hematocrit returns to normal within 4 weeks secondary to a postpartum diuresis.
- Serum creatinine, glomerular filtration rate, and BUN return to normal levels in less than 3 weeks.
- Mechanical effects of the gravid uterus on the gastrointestinal system resolve about 2 to 3 days after delivery; however, gastric emptying may be delayed for several weeks as serum progesterone levels slowly decrease.

**14. Discuss the pathways involved in labor pain.**

Pain during the first stage of labor is caused by uterine contractions and cervical dilation. This visceral pain is transmitted via sympathetic fibers entering the dorsal horn of the spinal cord at T10–L1. As labor progresses and the fetal head descends into the pelvis and during stage 2, pain is transmitted from the pelvic floor, lower vagina, and perineum via the pudendal nerve, entering the spinal cord at S2–S4.

**15. What are the three stages of labor?**

- **Stage 1.** Cervical dilation and effacement. It begins with the onset of regular, painful contractions and ends when dilation of the cervix is complete (or 10 cm). The latent phase is characterized by slow cervical dilation and effacement. The active phase is defined as the period of progressive cervical dilation, which usually begins around 4 to 5 cm.

- **Stage 2.** The second stage ends with delivery of the neonate.
- **Stage 3.** The third stage ends with delivery of the placenta.

#### 16. Describe the anatomy of the placenta and umbilical cord.

The maternal side of the placenta is made up of a basal plate. Within the basal plate are spiral arteries, which are divisions from the uterine arteries, and veins. The fetal side is the chorionic plate, made up of villi surrounded by chorion. The space where these two surfaces meet is the intervillous space. The villi contain divisions from two umbilical arteries, which carry blood to the placenta, and divisions from the single umbilical vein, which carries the nutrient-rich blood back to the fetal circulation.

#### 17. What factors influence uteroplacental perfusion?

- **Aortocaval compression:** When lying supine, the gravid uterus compresses the abdominal aorta, decreasing uteroplacental perfusion (UPP).
- **Hypotension:** A fall in maternal mean arterial pressure  $>25$  mm Hg decreases uterine blood flow.
- **Increased uterine vascular resistance:** Increases in uterine vascular resistance occur during contractions and parturition. Other causes include intravenous ketamine ( $>1.5$  mg/kg), oxytocin administration, and conditions such as preeclampsia and abruptio placentae.
- **Maternal hypoxia, hypercarbia, and hypocarbia:** These are associated with decreased UPP.
- **Catecholamines:** Increased maternal catecholamine levels (e.g., laboring patients) decrease UPP.

#### 18. How should hypotension associated with spinal anesthesia be treated in a cesarean section or laboring patient?

Historically ephedrine had been the preferred agent for treating hypotension associated with regional anesthesia during pregnancy because it was thought that other agents decreased uteroplacental blood flow, whereas ephedrine did not. Recent studies show that doses of ephedrine large enough to maintain homeostasis after induction of spinal anesthesia may be detrimental to the fetus. Problems observed with ephedrine are related to the  $\beta$ -agonist activity that causes increased fetal metabolism and include dose-dependent fetal metabolic acidosis, tachycardia, and abnormal FHR variability. Phenylephrine, a pure  $\alpha$ -agonist, is as effective as ephedrine in restoring and maintaining maternal blood pressure. Phenylephrine does not appear to cause fetal acidosis even in large doses. However, it is important to note that all of these studies were done in healthy parturients at term undergoing cesarean section. It is reasonable to infer that ephedrine would cause similar metabolic derangements in laboring patients and those with high-risk pregnancies. The routine use of prophylactic ephedrine to prevent any adverse effects of maternal hypotension following spinal anesthesia for cesarean delivery is also not supported by systematic reviews of the literature.

#### 19. What is the role of intravenous fluid preloading before regional anesthesia for cesarean delivery?

Intravenous crystalloid or colloid preload may prevent hypotension associated with neuraxial anesthesia for cesarean delivery. However, under urgent circumstances block placement should not be delayed to administer a preset volume of fluid.

#### 20. How are drugs and other substances transported across the placenta?

Placental transfer is accomplished by simple diffusion, active transport, bulk flow, facilitated diffusion, and *breaks* in the chorionic membrane. Anesthetic compounds cross the placenta mostly by simple diffusion. Compounds that are low in molecular weight, small in spatial configuration, poorly ionized, and lipid soluble have high rates of placental transfer. Most anesthetic drugs are highly lipid soluble and have molecular weights  $<600$ , and for this reason their rates of placental transfer are high.



## 21. What methods are used to evaluate fetal well-being during labor?

Measurement of FHR and uterine activity is important. The baseline (FHR) is measured between contractions and is normally 110 to 160 beats/min. Fetal tachycardia (>160) may indicate fever, hypoxia, use of  $\beta$ -sympathomimetic agents, maternal hyperthyroidism, or fetal hypovolemia. Fetal bradycardia (<110) may be caused by hypoxia, complete heart block,  $\beta$ -blockers, local anesthetics, or hypothermia. The beat-to-beat variability is thought to represent an intact neurologic pathway in the fetus. Increased variability is seen with uterine contractions and maternal activity. Decreased variability can be seen with central nervous system depression, hypoxia, acidosis, sleep, narcotic use, vagal blockade, and magnesium therapy for preeclampsia. Absence of beat-to-beat variability, especially in the presence of FHR decelerations or bradycardia, is a particular concern for fetal acidosis.

## 22. What is the significance of fetal heart rate decelerations?

- Early decelerations in FHR are caused by head compressions (vagal stimulation), are uniform in shape, begin near the onset of a uterine contraction with its nadir at the same time as the peak of the contraction, and are benign.
- Variable decelerations are caused by umbilical cord compression and are nonuniform in shape. They are abrupt in onset and cessation. The decrease is >15 beats/min. They last longer than 15 seconds but less than 2 minutes. Although they usually do not reflect fetal acidosis, repetitive variable decelerations can lead to fetal hypoxia and acidosis.
- Late decelerations are caused by uteroplacental insufficiency. They are uniform in shape. The onset and return to baseline are gradual. They often begin just after the onset of a contraction, with their nadir and recovery after the peak and recovery of the contraction. These decelerations are associated with maternal hypotension, hypertension, diabetes, preeclampsia, or intrauterine growth retardation. These are ominous patterns and indicate that the fetus is unable to maintain normal oxygenation and pH in the face of decreased blood flow.

The treatment for nonreassuring neonatal heart rate changes involves administering oxygen to the mother, maintaining maternal blood pressure, and placing the parturient in the left uterine displacement position (Figure 59-1).

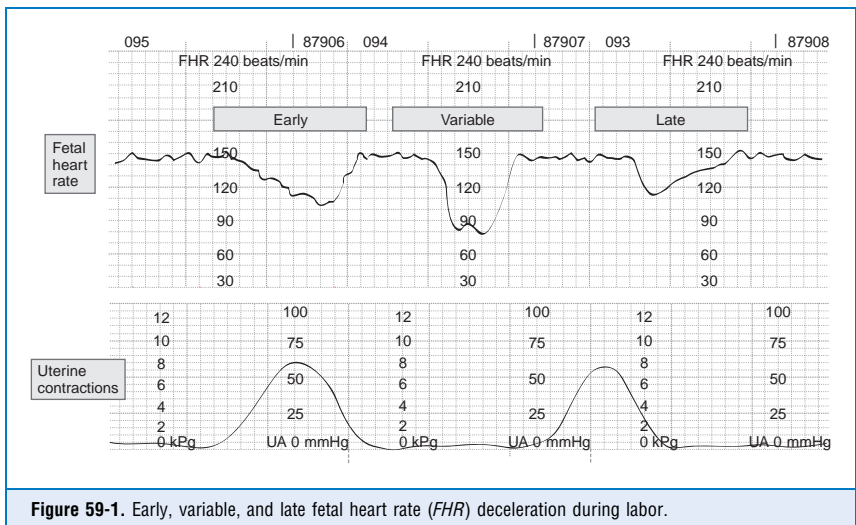


Figure 59-1. Early, variable, and late fetal heart rate (FHR) deceleration during labor.

**23. What is the Apgar score?**

The Apgar score is the most widely accepted and used system to evaluate the neonate, determine which neonates need resuscitation, and measure the success of resuscitation (Table 59-5). The score evaluates heart rate, respiratory effort, muscle tone, reflex irritability, and color, with heart rate and respiratory effort being the most important criteria. Each variable is given a score of 0 to 2, for a total score of 10. The Apgar score is measured at 1 and 5 minutes and then at 10 and 20 minutes as resuscitative efforts are continued. A score of 0 to 3 indicates a severely depressed neonate, whereas a score of 7 to 10 is considered normal.

**TABLE 59-5. APGAR SCORE**

Score	Heart Rate	Respiratory Effort	Muscle Tone	Reflex Irritability	Color
0	Absent	Apneic	Flaccid	No response	Pale or blue
1	<100	Irregular, shallow, or weak cry	Some flexion of extremities	Grimace or weak cry	Acrocyanosis
2	>100	Good and crying	Active motion	Sneeze, cough, or cry	Pink

**24. Describe the management of the pregnant patient undergoing nonobstetric surgery.**

Nonemergent surgery should be avoided to protect the developing fetus. If a procedure must be done, the second trimester is the safest time, avoiding organogenesis and minimizing the risk of preterm labor. Surgery during pregnancy increases perinatal mortality, and manipulation of the uterus should be minimized to decrease the risk of premature labor. The most common surgical condition during pregnancy is appendicitis, followed by torsion, rupture, or hemorrhage of ovarian cysts and cholecystectomy.

There is no evidence that any drug or technique is preferred over another as long as maternal oxygenation and perfusion are maintained. Nitrous oxide has been associated with deoxyribonucleic acid synthesis inhibition and probably should be avoided in the first trimester. If general anesthesia is chosen, the patient should receive an antacid regimen before rapid-sequence intubation with cricoid pressure. Use uterine displacement to avoid aortocaval compression. Treat hypotension with fluids and an appropriate vasopressor; an oxygen concentration of 100% is advisable to increase fetal oxygenation. When considering regional anesthesia, keep in mind the patient's altered responsiveness to local anesthetics. Fetal heart tones should be obtained before and after any procedure. Intraoperative FHR monitoring is rarely used before 26 weeks' gestation. The decision to use intraoperative FHR monitoring depends on maternal and fetal status, the procedure being performed, and the obstetric plan to act on abnormalities that occur. Since patients may be administered opioids, labor may not be recognized. After surgery the patient should be monitored for early onset of labor and tocolysis instituted in its presence.

## KEY POINTS: FUNDAMENTALS OF OBSTETRIC ANESTHESIA



1. Physiologic alterations in pregnancy of interest to the anesthesiologist include increases in cardiac output, heart rate, plasma volume, minute ventilation, and oxygen consumption; decreases in systemic vascular resistance; dilutional anemia; loss of FRC; and a hypercoagulable state.
2. Pregnant patients can pose airway management problems because of airway edema, large breasts that make laryngoscopy difficult, full stomachs rendering them prone to aspiration, and rapid oxygen desaturation caused by decreased FRC and increased oxygen consumption.
3. Pregnant patients are sensitive to both volatile and local anesthetics.
4. Nonemergent surgical procedures should be avoided if possible during pregnancy or ideally scheduled for the second trimester if necessary, and the patient should be monitored after surgery for the early onset of labor.

## WEBSITES



American College of Obstetricians and Gynecologists  
<http://www.acog.org>

American Society of Anesthesiologists  
<http://www.asahq.org>

## SUGGESTED READINGS

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# OBSTETRIC ANALGESIA AND ANESTHESIA

Ana M. Lobo, MD, MPH, and Joy L. Hawkins, MD

## 1. What are the most commonly used parenteral opioids for labor analgesia? Which side effects are of special concern to the parturient?

Table 60-1 summarizes commonly used parenteral opioids and their side effects. In general, intravenous medications help the parturient tolerate labor pain but do not provide complete analgesia. The incidence of side effects and efficacy of analgesia are dose dependent. Maternal sedation and nausea are common. Opioids easily cross the placenta and may cause a decrease in fetal heart rate variability. In addition, intravenous opioids may cause neonatal respiratory depression and neurobehavioral changes.

TABLE 60-1. INTRAVENOUS ANALGESICS FOR LABOR

Drug	Usual Dose	Onset	Duration	PCA Dosing
Meperidine	25–50 mg IV	5–10 minutes	2–3 hours	15 mg q10min
<i>Comments:</i> Normeperidine is an active metabolite that may last for 3 days; neonatal effects are most likely if delivery occurs between 1 and 4 hours after administration.				
Fentanyl	1–2 mc/kg IV	2–3 minutes	45 minutes	50 mc/kg q10min
<i>Comments:</i> Short acting, no active metabolites, potent respiratory depressant for mother, minimal sedation and nausea.				
Butorphanol	1–2 mg IV	5 minutes	2–3 hours	N/A
<i>Comments:</i> Sedating for mother, ceiling effect for both analgesia and respiratory depression, dysphoric reactions or withdrawal symptoms in opioid-dependent patients can occur.				
Nalbuphine	10 mg IV	5 minutes	2–3 hours	N/A
<i>Comments:</i> Similar profile as butorphanol.				
IV, Intravenously; N/A, not applicable; PCA, patient-controlled analgesia.				

## 2. What advantages does PCA offer over conventional intermittent bolus dosing?

Patient-controlled analgesia (PCA) has been associated with greater patient satisfaction, less risk of maternal respiratory depression, less need for antiemetic use, and better pain relief despite lower drug doses. PCA is especially useful if epidural anesthesia is contraindicated or not available. The most experience has been gained with meperidine and fentanyl using the regimens noted in Table 60-1.

### 3. Discuss the benefits of epidural analgesia for labor and delivery.

In most laboring women epidural analgesia provides the most effective pain relief and reduces maternal catecholamine levels, potentially improving uteroplacental perfusion. Epinephrine and norepinephrine secretion increase as a result of painful contractions and may prolong labor by decreasing uterine contractility through their  $\beta$ -agonist activity. Painful contractions may also lead to maternal hyperventilation and respiratory alkalosis, which in turn shifts the oxyhemoglobin dissociation curve to the left, decreasing delivery of oxygen to the fetus. Most important, the benefits of enhanced maternal well-being with adequate analgesia and the risk of posttraumatic stress symptoms caused by inadequate analgesia should not be underestimated.

### 4. What are the indications and contraindications for epidural analgesia during labor and delivery?

Relief of labor-induced pain is sufficient reason for placing an epidural catheter. *Analgesia* can be readily converted to *anesthesia* by increasing the local anesthetic concentration, thus facilitating forceps or cesarean delivery. Labor analgesia benefits patients with hypertension and some types of cardiac disease (e.g., mitral stenosis) because it blunts the hemodynamic effects that accompany uterine contractions (increased preload, tachycardia, increased systemic vascular resistance, hypertension, and hyperventilation). The contraindications to epidural anesthesia include patient refusal, coagulopathy, uncontrolled hemorrhage, and infection at the site of needle introduction. Relative contraindications include systemic maternal infection, elevated intracranial pressure, prior spinal instrumentation with hardware, and certain neurologic diseases.

### 5. Discuss the importance of a test dose and suggest an epidural test dose regimen. When and why is this regimen used?

The test dose is used to diagnose subarachnoid or intravenous placement of the epidural catheter, thereby preventing total spinal anesthesia or systemic toxicity from local anesthetics. A common test dose is 3 ml of 1.5% lidocaine (45 mg) with 1:200,000 epinephrine (15 mcg). If the test dose of local anesthetic is administered, subarachnoid, motor, and sensory block will appear within 3 to 5 minutes. If the test dose is injected intravenously (IV), tachycardia results within 45 seconds (increase in heart rate of 30 beats/min) because of the epinephrine additive. Every time an epidural catheter is injected, it is a test dose of sorts; always monitor for signs of possible intravenous or subarachnoid local anesthetic injection. Aspiration of the catheter may not be adequate to identify all intrathecal or intravascular catheters. If there is any doubt in the practitioner's mind about the exact location of the epidural catheter, the catheter should be removed and replaced.

### 6. What are the characteristics of the ideal local anesthetic for use in labor? Discuss the three most common local anesthetics used in obstetric anesthesia. How does epinephrine affect the action of local anesthetics?

The ideal local anesthetic for labor would have rapid onset of action, minimal risk of toxicity, minimal motor blockade with effective sensory blockade, and a minor effect on uterine activity and placental perfusion. Bupivacaine and ropivacaine are most commonly used for obstetric epidural analgesia. Lidocaine and chloroprocaine are most commonly used for obstetric surgical anesthesia.

Bupivacaine, an amide, is the most commonly used local anesthetic for obstetric analgesia. Pain relief after epidural injection is first noted by the patient after 10 minutes; 20 minutes is required to achieve peak effect. Analgesia usually lasts approximately 2 hours. Dilute solutions provide excellent sensory analgesia with minimal motor blockade. During early labor 0.125% bupivacaine or even lower concentrations is often adequate, whereas a 0.25% concentration may be required during the active phase of labor. Because bupivacaine is highly protein bound, its transplacental transfer is limited. Addition of epinephrine (1:200,000) to

bupivacaine speeds its onset and lengthens its duration of action but also increases the intensity of motor blockade (which is not desirable in laboring patients).

Lidocaine is also an amide local anesthetic used in concentrations of 0.75% to 1.5% for sensory analgesia, but it crosses the placenta more readily than bupivacaine and produces more motor block than bupivacaine; thus it is rarely used outside the operating room. Analgesia lasts approximately 45 to 90 minutes and is usually apparent within 10 minutes.

2-Chloroprocaine is an ester local anesthetic. Onset of analgesia is rapid and lasts approximately 40 minutes; this short duration limits its usefulness in labor. Chloroprocaine 3% is frequently used to increase the anesthetic level quickly for cesarean section or instrumental vaginal delivery. Chloroprocaine has a very short half-life in maternal and fetal blood because it is metabolized by plasma esterase; thus it may be the safest of the commonly used local anesthetics.

#### 7. Describe the properties and benefits of ropivacaine in obstetric anesthesia.

Ropivacaine is slightly less potent than bupivacaine; therefore concentrations of 0.1% to 0.2% are used during labor. Onset, duration, and sensory block are similar to equipotent doses of bupivacaine. Motor blockade is slightly less than bupivacaine and may be an advantage. It has less cardiotoxicity (if inadvertently injected intravenously) because it binds less avidly to sodium channels of cardiac conduction tissue. Ropivacaine costs significantly more than bupivacaine.

#### 8. Name three methods for administering epidural analgesia. State the concerns associated with each.

- **Intermittent injection** requires that the catheter be checked for migration into the subarachnoid space or a blood vessel via aspiration and a repeat test dose. After multiple injections the patient may develop intense motor blockade.
- Epidural analgesia may also be maintained by **continuous infusion** of dilute local anesthetic (with or without added opioid). The benefits of this method include:
  - Maintenance of a stable level of analgesia
  - Stable maternal hemodynamics
  - Improved patient satisfaction
- The patient should be assessed regularly for adequacy of analgesia and lack of motor blockade. The infusion pump should be different from that of intravenous infusion lines, and infusion tubing should be free of side ports to minimize the chance of accidental injection of other substances into the epidural space.
- With **patient-controlled epidural anesthesia (PCEA)**, the patient may deliver small incremental doses in addition to a programmed background infusion to control the level of analgesia. PCEA usually results in greater patient satisfaction and less total dosage of drug than other techniques. As with a continuous infusion, the patient should be checked frequently for degree of analgesia and motor blockade.

#### 9. Discuss the complications of epidural anesthesia and their treatments.

Hypotension (a decrease in systolic pressure of 20% to 30% from baseline) may accompany epidural local anesthetic administration and result in decreased uteroplacental perfusion and fetal distress. Hypotension results from sympathetic blockade, peripheral venodilation, and decreased venous return to the heart. Treatment includes volume expansion and placement of the mother in the full lateral position. Phenylephrine (50 to 100 mcg) or ephedrine (5 to 10 mg intravenously) should be administered if blood pressure does not promptly return to normal. In the absence of evidence of uteroplacental insufficiency, phenylephrine is currently the favored choice for many.

Limited spread or patchy blocks may occur as a result of septa within the epidural space, or the catheter may pass into spinal nerve foramina, similarly limiting spread.

Intravenous local anesthetic injection may produce dizziness, restlessness, tinnitus, seizures, and loss of consciousness. Cardiovascular (CV) collapse may follow central nervous

system (CNS) symptoms. Bupivacaine CV toxicity secondary to large intravenous doses is especially severe and may be fatal. To treat local anesthetic toxicity:

- Give the patient 100% oxygen and intubate if necessary (to oxygenate, hyperventilate, and protect the airway).
- Stop convulsions with a barbiturate or a benzodiazepine.
- Support blood pressure (intravenous fluids and pressors).
- Use cardiopulmonary resuscitation and advanced cardiac life support protocols as necessary.
- Treat bradycardia with atropine.
- Treat ventricular tachycardia with amiodarone.
- Treat ventricular fibrillation with vasopressin, epinephrine, and defibrillation.
- Consider administration of intralipid to act as a lipid “sink” to bind the local anesthetic and remove it from the maternal circulation.
- Deliver the fetus if an effective rhythm is not restored within 5 minutes so more effective cardiopulmonary resuscitation can be provided to the mother.

The incidence of unintentional dural puncture is about 1% to 8%. If cerebrospinal fluid (CSF) is noted, the needle may be removed, and the epidural catheter placed at an alternate interspace. Local anesthetic subsequently injected epidurally may pass into the subarachnoid space and result in a block that is unexpectedly high or dense. Alternatively the epidural catheter can be threaded through the dural hole at the time of puncture, and a continuous spinal anesthetic can be provided. Leaving the spinal catheter in place for 24 hours may decrease the incidence of headache.

The incidence of an unexpected high block or total spinal block is approximately 1 in 4500 lumbar epidurals during labor. Risk is minimized by aspirating the catheter and giving a test dose each time the catheter is bolused. The signs and symptoms of a total spinal block include hypotension, dyspnea, inability to speak, and loss of consciousness. Treatment includes intubation, oxygen administration, ventilation, and support of maternal circulation with pressors.

**10. Explain the mechanism of action of intrathecal and epidural opioids. What effect do they have on pain perception, sympathetic tone, sensation, and movement?**

Opioids administered intrathecally or epidurally provide excellent analgesia without appreciably affecting sympathetic tone, sensation, or voluntary motor function. Opioids given via these routes bind to presynaptic and postsynaptic receptor sites in the dorsal horn of the spinal cord (Rexed’s laminae I, II, and V), altering nociceptive transmission. Some of the effects of lipid-soluble opioids may be caused by their systemic absorption.

**11. What opioids are used to provide spinal and epidural analgesia during labor? Name their most common side effects. Do they provide adequate analgesia for labor and delivery when used alone?**

The most commonly used neuraxial (spinal and epidural) opioids are fentanyl and sufentanil (Table 60-2). Pruritus, nausea, and vomiting are the most common side effects; delayed respiratory depression is the most serious complication, although very uncommon in this

**TABLE 60-2. OPIOIDS USED TO PROVIDE INTRATHECAL (SPINAL) ANALGESIA DURING LABOR**

Drug	Dose
Fentanyl	25 mcg
Sufentanil	5 mcg
Morphine	0.25 mg
Meperidine	10 mg

population. Intrathecal or epidural opioids alone may provide adequate relief for the early stages of labor, but they are unreliable in producing adequate analgesia for the active phase of labor. Very high doses of epidural opioids are required, which leads to excessive side effects. Concurrent administration of local anesthetic is necessary for late cervical dilation and delivery of the infant.

**12. Is there a cause-and-effect relationship between epidural anesthesia and prolonged labor or operative delivery?**

No. This issue was highly controversial. It has been reported that epidural analgesia is associated with prolonged labor and increased operative delivery, but recent studies do not support this assertion. Although epidural labor analgesia may prolong the second stage by about 30 minutes, there appears to be no harm to mother or fetus, and the American College of Obstetricians and Gynecologists (ACOG) recommends allowing an extra hour of pushing for mothers with an epidural block in place. ACOG has stated that: "Neuraxial analgesia techniques are the most effective and least depressant treatments for labor pain . . . more recent studies have shown that epidural analgesia does not increase the risks of cesarean delivery."

**13. Relate the advantages and disadvantages of spinal anesthesia for cesarean section. Which drugs are frequently used in the technique?**

Spinal anesthesia produces a dense neural blockade; it is relatively easy to perform, has a rapid onset, and carries no risk of local anesthetic toxicity. The development of small-gauge, noncutting needles has significantly reduced the incidence of postdural-puncture headache (PDPH) to 1% or less. Hypotension can be treated by rapid hydration (1 L colloid or 1 to 2 L crystalloid), positioning to avoid aortocaval compression, and use of phenylephrine (50 to 100 mcg) or ephedrine (5 to 10 mg IV) if blood pressure does not improve with these measures. Commonly used drugs for spinal anesthesia are summarized in [Table 60-3](#).

**TABLE 60-3. DRUGS USED FOR SPINAL ANESTHESIA FOR CESAREAN SECTION**

	Dose	Duration (minutes)
Lidocaine	75 mg	45–75
Bupivacaine	11 mg	60–120
Tetracaine	7–10 mg	90–120
<b>Adjuvant Drugs</b>		
Epinephrine	200 mcg	
Morphine	0.1–0.3 mg	
Fentanyl	10–25 mcg	

**14. What are the advantages and disadvantages of cesarean section with epidural anesthesia vs. spinal anesthesia? What are the most commonly used local anesthetics?**

If epidural analgesia is used for pain relief during labor and delivery, higher concentrations of local anesthetics can provide surgical anesthesia. The local anesthetic should be given in increments, titrating to the desired sensory level. Titration of local anesthetic results in more controlled sympathetic blockade; thus the risk of hypotension and reduced uteroplacental flow may be decreased. Typically epidural anesthesia produces less intense motor and sensory blockade than spinal anesthesia.

Disadvantages of epidural anesthesia include slower onset, larger local anesthetic dose requirement, occasional patchy block unsuitable for surgery, and the risk of total spinal



anesthesia or systemic toxicity if the epidural catheter migrates subarachnoid or intravascular. Unintentional dural puncture may occur, and 50% to 85% of such patients experience headache. Drugs commonly used for cesarean section are 0.5% bupivacaine, 0.75% ropivacaine, 2% lidocaine, or 3% chloroprocaine. Epinephrine (1:200,000) may be added to prolong the duration of the block, decrease vascular absorption of the local anesthetic, and improve the quality of the block. The addition of epinephrine to a local anesthetic does not appear to affect uterine blood flow adversely, and it decreases the risk of maternal toxicity. Opioids enhance intraoperative analgesia and provide postoperative pain relief.

### 15. How is combined spinal/epidural anesthesia performed? What are its advantages?

The practitioner first finds the epidural space by loss-of-resistance technique with a Touhy needle. Subsequently a long (120 mm), small-gauge (24 to 27 G), noncutting spinal needle is advanced through the epidural needle until the dura is punctured and clear CSF is noted. A spinal dose of local anesthetic (plus narcotic, if desired) is injected into the subarachnoid space, and the spinal needle is removed. The epidural catheter is subsequently threaded into the epidural space. Small doses of spinal local anesthetics and opioids provide rapid and reliable analgesia for much of stage 1 labor. Epidural infusion of dilute local anesthetic and opioid will maintain analgesia. This technique does not increase the risk of PDPH over epidural analgesia alone.

## KEY POINTS: OBSTETRIC ANALGESIA AND ANESTHESIA



1. Opioids administered intravenously to the mother easily cross the placenta and may cause a decrease in fetal heart rate variability. In addition, intravenous opioids may cause neonatal respiratory depression and neurobehavioral changes.
2. Intravenous PCA has been associated with greater patient satisfaction, less risk of maternal respiratory depression, less need for antiemetic use, and better pain relief with lower drug doses.
3. In most laboring women epidural analgesia is effective and reduces maternal catecholamine levels, potentially improving uteroplacental perfusion. Pain management is an important component of obstetric care.
4. The contraindications to epidural anesthesia include patient refusal, coagulopathy, uncontrolled hemorrhage, and infection at the site of needle introduction. Relative contraindications include systemic maternal infection, increased intracranial pressure, back surgery with hardware placement, and certain neurologic diseases.
5. Bupivacaine, ropivacaine, lidocaine, and chloroprocaine are the most commonly used local anesthetics in obstetric anesthesia.
6. Spinal anesthesia for cesarean delivery produces dense sensory and motor blockade, is relatively easy to perform, has a rapid onset, and carries no risk of local anesthetic toxicity.

### 16. List the indications for general anesthesia for cesarean section.

- Extreme fetal distress (in the absence of a functioning epidural catheter)
- Significant coagulopathy
- Inadequate regional anesthesia
- Acute maternal hypovolemia/hemorrhage
- Patient refusal of regional anesthesia

### 17. What concerns the practitioner when administering general anesthesia for cesarean section? How is it performed?

The obstetric population is at greater risk for difficult intubation, rapid oxygen desaturation, and aspiration of gastric contents. The goal is to minimize maternal risk and neonatal depression. This goal is accomplished by following certain guidelines. After monitors are placed, while the patient is being preoxygenated, the abdomen is prepared and draped. When the obstetricians are scrubbed in and ready to make their skin incision, rapid-sequence induction with cricoid pressure is performed, and incision occurs after correct endotracheal tube placement is verified. Frequently used induction agents include thiopental, ketamine, propofol, or etomidate. Succinylcholine is the muscle relaxant of choice for most patients (1 to 1.5 mg/kg). To prevent maternal awareness until the neonate is delivered, a combination of 50% nitrous oxide in oxygen is used with a low end-tidal concentration of a halogenated agent (0.5 minimum alveolar concentration). Larger concentrations of a volatile agent may cause relaxation of the uterus and excessive bleeding.

After delivery of the child, the concentration of nitrous oxide is increased, and opioids are administered. Benzodiazepines and muscle relaxants may also be used at the practitioner's discretion. The concentration of the volatile agent is decreased if uterine atony appears to be a problem. Oxytocin (Pitocin) is also administered to facilitate uterine contraction. At the conclusion of the procedure the patient is extubated after thorough orogastric and airway suctioning and after the patient has demonstrated return of strength and mentation.

## WEBSITE



<http://www.acog.org>

## SUGGESTED READINGS

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# HIGH-RISK OBSTETRICS

Brenda A. Bucklin, MD

## 1. What is a high-risk pregnancy?

High-risk pregnancies include but are not limited to women with:

- Medical complications (e.g., preeclampsia, diabetes mellitus)
- Fetal complications (e.g., prematurity, intrauterine growth restriction, multiple gestations)
- Intrapartum complications (e.g., maternal fever, abnormal vaginal bleeding)

## 2. Describe the hypertensive disorders of pregnancy.

Hypertensive disorders occur in approximately 5% to 10% of all pregnancies. Preeclampsia, chronic hypertension, preeclampsia superimposed on chronic hypertension, and gestational hypertension are terms used to describe the hypertensive disorders of pregnancy. The term *pregnancy-induced hypertension* (PIH) is no longer used (Table 61-1).

TABLE 61-1. HYPERTENSIVE DISORDERS OF PREGNANCY\*

Type	Blood Pressure	Onset	Proteinuria
Preeclampsia	≥140/90 mm Hg	After 20 weeks' gestation	>300 mg/24hr
Chronic	≥140/90 mm Hg	Before 20 weeks' gestation Without resolution PP	Absent
Preeclampsia + chronic HTN	≥140/90 mm Hg	Before 20 weeks' gestation Sudden increase in HTN	Sudden increase
Gestational	≥140/90 mm Hg	After midpregnancy	Absent

\*National High Blood Pressure Working Group on High Blood Pressure in Pregnancy. Report of the national high blood pressure education program working group on high blood pressure in pregnancy. HTN, Hypertension; PP, postpartum.

## 3. What causes preeclampsia?

Preeclampsia is a disorder of unknown etiology. It is a systemic disorder with heterogeneous causes that are linked to maternal, paternal, fetal, and placental factors. In the first stage of the disease process abnormal placentation occurs in which the spiral arteries fail to dilate with or without atherosclerosis. This results in reduced placental perfusion and release of vasoactive substances.

## 4. What clinical findings are present in preeclampsia?

The principal features of preeclampsia include hypertension and proteinuria. Edema can be physiologic or pathologic and should not be used in the diagnosis of preeclampsia (see Table 61-1).

## 5. What conditions contribute to maternal and perinatal mortality in preeclampsia?

Complications result from cerebrovascular hemorrhage, stroke, renal or hepatic failures, liver hemorrhage, disseminated intravascular coagulation, abruptio placentae, and pulmonary edema. These complications occur more frequently in women who develop preeclampsia before 32 weeks' gestation and in those with preexisting medical comorbidities. Perinatal mortality most often results from prematurity.

## 6. What is HELLP syndrome?

HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) is a complication of preeclampsia. Patients develop a microangiopathic hemolytic anemia associated with thrombocytopenia and elevated liver enzymes. Ten to twenty percent of these patients will have normal blood pressure, making the diagnosis sometimes difficult. Although HELLP syndrome is not an indication itself for immediate cesarean delivery, delivery is the only definite treatment for preeclampsia. Patients who develop laboratory evidence of disseminated intravascular coagulation are delivered immediately, regardless of gestational age.

## 7. How is preeclampsia managed?

Magnesium sulfate is the drug of choice for seizure prophylaxis. Although magnesium has no substantial effect on blood pressure after a bolus dose and the mechanism for the anticonvulsant activity of magnesium is unknown, it attenuates the vascular responses to endogenous and exogenous pressor substances. It also dilates the vascular beds. Other anticonvulsants (e.g., phenytoin, diazepam) have been evaluated, but magnesium sulfate therapy is more effective in preventing recurrent seizures than either phenytoin or diazepam. The benefit of magnesium sulfate administration in women with mild disease is unclear. However, women with severe disease should receive magnesium sulfate prophylaxis during labor and after delivery. Acute severe hypertension should be treated to prevent cerebrovascular and cardiovascular complications. Blood pressures should not be *normalized*. However, blood pressures of at least 160/105 mm Hg should be treated with antihypertensive medications. Because uteroplacental perfusion is proportionate to blood pressure, precipitous decreases in blood pressure can cause fetal compromise.

Antihypertensive agents should be titrated. Although hydralazine is the most commonly administered agent, it was recently compared to intravenous labetalol or oral nifedipine in a metaanalysis of trials. In the systematic review labetalol or nifedipine therapies were as effective as hydralazine in controlling blood pressure with fewer side effects. Labetalol is representative of a class of drugs that act as competitive antagonists at both  $\alpha$ - and  $\beta$ -adrenergic receptors. Although systemic vascular resistance is reduced, cardiac output is maintained. Labetalol has also been shown to preserve uteroplacental perfusion. Hydralazine, an arteriolar vasodilator, remains a popular drug for patients with preeclampsia because it increases renal and uterine artery blood flow. The onset and duration are often unpredictable. Side effects include reflex tachycardia and ventricular dysrhythmias. Nifedipine is a calcium channel blocker that prevents the release of calcium, resulting in smooth muscle relaxation. Sodium nitroprusside is another alternative antihypertensive most often administered to patients with refractory hypertension and severe hypertension. Sodium nitroprusside administration requires placement of an arterial catheter to facilitate continuous assessment of maternal blood pressure. Advantages include a fast onset and short duration. It also preserves uteroplacental perfusion. Side effects include reflex tachycardia, cerebral vasodilation, and potential cyanide toxicity.

**8. What are the indications for invasive monitoring?**

In severe preeclampsia there is no proven benefit of invasive hemodynamic monitoring. Although the indications for invasive central monitoring remain controversial, most agree that the accepted indications include:

- Refractory hypertension.
- Pulmonary edema.
- Refractory oliguria unresponsive to fluid challenge.
- Severe cardiopulmonary disease (Table 61-2).

**TABLE 61-2. INDICATIONS FOR INVASIVE MONITORING IN PREECLAMPSIA**

Refractory pulmonary edema
Pulmonary edema
Refractory oliguria unresponsive to fluid challenge
Severe cardiopulmonary disease

**9. What potential problems may occur in patients receiving magnesium sulfate?**

The therapeutic range of magnesium sulfate is 4 to 8 mEq/L. As plasma concentrations increase, patients develop electrocardiogram changes with widening of the QRS complex and prolonged QT interval. Deep tendon reflexes are absent at 10 mEq/L; sinoatrial block and respiratory paralysis occur when concentrations are 15 mEq/L; cardiac arrest occurs at 25 mEq/L. In therapeutic doses magnesium sulfate increases sensitivity to muscle relaxants, especially nondepolarizing muscle relaxants. Because magnesium sulfate also crosses the placenta, newborns may demonstrate decreased muscle tone, respiratory depression, and apnea. Magnesium toxicity is treated with intravenous calcium.

**10. What are the anesthetic considerations in patients with preeclampsia?**

Before initiation of neuraxial anesthesia, evaluation of coagulation status is recommended. Because thrombocytopenia is the most common coagulopathy in preeclampsia, a screening platelet count is recommended. Although an arbitrary platelet count of 100,000 is often suggested, the actual platelet count safe for spinal or epidural placement is unknown.

Spinal anesthesia has been controversial in patients with severe preeclampsia because of the potential risk of sudden hypotension with rapid onset of sympathetic blockade, but there is growing support for its administration for cesarean delivery. It may be preferable to general anesthesia when the patient does not have an existing epidural catheter or there is insufficient time because of nonreassuring fetal heart rate tracing.

**11. What is eclampsia?**

Eclampsia is defined as peripartum convulsions and/or coma not caused by coincident neurologic disease. Eclampsia is usually preceded by preeclampsia. Symptoms of headache, visual disturbance, and epigastric pain often precede seizure activity. Seizure activity often begins with facial twitching and generalized tonic-clonic seizures developing within seconds.

**12. How are eclamptic seizures treated?**

Intrauterine resuscitation and maternal airway management are of overriding importance. The initial management of seizure activity includes:

- Supplemental oxygen
- Airway support vs. intubation

- Lateral positioning
- Sodium thiopental 50 to 100 mg (terminates seizure activity)
- Supplemental magnesium sulfate
- Intrauterine resuscitation

### 13. Discuss preterm labor.

Infants delivered between 20 and 37 weeks after the first day of the last menstrual period are defined as preterm. In the United States preterm delivery accounts for 69% to 83% of neonatal deaths. Preterm labor is associated with placental abruption, uterine abnormalities, multiple gestations, premature rupture of the membranes, urinary tract, systemic, or gynecologic infection.

### 14. What is the treatment of preterm labor?

Calcium channel blockers, magnesium sulfate, cyclooxygenase inhibitors and  $\beta$ -mimetic tocolytics have all been used to treat preterm labor. Nifedipine is being used more frequently because of its low incidence of significant maternal and fetal side effects and ease of administration.

### 15. Discuss antepartum hemorrhage.

Placenta previa, placental abruption, uterine rupture, and vasa previa are all causes of antepartum hemorrhage. Placental abruption is a separation of the placenta most often accompanied by vaginal bleeding, uterine tenderness, and increased uterine activity. Uterine rupture is a defect in the uterine wall that results in fetal distress and/or maternal hemorrhage. Vasa previa is of no threat to the mother; however, there is a velamentous insertion of the cord where the fetal vessels traverse the fetal membranes ahead of the presenting part. Rupture of these vessels can cause fetal exsanguination. Patients with antepartum hemorrhage are also at risk for postpartum hemorrhage. Underestimation of blood loss is a frequent problem in such cases.

### 16. What is placenta previa?

Placenta previa occurs when the placenta implants before the presenting part. Classification depends on the relationship between the cervical os and placenta. Several factors are associated with placenta previa: uterine trauma, multiparity, prior cesarean delivery or other uterine surgery, advanced maternal age, and a prior history of placenta previa. Painless vaginal bleeding occurs in the second or third trimester and is not related to any particular event. A lack of abdominal pain and no change in uterine activity differentiate it from placental abruption. The first episode of bleeding rarely causes shock or fetal compromise.

### 17. What is postpartum uterine atony? How is it managed?

Uterine atony is a failure of contraction and involution of the uterus. It can result in severe hemorrhage. It is frequently associated with the following conditions:

- Multiple gestations
- Macrosomia
- Polyhydramnios
- High parity
- Prolonged labor
- Chorioamnionitis
- Precipitous labor
- Augmented labor
- Tocolytic agents

Obstetric management includes bimanual compression, uterine massage, and uterotonics. Oxytocin is the first-line therapy. It is a synthetic hormone that is administered intravenously

(20 to 50 units/1000 ml crystalloid). Bolus administration (5 to 10 units intravenously) produces vasodilation that can result in hypotension in hypovolemic patients. Methylergonovine is an ergot alkaloid preparation and is administered intramuscularly in a dose of 0.2 mg. It is contraindicated in hypertensive disorders, peripheral vascular disease, and ischemic heart disease. 15-Methylprostaglandin  $F_{2\alpha}$  is administered intramyometrially or intramuscularly (250 mcg) for the treatment of refractory uterine atony. Side effects include bronchospasm, disturbed ventilation-perfusion ratios, increased intrapulmonary shunt fraction, and hypoxemia. Uterine atony refractory to these agents may require surgical ligation of arteries, embolization of arteries supplying the uterus, and hysterectomy.

**18. Discuss diabetes and its anesthetic considerations.**

Pregnant patients with diabetes are at risk for preeclampsia, polyhydramnios, fetal macrosomia, fetal malformations, and cesarean delivery. Pregestational diabetes is associated with preterm labor and delivery. Glycemic control and treatment of hypotension with nonglucose-containing crystalloids and ephedrine or phenylephrine are helpful in preserving fetal acid-base status during neuraxial anesthesia for labor and delivery.

**19. What causes disseminated intravascular coagulation in obstetric patients?**

Disseminated intravascular coagulation results from abnormal activation of the coagulation cascade with formation of large amounts of thrombin, depletion of coagulation factors, activation of the fibrinolytic system, and hemorrhage. In obstetrics, the most frequent causes are preeclampsia, sepsis, fetal demise, abruptio placentae, sepsis, and amniotic fluid embolism.

**20. What types of renal diseases are most frequently seen in obstetric patients?**

Two groups of disorders occur: glomerulopathies (nephritic and nephrotic syndromes) and tubulointerstitial diseases. Nephritic syndromes are disorders that involve necrotizing or inflammatory lesions. Nephrotic syndromes involve abnormal permeability to proteins. Tubulointerstitial disease is characterized by abnormal tubular function, resulting in abnormal urine composition and concentration.

**21. How is anesthetic management affected in patients with renal disease?**

Management is dependent on the extent of renal disease and severity of hypertension. Patients with mild-to-moderate disease, well-controlled hypertension, and stable renal function require minimal-to-no special considerations. However, patients with end-stage disease require careful monitoring of volume and cardiac status. In addition, these patients are at risk for hyperkalemia, hypoalbuminemia, hypertension, anemia, metabolic acidosis, hypocalcemia, and hyperphosphatemia.

**22. Which cardiac disease most commonly complicates pregnancy?**

Congenital heart disease is the most common cardiac disease in pregnant women in the United States. It accounts for approximately 60% to 80% of cardiac disease during pregnancy.

**23. How is congenital heart disease managed during pregnancy?**

Pulmonary artery catheterization is rarely required for most patients with congenital heart disease. Intrathecal opioid injections are good choices for labor analgesia when patients will not tolerate decreased systemic vascular resistance and decreased venous return. Epidural anesthesia is contraindicated in few, if any cardiac lesions, provided that the induction of anesthesia is slow and hemodynamic changes are treated promptly. Single-injection spinal for cesarean delivery are contraindicated in many patients with congenital heart disease.

## KEY POINTS: HIGH-RISK OBSTETRICS



1. Maternal morbidity and/or mortality from hypertensive disorders most often results from cerebrovascular and cardiovascular complications.
2. In preeclampsia hypertension should be treated, but blood pressure should not be *normalized*.
3. Indications for invasive central monitoring in preeclamptic patients include: (1) refractory hypertension, (2) pulmonary edema, (3) refractory oliguria unresponsive to fluid challenge, and (4) severe cardiopulmonary disease.
4. Uterine atony is the most common cause of postpartum hemorrhage and often results in substantial blood loss.

## WEBSITE



Society for Obstetric Anesthesia and Perinatology  
<http://www.soap.org>

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# GERIATRIC ANESTHESIA

*Gurdev S. Rai, MD*

## 1. What is geriatric anesthesia and why is it important?

- Geriatric anesthesia is defined as providing anesthetic care for patients older than 65 years old.
- The geriatric population of the United States exceeds 35 million people, 12% of the total population. This population accounts for 33% of all surgical procedures performed in the United States.
- Geriatric patients consume 50% of the U.S. Federal Health Care Budget.
- Their population is expected to double by the year 2050.

## 2. What are the overriding characteristics and principles governing age-related physiologic changes as they relate to anesthesia in geriatrics?

Basal function of most organ systems is relatively unchanged by the aging process per se, but the functional reserve and ability to compensate for physiologic stresses is reduced. However, because of the diversity of this population, it is difficult to predict the extent of age-related physiologic changes and reduction in functional reserve for any particular individual.

## 3. Review age-related changes to the cardiovascular system.

- Age-related wall thickening and stiffening of large elastic arteries reduces their compliance and increases afterload on the heart. These vascular changes can occur in the absence of atherosclerosis or hypertension and are independent predictors of mortality.
- Increased afterload (e.g., from hypertension) produces ventricular hypertrophy, leading to increases in wall stress, myocardial oxygen demand, and risk of ischemia.
- Diastolic dysfunction secondary to ventricular remodeling minimizes the ability to adjust stroke volume in response to changes in intravascular volume and tone.
- Stroke volume becomes more dependent on atrial preload for adequate end-diastolic volume.
- The atrium dilates as a result of impaired outflow secondary to ventricular remodeling, making the elderly more prone to atrial fibrillation. Fatty infiltration and fibrosis of myocardium manifests in conduction abnormalities and decreased heart rate variability.
- Down-regulation of  $\beta$ -adrenergic receptors magnifies the decreased ability of the heart to reach maximal cardiac output acutely in response to stress.

## 4. Describe age-related changes to the pulmonary system.

- Restrictive pulmonary changes are noted as increased thoracic stiffness increases the work of breathing and decreases maximal minute ventilation.
- Closing capacity surpasses functional residual capacity by age 65 years, increasing the risk of atelectasis.
- Decreased cough reflex, ciliary clearance, and compromised swallowing mechanics increase risk of perioperative aspiration and pneumonia.
- There is a centrally mediated decrease in ventilatory response to hypoxia and hypercapnia.
- Exposure time to environmental, genetic, and social factors increases the prevalence of lung diseases and further exaggerates the changes noted previously.

### 5. Discuss age-related changes to the nervous system.

- There is overall cerebral atrophy, decreased complexity of neuronal connections and decreased synthesis of neurotransmitters, increased fibrosis of peripheral sympathetic neurons, and impairment of cardiovascular reflexes.
- Decreased skeletal muscle innervation (and atrophy) results in decreased strength and fine motor control.
- There is increased sensitivity to all anesthetic agents.

### 6. How is baseline renal function impaired in the elderly?

There is progressive decrease in glomerular filtration rate (GFR) because of a decrease in renal blood flow and renal mass and diminishing tubular dysfunction, impairing sodium homeostasis and the ability to respond to acid loads. Under normal circumstances these have no real clinical implications other than subclinical hyponatremia. However, in the face of surgical stress, the failure to adapt to acute volume changes can lead to hemodynamic instability. Therefore meticulous attention needs to be paid to intraoperative fluid and electrolyte management in the elderly population.

### 7. How does serum creatinine change with aging?

Despite progressive decreases in GFR, because of an overall decrease in muscle mass in the elderly, serum creatinine should remain normal or decrease.

### 8. How do changes in renal function affect anesthetic management?

Decreases in GFR and renal blood flow lead to an increased risk for intraoperative fluid and electrolyte disturbances and an increased risk of acute renal failure. Intravascular volume must be replaced to maintain urine output at 0.5 ml/kg/hr or more. Moreover, many medications used intraoperatively and their metabolites that depend on renal clearance have prolonged elimination half-lives and longer durations of action. An example of these would be morphine and its metabolites, which, if not used with renal function in mind, can result in prolonged respiratory depression.

### 9. How is liver function affected by aging? What are some anesthetic implications?

- Liver mass, hepatic blood flow, and hepatic reserve decrease.
- Age-related loss of endoplasmic reticulum leads to decreased protein synthesis, including albumin. Thus the serum levels of protein-bound drugs increase.
- Because of the exceptional reserve of the liver, only in the presence of other comorbidities such as alcohol abuse and hepatitis are clinically relevant decreases in drug metabolism noted.

### 10. In what ways does body composition change with aging?

- Decreased basal metabolic rate leads to an overall increase in percentage of body fat.
- Muscle mass decreases with time, especially with inactivity.
- Total body water decreases by 20% to 30% with age, resulting in decreased total blood volume.

### 11. How do these changes in body composition affect anesthetic management?

- Increased body fat leads to an increased volume of distribution for lipid-soluble drugs. Thus elderly patients may have an extended elimination time and prolongation of effect.
- Loss of skeletal muscle leads to a decrease in maximal and resting oxygen consumption, a slightly lowered resting cardiac output, and diminished production of body heat (predisposing to hypothermia). Despite a smaller muscle mass, elderly patients are not more sensitive to muscle relaxants, probably because of fewer receptors at the neuromuscular junction.

- Decreased total body water leads to a smaller volume of distribution and higher-than-expected plasma concentrations of water-soluble drugs.
- Elderly patients may have a greater-than-anticipated response to drugs and thus appear to be more sensitive.

#### 12. Why are these patients prone to hypothermia?

Elderly patients have a reduced basal metabolic rate, produce less body heat, and have diminished reflex cutaneous vasoconstriction to prevent heat loss. Aging is also associated with a decrease in  $\beta$ -adrenergic receptors, which are integral to temperature homeostasis.

#### 13. What is the affect of aging on anesthetic requirements?

The minimum alveolar concentration for volatile anesthetics decreases 4% to 5% per decade after age 40. The alveolar concentration of a volatile anesthetic increases more rapidly because of decreased circulation time. The median effective dose ( $ED_{50}$ ) for intravenous agents decreases as well.

#### 14. How are the pharmacokinetics and quality of spinal anesthesia affected by age?

Elderly patients have decreased blood flow to the subarachnoid space, resulting in slower absorption of anesthetic solutions. They also have a smaller volume of cerebrospinal fluid, the specific gravity of which tends to be higher than that of younger patients. This leads to a higher final concentration for a given dose and may alter the spread of the anesthetic. Elderly patients may have accentuated degrees of lumbar lordosis and thoracic kyphosis, increasing cephalad spread and pooling in the thoracic segments. Thus one might see higher levels of spinal anesthesia accompanied by faster onset of action and prolonged duration. Older patients also have a lower incidence of postdural puncture headaches when compared with younger patients.

#### 15. Review the dynamics of epidural anesthesia change with age.

Older patients require a smaller local anesthetic dose to achieve the same level of block when compared with younger patients. This may be the result of narrowing of the intervertebral spaces.

#### 16. Do all elderly patients need extensive preoperative testing?

Preoperative testing should be tailored to the level of risk of planned surgery, underlying illnesses, and functional status. An electrocardiogram is recommended if the patient has had a recent episode of chest pain or ischemic equivalent, is at medium to high risk for cardiac complications during surgery, or is undergoing intermediate- or high-risk surgery. Appropriate laboratory testing should be determined by the patient's prior medical history, his or her medications, and the scope of the planned procedure. This topic is discussed further in Chapter 17.

#### 17. Is there a difference in outcome when performing regional vs. general anesthesia in the elderly?

Results of studies are mixed and depend on the outcome measured and the procedure. In repair of hip fractures, incidence of deep venous thrombosis, fatal pulmonary embolism, and 1 month mortality has been shown to be significantly reduced using regional anesthesia. On the other hand, other large studies of peripheral vascular surgeries have failed to consistently detect meaningful differences in outcome between elderly patients receiving epidural vs. general anesthetics. There is a theoretic benefit of improved graft patency with epidural anesthesia, but this has not been demonstrated consistently through clinical trials.

#### 18. What are the most common postoperative complications in elderly patients?

Adverse drug reactions are three times more likely in the elderly than young patients. Postoperative cognitive dysfunction (POCD) and delirium are very common among the elderly.

**KEY POINTS: GERIATRIC ANESTHESIA**

1. Implications of age-related changes on anesthetic management are profound, affecting almost every aspect of perioperative care.
2. Basal function of most organ systems is relatively unchanged by the aging process, but the functional reserve and ability to compensate for physiologic stress are reduced.
3. Not all elderly patients need an extensive preoperative workup; tailor it to their underlying illnesses and invasiveness of the surgery.
4. In general, anesthetic requirements are decreased in geriatric patients.
5. There is increased potential for a wide variety of postoperative complications in the elderly; POCD is arguably the most common.

**19. What is postoperative cognitive dysfunction and what are its risk factors?**

POCD is a disorder in thought processes, including memory, language comprehension, visuospatial abstraction, and attention. Risk factors include advanced age, lower educational level, alcohol use, a prior history of stroke, and Alzheimer's disease. Polypharmacy and delirium during hospitalization are also predictive of POCD.

The complexity of testing and lack of a standardized diagnostic battery of tests have challenged our understanding of POCD.

**20. What are the implications of postoperative cognitive dysfunction on patient mortality?**

The occurrence of POCD is associated with increased mortality during the first year after surgery. A rapid decline in cognitive function with a persistent course (greater than 3 months) further increases mortality in these patients. This is attributed to possible underlying health issues in patients with POCD, decreased compliance after surgery, and a higher rate of depression.

**21. What can anesthesiologists do to limit postoperative cognitive dysfunction in at-risk patients?**

There are not many well-powered studies laying out a plan for anesthetic management. We do know that POCD is not associated with any particular anesthetic technique and that deeper levels of anesthesia seem to be protective. There is also evidence that patient familiarity with the perioperative experience can be helpful. Other studies have hinted that involving a geriatrician in the preoperative evaluation of elderly patients might decrease the incidence of POCD. The most appropriate management would limit the use of drugs already associated with delirium in the elderly. These include but are not limited to long-acting opiates, benzodiazepines, and anticholinergic medications. It would also be appropriate to continuously reevaluate the elderly patient's list of medications with the purpose of eliminating unnecessary medications and considering undesirable synergistic effects.

**22. Is age itself a predictor of perioperative mortality in the elderly?**

Age itself has proven to be a poor predictor of mortality; more predictive risk factors include the following:

- Emergent abdominal or thoracic surgery
- A low preoperative albumin level (reflective of overall nutritional status)
- The number and severity of coexisting diseases
- POCD
- Lack of exercise tolerance and increased frailty

## WEBSITES



American Society of Anesthesiologists' Syllabus on Geriatric Anesthesia  
<http://www.asahq.org/clinical/geriatrics/syllabus.htm>

American College of Cardiology/American Heart Association Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery  
<http://www.acc.org/clinical/guidelines/perio/dirIndex.htm>

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# SEDATION AND ANESTHESIA OUTSIDE THE OPERATING ROOM

Mark H. Chandler, MD

## 1. What procedures outside the operating room require sedation or general anesthesia?

- Radiologic procedures, including computed tomography, magnetic resonance imaging (MRI), and interventional radiology; often a lack of patient cooperation necessitates the need for anesthesia assistance
- Cardiac catheterizations, insertion of implantable cardiac defibrillators, coronary arteriography, radiofrequency ablation, and cardioversions
- Surgical procedures in office settings
- Extracorporeal shock-wave lithotripsy and cystoscopy
- Upper and lower gastrointestinal endoscopy, liver biopsy, and endoscopic retrograde cholangiopancreatography
- Therapeutic radiation
- Electroconvulsive therapy
- Any number of pediatric procedures
- Invasive procedures outside the operating room, including central venous line insertion, percutaneous tracheostomy, diagnostic peritoneal lavage, thoracocentesis, pericardiocentesis, tube thoracotomy, vascular cut down, and bronchoscopy
- Emergency airway management anywhere in the hospital
- Anesthesia in military settings, including on the battlefield

## 2. What equipment and standards are necessary for safely conducting an anesthetic outside the operating room?

- A reliable source of oxygen with a backup supply (e.g., green oxygen E-cylinder)
- Suction
- If inhalation anesthetics are to be used, an anesthesia machine complete with scavenging capabilities
- A self-inflating hand resuscitator (Ambu) bag capable of delivering at least 90% oxygen
- Standard anesthetic drugs, airway equipment, and monitoring necessary for the intended anesthetic and the subsequent transport
- Sufficient electrical outlets, including clearly labeled emergency electrical outlets
- Illumination, including battery-powered backup illumination (not simply a laryngoscope)
- An emergency cart with a defibrillator, emergency drugs, and other equipment adequate to provide cardiopulmonary resuscitation
- Staff trained to support the anesthesiologist and transport the patient and a reliable means of two-way communication to request assistance
- Appropriate postanesthetic management

This can be remembered with the mnemonic **MAO IS SAME PEST**:

**M** = Machine (with scavenger)

**A** = Ambu bag

**O** = Oxygen (with backup supply)

**I** = Illumination

**S** = Suction

**S** = Space

- A = Anesthetic drugs and equipment
- M = Monitors
- E = Electricity
- P = Postanesthesia care unit
- E = Emergency cart
- S = Staff
- T = Telephone

### 3. What monitoring is necessary for administration of any anesthetic, regardless of whether it is in the operating room or elsewhere?

The American Society of Anesthesiologists (ASA) has established two basic monitoring standards for all anesthesia care, regardless of where it is administered:

1. Qualified anesthesia personnel must be present during the administration of any general anesthetics, regional anesthetics, and monitored anesthesia care.
2. Oxygenation, ventilation, circulation, and temperature shall be continually evaluated in any patient undergoing an anesthetic. Specifically the ASA requires the following:
  - **Oxygenation:** During all anesthetics a quantitative method of assessing oxygenation such as pulse oximetry shall be used. When using an anesthesia machine, an oxygen analyzer with a low oxygen concentration limit alarm shall be used.
  - **Ventilation:** At the very least, all patients undergoing an anesthetic will be assessed for qualitative clinical signs of ventilation such as observed chest excursion, movement of the reservoir breathing bag, or auscultation of breath sounds. When an endotracheal tube or laryngeal mask airway is inserted, its correct positioning must be verified by identification of carbon dioxide in the expired gas, and carbon dioxide must be monitored with capnography or capnometry.
  - **Circulation:** Every patient receiving anesthesia shall have an electrocardiogram (ECG) continuously displayed throughout the anesthetic and shall have blood pressure and heart rate evaluated at least every 5 minutes. In addition, every patient receiving general anesthesia will have circulatory function continually evaluated by one of the following methods: palpation of a pulse, auscultation of heart sounds, monitoring of a tracing of intra-arterial pressure, or pulse oximetry.
  - **Body temperature:** Whenever clinically significant changes in body temperature are expected, anticipated, or suspected, a patient receiving anesthesia shall have temperature monitored.

### 4. How might anesthesiologists be involved in establishing standards for sedation and analgesia conducted by nonanesthesiologists?

Given the rising cost of health care and the expense of operating room time, more and more procedures are now being performed in other areas of the hospital with nonanesthesiologists administering sedation and analgesia. Although this trend may help contain costs, it poses safety concerns. Anesthesiologists possess unique knowledge and expertise regarding the use of various pharmacologic agents and in the management of patients undergoing sedation and analgesia. For these reasons anesthesiologists are frequently called on (and indeed, necessary) to help establish hospital policies and procedures regarding sedation and analgesia by nonanesthesiologists.

### 5. Explain conscious sedation and the continuum of depth of anesthesia.

The ASA Task Force on Sedation and Analgesia by Nonanesthesiologists states that sedation and analgesia comprise a continuum of states ranging from minimal sedation to general anesthesia. Understanding the concept of the continuum of anesthesia is a critical first step for nonanesthesiologists to administer sedation and analgesia. The term *conscious sedation*, which is often used by nonanesthesiologists to refer to sedation administered in settings other than the operating room, is considered *moderate sedation/analgesia* and is defined in [Table 63-1](#).

TABLE 63-1. DEFINITION OF GENERAL ANESTHESIA AND LEVELS OF SEDATION/ANALGESIA\*

	Minimal Sedation (Anxiolysis)	Moderate Sedation/Analgesia (Conscious Sedation)	Deep Sedation/Analgesia	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response <sup>†</sup> to verbal or tactile stimulation	Purposeful response <sup>†</sup> following repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Adapted from American Society of Anesthesiologists, Task Force on Sedation and Analgesia by Nonanesthesiologists: Practice guidelines for sedation and analgesia by non-anesthesiologists, *Anesthesiology* 96:1004–1017, 2002.

\*Monitored anesthesia care does not describe the continuum of depth of sedation; rather it describes "a specific anesthesia service in which an anesthesiologist has been requested to participate in the care of a patient undergoing a diagnostic or therapeutic procedure."

<sup>†</sup>Reflex withdrawal from a painful stimulus is not considered a purposeful response.

## 6. What are some of the requirements for the administration of moderate sedation by nonanesthesiologists?

Not surprisingly the Joint Commission, an accrediting agency, makes no distinction between the general perioperative requirements for the administration of anesthesia in the operating room and the administration of moderate sedation such as might be delivered by nonanesthesiologists outside of the operating room. These requirements are as follows:

- A presedation or preanesthesia assessment must be performed for each patient before beginning sedation or anesthesia.
- Before undergoing anesthesia or sedation, each patient must be provided preprocedural treatment, services, and education according to his or her plan of care.
- Before administering sedating medications, a licensed independent practitioner must plan, or must concur with the plan, for sedation or anesthesia.
- A sufficient number of qualified staff must be on hand to evaluate the patient, provide sedation/anesthesia, help with the procedure, and monitor and recover the patient.
- Individuals administering sedation or anesthesia must be qualified and have credentials to manage and rescue patients at whatever level is achieved, either intentionally or unintentionally. Thus a practitioner administering *deep sedation/analgesia* to a patient



must be prepared for the patient to slip into general anesthesia, during which time the patient may require intubation, positive-pressure ventilation, and cardiovascular stabilization.

- Each patient's physiologic status (oxygenation, ventilation, and circulation) is monitored continuously during administration of sedation or anesthesia.
- The patient's postprocedure physiologic status is assessed as the patient recovers from sedation or anesthesia.

#### 7. Is it advisable to have nonanesthesiologists administer *deep sedation*?

Because of the possibility of slipping into a deeper level of sedation/analgesia, the ASA recommends that privileges to administer deep sedation should only be granted to practitioners who are qualified to administer general anesthesia.

#### 8. What is dexmedetomidine and what role does it serve in moderate sedation?

Dexmedetomidine (Precedex) is a relatively new, highly selective  $\alpha_2$ -agonist that has been shown to have excellent sedative and analgesic effects. The hypnotic effect of dexmedetomidine is thought to be from hyperpolarizing nonadrenergic neurons in the locus cereleus. Among the many qualities that make dexmedetomidine an excellent sedative for moderate sedation is that it has a predictable and stable hemodynamic effect, does not cause respiratory depression, and potentiates opioids and other sedatives. Moreover, when properly dosed, sedated patients are quickly aroused and oriented after the medication is discontinued, making it an ideal sedative for neurologic procedures and in the intensive care unit. Because it is also an antisialagogue, dexmedetomidine is especially favored in the setting of awake fiber-optic intubations, creating a dry field for the anesthesiologist. Its cost relative to other sedative medications has probably limited greater use.

#### 9. Why is soluble contrast media important to anesthesiologists?

Soluble contrast media have been used for years as a tool to aid radiologists in various radiologic studies. These media contain iodine, which, with its high atomic number (53), is particularly effective at absorbing x-rays. Despite higher costs, nonionized contrast media have recently begun to replace the older, toxic, hyperosmolar contrast media, thus significantly diminishing the occurrence of side effects. Nonetheless, side effects still do occur, ranging from fairly mild to severe life-threatening anaphylactic reactions. Most often these reactions occur within the first 5 to 10 minutes following the injection of contrast media. Thus it is advisable to keep the patient under close watch for at least 20 minutes following a contrast injection.

#### 10. Besides anaphylaxis, what is a major risk with regard to contrast media?

Renal failure is a well-documented, severe reaction long associated with soluble contrast media, particularly in patients with disorders predisposing them to renal failure such as renal disease, diabetes, jaundice, multiple myeloma, hypovolemia and diminished renal blood flow from severe cardiac or vascular disease. Adequate hydration is absolutely necessary to decrease the impact on the patient. Furthermore, the necessity of the contrast study should always be considered. Particular caution must be used in patients taking metformin since renal failure in these patients can lead to severe, life-threatening lactic acidosis. For this reason it is recommended that metformin be held for 48 hours before performing any radiologic study in which contrast media are to be used.

#### 11. Are there specific steps that can be taken to avoid and treat contrast media reactions?

Patients who have had adverse reactions to contrast media are at greater risk for more severe reactions with subsequent exposures. This risk can be somewhat mitigated by pretreatment

with 50 mg of prednisolone the night before and the morning of surgery and 50 mg of intravenous (IV) diphenhydramine immediately before the procedure. If a severe reaction occurs during the procedure, treatment is supportive: oxygen, IV steroids, and treatment of the patient's specific reaction (e.g., IV fluid and vasopressors for severe hypotension). Because reactions such as these are possible, all radiologic suites must be completely equipped with defibrillation and resuscitation equipment.

## 12. What are some of the more common manifestations of the reactions to soluble contrast media?

See Table 63-2.

Mild	Moderate	Life-Threatening
Nausea	Vomiting	Glottic edema/bronchospasm
Headache	Rigors	Pulmonary edema
Perception of warmth	Feeling faint	Life-threatening arrhythmias
Mild urticaria	Chest pain	Cardiac arrest
	Severe urticaria	Seizures/unconsciousness
	Bronchospasm	Renal failure
	Dyspnea	
	Abdominal pain	
	Arrhythmias	

## 13. How is radiation exposure measured?

The roentgen equivalent in humans (rem) is a measure of *equivalent dose* and relates the absorbed radiation dose in human tissue to the effective biologic damage of the radiation. Equivalent doses are often expressed in terms of thousandths of a rem, or mrem. The Centers for Disease Control and Prevention recommends that the general adult public limit their annual radiation dose to 5000 mrem/year. The equivalent doses from various sources are listed in Table 63-3.

Medical Procedures	Equivalent Doses
Chest x-ray	8 mrem
Extremities x-ray	1 mrem
Dental x-ray	10 mrem
Cervical spine x-ray	22 mrem
Pelvis x-ray	44 mrem
Upper gastrointestinal series	245 mrem
Lower gastrointestinal series	405 mrem
Computed tomography (whole body)	1100 mrem
<b>Background Sources of Radiation</b>	
Coast-to-coast airplane roundtrip	5 mrem
Average U.S. cosmic radiation	27 mrem/year

(continued)

**TABLE 63-3. EQUIVALENT RADIATION DOSES FOR MEDICAL PROCEDURES**  
(continued)

Medical Procedures	Equivalent Doses
Average U.S. terrestrial radiation	28 mrem/year
Average dose to U.S. public from all sources	360 mrem/year
<b>Recommended Radiation Exposure Limits</b>	
Occupational dose limit	5000 mrem/year
Occupational exposure limit for minors	500 mrem/year
Occupational exposure limits for pregnant females	500 mrem/gestation

*mrem*, Roentgen equivalent in humans (in thousandths).

#### 14. How can anesthesiologists protect themselves from radiation exposure?

Most institutions abide by the ALARA philosophy when it comes to protecting their workers: radiation exposure should be kept As Low As Reasonably Achievable. There are three basic strategies to the ALARA philosophy:

- Maximize the distance to the source:** Newton's inverse square law, which applies to any point source that spreads its influence in all directions (such as light, sound, gravitational field) tells us that the intensity of the radiation at a given radius is the source strength divided by the sphere area. Or, put more plainly, the intensity ( $I$ ) of radiation is inversely related to the square of distance ( $d$ ) from the source:

$$I = 1/d^2$$

Thus increasing the distance from an x-ray machine or a fluoroscope when in use can profoundly affect the intensity of radiation exposure. Six feet of air provides the equivalent protection of 9 inches of concrete or 2.5 mm of lead.

- Minimize the time of exposure:** Most medical occupational radiation exposure comes from x-rays scattered by both the patient and surrounding equipment. Obviously this scatter occurs only when the machine is on. A person's radiation exposure is directly proportional to the length of exposure; thus every reasonable effort to limit the time of exposure is beneficial.
- Use shields:** Most aprons contain the equivalent of 0.25 to 0.5 mm of lead, which is effective at blocking most scattered radiation in medical settings. Uncovered areas such as the lens of the eye still run the risk of radiation exposure. Other shields such as concrete walls and portable barriers should be used whenever possible. Lead aprons should be x-rayed periodically to determine if they are still effective barriers because they are known to deteriorate with lime particularly if mishandled.

#### 15. Define the unique problems associated with providing an anesthetic in the magnetic resonance imaging suite.

Difficulties in providing a safe anesthetic in the MRI suite arise from using a powerful magnetic field. The MRI suite is often located in a remote, isolated area of the hospital. The cylindrical large-bore magnet surrounding the body limits access to the patient. Ferromagnetic objects may be hurled toward the scanner, creating lethal projectiles. Large metal objects may interfere with the quality of the image. Many electronic instruments may not function normally when placed in close proximity to the magnet. Implantable ferrous magnetic devices such as older cerebrovascular clips, surgical clips, and pacemakers, are hazardous.

## 16. What modifications in the anesthesia machine, ventilator, and monitoring equipment must be made to provide an anesthetic in the magnetic resonance imaging suite?

All monitoring equipment is affected by the magnetic fields generated by the MRI machine. Monitors with ferromagnetic components must be located outside the magnetic field. The distance depends on the strength of the field and shielding in the suite. If the anesthesia machine, monitoring equipment, and ventilator are located several meters from the patient, long monitoring leads and ventilation tubing, with a large compressible volume in the circuit, are required, and risk of disconnection is increased. Anesthetic and monitoring equipment with nonferromagnetic components is available and allows much closer proximity to the patient and MRI machine. Many newer institutions have anesthesia machines built into the structure of the MRI suite, which allows easier and safer conduction of anesthesia. Nonferromagnetic ventilators are also available.

The lack of availability of a piped oxygen source into the MRI suite in older institutions may be a significant problem, because many standard gas cylinders are ferromagnetic and may become dangerous projectiles when introduced into the magnetic environment. Aluminum cylinders are a safe alternative, but they cannot be recharged because metal fatigue from repeated pressurization predisposes these tanks to rupture. Ferromagnetic cylinders can be distinguished from aluminum cylinders in that the whole ferromagnetic cylinder is painted with the identification color of the gas contained therein (e.g., green for oxygen, yellow for air). Aluminum cylinders have only the neck of the cylinder painted with the appropriate color.

Many MRI manufacturers now produce ECGs and respiratory monitors compatible with their equipment. Unfortunately they tend to provide limited qualitative ECGs (as for detecting ischemic changes), but for rhythm and heart rate they suffice. If such equipment is not available, modification of existing equipment is necessary because, when unshielded ferromagnetic wiring is used, the ECG demonstrates artifact, particularly in the early T waves and late ST segments, mimicking the changes seen in hyperkalemia and pericarditis. The rapidly changing magnetic fields also may cause spikes in the ECG trace, which may falsely elevate the heart rate display. Positioning the electrodes as close as possible to the center of the magnetic field, keeping the limb leads close together and in the same plane, and braiding or twisting the leads help to minimize the changes produced by the magnetic field.

When using pulse oximetry, signal distortion is also a risk; the use of nonferromagnetic probes and shielded wiring minimizes the artifact. To function properly the capnograph should be placed outside of the magnetic field. The long connecting tubing causes significant lags in alarm times. The waveform may show a prolonged upslope, even in patients with healthy lungs. However, trends and respiratory rate may be observed. Noninvasive blood pressure readings may be obtained if all ferrous connections are removed from the cuff and tubing. Invasive pressure readings may be obtained if the signal from the pressure transducer is passed through a radiofrequency filter. Dampening of the waveform is minimized by resting the transducer within 1.5 m of the patient.

## KEY POINTS: ANESTHESIA OUTSIDE THE OPERATING ROOM



1. Anesthesiologists are increasingly asked to administer anesthesia in nontraditional settings. Regardless of where an anesthetic is administered, the same standards exist for safety, monitors, equipment, and personnel.
2. Whenever a patient undergoes an anesthetic in any medical setting, qualified anesthesia personnel must be present, and oxygenation, ventilation, circulation, and temperature must be monitored.

3. Those medical professionals who administer moderate sedation (“conscious sedation”) must be well trained, prepared to evaluate and monitor their patient closely, and ready to manage their patient if their sedation and analgesia become deeper than intended.
4. Dexmedetomidine is a highly selective  $\alpha_2$ -agonist that has been shown to have excellent sedative and analgesic effects in a variety of settings.
5. Soluble contrast media can cause a whole range of reactions in patients, from the very mild such as urticaria and headaches to the severe and life threatening such as anaphylaxis, renal failure, and lactic acidosis.
6. Medical professionals keep their radiation exposure as low as reasonably achievable (ALARA), and below the CDC’s recommendation of less than 5000 mrem/year, by maximizing their distance to x-ray and fluoroscopes when in use, minimizing their time of exposure, and using shields.
7. Administering anesthesia to a patient undergoing an MRI poses several challenges, not the least of which is that any ferromagnetic object can become a projectile and that most monitors are affected by the powerful magnetic field.

## WEBSITES



American Society of Anesthesiologists  
<http://www.asahq.org>

American Society of Anesthesiologists  
<http://www.asahq.org/publicationsAndServices/standards/20.pdf>

American Society of Anesthesiologists  
<http://www.asahq.org/publicationsAndServices/standards/02.pdf>

Radiation Information Network of Idaho State University  
<http://www.physics.isu.edu/radinf>

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# PACEMAKERS AND INTERNAL CARDIOVERTER DEFIBRILLATORS

*Christopher M. Lowery, MD*

## 1. Explain the letters in the NBG coding system for pacemakers.

The first three letters refer to chamber paced, chamber sensed, and response to sensed events. The fourth letter generally refers to programmability and rate responsiveness. The fifth letter is rarely used (Table 64-1).

TABLE 64-1. CODING SYSTEM DESCRIBING CARDIAC PACEMAKERS

I Chamber Paced	II Chamber Sensed	III Mode of Response	IV Programmability	V Antitachycardiac Functions
O = none	O = none	O = none	O = none	O = none
A = atrium	A = atrium	T = triggered	P = simple programmable	P = pacing
V = ventricle	V = ventricle	I = inhibited	M = multiprogrammable	S = shock
D = dual (A + V)	D = dual (A + V)	D = dual (T + I)	R = rate responsive	D = dual (P + S)

## 2. What does AOO, VOO, or DOO mode mean?

AOO means pacing in the atrium alone, VOO means pacing in the ventricle only, and DOO means pacing in the atrium and ventricle without sensing or response. Such a device would simply pace at a set lower rate regardless of underlying rhythm.

These modes (ending in OO) are known as asynchronous modes and are useful in the operating room because they allow pacing to be maintained and prevent interference of electrocautery caused by the absence of sensing.

## 3. What is the result of VVI pacing?

This mode results in ventricular pacing, with sensing in the ventricle alone, and the response is inhibition. This means that the device will release a pacing stimulus unless a sensed event occurs before the expiration of a timer based on the lower rate. If a sensed event occurs, the only response by the device is to inhibit pacing, allowing for the intrinsic rhythm.

## 4. What is the result of DDI pacing?

DDI means pacing in the atrium and ventricle, sensing in the atrium and ventricle, and the response is constrained to inhibition. The device will thus pace at a set rate in the atrium unless a sensed event occurs at a faster rate in the atrium, which will result in inhibition. The device will then pace in the ventricle at a set rate unless sensing in that chamber occurs at a faster rate, leading to inhibition. This allows for some atrial and ventricular synchrony to be maintained. However, because the response is only inhibition, the pacemaker will not pace in the ventricle as a result of a sensed event in the atrium, which is known as a tracking or

triggered response. Thus competitive atrial pacing and variable atrioventricular (AV) timing can occur. This mode is helpful when atrial arrhythmias would lead to rapid heart rates if tracked and is a frequent default mode.

#### 5. What does DDD pacing mean?

DDD pacing means pacing in atria and ventricle, sensing in atria and ventricle, and a dual response (both triggered and inhibited). This is the most common pacing mode. A sensed atrial event occurring before the lower rate timer has expired will inhibit atrial pacing. If no event is sensed in the atrium above the lower rate, an atrial stimulus is released. Both events will initiate a timer expiring before ventricular pacing. If a ventricular-sensed event occurs before this timer expiring, ventricular pacing is inhibited, and intrinsic conduction is maintained. If the AV timer expires, a ventricular pacing stimulus is delivered and is triggered from the previous atrial paced or sensed event. This is known as tracking. If no underlying sensed events occur, atrial and ventricular sequential pacing occur at the lower programmed rate.

#### 6. Describe the difference between a unipolar and bipolar pacemaker.

Both scenarios detect electrical signals between two electrodes. In the case of unipolar pacemakers, one electrode is in the heart at the lead-tissue interface, and the other is comprised of the pacemaker generator. Sensing occurs from both electrodes. Thus sensing from the generator may lead to sensing extracardiac signals, muscle myopotentials, external noise, and interference. In the case of bipolar leads, the electrodes are closely spaced at the lead tip within the heart. Sensing between the electrodes is limited mainly to cardiac signals with much less oversensing or external interference.

#### 7. What is an implantable cardioverter defibrillator?

Implantable cardioverter defibrillators (ICDs) are devices much like pacemakers that can pace and support the heart rate in bradycardia. However, these devices have leads with shocking coils, usually one or two, that allow the device to administer internal shocks for tachyarrhythmias (which may be lifesaving). These devices also have complex programming. They allow rapid pacing to terminate regular, fast, more organized arrhythmias in a painless fashion. Algorithms in these devices may even allow differentiation of supraventricular arrhythmias from more serious arrhythmias from the ventricle. These devices are implanted for the treatment of life-threatening arrhythmias and prevention of sudden death.

#### 8. What are common indications for permanent pacing?

- In general patients with symptoms from slow heart rate of any type that are not reversible require pacing.
- Patients with AV block located below the AV node require pacing. These patients have wide escape complexes, and their escape mechanisms are unreliable and can lead to asystole or death.
- Patients with arrhythmias caused by bradycardia such as torsades de pointes responsive to pacing require pacing.
- Patients with syncope caused by carotid hypersensitivity require pacing.

#### 9. What are some common indications for implantable cardioverter defibrillator implantation?

- Cardiac arrest or ventricular fibrillation not from reversible causes
- Sustained ventricular tachycardia with associated structural heart disease
- Patients with left ventricular ejection fraction less than 35%, regardless of etiology
- Primary electrical disorders such as Brugada syndrome or long QT syndrome

#### 10. What is the effect of placing a magnet over a device?

The answer depends on the type of device and its programming. In general placing a magnet over a device prevents device sensing. In the case of pacemakers this usually leads to

asynchronous pacing at a preprogrammed rate, regardless of underlying rhythm. If the device is an ICD, the default is usually to prevent sensing leading to arrhythmia detection and therapy. This may be used emergently when device malfunction is occurring, leading to inappropriate shocks, or when external noise (i.e., electrocautery) is sensed as a tachyarrhythmia. Be certain that the device is not functioning appropriately at the time of ICD discharge when magnet application may lead to withholding of lifesaving therapy! Application of a magnet over a device may also be useful when emergency surgery is required and the ICD therapies cannot be deactivated in a timely manner.

#### 11. Do patients with devices need to avoid microwave ovens or other hospital electronics?

In general modern devices are shielded against routine electromagnetic interference. This shielding is inadequate for radiofrequency (intraoperative electrocautery) or transcutaneous electrical nerve stimulation units. This may lead to false detection of extracardiac *noise*, leading to inappropriate inhibition of pacing, or to defibrillation caused by inappropriate arrhythmia detection with ICDs. Other forms of strong magnetic fields such as arc welding and some short-wave radios may lead to device reprogramming or other malfunction. Cellular phones generally are not problematic unless in a pocket overlying the device; they should be used in the contralateral hand.

#### 12. Are there other responses to electromagnetic interference by devices?

Some devices are rate responsive. In this mode the device is programmed to respond to various stimuli by increasing or decreasing heart rate to correct for various metabolic demands of exertion in patients. Some of these sensors function with crystals that deform with impact, increase pacing with changes in chest impedance, or increase pacing in response to changes in momentum. With these sensors lithotripsy, certain electromagnetic monitoring equipment, or simply chest motion may trigger inappropriate rapid pacing. Rate responsiveness should always be programmed off before surgery.

#### 13. Can device leads be dislodged?

Generally after about 6 weeks the myocardium has begun to scar around the lead tip, which contributes to lead stability. However, new devices known as biventricular pacemakers and defibrillators have a special lead placed in a vein behind the left atrium and ventricle to improve symptoms of heart failure. These leads are placed in a vein with friction as the only mechanism of retention and may easily be displaced years after placement. The placement and withdrawal of intravascular monitoring catheters should be performed with extreme caution and probably with fluoroscopic guidance.

#### 14. Can device leads be damaged with intravascular access?

Device leads are generally wound wires surrounded by silicone that can be torn or damaged with an introducer needle. In general, access should be avoided in the veins where leads are in place.

#### 15. Do typical anesthetics and intraoperative medications affect the ability of implantable cardioverter defibrillators to defibrillate patients?

Fentanyl reduces the energy required from the device to convert a ventricular arrhythmia (defibrillation threshold). Most inhalational anesthetics do not appear to change the defibrillation threshold except for enflurane and pentobarbital, which appear to increase it.

#### 16. Can changes in the patient's clinical status affect pacemaker function?

In critically ill patients severe acidosis, hyperkalemia, and/or cardiac ischemia may lead to dramatic increases in pacemaker capture thresholds, resulting in apparent pacemaker malfunction.



**17. Can programming patients to a different mode lead to hemodynamic compromise?**

Certain patients may become hypotensive, diaphoretic and nauseated, or short of breath when programmed to modes that lead to AV dyssynchrony such as VVI setting in a patient with intact sinus mechanism. This may also occur when prolonged AV timing leads to atrial stimulation immediately following previous ventricular contraction. This is known as pacemaker syndrome and can on occasion be quite dramatic.

**18. Should patients with pacemakers or defibrillators be evaluated before and after surgery?**

Yes—to ensure that normal device function and adequate battery life remains. The physician should be aware if the patient is pacemaker dependent. This implies that the patient has no underlying cardiac rhythm when the pacemaker is not functioning. If this is the case or if electrocautery is to be used, the device should be programmed to an asynchronous mode to avoid inadvertent device inhibition by electromagnetic interference (EMI). Patients with ICDs should have the arrhythmia therapy feature turned off. This mandates that an external defibrillator be available for external defibrillation should an arrhythmia occur. After surgery, ICDs and pacemakers should be investigated to ensure that no programming errors were caused by EMI.

**19. Are there any precautions that can decrease the effect of electrocautery on devices?**

Yes. The dispersive electrode should be close to the area of the proposed cautery and as far from the device as possible. Bursts of electrocautery should be as brief as possible to avoid prolonged inhibition. The cautery electrode and dispersive pad should not be parallel to the presumed lead configuration and are best if perpendicular to the lead to avoid current traveling down the device leads. Devices with near end-of-life battery voltage may be permanently inhibited with electrocautery.

**20. If no underlying rhythm is seen when a pacemaker rate is rapidly decreased, does that mean that the patient is pacemaker dependent?**

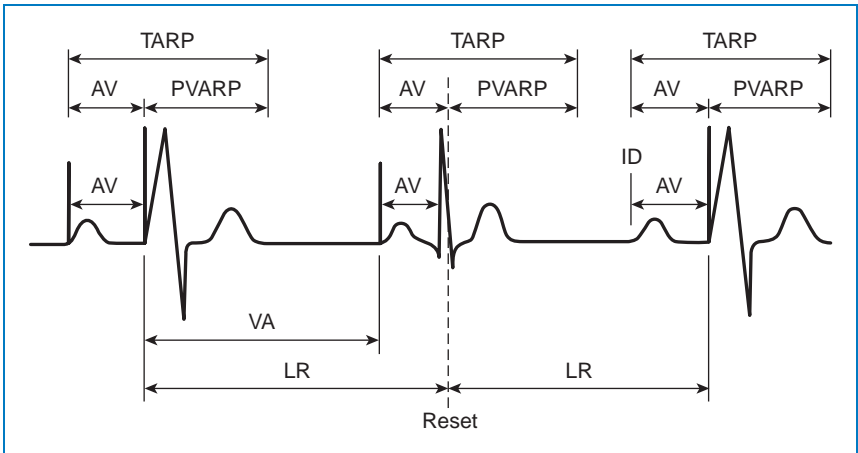
No. Many patients have their rhythm suppressed by pacing but when given time will have a hemodynamically tolerated underlying rhythm. To assess for this the pacing rate should be slowly reduced to allow for the patient's underlying rhythm to recover. If, after slow reduction in pacing rate, no underlying rate is seen above 30 to 40 beats/min, the patient is likely pacemaker dependent.

**21. No pacer spikes are seen on the monitoring system with your patient with a pacemaker. Does this mean that the pacemaker is not functioning properly?**

Not necessarily. The pacemaker may simply be inhibited because of the patient's underlying rhythm. However, it must be noted that with bipolar pacemakers the pacing spike is extremely small and may not be detected. In fact, with most digital recording systems the pacemaker spike seen is added to the strip by the recording system when electrical frequencies are detected that fall in the range of pacemaker stimuli. This sometimes leads to pacer spikes being seen on monitoring strips for patients without devices!

**22. Does failure of a pacemaker stimulus to capture the heart necessarily imply pacemaker malfunction?**

There are many reasons a pacemaker stimulus may not depolarize the tissue. Assess whether a stimulus is an atrial or ventricular stimulus (Figure 64-1). The tissue may have been refractory from a recent event such as a premature ventricular contraction, which is known as functional loss of capture. Occasionally the paced complex is not seen on a single-lead

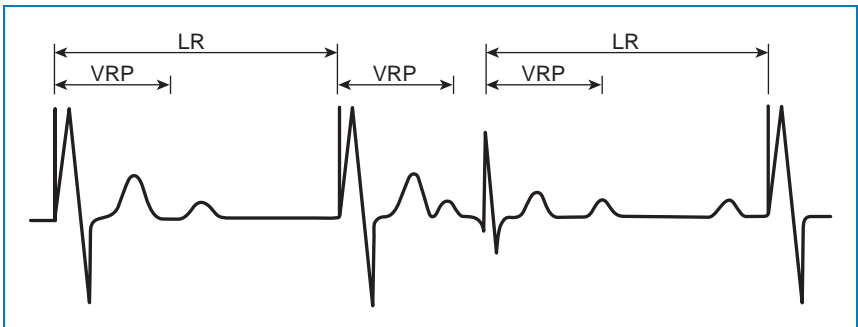


**Figure 64-1.** Normal atrioventricular pacing (sequential pacing). AV is Atrioventricular (paced) Interval, ID is Intrinsic Depolarization, LR is Lower Rate (of pacing), PVARP is Post Ventricular Atrial Refractory Period, TARP is Total Atrial Refractory Period. (From Zaidan JR: Pacemakers. In Barash PG, editor: *Refresher courses in anesthesiology*, vol. 21, Philadelphia, 1993, Lippincott, with permission.)

monitoring system because the axis of the paced rhythm is perpendicular to the monitoring lead. In this case the paced complex will not be visible on the lead viewed despite normal function and normal appearance on other leads if they were monitored. However, if repeated failure to capture is seen or the patient appears compromised, emergent evaluation of pacemaker function should be sought.

**23. If a pacemaker stimulus is superimposed on a native complex, is the pacemaker necessarily malfunctioning?**

No. There are many explanations for the previous finding. Most commonly this is a case in which the pacemaker timer times out before sensing an intrinsic event. In this case the device will release a stimulus. The intrinsic event may have started earlier on a surface lead but was not sensed by the device at the site of the lead until well into the complex. This is a common finding with normal VVI pacing (Figure 64-2). Other programmable behavior may also explain this finding, although inappropriate sensing must also be ruled out.



**Figure 64-2.** Normal VVI pacing. LR is Lower Rate (of pacing), VRP is Ventricular Refractory Period. (From Zaidan JR: Pacemakers. In Barash PG, editor: *Refresher courses in anesthesiology*, vol. 21, Philadelphia, 1993, Lippincott, with permission.)

## KEY POINTS: PACEMAKERS AND INTERNAL CARADIOVERTER DEFIBRILLATORS



1. A strong magnet leads to asynchronous pacing at a set rate in pacemakers and prevents inhibition; it also prevents sensing in ICDs and prevents tachycardia therapy.
2. In the pacemaker coding system, the first letter refers to the chamber paced, the second letter to the chamber in which sensing occurs, the third letter to the responses to sensing in chambers, and the fourth letter to rate responsiveness.
3. Bipolar versus unipolar pacing refers to the type of pacemaker and distance between distal sensing electrode and proximal electrode.
4. Unipolar pacemakers pace and sense with the distal electrode at the tip of the lead at the cardiac lead interface, and the proximal electrode generally is the pacemaker generator itself. Sensing occurs between these widely spaced electrodes, predisposing to oversensing of extracardiac noise, and generating large amplitude spikes on recording equipment with pacing.
5. Bipolar pacemakers pace and sense with the distal electrode at the tip of the lead at the cardiac tissue lead interface, and a proximal electrode located usually nearby within 3 cm. Sensing occurs between these closely spaced electrodes and is less susceptible to extra cardiac interference. Pacing spikes may not be visible on electrocardiographic recordings.

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# SPINAL ANESTHESIA

James Duke, MD, MBA

## 1. What are the advantages of spinal anesthesia over general anesthesia?

- The metabolic stress response to surgery and anesthesia is reduced by subarachnoid block (SAB).
- Particularly in elective hip surgery, there may be up to a 20% to 30% reduction in blood loss.
- SAB decreases the incidence of venous thromboembolic complications by as much as 50%.
- Pulmonary compromise appears to be less.
- Endotracheal intubation is avoided.
- Mental status can be followed.

## 2. What are the usual doses of common local anesthetics used in spinal anesthesia and the duration of effect?

See [Table 65-1](#).

TABLE 65-1. LOCAL ANESTHETIC DOSING FOR SPINAL ANESTHESIA

Usual Concentration	Suggested Doses (mg) (minutes)			Duration of Effect	
	Lower Extremities and Perineum	Low Abdomen	Upper Abdomen	Without Epinephrine	With Epinephrine
Lidocaine	5% in dextrose	30–50	75–100	60–75	75–90
Bupivacaine	0.75% in dextrose	5–10	12–17	90–120	100–150
Ropivacaine	0.25%–1%	8–12	16–18	90–120	90–120
Tetracaine	1% in dextrose	4–8	10–16	90–120	120–240
Ropivacaine	0.5% in dextrose	12–18	18–25	80–110	—
Levobupivacaine		8–10	12–20	90–120	100–150

## 3. Where are the principal sites of effect of spinal local anesthetics?

The principal sites are the spinal nerve roots and spinal cord. Interestingly nerve roots may have different anatomic configurations (rootlets vs. roots); and there may be variability in fascial compartmentalization of the roots, especially between the dorsal and ventral nerve roots, accounting in part for differences between motor and sensory blockade.

## 4. What factors determine the termination of effect?

Resorption of the agent from the cerebrospinal fluid (CSF) into the systemic circulation limits duration. Addition of a vasoconstrictor that slows resorption prolongs duration of effect. Vasoconstrictor efficacy decreases with local anesthetics with intrinsic longer durations of effect.

### 5. Describe the factors involved in distribution (and extent) of conduction blockade.

- Patient characteristics include height, position, intra-abdominal pressure, anatomic configuration of the spinal canal, and pregnancy. There is great interindividual variation in lumbosacral CSF volumes; magnetic resonance imaging has shown volumes ranging from 28 to 81 ml. Lumbar CSF volumes correlate well with the height and regression of the block. With the exception of an inverse relation with weight, no external physical measurement reliably estimates lumbar CSF volumes. CSF volumes are also reduced in pregnancy.
- Needle direction and site when anesthetic is injected are important.
- The total injected dose of local anesthetic is important, whereas the volume or concentration of injectant is unimportant.
- The baricity of the local anesthetic solution is important. *Baricity* is defined by the ratio of the density of the local anesthetic solution to the density of CSF. A solution with a ratio  $>1$  is hyperbaric and tends to sink with gravity within the CSF. An isobaric solution has a baricity of 1 and tends to remain in the immediate area of injection. A ratio  $<1$  is hypobaric solution, which rises in the CSF.

### 6. At what lumbar levels should a spinal anesthetic be administered? What structures are crossed when performing a spinal block?

The selected level should be below L1 in an adult and L3 in a child to avoid needle trauma to the spinal cord. As an anatomic landmark, the L3-L4 interspace is located at the line intersecting the top of the iliac crests. Either a midline or paramedian approach can be used. The anatomic layers passed through include skin, subcutaneous structures, supraspinous ligament, interspinous ligament, ligamentum flavum, dura mater, and arachnoid membrane.

### 7. What are the most common complications of spinal anesthesia?

Common complications include hypotension, bradycardia, increased sensitivity to sedative medications, nausea and vomiting (possibly secondary to hypotension), postdural puncture headache (PDPH), and residual back pain and paresthesias (usually associated with the use of lidocaine). Less frequent but more ominous complications include nerve injury, cauda equina syndrome, meningitis, total spinal, and hematoma/abscess formation. Particular issues associated with these complications are discussed subsequently.

### 8. What are the physiologic changes and risk factors found with subarachnoid block-associated hypotension?

Hypotension occurs as a result of a loss of sympathetically mediated peripheral vascular resistance. Arterial and central venous pressure decrease with only mild decreases in heart rate, stroke volume, and cardiac output. Hypovolemia, age greater than 40 years, sensory level greater than T5, baseline systolic blood pressure below 120 mm Hg, and performance of the block at or above L3-L4 increase the incidence of hypotension. Hypotension (and possibly decreased cerebral blood flow) may be responsible for nausea and vomiting observed with SAB. Patients should receive a bolus of crystalloid or colloid (250 to 1000 ml) before SAB. Because of the pattern of distribution, colloid is more effective, although more expensive. Volume expansion and intravenous sympathomimetics usually reverse hypotension should it occur. Trendelenburg position may raise the level of blockade and should be used with caution and vigilance. Volume loading should also be used cautiously in patients with limited cardiac reserve. In these patients, as the block recedes, vascular tone increases, raising the central blood volume, which may precipitate heart failure. Strategies to create a unilateral block may also decrease the hypotension associated with SAB.

**9. What are the etiology and risk factors for subarachnoid block–associated bradycardia?**

Bradycardia may occur secondary to unopposed vagal tone from a high sympathectomy, blockade of the cardioaccelerator fibers (T1-T4), and the Bezold-Jarisch reflex (slowing of the heart rate secondary to a decrease in venous return). Patients with underlying increased vagal tone (children and adults with resting heart rates <60) are at increased risk. Bradycardia may be treated with anticholinergic agents (atropine) or  $\beta$ -adrenergic agonists such as ephedrine.

**10. Why are patients who have received spinal anesthetics especially sensitive to sedative medications? What is deafferentation?**

Caplan and associates (1988) published a landmark review of healthy patients who, while undergoing elective surgery using spinal anesthesia, experienced a sleeplike state without spontaneous verbalization followed by respiratory and cardiac arrest. Despite the fact that these were witnessed arrests, the patients were difficult to resuscitate and either died or had severe neurologic deficits. Subsequently it has been determined that patients receiving spinal anesthetics are especially sensitive to sedative medications. The cause of this may be loss of peripheral input into the reticular activating system (RAS), that part of the brainstem responsible for maintaining arousal. It appears that motor spinal fibers and afferent sensory input into the RAS contribute to wakefulness and this input is diminished by spinal anesthesia, rendering the patient prone to oversedation. Spinal (and epidural) anesthesia increases the hypnotic potential of midazolam, isoflurane, sevoflurane, and thiopental.

**11. Review the clinical features of total spinal anesthesia.**

Total spinal anesthesia results from local anesthetic depression of the cervical spinal cord and brainstem. Signs and symptoms include dysphonia, dyspnea, upper extremity weakness, loss of consciousness, pupillary dilation, hypotension, bradycardia, and cardiopulmonary arrest. Early recognition is the key to management. Treatment includes securing the airway, mechanical ventilation, volume infusion, and pressor support. The patient should receive sedation once ventilation is instituted and the hemodynamics stabilize. The effects of total spinal anesthesia usually resolve by the conclusion of the surgical procedure, and, unless otherwise contraindicated, the patient can be extubated.

**12. If a patient has a cardiac arrest while having a subarachnoid block, how should resuscitative measures differ from standard advanced cardiac life support protocols?**

Since these patients have loss of sympathetic tone and decreased peripheral vascular resistance, rapidly escalating doses of epinephrine will be necessary to increase peripheral resistance and coronary artery perfusion. Until effective, consider doubling each subsequent dose of epinephrine (e.g., 1 mg, then 2 mg, then 4 mg, and so on).

**13. What are the clinical features of a postdural puncture headache and the treatment?**

A potentially severe headache may develop after dural puncture, presumably secondary to the rent in the dura and resultant CSF leak, which may cause traction on the meninges and cranial nerves. The headache typically occurs soon after the puncture. It is characteristically intense, often localized to the occipital region and neck, and worse in the upright position. Diplopia or blurred vision may occur. Newer pencil-point needles have reduced the incidence of PDPH to about 1%. Women, younger patients, parturients, and obese patients tend to have a higher incidence of PDPH. Hydration, analgesics, and caffeine mostly temporize the headache; epidural blood patching (administration of about 20 ml) has >75% success rate. It is important to rule out severe hypertension or central nervous system maladies as a cause of the symptoms before assuming that the patient has a PDPH.

**14. What is the risk of neurologic injury after spinal anesthesia?**

Direct trauma to nerve fibers may occur from the spinal needle and may be heralded by a paresthesia, for which the spinal needle should be redirected. Hematoma formation from epidural venous bleeding (from direct trauma or coagulopathy) or abscess formation is suggested by persistent neurologic deficits or severe back pain. Early recognition and management are imperative to avoid permanent neurologic sequelae. In patients who have received any medication with anticoagulant potential, it is important not to attribute persistent neurologic deficits to residual effects of local anesthesia. Adhesive arachnoiditis has been reported and is presumably caused by injection of an irritant into the subarachnoid space.

**15. What is the effect of spinal anesthesia on temperature regulation?**

Because patients become vasodilated and cannot shiver in response to decreases in body temperature, hypothermia is a risk. Curiously, patients may not perceive cold because the vasodilated extremities are warm. In addition, hypothermia may not be detected by the clinician because temperature monitoring is not widely practiced in patients receiving regional anesthesia and it would be necessary to monitor a site that reflects core body temperature such as the tympanic membrane. Patients receiving regional anesthetics should also be warmed using heated forced air devices.

**16. What are contraindications to spinal anesthesia?**

Absolute contraindications include local infection at the puncture site, bacteremia, severe hypovolemia, coagulopathy, severe stenotic valvular disease, infection at the site of the procedure, and intracranial hypertension. Relative contraindications include progressive degenerative (demyelinating) neurologic disease (e.g., multiple sclerosis), low back pain, and sepsis.

**17. Review the current recommendations for administering regional anesthesia to patients with altered coagulation caused by medications.**

The American Society of Regional Anesthesia and Pain Medicine has defined the risks of regional anesthesia in the anticoagulated patient. This and Questions 18 and 19 summarize key points:

- Patients on thrombolytic/fibrinolytic therapy should not receive regional anesthesia except in the most extreme circumstances. Patients who have had regional anesthesia before such therapy has been instituted should receive serial neurologic checks.
- Oral anticoagulants should be stopped 4 to 5 days before the planned procedure, and prothrombin time/International Normalized Ratio normalized.
- Concurrent administration of medications that affect bleeding by different mechanisms (e.g., antiplatelet drugs, aspirin, heparin) complicates the decision to perform regional anesthesia; therefore decisions must be individualized. Patients taking only nonsteroidal antiinflammatory drugs can safely have either single-shot or catheter regional anesthetics.
- Thrombocytopenia and an altered coagulation cascade are likely contraindications to regional anesthesia.

**18. Should spinal (or epidural) anesthesia be performed when unfractionated heparin is administered?**

- If heparin is to be administered, coexisting thrombocytopenia, antiplatelet medications, oral anticoagulants, and other bleeding dyscrasias suggest that regional techniques should be avoided.
- The subcutaneous administration of minidose unfractionated heparin is not contraindicated, but it is best to time performance of the block when the heparin effect is minimal. Similarly, a heparin dose should be held if it is scheduled soon after performance of the block.
- In vascular patients who will receive large doses of heparin, avoid regional techniques if other coagulopathies are present, delay heparin administration for at least 1 hour after the

procedure, and time removal of the catheter for when heparin effect has diminished (1 hour before subsequent doses or 2 to 4 hours after the last dose). There are no data to guide in decision making should a bloody tap occur.

- Prolonged therapeutic anticoagulation may increase the risk of spinal hematoma, especially if other coagulation abnormalities coexist.

### 19. Should spinal (or epidural) anesthesia be performed when low-molecular-weight heparin is administered?

- Patients who have received low-molecular-weight heparin (LMWH) should be believed to have altered coagulation, and a single-shot spinal injection is the safest procedure for these patients. As in the case with unfractionated heparin, other factors that increase the likelihood of bleeding will increase the risk of spinal hematoma when LMWH is administered.
- Timing of the neuraxial procedure and dosing LMWH is extremely important, as is the dose of LMWH. Needle placement should occur at least 10 to 12 hours after an LMWH dose. Neuraxial procedures should be delayed for 24 hours when the patient is receiving larger LMWH doses: enoxaparin 1 mg/kg q12h, enoxaparin 1.5 mg/kg daily, dalteparin 120 units/kg q12h, dalteparin 200 units/kg daily, or tinzaparin 175 units/kg.
- A bloody spinal tap should not cause cancellation of the surgery but should delay administration of LMWH by 24 hours.
- If a patient is to have an epidural catheter for postoperative pain management and is also to receive LMWH after surgery, twice daily dosing has a greater risk of spinal hematoma formation than single daily dosing, and the benefits of an epidural catheter in a patient receiving twice-daily dosing should be weighed against the risks. Although some authorities are more aggressive, a safe practice is to delay the first dose for at least 24 hours after surgery, and a catheter should be removed a minimum of 10 to 12 hours after the last dose of LMWH.

### 20. What are the sites of action, benefits, and side effects of intrathecal opioids?

Opioids produce intense visceral analgesia and may prolong sensory blockade without affecting motor or sympathetic function. The major sites of action are the opiate receptors within the second and third laminae of the substantia gelatinosa in the dorsal horn of the spinal cord. Lipophilic agents such as fentanyl and sufentanil have a much more localized effect than the hydrophilic agents such as the hydrophilic opioid morphine. Fentanyl and sufentanil have a rapid onset of action and an effective duration greater than 6 hours. Morphine lasts 6 to 24 hours. Side effects include respiratory depression (which may occur late with hydrophilic agents), nausea, vomiting, pruritus, and urinary retention. Opioid antagonists or agonist/antagonists reverse the complications but if given in large doses may also reverse analgesia.

### 21. What is transient neurologic syndrome and its cause?

Transient neurologic syndrome (TNS) was first described in 1993. Common findings include pain or dysesthesias in the buttocks radiating to the dorsolateral aspect of the thighs and calves. The pain has been alternatively described as sharp and lancinating or dull, aching, cramping, or burning. Usually symptoms improve with moving about, are worse at night, and respond to nonsteroidal antiinflammatory drugs. The pain is moderate to severe in at least 70% of the patients with TNS and diminishes over time, resolving spontaneously within approximately a week in about 90% of those affected. It is extremely rare for pain to continue beyond 2 weeks. It is significant to note that no objective neurologic findings are encountered.

TNS is associated with the use of spinal lidocaine in the majority of cases, and its incidence, although variable in studies, probably averages about 15%. Much more rarely TNS has been associated with the use of bupivacaine, prilocaine, procaine, and mepivacaine. The concentration of lidocaine does not appear to be a factor (TNS has been observed with 5% hyperbaric and 2% isobaric lidocaine). There is no association with the presence of dextrose, opioids, epinephrine, or the baricity or osmolarity of the solution. Further, neither gender,



weight, age, needle type, difficulty with, nor paresthesias during block placement are factors, although lithotomy positioning may have been a factor. Bupivacaine is not associated with TNS. Interestingly, pregnancy may protect against lidocaine-associated TNS.

## KEY POINTS: SPINAL ANESTHESIA



1. Loss of afferent sensory and motor stimulation renders a patient sensitive to sedative medications secondary to deafferentation. For the same reason neuraxial anesthesia decreases the minimum alveolar concentration of volatile anesthetics.
2. Vagal predominance suggests that a patient may be at risk for cardiovascular collapse during neuraxial anesthesia.
3. Patients with sympathectomies from regional anesthesia require aggressive resuscitation, perhaps with unfamiliarly large doses of pressors, to reestablish myocardial perfusion after cardiac arrest.
4. Suspect TNS in a patient who has received a lidocaine spinal anesthetic and has postanesthetic complaints of pain in buttocks and dorsal lower extremities. Note that there are no objective neurologic findings with this syndrome.

### 22. Since lidocaine is associated with TNS, what would be an appropriate local anesthetic selection for an ambulatory procedure?

Bupivacaine administered in 5- to 7.5-mg doses will achieve peak sensory blocks in the midthoracic region with durations of sensory blockade of about 2 hours, and duration of motor blockade of about an hour and time to discharge may not be appreciably different than if lidocaine had been used. Doses of bupivacaine greater than 10 mg will result in delays in voiding. This may not necessarily delay discharge to home if there is not a history of difficulty voiding and the procedure was in a nonpelvic area. Bladder ultrasound has been used to identify patients requiring catheterization.

### 23. Can continuous spinal anesthesia be performed?

Continuous spinal anesthesia is a technique regaining popularity. In the early 1990s many cases of cauda equina syndrome were noted after inappropriate dosing of spinal microcatheters. It appeared that the lack of turbulence associated with injecting through microcatheters led to a pooling of local anesthetic caudad to the lumbar lordotic curve, leading to repeated and inappropriate dosing of local anesthetics.

Continuous spinal anesthesia is safe and effective using 18- to 22-G epidural needles and catheters (and improved, specially designed kits). The incidence of hypotension is less, as is the need to rescue with vasopressors. This technique allows for titration of local anesthetics to effect and has been successfully used in elderly patients, patients with aortic stenosis, and trauma patients. This is an attractive technique for the elderly because they tend not to develop PDPH despite dural punctures with large-gauge epidural needles.

## WEBSITE



American Society of Regional Anesthesia and Pain Management  
<http://www.asra.com>

## SUGGESTED READINGS

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# EPIDURAL ANALGESIA AND ANESTHESIA

Joy L. Hawkins, MD

## 1. Where is the epidural space? Describe the relevant anatomy.

The epidural space lies just outside the dural sac containing the spinal cord and cerebrospinal fluid (CSF). As the epidural needle enters the midline of the back over the bony spinous processes, it passes through:

- Skin
- Subcutaneous fat
- Supraspinous ligament
- Interspinous ligament
- Ligamentum flavum
- Epidural space

Beyond the epidural space lie the spinal meninges and CSF. The epidural space has its widest point (5 mm) at L2. In addition to the traversing nerve roots, it contains fat, lymphatics, and an extensive venous plexus. Superiorly the space extends to the foramen magnum, where dura is fused to the base of the skull. Caudally it ends at the sacral hiatus. The epidural space can be entered in the cervical, thoracic, lumbar, or sacral regions to provide anesthesia. In pediatric patients the caudal epidural approach is commonly used (see Question 3).

## 2. Differentiate between a spinal and an epidural anesthetic.

When performing a spinal anesthetic, a small amount of local anesthetic drug is placed directly in the CSF, producing rapid, dense, predictable neural blockade. An epidural anesthetic requires a tenfold increase in dose of local anesthetic to fill the epidural space and penetrate the nerve coverings, and onset is slower. The anesthesia produced tends to be segmental (i.e., a band of anesthesia is produced, extending upward and downward from the injection site). The degree of segmental spread depends largely on the volume of local anesthetic. For example, a 5-ml volume may produce only a narrow band of anesthesia covering three to five dermatomes, whereas a 20-ml volume may produce anesthesia from the upper thoracic to sacral dermatomes. Placement of an epidural anesthetic requires a larger needle, often includes a continuous catheter technique, and has a subtle end point for locating the space. The epidural space is located by following the *feel* of the ligaments as they are passed through until there is loss of resistance, whereas the subarachnoid space is definitively identified by CSF flow from the needle.

## 3. How is caudal anesthesia related to epidural anesthesia? When is it used?

Caudal anesthesia is a form of epidural anesthesia in which the injection is made at the sacral hiatus (S5). Because the dural sac normally ends at S2, accidental spinal injection is rare. Although the caudal approach to the epidural space provides dense sacral and lower lumbar levels of block, its use is limited by major problems:

- Highly variable sacral anatomy in adults
- Risk of injection into a venous plexus
- Difficulty in maintaining sterility if a catheter is used

Caudal anesthesia is primarily used in children (whose anatomy is predictable) to provide postoperative analgesia after herniorrhaphy or perineal procedures. A catheter can be inserted for long-term use if desired.

#### 4. What are the advantages of using epidural anesthesia vs. general anesthesia?

- Avoidance of airway manipulation; useful for asthmatics, known difficult airways, and patients with a full stomach
- Decreased stress response; less hypertension and tachycardia and cortisol release
- Less thrombogenesis and subsequent thromboembolism; a proven benefit in orthopedic hip surgery
- Improved bowel motility with less distention; sympathetic blockade provides relatively more parasympathetic tone
- The patient can be awake during the procedure; desirable for cesarean deliveries and certain arthroscopic procedures
- Less postoperative nausea and sedation
- Better postoperative pain control, especially for thoracic, upper abdominal, and orthopedic procedures
- Less pulmonary dysfunction, caused by both better pain control and absence of airway manipulation
- Faster turnover at the end of the case because there is no emergence time

#### 5. What are the disadvantages of epidural compared with general anesthesia?

- Initiation is slower at the beginning of the case.
- It is less reliable, with higher failure rate.
- There are occasional contraindications, including coagulopathy, hemodynamic instability, spinal instrumentation, or patient refusal.

#### 6. What are the advantages of epidural anesthesia over spinal anesthesia?

- Epidural anesthesia can produce a segmental block focused only on the area of surgery or pain (e.g., during labor or for thoracic procedures).
- The gradual onset of sympathetic block allows time to manage associated hypotension.
- Duration of anesthesia can be prolonged by redosing through an indwelling epidural catheter.
- There is more flexibility in the density of block; if less motor block is desired (for labor analgesia or postoperative pain management), a lower concentration of local anesthetic can be used.
- Theoretically with no hole in the dura there can be no spinal headache; however, an inadvertent dural puncture occurs 0.5% to 4% of the time with the large-bore epidural needle, and about 50% of such patients require treatment for headache. Because newer technology in spinal needles has decreased the incidence of headache requiring treatment to less than 1%, this advantage is probably no longer true.

#### 7. What are the disadvantages of epidural compared with spinal anesthesia?

- The induction of epidural anesthesia is slower because of more complex placement, the necessity of incremental dosing of the local anesthetic, and the slower onset of anesthesia in the epidural space.
- Because a larger volume of local anesthetic is used, there is risk of local anesthetic toxicity if a vein is entered with the needle or catheter.
- Epidural anesthesia is less reliable; it is not as dense, the block can be patchy or one-sided, and there is no definite end point (comparable to seeing CSF in the needle) during placement.

#### 8. What factors should the anesthesiologist address in the preoperative assessment before performing an epidural anesthetic? Should special laboratory tests be performed?

In addition to the general preoperative assessment of every patient before surgery, the following specific items should be assessed before performing epidural anesthesia:

##### ■ History

- Previous back injury or surgery
- Neurologic symptoms or history of neurologic disease (e.g., diabetic neuropathy, multiple sclerosis)

- Bleeding tendencies or disease associated with coagulopathy (e.g., preeclampsia)
- Prior regional anesthesia and any associated problems

■ **Physical examination**

- Brief neurologic examination for strength and sensation
- Back examination for landmarks and potential anatomic abnormalities (scoliosis) or pathology (infection at the site of placement)

■ **Surgery**

- Expected duration and blood loss
- Positioning required
- Amount of muscle relaxation necessary

■ **General information**

- The patient should be given a detailed explanation of the procedure, risks, benefits, and options (including general anesthesia if the block fails).
- Discuss whether the patient desires sedation and how much.

■ **Laboratory tests**

- None is specifically necessary except as based on the history and physical examination.

**9. Describe the technique for performing a lumbar epidural anesthetic.**

- Resuscitation equipment must be immediately available: oxygen, equipment for positive-pressure ventilation and intubation, and pressors to treat hypotension.
- Place a well-running intravenous (IV) line and give an appropriate preload of fluid to protect against hypotension after sympathetic blockade.
- The patient may be sitting or in a lateral position. The spinous processes should be aligned in the same vertical or horizontal plane and maximally flexed. Administer sedation as deemed appropriate.
- For lumbar epidural placement, visualize a line between the iliac crests to locate the L4 spinous process. Palpate the L2-L3, L3-L4, and L4-L5 interspaces and choose the widest or the closest to the desired anesthetic level. For abdominal or thoracic surgeries, know the appropriate level for catheter placement.
- Make a skin wheal after sterile preparation and draping of the field. The anesthesiologist must wear a hat, mask, and sterile gloves.
- The epidural needle is inserted in the midline through the skin wheal until increased resistance from ligaments is felt. Remove the needle stylet and attach a syringe with 3 to 4 ml of air or saline. When the barrel of the syringe is tapped, it should feel firm and bounce back while the tip of the needle is in the ligament.
- Advance several millimeters at a time, tapping the syringe intermittently. The ability to recognize the feel of various layers of ligament comes with experience. Ligamentum flavum is often described as leathery, gritty, or producing a marked increase in resistance. This is the last layer before the epidural space.
- As the needle passes through ligamentum flavum and enters the epidural space, there is often a *pop* or *give*, and the air or fluid in the syringe injects easily; this marks the loss of resistance.
- The syringe is removed; and, while the nondominant hand grasps the hub of the needle to brace it, the dominant hand threads the catheter about 5 cm into the space.
- The epidural needle is withdrawn carefully so as not to dislodge the catheter. After attaching the injector port to the catheter, it is aspirated for blood or CSF; if negative, a test dose is given. The catheter is then taped in place.

**10. Are there any contraindications to epidural anesthesia?**

**Absolute contraindications**

- Patient refusal. Sometimes a more thorough explanation will allay the patient's fears and make the technique acceptable. Some common concerns include:
  - Having to watch surgery or remain wide awake

- Fear of a needle in the spinal cord
- Pain
- Reassure patients that a curtain will block their view and that the desired degree of sedation can be provided. For lumbar epidural placements, explain that the spinal cord ends at about L1 in adults and that the needle is placed below that level. Compare the procedure to the placement of the IV line, which also uses a 16- or 18-G needle, and explain that a local anesthetic will be used in the skin.
- Sepsis with hemodynamic instability. The induction of sympathetic blockade decreases systemic vascular resistance (SVR) even further. There is also a remote risk of epidural abscess if bacteremic blood is introduced into the epidural space without prior antibiotic coverage.
- Uncorrected hypovolemia. With ongoing hemorrhage the fall in SVR can produce severe refractory hypotension.
- Coagulopathy. If a vessel is injured within the epidural space, an epidural hematoma could form, causing neurologic damage by spinal cord compression.

#### Relative contraindications

- Elevated intracranial pressure
- Prior back injury with neurologic deficit
- Progressive neurologic disease such as multiple sclerosis
- Chronic back pain
- Localized infection at the injection site

### 11. What are the potential complications of epidural anesthesia? Can they be anticipated or prevented?

- Hypotension caused by sympathetic blockade, which may be prevented by fluid preload and patient positioning.
- Intravascular injection of local anesthetic, which can be prevented by aspirating the catheter for blood, injecting a marker such as epinephrine that will cause tachycardia if injected into a vessel, and using incremental dosing (no more than 5 ml at a time). If an intravascular injection occurs:
  - Stop convulsions with an induction agent or rapid-acting anticonvulsant. Intubate the trachea, if necessary, for ventilation and airway protection.
  - Treat cardiovascular collapse with pressors, inotropes, and advanced cardiac life support protocols.
  - Recent work in animals and case reports in humans have supported use of intralipid infusion to treat local anesthetic toxicity from bupivacaine. The lipid may act as a *sink* to remove circulating bupivacaine from the circulation.
- Subarachnoid injection of a large volume of local anesthetic (“total spinal”). This can be prevented by aspirating the catheter for CSF and giving a small initial dose of local anesthetic to look for rapid onset of sensory block if the drug enters the CSF. (Remember: the onset of an epidural anesthetic is slow.) If a total spinal occurs, treat hypotension with pressors and support ventilation with positive pressure by mask or intubation.
- Postdural puncture headache caused by accidental dural puncture with the large-bore epidural needle. Although not completely preventable, this can be treated in various ways, depending on the preference of the patient and anesthesiologist. Common therapies include analgesics, caffeine, or an epidural *blood patch*. Factors determining choice of treatment include severity of the headache and how aggressively the patient wishes to be treated. To provide a blood patch, up to 20 ml of the patient’s blood is placed in the epidural space to seal the dural hole and elevate low CSF pressure.
- Epidural hematomas, which are extremely rare and usually occur spontaneously in clinical settings outside of the operating room rather than following neuraxial procedures. When they are associated with regional anesthesia, there is almost always a preexisting coagulopathy. Epidural hematomas present as back pain and leg weakness and must be diagnosed by computed tomography (CT) or magnetic resonance imaging. If the hematoma is not surgically decompressed in 6 to 8 hours, neurologic recovery is rare.

## 12. What physiologic changes should be expected after successful initiation of an epidural anesthetic?

- **Decrease in blood pressure:** Afterload reduction can actually be useful for patients with hypertension or congestive heart failure if preload is maintained.
- **Changes in heart rate:** Tachycardia may occur as cardiac output increases to compensate for a drop in SVR. Bradycardia may occur if blockade above T4 disrupts the cardiac sympathetic accelerator fibers.
- **Ventilatory changes:** In normal patients ventilation is maintained as long as the diaphragm is not impaired (phrenic nerve: C3-C5), but patients may become subjectively dyspneic as they become unable to feel their intercostal muscles. Patients who are dependent on their accessory muscles of respiration may be impaired at lower levels of anesthesia. The ability to cough and protect the airway may be lost even if ventilation is adequate.
- **Bladder distention:** Sympathetic blockade and loss of sensation may require catheterization for urinary retention.
- **Intestinal contraction:** Sympathetic blockade with parasympathetic predominance contracts the bowel.
- **Change in thermoregulation:** Peripheral vasodilation lowers core body temperature if the patient is not covered. Shivering is common during epidural anesthesia.
- **Neuroendocrine changes:** Neural blockade above T8 blocks sympathetic afferents to the adrenal medulla, inhibiting the neural component of the stress response. Glucose control is better maintained.

## 13. How does one choose which local anesthetic to use?

The choice of local anesthetic is usually based on the onset, duration, safety profile, and the special clinical characteristics of the patient and surgical procedure (Table 66-1).

TABLE 66-1. LOCAL ANESTHETICS USED IN EPIDURAL ANESTHESIA FOR SURGICAL PROCEDURES

Anesthetic	Class	Concentration (%)	Onset	Duration	Maximal Dose with Epinephrine	Comments
Chloroprocaine	Ester	3	Rapid	45 minutes	15 mg/kg	Rapid metabolism; least toxic; intense sensory and motor block
Lidocaine	Amide	2	Intermediate	60–90 minutes	7 mg/kg	Intense sensory and motor block
Bupivacaine	Amide	0.75, *0.5 <sup>†</sup>	Slow	2–3 hours	3 mg/kg	Most cardiotoxic; motor < sensory block
Ropivacaine	Amide	0.75	Slow	2–3 hours	3 mg/kg	Less cardiotoxic than bupivacaine; most expensive

\*Not available for obstetric use.

<sup>†</sup>May not always produce adequate surgical anesthesia.

#### 14. Why is epinephrine sometimes combined with the local anesthetic? Should it be included in all cases?

Epinephrine is often added to local anesthetic solutions in a concentration of 5 mcg/ml (1:200,000) or less. There are several benefits to this practice:

- Vasoconstriction prolongs blockade by reducing uptake into the bloodstream and delaying metabolism
- Improves quality and reliability of blockade, either by increasing the available local anesthetic through decreased uptake or by an intrinsic anesthetic mechanism on central  $\alpha$ -adrenergic receptors
- Reduces peak blood levels and risk of toxicity by slowing vascular absorption
- Helps to identify an intravascular injection when used as the marker in a test dose. If the epinephrine-containing solution is unintentionally injected into a blood vessel, tachycardia usually results

Epinephrine may be added to the local anesthetic solution for all blocks except those involving end arteries (digits, penis) or for patients in whom the tachycardia and hypertension may be detrimental (coronary artery disease, preeclampsia).

#### 15. When should opioids be included in the epidural anesthetic?

Opioids may be combined with local anesthetic to improve the quality of the surgical block or to manage postoperative pain, either alone or with a dilute local anesthetic solution. Examples of epidural bolus doses are fentanyl 50 to 100 mcg, sufentanil 20 to 30 mcg, and morphine 2 to 5 mg. The opioids act at the mu receptors in the substantia gelatinosa of the spinal cord. The more lipophilic opioids such as fentanyl and sufentanil have fast onset (5 minutes), short duration (2 to 4 hours), and lower incidence of side effects. Morphine is hydrophilic and does not attach to the receptor as easily. It has a long onset (1 hour), long duration (up to 24 hours), and a high incidence of side effects such as itching and nausea. Respiratory depression, although rare, is the most serious concern and requires special monitoring for the duration of the drug.

### KEY POINTS: EPIDURAL ANALGESIA AND ANESTHESIA



1. Epidural anesthesia is segmental (i.e., it has an upper and a lower level). The block is most intense near the site of catheter or needle insertion and diminishes with distance.
2. Advantages include avoidance of airway manipulation, decreased stress response, less thrombogenesis, improved bowel motility, awake patient, less postoperative nausea and sedation, better postoperative pain control, and faster turnover.
3. Disadvantages include slower initiation and higher failure rate than general anesthesia.
4. Contraindications include coagulopathy, hemodynamic instability, some types of spinal instrumentation, and patient refusal.
5. Complications include hypotension caused by sympathetic blockade, intravascular injection of local anesthetic, subarachnoid injection of a large volume of local anesthetic (*total spinal*), postdural puncture headache, and neurologic injury.

#### 16. Why can some patients with epidural blocks move around and even walk, whereas others have a dense motor block?

Preserving motor function is especially important in postoperative patients and laboring women. The degree of motor block can be decreased by lowering the concentration of local anesthetic and by choosing a local anesthetic with favorable sensory-motor dissociation.



As local anesthetic concentration decreases, the intensity of the block decreases, and fewer motor nerves are affected. Sensory block can be augmented by the addition of epidural opioids if desired. Bupivacaine and ropivacaine provide relatively less motor block for a given amount of sensory block (so-called sensory-motor dissociation). This property accounts for much of their popularity in obstetric anesthesia. For example, a common epidural infusion for postoperative pain or labor analgesia is 0.1% bupivacaine with 2 to 5 mcg/ml fentanyl.

**17. When is analgesia preferable to anesthesia?**

Anesthesia implies an intense sensory and motor blockade, which is necessary to perform a surgical procedure. It is usually obtained by using the highest available concentration of local anesthetic (e.g., 2% lidocaine or 3% chlorprocaine). Analgesia implies sensory blockade only, usually for postoperative pain management or labor analgesia, and may be achieved with dilute local anesthetic or epidural opioids.

**18. How do you determine the level of anesthesia needed for different types of surgeries? What is a segmental block? When is it used?**

To provide adequate surgical blockade with an epidural anesthetic, it is necessary to know the innervation of the structures stimulated during the procedure. For example, a transurethral resection of the prostate requires a T8 level because the bladder is innervated by T8 through its embryologic origins. A laparotomy such as a cesarean delivery requires a T4 level to cover the innervation of the peritoneum.

Epidural anesthesia is segmental (i.e., it has an upper and lower level). The block is most intense near the site of catheter insertion and diminishes with distance. The needle and catheter should be placed as close to the site of surgery as possible (e.g., a thoracic injection is used for chest surgery, whereas a midlumbar injection is used for hip surgery). In labor the lower limit of block can be kept above the sacral nerve roots until the second stage of labor to preserve pelvic floor tone and the perineal reflex.

**19. How do you determine the amount of local anesthetic solution used for different procedures? What factors affect spread in the epidural space?**

The extent of epidural blockade is determined primarily by the volume of local anesthetic; more dermatomes are blocked by more milliliters of local anesthetic. To achieve a T4 level from a lumbar epidural catheter, 20 to 30 ml of solution is required. Other factors that may affect spread in the epidural space include:

- Age: older patients require less local anesthetic
- Pregnancy: requires less
- Obesity: may or may not require less
- Height: taller patients may require more

**20. What is a combined spinal-epidural anesthetic? Why use both?**

For a combined spinal-epidural anesthetic, a long spinal needle is passed through an epidural needle that has been placed in the epidural space, and the dura is punctured. When CSF is obtained from the spinal needle, a dose of local anesthetic is placed in the subarachnoid space, and the spinal needle is removed. The epidural catheter is then threaded into the epidural space, and the epidural needle is removed. This technique combines the advantages of both spinal and epidural anesthesia: fast onset of an intense spinal block so that the surgery can proceed quickly and an epidural catheter to extend the duration of the block if necessary for a long surgical procedure or for postoperative pain management.

**21. What is a combined epidural-general anesthetic? Why give the patient two anesthetics?**

In some surgical procedures controlled ventilation may be safer for the patient or necessary for the surgical procedure. Examples would be intrathoracic or upper abdominal operations.

Because these procedures often result in moderate to severe postoperative pain, an epidural anesthetic can be an ideal way to provide pain relief and aid in postoperative mobilization to prevent pulmonary and thromboembolic complications. The epidural anesthetic is placed before induction of general anesthesia. By using the epidural catheter intraoperatively, smaller amounts of general anesthetic agents are required, which may result in fewer hemodynamic effects and faster awakening. At the same time the patient's airway can be protected, ventilation controlled, and hypnosis and amnesia provided.

## 22. What should the anesthesiologist ask the patient postoperatively after an epidural anesthetic?

- **Satisfaction with the anesthetic:** Was there anything that the patient thought should have been done differently? Assess patient satisfaction and try to correct any misunderstandings.
- **Regression of sensory and motor block:** Is there any residual blockade? Can the patient ambulate? Does the patient have any problem with bowel or bladder function? Any of these complaints requires a thorough neurologic examination to localize the deficit. Although the complaint is usually caused by residual local anesthetic or nerve compression during the surgical procedure (which often resolves with time), in rare instances further evaluation may be needed. Depending on the pattern and severity of the neurologic dysfunction, a formal neurology consultation, electromyogram, or CT may be needed to rule out pathology in the epidural space (such as hematoma).
- **Complaints of back pain:** Examine the site for bruising, redness, or swelling.
- **Complaints of headache:** If an accidental dural puncture occurred, the patient should be followed for several days; such headaches can appear up to 1 week later.
- **Adequacy of postoperative pain relief:** Did any side effects of epidural narcotics (itching, nausea) require treatment?

## WEBSITES



American Society of Regional Anesthesia and Pain Medicine  
<http://www.asra.com>

New York Society of Regional Anesthesia  
<http://www.nysora.com>

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# PERIPHERAL NERVE BLOCKS

Ronald Valdivieso, MD

## 1. What are the advantages of peripheral nerve blocks?

Peripheral nerve blocks (PNBs) share many of their advantages with neuraxial (spinal and epidural) anesthetic and analgesic techniques, first of which is the lack of need for airway instrumentation. This feature makes PNBs useful in cases in which airway management will be difficult or in which the patient has borderline respiratory function. PNB allows for shorter discharge times in ambulatory settings because of the decreased incidence of nausea, vomiting, and severe pain. PNB may diminish or prevent the development of chronic pain syndromes because of the lack of central nervous system sensitization that occurs after acute injury. Finally, patients with PNB have minimal if any opioid requirements in the immediate postoperative phase.

## 2. What basic principles should be followed to ensure a safe and successful peripheral nerve block?

Patients should be informed about the potential risks and benefits of PNB and allowed to decide on the anesthetic they prefer. Not all patients are good candidates for regional anesthetics. For example, performing PNB after high-velocity trauma to a lower extremity might obscure the diagnosis of a compartment syndrome. Sedation should be carefully titrated while performing a PNB because the patient should be able to communicate and give feedback to the clinician. This helps in confirming correct needle placement and giving an early warning of local anesthetic toxicity.

The clinician must have knowledge of the anatomy, technique, and equipment necessary to perform the most appropriate block for a given situation. The use of aseptic technique, correct equipment (B-bevel needles, nerve stimulators, ultrasound), and basic physiologic monitoring is mandatory. The area in which the PNB is performed should have immediate access to resuscitative equipment and medications.

## 3. What are the risks of performing a peripheral nerve block?

- There may be inadvertent damage to anatomic structures by the advancing needle. Examples include direct trauma to the nerve or spinal cord by intraneural injection of local anesthetic, nerve laceration, vascular injury with resulting hematoma formation, or pneumothorax.
- The drugs that are injected may have undesirable local and systemic effects. Allergic reactions to local anesthetics are rare. Ester local anesthetics are derivatives of *para*-aminobenzoic acid, a known allergen, and therefore more likely to cause allergic reactions than the amide local anesthetics. Any local anesthetic injected intravascularly has the potential for systemic reactions, including seizures and cardiovascular collapse.

## 4. How can the risks from a peripheral nerve block be minimized?

It is essential to ensure correct needle placement. Knowledge of the anatomy of the target region and the surrounding structures is necessary. Knowledge of the equipment and the pharmacology of local anesthetics is also required. Do not perform a PNB with which you are unfamiliar or not trained to do.

### 5. Describe a good technique for advancing the needle and injecting the local anesthetic solution.

Continuous aspiration is mandatory while advancing the needle; flow of blood or cerebrospinal fluid is an obvious sign that the needle needs to be redirected and the landmarks reevaluated. Be attentive to reports of symptoms experienced by the patient. A paresthesia indicates close proximity to a nerve; and, depending on the technique being used, it might constitute the end point.

Once it is determined that the needle is correctly positioned, a 1-ml test dose is administered. Severe pain during injection might be a sign of intraneural needle placement. Evidence suggests that monitoring the injection pressure is useful in preventing intraneural injection. After the test dose is administered, slow incremental injection of the local anesthetic solution is started. This is a very important safety feature since it allows recognition of signs of local anesthetic toxicity before cardiac collapse occurs.

### 6. How are peripheral nerves localized?

Use of anatomic landmarks allows precise identification of correct skin insertion sites. After the needle is inserted, the nerves are localized by nerve stimulation. The clinician looks for a known motor response during electrical stimulation of 0.5 mA or less to signal correct needle position. A paresthesia of the targeted nerve is another useful identifying sign. Finally, with the use of ultrasound, the known relationship of nerves to other anatomic structures such as blood vessels and fascial planes allows for nerve localization.

### 7. Is one technique to localize nerves better or safer than any other?

Improvements in ultrasound equipment have made ultrasonic guidance more popular over the past few years. The safety of PNB may also have been improved by the introduction of ultrasound, although no study has demonstrated this. In experienced hands there seems to be no significant difference between nerve stimulator and landmark techniques and ultrasound-guided PNB in terms of success rate or complications. It is my belief that, if nothing else, ultrasound guidance is responsible for a resurgence of interest in regional anesthesia in many anesthesia practices.

### 8. When using ultrasound guidance, what is the difference between an in-plane and an out-of-plane approach?

The in-plane approach means that the shaft of the needle is visualized while the needle is advanced (Figure 67-1). This technique allows the operator to observe the tip of the needle as it advances through the different anatomic structures. The out-of-plane approach relies on known anatomic relationships and careful injection (which can be observed in real time) to evaluate the adequacy of needle placement. In the out-of-plane approach the short axis (transverse cut) of the needle is visualized.

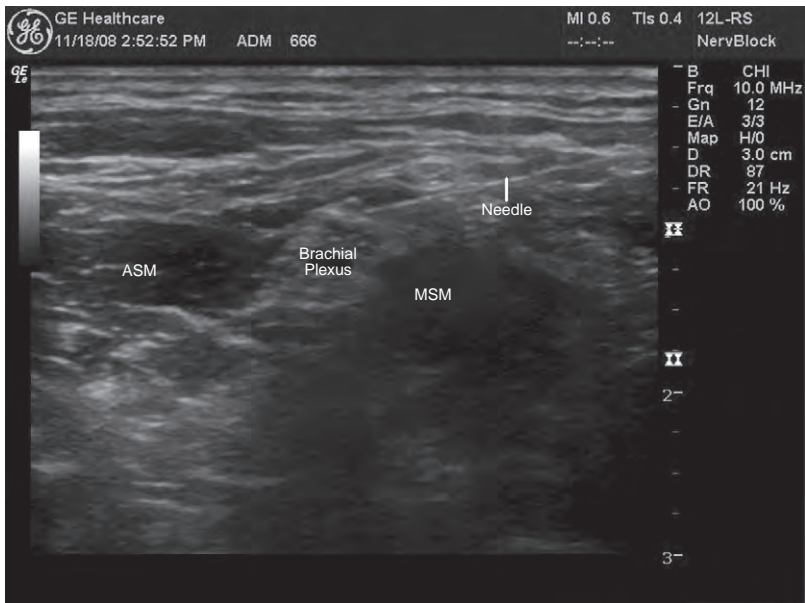
### 9. Review upper-extremity nerve blocks, including their indications, limitations, and complications.

See Table 67-1. The volumes of local anesthetic solutions for an adult are between 20 and 30 ml.

### 10. What is the Bier block and how is it performed?

The Bier block is also known as intravenous regional anesthesia. It is mostly used for anesthesia of the wrist and hand and usually for nonosseous procedures such as carpal tunnel release, trigger finger release, and ganglion resection. The Bier block works by local anesthetic diffusion from the intravenous space to the nerve fibers that travel in the vicinity of the veins in the upper extremity. The duration of the Bier block is up to 90 minutes, has a high patient satisfaction, and allows for rapid discharge of the patient.

The first step in performing a Bier block is securing intravenous (IV) access to the limb that is to be anesthetized. (The patient should also have an IV line in the opposite extremity for



**Figure 67-1.** A good example of an in-plane approach. Note the needle shaft and tip as it comes in contact with the brachial plexus between the anterior scalene muscle (ASM) and the middle scalene muscle (MSM).

administration of fluids and medications.) A small-gauge needle is enough, but care should be taken to place the IV line as distally as possible, usually in the back of the hand. A double tourniquet is placed around the upper arm. The arm is exsanguinated by elevating and wrapping it tightly with a wide elastic (Esmarch) band. The distal then proximal tourniquet is then inflated to 250 mm Hg. The Esmarch is removed, the distal tourniquet cuff is then deflated, and 40 to 50 ml of 0.5% lidocaine is injected through the IV line. Anesthesia sets in within minutes, and the surgical procedure might begin.

#### 11. How is local anesthetic toxicity avoided when performing a Bier block?

Local anesthetic toxicity will happen if the injected local anesthetic solution rapidly enters the central circulation. Local anesthetics can only gain access to the circulation if the tourniquet cuffs are purposefully or accidentally deflated. The anesthesiologists should have immediate access to the tourniquet, tubing, and pressuring device being used while performing a Bier block. Tubing should be secured and situated to avoid any accidental disconnection.

If the procedure lasts less than 30 minutes, the tourniquet is slowly and repeatedly deflated and reinflated. The brief deflations allow some of the local anesthetic into the circulation. The patient is quizzed for signs of local anesthetic toxicity. Perioral numbness, a metallic taste, and ringing in the ears are common early symptoms of mild toxicity. Should they occur, they should be allowed to resolve before further local anesthetic is released centrally. This should prevent more severe manifestations of local anesthetic toxicity such as seizures and cardiovascular collapse. Other mild symptoms include disinhibition as manifested by agitation and/or tearfulness.

TABLE 67-1. UPPER-EXTREMITY NERVE BLOCKS

	Interscalene	Supraclavicular	Infraclavicular	Axillary
Indications	Shoulder procedures (i.e., rotator cuff, total shoulder arthroplasty)	Complete anesthesia of the upper extremity; midhumerus to fingers	Anesthesia from the elbow down; peripheral nerve catheter placement	Anesthesia from the elbow down
Limitations	Ulnar nerve commonly missed; therefore should only be used for shoulder procedures	Difficult to perform without ultrasound guidance	Deep block that requires deeper sedation; could potentially miss the musculocutaneous nerve	Need to block the musculocutaneous nerve separately; might be difficult to perform in patients unable to move the upper extremity
Complications	Risk for intraspinal injection, injection into vertebral artery, 100% paralysis of ipsilateral phrenic nerve	Pneumothorax risk is somewhere between 3% and 6% when performed without ultrasound guidance	Puncture of the subclavian vessels	Puncture of the axillary vessels

## KEY POINTS: PERIPHERAL NERVE BLOCKS



1. There are multiple ways to localize peripheral nerves, including use of nerve stimulator, ultrasound guidance, paresthesia, and relationship to other structures such as arteries or fascial planes.
2. To date no particular technique to localize peripheral nerves has been demonstrated to produce fewer complications or a higher success rate when performed by appropriately trained personnel.
3. The correct use of PNB can decrease the incidence of perioperative complications such as pain, nausea, vomiting, and other opioid side effects caused by the decreased use of such drugs.

### 12. What peripheral nerve block can be performed for surgery of the lower extremity?

The first step in deciding what block is indicated for anesthesia or analgesia is appreciating the innervation of the lower extremity and the requirements of the proposed procedure. The lumbar plexus (L1-L4) gives origin to the ilioinguinal, genitofemoral, obturator, femoral, and

lateral femorocutaneous nerves and mainly innervates the inguinal region and the anterior aspect of the thigh. The rest of the lower extremity is innervated by the sacral plexus. This includes the posterior aspect of the thigh and all the area distal to the knee except for the medial aspect, which is the territory of the saphenous nerve, a branch of the femoral nerve. The main nerve arising from the sacral plexus is the sciatic nerve. The sciatic nerve is actually formed by union of the tibial and peroneal nerves. These two nerves separate in or slightly above the cephalad region of the popliteal fossa. Table 67-2 describes the most common indications, limitations, and complications of the most commonly performed PNB to the lower extremity.

TABLE 67-2. LOWER-EXTREMITY NERVE BLOCKS

	Lumbar Plexus	Femoral	Sciatic	Ankle
Indications	Hip procedures such as THA, hip fractures; in conjunction with a proximal sciatic block provides total anesthesia to the lower limb	Procedures in the anterior thigh, including TKA, and ACL reconstruction and analgesia for femur fractures	Below-the-knee procedures such as foot and ankle procedures, proximal and mid-tibia fractures, BKA	Foot procedures such as toe amputations, hammer toe corrections
Limitations	Difficult to perform, deep block that requires the patient to be placed in the lateral decubitus position	When trying to perform a three-in-one block (lateral femoro-cutaneous, femoral, and obturator) the obturator is frequently missed	Misses the internal aspect of the leg (saphenous nerve, branch of the femoral nerve)	Requires at least three different injections
Complications	Reports of retroperitoneal hematomas in patients on LMWH; epidural or spinal spread; injury to kidney or ureter	Injury to femoral vessels	Hematoma formation because of its deep position	Minimal

ACL, Anterior cruciate ligament; BKA, below-knee amputation; LMWH, low-molecular-weight heparin; THA, total hip arthroplasty; TKA, total knee arthroplasty.

### 13. What peripheral nerve block can be used to provide anesthesia or analgesia to the chest wall?

A thoracic paravertebral block can be performed to provide anesthesia for breast procedures such as lumpectomy or total mastectomy. Thoracic paravertebral analgesia is also used in patients undergoing VATS procedures and in patients with multiple unilateral rib fractures as an alternative to thoracic epidural catheter placement.

### 14. What peripheral nerve block can be used to provide anesthesia or analgesia to the anterior abdominal wall?

Anesthesia or analgesia to the lower quadrants or the inguinal region can be accomplished by performing intercostal blocks at the last three levels or blocking the genitofemoral and the ilioinguinal nerves. A more recently described approach, the transverse abdominis plane (TAP) block, is reported to cover the entire anterior abdominal wall, making it very useful in patients in whom epidural analgesia is impractical. TAPS block requires ultrasound guidance to ensure correct needle placement.

## WEBSITE



New York Society of Regional Anesthesia  
<http://www.nysora.com>

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# HEART TRANSPLANTATION

*Tamas Seres, MD, PhD*

## 1. What are the common diagnoses indicating heart transplantation in adults?

Although historically there has been an equal split between ischemic and nonischemic cardiomyopathy as the indication for transplantation, currently the incidence of nonischemic cardiomyopathy dominates. Valvular heart diseases (2%), retransplantation (3%), adult congenital heart diseases (3%), and miscellaneous conditions (3%) are the remaining indications for heart transplantation.

## 2. What is the bridge-to-transplant management of patients with heart failure?

At the time of transplant, 41% of adult recipients were receiving intravenous (IV) inotropic support and 29% were on some type of mechanical support device. This is a significant increase compared to the time period of 1999 to 2001 (34% and 19%, respectively). At the same time, substantially fewer adult recipients are now hospitalized immediately before transplant (47% compared with 72% in the period from 1999 to 2001). This reflects the current practice of outpatient management of patients on inotropic therapy with left ventricular assist devices.

## 3. What are the criteria for the selection of transplant recipients?

Patients with cardiac conditions not responding to maximal medical therapy follow:

- Severe heart failure (Grade D) and life expectancy less than 1 year
- Ischemic heart disease with intractable angina not amenable to interventional or surgical revascularization
- Intractable ventricular tachyarrhythmia
- Hypertrophic cardiomyopathy
- Congenital diseases without irreversible pulmonary hypertension (HTN)
- Management of cardiac tumor

## 4. What are the priority criteria for the selection of the recipients?

To ensure equitable distribution of donor hearts, the United Network for Organ Sharing (UNOS) has created an organ allocation system. Although many patients qualify for cardiac transplantation, actual donor heart allocation is based on UNOS priority status, ABO blood group compatibility, body-size match, and distance from the donor center. This policy resulted in a major decrease in mortality of patients on the waiting list. UNOS priority status reflects the urgency of the transplantation based on the severity and treatment modalities of the heart failure:

**Status 1A:** Inpatient with at least one of the following:

- Assisted mechanical support for acute decompensation
- Assisted mechanical circulatory support for >30 days with significant device-related complications
- Mechanical ventilation
- Continuous infusion of a single high-dose IV inotrope or multiple inotropes
- Life expectancy without transplantation of <7 days

**Status 1B:** Assisted mechanical circulatory support for >30 days

- Continuous infusion of IV inotropes

**Status 2:** A candidate who does not meet the criteria for Status 1A or 1B

**Status 7:** A candidate who is considered temporarily unsuitable to receive a thoracic organ transplant.

Thoracic organs are to be allocated locally first, then within one of the five zones in the sequence described by the UNOS allocation policy.

### 5. What is the significance of peak $VO_2$ measurement?

In general, the peak  $VO_2$  (maximum  $O_2$  uptake in ml/kg/min) appears to provide the most objective assessment of functional capacity in patients with heart failure (HF). Peak exercise capacity is defined as the maximum ability of the cardiovascular system to deliver  $O_2$  to exercising skeletal muscle and of the exercising muscle to extract  $O_2$  from the blood. As a result, exercise tolerance is determined by three factors: pulmonary gas exchange; cardiac performance; and skeletal muscle metabolism. Exercise capacity can be quantified clinically by measurement of  $O_2$  uptake ( $VO_2$ ), carbon dioxide production ( $VCO_2$ ), and minute ventilation. The  $VO_2$  eventually reaches a plateau despite increasing workload. At this point peak  $VO_2$  has a strong linear correlation with both cardiac output (CO) and skeletal muscle blood flow. The relationship between CO and  $O_2$  consumption also forms the basis for the Fick theorem to measure cardiac output:

$$CO = O_2 \text{ uptake} \div \text{Arteriovenous } O_2 \text{ difference}$$

### 6. What is the role of peak $VO_2$ in the decision-making process of heart transplantation?

Patients with a profoundly reduced exercise capacity of  $\leq 10$  ml/kg/min are likely to experience the most pronounced improvement in survival with transplantation; thus this patient can step forward on the priority list. With optimal pharmacologic and device therapy, the 1-year survival rate is increasing in low exercise capacity groups. However, observations suggest that persistent peak  $VO_2$  of 10 to 12 ml/kg/min may become criteria for referral for transplantation.

### 7. What are the absolute contraindications for the selection of the recipients?

Malignant tumor; active infection; human immunodeficiency virus–positive serology; irreversible, severe hepatic, renal, or pulmonary disease; and alcohol or IV drug abuse are absolute contraindications for heart transplantation. High, irreversible pulmonary vascular resistance (PVR) ( $>6$  Wood units/ $m^2$ ) and high transpulmonary gradient (mean pulmonary artery [PA] pressure – pulmonary capillary wedge pressure)  $>15$  mm Hg exclude patients also from heart transplantation.

### 8. What are the criteria for donor selection?

Acceptance of a potential organ donor requires confirmation of brain death and organ viability. Echocardiographic evaluation of cardiac function and coronary angiography for male donors older than 45 years and female donors older than 50 years are recommended. Although cardiac transplant recipients are screened before surgery for the percentage of reactive antibodies, donors and recipients are matched only on ABO blood group and weight ratio unless the percentage of reactive antibodies is greater than 20%.

### 9. How is anesthesia managed for organ harvesting?

Close attention is paid to monitoring of volume status and systemic arterial and central venous pressures. An inspired  $O_2$  concentration ( $FiO_2$ ) of 1 is optimal for organ viability unless the lungs are to be harvested. To decrease the possibility of  $O_2$  toxicity in the case of donor lung harvest, the lowest possible  $FiO_2$  that will maintain the  $PaO_2$  greater than 100 mm Hg should be used. Although intact spinal reflexes still may result in HTN, tachycardia, and muscle

movement, these signs do not indicate cerebral function or pain perception. Nondepolarizing muscle relaxants are commonly used to prevent spinal reflex-mediated muscle movement in response to noxious stimuli.

#### 10. How is the heart harvested and preserved for transplantation?

The donor heart is excised via median sternotomy. After initial dissection the patient is fully heparinized. Perfusion-sensitive organs (kidneys and liver) are removed via laparotomy before the heart if so planned. After excision the donor heart is placed in a plastic bag containing ice-cold saline and transported in an ice-filled cooler. Optimal myocardial function after transplantation is achieved when the donor heart ischemic time is less than 4 hours.

#### 11. In order of increasing acuity, review the physical status of patients awaiting heart transplantation.

- Patients with heart failure who are taking oral medications, including angiotensin converting enzyme inhibitors,  $\beta$ -adrenergic blockers, diuretics, vasodilators, digoxin, and warfarin, usually have low priority on the heart transplantation list.
- Patients may be on IV inotropes with or without vasodilators. The most frequently used inotropes are dobutamine and/or milrinone with or without nitroprusside. None of these medications can be used chronically because they decrease the long-term survival. The decision should be made to use mechanical assist devices or wait for a new heart for a limited time.
- Patients may be on a mechanical assist device. Intra-aortic balloon pump or ventricular assist devices can support left ventricular (LV) or right ventricular (RV) function or both. These patients have high priority for heart transplantation.
- Patients who have a failing transplanted heart and are waiting for retransplantation.

#### 12. What are the hemodynamic characteristics of the heart of the recipients?

Cardiac transplant recipients typically have hypokinetic, dilated, noncompliant ventricles sensitive to alterations in myocardial preload, afterload, and contractility.

#### 13. Describe an appropriate anesthetic induction for patients with heart failure.

Hemodynamic goals for anesthetic induction are to maintain heart rate (HR) and contractility, avoiding acute changes in preload and afterload. Inotropic support is often required during anesthetic induction and throughout the precardiopulmonary bypass (CPB) period. As a general rule, induction agents have negative inotropic effects on the heart. In clinical situations in which the sympathetic nervous system activated to maintain the hemodynamic stability of the patient, even etomidate or ketamine can promote cardiovascular collapse.

Rapid-sequence anesthetic induction is advisable in these cases. A full stomach and its risk for pulmonary aspiration should be considered because of short notice before the surgery. Furthermore, mask ventilation can be relatively ineffective, and the increasing CO<sub>2</sub> level elevates PA pressure, which decreases the CO in certain cases.

Etomidate in combination with fentanyl or sufentanil can be used in these patients with small doses of midazolam, ketamine, or scopolamine to ensure amnesia. Succinylcholine is appropriate for induction because of the concern of a full stomach. Timely administration of vasoactive agents is necessary in these patients because of the prolonged onset of the effect of medications. Epinephrine, phenylephrine, atropine, or glycopyrrolate vials should be available to keep the blood pressure (BP) and HR at the appropriate level for organ perfusion.

#### 14. How is anesthesia maintained for heart transplantation?

Patients with relatively stable hemodynamic status or on mechanical assist devices tolerate high-dose narcotics or a combination of anesthetic gases and narcotics. Patients with low CO

syndrome do not tolerate anesthetic gases well. Careful titration of narcotics can be the choice in this situation. Cardiostable muscle relaxants, including vecuronium, rocuronium, or *cis*-atracurium, can be used safely. Because of its vagolytic and mild sympathomimetic properties, the muscle relaxant pancuronium is commonly used to counteract high-dose narcotic-induced bradycardia.

#### 15. What monitors should be used for heart transplantation?

Noninvasive monitoring should include a standard five-lead electrocardiogram, noninvasive BP measurement, pulse oximetry, capnography, and nasopharyngeal and bladder temperature. Invasive monitoring should include systemic arterial, central venous, and PA pressure measurements. A PA catheter is helpful in the post-CPB period, permitting measuring of CO and ventricular filling pressures, and calculation of systemic and pulmonary vascular resistance. These indices are particularly useful for assessment and treatment of post-CPB pulmonary HTN and RV dysfunction. Intraoperative transesophageal echocardiography (TEE) is an important tool in evaluation of air in the transplanted heart and in monitoring LV and RV function.

#### 16. Are there specific preparations for cardiopulmonary bypass?

Many cardiac transplant recipients will have undergone previous cardiac surgery and are at increased risk for inadvertent trauma to the great vessels, myocardium, or preexisting coronary artery bypass grafts during repeat sternotomy.

Patients undergoing repeat sternotomy should have external defibrillation pads placed, and cross matched, irradiated, packed red blood cells should be available in the operating room before anesthetic induction.

The potential for a prolonged surgical dissection time in patients undergoing repeat sternotomy often necessitates that anesthesia be induced at an earlier than usual time to coordinate with donor heart arrival.

Femoral or axillary CPB cannulation may be necessary because of the potential for increased severe bleeding and trauma to the heart and great vessels through a previous sternotomy incision.

Moderate hypothermia (28° to 30° C) is commonly used during CPB to improve myocardial protection.

Hemofiltration is common during CPB, because patients with HF often have a large intravascular blood volume and coexistent renal impairment.

High-dose IV glucocorticoids such as methylprednisolone are administered before aortic cross-clamp release to reduce the likelihood of hyperacute rejection.

#### 17. Describe the etiology of coagulation disorders in these patients.

Potential etiologies include hepatic dysfunction secondary to chronic hepatic venous congestion, preoperative anticoagulation, CPB-induced platelet dysfunction, hypothermia, and hemodilution of clotting factors. Evaluation of prothrombin time, partial thromboplastin time, platelet number and/or the parameters of the thromboelastogram (TEG) can help to assess the coagulation status and plan the administration of appropriate blood products if there is clinical need.

#### 18. What antifibrinolytic agents can be used to decrease bleeding?

Antifibrinolytic medications such as tranexamic acid and  $\epsilon$ -aminocaproic acid are commonly administered after anesthetic induction to prevent postoperative bleeding. Aprotinin, a polypeptide protease inhibitor with platelet-preserving properties, has been shown to decrease perioperative blood loss in patients undergoing repeat sternotomy. However, this agent was removed from the market because of adverse effects on long-term survival and renal function.

**KEY POINTS: HEART TRANSPLANTATION**

1. Treatment modalities of heart failure include medical therapy, ventricular assist devices, and heart transplantation.
2. More and more patients with heart failure will be on ventricular assist device before heart transplantation.
3. Anesthesia for patients with heart failure requires assessment of hemodynamic status, invasive monitoring, and careful selection and titration of anesthetic agents.
4. There is a high risk for cardiovascular collapse during induction and maintenance of anesthesia because of the negative inotropic effect of anesthetic agents.
5. Before emergence from CPB, left and RV function, cardiac rhythm, and bleeding diathesis should be assessed and treated if necessary.
6. RV function plays a central role in successful emergence from CPB after heart transplantation.

**19. What preparation should be made before termination of cardiopulmonary bypass?**

Before CPB termination the patient should be normothermic, and all electrolyte/acid-base abnormalities corrected. Complete de-airing of the heart before aortic cross-clamp removal is essential because intracavitary air may pass into the coronary arteries, resulting in myocardial ischemia. TEE is particularly useful for assessing the efficacy of cardiac de-airing maneuvers. Inotropic agents should be commenced before CPB termination. An HR of 100 to 120 beats/min, a mean systemic arterial BP greater than 65 mm Hg, and ventricular filling pressures of approximately 12 to 16 mm Hg (central venous pressure [CVP]) and 14 to 18 mm Hg pulmonary capillary wedge pressure (PCWP) are goals for terminating CPB.

**20. What is the implication of autonomic denervation of the transplanted heart?**

During orthotopic cardiac transplantation, the cardiac autonomic plexus is transected, leaving the transplanted heart without autonomic innervation. The newly denervated heart does not respond to direct autonomic nervous system stimulation or to drugs that act indirectly through the autonomic nervous system (e.g., atropine). Instead, the denervated transplanted heart only responds to direct-acting agents such as catecholamines. Because transient, slow nodal rhythms are common after aortic cross-clamp release, a direct-acting  $\beta$ -adrenergic receptor agonist and/or epicardial pacing is commonly begun before CPB termination to achieve a HR of 100 to 120 beats/min. Infusions of dopamine, dobutamine, milrinone, or epinephrine are effective for inotropic support.

**21. What is the cause of the immediate left ventricular dysfunction after cardiopulmonary bypass?**

Post-CPB LV dysfunction may be a result of a prolonged donor heart ischemic time, inadequate myocardial perfusion, intracoronary embolization of intracavitary air, or surgical manipulation. The incidence of post-CPB LV dysfunction is greater in donors requiring prolonged, high-dose inotropic support before organ harvest.

**22. What is the cause of right ventricular failure after cardiopulmonary bypass?**

RV failure is a significant cause of early morbidity and mortality, accounting for nearly 20% of early deaths. Therefore prevention, diagnosis, and aggressive treatment of RV dysfunction

after CPB are essential. Acute RV failure after cardiac transplantation may be caused by preexistent pulmonary HTN in the recipient, transient pulmonary vasospasm, tricuspid or pulmonic valve insufficiency secondary to early postoperative RV dilation, and donor-recipient size mismatch. Additional factors that may contribute to postoperative RV dysfunction include a prolonged donor heart ischemic time, inadequate myocardial protection, and surgical manipulation of the heart.

### 23. How can right ventricular function be evaluated during the surgery?

RV distention and hypokinesis may be diagnosed by TEE or direct observation of the surgical field. Other findings suggesting RV failure include elevation in CVP, decreasing PA pressure, and high transpulmonary gradient (greater than 15 mm Hg). The pressure difference between CVP and mean PA pressure is a valuable parameter in evaluation of RV function. Decreasing difference or the difference  $<5$  mm Hg may indicate failing RV.

### 24. What are the treatment options for right ventricular failure?

Increased  $\text{FiO}_2$ , correction of acid-base abnormalities, and hyperventilation ( $\text{PaCO}_2$  of 25 to 30 mm Hg) may reduce pulmonary vascular resistance. RV function may be improved by inotropic support and pulmonary vasodilation (dobutamine, milrinone). Pharmacologic agents commonly used for pulmonary vasodilation include nitrates, prostacyclin (prostaglandin  $\text{I}_2$  [ $\text{PGI}_2$ ]),  $\text{PGE}_1$ , phosphodiesterase III inhibitors, and inhaled nitric oxide (NO).

### 25. What is the advantage of nitric oxide in the management of heart transplantation?

In contrast to nonselective vasodilators such as nitroglycerin and sodium nitroprusside that typically produce systemic hypotension, inhaled NO (20 to 40 ppm) selectively reduces PVR in the ventilated area of the lung, thus improving ventilation/perfusion mismatch. NO has little systemic effect because it is inactivated by hemoglobin and has a 5- to 10-second half-life.

### 26. What are the side effects of administration of nitric oxide?

NO administration results in the formation of nitrogen dioxide and methemoglobin, and the levels of these toxic metabolites should be monitored. In the presence of severe LV dysfunction, selective dilation of the pulmonary vasculature by NO may lead to an increase in PCWP and pulmonary edema. Thus agents producing both pulmonary and systemic vasodilation such as IV or inhaled  $\text{PGI}_2$  may be a better choice in this setting.

### 27. What are the concerns in anesthetic management of post-heart transplant patients for noncardiac surgery?

Cardiac denervation is an unavoidable consequence of heart transplantation, and reinnervation is absent or incomplete. Baseline cardiac function is normal, but the response to demands for increased cardiac output is altered. HR increases only gradually with exercise, and this effect is mediated by circulating catecholamines. Increases in cardiac output in response to exercise are mostly mediated via an increase in stroke volume. Therefore maintenance of adequate preload in these patients is crucial. Lack of parasympathetic innervation is responsible for the gradual decrease in HR after exercise. Drugs that act indirectly on the heart via either the sympathetic (ephedrine) or parasympathetic (atropine, pancuronium) nervous system will generally be ineffective.

## WEBSITE



United Network for Organ Sharing  
<http://www.unos.org/policiesandbylaws/policies.asp>

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# LIVER TRANSPLANTATION

Matthew J. Fiegel, MD

## 1. What is the Model for End-stage Liver Disease MELD?

The Model for End-stage Liver Disease (MELD) is a scoring system for prioritizing patients for liver transplantation. The MELD score is an objective model that predicts a patient's 90-day mortality while waiting for a liver transplant. It is a better predictor of perioperative mortality than the Child's scoring system and therefore has replaced it. MELD is calculated using bilirubin, international normalized ratio, and creatinine (the MELD calculator can be accessed at [www.UNOS.org](http://www.UNOS.org)). There are four listing status categories for patients with liver disease:

- **Status 1** includes patients with acute liver failure/disease with an estimated survival of less than 7 days (highest priority for liver transplantation).
- **Status 2a** (MELD score >29) includes patients with end-stage liver disease, severely ill, and potentially hospitalized.
- **Status 2b** (MELD score 24–29) includes patients with end-stage liver disease, severely ill, but not requiring hospitalization.
- **Status 3** (MELD score <24) includes patients with liver disease that is too early for cadaveric transplantation but may be a suitable live donor transplantation candidate.

## 2. Describe some indications and contraindications for liver transplantation.

Indications for liver transplantation include end-stage liver disease from hepatocellular disease, cholestatic disease, vascular disease, or polycystic disease. In addition, some nonresectable hepatic malignancies, metabolic liver diseases, and fulminant hepatic failure are indications (Table 69-1). Over time relative and absolute contraindications for liver transplantation have evolved (Table 69-2). Because MELD predicts 3-month survival, those with the highest scores have the greatest chance of dying from liver disease and thus have the best risk-benefit ratio for undergoing liver transplantation.

## 3. How does the cardiovascular physiology of a patient with end-stage liver disease differ from that of a normal patient?

Patients with end-stage liver disease have a hyperdynamic circulation, characterized by increased cardiac index and decreased systemic vascular resistance. This results in a consistently lower blood pressure and increased heart rate. Patients are significantly less responsive to catecholamines. Cirrhotic patients tend to be overloaded with total body water but arterially dehydrated. Pulmonary blood flow is increased and can result in increased pulmonary artery pressures; pulmonary vascular resistance usually remains normal. Coronary artery disease with resulting impaired myocardial function (previously thought to be uncommon in patients with liver disease) may be present, especially when the patient has diabetes. Coronary artery disease in liver transplant patients older than 50 years occurs in a range of 5% to 27%. Abnormalities in both systolic and diastolic function may be present and result in an inadequate cardiac output for the degree of vasodilation. This is especially true in patients with a history of alcohol abuse.

## 4. What are some preanesthetic considerations in a liver transplant patient?

Optimal anesthetic management of these complex, critically ill patients requires management of the pathophysiologic changes of liver disease, comorbid conditions, and the physiologic changes associated with the surgery. In some instances (e.g., pulmonary hypertension, hepatorenal



TABLE 69-1. INDICATIONS FOR LIVER TRANSPLANTATION

**Fulminant hepatic failure**

Viral hepatitis (e.g., A, B, delta)

Drug-induced

Metabolic disease (Wilson's disease, Reye's syndrome, organic acidurias)

**End-stage chronic liver disease**

Predominantly hepatocellular disease

Alcoholic, chronic viral, idiopathic autoimmune, and chronic drug-induced liver disease

Predominantly cholestatic disease

Primary biliary cirrhosis, primary sclerosing cholangitis, biliary atresia, and familial cholestatic syndromes

Predominantly vascular disease

Budd-Chiari syndrome and veno-occlusive disease

Polycystic disease

**Nonresectable hepatic malignancies**

Hepatocellular carcinoma, cholangiocarcinoma, and carcinoid

**Metabolic liver disease**

$\alpha$ 1-Antitrypsin deficiency, Wilson's disease, hemochromatosis, glycogen storage disease, etc.

TABLE 69-2. CONTRAINDICATIONS TO LIVER TRANSPLANTATION

**Absolute contraindications**

Sepsis outside hepatobiliary tree

Metastatic hepatobiliary malignancy

Advanced cardiopulmonary disease

Moderate to severe pulmonary hypertension refractory to vasodilator therapy

AIDS

**Relative contraindications**

Advanced chronic renal failure

Age >60 years

Portal vein thrombosis

Cholangiocarcinoma

Hypoxemia with intrapulmonary right-to-left shunts

Hepatitis: HBsAg and HBeAg positivity

Prior portocaval shunting procedure

Prior complex hepatobiliary surgery

Active alcohol and/or drug abuse

HIV positivity without clinical AIDS

Advanced malnutrition

Modified from Maddrey WC, Van Thiel DH: Liver transplantation: an overview, *Hepatology* 8:948, 1988. AIDS, Acquired immunodeficiency syndrome; HIV, human immunodeficiency virus.

syndrome), hepatic disease may be overshadowed by the severity of the comorbid conditions. Prior abdominal surgeries and encephalopathy are important features to note, as are coagulation deficits (factor deficiencies and thrombocytopenia). The thromboelastogram (TEG) provides valuable insight into the patient's entire clotting process. The TEG graphs the viscoelastic properties of a clot from the formation of the first fibrin strands to the full hemostatic plug. Thus the TEG is a dynamic test showing the evolution of clot formation. Because the TEG examines multiple phases of clot formation within a single test, it reflects information that is otherwise available only in multiple tests. The TEG is the best laboratory assessment of qualitative platelet function.

Electrolyte abnormalities are common. Hypokalemia is commonly seen in earlier stages of liver disease since hepatic injury leads to hyperaldosteronism. Hyperkalemia may be caused by the use of potassium-sparing diuretics to treat ascites and hepatorenal syndrome. Hyponatremia may result from diuretic use, hyperaldosteronism, or volume overload. Renal dysfunction should be assessed since intraoperative dialysis may be necessary. In fulminant hepatic failure, cerebral cytotoxic edema is a common complication, and there must be aggressive preoperative control of intracranial pressure to prevent brainstem herniation, a common cause of death. Patients with cerebral edema should have an intracranial pressure monitoring device.

Pulmonary hypertension associated with cirrhosis occurs in approximately 8% of patients and is a cause of significant intraoperative morbidity and mortality. Many liver failure patients are hypoxemic secondary to atelectasis and hepatopulmonary syndrome. All potential transplant candidates should undergo a screening transthoracic echocardiogram to assess pulmonary arterial pressures, left ventricular function, and intrapulmonary shunting. If pulmonary arterial pressures are elevated or right ventricular function is decreased, a right heart catheterization may be indicated.

#### 5. What is the significance of portal pulmonary hypertension? How are these patients managed in the pretransplant period?

In contrast to most transplant recipients, portal pulmonary hypertension (PPHTN) patients have an increased risk of death because of right ventricular failure in the peritransplantation period. Physicians are uncertain which PPHTN patients may undergo transplantation because there are no patient characteristics that clearly predict outcome. Patients with moderate to severe PPHTN should not be considered candidates until they undergo a trial of vasodilator therapy. The cause of pulmonary hypertension in liver failure patients is unknown, but the disease shares many similarities with primary pulmonary hypertension. Tissue hypoxia likely plays a role. The pulmonary circulation has increased vascular resistance that is transmitted back to the right heart and liver. The pulmonary vessels of patients with PPHTN are unable to accommodate increased blood flow during periods of aggressive blood transfusion and during the hyperdynamic postreperfusion phase, potentially resulting in acute right ventricular failure. Rapid dilation of the right ventricle can also compress the right coronary vessels, producing myocardial ischemia and infarction. Pulmonary hypertension will not resolve in all patients who were successfully transplanted with a new liver.

Vasodilators reduce pulmonary artery pressures and prolong survival in some pulmonary hypertension patients. The prostaglandin epoprostenol (Flolan) can reduce pulmonary artery pressures when given as a chronic infusion and has been used to bridge patients to transplantation. Nitric oxide inhaled in doses up to 80 ppm also acutely reduces pulmonary artery pressures in a small number of PPHTN patients and has been used in the operating room to reduce pulmonary artery pressures. More recently, sildenafil (Revatio) has been implemented as an oral agent to reduce pulmonary hypertension in transplant candidates.

#### 6. What are the concerns before anesthetic induction in the patient with end-stage liver disease?

- The room should be prewarmed because hypothermia will only worsen the preexisting coagulopathy.
- Preoxygenation should begin immediately on entering the operating room because hypoxemia is common in liver disease.

- Ascites, active gastrointestinal bleeding, gastroesophageal incompetency because of prior sclerotherapy, or hepatic encephalopathy may result in delayed gastric emptying. Therefore these patients are at risk for pulmonary aspiration, and a rapid-sequence induction is indicated.
- Plasma pseudocholinesterase levels are typically lower in this patient population, but a significant prolongation of the relaxant effect of succinylcholine is not common.
- Because of the risk of variceal bleeding and presence of coagulopathy, a naso/orogastric tube should be placed very carefully. Transesophageal echo is relatively contraindicated for the previous reasons.
- Liver disease affects drug distribution and metabolism. Patients with liver disease commonly have an increased volume of distribution, necessitating an increase in initial dose requirements. However, because the drug metabolism may be reduced, smaller doses are subsequently administered at longer intervals. The muscle relaxant cisatracurium has organ independent breakdown and thus is the preferred muscle relaxant for liver transplantation.
- Fentanyl, although completely metabolized by the liver, does not show a prolonged effect in cirrhosis. It also does not decrease hepatic blood or oxygen supply. Either fentanyl or remifentanyl are the opioids of choice during liver transplantation.

### 7. Describe the three stages of liver transplantation.

- The **preanhepatic (dissection) stage (stage 1)** begins with the surgical incision and dissection and mobilization of the patient's diseased liver. During this stage the surgeons identify the hepatic artery, portal vein, and the inferior vena cava, above and below the liver.
- The **anhepatic stage (stage 2)** isolates the liver from the circulation and commences with the occlusion of the hepatic artery and portal vein. Occlusion of the inferior vena cava above and below the liver is typically performed so the liver can be removed. During the anhepatic stage, the donated liver is reinserted into the circulation by anastomoses to the patient's vena cava, portal vein, and hepatic artery. The anhepatic stage concludes with removal of the vascular clamps, resulting in reperfusion of the donor liver graft.
- The **reperfusion stage (stage 3)** starts during portal vein reperfusion and extends to the conclusion of the operation. Biliary reconstruction takes place during this phase as does assessment of neohepatic function.

### 8. What is the role of venovenous bypass? Are there any alternatives?

During the anhepatic phase, after vascular clamps are placed on the inferior vena cava, venous return to the heart drops precipitously. To improve blood return, some physicians use a bypass circuit to return venous blood from the lower part of the body back to the thorax. However, some physicians control the decline in blood pressure that occurs during occlusion of the vena cava with vasopressors rather than with venovenous bypass. Another alternative is to place a cross-clamp over part of the vena cava and remove the liver with the part of the vena cava attached to the hepatic veins. Because part of the vena cava remains open to flow, venous return from the lower body is not compromised. Choice of technique depends on the amount of scarring surrounding the liver and surgeon preference.

### 9. List some of the anesthetic concerns during the preanhepatic (dissection) phase.

- Instituting warming measures early and maintaining normothermia are important because the metabolic activity of the liver contributes significantly to maintaining body temperature. Early temperature losses during the procedure are difficult to correct and potentiate coagulation disturbances.
- Hyperkalemia resulting from administration of blood products and impaired excretion caused by hepatorenal syndrome can be a life-threatening complication leading to cardiac arrest. The donor organ preservative solution contains 150 mEq/dl of potassium. On reperfusion, much of this potassium reaches the patient's circulation. Therefore it is important to control potassium early in the surgery, maintaining serum levels at

- approximately 3.5 mEq/dl. This is achieved with loop diuretics (furosemide) and hyperventilation. If these agents fail, intraoperative hemodialysis should be considered.
- Hyponatremia in patients with liver disease should not be corrected rapidly because fluctuations in the serum sodium during transplantation have produced pontine demyelination, resulting in debilitating disease or death.
  - Because citrate in banked blood normally undergoes hepatic metabolism, it accumulates during liver transplantation. Citrate binds calcium and can contribute to profound hypocalcemia.
  - Blood loss during this stage can be significant. It should be anticipated in any patient who has had previous intra-abdominal surgery, especially in the right upper quadrant.
  - Besides preexisting coagulopathies, mechanical reasons for excessive bleeding in liver failure patients include increased portal pressures with excessive splanchnic venous filling and hyperdynamic flow.
  - Patients with cirrhosis have splanchnic hypervolemia. Often splanchnic vasoconstrictors such as vasopressin are started in an attempt to return the splanchnic blood to the arterial circulation.
  - By the completion of this phase, patients should be warm, have coagulopathies and intravascular deficits corrected, display good urine output, and possess normal electrolytes.

#### 10. What are some anesthetic concerns that arise during stage 2, the anhepatic phase?

Once the dissection is finished, blood loss is usually minimal, but blood volume may be decreased from hemorrhage during the preanhepatic phase. Because the inferior vena cava is typically cross-clamped, half of the patient's blood volume is confined to the lower body. Therefore central filling pressures are a poor representation of total body blood volume. Most therapy in this phase is directed toward achieving hemodynamic stability and preparing for reperfusion by correcting potassium and pH. Steroids are also administered during this stage. Steroids are the initial step in rendering the patient immunosuppressed so he or she will not reject the new organ. They must be administered before reperfusion.

Hyperkalemia, hypocalcemia, and metabolic acidosis are common during the anhepatic stage and must be corrected since the anhepatic patient has no means of physiologic compensation. Hyponatremia caused by administration of sodium bicarbonate for metabolic acidosis is managed by administration of dextrose in water (D<sub>5</sub>W). Increases in PaCO<sub>2</sub> associated with bicarbonate administration also require adjustments in ventilation. Perhaps a better buffering agent is tromethamine (THAM). THAM is a low sodium buffer that does not increase sodium or PaCO<sub>2</sub>. As previously discussed, serum potassium must be aggressively lowered to <3.5 mEq/L to prevent hyperkalemia-induced asystole during reperfusion. Hyperventilation, alkalinizing agents, and insulin are all effective at doing this. The severity of these electrolyte abnormalities is related to the length of stage 2, severity of patient illness, hypotension, number of blood products administered, and renal function.

An acute decrease in venous return following caval occlusion leads to hypotension. There is relative hyperemia inferior to the cross-clamp and poor venous return above the cross-clamp. Distal anatomic shunts may act as capacitance vessels, sequestering intravascular volume and regulating rates of venous return. New vessel formation, in addition to enlargement of portosystemic connections, will influence central venous return and therefore cardiac output following caval occlusion. Although there are no reliable predictors of hemodynamic instability during venous occlusion, an accentuated hyperdynamic circulatory state, severe portal hypertension, and advanced age have been associated with adverse hemodynamic events.

#### 11. Define reperfusion syndrome. What are its clinical implications?

Reperfusion syndrome is characterized by either a decrease of 30% or more in mean arterial pressure (from baseline) for greater than 1 minute and occurring within the first 5 minutes of reperfusion or a mean arterial pressure less than 60 mm Hg under the same circumstances. Following portal vein unclamping, approximately 30% of patients will exhibit profound

cardiovascular collapse on reperfusion irrespective of attentive management during stage 2. This tends to be more profound with a histidine, tryptophan, ketoglutarate preservative solution as opposed to a University of Wisconsin preservative solution. The bradycardia, myocardial depression, and systemic vasodilation noted during reperfusion are secondary to rapid increases in serum potassium, decreases in temperature, acute acidosis, and release of vasoactive substances by the grafted liver. These vasoactive mediators include prostaglandins, kallikrein, platelet-activating factor, and leukotrienes. Increased age and larger donor organs also are considered risk factors.

Generally treatment with calcium, atropine, and/or epinephrine improves cardiovascular function. Fluid administration should be judicious because it can aggravate the already increased filling pressures (secondary to myocardial depression), resulting in impaired hepatic perfusion. Although the hemodynamic changes generally subside within 10 to 15 minutes, pulmonary hypertension, elevated central venous pressure, and hypotension may persist. Continuous vasopressors such as vasopressin or phenylephrine may be necessary to combat the persistent vasodilation.

## 12. Describe some of the major anesthetic management issues during the reperfusion stage (stage 3).

- Wide swings in blood pressure and arrhythmias can be expected. Hypertension may be caused by a large increase in blood flow from the lower body to the systemic circulation following unclamping of the inferior vena cava. Alternatively release of the portal vein clamp directs blood through the liver graft to the heart, and products of cell death and residual preservation fluid can cause severe hypotension, bradycardia, supraventricular and ventricular arrhythmias, electromechanical dissociation, and occasionally cardiac arrest. Many of these complications can be attenuated by meticulous management during stage 2.
- Hypotension may also be the result of surgical bleeding since the anastomotic sites are exposed to venous pressure.
- Mild to severe coagulation defects are commonly observed during stage 3 because the new liver requires time to resume its synthetic functions. Treatment should be guided by the TEG. Clotting variables gradually return to normal by a combination of specific replacement therapy and production by the allograft. Fibrinogen levels should be assessed in the setting of ongoing bleeding and lack of clot formation.
- Urine output typically improves, even in patients with prior hepatorenal syndrome, and inotrope requirements diminish.
- The procedure is completed by biliary reconstruction, either by direct bile *duct-to-duct* anastomosis or by a Roux-en-Y choledochojejunostomy.

## KEY POINTS: LIVER TRANSPLANTATION



1. The anesthesiologist should be a member of the hospital liver transplant team and play a critical role in the pretransplant evaluation and candidate selection process.
2. Although patients with end-stage liver disease have a hyperdynamic circulation characterized by increased cardiac index and decreased systemic vascular resistance, impaired myocardial function, coronary artery disease, and pulmonary hypertension are common.
3. Patients with liver disease commonly have an increased volume of distribution, necessitating an increase in initial dose requirements. However, because the drug metabolism may be reduced, smaller doses are subsequently administered at longer intervals.
4. Concerns during the preanhepatic stage of liver transplantation include aggressive rewarming; attention to serum potassium, sodium, and calcium levels; replacing significant blood losses; treating coagulation disturbances; and restoring effective arterial blood volume.

5. Concerns during the anhepatic stage include correction of hyperkalemia, hypocalcemia, and metabolic acidosis and restoration of intravascular volume in anticipation of vascular unclamping and reperfusion syndrome.
6. Wide swings in blood pressure and arrhythmias can be expected during the postanhepatic stage. Surgical bleeding and impaired coagulation are concerns. Urine output typically improves, the biliary tree is reconstructed, and graft function must be assessed.

### 13. What are indicators of graft function during stage 3?

An important part of the post anhepatic phase is the evaluation of graft function, as demonstrated by the following:

- The ability to maintain ionized calcium levels without supplementation (i.e., the liver is metabolizing citrate)
- Normalization of the base deficit, implying hepatic acid clearance
- Improving patient temperature toward normothermia
- Bile production noted before abdominal closure
- Clot production implying hepatic synthesis of clotting factors
- Signs suggestive of poor graft function include acute deterioration in urinary output with no other explanation, prolonged hypotension requiring pressor support, and recalcitrant coagulopathy.

## WEBSITE



United Network for Organ Sharing  
<http://www.unos.org>

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# CARDIOPULMONARY BYPASS

*Nathael Weitzel, MD*

## 1. What are the main functions of a cardiopulmonary bypass circuit?

A cardiopulmonary bypass (CPB) circuit functions as the temporary equivalent of the native cardiopulmonary system. The CPB circuit allows for perfusion of the patient's vital organs while oxygenating the blood and removing carbon dioxide (CO<sub>2</sub>). Isolation of the cardiopulmonary system allows for surgical exposure of the heart and great vessels along with cardiac electrical silence and a bloodless field.

## 2. What are the basic components of the cardiopulmonary bypass circuit?

A CPB circuit has a venous line, which siphons central venous blood from the patient into a reservoir. This blood is then oxygenated and has CO<sub>2</sub> removed before being returned to the patient's arterial circulation. Pressure to perfuse the arterial circulation is supplied by either a roller head or a centrifugal pump, usually resulting in nonpulsatile arterial flow, although some roller pumps can deliver pulsatile flow. The machine also has roller head pumps for cardioplegia administration, a ventricular vent to drain the heart during surgery, and a pump sucker to remove blood from the surgical field. In addition, the circuit contains filters for air and blood microemboli because both can cause devastating central nervous system injury if delivered to the arterial circulation. A heat exchanger is present to produce hypothermia on bypass and warm the patient before separating from CPB. The venous reservoir must never be allowed to empty while on CPB because a life-threatening air embolism could result.

## 3. Define the levels of hypothermia. What are adverse effects of hypothermia?

- **Mild:** 32–35° C
- **Moderate:** 26–31° C
- **Deep:** 20–25° C
- **Profound:** 14–19° C—This level of hypothermia is achieved if total circulatory arrest is planned.

Typical cardiopulmonary bypass temperatures range from 28° C to 33° C. Adverse effects of hypothermia include platelet dysfunction, reduction in serum ionized calcium concentration caused by enhanced citrate activity, impaired coagulation, arrhythmias, increased risk of infection, decreased oxygen unloading, potentiation of neuromuscular blockade, and impaired cardiac contractility.

## 4. Why is hypothermia used on cardiopulmonary bypass?

Systemic oxygen demand decreases 9% for every degree of temperature drop. Therefore hypothermia allows for lower CPB pump flows while providing adequate oxygen supply to vital organs. The main concern of CPB is the prevention of myocardial injury and central nervous system injury, along with renal and hepatic protection.

## 5. Discuss the common cannulation sites for bypass.

Venous blood is typically obtained through cannulation of the right atrium using a two-stage cannula that drains both the superior and inferior vena cava. Alternatively for open heart procedures bicaval cannulation is used with direct, separate cannulation of the superior and inferior vena cavae. Arterial blood is returned to the ascending aorta proximal to the

innominate artery. The femoral artery and vein can be used as alternative cannulation sites. Drawbacks to femoral bypass include ischemia of the leg distal to the arterial cannula, inadequate venous drainage, possible inadequate systemic perfusion secondary to a small inflow cannula, and difficulty in cannula placement because of atherosclerotic plaques. Axillary artery cannulation can be used for repeat sternotomies and is often carried out before the sternotomy itself to allow for arterial fluid or blood administration from the CPB machine during the sternal dissection if necessary.

#### 6. What are the basic anesthetic techniques used in cardiopulmonary bypass cases?

Historically many cardiac cases were managed using high-dose opioid anesthetic techniques for fear of cardiac depression with use of inhalational gases or induction agents such as propofol. During the past 20 years improvement in surgical technique and CPB circuit design, along with added experience using inhalation agents, has resulted in a moderate reduction in opioid dosing. The main benefit of lower opioid dosing is a decreased time to extubation on arrival in the intensive care unit—so-called *fast tracking*. Important details in determining anesthetic choice include degree of systolic dysfunction caused by coronary disease, degree of valvular involvement, and overall exercise tolerance. These critically ill cardiac patients require delicate anesthetic management. Patients undergoing CPB have been identified as a high-risk group for intraoperative awareness, likely a result of opioid-based techniques. Amnestic agents such as midazolam are routinely used along with inhalational agents, which can be administered by the perfusionist during CPB. Neuromuscular blocking agents prevent patient movement and shivering, decreasing systemic oxygen demand during bypass and diaphragmatic contraction during the surgical procedure.

#### 7. List the two basic types of oxygenators.

1. Bubble oxygenators work by bubbling oxygen ( $O_2$ ) through the patient's blood and then defoaming the blood to minimize air microemboli.
2. Membrane oxygenators use a semipermeable membrane that allows diffusion of  $O_2$  and  $CO_2$ . Membrane oxygenators have a lower risk of gas microemboli, cause less damage to blood elements, and are the main type used in clinical practice.

#### 8. What is meant by pump prime? What is the usual hemodynamic response to initiating bypass?

Priming solutions of crystalloid, colloid, or blood are used to fill the CPB circuit. When bypass is initiated, the circuit must contain fluid to perfuse the arterial circulation until the patient's blood can circulate through the pump. Priming volumes historically were 1.5 to 2 L, but newer CPB circuits can achieve priming volumes as low as 800 ml for an open circuit and even less with a so-called *closed* or *mini-bypass circuit*. Reductions in priming volume have resulted in decreased inflammatory response and a reduction in transfusion requirements. The acute hemodilution from the patient's circulating blood volume mixing with the prime volume can cause an acute reduction in mean arterial pressure and the hemoglobin concentration.

#### 9. Why is systemic anticoagulation necessary?

Contact activation of the coagulation system occurs when nonheparinized blood contacts the synthetic surfaces of the CPB circuit, resulting in widespread thrombosis, oxygenator failure, and death. In a dire emergency a minimum standard dose of 300 units/kg of heparin must be given through a central line before the initiation of bypass. Following separation from the CPB machine, protamine is used to bind heparin and reverse the anticoagulant effect.

#### 10. How is the adequacy of anticoagulation measured before and during bypass?

Activated clotting time (ACT) is measured about 3 to 4 minutes after heparin administration and every 30 minutes on CPB. An ACT of 400 seconds or longer is considered acceptable.



Heparin levels are measured frequently, but only the ACT is a measure of anticoagulant activity. This is particularly important in patients with heparin resistance (seen with preoperative heparin infusions) and antithrombin III deficiency.

### 11. What must be ascertained before placing the patient on cardiopulmonary bypass?

- Adequate arterial inflow of oxygenated blood with acceptable line pressures
- Sufficient venous return to the bypass pump
- ACT of at least 400 seconds
- Appropriate placement of retrograde cardioplegia cannula if being used.
- Arterial line monitor of mean blood pressure
- Core temperature monitoring
- Adequate depth of anesthesia

### 12. Why is a left ventricular vent used?

Left ventricular distention during bypass can be caused by aortic regurgitation or blood flow through the bronchial and thebesian veins. The resultant increase in myocardial wall tension can lead to myocardial ischemia by precluding adequate subendocardial cardioplegia distribution and elevating myocardial oxygen demands. A left ventricular vent, placed through the right superior pulmonary vein, decompresses the left side of the heart and returns this blood to the CPB pump.

### 13. What are the characteristics of cardioplegia?

Cardioplegia is a hyperkalemic solution containing various metabolic energy substrates. Perfused through the coronary vasculature, cardioplegia induces diastolic electromechanical dissociation. Myocardial oxygen and energy requirements are reduced to those of cellular maintenance. Cardioplegia is perfused either antegrade via the aortic root coronary ostia or retrograde through the right atrial coronary sinus.

### 14. Discuss myocardial protection during cardiopulmonary bypass. What elements should be in place to optimize myocardial protection?

Cellular integrity must be maintained during CPB to ensure cardiac performance after CPB. A critical factor to prevent cellular damage is intraoperative myocardial protection. Preservation of the balance between myocardial oxygen consumption and delivery is essential, and the following are key elements in achieving this:

- Adequate cardioplegia
- Hypothermia, specifically myocardial hypothermia with myocardial temperature goals below 12 to 15° C
- Topical cooling of the heart with icy saline slush
- Left ventricular venting to prevent distention
- Insulating pad on the posterior cardiac surface to prevent warming from mediastinal blood flow
- Minimizing bronchial vessel collateral flow (which rewarms the arrested heart)

Inadequate preservation manifests after CPB as impaired cardiac output, ischemic electrocardiogram (ECG) changes, and wall motion abnormalities on transesophageal echocardiogram (TEE), dysrhythmias, and the requirement for inotropic support.

### 15. What is the function of an aortic cross-clamp?

Clamping across the proximal aorta isolates the heart and coronary circulation. The arterial bypass inflow enters the aorta distal to the clamp. Cardioplegia is infused between the clamp and aortic valve, thus entering the coronary circulation. This isolation of the heart from the systemic circulation allows for prolonged cardioplegia activity, diastolic arrest of the heart, and profound myocardial cooling.

**16. Review the physiologic responses to cardiopulmonary bypass.**

- Stress hormones, including catecholamines, cortisol, angiotensin, and vasopressin, increase in part because of decreased metabolism of these substances.
- Exposure of blood to the CPB circuit results in complement activation, initiation of the coagulation cascade, and platelet activation. A systemic inflammatory response is also initiated.
- Platelet dysfunction associated with CPB may contribute to post-CPB bleeding.
- Hemodilution associated with onset of CPB decreases the serum concentrations of most drugs, but decreased hepatic and renal perfusion during CPB will eventually increase the serum concentration of drugs administered by continuous infusion.

**17. What are the pH-stat and  $\alpha$ -stat methods of blood gas measurement?**

There are differing opinions as to whether blood gases should be corrected for the temperature during CPB because the solubility of gases decreases with hypothermia. All blood gases are analyzed at 37° C. In pH-stat measurements, the obtained value is corrected on a nomogram, and the reported values refer to the partial pressure at the hypothermic temperatures. CO<sub>2</sub> is then added to the system to correct the acid-base status. More commonly blood gases are reported uncorrected for temperature, a method referred to as  $\alpha$ -stat blood gas management. Studies comparing the two methods show conflicting results, with the main concern being the alteration in cerebral vascular tone caused by the CO<sub>2</sub> management. In adults  $\alpha$ -stat management leads to improved outcomes and is commonly used. Neonatal data indicates a trend toward neurologic improvement using pH-stat management, which is therefore used in this population.

**18. Develop an appropriate checklist for discontinuing bypass.**

- Check acid-base balance, ensuring neutral pH, base deficit, PCO<sub>2</sub>, hematocrit, electrolytes, and platelet count.
- Ascertain adequate systemic rewarming, typically 37° C.
- Recalibrate (*zero*) all pressure transducers.
- Ensure adequate cardiac rate and rhythm (may require pacing).
- Reexamine the ECG for rhythm and ischemia.
- Evaluate TEE, looking for signs of ischemia (regional wall motion abnormalities) along with evaluation of valves, specifically in cases of valve replacement or repair.
- Remove intracardiac or intra-aortic air if the aorta or cardiac chambers were opened (TEE evaluation invaluable for this).
- Initiate ventilation of lungs.

**19. How is the heparin effect reversed? What are potential complications?**

Protamine, a positively charged protein molecule, binds the negatively charged heparin, and this complex is removed from the circulation by the reticuloendothelial system. Although there are different regimens to determine how much protamine should be administered, the simplest and most common method is to dose protamine based on the heparin administered (roughly 1 mg protamine per 100 units heparin). The efficacy of heparin reversal should be assessed by ACT but can also be determined using thromboelastography. Protamine has been associated with systemic hypotension because of histamine release or true anaphylaxis, along with catastrophic pulmonary hypertension due to anaphylactoid thromboxane release. Risk factors include preexisting pulmonary hypertension, patients with diabetes treated with NPH insulin preparations, bolus protamine administration, and central administration of protamine.

**20. Why is cardiac pacing frequently useful after bypass?**

Between the ischemic insult of bypass, the residual effect of cardioplegia, and effects from hypothermia, cardiac conduction may be impaired, and myocardial wall motion is suboptimal. Sequential cardiac pacing at a rate of 80 to 100 beats/min can significantly improve cardiac output.

**21. What are some therapies for the patient with impaired cardiac performance or difficulty weaning from cardiopulmonary bypass?**

From a surgical standpoint the adequacy of the surgical procedure (whether it be coronary artery bypass, valve replacement, or otherwise) should be reconsidered. TEE can evaluate regional wall motion abnormalities and valvular competency. Filling pressures should be assessed both by TEE and invasive monitors. Hemodynamic variables (cardiac index, mixed venous oxygen concentration, pulmonary artery pressure, pulmonary artery occlusion pressure, systemic vascular resistance) must be interpreted.

Typical scenarios encountered during the weaning process include reduced vascular resistance (so-called *vasoplegia*), which often requires vasopressor support. Contractility problems with the heart itself necessitate inotropic agents or possibly an aortic balloon pump to assist in the weaning from bypass. Right heart dysfunction and/or pulmonary hypertension may also complicate weaning from bypass. Agents such as nitric oxide or vasodilator therapy targeted toward the pulmonary system can be useful in this situation. TEE is invaluable in guiding these decisions along with interpretation of the pulmonary artery catheter. Inotropic and vasodilator therapies are discussed in Chapter 15.

**22. Review the central nervous system complications of cardiopulmonary bypass.**

There is about a 1% to 3% incidence of new neurologic events, defined as stroke (including vision loss), transient ischemic attack, or coma. There is also about a 3% incidence of deterioration in intellectual function, memory defects, or seizures, although close neurocognitive testing reveals a much higher incidence (20% to 60%) of cognitive dysfunction at 1- and 6-month intervals. Much of the cognitive dysfunction will resolve over a number of months. Cerebral microemboli, in particular platelet microemboli, are believed to be a contributing factor.

## KEY POINTS: CARDIOPULMONARY BYPASS



1. There are multiple approaches to the anesthetic technique during CPB. The overall cardiac reserve based on the exercise tolerance and severity of disease (valvular or ischemic) should guide the choice of anesthetic, using cardiac depressant agents cautiously.
2. Patients must be completely anticoagulated before initiating CPB or face the risk of massive intravascular clot formation.
3. The CPB reservoir should never be allowed to empty during CPB since massive air embolism is a consequence.
4. Factors involved in myocardial preservation include cardioplegia, myocardial hypothermia, and ventricular venting. Consequences of inadequate myocardial preservation include decreased cardiac output, ischemia, dysrhythmias, and failure to wean from CPB.
5. Always consider inadequate surgical technique (e.g., kinking of graft, valve failure) for the patient failing to wean from CPB.
6. Neurologic complications, in particular neurocognitive deficits, are distressingly common after CPB.

**23. What might be done to decrease the incidence of such complications?**

- Reversible factors may be identified before surgery. For instance, patients with significant carotid stenosis may require correction of this problem before CPB (perhaps at the same surgery). Significant aortic atherosclerosis is an independent risk factor for stroke. Therefore avoiding aortic cross-clamp is important; an *off-pump* surgical strategy may benefit these patients.

- Perioperative aspirin therapy and minimally invasive off-pump coronary artery surgery may also have some benefit.
- Meticulous attention intraoperatively to decreasing cerebral oxygen consumption through hypothermia, along with maintenance of perfusion pressure and mixed venous oxygen levels, may optimize cerebral supply and demand.
- Transesophageal echocardiography may identify patent foramen ovale, significant atheromatous disease at the site of aortic cannulation, left atrial thrombi, and intracardiac air and change subsequent management. Consider aortic ultrasound to help assess disease in the ascending aorta.
- Tight glucose control is likely beneficial.
- In the future some pharmacologic interventions may decrease neurologic complications.

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# LUNG ISOLATION TECHNIQUES

Mark D. Twite, MA, MB, BChir, FRCP

## 1. What are the indications for lung isolation?

There are five areas for which lung isolation may be required:

1. **Thoracic surgery**
  - Lung surgery: Thoracoscopy, lobectomy, pneumonectomy, lung transplantation, lung volume reduction
  - Bronchial surgery: Intraluminal tumors, bronchopleural fistula
  - Pleural surgery: Pleurectomy, pleurodesis, decortication
2. **Surgery on the great vessels, heart, and pericardium**
  - Heart: Via thoracotomy (as opposed to sternotomy) approach
  - Thoracic aorta: Descending aortic aneurysm
  - Pulmonary artery: Rupture, embolectomy
  - Pericardium: Pericardiectomy, pericardial window
3. **Esophageal surgery**
4. **Nonthoracic surgical procedures:** Anterior thoracic spinal fusion
5. **Nonsurgical procedures:** Pulmonary lavage, split lung ventilation, isolation of hemoptysis, or pulmonary infections

## 2. How can lung isolation be achieved while maintaining one-lung ventilation?

There are two basic techniques:

1. Double-lumen endotracheal tube (DLT), in which a bifurcated tube with both an endotracheal and endobronchial lumen can be used to isolate, selectively ventilate, or collapse the right or left lung independently according to the operative approach—the most common technique
2. Blockade of a bronchus to allow lung collapse distal to the occluding bronchial blocker

## 3. How do you choose the appropriate size double-lumen endotracheal tube?

There are right and left DLTs to account for the anatomic differences between the right and left main stem bronchi. Most commonly left-sided tubes are used. The optimal tube size for a particular patient is the largest tube that will pass atraumatically through the glottis, advance down the trachea, and fit in the bronchus with a small air leak detectable when the cuff is deflated. Using the largest possible tube is associated with the least airway resistance and ensures that a bronchial seal is obtained with small cuff volumes. A DLT that is too small requires a large endobronchial cuff volume, which may result in cuff herniation across the carina. Many anesthesiologists select 41-Fr and 39-Fr DLTs for tall and short men, respectively, and 39-Fr and 35- to 37-Fr DLTs for tall and short women, respectively. There is considerable variation in left main stem bronchi diameters and a relatively weak predictive value of gender and height. Other alternatives to predict the size of the optimal DLT are to measure the patient's trachea and left or right main stem bronchus diameters from preoperative radiologic studies such as chest x-ray films and computed tomography scans (Table 71-1).

TABLE 71-1. CONVERSION MEASUREMENTS OF TRACHEAL WIDTH BASED ON CHEST X-RAY AND BRONCHIAL DIAMETER MEASUREMENTS\*

Measured Tracheal Width (mm) at Clavicles on CXR	Measured Bronchial Diameter (mm)	Left-Sided DLT (Fr)
≥18	≥12	41
≥16	12	39
≥15	11	37
≥14	10	35
≥12.5	<10	32
≥11	NA	28

Data from Brodsky JB, Macario A, Mark JBD: Tracheal diameter predicts double-lumen tube size: a method for selecting left double-lumen tubes, *Anesth Analg* 82:861–864, 1996; and Hannallah M, et al: Evaluation of an approach to choosing a left double-lumen tube based on chest computed tomography scan measurement of left mainstem bronchial diameter, *J Cardiothorac Vasc Anesth* 11:168–171, 1997.  
 CXR, Chest x-ray; DLT, double-lumen endotracheal tube.

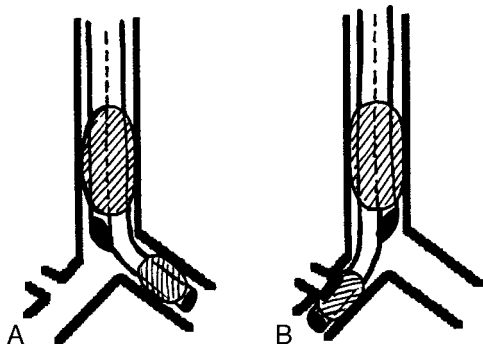
\*Bronchial diameter measurements based on computed tomography scan of the chest and the predicted left-sided double lumen endotracheal tube size.

#### 4. How is the right main stem bronchus different from the left and how does this affect right-sided double-lumen endotracheal tube design?

The adult trachea is 11 to 13 cm long and begins at the level of the cricoid cartilage (C6) and bifurcates behind the sternomanubrial joint (T5). The main differences between the right and left main stem bronchi include the following:

- The wider right bronchus diverges away from the trachea at a 25-degree angle, whereas the left bronchus diverges at a 45-degree angle.
- The right bronchus has upper, middle, and lower lobe branches, whereas the left bronchus divides into only upper and lower lobe branches.
- The orifice of the right upper lobe bronchus from the carina is 15 mm in women and 20 mm in men, whereas that of the left upper lobe is 50 mm from the carina.
- Therefore right-sided DLTs must have a slit in the bronchial cuff for ventilating the right upper lobe. It is more difficult to correctly position a right-sided DLT because of anatomic variations between individuals in the distance between the right upper lobe orifice and the carina, often resulting in difficulties ventilating the right upper lobe (Figure 71-1).

**Figure 71-1. A**, Double lumen endotracheal tube correctly positioned in the left main bronchus. **B**, Double lumen endotracheal tube correctly positioned in the right main bronchus but notice the position of the bronchial cuff on the endotracheal tube and the right upper lobe bronchus take off.



### 5. Describe the placement and positioning of double-lumen endotracheal tubes.

Using laryngoscopy, the DLT is passed with the distal curvature concave anteriorly and is rotated 90 degrees toward the side of the bronchus to be intubated after the tip passes the larynx. There are then two options to position the tube: auscultation or flexible fiber-optic bronchoscopy (FOB). With the auscultation method, the DLT is blindly advanced until resistance is felt as the endobronchial lumen enters the bronchus. The endobronchial and tracheal cuffs may then be inflated, and the lumens clamped in turn while auscultating the chest. However, auscultation alone is often unreliable for proper DLT placement.

Ovassapian (1996) described a reliable and reproducible method of placing DLTs on the first attempt. This technique requires advancing the tube only into the tracheal lumen. The FOB is then placed through the endobronchial lumen and advanced until the carina and main stem bronchi are identified. The FOB is then advanced into the appropriate bronchus and, using the FOB as a stylet, the DLT is slid over the FOB until its bronchial lumen comes into view just beyond the tip of the FOB. When positioning a right-sided DLT, it must be ensured that the endobronchial cuff does not block the right upper lobe orifice. Finally the FOB is passed through the tracheal lumen of the DLT to check for a carinal or subcarinal position of the bronchial cuff and ensure patency of the opposite main stem bronchus.

### 6. What complications may be caused by double-lumen endotracheal tubes?

- **Malposition:** Most often occurs when a patient is turned from the supine to the lateral position. Usually there is cephalad movement of the DLT by 1 cm. Malposition can be avoided by maintaining the head in a neutral position with folded blankets to avoid flexion and extension. After repositioning, the FOB should be used to confirm that the DLT is still in good position.
- **Airway trauma:** Inflation of the bronchial cuff beyond its resting cuff volume may result in high cuff pressures and bronchial rupture. The cuff volume depends on the size of the DLT. In a randomized, prospective controlled trial postoperative hoarseness and vocal cord lesions were significantly more frequent in patients intubated with a DLT compared to when an endobronchial blocker was used to achieve lung isolation. There was no difference in the incidence of bronchial injuries between the two groups.
- **Other complications:** Include stapling the endobronchial lumen in the bronchus during pneumonectomy (an argument for placing right-sided DLT for left pneumonectomy) and right upper lobe collapse when using right-sided DLTs.

### 7. Name three methods of bronchial blockade.

1. Univent tube, also known as a torque control blocker (Vitaid Airway Management)
2. Wire-guided endobronchial blocker (WEB), also known as an Arndt blocker (Cook Medical)
3. Fogarty embolectomy catheter (Baxter Healthcare)

### 8. Describe the Univent tube.

A Univent tube is a single-lumen tube with an incorporated channel for the bronchial blocker that can be used to block the left or right bronchus. The internal diameter of the Univent ranges from 3.5 to 9 mm, but the enclosed channel of the bronchial blocker makes the outer diameter larger than that of a standard endotracheal tube of the same internal size. The bronchial blocker catheter has a small internal lumen that can be used as a suction channel.

### 9. What are the advantages of using a Univent tube?

Since the shape of the Univent tube is similar to that of a standard endotracheal tube, it is useful in patients who have difficult airways for direct laryngoscopy. It may be used during awake fiber-optic intubation. Other features of the Univent tube are its efficiency as a selective lobar blocker and its ability to be used as a regular endotracheal tube without the need to exchange the tube if postoperative mechanical ventilation is contemplated.

**10. What are the advantages of a double-lumen endotracheal tube?**

DLTs are the best device for achieving absolute lung separation (e.g., bronchopulmonary lavage or presence of contamination of the other lung with massive bleeding or pus when a large suction lumen is needed). Although double-lumen tubes may be placed slightly more quickly than bronchial blockers (median times DLT 6.1 minutes, Univent 6.7 minutes, and Arndt blocker 8.6 minutes), there is no difference between DLTs and bronchial blockers in the success rate of accurate positioning by anesthesiologists with limited experience in thoracic anesthesia. The most critical factor in the successful placement of any lung isolation device is knowledge of endoscopic bronchial anatomy.

**11. Describe the placement and positioning of a Univent tube.**

Before use the bronchial blocker is lubricated to facilitate passage down the side channel. After the bronchial cuff is tested, the blocker is retracted, and standard endotracheal tube placement is performed. Once the tube is in the trachea, the bronchial blocker is advanced into the appropriate main stem bronchus under direct view of the FOB, which has been passed down the main lumen of the Univent tube. The optimal position of the bronchial blocker when fully inflated (6 to 8 ml of air) in the left main bronchus is when the inflated bronchial cuff is seen with the FOB 5 mm down the left main stem bronchus without any detectable air leak. For a right-sided bronchial blocker, the optimal position is when the cuff is seen above the origin of the right upper bronchus, with no leaks detectable when the cuff is inflated. (Check the Vitaid website for videos demonstrating Univent tube placement.)

**12. What complications can occur with the Univent tube?**

There are two serious complications with improper use of the Univent tube:

1. Inclusion of the bronchial blocker into the stapling line during right upper lobectomy
2. Obstruction of the tracheal lumen after the bronchial blocker is mistakenly inflated in the tracheal lumen

**13. Describe the wire-guided endobronchial blocker.**

The adult wire-guided endobronchial blocker (WEB) is a 9-Fr catheter that is available in 65- and 78-cm lengths. It has a small internal lumen measuring 1.4 mm in diameter, which contains a flexible wire that passes through the proximal end of the catheter, where it exits as a flexible wire loop. The wire loop allows the FOB and catheter to be coupled while they are guided into position. The WEB comes with a three-way multiport airway adapter, where the WEB, the FOB, and the anesthesia breathing circuit can be connected to the standard endotracheal tube. The smallest endotracheal tube that can accommodate both the WEB and an FOB is 7.0. After positioning the WEB, the wire guide is removed to convert the 1.4-mm channel into a suction port. However, once the wire is removed, it cannot be reinserted through the channel to allow repositioning of the catheter. There is a pediatric WEB that is a 5-Fr catheter, available in 50- or 65-cm lengths and 2.5 mm in diameter. When used with a 2.5-mm FOB, the pediatric WEB may be passed through a 5.0 endotracheal tube. (Check out the Cook website for links to videos and lectures on the WEB.)

**14. What are the advantages of the wire-guided endobronchial blocker?**

Like the Univent tube, the WEB can be used for selective lobar blockade. It is particularly useful in critically ill patients who are already intubated and ventilated who require single-lung ventilation. It is also useful in patients with difficult airways who can undergo awake fiber-optic intubation with a standard endotracheal tube followed by placement of the WEB. A final advantage is that the WEB may be used with patients who are nasally intubated.

**15. How can the Fogarty embolectomy catheter be used as a bronchial blocker?**

The most commonly used Fogarty catheter in adults is 8 Fr. The catheter comes with a wire stylet that can be curved at the distal end to facilitate guidance to the target bronchus. The



Fogarty catheter is passed through the standard endotracheal tube and guided into position using the FOB. An advantage of Fogarty catheters is that they can be passed through standard single-lumen endotracheal tubes, including pediatric sizes. A disadvantage is the lack of a hollow center so suction or oxygen insufflation is not possible and lung collapse takes longer because it is by absorption atelectasis.

**16. What tubes or bronchial blockers would you select for single-lung ventilation in children and adults?**

See [Table 71-2](#).

Age (years)	ETT (ID mm)	WEB (Fr)	Univent Tube	DLT (Fr)
0.5–1	3.5–4.0			
1–2	4.0–4.5			
2–4	4.5–5.0	5		
4–6	5.0–5.5	5		
6–8	5.5–6	5	3.5	
8–10	6.0 cuffed	5	3.5	26
10–12	6.5 cuffed	5	4.5	26–28
12–14	6.5–7.0 cuffed	5	4.5	32
14–16	7.0 cuffed	5	6.0	35
16–18	7.0–8.0 cuffed	5 or 9	7.0	35
Adult female	7.0–8.0 cuffed	9	7.0 or 8.0	35 or 37
Adult male	8.0–9.0 cuffed	9	8.0 or 9.0	39 or 41

*DLT*, Double-lumen endotracheal tube; *ETT*, endotracheal tube; *WEB*, wire-guided endobronchial blocker.

## KEY POINTS: LUNG ISOLATION



1. Always reassess optimal positioning of any lung isolation device after repositioning the patient.
2. A malpositioned tube is suggested by acute increases in ventilatory pressures and decreasing oxygen saturation.
3. Methods to improve oxygenation during one-lung ventilation include increasing  $\text{FiO}_2$ , adding PEEP to the dependent lung, adding CPAP to the nondependent lung, adjusting tidal volumes, and clamping the blood supply to the nonventilated lung.
4. To decrease airway pressures, always use the largest double-lumen endotracheal tube available.

**17. What are the standard ventilator settings for one-lung ventilation?**

Most anesthesiologists use approximately the same tidal volume for one-lung ventilation as for two-lung ventilation—typically around 10 ml/kg. Higher tidal volumes increase airway pressures and vascular resistance, which may cause more blood flow to the nonventilated lung and more

shunting. Lower tidal volumes may allow more atelectasis in the ventilated lung. The fractional concentration of oxygen in inspired gas ( $FiO_2$ ) will usually be 0.8 to 1.0, giving the greatest margin of safety against hypoxia. The respiratory rate is adjusted to maintain a normal  $PaCO_2$ .

### 18. Which volatile anesthetic agent would you use for single-lung ventilation?

Comparisons of desflurane and sevoflurane with isoflurane during single-lung ventilation demonstrated that the choice of volatile anesthetic does not significantly influence arterial oxygenation.

### 19. What pulmonary changes occur with one-lung ventilation?

Most thoracic surgery is performed in the lateral decubitus position. When ventilation is interrupted to the nondependent (operative) lung, a right-to-left shunt is created as blood flow continues to the now unventilated lung. However, several factors decrease the blood flow to the nondependent lung and therefore decrease this shunt:

- Gravity favors blood flow to the ventilated-dependent lung.
- Surgical compression and retraction decrease blood flow to the nondependent lung. The surgeon may also ligate the blood supply to the nondependent lung.
- Hypoxic pulmonary vasoconstriction (HPV)—hypoxia is a powerful stimulus for pulmonary vascular constriction (the opposite of its systemic effect). Factors that inhibit HPV will worsen the right-to-left shunt; they include hypocapnia and nitrovasodilators.

### 20. How should you manage hypoxia during one-lung ventilation?

During one-lung ventilation the change in  $PaO_2$  is usually greater than  $PaCO_2$  because of the greater diffusibility of  $CO_2$ . When the patient begins to desaturate on one-lung ventilation, a sequence of actions should happen:

- Increase the  $FiO_2$  to 1.0.
- Optimize tidal volumes and peak inspiratory pressures.
- Use the FOB to check your tube/blocker position.
- Add about 5 cm  $H_2O$  pressure of continuous positive airway pressure (CPAP) to the nondependent lung. This supplies oxygen to some of the alveoli that are perfused in the nondependent lung, therefore decreasing shunt.
- Consider adding 5 cm  $H_2O$  pressure of positive end-expiratory pressure (PEEP) to the dependent lung. This will help recruit any parts of the dependent lung that have developed atelectasis. However, be careful as the PEEP may have a negative effect by increasing vascular resistance in the dependent lung, causing more blood flow to the nondependent lung, thereby increasing shunt.
- If severe hypoxia continues, alert the surgeon. The surgeon may be able to help by ligating or clamping the pulmonary artery to the nondependent lung, thus eliminating the shunt. Alternatively, consider a return to two-lung ventilation.

## WEBSITES



Cook Medical  
<http://www.cookmedical.com>

VITAID Ltd.  
<http://www.vitaid.com>

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# SOMATOSENSORY-EVOKED POTENTIALS AND SPINAL SURGERY

*Daniel J. Janik, MD [Colonel (Retired), USAF, MC]*

## 1. What are somatosensory-evoked potentials?

Somatosensory-evoked potentials (SSEPs) are the electrophysiologic responses of the nervous system to the application of a discrete stimulus at a peripheral nerve anywhere in the body. They reflect the ability of a specific neural pathway to conduct an electrical signal from the periphery to the cerebral cortex.

## 2. How are somatosensory-evoked potentials generated?

Using a skin surface disc electrode or subcutaneous fine-needle electrode placed near a major peripheral mixed function (motor and sensory) nerve such as the median, a square-wave electrical stimulus of 0.2 to 2 ms is applied to the nerve at a rate of 1 to 2 Hz. The stimulus intensity is adjusted to produce minimal muscle contraction (usually 10 to 60 mA). The resulting electrical potential is recorded at various points along the neural pathway from the peripheral nerve to the cerebral cortex.

## 3. What major peripheral nerves are most commonly stimulated?

In the upper extremity the common sites of stimulation are the median and ulnar nerves at the wrist. In the lower extremity the common peroneal nerve at the popliteal fossa and the posterior tibial nerve at the ankle are used. Less commonly the tongue, trigeminal nerve, and pudendal nerve have been studied.

## 4. Trace the neurosensory pathway from the peripheral nerves to the cerebral cortex.

The axons of the peripheral sensory nerves enter the spinal cord via the dorsal spinal roots. These first-order neurons continue rostrally in the ipsilateral posterior column of the spinal cord until they synapse with nuclei at the cervicomedullary junction. Second-order neurons from these nuclei immediately decussate to the contralateral side of the brainstem, where they continue their ascent via the medial lemniscus through the midbrain, synapsing in the thalamus. Third-order neurons then travel via the internal capsule to synapse in the postcentral gyrus, the primary somatosensory cortex.

## 5. At what points along the neurosensory pathway are somatosensory-evoked potentials most commonly recorded?

After upper limb stimulation, potentials are recorded at the brachial plexus (Erb's point, 2 cm superior to the clavicular head of the sternocleidomastoid muscle), the cervicomedullary junction (posterior midline of the neck at the second cervical vertebra), and the scalp overlying the somatosensory cortex on the contralateral side.

After stimulation of the lower extremity, potentials are recorded at the popliteal fossa, lumbar and cervical spinal cord, and somatosensory cortex. It is important to record nerve and subcortical potentials to verify adequate stimulation and delineate anesthetic effects.

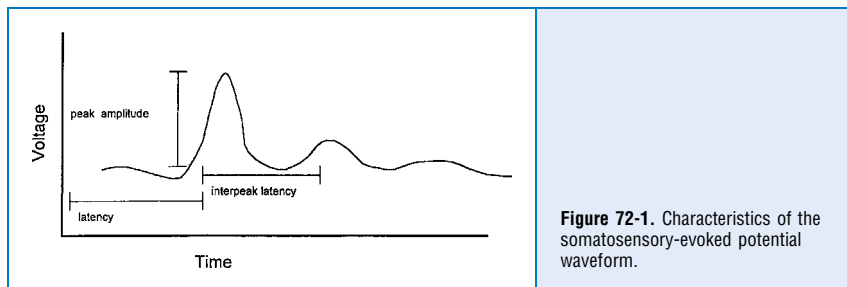
## 6. Describe the characteristics of the somatosensory-evoked potential waveform.

The SSEP is plotted as a waveform of voltage vs. time. It is characterized by:

- Amplitude (A), which is measured in microvolts from baseline to peak or peak to peak
- Latency (L), which is the time, measured in milliseconds, from onset of stimulus to occurrence of a peak or the time from one peak to another

- Morphology, which is the overall shape of the waveform, described as positive (P, below the baseline) or negative (N, above the baseline)

A waveform is identified by the letter describing its deflection above or below the baseline followed by a number indicating its latency (e.g., N20) (Figure 72-1).



## 7. Name several characteristic peaks important for the evaluation of somatosensory-evoked potentials.

See Tables 72-1 and 72-2.

**TABLE 72-1. CHARACTERISTIC PEAKS FOR EVALUATION OF MEDIAN NERVE STIMULATION**

Peak	Generator
N9	Brachial plexus (Erb's point)
N11	Dorsal root entry zone (cervical spine)
N13, 14	Posterior column (nucleus cuneatus)
P14	Medial lemniscus
N20	Somatosensory cortex

**TABLE 72-2. CHARACTERISTIC PEAKS FOR EVALUATION OF POSTERIOR TIBIAL NERVE STIMULATION**

Peak	Generator
N20	Dorsal root entry zone (lumbar spine)
N40	Somatosensory cortex

## 8. What is the central somatosensory conduction time?

The central somatosensory conduction time is the latency between the dorsal column nuclei (N14) and the primary sensory cortex (N20) peaks and reflects nerve conduction time through the brainstem and cortex.

### 9. What are the indications for intraoperative use of somatosensory-evoked potential monitoring?

SSEP monitoring is indicated in any setting with the potential for mechanical or vascular compromise of the sensory pathways along the peripheral nerve, within the spinal canal, or within the brainstem or cerebral cortex. SSEP monitoring has been used in the following:

#### ■ Orthopedic procedures

- Correction of scoliosis with Harrington rod instrumentation
- Spinal cord decompression and stabilization after acute spinal cord injury
- Spinal fusion

#### ■ Brachial plexus exploration

#### ■ Neurosurgical procedures

- Resection of a spinal cord tumor or vascular lesion
- Tethered cord release
- Resection of a sensory cortex lesion (e.g., aneurysm or thalamic tumor)
- Carotid endarterectomy

#### ■ Vascular surgery

- Repair of a thoracic or abdominal aortic aneurysm

### 10. What constitutes a significant change in the somatosensory-evoked potential?

Any decrease in amplitude greater than 50% or increase in latency greater than 10% may indicate a disruption of the sensory nerve pathways. The spinal cord can tolerate ischemia for about 20 minutes before SSEPs are lost.

### 11. Summarize the effects of anesthetic agents on the amplitude and latency of somatosensory-evoked potentials.

See [Table 72-3](#).

**TABLE 72-3. EFFECTS OF ANESTHETIC AGENTS ON AMPLITUDE AND LATENCY OF SOMATOSENSORY-EVOKED POTENTIALS**

Drug	Amplitude	Latency
<b>Premedication</b>		
Midazolam (0.3 mg/kg)	↓	0
Diazepam (0.1 mg/kg)	↓	↑
<b>Induction agents</b>		
Thiopental (5 mg/kg)	↑/0	↑
Etomidate (0.4 mg/kg)	↑↑↑	↑
Propofol (0.5 mg/kg)	0	↑
Ketamine (1 mg/kg)	↑	*
<b>Opioids</b>		
Fentanyl		↑
Sufentanil		↑
Morphine		↑
Meperidine	↑/↓	↑
<b>Inhaled anesthetics</b>		
Nitrous oxide	↓	↑
Isoflurane	↓	↑
Halothane	↓	↑

(continued)

TABLE 72-3. EFFECTS OF ANESTHETIC AGENTS ON AMPLITUDE AND LATENCY OF SOMATOSENSORY-EVOKED POTENTIALS (continued)

Drug	Amplitude	Latency
Enflurane	↓	↑
Desflurane	↓	↑
Sevoflurane	↓	↑
<b>Others</b>		
Droperidol	↓	↑
Muscle relaxants	0	0

↑, increase; ↓, decrease; 0, no change; \*, not known.

## 12. What is the take-home message of the effects of anesthetic agents on somatosensory-evoked potentials?

- All of the halogenated inhaled anesthetics probably cause roughly equivalent dose-dependent decreases in amplitude and increases in latency that are further worsened by the addition of 60% nitrous oxide. It is best to restrict the use of volatile anesthetics and nitrous oxide to levels below 1 minimum alveolar concentration (MAC) and not to combine the two.
- If possible, bolus injections of drugs should be avoided, especially during critical stages of the surgery. Continuous infusions are preferable.

## 13. What other physiologic variables can alter somatosensory-evoked potentials?

- **Temperature:** Hypothermia increases latency, whereas amplitude is either decreased or unchanged. For each decrease of 1° C, latency is increased by 1 ms. Hyperthermia (4° C) decreases amplitude to 15% of the normothermic value.
- **Hypotension:** With a decrease of the mean arterial blood pressure (MAP <40 mm Hg), progressive decreases in amplitude are seen. The same change is also seen with a rapid decline in MAP to levels within the limits of cerebral autoregulation.
- **Hypoxia:** Decreased amplitude caused by hypoxia has been reported.
- **Hypocarbica:** Increased latency has been described at an end-tidal CO<sub>2</sub> <25 mm Hg.
- **Isovolemic hemodilution:** Latency is not increased until the hematocrit is <15%, and amplitude is not decreased until the hematocrit is <7%. This effect is likely caused by tissue hypoxia.

## KEY POINTS: SOMATOSENSORY-EVOKED POTENTIALS AND SPINAL SURGERY



1. SSEPs are used when spinal cord or brain parenchyma is at risk for ischemia during surgery.
2. Volatile anesthetics have the most profound effects on SSEP waveforms.
3. An anesthetic technique that minimizes volatile anesthetic exposure is best—an opiate-based technique with low-dose (<1 MAC) volatile or a total intravenous anesthetic.
4. During distraction of the spinal column in scoliosis surgery (or other critical parts of surgery), minimize interventions that will lower mean arterial blood pressure or deepen anesthetic levels acutely to allow differentiation of changes in SSEP waveforms from anesthetic effect.

**14. If somatosensory-evoked potentials change significantly, what can the anesthesiologist and surgeon do to decrease the insult to the monitored nerves?**

■ The **anesthesiologist** can:

- Increase mean arterial blood pressure, especially if induced hypotension is used.
- Correct anemia, if present.
- Correct hypovolemia, if present.
- Improve oxygen tension.
- Correct hypothermia, if present.

■ The **surgeon** can:

- Reduce excessive retractor pressure.
- Reduce surgical dissection in the affected area.
- Decrease Harrington rod distraction, if indicated.
- Check positioning of associated instrumentation (e.g., screws, hooks).

If changes in the SSEPs persist despite corrective measures, a wake-up test may be performed to confirm or refute the SSEP findings. The patient's anesthetic level is lightened, and a clinical assessment of neurologic function is performed.

**15. Despite normal somatosensory-evoked potentials, can patients awaken with neurologic deficits?**

Although SSEP monitoring is a useful tool in preventing neurologic damage during spinal surgery, it is by no means foolproof. Because motor tracts are not monitored, the patient may awaken with preserved sensation but lost motor function. However, the reported incidence of false-negative monitoring in a large (>50,000) series of cases is 0.06% (1/1500). The monitoring of motor-evoked potentials along with SSEPs provides a more complete assessment of neural pathway integrity.

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# ANESTHESIA FOR CRANIOTOMY

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## 1. Are there particular anesthetic problems associated with intracranial surgery?

Space-occupying intracranial lesions are associated with disturbed autoregulation in adjacent tissue; vascular malformations and aneurysms are accompanied by altered vasoreactivity (particularly if preceded by subarachnoid hemorrhage [SAH]); and traumatic injuries sometimes require contradictory efforts to minimize brain swelling while maximizing systemic resuscitation. In addition, there are specific neurophysiologic concerns: control of cerebral blood flow and volume, anticipation of the effects of surgery and anesthetic management on intracranial pressure (ICP) dynamics, and maintenance of perfusion. In addition, as for any operative procedure, the patient should be unconscious and remain unaware of intraoperative stimuli; adrenergic responses of the patient to intraoperative events should be attenuated; and the surgeon's approach to the operative site should be facilitated.

## 2. How is the anesthetic requirement different in the brain and related structures?

During anesthesia for craniotomy the level of nociceptive stimulus varies greatly. Laryngoscopy and intubation require deep levels of anesthesia to block potentially harmful increases in heart rate, blood pressure, and brain metabolic activity, which may increase cerebral perfusion and brain swelling. Except for placement of pins in the skull for head positioning, considerable time may pass during positioning and operative preparation with no noxious stimulus. Incision of scalp, opening of the skull, and reflection of the dura provide increased surgical stimulus, only to be followed by dissection of the brain or pathologic tissue, which is almost completely free of nociceptive nerve fibers. Occasionally vascular structures of the brain may respond with an adrenergic surge during surgery, particularly if an SAH has occurred in the region of the procedure.

## 3. Should monitoring be different during a craniotomy?

The usual noninvasive monitors are used for every patient, including pulse oximetry, stethoscope, noninvasive blood pressure cuff, temperature, electrocardiogram, end-tidal and inspired gas monitors, and peripheral nerve stimulator. End-tidal anesthetic agent monitoring has some theoretic value, particularly in managing emergence. Continuous arterial pressure monitoring is often used to assess hemodynamic changes, which may develop acutely with cranial nerve root stimulation or slowly because of minimal intravascular volume repletion. Some forego the radial artery catheter for very superficial craniotomies such as mapping of the seizure focus directly with cortical electrodes; few anesthesiologists would use a central venous catheter unless there were a high risk of air entrainment in the venous system or a likelihood of using vasoactive infusions perioperatively. Occasionally continuous electroencephalography is used, not so much as an intraoperative monitor but rather as a means for the surgeon to localize diseased tissue. The various forms of processed electroencephalogram (EEG) monitors may facilitate the use of total intravenous anesthesia when indicated. Comparison of ipsilateral and contralateral evoked potentials has been reported during aneurysm surgery. Jugular bulb venous oxygen saturation and transcranial oximetry have been described as monitors of oxygen delivery and metabolic integrity of the

brain globally but are not used regularly in intraoperative settings. Some patients, especially after trauma, have subdural, intraventricular, or cerebrospinal fluid pressure monitors in use intraoperatively.

#### 4. Discuss the considerations for fluid administration during craniotomy.

Volume depletion from overnight fasting and volume redistribution from vasodilating anesthetic agents result in relative hypovolemia. Each patient should be evaluated individually to ensure adequate myocardial, central nervous system, and renal perfusion. Special attention must be directed toward stability of intracranial volume. Before opening of the dura, sudden increases in intravascular volume may cause deleterious increases in ICP, especially in situations involving intracranial masses or contusions or intraparenchymal, subdural, or epidural hematomas. Therefore, although fluids must be given to avoid hypovolemia and hypotension, exuberant bolus administration is to be avoided.

The content of the fluids used during a craniotomy is also important. An isosmolar intravenous fluid should be chosen. Unless hypoglycemia is documented, glucose-containing solutions should be avoided. In both clinical and experimental settings in which glucose is used in the resuscitation fluids after head injury, outcome is worse. Saline is the appropriate fluid for use during craniotomy. Balanced salt solutions may be used if their osmolality approximates or exceeds that of the serum. Ringer's lactate has a slight theoretic disadvantage because lactate is metabolized and the solution becomes hypotonic. Colloid solutions such as 5% albumin or 3% NaCl are equivalent solutions for acute volume replacement before packed red cell administration. Often 25% albumin is used for pressure support when blood replacement is not needed. Hetastarch solutions should be limited to 15 to 20 ml/kg body weight during craniotomies because of concerns that larger quantities are associated with impaired coagulation *in vitro*.

#### 5. When are measures for brain protection required?

*Brain protection* refers to the maneuvers by the anesthesiologist to maintain a balance between brain metabolism and substrate delivery and to prevent secondary injury to regions of the brain after an episode of ischemia. The need for brain protection should be anticipated after head trauma and brain contusion and during procedures for the correction of intracranial aneurysms or arteriovenous malformations. Of primary importance is adequate delivery of oxygen and energy substrates to brain tissue by ensuring optimal blood oxygen content and cerebral blood flow.

#### 6. How can the brain be protected?

Historically long-acting barbiturates have been used for metabolic suppression for refractory intracranial hypertension. The goal is suppression of brain activity with resultant reduction of metabolism, which is reflected by a flat EEG.

In the intraoperative setting metabolic suppression is needed when a major artery is temporarily clipped to facilitate access to an aneurysm. The EEG correlate is "burst suppression" in which the typical anesthetic slow-wave activity slows to random bursts of electrical activity. Burst suppression can be achieved by rapid infusion of thiopental, propofol, or etomidate. Hypothermia has long been known to reduce brain metabolism (and to slow the EEG). Mild to moderate hypothermia (32.5° to 34° C) has not been found to be useful for intraoperative brain protection. The global metabolic suppression secondary to hypothermia decreases not only neuronal electrical activity but also *housekeeping* functions, including cellular homeostasis and membrane integrity. Production of excitatory neurotransmitters during reperfusion of ischemic tissue may also be suppressed by modest hypothermia.

Much attention has been directed to suppression of the neuroexcitation that occurs with reperfusion after regional or global brain ischemia. Calcium influx into glial cells and vascular smooth muscle may be suppressed by calcium channel blockade; free radicals that are

generated may be *scavenged* by mannitol, and increased intracellular hyperglycemia may be prevented by avoiding systemic hyperglycemia. Cerebral protection remains a fruitful area of investigation.

## 7. How is the choice of anesthetic agent made?

Choice of anesthesia for craniotomy is based on an understanding of the pharmacologic properties of hypnotic agents, inhalation agents, opioids, and muscle relaxants and on a balancing of beneficial and potentially adverse effects. Whichever agents are chosen, the goals are postoperative hemodynamic stability associated with an awake, neurologically assessable patient.

- **Hypnotic agents:** Thiopental effectively blocks conscious awareness and reduces the functional activity of the brain, ICP, cerebral blood flow, and brain metabolism. Propofol has similar effects and is eliminated more rapidly. Etomidate and midazolam are only slightly less effective in metabolic suppression. An agent is selected on the basis of associated hemodynamic effects, anticipated difficulty of regaining consciousness, and cost.
- **Inhalation agents:** The differences between isoflurane, desflurane, and sevoflurane concerning metabolic suppression and cerebral blood flow are slight. All cause suppression of brain activity while preserving or enhancing cerebral blood flow. Cost and speed of elimination are concerns in selection. Nitrous oxide has been shown to increase ICP and cerebral blood flow in humans, although this effect is modified by the prior administration or coadministration of other hypnotic, analgesic, and anesthetic agents.
- **Opioids:** All opioids have negligible effects on cerebral blood flow and small effects on cerebral metabolism. Chiefly they block adrenergic stimulation, which increases brain activity. They are useful as part of a balanced anesthesia. More fat-soluble opioids such as morphine and hydromorphone may be eliminated so slowly that they cause respiratory depression after the procedure is completed. Respiratory depression that causes hypercarbia results in undesirable increases in cerebral blood flow and potentially ICP, which is to be avoided after a craniotomy. Newer short-acting synthetic opioids may also cause residual respiratory depression after prolonged infusion.
- **Muscle relaxants:** Depolarizing muscle relaxants are generally not used in the setting of intracranial pathology unless emergent control of the airway is necessary. Although theoretic hemodynamic differences exist among the nondepolarizing muscular relaxants, these are of little importance during a craniotomy. The main criteria for choosing a nondepolarizing muscular relaxant are the duration of neuromuscular blockade desired, route of elimination, and cost.

## 8. What are the concerns for patient positioning during a craniotomy?

Because craniotomies tend to be lengthy procedures, protecting vulnerable peripheral nerves and pressure-prone areas from injury is essential. Provisions must be made to prevent preparation solutions from entering the eyes. Generally the head is fixed in position with pins clamped against the outer table of the skull. Because the head is held in a fixed position, any patient movement will stress the cervical spine. Muscle paralysis must be maintained all the time the head is secured in the holding device.

In every craniotomy the risk of air entrainment into the venous system must be estimated. Whenever the head is positioned 10 cm above the midthorax (>20-degree elevation), a potential negative pressure exists between the venous sinuses of the head and the central venous system. Air entrained in the central venous system may collect in the right side of the heart and interfere with preload and pulmonary flow. Air can potentially cross the intra-atrial septum and, if a patent foramen ovale is present (20% of patients), become a paradoxical air embolus to the systemic circulation. This risk is very significant in sitting-position craniotomies. End-tidal CO<sub>2</sub>, end-tidal nitrogen, transesophageal echocardiography, and precordial Doppler are sensitive indicators of venous air. In high-risk situations a multiorificed right atrial catheter should be placed for removal of air bubbles.

### 9. Why do some patients awaken slowly after a craniotomy?

Continuous infusion of opioid as part of balanced anesthesia leads to prolonged redistribution and persistent sedation. Residual volatile anesthetic or barbiturate may contribute to slow awakening. However, all these residual anesthetic effects are overcome simply by waiting and providing respiratory support. Use of agents of short duration is beneficial. Slow awakening that persists for more than 2 hours is rarely an effect of residual anesthesia. The patient who is unresponsive for several hours after a craniotomy should be evaluated for increased ICP, embolic phenomenon, brainstem ischemia, or intracranial masses. Evaluation should be a joint effort of the neurosurgeon and anesthesiologist. The anesthetic technique should be tailored to facilitate a rapid emergence for early testing of neurologic function.

## KEY POINTS: ANESTHESIA FOR CRANIOTOMY



1. Always maintain a cerebral perfusion pressure of at least 50 mm Hg but preferably 70 mm Hg or higher.
2. If ICP is high, as evidenced by profound mental status changes or radiologic evidence of cerebral swelling, avoid volatile anesthetics and opt instead for a total intravenous anesthetic technique.
3. Remember that patients with profound mental status changes require little or no sedation before induction of general anesthesia.
4. Ensure deep anesthesia before intubation to avoid abrupt increases in cerebral blood flow.
5. Patients with large mass lesions may exhibit cardiovascular instability on induction of anesthesia because of intravascular volume reduction as a consequence of aggressive treatment of intracranial hypertension.
6. Rapid emergence from anesthesia facilitates early testing of neurologic function.

### 10. What anesthesia problems are unique to surgery on the intracranial blood vessels?

- **SAH:** Aneurysms of the intracerebral arteries may be diagnosed after SAH. Neurologic impairment after SAH ranges from headache and stiff neck (Hunt-Hess grade I) to deep coma (Hunt-Hess grade V). Initial resuscitation includes observation, tight control of blood pressure, and support of intravascular volume (hypervolemic, hyperosmolar, normotensive). The optimal time for surgical clipping of the aneurysm is within the first few days of hemorrhage. After 5 to 7 days following SAH the risk of rebleeding remains high, but the risk of vasospasm of the vessel feeding the aneurysm markedly increases because of irritation from the breakdown of old blood. Invasive monitoring of arterial pressure and central venous pressure is required to facilitate maintenance of hemodynamic stability and guide volume replacement. The minimal approach to brain protection is to maintain normal oxygen delivery to the brain tissue. Metabolic suppression by electroencephalographic burst suppression may be done at the time of temporary vessel clipping but may result in poor outcome when accompanied by hypotension.
- **Rebleeding:** Approximately 30% of intracranial aneurysms that have bled will rebleed at some time if untreated. In the initial few days the hydrodynamic forces on the aneurysm wall are caused by the systolic blood pressure resisted by the tension of the aneurysmal wall. Larger aneurysms have less wall tension for any part of the aneurysmal surface. Rebleeding of the aneurysm before the opening of the dura is catastrophic, requiring the surgeon to

approach the bleeding vessel blindly, perhaps temporarily clipping major feeding vessels. Although it might seem reasonable to induce hypotension during the opening of the dura, should a rebleed occur hypotension adversely affects regional perfusion and may promote vasospasm.

- **Vasospasm:** Vasospasm can occur after any SAH, regardless of clinical stage. The end result of persistent vasospasm is ischemic stroke in the region of distribution of the aneurysmal artery, resulting in permanent neurologic damage after SAH. Diagnosis is by angiography, and many times an angiogram is requested on the first postoperative day to guide therapy. Maintaining hypervolemic normotensive hemodynamic status is the first line of prevention of vasospasm and should be maintained intraoperatively. Physiologically vasospasm is caused by mediator release in the vascular smooth muscle in response to hemoglobin in the interstitium, ending in calcium influx into the cellular walls of the artery and causing persistent vasoconstriction. Calcium channel blockade has been advocated but has shown mixed results. Thromboplastin activators have been used experimentally by irrigation in the region of the aneurysmal bleed with some success. The main lines of prevention are intraoperative irrigation of the hematoma early in the SAH course and maintenance of favorable hemodynamics after surgery.

### 11. Are there special anesthetic problems associated with brain tumors?

Mass lesions of the brain cause problems for the anesthesiologist because of their size and location. Frontal tumors grow to large size without producing neurologic symptoms or increased ICP. Supratentorial tumors of the motor and sensory cortical regions present with seizures, localizing neurologic signs, and increased ICP. Posterior fossa masses in adults cause disturbances in gait, balance, proprioception, or cranial nerve impingement. There is a *penumbra* around all intracranial tumors where the adjacent brain loses autoregulatory function. Thus on induction regional blood flow in these areas may increase in response to aggressive fluid replacement or increased systolic blood pressure. After the resection is completed, this penumbra may respond to reperfusion with swelling. The end result may be either preincisional or postoperative increases in ICP. Infratentorial posterior fossa tumors cause particular problems for the anesthesiologist. Tumors are generally small but may surround complex vascular channels of the basilar, posterior communicating, and cerebellar arteries. Tumors may arise from the glia surrounding the cranial nerve roots or impinge on them. Simple dissection of a brainstem tumor can cause disturbance of heart rate and rhythm or blood pressure when nerve roots are retracted. The surgical approach to the posterior fossa involves awkward positioning, from sitting to lateral to prone to park bench. At the least, any of these positions requires careful attention to the position of the endotracheal tube to avoid migration to an endobronchial position or out of the glottis. Venous air embolism must be anticipated. The plan for anesthesia must also allow for intraoperative monitoring of auditory-evoked potentials, somatosensory-evoked potentials, or motor-evoked potentials if indicated. Any of these evoked potentials can be suppressed by hypnotic and inhaled anesthetic agents.

### 12. Are there other anesthetic concerns during craniotomies?

Transsphenoidal surgery, although not strictly a craniotomy, involves manipulation of ventilation to raise the PaCO<sub>2</sub> and ICP, which forces the pituitary into a more easily visualized position.

Rapidly deteriorating neurologic status after closed head injury often leads to emergency intubation, neuroradiologic studies, and emergent craniotomy. The increase in ICP that causes the clinical deterioration sometimes progresses to involve brainstem compression. The physiologic response to increased ICP is systemic hypertension and in the late stages bradycardia, known as the Cushing reflex. This reflex should be anticipated and treated by measures to reduce ICP rather than pharmacologic treatment of the hypertension *per se*. Typically, when the cranium is opened and brainstem pressure is reduced, the blood pressure

decreases, but if aggressive treatment of elevated blood pressure has been undertaken, the drop in blood pressure may have disastrous consequences.

Craniotomies in pediatric patients are in principle the same as in adults but fortunately rarer. The intracranial pathology that is most common in the pediatric group is the posterior fossa tumor, particularly cerebellar astrocytoma. Positioning, cranial nerve root stimulation, and venous air embolus are concerns during posterior fossa resections in children.

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# MINIMALLY INVASIVE SURGERY

*Prairie Neeley Robinson, MD*

## 1. What are the origins of modern laparoscopic surgery?

P. Bozzini developed the first self-contained endoscope in 1805, using candlelight for illumination. The first clinical laparoscopic examination in humans was performed by H. Jacobaeus in 1910. By the 1970s gynecologic laparoscopic surgery was being performed routinely. The first laparoscopic appendectomy was performed by Semm in 1983, and the first laparoscopic cholecystectomy was performed by Muhe in 1985. Since then the concept and techniques have rapidly expanded to include multiple surgical disciplines. Laparoscopic surgery has become the standard of care for some procedures.

## 2. What are some currently practiced laparoscopic, thoracoscopic, or endoscopic procedures?

- **General surgery:** Multiple procedures involving the appendix, colon, small bowel, gallbladder, bile ducts, stomach, esophagus, liver, spleen, pancreas, and adrenals. In addition, hernia repairs, diagnostic laparoscopy, adhesiolysis, gastric bypass, gastric banding, Nissen fundoplication, and feeding-tube placement can be performed laparoscopically
- **Gynecologic procedures:** Diagnostic procedures for chronic pelvic pain, hysterectomy, tubal ligation, pelvic lymph node dissection, hysteroscopy, myomectomy, oophorectomy, and laser ablation of endometriosis
- **Thoracoscopic procedure/video-assisted thoracic surgery:** Lobectomy, pneumonectomy, wedge resection, drainage of pleural effusions and pleurodesis, evaluation of blunt or pulmonary trauma, resection of solitary pulmonary nodules, tumor staging, repair of esophageal perforations, pleural biopsy, excision of mediastinal masses, transthoracic sympathectomy, splanchnicectomy, pericardiocentesis, pericardiectomy, and esophagectomy
- **Cardiac surgery:** Coronary artery bypass, valve repair
- **Orthopedics:** Joint arthroscopy, including knee, hip, shoulder, wrist, and elbow
- **Urologic procedures:** Laparoscopic nephrectomy/nephroureterectomy, pyeloplasty, orchiopexy, cystoscopy/ureteroscopy, and prostatectomy
- **Neurosurgery:** Ventriculoscopy, microendoscopic diskectomy, interbody fusion, anterior spinal surgery and scoliosis/kyphosis correction, and image-guided techniques to approach masses/tumors easily
- **Plastic/reconstructive surgery:** Breast augmentation, brow lift, face lift, and liposuction techniques
- **Transplant surgery:** Donor nephrectomy

Improvements in scope technology have allowed many procedures to be performed without large surgical incisions, affording the patient rapid recovery of function. However, the focus of this discussion will be the physiologic concerns associated with abdominal laparoscopy since they are of utmost importance to the anesthesiologist.

## 3. Are there any contraindications for laparoscopic procedures?

Relative contraindications for laparoscopy include increased intracranial pressure, patients with ventriculoperitoneal or peritoneojugular shunts, hypovolemia, congestive heart failure, or

severe cardiopulmonary disease and coagulopathy. Morbid obesity, pregnancy, and prior abdominal surgery were previously considered contraindications to laparoscopic surgery; however, with improved surgical techniques, technology, and experience, most patients with these conditions can safely undergo laparoscopic surgery.

#### 4. What are the benefits of laparoscopy when compared with open procedures?

- **Intraoperative benefits:** Decreased stress response with a reduction of acute phase reactants (C-reactive protein and interleukin-6), decreased metabolic response with reduced hyperglycemia and leukocytosis, decreased fluid shifts, better preserved systemic immune function, and avoidance of prolonged exposure and manipulation of abdominal contents.
- **Postoperative benefits:** Less postoperative pain and fewer analgesic requirements, improved pulmonary function (secondary to decreased pain, decreased atelectasis, and earlier ambulation), improved cosmesis because of smaller incisions, fewer wound infections, decreased postoperative ileus, decreased length of hospitalization, and a quicker resumption of normal daily activities.

#### 5. Why has carbon dioxide become the insufflation gas of choice during laparoscopy?

The choice of an insufflating gas for the creation of pneumoperitoneum is influenced by the blood solubility of the gas and its tissue permeability, combustibility, expense, and potential to cause side effects. The ideal gas would be physiologically inert, colorless, and capable of undergoing pulmonary excretion. Although a number of gases have been used (Table 74-1), carbon dioxide (CO<sub>2</sub>) has become the gas of choice since it offers the best compromise between potential advantages and disadvantages.

TABLE 74-1. COMPARISON OF GASES FOR INSUFFLATION

	Advantages	Disadvantages
CO <sub>2</sub>	Colorless Odorless Inexpensive Does not support combustion Decreased risk of air emboli compared with other gases because of its high blood solubility	Hypercarbia Respiratory acidosis Cardiac dysrhythmias, rarely resulting in sudden death More postoperative neck and shoulder pain resulting from diaphragmatic irritation (compared with other gases)
N <sub>2</sub> O	Decreased peritoneal irritation  Decreased cardiac dysrhythmias (compared with CO <sub>2</sub> )	Supports combustion and may lead to intra-abdominal explosions when hydrogen or methane is present Greater decline in blood pressure and cardiac index (compared with CO <sub>2</sub> )
Air		Supports combustion Higher risk of gas emboli (compared with CO <sub>2</sub> )
O <sub>2</sub>		Highly combustible
Helium	Inert Not absorbed from abdomen	Greatest risk of embolization



## 6. How does carbon dioxide insufflation affect PaCO<sub>2</sub>?

CO<sub>2</sub> insufflation increases the partial pressure of carbon dioxide (PaCO<sub>2</sub>). The degree of increase in PaCO<sub>2</sub> depends on the intra-abdominal pressure, the patient's age, underlying medical conditions, patient positioning, and the mode of ventilation. In healthy patients the primary mechanism of increased PaCO<sub>2</sub> is absorption via the peritoneum. Increases in intra-abdominal pressure also result in diaphragmatic dysfunction and increased alveolar dead space, leading to ventilatory impairment and subsequent increases in PaCO<sub>2</sub>. Spontaneous ventilation under local anesthesia does not result in a rise in PaCO<sub>2</sub>; however, other anesthetic techniques and ventilatory modes will result in hypercapnia unless ventilation is adjusted. PaCO<sub>2</sub> rises approximately 5 to 10 minutes after CO<sub>2</sub> insufflation and usually reaches a plateau after 20 to 25 minutes. The gradient between PaCO<sub>2</sub> and end-tidal pressure of CO<sub>2</sub> does not change significantly during insufflation, but it does increase during maintenance of pneumoperitoneum, especially in more compromised patients. The final PaCO<sub>2</sub> levels tend to be significantly higher in patients with cardiopulmonary disease than in healthy patients undergoing similar procedures.

## 7. How does patient positioning affect hemodynamics and pulmonary function during laparoscopy?

During laparoscopic surgery the patient is positioned to use gravitational displacement of the abdominal contents away from the surgical site to facilitate optimal surgical exposure.

- **Trendelenburg position:** Cardiac output (CO) and central venous pressure (CVP) increase, and patients with intact baroreceptor reflexes typically experience vasodilation and bradycardia. The Trendelenburg position decreases the transmural pressure in the pelvic organs, possibly decreasing blood loss but increasing the risk of gas emboli. Pulmonary effects include impaired diaphragmatic function secondary to the cephalad displacement of abdominal viscera, resulting in decreased functional residual capacity (FRC), total lung capacity, and pulmonary compliance, predisposing the patient to developing atelectasis. Cephalad migration of lungs and carina may result in main stem intubation.
- **Reverse Trendelenburg position:** Preload is decreased, resulting in decreased CO and mean arterial pressure (MAP). Blood pooling in the lower extremities may increase the risk of venous thrombosis and pulmonary emboli. Intraoperative sequential intermittent pneumatic compression of the lower extremities is recommended. Pulmonary function is improved compared to supine or Trendelenburg position secondary to downward positioning of the diaphragm.

## 8. What is considered a safe increase in intra-abdominal pressure?

The current recommendation for intra-abdominal pressure (IAP) during laparoscopy is less than 15 mm Hg, and most laparoscopic procedures are performed with IAPs in the 12- to 15-mm Hg range. In general IAPs less than 10 mm Hg have minimal physiologic effects. Insufflation pressures above 16 mm Hg result in undesirable physiologic changes (i.e., decreased CO, increased systemic vascular resistance [SVR] and decreased compliance of the lung and chest wall). At pressures greater than 20 mm Hg, renal blood flow (RBF), glomerular filtration rate, and urine output also decline. Insufflation pressures of 30 to 40 mm Hg have significant adverse hemodynamic effects and should be avoided. Many insufflation machines are set to alarm at 15 mm Hg. If the machine alarms when the surgeon is not insufflating with high pressure, the anesthesiologist should consider insufficient abdominal wall relaxation as one possible cause of the high-pressure alarm. Low-pressure pneumoperitoneum (7 mm Hg) and gasless laparoscopy have been advocated as means of decreasing the magnitude of hemodynamic derangement associated with higher IAP.

The observed changes in CO are biphasic: CO initially decreases with onset of CO<sub>2</sub> insufflation; within 5 to 10 minutes CO begins to increase, approaching preinsufflation values. At IAPs greater than 10 mm Hg, venous return decreases, but cardiac filling pressures increase most likely because of increased intrathoracic pressure; therefore with abdominal insufflation the usual

methods of measuring CVP or left ventricular end-diastolic pressure are inaccurate and overestimate true filling conditions. Adequate intravascular volume loading will help maintain CO. SVR and MAP also significantly increase during the initial stages of insufflation. Although these changes partially resolve approximately 10 to 15 minutes after insufflation, the changes in cardiac filling pressures and SVR increase left ventricular wall stress. Pulmonary vascular resistance is also increased. In healthy patients left ventricular function appears to be preserved; however, in patients with underlying cardiovascular disease, the changes could be deleterious (Table 74-2).

**TABLE 74-2. HEMODYNAMIC CHANGES DURING LAPAROSCOPY**

Increased	Decreased	No Change
SVR	Cardiac output (initially, then increases)	Heart rate (may increase because of hypercapnia or catecholamine release)
MAP	Venous return (at IAP >10)	
CVP		
PAOP		
Left ventricular wall stress		
Venous return (at IAP <10)		

*CVP*, Central venous pressure; *IAP*, intra-abdominal pressure; *MAP*, mean arterial pressure; *PAOP*, pulmonary artery occlusion pressure; *SVR*, systemic vascular resistance.

### 9. Describe pulmonary changes associated with pneumoperitoneum.

CO<sub>2</sub> insufflation and the resultant increase in intra-abdominal pressure result in cephalad displacement of the diaphragm, reducing FRC and compliance. Trendelenburg position further aggravates these changes. When the FRC is reduced relative to the patient's closing capacity, hypoxemia may result from atelectasis and intrapulmonary shunting. Positive end-expiratory pressure of 10 during pneumoperitoneum decreases CO and preload. Hypoxemia is uncommon in healthy patients but becomes a concern in obese patients or those with underlying cardiopulmonary disease since it can be difficult to ventilate against the pressure of the pneumoperitoneum adequately in compromised patients (Table 74-3).

**TABLE 74-3. PULMONARY CHANGES ASSOCIATED WITH LAPAROSCOPY**

Increased	Decreased	No Significant Change
Peak inspiratory pressure	Vital capacity	PaO <sub>2</sub> (in healthy patients)
Intrathoracic pressure	Functional residual capacity	
Respiratory resistance	Respiratory compliance	
PaCO <sub>2</sub>	pH	

### 10. What effect does the intra-abdominal pressure increase have on perfusion of intra-abdominal organs?

An IAP of 12 to 14 mm Hg decreases RBF, glomerular filtration rate, and urine output. The reduction in RBF is related to the decreased CO and/or compression of the renal vein.

Hepatoportal arterial and venous blood flow is gradually decreased with increasing IAP, and elevated liver enzymes have been noted after prolonged laparoscopic cases. Splanchnic microcirculation is decreased.

## KEY POINTS: ANESTHESIA FOR MINIMALLY INVASIVE SURGERY



1. PaCO<sub>2</sub> increases during CO<sub>2</sub> pneumoperitoneum in laparoscopy because of CO<sub>2</sub> absorption and ventilation-perfusion mismatch; if the patient is breathing spontaneously, ventilatory depression may also contribute to hypercarbia.
2. Hemodynamic changes during laparoscopy include increased SVR, MAP, and left ventricular wall stress. CO decreases initially and then gradually increases to baseline.
3. Pulmonary changes during laparoscopy include increases in peak inspiratory pressure, intrathoracic pressure, and respiratory resistance and decreases in vital capacity, FRC, and pulmonary compliance.

### 11. What are the neurohumoral responses associated with laparoscopy?

Plasma concentrations of dopamine, vasopressin, epinephrine, norepinephrine, renin, angiotensin, and cortisol all significantly increase. The increases correspond to the onset of abdominal insufflation. Serum levels of vasopressin and norepinephrine most closely parallel the changes noted in CO, MAP, and SVR. Hypercarbia, the mechanical effects of the pneumoperitoneum, and stimulation of the autonomic nervous system have all been implicated as possible causes of these observed changes. Preoperative  $\alpha_2$ -adrenergic agonists (clonidine/dexmedetomidine) have been shown to decrease the stress response.

### 12. Should nitrous oxide be used as an anesthetic adjuvant during laparoscopy?

There are no clinically significant differences in bowel distention and postoperative nausea and vomiting when nitrous oxide (N<sub>2</sub>O)-oxygen was compared to air-oxygen, and no conclusive evidence suggests that N<sub>2</sub>O cannot be used during laparoscopy.

### 13. What anesthetic techniques can be used for minimally invasive surgery?

Local anesthesia with intravenous (IV) sedation, regional techniques, and general anesthesia have all been used with favorable results. The unexpected conversion from a laparoscopic to an open procedure must be considered when choosing an anesthetic technique.

- **Local anesthetic with IV sedation:** Advantages include reduced anesthetic time, quicker recovery time, decreased postoperative nausea and vomiting, earlier recognition of complications, and fewer hemodynamic changes. Success depends on patient motivation, precise surgical technique, and short procedure time. This technique should be avoided in any procedure of long duration that requires multiple trocar sites, steep positioning, and large increases in IAP.
- **Regional anesthesia:** Advantages and disadvantages are similar to those of local anesthesia. However, the high level of sympathetic denervation in concert with abdominal insufflation and positioning extremes could be associated with adverse ventilatory and circulatory changes.

- General anesthesia:** General anesthesia is the most frequently used technique. Advantages include optimal muscle relaxation, amnesia, ability to position the patient as needed, ability to control ventilation, protection from gastric aspiration, and a quiet surgical field. The laryngeal mask airway (LMA) has been substituted for endotracheal intubation but does not protect against pulmonary aspiration of gastric contents. Controlled ventilation is also difficult with an LMA since peak inspiratory pressures increase with pneumoperitoneum. Urinary bladder and gastric decompression should be performed to decrease the risk of visceral puncture and improve the surgical field.

#### 14. Can laparoscopy be performed on children or pregnant women?

Laparoscopic surgery is now commonly performed in pediatric populations. Children undergo similar physiologic changes and experience similar benefits of laparoscopic procedures as adults. CO<sub>2</sub> absorption in infants may be faster and more profound than in adults because of a greater peritoneal surface area-to-body weight ratio.

Pregnancy was initially considered to be a contraindication to laparoscopic surgery because of concerns regarding decreased uterine blood flow, increased intrauterine pressure, and resultant fetal hypoxia and acidosis. Multiple reports have since determined that laparoscopic surgery is safe in pregnancy and does not result in increased rates of fetal morbidity or mortality. Since fetal acidosis is typically more severe than maternal acidosis, the end-tidal CO<sub>2</sub> concentration should be maintained between 25 and 33 mm Hg. Procedures should be performed in the second trimester if possible. Body positioning should avoid inferior vena cava compression. Abdominal insufflation pressure should be kept as low as possible in pregnant patients.

#### 15. What complications are associated with laparoscopic surgery and carbon dioxide pneumoperitoneum?

Complications are most likely to occur during placement of the trocar through the abdominal wall and CO<sub>2</sub> insufflation.

- Intraoperative complications:** Major vessel injury, hemorrhage, organ perforation, bladder and ureter injury, burns, cardiac arrhythmias (atrioventricular dissociation, nodal rhythms, bradycardia, and asystole), hypercapnia, hypoxemia, CO<sub>2</sub> subcutaneous emphysema, pneumothorax, gas embolism, endobronchial intubation, increased intracranial pressure, and aspiration are all risks. Other complications are possible, depending on the specific procedure performed.
- Postoperative complications:** Postoperative nausea and vomiting, pain, shoulder and neck pain secondary to diaphragmatic irritation, deep venous thrombosis, delayed hemorrhage, peritonitis, wound infection, pulmonary dysfunction, and incisional hernia have all been noted.

As laparoscopy has matured as a technique, procedures have become more complex, and patients are more likely to be older and more debilitated than in the past. Despite the increasing complexity of patients and procedures, complications and mortality have decreased for most procedures.

## WEBSITES



The Society of Laparoendoscopic Surgeons  
<http://www.sls.org>

The Society of Gastrointestinal and Endoscopic Surgeons  
<http://www.sages.org>

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# LASER SURGERY AND OPERATING ROOM FIRES

James Duke, MD, MBA

## 1. What is a laser?

*Laser* stands for *light amplification by stimulated emission of radiation*. Within a laser atoms, ions, or molecules are stimulated by an energy source and spontaneously radiate energy in the form of monochromatic light. The radiated light is then amplified and emitted as the laser beam. Laser light has three defining characteristics:

1. **Coherence:** All waves are in phase, both in time and in space.
2. **Collimation:** The waves travel in parallel directions.
3. **Monochromaticity:** All waves have the same wavelength.

Benefits of using lasers are that they are extremely precise in their excision margins and there is minimal dissipation of damaging heat and energy to surrounding tissues.

## 2. What makes lasers behave differently from each other?

When excited, the source of the laser radiates light of a certain wavelength. The longer the wavelength, the more strongly it is absorbed by the tissue target, and the more shallow is the overall lasing effect. Conversely, the shorter the wavelength, the higher the energy, and the deeper the penetration of the laser light. For example, a carbon dioxide (CO<sub>2</sub>) laser has a longer wavelength and is absorbed almost entirely at the tissue surface. As a result, precise excision of superficial lesions is possible. Conversely, a neodymium:yttrium-aluminum-garnet (Nd:YAG) laser has a shorter wavelength, deeper penetration, and is useful for heating large tissue masses and tumor debulking (Table 75-1).

TABLE 75-1. CHARACTERISTICS OF LASERS COMMONLY USED IN THE OPERATING ROOM

Laser Type	Wavelength	Absorber	Typical Applications
CO <sub>2</sub>	10,600 (invisible—far infrared)	All tissues, water	General, precise surgical cutting
Nd:YAG	1064 (invisible—near infrared)	Darkly pigmented tissues	General coagulation, tumor debulking
Nd:YAG-KTP*	532 (visible—emerald green)	Blood	General, pigmented lesions
Argon	488–514 (visible—blue-green)	Melanin, hemoglobin	Vascular, pigmented lesions
Krypton	400–700 (visible—blue-red)	Melanin	General, pigmented lesions

\*Neodymium:yttrium-aluminum-garnet:potassium-titanyl-phosphate.

### 3. What are the hazards of lasers?

- The vaporization of tissue and dispersion of diseased particulate matter are hazards for all operating room (OR) personnel. The smoke produced by vaporization of tissues with lasers may be mutagenic, transmit infectious diseases, and cause acute bronchial inflammation.
- A laser beam in contact with flammable materials such as endotracheal tubes, anesthetic gas tubing, surgical drapes, and sponges may cause fires or explosion. Fires result in minimal or no harm to the patient if the situation is handled swiftly but may be catastrophic if not.
- Although rare, venous gas embolism may occur, especially during laparoscopic or hysteroscopic procedures. Reported cases have been associated primarily with Nd:YAG lasers, in which coolant gases circulate at the probe tips. It is these coolant gases that embolize.
- Inappropriate energy transfer: Laser light vaporizes whatever tissue lies in its path. Precise aim by the surgeon and a cooperative (well-anesthetized, paralyzed) patient are mandatory. In addition, laser light is easily reflected by surgical instruments and may be hazardous to all OR personnel. Laser contact with the eyes may impair vision or cause blindness. The nature of ocular damage depends on the wavelength of the laser light. For example, CO<sub>2</sub> lasers cause corneal opacification, whereas Nd:YAG lasers cause damage to the retina. Any plastic lens protects against CO<sub>2</sub> laser injury; contact lenses do not. Other lasers require more specialized eye protection.
- Perforation: Misdirected laser energy may perforate a viscus or large blood vessel. Laser-induced pneumothorax after laryngeal surgery also has been reported. Sometimes the perforations do not occur until several days after surgery when edema and tissue necrosis are at a maximum.

### 4. What are some unique airway considerations for the patient having laser surgery of the airway?

- **Upper airway lesions:** In laser resection of upper airway lesions, tracheal intubation is optional. Techniques that do not involve an endotracheal tube allow better visualization of the operative field by the surgeon and also remove potentially flammable materials from the airway. Clearly the airway is being shared by surgeon and anesthesiologist, and a discussion of the operative course before the procedure begins is important.
- **Lower airway lesions:** The CO<sub>2</sub> laser beam is directed at the lesion through a rigid metal bronchoscope, coated with a matte finish to reduce reflected laser light. Ventilation is accomplished through the side arm of the bronchoscope, using saline-soaked gauze to form a seal around the bronchoscope. Jet ventilation is another option. In certain instances (e.g., lower tracheal and bronchial lesions) the laser approach is via fiber optic, and the Nd:YAG laser is required because it can travel through fiber-optic cables, whereas the CO<sub>2</sub> laser cannot.

### 5. Describe ventilation techniques commonly encountered during airway laser surgery

- **Jet ventilation:** In this technique the surgeon aims a high-velocity jet of O<sub>2</sub> at the airway opening. The high flow of O<sub>2</sub> entrains room air as a result of the Venturi effect, thus ventilating the lungs with a high volume of O<sub>2</sub>-air mixture. Ventilation is accomplished by attaching a suction catheter to wall O<sub>2</sub> and a Sanderson-type jet injector. This apparatus is mounted to the operating laryngoscope. Sometimes the mass of the airway lesion makes this method impossible. If the jet stream is not aimed in the trachea, gastric dilation may occur. Barotrauma to the airway and subsequent pneumothorax are also risks and may in turn lead to mediastinal or subcutaneous air. An intravenous anesthetic is necessary for this procedure.
- **Spontaneous ventilation:** Allowing the patient to inhale volatile agents via the operating laryngoscope is also an option, although it is not feasible for some procedures. It is difficult to control the depth of anesthesia during spontaneous ventilation, and it is often necessary to paralyze the patient during many airway procedures. Hypoventilation, hypercarbia, and aspiration (surgical debris, secretions, vomitus, and smoke) are additional complications related to both jet and spontaneous ventilation.

- **Endotracheal intubation:** This method allows excellent ventilation and airway protection of the anesthetized patient but often obscures the operative field and puts flammable materials in the path of the laser beam.

## 6. What are the three essential components necessary to create an operating room fire?

The *fire triad* consists of:

1. Oxidizers. Within the OR environment they are O<sub>2</sub> and nitrous oxide.
2. Ignition sources include electrosurgical or electrocautery devices, lasers, argon beam coagulators, fiber-optic light cables, defibrillator pads, heated probes, and drills and burrs. When not in use, electrocautery devices should remain within appropriate holders, not lying on the surgical drapes. The first three ignition sources listed are the most common ignition sources.
3. Fuel sources include the following: endotracheal tubes, sponges, drapes, gauze, alcohol-containing preparation solutions, the patient's hair, surgical dressings, gastrointestinal tract gases, and packaging materials. When using alcohol-containing preparation solutions, they should be allowed to dry before the patient is draped and ignition sources used. Surgical sponges, gauze, and the like are less likely to be fuel sources when they are wet rather than dry.

## 7. What are high-risk procedures for operating room fires?

They include but are not limited to tonsillectomies, tracheostomies, removal of laryngeal papillomas, cataract or other eye surgery, burr hole surgery, and removal of lesions about the head, neck, or face.

## 8. What strategies can reduce the incidence of airway fires?

- Laser-resistant endotracheal tubes should be chosen. The cuffs should be filled with saline, not air, and it is also recommended that the saline contain a small quantity of methylene blue to help identify rupture of the cuff, should this happen (as in an airway laser procedure). Many laser specialty tubes already have dye crystals within the cuffs. Cuffed tubes are also preferable to uncuffed tubes.
- Some authors advocate wrapping the endotracheal tube with metal tape; however, this method limits the pliability of the tube and increases the risk of a reflected laser beam and loss of metal tape fragments in the trachea.
- Nitrous oxide should not be used in high-risk procedures. Use only the lowest possible O<sub>2</sub> concentration necessary to maintain the patient's O<sub>2</sub> saturation.
- Ignition sources such as electrosurgical devices should not be allowed to enter the trachea. If they are required, the anesthesiologist should be warned of this by the surgeon, and a suitable period allowed to decrease the delivered O<sub>2</sub> concentration to the minimum amount tolerated by the patient.

## 9. What are signs that a fire has occurred?

A flame or flash may be noted; unusual sounds heard (*pop*, *snap* or *foomp*); and unusual odors, smoke, discoloration of the drapes or heat detected. Abnormal movements of the surgical drapes have also been noted in some fires.

## 10. Should an airway fire occur, what are the recommended practices for its management?

- Halt the procedure.
- Remove the endotracheal tube.
- Stop the flow of all airway gases.
- Flood the surgical field with saline and remove all flammable and burning materials.
- Mask-ventilate the patient with 100% O<sub>2</sub> and reintubate.



- Perform rigid laryngoscopy and bronchoscopy to assess the damage and remove debris.
- Monitor the patient for 24 hours.
- Use short-term steroids.
- Continue ventilatory support and antibiotics as needed.

## KEY POINTS: APPROPRIATE SCHEME TO MANAGE AN AIRWAY FIRE



1. Stop ventilation.
2. Disconnect the O<sub>2</sub> source, remove the endotracheal tube, and flood the surgical field with saline.
3. Mask-ventilate the patient with 100% O<sub>2</sub> and reintubate.
4. Perform rigid laryngoscopy and bronchoscopy (using Venturi jet ventilation) to assess the damage and remove debris.
5. Monitor the patient for 24 hours.
6. Use short-term steroids.
7. Continue ventilatory support and antibiotics as needed.

### 11. Are there additional recommendations for a fire not involving the airway?

For an intubated patient it is not necessary to halt the flow of ventilator gases. However, if the patient is receiving O<sub>2</sub> by nasal cannula or mask, stopping the flow of these gases may eliminate the oxidizing source. The burning drapes should be removed. Fire extinguishers of the CO<sub>2</sub> type may be needed. An out-of-control fire may require removal of the patient from the OR. The best way to manage any fire is to have a preestablished, practiced algorithm in which every member of the OR team understands his or her role.

## WEBSITE



Emergency Care Research Institute: The patient is on fire: Medical Device Safety Reports.  
<http://www.mdsr.ecri.org>

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# ELECTROCONVULSIVE THERAPY

*Philip R. Levin, MD, and Alma N. Juels, MD*

## 1. What are the major indications for electroconvulsive therapy treatment?

Electroconvulsive therapy (ECT) treatment plays an important role in treating severe and medication-resistant depression with psychotic features, manic delirium, and catatonia. ECT has been noted to result in a prompt improvement in symptoms of depression. Some studies have shown ECT to be more effective than antidepressant medications alone in treating the psychotic subtype of depression. ECT also remains a treatment option for patients with schizophrenia who do not respond to pharmacologic treatment.

## 2. What are the downsides of antidepressant medication?

Although antidepressant medications are effective for many patients, the rate of response to the first agent administered can be as low as 50%. The elderly may not be able to tolerate antidepressant medications because of the inability to tolerate the many side effects associated with antidepressant medications. In addition, certain neuronal changes in the elderly can decrease the response to medications.

## 3. What are the proposed mechanisms by which electroconvulsive therapy is effective?

Although its mechanism of action remains unclear, ECT increases cortical  $\gamma$ -aminobutyric acid concentration and enhances serotonergic function.

## 4. Has electroconvulsive therapy always been considered a good treatment for depression?

ECT was first used as a treatment for psychiatric disorders in the 1930s. However, complications such as fractures and cognitive impairment raised serious concerns. If not dangerous (use of insulin to cause a hypoglycemic seizure), it was barbaric (no anesthetic agents or muscle relaxants were used). Its use declined when antidepressant medications were introduced. In recent decades further research and technical advances have led to a renewed interest in the role of ECT.

## 5. How safe is electroconvulsive therapy?

It is estimated that death associated with ECT occurs in one of 10,000 patients. Interestingly, ECT appears to have less morbidity and mortality compared to many antidepressant medications. Because of this strong safety record, patients with significant comorbidities are often candidates for ECT.

## 6. What is the physiologic response to electroconvulsive therapy?

During ECT a generalized seizure is induced, leading to an acute increase in cerebral blood flow and an associated increase in intracranial pressure (ICP). Immediately following the ECT stimulus, there is a marked transient parasympathetic response that may induce sinus bradycardia, other bradyarrhythmias, asystole, premature atrial or ventricular contractions. This is rapidly followed by a more prominent sympathetic response, resulting in an increase in

heart rate of 20% or more and increases in blood pressure of 30% to 40% or more. Ventricular arrhythmias and ST-segment changes may be noted and tend to be self-limited. The duration of the tachycardia tends to correlate with the seizure duration as measured by electroencephalography (EEG), although hypertension often persists and requires therapy. Increases in adrenocorticotropic hormone, cortisol, epinephrine, vasopressin, prolactin, and growth hormone are noted. Intraocular pressure and intragastric pressure also transiently increase.

#### **7. What patients are at increased risk for complications after electroconvulsive therapy?**

ECT should be used cautiously if at all when the effects on cerebral blood flow, ICP, heart rate, and blood pressure may prove problematic to the patient because of coexisting disease. Thus patients with cerebral space-occupying lesions or cerebrovascular disease are at increased risk. Similarly patients with unstable cardiac disease, including patients with uncompensated congestive heart failure, severe valvular disease, unstable angina, recent myocardial infarction, and uncontrolled hypertension are all at increased risk of complications. Patients with pheochromocytoma should not receive ECT because massive amounts of epinephrine or norepinephrine may be released into the circulation. ECT has been used safely in persons with cardiac pacemaker or implantable cardioverter-defibrillators and during pregnancy.

#### **8. What type of preoperative evaluation is necessary before electroconvulsive therapy treatment?**

A standard preoperative anesthetic history must be taken, including identifying medications, allergies, and prior adverse anesthetic events. Presumably the patient has failed a course of antidepressant medications. The significant comorbidities discussed in Question 7 should be identified, and the stability of these conditions assessed. A prior history of response to ECT (both symptomatically and physiologically) is valuable. A physical examination is also considered extremely important. Remember to include an assessment of the patient's teeth and mouth, since the ECT stimulus will result in brief yet intense masseter contraction. There are no absolute requirements for laboratory testing. A decision to order laboratory tests should be based on the stability of the patient's comorbidities and medications. A pregnancy test in women of childbearing age is also reasonable. Optimal medical therapy in preparation for ECT is advised to minimize risk during and after treatment, although the patient's psychiatric condition may not allow this. In general, the patient's medications should be continued.

#### **9. Describe the technique of electroconvulsive therapy, including appropriate monitors and medications.**

Commonly a psychiatrist, anesthesiologist, and nurse attend the patient. An intravenous line is established, and routine monitors, including electrocardiogram, intermittent blood pressure, and pulse oximetry are placed. On rare occasions, predicated on the patient's comorbidities, arterial cannulation and continuous monitoring may be required. The psychiatrist places EEG leads to measure the cortical seizure. An additional blood pressure cuff is placed on a leg. This cuff will be inflated before administering muscle relaxants so the muscles are isolated from the circulation and after the ECT stimulus the duration of the motor seizure can be measured. Before inducing anesthesia, the patient is preoxygenated for a number of minutes with 100% oxygen.

Anticholinergic medications may be administered to lessen the effects of the initial parasympathetic discharge. In addition, they have antisialagogue properties. The medication most commonly used is glycopyrrolate, 0.2 to 0.4 mg intravenously.

Methohexital is the most common anesthetic induction agent used because it has a rapid, short duration of action, low cardiac toxicity, and, most important, minimal anticonvulsant properties. Side effects include hypotension, myoclonus, and pain on injection. A typical dose of methohexital is 0.75 to 1 mg/kg. In patients with left ventricular dysfunction, etomidate is an effective induction agent since it has minimal effects on myocardial contractility and cardiac output. Etomidate may also enhance seizure duration in patients who had prior ECT but whose seizure durations were thought inadequate to achieve a therapeutic effect. Side effects include pain on injection, nausea and vomiting, and delays in return of cognitive function. A typical dose of etomidate is 0.15 to 0.3 mg/kg.

Propofol has a rapid onset and a short duration of action and allows cognitive function to return soon. Although propofol use is associated with shorter seizure durations, recent investigations suggest that there is no difference in outcome when compared to methohexital. A typical dose of propofol is 0.75 to 1 mg/kg.

Although ketamine has also been used in ECT, compared with methohexital the EEG seizure duration is decreased; ketamine has the additional effects of increasing ICP and myocardial oxygen consumption. It does not seem to be an agent of choice.

The short-acting opioid remifentanyl has been used for its anesthetic-sparing effects, providing a stable anesthetic when swings in heart rate and blood pressure are undesirable while having no effect on seizure duration. Potent volatile anesthetic agents offer no advantage over intravenous agents, with the possible exception of late in pregnancy, during which time ECT has been noted on occasion to produce titanic uterine contractions.

After anesthetic induction, the blood pressure cuff on the leg is inflated and acts as a tourniquet. The patient is hyperventilated by Ambu bag to lower seizure threshold. Typically the short-acting muscle relaxant succinylcholine (0.5 to 1.5 mg/kg) is administered. Before administering the electroconvulsive stimulus, a compressible mouth oral guard protector is inserted to protect the patient's teeth, lips, and tongue from injury during the associated severe masseter contraction. Only rarely, based on patient circumstances, is the patient intubated. During the seizure itself the patient receives positive-pressure ventilation with 100% oxygen until spontaneous ventilation returns and the patient awakens. When stable, monitoring continues in the postanesthetic care unit until the patient is oriented and meets discharge criteria. Often the patient is confused or complains of a headache; benzodiazepines or opioids are appropriate treatments for these problems. However, benzodiazepines should be avoided before ECT because they increase seizure threshold.

Finally, it is common over a course of therapy that anesthetic medications require modification in their dosing; usually more medication is required. These adjustments must be made based on review of prior records and whether the patient experienced a seizure of therapeutic duration.

#### 10. What additional medications are used to address hypertension and tachycardia?

The cardioselective  $\beta$ -adrenergic blocker esmolol is sometimes given by either bolus or infusion to blunt the sympathetic response of ECT. The mixed  $\alpha$ - and  $\beta$ -adrenergic blocker labetalol is frequently administered for persistent hypertension.

Nitroglycerin (3 mcg/kg) IV can be given 2 minutes before ECT, or 2% nitroglycerin ointment applied 45 minutes before ECT to attenuate the increase in blood pressure and provide coronary vasodilation.

#### 11. What is an optimal seizure duration?

ECT-induced seizure activity lasting from 25 to 50 seconds is alleged to produce the best response. Patients experiencing an initial seizure lasting less than 15 seconds or greater than 180 seconds have been found to achieve a less favorable response to ECT.

**12. What can be done to prolong a seizure of inadequate duration or terminate a prolonged seizure?**

Etomidate is the induction drug of choice in patients experiencing inadequate seizure activity. The proconvulsant caffeine (500 mg) is often administered in situations in which the seizure duration during prior electroconvulsive treatments has been suboptimal. Aminophylline has also been used for this purpose. Prolonged ECT-induced seizures can be terminated with a benzodiazepine or bolus of propofol, 40 to 80 mg.

**13. How many electroconvulsive therapy treatments are usually necessary?**

ECT is given as a course of treatments. The total number needed to successfully treat psychiatric disturbance varies from patient to patient. For depression the typical range is from six to twelve treatments. Typically ECT is performed three times a week. In successful cases initial clinical improvement is usually evident after three to five treatments.

**14. What are some of the adverse effects of electroconvulsive therapy?**

An induced seizure lasting longer than 2 or 3 minutes is considered prolonged and can result in increased cognitive deficits. Prolonged apnea is said to occur if it takes longer than 5 minutes to regain spontaneous ventilations after ECT treatment and may be caused by a pseudocholinesterase deficiency, resulting in prolonged succinylcholine activity. Emergence delirium is characterized by restless agitation, aimless repetitive movements, grasping objects in view, or restless attempts to remove the monitors and intravenous line. It usually lasts from 10 to 45 minutes or more after the seizure and responds to benzodiazepines. Anterograde amnesia may occur immediately after an ECT treatment but tends to resolve usually within an hour. Retrograde amnesia is the most common persistent adverse effect of ECT. It is more commonly seen in elderly patients and those with preexisting cognitive impairment. Memory loss of events several months or years in the past can occur. Usually retrograde amnesia improves during the first few months after ECT, although many patients have incomplete recovery. Other adverse effects include headache, muscle aches, nausea, and fatigue.

## KEY POINTS: ELECTROCONVULSIVE THERAPY



1. ECT treatment is recommended for patients with depression with psychotic features, manic delirium, and catatonia and patients who cannot tolerate the side effects of antidepressant medications.
2. Typical physiologic responses to ECT include transient parasympathetic discharge resulting in bradyarrhythmias, followed by a sympathetic stimulus resulting in hypertension and tachycardia. Increases in cerebral blood flow and ICP are also noted.
3. Methohexital is the most common induction agent used during ECT because it has minimal anticonvulsant properties, a rapid onset, short duration of action, and low cardiac toxicity.
4. Succinylcholine is the most common muscle relaxant used during ECT because of its short duration of action.

**15. Is electroconvulsive therapy curative?**

ECT is an extremely effective acute treatment for major depressive episodes. However, a permanent cure is extremely rare. Maintenance therapy with occasional (weekly or monthly) ECT treatments in combination with antidepressant pharmacotherapy decreases the relapse rate, but more effective strategies for relapse prevention in mood disorders are urgently needed.

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# ACUTE PAIN MANAGEMENT

*Robin Slover, MD, and Heather Rachel Davids, MD*

### 1. Define acute pain.

*Pain* is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” Acute pain refers to pain of short duration (<3 months), usually associated with surgery, trauma, or an acute illness.

Acute pain differs from chronic pain because:

- Its cause is usually known.
- It is usually temporary and located in the area of trauma or damage.
- It resolves spontaneously with healing.

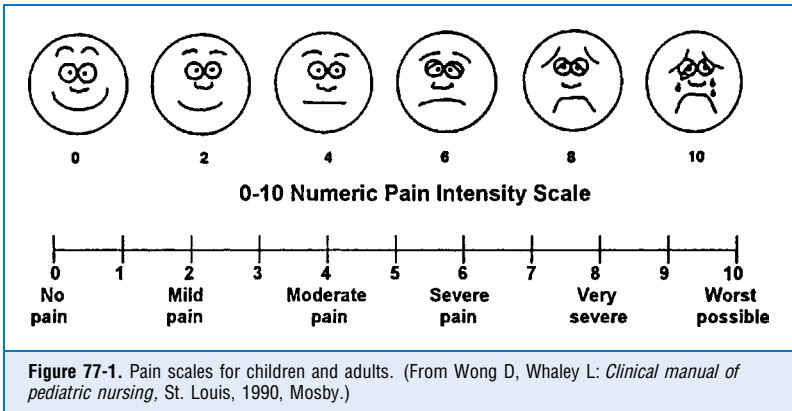
### 2. Why has acute pain been undertreated?

There are numerous reasons acute pain is typically undertreated. Physicians get very little education regarding pain management during the course of medical school and residency training. Many providers overestimate the risks associated with the use of opioids, such as respiratory depression and addiction. Health care providers are also often afraid of scrutiny from regulatory boards that they believe may result from regularly prescribing opioid narcotics. In reality, the fact that poorly treated pain may result in higher morbidity and mortality rates has become appreciated only recently. There is now a greater emphasis being placed on not undertreating pain; lawsuits have successfully been brought against physicians for not providing enough pain medication. Pain is now considered the fifth vital sign.

### 3. How is pain assessed?

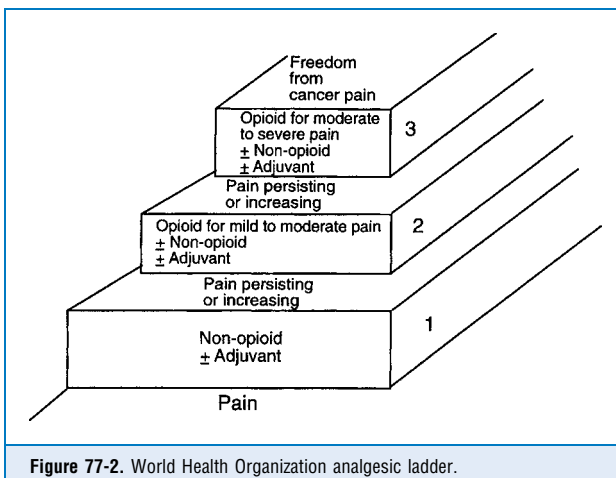
Pain is subjective and cannot be measured even with the most sophisticated medical equipment. Changes in vital signs such as blood pressure or heart rate correlate poorly with the degree of pain control.

The magnitude of pain and the response to treatment can be monitored in several ways. A visual analog scale may be used in which the patient chooses a mark on a 10-cm line corresponding with the perceived amount of pain being experienced. Scales using color (from blue for minimal pain through violet hues to bright red for maximal pain) or numbers (from zero for no pain through ten for maximal pain) have been devised for adults (Figure 77-1). A scale of 10 faces, ranging from very happy to very sad, can be used in young children. The child points to the face matching the way he or she feels. Verbal descriptive scales such as the McGill Pain Questionnaire are useful both for clinical and research purposes. Functional ability is also a useful measure of pain. In some patients, especially those who also have chronic pain, assessing ability to perform regular functions such as activities of daily living, performing at work, or ability to participate in leisure activities may be more useful than collecting pain scores. In a hospital setting the number of times a patient spontaneously leaves the room may provide a more accurate assessment than pain scores. Pain scores with activity may be a more sensitive measure of analgesia because it is easier to control pain at rest. The pain scale can be used to ensure that an intervention such as an increased dose of opioids is effective in decreasing the patient's pain.



#### 4. What medications are useful in treating acute pain?

The medications useful in treating acute pain are similar to those used in treating other types of pain. The World Health Organization analgesic ladder developed for treating patients with cancer pain also provides a useful approach to treating acute pain (Figure 77-2). At the lowest level (mild pain), nonopioid analgesics such as nonsteroidal antiinflammatory drugs (NSAIDs) (e.g., ibuprofen or acetaminophen) are useful. Such drugs have an analgesic ceiling; above a certain dose no further analgesia is expected. For moderate pain compounds combining acetaminophen or aspirin with an opioid are useful. The inclusion of acetaminophen limits the amount of such agents that should be used within a 24-hour period because toxic accumulations can occur. The next step to consider would be adding an agent such as tramadol. Tramadol has a dual mechanism of action as a weak  $\mu$ -opioid agonist and a weak inhibitor of reuptake of norepinephrine and serotonin. Care should be taken when concurrently prescribing with selective serotonin reuptake inhibitors since there is a potential increased incidence of serotonin syndrome (although there are very few reported cases). With severe levels of pain an opioid such as morphine or hydromorphone is a better choice; such opioids





have no analgesic ceiling. Most postoperative or trauma patients initially respond better to morphine or other opioids. Intravenous agents are usually faster, and patients report more satisfaction with analgesia after surgery or trauma. By the time the patient is eating and ready for discharge, opioid-acetaminophen agents or NSAIDs are often adequate.

#### 5. Do all types of pain respond equally to medication containing opioids?

Not all types of pain respond equally to the same medication. Opioid analgesics are helpful in controlling somatic or visceral pain. Bone pain may be helped partially by opioids. However, NSAIDs and steroids are highly effective in treating bone pain. The combination of NSAIDs and opioids is synergistic in controlling pain. Neuropathic pain, often described as pain with a burning, hyperesthetic quality, responds to a diverse group of drugs, including antidepressants (amitriptyline), anticonvulsants (carbamazepine or gabapentin), antiarrhythmics (mexiletine), muscle relaxants (baclofen), and  $\alpha$ -adrenergic agonists (clonidine). Opioids may also be helpful. Frequently pain control is improved after 1 to 2 days of using adjuvant drugs. Alternative medications may also help to control somatic or visceral pain. Drugs that control pain by different mechanisms may be synergistic when used together (such as NSAIDs and opioids). By using lower doses of two different agents, the patient may have good pain control with fewer side effects. Another option for mild to moderate pain is use of topical agents such as patches impregnated with lidocaine (Lidoderm) or diclofenac (Flector). In addition, topical gels or ointments can be considered, including 5% lidocaine ointment, 1% Voltaren gel, 1.3% diclofenac, or 4% ketamine compounded ointment. These patches and topical agents can also be used in conjunction with oral medications.

#### 6. What is the risk of addiction with opioids?

Addiction (or psychologic dependence) needs to be differentiated from physical dependence. Physical dependence, a physiologic adaptation of the body to the presence of an opioid, develops in all patients maintained on opioids for a period of several weeks. If the opioid is stopped abruptly without tapering, the patient may show signs of withdrawal. The patient can stop opioids at any time and avoid withdrawal symptoms by tapering down. Tolerance is the need for a higher dose of opioid to produce the same pharmacologic effect. Neither physical dependence nor tolerance indicates addiction. The psychologic dependence seen with addiction is characterized by a compulsive behavior pattern involved in acquiring opioids for nonmedical purposes (psychic effects) as opposed to pain relief. The risk of iatrogenic addiction is very low; several studies have shown it to be less than 0.1%. Patients who are inadequately treated may seem to be drug seeking, because they repeatedly request opioids and are concerned with the timing of their next dose. Such *pseudo addiction* may mimic addictive behavior but is caused by inadequate pain treatment. This iatrogenic condition can be avoided by listening to the patient and carefully assessing his or her pain. With proper doses of pain medication, pseudo addiction disappears. Current studies report that patients with a past history of other substance abuse are at higher risk for opioid addiction. About 4% of patients treated for trauma had problems with opioids but showed other indications of addictive behavior that correlated with their increased use.

#### 7. How should opioids be given? Are some opioids better than others?

Opioids can be given in various ways. Oral administration is usually the easiest and least expensive. Tablets should be provided on a schedule (e.g., oxycodone-acetaminophen tablets every 4 hours) rather than on an *as needed* (PRN) or *as requested* basis. Many studies have shown that PRN schedules usually provide only 25% of the maximal possible daily dose of opioids, despite the patient's repeated requests. If a patient cannot take medication orally, opioids can be administered intramuscularly, intravenously (including patient-controlled analgesia [PCA] pumps), subcutaneously, rectally, transdermally, epidurally, intrathecally, through iontophoresis, and through buccal mucosa. Because PCA pumps are safe and effective, they are often used when the patient cannot take oral medication.

Meperidine has the highest incidence of allergic reactions; in addition, its first metabolite, normeperidine, can accumulate and cause central nervous system excitation, including seizures. Normeperidine accumulation is dose dependent and more common in patients with renal impairment. Consequently meperidine has been removed from many hospital formularies and replaced with better opioid alternatives. Morphine has an active metabolite (morphine-6-glucuronide) that is analgesic and has a longer half-life than morphine. This metabolite can be useful in many cases because it allows a slow, sustained increase in analgesia. However, in patients with decreased renal function, the accumulation of an active metabolite may lead to increased side effects, including increased risk of respiratory depression. Fentanyl acts more rapidly than morphine or hydromorphone and has no active metabolites. It is a safer choice for patients with impaired renal or liver function. Hydromorphone also has no active metabolites. It is five times as potent as morphine and less dysphoric; however, its onset of action and duration are more similar to morphine than to fentanyl. Methadone can be given intravenously. The intravenous dose is equivalent to the oral dose, unlike other opioids, which are more potent intravenously. Oxycodone is a potent newer opioid that is only available orally. Tapentadol is a new oral opioid drug just approved by the Food and Drug Administration. It is approved for moderate to severe acute pain as a schedule II drug. Tapentadol is a combination of an opioid binding drug with a norepinephrine reuptake inhibitor. It is projected to be between tramadol and morphine in potency.

In a hospital setting the general guideline should be to schedule pain medications for the first 1 to 2 days after the surgery or injury. After that period of time the medication can be transitioned to an *as needed* status. As noted previously, assessment should continue by pain score and function to determine appropriate dosing. In an outpatient setting 1 day of scheduled pain medications is reasonable before transitioning to *as needed*.

#### 8. When treating acute pain in a chronic pain patient, how should the approach differ?

When a chronic pain patient has suffered an injury or undergone surgery, the general rule is that the typical dose of oral opioids should be tripled for the first 1 to 2 days. In the preoperative preparation for a chronic pain patient, a one-time dose of gabapentin (900 to 1200 mg) or pregabalin (75 to 100 mg) coupled with a one-time dose of celecoxib (Celebrex) (200 mg) has been shown to improve pain control. After surgery gabapentin or pregabalin can be continued as a regular oral dose, and celecoxib should be continued at 100 mg bid for 5 days. Regional blocks should be used whenever possible and continued at least 24 hours after surgery if possible. A low-dose ketamine (0.05 to 0.2 mg/kg/hr) infusion during the operation helps with pain control and can be continued after surgery by combining ketamine with the opioid in a PCA infusion.

#### 9. How should a patient-controlled analgesia pump be set?

Several decisions must be made in setting up a PCA pump. The first is what drug to use. As discussed previously, the most commonly used agents are morphine and hydromorphone. Meperidine has been removed from many hospital formularies and should only be used in rare circumstances. Fentanyl also can be used, particularly in patients with end-organ failure. Morphine comes prepackaged in a 1-mg/ml concentration; because hydromorphone is five times as potent, a 0.2-mg/ml concentration is equivalent to 1 mg of morphine. After choosing the drug, a decision should be made about the type of infusion: increment dosing only, basal (continuous) with incremental dosing, or incremental dosing with a basal dose only at night (between 10 PM and 6 AM) to help the patient sleep. Studies have shown no significant benefit to a basal rate, although anecdotally patients prefer a basal rate at night to help them sleep. Finally, the duration of the lock-out period needs to be determined. Lock-out refers to the time between actual delivery of opioid doses (e.g., if a 6-minute lock-out period is selected, the patient cannot receive opioid doses closer than 6 minutes apart, regardless of how often he or she activates the PCA pump). The lock-out period should be short enough to allow the

patient to titrate the opioid level but long enough to allow the patient to feel the effect of one dose before delivering another. The usual lock-out ranges are 6 to 10 minutes.

#### 10. What are common side effects of opioids? How are they treated?

The common side effects of opioids are sedation, pruritus, nausea and vomiting, urinary retention, and respiratory depression. In patients who have taken opioids previously, the risk of respiratory depression and sedation is less. Pruritus is treated by applying lotion to the affected area, by intravenous or oral delivery of diphenhydramine (25 to 50 mg), and in severe cases by using an opioid antagonist or agonist-antagonist (e.g., nalbuphine, 5 mg every 6 hours). Propofol, 10 mg every 6 hours, is also effective. Urinary retention is treated by urinary catheter drainage or nalbuphine. Nausea and vomiting respond to a decrease in opioid dose (elimination of a basal rate), nalbuphine, and antiemetics. Ondansetron, 4 mg intravenously, has proved to be a much more effective antiemetic than droperidol. Respiratory depression is treated by using a pure antagonist (naloxone) or agonist-antagonist (nalbuphine).

#### 11. How do neuraxial opioids work?

Opioid receptors are present in levels I and II of the substantia gelatinosa of the dorsal horn. Opioids given either intrathecally or epidurally bind to these receptors. The dose of morphine can be decreased to 10% of the usual intravenous dose when given epidurally and to 1% when given intrathecally. The clinical behavior of the opioid can be predicted by its lipid solubility. Highly lipid-soluble opioids such as fentanyl pass through membranes and bind quickly. Fentanyl has a rapid onset, short duration, and limited spread (five levels). Morphine, which is highly hydrophilic, moves through membranes more slowly and has a slower onset but longer duration because it stays suspended in solution and is released slowly to bind to the opioid receptors. Because of its poor lipid solubility, it spreads throughout the entire length of the spinal fluid and can help to control pain from several different anatomic sites. The termination of clinical activity of neuraxial opioids is caused by vascular absorption and breakdown. Local anesthetics such as lidocaine and bupivacaine can be used alone or in combination with opioids.

#### 12. How do agonist-antagonists differ from opioids such as morphine?

$\mu$ -,  $\delta$ -, and  $\kappa$ -opioid receptors have been identified in the central nervous system. Most morphine equivalent opioids are primarily  $\mu$ -agonists, with some  $\delta$ - and  $\kappa$ -effect. Agonist-antagonists are  $\mu$ -antagonists and  $\kappa$ -agonists. Because  $\kappa$ -receptors provide weaker analgesia, agonist-antagonists are adequate for mild to moderate pain, whereas  $\mu$ -agonists are adequate for moderate to severe pain. Suboxone is a newer oral combination of buprenorphine combined with naloxone. Patients using this agent can be given  $\mu$ -acting opioids but will need higher doses.

### KEY POINTS: ACUTE PAIN MANAGEMENT



1. Pain is the fifth vital sign. Use function and pain scales.
2. Good pain control may decrease postoperative complications.
3. Adjuvant drugs can be helpful.
4. Continuous infusions are as good as epidural infusions for postoperative pain control after knee procedures.
5. Doses of morphine differ by a factor of 10 between intravenous, epidural, and intrathecal routes.

### 13. How should patients with continuous infusions for analgesia or patient-controlled analgesia pumps be monitored?

Patients receiving analgesia do not need elaborate monitoring equipment. Pulse oximetry can be used if there is any concern for oxygen desaturation, but usually nurses are able to monitor patients safely by checking respiratory rate every hour and level of sedation every hour the patient is awake. Vital signs are taken as scheduled. The catheter site of the infusion should be checked daily for any signs of infection (redness, swelling) or leakage.

### 14. How is an oral agent chosen for a patient who previously received intravenous opioids?

Choice of an oral agent should be based on how much pain the patient still has and how much opioid was needed to control the pain. Opioid-acetaminophen compounds are adequate for patients whose pain requires 0 to 2 mg/hr of morphine. Hydrocodone-acetaminophen is a milder analgesic than oxycodone-acetaminophen and is useful for patients who require minimal opioids. An equal analgesic dosing chart (Table 77-1) can be used to select equivalent levels of analgesics.

TABLE 77-1. EQUIANALGESIC DOSES

Analgesic	Equianalgesic Doses		
	Parenteral (mg)	Oral (mg)	Dose Interval (hours)
<b>Opioid agonist</b>			
Morphine	10	30–60	3–6
Slow-release morphine	—	30–60	8–12
Hydromorphone (Dilaudid)	1.5	7.5	3–5
Fentanyl (Sublimaze, Innovar)	0.1	—	0.5–1
Transdermal fentanyl (Duragesic)	—	—	72
Levorphanol (Levo-Dromoran)	2	4	3–6
Meperidine (Demerol)	75	300	3–4
Methadone (Dolophine)	10	20	4–6
Oxymorphone (Opana)		10	3–6
Oxymorphone extended release (Opana ER)		10	12
Oxycodone		30	3–6
Codeine	130	200	3–6
Hydrocodone		30	3–4
<b>Agonist–antagonist</b>			
Nalbuphine (Nubain)	10	—	3–6
Butorphanol (Stadol)	2	—	3–4
Buprenorphine/Naloxone (Suboxone)			
<b>Oral Drugs Approximately Equianalgesic to Aspirin (650 mg)</b>			
Codeine	50 mg	Propoxyphene	65 mg
Hydrocodone	5 mg	Acetaminophen	650 mg
Meperidine	50 mg	Ibuprofen	200 mg
Oxycodone	5 mg	Naproxen	275 mg

**15. Which nonsteroidal antiinflammatory drug should be used?**

If the patient can take oral medication, an oral agent should be used. Most oral agents have the same degree of analgesia as antiinflammatory activity. The degree of potency of analgesia parallels the risk of gastric upset with oral agents. One or two specific agents may work better for a given patient, but their identification is usually a matter of trial and error. Price also may be a factor. Older, off-patent NSAIDs may be significantly cheaper and just as effective (e.g., naproxen, indomethacin, and ibuprofen).

For patients who cannot take oral medication, parenteral ketorolac is the available option. Ketorolac has a more potent analgesic than antiinflammatory effect. It may be given intravenously or intramuscularly. In patients over 65 years old who weigh less than 100 pounds or who are frail, half of the regular dose should be used. In patients with a serum creatinine above 1.3 ml/dl, alternatives to the use of ketorolac should be considered. The side effects of NSAIDs may be observed with either oral or parenteral use. Patients who have active gastric disease; are anticoagulated or hypovolemic; or have a history of asthma, congestive heart failure, or renal disease may have complications from NSAID use.

**16. Are cyclooxygenase-2 agents any better for pain than cyclooxygenase-1 agents?**

Cyclooxygenase-2 (COX-2) agents may have fewer gastrointestinal or platelet effects, but they are no better than COX-1 agents for pain control in most patients.

**17. What other techniques can be used for acute pain management?**

In addition to PCA pumps and epidurals, intrathecal opioids can be used, especially if spinal anesthesia is used for the procedure. Preservative-free morphine can be used for inpatients, and fentanyl for outpatients. Morphine doses of 0.1 to 0.3 mg are adequate for many lower extremity, urologic, and gynecologic procedures and have a minimal risk of respiratory depression. For thoracic procedures higher doses are needed (0.3 to 0.75 mg) and involve a risk of respiratory depression. Fentanyl can also be used intrathecally; 10 to 15 mcg of intrathecal fentanyl is equal to 0.1 to 0.3 mg of intrathecal morphine. Because fentanyl is more lipid soluble than morphine, it does not spread as far but still may be given through lumbar spinal injection.

Other types of blocks can be useful. Intercostal blocks decrease pain and improve ventilation in patients with rib fractures or flail chests. Continuous brachial plexus blocks increase blood flow in patients with collagen vascular diseases or arterial spasm (Burger's disease) and those who have digital reattachment, improving healing and providing good pain control. Single injections in the brachial plexus are helpful for shoulder or upper arm procedures. Recently continuous sciatic and/or femoral blocks have been useful for patients with knee or lower leg procedures. The use of ultrasound has improved the success rate of these catheters and allows other nerves to be blocked with continuous catheters.

**18. How does good acute pain management make a difference?**

Pain is a form of stress and produces an elevation in stress hormones and catecholamines. Good pain management has been shown to result in shorter hospital stays, improved mortality rates (especially in patients with less physiologic reserve such as those in the intensive care unit), better immune function, fewer catabolism and endocrine derangements, and fewer thromboembolic complications. In addition, specific benefits have been shown for patients undergoing specific procedures. Patients who undergo amputation under a regional block with local anesthetic have a decreased incidence of phantom pain. Patients in whom a vascular graft is placed have a lower rate of thrombosis. A decreased mortality rate has been shown in patients with flail chests who have epidural analgesia.

Recent studies have shown the value of preemptive analgesia in some surgical situations. The blockade of the pathways involved in pain transmission before surgical stimulation may decrease the patient's postoperative pain. Local infiltration along the site of skin incision in

patients having inguinal hernia repairs with general anesthesia is beneficial if the infiltration is done before the skin incision. Similar results have been found for preoperative local infiltration along the laparoscopic port sites. Several studies using intravenous or epidural opiates in patients having thoracotomies and hysterectomies have also shown a preemptive effect. The use of local anesthetic with spinal and epidural anesthetics has not been shown to be preemptive. NSAIDs have not shown a preemptive effect. Further studies with larger patient groups are needed to provide definitive answers regarding preemptive analgesia.

Proper pain management not only keeps patients more comfortable but also may decrease the risk of morbidity and mortality, thus improving use of health resources.

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# CHRONIC PAIN MANAGEMENT

Ronald Valdivieso, MD

## 1. What is the definition of pain?

The International Association for the Study of Pain defines *pain* as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” Acute pain is associated with an identifiable cause (e.g., surgery, trauma, acute illness) and usually resolves with healing. Chronic pain is more difficult to define. It is believed that pain becomes chronic if it persists beyond 1 month of the usual course of an acute problem. However, other authors do not believe that duration should be identified as one of the distinguishing features of chronic pain and point to cognitive-behavioral aspects as essential criteria in any chronic pain syndrome.

## 2. How does normal pain perception occur?

Nociceptors are structures located at the end of axons that are depolarized by noxious thermal, mechanical, or chemical stimuli. The distal ends of most A- $\delta$  and C fibers are nociceptors. These axons are the ones that carry nociceptive information to the dorsal root and trigeminal ganglion and enter the spinal cord via the posterior root. Once in the spinal cord these afferent fibers synapse with cells in Rexed's laminae I and V preferentially but also in laminae II and X. Axons from the previously mentioned neurons that travel to the contralateral side of the spinal cord will eventually form the spinothalamic tract, spinoreticular tract, and spinomesencephalic tract. Axons that enter the dorsal column will form the postsynaptic dorsal column tract. These ascending nociceptive tracts will eventually synapse with superior structures such as the periaqueductal gray, hypothalamus, and thalamus. The ventroposterolateral, ventroposteromedial, and ventroposteroinferior nuclei of the thalamus then send projections to the somatosensory cortex and cingulate cortices.

## 3. What is the classification of pain based on neurophysiologic mechanisms?

Pain can be classified according to its neurophysiologic mechanism:

- **Nociceptive pain:** Occurs when nociceptors are stimulated by noxious stimuli. This category is divided into somatic and visceral pain. Somatic pain sensation originates from trauma, burns, and ischemia, to name the most common ones. It is transmitted via somatic nerves. Visceral pain, as its name implies, originates from visceral structures. It is transmitted preferentially via the sympathetic fibers and is usually produced by distention, ischemia, or spasm of hollow viscera.
- **Neuropathic pain:** Is pain produced by an alteration in structure or function of the nervous system. Neuropathic pain can be divided into peripheral and central. Examples of peripheral neuropathic pain include CRPS II (causalgia), postherpetic neuralgia, diabetic neuropathy, and radicular pain from mechanical compression. Central neuropathic pain syndromes include poststroke pain, postparalytic pain, and pain syndromes from multiple sclerosis.
- **Psychogenic pain:** Is quite controversial in the sense that it is very difficult to define. One popular definition is that this pain is better described and understood in psychologic rather than physical language and is pain for which an adequate physical explanation cannot be found.

## 4. Name the most commonly used groups of medications for the treatment of chronic pain.

See Table 78-1.

TABLE 78-1. COMMONLY USED GROUPS OF MEDICATIONS FOR TREATMENT OF CHRONIC PAIN

Group	Drug Examples	Mode of Action	Potential Side Effects
TCAs	Amitriptyline	Norepinephrine and 5-hydroxytryptamine uptake inhibition	Anticholinergic actions
	Nortriptyline		Decreased seizure threshold
NSAIDs	Ibuprofen	Inhibit production of prostaglandin	Cardiac dysrhythmias
	Rofecoxib		Weight gain
SSRIs	Fluoxetine	Inhibit serotonin reuptake	Gastrointestinal bleeding
	Paroxetine		Platelet dysfunction
	Sertraline		Bronchospasm
Anticonvulsants	Carbamazepine	Reduce Na, K conductance	Coronary thrombosis
	Valproic acid	Increase GABA activity	Anxiety
	Gabapentin		Nausea
	Pregabalin		Weight loss
Neuroleptics	Fluphenazine	May alter perception of pain	Increase in levels of TCAs
	Haloperidol		Blood dyscrasias
Benzodiazepines	Diazepam	Reduce anxiety	Liver dysfunction
	Lorazepam		Gastrointestinal symptoms
Opioids	Morphine	$\mu$ -Receptor agonists	Sedation
	Meperidine		Ataxia
	Oxycodone		Extrapyramidal symptoms
	Methodone		Orthostatic hypotension
Muscle relaxants	Baclofen	Interaction with GABA receptor	Sedation
	Cyclobenzaprine		Anticholinergic action
Others	Mexiletine	Na-channel blocker	Orthostatic hypotension
	$\beta$ -blockers	$\beta$ -receptor blocker	Conduction block
			Bronchospasm
			Congestive heart failure

*GABA*,  $\gamma$ -Aminobutyric acid; *NSAID*, nonsteroidal antiinflammatory drug; *SSRIs*, selective serotonin reuptake inhibitor; *TCA*, tricyclic antidepressant.



### 5. How are nerve blocks helpful in the treatment of chronic pain?

- **Diagnosis:** Nerve blocks can help identify the nerve site responsible for the symptoms.
- **Therapy:** Nerve blocks temporarily reduce pain and therefore facilitate physical therapy. Based on the response to a diagnostic block, it might be possible to determine if a neuroablation procedure is appropriate to treat a given condition.

### 6. Are psychosocial factors important in the diagnosis and treatment of pain?

Painful disorders can present with associated psychologic or psychiatric symptoms. These can vary from mild depression to obvious substance abuse problems to suicidal thoughts. It is necessary to address such issues to improve the patient's chance for recovery.

### 7. How is pain of malignant origin treated?

Pain of malignant origin should be aggressively treated with a multiple therapeutic approach. This approach should initially be pharmacologic with introduction of short- and long-acting opioid preparations and some adjuvants. Adjuvants should be chosen according to the symptomatology and their side-effect profile. For example, nonsteroidal antiinflammatory drugs (NSAIDs) and steroids are very useful in the treatment of bone pain from primary or metastatic disease; anticonvulsants and tricyclic antidepressants (TCAs) can be used in the treatment of neuropathic pain from compression or from previous interventions such as chemotherapy or radiation therapy.

Diagnostic nerve blocks can be followed by either chemical or radiofrequency ablation procedures. For malignancies located in the abdomen, celiac plexus chemical ablation can be attempted; for malignancies located in the pelvis, a superior hypogastric plexus block can be beneficial, and perineal pain can be treated with a ganglion impar ablation. With the introduction of sophisticated intrathecal delivery systems, neuraxial ablative procedures are becoming less popular but are still very useful. As mentioned, intrathecal delivery systems and long-term epidural catheters can be used to deliver opioids, local anesthetics, and other potentially beneficial drugs to the neuraxis and therefore improve the patient's condition and decrease the side effects from other medications. Finally, radiation therapy and chemotherapy can also improve pain symptoms by reducing the extent of the disease.

### 8. Define CRPS I and II. What nerve blocks are commonly used to treat these conditions?

CRPS stands for *complex regional pain syndrome*. It is a painful condition usually centered in an extremity in which different degrees of sympathetic dysfunction can be identified. CRPS usually presents with spontaneous pain, hyperalgesia, hyperpathia, and allodynia that is not restricted to the territory of a single nerve. Sympathetic dysfunction presents as variations in regional blood flow that can cause edema and cyanosis. Localized sweating and trophic changes in the skin and nails of the affected part of the body can be seen as the disease progresses. CRPS I (formerly known as RSD) can follow minor trauma, venipuncture, or carpal tunnel surgery; sometimes no identifiable cause can be found. CRPS II (formerly causalgia) follows damage to a peripheral nerve. Sympathetic blocks are very useful since they can facilitate physical therapy and help the patient regain some function in the affected extremity. Upper-extremity sympathetic denervation is accomplished by blocking the stellate ganglion; for lower-extremity sympathetic block a lumbar sympathetic block is performed.

### 9. How is neuropathic pain treated?

Medical management that includes anticonvulsants and TCAs has been shown to improve symptomatology. Methadone, due to its *N*-methyl-D-aspartate receptor antagonism, is probably the most useful opioid in the treatment of neuropathic pain. Other agents such as

clonidine and mexiletine have also been used successfully. Injection of local anesthetics and steroids has a role in the treatment of isolated peripheral neuropathies. The introduction of peripheral and spinal cord stimulators is now an accepted therapy for very complex problems such as postlaminectomy pain syndromes and CRPS types I and II.

#### 10. Define myofascial pain syndrome.

Myofascial pain syndrome is a group of muscle disorders characterized by hypersensitive areas called *trigger points* that can occur in more than one muscle group. When trigger points are mechanically stimulated, they are painful and refer pain to an area called the *reference zone*. This reference zone does not correlate with any dermatome or peripheral nerve innervation area.

#### 11. Define fibromyalgia.

Fibromyalgia is a chronic pain condition characterized by widespread musculoskeletal pain, aches, and stiffness, soft tissue tenderness, general fatigue, and sleep disturbances. The most common sites of pain include the neck, back, shoulders, pelvic girdle, and hands, but any body part can be involved. Fibromyalgia patients experience a range of symptoms of varying intensities that wax and wane over time.

#### 12. How is fibromyalgia managed?

New research shows that fibromyalgia very likely has a central nervous system component. This theory helps explain the widespread nature of the patients' symptoms and its association with sleep disturbances. Pregabalin is the only Food and Drug Administration–approved medication for the management of fibromyalgia. In a randomized, double-blinded, placebo-controlled study, monotherapy with pregabalin showed statistically significant benefit in mean pain scores and Patient Global Impression of Change (PGIC). Aerobic conditioning and management of underlying depression are also very important in the management of these patients.

#### 13. List possible etiologies of low back pain.

Low back pain can arise from multiple anatomic structures located in the lower back; these include the following:

- Muscle strain in the paravertebral muscles or quadratus lumborum
- Posterior elements of the vertebral column such as the facet joints and ligamentous structures
- Anterior elements such as vertebral compression fractures and damage to the annulus fibrosis of the intervertebral disk
- Vertebral canal and foraminal stenosis, which can cause myelopathy or radiculopathy, respectively
- Sacroiliac joint dysfunction

#### 14. What is the rationale behind the use of epidural steroids in the treatment of radicular symptoms associated with a herniated disk?

Radiculopathy is pain that is present as a result of either mechanical or chemical (most of the time both) irritation of a nerve root and can lead to pain and edema of the same nerve. The site where this usually occurs is the neural foramen. Local injection of steroids will decrease the amount of time needed to recover from an acute episode of sciatica by three mechanisms:

1. Decreasing the inflammation of the nerve root due to the antiinflammatory properties of the steroids
2. Dilution of chemical irritants coming from a ruptured disc
3. Nerve membrane stabilizers

**15. Explain the gate theory of pain.**

In 1965 Melzack and Wall proposed that the substantia gelatinosa in the spinal cord was the primary gate in the transmission of noxious and nonnoxious stimulus to the central nervous system. The pain gate is opened by information coming from slow unmyelinated C fibers and closed by the impulses from faster myelinated fibers such as A- $\beta$ . Since pain is transmitted by slow A- $\delta$  and C fibers, they reason that, by activating faster fibers such as the ones that transmit proprioception, the gate will be closed, and the pain symptoms will improve. A practical application is the use of transcutaneous electrical nerve stimulation units and spinal and peripheral nerve stimulators for the treatment of pain.

**16. Name some indications for the use of spinal cord stimulators.**

The most common indication for use of spinal cord stimulation in the United States is in the treatment of postlaminectomy pain syndromes. In Europe the most common indication is in the treatment of peripheral vascular disease. Among other uses are CRPS I and II, arachnoiditis, and intractable angina pectoris.

**17. What are the most common medications used for intrathecal delivery via implantable delivery systems?**

The most common medications used in the implantable delivery systems are opioids in general and morphine and hydromorphone in particular. Local anesthetics are used, usually in combination with an opioid for the treatment of malignant pain. Baclofen is used for the treatment of spasticity and painful muscle contractions. Clonidine is used for the treatment of neuropathic pain. Recent studies have explored the potential for the use of ketamine, neostigmine, and some calcium channel blockers.

**WEBSITE**

International Association for the Study of Pain  
<http://www.iasp-pain.org>

**KEY POINTS: CHRONIC PAIN MANAGEMENT**

1. Chronic pain is best treated using multiple therapeutic modalities. These include physical therapy, psychologic support, pharmacologic management, and the rational use of more invasive procedures such as nerve blocks and implantable technologies.
2. Patients suffering from cancer pain often exhibit complex symptomatology that includes various forms of nociceptive and neuropathic pain.
3. In patients suffering from chronic pain, underlying psychologic/psychiatric conditions should be addressed if any meaningful recovery is to be achieved.
4. Neuropathic pain is usually less responsive to opioids than pain originating from nociceptors.

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