FIFTH EDITION

# Handbook of Neuroanesthesia

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COVER ART

By Frank D. Fasano, MAMS, BFA
Artistic rendition of neuronal apoptosis in brain hippocampus

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# FOREWORD

The inexorable march of technologic advance in both the clinical neurosciences and anesthesia makes the publication of successive editions of this handbook imperative. From the time of the first edition, dramatic innovations in CNS imaging, minimally invasive therapeutic interventions, and the pharmacology of anesthesia have increased the complexity of neurosurgical care. The reader's attention should be drawn to chapters on deep brain stimulation, awake craniotomy, intraoperative MRI imaging, and anesthesia for interventional radiologic techniques. These cutting-edge treatment paradigms cannot advance without the partnership between neuroanesthesia and neurosurgery.

Along with our ability to develop and implement technical advancements, we must seamlessly integrate initiatives that improve patient safety. Facilitating communication among all members of the OR team assumes primacy in this endeavor. The aviation industry has served as a model to be emulated. The surgical time-out evolved from the checklist methodology, which mandates information transfer among cabin crew. Although the isolated OR time-out serves an important purpose, a neurosurgical procedure can easily take longer than many airline flights. Information transfer remains integral to all phases of the flight/case. We may want to look at the principles of cockpit resource management for inspiration. These include, but are not limited to, team management, situational awareness, assertion and advocacy, stress and fatigue management, error reduction, and leadership strategies.

We remain indebted to Drs. Cottrell and Newfield for their continued efforts at advancing our interrelated disciplines.

**Steven Giannotta, MD**

# PREFACE

It is in the true spirit of cooperation, consultation, and collaboration among neuroanesthesiologists, neurosurgeons, neurointensivists, neurointerventionalists, neuropathologists, neuroradiologists, and neurologists that this fifth edition of the *Handbook of Neuroanesthesia* is offered as a concise and easily accessible compendium of neuroanesthesia and neurocritical care.

The chapters in this Fifth edition have not only been updated but now most feature clinically relevant illustrative cases along with summaries and chapter highlights. Several new chapters have been added including one on information technology that serves as a reader's guide to online medical resources and search modalities. Other additions include such topics as Parkinson's disease and deep brain stimulation, intraoperative imaging modalities, and the prevention of postoperative neuropathies and visual loss.

The advances in neuroanesthesia and neurocritical care over the past few years can be attributed to the intellectual curiosity, creativity, energy, and determination of the physicians who have worked tirelessly to improve the care of neurosurgical patients. We acknowledge the anesthesiologists who have devoted their careers to advancing the safe and enlightened practice of neuroanesthesia through teaching, research, and clinical care, especially those who have so generously contributed to this volume.

In the midst of our preparation of the Fifth edition of the *Handbook of Neuroanesthesia*, we were greatly saddened by the passing of Anne Minaidis who had shepherded the first four editions to completion with us. Our gratitude to Christine Waters is boundless for the way in which she stepped right into a foreign landscape, quickly familiarized herself with what had been done thus far, and then worked with the authors, editors, and publisher to see the process of writing and editing through to its conclusion. No detail escaped her notice, no e-mail went unanswered, and no author went uncontacted. We are in her debt for the thorough, professional, and good-humored way in which she approached the work.

In addition, we owe a debt of gratitude to our neurosurgical colleague, Dr. Steven Giannota, who wrote the Foreword to the fifth edition. His recognition of the need for interdisciplinary cooperation, clearly illustrated in his chapter entitled: "Anesthesia and Neurosurgery: A Communication Paradigm," underlines the importance of good communication and teamwork in the operating room, neurointerventional suite, and neurosurgical intensive care unit.

The blending of specialties for a systems-based approach toward total patient care is a goal to which we must all aspire.

**Philippa Newfield, MD**
**James E. Cottrell, MD, FRCA**

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PART I: GENERAL CONSIDERATIONS

# 1 Physiology and Metabolism of the Brain and Spinal Cord

**Yunfang Joan Hou and Ira S. Kass**

## Illustrative Clinical Case

Ms. Z is a 35-year-old healthy female without a history of hypertension. She was skiing and fell and bumped her head on a patch of ice. She was initially dazed but recovered quickly and felt fine; she continued skiing for an hour. When she went to the lodge for lunch, a headache developed and she took two Advil; this made her feel better. She mentioned her headache to a friend who convinced her to go to the first aid station in the lodge. Her blood pressure was elevated (180/100 mm Hg) and she complained about being tired; the nurse in the aid station recommended she be immediately transported to the hospital. In the ambulance she became increasingly confused and drowsy, her blood pressure reached 240/130 mm Hg, and her heart rate was 48 bpm. The ambulance radioed in for a neurosurgeon and anesthesiologist to be present on arrival of the patient. The patient deteriorated rapidly and was unconscious on arrival in the emergency room (ER). An immediate CT scan indicated a large epidural hematoma. The patient was sent immediately to the operating room for a craniotomy with evacuation of the hematoma.

The bleeding into the epidural space initially used up compliance and displaced volume from other compartments; thus, this increase in volume did not initially increase intracranial pressure (ICP). Once this compliance was exhausted, a small additional increase in volume caused a large increase in ICP. Since cerebral perfusion pressure (CPP) is equal to mean arterial pressure (MAP) minus ICP, blood flow to the brain is reduced. When cerebral blood flow (CBF) is reduced to ischemic levels, there is a strong sympathetic response (Cushing reflex) to increase blood pressure (with a compensatory decrease in heart rate) to maintain cerebral perfusion. This can compensate only up to a certain point beyond which CPP will fall further and lead to severe cerebral ischemia, coma, or even death if ICP is uncontrolled. The increased ICP from the expanding hematoma can also cause herniation of the brain, which can lead to rapid neurologic deterioration or death.

## Chapter Highlights

- Neurons maintain a membrane potential that is mainly influenced by the concentration difference of potassium (K) and sodium (Na) inside and outside of the neuron and the conductance of the membrane to

these ions. At rest, the cell has much greater permeability to K and a resting potential around −60 mV; with depolarization, the conductance to Na is increased and action potentials are generated.

- Neurons communicate with each other across a synapse by releasing neurotransmitters that activate receptors on the postsynaptic neurons and change the conductance of these neurons to ions. Glutamate, an excitatory transmitter, increases the conductance to Na, K, and calcium (Ca); this leads to depolarization and increased excitability. Gamma-aminobutyric acid (GABA), an inhibitory transmitter, increases the conductance to chloride (Cl); this leads to a hyperpolarization and decreased excitability. Anesthetics reduce excitability by enhancing GABA inhibitory activity and reducing glutamate excitatory activity.
- The brain and spinal cord need adenosine-5′-triphosphate (ATP) for energy-requiring processes such as ion pumps; transporting molecules, amino acids, and proteins; and synthesizing proteins and lipids. Most ATP formation comes from the metabolism of glucose in the presence of oxygen; when oxygen is limited, ATP production from glucose is much less and lactic acidosis occurs.
- When sufficient energy is not present, neurons die by either apoptotic or necrotic mechanisms. Apoptosis is programmed cell death that leads to normal cell death during development and excessive cell death with energy deprivation due to ischemia. Neurotrophic factors inhibit apoptotic cell death and enhance survival. Necrosis occurs when energy deprivation is more severe due to more prolonged or extreme ischemia; this leads to inflammation and more extensive damage of the surrounding brain tissue.
- CBF is highly regulated and coupled to metabolism. Blood flow is increased when carbon dioxide ($CO_2$) is increased (may be due to increased metabolism or hypoventilation) and reduced when $CO_2$ is decreased (may be due to decreased metabolism or hyperventilation); these changes in CBF are due to changes in brain pH. If blood pressure changes within a range (for normal patients 50 to 150 mm Hg perfusion pressure), the blood flow in the brain remains constant; this is termed autoregulation.
- Cerebrospinal fluid (CSF) is mainly formed in the choroid plexus of the cerebral ventricles and is absorbed in the arachnoid villi. Increased formation or decreased absorption of CSF can increase the volume of fluid in the cranium and lead to high ICP. Brain tissue swelling (cytotoxic edema) and/or increased extracellular fluid due to vasogenic edema or a bleed into the brain can also increase the volume in the cranium and lead to high ICP. High ICP can lead to decreased vascular perfusion of the brain or brain herniation, either of which can cause severe brain damage.

## I. BRAIN AND SPINAL CORD PHYSIOLOGY

To understand the effects of anesthesia and surgery on the nervous system, one needs to know basic cellular neurophysiology as well as organ-level physiologic function. This section briefly describes the basic principles of neurophysiology.

**A. Cellular neurophysiology.** The basic properties of neuronal excitability are due to a change in the membrane potential so that a threshold is reached and the neuron fires an action potential. This propagates to the axon terminal and leads to neurotransmitter release, which influences the membrane potential of a second neuron.

1. **Membrane potentials** are voltages measured across the cell membrane due to an unequal distribution of ions across that membrane. A combination of the equilibrium potential for a particular ion and the membrane's conductance (permeability) for that ion determines its contribution to the membrane potential.
   a. **The equilibrium potential *(E)*** for an ion can be calculated using the Nernst equation if the intra- ( for potassium, $K_i$) and extracellular ($K_0$) concentrations of that ion are known. For an ion with a single positive charge, the equation simplifies to $E_K = -61 \log[K_i/K_0]$ at 37°C. Under normal physiologic conditions in the nervous system, the equilibrium potential for potassium (K) is approximately −90 mV and for sodium (Na) +45 mV.
      1. The relative conductance of the neuronal membrane to different ions determines the membrane potential. This conductance ($g$) for the different ions varies with conditions, input to the specific neuron, and time. The membrane potential of a neuron at any point in time can be described by the following equation:

$$E_m = \frac{g_K(E_K) \pm g_{Na}(E_{Na}) \pm g_x(E_x)}{g_K + g_{Na} + g_x} \quad (1)$$

         where $g_x$ is the conductance for ion x and $E_x$ is the equilibrium potential for that ion. The resting membrane potential for a neuron is approximately −70 mV, which is closer to the $E_K$ (−90 mV) than the $E_{Na}$ (+45 mV) because $g_K$ is much greater than $g_{Na}$ in resting (unexcited) neurons.
      2. There are concentration-dependent and electrical field–dependent forces acting on ions; the sum of these forces determines whether the net movement of a particular ion will be into or out of that neuron. This is referred to as the electrochemical gradient for that ion.
2. **Action potentials** are regenerative changes in a neuron's membrane potential due to excitation of the neuron so that its membrane potential depolarizes past a certain threshold. During an action potential, a rapid initial increase in the $g_{Na}$ is followed by a return to baseline and a slower increase in the $g_K$. These conductance changes lead to a short and rapid depolarization followed by a repolarization. This is sometimes followed by a hyperpolarization after the action potential (Fig. 1.1).
   a. The Na conductance changes are due to the opening of a protein channel in the membrane that is selectively permeable to Na ions. This channel has one activation and one inactivation gate, both of which must be in the open configuration if the channel is to allow Na through it. The rapid opening and closing of this channel are in part responsible for the brief duration of the action potential.
   b. At rest, more K than Na channels are open. With the action potential, more Na channels open so that the $g_{Na}$ is greater than the $g_K$ and the neurons depolarize. The depolarization causes a slow opening of K channels, increasing $g_K$ and leading to a repolarization ($g_K > g_{Na}$). In the period after the action potential, when the Na channels have become inactivated, the increased $g_K$ can actually cause a hyperpolarization below the resting potential; this so-called afterhyperpolarization is frequently found in neurons.

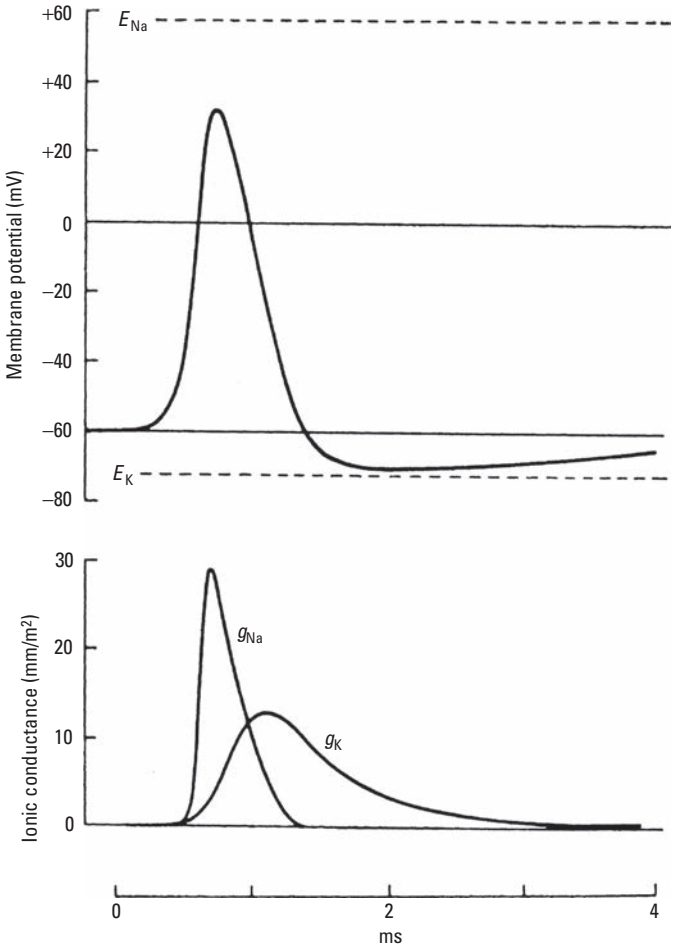


**FIGURE 1.1** Changes in the membrane potential and the sodium and potassium conductances ($g_{Na}$ and $g_K$) during an action potential. $E_{NA}$ and $E_K$ are the sodium and potassium equilibrium potentials. (From Aidley DJ. *The Physiology of Excitable Cells*. Cambridge: Cambridge University Press, 1989:65, as redrawn from Hodgkin AI, Huxley AT. A quantitative description of membrane and excitation in nerve current and its application to conduction. *J Physiol.* 1952;117:500–544.)

3. **Synaptic transmission** is the process by which one neuron (presynaptic neuron) influences the membrane potential and thereby the action potential generation in a second neuron (postsynaptic neuron). The axon terminals of a neuron contain vesicles with neurotransmitter molecules in them. When a terminal is depolarized, voltage-sensitive Ca channels open, increasing the Ca concentration in the terminal. This Ca increase causes the vesicles to release neurotransmitter into the synaptic

cleft. The transmitter diffuses across the synapse and binds to specific receptors on the postsynaptic neuron. Their effect on the postsynaptic neuron depends on the ion channels that are opened or the biochemical processes that are altered by the activation of that receptor.

a. **Ionotropic receptor** activation opens membrane channels for certain ions that can either hyperpolarize or depolarize the postsynaptic neuron, making it less or more likely to fire an action potential.
b. **Metabotropic receptors** can activate second messengers that alter neuronal biochemical parameters. This can lead to long-term changes in a neuron's activity.

4. **Glutamate** is a major excitatory neurotransmitter in the central nervous system (CNS). Its activation depolarizes neurons, increasing the number of action potentials generated.
   a. There are **three major ionotropic glutamate receptors**: alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid **(AMPA), kainate,** and *N*-methyl D-aspartic acid **(NMDA).** The AMPA and kainate receptors are attached to ion channels that allow Na and K to pass through them; a small number of AMPA receptors are also permeable to Ca. The NMDA channels, activated when neurons are already depolarized, are permeable to Na, K, and Ca. Activation of NMDA channels has been associated with long-term changes in neuronal activity that may be cellular correlates of learning and memory. Overactivation of glutamate receptors has been associated with neuronal injury from epilepsy, trauma, and ischemia.
   b. **Metabotropic receptors** are also activated by glutamate. These receptors act via guanosine-5′-triphosphate (GTP)-binding proteins (G proteins) to affect ion channels or second-messenger pathways (e.g., cyclic 3′,5′adenosine monophosphate [cAMP], inositol 1,4,5-trisphosphate), which in turn can alter ionic conductance, cell Ca levels, and other biochemical changes. The effect of metabotropic receptor activation is longer in duration than that of ionotropic receptor activation.
5. **Gamma-aminobutyric acid (GABA)** and **glycine** are major inhibitory neurotransmitters in the CNS. Their activation hyperpolarizes neurons, decreasing the number of action potentials generated. Inhibition is important for the brain and spinal cord to function. When inhibition is substantially reduced, seizures can occur and lead to complete loss of function and permanent brain damage.
   a. **GABA** is a major inhibitory transmitter in the brain and spinal cord. The $GABA_A$ receptor contains a chloride (Cl) channel that is opened when GABA binds. This activity is augmented by benzodiazepines, volatile anesthetics, and barbiturates. The $GABA_B$ receptor acts via a second messenger to open K channels.
   b. **Glycine** is a major inhibitory transmitter in the spinal cord that opens a ligand-gated Cl channel. Strychnine is an antagonist of the glycine receptor and causes convulsions and even death.
6. **Long-term potentiation (LTP)** is a cellular property associated with learning and memory and requires protein kinase activity. This is illustrated in Figure 1.2.
   a. LTP can be caused by a high-frequency train of stimuli and increases the response of postsynaptic neurons to subsequent single stimuli.
      1. The high-frequency stimuli cause an increase in NMDA receptor activity and cytosolic Ca levels. This activates kinases and increases AMPA channels in the membrane.

   **b.** LTP is considered a cellular neurophysiologic correlate of learning and memory.
   **c.** Protein kinase M zeta (PKM zeta) is important for maintenance of LTP and learning and memory.
      **1.** Its concentration increases following LTP.
      **2.** A peptide inhibitor of PKM zeta prevented the maintenance of LTP.
      **3.** This inhibitor when infused in the brain caused animals to forget a previously-learned task.

**7. Anesthetics,** like neurotransmitters, can act directly on ion channels (ionotropic actions) and/or alter cell metabolism and signaling pathways (metabotropic actions).
   **a. Ionotropic mechanisms of anesthetics**
      **1.** Anesthetics **bind to $GABA_A$ receptors** and enhance the inhibition caused by the activation of their associated Cl channels.
         **a. Barbiturates, volatile anesthetic drugs, propofol, and benzodiazepines** enhance $GABA_A$ transmission.
      **2.** Anesthetics can **bind to glutamate channels** and reduce their activity.
         **a. Barbiturates, volatile anesthetic drugs, and propofol** reduce glutaminergic transmission and thereby excitability.
   **b. Metabotropic effects** of anesthetics on cellular signaling pathways
      **1.** Anesthetics can **enhance the activity of protein kinases** that phosphorylate and thereby alter the activity of other proteins in the cell.

         Protein kinase C (PKC) and PKM zeta can affect cell metabolism and ion channel activity. These kinases also appear to play a role in anesthetic preconditioning protection of neurons.
      **2.** Anesthetics can **increase Ca concentrations in the cytosol,** which can alter cell signaling mechanisms and biochemical pathways.
      **3. Volatile anesthetic** drugs such as isoflurane and sevoflurane have been demonstrated to have metabotropic effects.
   **c.** Anesthetics can interfere with learning and memory.

**8. Active transport** maintains the ionic concentrations required for neuronal function. There is a constant leak of ions down their electrochemical gradients. If not corrected, this leak leads to a loss of these ion gradients. Ion pumps use energy to maintain the ion concentrations necessary for neuronal viability. During ischemia, a decrease in energy production and a loss of ion gradients occur (Fig. 1.2).
   **a. Adenosine-5′-triphosphate (ATP)** is a source of energy for many ion pumps. The Na–K ATPase pump maintains high intracellular K concentrations and low intracellular Na concentrations. The pump compensates for the leak of these ions in inactive neurons and the large changes in these ions during action potentials. If this pump is blocked, neurons quickly lose their ability to function. ATPase pumps in the plasma membrane and the endoplasmic reticulum maintain low cytosolic Ca concentrations in neurons.
   **b. The Na gradient** is a source of energy for ion pumps and amino acid transporters. These active transporters couple the energy of Na as it goes down its electrochemical gradient with the pumping of other ions and metabolites up their gradients. To maintain appropriate cellular levels of Ca and hydrogen (H), Na–Ca and Na–H exchangers are important transporters. The transport of glutamate and other amino acids from the extracellular to the intracellular compartment also uses the energy of the Na gradient. The gradient is maintained

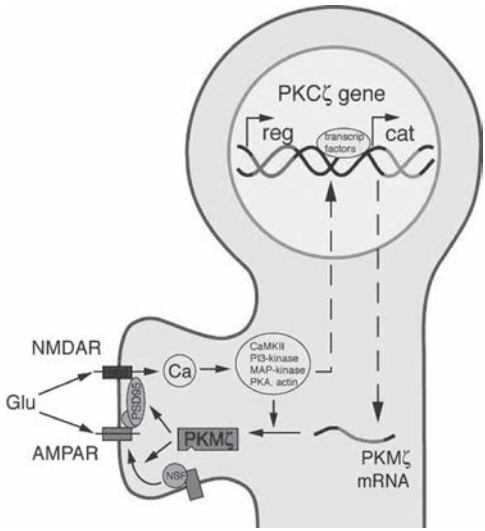


**FIGURE 1.2** Long-term potentiation (LTP) is caused by a high-frequency stimulus that releases the neurotransmitter glutamate (Glu) in large amounts activating AMPA receptors and NMDA receptors and causing an increase in cytosolic calcium levels (Ca). This activates kinases leading to the synthesis of Protein kinase M zeta (PKM zeta) from PKM zeta–specific mRNA; the active PKM zeta increases the insertion of AMPA receptor channels into the membrane. The maintained increase in AMPA receptor channels maintains the potentiation (increased response to a stimulus). NSF and PSD95 are two proteins important for channel insertion and anchoring to the membrane. Drugs that block these pathways not only block LTP but also impair learning and memory. (Hernandez AI, Blace N, Crary JF, Serrano PA, Leitges M, Libien JM, Weinstein G, Tcherapanov A, Sacktor TC. Protein kinase M zeta synthesis from a brain mRNA encoding an independent protein kinase C zeta catalytic domain. *J Biological Chemistry* 2003;278:403.)

by the Na–K ATPase pump; thus, the ultimate energy for this ion exchanger comes from ATP used to power the Na–K pump.

c. When energy fails due to **hypoxia or ischemia,** the pumps can no longer maintain the gradients, intra- and extracellular ion concentrations change, and the neurons depolarize, leading to a rapid and complete membrane depolarization and eventual cell death.

B. **Regional neurophysiology.** Different regions of the brain subserve different and distinct functions. We can provide only a very brief summary of them; for details, refer to *Principles of Neural Science* by Kandel et al. See Figure 1.3 for neuroanatomy.

1. **The primary somatosensory cortex** located on the postcentral gyrus is the cortical locus where somatic sensations converge. Association areas that aid in the interpretation of these sensations are located posterior to this gyrus.
2. **The primary motor cortex** is located on the precentral gyrus and has output to motor neurons in the spinal cord. Premotor association areas are located anterior to this gyrus and receive input from other important motor centers of the brain including the cerebellum, the basal ganglia,

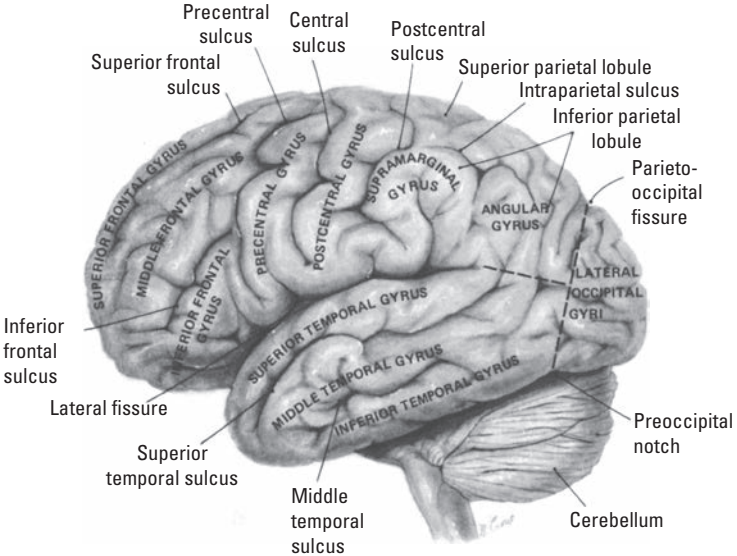


**FIGURE 1.3** Lateral view of the cerebral cortex. (From Gilman S, Newman SW. *Manter and Gatz's Essentials of Clinical Neuroanatomy and Neurophysiology,* 8th ed. Philadelphia, PA: FA Davis Co, 1992:7.)

and the red nucleus. The reticular formation also has important motor functions.

3. **The primary visual** and visual association areas are located in the occipital lobe.
4. **The primary auditory** and auditory association areas are located in the temporal lobe.
5. **Wernicke's area** is located on the angular gyrus in the dominant hemisphere. It is a multimodal association area. Lesions in this area are devastating and can lead to the loss of comprehension of written and spoken words.
6. **The frontal association areas** are important for controlling personality and directing intellectual activity through sequential steps toward a goal.
7. **The limbic areas** of the brain, not shown in Figure 1.3, are located medially. Limbic system structures include the hypothalamus, the amygdala, the hippocampus, and the limbic cortex. These areas are associated with feelings of reward and punishment, emotional behavior, learning, and memory. The hippocampus is essential for the transformation of short-term to long-term memory. The hypothalamus controls many bodily vegetative functions (cardiovascular, temperature, and water regulation).
   a. **The cerebellum** plays an important role in motor control, especially for rapid movements. It receives input from sensory systems and from other parts of the brain and spinal cord and integrates these inputs to fine-tune motor activity. It is involved in the coordination

and control of voluntary motor movement, as well as balance and muscle tone.

b. **The brain stem** consists of the midbrain, the medulla oblongata, and the pons. It is the part of the brain adjoining and structurally continuous with the spinal cord. It transmits ascending and descending pathways from peripheral nerves and the spinal cord to the higher centers in the brain. Cranial Nerves III to XII originate from the brain stem. The vasomotor areas located in the brain stem are important for the control of blood pressure and heart rate. The brain stem also controls other basic body functions such as swallowing and breathing. It contains the reticular activating system, which is responsible for maintaining alertness. Lesions in the brain stem can lead to coma.

8. **The spinal cord** is important as a pathway to convey information between the body and the brain and together with the brain makes up the CNS. It also contains neural circuits that can independently control numerous reflexes. Input to the spinal cord comes via the dorsal root to the dorsal horn; output from motor neurons, which are located in the ventral horn, is via the ventral root. Each level of the spinal cord corresponds to the motor output and sensory perception for a particular region of the body. Input to the brain via the spinal cord can be modified before transmission to the brain. Indeed, descending pathways can reduce pain input at the spinal level. These pathways are activated by periaqueductal and periventricular gray regions of the brain.

## II. BRAIN AND SPINAL CORD METABOLISM

### A. The overall metabolic rate for the brain

1. The cerebral metabolic rate of awake young adults at rest is 5.5 mg glucose/100 g/minute or 3.5 mL $O_2$/100 g/minute, whereas the metabolic rate of the body at rest is 10× less. This rate is virtually identical in healthy elderly people. Children have a higher cerebral metabolic rate, that is, 5.2 mL $O_2$/100 g/minute. The reason for the higher metabolic rate in children is unknown, but it may represent continuing growth and development of the nervous system.

### B. Energy utilization by neurons in the brain and spinal cord.

Neurons have a high metabolic rate and use more energy than other cells. Although the brain accounts for 2% of total body weight, it uses 20% of the body's total oxygen consumption. Most energy-requiring processes in cells use either ATP directly or energy stores indirectly derived from ATP such as ion gradients.

1. **Ion pumping** accounts for a large part of a neuron's energy requirement. The Na–K pump alone accounts for 25% to 40% of a neuron's ATP utilization. Calcium and the transport of other cations (e.g., H) or anions (Cl or $HCO_3$) also account for significant energy utilization. Some pumping of Ca and H is coupled with Na for an energy source and depletes the Na gradient; thus, Ca and H are indirectly coupled to ATP utilization via the Na–K pump. Energy is required to pump ions from the cytosol to intracellular organelles and to pump molecules across the plasmalemma.
2. **Transport of amino acids** and other essential small molecules **across the cell membranes** requires energy. Glutamate and many other neurotransmitters are removed from the extracellular space by active pumps that require energy. Reduced activity of the glutamate pump can lead to excessive excitability and neuronal damage.

3. **Neuronal structure and function** require the synthesis of proteins, lipids, and carbohydrates. These substances are continually being formed, modified, and degraded and require ATP for their synthesis.
4. **The transport of substances within cells** also requires energy. Most synthesis takes place in the cell body, and an energy-dependent transport system distributes these substances to the parts of the neuron that require them. The enormity of the task is apparent when one considers the length of the axons and dendrites of a typical neuron; diffusion is not sufficient, and active transport is required.

**C. Energy synthesis by neurons in the brain and spinal cord**

1. Efficient ATP production from glucose requires oxygen (Fig. 1.4).
   a. The major portion of energy is generated by glycolysis (breakdown of glucose), the citric acid cycle (a pathway that generates nicotinamide

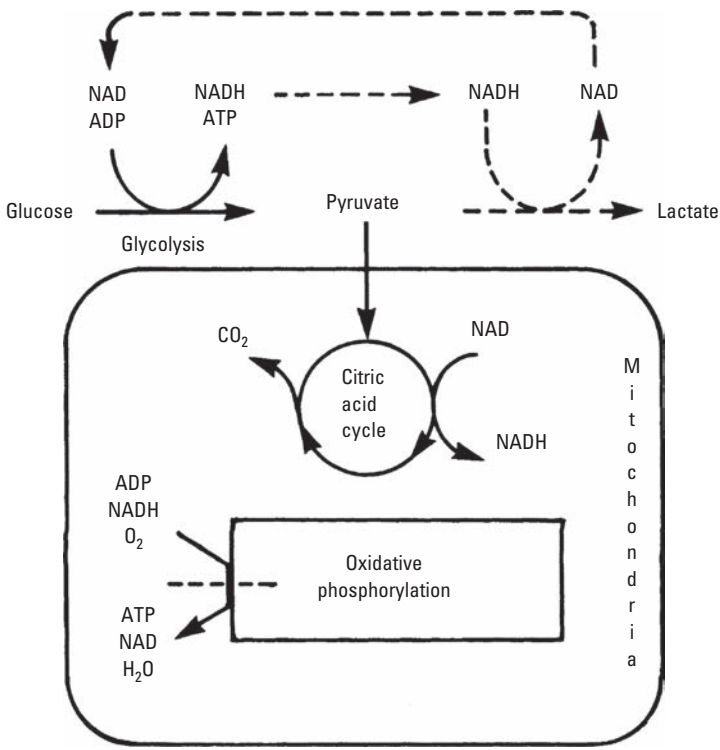


**FIGURE 1.4** Energy metabolism in the brain. Dotted lines indicate reactions that occur during ischemia. The dotted line across the oxidative phosphorylation reaction indicates that this reaction is blocked during ischemia. NAD, nicotinamide adenine dinucleotide; ADP, adenosine diphosphate; NADH, nicotinamide adenine dinucleotide, reduced form; ATP, adenosine-5′-triphosphate. (From Bendo AA, Kass IS, Hartung J, et al. Anesthesia for neurosurgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia,* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:746–789.)

adenine dinucleotide, reduced form [NADH], from nicotinamide adenine dinucleotide [NAD]), and oxidative phosphorylation (coupling of the regeneration of NAD from NADH to the production of ATP). The mitochondria and oxygen are critical for the efficient production of ATP from glucose. The yield from 1 glucose molecule ($C_6H_{12}O_6$) is a maximum of 38 ATP molecules:

$$C_6H_{12}O_6 + 6O_2 + 38ADP + 38P_i \rightarrow 6CO_2 + 6H_2O + 38ATP$$

**b.** In an actual neuron, other synthesis pathways use some of the energy and biochemical intermediates so that the average yield per glucose is between 30 to 35 ATP molecules.

**2.** In the absence of oxygen, the mitochondria cannot convert NADH to NAD by oxidative phosphorylation and thus lose much of the energy of glucose oxidation. Each molecule of glucose yields only two ATP molecules. This is insufficient to meet the energy demands of the brain.

$$\text{Glucose} + 2ADP + 2P_i + 2NAD \rightarrow 2\ \text{pyruvate} + 2ATP + 2NADH$$
$$\rightarrow 2\ \text{lactate} + 2H + 2NAD$$

The last step is required to regenerate the NAD from NADH; no energy is obtained from this step in the absence of oxygen. The H ion generated can lead to neuronal damage under certain circumstances.

**a.** High blood glucose before hypoxia or ischemia has been shown clinically and in animals to increase damage. The excess H ion production could partially explain this.

**3.** Emergency sources of energy during metabolic stress

**a.** There are **two immediate sources of ATP** when energy production does not meet the cell's demand for energy.

**1.** The enzyme **adenylate kinase** can convert adenosine diphosphate (ADP) to ATP.

$$ADP + ADP \leftrightarrows ATP + AMP$$

When energy production recovers, this process is reversed.

**2.** **Phosphocreatine (PCr)** acts as a store of high-energy phosphate that can be rapidly converted to ATP. Normally there are two to three times more PCr than ATP. Nevertheless, PCr levels fall rapidly during ischemia.

$$PCr + ADP + H \leftrightarrows ATP + Cr$$

**4.** Energy production and its reduced usage during ischemia

**a.** In addition to the **formation of ATP from 2ADP or PCr, anaerobic glycolysis** contributes to ATP maintenance. Anaerobic glycolysis leads to acidosis, which may be damaging to neurons. With ischemia that lasts for more than several minutes, ATP formation from 2ADPs and PCr is exhausted, and anaerobic glycolysis continues only so long as glucose is available. Some glucose is produced from the breakdown of glycogen.

**b.** Shortly after the onset of ischemia (in about 30 seconds), **spontaneous neuronal activity stops,** and the **electroencephalogram becomes quiet**. This reduces the neuron's metabolic rate and ATP utilization.

**D. Molecular aspects of neuronal metabolism, survival versus apoptosis**

**1.** Many more neurons are formed during mammalian development than the adult organism needs. In many areas of the brain and spinal cord, 50% of the neurons die as the animal matures.

a. **The target cells of a neuron**—those cells a neuron innervates—**secrete trophic factors** (e.g., nerve growth factor and brain-derived neurotrophic factor) in limited quantities. If the neuron receives enough of these trophic factors, it survives; if not, it dies. Because trophic factors are limited, on average 50% of the neurons do not receive enough trophic factors and die.

b. Neurons also receive **trophic factors from non-target sources** such as glia; this also promotes survival. The combination of trophic factors from all sources determines whether a neuron will survive or die.

c. **The trophic factors** work by **binding to external receptors** on membrane-spanning proteins. When their receptor is bound by a trophic factor, these proteins activate intracellular signals, which in some cases phosphorylate other intracellular proteins and alter cellular processes leading to neuronal survival (Fig. 1.5).

One example of such binding is the tyrosine receptor kinase (trk): it binds nerve growth factor, brain-derived neurotrophic factor, or other neurotrophins, dimerizes (combines two identical molecules), and then becomes active. It adds a phosphate group onto the amino acid tyrosine of certain proteins. This addition alters the activity of these proteins and inhibits cell death pathways.

d. **If a cell does not receive enough trophic factor,** certain proteins are not phosphorylated and a programmed cell death pathway is activated. This process is called **apoptosis** and causes cells to die in a way that does not cause inflammation. In the absence of trophic factor–induced phosphorylation, a molecule called *apoptosis activating factor 1*(Apaf-1) is activated, leading to the proteolysis of inactive procaspases to active caspases, which in turn splits other proteins and signals the cell to undergo programmed cell death (apoptosis).

2. **During and after ischemia, hypoxia, or other injury, neurons can die** by one of at least two pathways, necrosis or apoptosis.

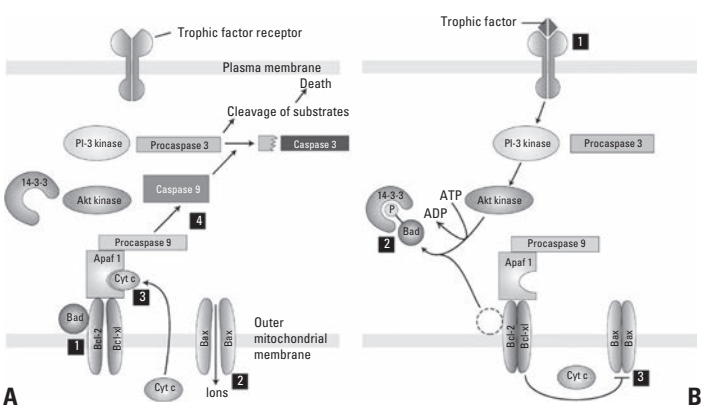


**FIGURE 1.5** Trophic factors and apoptosis. **A:** Absence of trophic factor: caspase activation. **B:** Presence of trophic factor: inhibition of caspase activation. ATP, adenosine-5′-triphosphate; ADP, adenosine diphosphate. (From Lodish H, Berk A, Kaiser CA, et al., eds. *Molecular Cell Biology*, 6th ed. New York, NY: W.H. Freeman & Co., 2008:943 as adapted from Pettmann B, Henderson CE. Neuronal cell death. *Neuron* 1998;20:633.)

a. **Necrosis** is caused by severe injury that causes neurons to swell and burst apart. In addition to causing the death of that neuron, inflammation and further cell death occur in that region of the brain.
b. If the injury is less severe and the neuron can recover its ability to make ATP, the neuron can activate the **apoptosis** pathway and die in a manner similar to the death of excess neurons during development. The advantage of this apoptosis is that the neuron does not break apart and the neurons around it are preserved, resulting in less overall brain damage.
   1. Apoptosis is triggered by ion flux into the mitochondria through an ion channel formed from the binding of two bax protein molecules together. The ion flux leads to the release of cytochrome c, which binds to Apaf-1, activates it, and initiates the caspase cascade of apoptosis (Fig. 1.5).
   2. Other apoptosis pathways are initiated that are independent of the mitochondria.

## III. CEREBRAL AND SPINAL CORD BLOOD FLOW

A. **Rate of cerebral blood flow (CBF)**. CBF rates are largely determined by the cerebral metabolic rate for oxygen consumption; there is exquisite coupling of blood flow and metabolism on a regional basis. The global blood flow to the brain remains fairly stable for a given physiologic state (e.g., awake adult). Anesthetics and hypothermia tend to decrease metabolism throughout the brain and thereby reduce global CBF.
   1. **The global CBF in adults** is approximately 50 mL/100 g/minute. This global measure is composed of flow from two very different regions: the gray matter, which is where neuronal cell bodies and synapses are located and has a blood flow of 75 mL/100 g/minute, and the white matter, which consists mainly of fiber tracts and has a blood flow of 20 mL/100 g/minute. The higher blood flow to gray matter is primarily due to its greater metabolic rate.
   2. **The global CBF of children** is approximately 95 mL/100 g/minute, which is higher than that of adults. In contrast, infants have a slightly lower CBF than adults (40 mL/100 g/minute).
   3. **Spinal cord blood flow** has been less extensively studied; the gray matter has a rate of 60 mL/100 g/minute and the white matter a rate of 20 mL/100 g/minute.

B. **Regulation of CBF**
   1. **Regional flow–metabolism coupling** depends on the buildup of metabolites that cause local dilatation of the microvessels.
      a. The precise mechanism of this coupling is unknown. It may be due to the buildup of K or H in the extracellular fluid surrounding the arterioles. Other drugs that may mediate flow–metabolism coupling include nitric oxide (NO), calcium, adenosine, and eicosanoids such as thromboxane and prostaglandin. A combination of these factors likely contributes to coupling.
   2. **NO** is a vasodilator that is released locally by the vascular endothelial cells. This vasodilatation is important for vascular regulation throughout the body, but the precise role of NO in the control of CBF remains to be determined. It is likely to be an important regulator of local CBF, perhaps by affecting arterioles upstream of the microvessels dilated by metabolic factors.
   3. **Carbon dioxide ($CO_2$)** enhances vasodilatation and increases CBF. $CO_2$ is hydrated with the help of carbonic anhydrase leading to acidification.

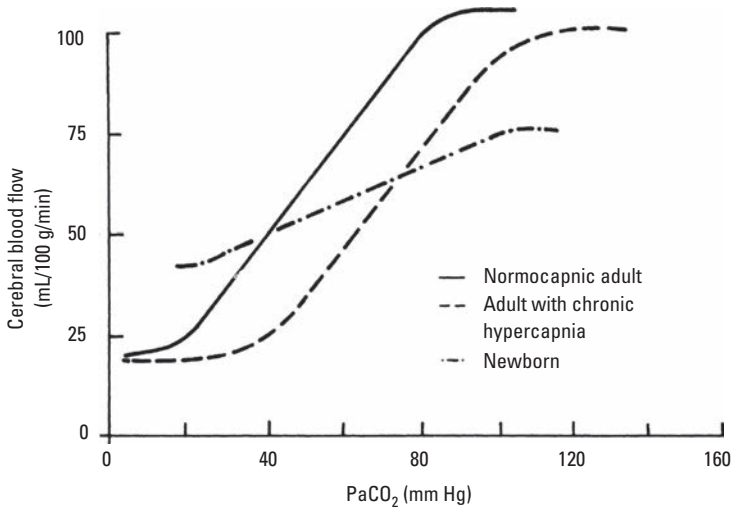


**FIGURE 1.6** Relationship between cerebral blood flow (CBF) and arterial carbon dioxide tension ($PaCO_2$) in the normocapnic adult, the hypercapnic adult, and the newborn.

This reduction in pH is thought to cause the vasodilatation. When $CO_2$ is halved from 40 to 20 mm Hg, the CBF is reduced by approximately half (Fig. 1.6).

a. **Hyperventilation** leads to a reduction in $CO_2$, an increase in pH, and thereby a reduction in CBF. If hyperventilation is maintained over a period of 6 to 8 hours, the pH returns to normal due to bicarbonate transport and CBF returns to its prehyperventilation levels. Thus, hyperventilation is useful for blood volume and ICP reduction for only short periods of time.
   1. If hyperventilation is discontinued abruptly, the increase in $CO_2$ to the normal level, in the presence of reduced $HCO_3$, leads to acidosis and an above-normal increase in CBF. This can be a critical problem when hyperventilation is used to reduce ICP.
   2. It is possible that extreme hyperventilation to levels below 20 mm Hg can lead to ischemia due to vasoconstriction; thus, hyperventilation to a $PaCO_2$ below 30 mm Hg is not recommended clinically.

4. **Autoregulation** allows CBF to remain constant if the CPP varies between 50 and 150 mm Hg. These values are only useful in normotensive patients without complicating pathologies. Signs of cerebral ischemia are seen below 50 mm Hg; above 150 mm Hg, disruption of the blood–brain barrier (BBB) and cerebral edema may occur. The adjustment of flow to abrupt changes in pressure requires 30 to 180 seconds (Fig. 1.7).
   a. **The mechanism of autoregulation** is not completely understood but is likely to be a combination of effects including myogenic and metabolic factors.
      1. **Myogenic activity** of the vessel wall musculature occurs in response to increased distending pressure. In isolated vessels, when the

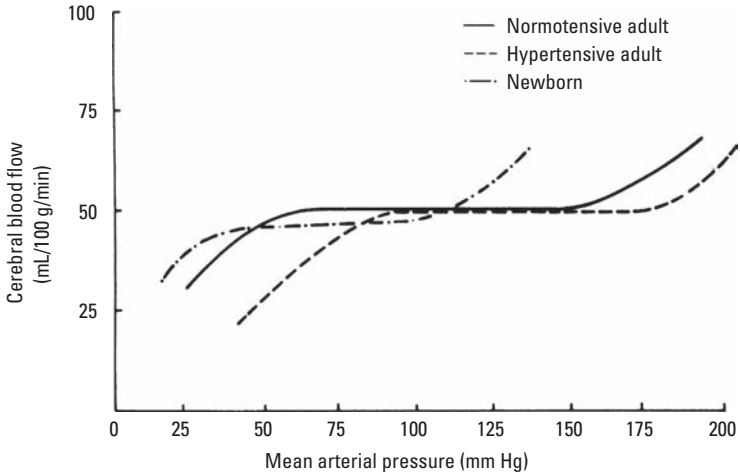


**FIGURE 1.7** Autoregulatory curve of the cerebral vasculature in the normotensive adult, the hypertensive adult, and the newborn.

vessel wall is stretched, as it would be by increased blood pressure, the smooth muscle contracts, causing a vasoconstriction that reduces flow. This balances out the increase in blood flow due to the increased pressure, resulting in little net change in blood flow.

2. **The metabolic theory** states that reduced pressure leads to reduced flow and the buildup of metabolites. This buildup in metabolites and the decrease in local pH lead to a local vasodilatation and thereby an increase in blood flow back to normal.
3. Autoregulation can be impaired by hypoxia, ischemia, hypercapnia, trauma, and certain anesthetic drugs.
4. Patients who are chronically hypertensive or have a high sympathetic tone have a shift in the autoregulatory curve to the right. They may demonstrate signs of ischemia due to reduced blood flow at pressures above the lower limit for normotensive individuals.

5. **The partial pressure of oxygen ($PaO_2$)** has little effect on global CBF until it falls below 50 mm Hg. At this point, a dramatic increase in blood flow with further reductions in $PaO_2$ occurs. Since the oxygen-carrying capacity of blood is high, a critical reduction in the oxygen content of the blood might not occur until the $PaO_2$ falls below a threshold of 50 mm Hg (Fig. 1.8).
6. **Neurogenic factors** including adrenergic, cholinergic, and serotonergic systems also influence CBF. Their greatest influence is on larger blood vessels.
7. **The hematocrit** alters blood viscosity and thereby can affect blood flow. A low hematocrit can increase blood flow by decreasing blood viscosity; however, it also reduces the blood's oxygen-carrying capacity.
8. **Hypothermia** decreases neuronal metabolism and thereby reduces CBF; hyperthermia has the opposite effect.
9. **The metabolic rate of neurons** surrounding the microvasculature regulates regional blood flow. If the activity of these neurons increases, their

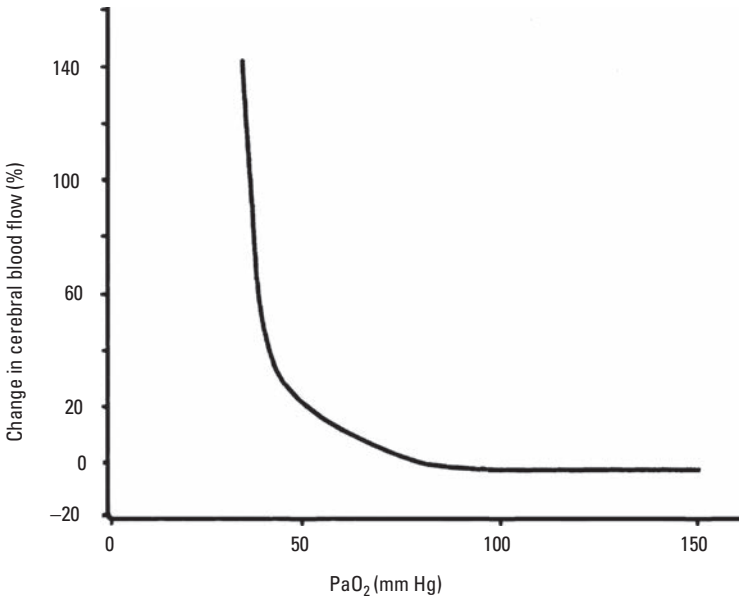


**FIGURE 1.8** Relationship between cerebral blood flow (CBF) and $PaO_2$, arterial oxygen tension.

metabolic rate increases, and the blood flow to that region increases to meet the demand for oxygen and glucose. This property has been exploited using positron emission tomography to functionally map brain activity. The increase in blood flow due to increased activity is frequently greater than the increase in metabolism. The reason for this is not known.

## IV. CEREBROSPINAL FLUID AND THE BLOOD–BRAIN BARRIER

**A. CSF formation:** CSF is formed in the choroid plexus of the cerebral ventricles (50% to 70%) and also produced around the blood vessels and along ventricular walls. The rate of CSF formation is 0.4 mL/minute (approximately 500 mL/day) and the total volume of CSF is between 100 and 150 mL.

1. **CSF** is an ultrafiltrate of plasma whose final composition is modified by active (mainly Na) and passive (most importantly glucose) transport of ions and other metabolites (Table 1.1). Proteins and other hydrophilic molecules are poorly permeable and excluded from the CSF. The capillary endothelium in the choroid plexus is freely permeable to substances. The epithelial cells of the choroid plexus contain tight junctions and are the site of the blood–CSF barrier.
   a. CSF formation is reduced by (1) decreased choroidal blood flow and capillary hydrostatic pressure, (2) hypothermia, (3) increased serum osmolarity, and (4) increased ICP.
2. **CSF flows** through the ventricles and out to the subarachnoid space of the brain and the spinal cord. It is reabsorbed into venous blood via the arachnoid villi. If reabsorption is impeded, CSF builds up and ICP increases.

B. **Blood–brain barrier.** The BBB isolates the brain from substances in the plasma and is important for normal brain function.
   1. The site of the BBB is the **capillary endothelial cells**. They are connected to each other via tight junctions that exclude the passage of substances between them. Any substance that crosses into the brain from the blood must cross the capillary epithelial cell. The tight junctions and therefore the BBB are not present in the choroid plexus and certain other small areas of the brain (e.g., restricted areas of the hypothalamus).
   2. Water, gases, and lipophilic substances are freely permeable to the BBB. Proteins and polar (hydrophilic) substances are poorly permeable to the BBB and cross this barrier only if there is a specific transport system for them. Glucose, ions, and certain amino acids are transported across the BBB. Because glucose is passively transported to and metabolized in the CNS, its concentration in the brain is usually 60% of its plasma level. This transport is saturable, so that large changes in glucose concentrations require time to equilibrate (Table 1.1).

## V. INTRACRANIAL COMPONENTS AND VOLUME

A. **Intracranial pressure (ICP)** is determined by the volume of the various intracranial components. Normal ICP is approximately 10 mm Hg. Because the cranium has a fixed volume, an increased volume of any intracranial component must be compensated for by a decrease in the volume of another component. Otherwise, the pressure in the cranium will increase.
   1. There are three **major intracranial components.**
      a. **Brain tissue** represents 80% to 85% of the intracranial volume and is composed of a cellular component that includes the neurons and glia, and an extracellular component consisting of the interstitial fluid.
      b. **The CSF volume** accounts for 7% to 10% of the intracranial volume.
      c. **The cerebral blood volume** accounts for 5% to 8% of the intracranial volume and includes the blood in the vascular space.
   2. There is an **elastance or compliance** to the components in the cranium such that a small increase in the volume of one component does not

TABLE 1.1 Composition of Cerebrospinal Fluid and Serum in Humans

| Component | CSF | Serum |
|---|---|---|
| Sodium (mEq/L) | 141 | 140 |
| Potassium (mEq/L) | 2.9 | 4.6 |
| Calcium (mEq/L) | 2.5 | 5.0 |
| Magnesium (mEq/L) | 2.4 | 1.7 |
| Chloride (mEq/L) | 124 | 101 |
| Bicarbonate (mEq/L) | 21 | 23 |
| Glucose (mg/100 mL) | 61 | 92 |
| Protein (mg/100 mL) | 28 | 7,000 |
| pH | 7.31 | 7.41 |
| Osmolality (mOsm/kg $H_2O$) | 289 | 289 |

Adapted with permission from Artru AA. Cerebrospinal fluid. In: Cottrell JE, Young WL, eds. Anesthesia and Neurosurgery. St. Louis, MO; Mosby,2010:60.

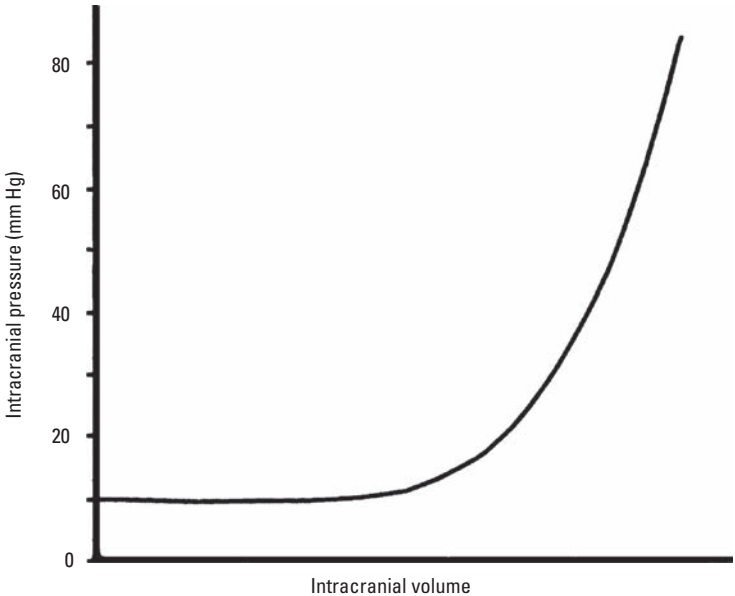


**FIGURE 1.9** Idealized intracranial pressure–volume curve

cause an increase in pressure. Once this compliance is exhausted, small increases in volume lead to large increases in ICP (Fig. 1.9).

3. **Increases in intracranial volume** can be caused by
   a. Increases in CSF volume due to blockage of the circulation or absorption of CSF
   b. Increased cerebral blood volume due to vasodilatation (intravascular) or hematoma (extravascular)
   c. Increased brain tissue volume due to a tumor or edema

B. **Brain edema.** Brain edema is classified as cytotoxic or vasogenic and can increase ICP.
   1. **Cytotoxic edema** is due to swelling of the neuronal and/or glial cellular component and is frequently the result of cerebral ischemia or trauma.
   2. **Vasogenic edema** can be caused by a breakdown of the BBB. The resultant extravascularization of protein increases interstitial water due to an increase in osmotic equivalents in the extravascular space.

C. **ICP pathophysiology.** An increase in ICP can have severe pathophysiologic consequences.
   1. **The cerebral perfusion pressure (CPP)** can be calculated by subtracting ICP from mean arterial pressure (MAP) (i.e., CPP = MAP – ICP).
      a. As ICP increases, CPP decreases. This leads to cerebral ischemia. Normally, cerebral ischemia leads to the Cushing reflex, which increases MAP. However, this can compensate only up to a certain point beyond which CPP will fall further, leading to severe ischemia, coma, and death if ICP is uncontrolled.
      b. Increased ICP can also cause herniation of the brain, which can lead to rapid neurologic deterioration and death.

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# 2 Effects of Anesthesia on Cerebral and Spinal Cord Physiology

**Rosemary Hickey**

## Illustrative Clinical Case

A 20-year-old man is involved in a high-speed motor vehicle accident. He suffers significant head trauma and is noted to have a large subdural hematoma on computed tomography (CT) scan with a midline shift. His other injuries include a moderate left pulmonary contusion, left-sided rib fractures, and a left femur fracture. Glasgow Coma Scale score on arrival is 7, BP 170/110 mm Hg, Pulse 120, R 24, and oxygen saturation ($SpO_2$) 92% on 100% oxygen ($O_2$) face mask. Mannitol (0.5 mg/kg) is initiated. His trachea is intubated in the emergency room (ER) following fentanyl (50 mcg), lidocaine (100 mg), propofol (150 mg), and rocuronium (10 mg). He is brought to the operating room for emergency evacuation of a subdural hematoma. A neuroanesthetic regimen must be selected on the basis of this patient's reduced intracranial compliance, the need for prompt surgical evacuation of the hematoma, the surgeon's request for postoperative neurologic evaluation, and the need for postoperative intubation and ventilation.

## Chapter Highlights

- A basic knowledge of cerebral and spinal cord physiology and the effects of anesthetic drugs on this physiology is necessary to make informed anesthetic choices for neurosurgical procedures.
- Barbiturates cause a dose-dependent reduction in cerebral blood flow (CBF) and cerebral metabolic rate ($CMRO_2$), with the $CMRO_2$ reduction due to the metabolic component associated with electrical brain function (as opposed to that associated with maintenance of cellular integrity). Large doses are capable of producing electroencephalogram (EEG) burst suppression, and they may be used clinically for this purpose. The intracranial pressure (ICP) reduction associated with thiopental has historically made this drug an integral part of neuroanesthesia practice.
- Propofol has become the popular alternative to thiopental for induction in the neurosurgical patient. Like barbiturates, it is associated with a reduction in CBF, $CMRO_2$, and ICP. The reduction in mean arterial pressure (MAP) associated with bolus doses of propofol necessitates caution in the elderly and volume-depleted patient. The favorable pharmacokinetic profile of propofol allows for prompt awakening following a continuous infusion, which makes this drug useful for intubated patients in whom sedation is desirable but intermittent evaluation of neurologic status is also required.
- Narcotics lack adverse effects on CBF, $CMRO_2$, and ICP as long as ventilation is maintained and thus have remained a valuable part of the neuroanesthetic regimen. Fentanyl has been the narcotic of choice for most

neuroanesthetics, but remifentanil has been added as a popular choice for many procedures. The context-sensitive half-time of remifentanil makes infusion of this drug an excellent choice to provide profound analgesia while maintaining the ability to awaken the patient promptly to evaluate neurologic status.

- Desflurane and sevoflurane have cerebral effects very similar to those of isoflurane, with the potential to cause cerebrovasodilation and an increase in CBF and ICP, particularly when used in higher doses. The reduction in $CMRO_2$ associated with these drugs is dose related, with a maximal reduction attained with the occurrence of EEG suppression. Despite the potential to increase CBF and ICP, these drugs are commonly used in neuroanesthesia in combination with other drugs that have more desirable cerebral effects. However, in patients in whom intracranial compliance is exhausted, the dose of these drugs is kept low (~1 minimum alveolar concentration [MAC] or less), or they are eliminated completely from the anesthetic regimen.
- Nitrous oxide has the potential to increase CBF and ICP with no change or an increase in $CMRO_2$. The recent use of desflurane and sevoflurane in neuroanesthesia, which have low blood-gas solubility coefficients and allow for more rapid awakening, has lessened the usefulness of nitrous oxide in neuroanesthesia.
- Muscle relaxants do not cross the blood–brain barrier and thus central nervous system (CNS) effects are secondary to systemic effects (such as histamine release). Vecuronium, rocuronium, and cis-atracurium are most commonly chosen, and these do not affect CBF or ICP. Succinylcholine causes a mild, transient increase in ICP. The ability of succinylcholine to cause significant hyperkalemia in certain neurosurgical patients (plegic patients, those with neuromuscular diseases, etc.) limits its use more than its effects on CBF or ICP.

The anesthetic management of neurosurgical patients is based on the knowledge of the selected drug's influence on the CNS physiology. The specific anesthetic regimen is a combination of drugs that favorably affects cerebral hemodynamics, cerebral metabolism, and ICP to provide good operating conditions and to enhance the probability of a quality outcome. Most anesthetic drugs have been studied in this regard and, as new drugs are developed, their effects on cerebral physiology will be elucidated. The effects of anesthetic drugs on cerebrospinal fluid (CSF) volume (as determined by the rate of formation and the resistance to reabsorption) have also been determined.

Fewer studies have addressed the effects of anesthetic drugs on spinal cord physiology. This could be in part because non-invasive methods of measuring various aspects of spinal cord physiology in the human are not available so that most of the data have been derived from animal studies. Although it has been assumed that the effects of anesthetics on the spinal cord mimic their effects in the brain (and this is likely to be qualitatively correct), to make true comparisons, investigators must examine both brain and spinal cord parameters simultaneously.

## I. INTRAVENOUS DRUGS

### A. Barbiturates

1. **Effect on CBF and cerebral oxygen consumption (Table 2.1).** Barbiturates were the first anesthetics to be examined for their cerebral vascular effects. Thiopental decreases CBF and cerebral metabolic rate for oxygen consumption ($CMRO_2$) in a parallel fashion up to the point of

TABLE 2.1 Effective of Anesthetic Drugs on Cerebral Blood Flow, Cerebral Metabolic Rate for Oxygen Consumption, and Intracranial Pressure

| Anesthetic | CBF | $CMRO_2$ | ICP |
|---|---|---|---|
| Thiopental | Decrease | Decrease | Decrease |
| Etomidate | Decrease | Decrease | Decrease |
| Propofol | Decrease | Decrease | Decrease |
| Fentanyl | 0/Decrease | 0/Decrease | 0/Decrease |
| Alfentanil | 0/Decrease/increase | 0/Decrease | 0/Decrease/increase |
| Sufentanil | 0/Decrease/increase | 0/Decrease | 0/Decrease/increase |
| Ketamine | Increase | 0/Increase | Increase |
| Midazolam | Decrease | Decrease | 0/Decrease |
| Nitrous oxide | Increase | 0/Increase | Increase |
| Isoflurane | Increase | Decrease | Increase |
| Desflurane | Increase | Decrease | Increase |
| Sevoflurane | Increase | Decrease | Increase |

CBF, cerebral blood flow; $CMRO_2$; cerebral metabolic rate for oxygen consumption; ICP, intracranial pressure.

isoelectricity on the EEG. The changes in CBF are thought to be secondary to the changes in $CMRO_2$ (a coupled decrease in flow and metabolism). The component of $CMRO_2$ that is affected is related to electrical brain function; there is minimal effect on the component of $CMRO_2$ associated with cellular homeostasis. At the point at which an isoelectric EEG occurs after the administration of thiopental, an approximately 50% decrease in $CMRO_2$ occurs with no cerebral metabolic evidence of toxicity. If barbiturates are used clinically for the purpose of cerebral protection, the endpoint of EEG burst suppression is often used to provide near-maximal metabolic suppression. The reduction in MAP associated with the high doses of thiopental needed to provide EEG burst suppression may require concomitant use of a vasopressor to maintain cerebral perfusion pressure (CPP), the difference between MAP and ICP. Methohexital differs from other barbiturates in regard to epileptiform activity in that it may induce seizures in patients who have epilepsy. If seizure activity occurs with methohexital, this results in an increase in $CMRO_2$ and CBF.

2. **Effect on autoregulation and $CO_2$ reactivity.** Thiopental, even in high doses, does not appear to abolish cerebral autoregulation or $CO_2$ reactivity.
3. **Effect on CSF dynamics** (Table 2.2). Low doses of thiopental cause no change in the rate of CSF formation ($V_f$) and either no change or an increase in the resistance to reabsorption of CSF ($R_a$). This would predict no change or an increase in ICP. High doses of thiopental cause a decrease in $V_f$ and either no change or a decrease in $R_a$ with a predicted decrease in ICP.
4. **Effect on ICP.** As a result of the reduction in both CBF and cerebral blood volume (CBV), barbiturates lower ICP. Barbiturates are used clinically for this purpose and may even be effective when other methods for reducing ICP have failed.
5. **Effect on spinal cord blood flow (SCBF) and metabolism.** Barbiturates produce a significant reduction in SCBF. Autoregulation of SCBF remains intact under barbiturate anesthesia (as demonstrated with thiopental) with an

TABLE 2.2 Effects of Intravenous Drugs on Rate of Cerebrospinal Fluid Formation, Resistance to Reabsorption of Cerebrospinal Fluid, and the Predicted Effect on Intracranial Pressure

| Intravenous Drug | $V_f$ | $R_a$ | Predicted ICP Effect |
|---|---|---|---|
| **Thiopental** | | | |
| Low dose | 0 | +, 0* | +, 0* |
| High dose | – | 0, –* | – |
| **Etomidate** | | | |
| Low dose | 0 | 0 | 0 |
| High dose | – | 0, –* | – |
| **Propofol** | 0 | 0 | 0 |
| **Ketamine** | 0 | + | + |
| **Midazolam** | | | |
| Low dose | 0 | +, 0* | +, 0* |
| High dose | – | 0, +* | –, ?* |

$V_f$, rate of CSF formation; $R_a$, resistance to CSF reabsorption; ICP, intracranial pressure; 0, no change; +, increase; –, decrease; *, effect dependent on dose; ?, uncertain.
Adapted from Artru AA, CSF dynamics, cerebral edema, and intracranial pressure. In: Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives*. New York, NY: McGraw-Hill, 1997:61.

autoregulatory range of approximately 60 to 120 mm Hg. Pentobarbital has been shown to decrease local utilization of glucose in the spinal cord, although the magnitude of this effect is smaller than that seen in the brain.

**B. Etomidate**

1. **Effect on CBF and $CMRO_2$.** Etomidate, like the barbiturates, reduces CBF and $CMRO_2$. An isoelectric EEG can be induced with etomidate, and, as with thiopental, there is no evidence of cerebral toxicity as reflected by normal brain metabolites. In addition, no further reduction in $CMRO_2$ occurs when additional doses are given after EEG burst suppression is achieved. Myoclonus produced by the drug has the disadvantage of being misinterpreted as seizure activity in neurosurgical patients. The use of etomidate may suppress the adrenocortical response to stress; however, this may not be an issue in patients who have intracranial tumors because they usually are already receiving steroids. Less cardiovascular depression with etomidate as compared to thiopental or propofol makes this drug advantageous for the induction of anesthesia in trauma patients who have a low blood volume and older neurosurgical patients who have multiple medical problems.
2. **Effect on autoregulation and $CO_2$ response.** Reactivity to $CO_2$ is maintained with the administration of etomidate. The effect of etomidate on autoregulation has not been evaluated.
3. **Effect on CSF dynamics.** Low-dose etomidate causes no change in $V_f$ and $R_a$ with no predicted effect on ICP. High-dose etomidate causes a decrease in $V_f$ and either no change or a decrease in $R_a$ with a predicted decrease in ICP.
4. **Effect on ICP.** Etomidate has been shown to reduce ICP without decreasing CPP and is clinically useful in neurosurgical patients for this purpose.

**C. Propofol**

1. **Effect on CBF and $CMRO_2$.** Propofol produces dose-related reductions in both CBF and $CMRO_2$. The pattern of regional CBF (rCBF) changes is different for propofol and thiopental. Using positron emission tomography (PET) in adult volunteers, propofol has been shown to decrease rCBF in the anterior brain regions, whereas thiopental decreases rCBF primarily in the cerebellar and posterior brain regions.

   A disadvantage of large bolus doses of propofol is a reduction in MAP, which can decrease CPP. In neurosurgical patients who are hypovolemic, the reduction in MAP might be substantial and either the intravascular volume of these patients should be restored before the administration of propofol or an alternative induction drug should be used. The more frequent maintenance of normovolemia in recent years in neurosurgical patients has made this less of an issue. A continuous infusion of propofol may be used intraoperatively as part of a total intravenous technique. The combination of an infusion of propofol and a narcotic (usually remifentanil) is particularly useful when the monitoring of evoked potentials precludes the use of other than low concentrations of inhalational drugs. The technique using propofol and remifentanil infusions along with a low-dose inhalational drug is also useful for providing good operating conditions when ICP is elevated. Another frequent use of propofol during neurosurgery is for sedation during awake craniotomies.
2. **Effect on autoregulation and $CO_2$ response.** Autoregulation and $CO_2$ response are preserved during the administration of propofol.
3. **Effect on CSF dynamics.** Propofol causes no change in $V_f$ or $R_a$ with no predicted effect on ICP.
4. **Effect on ICP.** Propofol reduces ICP. Because it also reduces MAP, its effect on CPP must be carefully monitored. Nonetheless, propofol's ICP-lowering effect makes it useful in the intensive care unit (ICU) for the sedation of patients in whom elevated ICP is a concern. Propofol has the advantage of allowing prompt awakening, which is advantageous in patients whose neurologic status needs to be evaluated serially. In the operating room, moderately deep sedation with propofol does not increase ICP in comparison to no sedation in patients undergoing stereotactic biopsy for brain tumors. During craniotomy for resection of brain tumors, ICP has been shown to be lower in patients who receive propofol–fentanyl in comparison to patients anesthetized with isoflurane–fentanyl or sevoflurane–fentanyl. The antinausea effect of propofol is also advantageous in neurosurgical patients because many of them receive moderate to large doses of narcotics, which are associated with a high incidence of nausea and vomiting. This can be particularly deleterious because nausea-induced retching and vomiting might increase ICP. Careful attention to sterile technique is essential when using propofol as an infusion because the solubilizing drug in which propofol is prepared provides an excellent medium for bacterial growth.
5. **Effect on spinal cord metabolism.** Propofol decreases local spinal cord metabolism in both the gray and the white matter, as expressed by local reductions in glucose utilization.

**D. Narcotics**

1. **Effect on CBF and $CMRO_2$.** The effects of narcotics on CBF are difficult to characterize accurately because of conflicting experimental reports. It appears, however, that low doses of narcotics have little effect on CBF

and $CMRO_2$, whereas higher doses progressively decrease both CBF and $CMRO_2$.

The baseline anesthetic state also plays a role. If a cerebral vasodilator is used to achieve the control anesthetic state to which a narcotic is added, a decrease in CBF and $CMRO_2$ occurs. If either an anesthetic possessing cerebral vasoconstricting properties or no anesthetic is used as the control, narcotics have little effect on CBF. The observed reductions in CBF and $CMRO_2$ parallel progressive slowing of the EEG. However, burst suppression and an isoelectric EEG are never achieved. High doses of narcotics have been shown to produce seizures in laboratory animals but rarely in humans. Seizures have been reported with high-dose fentanyl. Normeperidine, a metabolite of meperidine, is a known convulsant.

2. **Effect on autoregulation and $CO_2$ reactivity.** Cerebral autoregulation and $CO_2$ reactivity are maintained with narcotics.
3. **Effect on CSF dynamics (Table 2.3).** At low doses, fentanyl, alfentanil, and sufentanil cause no change of $V_f$ and a decrease in $R_a$ with a predicted decrease in ICP. At high doses, fentanyl decreases $V_f$ and causes either no change or an increase in $R_a$ with either a predicted decrease or an uncertain effect on ICP. At high doses, alfentanil causes no change in $V_f$ and $R_a$ with no predicted effect on ICP. High doses of sufentanil cause no change of $V_f$ and either no change or an increase in $R_a$, predicting either no change or an increase in ICP.
4. **Effect on ICP.** Under most conditions, narcotics produce either no change or a slight decrease in ICP. Narcotics can, however, increase ICP under certain study conditions. For example, the bolus administration of sufentanil has been shown to produce transient but pronounced increases in ICP in patients who have severe head injury. Likewise, the bolus administration of sufentanil and alfentanil has been shown to produce increases in cerebrospinal fluid pressure (CSFP) in patients who have supratentorial tumors. The autoregulation-induced vasodilatation of cerebral vessels from the decrease in MAP may explain the changes in CSFP. Thus, when narcotics are administered to the neurosurgical patient, they should be given in a manner that does not cause a sudden reduction in MAP. The narcotic antagonist naloxone, when carefully titrated, has little effect on CBF and ICP. When used in large doses to

TABLE 2.3 Effects of Narcotics on Rate of Cerebrospinal Fluid Formation, Resistance to Reabsorption of Cerebrospinal Fluid, and the Predicted Effect on Intracranial Pressure

| Narcotic | $V_f$ | $R_a$ | Predicted ICP Effect |
|---|---|---|---|
| Fentanyl, alfentanil, and sufentanil (low dose) | 0 | – | – |
| Fentanyl (high dose) | – | 0, +* | –, ?* |
| Alfentanil (high dose) | 0 | 0 | 0 |
| Sufentanil (high dose) | 0 | +, 0* | +, 0* |

$V_f$, rate of CSF formation; $R_a$, resistance to CSF reabsorption; ICP, intracranial pressure; 0, no change; –, decrease; +, increase; *, effect dependent on dose; ?, uncertain.

Adapted from Artru AA. CSF dynamics, cerebral edema, and intracranial pressure. In: Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives.* New York, NY: McGraw-Hill, 1997:61.

reverse narcotic effects, however, the administration of naloxone may be associated with hypertension, cardiac arrhythmias, and intracranial hemorrhage.

**E. Ketamine**

1. **Effect on CBF and $CMRO_2$.** Ketamine produces an increase in CBF and no change or a slight increase in $CMRO_2$. The mechanism of the increase in CBF may be several-fold: respiratory depression with mild hypercapnia in spontaneously ventilating subjects, regional neuroexcitation with a concomitant increase in cerebral metabolism, and direct cerebral vasodilatation as demonstrated by an increase in CBF during normocapnia and in the absence of changes in cerebral metabolism. The increase in CBF is more marked in certain regions of the brain, which might be related to the hallucinations associated with ketamine. Although seizures have been reported in epilepsy patients receiving ketamine, generally no epileptiform activity is seen on EEG analysis.
2. **Effect on autoregulation and $CO_2$ reactivity.** Cerebral autoregulation and $CO_2$ reactivity are maintained with ketamine.
3. **Effect on CSF dynamics.** Ketamine increases $R_a$ and causes no change in $V_f$, which would predict an increase in ICP.
4. **Effect on ICP.** During spontaneous ventilation, ketamine produces an increase in $PaCO_2$ and ICP, in both the presence and the absence of preexisting intracranial hypertension. Increases in ICP might also occur in the presence of normoventilation. Interestingly, ketamine is a noncompetitive *N*-methyl-D-aspartate antagonist. In one animal model of incomplete cerebral ischemia, ketamine was shown to reduce cerebral infarct size. In the clinical arena, however, ketamine is still avoided in most neurosurgical patients, particularly those who have mass lesions and the potential for increased ICP.

**F. Benzodiazepines**

1. **Effect on CBF and $CMRO_2$.** Benzodiazepines, including diazepam, midazolam, and lorazepam, produce small decreases in CBF and $CMRO_2$ in both small and large doses. A ceiling effect on these parameters is seen, which may represent saturation of receptor-specific binding sites. As with the barbiturates, some of the CBF-lowering effect of benzodiazepines is thought to be secondary to a reduction in $CMRO_2$. Electroencephalographic effects include a shift from alpha to low-voltage beta and then theta waves, although an isoelectric EEG is not produced. Benzodiazepines are known *anticonvulsants* and are used clinically for this purpose.
2. **Effect on cerebral autoregulation and $CO_2$ reactivity.** CBF autoregulation and $CO_2$ reactivity are maintained with benzodiazepines.
3. **Effect on CSF dynamics.** Midazolam causes no change in $V_f$ at low doses and a decrease in $V_f$ at high doses. $R_a$ is either not changed or increased. The predicted effect on ICP from these changes in CSF dynamics is uncertain.
4. **Effect on ICP.** ICP effects are small with benzodiazepines, which cause either no change or a slight reduction in ICP. Midazolam is commonly used as a premedication in neuroanesthesia, with small intravenous doses titrated to the patient's response, and as an anesthetic adjuvant. Large doses are generally avoided, however, because of the potential for prolonged sedation. Flumazenil is a receptor-specific benzodiazepine antagonist that can increase CBF and ICP when used in large doses to reverse midazolam sedation. Seizures scan also be precipitated by the administration of large doses of flumazenil.

## II. INHALATIONAL DRUGS

### A. Nitrous oxide ($N_2O$)

1. **Effect on CBF and $CMRO_2$.** Although many clinicians once thought $N_2O$ to be devoid of cerebrovascular effects, it is now known that it can cause large increases in CBF. The effects of $N_2O$ vary depending on the presence or the absence of other anesthetics. When administered alone or with minimal background anesthesia, $N_2O$ increases CBF. In contrast, when it is administered with certain intravenous anesthetics (barbiturates, narcotics), its effects on CBF may be attenuated. When the effects of a 1 MAC anesthetic produced by a volatile drug alone are compared to the effects of a 1 MAC anesthetic provided by the combination of 0.5 MAC volatile drug and 0.5 MAC $N_2O$, CBF is higher in the presence of $N_2O$. $CMRO_2$ may be unchanged or increased with $N_2O$. Although brain activity on EEG might be increased with $N_2O$, it does not cause seizures.
2. **Effect on $CO_2$ reactivity.** $CO_2$ reactivity is preserved during the use of $N_2O$.
3. **Effect on CSF dynamics (Table 2.4).** Either the addition to or the withdrawal of $N_2O$ from the inhalational drugs halothane and enflurane causes no change in either $V_f$ or $R_a$ with no predicted effect on ICP.
4. **Effect on ICP.** $N_2O$ can increase ICP in patients who have mass lesions. The ICP response can be attenuated if either intracranial compliance is improved first or drugs that decrease CBV such as barbiturates are administered concomitantly. $N_2O$ is known to diffuse rapidly into and expand closed air-filled spaces. Pneumocephalus produced by a recent craniotomy contraindicates the use of $N_2O$ for the repeat procedure. If a venous air embolism (VAE) occurs, $N_2O$ can increase the size of the air bubble and worsen the consequences of the air embolism. $N_2O$ should be discontinued if a VAE occurs. Some clinicians avoid the use of $N_2O$ altogether in procedures in which the likelihood of VAE is high, such as a posterior fossa craniectomy performed with the patient in the sitting position.
5. **Effect on spinal cord metabolism.** $N_2O$ increases the spinal cord's utilization of glucose, which is quantitatively similar to that effect produced in the brain (~25%).

TABLE 2.4 Effects of Inhaled Drugs on Rate of Cerebrospinal Fluid Formation, Resistance to Reabsorption of Cerebrospinal Fluid, and the Predicted Effect on Intracranial Pressure

| Inhaled Drug | $V_f$ | $R_a$ | Predicted ICP Effect |
|---|---|---|---|
| Nitrous oxide | 0 | 0 | 0 |
| Isoflurane | | | |
| Low dose | 0 | 0, +* | 0, +* |
| High dose | 0 | – | – |
| Desflurane | 0, +[a] | 0 | 0, +[a] |
| Sevoflurane | – | + | ? |

$V_f$, rate of CSF formation; $R_a$, resistance to CSF reabsorption; ICP, intracranial pressure; 0, no change; –, decrease; +, increase; *, effect dependent on dose; ?, uncertain.

[a]Effect occurs only during hypocapnia combined with increased CSF pressure.

Adapted from Artru AA. CSF dynamics, cerebral edema, and intracranial pressure. In: Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives.* New York, NY: McGraw-Hill, 1997:61.

**B. Isoflurane**

1. **Effect on CBF and $CMRO_2$.** Isoflurane is a cerebrovasodilator that increases CBF. Although it is one of the least potent cerebrovasodilators, it is the most potent depressant of $CMRO_2$. The techniques of CBF measurement may influence the interpretation of CBF studies with the different inhalational drugs. For example, cortical blood flow is higher with halothane than isoflurane. By contrast, the increase in CBF seen with isoflurane is higher in the subcortical areas. Therefore, if a technique of CBF measurement that selectively looks at cortical flow (radioactive xenon techniques, transcranial Doppler, and venous outflow) is used, halothane might demonstrate a greater effect on CBF than isoflurane. If whole-brain blood flow is measured (microspheres, PET, autoradiography), the effects might appear more similar among the different volatile anesthetics.

   Isoflurane initially causes EEG activation which is followed by EEG slowing that becomes more marked as the dose increases. It has the capacity to induce an isoelectric EEG at a concentration that is clinically relevant because it is tolerated hemodynamically. This occurs at approximately 2 MAC. The reduction in $CMRO_2$ plateaus at the point at which an isoelectric EEG is reached. A normal cerebral energy state is also present at this point.
2. **Effect on cerebral autoregulation and $CO_2$ reactivity.** Cerebral autoregulation is impaired with isoflurane in a dose-related manner. $CO_2$ reactivity is maintained with isoflurane. The achievement of hypocapnia may restore cerebral autoregulation impaired by isoflurane.
3. **Effect on CSF dynamics.** At low concentrations, isoflurane causes no change in $V_f$ and either no change or an increase in $R_a$ with either no change or an increase in ICP predicted. At high concentrations, isoflurane causes no change in $V_f$ and a decrease in $R_a$, predicting a decrease in ICP.
4. **Effect on ICP.** Isoflurane has the potential to increase ICP. However, it may not be necessary to induce hypocapnia before introducing isoflurane. The simultaneous introduction of hyperventilation and isoflurane may be sufficient to prevent an increase in ICP.
5. **Effect on SCBF and metabolism.** At both 1 and 2 MAC, isoflurane produces an increase in SCBF and an attenuation of autoregulation. The changes seen at 2 MAC are greater for the spinal cord than for either the cortex or the subcortex.

**C. Desflurane**

1. **Effect on CBF and $CMRO_2$.** The effects of desflurane on CBF and $CMRO_2$ appear to be very similar to those of isoflurane. The use of desflurane is associated with a dose-related decrease in $CMRO_2$ (although slightly less than with isoflurane) and, if the blood pressure is maintained, an increase in CBF. Desflurane produces EEG changes similar to those of isoflurane. At 2 MAC, EEG burst suppression can occur, but it may revert with the passage of time. Desflurane has a low blood-gas partition coefficient (0.4), which provides rapid titration of anesthetic depth and prompt emergence.
2. **Effect on cerebral autoregulation and $CO_2$ reactivity.** Cerebral autoregulation is impaired with concentrations of desflurane in excess of 1 MAC. The $CO_2$ reactivity is maintained at desflurane concentrations of between 0.5 and 1.5 MAC.
3. **Effect on CSF dynamics.** The effects of desflurane on CSF dynamics depend on CSF pressure and $PaCO_2$. Desflurane causes no change in

either $V_f$ or $R_a$ under conditions of normocapnia with either normal or increased CSF pressure. Likewise, with hypocapnia and normal CSF pressure, desflurane causes no change in either $V_f$ or $R_a$, predicting no effect on ICP. With hypocapnia and increased CSF pressure, however, desflurane increases $V_f$ with a predicted increase in ICP.

4. **Effect on ICP.** Like isoflurane, desflurane can produce an increase in ICP from general cerebrovascular dilatation. When hypocapnia is maintained, however, the effect on ICP is minimized. Altered CSF dynamics such as an increase in $V_f$ (as noted previously) may also play a role in desflurane's ability to decrease intracranial compliance.

**D. Sevoflurane**

1. **Effect on CBF and $CMRO_2$.** Sevoflurane's effects on CBF and $CMRO_2$ are similar to those of isoflurane. CBF increases with sevoflurane secondary to cerebral vasodilatation. $CMRO_2$ decreases and EEG burst suppression can be achieved with a clinically relevant concentration of approximately 2 MAC (similar to isoflurane). Epileptiform activity has been induced by sevoflurane during induction in pediatric patients who have a history of epilepsy. Anesthesia with high concentrations of sevoflurane has not provided any evidence of cerebral toxicity. Sevoflurane's relatively low blood-gas partition coefficient (0.6) provides for rapid induction and emergence. Unlike desflurane, sevoflurane is not irritating to the airway and can be used for inhalational induction. Inhalational inductions are avoided, however, in most neurosurgical patients because of the volatile drugs' potential for producing vasodilatation with a subsequent increase in CBF, CBV, and ICP and the potential for uncal, tentorial, or transforaminal herniation. Approximately 2% of the absorbed sevoflurane is metabolized with inorganic fluoride produced as one of the metabolites. Compound A, a degradation product from the interaction of sevoflurane with $CO_2$ absorbents, can also be produced. There is no agreement on the clinical significance of the levels of fluoride and Compound A so generated, but they are unlikely to be associated with renal injury in humans.
2. **Effect on cerebral autoregulation and $CO_2$ reactivity.** Cerebral autoregulation and $CO_2$ reactivity are preserved during the administration of low concentrations of sevoflurane.
3. **Effect on CSF dynamics.** Sevoflurane decreases $V_f$ and increases $R_a$. The predicted effect on ICP is uncertain.
4. **Effect on ICP.** The effect of sevoflurane on ICP is similar to isoflurane. A minimal change in ICP occurs in patients who have normal intracranial compliance. Caution should be exercised, however, when this drug is given to patients who have large mass lesions and reduced intracranial compliance because of the potential for cerebrovasodilatation and an increase in CBF, CBV, and ICP.

## III. MUSCLE RELAXANTS

Muscle relaxants do not cross the blood–brain barrier. Any cerebral effects are thus secondary to histamine release, systemic hemodynamic changes, actions of metabolites, and altered cerebral afferent input.

**A. Non-depolarizing muscle relaxants**

1. **Short-acting drugs.** Mivacurium is a short-acting relaxant that is metabolized by plasma cholinesterase (at about 88% of the rate of succinylcholine) and undergoes ester hydrolysis in the liver. It is commonly given by infusion because of its rapid metabolism. When large doses of mivacurium are given rapidly, some histamine release can occur. Therefore,

bolus doses should be given slowly over a period of 30 to 60 seconds to avoid histamine release and the potential for an increase in CBF and ICP.

2. **Intermediate-acting drugs. Atracurium** causes histamine release when given in large bolus doses. It is metabolized by ester hydrolysis and Hoffmann elimination and has an advantage in that with renal or liver dysfunction, atracurium does not alter its metabolism. Laudanosine, a metabolite of the Hoffmann elimination of atracurium, has been shown to cause seizures in laboratory animals although this has not been noted at the level obtained clinically. The newer analog of atracurium, *cis*-atracurium, does not cause histamine release and is not associated with the formation of toxic metabolites. The lack of dependence of *cis*-atracurium on renal or hepatic metabolism makes it very useful for neurosurgical procedures, particularly in patients in whom liver metabolism has been altered by the use of anticonvulsants.

   **Vecuronium** has the advantage of maintaining stable hemodynamics even when given in large doses. One possible exception is that bradycardia may occur when vecuronium is combined with large doses of narcotics for induction of anesthesia, leaving the vagotonic effect of the narcotic unopposed. Vecuronium does not alter ICP or CSF dynamics with no change in $V_f$ or $R_a$. Its stable hemodynamics and lack of cerebral effects have made vecuronium a popular choice in neuroanesthesia.

   **Rocuronium** is a non-depolarizing muscle relaxant that has a relatively stable hemodynamic profile (weakly vagolytic) and is excreted unchanged by the biliary system and the kidneys. Unlike vecuronium, it is not associated with the production of active metabolites. The rapid onset of rocuronium with larger doses makes it an excellent choice for intubation in the neurosurgical patient who is at risk for succinylcholine side effects but in whom rapid onset of action is desirable.

3. **Long-acting drugs. Pancuronium** decreases the MAC of volatile anesthetics, secondary to the decrease in cerebral input from paralyzed muscle spindles. Large doses of pancuronium may cause hypertension and tachycardia, which could increase CBF and ICP. These effects may not occur when pancuronium is combined with narcotics for induction or when it is given in smaller doses for maintenance of relaxation.

   **Doxacurium,** a long-acting muscle relaxant, is devoid of significant cardiovascular side effects and has not been shown to have any adverse cerebral effects. It is eliminated unchanged in the kidney and the bile. Doxacurium's lack of side effects and long duration of action could make this relaxant useful for extremely lengthy neurosurgical procedures.

**B. Depolarizing muscle relaxants**

**Succinylcholine** can cause an increase in CBF that is associated with an increase in ICP. This is secondary to increases in muscle spindle activity, which increase cerebral afferent input. These effects can be blocked by prior paralysis or pretreatment with a non-depolarizing muscle relaxant. The changes in ICP are modest and transient, however, and may be outweighed by the benefit of rapid and reliable onset of muscle relaxation in instances in which rapid control of the airway is necessary. Succinylcholine produces no change in either $V_f$ or $R_a$ and no predicted effect on ICP. Of greater concern than succinylcholine's effect on ICP in the neurosurgical patient is the exaggerated release of potassium that occurs with certain neurologic injuries such as closed head trauma, cerebrovascular accidents, hemiparesis, spinal cord trauma, and neuromuscular disorders.

## COMMENT ON ILLUSTRATIVE CASE

The patient presented at the first of the chapter presents an anesthetic challenge that is not infrequently encountered by the neuroanesthesiologist. If called to the ER for intubation, the challenge begins here. Considerations for intubation include the necessity of airway evaluation, the likelihood of a cervical spine collar in place, the inability of the patient to cooperate because of neurologic status, and the probable quick oxygen desaturation after induction drugs are given because of the associated lung injury. Propofol was chosen for induction in this case, but thiopental or etomidate is a suitable alternative, with etomidate's having the advantage of more cardiovascular stability. Lidocaine and narcotic (fentanyl) were given prior to induction to minimize the likelihood of an increase in ICP associated with intubation. The muscle relaxant chosen was rocuronium, because of its ability to provide suitable intubating conditions relatively quickly if given in a large intubating dose. Even though succinylcholine may cause a transient increase in ICP, it would also be suitable for intubation in this case. After the airway is secured, it is important to give additional anesthetic for transport to the operating room. This usually consists of midazolam and additional narcotic.

In the operating room, a propofol infusion is begun because of the beneficial effects of propofol on ICP in this patient with a mass lesion and midline shift on CT. Initially fentanyl is given to provide analgesia, but once time permits a remifentanil infusion is added. No nitrous oxide is used, and if the addition of an inhalational drug is chosen, low-dose sevoflurane, desflurane, or isoflurane may be used. Muscle relaxation is maintained with vecuronium, cis-atracurium, or rocuronium.

Shortly before the end of the surgical procedure, the remifentanil infusion is discontinued and additional fentanyl or morphine is given for postoperative pain relief. The patient is transported to the ICU with the propofol infusion running. This may be discontinued postoperatively for neurologic evaluation by the surgeons. The severity of the head injury and the associated pulmonary injury necessitates post-operative ventilation.

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# 3 Neurophysiologic Monitoring

**M. Sean Kincaid and Arthur M. Lam**

## Illustrative Clinical Case

A 72-year-old man is to undergo anesthesia for a right carotid endarterectomy (CEA) after experiencing temporary left hemiparesis thought to be due to a transient ischemic attack. Transcranial Doppler (TCD) monitoring of bilateral middle cerebral artery (MCA) flow velocities is planned. After induction of anesthesia and endotracheal intubation, anesthesia is maintained with a volatile drug. Bilateral MCA flow velocities remain about 55 cm/second. After the right internal carotid artery is occluded with a surgical clamp, the right MCA flow velocity loses its pulsatility and decreases to 12 cm/second. Increasing the patient's mean arterial pressure (MAP) with phenylephrine does not improve the velocity. Discussion of these changes with the surgeon prompts her to place a shunt in the right internal carotid artery. With placement of the shunt, MCA flow velocity returns to a pulsatile flow with a mean of 50 cm/second. The surgery proceeds uneventfully. Following surgical closure, the patient is allowed to emerge from anesthesia. Prior to tracheal extubation, the patient's blood pressure climbs to 176/95, and the right MCA flow velocity is 118 cm/second at end-tidal carbon dioxide ($CO_2$) of 40 mm Hg. Concerned about hyperemia and the risk of hyperperfusion syndrome, the anesthesiologist administers several doses of labetalol to normalize blood pressure. MCA flow velocity then falls to 60 cm/second. After removal of the endotracheal tube, the patient is taken to the postanesthesia care unit, where he complains of a headache. Blood pressure is now noted to be 183/101. The anesthesiologist brings the TCD machine to the patient's bedside and again discovers elevated MCA flow velocity > 110 cm/second (more than 100% of baseline). More labetalol is required to normalize the blood pressure, and the patient's headache resolves gradually. Multiple emboli were also observed during the first 10 minutes but were subsequently absent without treatment. The remainder of the patient's hospital course is unremarkable.

## Chapter Highlights

- Surgical patients are at risk for ischemic/hypoxic injury to the central nervous system (CNS).
- Intraoperative detection of insult to the CNS with neuromonitors may facilitate:
  - Early correction before injury becomes permanent.
  - Surgical procedure to be tailored to patient's physiology.
- Monitors of function:
  - Electroencephalography (EEG) records the electrical activity of the brain and can thus be used to detect insults, which compromise cerebral metabolism. It is particularly well suited for use in CEA surgery, and when drug-induced metabolic suppression is desired.
  - Bispectral analysis (BIS) is a derived value based on EEG recordings, on a normalized scale of 0 to 100, where appropriate hypnosis is thought to occur in the range of 40 to 60.

  - Evoked potential monitoring is used to assess the integrity of peripheral and central pathways, including ascending sensory pathways (sensory evoked potentials [SEP]), and descending motor pathways (motor evoked potentials). It is particularly useful during spine surgery where insult to the spinal cord is possible. More specialized evoked monitoring modalities include visual evoked potentials, assessing the visual system, and brain stem auditory evoked potentials, assessing Cranial Nerve VIII and brain stem pathways.
- Monitors of cerebral blood flow (CBF) and intracranial pressure (ICP):
  - Laser Doppler flowmetry (LDF) and transcranial Doppler (TCD) ultrasonography both measure relative changes in CBF. TCD measures flow velocity in large basal cerebral arteries, where velocity is proportional to flow. It has numerous applications, including CEA surgery, traumatic brain injury (TBI), stroke, and cerebral vasospasm.
  - ICP can be measured with various devices, including an intraventricular catheter, fiberoptic parenchymal device, or a subarachnoid bolt. Measurement of ICP facilitates optimization of cerebral perfusion pressure (CPP).
- Monitors of cerebral oxygenation and metabolism:
  - Brain tissue oxygenation ($PbtO_2$) is measured via an intraparenchymal monitor that can be placed in a region of concern, thus allowing localized monitoring of oxygenation.
  - Jugular bulb venous oximetry ($SjvO_2$) provides a global view of oxygen supply versus demand for the brain through analysis of cerebral venous drainage.
  - Microdialysis catheters are placed in the brain tissue and allow sampling of the interstitial fluid milieu. Excitatory amino acids suggest neuronal damage, glycerol indicates cellular membrane breakdown, and increased levels of lactate suggest ischemia.
  - Near-infrared spectroscopy (NIRS) measures cerebral oxygenation in a non-invasive fashion by light transmission through the scalp and skull, which is reflected off hemoglobin in the brain.

For patients who have neurologic disease, there is an increased risk of ischemic/hypoxic injury to the CNS during surgical procedures. This risk may be related to hemodynamic/embolic events associated with a non-neurosurgical operation (e.g., cardiopulmonary bypass [CPB] procedures in patients who have significant carotid stenosis) or the risk may be inherent in the neurosurgical procedure itself (e.g., temporary occlusion of a feeding artery during clip ligation of a cerebral aneurysm). Intraoperative neurophysiologic monitoring may improve patient outcome by facilitating early diagnosis of ischemia/hypoxia before irreversible damage occurs and enabling surgeons to provide optimal operative treatment as indicated by the monitoring parameter. Although not universally adopted, neurophysiologic monitoring has become routine for some surgical procedures in many centers.

Broadly speaking, the brain can be monitored in terms of function, blood flow, and metabolism (Tables 3.1 to 3.3).

## I. MONITORING OF FUNCTION

**A. EEG.** Summation of the excitatory postsynaptic potential generated by the pyramidal cells of the cerebral cortex gives rise to the electrical activity of the brain, which can be recorded as an EEG. The EEG comprises many underlying components that have different frequencies and harmonics. The component waves are typically classified according to their respective

TABLE 3.1 Monitoring of Function

**Electroencephalogram**
Ram electroencephalogram
Computerized processed
Compressed spectral array
Density spectral array
Aperiodic analysis
Bispectral Analysis

**Evoked Potentials**
Sensory evoked potentials:
Somatosensory EP
Brainstem auditory EP
Visual EP
Motor evoked potentials
Transcranial magnetic MEP
Transcranial electric MEP
Direct spinal cord stimulation

**Electromyography**
Cranial nerve functions (V, VII, IX, X, XI, XII)

EP, evoked potential; MEP, motor evoked potential.

frequencies (Table 3.4). This electrical activity is volume-conducted and can be recorded from the scalp and forehead using surface or needle electrodes.

1. **Recording techniques**
   a. Because the scalp has no electrically neutral area, the EEG is typically recorded using a montage (electrode arrangement) with bipolar recording. Thus, both electrodes are active and the polarity of the signal recorded depends on the arbitrary designation of the recording versus the referential electrode. Other electrical activities generated in the body such as electromyographic and electrocardiographic potentials are minimized but not eliminated using common-mode

TABLE 3.2 Monitoring of CBF and ICP

**Cerebral Blood Flow (CBF)**
Nitrous oxide wash-in
Radioactive xenon clearance
Laser Doppler blood flow
Transcranial Doppler sonography
Microvascular Doppler ultrasound
Indocyanine green videoangiography

**Intracranial Pressure (ICP)**
Intraventricular catheter
Fiberoptic intraparenchymal catheter
Subarachnoid bolt
Epidural catheter

TABLE 3.3 Monitoring of Metabolism

| |
|---|
| **Invasive Monitor** |
| Intracerebral $PO_2$ electrode (Paratrend, Licox) |
| **Non-invasive Monitor** |
| Transcranial cerebral oximetry (near-infrared spectroscopy) |
| Jugular venous oximetry |

$PO_2$, oxygen tension.

rejection that rejects the electrical signals that are measured in both recording sites (common) in comparison to a third "ground electrode."

The number of channels used and the placement of electrodes determine the specificity of the EEG as a monitor of the occurrence of regional ischemia. The gold standard for raw EEG recording is the 16-channel recording (eight channels for each hemisphere) with electrodes placed according to the International 10–20 System (Fig. 3.1). With the exception of monitoring in CEA in some centers, 16-channel EEG recording is seldom performed intraoperatively because of its relative complexity and the inaccessibility of recording sites during intracranial surgical procedures.

To simplify recording and interpretation of the EEG, most EEG machines designed for intraoperative monitoring use 2- to 4-channel recording with computer processing to simplify the output. Although different vendors use different algorithms, the basic premise is to filter out the high-frequency activity (likely to be artifacts or interference), typically at 30 Hz. The raw EEG is then separated into its component waves using Fast Fourier Transform, which are then grouped together according to the frequency spectrum. Thus, the raw EEG recorded in a time domain is displayed in a frequency domain. The resultant power (square of the amplitude of the EEG wave) spectrum can be displayed in a number of ways, the most common ones being compressed spectral array and density spectral array with either the peaks and valleys or the density of the gray scale representing the power of the spectrum. Aperiodic analysis is another method of EEG processing

TABLE 3.4 Electroencephalogram

| | | |
|---|---|---|
| Beta | 13–30 Hz | High frequency, low amplitude, dominant during awake state |
| Alpha | 9–12 Hz | Medium frequency, higher amplitude seen in occipital cortex with eyes closed while awake |
| Theta | 4–8 Hz | Low frequency, not predominant in any condition |
| Delta | 0–4 Hz | Very low frequency, low-to-high amplitude signifies depressed functions, consistent with deep coma (cause can be anesthesia, metabolic, or hypoxia) |

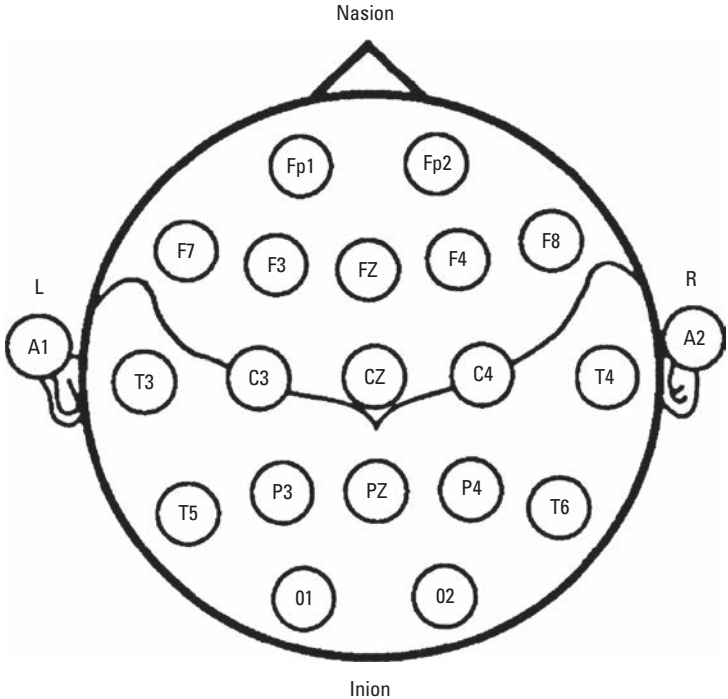


**FIGURE 3.1** The International 10–20 System for placement of EEG electrodes. It is based on dividing each head circumference (anteroposterior from nasion to inion over the vertex, coronal from tragus of one ear to the other) into two halves and then subdividing each half (50%) into 10%, 20%, 20% sectors. Fp, frontal pole; F, frontal; C, central; P, parietal; T, temporal; A, earlobe; M, mastoid (not shown). Odd number subscripts denote the left hemisphere and even numbers denote the right hemisphere.

that tracks each wave and plots it as a "telephone pole" with its height representing the amplitude or power of the wave.

**b.** Alternatively, direct electrocorticography (ECoG) can be recorded from the brain surface using strip electrodes placed intraoperatively by the neurosurgeon. This is typically utilized for monitoring seizure activity during epilepsy surgery. With placement of deep brain stimulator (DBS) leads for movement disorders, electrical activity is recorded from microelectrodes placed in the thalamic and subthalamic nuclei.

**2. Interpretation of the EEG**

**a.** The EEG is a random activity reflecting the state of arousal and metabolic activity. The generation of electrical activity is an energy-requiring process that depends on an adequate supply of substrates including oxygen and glucose. Thus, significant reductions of blood flow, oxygen, or glucose all lead to the depression of EEG activity. Gradual reductions of CBF can be correlated with characteristic

changes in the EEG. The possibility of a decrease in CBF constitutes the most frequent underlying indication for EEG monitoring.

b. **The awake EEG** is dominated by beta activity with high-frequency and low-amplitude waves. With **the onset of ischemia/hypoxia**, there is an initial transient increase in beta activity, followed by the development of slow waves (theta and delta) with large amplitude, disappearance of beta activity, and eventually the occurrence of delta waves with low amplitude. The ischemic changes can progress to suppression of electrical activity with an occasional burst of activity (burst suppression) and finally to complete electrical silence with a flat EEG, signaling the onset of irreversible damage. Thus, the sudden development of delta waves coincident with a surgical maneuver such as cross-clamping of the common carotid artery would warn the anesthesiologist and the surgeon that the patient is at risk of cerebral injury.

In the region of the ischemic penumbra where blood flow is inadequate to generate electrical activity but sufficient to maintain neuronal viability for a period of time, the EEG has poor predictive power for brain damage. Thus, EEG is sensitive to the occurrence of ischemia but lacks specificity as a diagnostic test for irreversible damage. In general, the faster the onset of the ischemic EEG changes, the higher the probability of irreversible damage.

3. **Confounding factors.** The changes in the EEG that are observed with ischemia/hypoxia are not unique; similar changes occur with anesthetic-induced metabolic depression, albeit in a reversible manner. Most intravenous (with the exception of ketamine) and inhalation anesthetics cause a dose-dependent depression of the EEG, and virtually all of them can produce a burst-suppression pattern. Similarly, hypothermia decreases cerebral metabolism and causes slowing of the EEG. EEG changes, therefore, should always be interpreted in the context of the clinical event, not in isolation.

4. **Indications for EEG monitoring**

a. All surgical procedures that potentially place the brain at risk are theoretically an indication for EEG monitoring. In practice, EEG monitoring is often difficult to perform during intracranial procedures because of the lack of access to scalp recording. The use of needle electrodes may ameliorate this problem. CEA, which places the ipsilateral hemisphere at risk during cross-clamping of the common carotid artery, is the most frequent indication for EEG monitoring. When EEG changes indicate that CBF is inadequate, induced hypertension may improve blood flow. The insertion of an intraluminal shunt will restore flow, albeit with an increased risk of embolic events.

b. Some anesthesiologists and surgeons utilize anesthesia-induced metabolic suppression to provide cerebral protection during risky procedures. EEG monitoring in these circumstances allows optimal metabolic suppression with anesthesia administered by titration to achieve burst suppression. The main indications for EEG monitoring are listed in Table 3.5.

c. Although uncommon in the anesthetized patient, occult seizures occur frequently in patients after TBI in the intensive care unit (ICU). These seizures, which may adversely affect the patient's outcome, are only detectable with continuous EEG monitoring. Although treatment of these seizures is likely beneficial, it is yet to

TABLE 3.5 Indications for Electroencephalogram Monitoring

1. Carotid endarterectomy
2. Cerebral aneurysm surgery when temporary clipping is used
3. Cardiopulmonary bypass procedures
4. Extracranial–intracranial bypass procedures
5. Deliberate metabolic suppression for cerebral protection

be determined whether continuous EEG monitoring in the ICU will improve outcome in a cost-effective manner. Furthermore, the use of continuous EEG monitoring in ICU patients at risk for cerebral ischemia, such as those experiencing post–subarachnoid hemorrhage (SAH) cerebral vasospasm, is a potential application of uncertain value.

5. **Bispectral analysis.** The bispectral index is a derived EEG parameter designed not to detect ischemia but to monitor the degree of hypnosis. Based on both power spectrum analysis and phase change or coherence of the different frequencies, the value is normalized to a range of 0 to 100. A value between 40 and 60 is considered adequate hypnosis to prevent possible recall, whereas a value above 80 is consistent with impending emergence from anesthesia. Strictly speaking, this is not a parameter used to preserve the integrity of the CNS but is derived from the raw EEG and, as such, it is potentially influenced by the occurrence of ischemia that results in changes in the EEG. The frontal location of electrode placement, however, renders the bispectral index less sensitive to the development of regional ischemia. Recent development of commercially available bilateral sensors with software that evaluates EEG symmetry may improve the utility of these monitors when a procedure, such as CEA, places one hemisphere at risk for ischemia.

**B. Evoked potential monitoring**

1. **Sensory evoked potential (SEP)** is a time-locked, event-related, pathway-specific electroencephalographic activity generated in response to a specific stimulus such as an electrical stimulus applied to the median nerve. The typical peaks and troughs are described by their polarity and latency (Fig. 3.2). For example, the cortical negative peak that typically occurs 20 ms after stimulation of the median nerve is called *N*20. Alternatively, peaks and troughs are numbered according to the sequence in which they are generated. Thus, the first positive wave that occurs after posterior tibial nerve stimulation is called *P*1. The amplitude of evoked potential waves is small relative to the conventional EEG and is not easily visualized without computer averaging of repetitive stimuli. SEPs are anatomically pathway specific and theoretically assess only the integrity of the pathway monitored. The contrast between conventional EEG and SEP is summarized in Table 3.6.
   a. SEP can be recorded in response to stimulation of any sensory nerve, cranial or peripheral. The common modalities of evoked potentials used in clinical practice are (i) somatosensory evoked potentials (SSEPs), (ii) visual evoked potentials (VEPs), and (iii) brain stem auditory evoked potentials (BAEPs). Of these three, VEP is profoundly influenced by inhalation anesthesia, difficult to perform, and

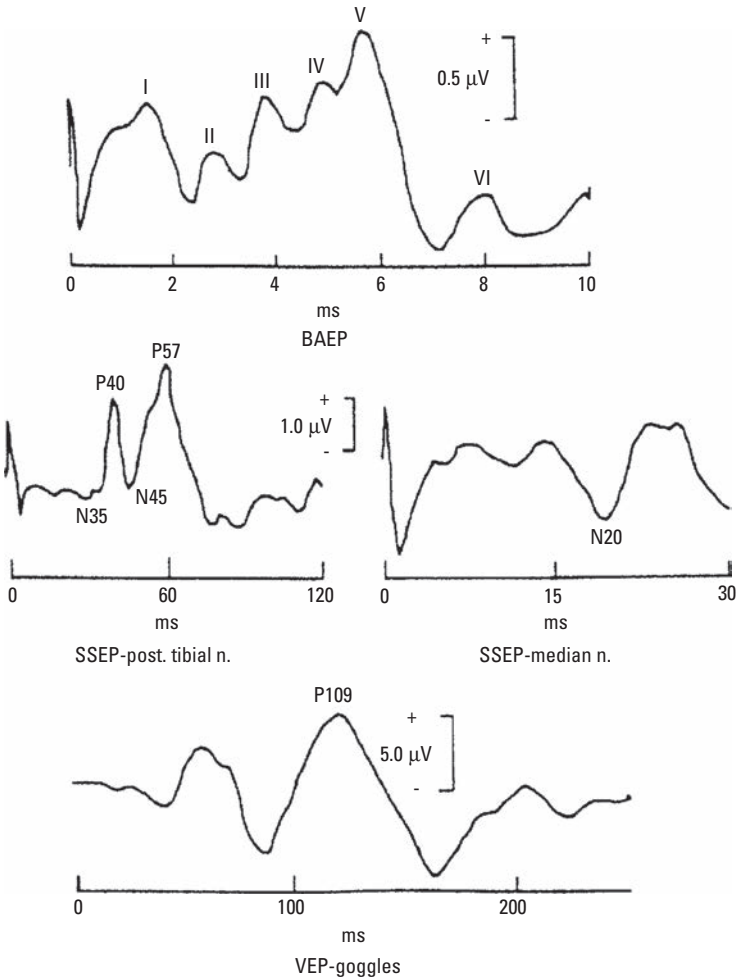


**FIGURE 3.2** Common modalities of sensory evoked responses. BAEP, brain stem auditory evoked potential; SSEP-median n., somatosensory evoked potential with median nerve stimulation; SSEP-post. tibial n., somatosensory evoked potential with posterior tibial nerve stimulation; VEP-goggles, visual evoked potential in response to stimulation with light-emitting diode goggles; μV, microvolt. (Reproduced from Lam AM. Monitoring neurologic evoked potentials. *ASA Refresher Course.* 1989;17(13):175–192, with permission.)

seldom utilized as an intraoperative monitor. However, it is potentially recordable during total intravenous anesthesia, and there is ongoing interest in VEP as a monitor to detect and prevent perioperative ischemic optic neuropathy.

TABLE 3.6 Difference between Sensory Evoked Potential (SEP) and Electroencephalogram (EEG)

| SEP | EEG |
|---|---|
| Event-related | Random |
| Anatomically pathway specific | Primarily cortical activity |
| Monitors integrity of the pathway | Monitors only the cortex |
| Small amplitude | Large amplitude |
| Requires computer averaging | No averaging required |
| Resistant to intravenous anesthetics | Abolished by high-dose intravenous or inhalation anesthetics |
| Recordable during inhaled anesthetics | |

The SSEPs recorded in response to stimulation of the median nerve, ulnar nerve, and posterior tibial nerve monitor the integrity of their respective pathways from the periphery to the cortex. They are a routine monitor for surgical procedures on the spinal column such as scoliosis surgery where there is potential risk to the spinal cord. SEPs are also used during CEA and cerebral aneurysm surgery. The theoretical advantage of SEPs over EEG is that even subcortical ischemia can be detected. Indications for different SEP-monitoring modalities are summarized in Table 3.7.

**b.** BAEPs include a series of seven short-latency peaks generated in response to stimulation of the auditory (VIII) nerve, typically with repetitive clicks delivered to the ears with a head phone or ear-inserted transducers. A specific neurogenerator produces each peak, numbered with a Roman numeral. Examination of the change in latency interval between the various peaks can localize the specific site of the injury. Monitoring BAEPs during acoustic neuroma surgery, when feasible, has been shown to help preserve the integrity of the auditory nerve. Although the neurogenerators are specific to the VIII nerve, BAEP monitoring has also been used to assess the general wellbeing of the brain stem in posterior fossa procedures.

**2. Interpretation of evoked potentials.** As with EEG, ischemia/hypoxia leads to depression of conduction with a resultant decrease in amplitude and increase in latency of the specific peaks. For SSEPs, a 50% reduction in amplitude from baseline in response to a specific surgical maneuver is generally accepted to be a significant change warranting alteration of

TABLE 3.7 Indications for Sensory Evoked Potential (SEP) Monitoring

| |
|---|
| **SSEP Monitoring** |
| Spinal column surgery |
| Carotid endarterectomy |
| Cerebral aneurysm surgery |
| **BAEP Monitoring** |
| Acoustic neuroma |
| Vertebral-basilar aneurysms |
| Other posterior fossa procedures |

SSEP, somatosensory evoked potential; BAEP, brain stem auditory evoked potential.

surgical strategy to avert potential damage. Some centers also consider a 10% increase in latency of SSEP signals to be significant. For BAEPs, an increase in latency of more than 1 msec, particularly in wave V, is considered to be clinically significant. In addition, a 50% decline in amplitude is of concern, and a loss of wave V is strongly predictive of postoperative hearing loss.

3. **Confounding factors.** As with EEG, anesthetic drugs influence cortical evoked potentials. Unlike EEG, SSEPs are relatively resistant to the influence of intravenous drugs. Although the amplitude may be slightly reduced and the latency increased, cortical SSEPs can be recorded even during deep barbiturate-induced coma when the EEG is isoelectric. In contrast, inhalation anesthetics cause a dose-related decrease in amplitude and increase in latency. With high doses, SSEP can become unrecordable. Nitrous oxide also has a profound depressant effect on the amplitude of SSEP, particularly when used in combination with an inhalation anesthetic. Therefore, the combination of inhalation anesthetic and nitrous oxide is avoided. **Intraoperative recording of SSEP is best accomplished using either an intravenous anesthetic technique or low-dose inhalation anesthetic (< 1 minimum alveolar concentration [MAC]).** Opioids have negligible effects on SSEP. Ketamine and etomidate have a paradoxical effect of augmenting the amplitude of SSEP and could make monitoring possible in patients whose SSEP might be otherwise unrecordable. BAEP, unlike cortical SSEP, resists the influence of anesthetic drugs and can be recorded even during high-dose inhalation anesthetics. For surgical procedures on the spinal column, evoked potentials can also be recorded directly from the epidural space; these potentials are robust and can be recorded regardless of the anesthetics used. As with EEG, hypothermia also decreases amplitude and increases latency.
4. **Motor evoked potentials.** Because SSEP monitors only the integrity of the sensory pathway, it is theoretically possible to miss an injury specifically affecting the motor pathway but sparing the sensory tracts. Thus, motor evoked potential (MEP) recording was introduced into clinical practice to complement SSEP recording. The MEP is basically an electromyographic potential recorded over muscles in the hand or foot in response to depolarization of the motor cortex (Fig. 3.3). Depolarization can be achieved using transcranial magnetic or electrical stimulation.

   Unfortunately, anesthetic drugs profoundly influence both modalities, rendering the transcranial magnetic stimulation essentially unrecordable during anesthesia and the electrical stimulation recordable optimally only during total intravenous anesthesia. The use of a train of four to six stimuli has augmented the amplitude of MEP and makes it easier to record under general anesthesia. In contrast to SSEP, the relatively large voltage of MEP abrogates the need for averaging and provides almost instant feedback. In many centers, MEP monitoring is used in addition to SSEP during operations on the spinal column, particularly for cervical spine and major scoliosis surgery, and is increasingly employed in skull base surgery including aneurysm surgery. MEPs are best recorded in the absence of neuromuscular blockade, although some centers advocate partial blockade to minimize patient movement during stimulation.
5. **Spontaneous electromyography.** Although not technically an evoked potential, spontaneous electromyography (EMG) is frequently recorded

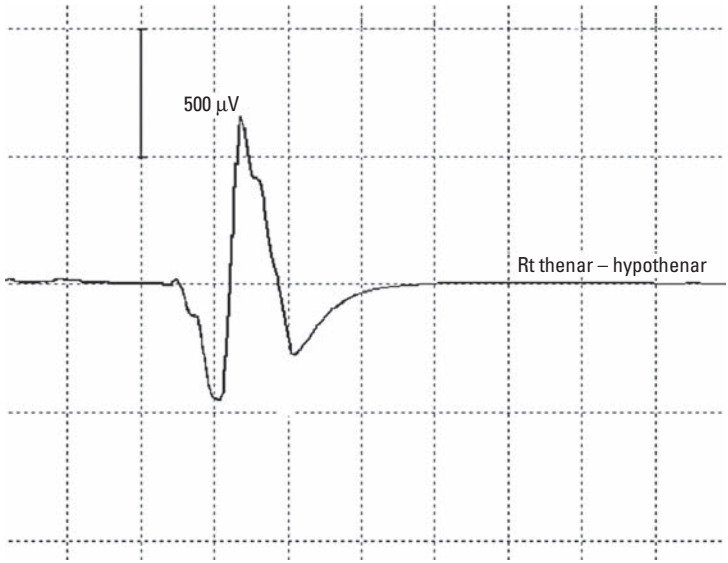


**FIGURE 3.3** Motor evoked potential from stimulation of left cranium. μV, microvolt.

during surgical procedures of both the cervical spine and lumbar spine. Irritation of peripheral nerves, such as spinal nerve roots, invokes immediate motor activity in muscles that should otherwise be silent under general anesthesia. Spontaneous EMG is particularly useful when the surgeon is working around nerve roots and needs immediate feedback regarding injury or irritation to them.

C. **Monitoring cranial nerve functions.** Operations in the posterior fossa and the lower brain stem are associated with potential injury to the cranial nerves. Monitoring the electromyographic potential of the cranial nerves that have motor components (V, VII, IX, X, XI, XII) can preserve the integrity of these cranial nerves. Two types of potentials can be recorded: spontaneous and evoked activity. Measuring spontaneous activity can detect injury potential, signifying accidental surgical trespass. Evoking the nerve with electrical stimulation facilitates identification and thus preservation of the cranial nerve. Although EMG theoretically can be recorded during partial neuromuscular blockade, it is best not to administer any muscle relaxants during cranial nerve monitoring.

## II. MONITORING OF CBF AND ICP

A. **Absolute CBF.** Most methods of CBF measurement are not applicable to intraoperative monitoring. Nitrous oxide wash-in is the classic method of measuring global hemispheric CBF, but it necessitates cannulation of the jugular bulb and clinically is cumbersome to use. Radioactive xenon clearance is a method that allows non-invasive measurement of regional CBF. Although some centers use it clinically to determine adequacy of hemispheric CBF during CEA, it is primarily a research tool. Thermal diffusion flowmetry is a quantitative technique for evaluating regional CBF based on

the thermal conductive properties of brain tissue, but it has not been implemented on a widespread basis.

B. **Relative CBF.** Other tools used for real-time evaluation of relative changes in CBF include **LDF** and **TCD sonography.** Modalities such as computed tomographic (CT) perfusion and single photon emission computed tomography (SPECT) are helpful in assessing ICU patients, but have a negligible role as intraoperative monitors.

1. **LDF** is a parenchymal or surface Doppler probe that measures local CBF in a quantitative manner. However, the flow can be expressed only in a relative manner in arbitrary units. Because the volume of tissue monitored is limited to 1 mm, its clinical use, both in the operating room (OR) and the ICU, remains limited. Insertion also requires a burr hole. Its incorporation into the intracranial monitor may increase its functionality.
2. **TCD sonography** allows non-invasive and continuous measurement of CBF velocity in the major vessels of the Circle of Willis. For intraoperative purposes, velocity in the MCA ($V_{mca}$) is measured transtemporally over the zygomatic arch. Although TCD sonography does not derive the absolute CBF, it can measure relative changes in CBF in a quantitative manner. The waveform profile also provides a qualitative assessment of ICP/CPP (the difference between the MAP and ICP). In addition, the presence of air or particulate emboli can be detected. TCD can be used to determine cerebral autoregulation and $CO_2$ reactivity.
   a. **Physiologic principles of TCD**
      1. **The diameter of the basal cerebral arteries is constant.** Flow velocity is proportional to CBF only when the diameter of the insonated vessel and the angle of insonation remain constant. There is considerable evidence to suggest that the basal cerebral arteries, as conductance vessels, do not dilate or constrict as the vascular resistance changes. Angiographic and $CO_2$ reactivity studies confirm that changes in $CO_2$ tension and blood pressure have negligible influence on the diameter of the proximal basal arteries. Intravenous and inhaled anesthetics do not constrict or dilate the MCA appreciably. Probably the only clinically important situation in which the basal cerebral vessels vasoconstrict is when **vasospasm** occurs as a complication of SAH. Vasospasm renders the relationship between CBF velocity and CBF invalid; as the vessel constricts, the flow velocity increases but the CBF actually decreases. This increase in flow velocity with constriction of the basal cerebral artery is the basis for one of the most important and established uses of the TCD. Once angiography confirms the diagnosis of vasospasm, TCD can track the patient's response to therapy and the time course of resolution of the vasospasm.
      2. **Changes in CBF velocity reflect relative changes in CBF.** Although correlation between absolute flow velocity and CBF in any given population is poor, good correlation exists between relative changes in flow velocity and CBF.
   b. **Clinical applications of intraoperative TCD monitoring**
      1. **Carotid endarterectomy**
         a. **Detection of ischemia.** TCD monitoring during CEA can detect cerebral ischemia during cross-clamping of the carotid artery and allows selective shunting. The correlation between changes in flow velocity and in EEG appears to be excellent in many studies. A decrease in $V_{mca}$ of more than 60% compared to preclamped baseline suggests inadequate CBF and the

need for an intraluminal shunt. TCD can also detect malfunctioning shunts due to kinking or thrombosis.

b. **Detection of microemboli.** Microemboli occur frequently during CEA; embolic events may outweigh hemodynamic events as an etiology of perioperative stroke. TCD can detect both air and particulate emboli.

c. **Diagnosis and treatment of postoperative hyperperfusion syndrome.** Approximately 1% of patients develop hyperperfusion syndrome after CEA, resulting in cerebral hemorrhage. TCD monitoring allows this diagnosis to be made and treatment to be implemented. Patients who develop the hyperperfusion syndrome show sustained elevation of flow velocities after release of carotid occlusion and often develop headaches. Prompt reduction of blood pressure is effective in normalizing the ipsilateral flow velocity and alleviating symptoms.

d. **Diagnosis and treatment of postoperative intimal flap or thrombosis.** Occlusion of the carotid artery postoperatively can occur from clot formation or the presence of an intimal flap. Sudden development of clinical symptoms in the postanesthesia care unit should prompt an immediate TCD examination. Emergent exploration may prevent an impending stroke.

2. **Cardiac surgery.** Stroke as a complication of cardiac surgical procedures occurs in up to 10% of patients. More subtle neurologic and cognitive dysfunction has been reported in 30% to 70% of patients. Adverse cerebral outcomes may be attributable to embolic events or hypoperfusion or both.

   a. **Cerebral emboli during CPB.** There is considerable evidence to suggest that the delivery of microemboli (air, platelet aggregate, and thrombus) into the cerebral circulation is responsible for the neuropsychological deterioration seen after bypass procedures. Patients who have the highest emboli counts have been observed to exhibit greater neurologic deterioration. Other studies have shown that the presence of arterial line filters reduces the incidence of emboli detected by TCD. Despite these published findings, TCD monitoring for emboli is still evolving and faces a number of technical challenges.

   b. **Cerebral perfusion during CPB.** Brain injury during CPB may also occur as a result of hypoperfusion. TCD has been used as a non-invasive tool for examining CBF in patients during cardiac surgical procedures performed under CPB. The validity of TCD as a surrogate estimate of CBF during CPB is unclear at present, however.

3. **Closed head injury.** TCD can be used to assess autoregulation and diagnose hyperemia and vasospasm as well as intracranial circulatory arrest. With elevation of ICP and cessation of CBF (intracranial circulatory arrest), a characteristic oscillating pattern is evident on TCD, with forward flow during systole and backward flow during diastole. In this context, although not widely used intraoperatively, TCD may be useful in monitoring head-injured patients who are undergoing non-neurosurgical procedures.

4. **Diagnosis of brain death.** When the oscillating pattern is persistent and reproducible, the American Academy of Neurology accepts it as a useful adjunct for the confirmation of brain death.

c. **Limitations of TCD as a routine intraoperative monitor**
   1. Most TCD monitors are designed for diagnostic rather than monitoring purposes. A fixation device is needed to allow continuous, reliable recording that does not interfere with the surgical procedure.
   2. Although most TCD equipment is fairly easy to operate, skill and training are nevertheless required and results are operator dependent.
   3. The successful transmission of ultrasound through the skull depends on the thickness of the skull, and the temporal bone thickness varies with gender, race, and age. The failure rate can be anywhere from 5% to 20%, depending on the patient population.

3. **Microvascular Doppler ultrasound** uses a 20-MHz probe applied directly to the surface of the vessel. This semi-quantitative technique allows the neurosurgeon to determine the patency of the vessel and whether flow is present in the sac during cerebral aneurysm surgery.
4. **Indocyanine green videoangiography** is the latest qualitative technique to assess blood flow. Using a software-enhanced microscope capable of reading near-infrared spectroscopy, blood flow can be visualized in the field under the microscope after intravenous injection of indocyanine green. This complements the microvascular Doppler ultrasound and has largely obviated the need for intraoperative angiography to determine both the patency of the parent vessel and the placement of the clip after aneurysm surgery. It has also been used successfully in surgery on the spine for vascular lesions.

C. **ICP**. Monitoring ICP facilitates the optimization of CPP and possibly prevents herniation. Monitoring methods currently available include ventriculostomy, subarachnoid bolt, epidural sensor, and fiberoptic intraparenchymal monitor; the latter is the most commonly used. The fiberoptic ICP monitors may allow simultaneous measurement of brain temperature, a function that is particularly useful in the ICU as fever exacerbates secondary brain injury. In addition, some monitors incorporate the measurement of LDF, arterial oxygen tension ($PaO_2$), arterial carbon dioxide tension ($PaCO_2$), and pH. Although the use of ICP monitoring is fairly common in the management of patients who have TBI in the ICU, the ICP monitor is available only as an intraoperative monitor when inserted preoperatively by the neurosurgeon.

## III. MONITORING CEREBRAL OXYGENATION AND METABOLISM

### A. Invasive monitoring

1. **Brain tissue oxygenation ($PbtO_2$).** In the setting of TBI, where secondary injury from ischemia/hypoxia is of concern, maintaining a reasonable CPP may not be adequate for brain preservation. Significant interpatient variability exists with respect to the CPP below which brain hypoxia is encountered. In this situation, monitoring $PbtO_2$ is useful for assessing the balance between oxygen supply and demand.

   The $PbtO_2$ monitor is placed intraparenchymally, typically in conjunction with an ICP monitor. As such, the monitor reveals regional or local, rather than global, oxygen tension, likely determined by a number of factors affecting the delivery of oxygen as well as local metabolic activity. These factors are not fully understood and may be counter-intuitive. For example, an increase in $PbtO_2$ may be achieved in a patient simply by increasing $PaO_2$, even without a significant increase in arterial oxygen content.

A brain tissue oxygen tension of 10 mm Hg is considered the threshold for brain hypoxia. This value can be increased either by increasing the supply of oxygen (supplemental $O_2$, raising CPP, treating anemia) or by decreasing demand (propofol or barbiturate therapy). In addition to identifying inadequate $PbtO_2$, this monitor may demonstrate hyperoxia, which could occur with absolute or relative cerebral hyperemia such as from loss of cerebral autoregulation.

Most studies have suggested that the use of $PbtO_2$ monitoring improves outcome in patients after TBI and subarachnoid hemorrhage. Some controversy exists regarding whether $PbtO_2$ monitors should be placed within a region of normal brain parenchyma or adjacent to the injured brain area.

2. **Jugular bulb venous oximetry monitoring.** In contrast to the *regional* information that the $PbtO_2$ monitor provides, the jugular bulb oximeter offers a continuous or intermittent estimate of the *global* balance between cerebral oxygen demand and supply. Provided the cerebral metabolic rate for oxygen consumption ($CMRO_2$) remains constant, calculation of the arteriovenous oxygen content allows estimation of the relative CBF. Even if $CMRO_2$ does not stay constant, the arteriovenous oxygen content difference always reflects the balance between the brain's oxygen demand and supply. Because arterial oxygenation is usually 100%, provided that hematocrit remains constant, the jugular venous oxygen saturation ($SjvO_2$) equally reflects this balance. The physiologic principle behind jugular venous oximetry is shown in Figure 3.4.
   a. Intraoperative cerebral ischemia from inadequate perfusion pressure or excessive hyperventilation can be diagnosed readily with $SjvO_2$. The influence of jugular venous desaturation on prognosis in patients after TBI has been documented, and continuous jugular venous oximetry has become a routine monitor in many neurointensive care units. The thermistor-tipped catheter also measures temperature approximating that of the brain. Its major limitations include its global nature and therefore inability to detect focal cerebral ischemia and its

$$CMRO_2 = CBF \times AVDO_2$$

$$AVDO_2 = CMRO_2 \div CBF$$

$$\begin{aligned} AVDO_2 &= \text{arterial } O_2 \text{content}(CaO_2) - \text{jugular venous } O_2 \text{ content}(CjvO_2) \\ &= (Hgb \times 1.39 \times SaO_2 + 0.003 \times PaO_2) - (Hgb \times 1.39 \times SjvO_2 + 0.003 \times PjvO_2) \\ &= Hgb \times 1.39(SaO_2 - SjvO_2) + 0.003(PaO_2 - PjvO_2) \\ &= Hgb \times 1.39(SaO_2 - SjvO_2)(\text{ignoring the amount of dissolved } O_2) \end{aligned}$$

Since, under most circumstances, $SaO_2 = 1$, thus $AVDO_2 \propto 1 - SjvO_2$ where $AVDO_2$ = arteriovenous $O_2$ content, $SjvO_2$ = jugular venous $O_2$ saturation, $PjvO_2$ = jugular venous $O_2$ tension, $SaO_2$ = arterial $O_2$ saturation, $PaO_2$ = arterial $O_2$ tension. Therefore, a change in $SjvO_2$ will reflect corresponding change in $AVDO_2$ provided hemoglobin saturation stays constant.

**FIGURE 3.4** Physiologic principles of jugular venous oximetry.

invasive nature. The advent of $PbtO_2$ monitoring has superceded the use of jugular venous oximetry in many centers.

b. **Interpretation of $SjvO_2$.** The normal arteriojugular difference for $O_2$ ($AVDO_2$) is 2.8 mcmol/mL or 6.3 vol% of oxygen (Range: 2.2 to 3.3 mcmol/mL, or 5 vol% to 7.5 vol%), and $SjvO_2$ is between 60% and 70%. When oxygen delivery is higher than oxygen demand, as in hyperemia, $AVDO_2$ decreases and $SjvO_2$ increases. During periods of global cerebral ischemia, $AVDO_2$ widens and $SjvO_2$ decreases.

   1. **Increased values.** An $SjvO_2$ value of more than 90% indicates absolute or relative hyperemia. This can occur as a result of reduced metabolic need (e.g., a comatose or brain-dead patient) or from excessive flow (e.g., severe hypercapnia). Patients who have cerebral arteriovenous malformations have a direct arterial shunt into the venous circulation and thus have an abnormally increased $SjvO_2$. Extracranial contamination, either from the facial vein or from rapid withdrawal in blood sampling (as for intermittent measurement), also results in an elevated value.
   2. **Normal values.** Although a normal balance between flow and metabolism results in a normal $SjvO_2$, it does not exclude the presence of focal ischemia. Because the blood in the jugular veins drains all areas of the brain, a discrete area of ischemia or infarction might not influence the overall level of saturation.
   3. **Decreased values.** On the other hand, $SjvO_2$ is sensitive to global cerebral ischemia. A value of < 50% reflects increased $O_2$ extraction and indicates the potential risk of ischemic injury. This may be from either an increase in metabolic demand, as in fever or seizure, that is not matched by an equivalent increase in flow or an absolute reduction in flow. A significant decrease in $O_2$-carrying capacity due to a decrease in hematocrit also leads to desaturation. Ischemia may also alter $CMRO_2$ and affect the interpretation of $SjvO_2$. As ischemia progresses to infarction, oxygen consumption decreases and $SjvO_2$ normalizes.

3. **Microdialysis catheters.** A small catheter, typically inserted in conjunction with an ICP or $PbtO_2$ monitor, allows sampling of small molecules in the interstitial fluid. The catheter, 0.6 mm in diameter, has a 10-mm dialysis membrane. Artificial cerebrospinal fluid (CSF) circulates through the catheter, allowing equilibration with the extracellular fluid and subsequent analysis of its chemical composition.

   a. **The value of microdialysis catheters is in determining the metabolic state of the brain and assessing the local cellular integrity.** Various markers are used in this task. Evaluation of the dialysate for glucose provides an assessment of the availability of energy substrate. An increasing lactate concentration and lactate/pyruvate ratio demonstrate the presence of anaerobic metabolism; these markers are sensitive to the onset of ischemia. High levels of glycerol suggest inadequate energy to maintain cellular integrity and the resultant breakdown in membrane integrity. Excitatory amino acids, such as glutamate, are both a marker for neuronal injury and a factor in its exacerbation. Finally, novel markers such as cytokines are under investigation for the information they may provide on the inflammatory status of the brain.

   b. Currently, the microdialysis catheter is primarily used in two situations: (i) extensive SAH where subsequent vasospasm is likely and (ii) TBI of sufficient severity to warrant ICP/CPP monitoring. In both situations, a significant risk exists for the development of secondary injury due to cerebral ischemia.

c. **Location of the microdialysis catheter** is important because it provides information regarding only a small surrounding region of brain. With **SAH**, the catheter should be placed in the region of the brain perfused by the vessel most likely at risk for vasospasm. Placement in **TBI** depends on the nature of the injury. With diffuse injury, the recommendation is to place the catheter in the right frontal region. A focal contusion warrants one catheter in the pericontusional area but not within the contusion and a second catheter in the normal brain.

B. **Non-invasive monitoring. NIRS or transcranial oximetry** measures cerebral regional oxygen saturation by measuring the near-infrared light that is reflected off the chromophobes in the brain, the most important of which are oxyhemoglobin, deoxyhemoglobin, and cytochrome A3. NIRS has been studied in a variety of clinical settings including CEA and hypothermic circulatory arrest. Its **major limitations** include the intersubject variability, the variable length of the optical path, the potential contamination from extracranial blood, and most important, the lack of a definable threshold. Because of the thin scalp and skull in the neonate and infant, NIRS holds promise in this patient population but remains an investigative tool in its present form.

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# 4 Improving Neurologic Recovery from Cerebral Ischemia

**Yunfang Joan Hou, James E. Cottrell, Baiping Lei, and Ira S. Kass**

## Illustrative Clinical Case

Madame X is a 60-year-old right-handed female who has a history of hypertension (HTN), diabetes, and hyperlipidemia. She was brought to the Emergency Department in an ambulance at 09:50 at which time she was noted to have right-sided weakness and drooping of her right lower face. She was conscious but unable to answer questions correctly. Her husband stated she was normal and talking with him at 09:00 during breakfast but when he returned from getting dressed for work at 09:30, she was lying on the couch and unable to move her right arm. When he asked what was wrong, she spoke but her words made no sense. He called 911. The ambulance took the patient to a hospital that had a dedicated Stroke Unit. A stroke code was called at 09:55 after immediate evaluation in the Emergency Department.

**Vital signs:** temperature, 36.4°C; heart rate, 98 beats/minute; respiratory rate, 18 breaths/minute; blood pressure, 180/90 mm Hg. General physical exam: unremarkable. Neurologic exam: awake and alert; could not answer questions about herself, place, or date; answered questions with words that did not make sense or go together ( fluent aphasia); right-sided weakness, right lower face droop, positive Babinski sign; left side normal.

**Diagnosis:** possible stroke of left middle cerebral artery; workup for administration of recombinant tissue plasminogen activator (rtPA) initiated. (See Table 4.1 for criteria to determine the eligibility of a patient for rtPA.) Important exclusion criteria include (1) history of intracranial hemorrhage, (2) blood pressure > 185/110 mm Hg, (3) evidence of active bleeding or acute trauma ( fracture), (4) stroke or head trauma in preceding 3 months, and (5) signs and symptoms suggestive of subarachnoid hemorrhage (SAH). IF EXCLUSION CRITERIA ARE NOT MET THEN: obtain computed tomographic (CT) scan of the head to rule out hemorrhagic stroke. IF GUIDELINES FOR rtPA ARE MET (see Table 4.1) AND ONSET OF SYMPTOMS WAS LESS THAN 3 HOURS BEFORE EVALUATION ( for Madame X, must be before 12:00 as she was last witnessed to be normal at 09:00 by her husband), THEN ADMINISTER rtPA. The time to treatment has been extended in some cases to 4.5 hours after the onset of symptoms (see Section IV-C.2). The sooner the treatment, the less the brain damage; *time = brain loss*. The goal is to start rtPA within 1 hour of entry into the Emergency Department.

## Chapter Highlights

- The best way to improve neurologic recovery from ischemia is to reduce the degree or the duration of the ischemia.
- Ischemia leads to acidosis, glutamate-induced neurotoxicity, sodium (Na) and calcium (Ca) influx, potassium (K) efflux, depolarization, loss of energy production, and free-radical formation. These changes in neurons

cause cell death by either necrosis (severe ischemia) or apoptosis (less severe ischemia).

- A focal ischemic lesion is induced by the obstruction of blood flow through a cerebral artery. This leads to two areas of insult: the core that is severely ischemic and the penumbra that receives some collateral blood flow and is less ischemic. Neurons die quickly in the core, mainly by necrosis; death in the penumbra is slower and is mainly by apoptosis. Reperfusion and drug therapy are targeted at reducing death in the penumbra of an ischemic lesion.
- rtPA has been demonstrated to improve outcome from ischemic stroke if administered within 3 hours of stroke onset. In certain patients, this has been extended to within 4.5 hours of onset. rtPA will exacerbate hemorrhagic stroke significantly and lead to uncontrolled bleeding in trauma patients. (See Table 4.1 for contraindications.)
- Maintaining physiologic parameters in the normal range can dramatically reduce ischemia and the damage it causes. It is important to avoid hyperthermia, hyperglycemia, hypotension, hypoxia, hypercapnia, and acidosis. Seizures must be rapidly and effectively treated as they clearly worsen outcome. High intracranial pressure (ICP) should also be avoided and treated if present.
- Mild hypothermia (32°C to 35°C) is recommended after cardiac arrest or neonatal asphyxia.
- The effectiveness of drugs for improving clinical outcome from ischemia has not been demonstrated. Barbiturates (thiopental) appear to be most beneficial although the clinical evidence is somewhat equivocal. Some animal evidence exists for beneficial effects of propofol and dexmedetomidine. Volatile anesthetics (isoflurane, sevoflurane, and desflurane) induce preconditioning protection in animals and this may be of benefit to patients. Xenon, erythropoietin, lidocaine, and magnesium have been effective in animal studies and are currently undergoing clinical trials.

## I. IMPORTANT QUESTIONS CONCERNING CEREBRAL PROTECTION

Neurosurgical, cardiac, and vascular procedures carry considerable risk of ischemic/hypoxic injury to the brain and may subject patients to perioperative stroke, long-term adverse neurocognitive outcome, or death.

**A. Outcome improvement.** In this chapter, we will discuss a number of drugs and measures that may provide cerebral protection. The fundamental question is **do they improve clinical outcome?**

1. It is important to note that the only treatment proven to improve outcome after ischemic stroke is reperfusion with **rtPA** within 3 hours of the onset of symptoms.
2. **Hypothermia** after cardiac arrest and neonatal birth asphyxia has been promising.
3. Most **clinical drug trials** have failed to improve outcome.
4. **Preventing the occurrence of ischemia** and **reducing the duration and the extent** of the ischemia have been the **most productive clinical strategies.**

**B. Importance of mechanisms.** In order to understand what may protect against and improve recovery from ischemic brain damage, it is first important to understand the cellular and the molecular mechanisms that cause neuronal damage from ischemic insults.

## II. THE ISCHEMIC BRAIN

**A. Cerebral ischemia** is defined as **perfusion *insufficient* to provide the supply of oxygen and nutrients needed for maintenance of neuronal integrity** (which utilizes 40% to 45% of the total cerebral metabolic rate for oxygen consumption [$CMRO_2$]) and **neuronal function** (which utilizes 55% to 60% of $CMRO_2$).

1. **Cellular integrity** involves basic cellular activities such as carbohydrate, lipid, and protein synthesis and the maintenance of ionic gradients and membrane integrity.
2. **Neuronal function** involves the generation and the transmission of nerve impulses and is manifested by the presence of electroencephalographic (**EEG**) activity.
3. **Ischemia leads to the depletion of adenosine triphosphate** (ATP), which is required for all active cellular processes. There is a hierarchy of ischemic damage in which **neuronal function is abolished *before* cellular integrity is lost.**

**B. Types of cerebral ischemia**

1. **Global cerebral ischemia**
   a. **Complete global ischemia** is the **complete cessation of blood flow to the brain** as is seen with cardiac arrest. Neuronal depolarization occurs in a few minutes. The hippocampus and the cerebral cortex are most vulnerable and the neurons in these regions die rapidly.
   b. **Incomplete global ischemia** occurs with hypotension or shock. The level of cerebral blood flow (CBF) is less than that required for normal function.
2. **Focal cerebral ischemia** involves the **occlusion of a single cerebral artery** leading to ischemia that is confined to a specific region in the brain.
   a. The **ischemic region** is composed of a severe ischemic area, **the core,** which is surrounded by a less severe ischemic area, **the penumbra.**
   b. The **neurons in the core die rapidly** whereas **those in the penumbra can survive for a longer period of time** and **can be rescued from infarction** if recanalization (i.e., reperfusion) occurs early. This provides a window of opportunity for therapeutic intervention.
   c. If the blood flow is not restored, however, the infarct core will grow progressively and the neurons in the penumbra will also die.

**C. The ischemic cascade (Fig. 4.1).** The ischemic insult evokes a cascade of pathophysiologic processes involving a multitude of chemical mediators of neuronal damage.

1. The **decreased availability of oxygen and glucose results in depletion of ATP.** This depletion occurs within 2 to 4 minutes of the onset of complete ischemia.
   a. **Phosphocreatine (PCr)** is a source of high-energy phosphate that allows the resynthesis of ATP from adenosine diphosphate (ADP). Brain PCr levels are normally three times those of ATP.
   b. PCr levels decrease first with the onset of ischemia and act as a buffer to maintain ATP levels. Once PCr levels fall, ATP levels diminish rapidly thereafter.
2. **Lactate levels increase** as a result of the anaerobic metabolism of glucose. Lactic acidosis aggravates ischemic damage and **promotes free-radical formation.** This is followed by the lipid peroxidation of cell membranes.
   a. The **continued supply of glucose** associated with **incomplete ischemia** contributes to **anaerobic glycolysis.** Lactic acid production is increased, which is thought to be the mechanism for the **heightened damage** seen with incomplete ischemia.

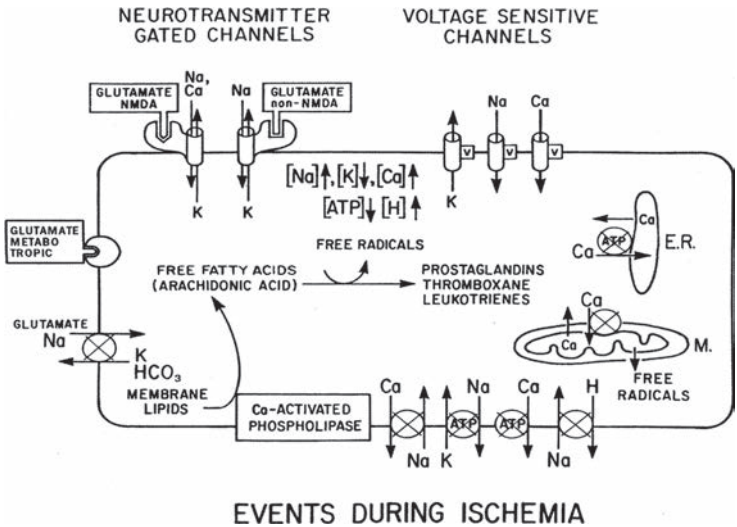


**FIGURE 4.1** Effect of ischemia on ion and metabolite levels in neurons. For clarity, ion channels are shown on the top membrane and ion pumps on the bottom membrane; their actual location can be on any membrane surface. Circles indicate energy-driven pumps; an x through the circle indicates that this pump is blocked or has reduced activity during ischemia. V indicates a voltage-dependent channel. NMDA, *N*-methyl-D-aspartic acid; ATP, adenosine triphosphate. (From Bendo AA, Kass IS, Hartung J, et al. Anesthesia for neurosurgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:746–789, with permission.)

- **b.** In contrast, **complete ischemia** results in the complete cessation of glycolysis and **no additional lactic acid production** once all the glucose and the glycogen have been depleted.
- **c.** **Hyperglycemia** is an independent risk factor for exacerbating ischemic damage. The primary mechanism for the increased damage appears to be the **enhanced production of lactate and intracellular acidosis.**

**3.** Cerebral ischemia increases the release of the excitatory amino acid (EAA) neurotransmitters **glutamate** and **aspartate.**

- **a.** Three **receptors for the excitatory neurotransmitters** are currently identified.
  - **1.** ***N*-methyl-D-aspartate (NMDA) receptors** mediate the influx of Na and Ca and the efflux of K through receptor-coupled ion channels. These channels are important for long-term potentiation, learning, and memory. The presence of **glycine** is necessary for activation of NMDA receptors by glutamate. **Magnesium** (Mg) blocks the channel at its physiologic concentration. This block can be overcome, however, by neuronal depolarization. The **NMDA channels open during hypoxia and ischemia. This leads to a large influx of Na and Ca,** which contributes to neuronal damage.
  - **2.** Alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid **(AMPA) receptors** mediate the influx of Na and the efflux of K. A small percentage of these channels have a subunit composition that can also allow Ca to pass through them. These channels **contribute**

**to damage by allowing Na into the cell,** which when the water comes with it, causes cell swelling and death and also **leads to depolarization, which facilitates the activation of the NMDA channels.**

3. **Kainate** receptors also mediate the influx of Na and the efflux of K.

b. **Glutamate** stimulates all three receptors, but **aspartate** affects only the NMDA receptor.

c. **Glutamate causes neuronal cell death** from immediate and delayed neurotoxicity.

1. In **immediate neurotoxicity,** glutamate activates the NMDA receptor, leading to the influx of Ca, Na, chloride (Cl), and water ($H_2O$), which results in cellular edema, membrane lysis, and cell death.
2. In **delayed neurotoxicity** (24 to 72 hours), the activated NMDA receptor promotes a cycle of damage initiated by the influx of Ca. This leads to the activation of phospholipases and proteases, the formation of free radicals and free fatty acids (FFAs) including arachidonic acid, and cell death.

4. **The increased cytosolic Ca concentration** is an important event in the ischemic cascade leading to cell death and is caused by several mechanisms.

a. **Depletion of ATP** results in failure of the energy-requiring Na/K ATPase-dependent ion pumps. Na and Cl build up intracellularly and K extracellularly. Influx of $H_2O$ and edema occur secondary to the intracellular ion level increase. The resulting **membrane depolarization leads to opening of voltage-sensitive Ca channels and Ca influx.**

b. The increase in intracellular Na leads to the **loss of the Na gradient,** which is an energy source for the **Na/Ca exchanger** that pumps Ca out of the cell.

c. Depletion of ATP results in the **failure of the plasma membrane Ca ATPase pump** and reduced pumping of Ca out of the cell.

d. Decreased ATP leads to **reduced activity of the Ca ATPase pump** in the endoplasmic reticulum (ER), which removes Ca from the cytosol and pumps it into the ER. The reduced pumping leads to a net loss of Ca from the ER.

e. EAA levels increase during ischemia, leading to stimulation of glutamate receptors and the **opening of NMDA-mediated Ca channels.**

5. Numerous effects of **high cytosolic Ca** form a common pathway **leading to neuronal cell destruction.**

a. **Increased intracellular Ca activates phospholipases $A_1$, $A_2$,** and **C,** which lead to the hydrolysis of membrane phospholipids and the release of FFAs. The loss of membrane phospholipids also results in mitochondrial and cell membrane damage.

1. **Arachidonic acid,** a major FFA, is a precursor to prostaglandins, leukotrienes, and free radicals.
2. Both **prostaglandins** (via the cyclooxygenase pathway) and **leukotrienes** (via lipoxygenase) lead to cerebral edema.
3. **Thromboxane $A_2$,** a prostaglandin derived from arachidonic acid with potent vasoconstrictor and platelet aggregation properties, potentiates ischemia and has been implicated in reperfusion injury.
4. **Free radicals cause lipid peroxidation** within neuronal cell membranes. This alters membrane function and damages cellular membranes.

b. Ca-activated proteases called **calpains** break down essential proteins and lead to damage.

c. **Ca influx into mitochondria** during ischemia can lead to mitochondrial dysfunction and damage.

6. **Free-radical formation**
   a. Free radicals can be formed independent of Ca activation **by incomplete oxidation in the mitochondria or by arachidonic acid metabolism** after ischemia and acidosis.
   b. Free radicals **damage proteins and membranes** and inhibit their function.
7. **Activation of cell death pathways: necrosis versus apoptosis**
   a. **Apoptosis is orderly programmed cell death** that requires energy to be carried out. It can be modulated and reversed by trophic factors (Fig. 4.2) and involves:
      1. **Milder ischemia**
      2. Mitochondria cytochrome C release and activation of caspase and endonuclease
      3. Compartmentalization of cell contents **(apoptosomes)**
      4. Reduced exposure of cell contents to outside, **which limits inflammation**
      5. **Primary form of cell death in the penumbra** of a region of focal ischemia
   b. **Necrosis leads to cell disintegration** and involves:
      1. **More severe ischemia**
      2. Cell and mitochondria **swelling** and rupture of lysosomes
      3. **Cell lysis and bursting**
      4. **Exposure of intracellular contents, which causes inflammation and damage to surrounding cells**
      5. **Primary form of cell death in the core** of an ischemic region

D. **Clinical aspects of ischemia**
   1. Of all body organs, **the brain is the most vulnerable to ischemia.** Loss of consciousness occurs within 15 seconds of cardiac arrest. Brain PCr

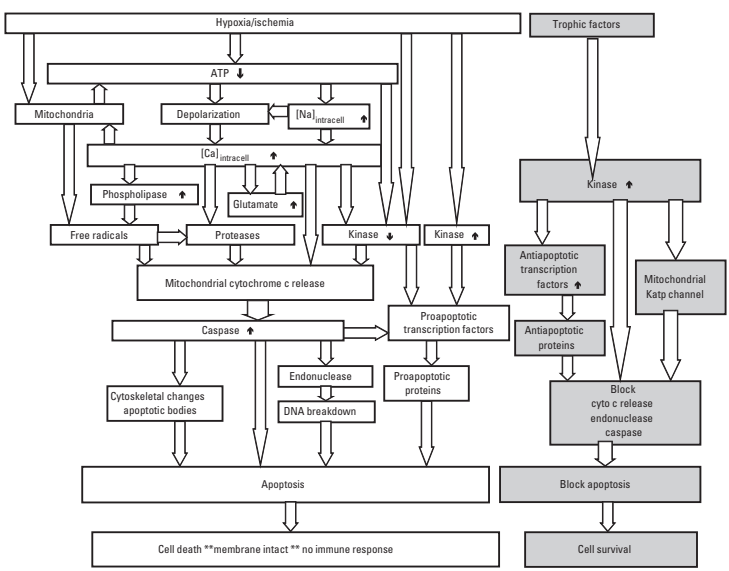


**FIGURE 4.2** Ischemic cascade leading to apoptosis. ATP, adenosine triphosphate. (From Kass IS. Brain metabolism and mechanisms of cerebral ischemia. In: Schwartz A, Butterworth J, Gross J, eds. *Refresher Courses in Anesthesiology.* Philadelphia, PA: Lippincott Williams & Wilkins, 2006;34:85–93.)

levels fall to very low levels within 1 minute. Glucose and ATP stores are exhausted within 4 to 5 minutes. Critical levels for CBF, cerebral perfusion pressure (CPP, the difference between the mean arterial pressure [MAP] and the intracranial pressure [ICP]), and the partial pressure of arterial oxygen ($PaO_2$) have been determined below which cerebral ischemia occurs with characteristic EEG changes. With prolongation of the cerebral ischemia, progression to isoelectricity in the EEG occurs quickly.

2. **Critical CBF** is 18 to 20 mL/100 g of brain/minute. The EEG becomes isoelectric at a CBF of 15 mL/100 g/minute. Metabolic failure occurs at a CBF of 10 mL/100 g/minute. The **penumbra** is a hypoperfused region that may remain viable for a period of time after the insult occurs.
3. **Critical CPP** is 50 mm Hg in the normal individual.
4. **Critical $PaO_2$** is 30 to 35 mm Hg in healthy awake patients.

E. **Reperfusion injury** refers to damage that occurs after the restoration of cerebral perfusion.
1. This can be due to **processes activated during ischemia that require energy or oxygen** for their culmination.
   a. **Free radicals** are increased in the period immediately after ischemia.
   b. **Apoptosis** requires energy-using processes to be completed. In the absence of energy, these cells die of necrosis.
2. Reperfusion injury can also be due in part to the inflammatory response of damaged tissue. In response to tissue damage, **white blood cells, carried to the area by the newly restored blood flow, release inflammatory mediators as well as free radicals,** which may exacerbate the neuronal damage.

## III. PATIENTS WHO WOULD BENEFIT FROM CEREBRAL PROTECTION

A. **Patients who require resuscitation from cerebral ischemic damage** include:
1. Intensive care unit (ICU) patients who have **traumatic but non-operative brain injury** such as diffuse axonal injury (DAI) with increased ICP and cerebral edema who may be candidates for barbiturate coma.
2. Patients who have **Reye's syndrome and cerebral edema with increased ICP.**
3. **Near-drowning** victims who have **anoxic encephalopathy,** cerebral edema, and intracranial hypertension.
4. Stroke patients who have **non-hemorrhagic stroke** who may be candidates for fibrinolytic therapy with rtPA (see Section IV-C).
5. Patients who have had a **cardiac arrest with re-establishment of circulation.**
6. Patients who have **neonatal birth asphyxia.**

B. **Candidates for cerebral protection also include patients who are at risk for cerebral ischemia/reperfusion injury:**
1. Patients who have an **increase in intracranial volume** from tumor, abscess, hematoma, hydrocephalus, or chronic cystic fluid collections with or without increased ICP who are scheduled for neurosurgical procedures.
2. Patients who are **scheduled for intracranial vascular procedures,** such as cerebral aneurysm coiling/clipping, excision of arteriovenous malformation (AVM) and cavernous angioma, and extracranial vascular procedures including carotid endarterectomy (CEA) and superficial temporal artery to middle cerebral artery (STA-MCA) bypass, which involve temporary vessel occlusion and the possibility of focal ischemia.
3. Patients who are **scheduled for the clipping or coiling of giant or complex basilar artery aneurysms.**
4. **Cardiopulmonary bypass (CPB) patients** who are at risk for either global cerebral ischemia from low-flow states or focal cerebral ischemia from multiple small emboli.

**C. Patients who are at risk for cardioembolic strokes**

Cardioembolism accounts for about 20% of all ischemic strokes. Cardioembolic strokes have a high recurrence rate and are often preventable, so that primary and secondary prevention strategies are important.

1. **Clinical features** of cardioembolic stroke may be helpful in distinguishing cardioembolism from other causes of cerebral ischemia, but they are not very sensitive. These include short time from sudden onset to maximal deficit, rapid recovery from symptoms, simultaneous or sequential strokes in different cerebral arterial territories, and onset of symptoms after a Valsalva-provoking activity.
2. **Antiplatelet** and **anticoagulant therapies** are mainstays in the prevention of cardioembolic stroke.
   a. Clinical trials demonstrated that **anticoagulation** is more effective than aspirin. Adjusted-dose warfarin (to maintain international normalized ratio [INR] at 2 to 3) is associated with a 60% reduction in the incidence of stroke. The reduction with aspirin is 20%.
   b. **Warfarin** is the first-line anticoagulant for most causes of cardioembolic stroke. Its use requires close monitoring of the INR. The beneficial effect of warfarin in reducing the risk of stroke must be balanced against the attendant risk of hemorrhagic complications.
   c. **Dabigatran**, 150 mg twice a day, has been approved for the prevention of stroke in patients with non-valvular atrial fibrillation. Its efficacy is similar to warfarin but does not require frequent blood tests for INR monitoring.
   d. Among antiplatelet drugs, **aspirin** has been proven in clinical trials to reduce the risk of cardioembolic stroke.
      1. Aspirin carries a **lower risk of bleeding** and requires **less medical monitoring** than do anticoagulants, but has a **lower stroke risk reduction.**
      2. Aspirin, 81 to 325 mg daily, is **recommended** as an alternative to vitamin K antagonists **in low-risk patients** and in **those who have contraindications to oral anticoagulation** (level of evidence A).
3. **Atrial fibrillation** accounts for up to 50% of all cardioembolic strokes, and is a major cause of stroke in the elderly.
   a. Both paroxysmal and chronic atrial fibrillation are associated with an increased risk of stroke.
   b. **Guidelines for stroke prevention** recommend the use of **anticoagulation** in patients who have more than one moderate risk factor (age: 75 years or older, hypertension, heart failure, ejection fraction < 35% or fractional shortening < 25, and diabetes mellitus) (level of evidence A).

## IV. CLINICAL CEREBRAL PROTECTION

**A. Rationale.** The goal is to maximize the available oxygen by **increasing oxygen supply (delivery)** and **decreasing oxygen demand.** Preservation of CBF and avoidance of hypoxia and hypoxemia are critical.

**B. Maintain physiologic parameters**

1. **Avoid hyperthermia** as there is clear evidence that above-normal temperatures markedly increase $CMRO_2$ and exacerbate ischemic damage. Mild hypothermia (around 34°C) may be beneficial in certain circumstances, but the clinical evidence for this is not conclusive.
2. **Avoid hyperglycemia and hypoglycemia.**
   a. The current recommendation is to keep the **serum glucose < 150 mg/dL,** as **hyperglycemia aggravates ischemia by worsening lactic acidosis.**

   b. However, **hypoglycemia** (serum glucose < 60 mg/dL) can also exacerbate ischemic brain injury by reducing ATP formation. The persistence of hypoglycemia results in seizure activity and neuronal injury. Thus, serum glucose should be monitored frequently, and hypoglycemia is scrupulously avoided.
3. **Avoid hypotension, hypoxia, and hypercapnia.** Induced hypotension can be detrimental in patients at risk for vasospasm.
4. **Normalization of increased ICP can be achieved by the following measures:**
   a. **Moderate hyperventilation** to a partial pressure of arterial carbon dioxide ($PaCO_2$) of 25 to 30 mm Hg. Hyperventilation is, however, only a **temporary measure to reduce CBF** by increasing the interstitial brain fluid pH, as $HCO_3$ transport leads to the normalization of pH and CBF within 8 hours.
   b. **Head elevation** to 30° in the neutral position
   c. **Mannitol and/or furosemide diuresis**
   d. Cerebrospinal fluid (**CSF**) **drainage** via ventriculostomy
   e. **Limited fluid restriction**
   f. **Barbiturate coma** in patients unresponsive to these techniques
5. **Prompt correction of acidosis and electrolyte imbalance** including Na and K abnormalities
6. **Avoid high hematocrit and hypercoagulated state**
   a. **Hemodilution** to a hematocrit of 32% to 34% increases CBF by decreasing viscosity, thereby improving oxygen delivery. However, excessive hemodilution decreases the oxygen-carrying capacity of blood.
   b. **Anticoagulation** may be beneficial if the risk of stroke is high.

C. **Recombinant tissue plasminogen activator (rtPA)**
1. **General guidelines:** Intravenous rtPA is the **only recognized treatment to improve outcome** from ischemic stroke.
   a. **Class I recommendations**
   1. **Intravenous rtPA,** 0.9 mg/kg; maximum dose = 90 mg, is recommended for selected patients who may be treated **within 3 hours of onset of ischemic stroke** (Class I, level of evidence A).
      2. Physicians should review the criteria outlined in Table 4.1 (which are modeled after those used in the NINDS trial) to determine the eligibility of the patient.
      3. A recommended regimen for observation and treatment of the patient is described in Table 4.2.
      4. This recommendation has not changed from previous statements.
      b. Besides **bleeding complications,** physicians should be aware of the potential side effect of **angioedema,** which may cause partial airway obstruction (Class I, level of evidence C). This recommendation has been added since publication of the previous guidelines.
2. **Recent updates. The time period for certain patients has been expanded to 4.5 hours after onset of symptoms.**
   a. Class I recommendation, level of evidence B
      **rtPA should be administered** to eligible patients who can be treated **within 3 to 4.5 hours after the onset of the stroke.**
   b. The eligibility criteria for treatment within 3 to 4.5 hours are similar to those for treatment within the earlier time frame, but there are **additional exclusion criteria:**
      1. Patients older than 80 years
      2. Patients taking oral anticoagulants who have an INR ≤ 1.7.
         For the 3 to 4.5–hour window, all patients receiving oral anticoagulants are excluded regardless of their INR.

TABLE 4.1 Criteria for Determination of Patients' Eligibility for rtPA

Diagnosis of ischemic stroke causing measurable neurologic deficit
The neurologic signs should not be clearing spontaneously
The neurologic signs should not be minor and isolated
Caution should be exercised in treating a patient who has major deficits
The symptoms of stroke should not be suggestive of subarachnoid hemorrhage
Onset of symptoms < 3 hours before beginning treatment
No head trauma or prior stroke in the previous 3 months
No myocardial infarction in the previous 3 months
No gastrointestinal or urinary tract hemorrhage in previous 21 days
No major surgery in the previous 14 days
No arterial puncture at a non-compressible site in the previous 7 days
No history of previous intracranial hemorrhage
Blood pressure not elevated (systolic < 185 mm Hg and diastolic < 110 mm Hg)
No evidence of active bleeding or acute trauma (fracture) on examination
Not taking an oral anticoagulant or, if anticoagulant being taken, INR ≤ 1.7
If receiving heparin in previous 48 hours, aPTT must be in normal range
Platelet count ≥ 100,000 $mm^3$
Blood glucose concentration ≥ 50 mg/dL (2.7 mmol/L)
No seizure with postictal residual neurologic impairments
CT does not show a multilobar infarction (hypodensity > 1/3 cerebral hemisphere)
Patient or family members understand the potential risks and benefits of treatment
INR indicates international normalized ratio; aPTT, activated partial thromboplastin time

Reprinted with permission Adam HP Jr, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke. *Stroke*. 2007;38:1655–1711.
CT, computed tomography; rtPA, recombinant tissue plasminogen activator.

TABLE 4.2 Treatment of Acute Ischemic Stroke with rtPA: Recommended Regimen

Intravenous infusion of rtPA at 0.9 mg/kg (maximum dose, 90 mg) over 60 min with 10% of the dose given as a bolus over 1 minute
Admit the patient to an intensive care or a stroke unit for monitoring
Perform neurologic assessments every 15 min during the infusion and every 30 min thereafter for the next 6 hours and then hourly until 24 hours after treatment
If the patient develops severe headache, acute hypertension, nausea, or vomiting, discontinue the infusion (if rtPA is being administered) and obtain emergency CT scan. Measure blood pressure every 15 min for the first 2 hours and subsequently every 30 minutes for the next 6 hours and then hourly until 24 hours after treatment
Increase the frequency of blood pressure measurements if the systolic blood pressure is > 180 mm Hg or if the diastolic blood pressure is > 105 mm Hg; administer antihypertensive medications to maintain blood pressure at or below these levels
Delay insertion of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters
Obtain a follow-up CT scan at 24 hours before starting to administer anticoagulants or antiplatelet drugs

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rtPA, recombinant tissue plasminogen activator; CT, computed tomography.

3. Patients who have a baseline National Institutes of Health (NIH) Stroke Scale score > 25
4. Patients who have a history of both stroke and diabetes

c. The relative utility of rtPA in this time frame as compared with other methods of thrombus dissolution or removal has not been established.

d. Class IIb Recommendation, Level of Evidence C
The efficacy of intravenous treatment with rtPA within 3 to 4.5 hours after stroke in patients who have these additional exclusion criteria is not well established and requires further study.

D. **Hypothermia** may be beneficial.

1. **Hypothermia** decreases both metabolic and functional activities of the brain.

a. The **temperature coefficient** (***$Q_{10}$***) represents the factor by which the $CMRO_2$ changes for every ten-degree change in temperature. For most biologic reactions, the $Q_{10}$ is approximately two (a 50% decrease in $CMRO_2$ for every 10°C decrease in temperature). Thus, if the normothermic brain (37°C) can tolerate 5 minutes of complete ischemia, at 27°C the brain should tolerate 10 minutes of ischemia.

b. Although hypothermia reduces $CMRO_2$ by roughly 7% for each degree Celsius, the mechanism is not uniformly linear.

1. The actual $Q_{10}$ is 2.2 to 2.4 **between 37°C and 27°C**, resulting in a reduction of > 50% in $CMRO_2$ at 27°C.
2. **Between 27°C and 17°C**, the $Q_{10}$ is approximately 5. This correlates with the gradual loss of neuronal function, as demonstrated by an isoelectric EEG (which occurs between 18°C and 21°C) and the ability of the brain to tolerate more prolonged ischemia than would be predicted based on a linear model.
3. **Below 17°C**, the $Q_{10}$ is 2.2 to 2.4 again.

2. **Neuroprotection from mild to moderate hypothermia** has been demonstrated in different **laboratory models** of brain injury. The **mechanism** is multifactorial and correlates with reduction in the cerebral metabolic rate and metabolism down-regulation, decreased Ca influx, decreased EAA release, preservation of protein synthesis and the blood–brain barrier, prevention of lipid peroxidation, a decrease in edema formation, neuroprotection of the white matter, and modulation of the inflammatory response and apoptotic cell death.

3. **Hypothermia shows promise clinically.**

a. Hypothermia at present is **recommended only for postcardiac arrest survivors** and **for neonatal birth asphyxia**. In these patients, mild hypothermia (32°C to 35°C) has been shown to improve survival rates and neurologic outcomes and is recommended by the European Resuscitation Council and American Heart Association guidelines.

b. The use of **induced hypothermia** in patients after traumatic brain injury (TBI), stroke, CPB, and intracranial aneurysm surgery may have beneficial effects in terms of both ICP reduction and possible neuroprotection. Clinical studies to date, however, do not yet justify the use of hypothermia for brain protection in these circumstances.

1. To achieve maximum benefit, hypothermia needs to be **instituted early**, directed to a defined endpoint, and maintained for a prolonged period.
2. The patients who have been shown to be **more responsive to therapeutic hypothermia** in clinical trials include younger patients

(< 45 years of age) and those who have severe TBI with a Glasgow Coma Scale score of four to seven on admission to the hospital.

3. In the case of ischemic stroke, hypothermia should be instituted in combination with the re-establishment of cerebral perfusion.
4. Evidence for the efficacy of mild hypothermia is absent for cerebral aneurysm clipping and CEA.

c. Although clinical research has not demonstrated an improvement in outcome, mild (32°C to 35°C) and moderate (26°C to 31°C) hypothermia have been used in heart procedures for many years. Similarly, deep hypothermia (18°C to 25°C) during circulatory arrest has also been induced in the repair of congenital heart disease, adult thoracic aortas, and giant or complex intracranial aneurysms.

d. There are numerous **serious complications** from hypothermia that limit its beneficial effect in preserving neuronal function. This is most evident during deep and moderate hypothermia.

1. **Cardiovascular complications** include myocardial depression, dysrhythmia, hypotension, and inadequate tissue perfusion.
2. **Coagulation disorders** include thrombocytopenia, fibrinolysis, and platelet dysfunction.
3. **Metabolism of drugs is delayed** with hypothermia.
4. **Shivering** can lead to oxygen desaturation, hemodynamic instability, and an increase in oxygen demand and carbon dioxide production.

E. **Anesthetics and adjuvant drugs**. No pharmacologic drug besides rtPA has been conclusively shown in a large clinical trial to improve outcome after ischemia. However, the results from small clinical trials and animals studies indicate certain drugs may be beneficial.

1. **Barbiturates** are useful for treating cerebral edema that does not respond to other approaches. They can produce isoelectricity of the EEG and have been considered to be effective cerebral protectants. Barbiturates are indicated for **elevated ICP or seizures that are unresponsive to other treatments**.

a. **Thiopental** decreases $CMRO_2$, CBF, cerebral blood volume (CBV), and ICP. $CO_2$ reactivity is preserved.

1. Thiopental has been found to **reduce the extent of cerebral injury in focal ischemia** in animal models, but has not been shown to improve outcome after global ischemia from cardiac arrest.
2. In humans, the ability of thiopental to improve neurologic outcome after heart surgery with CPB has only been demonstrated in one old study and this result has not been duplicated.
3. Protection involves the **reduction in $CMRO_2$** of up to 55% to 60% from blockade of neuronal activity. At this point, the EEG becomes isoelectric.
4. Thiopental may cause an **inverse steal** phenomenon whereby vasoconstriction in normal tissue improves perfusion of ischemic areas that do not vasoconstrict.
5. Thiopental is an effective **anticonvulsant**. Seizures drastically increase energy requirements and neuronal damage.
6. Other possible **protective mechanisms** include gamma-amino butyric acid (GABA) agonism, free-radical scavenging, reduced membrane lipid peroxidation and damage, NMDA antagonism, Ca channel blockade, and maintenance of protein synthesis.
7. The dose of thiopental used for focal ischemia is 3 to 5 mg/kg every 5 to 10 minutes titrated to EEG burst suppression up to a total of 15 to 20 mg/kg.

a. The need to maintain cardiovascular stability and avoid hypotension will determine the rate of administration.
b. The duration of action is short with the smaller dose delineated above. Larger doses can lead to a substantially prolonged duration of action.

b. The cerebral effects of **pentobarbital** are similar to those of thiopental.
1. Pentobarbital is **longer acting** with a duration of action of 3 to 4 hours. The elimination $t_{1/2}$ = 15 to 50 hours.
2. The **current clinical indication** for pentobarbital is limited to **barbiturate coma** in patients who have increased ICP resistant to standard therapy.
3. A loading **dose** of 3 to 10 mg/kg over 0.5 to 3 hours is given, followed by a maintenance infusion of 0.5 to 3 mg/kg/hour titrated to EEG burst suppression. The currently accepted therapeutic plasma concentration of pentobarbital is 2.5 to 4 mg/dL.

2. **Etomidate** is a short-acting imidazole compound that, like barbiturates, **causes cerebral vasoconstriction**. EEG burst suppression occurs with higher doses. The administration of induction doses of etomidate has been associated with cerebral desaturation. Studies have not shown any beneficial effect when etomidate is given after cerebral ischemia.
a. **Etomidate reduces $CMRO_2$ (by as much as 50%), CBF, and ICP** while maintaining cardiovascular stability and CPP. $CO_2$ reactivity is preserved.
b. Although etomidate significantly reduces brain metabolism, experimental studies have shown that etomidate increases the brain infarct size in certain circumstances. Thus, etomidate is not used to reduce injury from cerebral ischemia.
c. Etomidate can cause **adrenocortical suppression** for up to 24 hours after a single induction dose through inhibition of 11 beta-hydroxylase. This may be of clinical concern when etomidate is used as an infusion, especially in patients who are not concomitantly receiving steroids.
d. Myoclonic activity has been reported with etomidate and seizures may occur.

3. **Propofol** (2,6-diisopropylphenol), a short-acting drug used for induction and maintenance of anesthesia, has a cerebrovascular profile that is similar to that of barbiturates.
a. **Propofol decreases $CMRO_2$, ICP, and CBF**. The reduction of CBF is larger than the reduction of $CMRO_2$ (via possible direct cerebrovasoconstriction). Hemodynamic depression decreases CPP more than with barbiturates. Therefore, it is important to maintain MAP and CPP when propofol is given to treat intracranial hypertension.
b. Propofol has been shown to **protect the brain against focal cerebral ischemia in animal models** when initiated concurrently with a stroke or delayed up to 2 hours after the onset of ischemia. The neuroprotection is not sustained, however, beyond a period of 1 week. The beneficial effects of propofol after brain ischemia have not been examined in patients. The **possible neuroprotective mechanisms** include reduction in the $CMRO_2$, potentiation of GABA-mediated inhibition, and altered CBF, which may involve a beneficial redistribution of flow.
c. **Propofol interferes minimally with electrophysiologic monitoring**, including motor evoked potentials. Burst suppression of the EEG occurs with large doses of propofol. Thus, propofol seems to be **a favorable anesthetic for a variety of neurosurgical procedures.**

4. **Benzodiazepines** are sedative-hypnotic drugs most commonly used as anesthetic adjuncts.
   a. **General effects**
      1. Benzodiazepines **enhance the inhibitory GABA neurotransmission and decrease $CMRO_2$ and CBF while preserving $CO_2$ reactivity.** ICP may be decreased slightly.
      2. Benzodiazepines are potent **anticonvulsants**. Preventing or stopping seizures when they occur clearly improves neurologic outcome.
      3. They also produce **amnesia and anxiolysis**.
   b. **Diazepam** is used as an oral premedicant at a dose of 0.1 to 0.25 mg/kg.
      1. Its prolonged **elimination $t_{½}$ of 21 to 37 hours limits its use in neurosurgical patients** in whom prompt emergence and postoperative neurologic assessment are critical.
      2. Diazepam is an effective treatment for **status epilepticus**.
   c. **Midazolam** has an elimination $t_{½}$ of 1 to 4 hours. The intravenous dose of midazolam for premedication is 0.5 to 2.5 mg up to 0.1 mg/kg. Excessive sedation and the possibility of **hypoventilation-induced hypercapnia should be avoided** especially in patients at risk for increased ICP.
   d. **Lorazepam** is an effective premedicant in doses of either 0.5 to 4 mg by mouth or 2 to 4 mg intravenously or intramuscularly. Like diazepam, its **use is limited in neurosurgery by an elimination $t_{½}$ of 10 to 20 hours**.
5. **Dexmedetomidine,** an alpha 2 agonist, decreases central sympathetic activity by decreasing plasma norepinephrine release. It has **sedative, analgesic, sympatholytic, and anxiolytic effects *without* causing significant respiratory depression.**
   a. Dexmedetomidine provides effective sedation and shortens the time to extubation when compared to midazolam. It is **indicated for sedation of critically ill ICU patients**.
   b. Dexmedetomidine **decreases the minimum alveolar concentration (MAC) for halothane and isoflurane.** It is used as an adjunct for sedation and general anesthesia.
   c. Dexmedetomidine has been found to be **neuroprotective in animal models** of focal ischemia, perhaps because excess catecholamine levels correlate with increased neuronal damage from an ischemic insult.
   d. **In animal studies, dexmedetomidine decreases CBF without significantly altering $CMRO_2$.** However, the decrease in the CBF/$CMRO_2$ ratio is not observed in humans.
6. **Ketamine,** a phencyclidine derivative, produces dissociative anesthesia.
   a. Ketamine **markedly increases ICP and CBF** (60%) via cerebrovasodilatation. The $CMRO_2$ is unchanged or slightly increased. Autoregulation is abolished. Thus, ketamine is not a first choice in patients who have intracranial hypertension.
   b. **Seizures** can occur.
   c. Although it is a non-competitive NMDA antagonist, ketamine is **not recommended for patients who have intracranial pathology**.
7. **Lidocaine**, a Na channel-blocking drug, is commonly used as an adjuvant in neuroanesthesia. There is evidence that it improves neurologic outcome.
   a. Lidocaine's **clinical effects are determined by the blood concentration**. It causes sedation at low concentrations, but seizures occur at toxic doses, which clearly worsen outcome.

b. Lidocaine **reduces $CMRO_2$** with non–seizure-inducing doses. When administered after EEG isoelectricity induced by pentobarbital, lidocaine may decrease $CMRO_2$ by an additional 15% to 20%.
c. At a clinically recommended antiarrhythmic dose (1.5 mg/kg), lidocaine has been shown to **reduce ischemic damage in animals**. Clinical studies are not consistent: some show protection and others do not.
d. Lidocaine also **blunts the hemodynamic response to intubation** and other stressful manipulations by increasing anesthetic depth. As a result, it prevents an elevation in ICP in these situations.

8. **Inhaled anesthetics**
All potent inhaled anesthetics are **cerebrovasodilators** and thereby **increase CBF and ICP** to different degrees. This effect can be attenuated by prior hyperventilation. The volatile anesthetics also **decrease $CMRO_2$** while uncoupling CBF and $CMRO_2$. **Autoregulation is impaired,** but **$CO_2$ reactivity is preserved**. Volatile anesthetics have been shown to **delay neuronal death and reduce ischemic cerebral injury** in a variety of ischemic models.
a. **Isoflurane** causes **a large decrease in $CMRO_2$** (40% to 50%) and only a small increase in CBF.
1. The EEG becomes isoelectric at 2 MAC or 2.4%.
2. Isoflurane has no effect on the production of CSF but does increase CSF resorption.
3. Isoflurane may also offer **protection after brain ischemia**.
a. Studies of isoflurane **in animal models** of ischemia and hypoxemia have shown some limited protection from isoflurane.
b. **Preconditioning** with isoflurane seems to confer tolerance to ischemia and some neuroprotection in animal models.
b. The **cerebral effects** of **sevoflurane** are similar to those of isoflurane.
1. Both cause a **slight increase in CBF and ICP** and **a decrease in $CMRO_2$**.
2. **Nephrotoxic inorganic fluoride may accumulate** when patients receive sevoflurane for prolonged periods of time.
3. **Induction** and **emergence** are **rapid**.
4. **Preconditioning** with sevoflurane and subsequent cerebral protection after brain ischemia have been demonstrated in animals.
c. **Desflurane** is **similar to isoflurane** in its cerebrovascular profile.
1. **Induction** and **emergence** with desflurane are **rapid**.
2. Unlike isoflurane**, ICP may increase** despite normocapnia with desflurane.
3. Desflurane may also be **protective after brain ischemia**. Studies with hypoxia and incomplete cerebral ischemia in rats have shown cerebral protective effects from desflurane, which are similar to those with isoflurane and sevoflurane.

9. **Nitrous oxide**
a. Nitrous oxide **increases CBF, $CMRO_2$, and ICP**. The increase in CBF is attenuated by hypocapnia and intravenous drugs including barbiturates, opioids, benzodiazepines, and propofol.
b. Nitrous oxide is **32 times more soluble in blood than nitrogen** and is capable of diffusing into air-containing body cavities with extreme rapidity. Thus, nitrous oxide can **enlarge an air embolus**.
1. Nitrous oxide is **avoided** in the presence of pneumocephalus and in any surgical procedure within 2 weeks of a craniotomy in which nitrous oxide was used.
2. Nitrous oxide is also discontinued immediately if air embolism is suspected and may increase neurologic deficits after brain injury.

10. **Anticonvulsant drugs** are indicated in patients at risk for seizures including individuals who have epilepsy, head trauma, or craniotomy, and their administration is continued into the postoperative period.
    a. **Seizure activity exacerbates the effects of ischemia,** which can worsen outcome. CBF, $CMRO_2$, and intracellular Ca increase during seizures, and EAA neurotransmitters, including glutamate, are released.
    b. Once a seizure occurs, the patient's **airway must be immediately secured** and adequate ventilation ensured to prevent hypoxemia and hypercapnia.
    c. Anticonvulsant therapy is administered promptly:
        1. **Diazepam,** 2 to 20 mg; **midazolam,** 1 to 5 mg; **thiopental,** 25 to 100 mg; and **pentobarbital,** 100 mg (after 1 minute additional doses may be given up to 500 mg), are effective for treating seizures.
        2. **Fosphenytoin,** 15 to 20 mg phenytoin equivalents (PE)/kg, or **phenytoin**, 15 mg/kg, may be administered to prevent further seizure activity once the acute episode has been terminated.
            a. Fosphenytoin, 75 mg, is equivalent to phenytoin, 50 mg, and has the advantage of increased speed of administration (up to 150 mg PE/minute).
            b. Phenytoin administration is limited to 50 mg/minute because it may induce hypotension.
            c. The loading dose of fosphenytoin can be given in 5 to 7 minutes, whereas the equivalent dose of phenytoin would require 15 to 20 minutes.

F. **Other pharmacologic approaches**
1. **Calcium channel-blocking drugs** should theoretically provide cerebral protection by vasodilatation and diminution of the consequences of Ca influx. However, their use was not shown to improve outcome from ischemia. They are recommended for prophylaxis against cerebral vasospasm after aneurysmal SAH.
    a. **Nimodipine decreases the incidence and the severity of vasospasm** after aneurysmal SAH. This is an approved use for the drug.
        1. The dose of nimodipine, presently available **only in oral form**, is 60 mg every 4 hours for 21 days after SAH. Hypotension may occur with the administration of nimodipine.
        2. **Do not give nimodipine intravenously** as it can cause life-threatening adverse events or death.
        3. Nimodipine presumably **reduces vasospasm** by blocking Ca influx into the vascular smooth muscle and thereby preventing its hypercontraction.
    b. **Nicardipine,** available for intravenous administration, has decreased ischemic damage in animal studies, but clinical trials have not shown improved neurologic outcome after ischemia.
    c. **Magnesium (Mg)** also reduces Ca influx into cells by blocking channels and pathways in addition to the voltage-sensitive Ca channels blocked by nimodipine and nicardipine. Mg also blocks transmitter release and NMDA channels (see below).
        1. **Mg** is the recommended the **treatment for pre-eclampsia and eclampsia**.
        2. **Mg** has shown **neuroprotection** in different models of focal cerebral ischemia. A clinical trial is currently underway examining its use for neuroprotection.

2. **Glutamate-receptor antagonists** were developed to prevent neuronal damage from the excessive accumulation of the excitatory neurotransmitter glutamate. The NMDA receptor antagonists have not demonstrated consistent neuroprotection in clinical studies. One of the difficulties has been the development of drugs that effectively penetrate the blood–brain barrier.
   a. **Dizocilpine maleate (MK-801)** is a non-competitive NMDA receptor antagonist whose beneficial effects in laboratory experiments may be partially attributable to drug-induced hypothermia. Dizocilpine is not approved for use in humans and does not appear to be promising.
   b. **Mg,** a non-competitive NMDA antagonist, binds within the ion channel, preventing ion flux, and may be helpful after brain injury.
   c. **Glycine binding-site antagonism** with HA-966 and 7-chlorokynurenic acid is still in the investigational stage but shows promise.
   d. **AMPA receptor antagonism** with 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo (f)quinazoline **(NBQX)** has proven beneficial when given after the ischemic insult in experimental models.
   e. **Xenon** is a non-competitive antagonist of the NMDA receptor and has been used as an anesthetic adjunct in general anesthesia. Unlike most general anesthetics, xenon has little or no effect on GABA receptors. It has shown **significant neuroprotective efficacy** in a variety of models.
3. **Sodium-channel blocking drugs**
   a. **Riluzole,** a sodium-channel blocking drug, may reduce glutamate release during ischemia.
   b. **Lamotrigine,** an anticonvulsant with sodium-channel blocking activity, is known to reduce glutamate release and may reduce ischemic damage.
   c. **Lidocaine** at a low antiarrhythmic dose has been shown to improve neurologic recovery in animals. Clinical studies with lidocaine have been ambiguous and a large study examining lidocaine protection is currently underway.
4. **Tirilazad** has been proposed for use in the treatment of stroke.
   a. A lipid-soluble 21-aminosteroid, tirilazad crosses the blood–brain barrier and acts as a lipid antioxidant, inhibiting free-radical formation and lipid peroxidation.
   b. Studies in animal models of stroke indicate protection only when tirilazad is administered before the ischemic event.
   c. No clinical trials with tirilazad have shown improved outcome after stroke to date. It even appeared to **worsen outcome marginally** when given to patients after an acute ischemic episode.
5. **Free-radical scavengers** including **superoxide dismutase (SOD), deferoxamine, vitamin E, mannitol,** and **glucocorticoids** all possess free-radical scavenging activity. The utility of SOD has been limited by its **short elimination** $t_{1/2}$ (8 minutes) and **poor blood–brain barrier penetration**. While glucocorticoids have membrane-stabilizing properties and decrease cerebral edema from brain tumors, they have not been shown to improve outcome in cerebral ischemia. The clinical usefulness of free-radical scavengers is still under investigation.
6. **Modification of arachidonic acid synthesis.** Ischemia-induced excess of the vasoconstrictor thromboxane relative to the vasodilator prostacyclin ($PGI_2$) has led to the development of **thromboxane-synthetase inhibitors** and **$PGI_2$-synthetase stimulation** to prevent excessive cerebral vasoconstriction.

7. **Nitric oxide (NO)** is a free radical with complex neuronal activity. **Nitric oxide synthase (NOS)** catalyzes the formation of NO from the amino acid L-arginine, which itself decreases neuronal damage in experimentally induced focal ischemia. Three forms of NOS have been discovered:
   a. **Neuronal NOS (nNOS)** enhances glutamate release and NMDA-mediated neurotoxicity. Selective nNOS inhibition has been shown to be neuroprotective.
   b. **Immunologic NOS (iNOS)** is not detectable in healthy tissue. Induction of iNOS causes delayed neuronal cell death and can exacerbate glutamate excitotoxicity. Inhibition of iNOS by **aminoguanidine** reduces ischemic damage in experimental models.
   c. Stimulation of **endothelial NOS (eNOS)** by an ischemia-induced increase in intracellular Ca improves CBF by dilatation of cerebral blood vessels and has been shown to reduce ischemic damage in a rodent model.
8. **Erythropoietin (EPO)** is a substance produced in the brain after hypoxic or ischemic insults. Primarily elaborated in adult mammalian astrocytes in the ischemic penumbra, EPO is thought to **reduce inflammation, inhibit neuronal apoptosis, and stimulate neurogenesis, angiogenesis, and production of the proteins of repair**. EPO may be effective when given after a stroke. It may be more effective, however, as a prophylactic protectant when given preoperatively. The neuroprotective property of EPO appears to be independent of its hematopoietic action. Non-hematopoietic analogs of EPO, such as asialoEPO, have been developed and are showing equivalent potency as neuroprotectants in the laboratory. These analogs do not increase the hematocrit and thus do not exacerbate the ischemic injury through an increase in blood viscosity.

G. **Neurogenesis**. Ischemia also stimulates neurogenesis. The new neurons migrate to the site of tissue injury and may participate in functional recovery. Activated neuronal stem cells contribute to stroke-induced neurogenesis and the migration of neuroblasts toward the infarct boundary in adult rats. Therapy for stroke in rats with a NO donor and human bone marrow stromal cells enhances angiogenesis and neurogenesis subsequent to middle cerebral artery occlusion.

## V. ISCHEMIC PRECONDITIONING

A. **Cerebral ischemic preconditioning** is induced by a short period of ischemia that is not severe enough or long enough to cause damage. This short-term exposure causes changes in the neurons that allow them to survive a longer and normally damaging period of ischemia.
   1. Preconditioning induces the formation of proteins that reduce damage and enhance repair in animal models of cerebral ischemia.
   2. Prodromal transient ischemic attacks (TIAs) may protect the brain during subsequent ischemic strokes.
   3. Ischemic preconditioning is not induced clinically due to its potential for causing ischemic damage in patients. A period of ischemic preconditioning that may be enough to induce damage in some patients might not be harmful in other patients. Indeed, certain vulnerable regions of the brain may always be at risk from ischemic preconditioning.

B. **Volatile anesthetics** have been shown to **induce preconditioning** and reduce neuronal damage in animals.
   1. Most of the studies have examined isoflurane or sevoflurane.
   2. These anesthetics may work by a metabotrophic mechanism that activates protein kinases, which in turn activate the proteins that reduce

ischemic damage. Isoflurane and sevoflurane may also cause the formation of proteins that reduce damage and enhance repair.

C. **Other experimental modalities induce preconditioning.** Experimental results with hyperbaric oxygen, normobaric 100% oxygen exposure, electroconvulsive shock, and the K channel-opening drug, diazoxide, have shown that all of these modalities can induce cerebral ischemic preconditioning in animals.

## VI. OTHER ANESTHETIC CONSIDERATIONS

A. Anesthesiologists may be consulted about the **management of cerebral edema** and **increased ICP** or the **induction and the maintenance of barbiturate coma.** These patients may also require sedation, analgesia, and neuromuscular blockade.

B. **Anesthesia duration and depth.** Minimizing the duration of the time during which the patient is deeply anesthetized may reduce neuronal damage by attenuating neuronal apoptosis. A growing body of evidence indicates that cumulative deep anesthesia time is an independent predictor of increased postoperative morbidity and mortality in adult patients.

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# 5 The Management of Pain in the Neurosurgical Patient

**Timothy R. Deer and Jason E. Pope**

## Illustrative Clinical Case

The patient is a 38-year-old female who underwent anterior fusion for the treatment of cervical disc C4–C5 herniation. The procedure was performed under general anesthesia with the patient in the supine position without incident. In the postoperative period, she complained of severe pain in her right arm and shoulder. Pain treatment was initiated with hydromorphone by patient-controlled analgesia (PCA), demand dosing only with an appropriate dose and dosing interval. Despite increased doses of the drug overnight, the patient rated her pain at 10/10. Her anxiety level became a major complaint, and she became tachycardic and hypertensive. The anesthesiologist was called for additional instructions.

Two milligrams of midazolam were given as an anxiolytic to assist in her comfort. Thirty minutes after this intervention, the nurse found the patient unresponsive, apneic, and without a pulse. Appropriate advanced cardiac life support was performed, and her airway was secured although, as suspected, the intubation was difficult secondary to the reduced neck extension from the recent fusion. She was transferred to the intensive care unit (ICU) where it was determined that the patient had suffered an extensive hypoxic insult to the brain and she was taken off life support 4 days later.

### ISSUES TO CONSIDER

1. Neuropathic pain before or after surgical correction may not respond well to opioids. The use of additional opioids can lead to respiratory depression, confusion, and in some cases hyperalgesia if the dose is sufficiently elevated.
2. The trachea of a patient undergoing cervical fusion may be very difficult to reintubate in the immediate postoperative period. Care should be taken in extubation and with sedation.
3. Opioids and benzodiazepines act synergistically to shift the carbon dioxide ($CO_2$) response curve down and to the right, requiring a higher level of $CO_2$ to initiate a breath. This can lead to clinically significant hypoventilation and apnea.
4. When treating acute postoperative neuropathic pain, the physician should consider a multimodal approach, employing neuropathic pain medications, including antidepressants, anticonvulsants, intravenous steroids, and low-dose opioids.

## Chapter Highlights

- The patient undergoing neurologic surgery should be evaluated closely before surgery for past pain history and previous responses to pain interventions with special attention to pain medications.

- A pain treatment plan should be developed collaboratively among the patient, anesthesiologist, and neurosurgeon before surgery. Multimodal and regional/neuraxial techniques, when appropriate, can lessen systemic side effects, improve postoperative pulmonary function, and shorten hospital stays.
- In many cases, the knowledge base for pain treatment exists, but clinical implementation is often limited. Because of these challenges, many patients have less than optimal treatment in the perioperative period.

## INTRODUCTION

The successful treatment of pain in the postoperative patient is important with all surgical specialties, but in many instances, it is more critical in the patient undergoing neurosurgical or spinal surgery. As illustrated above, pain can very commonly increase sympathetic tone, leading to hypertension, tachycardia, increased intracranial pressure (ICP), and changes in the vasomotor response, while misguided non-vigilant medication administration can also have deleterious effects.

Previously, Dunbar performed a comprehensive look at the issue of postoperative pain in the patient undergoing intracranial surgery, leading to some clarification of the issue. He compared those undergoing intracranial surgery to those who had select extracranial procedures. In this 200-patient retrospective study, the intracranial group did have significantly less pain than the comparison group ($p < 0.05$). A subset of intracranial patients did, however, have significantly more pain than others in the group: those requiring frontal craniotomies required more opioids and had elevated heart rates, blood pressure, and ICP. This analysis was inconclusive regarding those undergoing intracranial procedures. It is well substantiated that recovery from spinal surgery is more painful than from a craniotomy. In a recent presentation at the European Society of Regional Anesthesia in 2010, data suggested that a high-volume local anesthetic block in the cranium before incision may lower the overall opioid requirements in the postoperative period. This has not been substantiated in a prospective fashion.

In addition, there are inherent difficulties with managing postoperative pain in neurosurgical patients. The other factor that makes this issue more complex is the desire to limit postoperative sedation, as it is clinically imperative to obtain an accurate neurologic exam to guide treatment, as surrogate objective monitors are secondary and have inherent flaws. This gold-standard monitor can be affected adversely if the patient is sedated or obtunded. This conflict of treatment goals can lead to withholding pain medication and techniques, which is also deleterious to patient outcome. This has led to the increased use of mixed agonist/antagonist or partial agonist opioids and decreased use of traditional opioids, like morphine, in some neurosurgical ICUs. Opioids used inappropriately can, because of their known side-effect profiles of cough, nausea, vomiting, constipation, and respiratory depression, increase patient morbidity and mortality. However, recent studies have demonstrated that, when morphine and other potent opioids are titrated appropriately in the presence of postsurgical monitoring, the outcome is not altered.

It is not uncommon to awaken the patient in the operating room to demonstrate intact (or improved) motor and cognitive function, even with the use of intraoperative sensory and motor-system evoked potential monitors (SSEPS, MEPS). The use of short-acting inhalation or intravenous anesthetics has commonly produced an awake patient with poor analgesia. With the recent focus on pain as the fifth vital sign, it is imperative to treat the pain promptly and mindfully when the visual analog scale (VAS) exceeds 5/10. The anesthesia plan should

include both intraoperative and postoperative planning to ensure adequate analgesia and a reliable neurologic assessment. One does not preclude the other.

It is critical to realize that the treatment of pain in the neurosurgical patient may influence outcome in a variety of ways. The treatment focus needs to rest on alleviation of pain as the primary goal. Although the hemodynamic consequences of pain, including tachycardia and hypertension, can be treated with sympatholytics (e.g., beta-blocking drugs), this obviously does not provide analgesia. Studies have shown that pain in the postoperative period can adversely influence outcome independent of hemodynamic or intracranial endpoints. Proper pain control may stabilize hemodynamics, reduce blood pressure, and lower cerebral metabolic rate for oxygen consumption ($CMRO_2$), as well as lower the ICP.

In addition to pain issues, the perioperative period for the craniotomy patient is complex, and needs to be considered systemically, as the question becomes: how much is the intracranial compliance compromised? The surgical stress response causes elevations in total body oxygen consumption and serum catecholamine concentrations. Systemic hypertension is often present after neurosurgical procedures and has been linked to intracranial hemorrhage. Bleeding in the postoperative period can increase mortality, morbidity, and hospitalization. The cerebral consequences of hypertension in the recovery period include cerebral hyperemia and increased ICP. Prevention or control of pain is one of the major factors in limiting these adverse systemic effects.

Over the past decade, developments in intravenous opioids, new regional techniques, and local anesthetics have greatly enhanced our ability to treat this patient group. Pre-emptive analgesia improves the stability of the patient throughout the surgical experience. To minimize pain and decrease the stress response and hemodynamic changes, the surgeon and the anesthesiologist must work as a team. The importance of the anesthesiologist in decreasing anxiety, creating a treatment plan, and executing the plan is crucial to a successful surgical experience.

The surgeon can help reduce the immediate postoperative pain by infiltrating local anesthetic when appropriate, limiting surgical tissue trauma, and participating in the preoperative planning for postsurgical treatment.

Modern pain treatment methods have enabled neuroanesthesiologists to offer their patients numerous modalities for treating the mechanisms that cause pain. The options for interrupting the pain pathway can be divided into four components: transduction, transmission, modulation, and perception. Transduction occurs when one type of energy (temperature, mechanical) is converted to electrical energy via ionic charge separation (i.e., action potentials). Transmission is the transfer of a pain impulse through the nervous system by the first-order, second-order, and third-order neurons via the C and A delta fibers in the spinothalamic tracts to the thalamus and the cortex. Pain modulation describes the alteration of the pain signal by either augmentation or diminution as it travels. Perception is the subjective and emotional interpretation of pain, occurring in the somatosensory cortex and the limbic system. The patient's genetic, social, and cultural background influences this interpretation. By understanding this complex neural network and its interconnections, the opportunity to affect the pain response is great. The method chosen depends on the surgical procedure and the patient's comorbidities. The remaining sections of this chapter focus on the key points necessary to enhance outcome, patient satisfaction, and patient safety.

## I. PREOPERATIVE ASSESSMENT

### A. Preadmission and preoperative considerations

1. **Reducing anxiety.** Recent studies have shown that reducing anxiety preoperatively or in the immediate postoperative period enhances the

ease of controlling pain, blood pressure, and subsequent anxiety, reducing the need for pharmacologic intervention. It is important for the anesthesiologist to have an open dialogue with the patient, using part of the preoperative interview to discuss the plan for intraoperative pain treatment (if an awake test is used), along with postoperative pain management. Studies have demonstrated that a discussion of the patient's previous experiences, expectations, and fears can be as useful as some anxiolytic medications.

2. **Pain treatment history.** The prolonged use of oral opioids for chronic pain makes determining the baseline dose of opioids in chronic-pain patients somewhat difficult. The analgesic tolerance to opioid medication can influence dosing in both the intraoperative anesthetic and the postoperative periods. It is important to realize that the use of chronic medications is for a stable pain condition, and it will be necessary to supplement this baseline dose with additional medication. It is helpful to obtain a history of previous experiences with postoperative pain treatment, complications, and adverse reactions. The anesthesiologist should explain in detail the pain treatment plan; patient reassurance should be a high priority. It is well established that patients who have a history of chronic opioid use become tolerant to the opioid effects of nausea, vomiting, sedation, euphoria, and respiratory depression, whereas there is minimal tolerance to pupillary constriction and constipation.
3. **Understanding the procedure.** The physician providing the postoperative pain relief should understand the procedure being performed. An understanding of the patient's postsurgical mental status is helpful when the physician chooses a pain treatment plan. Techniques that require an alert patient, such as PCA, should be offered only to those who are able to comply with instructions. Regional anesthesia is possible if the procedure involves only limited portions of the spine.
4. **Role of coexisting disease.** The patient's non-surgical disease processes must be considered when tailoring a pain treatment plan. The review of systems is critical in determining what recommendations should be made. The following factors should be considered as part of the preoperative assessment.
   a. **Neurologic system.** The site of surgery and the perioperative morbidity should be considered. The patient's baseline cognitive and neurologic function also determines whether PCA can be used, and may provide insight regarding intracranial compliance. PCA can be used in children as young as 5 years of age but should be instituted with caution and requires the education of both patients and their parents.
   b. **Renal system.** A patient who has renal disease is prone to complications from drugs that are metabolized by the kidneys. Meperidine, for example, breaks down to normeperidine, which can cause seizures in these patients. Meperidine should be used in a limited fashion in any postsurgical patient, but the risk is high in those who have renal impairment. Morphine and hydromorphone are metabolized to M3G/M6G and H3G/M6G, respectively, and are renally excreted. The 6-glucuronide metabolite is pharmacologically active at the mu receptor, while the 3G metabolite has been implicated in lowering the seizure threshold.
   c. **Infectious disease.** Neuraxial procedures may be contraindicated in the patient who has either a systemic infection or a local infection at

the site of the proposed procedure. If a patient is bacteremic or has an infection at the surgical site, regional anesthesia is contraindicated.

d. **Hematologic system.** An epidural hematoma is a rare but disastrous complication of regional anesthesia. Factors that may contribute to this adverse outcome include abnormalities of the clotting cascade, a history of bleeding during previous surgery, and the use of low molecular weight heparin and other anticoagulants during the postoperative period. This condition may be evaluated both by history and by laboratory examination. If anticoagulation is continued perioperatively, care and timing of neuraxial regional anesthesia procedures, including catheter removal, require vigilance and an appreciation of the regional anesthesia complication rate and the anticoagulant's kinetics and pharmacodynamics. The reader is referred to the American Society of Regional Anesthesia (ASRA) 2010 Third Edition Guidelines.

e. **Cardiovascular system.** As noted in a previous section, the physiologic response to intracranial surgery includes hypertension, tachycardia, and catecholamine surges. An increase in blood pressure, heart rate, and catecholamines results in an increase in cardiac workload and may lead to ischemia in those who have perioperative risk factors. When in doubt, a cardiology consultation may be useful in planning the postoperative pain treatment plan. The other risk of the anesthetic and pain treatment is the issue of patients who are cardiovascularly unstable and require support. Furthermore, care must be taken regarding reduction of blood pressure in the presence of intracranial hypertension, as this could result in ischemic insults.

f. **Gastrointestinal system.** A history of ileus may be a cause for concern in regard to the use of narcotics and an epidural infusion of local anesthetic. Opioids can cause constipation, sympathectomy can cause increased peristalsis, and surgical neuraxial anesthesia can exacerbate ileus. In these cases, it is important to implement a bowel support regimen as a standard part of the program when using intravenous or oral opioids or epidural infusions.

g. **Genitourinary system.** A history of urinary retention may cause concern for regional neuraxial analgesia as neuraxially administered opioids and local anesthetics can cause urinary retention. In these cases, it is important to implement a urinary support regimen as a standard part of the program when using intravenous or oral opioids or epidural infusions.

B. **Summary of the preoperative period.** Appropriate preparation in the preoperative period is crucial to the overall success of the neurosurgical pain treatment program. The clinician should develop a mental checklist of assessment points before bringing the patient to the operating theater.

## II. THE IMPORTANCE OF PAIN TREATMENT

A. The patient undergoing neurosurgical intervention may develop many perioperative changes that can affect the overall outcome in the absence of pain management. The stress response, which is somewhat dependent on the complexity and the site of surgery, can affect the immunologic response, coagulation, cardiac function, hormonal response, oxygen consumption, and other systems crucial to the neurosurgical patient's recovery. The anesthesiologist has several options to blunt the stress

response, but these methods are successful only when the appropriate procedure is matched with the right patient.

**B.** The technique of postoperative pain control has been shown to have a major impact on outcome and pain reduction, as demonstrated in thoracic surgery. At the current time, no studies exist in the neurosurgical patient, and the significance of postoperative pain is unclear. Recent studies have suggested that total intravenous anesthesia (TIVA) may be associated with a lower incidence of nausea, vomiting, and pain, as compared to maintenance with volatile anesthetics alone.

## III. THE STRESS RESPONSE: AN OVERVIEW

**A. Changes in other organ systems.** The patient undergoing neurologic surgery is often very sensitive to subtle changes in other organ systems. The pathophysiologic changes associated with the stress response from surgical trauma can greatly affect the outcome from procedures with high risk of morbidity and mortality.

**B. Physiologic effects of the stress response.** The stress response includes an initial depressed phase and a subsequent hyperdynamic phase.

1. **The depressed phase.** In the initial portion of the stress response, the body responds by depressing most physiologic functions. This phase is brief in the surgical patient and might even be unidentifiable in some patients.
2. **The hyperdynamic phase.** The portion of the stress response of most concern to the anesthesiologist and most implicated in morbidity and mortality in the neurosurgical patient is the period of recovery after surgery. The duration of this phase is directly related to the amount of tissue trauma and the patient's pre-existing disease state. A characterization of this response is given below.
   a. **Endocrinologic changes.** Both catabolic and anabolic responses occur during this phase of the response.
      1. **Catabolic changes** include increases in several hormones: catecholamines, renin, angiotensin II, aldosterone, glucagon, cortisol, tumor necrosis factor, adrenocorticotropic hormone (ACTH), growth hormone, and interleukin (primarily IL-1 and IL-6). These changes lead to hemodynamic instability in some patients and perhaps to changes in cerebral blood flow (CBF) and ICP.
      2. **Anabolic changes** include decreases in insulin and testosterone. The changes can lead to hyperglycemia and imbalances in the hormonal axis, which impact wound healing and response to tissue trauma.
   b. **Metabolic changes.** The stress response's overall impact on patient outcome may be understood by considering the metabolic balance during this tumultuous time.
      1. The catabolic and the anabolic effects noted here create intense changes that adversely affect the patient's physiologic stability. These changes include breakdown of muscle and fat, shifts in insulin resistance, glucose intolerance, hyperglycemia, increased tissue oxidation with the creation of free radicals, sodium and water retention, increased acute-phase proteins, and fluid shifts and third spacing.
      2. The end effect is a change in fluid balance and protein, fat, and carbohydrate metabolism.

**C. Body system responses to the stress response**

1. Mechanisms to block the stress response have focused on beta blockade and blockade of other receptors. While these mechanisms are important,

the physician should not forget the importance of impacting the pain pathways. Using both techniques enhances the chance of blocking the stress response and limiting instability. The uninhibited stress response has been shown to increase cardiac workload, vascular tension, and oxygen consumption; adversely affect platelet function; and decrease fibrinolysis, renal perfusion, the urinary excretion of water, wastes, and electrolytes, hepatic function, immunocompetence, and the centrally mediated temperature regulation mechanisms.

2. Considering these enormous changes attendant upon the unbridled stress response, the importance of blunting this response in enhancing outcomes becomes critical. Pain treatment mechanisms utilized in limiting this systemic response are detailed. Although there are no randomized, controlled studies with clear outcome data, anecdotal evidence is overwhelmingly in support of treating pain to improve postsurgical outcomes, which are better than with tight control of hemodynamics alone.

## IV. MECHANISMS FOR BLUNTING THE STRESS RESPONSE TO SURGERY

A. **General anesthesia.** The use of inhalational anesthetics and intravenous anesthesia has been responsible for tremendous advances in improving the surgical experience and reducing pain during surgery. Unfortunately, although interrupting pain at the time of surgical insult, most anesthetic drugs have not been shown to block the metabolic and endocrine response to tissue trauma. A few anesthetic drugs have shown promise when compared to alternatives.

1. **Etomidate.** Intravenous etomidate may have some ability to blunt the adrenocortical system's response to stress. This effect is seen by a smaller rise in cortisol than expected with similar tissue trauma. Etomidate is thought to accomplish this by blocking enzymes in the cortisol synthesis pathway. The clinical benefit of this drug has not been proven in prospective randomized trials. Its prolonged recovery may also limit its use as a neuroanesthetic drug. Long-term administration can cause an Addisonian response and should be avoided.
2. **Inhalational drugs.** Sevoflurane and isoflurane are both useful drugs in low concentrations for intracranial surgery. Their usefulness in minimizing the stress response is limited, however, because they increase CBF, cerebral blood volume (CBV), and ICP in higher concentrations.
3. **High-dose opioids.** Recent years have shown a dramatic increase in the utilization of high-potency, short-acting opioids. Remifentanil, a compound of the 4-anilidopiperidine derivatives, is an ideal drug because of its ultrashort duration of action and metabolic independence of both hepatic and renal functions. The advantages of this drug may also lead to poor outcomes in regard to postprocedural pain complaints. The rapid increase in serum levels leads to an initial blunting of the stress response, but when the drug is discontinued, the patient is at risk for hyperalgesia and substantial increases in the stress response. It is critical that longer-acting opioids be administered when the intravenous infusion of short-acting opioids is discontinued. Remifentanil, like other intravenous opioids, often provides hemodynamic stability intraoperatively.
4. **Propofol.** Propofol has been used to reduce the wake-up time from general anesthesia and to blunt the initial stress and pain responses. Limited studies provide no evidence that this drug changes the immediate stress response, even when a slow reduction of dosage lengthens the wake-up phase until the patient has recovered baseline cognitive function.

Long-term administration needs to be used cautiously, as propofol infusion syndrome can occur, heralded by metabolic acidosis, rhabdomyolysis, acute renal failure, and cardiac failure. This can occur when doses as small as 4 to 5 mg/kg/hour are given for as little as 48 hours. The treatment is supportive and includes cessation of propofol.

5. **Alpha 2-adrenergic agonists.** Dexmedetomidine is a highly selective alpha 2 agonist (1620:1), as compared to clonidine (220:1), alpha 2 to alpha 1. Both clonidine and dexmedetomidine attenuate the response to laryngoscopy and reduce the minimum alveolar concentration (MAC), but both can cause hypotension. This effect needs to be mitigated in the presence of diminished intracranial compliance when CBF is pressure dependent. Dexmedetomidine provides sedation, anxiolysis, potent analgesia, and spontaneous breathing.

B. **Regional anesthesia: neuraxial.** Regional anesthetic techniques appear to have the greatest ability to block the stress response. The use of regional anesthetics in the neurosurgical patient is appropriate for only a few surgical techniques. Possible opportunities include spinal instrumentation, spinal repair, plexus operations, and surgery on peripheral nerves. The use of regional anesthesia is also limited in surgery of the neuraxis because it may delay the ability to do postoperative neurologic checks. While studies have shown epidural or intrathecal analgesia has decreased cardiac work load and improved postoperative nitrogen balance, renal function, glucose metabolism, oxygen consumption, coagulation and fibrinolysis, and hepatic and immunologic function, it has very little application in the neurosurgical patient.

C. **Peripheral nerve blockade.** Peripheral nerve blocks can blunt the initial response to surgery and may be used as the sole anesthetic. Common locations for peripheral nerve blockade include the brachial plexus, the cervical plexus, the femoral nerve, and peripheral nerves of the lower extremities. Their use in neurosurgical patients is limited, however, owing to the need to assess nerve function in the immediate postoperative period.

D. **Adrenergic blockade.** Clonidine has been used to blunt the stress response in patients after traumatic brain injury and after extensive neurologic surgery. The drug has also been shown to limit the development of vasogenic edema. The use of spinal or epidural alpha-adrenergic blockade has also been shown to reduce the stress response. It is unclear whether the reduction in adrenergic response with epidural or intrathecal clonidine is a direct effect of the alpha-adrenergic blockade or a response to the clonidine-induced analgesia. The use of systemic beta-adrenergic and alpha-adrenergic drugs has been shown to stabilize the hemodynamic response and the cerebral circulation.

E. **Non-steroidals.** The perioperative use of non-steroidal anti-inflammatory drugs (NSAIDs) may enhance the effectiveness of other techniques such as regional analgesia and anesthesia in blocking the stress response. The enhancement of regional analgesia and anesthesia is related to the NSAIDs' action at peripheral receptors involved in the tissue trauma cascade, along with central mechanisms including prostaglandin reduction. Caution needs to be exercised in treating patients who have known renal, cardiovascular, or gastrointestinal comorbidities. NSAIDs can interfere with platelet aggregation. NSAIDs may also adversely affect bone healing and have been implicated in failed lumbar fusions although retrospective reviews failed to demonstrate significance. Cyclooxygenase-2 (COX-2) inhibitors have been associated with increased cardiac morbidity when taken long-term. Data on acute perioperative administration of NSAIDs are lacking, however.

F. **Intravenous opioids.** The use of PCA has led to markedly improved patient satisfaction and improved pain scores. Studies have shown that opioid-induced pain control can improve immunologic function in the neurosurgical patient, which may lead to improved outcomes.
G. **Transcutaneous electrical nerve stimulation (TENS).** TENS has been used to treat postoperative pain. Current data do not support its efficacy in blunting the stress response.
H. **Psychological counseling.** As noted earlier in this chapter, biofeedback, music therapy, relaxation training, and simple conversation have been shown to lessen the stress response to surgery and reduce the overall stress response.

## V. INTRAOPERATIVE AND POSTOPERATIVE PAIN TREATMENT INTERVENTIONS

A. **Pre-emptive analgesia.** The effectiveness of pre-emptive analgesia lacks sound evidence as a study endpoint, and the implementation and the maintenance of therapy lack standardization. However, anecdotal evidence, largely from observational and retrospective reviews, supports the use of pre-emptive analgesia if the surgeon is amenable to its preoperative implementation.
   1. **Preoperative local anesthetic infiltration of the surgical field.** Diminishing the response to the initial incision may be crucial to the overall ability to provide effective postoperative pain relief, lessen the amount of anesthetic, and blunt the initial stage of the surgical stress response. Combining local anesthesia with general anesthesia can lower minimum alveolar concentration (MAC) when compared with using general anesthesia alone. Recovery is also superior with this technique. The combined use of general and local anesthesia may reduce the afferent barrage of surgical stimulation, and may also decrease postoperative pain and blunt the stress response. For these reasons, local anesthesia at the operative site should be considered even when the patient is scheduled to receive general anesthesia.
   2. **Anesthetics and systemic opioids.** There is no evidence that use of either high-dose opioids or inhalational drugs results in any variation in postoperative pain levels or differentially affects the need for pain medications.
   3. **Neuraxial anesthetic techniques.** Randomized controlled studies in the Japanese literature show that using epidural anesthesia for spine surgery has a pre-emptive effect on postoperative pain and leads to less perioperative bleeding. An understanding of these techniques is important to be able to use them properly.
B. **Neuraxial infusion therapy: epidural.** The use of epidural infusion therapy has increased in recent years as the primary method of acute pain control in patients undergoing surgical procedures involving peripheral nerves. The effective use of an epidural infusion requires a working knowledge of dermatomal anatomy, drug pharmacokinetics, drug synergies, and postoperative follow-up requirements.
   1. **Epidural location.** This is important in the dosage requirement and the infusion rate required for effective analgesia. Epidural placement should ideally be within two levels of the nerve root of primary focus for the surgical procedure.
   2. **Lipophilia.** This is crucial in drug selection for control of postoperative pain. A lipophilic drug such as fentanyl requires placement of the catheter at a level near the nerve innervating the surgical site. With morphine, which is much less lipid soluble, the catheter placement is less critical because the drug may spread over several interspaces before being absorbed. Hydromorphone has intermediate properties.

3. **Drug synergies.** For more than a decade, data have demonstrated an antinociceptive synergy between intrathecal morphine and local anesthetics during visceral and somatic nociception at dosages that do not impair motor function. The combination of local anesthetics and opioids offers a synergistic effect that leads to better analgesia than either drug infused alone. The infusion of local anesthetics has been shown to be the most effective method of blunting the stress response to tissue trauma. The addition of opioids helps eliminate the problem of tachyphylaxis that may develop with local anesthetics alone.

C. **Neuraxial infusion therapy: subarachnoid.** The use of spinal blockade in neurosurgical procedures is somewhat limited. Continuous spinal infusion therapy is generally discouraged because of the risk of cerebrospinal fluid leaks and infection as well as the confusion of the neurologic examination.

D. **Peripheral nerve blockade.** Peripheral nerve infusions of local anesthetic can be beneficial in the intraoperative period as well as for postoperative pain control. Common sites for continuous infusion include the brachial plexus and the femoral nerve. The use of a nerve stimulator or ultrasound guidance is helpful in assuring proper placement of the catheter. In general, a blunt-tipped needle is preferable to a sharp-beveled needle to reduce the risk of nerve injury.

E. **PCA.** The use of patient-controlled opioid administration may be applied to either intravenous or epidural delivery of medications. The neurosurgical patient presents a dilemma in the decision-making process. Careful attention must be given equally to the baseline preoperative function in regard to the ability to understand the use of a PCA system and to the expected postoperative cognitive function and the ability to utilize the system. A team approach involving the surgeon, anesthesiologist, and patient is needed when this mode of treatment is considered.

F. **Nurse-administered intermittent analgesia.** The classic method of postoperative pain relief in the neurosurgical patient is to have a nurse administer intravenous medications. This involves administration either on the patient's demand or at scheduled times at the request of the surgeon or the anesthesiologist. This mode of treatment is most appropriate in the patient with altered preoperative or postoperative cognitive function. The disadvantages of this method include delay in treatment, unnecessary suffering, and excessive sedation. It is also labor intensive.

G. **TENS.** There are no current data to support any change in postoperative outcome with the use of TENS for incisional pain. This method is difficult to use in the neurosurgical population because of the technical difficulties of application.

H. **Psychological counseling.** The addition of a psychologist to the postoperative acute pain team is helpful in improving the patient's ability to cope with the emotional stress of pain and disease. Unfortunately, because no good studies on the cost-effectiveness of adding this service exist, reimbursement may be difficult to obtain.

I. **Adjuvant drugs.** Anticonvulsants are often used after intracranial surgery to prevent seizures. These drugs may also offer some improvement in neuropathic pain syndromes and reduce the opioid requirements. The classic anticonvulsant drugs used for treating neuropathic pain include gabapentin, pregabulin, carbamazepine, oxycarbazepine phenytoin, lamictal, and topiramate. Baclofen, a GABA B agonist, has been used to treat spinal-induced spasticity and has been reported in some patients to improve pain of neuropathic origin. NSAIDs may reduce the opioid

requirement and improve outcome (Vide supra). Ziconitide, an alpha 2-delta postsynaptic calcium-channel blocking drug, commonly used for neuropathic pain, has been demonstrated to be effective in nociceptive pain, although a small therapeutic window and slow titration preclude its use as a given-as-needed medication. Ketamine, an NMDA receptor antagonist, is an excellent analgesic at subanesthetic doses, but as it increases $CMRO_2$, it should be avoided in patients at risk for extension of the ischemic penumbra.

**J.** The addition of antiemetics may reduce the postoperative nausea that can accompany opioids. Ondansetron is an attractive choice because it does not tend to potentiate the neurologic cognitive changes of the opioids and other pain medications, whereas droperidol and other dopaminergic medications may affect cognitive assessment. Tramadol is a mu-selective drug that has been shown in a few randomized studies to be less effective in the neurosurgical patient than either codeine or morphine. At higher doses of up to 75 mg, tramadol had improved efficacy but was not tolerated because of nausea and vomiting.

## VI. CREATING A CASE-SPECIFIC PAIN MANAGEMENT PLAN

**A. Intracranial procedures.** The patient who has had an intracranial procedure presents one of the most difficult problems in pain management. The use of regional anesthesia is not an option. Oversedating the patient can lead to hypercarbia and hypoxemia, reducing intracranial compliance. The cognitive function might be impaired because of the surgical area involved. Despite these limitations, controlling pain in this group is crucial because of the increased morbidity and mortality associated with uncontrolled hemodynamic response to pain and surgery.

**B. Procedures of the extremities.** The patient requiring surgery of the extremities gives the anesthesiologist many options. A discussion should occur regarding the patient's postoperative neurologic function and the need for serial functional checks. If the issue of sensory loss is minimal, the use of regional anesthesia is optimal because of the blunting of both pain and the stress response. Other techniques are also acceptable in this population. Care must be taken when regional anesthesia is employed, as vigilance is required for early indication of compartment syndrome.

**C. Procedures involving the spine.** When neurosurgery is performed on the spine, regional anesthesia may result in improved outcomes with a salutary effect on both postoperative pain and blood loss. These surgeries have no effect on the patient's cognitive response and are appropriate for postoperative PCA.

## VII. COMPLICATIONS OF PAIN MANAGEMENT IN NEUROSURGERY

**A. Mental status changes.** Serial neurologic checks are often an essential part of the postoperative course. If pain treatment interferes with this assessment, the overall benefit of the pain treatment may be lost. Establishing a team approach with the surgical team and the nursing team to balance the risks and benefits of pain therapies is crucial.

**B. Elevation of arterial carbon dioxide ($CO_2$).** The importance of ICP varies in the neurosurgical population. In patients in whom this is a significant factor, it is crucial to have some method of monitoring postoperative respiration and $CO_2$. While treating pain may improve hemodynamics and ensure the stability of the patient who has elevated ICP, the risk of excessive sedation and hypercarbia could be a possible problem, necessitating close observation. An increase in arterial $CO_2$ and a concomitant decrease in pH may be early indicators of impending problems from hypoventilation.

C. **Reduction of arterial oxygen ($O_2$).** Hypoxemia may create multiple problems in the patient who has sustained neuronal tissue trauma. Anaerobic metabolism occurs when neurons do not have enough $O_2$ substrate, which can result in a reduction of adenosine triphosphate and subsequent cell death. The use of supplemental $O_2$ and $O_2$ saturation monitoring as well as serial arterial blood gas measurement is essential in patients who are receiving systemic opioids.

D. **Hypotension.** In the patient who has had possible spinal cord trauma, the use of regional anesthesia can be helpful in controlling the stress response and subsequent systemic changes. The stress response-related fall in mean arterial pressure can decrease perfusion to the neurologic tissue and create ischemia. Careful attention to blood pressure is also crucial when using local anesthetics postoperatively.

E. **Cerebrospinal fluid leak.** The possibility of subarachnoid puncture when inserting an epidural catheter must be weighed against the benefit of the catheter. The risks of brain herniation from such a puncture must also be discussed with the surgeon if intracranial hypertension is part of the disease process.

F. **Nerve injury.** When using regional techniques in patients who have coexisting neurologic disease, the risk of nerve injury exists if the patient has abnormal nociception in the area of the proposed neural blockade. This risk also exists for the anesthetized or the heavily sedated patient who may be unable to respond to an inadvertent intraneural injection.

G. **Infection**

1. In the sedated patient, aspiration precautions should be ordered. This should be accompanied by frequent neurologic checks. If aspiration is a risk, sedating medications should be used with caution.
2. Regional anesthesia should be avoided in the patient with local infection at the site of the proposed regional procedure or in the patient with untreated or uncontrolled systemic infection.
3. The site of indwelling regional catheters should be checked regularly for infection. If the catheter is tunneled through a gel coat catheter, the risk of infection is more likely to be skin related.

## VIII. NEURAXIAL PAIN RELIEF PROCEDURES

A societal emphasis on the importance of treating patients who have chronic pain has led to an increase in the number of physicians who perform pain-relief procedures requiring anesthesia. Neurosurgeons, anesthesiologists, physiatrists, orthopedic surgeons, and neurologists now perform these procedures. Regardless of the specialty of the procedural physician, the anesthetic issues are the same in assuring achievement of a stable perioperative course.

A. **Spinal cord stimulation (SCS).** This procedure is most commonly performed for neuropathic or ischemic pain. Conditions that have the potential for successful treatment with SCS include postherpetic neuralgia, intercostal neuralgia, postlaminectomy pain ( failed back surgery syndrome), complex regional pain syndrome, phantom limb pain, angina, painful peripheral neuropathy, focal peripheral neuropathies, ischemic limb pain, and radiculitis/radiculopathy. The procedure is often separated into stages.

1. **The percutaneous trial.** In either the operating room or the radiology suite, a temporary stimulation system is inserted percutaneously under fluoroscopic guidance. Anesthesia is difficult because many of these patients have taken oral opioids for long periods and are tolerant to this class of drugs. The patients may require analgesia for insertion of the lead in either the lumbar or the cervical region, but they should remain

alert and responsive to avoid nerve root injury. They also need to be cognitively functional for the computer screening, which involves connecting the epidural lead to a handheld computer and electrically stimulating the nerve to obtain a paresthesia. As continued patient communication with the surgeon is required for accurate placement of the lead, conscious sedation is a necessity. Regional or general anesthesia is contraindicated in this setting.

2. **The surgical lead.** A surgical lead must be inserted in some patients who have more anatomically difficult spines or in whom a percutaneous lead has failed. This procedure usually requires general anesthesia and a wake-up period so the patient can discuss the perception of stimulation. The choice of anesthetic is challenging because the procedure itself requires a hemilaminectomy. Some surgeons request a general anesthetic with evoked potential monitoring for this procedure. NSAIDs should be avoided in this population because of the increased risk of bleeding.
3. **The permanent lead.** In most cases, the permanent implant involves the placement of both the lead and a generator. The permanent implant requires a complex anesthetic because the patient needs to be conversant during insertion of the lead and then more sedated for the tunneling and the creation of the generator pocket. In some cases, the lead from the trial procedure is used as a permanent lead. If that is the case, the patient returns to the operating room 1 to 4 weeks later for connection of the lead to a permanent generator. This procedure is most often performed under monitored anesthesia care (MAC) or general anesthesia as this stage requires no discussion. In either method, the location of the generator pocket determines the patient's positioning. If the generator is to be inserted in a different part of the body, then repositioning and draping may be necessary, affecting the anesthetic requirement.

B. **Peripheral field stimulation.** Advances in neurostimulation have broadened the scope and the application of peripheral nerve stimulation. Occipital nerve stimulation, for example, has been used in the treatment of headaches, including occipital neuralgia and migraine. As with SCS, the patient undergoes a percutaneous trial, and, if successful, a permanent implant. Anesthetic implications are similar between the two, although MAC or general anesthesia may be required for facial peripheral nerve stimulation or the insertion of leads directly over peripheral nerves.

C. **Intrathecal and epidural drug infusion systems.** The use of neuraxial infusions to treat pain that is unresponsive to oral or transdermal medications is becoming more common. Catheters may be tunneled and connected to an external infusion source or may be connected to an implantable system that is placed in the subcutaneous tissue.

1. **Totally implantable infusion systems.** Placing an intrathecal or epidural pump in the subcutaneous tissue involves two steps. First, a catheter must be inserted in the epidural or intrathecal space. The catheter is then connected to an infusion source. Anesthesia for these procedures might entail sedation with local anesthetic infiltration, or rarely neuraxial or general anesthesia. Each method has its risks and benefits. With general anesthesia, the patient is less likely to move, and the risk of nerve injury may be diminished. The risk of nerve injury may be increased, however, in the patient who is unresponsive and cannot report the development of a parasthesia. Spinal or epidural anesthesia avoids the general anesthetic, which may be advantageous for someone at high risk for pulmonary or cardiac complications. The use of sedation

with local anesthetic infiltration reduces the risk of undiagnosed nerve injury at the time of catheter insertion. In some patients, the stimulation involved in the tunneling and pocketing component of the procedure might not be successfully diminished with sedation and local infiltration alone, and a conversion to general anesthesia might be required during the course of the procedure.

2. **Externalized infusion systems.** In patients in whom the need for infusion is short term or in those with a life expectancy of < 3 months, an externalized system is often selected. The need for general anesthesia in this population is rare because of the lack of pocket creation. Although this procedure could be completed under neuraxial blockade or general anesthesia, the more common scenario is to use MAC with sedation and local infiltration.

D. **Radiofrequency nerve ablation.** The cost-effectiveness of radiofrequency (RF) ablation has led to a vast increase in the number of procedures performed annually in the United States and Europe. Traditional RF uses heat to destroy neural targets. Permutations of the traditional thermal ablation include pulsed RF and cooled RF. Pulsed RF was first introduced in 1998 and involves a neuromodulatory mechanism of action, which creates a histologic destructive lesion. Cooled RF is a thermal technique, like the traditional RF, but it creates a larger lesion that can compensate for the anatomic variability of the ablation target, achieving better outcomes, although this has recently come into question. The anesthetic in these cases is difficult. The patient must be sufficiently sedated to permit the placement of a large RF cannula and then allowed to awaken rapidly to be able to answer questions involving sensory, motor, and nociceptive input. The risks of nerve injury greatly increase in the patient who is not able to discern the computer stimulation pattern adequately. Because of these issues, the infusion or the bolus injection of kinetically-attractive medications that have short durations of action is often utilized.

E. **Spinal endoscopy.** In 1997, the United States Food and Drug Administration (FDA) approved the use of spinal endoscopy. In this method, the physician uses a fiberoptic scope to visualize and treat diseases of the spine by an epidural route. This procedure is stimulating and requires sedation in most cases. The use of general anesthesia is avoided, however, because of the risks of nerve damage in the patient who is unable to report a paresthesia.

F. **Minimally-invasive disc procedures.** New minimally invasive procedures are available to treat discogenic pain and herniations after appropriate diagnostic discography has demonstrated concordant pain reproduction. The use of percutaneous techniques to treat contained disc herniations and leaks of the annulus is a valuable option for patients who would like to avoid more invasive techniques such as fusion or artificial disc replacement. During these procedures, the physician needs to converse with the patient at all times. Anesthesia consists of local infiltration with or without mild sedation. These percutaneous procedures include biaculoplasty, intradiscal radiofrequency thermocoagulation, percutaneous nucleotomy, percutaneous decompression, ozone discolysis, and nucleoplasty,

G. **Minimally invasive lumbar decompression (MILD).** Recently, neurogenic claudication secondary to multiple etiologies, with significant ligamentum flavum hypertrophy, has been treated by percutaneous lumbar decompression. With the MILD procedure, the posterior portion of the hypertrophied ligamentum flavum is resected, enlarging central canal stenosis and improving multidimensional outcomes. There have been no reported complications and outcome data at 6 months have been

excellent. Conscious sedation or MAC is recommended. General anesthesia is contraindicated.

## IX. SUMMARY

**A.** The neurosurgical patient is a tremendous challenge to the team providing pain relief. Achieving balance between controlling pain and maintaining safety for the patient in the postoperative period is a difficult task. It is critical that the anesthesiologist, surgeon, and nursing staff work together to obtain a good result.

**B.** For neuraxial percutaneous procedures, it is crucial to provide analgesia while maintaining the patient's ability to be conversant. This not only ensures proper device placement, but also provides a necessary safety precaution in avoiding nerve injury.

**C.** As new drugs and techniques become available, it will be important to update our knowledge of the best methods by which to achieve safe and effective relief of pain in the neurosurgical patient.

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# 6 Anesthesia and Neurosurgery: A Communication Paradigm

**Eugenia Ayrian, Chelsia L. Varner, Yvette Marquez, and Steven L. Giannotta**

## Illustrative Clinical Case

A 43-year-old male with a past medical history of hypertension, antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, Hepatitis A, and renal failure presents with subarachnoid hemorrhage due to a ruptured right middle cerebral artery (MCA) aneurysm. The trachea was intubated for respiratory failure and a subclavian central line was placed in the intensive care unit (ICU). A cerebral angiogram and attempted coiling were performed prior to his presentation in the operating room (OR). The neurosurgeon then decided to pursue surgical intervention, and the patient was brought to the OR for right frontotemporal decompressive craniotomy and right MCA aneurysm clipping. Sevoflurane at 0.5 minimum alveolar concentration (MAC) inspired with oxygen ($O_2$) and propofol at 75 mcg/kg/minute were started. A radial arterial line was then placed.

After careful retraction and delicate dissection, the MCA aneurysm was located. A temporary clip was then placed on the proximal MCA. The patient was maintained on $FiO_2$ of 100% and in burst suppression using a high-dose propofol infusion while the temporary clip was in place. Spontaneous rupture of the right internal carotid artery (ICA) proximal to the temporary clip occurred during blunt dissection and further isolation of the vascular defect. Approximately 4 L of blood were lost before a temporary clip was successfully applied proximal to the ICA rupture. Nine units of PRBCs and four units of fresh frozen plasma (FFP) were transfused in addition to rapid colloid and crystalloid resuscitation. The propofol infusion was stopped during the massive blood loss and resuscitation. As a result of the patient's severe vasculitis and the friable vasculature, placement of a permanent clip was very challenging. With each attempt to place a clip, the artery wall would rupture. Accordingly, a decision was then made to place the clip on the right ICA permanently. Once resuscitated, the patient was returned to the ICU.

Despite permanent clipping of the right ICA, the patient began to follow simple commands on postop day one although he did have significant left-sided paralysis. His trachea was extubated on postop day two. He remained hospitalized for several weeks before being discharged to a rehabilitation facility.

## Chapter Highlights

Intracranial pressure (ICP) and Blood Pressure Management during Intracranial Hematoma Evacuation

- *Understanding intracranial hypertension*
- *Evaluation of ICP in the operating room*
- *Treatment of intracranial hypertension*

Management of Cerebral Aneurysm Rupture

- *Pre-exposure rupture*
- *Neurophysiologic monitoring*
- *Intraoperative rupture (IOR)*
- *Temporary clips and cerebral protection*

Bleeding During Excision of Spinal Cord Tumor

- *Preoperative evaluation*
- *Intraoperative management*

## INTRODUCTION

As technology in both anesthesia and neurosurgery advances, the need for a systems-based approach to operative procedures has become critical to the success of each operation. Strategies to improve safety and outcome in the OR environment must include **effective and efficient communication** among all physicians and personnel. Impediments to this level of communication in the OR include stress, differing knowledge base, and a steep hierarchy, among others. The aviation industry has successfully addressed deficits in information exchange, prompting the healthcare industry to adopt similar best practices. One of the more effective communication methodologies responsible for reducing error in the cockpit is the checklist.

In this chapter, we have introduced and discussed several critical intraoperative scenarios that demand coordinated responses from the neurosurgical and anesthetic teams. The physiologic rationale for appropriate action is presented in the context of efficient communication. We conclude each scenario with a simple checklist that can serve as a prompt to ensure human error remains at a minimum and to empower all members of the team to take ownership of their roles within this hierarchical structure.

### I. INTRACRANIAL AND BLOOD PRESSURE MANAGEMENT DURING INTRACRANIAL HEMATOMA EVACUATION

The intraoperative interaction between the neurosurgeon and the anesthesiologist requires communication that is at once clear, engaging, and open. During operative neurosurgical procedures, special attention to multiple factors on the part of the anesthesiologist is necessary to ensure that the patient does well from a neurologic standpoint. The anesthesiologist's management of both ICP and blood pressure (BP) in these cases goes beyond the general anesthesia protocol for general surgery procedures. Specifically, the control of increases in ICP and BP during the evacuation of an intracranial hematoma is a very important illustration of the necessity for close collaboration between the neurosurgeon and the anesthesiologist. To accomplish this, the anesthesiologist should focus on the following:

- Understanding of ICP dynamics
- Evaluation of ICP in the OR
- Treatment of intracranial hypertension

#### A. Intracranial hypertension

1. The **Monro–Kellie hypothesis** states that the sum of the intracranial volumes of blood, brain, cerebrospinal fluid (CSF), and other components (such as tumor, hematoma, and abscess) is stable. An increase in one of these components results in an equal decrease in another component or the pressure inside the intracranial compartment will begin to rise. The normal ICP in adults is < 10 to 15 mm Hg. Intracranial hypertension

produces pressure gradients that, if not treated emergently, result in herniation of brain tissue. Often, Cushing's Triad can be used as an indicator of elevated ICP before the actual measurement of ICP. The **hallmarks of Cushing's Triad are hypertension, bradycardia, and respiratory irregularities.** Intracranial hypertension can be caused by traumatic brain injury (TBI) with resultant cerebral edema, hyperemia, mass lesions (such as epidural and subdural hematoma), intraparenchymal hemorrhage, hemorrhagic contusion, foreign body, and depressed skull fracture. Other etiologies include hydrocephalus, hypoventilation, systemic hypertension, and venous sinus thrombosis. Specifically, when intracranial hematoma is the cause of the elevation in ICP, the goal is to ensure that tight control of ICP and BP is coupled with urgent removal of the mass lesion.

2. It is also important to ensure that **cerebral blood flow** (CBF) is not compromised to the point of neuronal loss, infarction, or even brain death. However, CBF is difficult to quantify as it requires specialized equipment for careful measurement at the bedside. In addition, assessment of intracranial dynamics by means of CBF is a relatively complex undertaking. While increasing ICP may be associated with decreases in CBF, other physiologic changes occur as well. Mean arterial pressure (MAP) may increase as the ICP increases. The cerebral vascular resistance (CVR) adjusts to the increase in MAP with a decrease in cerebral perfusion pressure (CPP), the difference between the MAP and the ICP, until vasodilatation reaches its peak, which usually occurs when CPP ≤ 50 mm Hg. An appropriate expedient is to view CPP as a predictor of CBF. Because of **cerebral autoregulation,** the mechanism whereby large changes in systemic BP produce only small changes in CBF, CPP would have to drop to below 40 mm Hg in the normal brain before CBF is impaired. This is the lower limit of autoregulation. In TBI, ICP ≥ 20 mm Hg may be more harmful than changes in CPP as long as CPP > 60 mm Hg.

**B. Measurement of ICP**

1. While various methodologies for measuring ICP are available, the gold standard is the **external ventricular drain** (EVD) or ventriculostomy. Depending on the rapidity of evacuation from the field to the hospital, EVDs are indicated for management of severe TBI when the Glasgow Coma Scale (GCS) score ≤ 8 after cardiopulmonary resuscitation and there is either an abnormal computed tomographic (CT) scan of the brain or a normal CT scan with ≥ 2 risk factors including age > 40 years, systolic BP < 90 mm Hg, and decerebrate or decorticate posturing on motor exam.
2. **ICP waveforms**
   a. The ICP **waveform is affected by BP and respiratory patterns.** Specifically, alterations in the normal ICP tracing are derived from small pulsations transmitted from the systemic BP to the intracranial cavity. These BP pulsations are superimposed on slower oscillations caused by the respiratory cycle. In mechanically ventilated patients, the superior vena cava pressure increases during inspiration, which reduces venous outflow from the cranium, causing an elevation in ICP.
   b. **Pathologic waveforms** appear as the ICP increases, cerebral compliance decreases, arterial pulses become more pronounced, and venous components disappear. Pathologic waveforms include Lundberg A, B, and C types. **Lundberg A waves or plateau waves** are ICP elevations to > 50 mm Hg lasting 5 to 20 minutes. These waves are accompanied by a simultaneous increase in MAP, but it is not clearly understood if the change in MAP is the cause or effect. **Lundberg B waves or pressure pulses** have an amplitude of 50 mm Hg and occur every 30 seconds to 2 minutes. Lundberg C waves have an amplitude of 20 mm Hg and

a frequency of four to eight per minute; they are seen in the normal ICP waveform, but high-amplitude C waves may be superimposed on plateau waves. Regardless of the waveform, if the ICP > 20 mm Hg, the anesthesiologist should alert the neurosurgeon of the elevation to determine how and when to proceed.

**C. Treatment of intracranial hypertension**

The current practice for managing intracranial hypertension is to use an ICP of 20 to 25 mm Hg as the upper limit of normal. If the patient has an EVD, it is important to zero the transducer at the level of the external auditory canal as this approximates the level of the foramen of Monroe. The following ways to control ICP should be initiated by the anesthesiologist:

1. Elevate the head to approximately 30 degrees.
2. Ventilate to normocarbia: arterial carbon dioxide tension ($PaCO_2$) of 35 to 40 mm Hg.
3. Hyperventilate to $PaCO_2$ of 30 to 35 mm Hg if ICP > 20 to 25 mm Hg.
4. Use sedation and pharmacologic paralysis with thiopental, propofol, or fentanyl and a non-depolarizing muscle relaxant.
5. Drain 3 to 5 mL CSF if a ventriculostomy is present.
6. Give mannitol, 0.25 to 1 g/kg; then 0.25 g/kg every 6 hours; increase dose if needed and serum osmolality < 320 mOsm/L
   a. Mannitol increases the osmolality of the blood relative to the brain, which in turn pulls water from the brain to the intravascular compartment to restore osmolar balance.
   b. **Furosemide** is often given concomitantly as it induces systemic diuresis, decreases CSF production, and reduces cerebral edema by enhancing water transport. In other words, furosemide reduces ICP without increasing cerebral blood volume (CBV) or blood osmolality.
7. Control fever, which can cause brain swelling; maintaining normothermia decreases the cerebral metabolic rate for oxygen consumption ($CMRO_2$)
8. Increase MAP.
9. Infuse 3% hypertonic saline (HS) in boluses of 250 mL.

**ICP MANAGEMENT CHECKLIST**

1. **HEAD POSITION**
2. **$PaCO_2$ CONTROL**
3. **SEDATION AND PHARMACOLOGIC PARALYSIS**
4. **CSF DRAINAGE VIA VENTRICULOSTOMY OR LUMBAR SUBARACHNOID DRAIN**
5. **MANNITOL AND/OR FUROSEMIDE AND/OR HS**
6. **FEVER CONTROL**

## II. MANAGEMENT OF CEREBRAL ANEURYSMAL RUPTURE

The preoperative or IOR of a cerebral aneurysm is one of the most catastrophic events that can occur in the OR environment. The **incidence of IOR** has been documented to range between 11% and 19% with the majority of ruptures occurring during either dissection or clipping of the aneurysm. The clinical outcome after rupture during the predissection interval is poor in that only one of four patients survives. Thus, the lines of communication between the surgical team and the anesthesia team need to be open

and reciprocal even before the patient enters the OR. Factors that predispose to premature rupture and appropriate preventive/management techniques can be organized into a checklist to facilitate communication and strategic planning.

**A. Pre-exposure rupture** is associated with a high morbidity and mortality. Thus, **continual communication** between the anesthesiologist and the neurosurgeon is essential. For example, destabilization of the BP before the surgical incision can be the cause of premature rupture. Painful procedures may trigger swings in systolic pressure. Abrupt changes in intracranial dynamics, especially when associated with placement of a lumbar subarachnoid drain or a ventriculostomy, may also lead to premature rupture of the aneurysm.

1. The **goal of anesthetic and surgical management** in craniotomy for aneurysmal clip ligation is to prevent aneurysmal rupture, maintain CPP, and provide a brain that is neither tight nor taut. In this context, the maintenance of hemodynamic stability with a MAP between 80 and 90 mm Hg during stimulation of the patient is crucial. There are **five periods during the procedure that threaten hemodynamic stability:** Laryngoscopy and endotracheal intubation; Insertion of the skull pin fixation; Scalp incision; Turning the bone flap; and Opening the dura. These maneuvers require a deep plane of anesthesia and the use of anti-hypertensive medications in order to avoid a hypertensive response. The presence of subarachnoid blood can also increase ICP which, as described, often leads to systemic hypertension and dysrhythmias. Aneurysmal surgery requires significant intravascular volume shifts because of the initial diuresis followed by volume loading as well as extensive systemic BP manipulation owing to the need for deliberate hypotension and hypertension, depending on the situation.
2. **Aneurysmal rupture during the induction of anesthesia** occurs in 1% to 2% of cases, but carries a mortality that approaches 75%. A number of factors require consideration during induction. To minimize the risk of systemic and intracranial hypertension and aneurysmal rupture, intravenous lidocaine and labetalol, nicardipine, or (most commonly) the beta-1 adrenergic antagonist esmolol may be given in addition to induction drugs (propofol, etomidate, or thiopental in combination with an opioid such as fentanyl and a non-depolarizing muscle relaxant) for laryngoscopy. If the patient requires a rapid-sequence induction, succinylcholine is used although there are studies demonstrating an increase in ICP after injection. A defasciculating dose of a non-depolarizing muscle relaxant is recommended to diminish the increase in ICP. When the patient is known to have intracranial hypertension, mild hyperventilation is initiated. If the ICP is normal, then normocarbia is recommended.
3. After induction, ventilation is controlled to maintain normocarbia if the ICP is normal. The $PaCO_2$ may be reduced to 30 to 35 mm Hg when there is an increase in ICP. **Aneurysmal rupture** before the opening of dura mater is manifested by a sudden severe increase in ICP or an abrupt and dramatic increase in BP, which can be accompanied by bradycardia. At this point, it is essential to discuss the change in vital signs with the neurosurgeon and diagnose the rupture immediately. Transcranial Doppler ultrasound is helpful. The CPP is maintained and control of the intracranial hypertension is necessary to reduce the transmural pressure gradient across the wall of the aneurysm. In this situation, thiopental has been shown to protect the brain against focal ischemia.

4. The **anesthesiologist must always be prepared to take appropriate action** before the rupture occurs by having the necessary drugs available and ready for administration including propranolol, labetalol, and esmolol, which do not affect CBF or ICP. Mannitol is used with caution before the dura is opened because the resultant abrupt increase in intravascular volume and MAP coupled with a decrease in ICP can cause a change in the transmural pressure gradient and subsequent aneurysmal rupture. Once the skull is opened, the brain must remain slack to decrease the pressure under the retractors and avoid the risk of stretching and tearing the adjacent vessels.
5. The **anesthesiologist can provide the following:** hyperventilation, osmotic diuresis, barbiturate or propofol administration, and CSF drainage during the procedure from the lumbar subarachnoid drain, which had been inserted after the induction of anesthesia. Drugs for the maintenance of anesthesia include propofol and fentanyl or remifentanil in conjunction with an inhalational anesthetic (sevoflurane or desflurane) ≤ 0.5 minimum alveolar concentration (MAC) in air/oxygen. In some centers, thiopental or propofol is administered to achieve electroencephalographic burst suppression for cerebral protection. This may require BP support with pressors and fluid administration.

**B. Neurophysiologic monitoring**

1. Intraoperative **neurophysiologic monitoring** has become an indispensable tool in the ongoing attempt to improve outcome after neurosurgical procedures. The monitoring of somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) is the standard technique for detecting selective subcortical ischemia of the motor or sensory pathways during temporary occlusion of the parent vessel and after permanent clipping of the aneurysm and for assessing the effectiveness of cerebroprotective anesthesia. Evoked potentials record the electrical potentials produced after stimulation of specific neural tracts. Based upon the patient's response to such stimulation in comparison to the patient's baseline tracings, impending neural compromise can be identified quickly. The neurosurgeon and the anesthesiologist are thus able to take immediate action and possibly prevent permanent damage.
2. The use of intraoperative neurophysiologic monitoring requires **close communication** among the neurophysiologist, the neurosurgeon, and the anesthesiologist. Surgical, anesthetic, and monitoring issues need to be discussed before the start of the operation to facilitate the selection of an appropriate monitoring technique and an appropriate anesthetic plan especially as different anesthetics may adversely affect the ability to perform intraoperative monitoring. In general, the inhalational anesthetics desflurane, isoflurane, and sevoflurane will increase the latency and decrease the amplitude of SSEPs and MEPs. With regard to brain stem auditory evoked potentials (BAEPs), these anesthetics increase latency but have no effect on the amplitude. Intravenous anesthetics such as propofol have a milder effect and can be used intraoperatively as they cause little interference with the monitoring. Dexmedetomidine as an adjunct to a propofol-based total intravenous anesthetic (TIVA) technique has been studied with respect to the effect of the combination on transcranial electric MEPs and SSEPs with mixed results. Neuromuscular blocking drugs impair or prevent MEP and electromyographic (EMG) monitoring but have virtually no effect on SSEPs.

3. In addition, many **patient characteristics** may affect the neurophysiologist's ability to obtain adequate signals for comparison. The identification of these characteristics would alert the anesthesiologist that perhaps a technique such as TIVA may be necessary to facilitate monitoring. Hypertension and diabetes are independent predictors of monitoring failure, and these are preferentially sensitive to inhalational anesthetics. Intraoperative conditions such as hypothermia, hypotension, hypoxia, and profound anemia may also make neurophysiologic monitoring difficult to impossible to accomplish.

C. **IOR correlates with several factors** that are out of the anesthesiologist's control. These include the size, shape, and location of the aneurysm; experience of the surgical team; number of previous ruptures; use of temporary clips; and amount of blunt versus sharp dissection. Aneurysmal rupture during dissection can be attributed to blunt dissection techniques in 75% of cases and to sharp dissection in 25%. The outcome after IOR has been noted to be favorable in only 50% of the patients sustaining blunt dissection errors, whereas all patients sustaining IOR during sharp dissection recover well. Rupture during clip application has been attributed to incomplete dissection in 65% of cases, poor clip application in 31%, and only very rarely to mechanical clip failure. Eighty-eight percent of the patients who undergo uneventful operative procedures have favorable outcomes, whereas only 62% of the patients suffering IOR recover well.

1. The **incidence of IOR** is affected by several factors. The highest rate of IOR has been recorded for aneurysms of the anterior cerebral artery (specifically, the anterior communicating artery). The incidence of IOR increases as the size of the aneurysm increases. A significant increase in the incidence of IOR has been documented in aneurysms that have diverticula ($p = 0.004$) and wide necks ($p = 0.04$). The occurrence of IOR in the patients operated within the first 3 weeks after subarachnoid hemorrhage (SAH) was three times greater than in those operated outside of this period. The incidence of IOR is low in the treatment of asymptomatic or unruptured aneurysms (2.5%). The risk for IOR is higher in patients who have had multiple prior hemorrhages. Temporary proximal occlusion of the parent vessel substantially lessens the risk of IOR.

D. **Temporary clips and cerebral protection**

Advanced cerebrovascular teams have well-rehearsed scripts delineating the use of temporary clips and cerebral protective drugs in conjunction with neurophysiologic monitoring. The monitoring of either MEPs or SSEPs and a form of pharmacologic protection are used during temporary clip application. The anesthesiologist advises the surgeon of the elapsed time of temporary occlusion and the status of both the BP and the latency and amplitude of the evoked potential waveforms. This communication is integral to the success of the operation.

1. **If the aneurysm ruptures prematurely**, either at the time of exposure or during clipping, it is imperative that CLEAR COMMUNICATION EXISTS RELATIVE TO THE NEED FOR INDUCED HYPOTENSION. Surgical results are downgraded by lowering the BP during aneurysmal bleeding because of exacerbation of the resulting cerebral ischemia. If the surgeon can regain control quickly, there may not be any need for profound hypotension. If, however, the rupture is life threatening, it is incumbent on the surgeon to give explicit instructions as to the level of the BP necessary to effect control of the bleeding. In this case, MAP should be ≤ 50 to 60 mm Hg and the brain rendered as slack as possible in order to

facilitate either direct clipping of the aneurysm or temporary clipping of both ends of the parent vessel. There may even be a rationale for carotid compression until the temporary clips are in place. After permanent clipping, the BP is increased to enhance collateral blood flow to the parts of the brain distal to the temporary clips.

2. The IOR of an aneurysm requires that the anesthesiologist be prepared to **keep up with the blood loss through transfusion**. If hemorrhage is excessive, aggressive volume resuscitation must commence immediately. The potential for major ischemic damage results from hypotension in the face of hypovolemia from blood loss and also the surgical efforts to control the bleeding. If the leak is small and the dissection is complete, a permanent clip can indeed be applied. However, if temporary clips are necessary for rapid control of the hemorrhage, thiopental may be given just before clip placement for neuroprotection.

**PREMATURE ANEURYSMAL RUPTURE CHECKLIST**

1. **BLOOD PRESSURE AND PAIN CONTROL PREINDUCTION**
2. **BLOOD PRESSURE AND PAIN CONTROL PRE-EXPOSURE**
3. **SUBARACHNOID LUMBAR DRAIN OR VENTRICULOSTOMY**
4. **COMPLEXITY OF THE ANEURYSM**
5. **NEUROPHYSIOLOGIC MONITORING**
6. **CEREBRAL PROTECTION**
7. **TEMPORARY CLIPS**
8. **INDUCED HYPOTENSION AND TRANSFUSION**

## III. BLEEDING DURING RESECTION OF SPINAL CORD TUMORS

Significant blood loss during resection of spinal cord tumors is one of the more serious complications of this procedure. In order to prevent or minimize the sequelae of this occurrence, communication among neurosurgeon, anesthesiologist, and all members of the OR team is of tremendous importance.

### A. Preoperative evaluation and preparation

1. Before the patient is brought to the OR, a **discussion between the surgeon and the anesthesiologist** about the patient's history, probable diagnosis, and management throughout the operation is strongly recommended. The neurologic status of the patient is addressed in order to avoid further neurologic deterioration during endotracheal intubation, patient positioning, and other aspects of intraoperative management. If the patient is wheelchair bound, the cardiovascular status may be difficult to evaluate. Minimum investigations in this case include electrocardiogram (ECG), echocardiogram, and a dobutamine stress test. The possibility of complications in cancer patients must also be considered including side effects of chemotherapy, difficulty with endotracheal intubation from radiation therapy to the cervical spine, and metastasis to different organs.
2. While the intraoperative determination of the preliminary pathology of a newly diagnosed tumor is imperative, neuroimaging and the patient's presentation enable the neurosurgeon to **formulate a differential diagnosis**

**preoperatively**. This is then communicated to the anesthesiologist before the start of the procedure. In addition, if the tumor is a recurrence, the neurosurgeon can alert the anesthesiologist as to the extent of the tumor. For example, malignant metastatic tumors usually spread through local vasculature or stimulate the development of new collaterals. Such angioneogenesis increases the difficulty of the tumor resection and contributes substantially to the additional risk of major blood loss. Some benign tumors, such as hemangiomas, are also extremely vascular. Therefore, it is very important to predict and be prepared for the possibility of excessive bleeding and the need for transfusion during the operation.

3. **Excellent venous access and additional cardiovascular monitoring** to facilitate dynamic assessment of volume status and cardiovascular stability are essential to the management of volume resuscitation. The anesthesiologist should advise the surgeon of *and the surgeon should appreciate* the fact that this often entails extensive preparation for direct arterial BP and central venous pressure (CVP) monitoring. Typed and cross-matched blood and intraoperative blood salvage equipment should also be readily available.
4. To minimize blood loss and facilitate surgical resection, neurosurgeons and interventional radiologists commonly **embolize spinal cord tumors** before the operative procedure. For huge, highly vascular neoplasms, preoperative embolization may be essential in order to achieve total excision of the tumor. A number of neoplasms including sacral chordomas, giant thoracic sarcomas, and metastatic tumors such as renal cell carcinoma are very vascular and can benefit from embolization. Preoperative embolization of spinal cord tumors is a safe procedure. Multiple studies have shown that there is a significant difference in blood loss and transfusion requirements in patients who undergo preoperative embolization as compared to non-embolized patients. Even partial embolization can reduce blood loss during the surgical procedure significantly. If the patient has had an angiogram, the anesthesiologist needs to know the extent of the tumor's vascularity and whether embolization of the tumor was successful.

**B. Intraoperative management**

1. **Positioning**. It is imperative for everyone in the OR to be familiar with the position of the patient for every procedure and the best way to achieve that position. The positioning of the patient on the operating table is always performed with the surgeon's assistance. Critical to positioning is avoiding displacement of unstable spinal fractures and ensuring that pressure points are adequately padded. The orbits, the superior orbital nerve, and the skin over the maxilla are at particular risk of ischemic injury if positioned incorrectly. Postoperative visual loss can be a devastating sequela of the prone position, especially when coupled with intraoperative hypotension.
2. The **intraoperative monitoring of SSEPs and MEPs** is a common practice during spinal cord tumor resection. The operating surgeon arranges for neurophysiologic monitoring and advises the anesthesiologist as the use of neurophysiologic monitoring affects the choice of anesthetic drugs. However, maintenance of the patient's stability throughout the procedure takes precedence over the selection of a specific anesthetic technique to facilitate neurophysiologic monitoring. The combination of hemodynamic homeostasis and a stable level of anesthesia enables the neurophysiologist to detect subtle changes in the patient's status.

The anesthesiologist continually advises the neurophysiologist of any major shifts in the anesthetic requirement or delivery to facilitate accurate interpretation of the results.

3. **Fluid management** is a matter of major importance. The patient's preoperative volume status should be optimized and then the intravascular volume and the hemoglobin level maintained throughout the procedure. Vasopressors should be used only if necessary to maintain the spinal cord perfusion pressure. Blood transfusion, hemodilution, autologous blood donation, intraoperative blood salvage, and deliberate hypotension are all utilized to handle blood loss and replacement intraoperatively.
   a. **Autologus normovolemic hemodilution** is the process whereby blood is collected from the patient and stored until the end of operation. In order to maintain normovolemia, the intravascular volume is replenished by administration of colloid and crystalloid solutions. At the conclusion of the procedure, the collected blood is reinfused into the patient. Hemodilution is usually well tolerated by patients to a hemoglobin concentration of seven; below this level there may be problems with hemodynamics and coagulation, so it is important to proceed with caution. This technique can be applied only to those patients who can tolerate a marked reduction in hemoglobin. The patients who have cardiovascular instability or a low hemoglobin preoperatively are excluded. It is important to consider the fact that the blood supply to the thoracolumbar spine is limited. Patients could become paraplegic because of the decrease in oxygen delivery to the spinal cord attendant upon a drop in the hemoglobin concentration. The quantity and quality of fluid administration should be guided by the monitoring of preload and blood oxygen levels.
   b. **Autologus blood donation** by the patient before the operation decreases the risk of heterologous blood transfusion. However, the operative blood loss is usually significantly more than the amount of blood a patient would be physically able to donate before surgery. Therefore, autologous blood donation is rarely used.
   c. **Intraoperative blood salvage** cannot be used in patients who have malignancies, because of the risk of tumor dissemination. Only in cases of benign tumors should intraoperative blood salvage be employed.
   d. **Deliberate hypotension** helps to reduce blood loss and provides a better surgical field. This technique is very controversial in that it can decrease the oxygen supply to the spinal cord and increase the possibility of **postoperative paraplegia**. The vascular anatomy of the spinal cord is a very important factor in the development of paraplegia after spinal surgery. In regard to the anterior spinal artery, C3–C5 and T12–L2 are the most vulnerable segments; for the posterior spinal arteries, the segments from C8 to T4 are the most vulnerable to ischemia. **Postoperative visual loss** (POVL) is also a risk of spine surgery in the prone position although it has been described after operations in the lateral position as well. The risk is believed to be increased if deliberate hypotension is used. Hypotension, peripheral vascular disease, and anemia (hemodilution) are the biggest risk factors for the development of ischemic optic neuropathy and POVL. Therefore, many surgeons and anesthesiologists maintain a MAP > 80 to 85 mm Hg in normotensive patients operated in the prone position to preserve adequate blood flow to the spinal cord and optic nerve even in the face of severe blood loss. The risk of hypotension may outweigh

its benefits, but if the surgeon and the anesthesiologist decide to implement deliberate hypotension, then careful hemodynamic assessment and spinal cord monitoring are employed throughout the procedure.

**C. Postoperative care**

1. It is very important for patients to regain consciousness and be able to respond to commands immediately after anesthesia to permit early neurologic assessment.
2. It is important that techniques of acute pain management render the patients comfortable and hemodynamically stable yet still able to respond appropriately to serial neurologic testing.

**PREVENTION AND TREATMENT OF INTRAOPERATIVE BLEEDING DURING EXCISION OF SPINAL CORD TUMORS**

1. **PREOPERATIVE TUMOR EMBOLIZATION**
2. **PRE/INTRAOPERATIVE TRANSFUSION**
3. **MAINTENANCE OF ADEQUATE MAP INTRAOPERATIVELY**
4. **BLOOD TRANSFUSION, HEMODILUTION, INTRAOPERATIVE BLOOD SALVAGE FOR VOLUME RESUSCITATION**
5. **INDUCED HYPOTENSION**
6. **EVOKED POTENTIAL MONITORING**

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# 7 Anesthetic Management of Head Trauma

**Kishore Tolani, Audrée A. Bendo, and Takefumi Sakabe**

## Illustrative Clinical Case

A 28-year-old male is brought to the emergency department (ED) after sustaining a severe closed head injury in a motor vehicle accident. His Glasgow Coma Scale (GCS) score is 7 on admission. You are called to the ED for intubation and find a combative, uncooperative patient who has facial injuries and a cervical collar. His oxygen saturation is 90% to 92% on face mask oxygen. His vital signs are BP 100/50, P 110, and RR 24.

## Chapter Highlights

The **major goal of the perioperative management** of patients who have head injuries is to **prevent secondary damage**. Therapeutic measures based on established guidelines and recommendations must be instituted promptly and continued throughout the perioperative course. Appropriate selection of anesthetics and meticulous general management of respiration, circulation, metabolism, fluid replacement, and temperature are all essential to improve outcome after traumatic brain injury (TBI).

Head trauma or TBI is one of the most serious, life-threatening conditions in trauma victims. Prompt and appropriate therapy is necessary to obtain a favorable outcome. Anesthesiologists care for these patients throughout their perioperative course, taking them from the ED to the neuroradiology suite, the operating room (OR), and the neurointensive care unit (N-ICU).

The perioperative management of patients who have TBI focuses on aggressive stabilization of the patient's physiologic condition and avoidance of systemic and intracranial insults that cause secondary neuronal injury. These secondary insults, while potentially preventable and treatable, can complicate the course of patients after TBI and adversely affect outcome.

### I. HEAD INJURY PRACTICE GUIDELINES

In 1995, the Brain Trauma Foundation approved guidelines for the initial resuscitation and treatment of intracranial hypertension in the severely head-injured patient, recognizing the need to standardize care to improve outcome in these patients. A task force was formed in 1998 to review and

update the scientific evidence for the guidelines. These **evidence-based guidelines for the management of severe TBI** were published in 2000 and were updated in 2007 (Table 7.1). This comprehensive review of the literature recommends three standards based on Class I evidence and several guidelines based on Class II evidence.

**Evidence-based guidelines** for **prehospital management of TBI** and for **pediatric brain injury** have also been published, and in March 2006, **surgical management guidelines** were published. Compared with the evidence informing *Guidelines for the Management of Severe Traumatic Brain Injury,* however, there are no controlled clinical trials in the literature to support different forms of surgical management or surgical versus conservative therapy. As with the other guidelines in severe TBI, the authors of the surgical management guidelines stated in 2006 that "*this is a document in evolution*," and revisions will be made as new knowledge is gained.

## II. CLASSIFICATION OF HEAD INJURY INTO PRIMARY INJURY AND SECONDARY INJURY IS USEFUL WHEN CONSIDERING THERAPEUTIC STRATEGIES

**A. Primary injury** is the damage produced by the direct mechanical impact and the acceleration–deceleration stress onto the skull and the brain tissue,

**TABLE 7.1** Recommendations from Guidelines for the Management of Severe Traumatic Brain Injury

***Standards based on Class I evidence:***

If ICP is normal, avoid chronic prolonged hyperventilation therapy ($PaCO_2 < 25$ mm Hg).
The use of steroids is not recommended for improving outcome or reducing ICP.
Prophylactic use of anticonvulsants does not prevent late post-traumatic seizures.

***Guidelines based on Class II evidence:***

All regions should have an organized trauma care system.
Avoid or correct immediately hypotension (systolic blood pressure < 90 mm Hg) and hypoxia ($SaO_2 < 90\%$ or $PaO_2 < 60$ mm Hg).
Indications for intracranial pressure (ICP) monitoring include GCS score 3 to 8 with abnormal CT scan or two or more of the following adverse features: age > 40 y, motor posturing, and systolic blood pressure < 90 mm Hg.
Initiate treatment for ICP at an upper threshold above 20 mm Hg.
CPP value to target lies within the range of 50 to 70 mm Hg. Aggressive attempts to maintain CPP > 70 mm Hg should be avoided because of the risk of ARDS.
Avoid the use of prophylactic hyperventilation ($PaCO_2 \leq 25$ mm Hg) during the first 24 h after severe TBI.
Mannitol is effective for control of raised ICP after severe TBI in doses ranging from 0.25 to 1 g/kg body weight.
High-dose barbiturate therapy may be considered in hemodynamically stable salvageable severe TBI patients who have intracranial hypertension refractory to maximal medical and surgical ICP lowering therapy.
Provide nutritional support (140% of resting energy expenditure in non-paralyzed patients and 100% of resting energy expenditure in paralyzed patients) using enteral or parenteral formulas containing at least 15% of calories as protein by day 7 after injury.

Data adapted from Bullock RM, et al. and Guidelines, 3rd ed.
$PaCO_2$, arterial carbon dioxide tension; $SaO_2$, arterial oxygen saturation; $PaO_2$, arterial oxygen tension; GCS, Glasgow Coma Scale; CT, computed tomography; CPP, cerebral perfusion pressure; ARDS, adult respiratory distress syndrome; TBI, traumatic brain injury.

which results in skull fractures (cranial vault, skull base) and intracranial lesions. The intracranial lesions are further classified into two types: diffuse injury and focal injury.

1. **Diffuse brain injury**
   a. **Brain concussion**: loss of consciousness lasting < 6 hours
   b. **Diffuse axonal injury**: traumatic coma lasting > 6 hours
2. **Focal brain injury**
   a. **Brain contusion**: located either below or opposite the region of impact
   b. **Epidural hematoma (EDH)**: often caused by skull fracture and laceration of the middle meningeal artery
   c. **Subdural hematoma (SDH)**: usually caused by the tearing of the bridging veins between the cerebral cortex and the draining sinuses. Acute SDH is often associated with high mortality.
   d. **Intracerebral hematoma** is usually located in the frontal and the temporal lobes and visualized as a hyperdense mass on a computed tomographic (CT) scan. Brain tissue destroyed by the primary impact will not be saved. Therefore, functional outcome is improved by prompt surgical intervention and medical therapy.
3. **Indications for surgery.** Presently, no definitive therapeutic measure exists to treat diffuse axonal injury. Most open and depressed skull fractures and compound **skull fractures** with dural laceration require early surgical repair. Uncomplicated basal fractures usually do not require operation. The presence of **compression of the basal cisterns** from a brain contusion necessitates operative intervention because of the risk of herniation (usually of the temporal lobe). **Intracranial hematoma** is the most common sequela of head trauma requiring surgical treatment. An EDH > 30 $cm^3$ should be surgically evacuated regardless of the GCS score. Patients who have an acute EDH, a GCS score < 9, and anisocoria (inequality of pupillary diameter) should undergo urgent surgical evacuation. An acute SDH > 10 mm thick or a midline shift > 5 mm on CT scan requires evacuation. If the GCS score is < 9 in patients who have an SDH < 10 mm thick, intracranial pressure (ICP) monitoring must be instituted.

B. **Secondary injuries** develop within minutes, hours, or days of the initial injury and cause further damage to nervous tissue. The common denominators of secondary injury are **cerebral hypoxia and ischemia**. Secondary injuries are caused by the following disorders:
   1. Respiratory dysfunction: hypoxemia, hypercapnia
   2. Cardiovascular instability: hypotension, low cardiac output (CO)
   3. Elevation of ICP
   4. Metabolic derangements

## III. PATHOPHYSIOLOGY OF HEAD TRAUMA

### A. Systemic effects

1. **Cardiovascular responses** commonly observed in the early stage after TBI include hypertension, tachycardia, and increased CO. Patients who have severe TBI and those suffering from multiple systemic injuries with substantial blood loss may, however, develop hypotension and a decrease in CO. Systemic hypotension (systolic blood pressure [SBP] < 90 mm Hg) at the time of hospital admission is associated with significantly increased morbidity and mortality.
2. **Respiratory responses** to head trauma include apnea and abnormal respiratory patterns. Respiratory insufficiency and spontaneous hyperventilation often occur. Patients may also suffer from central

neurogenic pulmonary edema and aspiration of blood, teeth, and vomitus.

3. **Temperature regulation** may be disturbed, and hyperthermia, if it occurs, can provoke further brain damage.

B. **Changes in cerebral circulation and metabolism**

1. In **focal brain injury**, cerebral blood flow (CBF) and cerebral metabolic rate for oxygen consumption ($CMRO_2$) decrease in the core area of injury and in the penumbra, the area of hypoperfused tissue that surrounds the damaged tissue. When ICP increases, the cerebral perfusion pressure (CPP), the difference between the mean arterial pressure (MAP) and the ICP, decreases and diffuse and more marked hypoperfusion and hypometabolism ensue.
2. In **diffuse brain injury**, hyperemia may occur. In most cases, however, CBF decreases within a few hours of head trauma. The combination of hypotension and impaired autoregulation exacerbates cerebral ischemia. The chemical-metabolic regulation of CBF may also be impaired.

C. **Acute brain swelling and cerebral edema**

1. **Acute brain swelling** is provoked by a decrease in vasomotor tone and a marked increase in the volume of the cerebral vascular bed. In this situation, increases in BP can easily lead to further brain swelling and an increase in ICP.
2. **Cerebral edema** after head trauma is often a mixture of vasogenic and cytotoxic types caused by blood–brain barrier (BBB) disruption and ischemia, respectively.

   Both acute brain swelling and edema ensue concurrently after TBI. When these pathologic conditions occur in association with an intracranial hematoma, the resultant intracranial hypertension causes a further reduction in CBF and exacerbation of cerebral ischemia. Eventually, intracranial hypertension, if untreated, leads to herniation of the brain stem through the foramen magnum.

D. **Excitotoxicity.** Head trauma causes **excessive release of glutamate** from neurons and glia, increasing the concentration of glutamate in the cerebrospinal fluid (CSF). The biochemical changes associated with the excessive release of glutamate and the activation of glutamate receptors are closely related to an **increase in intracellular calcium,** which triggers a number of events that lead to cellular damage. These include the activation of phospholipase, protein kinase, proteases, nitric oxide synthase (NOS), and other enzymes. Activation of these enzymes also leads to lipid peroxidation, proteolysis, free-radical formation, deoxyribonucleic acid (DNA) damage, and, finally, neuronal death (Fig. 7.1).

E. **Inflammatory cytokines and mediators.** The cytokines are **major mediators in the initiation of inflammatory and metabolic responses to injury**. Cytokines increase in response to cerebral ischemia. Interleukin-6 (IL-6) and tumor necrosis factor alpha are known to be released after TBI. Patients who have GCS scores < 8 show a higher and more sustained elevation of IL-6. The cytokines released after TBI stimulate the production of free radicals and arachidonic acids and upregulate the activity of the adhesion molecules, which produce disturbances in the microcirculation. All of these changes contribute to secondary brain injury.

## IV. EMERGENCY MANAGEMENT

A. **Initial assessment of the patient's condition**

1. **Neurologic assessment.** There is usually little time initially for thorough evaluation of the patient's neurologic condition. However, a quick neurologic assessment can be performed while achieving adequate

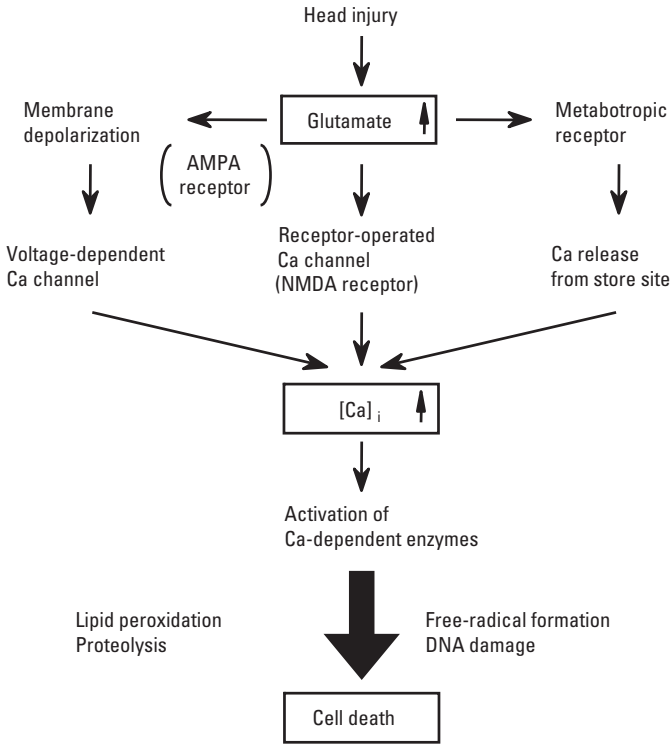


**FIGURE 7.1** Excitotoxicity in head injury. AMPA, alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionate; NMDA, *N*-methyl-D-aspartate; [Ca]i, intracellular calcium; DNA, deoxyribonucleic acid.

ventilation (oxygenation and carbon dioxide [$CO_2$] elimination) and hemodynamic stability.

a. **GCS** (Table 7.2) is a simple and universally accepted method for assessing consciousness and neurologic status in patients after TBI. The GCS has low interobserver variability and is a good predictor of outcome. Even patients who have good GCS scores need to be closely monitored. Patients may deteriorate rapidly, especially those who have medial temporal lesions as even slight expansion in this region may result in herniation. CT scans are obtained in patients who have GCS score < 15 or if loss of consciousness has occurred.
   1. GCS score < 8 characterizes severe head injury.
   2. GCS score of 9 to 12 represents moderate injury.
   3. GCS score of 13 to 15 represents mild injury.

b. **Pupillary responses** (size, light reflex, accommodation) and **symmetry of motor function in the extremities** should be quickly assessed.

2. **Assessment of injuries to other organs.** Trauma patients often suffer from injuries to multiple organ systems, and therefore require early diagnosis of intrathoracic and intraperitoneal (intrapelvic) injuries. If bleeding is suspected, the thorax or the abdomen should be explored without delay. **Treatment of hemorrhagic shock takes precedence over neurosurgical**

TABLE 7.2 Glasgow Coma Scale

| Adult Scale | | Pediatric Scale | | |
|---|---|---|---|---|
| **Parameter** | **Score** | **Parameter** | **Score** | |
| **Eye Opening** | | **Eye Opening** | | |
| Spontaneously | 4 | Spontaneously | 4 | |
| To speech | 3 | To speech | 3 | |
| To pain | 2 | To pain | 2 | |
| None | 1 | None | 1 | |
| **Best Verbal Response** | | **Best Verbal Response**[a] | | |
| Oriented | 5 | Oriented to place | 5 | > 5 y |
| Confused | 4 | Words | 4 | > 12 mo |
| Inappropriate | 3 | Vocal sounds | 3 | > 6 mo |
| Incomprehensible | 2 | Cries | 2 | < 6 mo |
| None | 1 | None | 1 | |
| **Best Motor Response** | | **Best Motor Response in Upper Limbs**[a] | | |
| Obeys commands | 6 | Obeys commands | 6 | > 2 y |
| Localizes to pain | 5 | Localizes to pain | 5 | 6 mo–2 y |
| Withdraws from pain | 4 | Normal flexion to pain | 4 | > 6 mo |
| Flexes to pain | 3 | Spastic flexion to pain | 3 | < 6 mo |
| Extends to pain | 2 | Extension to pain | 2 | |
| None | 1 | None | 1 | |

[a]Score highest appropriate for age.

**procedures.** The patient's hemoglobin must be measured immediately and blood and fresh-frozen plasma ordered for infusion.

**B. Establishment of airway and ventilation**

1. **Tracheal intubation.** The first step in emergency therapy is to secure an open airway and ensure adequate ventilation. Because all trauma patients are considered to have a "full stomach" and approximately 10% have an associated cervical spine injury as well, **cricoid pressure** and **manual inline stabilization** of the cervical spine are used during laryngoscopy and intubation.

   If facial fractures and soft tissue edema prevent direct visualization of the larynx, either **fiberoptic intubation** or intubation with an **illuminated stylet** may be attempted. In the presence of either severe facial injuries or laryngeal trauma, a **cricothyrotomy** may be required. **Nasal intubation is avoided** in the presence of a suspected basilar skull fracture, severe facial fractures, and a bleeding diathesis. Nasal intubation also adds the risk of introducing contaminated material into the brain when there is a basilar skull fracture. Hemorrhage of the tympanic cavity, otorrhea, petechiae on the mastoid process (Battle's sign), and petechiae around the eyes (panda sign) are all indications of a basilar skull fracture.
2. **Drugs to facilitate laryngoscopy and intubation** (see Section **V**)
3. **Mechanical ventilation.** As soon as the trachea has been intubated, a nondepolarizing muscle relaxant is administered and mechanical ventilation to an arterial carbon dioxide tension ($PaCO_2$) of approximately 35 mm Hg is instituted. Aggressive hyperventilation to a $PaCO_2$ < 30 mm Hg is avoided unless transtentorial herniation is suspected. Hypoxemia, if present, is corrected immediately. Hyperoxia may be

recommended. If massive aspiration is suspected, bronchial suctioning using a fiberscope is advisable before transferring the patient to either the neuroradiology suite or the OR.

C. **Cardiovascular stabilization.** Systemic hypotension is one of the major contributors to poor outcome after head trauma. When necessary, fluid resuscitation is initiated immediately and inotropic and vasopressor drugs are administered as required to stabilize the BP.

1. **Fluid resuscitation.** Hypovolemia is often masked by a relatively stable BP secondary to either sympathetic hyperactivity or the reflex response to increased ICP. Therefore, fluid resuscitation should be guided not only by BP but also by urinary output and central venous pressure (CVP). **Total osmolality** is the most important factor in determining brain edema formation. Colloid oncotic pressure has a very minor effect on pressure gradients for diffusion of water across the BBB. Care should be taken during fluid resuscitation as these patients are at risk for pulmonary edema, which may worsen hypoxia.

   a. **Crystalloid and colloid solutions.** Isotonic and hypertonic crystalloid solutions and colloid solutions may be given to maintain adequate intravascular volume. **Normovolemia** is the intended fluid management goal. Any negative fluid balance from the use of diuretics may have a deleterious effect on a brain that has impaired autoregulation.

      1. **Lactated Ringer's solution** is slightly hypotonic (273 mOsm/L) relative to plasma, which precludes the use of a substantial amount. If administered, serum osmolality should be measured periodically. When large-volume resuscitation with crystalloid is required, an isotonic crystalloid, such as normal saline (308 mOsm/L), is preferable.
      2. **Hypertonic saline (HS)** (3%, 7.5%) can be beneficial in small amounts after TBI. HS was shown to reduce brain water content in non-traumatic brain tissue in an animal model. A rebound phenomenon, as occurs with mannitol, is not seen with HS given to patients after TBI. Pre-existing hyponatremia should be excluded as there is a risk of central pontine myelinolysis after rapid correction with HS. Infusion of HS should be carefully monitored in patients who have cardiac problems as it may aggravate pulmonary edema. HS may be more effective in patients who have refractory intracranial hypertension. Research is still needed to determine the optimal administration and concentration of HS.
      3. **Hydroxyethyl starch (HES) and albumin** can be administered to maintain intravascular volume for longer periods. **No more than 1.5 L of HES should be administered** in conjunction with careful monitoring of coagulation parameters. The incidence of coagulopathy in patients after TBI is approximately 20%, and HES in large amounts is known to interfere with clotting. The reported incidence of coagulopathy is less with pentastarch. **Dextrans are usually avoided** owing to their effect on platelet function. **Hypertonic saline/dextran** combinations have been shown to reduce mortality and decrease the incidence of adult respiratory distress syndrome (ARDS) in the trauma patient.

   b. **Blood and blood products.** Patients who have a low hematocrit may require a transfusion to optimize oxygen delivery; the hematocrit ideally is maintained at > 30%. Children require special attention because they can easily become hypovolemic by losing large but

unsuspected volumes of blood into an intracranial or a subgaleal hematoma or through a scalp laceration, even without blood loss from other organs. Release of brain tissue thromboplastin may trigger disseminated intravascular coagulation (DIC) in which case fresh-frozen plasma, platelets, and cryoprecipitate may be required.

c. **Adverse effect of glucose-containing solutions.** Glucose-containing solutions are avoided because **hyperglycemia is associated with worsening of neurologic outcome**. Glucose should be used only to treat hypoglycemia. A plasma level of 80 to 150 mg/dL is desirable; values > 200 mg/dL should be avoided and treated with insulin. When insulin protocols are used, care is also taken to avoid hypoglycemia as it may have an even more harmful effect on outcome.

2. **Inotropes and vasopressors.** If the BP and CO cannot be restored through fluid resuscitation, the administration of intravenous inotropic and vasopressor drugs may be necessary. An infusion of either phenylephrine or dopamine is recommended to maintain the CPP above 60 mm Hg.

D. **Management of elevated ICP.** The reduction of elevated ICP and the maintenance of BP are crucial in the management of intracranial hypertension because CPP is directly related to both MAP and ICP. ICP monitoring is recommended in patients who have CT evidence of elevated ICP including midline shift, effaced ventricles, compressed basal cisterns, or the presence of an intracranial space-occupying lesion.

1. **Hyperventilation.** When evidence of transtentorial herniation in patients who have severe TBI exists, hyperventilation to a $PaCO_2$ of 30 mm Hg should be instituted because hyperventilation **can reduce ICP rapidly and effectively**. However, there is clinical evidence that the initial response of both adult and pediatric patients to TBI is more often hypoperfusion. **Aggressive hyperventilation to a $PaCO_2$ < 30 mm Hg can therefore aggravate ischemia through excessive vasoconstriction.** To avoid this risk, other measures including CSF drainage and diuretic and barbiturate therapy should be instituted. The $PaCO_2$ is allowed to return toward normal as soon as possible. Further trials are needed to determine the effect of short-term hyperventilation on outcome.
2. **Diuretic therapy.** Mannitol, 1 g/kg infused over 10 minutes, is administered to patients in whom transtentorial herniation is suspected. In less acute cases, an infusion of 0.25 to 1 g/kg may be administered over 10 to 20 minutes and repeated every 3 to 6 hours. The serum **osmolality is monitored frequently** and should not exceed 320 mOsm/kg.
3. **Posture.** A **head-up tilt** of 10° to 30° facilitates cerebral venous and CSF drainage and lowers ICP. This ICP-reducing effect is negated if systemic BP is decreased by this maneuver.
4. **Corticosteroids are not recommended for the treatment of cerebral edema and ICP in head-injured patients.** The results of the Corticosteroid Randomization After Significant Head Injury (CRASH) trial, an international randomized prospective placebo-controlled trial on the effect of early administration of methylprednisolone on the risk of death and disability after head injury, published in 2005, revealed a higher risk of death within 2 weeks of injury in the corticosteroid group versus placebo as well as a higher risk of subsequent death or severe disability. In addition, steroid administration increases blood glucose levels, which can adversely affect the injured brain, and is associated with an increased risk of gastrointestinal hemorrhage.

5. **Barbiturates** are known to **exert cerebral protective and ICP-lowering effects**. High-dose barbiturate therapy may be considered in severely head-injured patients whose intracranial hypertension is refractory to maximal medical and surgical ICP-lowering therapy. Hemodynamic stabilization of the patient is a prerequisite. The hypotensive effect of barbiturate therapy will offset any improvement in CPP attendant upon lowering the ICP. Although high-dose barbiturate therapy is recommended as a second-tier therapy for refractory intracranial hypertension, no clear benefit or improved outcome has been shown in clinical trials. The prophylactic use of barbiturate coma is not indicated.
6. **Decompressive craniectomy** is an advanced treatment option for ICP control in severe TBI. There are two ongoing randomized controlled trials, the RESCUEicp study in Europe (http://www.rescueicp.com) and the DECRA study in Australia (http://www.ntri.com.au/research/clinical/projects.asp), to determine whether decompressive craniectomy is more effective in improving outcome after TBI than maximal medical therapy in adults.

E. **Anticonvulsants.** Diphenylhydantoin, usually administered to patients who have significant head injury, has been shown to prevent early-onset seizures. However, the prophylactic use of anticonvulsants does not prevent late post-traumatic seizures. When given as an infusion, the rate should be limited to 50 mg/minute owing to the risk of cardiovascular depression.

F. **Cerebral protection: hypothermia.** A reduction of body temperature to 33°C to 35°C may confer cerebral protection. **Protective mechanisms** include a reduction in metabolic demand, excitotoxicity, free-radical formation, and edema formation. In an animal ischemia model, mild hypothermia of approximately 34°C to 36°C markedly attenuated ischemic injury. In clinical practice, controversy concerning the effectiveness of hypothermia in TBI is ongoing. A meta-analysis of various trials of hypothermia in TBI indicates that **hypothermia may be associated with better neurologic outcome**, defined as a Glasgow Outcome Scale (GOS) score of 4 or 5. Preliminary results also indicate that maintaining hypothermia for more than 48 hours may increase the chance of reducing mortality. However, certain confounding factors such as patients' temperatures on admission limit support for recommending hypothermia to **Level III** only (Brain Trauma Foundation, 2007).

When induction of hypothermia is elected, meticulous care is necessary to **avoid adverse side effects** such as hypotension, cardiac arrhythmias, coagulopathies, and infections. **Rewarming** should be carried out slowly. Temperature monitoring at two or more sites is recommended including tympanic membrane, nasopharyngeal area, esophagus, and blood.

## V. ANESTHETIC MANAGEMENT

The **major goals** of anesthetic management are to optimize cerebral perfusion and oxygenation, avoid secondary damage, and provide adequate surgical conditions. General anesthesia is recommended to facilitate control of respiratory and circulatory function.

A. **Induction of anesthesia.** Most severely head-injured patients have already had an endotracheal tube inserted in the field, during triage in the ED, or before their CT examination. The patient who comes to the OR without endotracheal intubation is treated with **immediate oxygenation and securing of the airway**. Anesthesiologists must be aware that these patients often have a full stomach, decreased intravascular volume, and a potential

cervical spine injury. **Direct arterial pressure monitoring** by arterial cannulation before the induction of anesthesia is recommended. Either the radial artery or the dorsalis pedis artery may be cannulated, depending on the other sites of injury.

The patient's presentation and hemodynamic stability determine the choice of induction technique.

1. **Rapid sequence induction** may be desirable in **hemodynamically stable patients**, although this technique can produce an elevation in BP and ICP. During administration of 100% oxygen, thiopental, 3 to 4 mg/kg, or propofol, 1 to 2 mg/kg, and succinylcholine, 1.5 mg/kg, are administered and the trachea is intubated. In **hemodynamically unstable patients**, the dose of induction drugs is substantially decreased or even omitted. However, cardiovascular depression is always a concern, especially in hypovolemic patients.

   **Succinylcholine** has been shown to increase ICP. The prior administration of small doses of a non-depolarizing muscle relaxant may prevent this increase but not predictably. In the presence of airway compromise and a full stomach, however, succinylcholine remains a good choice to facilitate laryngoscopy for rapid airway control. Rocuronium, 0.6 to 1 mg/kg, is an excellent alternative because of its rapid onset of action and lack of effect on intracranial dynamics.
2. **Intravenous induction.** When the patient is stable and does not have a full stomach, anesthesia can be induced by titrating the dose of either **thiopental or propofol** to minimize circulatory instability. An intubating dose of a non-depolarizing muscle relaxant is given with or without priming to facilitate intubation within a short period of time. For example, **rocuronium**, 0.6 to 1 mg/kg, allows satisfactory intubating conditions within 60 to 90 seconds. **Fentanyl**, 1 to 4 mcg/kg, is administered to blunt the hemodynamic response to laryngoscopy and intubation. An opioid given as premedication can cause respiratory depression, increasing $PaCO_2$ and leading to a further rise in ICP. **Lidocaine**, 1.5 mg/kg, given 90 seconds before laryngoscopy, can help prevent the increase in ICP. There is some animal evidence that lidocaine may reduce ischemic damage in the penumbra by blocking the apoptotic cell death pathways.

   A large-bore oral gastric tube is inserted after intubation, and gastric contents are initially aspirated and then passively drained during the operation. Nasal gastric tubes are avoided because of the potential presence of a basilar skull fracture.

B. **Maintenance of anesthesia.** The **ideal drug** for maintenance of anesthesia **should reduce ICP, maintain adequate oxygen supply to cerebral tissue**, and **protect the brain against ischemic-metabolic insult**. No gold-standard anesthetic drug fulfills these requirements for head injury. The selection of anesthetic drugs is based on a consideration of the intracranial pathology as well as systemic conditions such as cardiopulmonary disturbances and the presence of multisystem trauma.

1. **Anesthetics**
   a. **Intravenous anesthetics** all have a minor effect on cerebral autoregulation and $CO_2$ responsiveness.
      1. **Barbiturates.** Thiopental and pentobarbital **decrease CBF, cerebral blood volume (CBV), and ICP**, even in patients whose $CO_2$ response is impaired. The reduction in ICP with these drugs is related to

the reduction in CBF and CBV coupled with metabolic depression. Although thiopental and pentobarbital have been shown in animal models to protect against focal brain ischemia and thus might be effective in head injury where ischemia is a common sequela, no prospective randomized clinical trial has demonstrated that they definitely improve outcome after TBI. In addition, barbiturates can be detrimental in head-injured patients because of their **cardiovascular depressant effect**. Also, when administered for prolonged periods, neurologic recovery is delayed because of the **persistent sedative effect**.

2. **Etomidate.** As with barbiturates, etomidate **reduces CBF, $CMRO_2$, and ICP**. Systemic hypotension occurs less frequently than with barbiturates. Prolonged use of etomidate may, however, suppress the adrenocortical response to stress. There is no evidence in animal or human studies of cerebral protection with etomidate.
3. **Propofol.** The **cerebral hemodynamic and metabolic effects** of propofol are **similar to those of barbiturates**. Propofol might be useful in patients who have intracranial pathology, if hypotension is avoided. Because the context-sensitive half-life is short, **emergence from anesthesia is rapid**, even after prolonged administration. This may offer an advantage over other intravenous anesthetics in providing the opportunity for early postoperative neurologic evaluation. Another advantage of propofol infusion is a **reduced incidence of postoperative nausea and vomiting**, which may have harmful effects on ICP. Because of propofol's **potent circulatory depressant effect**, however, meticulous care should be exercised to maintain adequate CPP, including the **correction of hypovolemia before administering propofol**. Recent studies have shown a reduction in jugular bulb oxygen saturation during propofol anesthesia. Propofol can also reduce CBF more than $CMRO_2$, producing ischemia under certain conditions. Therefore, care should be taken when hyperventilating patients during propofol anesthesia.
4. **Benzodiazepines** may be useful for sedating patients and inducing anesthesia because these drugs have **minimal hemodynamic effects** and are **less likely to impair cerebral circulation. Diazepam**, 0.1 to 0.2 mg/kg, may be used to induce anesthesia and repeated, if necessary, up to a total dose of 0.3 to 0. 6 mg/kg, although it is usually avoided because of its long duration of action. **Midazolam**, 0.2 mg/kg, can also be used for induction and repeated as necessary. Care should be taken when administering these drugs as they **may interfere with further neurologic assessment** and are avoided in an already lethargic patient.
5. **Narcotics** produce a **minimal- to-moderate decrease in CBF and $CMRO_2$** in clinical doses. When ventilation is adequately maintained, narcotics probably have a minimal effect on ICP. Despite its small ICP-elevating effect, **fentanyl** provides satisfactory analgesia and permits the use of lower concentrations of inhalational anesthetics. Some reports have shown that **sufentanil** increases ICP in severely head-injured patients. This could result from the autoregulatory response (i.e., cerebral vasodilatation) to the sudden decrease in systemic BP. **When narcotics are used, measures to maintain systemic BP need to be implemented**. In the perioperative period,

persistent opioid effects can **alter pupillary responses** and interfere with adequate monitoring of neurologic status.

6. **Ketamine** is usually avoided in the head-injured patients because of the risk of sympathetic response, psychomimetic effects, and delayed recovery. However, it may be beneficial in patients who are hemodynamically compromised. Its *N*-methyl D-aspartate (NMDA) receptor antagonism, which may have some neuroprotective effects, has renewed interest in this drug in neurologic patients.

b. **Inhalational anesthetics increase CBF** because of cerebral vasodilatation and **decrease $CMRO_2$**, thus uncoupling the relationship between them. Hence, the concentration of inhalational anesthetics is usually limited to < 1 minimum alveolar concentration (MAC). In instances where patients have evidence of raised ICP, as in stuporous patients or those whose ventricles are obliterated on CT scan from mass effect, the use of inhalational anesthetics should be limited, and a predominantly intravenous technique is recommended.

1. **Isoflurane,** a potent metabolic depressant, has less effect on CBF and ICP than halothane. Because isoflurane **depresses cerebral metabolism**, it may have a cerebral protective effect when the ischemic insult is not severe. Isoflurane is avoided in concentrations >1 MAC, however, because it can cause substantial increases in ICP from its ability to dilate cerebral vessels and **increase CBF**.
2. **Sevoflurane**, in clinical studies, has a demonstrated **effect on cerebral hemodynamics that is either similar to or milder than isoflurane**. The **disadvantage** of sevoflurane is that its biodegraded metabolite may be toxic in high concentrations. There is no evidence of an adverse effect at clinically-used concentrations, however, unless sevoflurane is administered in a low-flow circuit for prolonged periods. **Rapid emergence** from anesthesia with sevoflurane may be an advantage because it facilitates early postoperative neurologic evaluation. Sevoflurane has also shown some promise in animal models as a **cerebral protectant** through a preconditioning effect. The potential may also exist for sevoflurane as a direct cerebral protectant.
3. **Desflurane** at high concentrations appears to **increase ICP**. This may be related to the sympathetic stimulation, which occurs with the use of such high concentrations.
4. **Nitrous oxide ($N_2O$) dilates cerebral vessels**, thereby **increasing ICP**. Patients who have intracranial hypertension or a decrease in intracranial compliance should, therefore, not receive this drug. $N_2O$ should also be **avoided in the presence of pneumocephalus or pneumothorax** because it diffuses into an air space more rapidly than the nitrogen diffuses out, thereby increasing the volume within the air space.

c. **Local anesthetics.** The infiltration of either **lidocaine 1%** or **bupivacaine 0.25%,** with or without epinephrine, in the skin around the scalp incision and the insertion sites for the pin head holder is helpful in preventing systemic and intracranial hypertension in response to these stimuli and avoiding the unnecessary use of deep anesthesia. In order to block the entire scalp, a circumferential injection of local anesthetic is given starting above the ears and passing over the occiput and above the glabella.

d. **Muscle relaxants.** Adequate muscle relaxation facilitates appropriate mechanical ventilation and reduces ICP. The avoidance of coughing and straining is crucial because both can produce cerebral venous engorgement. Muscle relaxants that cause histamine release are not used because of the risk of cerebral vasodilatation.
   1. **Vecuronium** appears to have **minimal or no effect on ICP**, blood pressure, or heart rate and, as such, is effective in head-injured patients. This drug is given as an initial dose of 0.08 to 0.1 mg/kg followed by a maintenance dose of 0.012 to 0.018 mg/kg.
   2. **Pancuronium** does not increase ICP but can cause **hypertension and tachycardia** because of its vagolytic effect. **Disadvantages** are prolonged duration and dependence on renal and hepatic elimination.
   3. **Cis-atracurium** has **little effect on ICP** as it does not cause histamine release when compared to its parent drug, atracurium. Cis-atracurium does not depend on renal and hepatic elimination.
   4. **Rocuronium** is useful for intubation because of its **rapid onset** of action and **lack of effect on intracranial dynamics**.

C. **Intraoperative respiratory and circulatory management**
1. **Mechanical ventilation** is adjusted to maintain a **$PaCO_2$ of around 35 mm Hg**. The fraction of inspired oxygen ($FiO_2$) is adjusted to maintain a **$PaO_2$ of > 100 mm Hg**. Patients, especially those who have pulmonary contusion, aspiration, or central neurogenic pulmonary edema, may require **positive end-expiratory pressure (PEEP)** to maintain adequate oxygenation. Excessive PEEP should be avoided, however, because the elevation in intrathoracic pressure can compromise cerebral venous drainage and increase ICP. Similarly, it is imperative to **avoid any increase in peak airway pressure** from secretions, kinking of the endotracheal tube, or bronchospasm.

   Adult respiratory distress syndrome (ARDS) is a risk in head-injured patients in which case **lung-protective ventilation** may be required. An ICU ventilator should be available in the OR for this purpose.
2. **Circulatory management. CPP** should be maintained at a **minimum level of 60 mm Hg**. A higher CPP may be necessary for elderly patients and those who have hypertension or cerebrovascular disease. The **transducer for direct monitoring of arterial BP is zeroed at the level of mastoids to reflect the cerebral perfusion**.
   a. When **hypotension** persists despite adequate oxygenation, ventilation, and fluid replacement, careful elevation of the BP through the use of a continuous infusion of an inotrope or a vasopressor may be necessary. **Phenylephrine**, 0.1 to 0.5 mcg/kg/minute, and **dopamine**, 1 to 10 mcg/kg/minute, are appropriate drugs in this setting. Bolus doses of vasopressor can be problematic as abrupt increases in BP can elevate ICP to dangerous levels, especially in patients who have disordered autoregulation.
   b. **Hypertension** is treated cautiously because the elevation in BP may reflect compensatory hyperactivity of the sympathetic nervous system in response to elevated ICP and compression of the brain stem (Cushing's reflex). The adequacy of oxygenation, ventilation, volume replacement, and analgesia should be first assessed and corrected. When necessary, anti-hypertensive drugs such as **labetalol** and **esmolol**, which have minimal cerebral vasodilating effects, should be administered. The maintenance of CPP is of major concern whenever hypertension is treated.

D. **Intraoperative management of elevated ICP**
   1. **Patient's position.** A slight head-up tilt of 10° to 30° is desirable. CPP might not be improved, however, if systemic BP decreases substantially. When the surgeon requests either rotation or flexion of the head and the neck, the anesthesiologist must ensure the adequacy of venous return.
   2. **Ventilation.** The $PaCO_2$ is maintained at around 35 mm Hg. Hyperventilation is best avoided because of its cerebrovasoconstrictive effect.
   3. **Circulation.** Both hypotension (systolic BP < 90 mm Hg) and hypertension (systolic BP > 160 mm Hg) should be corrected when indicated.
   4. **Diuretics**
      a. **Mannitol decreases cerebral volume and reduces ICP**. The immediate plasma expanding effect reduces viscosity, increases CBF, and hence, improves cerebral oxygen delivery. The increased deformability of erythrocytes may help in reducing ICP. The osmotic effect is delayed for 15 to 30 minutes and may persist for a variable period of 90 minutes to 6 hours. A multicenter trial is needed to determine the effect of a single administration of high-dose mannitol on outcome after TBI.
      b. **Furosemide** may be coadministered in severe cases as well as in the patient who has compromised cardiac function and the potential for heart failure. Furosemide, 0.1 to 0.2 mg/kg, is given 15 minutes before mannitol administration. When furosemide and mannitol are administered together, careful monitoring of intravascular volume by either CVP or pulmonary artery (PA) pressure is necessary. The combination of mannitol and furosemide has a synergistic effect as furosemide excretes the water load and helps maintain the osmotic gradient established by mannitol. Also, furosemide has a role in preventing the rebound phenomenon by blocking chloride channels.

E. **Acute brain swelling.** Ventilation, oxygenation, depth of anesthesia, and last dose of diuretics should be assessed when the brain is observed to protrude during craniotomy. Other factors that can contribute to brain swelling and require identification and correction are direct jugular compression, increase in airway pressure from secretions or bronchospasm, and the use of vasodilating drugs including volatile anesthetics. If all are adequate, additional thiopental (or pentobarbital) may be indicated. More vigorous hyperventilation is also an option with careful monitoring of brain oxygenation. If these measures fail, decompressive craniectomy may be necessary.

F. **CSF drainage.** If an intraventricular catheter is in place, CSF drainage is an effective and reliable technique for reducing ICP. Drainage of even amounts of CSF as small as 10 to 20 mL can effectively reduce brain tension.

G. **Monitoring**
   1. **Standard monitoring** includes heart rate and rhythm (electrocardiogram), non-invasive and direct arterial BP measurement, pulse oximetry, end-tidal $CO_2$, body temperature, urinary output, CVP, and neuromuscular blockade. Arterial blood gases, hematocrit, electrolytes, glucose, and serum osmolality should be measured periodically.
   2. **Monitoring for air embolism.** Detection of venous air embolism by Doppler ultrasound should be considered for surgical procedures in which veins in the operative site are above the level of the heart.
   3. **Brain monitoring** options include electroencephalogram (EEG), evoked potentials, jugular bulb venous oxygen saturation ($SjO_2$), flow velocity

measured by transcranial Doppler (TCD), brain tissue oxygen tension ($btPO_2$), and ICP.

a. **$SjO_2$.** The $SjO_2$ provides continuous information about the **balance between global cerebral oxygen supply and demand**. However, this is an invasive technique requiring retrograde cannulation of the internal jugular vein. Vessel wall abutment causing a decrease in light return is a problem. Significant false-positive rates are also seen. Normal $SjO_2$ is 60% to 70%. A $SjO_2 < 50\%$ for > 15 minutes is a poor prognostic sign and is often associated with poor neurologic outcome. The decrease in $SjO_2$ could be caused by excessive hyperventilation, decreased CPP, cerebral vasospasm, or a combination. The major causes of a decrease in $SjO_2$ and their treatment are listed in Table 7.3.

b. **Flow velocity** of basal cerebral arteries as measured by the TCD technique is useful for evaluating the cerebral circulatory state at the bedside. Although TCD does not provide an absolute value for CBF, it does **help to assess $CO_2$ reactivity and autoregulation and estimate CPP**. High-normal values for flow velocity may indicate hyperemia or vasospasm. The TCD waveform can differentiate between these two conditions. Disadvantages of TCD as a monitor are subjective variations in the measurements and difficulties in applying the Doppler probe during surgical procedures.

c. **Near-infrared spectroscopy,** currently available in clinical practice, provides relative **information about changes of oxy- and deoxyhemoglobin and the cytochrome oxidase redox status** in the brain tissue of interest in a non-invasive and continuous fashion. Limitations are lack of a definitive threshold and problems of contamination with extracranial blood.

d. **ICP.** The association between severity of ICP elevation and poor outcome is well known. Monitoring ICP is useful, therefore, not only as a guide to therapy, but also for assessing the response to therapy and determining the prognosis. The **ventricular catheter** is the most reliable monitor of ICP and allows ease of calibration and also drainage of CSF. ICP monitoring helps assess CPP and determine the risk of herniation. Treatment is usually initiated when ICP is > 20 mm Hg. However, this threshold should be closely correlated with clinical

TABLE 7.3 Major Causes of Decreased $SjO_2$[a] and Treatment

| Cause | Clinical Condition | Treatment |
|---|---|---|
| $CaO_2 \downarrow$ | Hypoxemia | Correction of hypoxemia |
| | Anemia | Blood transfusion |
| CBF ↓ | Hypotension | Fluid replacement; inotropics and vasopressors |
| | Hyperventilation | Correction of $PaCO_2$ |
| | Intracranial hypertension | Mannitol, furosemide, barbiturate, propofol |
| $CMRO_2 \uparrow$ | Hyperthermia | Cooling |
| | Seizures | Barbiturate, propofol |

$CaO_2$, oxygen content in arterial blood; CBF, cerebral blood flow; $CMRO_2$, cerebral metabolic rate for oxygen consumption; $SjO_2$, jugular bulb venous oxygen saturation.
[a]$SjO_2 \propto [CaO_2 - CMRO_2/CBF]$.

examination and CT results because the location of the mass lesion may also be a determinant of the risk of herniation.

e. **Brain tissue oxygen tension ($btPO_2$).** A probe for the determination of $btPO_2$ is available. A brain tissue $PO_2 < 10$ to 15 mm Hg for greater than 30 minutes is associated with a higher risk of mortality. The disadvantages of monitoring $btPO_2$ are that it (i) only provides focal monitoring, (ii) cannot be used in the surgical field during operation, and (iii) has a critical threshold that is not well determined. Future trials should investigate the role of therapeutic interventions aimed at preventing a fall in $btPO_2$ to see whether they are associated with an improvement in outcome.

## VI. POSTOPERATIVE MANAGEMENT

A. **Emergence and extubation.** Anesthesiologists often receive requests to awaken patients promptly to allow early postoperative neurologic assessment. Patients who had a normal level of consciousness before the operation and who have undergone an uneventful procedure can be awakened and their tracheas extubated in the OR, assuming that emergence criteria have been satisfactorily met. **Smooth emergence with control of systemic BP and avoidance of coughing is necessary to prevent postoperative cerebral edema and hematoma formation.** Administration of lidocaine and remifentanil, a short-acting opioid, are effective in suppressing the cough and even the hypertensive response. Drugs such as labetalol, esmolol, and hydralazine may also be given to prevent the hypertensive response to emergence and extubation.

Extubation in the OR is discouraged for patients whose level of consciousness was depressed preoperatively and in whom brain swelling is either marked during operation or expected to occur postoperatively. Patients who have sustained multiple traumatic injuries are also candidates for postoperative ventilation. Patients who are hypothermic during emergence should be mechanically ventilated postoperatively and their tracheas extubated after careful rewarming.

B. **Delayed awakening** is a major neurologic problem faced in the OR after surgery in head-injured patients. The most important determinant of ability to awaken promptly is the preoperative GCS score. Other causes such as residual drug effects, metabolic or electrolyte disturbances, and hypothermia should be identified and treated. Seizures or persistent ICP elevation from residual hematoma, cerebral edema, or pneumocephalus may also act as factors in delaying arousal.

C. **Systemic complications.** Head injury patients often suffer the systemic effects of trauma including massive bleeding and insufficiency or failure of multiple organ systems. Respiratory failure may occur as a result of aspiration, pulmonary edema, and ARDS. Endocrine manifestations include diabetes insipidus (DI) leading to hypernatremia, the syndrome of inappropriate antidiuretic hormone (SIADH) secretion, and cerebral salt wasting (CSW) syndrome leading to hyponatremia. DIC, stress ulcers, and non-ketotic hyperosmolar coma are other complications that may occur in the postoperative period. Patients may require chronic ventilator support and enteral nutrition therapy, as well.

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# 8 Anesthesia for Supratentorial Tumors

**Nicolas J. Bruder and Patrick A. Ravussin**

## Illustrative Clinical Case

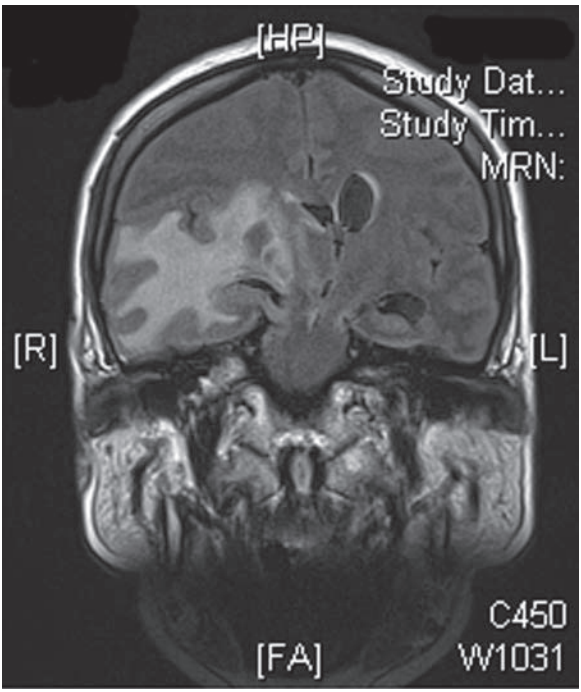
A 52-year-old woman, with a history of arterial hypertension treated with nicardipine, is admitted in the neurosurgical unit for headaches and left-sided hemiparesis. The magnetic resonance imaging (MRI) (see figure) reveals a temporal and parietal tumor. Surgery is planned 2 days later, but during the night, the patient becomes lethargic with vomiting and complete hemiplegia. Emergency surgery is planned for tumor removal.

The symptoms are due to intracranial hypertension. The MRI shows mass effect and temporal herniation. The primary objectives are to maintain perfusion to the brain, avoid aspiration during induction, and avoid blood pressure bursts during recovery.

Rapid-sequence induction of anesthesia is indicated (propofol or thiopental as hypnotic). Succinylcholine can be used despite its effect on intracranial pressure (ICP). Vasopressors (phenylephrine or ephedrine) should be immediately available to treat any hypotension (and decrease in cerebral perfusion pressure [CPP]). Infuse 500 mL of isotonic crystalloid to limit hypotension due to hypovolemia. Infuse mannitol 20% 300 mL during surgical preparation and compensate urinary losses with isotonic fluids. A large dose of corticosteroids to reduce peritumoral edema is indicated if not given immediately before anesthesia (methylprednisolone 120 mg). Antibioprophylaxis (first- or second-generation cephalosporin) is indicated. Invasive arterial pressure monitoring is required.

Maintenance of anesthesia will use a continuous infusion of propofol and sufentanil or remifentanil without nitrous oxide (air–oxygen mixture). Deep neuromuscular blockade is useful during tumor removal to avoid coughing due to inadequate anesthesia. Mild hypocapnia (arterial carbon dioxide [$CO_2$] partial pressure 30 to 35 mm Hg) is indicated because intracranial hypertension is present. More profound levels of hypocapnia should be used only on request by neurosurgeons. Before skull opening, mean arterial pressure has to be maintained in the high range (> 85 mm Hg) because ICP may be over 30 mm Hg and CPP should be above 60 mm Hg. Use continuous infusion of phenylephrine after excluding hypovolemia. After opening the dura, the ICP is equal to 0 and arterial pressure has to be kept in the normal range. Warm the patient to avoid hypothermia.

After completion of surgery, prevent edema formation with corticosteroids, prevent postoperative epilepsy (phenytoin), prevent postoperative pain (depending on the amount and the type of narcotics used for maintenance), and prevent nausea and vomiting with ondansetron. Emergence from anesthesia requires hemodynamic stability: short-acting beta-blocker (esmolol) and/or nicardipine on request. Assess neurologic status as soon as possible but consider resuming sedation to transfer the patient in the intensive care unit (ICU) if criteria for tracheal extubation are not met.




## CHAPTER HIGHLIGHTS

- Assess brain compliance preoperatively (CT scan) and risk of intracranial hypertension during anesthesia.
- Avoid oversedation with premedication before anesthesia.
- Maintain hemodynamic stability and avoid hypercapnia during induction of anesthesia.
- Antibioprophylaxis is indicated for tumor surgery.
- Consider mannitol infusion, 0.75 g/kg, before skin incision in agreement with neurosurgeons.
- Large meningiomas may be associated with significant blood loss.
- Hypocapnia improves operative conditions but reduces cerebral blood flow. Its use should be limited to the time of surgical dissection.
- Total intravenous anesthesia is associated with reduced ICP and brain bulk. Inhalation anesthesia is associated with a more predictable delay for tracheal extubation.
- Movement and coughing must be prevented during surgery (may need neuromuscular blocking drug [NMB]).
- Check if corticosteroids (malignant tumors) and antiepileptic drug are required before emergence. Infuse analgesics if remifentanil is used for maintenance.
- Maintain stable blood pressure during recovery (risk of intracranial bleeding). Plan early tracheal extubation and rapid neurologic evaluation but avoid restlessness and respiratory depression.

## I. ANESTHESIA FOR SUPRATENTORIAL TUMORS

**A. Background.** Approximately 51,410 new brain tumors are diagnosed each year in the United States. The majority of tumors (> 80%) are supratentorial and half of these are malignant. The most common primary brain tumors are gliomas (36%), meningiomas (32%), and pituitary adenomas (8%). The incidence of brain metastases increases with age and may reveal the primary cancer. The five most common sources of brain metastases are breast, colorectal, kidney, lung, and melanoma. Within 1 year of diagnosis of the primary cancer, approximately 6% of patients develop brain metastasis.

**B. General considerations**

1. **Concerns and problems**
   a. **Signs and symptoms** result from local mass effect and generalized increased ICP.
   b. **Main surgical concern** is brain exposure without damage from retraction pressure or mobilization.
   c. **Main anesthetic concern** is the avoidance of secondary brain damage (Table 8.1). Therefore, understanding the following is vital: pathophysiology of ICP and cerebral perfusion; effects of anesthesia on ICP, cerebral perfusion, and cerebral metabolism (the cerebral metabolic rate for oxygen consumption [$CMRO_2$]); and therapeutic options for decreasing ICP, brain bulk, and tension perioperatively.
   d. **Specific challenges** include intraoperative hemorrhage, seizures, air embolism (seen with head elevation, sitting position, or entry into venous sinuses), monitoring brain function and environment, and rapid versus prolonged emergence from anesthesia. Intracranial pathology may also be complicated by the concurrence of extracranial issues including cardiovascular and pulmonary disease, paraneoplastic phenomena with metastases, and the effects of chemo- and radiation therapy.
2. **Pathophysiology of elevated ICP.** The usual intracranial space-occupying components—brain tissue, intravascular blood, cerebrospinal fluid (CSF)—are contained in an unyielding skull. Any volume increase (tumor, abscess, hematoma) must be compensated by the parallel volume reduction of one or more of these components,

TABLE 8.1 Secondary Insults to the Already-Injured Brain

| Intracranial | Systemic |
|---|---|
| ■ Increased intracranial pressure | ■ Hypercapnia/hypoxemia |
| ■ Epilepsy | ■ Systemic hypotension/hypertension |
| ■ Cerebral vasospasm | ■ Low cardiac output |
| ■ Herniation: falx, tentorium, foramen magnum (vessel compression and ischemia), craniotomy (brain injury on skull edge) | ■ Hypo/Hyperglycemia |
| ■ Midline shift: tearing of cerebral vessels | ■ Osmolality < 280 or > 320 mOsm |
| | ■ Shivering/hyperthermia |

mainly either CSF or blood as the brain is largely incompressible. The brain's ability to compensate for the presence of a mass and still maintain homeostasis depends on the volume of the mass and its rate of growth as the intracranial pressure–volume curve shifts to the left for rapidly expanding masses. Homeostatic mechanisms include *early* (limited capacity)—intracranial to extracranial blood shift; *late* (larger capacity)—CSF displacement (ineffective if CSF flow is obstructed); and *exhaustion*—rapid ICP rise → impaired cerebral circulation → brain herniation as the end stage when there is no more compensation.

3. **Cerebral perfusion and cerebral blood flow**
   a. **Regulation of cerebral blood flow (CBF)** is accomplished through gradients in the mural pressure of cerebral arterioles. These gradients are affected by the cerebral perfusion pressure (CPP = mean arterial pressure [MAP] – ICP) and the partial pressure of arterial carbon dioxide ($PaCO_2$), which is the result of ventilation (Fig. 8.1).
   b. **Autoregulation of CBF** keeps the CBF constant despite changing CPP via alterations in cerebral vasomotor tone (i.e., cerebrovascular resistance [CVR]). Characteristics are (1) dominant to ICP homeostasis; (2) normally functional for CPP of 50 to 150 mm Hg; and (3) impaired or affected by intracranial (e.g., blood in CSF, trauma, tumors) and extracranial (e.g., chronic systemic hypertension) pathologies and anesthetic drugs. Autoregulation is also not an immediate response in that a sudden increase in blood pressure will give rise to a temporary increase in CBF.

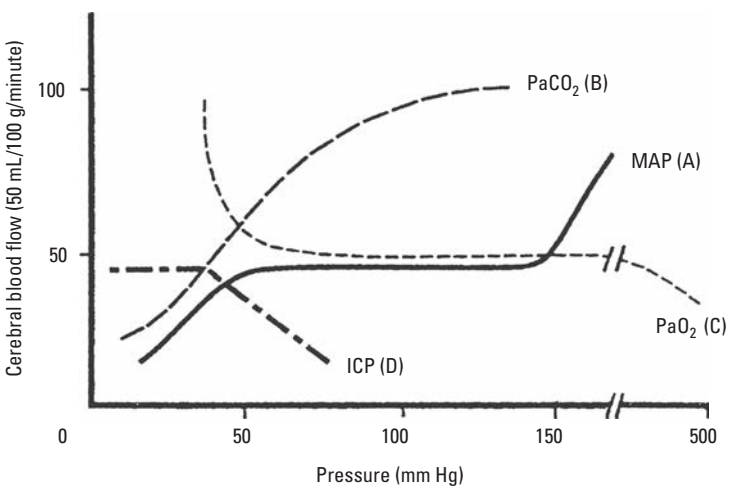



**FIGURE 8.1** Pressure–cerebral blood flow relationships. **(A)** Cerebral blood flow (CBF) autoregulation. CBF is maintained at 50 mL/100 g/minute for mean arterial pressure (MAP)/cerebral perfusion pressure = 50 to 150 mm Hg. **(B)** Linear relationship between partial pressure of arterial carbon dioxide ($PaCO_2$) and CBF for $PaCO_2$ = 20 to 80 mm Hg. **(C)** Partial pressure oxygen ($PaO_2$) and CBF. **(D)** Intracranial pressure (ICP) and CBF.

c. **Formulas.** CBF = CPP/CVR (cerebrovascular resistance), CPP = MAP – ICP. Note that normally ICP ≈ CVP (central venous pressure).
d. **Inadequate perfusion** occurs when CBF falls below 20 mL/100 g/minute and depends on both the reduction of CBF and its duration. Inadequate perfusion is also linked to CPP < 50 mm Hg with intact autoregulation. Treatment is to restore CPP and CBF by increasing MAP and cardiac output and decreasing ICP and cerebral metabolic demand, the latter through deepened anesthesia, hypothermia, and anticonvulsant therapy.
e. **Vasodilatory and vasoconstrictive cascades.** If autoregulation is intact: ↓ MAP → cerebral arteriolar vessel dilatation →↑ CBV (cerebral blood volume) →↑ ICP →↓ CPP (vicious circle!). Conversely, ↑ MAP →↑ CPP →↓ ICP via cerebral vasoconstriction (positive circle).
f. **$PaCO_2$.** Hypocapnia results in vasoconstriction, reducing CBF, CBV, and therefore ICP, making hyperventilation a favorite tool for the acute control of cerebral hyperemia, elevated ICP, and intraoperative expansion of brain bulk. However, the reduction of CBF induces the risk of cerebral ischemia.

4. **Anesthesia and ICP, cerebral perfusion, and metabolism.** Anesthesia affects the intracranial environment through pharmacologic and mechanical effects, all of which are sensitive to intra- and extracranial conditions including cerebral compliance, intracranial pathology, volume status, and coexisting diseases.
   a. **Intravenous anesthetics** (barbiturates, propofol, etomidate) reduce $CMRO_2$ in a dose-dependent fashion by depressing electrical and neurotransmitter synthesis (not basal metabolic) activity of the neurons with a ceiling effect at electroencephalographic (EEG) burst suppression. The intravenous anesthetics are cerebral vasoconstrictors →↓ CBF, CBV, and ICP. Cerebral flow-metabolism coupling, autoregulation, and $PaCO_2$ vessel reactivity remain intact. In contrast to volatile anesthetics, propofol suppresses the cerebrostimulatory effects of nitrous oxide ($N_2O$).
   b. **Volatile anesthetics** (isoflurane, sevoflurane, desflurane) decrease $CMRO_2$. They are all cerebral vasodilators (desflurane > isoflurane > sevoflurane). For minimum alveolar concentration (MAC) < 1 to 1.5 in the normal brain (with flow/metabolism coupling intact), CBF decreases as compared to the awake state and autoregulation is maintained. Above 1 to 1.5 MAC, there is a dose-related increase in CBF and impairment of autoregulation (Figs. 8.2 and 8.3). Maintenance of $PaCO_2$ reactivity allows hypocapnic control of this type of vasodilatation. A situation to avoid is the combination of brain pathology + high volatile MAC → impaired or abolished $CO_2$ reactivity.
   c. **Nitrous oxide** is cerebrostimulatory →↑ $CMRO_2$, CBF, and sometimes ICP, particularly in combination with a volatile anesthetic. For the normal brain, the $N_2O$-induced cerebral vasodilatation can be controlled by hypocapnia or intravenous anesthetics, but volatile anesthetics offer *no* attenuating effect. $CMRO_2$ and CBF are higher for 1 MAC anesthesia with $N_2O$ and a volatile anesthetic versus volatile anesthesia only.
   d. **Opioids** have been associated with a short-term ↑ ICP when given in large doses. However, opioids are only modest direct cerebral vasodilators. Therefore, it is probably the reflex cerebral vasodilatation after

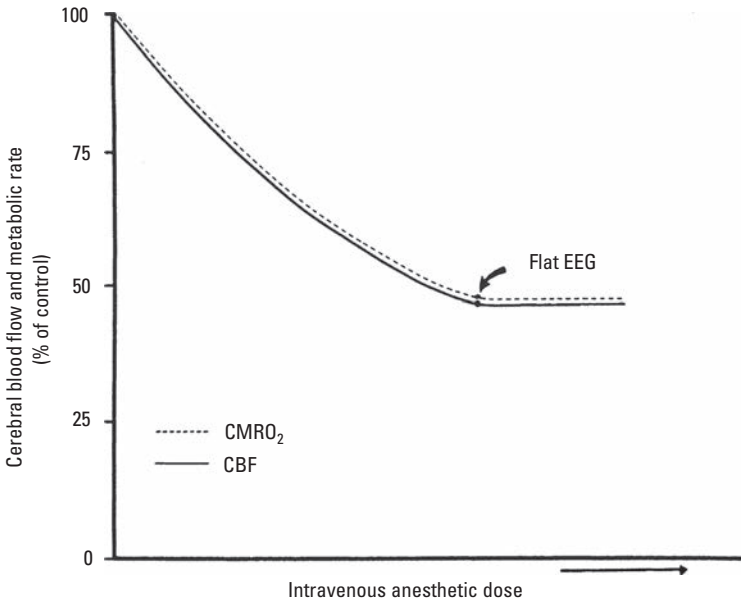



**FIGURE 8.2** Cerebral blood flow (CBF)—cerebral metabolic rate for oxygen consumption ($CMRO_2$) coupling during increasing dose of an intravenous anesthetic. A normal $CMRO_2$ of 4 mL/100 g/minute is coupled to a CBF of 50 mL/100 g/minute. EEG, electroencephalogram.

↓ MAP/CPP that causes the transient ↑ ICP. Opioids modestly ↓ $CMRO_2$ without affecting flow-metabolism coupling, autoregulation, or vessel $CO_2$ reactivity. Remifentanil is particularly suitable for rapid emergence from anesthesia, but discontinuation of the remifentanil infusion requires the addition of a longer-acting analgesic for postoperative pain control.

e. **Neuromuscular blocking drugs (NMB).** The effect of succinylcholine on ICP is controversial, but fasciculations may increase ICP. Succinylcholine may be used, however, for the difficult intubation or rapid-sequence induction in patients who have brain injuries. Other NMB have no effect on ICP.

f. **Other drugs.** Avoid vasodilating anti-hypertensive drugs (nitroglycerin, nitroprusside, hydralazine) as they may lead to cerebral vasodilatation. Take into account pharmacologic interactions, particularly with antiepileptic drugs.

5. **Reducing ICP, brain bulk, and tension** (Table 8.2). The effectiveness of these techniques depends on intact intracerebral homeostatic mechanisms and/or structures.

a. **Intravenous anesthetics**→↓ $CMRO_2$, CBF →↓ CBV, ICP →↓ brain bulk. Cerebral vasoconstriction depends on intact $CMRO_2$-CBF coupling (Fig. 8.2) and is dose related up to neuronal electrical silence (EEG burst suppression). As with autoregulation, $CMRO_2$-CBF coupling is impaired by brain contusion and other intracerebral pathologies.

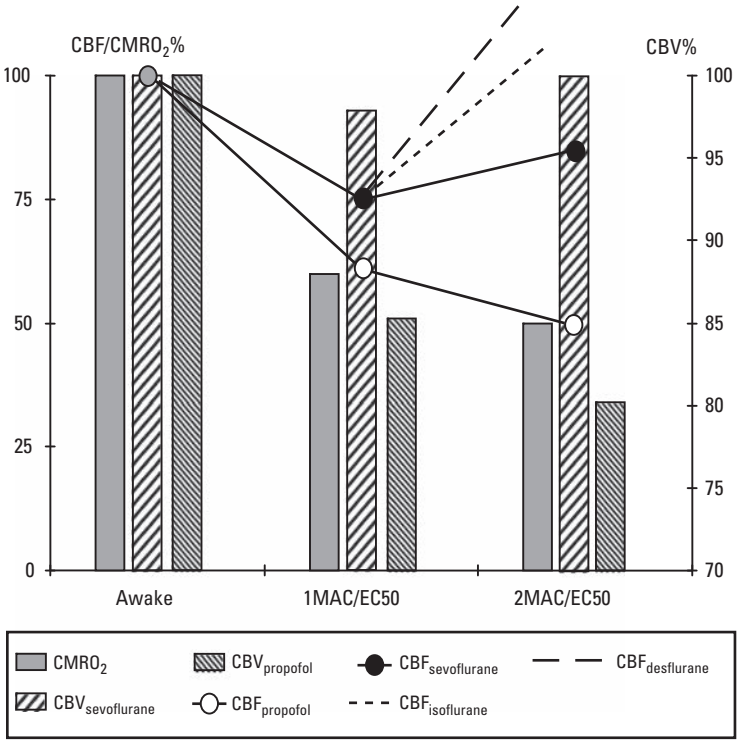



**FIGURE 8.3** Cerebral blood flow (CBF)—cerebral metabolic rate for oxygen consumption ($CMRO_2$)—cerebral blood volume (CBV) during increasing doses of intravenous (propofol) and volatile anesthetics. Changes are noted as a percentage value from the awake state. Despite similar changes in $CMRO_2$, changes in CBF and CBV are markedly different between intravenous and volatile drugs and among sevoflurane, isoflurane, and desflurane above 1.5 minimum alveolar concentration (MAC). EC50, median effective concentration.

b. **Hyperventilation**→ hypocarbia → cerebral vasoconstriction. The acute effect lasts for a maximum of 24 hours. When autoregulation is intact, CBF is linearly related to $PaCO_2$ from 20 to 70 mm Hg so that there is a 3% to 4% change/mm Hg $PaCO_2$. Factors impairing $CO_2$ reactivity are head injury, other intracranial pathology, high-inspired volatile anesthetic concentrations, and $N_2O$ (especially when cerebral vessels are already dilated). The typical target for ventilation is a $PaCO_2$ of 30 to 35 mm Hg as measured by arterial blood gas analysis rather than end-tidal $CO_2$ ($ETCO_2$) as neurosurgical patients may have large arterioalveolar $CO_2$ gradients. Side effects of hyperventilation include reduction in coronary artery flow and cardiac venous return as well as hypokalemia.

c. **Hyperosmolar drugs.** *Osmolality*: 20% Mannitol 1,100 mOsm/kg; 7.5% sodium chloride (NaCl) 2,567 mOsm/kg. Osmotic diuretics (mannitol, hypertonic saline) → acutely ↑ blood osmolality →↓ brain water

TABLE 8.2 Intracranial Hypertension and Brain Bulging: Prevention and Treatment

| Prevention | Treatment |
|---|---|
| ■ Preoperative adequate anxiolysis and analgesia<br>■ Preinduction: hyperventilate on demand, head-up position, head straight, no jugular vein compression<br>■ Avoid overhydration<br>■ Osmotic diuretics (mannitol, hypertonic saline); steroids for tumor<br>■ Optimize hemodynamics: MAP, CVP; remifentanil or beta-blockers to prevent hypertension<br>■ Ventilation: $PaO_2$ > 100 mm Hg; $PaCO_2$ 35 mm Hg; low intrathoracic pressure (no PEEP)<br>■ Intravenous anesthetics for induction and maintenance | ■ Cerebrospinal fluid drainage<br>■ Osmotic diuretics<br>■ Hyperventilation ($PaCO_2$ 25–28 mm Hg)<br>■ Increase depth of anesthesia using intravenous anesthetics (propofol, thiopental)<br>■ Muscle relaxation<br>■ Control head position and correct excessive rotation (avoid jugular compression)<br>■ Mild controlled hypertension (MAP 100 mm Hg) with phenylephrine if cerebral autoregulation intact |

MAP, mean arterial pressure; CVP, central venous pressure; $PaCO_2$, arterial carbon dioxide tension; $PaO_2$, arterial oxygen tension; PEEP, positive end-expiratory pressure.

content (occurs mainly in healthy brain tissue with intact blood–brain barrier) →↓ brain bulk, ICP, ↑ intracranial compliance. Blood rheology is also improved because of ↓ endothelial edema and ↓ erythrocyte edema →↑ erythrocyte deformability with augmentation of perfusion, especially through the microvasculature. A typical regimen is mannitol, 0.5 to 1 g/kg intravenously. This may be divided between a rapid precraniotomy dose and a subsequent slower infusion until brain dissection is complete. The ICP-lowering effect is prompt, lasts for 2 to 3 hours, and removes approximately 90 mL of brain water at peak effect. Problems with mannitol include hypernatremia and acute hypervolemia, which prompts caution in patients who have heart disease. Urinary losses from mannitol are replaced with isotonic crystalloid solutions.

d. **CSF drainage** can be accomplished either by direct puncture of the lateral ventricle by the surgeon or preoperative insertion of a lumbar subarachnoid catheter, which is effective only in the absence of a caudal block to CSF outflow. As acute brain herniation might occur if the ICP is elevated, lumbar CSF drainage should be used cautiously and only when the dura is open and the patient is at least mildly hyperventilated. Draining 10 to 20 mL of CSF effectively reduces brain tension; up to 50 mL can be drained if necessary.

e. **Use the vasoconstrictive cascade.** Mild ↑ MAP →↑ CPP →↓ CBV from cerebrovasoconstriction.

f. **Avoid other factors** causing cerebral vasodilatation or hypotension. These include hypovolemia, hypoxia, poor patient positioning (head-down; extreme flexion of the neck →↓ cerebral venous drainage; rotation of the head on one side and jugular venous thrombosis

on the other side → major brain swelling), and volatile anesthetics > 1 to 1.5 MAC.

**C. General anesthetic management**

1. **Preoperative assessment.** Anesthetic strategy is based on the patient's neurologic and general state and the planned operation. Both should be discussed with the neurosurgeon before surgery.
   a. **Neurologic state of the patient** (Table 8.3) (1) Assess the level of consciousness clinically (if ↓, then suspect ↑ ICP), Glasgow Coma Scale score, presence of focal neurologic deficits (including speech deficit), pupil size and reactivity; (2) Note treatments and their side effects (especially antiepileptic drugs); (3) Review diagnostic radiology for signs of ↑ ICP (mass effect, midline shift, temporal or frontal herniation, reduced or absent CSF around brain stem, disappearance of subarachnoid spaces).
   b. **General state of the patient.** (1) Cardiovascular system: brain perfusion/oxygenation depend on it; acute intracranial pathologies affect cardiac and lung function (worst situation: neurogenic pulmonary edema); supratentorial surgery (meningioma, metastasis) may cause significant bleeding. (2) Respiratory system: hyperventilation to ↓ ICP, CBF, CBV, and brain tension depend on it; 40% of brain metastases are from lung (primary tumor, chemotherapy/radiation therapy). (3) Other systems: paraneoplastic or chemotherapy-/radiation therapy–associated syndromes (hypercalcemia, aplasia, cardiotoxicity of chemotherapy); renal system; altered endocrine system (intracranial processes; pituitary adenoma or its therapy; steroids); gastrointestinal tract (nausea and vomiting, steroids, and mucosal irritation). Coagulation profile must be normal: stop aspirin 7 days and clopidogrel 10 days before surgery.

**TABLE 8.3** Preoperative Neurologic Evaluation

**History**
- Seizures
- ↑ ICP: headache, nausea, vomiting, blurred vision
- Focal neurologic deficit: motor or sensory deficit
- Hydration: fluid intake, diuretics
- Medication: steroids, antiepileptic drugs, and their adverse effects
- Associated medical conditions

**Physical Examination**
- Mental status, level of consciousness
- Papilledema, Cushing's response (hypertension, bradycardia)
- Pupil size, speech deficit, Glasgow Coma Scale score, focal deficit

**Radiology (CT or MRI Scan)**
- Size and location of the tumor (proximity to large vessels or eloquent brain areas)
- Mass effect: midline shift, temporal or frontal herniation, absent basal CSF cisterns, hydrocephalus

ICP, intracranial pressure; CT, computed tomography; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid.

c. **Biology.** Coagulation, hemoglobin, platelet count, potassium, sodium, calcium.

d. **Planned operative intervention.** Clarify surgical approach and planned duration (tumor size/position, proximal structures and likelihood of vascular involvement, radical excision) with attention to patient positioning (supine, prone, sitting, lateral) and tumor type.

1. **Meningiomas.** The combination of large size, difficult location, and radical excision (total resection is virtually curative) makes for long, technically-demanding operations, often with significant bleeding. Anesthetic priority: maximal reduction in brain tension to facilitate surgical access. Replace blood loss with blood products, isotonic crystalloid, or colloid to keep the hematocrit above 28%.
2. **Gliomas.** The operative approach is often simple debulking with easy surgical access and little risk of bleeding. There may be postoperative intracranial hypertension from edema.
3. **Others.** Third-ventricle colloid cysts with resultant obstructive hydrocephalus may be associated with ↑ ICP at induction. Colloid cysts, basal cisternal epidermoids, and transcranially-resected pituitary tumors need maximal brain relaxation for optimal exposure at the base of the skull.
4. **Pituitary adenoma by trans-sphenoidal resection.** Essentially an extracranial operation in a head-up position.

e. **Determination of anesthetic strategy**

1. **Vascular access.** Consider the risk of bleeding or venous air embolism and the need for hemodynamic and metabolic monitoring, replacement of intravascular volume, and infusion of vasoactive and anesthetic drugs.
2. **Fluid therapy.** Target normovolemia/normotension as the goal of fluid replacement. Avoid hypo-osmolar (Ringer's lactate) and glucose-containing solutions as hyperglycemia →↑ ischemic brain injury.
3. **Anesthetic regimen.** "Simple" procedures (low risk of ICP problems or ischemia, little need for brain relaxation): volatile-based technique (< 1.5 MAC) alone or in combination with intravenous anesthetics. "High-risk" procedures (anticipated ICP problems, significant risk of intraoperative cerebral ischemia, need for deep brain relaxation): total intravenous anesthesia (TIVA) with propofol.
4. **Extracranial and intracranial monitoring.**

2. **Preoperative preparation**

a. **Premedication.** Risk assessment: *sedation* → hypercapnia, hypoxemia, upper-airway obstruction →↑ ICP whereas *stress* →↑ CPP/CBF/$CMRO_2$, ↑ ICP, and the development of vasogenic edema. Best: titrated intravenous analgesia/sedation (e.g., midazolam, 0.5 to 2 mg, ± fentanyl, 25 to 100 mcg, or sufentanil, 2.5 to 10 mcg) for vascular access placement under the direct and continuous supervision of the anesthesiologist. Patients who do not have signs of ↑ ICP may benefit from oral premedication with a small benzodiazepine dose before surgery. Continue steroids and other regular medication (anticonvulsants, anti-hypertensives except ACE inhibitors, other cardiac drugs). Consider starting anticonvulsant therapy if not already initiated (e.g., loading dose of phenytoin, 15 mg/kg, or fosphenytoin, 20 mg/kg, over 30 minutes).

b. **Vascular access.** Two large-bore peripheral intravenous catheters are essential for full craniotomy and major spinal column operations.
   1. **Central venous access.** Recommended for long operations (> 6 hours), for patients who have significant cardiovascular compromise (if severe, consider pulmonary artery catheter or transesophageal echocardiography), or when there is significant risk of venous air embolism (catheter tip is positioned at the point at which the vena cava transitions into the right atrium) or bleeding or the need for continuous infusion of vasoactive drugs. The technique of jugular cannulation (conventional or retrograde) must be meticulous as impairment of cerebral venous drainage from hematoma or head-down position $\rightarrow\uparrow$ ICP.
   2. **Arterial cannulation.** Obligatory for full craniotomy owing to the need for close monitoring and control of CPP. The CPP can be obtained by positioning the arterial pressure transducer at the mid-ear/circle of Willis level (CPP = MAP – ICP). Arterial cannulation also facilitates the frequent determination of arterial $PaCO_2$ as a guide to hyperventilation as well as measurement of plasma glucose, potassium, and sodium. Note that $ETCO_2$ monitoring is no substitute for $PaCO_2$ measurement as they often correlate poorly, especially when there is ventilation–perfusion mismatch.

c. **Monitoring**
   1. **Cardiovascular.** Electrocardiographic for detection of myocardial ischemia and arrhythmias; arterial and CVP (see preceding text); transesophageal echocardiography; pulse oximetry; urinary catheter.
   2. **Air embolism.** Sensitively detected by precordial Doppler, end-tidal nitrogen; $ETCO_2$ with transesophageal echocardiography as an alternative.
   3. **Neuromuscular blockade.** Do not monitor hemiplegic extremities. There is an increase in the density of acetylcholine receptors of lower-motor-neuron units innervated by dysfunctional or nonfunctional upper-motor neurons. This causes resistance to nondepolarizing muscle relaxants, which may lead to an effective overdose for normal neuromuscular units. Contralateral hemiparesis from a supratentorial tumor is not associated with hyperkalemia as in paraplegic or burned patients. Succinylcholine is therefore not contraindicated.
   4. **Metabolic.** Monitor glucose regularly in diabetic patients and patients receiving steroids to avoid hyperglycemia (> 1.4 g/dL) or hypoglycemia (< 0.8 g/dL). Monitor temperature via esophageal or bladder thermistor and measure hematocrit, coagulation profile, and serum sodium, potassium, and osmolality as needed.
   5. **Intracranial environment, cerebral function.** Evoked potentials monitor the intactness of specific central nervous system (CNS) pathways. Electroencephalogram (EEG) provides information on the adequacy of cerebral perfusion, presence of ischemia, and "depth of anesthesia."
   6. **ICP monitoring.** Currently rare for elective neurosurgery because of improvements in perioperative ICP control but still has an important role in neurotraumatology and intensive care.

TABLE 8.4 Suggested Anesthesia Induction and Maintenance Regimen

**Induction**
- Adequate preoperative anxiolysis
- ECG, capnograph, pulse oximeter, noninvasive blood pressure
- Venous, arterial lines (under local anesthesia)
- Preoxygenation, then remifentanil, 0.1 mcg/kg/min, or TCI (target: 3–5 ng/mL) or sufentanil bolus, 0.15–0.30 mcg/kg
- Propofol, 1.25–2.5 mg/kg, or thiopental, 3–6 mg/kg
- Nondepolarizing muscle relaxant
- Hyperventilation ($PaCO_2$ 35 mm Hg)
- Intubation

**Maintenance**
- Sevoflurane 0.5%–1.5%, desflurane 3%–6%, propofol 50–150 mcg/kg/min
- Analgesia: remifentanil 0.1–0.15 mcg/kg/min (or target 3–6 ng/mL) or sufentanil
- Pin head holder placement: local anesthesia or remifentanil 0.5–1 mcg/kg
- Position: head up 10°–20°, jugular veins free
- Mannitol 0.5–0.75 g/kg or lumbar CSF drainage
- Normovolemia: isotonic crystalloids or 6% hydroxyethyl starch to replace blood losses
- Brain dissection: decrease narcotic dosage (remifentanil 0.05–0.1 mcg/kg/min or target 2–4 ng/mL)

ECG, electrocardiogram; $PaCO_2$, arterial carbon dioxide tension; TCI, targeted infusion.

3. **Induction of anesthesia**
   a. **Goals.** Ventilatory control (early mild hyperventilation; avoid hypercapnia, hypoxemia); sympathetic/blood pressure control (adequate pain control and hypnosis, treat postinduction hypotension); optimal head and neck position (avoid venous outflow obstruction).
   b. **Typical induction scheme.** See Table 8.4.
   c. **Muscle relaxants.** Modern non-depolarizing drugs have minimal effects on intracranial hemodynamics. The interaction between pancuronium/vecuronium/ rocuronium/cis-atracurium and chronic (> 7 days) phenytoin/carbamazepine treatment from induced resistance to muscle relaxants necessitates increasing the dose of muscle relaxant by 50% to 60%. Neuromuscular blockade monitoring on hemiplegic extremities is avoided (see preceding text). Note that because neurosurgical patients are susceptible to muscle relaxant "hangover," which is difficult to detect by manual relaxometry, long-acting muscle relaxants (such as pancuronium) are avoided in favor of medium- to short-acting drugs (e.g., vecuronium, rocuronium, atracurium, cis-atracurium, mivacurium).
   d. **Patient positioning.** Pin holder application is a maximal nociceptive stimulus that can be blocked by increasing analgesia (remifentanil, 0.25 to 1 mcg/kg; fentanyl, 1 to 3 mcg/kg; sufentanil, 0.2 to 0.3 mcg/k; alfentanil 10 to 20 mcg/kg) and anesthesia (propofol, 0.5 mg/kg) and infiltrating pin site with local anesthetic before application. Alternatively, anti-hypertensives (esmolol, 0.5 to 1 mg/kg; labetalol, 0.075 to 0.15 mg/kg) may be administered. Remember that pin insertion can introduce venous air embolism through sinuses in the skull! Extreme

positions are avoided. Areas of the body that are susceptible to pressure, abrasion, or movement injury are secured and padded. The endotracheal tube is fixed securely to avoid accidental extubation with movement. The eyes are taped occlusively to prevent corneal damage.

A mild head-up position helps venous drainage. Mild knee flexion decreases back strain. Severe lateral extension or flexion of the head on the neck is avoided by maintaining more than two fingers' space between the chin and the nearest bone. Extreme flexion of the head may induce quadriparesis or massive swelling of the face and the tongue, which mitigates against early extubation. If the head is turned laterally, the contralateral shoulder is elevated with a wedge or a roll to prevent brachial plexus stretch injury and limit head rotation. Specific precautions are indicated for the lateral, sitting, and prone positions. All potential pressure points are protected and padded including the eyes, peripheral arterial pulses, and peripheral nerves and are checked frequently during the procedure to avoid compression.

4. **Maintenance of anesthesia (Table 8.4)**
   a. **Goals**
      1. **Control of brain tension through control of $CMRO_2$ and CBF.** CNS arousal is prevented by adequate anesthesia and antinociception. The consequences of CNS arousal are treated with sympatholysis and anti-hypertensive drugs. The concept of the "chemical brain retractor" is illustrated in Table 8.5.
      2. **Neuroprotection.** Maintenance of an optimal intracranial environment ensures adequate CPP, $PaCO_2$, and arterial oxygen saturation ($SaO_2$) and matching cerebral substrate demand and supply. The use of specific drugs for neuroprotection is controversial and should not induce adverse effects or delay recovery.
      3. **Normothermia.** Hypothermia increases blood loss and the risk of infection. Normothermia is maintained except when hypothermia is indicated for brain protection.
   b. **Choice of technique.** Whether intravenous or volatile anesthesia should be used for neurosurgery is controversial. No study to date has shown significant differences in outcome for intravenous versus volatile neuroanesthesia. Operative conditions are worse, however, when the expired concentration ($F_e$) of the volatile anesthetic is > 1.5 MAC.

TABLE 8.5 The Chemical Brain Retractor Concept

- Mild hyperosmolality[a]
- Mild hyperventilation
- Adequate head-up positioning (10°–20°)
- Intravenous anesthetic drug (propofol)
- Normotension or mild hypertension[b]
- Lumbar cerebrospinal fluid drainage
- Venous drainage: jugular veins free
- Avoidance of brain retractors

[a]Before bone flap removal, give 20% mannitol, 0.5–0.75 g/kg, or 7.5% NaCl, 2–3 mL/kg.
[b]Mean arterial pressure 100 mm Hg.

1. **Volatile anesthetics.** *Con*: CBF-$CMRO_2$ uncoupling; ↑ CBF, ICP, and brain bulk. *Pro:* easy to use and control, extensive experience with successful outcomes; predictability facilitates early awakening. *Recommendation*: (a) use for straightforward cases for which no ischemia, ICP, or brain-bulk problems are anticipated; (b) early institution of moderate hyperventilation; (c) $F_e$ < 1.5 MAC; (d) avoid combination with $N_2O$, which will ↑ cerebrostimulation.
2. **Intravenous techniques.** *Con*: more difficult to use; prolonged and unpredictable awakening, which may be mitigated by target-controlled infusion (TCI) with a combination of propofol and remifentanil. *Pro*: intact CBF-$CMRO_2$ coupling; ↓ CBF, ICP, and brain bulk; propofol blunts $N_2O$ cerebrostimulation. *Recommendation*: (a) use for cases with high probability of elevated ICP and brain-bulk problems; (b) use TCI and short-acting drugs.

c. **Management of increases in ICP and brain bulk** (Table 8.2)

d. **Other measures.** When CNS arousal and hemodynamic hyperdynamism are evident despite adequate anesthesia/analgesia, consider sympatholysis with esmolol, 0.5 to 1 mg/kg, or labetalol, 0.075 to 0.15 mg/kg.

e. **Antibiotic prophylaxis.** Vancomycin or a second-generation cephalosporin is administered before the skin incision. Clindamycin may be given if the patient is allergic to beta-lactam.

f. **Fluid therapy.** Goals: normovolemia, normotension, normoglycemia, low-normal hematocrit of approximately 30%, mild hyperosmolality (< 320 mOsm/kg at end of procedure). *Recommendations*: (1) avoid glucose-containing solutions, Ringer's lactate (hypo-osmolar); (2) use isotonic crystalloids or 6% hydroxyethyl starch.

5. **Emergence from anesthesia** causes respiratory, cardiovascular, metabolic/endocrine, and neurologic changes. Emergence is associated with hemodynamic arousal lasting from 10 to 25 minutes, weakly correlating with a rise in oxygen consumption and mediated by elevated catecholamine levels and nociceptive stimuli. Treatment includes antinociception and sympatholysis. Oxygen consumption is increased up to five times by pain and by shivering and non-shivering thermogenesis during rewarming. As a result of all of these factors, 20% of elective craniotomy patients develop intracranial hypertension in the early postoperative period. Systemic hypertension is also a frequent occurrence and has been associated with an increased risk of postoperative intracranial hemorrhage.

a. **Aims of emergence.** (1) maintain intra- and extracranial homeostasis for MAP, CPP, CBF, ICP, $CMRO_2$, $PaCO_2$, $PaO_2$, and temperature; (2) prevent postcraniotomy pain; (3) avoid factors leading to intracranial bleeding such as coughing, tracheal suctioning, straining against the ventilator, and increased blood pressure. The patient should be calm, cooperative, and responsive to verbal commands soon after emergence.

b. **Early versus delayed emergence.** Ideal: rapid emergence to permit immediate postoperative neurologic examination and early assessment of surgical results. However, early emergence is not appropriate for some categories of patients (see below and Tables 8.6 and 8.7).

c. **Indications for delayed emergence.** Awakening is delayed in patients who have obtunded consciousness or inadequate airway control preoperatively; intraoperative catastrophe; or significant risk of

TABLE 8.6 Early Versus Delayed Awakening: Pros and Cons

| Early Awakening | Delayed Awakening |
|---|---|
| ***Pros*** | ***Pros*** |
| ■ Earlier neurologic examination and reintervention<br>■ Baseline assessment for subsequent changes<br>■ Less hypertension, catecholamine burst<br>■ Performed by anesthesiologist in charge of the patient<br>■ Decreased costs, less use of ICU resources | ■ Less risk of hypoxemia and hypercapnia<br>■ Better respiratory and hemodynamic control<br>■ Time for stabilization and potentially better hemostasis |
| ***Cons*** | ***Cons*** |
| ■ Increased risk of hypoxemia and hypercapnia<br>■ Less time for stabilization | ■ Less neurologic monitoring<br>■ Delay in the treatment of pain<br>■ More hypertension, catecholamine release |

ICU, intensive care unit.

brain edema and increased ICP. Risk factors for intracranial hypertension include long (> 6 hours) procedures with extensive dissection and major blood loss; repeat surgery; operations involving or close to vital brain areas; and surgery associated with significant brain ischemia (e.g., long vascular clipping times, extensive retractor pressure). If delayed emergence is chosen, adequate sedation and analgesia are assured, preferably with short-acting drugs.

TABLE 8.7 Check List Before Attempting Early Awakening

**Precondition**
- Adequate preoperative state of consciousness
- Cardiovascular stability, normal body temperature, adequate oxygenation
- No major brain laceration or complication during surgery
- No injury to Cranial Nerves IX, X, XII
- No removal of large arteriovenous malformation

**Preparation**
- Anticipate need for analgesia especially if remifentanil used
- Check adequacy of seizure prophylaxis
- Continue steroids if malignant tumor
- Prevent PONV in high-risk patients
- Prepare or infuse anti-hypertensive drugs for hypertension at extubation

PONV, postoperative nausea and vomiting.

d. **Preconditions for early emergence.** Early awakening necessitates advanced planning (Table 8.7) and the use of a pharmacologically-appropriate anesthetic technique. It is important to pay meticulous attention to intraoperative homeostasis including oxygenation, temperature, intravascular volume, cardiovascular function, and CNS metabolism.

e. **Pain control.** Craniotomy is painful after the operation. The need for postoperative **analgesia** is anticipated before awakening, especially if remifentanil is used for maintenance, by adding a longer-acting opioid as the remifentanil infusion is discontinued. Scalp infiltration with local anesthetics is also helpful during the early postoperative period. First-line intravenous analgesics include morphine and fentanyl, which are titrated to avoid respiratory depression and excessive somnolence, and intravenous acetaminophen (paracetamol). For patients taking medication by mouth, acetaminophen is a good first choice. Tramadol is less helpful as it decreases the seizure threshold and is associated with postoperative nausea and vomiting (PONV). The non-steroidal anti-inflammatory drugs (NSAIDs) such as ketorolac are effective but may theoretically increase the risk of bleeding owing to their antiplatelet effect.

f. **Differential diagnosis of unplanned delayed emergence.** Within 10 to 20 minutes of cessation of pharmacologically-adequate anesthesia using short-acting drugs, the patient should be awake enough to obey simple verbal commands. If not, consider using transcranial Doppler ultrasound to assess cerebral perfusion and a computed tomographic scan to identify neurosurgical complications including intracranial hematoma, cerebral edema, and tension pneumocephalus. If these studies are normal, the patient is transferred to the ICU for an electroencephalgram (EEG) to diagnose non-convulsive seizures and to identify metabolic or electrolyte disturbances.

g. **Neurologic evaluation.** A simple baseline neurologic examination is performed to assess motor responses of arms and legs, size of pupils and reactivity to light, adequate understanding of simple words and verbal response, and orientation to time and space. If delayed extubation is planned, temporary awakening for assessment of neurologic status should be considered under close hemodynamic control.

D. **Specific anesthetic management**

1. **Predicted difficult airway.** Avoiding hypoxia is more important than preventing ICP increases. The method of choice for a difficult intubation is fiberoptic intubation or videolaryngoscopy. The technique requires that the patient be a well-prepared, informed, and cooperative patient. Good local anesthesia of the nasopharynx and airways plus judicious light sedation with midazolam, 0.5 to 1 mg, ± fentanyl, 25 to 50 mcg, facilitate the process. Alternatively, a low-dose propofol infusion at 1 to 2 mg/kg/hour may be used but deep sedation and hypercapnia are avoided. Hypertension is treated promptly with esmolol, labetalol, or clonidine.

2. **Infectious tumors or abscesses** are part of the differential diagnosis of supratentorial mass lesions. They are often accompanied by low-grade fever. Risk factors include contiguous infections (sinus, ear); right-to-left cardiac shunt; immunosuppression (extrinsic/intrinsic); and intravenous drug abuse. Initial treatment is with antibiotics for the infection and corticosteroids for the brain swelling. Definitive diagnosis and treatment are craniotomy with evacuation of the

abscess. Surgical and anesthetic techniques are the same as for supratentorial neoplasms. Aseptic precautions and sterile technique are vital for immunocompromised patients who have acquired immunodeficiency syndrome.

3. **Craniofacial/skull-base surgery.** A complex, multidisciplinary approach is used increasingly for tumors of the orbit and the posterior nasal sinus wall. Tracheotomy or oral intubation is possible. The extensive bony involvement leads to increased bleeding, hemorrhagic diathesis, and venous air embolism from the head-up position. Sensory ± motor neurophysiologic cranial nerve monitoring is common; for motor monitoring, neuromuscular blockade is avoided. Repeat procedures may be necessary and difficulty with intubation may be encountered with subsequent operations because the skull-base exposure requires extensive temporalis muscle mobilization, which can lead to mandibular pseudoankylosis and limited mouth opening.

## II. ANESTHESIA FOR INTRACRANIAL HEMATOMAS

**A. General considerations.** The effects of intracranial hematomas on neurostatus and ICP depend particularly on the speed with which they arise. *Slow*: chronic subdural hematomas involve subtle neurologic signs and a small increase in ICP. The anesthetic technique is similar to that for supratentorial tumors. Chronic subdural hematomas occur mostly in elderly patients (> 70 years). *Fast*: acute epidural (e.g., traumatic), subdural, and intracerebral hematomas cause massive neurologic impairment and have the potential for leading to an acutely life-threatening increase in ICP. *Anesthetic technique:* involves aggressive measures to decrease ICP and preserve brain oxygenation and perfusion as the prelude to urgent surgical decompression. This is applicable to bleeding from head trauma and from anticoagulation with coumadin or antiplatelet drugs. Coagulation is corrected before operation by the administration of factors II, VII, IX, and X. Patients treated with vitamin K antagonists receive vitamin K. Platelet transfusion may be necessary for patients taking clopidogrel. *Priority*: rapid transfer to the operating room to limit the delay between hematoma accumulation and removal in view of the possibility of impending herniation.

**B. Anesthetic management of acute intracranial hematomas**

1. **Induction**

   a. **Basics.** Ensure oxygenation and then secure the airway, hyperventilate with 100% $O_2$, and perform a brief, atraumatic intubation with minimal rise in ICP. It is essential to avoid coughing and arterial hypertension from light anesthesia. Hypotension is treated immediately as low blood pressure in the context of elevated ICP is equivalent to circulatory arrest for the brain. In patients who are hypotensive and hypovolemic after sustaining multisystem trauma, the dose of hypnotic and analgesic drugs is decreased and circulating blood volume is restored. If the patient has a full stomach, aspiration prophylaxis and cricoid pressure are used but caution is indicated if a fracture of the cervical spine is suspected.

   b. **Pharmacologic options.** Intubation without further use of drugs in the deeply comatose patient is acceptable. A judicious dose of a sedative–hypnotic such as etomidate, 0.2 to 0.5 mg/kg; propofol, 0.5 to 1.5 mg/kg; or thiopental, 2 to 4 mg/kg, and muscle relaxation are appropriate in the semiconscious, struggling patient. A "classical" rapid-sequence induction is indicated for the (still) conscious

and stable patient. *Controversy*: what muscle relaxant should be used? Succinylcholine, perhaps preceded by a small dose of non-depolarizing muscle relaxant, remains the time-tested choice with rocuronium, 1 mg/kg, as an alternative.

c. **Control of ICP and brain swelling.** The next priority after securing the airway and instituting controlled ventilation is to control the ICP. This is instituted as quickly as possible and continued into the ICU. The initial treatment after hyperventilation is a large dose of mannitol, 0.7 to 1.4 g/kg (Table 8.2).

2. **Anesthesia maintenance.** During this phase, it is important to control ICP and brain swelling and maintain cerebral perfusion and oxygenation by avoiding hypotension and hyperthermia.

a. **Monitoring**

1. **Cardiovascular monitoring** for these frequently hemodynamically-unstable patients includes direct arterial-pressure monitoring, preferably commenced before induction. Electrocardiographic monitoring is important because of the interaction between brain damage and myocardial injury and the risk of arrhythmias.
2. **ICP monitoring.** Generally initiated once the hematoma has been evacuated, and used mainly as a guide to the state of the patient and the effectiveness of treatment in the ICU.
3. **Laboratory analyses.** Measurements include blood-gas analysis (acid–base balance, ventilation), glucose (hyperglycemia exacerbates brain ischemia), coagulation profile (brain-tissue damage can release circulating thromboplastin), blood osmolality as guide for use of osmotic diuretics. With mannitol, maximum osmolality should be 320 mOsm/kg.

b. **Anesthetic technique.** Intravenous anesthetics are the mainstay of anesthesia for acute intracranial hematoma. Volatile anesthetics are *not* recommended because of risk of markedly increasing ICP and brain tension to the point of acute transtentorial herniation or herniation through the craniotomy site, even with pre-existing hypocapnia.

The following situations must be evaluated and treated:

1. Deep coma and signs of brain herniation: use muscle relaxation and repeated small doses of thiopental titrated to blood pressure with 100% oxygen.
2. Coma but no signs of herniation or increased ICP: use propofol TCI or small doses of thiopental and opioids titrated to blood pressure and muscle relaxation with air/oxygen.
3. Conscious patient but mass effect on CT scan: use rapid sequence induction, followed by propofol TCI, opioids, and muscle relaxation with air/oxygen.

c. **Cardiovascular control.** Avoid arterial hypotension by using judicious doses of intravenous anesthetics to prevent a decrease in CPP. *Controversy*: control of arterial hypertension in the presence of acute intracranial hematoma (Table 8.2): carefully balance maintenance of CPP to areas of the brain rendered ischemic from compression by the hematoma against the risk of more vasogenic brain edema or bleeding from arterial hypertension. Jugular venous bulb oxygen-saturation monitoring may help assess adequacy of global CPP but its institution should not delay surgery. Globally-adequate CPP does not rule out regional ischemia. Transcranial Doppler examination

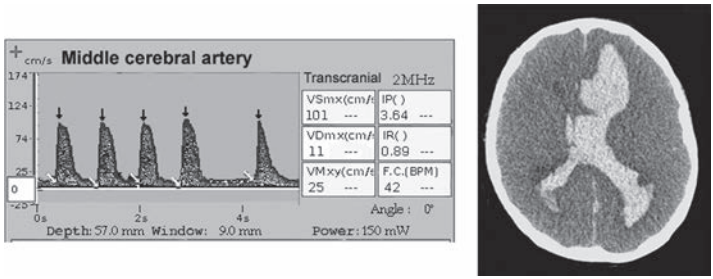



**FIGURE 8.4** Large intracerebral hematoma associated with impaired cerebral perfusion on transcranial Doppler (high pulsatility index, low diastolic flow). In this case, blood pressure should not be reduced and mannitol is indicated before surgery.

may be useful (Fig. 8.4). If arterial pressure requires a reduction in systemic arterial pressure (SAP < 180 mm Hg), first improve analgesia with opioids and/or deepen anesthesia with propofol, barbiturates, or etomidate before instituting specific anti-hypertensive treatment with antisympathetic drugs such as esmolol, labetalol, and clonidine. Avoid cerebral vasodilators. The decrease in blood pressure should not exceed 15% to 20%. *Anticipate severe hypotension after brain decompression due to disappearance of Cushing's response* and treat with rapid fluid loading and phenylephrine, noradrenaline, or epinephrine, all immediately available.

d. **Emergence.** After evacuation of an acute cerebral hematoma, patients still have significant brain injury with significant potential for and actual brain swelling. They should therefore undergo slow weaning and delayed extubation in the ICU. Seizure prophylaxis is usually indicated but corticosteroid use is not universal. Chronic subdural hematoma patients frequently have minimal neurologic impairment preoperatively and can therefore often be awakened and their tracheas extubated immediately after surgery.

## III. CONCLUSIONS

The main objectives of anesthesia for excision of a cerebral tumor include the following:

- Preserving uninjured cerebral territories by global maintenance of metabolic, cardiovascular, and respiratory stability.
- Balancing CBF autoregulation and MAP and preserving cerebral vasoreactivity to $PaCO_2$.
- Achieving and maintaining brain relaxation by means of
  - ↓ $CMRO_2$, CBF, and CBV
  - Moderate hyperventilation ($PaCO_2$ 35 mm Hg)
  - Inhaled anesthetics less than 1 to 1.5 MAC or intravenous anesthesia
  - Strict maintenance of CPP
  - Osmotherapy and/or CSF drainage
- Timely awakening to facilitate early and ongoing neurologic assessment and permit prompt diagnosis and treatment of complications.

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# 9 Anesthesia for Posterior Fossa Surgery

**Deborah S. Pederson and Robert A. Peterfreund**

## Illustrated Clinical Case

A middle-aged woman is scheduled for an elective craniectomy. She presents with 5 years of decreased hearing in her right ear, occasional right facial twitching, and balance difficulties. Imaging revealed a 4 cm × 4 cm mass in the right cerebellopontine angle (Figs. 9.1 and 9.2). She takes levothyroxine for a history of hypothyroidism but is otherwise healthy. She has had no complications from general anesthesia in the past.

This presentation is consistent with an acoustic neuroma, without associated neurofibromatosis Type II. Preparation for this case can be aided by review of the Six Questions for Posterior Fossa Surgery (Fig. 9.3).

1. Does the patient have preoperative evidence of brain stem or cranial nerve dysfunction? Yes. This patient has evidence of sensorineural hearing loss and dizziness as a result of the disturbance of vestibular–cochlear function in Cranial Nerve VIII. The occasional facial twitching is an indication that the tumor is causing local compression of Cranial Nerve VII.
2. Does the patient have elevated intracranial pressure (ICP)? She has evidence of obliteration of the fourth ventricle on imaging but is not exhibiting clinical symptoms of hydrocephalus or elevated ICP.
3. What is the proposed patient position for operation? Supine, with the head turned to the left.
4. Is the patient at risk for venous air embolus (VAE)? Moderate risk. The risk for VAE in the horizontal patient undergoing posterior fossa surgery is approximately 15% (range: 0% to 17%). The time of increased risk is during craniectomy when non-compressible skull veins are exposed and during dissection near the sinuses.
5. Is there potential for large blood loss? Low-to-moderate risk. The location and the characteristics of the tumor do not suggest large blood loss. One must consider the involvement of sinuses, vascularity of the mass, and the skill of the surgeon when assessing this component of the case.
6. Will the surgery involve intraoperative central nervous system (CNS) monitoring? Yes. Electromyographic (EMG) monitoring of Cranial Nerves V and VII is often used to help identify structures and to minimize facial weakness resulting from dissection near these delicate structures. For large lesions at the cerebellopontine angle threatening the lower cranial nerves, Cranial Nerve X may also be monitored by EMG. Brain stem auditory evoked response (BAER) monitoring of Cranial Nerve VIII may be used to help preserve residual hearing.

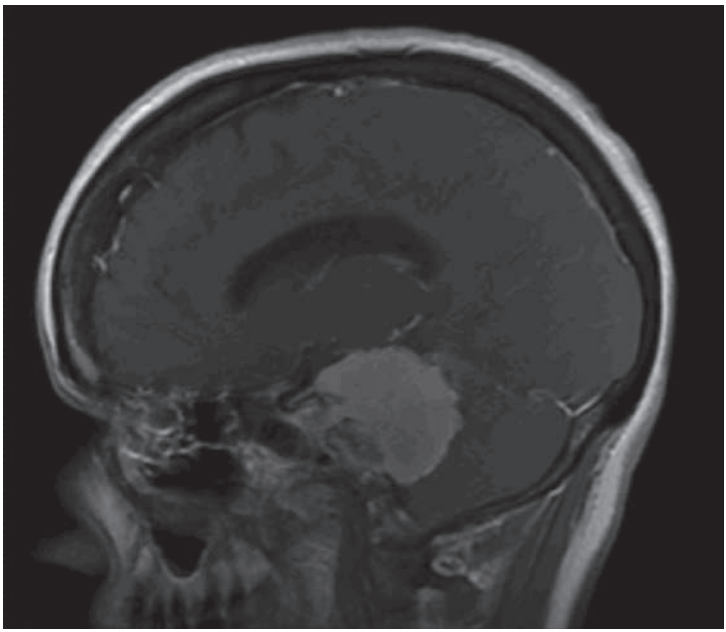

**FIGURE 9.1** Sagittal image of a middle-aged woman who has a 4 cm × 4 cm mass in the cerebellopontine angle.

## CHAPTER HIGHLIGHTS

This chapter reviews the anesthetic considerations for posterior fossa surgery. Key points include the following:

- Venous air embolus (VAE)
- Intraoperative monitoring techniques
- Positioning
- Pathophysiology associated with brain stem dysfunction

## ANESTHESIA FOR POSTERIOR FOSSA SURGERY

Operations in the posterior fossa are often demanding, delicate, and long. Anesthesia for these cases can also be challenging. In addition to the anesthetic management issues that apply to supratentorial surgery, operations in the posterior fossa present special problems related to brain stem dysfunction, patient positioning, intraoperative neurophysiologic monitoring, and the potential for VAE.

### I. ANATOMICAL CONSIDERATIONS

**A.** The posterior fossa is a **small, rigid compartment** containing the midbrain pons, medulla, cerebellum, and fourth ventricle. Surgery within the posterior fossa may be indicated for resection of vascular lesions or tumors, decompression of cranial nerves, and correction of craniocervical

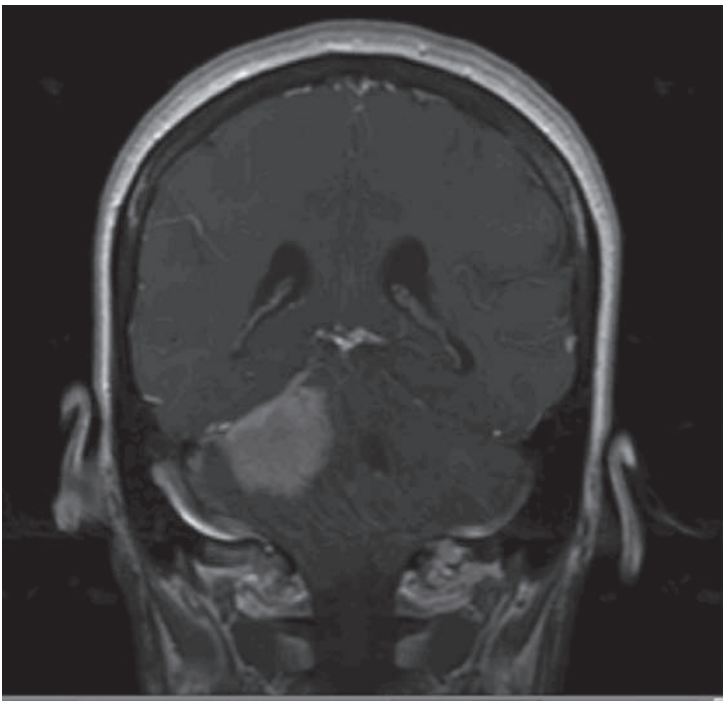

**FIGURE 9.2** Coronal image of a middle-aged woman who has a 4 cm × 4 cm mass in the cerebellopontine angle.

abnormalities. The common goal of the surgeon and the anesthesiologist is to facilitate safe exposure with minimal retraction and consequent tissue damage and edema.

**B.** The reticular activating system, cranial nerves, and structures vital for control of the airway and cardiovascular and respiratory systems are contained within a very small space in the posterior fossa. Accordingly, patients may present with dysphagia, laryngeal dysfunction, respiratory irregularities, cardiac rhythm disturbances, or altered states of consciousness. In some cases, chronic aspiration owing to loss of airway reflexes can further compromise respiratory function. These abnormalities may be encountered intraoperatively, associated with traction or nerve manipulation, and postoperatively as a result of mechanical trauma, edema, or bleeding in this confined space.

**C.** **Hydrocephalus** from obstruction of ventricular outflow is a common cause of increased ICP with posterior fossa lesions. This is evident on the preoperative computed tomographic (CT) or magnetic resonance imaging (MRI) scan as obliteration of the fourth ventricle or loss of the cerebellar folds. It can be **treated** by ventricular drainage, endoscopic third ventriculostomy, or hypertonic osmotherapy with mannitol and furosemide administered either pre- or intraoperatively.

1. Does the patient have preoperative evidence of brain stem or cranial nerve dysfunction?
2. Does the patient have elevated intracranial pressure (ICP)?
3. What is the patient's proposed operative position?
4. Is there a significant risk of venous air embolism (VAE)?
   a. Is the patient at risk for paradoxical air embolism (PAE)?
5. Is there potential for large blood loss?
6. Will the surgery involve intraoperative central nervous system (CNS) monitoring?

**FIGURE 9.3** Six Questions For Posterior Fossa Surgery. Six questions to consider before caring for patients undergoing posterior fossa surgery.

## II. POSITIONING

**A. General issues.** Posterior fossa surgery often requires unusual patient positioning. The prone, lateral, park bench, and sitting positions are commonly used. Regardless of the position chosen, care in positioning is of utmost importance because most problems are presumably avoidable with careful positioning and padding of vulnerable areas.

1. In the **prone position**, facial skin **ulcerations** can occur from uneven pressure distribution when head rests are used, and **blindness** can result from pressure on the globe of the eye. **Ischemic optic neuropathy** is associated with prolonged procedures in the prone position even when direct pressure on the eye is absent. **Risk factors** associated with this condition include significant blood loss, anemia, and hypotension.
2. In the **lateral and the park bench positions**, there is a **risk of brachial plexus injury** if the up arm is pulled caudally to gain access to the retromastoid area. There can also be **nerve compression** on the dependent side from pressure on the axillary contents or the peroneal nerve at the knee.
3. Excessive neck rotation can also stretch and damage the brachial plexus. **Extreme neck flexion** is associated with **the risk of quadriplegia,** especially in the sitting position (see below). As this can be exacerbated by hypotension, measurement of the blood pressure (BP) at the level of the cervical spine is recommended.

**B. The sitting position**

1. **Advantages** of the sitting position include good surgical exposure, improved ventilation, better access to the airway, greater comfort for the surgeon, and possibly reduced blood loss.
2. **Disadvantages** of the sitting position include the risk of VAE, increased chance of pneumocephalus, and the potential for hemodynamic instability. **Additional complications** include sciatic nerve injury from extreme flexion of the hip, massive swelling of the face and tongue from extreme neck flexion and/or rotation, and midcervical quadriplegia. The cause has been attributed ostensibly to a combination of stretch and compression

of the spinal cord by extreme neck flexion in conjunction with hypotension.

3. The **main contraindication** to the use of the sitting position is the presence of a documented right-to-left intracardiac or pulmonary shunt, which would facilitate systemic embolization of air.
4. When caring for patients in the sitting position, BP is measured at the level of the head. BP measured at the level of the heart will underestimate the perfusion pressure for the brain by about 2 mm Hg for every inch the head is above the heart.

## III. VENOUS AIR EMBOLISM

**A.** VAE can occur whenever **pressure within an open vessel is subatmospheric**. This situation is more likely to be encountered when the **surgical site is above the level of the heart.** Hence, VAE is a particular problem during surgery in the seated position, but it also occurs, albeit less frequently, in patients operated in the lateral or the prone position.

**B.** **When open vessels cannot collapse,** which is the case with major venous sinuses as well as bridging and epidural veins, the **risk of VAE increases** substantially. Most studies indicate that the incidence of VAE during posterior fossa procedures in the sitting position is 40% to 45% (range: 0% to 70%). For seated cervical laminectomy or operations in the prone or the lateral position, VAE occurs in approximately 10% to 15% of cases.

**C.** VAE can occur in varying amounts and duration with varying effects.

1. **Massive air embolism** produces abrupt and catastrophic hemodynamic changes. Fortunately, this type of VAE is rare.
2. More commonly, **air entrainment occurs slowly** over a longer period of time. This may produce little or no respiratory or hemodynamic compromise. However, it may result in increased right-sided cardiac pressures, increased dead-space ventilation, and hypoxemia.
   - **a.** As **air is cleared to the pulmonary circulation**, pulmonary vascular resistance and pulmonary artery (PA) and right atrial pressures increase. If unchecked, cardiac output can decrease as a result of right-heart failure and/or reduced left ventricular filling.
   - **b.** This **vascular obstruction increases dead-space ventilation**, resulting in a **decrease in end-tidal carbon dioxide tension ($ETCO_2$)** with an **increase in arterial carbon dioxide tension** ($PaCO_2$). Both of these features are characteristic of VAE.
   - **c.** **Hypoxemia** develops owing to the partially occluded pulmonary vasculature and the local release of vasoactive substances.

**D.** **Monitoring for VAE.** Multiple modalities are available for VAE monitoring including hemodynamic monitors (BP, central venous pressure [CVP], and PA pressure), precordial Doppler ultrasound, end-tidal gas monitoring, and transesophageal echocardiography (TEE). For high-risk cases, Doppler and $ETCO_2$ monitoring are considered the acceptable minimum (Table 9.1).

1. **Hemodynamic changes.** Monitoring of hemodynamics may not provide sufficient advanced warning in the case of massive air embolism because the hemodynamic changes are abrupt and catastrophic.
   - **a. CVP**
     1. As a monitor for VAE, the CVP is insensitive and easily superseded by other devices. It is, however, **useful in confirming the diagnosis and treating VAE** via aspiration of air from the right side of the circulation. It can also be used to aid in the positioning of the precordial Doppler.

TABLE 9.1 Comparison of VAE Detection Methods

| VAE Detection Method | Sensitivity | Limitations |
|---|---|---|
| TEE | High (0.02 mL/kg) | Invasive, requires expertise, requires constant vigilance |
| Precordial Doppler | High (0.05 mL/kg) | Obesity, COPD |
| PA catheter | High (0.25 mL/kg) | Unable to treat due to small diameter |
| End-tidal nitrogen | Moderate (0.5 mL/kg) | Not widely available |
| End-tidal $CO_2$ | Moderate (0.5 mL/kg) | Not specific |
| Oxygen saturation | Low | Late indicator |

VAE, venous air embolism; TEE, transesophageal echocardiography; PA, pulmonary artery; $CO_2$, carbon dioxide; COPD, chronic obstructive pulmonary disease.

2. To facilitate rapid aspiration of air, a **multiorificed catheter** is recommended. Because air tends to localize at the junction between the superior vena cava and the right atrium, greatest air retrieval occurs when the catheter orifices traverse this region.
3. The **catheter position can be confirmed** in a number of ways. The catheter can be advanced until a right ventricular pressure trace is obtained and then withdrawn several centimeters. Alternatively, a chest x-ray can be obtained to confirm position. One method involves using the electrocardiogram, but its use has a risk of microshock. The right arm lead is connected to the catheter by a fluid column of sodium bicarbonate or via the *J* wire used to place the catheter. The tip is advanced until a biphasic *P* wave appears, at which point the catheter is withdrawn a few centimeters.
4. One should always attempt to insert a CVP catheter in posterior fossa cases requiring the sitting position, but whether the inability to do so should result in cancellation of the case or using a different position for surgery is controversial.

b. **PA pressure**
   1. The PA catheter is **useful for diagnosis** because PA pressures rise with significant VAE. However, it is **not useful for treatment** of VAE. It is difficult to aspirate air from the distal port of a PA catheter given the small diameter and associated resistance. Furthermore, the port may not be in a location that has air. Aspiration is more effective with a CVP catheter.
   2. In addition, as a diagnostic tool, the PA catheter **offers no advantage over $ETCO_2$** monitoring.

2. **Precordial Doppler ultrasound**
   a. This device can detect 0.25 mL of air (0.05 mL/kg), which makes it more **sensitive** than any other monitor except TEE. The Doppler is **not quantitative**, however, and it requires experience to recognize which of the various sounds it emits is indicative of air.
   b. The Doppler probe should be **placed after the patient is in the operative position.** The probe is usually positioned at the middle third of the sternum on the right side but, because the position of the right

atrium varies with the patient's position, proper placement must be confirmed. Hearing heart tones is not enough.

c. To **test for proper placement of the probe**, agitated saline or blood is injected through the right atrial catheter or peripheral intravenous line; alternatively, the injection of 0.5 to 1 mL of air, carbon dioxide ($CO_2$), or circuit gas is acceptable. The probe is properly placed if this maneuver produces characteristic Doppler sounds signaling air embolism.

d. Because of its sensitivity, a **properly positioned Doppler probe, combined with end-tidal gas monitoring**, is **essential for all posterior fossa procedures in the seated position**.

3. **End-tidal gas monitoring**

a. **$ETCO_2$.** For reasons already stated, VAE is associated with a **decrease in $ETCO_2$**.

1. $ETCO_2$ monitoring is of **intermediate sensitivity** but provides a **qualitative estimate of the size of a VAE**. In general, the larger the embolus, the greater the decrease in $ETCO_2$. A decrease in $ETCO_2$ is **not specific for VAE**, however, because a decrease in cardiac output from any cause has the same effect.

2. $ETCO_2$ monitoring is particularly **useful for corroborating evidence of VAE from the Doppler** and judging the clinical and physiologic significance of the embolus.

b. **ET nitrogen ($N_2$).** Monitoring for $ETN_2$ is not routinely available. However, it is **both sensitive and specific** (if not utilizing air as part of the fresh gas flow admixture). $ETN_2$ monitoring is more sensitive and can detect a large-volume VAE sooner than $ETCO_2$ monitoring. It is equivalent to $ETCO_2$ for smaller VAE with slower entrainment.

4. **Transesophageal echocardiography (TEE)**

a. TEE is **more sensitive than Doppler ultrasound**, detecting 0.02 mL/kg of air. Its specificity is dependent on the operator and his/her ability to differentiate air from other embolic materials ( fat, thrombus, etc.) that also create echocardiographic image changes.

b. TEE is expensive, requires special expertise, and demands near-constant attention. For these reasons, in most centers it is not a routine monitor for VAE.

c. TEE and transcranial Doppler ultrasound **can detect paradoxical air embolus** (PAE).

E. **Prevention of VAE**

1. **Positive end-expiratory pressure (PEEP)**

a. The use of PEEP to prevent VAE in the sitting position is controversial. High levels of PEEP (> 10 cm $H_2O$) are needed to increase venous pressure at the head, and studies are inconsistent as to whether PEEP decreases the incidence of VAE. PEEP can, however, reduce venous return, cardiac output, and mean arterial blood pressure (MAP), which is detrimental in the setting of VAE.

b. Experimental data also indicate that the discontinuation of PEEP is associated with the entrainment of venous air and promotes right-to-left shunting of air. Overall, **PEEP is not recommended**.

2. **Volume loading.** Although hypovolemia has been proposed as a predisposing factor for VAE, evidence for a prophylactic effect of volume loading on reducing the incidence of VAE and PAE is not strong enough to warrant its routine use. Adequate hydration is the goal.

3. **Deliberate hypoventilation**

a. While some studies suggest that moderate hypoventilation may reduce the risk of VAE, hypoventilation also increases cerebral blood

flow (CBF) and cerebral blood volume (CBV), which may impair surgical exposure.

b. Until the benefits of hypoventilation are confirmed, mild hyperventilation is the more common practice.

4. **Position.** Despite firmly held opinions and anecdotes and the documented increase in the incidence of VAE, there is little evidence that the sitting position—at least when used in large centers doing large numbers of sitting cases—is less safe than alternative operative positions. It is therefore difficult to argue that the sitting position should be abandoned purely because of the risk of VAE.

F. **Treatment of VAE**

1. **Prevention of further air entrainment**
   a. Alert the surgeon. This will allow flooding of the surgical field with saline and application of occlusive pads and bone wax.
   b. Consider gentle compression of bilateral jugular veins to minimize air entrainment.
   c. Consider changing the patient position so the site of entrainment is lower than the patient's heart. This can be complicated with a patient in Mayfield pins undergoing craniectomy.
2. **Relief of obstruction**
   a. Aspirate the right atrial catheter. Aspiration via a multiorifice catheter has a success rate of 30% to 60%.
   b. Discontinue nitrous oxide ($N_2O$) immediately if in use.
3. **Supportive therapy**
   a. Administer 100% oxygen.
   b. Begin inotropic support, especially to promote right heart contractility.
   c. Enhance volume administration.
   d. Consider cardiopulmonary resuscitation (CPR).

## IV. PARADOXIC AIR EMBOLISM (PAE)

A. When air enters the venous circulation, there is a risk that the **air could pass via the pulmonary vascular bed or a patent foramen ovale (PFO) to the arterial side and embolize to coronary and cerebral vessels.** The incidence of clinically significant PAE is unknown, and only a handful of cases have been reported most of which were without complications.

B. Approximately 25% of the population has a probe-patent foramen ovale. The reported incidence of VAE in craniotomies is approximately 40% (range: 0% to 70%.) Therefore, the risk of potential PAE in patients operated in the sitting position is not inconsequential and thus should be considered.

C. **Detection of PFO**

1. **Precordial echocardiography** has been used preoperatively to identify patients at risk of PAE from a PFO. While detection of a PFO indicates that a patient is at risk for PAE, failure to identify a PFO is not reassuring because precordial echocardiography has a high false-negative rate. While **transesophageal echocardiography** (**TEE**) is more sensitive, it is also less practical given the invasive nature of the study. Hence, neither precordial echocardiography nor TEE is presently recommended as a routine part of the preoperative evaluation of patients scheduled for craniectomy in the sitting position.
2. **Transcranial Doppler (TCD)** has a sensitivity of 91% and has been used preoperatively to identify patients who have a PFO. This technique is useful as it is **non-invasive** and **almost as sensitive as TEE**.

D. **Preoperative closure of PFO.** With the increasing safety and efficacy of percutaneous PFO closure, treating the PFO before a neurosurgical

procedure is increasingly an option. Antithrombotic therapy is recommended after the closure and remains the only controversy in the setting of neurosurgery. Further studies will need to be done to assess the need and the duration of antithrombotic therapy.

## V. ANESTHETIC TECHNIQUE

**A.** There is no evidence that any one anesthetic drug or technique is superior to another for posterior fossa surgery. Moreover, hemodynamic changes associated with the assumption of the sitting position can be managed regardless of the anesthetic technique.

**B.** The **use of $N_2O$** is controversial. Because of the risk of VAE and the ability of $N_2O$ to expand air bubbles, some practitioners argue that $N_2O$ should be avoided entirely. In addition, the surgical site may be below the vertex of the head (e.g., pineal surgery) so that achieving evacuation of residual pneumocephalus at the conclusion of the case is difficult. The risk/benefit analysis must be done for each patient as there are currently no definitive studies to guide recommendations. If used, $N_2O$ should probably be discontinued during closure if the dural incision is below the top of the head.

**C.** The **airway** requires special attention. Often with posterior fossa cases, **substantial neck flexion or rotation is required** for optimal surgical exposure. Flexion can advance the tip of the endotracheal tube into a mainstem bronchus or cause kinking of the endotracheal tube in the posterior pharynx.

1. Clinicians may use standard oral intubation, oral intubation with a wire-reinforced tube, or nasotracheal intubation. Regardless of the technique used, **careful assessment of tube patency and position** is required after surgical positioning.
2. If evidence of **partial obstruction of the tube** (e.g., high airway pressures, slow upstroke of the $ETCO_2$ tracing) exists, demonstrate that a suction catheter passes freely through the endotracheal tube, and insist on repositioning of the head and the neck if it does not.

**D.** In most cases, **controlled mild hyperventilation** is desirable to improve surgical exposure and reduce retraction pressure on the brain. However, changes in respiration may be more sensitive to brain stem manipulation than hemodynamic changes. Consequently, the use of **spontaneous ventilation** may be appropriate in rare circumstances, as when manipulation or ischemia of respiratory centers is likely. This should only be undertaken after discussion with the surgeon as the hypoventilation that occurs with spontaneous ventilation during general anesthesia may cause brain engorgement and make surgical exposure more difficult.

**E. Brain stem monitoring**

1. **Cranial nerve injury** is a significant risk of operations in the area of the cerebellopontine angle and lower brain stem. Therefore, intraoperative stimulation and recording from Cranial Nerves V, VII, VIII, X, XI, and XII are often utilized.
2. **Monitoring techniques** include somatosensory evoked potentials (SSEPs), BAERs, and the spontaneous and evoked electromyogram (EMG).
3. Monitoring can pose challenges for the anesthesiologist because **anesthetic drugs affect evoked potentials and the EMG**. Muscle relaxants complicate interpretation of the EMG, and $N_2O$ and high-dose inhalation anesthesia may interfere with SSEPs. The BAERs are robust and minimally influenced by anesthetics.
4. Although direct intracranial stimulation of the facial and the trigeminal nerves produces facial movement even in well-paralyzed patients, **"spontaneous" (i.e., surgical manipulation-induced) EMG**

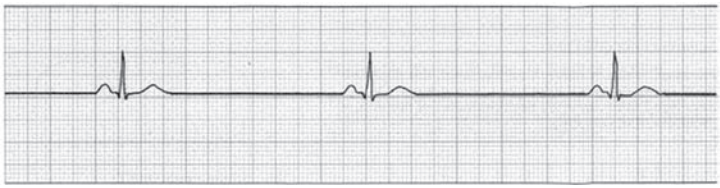

**FIGURE 9.4** Intraoperative bradycardia associated with surgical manipulation. Note sinus mechanism despite the very low heart rate.

**discharges are subtle.** Hence, some electrophysiologists request that, with the exception of succinylcholine for intubation, no muscle relaxants be given. The clinical necessity for this "pure" state has not been documented, however, and some centers are satisfied with a **continuous infusion of relaxant** to maintain a constant level of modest twitch suppression.

F. **Cardiovascular reflexes**
   1. Operations on or near the brain stem (e.g., during acoustic neuroma surgery) can produce abrupt, often profound, **cardiovascular responses** that may signal potential damage to the brain stem.
   2. Stimulation of the floor of the fourth ventricle, medullary reticular formation, or trigeminal nerve results in **hypertension**, usually in association with **bradycardia**. Bradycardia also results from opening of the dura, retraction of the cerebellum, instillation of cool irrigation fluid, stimulation of the trigeminal or vagus nerve, and other surgical actions (Fig. 9.4).
   3. If such changes occur, the **surgeon should be alerted immediately** so that he or she can avoid the manipulation that provokes the response.
   4. **Masking bradydysrhythmias with pharmacologic treatment is undesirable** unless the changes are recurrent and severe. Bradycardic responses are typically so abrupt and transient that by the time a drug is administered, the stimulus is gone and treatment becomes unnecessary. Bradydysrhythmias also serve as a **warning sign of potentially harmful surgical manipulation.** If treatment is deemed necessary, consider **short-acting, titratable/reversible drugs and techniques** such as bolus doses of phenylephrine or ephedrine, brief infusions of dopamine or isoproterenol, and transesophageal or transvenous pacing. Consider reserving glycopyrrolate or atropine for extreme circumstances or prolonged episodes of bradycardia that are refractory to other therapy.
   5. **Hypertension**, particularly at the conclusion of the operation, may be marked and refractory to treatment. Surprisingly aggressive treatment with high doses of multiple drugs may be required to reduce the BP to acceptable levels.

G. **Emergence from anesthesia**
   1. As with other types of intracranial neurosurgery, **prompt, smooth emergence** and avoidance of coughing, straining, and abrupt increases in BP are desirable.
   2. The **feasibility of extubation** depends on the usual factors plus pre-existing neurologic impairment, the nature and the extent of the surgery, intraoperative complications, and the likelihood of brain stem edema or injury. Even if extubation is not planned, one should attempt to awaken the patient for postoperative neurologic evaluation.

3. Ventilation/airway abnormalities
   a. **Longer-term ventilation and airway protection** might be required in some patients because of disease- or surgery-induced dysfunction of cranial sensory or motor nerves. Patients may have difficulty in swallowing, vocalizing, or protecting the airway. In addition, damage to, or edema of, the respiratory centers from intraoperative manipulation can result in hypoventilation or erratic respiratory patterns.
   b. Severe **tongue and facial edema** can occur owing to position-induced venous or lymphatic obstruction. The endotracheal tube should be left in place until the edema resolves.
   c. **Pulmonary edema** may result from large VAE. Although pulmonary edema is usually responsive to conservative measures such as supplemental oxygen and diuretics, continued postoperative ventilation may be appropriate until evaluation is completed.

**H. Postoperative considerations**

1. **Hypertension** is common after posterior fossa surgery and may contribute to edema formation and intracranial hemorrhage. Hence, one should be prepared for rapid control of postoperative hypertension.
2. A **variety of untoward neurologic complications** can occur after posterior fossa operations. These include altered levels of consciousness, varying degrees of paresis, and specific cranial nerve deficits including visual disturbances, facial nerve paresis, and impaired swallowing and phonation. Treatment is supportive, but **evaluation of delayed emergence should proceed** lest a treatable non-anesthetic cause go unrecognized. If cerebral paradoxical air embolism is suspected, hyperbaric oxygen therapy may be warranted.
3. **Pneumocephalus**
   a. **Air is retained in the cranial cavity after all craniotomies** regardless of position. When the patient is in the sitting position, cerebrospinal fluid drains easily, and a larger amount of air may be trapped when the wound is closed. In most cases, the air is reabsorbed uneventfully over several days and no treatment is necessary.
   b. **Tension pneumocephalus** can occur when the brain re-expands and compresses the air. This situation is difficult to diagnose but **should be suspected if emergence is delayed** after an otherwise uneventful operation or if either cardiovascular collapse or neurologic deterioration occurs postoperatively.
   c. In such rare circumstances, surgical evacuation and either an emergent CT scan or radiograph of the skull may be indicated.

In **summary**, providing anesthesia for posterior fossa surgery requires appropriate planning, vigilance for unique physiologic events, good communication with the surgical team, and the ability to adapt to quickly changing circumstances.

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# 10 Anesthetic Management of Cerebral Aneurysms and Arteriovenous Malformations

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## Illustrative Clinical Case

A 42-year-old woman comes to the emergency department complaining of the worst headache of her life. Computer tomographic scan of the brain reveals a subarachnoid hemorrhage from a ruptured aneurysm of the middle cerebral artery. The patient is judged to be World Federation of Neurological Surgeons (WFNS) clinical Grade I, and the aneurysm is successfully clipped within 48 hours of admission. Postoperatively, however, the patient develops a focal neurologic deficit. Hypertensive, hypervolemic hemodilution treatment is initiated and the patient is brought to the interventional neuroradiology suite for endovascular dilatation of the vasospastic arterial segments after which the neurologic deficit begins to resolve.

## Chapter Highlights

- **CEREBRAL ANEURYSMS**
  - **Epidemiology**
  - **Types of Aneurysms**
  - **Pathophysiology**
  - **Genetics and Associated Conditions**
  - **Clinical Presentation and Grading**
  - **Diagnosis of Cerebral Aneurysms**
- **SUBARACHNOID HEMORRHAGE (SAH)**
- **COMPLICATIONS OF SUBARACHNOID HEMORRHAGE**
  - **Rebleeding**
  - **Vasospasm**
  - **Central Nervous System Complications**
    1. **Hydrocephalus**
    2. **Seizures**
  - **Systemic Sequelae**
    1. **Fluid and electrolyte disturbance**
    2. **Cardiac abnormalities**
    3. **Pulmonary abnormalities**
    4. **Other medical complications**
- **OPERATIVE ANEURYSMAL OBLITERATION**
  - **Anesthesia for Aneurysm Surgery**
  - **Temporary Proximal Occlusion**
  - **Intraoperative Aneurysmal Rupture**

- **ENDOVASCULAR TREATMENT**
- **ARTERIOVENOUS MALFORMATIONS (AVMs) OF THE BRAIN**
  - **Definition**
  - **Presenting Signs and Symptoms**
  - **Neurologic Damage**
  - **Unfavorable Prognostic Features**
  - **Imaging**
  - **Treatment**
  - **Management of Associated Aneurysms**
  - **Anesthetic Management**
  - **Cerebral Circulatory Changes**
  - **AVMs and Pregnancy**
  - **Vein of Galen AVMs**

## I. CEREBRAL ANEURYSMS

The anesthetic and perioperative management of the surgical and the endovascular treatment of intracranial aneurysms, which are abnormal focal dilatations of cerebral arteries usually located at branch points, is designed to facilitate the conduct of the procedure and the patient's recovery. The goal of management is to improve functional survival while minimizing the risk of aneurysmal rupture, cerebral ischemia, neurologic deficit, and associated systemic morbidity.

### A. Epidemiology

Cerebral aneurysms have been reported to occur in every racial group in the world with an age range from 7 to 70 years. The size of an intracranial aneurysm is directly correlated with the risk of rupture and also of treatment. The annual incidence of aneurysmal subarachnoid hemorrhage (SAH) is approximately 6 to 8/100,000 in most western populations. The rate of rupture of an intracranial aneurysm is 0.05% to 6% per year, depending on the size and the location. Aneurysms are 11 times more likely to rupture in patients who have had a previous SAH than in those who have an asymptomatic aneurysm. Smoking and hypertension are risk factors. The incidence in men outnumbers women until age 50; women predominate thereafter. Aneurysms commonly present in the sixth decade of life. Approximately 20% of patients have more than one aneurysm. Aneurysmal SAH accounts for 10% of all cerebrovascular accidents.

### B. Types of aneurysms

1. **Saccular aneurysms** are < 2.5 cm in diameter and are by far the most common. These are formed by the disintegration of the elastic layer of the artery at the flow separator region due to the pressure of the arterial pulse wave.
2. **Giant aneurysms** are up to 10 cm in diameter and represent 5% of all aneurysms.
3. **Other types of aneurysms** include dissecting ( from a tear in the luminal endothelium that permits a blood column to dissect between the endothelium and the media), fusiform (associated with severe atherosclerosis or degenerative processes in childhood), traumatic (develop within 2 to 3 weeks after severe head injury), dolichoectatic, mycotic (infectious), and serpentine (with or without internal thrombosis).

### C. Location

Ninety percent of aneurysms occur on the anterior circulation, most commonly the internal carotid-posterior communicating artery (more common in women), anterior communicating artery (more common

in men), and middle cerebral artery (MCA) bifurcation. Ten percent occur on the posterior circulation, most commonly at the basilar apex. The internal carotid artery is affected in children. Complication rates are reported to be highest for anterior communicating artery (ACA) aneurysms in the anterior circulation and aneurysms of the basilar bifurcation in the posterior circulation.

**D. Natural history**

One patient in six will die within minutes of an SAH. Of the patients who survive to be admitted to the hospital, 25% will die thereafter, and just over 50% will recover partially or completely. Without treatment, at least 50% of ruptured aneurysms will rerupture within 6 months and then at a rate of 3% per year.

**E. Prognostic factors**

The rate and the volume of bleeding affect the patient's neurologic condition at hospital admission and determine outcome. Patients who remain conscious and complain only of severe headache after SAH do better than patients who are comatose upon arrival at the hospital. Older age, poor general health, evidence of clots in either the brain substance or the ventricles, and repeat hemorrhage all affect outcome adversely (Table 10.1).

**F. Genetics and associated diseases**

Of patients who have SAH, 5% to 10% will have one or more first-order relatives who have also had a ruptured aneurysm. The inheritance is probably dominant with variable penetrance. Conditions associated with intracranial aneurysms include polycystic kidney disease (5% of aneurysms series, 33% of polycystic kidney series), coarctation of the aorta (1% of aneurysm patients, 5% of coarctation patients, all of whom are hypertensive), sickle cell disease, drug abuse (cocaine: generalized vasoconstriction and hypertension; intravenous use: mycotic aneurysms), and hypertension (30% to 40% of patients who have SAH). More rarely associated conditions include fibromuscular dysplasia, Marfan's syndrome, tuberous sclerosis, Ehlers-Danlos syndrome, hereditary hemorrhagic telangiectasia, moyamoya disease, and pseudoxanthoma elasticum. Choriocarcinoma and cardiac myxomas are associated with multiple cerebral aneurysms.

The cost-effectiveness of screening asymptomatic individuals, even when there is a familial history of intracranial aneurysms, has not been demonstrated so that screening with magnetic resonance angiography (MRA) combined with computed tomography angiography (CTA) should be considered on a case-by-case basis although catheter angiography remains the gold standard for aneurysm detection.

TABLE 10.1 Predictors of Mortality after Subarachnoid Hemorrhage

| |
|---|
| Poor neurologic condition at hospital admission, a function of rate and volume of bleed |
| Depressed level of consciousness after initial bleed |
| Older age |
| Pre-existing illness |
| Elevated blood pressure |
| Thick clot in the brain substance or ventricles on initial computed tomographic scan |
| Repeat hemorrhage |
| Basilar aneurysmal location |

## II. SUBARACHNOID HEMORRHAGE

Most intracranial aneurysms remain asymptomatic until they rupture. Aneurysmal SAH from rupture of an intracranial aneurysm is reported to occur during physical exertion or stress but can happen at any time. **Risk factors** for SAH include hypertension, smoking, alcoholism, sympathomimetic drug use, polycystic kidney disease, Ehlors-Danlos syndrome, and a family history of SAH (Table 10.2).

**A.** The **clinical presentation** of patients after aneurysmal SAH is classic, with 80% of awake patients complaining of a severe throbbing headache which they describe as "the worst headache of my life." A warning or a sentinel headache is also described by approximately 20% of patients. The headache may be accompanied by malaise, nausea and vomiting, and neck stiffness. This "warning leak" or "sentinel bleed" is reported to precede a major SAH in approximately 40% of patients (range: 5% to 70%). Approximately half of these patients seek medical attention before their major SAH, and 16% to 60% of them are misdiagnosed. Common misdiagnoses include flu, meningitis, cervical disc disease, migraine, cluster headaches, myocardial infarction, malingering, and intoxication. This is of significance because the overall clinical course and outcome are worse in misdiagnosed patients. Misdiagnosis was reported to be associated with a nearly fourfold greater likelihood of death or disability at 1 year in patients who had minimal or no neurologic deficit at the initial visit. More serious sequelae of SAH include change in mental status (combativeness, irritability) and level of consciousness, collapse, seizures, cranial nerve palsy, and intracranial hypertension from mass effect.

**B.** SAH is a **true medical emergency**. Rupture of an intracranial aneurysm accounts for approximately 80% of cases with a high rate of complications and death. An estimated 10% to 15% of patients die before reaching the hospital. The 30-day mortality rate approaches 45% and approximately half of the patients die within the first 6 months. Mortality and morbidity increase with age and poorer overall health and more than half the survivors have major neurologic deficits. Physical examination and laboratory studies identify changes in level of consciousness, focal neurologic deficits, intracranial hypertension, fever, meningismus, nuchal rigidity (may be absent early after SAH), photophobia, ophthalmic hemorrhages (poor prognostic sign), and fluid (hypovolemia) and electrolyte (hyponatremia) imbalance.

**C. Grading.** In 1956, **Botterell** introduced a system for grading patients after SAH to facilitate assessment of surgical risk, prediction of outcome, and prompt evaluation of the patient's condition. Grades I to V describe the patient's level of consciousness and degree of neurologic impairment, with

TABLE 10.2 Risk Factors for Aneurysmal SAH

1. Hypertension
2. Smoking
3. Heavy alcohol use
4. Sympathomimetic drugs including cocaine and phenylpropanolamine
5. Autosomal dominant polycystic kidney disease
6. Type IV Ehlers-Danlos syndrome
7. Family history, an independent risk factor for SAH

SAH, subarachnoid hemorrhage.

TABLE 10.3A Clinical Grading after Subarachnoid Hemorrhage: Hunt and Hess Modification

| Grade | Description | Mortality (%) |
|---|---|---|
| Grade 0 | Unruptured aneurysm | — |
| Grade I | Asymptomatic or minimal headache with normal neurologic examination | 2 |
| Grade II | Moderate to severe headache, nuchal rigidity, no neurologic deficit other than cranial nerve palsy | 5 |
| Grade III | Lethargy, confusion, or mild focal deficit | 15–20 |
| Grade IV | Stupor, moderate to severe hemiparesis, possible early decerebrate rigidity, vegetative disturbances | 30–40 |
| Grade V | Deep coma, decerebrate rigidity, moribund appearance | 50–80 |

Serious systemic diseases (hypertension, coronary artery disease, chronic pulmonary disease, diabetes) and severe vasospasm on angiography cause assignment of the patient to the next less favorable category. From Hunt WE, Hess EM. *J Neurosurg.* 1968;28:14, with permission.

each higher grade representing greater severity. **Hunt and Hess** modified Botterell's system in 1968 to include a provision for the effect of serious systemic illness (Table 10.3A).

The **World Federation of Neurological Surgeons** (WFNS) 1988 grading scale, based on the Glasgow Coma Scale, demonstrated that the preoperative level of consciousness correlated most directly with outcome (Table 10.3B).

**D. Diagnosis of cerebral aneurysms**

1. **Computed tomography (CT) and angiography (CTA):** A non-contrast cranial CT scan to assess the amount of subarachnoid, intracerebral, and intraventricular blood is the first step in the diagnosis of SAH. The probability of detecting hemorrhage is proportional to the timing and the clinical grade of the bleed. The sensitivity of the CT scan for identifying SAH is 98% to 100% in the first 12 hours after SAH. This declines in the next 24 hours to 93% and then to 57% to 85% in the 6 days after the initial SAH.

   CTA is a non-invasive, rapid, and readily available modality that is fairly sensitive for large-size cerebral aneurysms. Although effective in diagnosing severe vasospasm, CTA is less accurate in detecting moderate and mild vasospasm and not useful at all in patients who have

TABLE 10.3B World Federation of Neurological Surgeons Clinical Grading Scale

| WFNS Grade | GCS Score | Motor Deficit |
|---|---|---|
| I | 15 | Absent |
| II | 14–13 | Absent |
| III | 14–13 | Present |
| IV | 12–7 | Present or absent |
| V | 6–3 | Present or absent |

WFNS, World Federation of Neurological Surgeons; GCS, Glasgow Coma Scale.
From Drake CG, Hunt WE, Kassell N, et al. *J Neurosurg.* 1988;68:985, with permission.

already had clipping or coiling of an aneurysm owing to artifacts from the metal in aneurysm clips and coils.

When combined with catheter angiography, CTA is able to define intraluminal aneurysmal thrombosis and demonstrate calcification of the aneurysmal wall and its relation to intracerebral hemorrhage and the bony landmarks. The sensitivity and the specificity of CTA for aneurysmal detection depend on the quality of the images obtained, expertise of the radiologist, and size and location of aneurysms. The reported sensitivity of CTA for aneurysms is 70% to 100%; the specificity is 79% to 100%. When aneurysmal size is considered, CTA sensitivity for aneurysms ≥ 5 mm is 95% to 100%; for aneurysms < 5 mm, the sensitivity is 64% to 83%. Both the sensitivity and the specificity of CTA for aneurysm diagnosis increase with the experience of the radiologist. CTA is considered equal to catheter angiography in 80% to 83% of cases while in 74% of patients, catheter angiography performed after CTA did not add any new information. Thus, when the aneurysm is demonstrated on CTA, many neurosurgeons opt to operate on the basis of CTA alone in cases where the risk of delaying surgery for catheter angiography is too great.

2. **Lumbar puncture** is recommended for diagnostic analysis of cerebrospinal fluid (CSF) if the CT scan is negative as the sensitivity of the CT scan is not 100% even in the first few hours after SAH. Technique, timing, and interpretation of the **CSF** sample are vital to the accurate diagnosis of SAH. The sample is studied for red blood cells, white blood cells, xanthochromia, and the presence of bilirubin. A "warning leak" can be excluded and a favorable outcome expected if both CT and CSF results are negative after a history of severe headache.
3. **Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA)** demonstrate the true size of the aneurysm, its relation to important anatomic structures, the size, shape, and amount of clot in the lumen of aneurysm, and any recent or old hematoma. MRI and MRA images may also indicate other possible causes of SAH in patients who have a negative CT scan and an equivocal CSF examination.

   MRA does not require iodinated contrast and ionizing radiation and thus is useful in evaluating pregnant patients. MRA is not, however, sufficiently sensitive for detecting small aneurysms. The sensitivity of MRA with aneurysms ≥ 5 mm is 85% to 100%; this decreases to 56% for aneurysms < 5 mm in size. The sensitivity of 3-dimensional (3D) time-of-flight MRA for cerebral aneurysms is between 55% and 93%.
4. **Cerebral angiography**, although invasive, still remains the gold standard for the diagnosis of a cerebral aneurysm as the cause of SAH. This modality gives the exact location, size, and configuration of the aneurysm with good visualization of the neck of the aneurysm.

## III. COMPLICATIONS OF ANEURYSMAL SAH (TABLE 10.4)

### A. Rebleeding after SAH

The occurrence of further hemorrhage after the initial SAH is **one of the major causes of neurologic deterioration after SAH**. The size of the hematoma from the episode of rebleeding is the most critical factor in determining outcome. Patients who have a large subdural hematoma and a marked midline shift on CT scan have a poorer prognosis, as do those who have associated intracerebral and intraventricular hemorrhage (See Table 10.5).

1. The **cardinal signs** are deterioration in the level of consciousness, development of focal neurologic deficits (aphasia, hemiplegia), abnormal vital

TABLE 10.4 Complications of Aneurysmal Subarachnoid Hemorrhage

| |
|---|
| **Central Nervous System** |
| Rebleeding |
| Vasospasm |
| Disordered autoregulation |
| Intracranial hypertension |
| Hydrocephalus |
| Seizures |
| **Systemic Disorders** |
| Hypovolemia |
| Hyponatremia, hypokalemia, hypocalcemia |
| Electrocardiographic abnormalities |
| Respiratory abnormalities: pulmonary edema, pneumonia, pulmonary embolus |
| Hepatic dysfunction |
| Renal dysfunction |
| Thrombocytopenia |
| Gastrointestinal bleeding |

signs (hypertension, bradycardia, arrhythmias, irregular respirations), and the presence of hemorrhage on ophthalmic examination.

These subsequent episodes of aneurysmal rupture are usually more severe than the first hemorrhage. The mortality associated with a second hemorrhage rises precipitously with significant morbidity in the surviving patients. Late rebleeding is fatal in 67% of cases. All rebleeding accounts for 22% of the mortality from SAH. Several factors predispose to rebleeding (Table 10.5). Increasing admission Hunt-Hess grade and aneurysm size are independent predictors of rebleeding.

2. The **incidence** of rebleeding is highest (4%) during the first 24 hours after SAH and then declines to 1% to 2% per day for the next 13 days. Approximately 20% to 30% of ruptured aneurysms rebleed within the first 30 days after SAH. The cumulative risk of rebleeding is 19% at 2 weeks, 50% at 6 months, and then decreases to 3% per year for up to 15 years. During the

TABLE 10.5 Factors Predisposing to Rebleeding after SAH

1. Large volume of blood in the subarachnoid space
2. Poor neurologic state from initial SAH
3. Short interval from initial bleed
4. Female gender: women bleed twice as frequently as men
5. Older age and poor general medical condition
6. Systemic hypertension: rebleeding directly related to systolic pressure
7. Multiple rebleeds that increase chance of rupture and death
8. Presence of intracerebral or intraventricular hematoma
9. Abnormal clotting parameters
10. Posterior circulation aneurysms
11. Increased time to treatment
12. Transfer to another facility after initial SAH

SAH, subarachnoid hemorrhage.

ensuing 5 months after the initial SAH, 10% to 15% of patients will rebleed. The overall incidence of rebleeding is 11%. The incidence of aneurysmal rupture during induction of anesthesia is 0.5% to 2% and carries a mortality of 75%. The incidence of intraoperative aneurysmal rupture varies from 6% to 18%, depending on the institution and the size and the location of the aneurysm. In order of decreasing incidence, the causes of rupture during operation include aneurysmal dissection, brain retraction, hematoma evacuation, and dural and arachnoid opening.

3. **Pathophysiologic sequelae** of rebleeding include intracranial hypertension and compromised cerebral perfusion; acute hydrocephalus from the sudden deposition of subarachnoid clot that obstructs the flow of CSF through the basal cisterns; cerebral infarction from either direct, hematoma-induced destruction of tissue or shifts in the intracranial contents with vascular compromise; impaired autoregulation (the ability of the normal brain to maintain cerebral blood flow [CBF] at a fairly constant level between a mean arterial pressure [MAP] of 50 and 150 mm Hg); and a reduction in the cerebral metabolic rate for oxygen consumption ($CMRO_2$).
4. **Prevention of rebleeding** (Table 10.6) is only accomplished definitively by early surgical or endovascular obliteration of the aneurysm. Either operation or endovascular obliteration within 24 to 48 hours of SAH is, therefore, favored because of the association with improved outcome. At 1-year follow-up, the results of the International Subarachnoid Aneurysm Trial comparing operative aneurysmal clip ligation with endovascular metal coiling demonstrated that the risk of rebleeding was low in both groups: 1% for the surgical group and 2.4% for the endovascular group. The effects of rebleeding were taken into account in determining that the relative risk of either death or significant disability for endovascular patients is 22.6% lower than for surgical patients. This represented an absolute risk reduction of 6.9%. Most of the 2,143 patients randomized into the trial were in good condition (WFNS Grades I and II) after SAH and had small anterior-circulation aneurysms (92% < 11 mm in size) for which both endovascular coiling and neurosurgical clipping were considered therapeutic options.

**TABLE 10.6** Prevention of Rebleeding after SAH

1. Control of blood pressure to avoid hypertension
2. Maintenance of cerebral perfusion pressure
3. Bedrest as component of broader treatment plan
4. Early treatment with a short course of antifibrinolytic drugs combined with early aneurysm treatment and prophylaxis against hypovolemia and vasospasm followed by discontinuation of the antifibrinolytic drugs
5. Appropriate control of pain and anxiety
6. Treatment with nimodipine, a calcium-channel blocking drug
7. Adequate control of ICP
8. Maintenance of euvolemia, avoidance of hypovolemia with consequent vasospasm and ischemia
9. Adequate control of seizures
10. Early surgical or endovascular obliteration of the aneurysm

SAH, subarachnoid hemorrhage; ICP, intracranial pressure.

All protocols designed for prevention of rebleeding after SAH include bedrest as part of the therapeutic package. Control of systolic hypertension and prevention of increases in the transmural pressure gradient (TMPG) across the wall of the aneurysm (MAP minus intracranial pressure [ICP]) are recommended. This can be achieved by the intravenous infusion of short-acting drugs (e.g., esmolol, labetalol), which have a good safety profile and a reliable dose–response relationship, to control either labile hypertension or transient spikes in blood pressure from therapeutic interventions. The routine use of nimodipine as prophylaxis against vasospasm needs to be taken into consideration as it also contributes to the lowering of systemic blood pressure.

It is equally important to avoid hypotension and to maintain the patient's "normal" blood pressure as the lower acceptable limit as means of preventing either initiation or exacerbation of vasospasm from a decrease in cerebral perfusion pressure (CPP), the difference between MAP and ICP. The use of narcotic analgesics and sedatives is recommended in titrated doses to reduce pain and anxiety while avoiding oversedation, hypoventilation, and hypercarbia with a consequent rise in ICP.

Avoiding hypovolemia and ensuring normovolemia are crucial to the successful treatment of hypertension and the prevention of hypotension, vasospasm, hypoperfusion, and the consequent development of cerebral ischemia, infarction, and new neurologic deficit. Control of any seizure activity is also vital as seizures may themselves lead to hypertension and an increase in the cerebral oxygen requirement.

Control of ICP is important in poor-grade patients who may have intracranial hypertension after SAH. The rapid drainage of cerebrospinal fluid (CSF) from either lumbar or ventricular puncture is avoided, however, as this may lead to a deleterious fall in ICP with a relative rise in transmural pressure and the potential for aneurysmal rerupture. When cerebral perfusion is seriously compromised because of intracranial hypertension from intracranial hematoma or cerebral swelling, CSF drainage may be instituted to reduce ICP, along with other strategies.

The use of **antifibrinolytic drugs** such as tranexamic acid and epsilon–aminocaproic acid has been shown to reduce the rate of rebleeding in the initial 2 weeks after SAH. There was, however, an increase in the incidence of cerebral ischemia and infarction that was shown to offset any improvement in overall outcome in the older studies. Recent studies, however, have demonstrated a reduction in the rate of early rebleeding and adverse outcome when tranexamic acid is given immediately after making the diagnosis of SAH. Newer recommendations thus include the early administration of a short course of antifibrinolytic therapy in combination with early treatment of the aneurysm by either endovascular obliteration or craniotomy for clip ligation, depending on the clinical situation. This mandates the rapid and efficient accomplishment of diagnosis, evaluation, and initial treatment. Administration of the antifibrinolytic drug is discontinued after the aneurysm is secured and prophylaxis against hypovolemia and vasospasm is instituted. Antifibrinolytic therapy is also recommended in patients who are at low risk of vasospasm and for whom there may be a beneficial effect from delaying surgery.

5. **Management of rebleeding** after SAH is designed to maintain CPP, limit intracranial hypertension, decrease intracranial volume, control systemic blood pressure, reduce transmural pressure across the wall of the aneurysm, and maintain cerebral oxygen delivery through normal arterial oxygen saturation and hemoglobin concentration.

**B. Vasospasm or delayed ischemic deficit**

Vasospasm is the reactive narrowing of the larger conducting arteries in the subarachnoid space that are surrounded by clots after SAH and affected by spasmogenic breakdown products of the red blood cells within the clot. The subsequent delayed ischemic deficit and infarction caused by vasospasm are major causes of disability and death after SAH, accounting for 30% of SAH-induced morbidity and mortality. Vasospasm has been considered the causative factor in 28% of all deaths and 39% of all disability after SAH and is, therefore, responsible for the great human cost and extensive utilization of limited health care resources.

Patients of all neurologic grades have a 50:50 chance of developing significant angiographic vasospasm. Symptoms of delayed ischemia occur in 20% to 25% of patients, and 30% to 50% of patients have evidence of infarction from vasospasm on CT scan. Death from vasospastic infarction occurs in 5% to 17% of patients.

The incidence of vasospasm peaks between the fourth and the ninth day after SAH and decreases over the next 2 to 3 weeks.

Vasospasm is directly related to the severity of the hemorrhage from the aneurysmal rupture, which correlates well with the location and the volume of blood noted on the post-SAH CT scan. The risk of vasospasm is increased by SAH-induced cerebral dysautoregulation and abnormal carbon dioxide ($CO_2$) responsiveness, a Glasgow Coma Scale score of < 14 on hospital admission, an early increase in mean MCA flow velocity on transcranial Doppler (TCD) ultrasonography, and anterior cerebral and internal carotid artery aneurysms. The timing of surgery and the method of occlusion—surgical versus endovascular—have no effect on the subsequent development of vasospasm. The intraoperative transfusion of packed red blood cells is a risk factor for poor outcome, and postoperative transfusion is correlated with the development of angiographically-confirmed vasospasm. The mechanism may involve either the depletion or the inactivation of nitric oxide, an endogenous vasodilator, which transfused red cells lack.

1. **Diagnosis of vasospasm**
   a. **Clinical signs** include either progressive impairment in the level of consciousness or the appearance of new focal neurologic deficits > 4 days after the initial SAH that are not associated with any other structural or metabolic cause. The onset may be either sudden or insidious and accompanied by increased headache, meningismus, and fever.
   b. **TCD ultrasonography** may be used to determine the efficacy and the duration of treatment. Both a large increase in blood flow velocity (MCA velocity > 120 cm/second) and a rapid rise in blood flow velocity (> 50 cm/second in 24 hours) reflect a reduction in vessel caliber. A peak flow velocity of 140 to 200 cm/second indicates moderate vasospasm; a peak flow velocity > 200 cm/second is associated with severe vasospasm. Critically high blood flow velocities (>120 cm/second) correlate strongly with vasospasm on angiography. Because TCD is operator dependent and reflects technical factors, ICP, cardiac output, and the artery being assessed, it is important to correlate TCD results with sequential neurologic examination and ICP, blood pressure, and cardiac output. In addition, absolute values for TCD can be misleading in the setting of "Triple-H" therapy (hypertension/hypervolemia/hemodilution). The Linegaard ratio (ratio of the velocity in the vessel in question to the velocity in the

ipsilateral internal carotid artery) has been shown to be helpful in following the TCD trends and as a guide to therapy.

c. **Cerebral angiography** is the most reliable modality for diagnosing and evaluating vasospasm. Although some angiographic evidence of vasospasm occurs in 70% to 80% of cases, only one-third of patients develop the clinical picture. Signs and symptoms of decreased CBF usually occur when the reduction in the diameter of the arterial lumen exceeds 50%, the definition of angiographically-severe vasospasm.

d. **Xenon-enhanced CT,** a relatively inexpensive technique, demonstrates the decrease in regional cerebral blood flow (rCBF) in patients who have clinical vasospasm. This technique can quantify rCBF accurately, be repeated within 20 minutes, fuse rCBF data with conventional CT scan anatomy, and distinguish ischemia from other causes of neurologic deterioration after SAH.

e. **Jugular bulb oximetry** detects changes in cerebral oxygen extraction ($AVDO_2$). Patients who develop clinical vasospasm have a significant rise in $AVDO_2$ approximately 1 day before the onset of signs of neurologic deficit. Increases in $AVDO_2$ may therefore predict impending clinical vasospasm, while an improvement in $AVDO_2$ reflects the patient's response to treatment.

f. **CBF-measuring modalities** include positron emission tomography, which demonstrates a fall in $CMRO_2$ after SAH, and single photon emission computed tomography (SPECT). Angiographic vasospasm, delayed ischemic deficit, and increased TCD velocities are associated with regions of hypoperfusion on SPECT.

2. **Treatment of vasospasm** involves pharmacologic and mechanical modalities.

a. **Early operation** for clip ligation of the aneurysmal neck permits the removal of a fresh clot by irrigation and suction. The surgeon may instill recombinant tissue plasminogen activator (rtPA) directly into the subarachnoid space to dissolve the remaining clot. This fibrinolytic drug can reduce vasospasm, but it also may cause bleeding by dissolving normal clots. Therefore, only patients at great risk of developing clinically-significant vasospasm are candidates for this treatment.

b. **Timely securing of the aneurysm facilitates the subsequent treatment of vasospasm** with hemodynamic and pharmacologic therapies. While better-grade patients (WFNS Grades I to III on hospital admission) whose aneurysms were occluded endovascularly were less likely to develop symptomatic vasospasm as compared with those undergoing surgical clip ligation, there was no significant difference in overall outcome between the two groups at the longest follow-up period.

c. The prophylactic use of the **calcium antagonist nimodipine** within 96 hours of SAH is now a standard aspect of care after SAH. Although nimodipine reduces the incidence of vasospasm, the improvement in mortality has not been statistically significant when compared with control groups. Because nimodipine tends to decrease blood pressure, patients may require hydration and the administration of pressor drugs during the induction of anesthesia and careful attention to fluid balance intra- and postoperatively.

d. **Enoxaparin,** a low-molecular-weight heparin given as one subcutaneous injection of 20 mg/day, has been shown to improve overall outcome at 1 year after SAH by reducing delayed ischemic deficit and cerebral infarction. Patients receiving enoxaparin also had fewer intracranial bleeding events and a lower incidence of severe shunt-dependent hydrocephalus.

e. **Other drugs** used to treat vasospasm include tirilazad, an antioxidant and free-radical scavenger whose clinical trials have demonstrated mixed results; nicaraven, a free-radical scavenger associated with a trend toward improved mortality, good outcome, and smaller infarct size at 3 months; ebselen, an antioxidant and anti-inflammatory drug whose neuroprotective properties have caused it to be effective in the treatment of acute stroke; and fasudil, a kinase inhibitor used intra-arterially to treat vasospasm. The use of endothelin antagonists has been associated with an increase in the incidence of pneumonia and hypotensive episodes. Preliminary studies have suggested that statins (e.g., simvastatin and pravastatin) may reduce vasospasm and improve mortality.

f. **"Triple-H therapy,"** hypertensive hypervolemic hemodilution, is thought to augment cerebral perfusion in vasospastic areas of the brain in which autoregulation is impaired through increases in blood pressure, cardiac output, and intravascular volume. Relative hemodilution to a hematocrit of 30% to 35% should promote blood flow through the cerebral microvasculature. The early institution of Triple-H therapy has been an accepted treatment to prevent the progression from vasospasm-induced mild ischemia to infarction. The need to expand intravascular volume after SAH is considered important because the total circulating blood volume and the total circulating red cell volume are reduced secondary to supine diuresis, peripheral pooling, negative nitrogen balance, decreased erythropoiesis, iatrogenic blood loss, and increased natriuresis from the elaboration of natriuretic hormone. However, the efficacy of Triple-H therapy has not been proven in controlled trials, and it has been associated with side effects, such as pulmonary edema and cardiac arrhythmias and other complications as described below.

1. The guidelines for optimal volume expansion include a central venous pressure (CVP) of 10 mm Hg and a pulmonary capillary wedge pressure (PCWP) of 12 to 16 mm Hg. The vagal and diuretic response to intravascular volume augmentation may necessitate the administration of atropine, 1 mg intramuscularly (i.m.) every 3 to 4 hours, and aqueous vasopressin (Pitressin), 5 units i.m., to reduce urine output to < 200 mL/hour. Hydrocortisone has also been used to attenuate the excessive natriuresis and consequent hyponatremia seen in patients after SAH, and to prevent the decrease in total blood volume. The use of 5% albumin to augment intravascular volume after the administration of normal saline has failed to increase the CVP above 8 mm Hg, but may improve clinical outcome at 3 months and reduce hospital costs.
2. Vasopressor drugs, including dopamine, dobutamine, and phenylephrine, may be necessary to increase blood pressure. If the aneurysm has not been secured, systolic pressure is maintained at 120 to 150 mm Hg. After the aneurysm has been secured, systolic blood pressure may be increased to 160 to 200 mm Hg. Invasive hemodynamic monitoring including the direct measurement of systemic arterial blood pressure, CVP, pulmonary artery pressure, PCWP, and cardiac output improves the safety and the efficacy of treatment with induced hypertension.
3. The complications of Triple-H therapy include rebleeding, transformation to hemorrhagic infarction, cerebral edema, intracranial hypertension, hypertensive encephalopathy,

myocardial infarction, pulmonary edema, congestive heart failure, coagulopathy, dilutional hyponatremia, and the complications of central venous catheterization.

g. **Transluminal balloon angioplasty,** the mechanical dilatation of a cerebral vessel at a segment of spastic narrowing by the use of an inflatable intravascular balloon, may effect improvement in the patient's level of consciousness and focal ischemic deficits. Early intervention is crucial to success. The superselective intra-arterial infusion of papaverine has also been successful in dilating distal vessels, but because papaverine can be neurotoxic, verapamil, nimodipine, and nicardipine are being used instead. The complications of angioplasty include rupture of the aneurysm, rupture of intracranial vessels, intimal dissection, and cerebral ischemia and infarction.

3. **Prevention of vasospasm** requires attentive critical care to prevent secondary cerebral insults and medical complications, maintain normovolemia and electrolyte balance, and monitor the level of consciousness and neurologic function in a critical care area until the peak time for the development of vasospasm has passed. After SAH, patients require 3 to 4 L of fluid per day to maintain normovolemia. Hypotonic solutions (e.g., lactated Ringer's solution) are avoided and hyponatremia is treated with either normal or hypertonic saline as necessary. The blood pressure is controlled before the aneurysm has been secured but not treated thereafter unless the elevation reaches critically high levels. Mannitol, ventricular drainage (with avoidance of a sudden drop in ICP and consequent rise in transmural pressure), and mild hyperventilation are used to maintain ICP in the normal range. The goal is to keep the CPP above 60 to 70 mm Hg.

**C. Central nervous system complications**

The CNS is directly affected by SAH and the resultant hematoma, vascular disruption, and edema, all of which decrease CBF and $CMRO_2$. The patient's clinical grade correlates with the extent of neurologic impairment caused by the intracranial derangement. The cerebral vasculature's **responsiveness to changes in $CO_2$ tension ($PaCO_2$) is preserved** after SAH. A decline in $CO_2$ reactivity usually does not occur without extensive disruption of cerebral homeostasis. **SAH interferes with cerebral autoregulation.** The upper and the lower limits of autoregulation are higher in hypertensive patients.

Intracranial aneurysms themselves, particularly giant ones, and the SAH-induced hematoma and edema all have the potential for causing **intracranial hypertension** with a resultant decrease in the patient's level of consciousness and the potential for brain stem herniation and death. After SAH, the patient's Hunt and Hess clinical grade reflects the ICP. Grade I and II patients have normal ICP (but not necessarily normal elastance), whereas Grade IV and V patients have intracranial hypertension.

1. **Hydrocephalus** occurs in 10% of patients after SAH from obstruction of the CSF drainage pathways by either intraventricular or intraparenchymal blood and the subsequent development of arachnoidal adhesions that prevent reabsorption of CSF. Whether the aneurysm has been occluded by either surgical or endovascular means does not affect the patient's subsequent risk for the development of hydrocephalus.

   **Acute hydrocephalus**, defined as ventricular enlargement within 72 hours of SAH, is reported to occur in approximately 20% to 30% of patients. Characterized by the early onset of lethargy and coma, acute hydrocephalus is associated with poor clinical grade on admission, a

higher Fischer Scale score, either thick subarachnoid blood or intraventricular hemorrhage on initial CT scan, alcoholism, female gender, older age, increased aneurysm size, pneumonia, meningitis, and a pre-existing history of hypertension. The development of acute ventricular dilatation immediately after SAH, contributing to assignment of poor neurologic grade, may require external ventricular drainage (EVD) to normalize ICP, especially if the patient's level of consciousness is depressed. Good results have been achieved when EVD is performed in conjunction with early occlusion of the aneurysm. While half of the patients who develop acute hydrocephalus go on to require a ventriculoperitoneal (VP) shunt, an EVD can reduce the need for permanent shunting. Other predictors of the need for permanent shunting are poor grade on admission, rebleeding, and intraventricular hemorrhage.

**Chronic hydrocephalus,** which develops weeks later in 25% of patients who survive SAH, is an important cause of failure to improve in patients who are initially comatose and of secondary slow decline in those who were originally in good condition. Symptoms include impaired consciousness, dementia, gait disturbance, and incontinence. Chronic ventriculomegaly requiring a permanent CSF shunting procedure is reported to occur in 18% to 26% of surviving patients. The need for permanent CSF diversion is associated with older age, early ventriculomegaly, intraventricular hemorrhage, poor clinical condition on presentation, and female sex. A follow-up CT scan is indicated a month after SAH to ascertain the ventricular size.

2. **Seizures** are detrimental after SAH because they increase CBF and $CMRO_2$ and may precipitate rebleeding from the attendant rise in blood pressure. The post-SAH incidence of seizures ranges from 3% to 26%. Early seizures occur in 1.5% to 5% of patients; delayed seizures occur in 7% of patients. Patients at highest risk for the development of seizures have either thick cisternal blood or lobar intracerebral hemorrhage on CT scan. Other risk factors include rebleeding, vasospasm and delayed ischemic deficit, MCA aneurysms, subdural and intraparenchymal hematoma, cerebral infarction, a history of hypertension, and chronic neurologic impairment.

   The value of prophylactic anticonvulsant therapy is controversial because most seizures occur in the first 24 hours after SAH and frequently before hospitalization. Neurosurgeons usually do administer phenytoin, fosphenytoin, or levetiracetam for 1 to 2 weeks after SAH, although a recent study investigating the effect of the prophylactic use of phenytoin on cognitive outcome reported that phenytoin was independently associated with worse cognitive function at 3 months after SAH.

   Although in-hospital seizures are rare in patients who receive prophylactic anticonvulsants after SAH, non-convulsive seizures have been reported. Continuous EEG monitoring revealed the presence of non-convulsive seizures in 19% of patients who were still either stuporous or comatose an average of 18 days after SAH despite anticonvulsant therapy and all died. Patients who have either an intracranial hemorrhage or more than one early seizure receive anticonvulsants for at least 6 months.

**D. Systemic sequelae of SAH**

1. **Fluid and electrolyte balance**

   Most patients (30% to 100%) develop a **decrease in intravascular volume** after SAH that correlates with clinical grade and the presence of intracranial hypertension. **Hyponatremia** occurs from the release of atrial natriuretic factor from the hypothalamus. Treatment includes hydration

with either normal or hypertonic (3%) saline to improve cerebral perfusion. The administration of 5% albumin has also been shown to prevent sodium and fluid losses associated with cerebral salt wasting. Many patients (50% to 75%) develop **hypokalemia** and **hypocalcemia** and require replacement. **Hypomagnesemia**, not uncommon after SAH, has been associated with vasospasm and poor outcome. A large placebo-controlled trial of treatment with a 14-day continuous infusion of magnesium suggested that administration of magnesium may reduce delayed cerebral ischemia by as much as 34% and decrease poor outcome at 3 months by 23%.

2. **Cardiac abnormalities**

Electrocardiographic (ECG) abnormalities occur in 50% to 100% of patients after SAH. The most common are T-wave inversion and ST-segment depression. Other changes include U waves, QT interval prolongation, and Q waves. These abnormalities are similar to those seen with cardiac ischemia and infarction and may predispose the patients to life-threatening arrhythmias. Prolongation of the corrected QT interval (QTc) makes patients particularly vulnerable to ventricular arrhythmias. The routine measurement of QTc may identify patients at risk for potentially lethal arrhythmias, a risk exacerbated by hypokalemia.

Rhythm disturbances, seen in 30% to 80% of patients, include premature ventricular complexes (most commonly), sinus bradycardia and tachycardia, atrioventricular dissociation, atrial extrasystole, atrial fibrillation, brady- and tachyarrhythmias, and ventricular tachycardia and fibrillation. Arrhythmias occur most frequently within the first 7 days of SAH. The peak occurrence is between the second and the third day. The etiology has been attributed to injury to the posterior hypothalamus with release of norepinephrine and resultant subendocardial ischemic changes and electrolyte disturbances. This increase in sympathetic tone can persist for the first week after SAH.

The extent of myocardial dysfunction correlates with the severity of the neurologic injury after SAH. Prophylactic adrenergic blockade has improved cardiac outcome in some patients. In determining whether to proceed with operation on an emergent basis after SAH, the measurement of serial cardiac isoenzymes and the assessment of ventricular function by echocardiography help elucidate the degree of ischemia especially as increases in serum cardiac troponin concentration after SAH reflect myocardial damage and are associated with a poor outcome. The urgency of the operation usually takes precedence over further cardiac testing so that patients who have physical and ECG findings of cardiac impairment are considered as having true cardiac damage and their anesthetic management adjusted accordingly. In terms of endovascular versus surgical occlusion, the type of therapy does not seem to affect the incidence of cardiac dysfunction and myocardial injury.

The use of a pulmonary artery catheter to monitor PCWP and cardiac output may facilitate management of both the patient's cardiac dysfunction and the response to Triple-H therapy for the treatment of vasospasm.

The presence of either a severe arrhythmia, as occurs in 5% of the patients who have arrhythmias, or significant cardiogenic pulmonary edema may necessitate the postponement of surgery until treatment has been instituted although delay could put patients at risk for rebleeding and compromise the treatment of vasospasm.

3. **Pulmonary abnormalities**
   Pulmonary conditions including cardiogenic and neurogenic pulmonary edema, pneumonia, adult respiratory distress syndrome, and pulmonary emboli account for 50% of deaths from medical complications at 3 months after SAH. Medical complications themselves cause 23% of all deaths.

   The majority (60%) of patients become symptomatic from pulmonary edema between days 0 and 7 after SAH; the largest number of cases presents on day 3. The incidence of pulmonary edema is greater in patients older than 30 years. Poor clinical grade at the time of admission also correlates with more respiratory dysfunction, suggesting neurogenic influences. Treatment includes antibiotics, supportive care, and correction of intracranial (intracranial hypertension, cerebral edema, hydrocephalus) and fluid and electrolyte abnormalities.
4. **Other medical complications**
   a. **Hepatic dysfunction** (hepatic failure and hepatitis) occurs in 25% of patients after SAH, correlates positively with poor clinical grade, and is frequently observed in patients who develop pulmonary edema.
   b. **Renal dysfunction** is noted in 8% of patients after SAH and occurs more frequently in septic patients who are receiving antibiotics.
   c. **Thrombocytopenia** occurs in 4% of patients after SAH and is associated with sepsis, severe neurologic deficits, and antibiotic use. Disseminated intravascular coagulation and leukocytosis have also been reported.
   d. **Gastrointestinal bleeding** occurs in almost 5% of patients and should be part of the differential diagnosis of any unexpected episode of hypotension and tachycardia.

## IV. OPERATIVE ANEURYSMAL OBLITERATION

The major determinant of outcome after surgical or endovascular treatment of a ruptured aneurysm is the preoperative neurologic status of the patient as determined by the severity of the initial hemorrhage.

A. **Early operative clip ligation of the neck of the aneurysm** to prevent flow into the aneurysmal sac has advantages when performed in the first 24 to 48 hours after SAH. These include prevention of rebleeding, reduction in vasospasm from removal of blood from the subarachnoid space ("intracranial toilet"), ability to treat vasospasm through volume expansion and deliberate hypertension with relative safety, and a reduction in medical complications, patient anxiety, and the cost of hospitalization. Clip ligation requires a craniotomy and runs the risk of intraoperative rupture of the aneurysm. The International Study on the Timing of Aneurysm Surgery, published in 1990, documented that early (0 to 3 days after SAH) and late (11 to 14 days) surgery yielded similar overall morbidity and mortality. The fact that results were better in the subset of North American patients who were alert and underwent early operation has made early surgical intervention a common practice.

   The **risk** associated with craniotomy for aneurysmal clip ligation is higher if the aneurysm has already ruptured. The morbidity and the mortality of operating on unruptured aneurysms are 4% to 10% and 1% to 3%, respectively. Surgical morbidity is increased with larger aneurysms, certain locations (e.g., vertebral, anterior communicating), and older and sicker patients. The experience of the surgeon and the center plays a role, as well, in that high-volume surgeons who work at high-volume institutions have better outcomes.

**B. Anesthesia for operative intervention**

Anesthesia for craniotomy for aneurysmal clip ligation of an intracranial aneurysm is tailored to ensure preservation of cerebral perfusion and oxygenation, avoidance of sudden changes in blood pressure and ICP to control the transmural pressure gradient across the wall of the aneurysm, satisfactory surgical exposure, and prompt emergence to facilitate early neurologic evaluation.

1. **Preoperative evaluation** includes (a) Review of neurodiagnostic studies (MRI, MRA, CT scan, cerebral angiogram); (b) History and focused physical and neurologic examinations; (c) Notation of ward blood pressures and association between blood pressure decrease and neurologic deterioration; (d) Assessment of fluid and electrolyte balance; (e) Cardiac history and ECG with determination of need for echocardiogram, cardiac isoenzymes, cardiac nuclear scanning, perioperative cardiovascular monitoring; and (f) Notation of current drug regimen.
2. **Premedication** involves continuation of calcium channel-blocking drugs, anticonvulsants, and steroids. In addition, drugs to reduce gastric acidity (cimetidine, ranitidine) and speed gastric emptying (metoclopramide) are given before the induction of anesthesia. Sedatives, hypnotics, anxiolytics, and narcotics are used sparingly to avoid respiratory depression and the masking of neurologic deterioration. Good-grade patients may receive small doses of intravenous narcotic (morphine, 1 to 4 mg; fentanyl, 25 to 50 mcg) and benzodiazepine (midazolam, 1 to 2 mg) when under the anesthesiologist's direct supervision. Poor-grade patients do not receive premedication unless an endotracheal tube is in place, in which case they could require muscle relaxation, sedation, and blood pressure control.
3. **Monitoring** during anesthesia includes the usual monitors plus: (a) Direct intra-arterial blood pressure with pressure transducer at brain level to reflect cerebral perfusion; (b) CVP through the antecubital, jugular, or subclavian route; (c) PCWP and cardiac output in patients who have cardiac compromise or severe vasospasm; (d) Transesophageal echocardiography as a guide to volume status; (e) Intermittent arterial blood gases, glucose, electrolytes, osmolality, hematocrit; (f) Brain temperature by tympanic or nasopharyngeal thermistor; (g) CBF velocity by TCD ultrasonography; (h) Electrophysiologic monitors: electroencephalogram (EEG); brain stem, auditory, somatosensory, and motor evoked potentials (for which total intravenous anesthesia [TIVA] is superior to inhalational drugs); and (i) Jugular bulb cerebral venous oxygen saturation (a global measure that may not reflect regional imbalances).
4. **Intravenous access.** The need for adequate intravenous access mandates the insertion of two large-bore intravenous catheters in addition to the CVP or pulmonary artery catheter before positioning for operation. Operative position may limit access to arteries and veins. In addition, interventions occurring during positioning can affect blood pressure, ICP, and transmural pressure of the aneurysm and require that venous access and monitoring be in place for assessment and treatment, as necessary.
5. **Induction of anesthesia** is critical because the rupture of the aneurysm at this juncture can be fatal (Table 10.7). A smooth induction requires limitation of the hypertensive response to laryngoscopy and intubation through adequate anesthesia and beta blockade (e.g., metoprolol, esmolol), prevention of coughing and straining on the endotracheal tube, and

TABLE 10.7 Induction of Anesthesia for Endovascular and Operative Treatment of Intracranial Aneurysms

| | |
|---|---|
| Optimal head position | |
| Deep plane of anesthesia | |
| Fentanyl | 0.5–1 mcg/kg |
| Remifentanil | 0.5 mcg/kg |
| Thiopental | 3–5 mg/kg |
| Propofol | 1–2 mg/kg |
| Vecuronium | 0.1 mg/kg |
| Low-dose inhaled anesthetic | 0.5 MAC |
| Controlled ventilation | 100% oxygen |
| $PaCO_2$ 35–40 mm Hg (normal ICP) | |
| $PaCO_2$ 30–35 mm Hg (elevated ICP) | |
| Before laryngoscopy | |
| Lidocaine | 1.5 mg/kg |
| Thiopental | 2–3 mg/kg |
| Propofol | 0.5 mg/kg |
| Brief, gentle laryngoscopy | |
| Intubation | |

ICP, intracranial pressure; MAC, minimum alveolar concentration; $PaCO_2$, arterial carbon dioxide tension.

maintenance of adequate CPP while minimizing the change in transmural pressure across the wall of the aneurysm. A moderate decrease in blood pressure at this juncture is acceptable in good-grade patients (Grades 0, I, II). The poor-grade patients (Grades IV and V) are less likely to tolerate any hypotension.

**a.** The ICP of good-grade patients is usually not elevated, and therefore these patients can tolerate a decrease in blood pressure of 20% to 30% below normal value, if there is no evidence of cerebral ischemia. Poor-grade patients already have the potential for ischemia secondary to intracranial hypertension and impaired perfusion. Decreasing the blood pressure of these patients may exacerbate the cerebral ischemia. Measures are still necessary, however, to blunt the sympathetic response to laryngoscopy and intubation.

**b.** Good-grade patients do not require hyperventilation during induction ($PaCO_2$ 35 to 40 mm Hg) because they have normal intracranial elastance. Poor-grade patients who have intracranial hypertension benefit from moderate hyperventilation to a $PaCO_2$ of 30 mm Hg during induction. Cerebrovascular reactivity to $CO_2$ is preserved with all anesthetic drugs.

**c.** The intravenous induction of anesthesia confers loss of consciousness while maintaining cardiovascular and intracerebral homeostasis during catechol-releasing maneuvers (e.g., laryngoscopy and intubation followed shortly by application of the pin head-holder, positioning, elevation of the bone flap) by the administration of propofol, 1 to 2 mg/kg, or thiopental, 3 to 5 mg/kg; fentanyl, 3 to 5 mcg/kg, or remifentanil, 0.5 mcg/kg; lidocaine, 1.5 mg/kg; and midazolam, 0.1 to 0.2 mg/kg. The patient is ventilated by mask with 100% oxygen.

d. If the patient does not have an increase in intracranial elastance, the introduction of isoflurane or sevoflurane before laryngoscopy deepens the anesthesia.
e. Additional fentanyl, 1 to 2 mcg/kg; propofol, 0.5 mg/kg; or lidocaine, 1.5 mg/kg, is given before brief gentle laryngoscopy and intubation to preserve hemodynamic and intracranial stability.

6. **Muscle relaxants. Vecuronium,** 0.1 mg/kg, a non-depolarizing muscle relaxant of intermediate duration, does not increase the heart rate (and blood pressure) or the ICP in the presence of a reduction in intracranial compliance. **Rocuronium and cis-atracurium** are shorter- and longer-acting alternatives to vecuronium, respectively. **Succinylcholine** has increased ICP and caused ventricular fibrillation in patients after SAH. Susceptible patients include those who are comatose but non-paretic; have flaccid paralysis, spasticity, or clonus; or move their extremities in response to pain but not command. For these patients, rocuronium, 0.6 mg/kg, which does not adversely affect CBF or ICP, is useful for rapid-sequence induction.
7. **Cardioactive drugs** counteract the hypertensive response to laryngoscopy and intubation. Esmolol, 0.5 mg/kg; labetalol, 2.5 to 5 mg; and metoprolol, 2 to 5 mg, block the chronotropic and the inotropic effects of sympathetic stimulation without affecting CBF or ICP. Intravenous lidocaine is also useful for this purpose. **Nitroglycerin** increases CBV from the dilatation of capacitance vessels and therefore may increase ICP. The **calcium channel-blocking drugs** nicardipine, 0.01 to 0.02 mg/kg, and diltiazem, 0.2 mg/kg or 10 mg, facilitate rapid control of hypertension intraoperatively. Neither drug decreases local CBF or blood flow velocity (BFV).
8. **Maintenance of anesthesia** is geared toward ensuring cerebral perfusion while avoiding changes in the transmural pressure gradient and aneurysmal rupture by maintaining the blood pressure at preoperative levels until the aneurysm has been clipped.
   a. **Intravenous drugs** including propofol, narcotics, and non-depolarizing muscle relaxants are used together or in combination with 0.5 minimum alveolar concentration (MAC) of a volatile anesthetic for maintenance of anesthesia.

      **Fentanyl** and **remifentanil** improve cerebral relaxation during craniotomy in hyperventilated patients receiving isoflurane. Either fentanyl (bolus: 25 to 50 mcg; infusion: 1 to 2 mcg/kg/hour) or remifentanil (bolus: 0.25 mcg/kg; infusion: 0.05 to 2 mcg/kg/hour) may be combined with isoflurane or sevoflurane or administered with an infusion of propofol, 40 to 60 mcg/kg/minute, for the maintenance of anesthesia.

      **Thiopental** may be useful as the primary anesthetic in a dose of up to 3 mg/kg/hour when the brain is "tight." The disadvantages of this approach are the potential for slow recovery from anesthesia and for systemic hypotension, which may be counteracted by volume expansion and enhancement of cardiac performance by monitoring pulmonary artery pressure and cardiac output. **Propofol** has largely supplanted thiopental both for induction and maintenance of anesthesia.
   b. All **inhalational anesthetics** are cerebral vasodilators and have the potential for increasing CBF and ICP. These drugs are avoided in patients who have cerebral injury accompanied by a decrease in cerebral compliance and an increase in ICP. All the inhalation anesthetics, with the exception of nitrous oxide ($N_2O$), depress cerebral

metabolism. Nitrous oxide is avoided in patients who have poor intracranial compliance because its use will further increase ICP.

**Isoflurane** increases CBF minimally but has increased ICP despite hypocapnia in patients who have space-occupying lesions. Isoflurane is therefore used in low concentrations or avoided altogether in patients known to have a decrease in intracranial compliance. The cerebral vascular effects of **desflurane** (4% to 6%) are similar to those of isoflurane. **Sevoflurane** is also a cerebral vasodilator with minimal effects on ICP when administered after the establishment of hypocapnia. The low blood-gas solubility coefficient of desflurane and sevoflurane permits rapid emergence and prompt postoperative neurologic evaluation.

9. **Emergence**
   a. Good-grade patients may be awakened in the operating room and their tracheas extubated at the end of the operation. The avoidance of coughing, straining, hypercarbia, and hypertension is essential. Hypertension in the immediate postoperative period, secondary to preexisting hypertension, pain, urinary retention from a malfunctioning catheter, and $CO_2$ retention from residual anesthesia, usually returns to baseline within 12 hours. Antihypertensive drugs are administered as necessary to avoid intracranial hemorrhage and cerebral edema. Patients at risk for the development of delayed ischemic deficit may benefit from a blood pressure that is 10% to 20% above their preoperative values.
   b. If patients have received remifentanil intraoperatively, longer-acting narcotics are administered before the conclusion of the operation to confer analgesia in the immediate postoperative period.
   c. The blood pressure of patients whose aneurysms have been wrapped rather than clipped or who have other untreated aneurysms is maintained within 20% of their normal range (120 to 160 mm Hg systolic) to avoid aneurysmal rupture during emergence.
   d. Hypervolemia and relative hemodilution are maintained in the postoperative period.
   e. Both poor preoperative status (Grades III to V) and a catastrophic intraoperative event (e.g., brain swelling, aneurysmal rupture, ligation of a feeding vessel) mandate continued intubation, sedation, and postoperative ventilatory support.
   f. When the patient either fails to awaken or has a new neurologic deficit at the conclusion of the operation, the residual effects of sedatives, narcotics, muscle relaxants, and inhalational drugs should be reversed or dissipated, the $PaCO_2$ normalized, and other causes of depressed consciousness (e.g., hypoxia, hyponatremia) ruled out or treated. Both the persistence of diminished responsiveness and a new neurologic deficit for 2 hours after surgery necessitate a CT scan to diagnose the presence of hematoma, hydrocephalus, pneumocephalus, cerebral infarction, or edema. An angiogram is helpful in demonstrating vascular occlusion.

C. **Intraoperative management**
   1. **Fluid administration**
      a. Patients have an SAH-induced decrease in circulating blood volume and therefore require hydration with isotonic crystalloid solution before the induction of anesthesia to preserve cerebral perfusion. The decrease is greater at 72 hours after SAH than at 6 hours so that patients operated "early" (within the first 24 hours) after SAH will

require less fluid to maintain normovolemia than those operated later on.

**b.** Normovolemia is maintained in good-grade patients who have no evidence of delayed ischemic deficit until the aneurysm has been clipped. Patients who have evidence of delayed ischemic deficit preoperatively require volume loading, preferably guided by invasive monitoring of volume status, with induction of moderate hypertension once the aneurysm has been clipped or continuation of the hypertension intraoperatively if induced preoperatively.

**c.** Full restoration of the intravascular volume to a state of modest hypervolemia occurs after the aneurysm has been clipped. Glucose-free crystalloid solutions are administered because both focal and global ischemic deficits can be exacerbated by hyperglycemia. Normal saline and other isotonic solutions are preferable to lactated Ringer's solution, which is hypo-osmolar to plasma and can lead to cerebral edema, if the blood–brain barrier is disrupted.

**d.** Blood and blood products are indicated to maintain the hematocrit at 30% to 35%. Blood is available in the operating room when the dissection of the aneurysm commences. The use of 5% albumin can confer some rheologic advantage. The administration of > 500 mL of hetastarch can, however, interfere with hemostasis and cause intracranial bleeding.

**2. Cerebral volume reduction:** The volume of the intracranial contents is reduced and brain relaxation improved to facilitate the surgical approach to the aneurysm after the dura is opened and to reduce the pressure required for brain retraction.

**a.** Moderate hyperventilation to a $PaCO_2$ of 30 to 35 mm Hg is maintained throughout the procedure. Hyperventilation to a $PaCO_2$ of 25 to 30 mm Hg is induced only if necessary to reduce brain bulk. With a preoperative increase in intracranial elastance, the $PaCO_2$ can be reduced to 25 to 30 mm Hg during induction. In patients who have vasospasm, higher $PaCO_2$ values are necessary to promote CBF.

**b.** Mannitol starts working within 10 to 15 minutes of the administration of 0.25 to 1 g/kg, which should occur after the dura is opened to avoid any decrease in CBV and ICP. Once the serum osmolality exceeds 330 mOsm/kg, additional mannitol will have little effect on ICP. Furosemide, 0.25 to 1.0 mg/kg, potentiates the action of mannitol by decreasing brain water content and diminishes the dose. The therapeutic effect of mannitol and furosemide together on ICP and brain bulk is greater and more prolonged than with either drug alone but requires close monitoring of intravascular volume, serum electrolytes and osmolality, and acid-base balance.

**c.** CSF may be drained through a lumbar subarachnoid catheter inserted after the induction of anesthesia, a ventricular catheter, or intraoperative cannulation of the basal cisterns. Leakage of CSF is avoided while the cranium is closed to prevent a decrease in ICP, the concomitant rise in transmural pressure, and potential rupture of the aneurysm. If the ICP is elevated preoperatively (as with an intracerebral hematoma), the escape of CSF from the subarachnoid puncture before craniotomy may also cause tonsillar herniation. Lumbar CSF drainage may be contraindicated in this situation.

**d.** Pharmacologic reduction of brain bulk may be achieved after the dura is opened by replacing inhalational drugs and $N_2O$ (if in use)

with intravenous anesthetics. Thiopental as a bolus (2 to 3 mg/kg) or infusion (4 to 5 mg/kg/hour) may decrease brain bulk by cerebral vasoconstriction but will prolong awakening and may require blood pressure support.

3. **Temporary proximal occlusion**
   a. **Induced hypotension** during microscopic dissection of the aneurysm had been advocated in the past to reduce the risk of rupture by decreasing aneurysmal wall tension. As regional CBF (rCBF) and even outcome are adversely affected in patients who have SAH-induced dysautoregulation and a higher incidence of cerebral vasospasm, ischemia, infarction, and postoperative neurologic deficit, neurosurgeons prefer to avoid the use of induced hypotension. An exception may be made to gain control of the parent vessel if the aneurysmal sac ruptures during surgical manipulation. Relative contraindications to induced hypotension include intracerebral hematoma, occlusive cerebrovascular disease, coronary artery disease, renal dysfunction, anemia, and fever.
   b. Neurosurgeons now use **temporary proximal occlusion** of the aneurysm's parent vessel to reduce the risk of rupture during aneurysmal dissection and manipulation. The application of temporary clips decreases the turgor of the aneurysmal sac through "local hypotension" and a reduction in blood flow. To **enhance collateral circulation** during temporary proximal occlusion, the patient's blood pressure is maintained in the high-normal range. This may require dopamine or phenylephrine, although patients who have coronary artery disease may be at risk for the development of cardiac ischemia. Blood pressure is quickly returned to the low-normal range whenever the clip is removed without the neurosurgeon's having secured the aneurysm.

      The **duration of temporary occlusion** is 20 minutes or less as the **risks** of distal ischemia and infarction, cerebral edema, and damage to the parent vessel are directly related to the duration of temporary occlusion and the integrity of the collateral circulation. Some neurosurgeons even recommend removal of the temporary clip at 10 minutes of occlusion to re-establish perfusion and then reapplication after an additional dose of thiopental. The chance of developing a new neurologic deficit after temporary proximal occlusion is exacerbated by older age, poor preoperative neurologic status, and aneurysms involving the distributions of the basilar and the middle cerebral arteries.

      Drugs suggested for **cerebral protection** during temporary occlusion include mannitol, vitamin E, and dexamethasone although no evidence exists for their effectiveness. Thiopental or propofol may be administered to achieve electroencephalographic burst suppression immediately before temporary occlusion.

      **Mild hypothermia** to 32°C to 34°C has been investigated as a cerebral protective adjunct during aneurysm surgery. For good-grade patients, the results failed to demonstrate any statistically significant effect of hypothermia on the duration of stay in the intensive care unit, total hospital stay, rates of death at follow-up, disposition at discharge, or neurologic outcome. There was also an increased incidence of bacteremia in the hypothermia group.
4. **Intraoperative aneurysmal rupture**
   a. **Rupture** of the aneurysm during induction of anesthesia and operation (7% before dissection, 48% during dissection, 45% during clip ligation) markedly increases mortality and morbidity because of

ischemia from the hypotension and surgical maneuvers necessary to secure the aneurysmal neck (e.g., temporary proximal and distal occlusion of the parent vessel). The cause is usually a sudden increase in the transmural pressure gradient across the wall of the aneurysm from either an abrupt decrease in ICP or a sudden increase in blood pressure. Intraoperative rupture was reported to occur in 11% of patients whose aneurysms had previously ruptured as compared with 1.2% of patients whose aneurysms were intact before operation. The prognosis is worse if the rupture occurs while the skull is still intact (e.g., induction of anesthesia).

b. **Diagnosis** of rupture during or after induction is based on an abrupt increase in blood pressure with or without bradycardia. The ICP might increase as well. The TCD may demonstrate the rupture and the efficacy of management.

c. **Therapy** is designed to (1) restore intravascular volume with isotonic crystalloid, colloid, blood, and blood products; (2) maintain cerebral perfusion; (3) control ICP; and (4) reduce bleeding. Bleeding can be reduced by lowering the systemic pressure with thiopental or sodium nitroprusside (SNP) after establishing normovolemia.

d. Intraoperative rupture of the aneurysm requires **rapid surgical control**. After restoration of intravascular volume, the MAP may be reduced briefly to 40 to 50 mm Hg to facilitate clip ligation of the aneurysmal neck. Alternatively or in addition, temporary occlusion of the parent vessel proximal and distal to the aneurysm may enable the surgeon to gain control of the aneurysm. The use of temporary occlusion may cause less cerebral ischemia than lowering the blood pressure in the face of hypovolemia.

## V. ENDOVASCULAR TREATMENT (SEE CHAPTER 16A)

**A.** Interventional neurosurgeons and neuroradiologists are now able to treat aneurysms with **endovascular coiling technology** as an alternative to operation, depending on the age of the patient and the size and the location of the aneurysm. The goal of the procedure is to fill the aneurysmal lumen with the Guglielmi Detachable Coil (GDC), which then sets up secondary thrombosis of the aneurysm. The coil is threaded into the aneurysmal sac by means of a catheter inserted into the cerebral vascular tree through the femoral artery, cannulation of which can be extremely stimulating.

**B. Endovascular coiling may be indicated when the:**

1. aneurysm is determined to be unclippable by the neurosurgeon; (Location is also important as outcome is better after clipping of middle cerebral artery aneurysms than after coiling. Clinical results were similar from both techniques with aneurysms of the anterior communicating and anterior cerebral arteries.)
2. patient is unable to tolerate surgery owing to poor clinical grade (Hunt and Hess IV or V) or poor medical condition; (The patient's age is also an important consideration as coiling has been associated with better functional outcome than clipping in patients > 65 years of age who were in good condition after SAH from a small internal carotid or posterior communicating artery aneurysm. Younger patients (< 40 years of age) may benefit from definitive clipping as they can tolerate the surgery and achieve better long-term protection without the risk of late rebleeding.)
3. aneurysm has been partially clipped;
4. the patient refuses operation.

GDC therapy has been most successful in treating smaller aneurysms that have relatively large dome-to-neck ratios, which allow for maximal packing of the coil within the lumen of the aneurysm. For large aneurysms and wide-necked aneurysms that have dome-to-neck ratios of < 2 (making it difficult to achieve and retain maximal coil packing), the incidence of complete treatment is significantly lower with higher rates of rerupture after GDC therapy.

The results of the International Subarachnoid Aneurysm Trial (2005) and long-term follow-up (2009) comparing outcome after clipligation and endovascular coiling favored endovascular coiling because of absolute (7.4%) and relative (23.9%) risk reductions at 1 year. The benefit of coiling on functional outcome remained significant for a mean of 9 years, despite a greater risk of rebleeding with coiling than with clipping. It is recommended that patients treated with coiling have regular follow-up angiograms to facilitate timely identification and treatment of a recurrence. There is, however, no significant difference in the incidence of symptomatic vasospasm between clipping and coiling.

**C. Complications of endovascular coiling** include the possibility of: (1) aneurysmal perforation, (2) thromboembolic events, (3) occlusion of the parent vessel from coil herniation.

Institutions that offer endovascular services have lower rates of in-hospital mortality for both endovascular and operative cases. New technologies including enhanced coil construction, intracranial stents, balloon remodeling, and the two-catheter technique have been developed to enhance safety.

**D.** The **challenges of anesthesia** for interventional neuroradiology include work in a location remote from the operating room, the need for communication with a team perhaps unfamiliar with the requirements of patients undergoing anesthesia for neurosurgical procedures, and the need for the anesthesiologist to have a thorough understanding of the technicalities, pace, and interventions planned by the interventional neuroradiologists. The anesthesiologist must also be familiar with the plan for anticoagulation (degree, duration, timing of reversal) and need for baseline anticoagulation studies, the use of intravenous contrast drugs and need for determination of baseline renal function, and the potential intraprocedural requirement for induced hypotension, hypertension, and hypercapnia.

Above all, the attention to the patient's comfort and safety, the precautions (two large-bore intravenous catheters, comfortable pillow, padding of all pressure points), and the monitoring (standard monitors plus direct intra-arterial blood pressure measurement when manipulation of blood pressure is required) for both conscious sedation and general anesthesia in the interventional suite must be identical to those indicated when patients are anesthetized in the operating room. Electrophysiologic monitoring may be considered in complex cases as these monitoring techniques may help to reduce the incidence of ischemic complications.

**E. Anesthesia** for endovascular procedures includes **conscious sedation** and **general anesthesia**. Conscious sedation enables interventionalists and anesthesiologists to perform intermittent neurologic examinations. Some interventionalists prefer general anesthesia, however, as the quality of the images improves when patients are immobile. Because access to the airway is limited, it is important to secure the airway before the procedure begins. Endotracheal intubation offers the combination of absolute

control of ventilation and adequate conditions for intracranial manipulation, which result in better images. The **choice of anesthetic drugs** includes either TIVA or a combination of intravenous and inhalational anesthetics with or without muscle relaxation. The choice of drugs depends on the patient's clinical condition. If ICP is elevated, TIVA may be preferable. Achieving hemodynamic stability is of paramount importance. The systemic blood pressure is adjusted to maintain the cerebral perfusion pressure while avoiding the wide swings in blood pressure that can cause the aneurysm to rerupture. Controlled hypertension may also be indicated if the patient requires treatment for vasospasm. Heparin is administered to prevent thromboembolic events and then reversed at the conclusion of the procedure.

F. **Complications** include both hemorrhagic and occlusive catastrophes. Differentiation between these two is important. If the problem is **hemorrhagic**, patients may have signs of increased ICP including headache, nausea, vomiting, hypertension and bradycardia, and a change in the level of consciousness. Treatment includes immediate administration of protamine to reverse the anticoagulation and maintenance of the blood pressure in the low-normal range is indicated. **Occlusive** problems, both thromboembolic and vasospastic, require deliberate hypertension titrated to the neurologic examination either with or without direct thrombolysis or angioplasty to improve distal perfusion. Other emergent interventions include volume expansion, head-up tilt, hyperventilation, diuretics, anticonvulsant drugs, hypothermia to 33°C to 34°C, the infusion of thiopental to achieve electroencephalographic (EEG) burst suppression for cerebral protection, and vasodilating drugs for cerebral vascular dilatation.

## VI. ARTERIOVENOUS MALFORMATIONS OF THE BRAIN

A. **Definition**: Arteriovenous malformations (AVMs) are congenitally malformed focal conglomerations of dilated arteries and veins within the brain parenchyma, which produce low-flow, high-resistance shunts that conduct arterial blood directly into the venous system without passage of the blood through a high-resistance capillary bed.

1. Lack of intervening capillaries causes abnormal shunting via fistulous connections between arteries and veins
2. High-pressure vascular channels created by **direct arteriovenous connections at the nidus (or center) pose risk of rupture, especially in veins that have fibromuscular thickening and incompetent elastic lamina**
3. Location: supratentorial (70% to 97%); infratentorial (3% to 30%); deeper brain structures (5% to 18%)
4. Aneurysms are found in more than 50% of patients who have AVMs
5. AVMs occur in 0.01% of the general population
6. Seen with Osler-Weber-Rendu disease and Sturge-Weber syndrome
7. Hemorrhage (overall risk: 2% to 4% per year; annual risk of subsequent hemorrhage: 6% during first year with return to baseline risk thereafter) is associated with a 5% to 10% chance of death and a 30% to 50% chance of either permanent or disabling neurologic deficit

B. **Presenting signs and symptoms**: (1) intracranial hemorrhage: 42% to 72% of adults; 75% to 80% of children; (2) seizures: 8% to 46%; (3) focal neurologic deficits: 4% to 23%; (4) hydrocephalus; (5) congestive heart failure. Patients commonly present between 20 and 40 years of age.

C. **Neurologic damage** may be caused by (1) mass effect from direct compression or swelling; (2) ischemic "steal" from preferential low-resistance flow through the AVM with hypoperfusion of adjacent structures; (3) hemor-

rhagic infarction; (4) cerebral atrophy; (5) hydrocephalus; (6) headaches (migraine pattern); (7) seizures.

D. **Unfavorable prognostic features**: (1) history of a previous hemorrhage; (2) proximity to eloquent areas of the brain; (3) diameter of AVM > 20 cm; (4) transcranial Doppler estimation of shunt flow > 120 cm/second and pulsatility index < 0.5; (5) presence of deep feeding vessels and deep draining system.

E. **Imaging**: (1) **angiography** is the standard for identifying the architecture of the AVM, presence or absence of associated aneurysms and venous outflow obstruction, and pattern of venous drainage; (2) **magnetic resonance imaging** (MRI) and **magnetic resonance angiography** (MRA) permit better visualization of the AVM in relation to surrounding cerebral structures; **functional MRI** helps identify functional brain tissue; (3) **computerized tomography** (CT) is best for acute hemorrhage; **computerized tomographic angiography** (CTA) offers better vascular detail than MRA; can also identify feeding vessels not visualized on conventional angiography; (4) **diffusion tensor MR tractography** (MRT) identifies major white-matter neural tracts.

F. **Treatment**: the goal is complete obliteration of the AVM as partial obliteration does not protect against hemorrhage and may even increase the risk of subsequent bleeding. A secondary goal is the control of seizures.

1. **Surgical resection**: The three characteristics most predictive of surgical outcome—(a) maximum diameter of AVM; (b) location (within or outside eloquent areas); (c) presence or absence of deep venous drainage—comprise the **Spetzler-Martin grading system** (the sum of the scores for the three characteristics), which guides decisions regarding lesions that may be surgically resected. As operation on higher-grade AVMs is associated with greater morbidity and mortality, other treatment options are considered.

   **Complicating the resection** and increasing the risk of intraoperative hemorrhage are the presence of (a) high pressure in the nidus or feeding artery; (b) a deep perforating artery supply; (c) a single draining vein; (d) deep venous drainage; and (e) feeding artery aneurysms.

   **Intraoperative neuromonitoring modalities** are available. (a) **Digital-subtraction angiography** is helpful for identifying missing arterial feeding vessels and unsecured remnants of the nidus and determining the real-time hemodynamic status of the lesion. (b) **Image-guided navigational systems** aid in confirming complete resection of the AVM. This does, however, require good renal function and adequate hydration to maintain urine output. (c) **Measurement of cerebral blood flow** in patients who have large AVMs is helpful in detecting an increase in blood flow around the nidus. If this increase in local blood flow is present at the time of dural closure, significant lowering of the blood pressure is recommended postoperatively. (d) **Color Doppler ultrasound** aids in locating the nidus; spectral Doppler ultrasound is used to distinguish feeding arteries from normal vessels. (e) **Electrocorticograms** help to identify epileptogenic areas in patients who have seizures.

2. **Radiosurgery**: recommended for small AVMs (< 3 cm) located in eloquent areas of the brain where operation might cause a neurologic deficit. As there is a lag time of 1 to 3 years from treatment to complete obliteration of the AVM, the risk of hemorrhage is greatly reduced but not eliminated. Cure rates are reported to be 70% to 90% for lesions < 3 cm in diameter. Early (seizures, nausea, vomiting, headaches) and delayed (radionecrosis, hemorrhage, seizures, edema, venous

congestion) complications comprise a 5.2% incidence of transient neurologic problems and a 1.4% incidence of permanent neurologic deficits. Staged radiosurgery, which treats different sections of the AVM during different sessions, may be useful for larger and higher-grade lesions alone or in combination with embolization and operation.

3. **Embolization**: occlusive material delivered to feeding arteries and the nidus of AVMs via endovascular catheters, which may either completely obliterate AVMs of < 1 cm fed by a single artery or decrease blood flow to an AVM before surgical resection. Complications reported in 6% to 14% of cases include hemorrhage, stroke, and death.

G. **Management of associated aneurysms**: microsurgical clip ligation or endovascular coiling of feeding-artery aneurysms precedes treatment of the AVM. Intranidal aneurysms are treated in conjunction with the AVM.

H. **Anesthesia**

1. **Monitoring**: (a) **cardiovascular**—direct measurement of arterial pressure and central venous pressure; (b) **neurophysiologic**—corticography and stimulation mapping to evaluate motor, sensory, and language cortex; somatosensory evoked potentials; brain stem auditory evoked potentials; compressed spectral array; (c) **transduction of vascular pressures in the operative field** including proximal arterial pressure
2. **Medications**: osmotic diuretics (given at the time of the skin incision), steroids, antibiotics, antiepileptics, and antihypertensives (as necessary)
3. **Mild hyperventilation** to a $PaCO_2$ of 30 to 35 mm Hg
4. **Mild hypothermia** to 34°C to 35°C (with active rewarming as the operation concludes). Temperature monitoring is maintained in the postoperative period and hyperthermia is avoided as it can aggravate ischemic damage.
5. **Blood pressure management**: during the operation blood pressure (BP) remains at low-normal levels (100 to 120 mm Hg systolic) as hypotension may increase risk of postoperative hemorrhage from unrecognized inadequate hemostasis. Strict blood pressure control may reduce the risk of intraoperative bleeding, however; induced hypotension can be useful when the arterial supply of the AVM is deep within the brain. It is important to maintain adequate intravascular volume throughout the procedure, especially when the blood pressure is reduced. After resection of the nidus (but before closure), the BP is elevated to identify bleeding from unrecognized areas of residual AVM. Hypertension is strictly avoided, however, during emergence and in the postoperative period to prevent hemorrhage and cerebral swelling.
6. **Anesthetic technique**: the choice of anesthetic is governed by the need to avoid cerebral vasodilators in the presence of decreased intracranial compliance. Rapid emergence from anesthesia and early neurologic examination postoperatively may be facilitated by the use of either TIVA or a combination of inhalational and intravenous drugs. Both hypertension and hypotension are detrimental during emergence from anesthesia. Blood pressure support may be necessary with phenylephrine; control of high blood pressure may require the use of labetalol or esmolol. The goal is to achieve rapid but controlled emergence from anesthesia to facilitate early neurologic examination. Close observation and careful blood pressure management are continued into the postoperative period. When staged operation is recommended for large AVMs, the patient remains anesthetized overnight in the intensive care unit with strict blood pressure control.

7. **Cerebral protection:** may be achieved through **metabolic suppression** with barbiturates, propofol, or etomidate but at the cost of delayed emergence. There is also no evidence that the outcome is affected although metabolic suppression may be helpful if there is an intraoperative catastrophe (e.g., uncontrolled bleeding, malignant cerebral swelling). **Nonpharmacologic methods** of cerebral protection include (a) maintenance of stable systemic hemodynamics and cerebral perfusion pressure; (b) cerebral relaxation to decrease retractor pressure (via neutral head position, cerebral spinal fluid drainage, diuretics, modest hypocapnia); (c) euglycemia and isotonicity; (d) euvolemia; (e) mild hypothermia; and (f) controlled emergence from anesthesia. As glucose may exacerbate cerebral injury, glucose-containing solutions are avoided and glucose is monitored intraoperatively.

**I. Cerebral circulatory changes**

1. An increase in the rate of blood flow through the AVM increases the total amount of blood passing through the shunt. This causes a progressive decrease in arterial pressure from the circle of Willis to the nidus of the AVM with a concomitant decrease in the pressure perfusing circulatory beds paralleling the AVM. These hypotensive regions within areas of normal brain may, however, demonstrate normal rates of tissue perfusion and no focal ischemic symptoms as a result of **adaptive autoregulatory displacement**. The lower limit of autoregulation in these regions is markedly reduced (below the lower limit assumed for normal brains) so that the presence of hypotension does not lead to vasoparalysis in the arteriolar resistance bed. Responsiveness to $CO_2$ is also preserved before and after resection of the AVM. Focal neurologic deficits (unrelated to intracerebral hemorrhage or seizures) are thus more likely caused by local mass effect from the abnormal AVM vasculature than by cerebral arterial hypotension.
2. The hyperemic complications of hemorrhage and cerebral swelling occurring after resection of an AVM have been explained by **normal perfusion-pressure breakthrough (NPPB)** attributed to cerebral hyperemia caused by an increase in blood flow and perfusion pressure in previously hypotensive areas after obliteration of the AVM. NPPB assumes that chronic dilatation of vessels in hypotensive areas causes a loss of autoregulation, but the fact is that autoregulation (albeit with a leftward shift of the autoregulatory curve) and $CO_2$ responsiveness are actually preserved. Regardless of the etiology of cerebral swelling and bleeding after ablation of the AVM, strict blood pressure control and even the institution of induced hypotension are indicated during emergence from anesthesia and in the postoperative period to prevent and treat these serious complications.
3. **Brain swelling during operation** may also be caused by (a) obstruction of venous drainage by vascular kinking or compression in the surgical field or compression of the jugular veins through inappropriate positioning of the patient; (b) cerebral spinal fluid (CSF) retention; or (c) hemorrhage below the lesion or within the ventricle. If brain swelling continues despite correction of these issues, then the blood pressure may be lowered and measures for cerebral protection instituted (e.g., barbiturates, hypothermia).

**J. AVMs and pregnancy**

1. The most common presentation of AVMs in pregnancy is rupture with subsequent hemorrhage although the risk of hemorrhage from an unruptured AVM during pregnancy is the same as for the general

population. Bleeding from an AVM during pregnancy is (a) increased with younger age (20 to 25 years) and primigravida status; (b) associated with headache, meningismus, and photophobia; and (c) a leading cause of non-obstetrical morbidity.

2. Patients who have unruptured AVMs or who are stable after a rupture are permitted to come to term and deliver before surgical or endovascular intervention. The superiority of vaginal versus cesarean delivery in the presence of an unruptured AVM remains controversial.
3. General anesthesia is indicated when cesarean section immediately precedes treatment of the AVM. Normocarbia, normovolemia, and strict blood pressure control are maintained intraoperatively.

**K. Vein of Galen AVMs**

1. Commonly present in infancy with congestive heart failure ( from pressure and volume overload) and hydrocephalus. Older children and adults can have hydrocephalus, hemorrhage, neurologic deterioration, or intracranial hypertension. The morbidity and the mortality rates are high even with treatment.
2. Signs and symptoms may be secondary to (a) local compression of brain tissue and obstruction of the flow of CSF and (b) systemic cardiovascular decompensation ( from left and /or right heart failure) and pH and electrolyte imbalance.
3. Pharmacotherapy with digoxin, furosemide, and inotropes is continued during endovascular treatment as the systemic vascular resistance is often low. Sedatives are avoided in the absence of mechanical ventilation. The need for maintenance of euvolemia may necessitate the use of central venous pressure monitoring or transesophageal echocardiography.
4. Veins of Galen AVMs have a very large shunt. Treatment is frequently staged with endovascular embolization through the femoral vein or a combination of endovascular and open surgical techniques. An important endpoint is improvement in cardiac function rather than complete obliteration of the AVM. Postoperative ventilation is considered until the patient is deemed cardiovascularly and neurologically stable.

## *Suggested Readings*

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# 11 Ischemic Cerebrovascular Disease

**Ian A. Herrick and Adrian W. Gelb**

## Illustrative Clinical Case

A 68-year-old, right-handed woman presents for left carotid endarterectomy (CEA). She is a retired factory worker who lives independently in her home. She has experienced two episodes of numbness and incoordination involving her right hand and forearm over the past three weeks, each lasting several minutes before resolving completely. She was started on aspirin following the second episode and has experienced no further events. Historically, she has smoked since the age of 15 years and is known to have hypertension, which is satisfactorily treated. She has no history of symptomatic systemic vascular disease but notes that her father developed heart disease in his fifties. Neurologic examination is unremarkable with no deficits. Computerized tomographic angiography of the head and the neck demonstrates severe bilateral carotid stenoses and a patent anterior communicating artery and posterior cerebral circulation. Surgery proceeds uneventfully under desflurane/remifentanil anesthesia. The surgeon opts to insert an intracarotid shunt in response to low carotid stump pressure and a 15% to 20% decline in left cerebral oximetry values (positioned over the left forehead) that accompany carotid cross-clamping. Oximetry values recover following placement of the shunt and endarterectomy is completed uneventfully. As the shunt is removed, the patient's blood pressure increases abruptly accompanied, in short order, by a modest decline in the left cerebral oximeter readings. The surgeon and the anesthesiologist, concerned that the circumstances reflect an evolving embolic stroke, must determine an appropriate course of action to manage the acute event, close the arteriotomy, complete the procedure, and arrange for appropriate postoperative assessment and care.

## Chapter Highlights

- Patients presenting for CEA and carotid angioplasty and stenting (CAS) procedures are often elderly, have advanced cerebrovascular disease, and frequently have significant coexisting diseases involving other organ systems.
- Anesthetic management of these patients requires both an understanding of the physiologic stress imposed by the surgical procedure (disruption of the major cerebral hemispheric blood supply) and an appreciation of the physiologic constraints imposed by coexisting diseases.
- Current guidelines for CEA are based on large multicenter prospective studies that confirm the efficacy of CEA as a surgical procedure for the prevention of stroke in appropriately selected patients.
- Numerous studies emphasize the important role that patient selection, preoperative optimization of comorbidities, and the experience and the expertise of the surgeon, surgical team, and institution play in mitigating risk associated with CEA.

- A large body of evidence supports the premise that, in experienced centers, the procedure can be performed safely under regional or general anesthesia.
- Although use is not linked to evidence of improved outcome, many centers employ intraoperative neurologic monitoring to guide the management of patients who develop cerebral ischemia in response to carotid occlusion.
- Stroke and myocardial infarction remain the most prominent causes of postoperative morbidity and mortality emphasizing the importance of appropriate patient selection and preoperative optimization.
- CAS procedures are associated with a higher risk of stroke and death compared to CEA and current recommendations do not support the use of these procedures in asymptomatic patients or routinely in symptomatic patients. CEA remains the "gold standard" surgical procedure for the prevention of stroke.

## I. GUIDELINES FOR PERFORMING CEA

**A.** Overwhelming evidence over the past two decades supports the efficacy of CEA, combined with best medical therapy, for the prevention of stroke among appropriately selected, medically stable patients who have symptomatic carotid stenosis (Table 11.1).

**B.** Current American Heart Association (AHA) guidelines[1,2] recommend CEA for patients who have symptomatic carotid stenosis of 50% to 99% if the perioperative risk of stroke or death is < 6% and for asymptomatic patients who have stenosis of 60% to 99% if the risk of perioperative stroke or death is < 3% (Table 11.2). These recommendations are based on clinical trials that incorporated stringent inclusion criteria and note has been made that the risk associated with CEA is also influenced by clinical conditions that bear on outcome, such as life expectancy, gender, comorbidity, and surgical experience.

TABLE 11.1 Number of Patients Needed to Treat with CEA (NNT) to Prevent Death or Stroke

| Characteristic | NNT | 95%CI |
|---|---|---|
| Symptomatic carotid stenosis ≥ 70% (ipsilateral stroke or death within 5 y) | 6 | 5–9 |
| Symptomatic carotid stenosis of 50%–69% (ipsilateral stroke or death within 5 y) | 22 | 12–80 |
| Asymptomatic carotid stenosis > 60% (any stroke or death within 5 y) | 20 | 14–50 |
| **Overall Results for Symptomatic Carotid Stenosis > 50%** | | |
| Male | 9 | |
| Female | 36 | |
| Age ≥ 75 y | 5 | |
| Age < 65 y | 18 | |
| Surgery within 2 wk of last TIA | 5 | |
| Surgery more than 12 wk after last TIA | 125 | |

CEA, carotid endarterectomy; NNT, number needed to treat; CI, confidence intervals; TIA, transient ischemic attack. Adapted from Rothwell PM, Eliasziw M, Gutnikov SA, et al. *Lancet.* 2003;361:107–116 and *Lancet.* 2004;363:915–924. Based on post-hoc analysis of 5-year pooled data from major CEA trials assuming a risk of stroke or death following CEA of 6% or less for symptomatic patients and 3% or less for asymptomatic patients.

TABLE 11.2 Candidates for Carotid Endarterectomy

**Established Benefit**

- Severe (70%–99%) symptomatic carotid stenosis
  - TIA or non-disabling stroke
  - Surgically accessible lesion
  - Perioperative risk of stroke or death < 6%

**Potential Benefit**

- Moderate (50%–69%) symptomatic stenosis
  - Benefit for males > females
  - TIA or non-disabling stroke
  - Surgically accessible lesion
  - Perioperative risk of stroke or death < 6%
- 60%–99% asymptomatic stenosis
  - Benefit for males > females
  - Surgically accessible lesion
  - Perioperative risk of stroke or death < 3%

**No Benefit**

- Asymptomatic stenosis < 60%
- Symptomatic stenosis < 50% (< 30% harmful)

TIA, transient ischemic attack.
Adapted from Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Carotid Endarterectomy—an evidence-based review. *Neurology.* 2005;65:794–801.

**C.** Subgroup analyses of the pooled results of the major North American and European CEA trials report that CEA is of greatest benefit for elderly males (≥ 75 years) with a high-grade (≥ 70%) symptomatic stenosis who proceed to surgery within 2 weeks following the last ischemic event (TIA).[3]

**D.** Endovascular treatment for carotid stenosis—CAS—has advanced markedly over the past two decades. Endovascular approaches to carotid revascularization are currently widely employed around the world. However, despite numerous clinical trials, definitive evidence demonstrating superior outcome relative to CEA has not been forthcoming.[4]

**E.** CEA remains the preferred surgical intervention for the prevention of stroke for patients who have extracranial cerebrovascular disease.

## II. PHYSIOLOGIC CONSIDERATIONS

### A. Cerebral blood flow (CBF) and metabolism

1. The brain is highly active metabolically but is essentially devoid of oxygen and glucose reserves, making it dependent on the continuous delivery of oxygen and glucose by the cerebral circulation.
2. CBF is provided by the internal carotid arteries (approximately 80%) and the vertebral arteries (approximately 20%), which anastomose at the base of the brain to form the circle of Willis.
3. Patients who have advanced occlusive cerebrovascular disease may be dependent on other collateral channels to maintain adequate CBF.
4. Normally, CBF is autoregulated to match the brain's metabolic requirements and maintain normal neuronal function.

**B. Cerebral perfusion**

1. CBF is related directly to cerebral perfusion pressure (CPP) and inversely to cerebrovascular resistance (CVR).
   a. CPP is defined as the difference between mean arterial blood pressure (MAP) and intracranial pressure or central venous pressure, whichever is higher.
   b. CVR is related to blood viscosity and the diameter of the cerebral resistance vessels.
2. Optimization of CBF during CEA is managed indirectly through the factors most amenable to intraoperative manipulation—arterial blood pressure and arterial carbon dioxide tension ($PaCO_2$), which impact CPP and CVR, respectively.

**C. Carbon dioxide tension $PaCO_2$**

1. Within the range of $PaCO_2$ from 20 to 80 mm Hg, CBF changes by 1 to 2 mL/100 g/minute for every 1 mm Hg change in $PaCO_2$.
2. Coexisting disease processes such as diabetes mellitus and severe chronic obstructive lung disease may impair the cerebrovascular response to carbon dioxide.
3. In the absence of demonstrable benefit associated with hypercarbia or hypocarbia during CEA, the most common approach to ventilatory management during these procedures is to maintain normocapnia. This is achieved by ventilation to a $PaCO_2$ that produces a normal pH in the absence of coexisting metabolic acidosis.

**D. Blood pressure**

1. Normally, CBF remains stable within the range of MAP from 50 to 150 mm Hg. Beyond this range, the limit of vasomotor activity is exceeded and CBF directly depends on changes in CPP.
2. In patients who have chronic hypertension, both the upper and the lower limits of autoregulation are shifted to higher pressures.
3. In patients who have cerebrovascular disease, the CBF response to changes in $PaCO_2$ during carotid cross-clamping is impaired. Under these conditions, improvement in CBF is likely to depend largely on increases in CPP, emphasizing the relatively greater importance of blood pressure control during CEA surgery.
4. During CEA, blood pressure should be maintained within the normal preoperative range. Mild increases in systolic blood pressure of up to 20% above normal at the time of cross-clamping are acceptable, but hypotension and severe hypertension should be avoided.

## III. PREANESTHETIC ASSESSMENT

**A.** The patient's state of health is determined from the medical history, pertinent physical examination, and chart review.

**B.** Coexisting diseases are assessed and optimized. Common coexisting diseases include coronary artery disease, arterial hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes mellitus, and renal insufficiency.

**C.** For patients who have diabetes mellitus, perioperative blood glucose should be carefully managed to avoid both hypo- and hyperglycemia. Current evidence suggests that perioperative hyperglycemia (blood-glucoses level > 200 mg/dL) adversely affects outcome following CEA.[5] Hypoglycemia is also neurologically deleterious. As a consequence, perioperative glucose management should probably be targeted at glucose levels that are consistent with the AHA guidelines for the management of acute stroke (140 to 185 mg/dL).[6]

**D.** Cardiac complications remain a prominent source of mortality after CEA. The benefit associated with CEA is premised on evidence that the risk of stroke in the absence of treatment is higher than the risk of stroke or death as a consequence of treatment. Minimizing perioperative risk by optimizing cardiovascular comorbidities (e.g., hypertension, coronary artery disease, and congestive heart failure) represents a key determinant of outcome.

**E.** Cerebral angiograms, including computed tomographic or magnetic resonance angiography studies, should be reviewed to identify patients at increased risk from the presence of significant contralateral carotid artery disease or poor collateral circulation.

**F.** A risk stratification scheme for perioperative complications has been proposed for patients undergoing CEA (Table 11.3). Recently, several other risk indices for CEA have been developed and variably validated. Key common features suggest that active coronary artery disease, a history of congestive heart failure, significant contralateral carotid disease (particularly occlusion), and unstable neurologic ischemic symptoms merit particular caution in patients presenting for CEA.

## IV. ANESTHETIC MANAGEMENT

CEA can be safely performed under general anesthesia, regional anesthesia, or local anesthetic infiltration. Experienced centers report similar morbidity and mortality. Despite enormous interest, available evidence, including the results from a recent large prospective trial (GALA), subgroup analyses of data from the prospective CEA trials, and meta-analyses of the published literature, remains insufficient to establish the definitive superiority of any one technique.[7,8] As a consequence, it is likely that outcome following CEA is more likely to be favorably influenced by patient selection, optimization of concurrent disease, and meticulous surgical technique than by the choice of anesthetic.

### A. Regional anesthesia

1. Superficial or deep cervical plexus blocks are the most commonly used regional anesthetic techniques for CEA.
   - **a.** A superficial cervical plexus block is performed by injecting a local anesthetic subcutaneously along the posterior border of the sternocleidomastoid muscle where the cutaneous branches of the plexus fan out to innervate the skin of the lateral neck.
   - **b.** A deep cervical plexus block is a paravertebral block of the C2–C4 nerve roots. This technique involves injecting local anesthetic at the vertebral foramina (transverse processes) of the C2–C4 vertebrae to block the neck muscles, fascia, and greater occipital nerve.
   - **c.** The two blocks are reported to be equally effective for CEA. However, deep cervical plexus block has been reported to have a higher failure rate (inadequate block) and to represent the exclusive source of serious, although rare, complications associated with these blocks. As a consequence, superficial cervical plexus block has been advocated as the regional technique of choice for CEA.[9]
   - **d.** Many regional anesthesia textbooks describe these techniques in detail and should be reviewed before performing the blocks.
   - **e.** With experience and patience, CEA can also be performed satisfactorily under local anesthetic infiltration of the surgical field and underlying tissue planes.
2. Intraoperative monitors include intra-arterial blood pressure measurement, continuous electrocardiogram (ECG), pulse oximetry, and capnography—often sampled via nasal prongs to monitor respiratory

TABLE 11.3 Preoperative Risk Stratification for Patients Undergoing CEA

| Risk Group | Characteristics | Total Morbidity and Mortality (%) |
|---|---|---|
| 1 | Neurologically stable, no major medical or angiographic risk | 1 |
| 2 | Neurologically stable, significant angiographic risk, no major medical risk | 2 |
| 3 | Neurologically stable, major medical risk, major angiographic risk | 7 |
| 4 | Neurologically unstable, major medical or angiographic risk | 10 |

| Type of Risk | Risk Factors |
|---|---|
| Medical risk | Angina |
| | Myocardial infarction (< 6 mo) |
| | Congestive heart failure |
| | Severe hypertension (> 180/110 mm Hg) |
| | Chronic obstructive lung disease |
| | Age > 70 y |
| | Severe obesity |
| Neurologic risk | Progressing deficit |
| | New deficit (<24 hrs) |
| | Frequent daily transient ischemic attacks |
| | Multiple cerebral infarcts |
| Angiographic risk | Contralateral carotid artery occlusion |
| | Internal carotid artery siphon stenosis |
| | Proximal or distal plaque extension |
| | High carotid bifurcation |
| | Presence of soft thrombus |

Adapted from Sundt TM Jr, Sandok BA, Whisnant JP. Carotid endarterectomy. Complications and preoperative assessment of risk. *Mayo Clinic Proc.* 1975;50:301–306. Used from Herrick IA, Gelb AW. Occlusive cerebrovascular disease: anesthetic considerations. In: Cottrell JE, Young WL, eds. *Anesthesia and Neurosurgery.* 5th ed. St Louis: Mosby, 2010:282, with permission.

rate when the patient's head and neck may not be entirely visible under the surgical drapes.

3. Supplemental oxygen should be provided through a mask or nasal prongs positioned to avoid the site of surgery.
4. Carefully titrated sedation using small, repeated, intravenous doses of fentanyl, 10 to 25 mcg, and/or midazolam, 0.5 to 2 mg, should render the patient comfortable and cooperative during the operation. Propofol is a reasonable alternative administered typically as a low-dose continuous infusion at 10 to 75 mcg/kg/minute and can be supplemented with a low-dose infusion of remifentanil (0.04 to 0.08 mcg/kg/minute).
5. The alpha 2-agonists, dexmedetomidine and clonidine, have also been reported to provide sedation and modest analgesia with minimal respiratory depression.[10] Limited experience with these drugs during CEA suggests they are associated with reduced intraoperative hypertension but a higher incidence of postoperative hypotension. Careful attention is necessary during the administration of dexmedetomidine to avoid hemodynamic instability (i.e., transient hypertension, hypotension, and bradycardia).

6. Equipment should be immediately available to convert to general anesthesia if intraoperative conditions warrant.
7. Advantages of regional anesthesia include the following:
   a. Superior neurologic monitoring associated with an awake patient
   b. Potential to optimize interventions such as shunt insertion based on the presence or the absence of neurologic symptoms at cross-clamping
   c. Less expensive
   d. Reports of more rapid recovery and shorter hospitalization
8. Disadvantages of regional anesthesia include the following:
   a. Requires an operating room staff committed to working with patients under regional anesthesia, which necessitates patience, gentle technique, and reinforcement of the block as needed. Staff commitment has been identified as a key feature of a successful CEA surgery program using regional anesthesia.[11]
   b. Lack of airway and ventilatory control
   c. Potential need to deal with complications in an awake patient: stroke or transient cerebral ischemia, cross-clamp intolerance, seizure, airway obstruction, hypoventilation, confusion, agitation, and angina
   d. Complications associated with cervical plexus blocks: local anesthetic toxicity, inadvertent injection into either the subarachnoid space or the vertebral artery, and phrenic or recurrent laryngeal nerve block

**B. General anesthesia**

1. General anesthesia represents the most common anesthetic technique for CEA.
2. Intraoperative monitors are the same as those used during regional anesthesia.
   a. Monitoring central venous or pulmonary artery pressure is used very infrequently. A central venous catheter facilitates the management of intraoperative fluid administration and provides central access for drug administration or resuscitation. A pulmonary artery catheter may be helpful in patients who have high-risk cardiovascular disease (e.g., unstable angina, poor left ventricular function, recent myocardial infarction). Care should be exercised to avoid carotid puncture when inserting these catheters into the jugular vein. Transesophageal echocardiography is viewed by many as a better alternative to a pulmonary artery catheter.
3. The key consideration during the induction of anesthesia is the maintenance of stable hemodynamic conditions during intubation, positioning, and draping.
4. Thiopental, midazolam, propofol, and etomidate are all appropriate induction drugs and should be supplemented with opioid. Propofol and etomidate are probably currently the most popular choices.
5. All of the non-depolarizing neuromuscular-blocking drugs facilitate tracheal intubation. Succinylcholine is a reasonable alternative. However, its use is contraindicated in patients who have had a recent paretic cerebral infarct.
6. General anesthesia is usually maintained with a combination of volatile anesthetic (typically isoflurane, desflurane, or sevoflurane) and opioid.[12] Neuromuscular blockade is typically maintained throughout the procedure. A propofol infusion is a reasonable alternative to the use of a volatile anesthetic. The use of remifentanil, an ultrashort-acting opioid, has also become popular as an adjunct to general anesthesia for

CEA. Its short duration of action facilitates titration of anesthesia and promotes early emergence, particularly when used in combination with a short-acting volatile anesthetic drug such as desflurane or sevoflurane.

7. The administration of nitrous oxide during CEA is declining in popularity as a result of controversial reports of adverse effects on cerebral metabolism and increased risk of postoperative complications including nausea and vomiting. In addition, many of the historic advantages attributed to nitrous oxide have been supplanted by other short-acting anesthetics such as desflurane, sevoflurane, and remifentanil.[13]
8. Blood pressure is maintained at preoperative levels. Small bolus doses of vasopressor (e.g., phenylephrine, 40 to 100 mcg, or ephedrine, 5 to 7.5 mg) can be administered to support blood pressure if necessary. Some anesthesiologists use infusions of phenylephrine to maintain or increase blood pressure, especially during cross-clamping. However, evidence suggests that this practice may be associated with an increased risk of perioperative myocardial ischemia.
9. Ventilation is adjusted to maintain normocapnia.
10. Advantages of general anesthesia include the following:
    a. Potentially more comfortable for patients and operating room staff
    b. Facilitates intraoperative control of ventilation, airway, and sympathetic responses
    c. Facilitates management of complications (e.g., cross-clamp intolerance and transient cerebral ischemia) through the use of induced hypertension or pharmacologic suppression of electroencephalographic (EEG) activity
    d. Reduces the need for expedience in performing surgery because patient tolerance is not a factor
11. Disadvantages of general anesthesia include the following:
    a. There is the need for an alternate method for monitoring cerebral function.
    b. In the absence of a completely reliable cerebral function monitor, it is possible that some remediable complications will not be detected before the occurrence of irreversible neuronal injury (e.g., cross-clamp intolerance, kink in carotid shunt).
    c. Prolonged emergence might confuse postoperative evaluation.
    d. It is more expensive.

**C. Carotid cross-clamping**

1. Before cross-clamping, heparin, 75 to 100 U/kg, is administered intravenously.
2. Carotid cross-clamping is often associated with an increase in blood pressure of up to approximately 20% above preoperative levels. Excessive increases can reflect cerebral ischemia. This should be considered before controlling the increase in blood pressure pharmacologically.
3. **Neurologic monitoring**
    a. The purpose of neurologic monitoring is to identify patients at risk for developing neurologic ischemia during CEA, particularly during carotid cross-clamping.
    b. An awake patient represents the least expensive and most sensitive neurologic function monitor during CEA.
    c. Because patients are not awake during general anesthesia, other techniques have been employed to monitor neurologic function.

EEG, carotid stump pressure measurements, transcranial Doppler (TCD), cerebral oximetry, evoked potential monitoring, and CBF measurements are used most commonly, either individually or in combination (e.g., EEG and TCD).

**d.** Each of these techniques can identify conditions (changes in perfusion, oxygenation, or metabolism) that may place the patient at increased risk of ischemia. However, controversy continues regarding the reliability of these monitors, individually or in combination, to predict outcome accurately (i.e., to identify the subgroup of patients who will progress to irreversible neurologic injury).[14]

**e.** A number of interventions have been used during CEA in response to evidence of an increased risk of ischemic cerebral injury although the efficacy of each remains unproven in clinical trials.[15,16] Interventions include:

1. Increasing CPP by administering systemic vasopressor drugs (e.g., phenylephrine)
2. Reducing the risk of ischemia by pharmacologic suppression of cerebral metabolic requirements (e.g., thiopental, propofol, etomidate)
3. Restoring internal carotid artery blood flow by inserting a carotid shunt

**f.** While the use of intraoperative neurologic monitoring remains popular, there is little evidence that the practice, including awake monitoring under regional or local anesthesia, contributes to improved outcome. As a consequence, the decision to employ these techniques and technologies remains largely a preference of the surgeon and surgical team.

**D. Emergence**

1. Emergence should be designed to avoid excessive coughing or straining and surges in systemic blood pressure, which might open the freshly closed arteriotomy.
2. Heparin may be partially reversed at the time of wound closure.
3. Many surgeons prefer patients to be awake and their tracheas extubated at the conclusion of the procedure to facilitate neurologic examination in the early postoperative period.

## V. POSTANESTHETIC MANAGEMENT

**A.** The intra-arterial cannula is maintained during the initial postoperative period to permit continuous blood pressure monitoring.

**B.** All patients receive supplemental oxygen postoperatively and oxygenation is monitored with pulse oximetry. Although uncommon, bilateral CEA is associated with the abolition of the ventilatory and cardiovascular responses to hypoxemia. Providing supplemental oxygen and closely monitoring ventilatory status are particularly important in these patients.

**C.** Postoperative hemodynamic instability occurs in 40% of patients after CEA and is postulated to be related, at least in part, to carotid baroreceptor dysfunction.[17,18]

1. CEA performed using a carotid sinus nerve-sparing technique is associated with a higher incidence of postoperative hypotension, most likely because of increased exposure of the carotid sinus after removal of the atheromatous plaque. The condition is associated with a marked decrease in systemic vascular resistance, and can be prevented or treated with local anesthetic blockade of the carotid sinus nerve, the

administration of intravenous fluid, or, if necessary, the administration of vasopressor drugs such as phenylephrine.

2. Hypertension after CEA is less well understood and has been reported to be more common in patients who have preoperative hypertension and in patients who undergo CEA with denervation of the carotid sinus. Mild increases in postoperative blood pressure of up to 20% above preoperative levels are acceptable, but marked increases are treated with antihypertensive drugs. Persistent postoperative hypertension should be distinguished from cerebral ischemia.
3. Other causes of hemodynamic instability after CEA include stroke, myocardial ischemia or infarction, arrhythmias such as atrial fibrillation, hypoxia, hypercarbia, pneumothorax, pain, confusion, and distention of the urinary bladder.

**D.** In most hospitals, patients are discharged from the postanesthetic care unit to a high-acuity environment in which intensive neurologic and cardiovascular monitoring is available (e.g., intensive care unit or neurosurgical observation unit).

## VI. COMPLICATIONS

Major postoperative complications after CEA include stroke, myocardial infarction, and hyperperfusion syndrome.

### A. Stroke

1. Approximately two-thirds of CEA-related strokes occur in the postoperative period. Most of these appear to be related to surgical factors that result in either carotid occlusion (e.g., thrombosis, intimal flap) or emboli originating at the surgical site.
2. Approximately one-third of CEA-related strokes occur intraoperatively. Most intraoperative strokes arise at the time of carotid cross-clamping or manipulation and are either technical (i.e., shunt malfunction) or embolic, rather than hemodynamic (< 10%), in origin.[19]
3. Monitoring intraoperative neurophysiologic function is directed to identifying the relatively small group of patients who develop hemodynamically induced ischemia, which is potentially reversible with early recognition and intervention.
4. Patients who have unstable neurologic ischemic symptoms, such as crescendo TIA or stroke-in-evolution, represent particularly high-risk candidates for CEA with the combined risk of stroke and death reported to exceed 10% and 20%, respectively.[20]

### B. Myocardial infarction

1. Second only to stroke, myocardial infarction, reported to occur in approximately 2% of patients, represents a major cause of mortality after CEA.
2. Despite the high incidence of coronary artery disease among patients undergoing CEA, little evidence supports routine preoperative coronary angiography in these patients. It is more reasonable to assume that all patients presenting for CEA have atherosclerotic disease involving the coronary arteries and to gauge perioperative risk in relation to the patient's functional status.
3. Extensive evidence-based guidelines have been developed to guide the preoperative assessment and management of patients who have cardiac disease who are scheduled to undergo non-cardiac surgical procedures, including CEA. Clinicians providing preoperative care and consultation to patients presenting for CEA should be familiar with the AHA guidelines[21,22] including recommendations for the continuation of beta-adrenergic antagonist medications, statin therapy, and aspirin.

3. High-risk cardiac patients including those who have unstable angina, recent myocardial infarction, or recent heart failure may be considered more appropriate candidates for CEA staged or combined with a coronary artery bypass graft (CABG) procedure.[2,4]
4. CEA staged or combined with CABG should be considered for a patient who has symptomatic carotid stenosis > 50% or asymptomatic stenosis > 80% who requires urgent coronary revascularization surgery.[4,23] Current recommendations suggest that the risk of stroke is lower if CEA precedes or is combined with urgent CABG than when CABG is performed before CEA. Cardiac mortality following the combined procedure has been reported to be similar to the risk of death following cardiac surgery alone. However, the risk of stroke following the combined procedure is significantly higher than that associated with CABG alone (approximately 6% vs. 1.5%, respectively) and the combined risk of stroke and death for the combined procedure is reported to be approximately 10%.

**C. Hyperperfusion syndrome**

1. An increase in CBF (typically < 35%) occurs frequently after CEA and has been reported following interventional revascularization (i.e., angioplasty and/or stenting, CAS) procedures as well. In severe cases, increases in CBF can exceed 200% of preoperative levels and can be associated with increased morbidity and mortality in the early postoperative period.[24]
2. The syndrome, with features similar to hypertensive encephalopathy, is thought to result from restoration of perfusion to an area of the brain that has lost its ability to autoregulate as the result of a chronic decrease in CBF. Patients at greatest risk include those who already have a preoperative reduction in hemispheric CBF due to a combination of bilateral high-grade carotid stenoses and/or poor collateral cross-flow.
3. Diagnosis is based on clinical features including headache (usually unilateral), face and eye pain, cerebral edema, seizures, and intracerebral hemorrhage. Patients at risk for this syndrome should be monitored closely in the postoperative period and blood pressure should be meticulously controlled.

**D. Other complications.** Other complications associated with CEA include wound hematoma formation and cranial nerve palsies.

1. Wound hematoma is associated with an increased risk for postoperative stroke or death and can lead to airway compromise as a result of mass effect. An expanding hematoma at the operative site should be managed as an emergency with reintubation and surgical evacuation.
2. Nerve palsies involving the hypoglossal, vagus, facial, and laryngeal nerves have been reported to occur in 5% to 12% of patients following CEA. They may be manifest as altered gag reflex or unilateral vocal cord dysfunction and are typically temporary.

## VII. CAROTID ANGIOPLASTY AND STENTING (CAS) PROCEDURES

**A. General considerations**

1. Carotid angioplasty with or without the deployment of an endovascular stent is widely employed around the world for the treatment of carotid stenosis. The safety and the efficacy of these procedures, relative to CEA, have been a topic of enormous interest and the focus of numerous prospective comparative trials over the past two decades.

2. CAS techniques have been evolving progressively over this interval as new technologies become available such as self-expanding stents and embolic-protection devices.
3. Despite great enthusiasm, investigators have had difficulty establishing the superiority of CAS relative to CEA.[4,25,26] Although some studies have reported a lower incidence of perioperative myocardial infarction associated with CAS, many have also reported inferior outcome in relation to stroke and death. Capping these studies, the long-awaited Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)[27] recently reported a lower incidence of myocardial infarction (1.1% vs. 2.2%) with carotid stenting but a higher incidence of stroke and death (CAS, 6.4%, vs. CEA, 4.7%) among 2,500 symptomatic and asymptomatic patients randomized to CEA or carotid stenting. Despite a combined rate of death, myocardial infarction, and stroke that was similar between treatment groups, CREST reported that neurologic risk was higher in patients randomized to CAS.
4. CEA remains the "gold standard" surgical treatment for the prevention of stroke. CAS may be an appropriate treatment for symptomatic patients who are unsuitable candidates for CEA due to technically inaccessible disease (e.g., previous neck irradiation) or who are medically unfit.[28] Current recommendations do not support the use of CAS procedures in asymptomatic patients. CAS is actually worse for intracranial arterial stenoses than aggressive medical management including the addition of aspirin to clopidogrel.

**B. Anesthetic considerations**

1. Preoperative assessment is consistent with the assessment of patients scheduled for CEA.
2. CAS can be performed under either general anesthesia or local anesthesia with sedation although the latter technique is employed more commonly. Patients generally complete the procedure without significant difficulty provided they can tolerate supine positioning. The fact that the procedure is typically performed conveniently under local anesthesia is often promoted as an advantage.
3. Monitoring should be consistent with operating room standards including intra-arterial blood pressure measurement, pulse oximetry, ECG, and capnography.
4. Hemodynamic changes may accompany carotid distension at the time of angioplasty or stent expansion and can be profound—especially bradycardia and asystole. A small dose of atropine or glycopyrrolate can be administered to attenuate this response. Equipment for transthoracic pacing should be immediately available.

## VIII. SUMMARY

This chapter focuses on the anesthetic management of patients undergoing CEA and briefly reviews the current status of CAS procedures. Physiologic concepts that form the basis for current recommendations regarding the choice of anesthetic technique, anesthetic drugs, monitoring, and hemodynamic and ventilatory management are discussed. Current evidence confirms CEA as the gold standard for the operative prevention of stroke. CAS procedures may be appropriate for a limited group of symptomatic patients who are unsuitable candidates for CEA. Challenges for the coming decade will focus on improving outcome through refining patient selection criteria, ensuring timely intervention, and optimization of comorbid high-risk conditions.

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# 12 Neuroendocrine Procedures

**David L. Schreibman and Mary K. McHugh**

## Illustrative Clinical Case

A 49-year-old female presents to the emergency department (ED) with a sharp, constant throbbing right retro-orbital headache. Past medical history is significant for a 3-month history of headaches and visual changes (bitemporal hemianopsia). Previously, the patient's headache would dissipate in 30 minutes but was continuous last night associated with worsening visual acuity in the left eye, photophobia, double vision, nausea, and vomiting. The patient denied galactorrhea or endocrine abnormalities. Prior workup by her ophthalmologist revealed a suprasellar mass on magnetic resonance imaging (MRI). At presentation to the ED, an MRI scan demonstrated a large cystic sellar/suprasellar mass causing mass effect on the optic chiasm and the floor of the third ventricle. The patient will be operated today for trans-sphenoidal decompression of her suprasellar mass because of the deterioration of her vision.

## Chapter Highlights

- Anatomy
- Endocrine physiology
- Pituitary pathology
  - Pathophysiology of mass effect
  - Pathophysiology of endocrine hypersecretion
- Therapy
- Perioperative management
- Complications

### I. ANATOMY

The **pituitary gland** is housed within the sella turcica, a boney alcove of the sphenoid. Critical structures surrounding the pituitary gland and sella turcica (Fig. 12.1) include

**A.** Optic nerve and chiasm, which lie superior to the diaphragma sella

**B.** Cavernous sinus, which surrounds the sella turcica laterally

1. Internal carotid artery
2. Occulomotor (III) Nerve
3. Trochlear (IV) Nerve
4. Ophthalmic division of the Trigeminal (V1) Nerve
5. Maxillary division of the Trigeminal (V2) Nerve
6. Abducens (VI) Nerve

### II. ENDOCRINE PHYSIOLOGY

**A.** Hypothalamus

1. The hypothalamus serves two primary physiologic roles within the body:

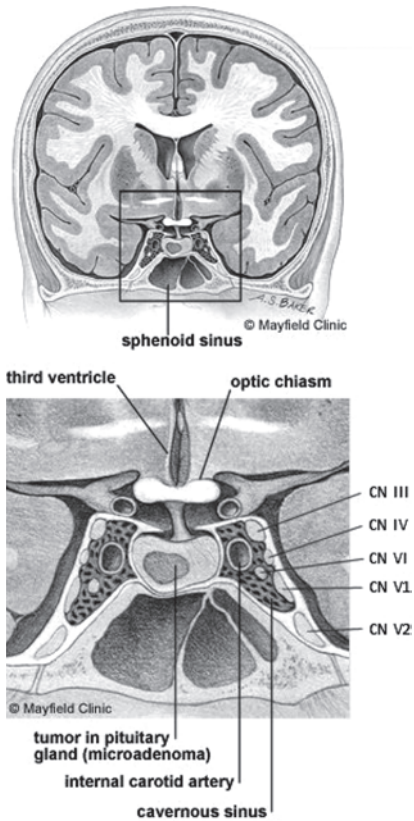


**FIGURE 12.1** Anatomy of pituitary gland, cavernous and sphenoid sinuses. CN, cranial nerve. Copyright permission pending.

   **a.** Regulation of the anterior pituitary gland through the synthesis of releasing and inhibiting factors
   **b.** Production of oxytocin and vasopressin
2. Releasing and inhibiting factors, produced in response to feedback from target organs, travel to the pituitary gland via the hypothalamohypophyseal portal system.
3. At the level of the pituitary gland, releasing factors stimulate the synthesis and the secretion of hormones into the systemic circulation. Inhibiting factors modulate further hormone production.

**B.** Anterior pituitary gland (adenohypophysis)
1. The anterior pituitary gland produces hormones in response to a variety of intrinsic and extrinsic stimuli. The body's diurnal rhythms and emotional wellbeing affect hormone production as do anesthetic drugs, surgical stress, and the hypothalamus.
2. Adenomas involving the anterior pituitary gland may lead to excessive production and secretion of one or more hormones. Those most commonly affected are adrenocorticotrophic hormone (ACTH), growth hormone (GH), and prolactin.

3. Radioimmunoassays detect and measure all anterior pituitary hormones in the systemic circulation.
4. Anterior pituitary gland hormones (Table 12.1)
   a. ACTH
   b. Follicle-stimulating hormone (FSH)
   c. GH
   d. Luteinizing hormone (LH)
   e. Prolactin (PRL)
   f. Thyroid-stimulating hormone (TSH)

TABLE 12.1 Anterior Pituitary Gland Hormones

| Hormone | Stimulating Factor | Inhibiting Factor | Effect |
|---|---|---|---|
| Growth hormone | GHRH | Somatostatin | Release glucose from glycogen<br>Increase protein synthesis for muscle and growth |
| ACTH | CRH<br>Acetylcholine<br>Serotonin | Cortisol<br>Norepinephrine | Stimulate adrenal to release cortisol |
| TSH | TRH | Thyrotropin | Increase metabolic rate of cells; ATP, heat production<br>Breakdown of liver glycogen |
| FSH<br>LH | GnRH | Estrogen<br>Testosterone<br>Progesterone<br>Inhibin | FSH—stimulate ovulation, spermatogenesis<br>LH—stimulate corpus luteum development and ovarian release of estrogen and progesterone, secretion of testosterone in males |
| Prolactin | PRH<br>TRH<br>Serotonin | PIH | Lactation |
| Melanocyte-stimulating hormone | MRH | MIH | Skin darkening, increase skin melanin |

GHRH, growth hormone-releasing hormone; ACTH, adrenocorticotrophic hormone; TSH, thyroid-stimulating hormone; TRH, thyroid-releasing hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; GnRH, gonadotrophin-releasing hormone; PRH, prolactin-releasing hormone; PIH, prolactin-inhibiting hormone; MRH, melanocyte-releasing hormone; MIH, melanocyte-inhibiting hormone; CRH, cortisol-releasing hormone.

- **C.** Posterior pituitary gland
  - **1.** Posterior pituitary gland hormones
    - **a.** Antidiuretic hormone (ADH) also known as vasopressin
    - **b.** Oxytocin
  - **2.** Both ADH and oxytocin are produced in the supraoptic and the paraventricular nuclei of the hypothalamus. Oxytocin differs from ADH in two of the nine amino acids.
  - **3.** Transport to the posterior pituitary gland occurs by way of axonal flow through the median eminence and pituitary stalk. The posterior pituitary gland serves as a reservoir for ADH and oxytocin. Both hormones are packaged into granules and secreted along with carrier proteins called neurophysins.
  - **4.** Numerous physiologic and pharmacologic factors influence ADH synthesis and secretion although hypovolemia has the greatest effect. (See Section IV for discussion of diabetes insipidus [DI])

## III. PITUITARY ADENOMA: EPIDEMIOLOGY AND CLASSIFICATION

- **A.** Epidemiology
  - **1.** The incidence of pituitary adenomas is difficult to determine. Clinically, they represent up to 10% of neoplasms affecting the brain. However, 27% of autopsies reveal a previously undiagnosed pituitary adenoma.
  - **2.** Forty percent of diagnosed pituitary adenomas are prolactinomas. Thirty-five percent are endocrine non-functioning pituitary adenomas.
  - **3.** Presentation and diagnosis typically occur between 30 and 50 years of age. Ten percent of diagnosed adenomas involve adolescents.
- **B.** Classification
  - **1.** Size
    - **a.** Microadenomas measure less than 10 mm in diameter.
    - **b.** Neoplasms that are greater than 10 mm at the time of diagnosis are considered macroadenomas.
  - **2.** Location
    - **a.** Microadenomas generally remain within the confines of the sella turcica and are considered extracranial or extra-arachnoid.
    - **b.** Macroadenomas often disrespect the normal boundaries of the pituitary gland, extending into the intracranial space to reach the cavernous sinus, sphenoid sinus, and suprasellar area.
  - **3.** Functional versus non-functional
    - **a.** Functional adenomas often result from the neoplastic growth of a single cell type. Excessive production of one pituitary hormone occurs and accounts for presentation and diagnosis.
    - **b.** Macroadenomas are generally larger at the time of diagnosis. Such non-functional adenomas present secondary to signs and symptoms of mass effect.
    - **c.** Differential diagnosis
      - **1.** Adenoma
      - **2.** Craniopharyngioma
      - **3.** Meningioma
      - **4.** Carotid aneurysm
      - **5.** Optic glioma
      - **6.** Empty sella syndrome
      - **7.** Neoplasms
        - **a.** Dermoid
        - **b.** Germinoma
        - **c.** Metastatic lesion

8. Inflammatory disease
   a. Infection
   b. Sarcoid
   c. Hemochromatosis
   d. Amyloid

## IV. PITUITARY ADENOMA: PATHOPHYSIOLOGY OF MASS EFFECT

Pituitary adenomas that extend beyond the normal boundaries of the sella turcica often produce symptoms secondary to mass effect, which causes the compression of surrounding structures. Signs and symptoms include:

A. Headache
   Patients frequently complain of bitemporal or bifrontal headaches secondary to
   1. Dural stretch of the diaphragma sella
   2. Disruption of normal cerebrospinal fluid (CSF) flow through the third ventricle (with resultant hydrocephalus)

B. Visual field defects
   1. Occur secondary to compression of the optic chiasm
   2. Bitemporal hemianopsia is the classic presentation but decreased visual acuity is not uncommon

C. Cranial nerve palsy
   1. May occur secondary to encroachment on the cavernous sinus by an enlarging mass
   2. Double vision due to effect on Cranial Nerves III, IV, and VI
   3. Facial numbness due to effect on Cranial Nerve V (V1 and V2)

D. Panhypopituitarism/hypothalamic dysfunction
   1. Compression of normal pituitary tissue and/or disruption of the normal communication pathways between the hypothalamus and the pituitary gland may produce signs and symptoms of panhypopituitarism or DI.
   2. Panhypopituitarism may include hypothyroidism, hypoadrenalism, and/or hypogonadism.

E. Diabetes insipidus
   1. DI occurs when either mass effect or neoplastic infiltration compromises function of the supraoptic nuclei of the hypothalamus, resulting in diminished or absent ADH release. Under normal conditions, osmoreceptors in the supraoptic nuclei and stretch receptors in the left atrium respond, respectively, to an increase in osmolality or a decrease in the volume of the extracellular fluid compartment with the synthesis and the release of ADH. In the systemic circulation, ADH binds to specific receptors in the collecting tubules of the kidney, modulating water permeability.
   2. Absent or diminished ADH produces:
      a. Polydipsia
      b. Hyperosmolality (> 320 mOsm/kg)
      c. Hypernatremia (serum Na > 150 mEq/L)
      d. Polyuria (> 3 L/day)
      e. Dilute urine (urine specific gravity < 1.005 and osmolality < 200 mOsm/L)
   3. Diagnosis relies upon recognition of the above signs and symptoms. Confounding conditions include diuresis secondary to hyperglycemia, osmotic diuretics such as mannitol, and overhydration.
   4. Management of DI intraoperatively includes:
      a. Determination of serum and urine electrolytes
      b. Replacement of total body water deficit
      c. Administration of aqueous vasopressin (see Section V below)

**F.** Hydrocephalus

**G.** Pituitary apoplexy

1. Pituitary apoplexy describes a condition of marked and often rapid expansion of a pituitary neoplasm and/or normal gland tissue secondary to hemorrhage, infarction, or necrosis.
2. Signs and symptoms of pituitary apoplexy include retro-orbital headache, ophthalmoplegia, visual deficits including blindness or decreased acuity, altered mental status from hydrocephalus, meningismus, and panhypopituitarism.
3. Addisonian crisis may occur in the face of acute ACTH deficiency leading to stupor, cardiovascular collapse, hyponatremia, and hyperkalemia.
4. Acute and symptomatic pituitary apoplexy with evidence of either hydrocephalus or visual defects requires surgical decompression. Adjunctive therapy includes corticosteroids.

## V. PITUITARY ADENOMA: PATHOPHYSIOLOGY OF ENDOCRINE HYPERSECRETION

**A. Cushing's disease:** ACTH hypersecretion

1. Cushing's disease occurs in the setting of both neoplastic hypersecretion of ACTH and failed autoregulation of hormone production. Cushing's syndrome encompasses a number of disease states producing hypercortisolism. Possible sources of excess cortisol production include
   - **a.** Pituitary adenoma (Cushing's disease)
   - **b.** Adrenal gland production secondary to carcinoma or adenoma
   - **c.** ACTH-producing neoplasms of the lung or the pancreas
   - **d.** Exogenous administration of steroids
2. Under normal conditions, ACTH is secreted by the anterior pituitary in response to corticotrophin-releasing factor, acetylcholine, and serotonin. Norepinephrine inhibits release of ACTH at the level of the hypothalamus. The adrenal gland responds to ACTH stimulation by secreting 17-hydroxycorticosteriod (cortisol) and 17-ketosteroids. Circadian rhythm profoundly affects cortisol levels, with peak secretion occurring between 4 am and 8 am (4 am to 8 am: 25 mcg/dL; 4 pm to 8 pm: 10 mcg/dL). Cushing's disease eliminates diurnal cortisol secretion and elevated levels occur in both morning and evening.
3. **Signs and symptoms** of Cushing's disease/syndrome
   - **a.** Centripedal fat distribution—moon facies, posterior cervical fat pad, supraclavicular fat, obesity
   - **b.** Hypertension
   - **c.** Osteoporosis
   - **d.** Acne
   - **e.** Abdominal striae
   - **f.** Hirsuitism
   - **g.** Glucose intolerance
   - **h.** Emotional disturbance
   - **i.** Easy bruisability with thin skin
   - **j.** Hyperpigmentation from cross reactivity of melanocyte-stimulating hormone (MSH) with ACTH
   - **k.** Menstrual irregularity/decreased libido/impotence
   - **l.** Generalized weakness and fatigability
   - **m.** Adrenal hyperplasia. In the past, many patients had bilateral adrenalectomy to treat what was thought to be a primary adrenal condition (Nelson's syndrome). These patients would then come for surgery later to remove what was actually a primary pituitary tumor.

4. **Diagnosis** of Cushing's disease rests upon evidence of cortisol hypersecretion (elevated levels of serum cortisol and urinary 17-hydroxycorticosteroid and 17-ketosteroid), loss of diurnal variation, and evidence of deregulated ACTH release.
   a. High-dose dexamethasone suppression test generally produces a fall in ACTH levels. This is not true in adrenally- or ectopically-mediated hypercortisolism.
   b. Metyrapone blocks conversion of cortisol precursors to their end product. A state of hypocortisolism ensues and stimulates ACTH release and further cortisol secretion. Metyrapone administration generally heralds an increase in ACTH levels and cortisol secretion in Cushing's disease. As with the dexamethasone suppression test, hypercortisolism secondary to adrenal or ectopic sources is impervious to pharmacologic manipulation.
   c. Gadolinium-enhanced MRI is the preferred imaging method. Most tumors are microadenomas and are discovered because of their endocrine effects.
   d. For tumors that are not evident on MRI, bilateral petrosal sinus sampling may be employed to identify their location.

B. **Prolactinoma:** Prolactin hypersecretion
   1. Under normal circumstances, the hypothalamus inhibits prolactin secretion through the release of prolactin inhibitory factor (PIF) or dopamine. Disease states that disrupt normal communication between the hypothalamus and the pituitary gland often produce signs and symptoms of hyperprolactinemia secondary to loss of hypothalamic inhibition. The role of prolactin-releasing factors like estrogen, thyroid-releasing hormone, and serotonin remains poorly described.
   2. **Signs and symptoms** of hyperprolactinemia
      a. Female patients present with complaints of amenorrhea, galactorrhea, infertility, and decreased libido.
      b. Male patients may also experience galactorrhea as well as decreased libido, impotence, premature ejaculation, and erectile dysfunction.
      c. Prolactin-secreting tumors are larger in men than women because women tend to seek medical attention sooner because of infertility.
   3. **Diagnosis** of a prolactinoma is confirmed by elevated serum levels of prolactin in conjunction with radiographic evidence of a sellar mass. Prolactin levels > 200 ng/mL (normal 3 to 20 ng/mL) suggest a prolactinoma even if its presence is not demonstrated radiographically. Prolactin levels < 150 ng/mL may reflect impingement on the pituitary stalk and interruption of the secretion of prolactin-inhibiting factors.

C. **Acromegaly/Gigantism:** Growth hormone hypersecretion
   1. GH hypersecretion leads to acromegaly or gigantism. Gigantism occurs if the onset of the disease occurs before the closure of the epiphyseal plates.
   2. The hypothalamus plays a critical role in GH regulation through the synthesis and the secretion of two releasing factors: GH-releasing factor (GHRF) and GH release-inhibiting factor (GHRIF) or somatostatin. External forces such as exercise and hypoglycemia affect GH levels by modifying stimulation from the hypothalamus.
   3. **Signs and symptoms** of acromegaly
      a. Hypertrophy of facial bones: prognathia and enlarged brow
      b. Macroglossia and enlarged nose, lips, and spaces between teeth
      c. Obstructive sleep apnea (OSA), upper airway obstruction, and laryngeal stenosis involving both true and false vocal cords from soft tissue over growth

d. Hoarseness from soft tissue stretching of Cranial Nerve X
e. Goiter
f. Acral enlargement (increased ring, glove, shoe size) and arthritis
g. Thickened skin, especially palms and soles of feet
h. Acne
i. Cardiovascular disease: hypertension, congestive heart failure, coronary artery disease, and cardiomyopathy from lymphocytic infiltration
j. Neuropathy: carpal tunnel syndrome from soft tissue hypertrophy; cervical and lumbar spinal stenosis from boney overgrowth; hoarseness secondary to stretch of Cranial Nerve X
k. Glucose intolerance
l. Heat intolerance and hyperhidrosis
m. Hyperprolactinemia
n. Visceromegaly and increased incidence of polyps of the colon

4. **Diagnosis** rests upon several laboratory indicators including elevated 24-hour GH levels, aberrant response to glucose tolerance test, and elevated levels of somatomedin C.

D. **Diagnosis** of pituitary adenoma

1. **Gadolinium-enhanced MRI** represents the gold standard for radiographic demonstration of a pituitary adenoma. Most microadenomas appear hypointense on T1-weighted images and hyperintense on T2-weighted images. The successful use of gadolinium requires exquisite timing as enhancement of neoplastic tissue occurs within 5 minutes of contrast administration. Tumor invasion into surrounding structures including the cavernous sinus and the carotid arteries is also demonstrated by MRI.
2. Once the diagnosis of an adenoma has been confirmed, pituitary **endocrine function is evaluated**. The diagnosis of functional pituitary adenomas relies upon detection of aberrant hormone production as defined above.

## V. TREATMENT MODALITIES

A. Medical management

The goals of medical management of functional pituitary adenomas include symptomatic relief, tumor regression, and prevention of end-organ damage.

1. Cushing's disease
   a. Ketoconazole, which blocks peripheral conversion of steroid precursors to cortisol, represents first-line therapy.
   b. Cyproheptadine, a serotonin antagonist, and mitotane, an adrenal suppressant, are alternative drugs for medical management. Poor patient tolerance, however, limits the use of both.
2. Prolactinoma
   a. Most prolactinomas respond to treatment with bromocriptine, a dopamine agonist. Decreased tumor size as well as decreased serum levels of prolactin are achieved. Prolonged treatment with bromocriptine may induce fibrosis, diminishing the chance for total surgical excision.
3. Acromegaly
   a. Bromocriptine remains the first-line therapy because of its low side-effect profile and cost, although it is less successful than other therapies.
   b. Octreotide, a somatostatin analog, profoundly decreases GH secretion in the majority of patients. Unsavory side effects prevent its widespread utilization.

c. Pegvisomant is a GH analog that functions as a GH receptor antagonist. Its use is indicated in patients who have an inadequate response to surgical, medical, or radiation therapy. Therapy is measured by normalization of serum insulin-like growth factor (IGF-1) levels.

4. Dismal success rates, the long lag time for clinical effect, and a plethora of side effects including panhypopituitarism, blindness, cranial nerve palsies, and apoplexy prevent greater utilization of radiation therapy in the management of pituitary adenomas. Radiotherapy has been used primarily for control of residual tumor after incomplete excision.

B. Surgical management

With the exception of prolactinomas, surgical management offers the only definitive cure. The two principal approaches for the resection of pituitary adenomas are trans-sphenoidal hypophysectomy and craniotomy.

1. Trans-sphenoidal hypophysectomy includes both the transnasal and the translabial–trans-septal approaches.
   a. The extra-arachnoid approach to trans-sphenoidal surgery obviates the need for brain retraction while still providing microscopic, multidimensional visualization of the adenoma.
   b. Both microadenomas and macroadenomas are amendable to trans-sphenoidal resection. Invasion into the cavernous and sphenoid sinus and suprasellar extension may require an alternative approach.
2. Endoscopic transnasal sphenoidotomy
   a. Endoscopic surgery utilizes an approach to the pituitary that is similar to trans-sphenoidal hypophysectomy. The use of the endoscope, however, minimizes dissection of the nasal septum while providing a more extensive and complete view of the sphenoid sinus and its abutting structures.
   b. Advantages of the endoscopic approach:
      1. Less surgical dissection translates to less operating room time, shorter hospital stays, and improved patient tolerance.
      2. The endoscope also provides better visualization of the superior and the lateral surgical fields.
   c. Disadvantage of the endoscopic approach is that it requires a unique surgical skill set that differs greatly from that for other microsurgical techniques.
3. Craniotomy
   a. Three approaches
      1. Subfrontal
      2. Pterional
      3. Subtemporal
   b. The pterional and the subtemporal approaches provide greater visualization of critical surrounding structures including the optic chiasm and the carotid arteries.

## VI. PERIOPERATIVE MANAGEMENT

A. Preoperative evaluation

1. Evaluation for endocrine abnormalities ranging from panhypopituitarism to hypersecretory syndromes is paramount in the preoperative period.
2. Hormone replacement for patients who have panhypopituitarism should commence before operation with daily prednisone and levothyroxine as necessary. Intraoperative administration of an intravenous stress dose of steroids is prudent.

**B.** Airway assessment in acromegaly
1. Anticipate difficulty with mask fit because of hypertrophy of facial bones, nose, tongue, and lips.
2. Hypertrophy of upper airway structures including soft palate, tongue, epiglottis, and tonsils as well as glottic stenosis, vocal cord paralysis, and goiter account for the possibility of a difficult intubation.
3. Although no single approach to intubation is recommended in this population, the availability of several airway management modalities including intubating laryngeal mask, videolaryngoscopy, and fiberoptic laryngoscopy is advisable.

**C.** Intraoperative management
1. Monitoring
   a. In addition to standard monitoring, radial artery catheterization is performed in most patients. Acromegalic patients warrant special caution during the placement of arterial lines as up to 50% will have an incomplete palmar arch.
   b. Most patients are positioned with modest head elevation to facilitate venous return. Theoretical risks for venous air embolus (VAE) exist with head elevations in excess of 15°. Preparation for diagnosis of VAE with precordial Doppler, central venous access, and end-tidal carbon dioxide and nitrogen monitoring (if available) is recommended, especially in the setting of cavernous sinus invasion.
2. Most practitioners consider peripheral venous access adequate for trans-sphenoidal surgery. The need for central venous access is determined by the size and the location of the tumor and/or by the patient's medical condition. Cavernous sinus invasion with evidence of carotid artery involvement suggests the possibility of significant bleeding. Adequate intravenous access is mandated and central venous access should be considered.
3. A stress dose of steroids and antibiotic prophylaxis (usually cefazolin, ampicillin/sublactam, or vancomycin) is warranted before incision.
4. Mucosal surfaces are often pretreated with combinations of local anesthetics and vasoconstrictors including lidocaine with epinephrine and cocaine. Patients who have a history of essential or disease-related hypertension, especially those treated with beta blockade, may experience a hyperdynamic response to the epinephrine and cocaine from an unopposed alpha sympathetic effect. Short-acting drugs to reduce afterload (e.g., nitroprusside, nitroglycerine) should be readily available.
5. Several techniques exist to facilitate exposure and visualization of a tumor that involves suprasellar extension. Hyperventilation should be avoided and mild permissive hypercarbia or an occasional Valsalva maneuver may seat a tumor with superior extension back into the sella. Injection of saline, air, or nitrous oxide into the lumbar subarachnoid drain will produce a similar effect.
6. Choice of anesthetic
   As for other neurosurgical procedures, a brief but directed neurologic examination is performed at the conclusion of trans-sphenoidal hypophysectomy. Accordingly, anesthetic plans should allow for rapid emergence; shorter-acting drugs such as propofol, remifentinil, and sevoflurane are popular choices.

**D.** Postoperative management
Immediate postoperative concerns include airway management, nausea, vomiting, and pain control.

1. Most patients emerge from anesthesia with hemostatic packing in both nares. A pre-emptive preoperative discussion concerning the need to mouth breath upon awakening is of paramount importance.
2. The high incidence of OSA and difficult airway in the acromegalic patient requires that special caution be exercised during extubation.
3. A relatively high incidence of nausea and vomiting accompanies these procedures. Pre-emptive pharmacologic management is highly desirable to avoid the potentially damaging sequelae of vomiting (e.g., bleeding and an increase in intracranial pressure) upon surgical outcome.
4. Management of pain after trans-sphenoidal surgery includes narcotics and non-steroidal anti-inflammatory drugs. Given the strong association between acromegaly and OSA, narcotics should be titrated cautiously in this patient population.
5. Postoperative considerations include hypopituitarism, DI, cerebrospinal fluid (CSF) leaks, and infectious complications.
   a. Postoperative replacement with intravenous mineralocorticosteroids such as hydrocortisone, 50 to100 mg every 6 to 12 hours, is usually warranted until endocrine testing is complete and then tapered accordingly.
   b. Preoperative hormone replacement with levothyroxine and/or vasopressin is reinstituted as soon as possible.
   c. Fluid intake, urine output, urine specific gravity, and serum electrolytes are closely monitored. The diagnosis of DI is confirmed by the presence of hypotonic polyuria (> 250 mL/hour) along with hypernatremia and hyperosmolality.
   d. The use of nasogastric tubes, incentive spirometry, and drinking straws is avoided. To ascertain the possibility of a CSF leak, ask the patient about nasal dripping or a "salty" taste in the throat. Lumbar drains have been employed to treat CSF leaks.

E. Complications
1. An overall **mortality rate** ≤ 1% is reported in most series.
2. Trans-sphenoidal hypophysectomy complications
   a. Overall complication rate for trans-sphenoidal hypophysectomy is around 3.5%. Serious morbidities including ischemic stroke, vascular injury, intracranial hemorrhage, blindness, CSF leak, and meningitis complicate 1.5% of trans-sphenoidal operations.
   b. Panhypopituitarism
      1. The incidence of postoperative panhypopituitarism is around 20%.
      2. Up to 27% of patients who experience postoperative panhypopituitarism will regain some or all function of the anterior pituitary gland.
   c. CSF rhinorrhea
   d. Diabetes insipidus
      1. DI affects approximately 20% of patients undergoing trans-sphenoidal surgery.
      2. There are three postoperative patterns
         a. Transient DI (12% in one series)—most patients will experience spontaneous recovery
         b. Permanent DI
         c. Triphasic DI (rare) reflects destruction of the majority of ADH-producing neurons of the pituitary stalk.
            i. Initial phase ( first 5 to 7 days) is caused by damage to the vasopressin-secreting neurons of the hypothalamus leading to polyuria and hypernatremia.

ii. Normalization or antidiuretic phase (7 to14 days) involves the release of the remaining ADH from the posterior pituitary or the hypothalamus leading to hyponatremia and increased urine osmolality. This can be exacerbated by treatment of the hypernatremia in the first phase.

iii. Chronic phase of hypernatremia occurs after the release of the remaining ADH, which leads to permanent DI.

3. Treatment
   a. Calculate free water deficit (FWD)

$$FWD = Weight\ (kg) \times 0.6 \times ([Serum\ Na/140] - 1)$$

   b. Replace FWD in addition to maintenance and other losses with hypo-osmolar fluids over 24 hours. Hypernatremia should not be corrected at a rate greater than 1 mEq/L/hour. Hypovolemia should be treated with iso-osmolar fluids.
   c. When the patient can tolerate oral intake, liberal oral intake should be allowed and thirst should be utilized as a guide to therapy.
   d. Methods of ADH administration
      i. Desmopressin (DDAVP), 1 to 2 mcg every 12 to 24 hours intravenously or subcutaneously
      ii. Vasopressin, 0.2 to 1.0 microunits/kg/hour, as an intravenous infusion
         A. Short half-life (10 to 20 minutes)
         B. May cause a hypertensive response; contraindicated in patients who have coronary artery disease
      iii. Aqueous vasopressin, 5 to10 units every 4 to12 hours intravenously, intramuscularly, or subcutaneously
      iv. Intranasal DDAVP, 2.5 to 20 mcg by insufflation twice a day
   e. Follow the specific gravity of the urine and administer the next dose of DDAVP when the specific gravity has fallen to less than 1.008 and the urine output has increased.
   f. Overdose of drugs will lead to an iatrogenic syndrome of inappropriate antidiuretic hormone (SIADH) secretion.

e. Sinusitis
f. Epistaxis
g. Meningitis
h. Ophthalmoplegia
i. Hydrocephalus
j. Internal carotid artery (ICA) injury—rare
   1. Occurs with deviation from midline approach and entrance into the cavernous sinus
   2. Requires intraoperative compression with surgical packing to achieve tamponade of ICA at the point of injury
   3. May result in delayed epistaxis, cranial nerve deficit, cerebral ischemia, blindness, death
   4. Recommend postoperative angiographic evaluation and treatment if necessary

3. Craniotomy complications
   a. Greater morbidity and mortality are associated with the craniotomy than trans-sphenoidal approach.
   b. Cranial nerve neuropathy
   c. Vision loss
   d. Anosmia

**e.** Internal carotid artery damage
**f.** DI
**g.** Cerebral edema from retraction

## *Suggested Readings*

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Yaniv E, Rappaport ZH. Endoscopic transseptal transsphenoidal surgery for pituitary tumors. *Neurosurgery.* 1997;40:944.

## *Internet Resources*

The National Endocrine and Metabolic Diseases Information Service http://endocrine.niddk.nih.gov/info/index.htm
The Hormone Foundation http://www.hormone.org/pituitary
Pituitary Network Association http://www.pituitary.org
Mayfield Clinic, University of Cincinnati Department of Neurosurgery http://www.mayfieldclinic.com/PE-surgpit.htm

# 13 Epilepsy, Epilepsy Surgery, Awake Craniotomy for Tumor Surgery, and Intraoperative Magnetic Resonance Imaging

**Pirjo Hellen Manninen and Jee Jian See**

## Illustrative Clinical Case

A 31-year-old female who had a history of complex partial seizures that were increasing in frequency was admitted to the epilepsy unit for assessment. She was taking phenobarbital, topamax, carbamazepine, and clonazepam. Investigations for the localization of her epileptic focus included magnetic resonance imaging (MRI), electroencephalogram (EEG), and WADA test. To define her seizures further, the patient received a general anesthetic for burr holes for the insertion of surface and depth EEG electrodes. She was observed for 2 weeks with EEG video and cerebral function imaging and was found to have seizure activity predominately in the left temporal region. The electrodes were removed under sedation. She was scheduled for resection of a temporal lobe lesion as well as the hippocampus and amygdala.

As her seizure focus was in the dominant hemisphere, surgical resection would present a possible risk to her speech and memory. An awake craniotomy was recommended to allow for intraoperative mapping of EEG, speech, and memory in order to preserve these areas of eloquent function. The anesthetic management was with a conscious sedation technique. Local anesthesia (bupivacaine) was used for the placement of the rigid head frame and for infiltration of the surgical incision. Sedation included midazolam and infusions of propofol and remifentanil. Non-invasive monitoring was used and supplemental oxygen ($O_2$) was delivered via nasal prongs with a carbon dioxide ($CO_2$) outlet.

After craniotomy and at the time of opening of the dura, the propofol was stopped but remifentanil was continued at a low infusion rate. Cortical electrode EEG mapping was performed. During stimulation testing for speech, the patient suddenly developed a seizure. Initial treatment was with a small dose of propofol. The seizures continued and required multiple doses of propofol. The patient then became very drowsy and uncooperative. What is the best plan for proceeding with the mapping and the operation? Should the team wait for the patient to recover from the effects of propofol and her seizures or abandon the mapping process? Should the procedure continue under general anesthesia and if so, what is the best way to secure the patient's airway?

## Chapter Highlights

- Epileptic seizures
  - Classification
  - Status epilepticus
  - Medical treatment of epilepsy
  - Anesthesia for non-epilepsy surgery
- Pro- and anticonvulsant effects of anesthetic drugs

- Epilepsy surgery
  - Preoperative evaluation, localization of epileptogenic focus, and preparation for surgery
  - Techniques of anesthesia: Conscious sedation, asleep–awake–asleep, general anesthesia
- Awake craniotomy for tumor
- Anesthesia for intraoperative MRI

## SUMMARY

1. Management of patients who have epilepsy for any operation requires an understanding of the disease, its treatment, and possible drug interactions during anesthesia.
2. Operation for intractable epilepsy involves extensive assessments and preparation. Various techniques of anesthesia are used depending on the nature and requirements of the operation.
3. Awake craniotomy for tumor surgery is used to protect areas of eloquent brain function during tumor resection.
4. Providing anesthesia in an intraoperative MRI suite requires preparation and knowledge of the effects of MRI on anesthesia equipment.

### I. EPILEPSY

#### A. Definitions

1. **Epileptic seizures** are the clinical manifestations (signs and symptoms) of excessive and/or hypersynchronous abnormal activity of neurons in the cerebral cortex. This activity is usually self-limited. The features of the seizure reflect the functions of the cortical areas from which the abnormal activity originates and to which it spreads. Epileptic seizures have electrophysiologic correlates that can be recorded on a scalp EEG.
2. **Epilepsy** is a chronic disorder caused by a variety of pathologic processes in the brain and is characterized by epileptic seizures. The incidence of epilepsy ranges from 0.5% to 2% of the total population; 25% to 30% of persons who have epilepsy experience more than one seizure a month.

#### B. Classification of epileptic seizures

1. **Partial seizures** have an onset that is localized or focal within the brain.
   a. **Simple partial.** Alteration in consciousness does not occur during these seizures. They are classified according to signs and symptoms: motor, sensory, autonomic, and psychic. **Auras** are the sensory, autonomic, or psychic symptoms that precede a progression to impaired consciousness or motor seizure.
   b. **Complex partial.** These seizures spread into multiple areas of the brain and alter consciousness; they are also called **psychomotor** or **temporal lobe** seizures. A simple partial seizure can progress to become complex.
   c. **Convulsive.** These seizures have a partial onset but then spread to involve most areas of the brain and brain stem. They are not easily distinguishable from generalized seizures.
2. We speak of **generalized seizures** when the EEG shows simultaneous involvement of both cerebral hemispheres and consciousness is impaired. These seizures can be
   a. Inhibitory or non-convulsive, such as atonic or absence seizures (petit mal)
   b. Excitatory or convulsive, which produce myoclonic, tonic, or clonic seizures
3. **Unclassified seizures**

C. **Mechanisms of epilepsy** are diverse and include abnormalities in the regulation of neural circuits and the balance of neural excitation and inhibition. Factors that influence the appearance of epilepsy can be genetic, environmental, or physiologic.

D. **Associated medical problems** include (1) psychiatric disorders; (2) rare syndromes: tuberous sclerosis, neurofibromatosis, and multiple endocrine adenomatosis; (3) history of trauma; and (4) sleep deprivation.

E. **Treatment of epilepsy**

1. **Medical therapy** involves various antiepileptic drugs:
   a. **First generation:** phenytoin, phenobarbital, primidone, carbamazepine, clonazepam, valproic acid, and benzodiazepines. These have more adverse effects and drug interactions.
   b. **Second generation:** gabapentin, lamotrigine, topiramate, felbamate, vigabatrin, oxcarbamazepine, zonisamide and pregabalin. These have a safer profile and fewer drug interactions.
   c. Treatment consists of either a single medication or multiple-drug therapy.
   d. The choice depends on considerations of the pharmacokinetics, clinical toxicity, efficacy, and type of epilepsy.
2. **Adverse effects of antiepileptic drugs** are dose dependent and are usually associated with long-term therapy:
   a. Many drugs have neurologic side effects including sedation, confusion, learning impairment, and ataxia as well as gastrointestinal problems such as nausea and vomiting.
   b. Most anticonvulsants are metabolized by the liver. Therefore, long-term usage may cause induction of liver enzymes, which increases the rate of metabolism of other drugs, particularly anesthetics.
   c. Long-term therapy with phenytoin causes gingival hyperplasia with poor dentition and, potentially, difficulties with airway management.
   d. Carbamazepine can depress the hemopoietic system and, in rare cases, causes cardiac toxicity.
   e. Valproic acid may occasionally lead to thrombocytopenia and platelet dysfunction.
3. **Surgical treatment**
   a. Epilepsy is deemed refractory in up to 30% of patients when there is a failure to obtain adequate seizure control or there are unacceptable side effects associated with antiepileptic drugs. Approximately 15% to 20% of these patients are candidates for surgical treatment.
   b. There should be reasonable evidence that the treatment will benefit the patient. A surgical cure occurs in 50% to 80% of patients who either remain seizure free or have a significant reduction in the frequency of their seizures.
   c. Cognitive improvement also results because the dose of anticonvulsant drugs is either reduced or eliminated.

F. **Status epilepticus**

1. Status epilepticus is defined as epileptic seizures that are so frequently repeated or so long in duration that they create a fixed and lasting epileptic condition, either convulsive or non-convulsive. This is considered a neurologic emergency.
2. **Treatment.** To prevent brain damage, seizures must be stopped as quickly as possible. Emergent treatment includes the following:
   a. Secure the airway, provide oxygen, and maintain circulation.
   b. Protect the patient from traumatic injury from involuntary motor movements.

c. If hypoglycemia is present or cannot be ruled out, administer 50% glucose, 50 mL intravenously, and thiamine, 100 mg intravenously.
d. There are different approaches, but the initial drugs of choice usually include phenobarbital, phenytoin, and benzodiazepines. One regimen is diazepam, 0.2 mg/kg intravenously, or lorazepam, 0.1 mg/kg intravenously, followed by phenytoin, 15 to 20 mg/kg intravenously, given slowly at a rate of no > 50 mg/minute.
e. Seizures that continue to be refractory to drug therapy might require barbiturate coma titrated to EEG effect.
f. Other anesthetic drugs that have been used include etomidate, ketamine, propofol, halothane, enflurane, isoflurane, and desflurane.

G. **Pro- and anticonvulsant effects of anesthetic drugs.** Numerous reports describe how anesthetic drugs can paradoxically exhibit proconvulsant and anticonvulsant properties with different doses, under different physiologic situations, and in different species.
1. The inhalation drugs isoflurane and desflurane are effective anticonvulsants. Although controversial, sevoflurane has been shown to produce epileptiform activity. Nitrous oxide ($N_2O$) does not have any anticonvulsant properties and tends to inhibit seizure spikes on EEG.
2. Barbiturates are anticonvulsants, but, when given in small doses, thiopental and methohexital activate the epileptiform activity from a seizure focus, as indicated by EEG monitoring. Etomidate and ketamine can activate the epileptogenic focus and have also been used to treat status epilepticus. Benzodiazepines are effective anticonvulsants. Propofol is an anticonvulsant but there have been controversial reports of seizure and seizure-like activity after its use in patients who have and do not have epilepsy.
3. Opioids (e.g., fentanyl, alfentanil, and remifentanil) can activate the epileptiform activity from a seizure focus in patients who have epilepsy.
4. Local anesthetic drugs are anticonvulsant in low doses but, at higher serum concentrations, can produce central nervous system (CNS) excitation.

H. **Interaction between anesthetic and antiepileptic drugs**
1. The requirements for muscle relaxants, opioids, and barbiturates increase in patients taking most anticonvulsants, particularly phenytoin and phenobarbital, on a long-term basis owing to the enhanced activity of hepatic microsomal enzymes, which accelerates hepatic biotransformation.
2. Interactions with endogenous neurotransmitters and changes in the number of receptors, including opioid, may occur.

I. **Anesthetic management of an epileptic patient for non-epilepsy surgery**
1. **Preoperative assessment** focuses on general assessment and preparation. Specific concerns with an epileptic patient include:
   a. Medical problems including psychiatric disorders associated with epilepsy
   b. Complications from anticonvulsant therapy
   c. Continuation of anticonvulsant therapy
2. **Anesthetic management and monitoring** depend on the needs of the patient and the procedure.
   a. Drugs that potentiate seizure activity should be avoided.
   b. The requirement for anesthetic drugs may increase.
   c. Seizures can occur postoperatively because anesthetic drugs and changes in body physiology during the operation can significantly affect blood levels of anticonvulsants.

d. Consideration should be given to the administration of additional doses of antiepileptic drugs during prolonged procedures.
e. Hyperventilation might potentiate seizure activity and should be avoided unless necessary for the operation itself.

## II. SURGERY FOR EPILEPSY

### A. Procedures

1. Craniotomy for surgical resection of the epileptogenic focus is used mostly for patients who have partial epilepsy disorders with discrete structural lesions showing sclerosis or gliosis and with specific syndromes such as mesial temporal lobe epilepsy.
2. Other surgical treatment modalities include insertion of a vagus-nerve stimulator or a deep-brain stimulator. Both have been shown to improve frequency and duration of seizures and/or severity. Vagus-nerve stimulator insertion is usually performed under general anesthesia. Deep-brain stimulators are usually inserted under monitored anesthesia care/conscious sedation but general anesthesia may also be used.
3. Generalized seizures are treated by interrupting the seizure circuits by means of a corpus callosotomy or a hemispherectomy.

**B. Patient suitability for epilepsy surgery.** A complete multidisciplinary evaluation is needed to assess whether the patient is a candidate for epilepsy surgery. Invasive and non-invasive investigations identify the origin of seizure activity and evaluate the feasibility of performing surgery safely with minimal risk of neurologic and cognitive injury. Advances in neuroimaging techniques have reduced the need for invasive evaluation.

1. **Non-invasive evaluations**
   a. This includes **medical history**; assessment of the frequency, severity, and type of seizures; physical examination; and psychosocial and neuropsychiatric testing.
   b. Surface-electrode monitoring of **EEG** activity may also be combined with video-camera monitoring of the seizures.
   c. **Radiologic imaging** can supplement EEG data. Computed tomographic (CT) scanning and MRI help identify areas of sclerosis and the presence of low-grade intracranial neoplasms.
   d. **Functional imaging** facilitates assessment of brain activity, cerebral blood flow (CBF), and the metabolic effects of resection of the seizure focus. Modalities include positron-emission tomography, single-photon emission CT scan, functional MRI, subtraction ictal single-photon emission CT scan, and spectroscopy.
2. **Invasive evaluations**
   a. **Thiopental testing** may be performed to assist in EEG localization of the seizure focus. The technique is accomplished by producing a gradual increase in the blood level of thiopental during EEG recording. This causes an increase in beta activity in normally functioning neural tissue but not in the seizure focus.
   b. **Intracarotid sodium amytal injection (WADA test)** is used to test for lateralization of language and memory.
   c. **Insertion of intracranial electrodes.** Epidural electrodes are inserted through multiple burr holes. Subdural grids, depth electrodes, or strip electrodes are inserted through a full craniotomy. Stereotactic techniques can also be used. These electrodes are inserted several weeks before the definitive operation to monitor the patient for an adequate period of time. The patient's behavior and EEG are recorded continuously and displayed on a television monitor in specialized units.

d. **Placement of intracranial electrodes or grids** is usually performed under general anesthesia. The anesthetic plan should consider the concerns of a patient who has epilepsy and the precautions that apply to any craniotomy. Routine non-invasive monitoring is required with the addition of intra-arterial blood pressure measurement as indicated. The choice of anesthetic drugs is not limited as the EEG is not recorded. Electrode plates and large grids are quite bulky, however, so that brain shrinkage might be required through the use of mannitol, hyperventilation, and intravenous anesthetics. These patients may develop brain edema postoperatively and require urgent removal of the grid because of the development of intracranial hypertension.

e. Removal of electrodes may be performed in the operating room under sedation or general anesthesia either separately or in conjunction with the surgical resection.

C. **Intraoperative localization of epileptogenic focus**

1. **Electrocorticography (ECoG) is performed** during surgery after opening of the dura by placing electrodes directly on the cortex over the area predetermined to be epileptogenic and on the adjacent cortex. Additional recordings can be obtained from microelectrodes inserted into the cortex or depth electrodes inserted into the amygdala and the hippocampal gyrus.
2. **Pharmacologic stimulation of the epileptogenic focus is possible** if insufficient information is obtained to define the seizure focus adequately during routine ECoG. Drugs used in adults include methohexital, 10 to 50 mg; thiopental, 25 to 50 mg; propofol, 10 to 20 mg; or etomidate, 2 to 4 mg. If the patient is under general anesthesia, other drugs such as alfentanil, 20 to 50 mcg/kg, and enflurane can be used with or without hypocarbia.
3. **Direct electrical stimulation of the cortex delineates eloquent areas** of brain function, such as speech, memory, and sensory and motor function. This allows these areas to be preserved during resection of the seizure focus. Only motor testing can be done when the patient is under general anesthesia.

D. **Preoperative preparation for epilepsy surgery.** Communication among all members of the team, including the neurologist, neurosurgeon, and anesthesiologist, is vital to the successful management of the patient throughout the perioperative period.

1. Routine and specific epilepsy assessment is carried out.
2. Appropriate preparation of the patient for the anesthetic technique selected is carried out.
3. Anticonvulsant drugs are administered before surgery in consultation with the neurologist and surgeon.
4. Premedication for the purpose of sedation is not routinely required. Drugs that may affect the EEG should be avoided.

E. **Techniques of anesthesia.** Anesthetic management for epilepsy surgery may include **conscious sedation/monitored anesthesia care, general anesthesia, or a combination** of both techniques. Awake craniotomy is performed with conscious sedation/monitored anesthesia care or with an "asleep–awake–asleep" technique. The decision as to whether the craniotomy will be performed "awake," "asleep–awake–asleep," or under general anesthesia depends on the location of the seizure focus, the need for intraoperative ECoG and testing of eloquent function, and the patient's ability to tolerate an awake procedure.

1. **Conscious sedation**
   a. **The reasons for having an awake patient** are as follows:
      1. Better ECoG localization of the seizure focus without the influence of general anesthetic drugs
      2. Availability of immediate responses from the patient to direct electrical stimulation of the cerebral cortex for delineation of eloquent areas of brain function such as speech and motor function and to facilitate real-time neurocognitive testing to preserve those areas during surgical resection
      3. Continuous clinical neurologic monitoring of the patient throughout the procedure
   b. **Benefits:** (1) better speech preservation; (2) more accurate prediction of seizure-free outcome; (3) decreased incidence of postoperative complications such as nausea and vomiting; and (4) shorter hospital stay.
   c. The **challenge** is to render the patient comfortable enough to remain immobile through a long procedure but sufficiently alert and cooperative to comply with testing. The analgesic and sedative drugs employed must have minimal interference with ECoG, electrical cortical stimulation, and testing.
   d. **Specific preoperative preparation**
      1. The **patient's suitability** for an awake craniotomy is assessed with regard to cooperativeness and ability to understand and follow commands for testing.
      2. The patient is prepared psychologically and informed about the complexities and demands of an awake craniotomy such as the requirements for stimulation testing which may involve speech, memory, and motor function.
      3. The establishment of **good rapport** between the anesthesiologist and the patient is absolutely essential.
      4. The anesthesiologist should be aware of the signs and symptoms that may herald the onset of a seizure.
      5. **Airway assessment**: In case of difficulties with anesthesia or surgery, the patient may require urgent tracheal intubation to secure the airway.
   d. **Preparation of the operating room.** An awake craniotomy may add additional stressors for the patient and the entire team.
      1. All preparations should be completed before the patient arrives in the room so that the patient can receive the full attention of all team members.
      2. Anesthetic drugs and equipment for conscious sedation, induction of general anesthesia, and the treatment of complications are available.
      3. Room environment is at normal room temperature with a quiet, reassuring atmosphere. It is essential to prevent unnecessary traffic by placing a sign on the door advising people of the procedure within.
   e. **Patient management**
      1. The patient may be placed in the lateral decubitus or supine position. For the supine position, the head should be turned slightly to face the anesthesiologist.
         a. Extra pillows and blankets are utilized for comfort, additional support, and warmth.
         b. Patients should be positioned in such a way as to have some freedom of movement of the extremities to allow for comfort and for testing of motor function.

c. Rigid skull pin-fixation systems are frequently used to accommodate neuronavigation for imaging and a still surgical field. Some procedures may be performed with the patient's head on a pillow of appropriate size and shape.
d. If head fixation is accomplished under general anesthesia, the patient is allowed to awaken afterward to ensure comfort of the patient's head and neck and good airway access (good mouth opening) in the event that manipulation of the airway becomes necessary.
e. The placement of the surgical drapes should allow for maximum visibility of the patient's face by the anesthesiologist. It is also essential for the patient to be able to see the anesthesiologist continuously and not to feel claustrophobic.
f. Stimulation testing of the patient may involve the help of other members of the neuropsychological team.

2. **Local anesthesia and regional scalp block**
   a. Local anesthesia is required for the skull-fixation pin sites and for the site of the surgical incision.
   b. This can be achieved by local infiltration of pin and surgical sites or by a regional scalp block using infiltration of six nerves: greater and lesser occipital, supraorbital, supratrochlear, zygomaticotemporal, auriculotemporal, and greater auricular.
   c. Long-acting local anesthetics, such as bupivacaine, ropivacaine, and levobupivacaine, with the addition of epinephrine are used.
   d. Lidocaine, which has a fast onset, may be used to infiltrate areas that are still painful during the procedure, such as the dura.
   e. The maximum doses: bupivacaine = 3 mg/kg, lidocaine = 5 to 7 mg/kg, ropivacaine = 3 to 4 mg/kg.
   f. Both local infiltration and scalp blocks are painful. The patient might need analgesia and sedation at that time.
3. **Monitors**
   a. Electrocardiogram (ECG), non-invasive blood pressure cuff, pulse oximeter, and end-tidal $CO_2$ via nasal prongs used to deliver supplemental $O_2$. Invasive monitoring such as an intra-arterial catheter is not routinely required for all patients.
   b. A urinary catheter is not routinely needed for all patients. If not used, fluids should be kept to a minimum. Dextrose-containing fluids are avoided.
4. **Anesthetic drugs**
   a. The techniques of drug administration and dose requirements vary greatly and need to be titrated to each patient.
   b. The drugs may be administered by intermittent bolus, continuous infusion, target-controlled infusion, patient-controlled analgesia, or a combination.
   c. Depth of anesthesia monitoring devices may be used to guide sedation such as Bispectral Index $\geq 60$. The goal of clinical monitoring is to maintain the patient at a score of $\geq 3$ on the Observer's Assessment of Alertness/Sedation Scale at which the patient will respond to name calling.
   d. Traditionally, intermittent boluses of fentanyl and droperidol were used. Now the most common combination is an infusion of propofol (25 to 100 mcg/kg/minute) with either intermittent boluses of fentanyl (0.5 to 1 mcg/kg) or an

infusion of remifentanil (starting at 0.0125 mcg/kg/minute). Other opioids (e.g., sufentanil and alfentanil) have also been used.

e. Dexmedetomidine, an alpha 2-adrenoreceptor agonist, is another choice as it provides sedation, analgesia, and anxiolysis with minimal risk of respiratory depression. Dexmedetomidine may be used alone with an initial infusion rate of 0.2 mcg/kg/hour or as an adjunct with lower starting rate of 0.01 mcg/kg/hour.

f. Infusions of propofol and dexmedetomidine must be discontinued at least 20 minutes before the start of ECoG recording.

g. During prolonged stimulation testing in some patients, low infusion rates of remifentanil or dexmedetomidine may be continued to provide analgesia.

h. Antiemetic drugs including dimenhydrinate, prochlorperazine, metoclopramide, ondansetron, dolasetron, and granisetron may also be needed and do not affect the ECoG.

5. **Non-pharmacologic measures** are very useful to help the patient through the procedure. These include frequent reassurance, allowing the patient to move intermittently, warning the patient in advance about loud noises (drilling and rongeuring of bone) and painful interventions, providing ice chips and a cold cloth to the face, and just holding the patient's hand.

2. **Asleep–awake–asleep** is another technique of anesthesia for awake craniotomy.

a. **General anesthesia** is used for the craniotomy and closure. Either intravenous or inhalation anesthetic drugs with or without controlled ventilation may be used.

b. Appropriate **airway devices** include endotracheal tube, special oral airway, but, most commonly, the laryngeal mask airway, which has the advantages of easier placement and decreased coughing and laryngospasm.

c. The patient is **awakened completely** and the airway device removed for the period of intraoperative neurologic evaluation.

d. For resection of the lesion and for closure, **general anesthesia is again induced** with reinsertion of the airway device.

e. This **technique requires intraoperative airway manipulation,** while the head is fixed in the pin head-holder device.

f. **Advantages** include increased patient comfort and tolerance during craniotomy and a secured airway with ability to control ventilation and prevent hypercapnia.

g. **Intraoperative complications**

1. **Pain/discomfort.** At certain times, patients might feel either pain or discomfort and should be warned about this (e.g., the scalp block) in advance. Patients may also experience pain during the bone work if dural vessels come in contact with instruments and during the manipulation of the dura mater and the major vessels within brain tissue. The loud noises of drills and rongeurs can be frightening if not actually painful.

2. **Nausea/vomiting.** Many factors may be responsible for occurrence of nausea and vomiting including anxiety, medications, and surgical stimulation, especially the stripping of the dura and the manipulation of the temporal lobe and meningeal vessels. The use of propofol has diminished the incidence of nausea and vomiting.

3. **Seizures** can occur at any time.
   a. Short, mild seizures may not require any treatment. Convulsive or generalized seizures need to be treated immediately.
   b. The patient should be protected from injury.
   c. A patent airway, adequate oxygenation, and circulatory stability must be assured.
   d. Seizures can be treated with small intravenous doses of either thiopental, 25 to 50 mg, or propofol, 10 to 20 mg, and midazolam, 1 to 2 mg, after ECoG recordings. After dural opening, the surgeon can treat seizures by the placement of iced saline on the cortical surface.
   e. If repeated treatments are required, the patient may become very drowsy and need airway support.
4. **Respiratory.** Oxygen desaturation and airway obstruction may result from oversedation, seizures, mechanical obstruction, or loss of consciousness from an intracranial event. Treatment needs to be immediate and includes decreasing sedation and jaw thrust or the insertion of an oral airway, laryngeal mask, or endotracheal tube.
5. **Induction of anesthesia.** If a patient becomes uncooperative or complications such as hemorrhage or continuous seizures develop, the induction of general anesthesia may be required. To do this safely, a plan of action is necessary. Airway assessment determines the best approach.
   a. The laryngeal mask airway may be used temporarily or for completion of the procedure.
   b. Occasionally, **endotracheal intubation** will be required. This can be accomplished with the patient in either the supine or lateral position. With adequate assistance, the anesthesiologist comes to the patient's head while the surgeon protects the sterile brain field. After preoxygenation, anesthesia can be induced if necessary with a small dose of propofol (with or without opioids and muscle relaxant). Intubation may be accomplished with whichever airway technique the anesthesiologist favors including direct laryngoscopy, video-assisted laryngoscopy, fiberoptic bronchoscopy, or intubating laryngeal mask.
   c. If any difficulty in securing the airway is anticipated, an awake intubation with local anesthesia should be performed.
6. Other **less common complications** include excessive blood loss, hypertension, hypotension, air embolism, new neurological deficits, and a tight brain, which may also result from hypoventilation.

h. **Resection of lesion and closure.** After all testing is complete, sedation of the patient may resume with similar technique and drugs.

i. **Recovery of the patient** takes place in an intensive care or specialized observation unit. Postoperative complications are the same as for any patient after a craniotomy. Analgesia needs to be titrated to patient needs. Seizures might still occur and may require treatment.

3. **General anesthesia**
   a. The **reason for choosing general anesthesia** depends on the preference of the neurosurgeon and the patient's ability to tolerate an awake craniotomy. Many procedures such as the resection of structural

lesions, amygdala and hypothalamus, or an entire temporal lobe may be performed under general anesthesia.

b. The **advances** in preoperative neuroimaging, functional testing, and the use of frameless stereotactic surgery for localization of the epileptic focus have lessened the need for the patient to be awake during the procedure.

c. The **challenge** with general anesthesia, if intraoperative localization is needed, is to provide good conditions for EEG, ECoG, and motor testing by keeping the influence of the anesthetic drugs to a minimum while avoiding long periods of potential awareness on the part of the patient.

d. **Specific preoperative preparation** involves informing patients of the possibility that awareness might occur at the time of ECoG recording and testing but reassuring them that it will be brief and painless.

e. **Preparation** of the operating room, anesthetic equipment and drugs, and positioning supplies is the same as for any craniotomy. In addition to routine monitors, intra-arterial and urinary catheters are frequently used.

f. **Anesthetic management**

1. **Specific concerns** include the increased dosage requirements for opioids and neuromuscular blocking drugs as a result of long-term anticonvulsant therapy.
2. **$N_2O$.** If the patient has had a recent craniotomy or burr holes for electrode placement, intracranial air might still be present. $N_2O$ should be avoided to prevent complications from an expanding pneumocephalus.
3. **Anesthetic drugs**
   a. Drugs should be short acting with minimal influence on EEG and ECoG and no seizure-producing activity.
   b. A balanced technique may be used with opioids, muscle relaxant, and low concentrations of inhalation drugs.
   c. Total intravenous anesthesia with propofol and an opioid may also be used.
   d. Inhalation drugs and propofol must be discontinued at least 20 minutes before ECoG recording.
4. **Motor testing** is possible during general anesthesia by discontinuing all inhalation drugs and propofol and either reversing or allowing the muscle paralysis to wear off. This testing demands very careful planning and care of the patient. The addition of either opioids or lidocaine might decrease the chance of the patient's coughing.

g. **Complications**

1. Craniotomy-related complications
2. The possibility of awareness
3. Movement from seizures, especially during any stimulation testing

h. **Recovery** is the same as for awake patients.

F. **Pediatric surgery.** The considerations for epilepsy surgery in pediatric patients are similar to those for adults, except that younger children are not able to tolerate an awake craniotomy. Cerebral hemispherectomy is a common procedure. Vagal nerve stimulators have also been used in children.

1. **General anesthesia** is used for most procedures.
2. **Awake craniotomy** may be tolerated by an older child.
3. **Asleep–awake–asleep** technique with the use of a laryngeal mask airway is an alternative.

4. **Coexisting conditions** with multiple organ-system involvement and significant psychological and behavior problems may be present.
5. **Parents** may be very actively involved in the patient's management and also require consideration and education.

G. **Cerebral hemispherectomy and corpus callosotomy.** Treatment of diffuse generalized seizures might require either resection of substantial portions of the entire cerebral hemisphere or section of the corpus callosum and functional hemispherectomy. These procedures are usually performed under general anesthesia because they involve a large craniotomy and most of the patients are children. The major concern with these lengthy procedures is the possibility of extensive blood loss and air emboli because the surgical site is close to major vessels and sinuses.

## III. AWAKE CRANIOTOMY FOR TUMOR

The awake craniotomy has been adapted from epilepsy surgery for the resection of tumors located either in or close to areas of eloquent brain function, especially those involving speech, motor, and sensory pathways.

### A. Reasons for awake craniotomy

1. The accurate localization of eloquent brain function through intraoperative mapping allows for optimal tumor resection and minimization of the risk of neurologic injury.
2. Though awake craniotomy is perceived to be stressful, with good preoperative preparation and adequate local anesthesia, patients tolerate the procedure well and have less pain, anxiety, and discomfort.
3. This technique facilitates more efficient use of high-dependency facilities with earlier discharge from the hospital.

### B. Patient selection

1. Cooperative and alert patients who are able to understand the demands of the procedure are ideal candidates.
2. Confused, demented, or agitated patients are poor candidates.
3. Tumor size and location influence selection. Supratentorial tumors that have minimal dural involvement are amenable to resection under awake craniotomy.
4. Patients who have increased intracranial pressure (ICP) may not be suitable as spontaneous ventilation may result in further increases in ICP.

C. **Anesthesia.** The aim is to provide adequate sedation and analgesia with stable respiratory and hemodynamic control during craniotomy but an awake and cooperative patient for the period of neurologic testing.

1. **Preoperative management**
   a. The preoperative assessment and preparation are tailored to patients who have intracranial tumors but are similar to what is done for patients who have epilepsy.
   b. The establishment of good rapport between the anesthesiologist and the patient is crucial.
   c. The patient is prepared psychologically and informed about the complexities of an awake craniotomy.
   d. Medications such as dexamethasone and anticonvulsant drugs are reviewed and continued because some patients may have presented with seizures.
   e. Premedication with drugs such as clonidine, ranitidine, antiemetics, and benzodiazepines is occasionally administered.
   f. Obese patients and those who have either a known difficult airway or a large vascular tumor may pose additional challenges.

2. **Operating room preparation and setup** are similar to epilepsy surgery.
   a. Positioning may be lateral, supine, or semisitting.
   b. Neuronavigation for imaging is usually used, necessitating rigid three-point pin fixation of the head.
   c. Monitoring depends on the needs of the patient. Routine invasive monitoring is not required for all patients.
   d. Monitoring of depth of anesthesia may help in regulating doses of anesthetic drugs.
3. **Anesthetic techniques**
   a. **Local anesthesia and regional scalp block** are similar to the management of patients for epilepsy surgery. For a smaller craniotomy, local infiltration of the surgical site with a "ringblock" is frequently used.
   b. **Sedation techniques** are similar to those discussed for epilepsy surgery, but, because EEG and ECoG are not performed, the choice of anesthetic drugs is more flexible.
      1. **Conscious sedation**: Commonly-used drugs include midazolam, propofol, fentanyl, remifentanil, and dexmedetomidine.
         a. The method of drug administration may be infusion, bolus injection, or target or patient controlled.
         b. Non-pharmacologic measures are useful including frequent reassurance, warning the patient in advance about loud noise (drilling of bone) and pain, and holding the patient's hand.
      2. **Asleep–awake–asleep** is a technique commonly used for tumor surgery.
         a. General anesthesia with some technique for securing the airway such as laryngeal mask airway is used for the craniotomy, tumor resection, and closure. Either inhalation or intravenous anesthetic drugs may be used with or without controlled ventilation.
         b. The patient is fully awakened for the cortical mapping.
         c. Advantages include increased patient comfort and tolerance during craniotomy, especially for longer procedures, and a secured airway with the ability to use hyperventilation.
4. **Intraoperative cortical mapping** for speech, motor, and sensory functions is accomplished by placing a stimulating electrode directly on the cortex. The patient needs to be alert and cooperative during this time. For some patients, such continuous monitoring is also helpful during tumor resection.
5. **Postoperative care** is the same as for any craniotomy for tumor surgery. Postoperative analgesia needs to be titrated to the patient's needs during emergence and recovery. However, shorter hospital stays are often possible.
6. **Common problems**
   a. **Airway complications**
      1. Oxygen desaturation and airway obstruction may result from oversedation, seizures, mechanical obstruction, or loss of consciousness from an intracranial event.
      2. Treatment needs to be immediate and can include stopping or decreasing sedation and jaw thrust or securing of the airway with an oral or nasal airway, laryngeal mask, or endotracheal tube.
   b. **Pain** may occur during pin fixation, dissection of the temporalis muscle, traction on the dura, and manipulation of the intracerebral blood vessels.
   c. **Seizures** may occur in patients whether or not they have had seizures preoperatively, most commonly during cortical stimulation. Initial

treatment may be with the placement of iced saline on the cortex by the surgeon. Other treatment includes propofol, 10 to 20 mg, or midazolam, 1 to 2 mg.

d. Other **less common problems** are an uncooperative or disinhibited patient, a tight brain, air embolism, hypertension, hypotension, and nausea and vomiting (less frequent during tumor surgery).

e. **Induction of general anesthesia** may be required for the management of ongoing complications and catastrophic intracranial events including loss of consciousness, recurrent seizures, and bleeding.

## IV. INTRAOPERATIVE MAGNETIC RESONANCE IMAGING

The introduction of MRI into the operating room to provide intraoperative real-time imaging during surgery is steadily gaining acceptance. Intracranial anatomy changes constantly during neurosurgical procedures with fluctuations of cerebrospinal fluid and shifting of the brain tissue. The advantage of intraoperative MRI is the ability to assess brain parenchyma immediately before, during, and after the operation; to determine the extent of surgical removal of the tumor; to identify areas of eloquent brain; and to avoid the transfer of the patient to another suite should urgent imaging be needed during operation.

### A. Preparation and safety considerations

1. **Safety** concerns in the operating room are the same as in any MRI suite as a magnetic field is constantly present and extends beyond the magnet.
2. The **design of the intraoperative MRI room** and the layout of all essential equipment must be planned in advance to assure the safety of patients and personnel.
3. The **location of the intraoperative MRI suite** may be remote from the main operating rooms.
4. A **5 Gauss line** should be clearly indicated on the floor as the area between this line and the magnet core has a static magnetic field greater than 5 Gauss.
5. The **intraoperative MRI suite provides a unique interactive working environment** for the anesthesiologists, neurosurgeons, radiologists, nurses, and technologists.
6. **Personnel training and education** are necessary before the inception of the program.
7. The **greatest hazard** of the magnetic field is that any ferromagnetic object brought close to the magnet can be forcibly sucked into the magnetic field. This can cause serious injury to patients and healthcare personnel.
8. **Patient selection and screening** are critical. Patients who have ferromagnetic implants such as older cerebral aneurysm clips, defibrillators, and pacemakers are not candidates for MRI.

### B. Intraoperative MRI systems

. The specifications and the layout of each intraoperative MRI system vary greatly. Each system has its own particular set of anesthetic concerns.

1. The strength of the MRI ranges from 0.2 to 3 T.
2. The MRI scanner can be fixed in place or mobile.
3. A mobile unit may be permanently mounted in the room or available to be transported into the operating room when needed.
4. The location of the operating field affects the anesthetic plan.
   a. Within the magnet itself
      1. Real-time imaging is possible.

2. Minimal patient transport is needed.
3. All equipment, anesthetic and surgical, must be MRI compatible.
4. Disadvantages include space constraints for the surgeons and limited access to the patients for the anesthesiologist.

b. In close proximity to a fixed MRI scanner
1. Allows the use of equipment and technologies (e.g., surgical instruments and the operating microscope) that are not MRI compatible
2. Requires transfer of the patient to the scanner
3. Still requires all anesthesia equipment to be MRI compatible
4. Must shield equipment that is not MRI compatible
5. Limits the number of images taken

c. In close proximity to a mobile MRI scanner
1. A mobile ceiling-mounted scanner is placed over the patient when scanning is needed.
2. A mobile, compact, low field-strength MRI system is positioned and shielded under the operating room table.

**C. Equipment considerations**

1. MRI-compatible anesthetic, surgical, monitoring, and imaging equipment should ideally be available, but the equipment actually used depends on the strength of the magnet and the proximity to the magnetic system with which that equipment will be used.
   a. The magnetic field decreases in strength from the core of the magnet outward. Safety zones and Gauss lines should be marked on the floor.
   b. All equipment must be tested before use.
2. Physiologic monitors, anesthesia machines, and ventilators need to be fully MRI compatible. They also must not distort the images.
3. The location of the patient and the need for movement within the room may require extra-long circuits, intravenous tubing, and monitoring cables.
4. Conventional ECG monitors will not function properly in the MRI due to distortion generated by the magnetic field. Precordial MRI-compatible leads are placed close together to minimize the distortion. This system is not capable of monitoring the ST segment for cardiac ischemia.
5. Because they are potential sources of skin burns, wires and cable must not be looped and not have direct contact with the skin. Procedures to prevent burns must be developed and set in place.
6. Visual as well as audio alarms are necessary because the loud noise generated by the scanner may mask the sound of the audio alarms.

**D. Anesthetic management**

1. Advanced planning by and communication among all members of team are crucial.
2. Preoperative evaluation involves thorough assessment of the patient for the surgical procedure and eligibility for the MRI.
3. Anesthetic management includes considerations for the patient and the surgical procedure as well as for MRI scanning.
4. Induction of anesthesia
   a. Induction in a separate room adjacent to the MRI operating room allows the use of non–MRI-compatible equipment such as the fiberoptic bronchoscope and facilitates management of the anticipated and unanticipated difficult airway.
   b. When anesthesia is induced in the MRI suite itself, it is essential to use only MRI-compatible equipment.

5. The anesthesiologist has limited access to and visualization of the patient during scanning.
6. The patient and healthcare personnel need protection from the MRI's noise to prevent damage to hearing. The use of foam ear plugs by all is recommended.
7. Anesthesiologists need to interact not only with the surgical team but also with the radiologist and the MRI technologist.
8. Patient temperature control may be difficult. The MRI suite is kept cold to avoid overheating of the computers, but radio frequency waves from imaging may produce heat and increase body temperature.
9. Anesthesiologists are frequently requested to administer gadolinium-based contrast drugs for imaging. There is a risk of additional renal impairment in patients who have renal insufficiency.
10. At the completion of the procedure, safe transfer to a recovery or intensive care unit must be planned. Because this may involve travel over a relatively long distance, the use of appropriate monitoring during the transfer is indicated.

E. **Anesthetic techniques.** The choice of anesthetic technique depends on the procedure, the patient, and the preference of the surgeon and the anesthesiologist.
   1. **Conscious sedation** is similar to the technique for awake craniotomy for tumor but
      a. Visibility of and access to the patient are limited.
      b. Monitoring and communication are more difficult.
      c. Sedation may be unacceptable to the patient because of the scanner's confined nature and noise.
      d. Transfers may be uncomfortable for the patient.
   2. **General anesthesia** has these characteristics:
      a. Principles and concerns are similar to those for any patient undergoing a neurosurgical procedure.
      b. Working around the MRI constrains equipment and access.
      c. There is no best technique or drug.

## *Suggested Readings*

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# 14 Spinal Cord: Injury and Procedures

**Gary R. Stier, Daniel J. Cole, and Elie Fried**

## Illustrative Clinical Case

A 38-year-old male police officer involved in a motorcycle accident was transported to the emergency department (ED) of a large regional medical center. Upon arrival in the ED, the patient demonstrated severe respiratory distress and underwent emergency endotracheal intubation with manual inline immobilization of the neck. Initial neurologic examination revealed absence of motor function below the C5 spinal level, but with evidence of sacral sparing. No other injuries were clinically noted. An emergency CT scan of the cervical spine revealed a burst fracture of the C5 vertebral body with subluxation. During the initial care, the vital signs disclosed a blood pressure of 85/50 mm Hg (mean arterial pressure [MAP] 61 mm Hg) and a heart rate was 60/minute. Isotonic fluids and vasopressor medications were emergently administered through a central venous pressure (CVP) line placed to guide fluid management. Initial goals of therapy included achieving a CVP of 10 mm Hg and a MAP of ≥ 85 mm Hg. The patient was transferred to the intensive care unit (ICU) where a discussion among the patient's family, neurosurgeon, and intensivist culminated in agreement for early (< 12 hours) surgical cervical spine decompression and stabilization. During surgery, the patient's blood pressure was supported to maintain a MAP of ≥ 85 mm Hg and a CVP of 10 mm Hg with continued fluids and vasopressor medications, as needed.

Following the surgical procedure, the patient was transferred back to the ICU where medical management goals included maintaining a MAP of ≥ 85 mm Hg for 7 days, sustaining a CVP of 10 mm Hg, hemoglobin of 10 g/dL, serum glucose levels of 80 to 150 mg/dL, normothermia, antiulcer prophylaxis, and serial neurologic examinations every 12 hours for the first 48 hours of hospitalization, utilizing the American Spinal Injury Association (ASIA) Impairment Scale. During this period, the patient remained on mechanical ventilation with incorporation of lung protection strategies. Thromboprophylaxis was instituted early after surgery with the use of intermittent pneumatic compression (IPC) stockings; low-molecular-weight heparin (LMWH) was initiated at 72 hours when there was no longer a risk of further spinal hemorrhage. Enteral nutrition, delivered through a small bowel flexible feeding tube, was started at 48 hours following surgery. Evidence of ventilator-associated pneumonia was diagnosed clinically at day 4 of hospitalization and broad-spectrum antibiotics were administered for a total of 8 days, with marked improvement in oxygenation and chest radiographic appearance. A rehabilitation medicine consultation was requested early in the hospital course to facilitate a coordinated multidisciplinary care team approach following discharge from the ICU. At day 6 following injury, the patient underwent a percutaneous tracheostomy, with transition to a tracheostomy oxygen mask at day 17 of hospitalization. The patient was successfully transferred to the rehabilitative center on day 20 following injury.

## Chapter Highlights

**I. GENERAL CONSIDERATIONS**

**A. Spinal anatomy and physiology**

1. Structure
2. Blood supply
3. Regulation of blood flow

**II. SPINAL CORD INJURY**

**A. Introduction**

**B. Pathogenic correlates of spinal cord injury**

**C. Anatomical correlates of spinal cord injury**

**D. Clinical correlates of spinal cord injury**

1. Spinal shock
2. Neurogenic shock
3. Disturbances of cardiac rhythm
4. Left ventricular impairment
5. Autonomic dysreflexia

**E. Acute care of the patient after spinal cord injury**

1. External splinting and immobilization
2. Neurologic examination
3. Radiologic evaluation
4. Medical management
   - **a.** Airway
   - **b.** Pulmonary system
   - **c.** Cardiovascular system
   - **d.** Gastrointestinal
   - **e.** Genitourinary
   - **f.** Temperature control
   - **g.** Deep vein thrombosis
5. Neuroprotective strategies
   - **a.** Spinal alignment
   - **b.** Surgical therapy
   - **c.** Physiologic therapy
   - **d.** Pharmacologic therapy

**F. Prognosis after spinal cord injury**

**G. Anesthetic management of acute spinal cord injury**

1. Preoperative evaluation
2. Monitoring
3. Anesthetic technique

**H. Chronic spinal cord injury**

1. Preoperative
2. Intraoperative
3. Postoperative

**I. GENERAL CONSIDERATIONS**

**A. Spinal anatomy and physiology**

1. **Structure**
   - **a.** The **vertebral column consists of 33 superimposed vertebrae,** which are divided into 7 cervical (C), 12 thoracic (T), 5 lumbar (L), 5 sacral (fused), and 4 coccygeal (fused) bones. Each individual vertebra (Fig. 14.1) is composed of a ventral vertebral body and a dorsal bony neural arch composed of a pedicle on either side of the vertebral body, each supporting a lamina, which combine posteriorly to form a spinous process. The vertebral foramen is formed by the posterior vertebral body, pedicles, and lamina. The neural laminar arches bear lateral transverse processes and superior and inferior articular facets.

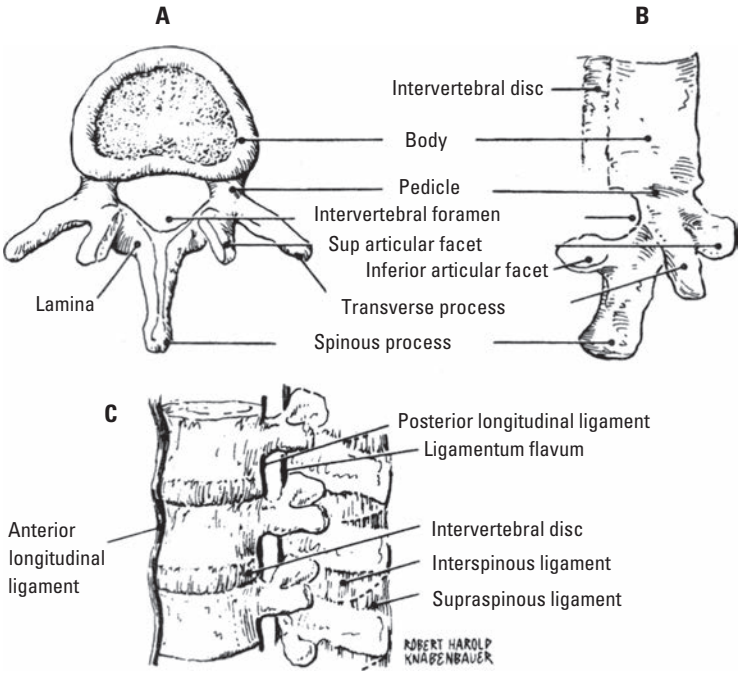


**FIGURE 14.1** **A**: View of a typical vertebra from above; (**B**) Lateral view; (**C**) Ligaments of the spine. (Reprinted from Stier GR, Schell RM, Cole DJ. Spinal cord injury. In: Cottrell J, Smith D, Eds. *Anesthesia and Neurosurgery.* 4th Ed. Philadelphia, PA: Mosby Inc., 2001, with permission.)

b. The **vertebral column is stabilized** by (from posterior to anterior) the supraspinous, interspinal, ligamentum flavum, posterior longitudinal, and anterior longitudinal ligaments (Fig. 14.1). The ligaments provide flexibility and limit excessive movement that could damage the cord.

c. The **spinal cord** begins at the foramen magnum and terminates at the conus medullaris (L2 in adults). Below the termination of the spinal cord, the lumbar and sacral roots form the cauda equina. The spinal cord is surrounded by the meninges, which are layers of tissue (the dura mater and arachnoid membranes) that have cerebrospinal fluid (CSF) between them providing further protection for the spinal cord. The anterior portion of the cord gives rise to the motor nerves. Nerves that originate posteriorly are sensory in function.

2. **Blood supply**

a. **Anterior spinal artery.** A single vessel, formed from the union of the two anterior spinal branches of the vertebral arteries, descends down the entire length of the anterior portion of the spinal cord. This artery supplies perfusion to the anterior two-thirds of the cord (the anterior column and most of the lateral column).

b. **Posterior spinal arteries.** Two vessels originating from the posterior inferior cerebellar arteries supply the posterior one-third of the cord (the entire posterior column and the balance of the lateral column).

c. **Radicular arteries.** These vessels originate from branches of the vertebral, deep cervical, intercostal, and lumbar arteries. They anastomose with the anterior and posterior spinal arteries. The artery of Adamkiewicz (arteria radicularis magna), the major radicular artery, is most commonly located in the lower thoracic or upper lumbar region and provides most of the blood supply to the lower cord distal to its level of entry.

3. **Regulation of spinal cord blood flow (SCBF)** (Fig. 14.2). Average SCBF is estimated at 60 mL/100 g/minute, with a three- to four-fold gray matter to white matter blood flow differential. Autoregulation maintains SCBF by altering vascular resistance in response to changes in MAP.
   a. Normally, autoregulation exists for a MAP between 60 and 120 mm Hg.
   b. Failure of autoregulation occurs below a MAP of 50 mm Hg, leading to progressive tissue ischemia.
   c. Above a MAP of 120 mm Hg, SCBF increases, leading to progressive tissue edema and cellular disruption.
   d. The autoregulatory range of individuals who have chronic hypertension is shifted to the right (higher range of MAP).
   e. Alterations in the partial pressure of carbon dioxide ($PaCO_2$) and oxygen ($PaO_2$) affect SCBF in the spinal cord much as they do in the brain. Between 20 and 80 mm Hg, SCBF is linearly related to $PaCO_2$. SCBF is well maintained at varying degrees of oxygenation until $PaO_2$ falls to 50 mm Hg; below this value, SCBF increases significantly.

## II. SPINAL CORD INJURY

A. **Introduction.** The reported annual incidence of traumatic spinal cord injury (SCI) in the United States is estimated at 12 to 55 patients per million population, with approximately 11,000 new cases of SCI per year. The estimated prevalence of SCI is within a range of 225,000 to 296,000 cases. SCI occurs with greatest frequency in those individuals between the ages of 15 and

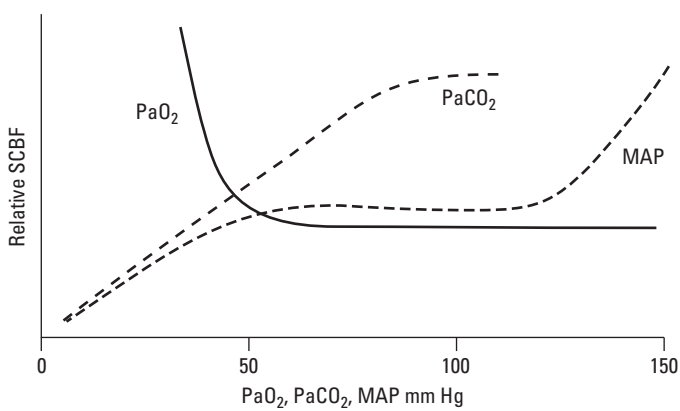


**FIGURE 14.2** Effect of changes in $PaCO_2$, $PaO_2$, and MAP on SCBF. (Reprinted from Stier GR, Schell RM, Cole DJ. Spinal cord injury. In: Cottrell J, Smith D, Eds. *Anesthesia and Neurosurgery.* 4th Ed. Philadelphia, PA: Mosby Inc., 2001, with permission.)

34 years of age, with a male-to-female ratio of approximately 4:1. Common causes of SCI include motor vehicle accidents (40% to 56%), falls (15% to 20%), violence (5% to 20%), sports injuries (5% to 16%), and other causes (5% to 10%). Among persons age 65 and older, falls cause most SCIs. SCI from spinal trauma occurs most frequently in the cervical spine (55%), followed by the thoracic spine (30%) and the lumbar spine (15%). Most injuries occur at the midcervical (C4–C6) or thoracolumbar (T12) region and are often associated with concomitant injuries. Isolated SCI is present in only 20% of cases, while additional injuries, typically of the head, thorax, and abdomen, are present in 20% to 50% of cases. It has been estimated that up to half of all patients who sustain an acute SCI have an associated head injury, while 5% to 10% of head-injured patients have an associated acute SCI. Of those individuals sustaining an SCI, the distribution of injury consists of incomplete tetraplegia, 34.5%; complete paraplegia, 23.1%; complete tetraplegia, 18.4%; and incomplete paraplegia, 17.5%. The probability of death during the first year after an SCI is 6.3%, decreasing to 1.8% during the second year. The 12-year survival rate in SCI-injured patients is 85%. Determinants of survival include Glasgow Coma Scale score on admission, age, level of injury, presence of multiple injuries, respiratory failure, cardiac complications, pulmonary emboli, and infection.

The perioperative medical care of patients during the acute phase of SCI is of extreme importance in determining the outcome. Thus, strategies that prevent further SCI, limit the extension of an existing SCI injury, or salvage even a few dermatomal levels can affect morbidity, mortality, long-term disability, quality of life, and health-care costs significantly. Surgical treatment for SCI is aimed at immobilization, operative decompression, and spinal stabilization. Care during the intermediate and chronic phases of SCI is also important.

**B. Pathogenic correlates of spinal cord injury**

1. **Primary SCI,** caused by the mechanical forces of the trauma, results in direct neuronal disruption and destruction from shearing forces, lacerations, acute stretching of axonal fibers, and sudden acceleration–deceleration injuries. Petechial hemorrhages and hematomyelia also occur. Histologic changes consist of hemorrhage and protein extravasation into the central gray matter that spread to the adjacent white matter. Primary injury rarely causes actual transection of the cord.
2. **Secondary SCI** is due to microvascular damage in combination with the activation of biochemical and enzymatic processes. The severity of damage is in proportion to the magnitude of the initial injury. Progressive hemorrhagic necrosis, loss of cellular membrane integrity, vasogenic and cytotoxic edema, inflammation, arachidonic acid release, lipid peroxidation, and loss of vascular autoregulation all contribute to and determine the extent of secondary SCI. This is manifest as vascular stasis, decreased SCBF, ischemia, and cell death. The traumatized areas eventually undergo cavitating necrosis and ultimately glial scar formation. Spinal cord edema is maximal at 48 hours and may persist for up to 2 weeks.

**C. Anatomical correlates of spinal cord injury (**Table 14.1**).** Flexion injuries may cause anterior subluxation or fracture dislocations of the vertebral bodies, traumatic disk herniation, and disruption of the posterior longitudinal ligament. Hyperextension injuries are associated with transverse fractures of the vertebrae, disruption of the anterior longitudinal ligament, and posterior dislocations. Vertical compression produces burst fractures, teardrop fractures, and ligamentous rupture. Rotational injuries may result in fractures of the vertebral peduncles and facets. The designation of an

TABLE 14.1 Spinal Injury, Clinical Finding, and Indicated Treatment

| Spinal Injury | Clinical Finding | Treatment |
|---|---|---|
| Atlanto-occipital dislocation | Usually unstable; commonly fatal | Reduction, immobilization, fusion |
| **Atlantoaxial Injury** | | |
| Isolated atlas fracture | Usually stable/no neurologic injury | Philadelphia collar |
| Isolated odontoid fracture | Usually neurologically intact | Immobilization |
| Displaced fracture C1–C2 | Commonly fatal or quadriplegic | Immobilization and reduction |
| Posterior subluxation C1–C2 | Usually neurologically intact | Immobilization |
| Axis pedicle fracture | Can be neurologically intact | Immobilization |
| Hyperflexion dislocation C3–T1 | Any subluxation is unstable | If neurologic deficit, decompression |
| Dislocated facets | Neurologically variable | Traction and surgery |
| Flexion–rotation injuries | Neurologically variable | Surgical reduction and fusion if anterior subluxation and jumped facet |
| **Compression Fractures C3–T1** | | |
| Wedge compression/burst fractures | Frequent neurologic damage | Surgical decompression |
| Teardrop fractures (vertebra dislocated anteriorly with inferior vertebral fracture) | Usually unstable | Posterior fusion |
| Hyperextension injuries | Geriatric patients who have spondylosis producing central cord syndrome | Immobilization; if significant spinal canal narrowing, decompression |
| Thoracic spine injuries | Incomplete neurologic injury most common | Realignment and stabilization |
| Thoracolumbar injuries | Neurologic deficits complex | Decompression and fusion |
| Lumbar injuries | Incomplete neurologic injury | Realignment and decompression |
| Penetrating injuries | Neurologic deficit variable | Decompression/ foreign body removal |

SCI as stable or unstable considers the potential for further spinal injury and the failure to heal properly, if untreated.

**D. Clinical correlates of spinal cord injury** (Table 14.2). SCI can result in complete (total loss of sensory and motor function distal to the injury) or incomplete (presence of any non-reflex function distal to the injury; see Table 14.2) loss of neurologic function. A complete SCI has less than a 10% chance of full

TABLE 14.2 Incomplete SCI Syndromes

| Syndrome | Clinical Findings |
|---|---|
| Anterior cord syndrome | Motor, sensory, temperature, and pain lost; vibration/position intact |
| Central cord syndrome | Motor impairment of upper more than lower extremities |
| Posterior cord syndrome | Loss of fine, vibratory, and position sensation; preserved motor function |
| Brown-Séquard (hemicord) syndrome | Ipsilateral paralysis, loss of proprioception, touch, and vibration; contralateral loss of pain and temperature |
| Conus medullaris syndrome | Areflexic bladder, bowel, and lower extremities; sacral reflexes can be preserved; reduced rectal tone and perirectal sensation |
| Cauda equina syndrome | Sensory loss with flaccid weakness; sacral reflexes abnormal or absent |

return of normal neurologic function. An incomplete SCI has a 59% to 75% chance of recovering lost function. The degree of cardiac and respiratory dysfunction is dependent on the spinal level of the acute SCI (Table 14.3). Medical problems include the following:

*Cardiovascular*
- Hypotension
- Bradycardia
- ↓Myocardial contractility
- Deep vein thrombosis
- Hypothermia

*Respiratory*
- Respiratory impairment
- Poor cough
- Viscous mucous

*Gastrointestinal*
- Atony
- Aspiration risk

*Genitourinary*
- Bladder distension
- Infection

*Electrolytes*
- Hypercalcemia
- Hyperphosphatemia
- Hyponatremia
- Hyperkalemia

The **cardiovascular effects** of an acute SCI depend on the level of injury (Table 14.3). For SCIs below T6, the major problem involves varying degrees of hypotension resulting from the functional sympathectomy. With complete SCI above T6, more significant cardiovascular abnormalities occur including bradycardia, hypotension, ventricular dysfunction, and dysrhythmias.

1. **Spinal shock,** seen most commonly with physiologic or anatomic transection of the spinal cord above C7, results from a total loss of impulses from higher central nervous system (CNS) centers as an immediate consequence of injury.
   - **a.** Spinal shock is characterized by flaccid paralysis, paralytic ileus, and loss of reflexes below the level of the lesion, visceral and somatic sensations, vascular tone, and the vasopressor reflex.
   - **b.** This syndrome, including the signs and symptoms of autonomic dysfunction, lasts from days to weeks and is prolonged by serious infection.

TABLE 14.3 Level of SCI and Pulmonary/Cardiac Function

| Level of Spinal Cord Injury | Pulmonary Function Ventilatory Function | Cough | Cardiovascular Function Sympathetic Function | Cardiovascular Reserve |
|---|---|---|---|---|
| C1–C2 | 0 | 0 | Minimal | Minimal |
| C3–C4 | 0 | 0 | Minimal | Minimal |
| C5–C6 | + | + | Minimal | Minimal |
| C7 | + to ++ | + to ++ | Minimal | + |
| High thoracic | ++ | ++ | + to ++ | ++ |
| Low thoracic | ++ to +++ | ++ to +++ | ++ to +++ | ++ to +++ |
| Lumbar | +++ | +++ | +++ | +++ |
| Sacral | +++ | +++ | +++ | +++ |

Scale is 0 (no function) to +++ (normal); SCI, spinal cord injury.

2. **Neurogenic shock** refers to the cardiovascular manifestations of SCI, particularly above T6, which include hypotension, bradycardia, and hypothermia. The higher the spinal level of injury, the more severe the physiologic derangements encountered. Neurogenic shock is caused by the loss of supraspinal sympathetic control of cardiovascular functions including coronary blood flow, cardiac contractility, and heart rate. The disruption of vascular tone and blood pressure control leads to low resting blood pressure, orthostatic hypotension, and bradycardia from unopposed vagal tone. Cardiovascular abnormalities after an acute cervical SCI include the following:

| | |
|---|---|
| Marked bradycardia (< 45 beats/min) | 71% |
| Episodic hypotension | 68% |
| Need for intravenous pressors | 35% |
| Use of atropine or temporary transvenous pacemaker | 29% |
| Primary cardiac arrest | 16% |
| Autonomic dysreflexia | 6% |

These cardiovascular derangements remain most problematic during the first 2 weeks after acute cervical SCI and may persist for up to 5 weeks after injury.

1. **Bradycardia,** nearly universal after complete acute cervical SCI, results from the functional sympathectomy with interruption of cardiac accelerator nerves (T1–T4) and unopposed vagal innervation. Bradycardia usually resolves over a 2- to 5-week period. More profound degrees of bradycardia, as well as cardiac arrest, may occur during stimulation of the patient (e.g., turning the patient, tracheal suctioning). Familiarity with the factors precipitating bradycardia should lead to institution of preventive interventions such as sedation, anticholinergics, 100% oxygen before suctioning, and limiting the time allowed for suctioning. Although severe bradycardic episodes may be effectively treated with atropine alone, in some instances (30%) a temporary pacemaker is necessary. In the context of traumatic hemorrhage, it is

important to remember that the heart rate will be less useful in differentiating between neurogenic shock (bradycardia) and hemorrhagic shock (tachycardia). Thus, in patients who have evidence of hemorrhage, an inappropriately slow heart rate should prompt suspicion of an associated SCI.

2. **Hypotension,** defined as a systolic blood pressure < 90 mm Hg or systolic blood pressure of 30% below baseline, is seen in 60% to 80% of patients after acute cervical SCI. Hypotension occurs because the loss of sympathetic tone causes peripheral vasodilatation with vascular pooling of blood. Early intervention to maintain MAP at 85 mm Hg for the first 7 days after injury is recommended to preserve neurologic function as autoregulation is impaired. **Hypovolemia** from coexisting hemorrhagic shock should be treated with prompt blood replacement and administration of isotonic crystalloid. Strict attention to the total volume of fluid administered is warranted, however, as pulmonary edema and cardiac decompensation are more likely to occur in the setting of an acute cervical SCI.
   a. If hypotension persists despite adequate fluid administration, **vasopressor therapy** is indicated. The vasopressor should have beta-agonist properties (e.g., dopamine or dobutamine). Supplementation with an alpha 1 agonist such as phenylephrine might be necessary. Caution should be exercised, however, when selecting a more potent alpha agonist, such as norepinephrine, because the potent vasoconstricting properties may substantially increase cardiac afterload, diminish cardiac output, and precipitate frank left ventricular failure.
   b. **Invasive central hemodynamic monitoring** is recommended in acute cervical SCI as an aid in guiding fluid therapy. A CVP of 8 to10 mm Hg or a pulmonary artery occlusion pressure of 12 to 16 mm Hg appears to optimize spinal cord perfusion most effectively. Newer technologies that analyze the arterial pulse wave contour and record stroke volume variation are also useful as tools in guiding fluid management. In patients who have suffered multiple traumatic injuries, the presence of neurogenic shock might conceal the symptoms of hemorrhagic shock making invasive hemodynamic monitoring an appropriate choice. Operative intervention for SCI should be postponed until the patient's hemodynamic status has been stabilized.
3. **Disturbances of cardiac rhythm** are common after SCI above the T6 level, and include bradycardia, primary asystole, supraventricular dysrhythmias (atrial fibrillation, re-entry supraventricular tachycardia), and ventricular dysrhythmias. An acute autonomic imbalance resulting from a disruption of sympathetic pathways in the cervical cord is causative. The arrhythmias typically resolve within 2 to 3 weeks after the SCI.
4. **Left ventricular impairment** has been noted in complete cervical SCI and is attributed to the functional sympathectomy and resulting autonomic imbalance. These patients are also more prone to the development of pulmonary edema.
5. **Autonomic dysreflexia** occurs in 85% of patients who have spinal cord transection above T6. The onset of signs and symptoms occurs 5 days to 3 weeks after injury. This syndrome is secondary to autonomic vascular reflexes, which usually begin to appear as spinal shock resolves.

a. Afferent impulses originating from cutaneous, proprioceptive, and visceral stimuli (bladder or bowel distention, childbirth, manipulations of the urinary tract, or surgical stimulation) are transmitted to the isolated spinal cord. These impulses elicit a **massive sympathetic response** from the adrenal medulla and sympathetic nervous system which is no longer modulated by the normal inhibitory impulses from the brain stem and hypothalamus. Vasoconstriction occurs below the level of the spinal cord lesion. Reflex activity of carotid and aortic baroreceptors produces vasodilatation above the lesion, which is often accompanied by bradycardia, ventricular dysrhythmias, and even complete heart block.
b. **Common signs and symptoms** include extreme hypertension, bradycardia, hyper-reflexia, muscle rigidity and spasticity, diaphoresis, pallor, flushing above the lesion, and headache. Horner's syndrome, pupillary changes, anxiety, and nausea occur less frequently. Systolic pressures in excess of 260 mm Hg and diastolic pressures of 220 mm Hg have been reported.
c. **Adverse effects** of autonomic dysreflexia include myocardial ischemia, intracranial hemorrhage, pulmonary edema, seizures, coma, and death.
d. **Treatment** involves cessation of the offending stimulus and a change to the upright position to enhance pooling of blood in the lower extremities. Pharmacologic intervention includes direct-acting vasodilators (e.g., sodium nitroprusside), beta blockers (e.g., esmolol), combination of alpha and beta blockers (e.g., labetalol), calcium channel blocking drugs (e.g., nicardipine), and ganglionic blocking drugs. As the attacks are often paroxysmal, drugs of rapid onset and short duration are preferred.

E. **Acute care of the patient after spinal cord injury.** Preservation of spinal cord function involves maintaining adequate oxygenation and MAP, stabilizing the spine, decreasing spinal cord edema, and decreasing secondary biochemical processes that worsen neurologic injury. The initial care of the patient who has an SCI is as follows:
1. **External splinting and immobilization.** Immobilization of the spine is accomplished in the field by placing the patient on a spine board with sandbags on either side of the head to prevent rotation.
2. **Neurologic examination.** In patients who have sustained spinal trauma, a neurologic examination is important to establish the patient's baseline neurologic function and to facilitate management decisions. Performed after the primary trauma survey, the neurologic evaluation includes an appraisal of mental status, an examination of the spinal column, and an assessment of the sensorimotor function of the extremities. During examination, it is important to take spinal precautions at all times (e.g., log rolling, neutral neck position). The neurologic examination should be accurately detailed in the medical record preferably by using the American Spinal Injury Association (ASIA) Impairment Scale (Fig. 14.3). The use of the ASIA chart standardizes the neurologic evaluation process and ensures the accuracy of the neurologic examination, which includes the following:
   a. **Mental status**: The Glasgow Coma Scale score is determined by considering the following—does the patient follow commands, open his/her eyes, track appropriately, and speak coherently? Altered mental status may signify coexisting brain injury.

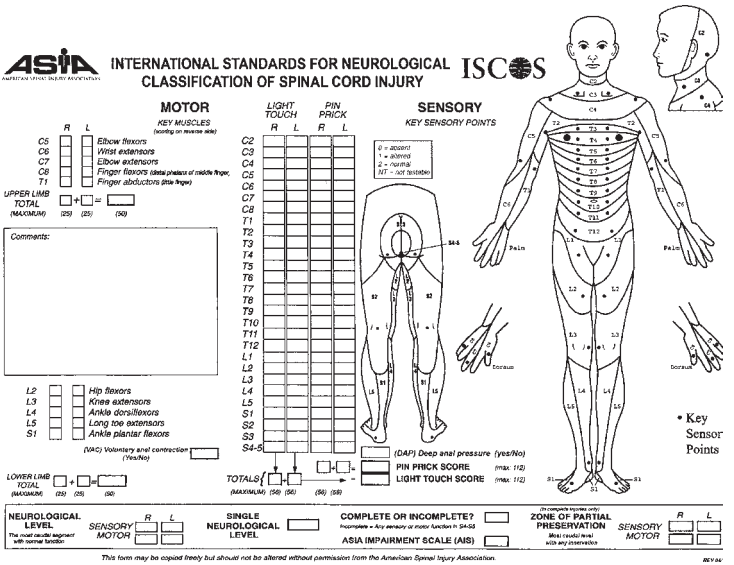


**FIGURE 14.3** American Spinal Injury Association. (Reprinted from International Standards for Neurological Classification of Spinal Cord Injury, revised 2011, Atlanta, GA, 2011, with permission.)

b. **Determination of sensorimotor function:** In the ASIA evaluation method, neurologic assessment is performed by testing key muscles and sensory points. For motor testing, 10 groups of muscles are tested. The function of these muscles is graded on a 6-point scale, with 0 assigned for total paralysis and 5 points assigned for normal strength. In total, there are 100 points when the right and left sides are assessed. The second part of the ASIA neurologic examination is the sensory score, which is based on the evaluation of 28 sensory dermatomes on the right and left sides of the body. At each of these key points, both sensitivity to pin prick and to light touch are tested and scored on a scale of 0 to 2 (0—absent sensation; 1—impaired sensation; 2—normal sensation). In addition, voluntary motor contraction of the external anal sphincter is tested by digital examination. Perirectal sensation and the bulbocavernosus reflex (anal cutaneous reflex) are also tested. A normal response indicates the preservation of distal function, known as "sacral sparing." This identifies the SCI as incomplete and is thus indicative of a more favorable prognosis.

c. **The ASIA Impairment Scale** is used to identify the severity of the SCI (Table 14.4). The terms *sensory level* and *motor level* are used to define the most caudal segment of the cord that has normal sensory and motor function, respectively, on both sides of the body.

3. **Radiologic evaluation.** The goal of radiologic imaging after spine trauma is to recognize and determine the extent of the spinal injury, as well as to aid in prognosis. Although plain radiography has been the traditional modality used to identify spine injuries, CT is rapidly supplanting plain radiography as the primary screening modality for spinal imaging.

TABLE 14.4 Muscle Group with Corresponding Level of Innervations

| Injury Level | Sensory Deficit | Affected Muscle Group |
|---|---|---|
| C4 | Acromioclavicular joint | Diaphragm |
| C5 | Antecubital fossa (lateral) | Shoulder rotators and abductors, elbow flexors |
| C6 | Thumb | Supinators, pronators, wrist extensors |
| C7 | Middle finger | Elbow extensors, wrist flexors |
| C8 | Little finger | Finger flexors, distal phalanx |
| T1 | Antecubital fossa (medial) | Intrinsic hand muscles |
| L2 | Upper anterior thigh | Hip flexors |
| L3 | Medial femoral condyle | Knee extensors |
| L4 | Medial malleolus | Ankle dorsiflexors |
| L5 | Dorsum of foot | Toe extensors |
| S1 | Lateral heel | Plantar flexors |
| S2–S5 | Popliteal fossa, ischial tuberosity, perianal area | Sphincter ani, bulbocavernosus reflex |

Regardless of the technique utilized, the results of radiologic imaging and the identified neurologic deficits are combined with knowledge of the mechanism of injury to determine the final pathologic state. The incidence of cervical spinal injury in comatose trauma patients is 7%. Therefore, radiologic assessment of the spine is essential after traumatic head injury, particularly in those individuals who also have signs and symptoms referable to a spinal injury.

a. **Plain radiographs**. The three-view cervical spine series composed of lateral, anteroposterior (AP), and open-mouth odontoid view, will detect most cervical spinal injuries. However, the abnormality will not be detected on the plain film in as many as 15% to 20% of patients who have a cervical SCI. When clinical suspicion is high, a more comprehensive radiologic evaluation is often indicated. For cervical spine injuries, a useful method of analysis of the plain radiographs is as follows:
   1. *Adequacy* and quality of the occipital–cervical junction (C1–C2), C3–C7, and the C7–T1 junction.
   2. *Alignment* of the anterior edge of the vertebral body, the posterior edge of the vertebral body, the spinolaminar junction, and the tips of the spinous processes (Fig. 14.4).
   3. *Bones*. Look for fractures of the vertebral body, pedicle, lamina, and spinous process.
   4. *Cartilage*. Analyze the disk space and the facet joints.
   5. *Soft tissue space*. Observe for edema and other abnormalities.

b. **Computerized tomography (CT)** has superior spatial resolution of the spine as compared with plain radiographs, and the axial format provides better evaluation of the spinal canal. CT imaging of C1 and C2 and the lower cervical spine is indicated when there are poorly visualized or suspicious areas on plain films. The negative predictive value of the combination of a normal three-view cervical spine series supplemented with CT through "suspicious" areas and areas that are difficult to visualize is 98% to100%. CT is therefore more helpful to:

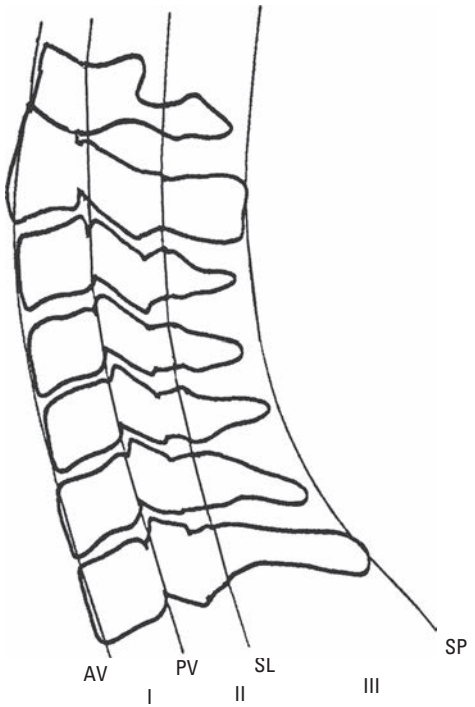


**FIGURE 14.4** The lateral cervical spine. Spinal column stability after traumatic injury is often based on a system that divides the spine into four longitudinal lines from anterior to posterior, starting with the anterior edge of the vertebral body (AV), the posterior edge of the vertebral body (PV), the spinolaminar junction (SL), and the tips of the spinous process (SP). Each line provides the border for three columns (I, II, and III). Disruption of two or more of these columns indicates spinal instability.

1. Define bony and soft tissue abnormalities
2. Evaluate the lower C-spine
3. Measure spinal canal and neuroforaminal diameter
4. Provide detailed anatomy of the facet joints
5. Detect hematoma formation
6. Determine compression of the spinal canal and spinal stability
7. Detect a unilateral jumped facet or bone fragments in the canal or root foramen
8. Confirm complete reduction of a dislocation
9. Demonstrate hyperdense acute blood or retropulsed vertebral body fragments

c. **Magnetic resonance imaging (MRI)** has inherent advantages in the setting of spinal trauma, including the ability to image the spinal cord in any orientation and to visualize soft tissues and spaces. MRI is indicated within 48 hours of injury for symptomatic SCI and in comatose trauma patients who may have a cervical spine or ligamentous injury. MRI is helpful to:

1. Determine the degree of injury to the spinal cord parenchyma such as hemorrhage, edema, myelomalacia, and lacerations
2. Identify ligamentous injury, nerve root compression, and spinal canal size
3. Visualize the epidural and subarachnoid spaces
4. Detect elevation of the anterior or posterior longitudinal ligaments
5. Predict functional neurologic outcome in the subacute stage of SCI

d. **Flexion–extension films** performed under fluoroscopic guidance are recommended as an alternative to MRI to evaluate ligamentous stability in awake patients who have symptoms of cervical spinal injury or in comatose trauma patients.

4. **Medical management.** Identification of associated injuries is crucial. These include the following:

*Cervical Spine Injury*
- Head
- Airway
- Esophagus

*Lumbar Spine Injury*
- Abdominal
- Pelvic

*Thoracic Spine Injury*
- Myocardial
- Pulmonary
- Ribs
- Major vascular

a. **Airway**
1. SCI presents several problems in airway management. Many maneuvers used for intubation can cause displacement and worsening of the injury, especially at the level of the cervical spine (C-spine). For this reason, all patients who have head trauma, multiple traumatic injuries, or decrease in level of consciousness should be considered as having a spinal injury until proven otherwise and the airway managed appropriately (Fig. 14.5).
2. Patients who have a normal level of consciousness, an intact "gag reflex," and a patent airway may be managed conservatively with supplemental oxygen. However, these patients should be observed closely to detect progressive loss of ventilatory ability as a result of developing diaphragmatic or intercostal paralysis. As profound reductions in forced vital capacity (FVC) and expiratory flow rates are observed immediately after injury, nearly all patients who have an acute cervical SCI will require mechanical ventilation within 24 to 48 hours of hospital admission.
3. The initial airway management of the cervical spine-injured patient includes consideration of the following issues:
   a. The urgency of the need for airway intervention
   b. Whether there is time available for radiologic evaluation of the spinal injury
   c. The presence of associated facial injuries or soft tissue injuries
   d. The presence of basilar skull fracture or midface fractures that would contraindicate nasal intubation
   e. Whether or not the patient is awake and cooperative
   f. The skill of the operator in using different airway techniques
4. Maintenance of a patent airway and adequate oxygenation in a patient who has a cervical spine injury may require bag and mask ventilation, an oral or nasal airway, or oral or nasotracheal intubation.

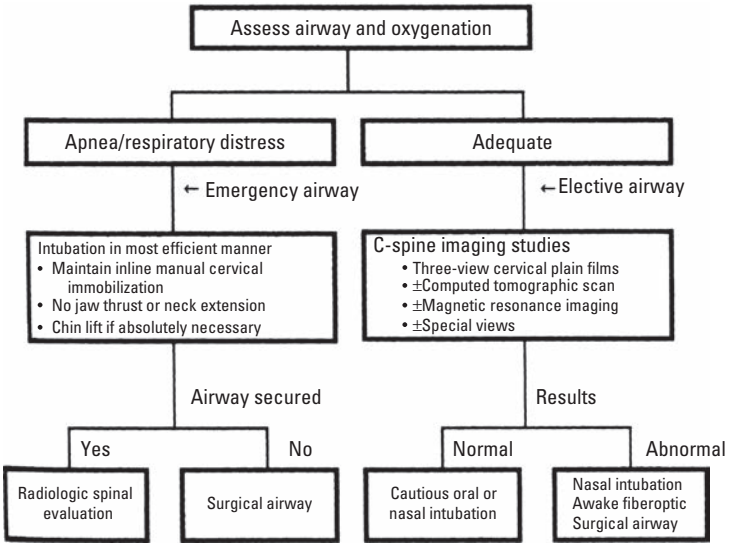


**FIGURE 14.5** Airway management algorithm for the patient who has suspected C-spine injury.

5. Direct laryngoscopy remains the method of choice for emergent airway control in patients who have confirmed or possible C-spine injuries. Mouth opening for laryngoscopy may be facilitated by removing the cervical collar and neck movement minimized by manual inline immobilization (MILI) without axial traction. During direct laryngoscopy, minimal displacement of the cervical spine typically occurs in the subaxial segments (C2–C5), while some extension occurs at the C1–C2 articulations. Thus, the upper cervical spine may be at greater risk for secondary injury during laryngoscopy than the lower cervical spine. The use of cricoid pressure may be utilized to reduce the risk of pulmonary aspiration of gastric contents.
   a. Specific blades available for direct laryngoscopy have minimal differences with respect to the effects on spinal movements. However, a newer laryngoscopic device, the Glidescope, utilizes a video camera at the tip of the blade that transmits images to a display monitor. Compared with a Macintosh blade, the Glidescope improves the typical laryngeal view by one grade in patients who have cervical collars and reduces associated spine movements by 50%, although time to intubation is lengthened.
   b. Neck-stabilizing cervical orthotic devices, such as soft and hard collars, do not limit spinal movements or offer significant spine protection; in addition, such collars interfere with mouth opening. As such, these collars should be removed in combination with MILI to facilitate tracheal intubation.
   c. Excessive flexion and extension of the neck during maintenance of the airway and intubation might lead to catastrophic exacerbation of the spinal injury. Therefore, MILI should be

utilized whenever traditional laryngoscopy is indicated. MILI is accomplished by having an assistant hold the sides of the neck and the mastoid process, preventing significant movement of the neck during direct laryngoscopy. If necessary, the airway can be opened using a careful jaw thrust technique with the head maintained in a neutral position through prevention of significant flexion and extension.

6. Blind nasal intubation has been utilized for airway management in patients who have a SCI. The benefit of this technique is minimal head movement, while potential disadvantages include an extended period of time to accomplish the intubation and trauma to the nasal passage. Nasotracheal intubation is contraindicated in the presence of a basilar skull fracture and extensive facial trauma. Compared to traditional direct laryngoscopy, nasal intubation provides no benefits and places the patient at increased risk of developing nasal erosions and eventual sinusitis (after 5 days).
7. Fiberoptic intubation is appropriate in non-emergent situations where the airway is free of blood and stomach contents. This technique may facilitate intubation of the trachea with the least amount of neck movement.
8. Retrograde intubation may be warranted to secure a particularly difficult airway. In such patients, a catheter is passed through a needle first inserted through the cricothyroid membrane and directed cranially, emerging from the nose or mouth. This catheter can be used as a guide for antegrade intubation.
9. SCI frequently results in gastric atony and paralytic ileus. These patients are considered to have a full stomach and are at increased risk for regurgitation and aspiration. Cricoid pressure should be administered with minimum force to avoid inadvertent further injury to the cord. As neck displacement of up to 9 mm can occur with the application of cricoid pressure, the risk of causing or exacerbating C-spine injury should be weighed against the risk of pulmonary aspiration.
10. Airway adjuncts, like the laryngeal mask airway (LMA), should be available, if needed, for an anticipated difficult airway (Fig. 14.4). While the LMA is helpful in maintaining oxygenation during a particularly difficult laryngoscopy, it should not be relied on as a long-term solution.
11. Cricothyroidotomy is an appropriate choice when faced with an anatomically abnormal airway in an emergent situation. While excessive movement of the spine is to be avoided, hypoxia secondary to a failure to intubate has a worse prognosis, and intubation should be accomplished as expeditiously as possible, including the use of a surgical airway technique.
12. A brief neurologic examination after intubation of the trachea will reveal any further deterioration in the patient's neurologic condition that may have occurred from manipulation of the airway or positioning.
13. There is a paucity of evidence to suggest that any one particular airway management technique is superior to another technique in a patient who has an unstable cervical spine injury. Most important is the skill of the operator.

b. **Pulmonary system.** SCI can have a profound effect on the respiratory system, including paralysis of the abdominal, intercostal, diaphragmatic,

and accessory muscles. The magnitude of the effect depends on the level and degree of SCI. Problems include respiratory failure, recurrent lobar atelectasis, hypoventilation, ventilation–perfusion mismatching, pulmonary edema (neurogenic, cardiogenic), bacterial pneumonia, aspiration pneumonitis, and coexisting blunt chest trauma.

1. Respiratory failure is present in nearly all patients who have SCI above C7. The resultant abnormality in respiratory mechanics leads to a reduction in lung volume (tidal volume, expiratory reserve volume, functional residual capacity), impairment of respiratory function (decreased FVC, forced expiratory volume in one second [$FEV_1$], peak forces, peak flows), and retention of pulmonary secretions with progressive hypoxemia and $CO_2$ retention. In addition, patients may have abdominal distention secondary to gastric atony, which further impairs pulmonary function.
2. Patients require frequent assessment of respiratory function as significant declines in pulmonary reserve can occur before overt clinical signs of respiratory failure appear. Frequent measurements of vital capacity (VC) and negative inspiratory force are helpful in the early identification of deterioration in respiratory function. When the VC decreases to < 1 L, especially if the patient is dyspneic and hypoxemic, endotracheal intubation should be performed.
3. The intention of mechanical ventilation in patients who have cervical SCI is to minimize the degree of respiratory muscle fatigue, decrease oxygen consumption, and facilitate optimal secretion clearance. The cervical SCI patient is effectively managed using a volume-control ventilation mode, either assist-control or synchronized intermittent mandatory ventilation with pressure-support ventilation.
   a. Initial ventilator settings should consider parameters that limit ventilator-induced lung injury: tidal volume of 6 to 8 mL/kg adjusted to limit plateau pressure to ≤ 30 cm $H_2O$, positive end-expiratory pressure (PEEP) of 5 cm $H_2O$, an initial rate of 8 to 15 breaths per minute, and an $FiO_2$ titrated to keep oxygen saturation > 90% (being careful to maintain an $FiO_2$ ≤ 60%). Including intermittent "sigh" breaths (e.g., 1 to 2 "sigh" breaths per minute at 10 mL/kg) might also enhance alveolar recruitment.
   b. Weaning from mechanical ventilation after cervical SCI is facilitated by the development of spasticity of the respiratory muscles (at about 3 weeks). Spasticity of the chest wall muscles stabilizes the thorax sufficiently to cause improvement in lung volume and overall ventilatory effectiveness. The VC doubles in volume within 5 weeks of injury in patients who have injuries at the C4–C5 level. Respiratory dynamics in the supine position are optimized due to the more cephalad position of the diaphragm. This position is most effectively used during weaning.
4. Lobar atelectasis, common in SCI above C7, requires aggressive pulmonary therapy emphasizing the prevention, recognition, and treatment of secretion retention. This regimen, instituted at the time of hospitalization, includes frequent nasotracheal or endotracheal suctioning, frequent repositioning or the early use of

kinetic therapy (i.e., continuous lateral rotation to ≥ 45°), chest percussion, bronchodilator therapy, deep breathing exercises, incentive spirometry, and cough-assist devices (e.g., mechanical insufflator–exsufflator devices). Even with the most aggressive pulmonary care and management, retained secretions result in repeated lobar collapse during the first 2 weeks of hospitalization. Therapeutic bronchoscopy (sometimes repeated daily) is often required for optimal secretion clearance and re-expansion of atelectatic areas of the lung.

5. Pulmonary edema is observed in patients who have acute SCI. Neurogenic causes of pulmonary edema may be related to autonomic dysfunction with sympathetic discharge at the time of injury which causes transient extreme elevations in blood pressure with resultant increases in extravascular lung water. Cardiogenic pulmonary edema might also occur because of a reduction in myocardial systolic function combined with over-zealous fluid administration. Accordingly, meticulous fluid management guided by central venous monitoring is essential in limiting pulmonary complications.
6. Pneumonia is observed in 70% of cervical and high thoracic spinal cord injuries. Pneumonia might result from aspiration of gastric contents at the time of the initial injury or might occur later on from nosocomial bacterial infection. Interventions suggested to reduce the incidence of pneumonia include elevation of the head of the bed by > 30°, use of antiulcer prophylaxis, regular suctioning of the posterior pharynx, and daily interruption of sedation.
7. Chest trauma and resulting hemothorax, pulmonary contusions, and rib fractures are frequently present in patients who have SCI. These injuries are often associated with prolonged mechanical ventilation, difficulty in weaning, and delayed operative intervention to stabilize the spine.

c. **Cardiovascular support.** For the first few minutes after SCI, there is a brief and substantial autonomic discharge from direct compression of sympathetic nerves. This results in severe hypertension and arrhythmias, which can cause left ventricular failure, myocardial infarction, and pulmonary capillary leak. This transient phase will have typically resolved by the time the patient arrives at the hospital, when hypotension from neurogenic shock and traumatic hypovolemia are more common. Optimal hemodynamic support to a target mean arterial blood pressure of ≥ 85 mm Hg is achieved by first assuring adequate volume resuscitation, guided by central venous monitoring (CVP 8 to 10 cm $H_2O$). Once adequate intravascular volume is assured, additional blood pressure support may be achieved through the use of dopamine (vasopressor and chronotropic effects), dobutamine, and/or potent $alpha_1$-specific vasoconstrictors (e.g., norepinephrine).

d. **Gastrointestinal.** During the acute stages of SCI, the gastrointestinal tract loses autonomic neural input and becomes atonic. Intestinal ileus (especially after thoracic and lumbar SCI) and gastric atony result in gastric distention and place the patient at risk for aspiration. Moreover, the dilatation might cause upward pressure on the diaphragm, adversely affecting ventilation. Insertion of a nasogastric tube will limit distention and reduce the risk of regurgitation.

1. A hypochloremic metabolic alkalosis may occur with excessive gastric suctioning. Thus, careful monitoring of fluid and electrolyte balance is indicated.
2. Gastritis and gastric ulceration and hemorrhage can occur after SCI, especially in patients requiring mechanical ventilation or as a result of administration of corticosteroids. Preventive techniques include monitoring of gastric pH and the use of antacids, $H_2$ blocking drugs, and proton-pump inhibitors (PPI). Therapy with either $H_2$ blocking drugs or PPIs should be continued for 4 weeks after SCI.
3. Other diseases occurring in critically ill patients after SCI include pancreatitis, acalculous cholecystitis, and gastric perforation (especially in patients receiving corticosteroids).
4. Patients who have acute SCI characteristically are catabolic and require nutritional supplementation within the first few days after injury. Enteral feedings are preferred over parenteral formulations, if possible.

e. **Genitourinary.** During the acute stages of SCI, the bladder is flaccid. Insertion of an indwelling urinary catheter is often necessary. Adequate hydration is likely if the urine output is > 0.5 mL/kg/hour in the absence of renal dysfunction.
   1. Bladder spasticity occurs after bladder flaccidity. The abnormalities with bladder emptying predispose the patient to recurrent urinary tract infections, bladder stones, nephrocalcinosis, and urosepsis.
   2. An indwelling urinary catheter is often required during the initial 2 to 3 weeks after injury. To prevent urinary tract infection, intermittent straight catheterization of the bladder is instituted as soon as feasible.
   3. Acute renal failure is uncommon but can occur as a result of hypotension, dehydration, sepsis, or associated trauma.

f. **Temperature control.** The body temperature of patients who have injuries above C7 tends to approach that of the environment (poikilothermia) due to their inability to conserve heat in cold environments through vasoconstriction. Consequently, SCI patients are at an increased risk of developing hypothermia, particularly if the ambient temperature is lower than normal body temperature. While hypothermia can provide some degree of spinal cord protection, it can also increase the incidence of arrhythmias, adversely affect the coagulation system, and prolong the effects of medications, particularly anesthetic drugs. Delayed awakening after operation can be especially problematic as it interferes with prompt neurologic examination.

g. **Deep vein thrombosis (DVT).** In the absence of prophylaxis, patients who have acute SCI have an incidence of asymptomatic DVT of 60% to 100% with positive venograms appearing 6 to 8 days after injury. Risk factors for DVT include increasing age, level of injury (paraplegia vs. tetraplegia), degree of injury (complete vs. incomplete), lower-extremity fractures, cancer, and delayed initiation of thromboprophylaxis. Despite an increased awareness of DVT as a complication of SCI, pulmonary embolism (PE) occurs in 0.5% to 5% of SCI patients and ranks as the third leading cause of death.

   The diagnosis of DVT or PE is made by clinical suspicion combined with the results of diagnostic testing: elevation in D-dimer

levels; color flow duplex imaging (CFDI); CT angiography; venography; and pulmonary angiography. Given the high risk of DVT and PE after SCI, a multimodal prophylactic medical treatment plan is recommended. With an effective treatment plan, the occurrence of DVT can be decreased to 5%. The American College of Chest Physicians (ACCP) consensus guidelines on the prevention of DVT in the SCI patient published in 2008 serve to guide therapy. They include the following:

1. Thromboprophylaxis is recommended for all patients after acute SCI with low molecular weight heparin (LMWH), once primary hemostasis is assured. Alternative therapies include IPC and either low-dose unfractionated heparin (LDUH) or LMWH.
2. Where anticoagulant thromboprophylaxis is contraindicated after acute SCI because of the high risk of bleeding, the use of IPC and/or graded compression stockings (GCS) is recommended. When the risk of bleeding decreases, pharmacologic thromboprophylaxis should be added.
3. In patients who have an incomplete SCI and evidence of a spinal hematoma on CT or MRI, mechanical thromboprophylaxis alone is recommended for the first few days after injury.
4. LDUH alone is not recommended after acute SCI.
5. An inferior vena caval filter should not be used as primary thromboprophylaxis against PE but is indicated when anticoagulation is contraindicated or after a documented PE in a patient who is already receiving anticoagulant therapy.
6. During the rehabilitation phase after acute SCI, the continuation of LMWH prophylaxis or conversion to an oral vitamin K antagonist (INR target of 2 to 3) is recommended. DVT prophylaxis should be continued for 3 months or until completion of the in-patient phase of rehabilitation.

5. **Neuroprotective strategies**
   a. **Spinal alignment**
      1. Studies have shown that movement of an injured spinal segment leads to exacerbation of the initial injury. Thus, an important neuroprotective strategy is to relieve cord compression through immediate and effective immobilization of the spine. Time to decompression is important. Failure to achieve adequate cord decompression in a timely manner may lead to progressive loss of residual neurologic function and worsen the ultimate outcome.
      2. Patients who have unstable injuries, particularly involving spinal cord compression, are placed in traction to realign the spine, decompress neural structures, and prevent further injury. Immobilization of the spine is accomplished through the use of tongs or a halo-traction device. Diminished pressure on the cord improves microvascular circulation, which might limit spinal cord edema. If there is no bony instability, as with penetrating injuries, traction is typically not needed.
      3. Thoracic and lumbar fractures and dislocations may initially be managed by restricting the patient to bed rest and "log rolling," to keep the spine protected. In fact, many stable thoracic and lumbar fractures may be treated without surgery, using a spinal orthotic device such as a thoracic-lumbar-sacral orthosis (TLSO). Significant spine distractions and/or compression fractures (> 50% loss of vertebral body height), particularly in the context of neurologic injury, are best stabilized by surgical intervention.

b. **Surgical therapy.** Surgical interventions, including spinal decompression and stabilization, are appropriate treatment for patients who have spine dislocations or unstable spine injuries with progressive neurologic injury. Animal and clinical studies increasingly suggest that early surgical decompression (< 24 hours) may lead to a more favorable neurologic outcome, particularly in patients who have incomplete SCI. Late surgical decompression (> 48 hours) offers no particular neurologic benefits other than stabilizing the spinal column, which facilitates early rehabilitation therapy. The ultimate decision as to the timing of surgery after spinal injury considers the following:
   1. Assessment of the underlying injury
   2. Failure of medical, manipulative, and bracing procedures to achieve adequate alignment
   3. Benefit of early decompression or stabilization of the spine
   4. Presence of progressive neurologic deficits and/or refractory pain
   5. Severity of any coexisting illnesses, infections, or trauma
   6. Documented benefit of earlier patient mobilization and rehabilitation facilitated by earlier surgical intervention (within 8 to 72 hours after injury)

c. **Physiologic therapy**
   1. Cooling may play a role in the treatment of SCI, but little therapeutic benefit from **modest hypothermia** after SCI has been demonstrated in humans thus far. The high mortality rate and significant circulatory, pulmonary, metabolic, and immunologic side effects coupled with the limitations of the clinical studies (small cohort size and lack of adequate controls) are all deterrents to the clinical use of hypothermia after SCI. While modest hypothermia after SCI remains an option and its effect on spinal recovery continues to be evaluated, the routine use of hypothermia as a spinal cord protectant in the setting of traumatic SCI cannot be considered standard therapy. Conversely, hyperthermia is definitely deleterious after traumatic SCI. Aggressive measures to prevent hyperthermia should be taken to minimize the propagation of secondary neuronal damage.
   2. **Maintenance of high-normal blood pressure** is recommended after SCI to improve spinal cord perfusion, as autoregulation is impaired and the risk of hypoperfusion consequently increased. Although definitive human data are not available, the MAP should be kept in the normal to high-normal range (MAP ≥ 85 mm Hg) with volume replacement (non–dextrose-containing crystalloid, colloid, or blood products) and/or inotropes and vasopressors. Aggressive blood pressure support may, however, increase the risk of intramedullary hemorrhage and further edema.
   3. **Dextrose-containing solutions should be avoided**. Studies in experimental models have shown that even minimally increased blood glucose levels worsen neurologic outcome. Serum glucose levels should be maintained ≤ 150 mg/dL.

d. **Pharmacologic therapy**
   1. The administration of **corticosteroids** after acute SCI was previously considered to be standard of care. The rationale for steroid use in SCI was the potential to stabilize membrane structures, maintain the blood–spinal cord barrier, enhance SCBF, alter electrolyte concentrations at the site of injury, inhibit endorphin release, scavenge damaging free radicals, and limit the inflammatory response

to injury. The recommendation for the use of corticosteroids came from two prospective, placebo-controlled, randomized trials: the National Acute Spinal Cord Injury Study (NASCIS) II reported in 1990 and NASCIS III published in 1997. Both studies compared high-dose methylprednisolone (MP) to naloxone and placebo in patients who had complete and incomplete acute SCI. In NASCIS II, methylprednisolone was associated with improvement in motor function and in sensation at 6 months of follow-up. The data from NASCIS III showed that if MP were given within 3 hours of SCI, the required duration of the steroid infusion was shorter than when therapy was initiated between 3 and 8 hours of injury, Both studies demonstrated an increase in medical complications in the steroid-treated patients—longer hospitalizations and a higher incidence of wound infections, pneumonia, gastrointestinal bleeding, and severe sepsis.

Subsequent re-examination of the NASCIS II and III data has led to significant criticism of each study. Specifically, NACIS II had flaws in study design and statistical analysis. The NASCIS III results have been questioned because of concerns regarding the timing of surgery, the process of neurologic assessment, and the fact that there were negligible differences in motor scores and functional outcome among the groups. Consequently, steroid use after SCI is now best considered a treatment option rather than the standard of care.

2. **Mannitol,** 0.25 to 1 g/kg, may be used to treat cord edema. The ensuing osmotic diuresis necessitates close attention to the patient's fluid and electrolyte balance.
3. **Hypertonic saline (HTS)** use in experimental models of acute SCI has suggested that it may enhance the delivery of methylprednisolone and prevent immunosuppression, leading to improvements in overall neurologic function and survival rates after injury. In addition, the use of HTS has reduced spinal cord edema in animal models of SCI. As the demonstration of benefit in clinical studies has so far remained elusive, HTS in the setting of acute SCI remains largely experimental.
4. Other **pharmacologic drugs** have been studied in the context of acute SCI to limit secondary injury or to enhance neurologic recovery including GM-1 ganglioside, tirilazad, naloxone, thyroid releasing hormone, and nimodipine. None of them has clearly demonstrated an improvement in outcome after acute SCI so that their use is not currently recommended. Other therapies, including transplantation of progenitor or stem cells into the injured cord, electric field gradients to stimulate nerve regrowth, monoclonal antibodies, minocycline (a metalloproteinase inhibitor), Rho inhibition (Cethrin), and local injection of activated macrophages into the injured cord are all currently under study and may hold promise in reducing the magnitude of secondary injury after SCI.

F. **Prognosis after SCI:** The major factors in predicting recovery in the first year after traumatic SCI include the initial neurologic level of injury, the patient's initial motor strength, and, most importantly, whether the injury is classified as neurologically complete or incomplete.

1. Complete tetraplegia: Most upper-extremity (UE) recovery occurs during the first 6 months after injury, with the greatest rate of change in the

first 3 months. Motor recovery can continue to occur, however, into the second year. Most patients who have complete cervical lesions will recover one root level of function.

2. Incomplete tetraplegia: The UE motor recovery is significantly better in incomplete tetraplegia than in complete tetraplegia. For patients who demonstrate some sensation initially, the prognosis for motor recovery is more favorable in those who have sparing of pinprick sensation as compared with light-touch sensation alone. Most motor recovery occurs within the first 6 months after injury; early recovery of some motor function suggests a better functional outcome.
3. Complete paraplegia: The greater the potential for lower-extremity (LE) motor recovery, the more caudad the initial neurologic level of injury: 15% of patients who have a neurologic level of injury between T9 and T11 regain some strength in the LE, while 55% of those who have an initial neurologic level of injury below T12 recover some strength in the lower limbs.
4. Incomplete paraplegia: The prognosis for LE motor recovery and ambulation is best in this group. Eighty percent of people who have incomplete paraplegia regain antigravity hip flexors and knee extensors at 1 year.
5. Overall, 16% of those classified as a complete SCI improve one classification grade by 1 year of follow-up. The initial presence of spinal shock portends a more severe injury and a less optimistic prognosis.

**G. Anesthetic management of acute SCI**

1. **Preoperative evaluation.** The SCI patient frequently has multiple medical complications that may impact the anesthetic plan.
   a. Indicated **studies** include complete blood count, serum electrolytes, blood urea nitrogen, creatinine, glucose, liver function tests, and urinalysis. A preoperative electrocardiogram (ECG), arterial blood gas, chest x-ray, and pulmonary function tests may also be indicated.
   b. **Airway evaluation**. Patients presenting for elective or emergency spinal surgery under general anesthesia require meticulous evaluation regarding the limitation of neck motion from an unstable spine, cervical collar, or spinal immobilization device and the presence of any neurologic deficits. The initial airway assessment consists of a general survey of the patient's head and neck. Obvious problems such as morbid obesity, short neck, cervical collar, full beard, and any breathing difficulties (e.g., stridor) should be noted. Mouth opening is assessed to determine the laryngoscopic visualization grade.

      The oral pharynx is examined with special attention to the size of the tongue in relation to mouth opening. The ability to visualize the structures of the oral cavity (Mallampati examination) is an accurate predictor of difficulty with direct laryngoscopy. Patients who have SCI are at increased risk for further neurologic injury if the airway is not approached with care. The patient who has moderate to severe limitation from mechanical or neurologic restrictions should be considered as a candidate for an awake intubation under local anesthesia to minimize movement of the head and neck. If an awake fiberoptic intubation is chosen, the patient needs to be advised about the process.

      The patient who has mild limitation of neck movement and in whom a difficult intubation is not anticipated may undergo anesthetic induction before intubation. For patients who have spinal trauma and are scheduled for elective or urgent surgery, the cervical spine should be "cleared" before induction, if at all possible. In any

patient presenting for spine surgery, several alternate means of intubating the trachea should be available (e.g., fiberoptic bronchoscope, transtracheal cannula, specialized laryngoscopes) in the event that airway management becomes difficult.

c. **Neurologic evaluation** is performed preoperatively and any pre-existing neurologic deficits are documented. Regional anesthesia for procedures below the level of injury should be chosen only after careful evaluation of the level of injury, the risk of extreme hypotension, and the potential for neurotoxicity in the context of injured neural tissue. To avoid confusion regarding neurologic changes, general anesthesia is the preferred technique for surgical procedures in patients who have SCI.

d. **Pulmonary evaluation** must take into consideration the level of SCI. Patients who have C-spine injury have restrictive pulmonary abnormalities and marked reductions in lung volume that predispose them to hypoxemia. Injuries of the cervical and high thoracic spine also create difficulties with clearance of secretions, which might also predispose patients to hypoxemia and hypercarbia.

e. **Cardiac evaluation** is essential to elicit evidence of cardiovascular dysfunction due to acute SCI or to any pre-existing cardiovascular comorbidities. In addition, preoperative assessment of the degree of orthostatic hypotension, the use of vasoactive drugs, and the risk of autonomic hyper-reflexia should be made.

2. **Monitoring.** Decisions regarding the utilization of advanced monitoring techniques are based on the level of injury and neurologic deficits, the complexity and length of the surgical procedure, and any pre-existing underlying medical conditions.

a. **Routine monitors** including ECG, pulse oximetry, capnography, noninvasive blood pressure, and temperature are employed for every procedure. A urinary catheter is used to track the patient's volume status.

b. **Invasive monitors** are generally indicated for surgical procedures in the context of SCI. In patients who have neurogenic shock, the institution of direct blood pressure monitoring is appropriate, ideally before induction. The arterial access is also useful for blood gas measurements and other laboratory determinations that might be necessary intraoperatively. CVP monitoring or the use of a pulmonary artery catheter (PAC) during the period of neurogenic shock is also appropriate.

Measurement of intracardiac pressure and volume (CVP, pulmonary capillary wedge pressure [PCWP], left ventricular end-diastolic pressure [LVEDP], transesophageal echocardiography) in conjunction with cardiac output (CO) and blood pressure is necessary to differentiate hypovolemia from low systemic vascular resistance (SVR). Although the absolute values for indicators of cardiac volume such as CVP and PCWP are inaccurate when compared with volume estimates utilizing transesophageal echocardiography, the trend of the values is helpful in determining the appropriate management (fluid vs. vasopressors) and in monitoring the response to therapy.

1. Patients who have **low SVR** may be treated with titrated infusions of a direct-acting alpha agonist (e.g., norepinephrine, dopamine, phenylephrine).
2. Patients who are **volume depleted** (as indicated by a decreasing CVP) receive isotonic fluid (5 to 7 mL/kg) in 250 to 500 mL increments over 10 minutes. The achievement of optimal intravascular

volume can be estimated from the changes in intracardiac pressures (CVP, PCWP, LVEDP), CO, and blood pressure in response to the fluid administration.

c. **Neurophysiologic monitoring** may be appropriate for particular types of spinal surgery, including operations for stabilization and fusion of an unstable spine. In general, several methods are used to monitor spinal cord function during operations where injury to the spinal cord may be increased. These include the intraoperative wake-up test, somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), and electromyographic potentials (EMG).

1. **SSEPs** are recorded in response to repeated stimuli applied to the peripheral sensory nervous system. SSEP signals reflect the integrity of the posterior spinal sensory pathways and large peripheral nerves. An intact cerebral cortex also is necessary. Baseline recordings are generated after surgical incision and these signals are used for comparison during the operative procedure.

   Anesthetic depth using drugs that do not adversely affect SSEP is stable at the time of initial baseline recordings. Inhalational anesthetics and nitrous oxide ($N_2O$) interfere with SSEP signals in a dose-dependent fashion but effective SSEP responses are present with 0.5 minimum anesthetic concentration (MAC) isoflurane in 60% $N_2O$. Newer volatile drugs such as sevoflurane and desflurane have a similar effect on SSEPs at doses up to 1 MAC. Nitrous oxide potentiates the negative effects of volatile anesthetics on latency and amplitude of evoked potentials so that it is best to omit the use of $N_2O$ during SSEP monitoring. Although intravenous drugs such as propofol and benzodiazepines can also adversely affect SSEP recordings, these drugs have comparatively minimal effects on SSEP wave morphology as compared with volatile anesthetics and can be safely utilized during SSEP monitoring. Opioid analgesics are also compatible with evoked potential monitoring so that the combination of an opioid infusion and an infusion of an intravenous anesthetic such as propofol is recommended.

   During surgery, SSEP responses are obtained repeatedly. Comparison is made of the SSEP wave amplitude, wave latency, and wave morphology. Changes in SSEP wave morphology that indicate possible disruption of the sensory pathway include an increase in the wave latency and a decrease in the wave amplitude. Such changes can be caused by ischemia, injury, or compression of neural structures.

2. **MEPs** assess the integrity of the motor pathways during complex spine procedures such as operations on the cervical spine. Intraoperatively, MEPs are typically produced by transcutaneous electrical stimulation of the motor cortex. The resulting myogenic responses are recorded in the peripheral muscles distal to the surgical level. MEPs measure the functional integrity of the spinal motor tracts, as opposed to the sensory tracts measured by the SSEPs. Cortical evoked responses are more sensitive to the effects of anesthetics than are SSEP responses. Volatile anesthetics in particular cause significant dose-dependent depression of motor-response amplitudes at clinically relevant concentrations (> 0.5 MAC). The anesthetic regimen most compatible with preservation of MEP signals consists of total intravenous anesthesia

(TIVA) and the avoidance of volatile drugs. The combination of a modest infusion of propofol (< 50 mcg/kg/minute) and an infusion of a short-acting opioid (e.g., remifentanil) is recommended when MEP monitoring is used.

d. Intracranial pressure monitoring should be considered for patients who have severe head injuries (Glascow Coma Scale [GCS] score < 9) and who are scheduled for prolonged surgical procedures where neurologic evaluation is not practical.

3. **Anesthetic technique**
   a. **Securing the airway** without causing or exacerbating SCI is the principal concern. The specific choice of technique should consider the risk of delayed gastric emptying, the need to assess neurologic function after intubation (particularly with an unstable spine and incomplete SCI), and the presence of a neck-immobilization device (e.g., halo traction), which hinders adequate airway access.
      1. **Direct laryngoscopy** may be appropriate if airway difficulties are not anticipated and progression of the neurologic injury is unlikely. However, care should be taken to limit extreme degrees of extension or flexion during intubation as such maneuvers cause excessive spine movement. Manual inline stabilization should be provided during laryngoscopy to minimize spinal column motion.
      2. The advantage of an **awake intubation** is that the patient acts as a monitor to avoid exacerbation of the spinal cord condition. In addition, a neurologic evaluation immediately after intubation can identify the presence of new neurologic changes. An awake intubation also avoids the use of succinylcholine with the attendant risk of hyperkalemia.
      3. **A *blind* nasal endotracheal intubation** has been recommended as an option that best avoids spinal manipulation during intubation. This approach is contraindicated, however, if there is facial trauma or a basilar skull fracture. Topical application of 0.2% phenylephrine hydrochloride in 4% lidocaine is helpful to shrink nasal tissues and limit bleeding. Anesthesia of the tongue can be achieved using 2% lidocaine ointment or local anesthetic sprays. Vocal cord and laryngeal anesthesia is provided with the combination of transtracheal injection of 4% lidocaine via percutaneous puncture of the cricothyroid membrane and superior laryngeal nerve blocks with bilateral injection of 2 to 4 mL of 1% lidocaine injected bilaterally just below the cornu of the hyoid bone into the thyrohyoid membrane. An alternative and effective technique utilizes nebulized 4% lidocaine with the patient receiving no more than 4 to 5 mg/kg.
      4. **Fiberoptic endotracheal intubation** may be used in a non-emergent situation after local anesthetic topicalization of the airway is achieved. If the oral route is chosen, a bite block or large oral airway with a central passageway for the fiberoptic scope is essential. Fiberoptic intubation often mandates the use of mild sedation to elicit patient acceptance and cooperation. Intravenous dexmedetomidine has been utilized successfully in this setting.
      5. In situations where severe facial trauma or neck instability exists, or if the airway is lost, a **surgical airway** via cricothyrotomy or tracheotomy should be considered. At a minimum, all instrumentation and personnel necessary for an emergency surgical airway should readily be available in the event that the airway is lost.

b. **Induction**
   1. In the presence of SCI, the induction of anesthesia should proceed very carefully as the functional sympathectomy and hypovolemia (relative or absolute) may combine to produce profound degrees of hypotension. A rapid-sequence induction is appropriate when the patient has a full stomach, but it may lower the blood pressure even further.
   2. **Intravenous induction drugs** are generally appropriate in all patients who have SCI, with the possible exception of the patient who has an extremely unstable spine or a unique anatomical airway issue (e.g., swelling or edema). While depolarizing muscle relaxants have the potential for inducing a hyperkalemic response, the use of succinylcholine within the first 24 hours after SCI is not associated with hyperkalemia. Succinylcholine should not, however, be used beyond 24 hours after the injury. The use of short-acting nondepolarizing muscle relaxants is appropriate for induction as this allows for subsequent neurophysiologic spinal cord monitoring.
      a. **Ketamine** (1 to 2 mg/kg) may provide a more stable hemodynamic profile during induction. Although ketamine has the added advantage of amplifying the electrophysiologic signal amplitude, its use is generally contraindicated in the presence of intracranial hypertension.
      b. **Etomidate** provides cardiovascular stability during induction but can cause myotonic muscle movements.
      c. **Propofol** and thiopental are acceptable choices for induction of anesthesia if hemodynamic stability has been achieved.
   3. **Hemodynamic stability is essential** during induction. The maintenance of a MAP ≥ 85 mm Hg will provide optimal spinal cord perfusion. If the patient is in the early phase of neurogenic shock, the risk of severe bradycardia and/or asystole with manipulation of the airway is increased. Accordingly, the prophylactic use of an anticholinergic should be considered.
   4. Hemodynamic lability with **hypotension** during induction is treated with direct-acting alpha and beta agonists. These drugs should be short acting and delivered via an intravenous infusion.

c. **Maintenance.** The selection of anesthetic technique for surgical procedures on the spine is based primarily on the patient's underlying medical condition, the anticipated intraoperative requirements, and the preference of the anesthesiologist. If neurophysiologic monitoring is planned, the selection of anesthetic drugs is based on their effects on neurophysiologic testing. Most importantly, a **stable intraoperative anesthetic depth is essential** so that any changes in evoked responses (SSEPs or MEPs) can be explained appropriately. Volatile anesthetics reduce evoked responses in a dose-dependent fashion thus favoring the use of balanced anesthesia.

An appropriate **anesthetic technique** for when **SSEP monitoring** is utilized would include a combination of a low-dose volatile drug (< 0.5 MAC), an opioid, and a muscle relaxant. **Motor evoked potentials (MEPs)** are more sensitive to the effects of volatile drugs and to $N_2O$. Therefore, these drugs should be avoided during MEP recordings. In addition, as the use of muscle relaxants may prevent adequate monitoring of intraoperative motor responses, relaxants should be either avoided or carefully titrated to partial twitch suppression. In the setting of intraoperative MEP recordings, the preferred anesthetic

technique utilizes **total intravenous anesthesia** (TIVA), such as an infusion of propofol combined with an infusion of a short-acting opioid (e.g., remifentanil), with/without a non-paralytic dose of a muscle relaxant (although it is probably better to avoid its use altogether). The TIVA regimen has been demonstrated to be better at preserving intraoperative MEP recordings than other anesthetic techniques.

d. **Muscle relaxants.** Patients suffering a complete or nearly complete SCI develop a proliferation of the number of perijunctional nicotinic acetylcholine receptors on denervated skeletal muscles as well as a denervation myopathy. Consequently, these patients develop **hypersensitivity to depolarizing muscle relaxants**. The use of succinylcholine stimulates the opening of pores on the neuromuscular junction and precipitates acute muscle injury (rhabdomyolysis). This causes a massive egress of stored intracellular potassium. The magnitude of the potassium release is more a function of the amount of muscle mass affected by the injury than the dose of depolarizing drug given. Even small doses of succinylcholine have triggered significant hyperkalemia. The resulting acute hyperkalemic response may induce changes in myocardial cell repolarization and cardiac arrest. As the time course for the development of the extrajunctional receptors is not clear (but may begin within 24 hours of injury), succinylcholine is best avoided beyond 24 hours after injury.

e. **Positioning.** Spinal operations are often performed in the **prone** position. In such instances, patients may be initially anesthetized and/or their tracheas intubated on the stretcher, and then log rolled into the prone position on the operating bed. Important **goals during positioning** include maintaining the head and neck in neutral position; providing adequate padding to the chest, abdomen, head, and extremities; and avoiding excessive neck flexion or extension during positioning. Special attention should be given to the endotracheal tube as significant movement or obstruction can occur with positional changes. All positioning maneuvers are accomplished with extreme care as such movements are associated with hemodynamic lability from the lack of adequate compensatory mechanisms that preserve venous return and cardiac output.

When prone, the head is positioned to avoid injury to bony prominences and prevent pressure on the eyes, ears, and nose. Head position may be adjusted slightly every 15 minutes or so throughout the procedure to prevent pressure-related injuries.

When an awake intubation is employed, the use of local anesthetic nerve blocks and topicalization of the airway will reduce the need for supplemental sedatives. The awake patient may then achieve the prone position himself after intubation, facilitating neurologic assessment.

4. **Fluid management** is based on estimated preoperative fluid deficits, intraoperative blood and fluid losses, and knowledge of the effect of the level of SCI on cardiac and pulmonary function. Meticulous fluid management is essential as patients who have high thoracic and cervical spine injuries have an increased propensity for developing pulmonary edema. In addition, cervical spine injury can cause cardiac dysfunction with decreased inotropy and chronotropy from reduced sympathetic neural input to the heart. Dextrose-free isotonic crystalloid is the preferred replacement fluid. Lactated Ringer's solution should be avoided

as it is relatively hypotonic (sodium, 130 mEq/L) and may increase tissue edema. Hemoglobin levels should be maintained at around 10 g/dL to optimize SCBF and tissue oxygen delivery. In the context of SCI, the use of acute normovolemic hemodilution to reduce loss of red cell mass is not recommended. Intraoperative blood glucose levels are kept below 150 g/dL and checked every 1 to 2 hours.

5. **Temperature regulation.** SCI patients have impaired thermoregulation below the level of injury. Prophylactic measures to prevent profound intraoperative hypothermia (i.e., < 34°C) should be aggressively instituted. These include a warm ambient environment, warm intravenous fluids, standard warming mattress, humidification of the respiratory circuit, and forced hot-air blankets. Conversely, hyperthermia should be avoided as it worsens neurologic injury.
6. **Postoperative care.** Even patients who had adequate respiratory function before operation might require a weaning period postoperatively before extubation due to the residual effects of the anesthetics. Because of the potential difficulty in reintubating the trachea, a conservative approach to extubation is recommended. Facial and airway edema are also likely, particularly after prolonged surgery in the prone position. It is therefore imperative that the patient be fully awake and have an air leak around the endotracheal tube cuff before any consideration of extubation. Finally, in patients who have a high thoracic or cervical SCI, extubation should be delayed until there is solid evidence demonstrating the ability to maintain the airway.

   Extubation criteria include the following:

   a. **Blood gases**
      1. pH > 7.3
      2. $PaO_2$ > 60 mm Hg
      3. $PaCO_2$ < 50 mm Hg
      4. Ratio of partial pressure of arterial oxygen to fraction of inspired oxygen ($PaO_2/FiO_2$) > 200
   b. **Respiratory functions**
      1. Maximal negative inspiratory forces <–25 cm $H_2O$
      2. VC > 15 mL/kg
      3. Respiratory rate < 25/minute
   c. **Others**
      1. Patient is conscious and oriented
      2. Unlabored or minimally labored breathing
      3. Ability to generate an effective cough
      4. Minimal volume of tracheal secretions
      5. Stable cardiac function
      6. Optimal intravascular fluid volume and electrolyte status
      7. Absence of infection

H. **Chronic spinal cord injury.** As improved emergent medical care increases the survival of patients after high-level spinal cord injuries, more patients who have chronic SCIs will require surgical procedures for spinal and other indications. Many of the issues regarding acute spinal cord injuries apply equally to patients who have chronic injury. There are, in addition, a number of medical problems (Table 14.5).

1. **Preoperative.** Respiratory complications are the most common cause of morbidity in spinal-injury patients. Pneumonia is second only to anoxia at the time of injury as a cause of death. Any fever with a leukocytosis or physical or radiographic evidence of pneumonitis should be treated aggressively.

TABLE 14.5 Medical Problems of the Patient Who Has Chronic SCI

| System | Abnormality | Relevant Comment |
|---|---|---|
| Cardiovascular | ■ Autonomic hyper-reflexia<br>■ ↓ Blood volume<br>■ Orthostatic hypotension | Susceptible to hypertensive crisis if SCI level is above T6. Positional changes and intrathoracic pressure can cause hypotension. |
| Respiratory | ■ Muscle weakness<br>■ ↓ Respiratory drive<br>■ ↓ Cough | SCI patient is susceptible to postoperative pneumonia and can be difficult to wean from mechanical ventilation. |
| Muscular | ■ Proliferation of acetylcholine receptors<br>■ Spasticity | Hyperkalemia from succinylcholine. |
| Genitourinary | ■ Recurrent urinary tract infections<br>■ Altered bladder emptying | Can lead to renal insufficiency, pyelonephritis, sepsis, or amyloidosis. Frequent catheterization can cause latex allergy. |
| Gastrointestinal | ■ Gastroparesis<br>■ Ileus | Susceptible to aspiration. |
| Immunologic | ■ Urinary tract infection<br>■ Pneumonia | Watch for subtle signs of infection and sepsis. Questionable risk of seeding an infection from invasive monitoring. |
| Skin | ■ Decubitus ulcers | Prevention. |
| Hematologic | ■ Anemia<br>■ Risk of DVT | DVT prophylaxis. |
| Bone | ■ ↓ Bone density | Osteoporosis, hypercalcemia, heterotopic ossification, muscle calcification, pathologic fractures. |
| Nervous system | ■ Chronic pain | Perioperative pain can be difficult to control. |

SCI, spinal cord injury; DVT, deep vein thrombosis.

Patients who have chronic injury are more prone to episodes of hypertension secondary to autonomic hyper-reflexia, especially with lesions above T6. Muscle spasms also occur because of hyper-active spinal reflexes without the modulating effect of cortical, brain stem, and cerebellar centers. The treatment of this "mass reflex" might require the therapeutic use of skeletal muscle relaxants in the awake patient.

2. **Intraoperative**
   a. **Regional anesthesia** may offer some advantage for patients who still have instability of the cervical spine or whose initial repair limits their cervical range of motion. The level of block desired must be evaluated in the context of the impaired hemodynamic reserve common in patients after SCI.

**b.** General anesthesia and regional anesthesia are equally effective in preventing **autonomic hyper-reflexia**. A technique based on the use of oxygen/$N_2O$ /narcotics seems, however, to be less efficacious in this regard. The patient's underlying hemodynamic status should also be taken into account. Regardless of the technique, direct-acting vasodilators (e.g., nitroprusside, nicardipine), alpha-adrenergic blocking drugs (e.g., hydralazine, phentolamine), antiarrhythmics (e.g., lidocaine, esmolol), atropine, and other antihypertensives (e.g., labetalol) should be readily available.

**c.** Chronic SCI increases the risk of a hyperkalemic response to depolarizing muscle relaxants. Decreasing the dose does not reliably prevent the response. Therefore, succinylcholine is best avoided for at least 6 months after injury and perhaps longer. Nor can the dose of a non-depolarizing muscle relaxant be based on twitch response from a denervated limb. As receptors at the neuromuscular junction of denervated muscle are up-regulated, this may lead to the administration of an excessive dose. Thus, the use of all muscle relaxants in chronic SCI patients and the determination of the completeness of reversal after neuromuscular blockade require significant consideration.

**d.** Urinary retention and urinary tract infections are a persistent problem. A distended bladder can also trigger the hypertensive response of autonomic hyper-reflexia. Therefore, an indwelling urinary catheter is inserted for most procedures.

3. **Postoperative** management, including the timing of tracheal extubation, should be guided primarily by the requirements of the surgical procedure, level of SCI, and comorbidities

## III. SPINAL CORD TUMORS

Tumors of the spinal cord are primary or metastatic in origin. The medical problems associated with the patient will be determined by the level of the spinal cord lesion and the location of the primary tumor in metastatic lesions. Depending on how much time has elapsed since the appearance of the spinal cord lesion and its associated signs and symptoms, these patients might present with many of the same complications as patients who have traumatic injury of the cord.

### A. Preoperative management

1. Lesions of the upper spinal cord are the most damaging physiologically. **Respiratory impairment** secondary to loss of intercostal muscle and/or diaphragmatic activity is common; blood gas measurement is indicated to determine the patient's baseline respiratory status. In addition, the decreased ability to clear secretions may frequently result in pneumonitis, which may require further evaluation and intervention. Such infections might not always be associated with elevated temperature, nor will elevated temperature always point to an infection as temperature regulation is frequently impaired.
2. **Cardiovascular tone might be diminished** with resulting hypotension, as occurs in patients after acute SCI. One must differentiate neurogenic hypotension from the hypotension caused by dehydration and malnutrition, which is commonly associated with cancer patients. Such dehydration might be exacerbated by diagnostic radiographic tests that involve the use of contrast dyes as these usually act as diuretics.
3. In addition to the basic chemistries, preoperative blood tests should include liver function studies to identify the presence, if any, of metastasis

to the liver. The possibility of pituitary and adrenal insufficiency should also be considered as these are also frequent sites of metastatic lesions.

4. **Premedication** should be kept to a minimum as it is useful to be able to reassess neurologic function immediately before surgery. Sedatives are avoided in situations where the respiratory status is already impaired.

**B. Intraoperative management**

1. The choice of **monitors**, beyond the routine, will be dictated by the planned procedure and the location of the lesion. Patients who exhibit signs of spinal shock will be managed more effectively with the cardiovascular information provided by a pulmonary artery catheter and an arterial line. Those patients at risk for autonomic hyper-reflexia may also require the "beat-to-beat" blood pressure monitoring provided by an arterial line.
2. **Positioning** of these patients frequently places the surgical site above the level of the heart. This increases the risk of venous air embolism. A monitor for the detection of air embolism (e.g., precordial Doppler, transesophageal echocardiography, pulmonary artery pressure), as well as an appropriately positioned CVP line to aspirate entrained air, should be incorporated into the anesthetic plan.
3. The risk of hyperkalemia with the use of succinylcholine is increased as it is for the patient after SCI. The use of **non-depolarizing relaxants** is recommended to ensure a quiet surgical field. However, because of up-regulation of receptors in the neuromuscular junction secondary to denervation, care should be taken to select an appropriate site for the monitoring of twitch suppression via the nerve stimulator.
4. **Maintenance of anesthesia** can be accomplished with any general anesthetic technique. However, in procedures where the use of SSEPs is anticipated, drugs that suppress the monitored potentials are avoided in favor of a $N_2O$/narcotic technique. Frequent changes of anesthetic depth are avoided as they will interfere with SSEP interpretation.

**C. Postoperative management**. The decision regarding early extubation is made on a case-by-case basis. Early extubation in a fully awake patient facilitates postoperative neurologic examination. The appropriateness of early extubation will depend on baseline respiratory function, location and size of the tumor, and duration and degree of difficulty of surgical dissection. Patients who were operated for high-level lesions require close monitoring for up to 48 to 72 hours postoperatively. During this time, edema at the surgical site can cause renewed compression of the spinal cord and lead to progressive respiratory compromise and loss of protective gag reflexes. Reintubation, when necessary, should be done early in the course of respiratory deterioration. This allows control of the airway in a patient who has a potentially unstable neck to be accomplished in as non-emergent an environment as possible.

## IV. SCOLIOSIS

**A. Scoliosis is a structural disease of the vertebral column** involving lateral curvature of the spine with rotation of the vertebra.

1. Scoliosis most frequently involves the **thoracic and lumbar** regions.
2. The **severity of the disease** is expressed in "degrees of lateral angulation." A larger degree of angulation represents more severe disease. The side of convexity of the curve designates it as a right or left curvature.

3. **Idiopathic scoliosis**, accounting for almost 75% of cases, occurs most frequently in adolescent girls. Other types are classified as non-structural (caused by gait/posture), congenital, neuromuscular, and traumatic.
4. The degree of severity of scoliosis correlates directly with the degree of **respiratory dysfunction**. Curvatures < 60° are not usually associated with significant pulmonary involvement, whereas patients who have curvatures > 100° are typically severely impaired.
5. **Pulmonary function testing** typically reveals a restrictive pattern due to the decrease in chest wall compliance, with reductions in all measures of lung capacity and volume. The greatest decrease is noted in the VC. Blood gas analysis will reveal a lowered $PaO_2$, which is primarily due to ventilation–perfusion mismatch. $PaCO_2$ is not usually altered unless an obstructive pulmonary component has also developed which is more common in the elderly.
6. In patients who have more severe thoracic disease, rib cage deformities lead to underdevelopment of the pulmonary vasculature. This is exacerbated by hypoxic pulmonary vasoconstriction and can lead to potentially significant elevations in pulmonary vascular resistance. Right ventricular hypertrophy and right atrial enlargement can occur as a result of the increase in pulmonary vascular resistance. Eventually, patients develop irreversible pulmonary hypertension.

**B. Preoperative management**

1. The preoperative assessment should include information about the location and degree of scoliosis as well as its etiology. Both location and degree of disease will play a role in determining the amount of pulmonary/cardiac involvement one can expect to find. Scoliosis from concurrent neurologic motor deficits may alter the choice of muscle relaxants.
2. Physical exam will indicate necessary testing. Patients who have limited exercise tolerance require further pulmonary function testing to ascertain the extent of pulmonary insufficiency. Patients who have vital capacities < 25 mL/kg are high operative risks.
3. Preoperative sedation is avoided in patients who have significant pulmonary compromise.

**C. Intraoperative management**

1. Decisions regarding **monitoring** are guided by the extent of pulmonary and cardiac involvement. One should consider an arterial line for blood gas measurement in any patient who has an even moderate reduction in pulmonary reserve. An arterial line is also necessary for closer monitoring of blood pressure when "deliberate hypotension" is employed to reduce intraoperative blood loss.
2. Pulmonary artery catheter monitoring is reserved for those patients who have pulmonary hypertension or significantly diminished right ventricular output.
3. No advantage can be demonstrated for any particular anesthetic induction or maintenance regimen. The underlying hemodynamic condition of the patient should be used to guide the choice and dose of drugs.
4. Placement of spinal instrumentation involves traction to correct the curvature. Frequently, SSEPs are utilized to monitor the sensory component of the spinal cord. However, SSEPs reflect only the posterior cord. It is possible that anterior cord elements might be damaged despite normal SSEPs. When SSEP monitoring is utilized, one should limit the

concentration of inhalation anesthetics as they will interfere with signal interpretation (see above).

5. A positive wake-up test definitively confirms adequate blood flow to, and thus the function of, the anterior motor portion of the spinal cord. This is accomplished by having the patient awaken and move the lower extremities in response to verbal command. With a multitude of short-acting muscle relaxants and maintenance anesthetics, it has become relatively simple to maintain a deep level of anesthesia until the time of the wake-up test and yet allow for a quick awakening at the appropriate time during the procedure.

D. **Postoperative management.** The spinal fusion and rodding procedure prevents further deterioration of pulmonary and cardiac parameters. These abnormalities are not typically corrected by the procedure. Careful consideration of the patient's baseline status helps to determine which patients are suitable candidates for early extubation.

## *Suggested Readings*


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### *Internet Resources*

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# 15 Pediatric Neuroanesthesia

**Nadeem A. Hamid, Rukaiya K. A. Hamid, and Philippa Newfield**

## Illustrative Clinical Case

A healthy 4-month-old male presented for a craniotomy and "barrel-stave" osteotomy with contouring secondary to craniosynostosis. He was a 6.9 kg full-term infant born via normal spontaneous vaginal delivery. After standard monitors and an arterial line were placed, the patient underwent the aforementioned 4-hour procedure. In the intraoperative period, the patient was transfused with 20 mL/kg of packed red blood cells (PRBCs) due to surgical blood loss of approximately 100 mL (> 10 mL/kg). The postoperative hemoglobin concentration was 11.2 g/dL and after extubation the patient was transported to the pediatric intensive care unit (ICU) in stable condition.

## Chapter Highlights

- Intracranial physiology
- Pediatric anesthetic requirements
- The pediatric airway and pulmonary physiology
- Anesthetic considerations
- Neuroanesthetic management for special procedures
  - Hydrocephalus
  - Craniosynostosis
  - Intracranial tumors
  - Surgery for epilepsy
  - Head trauma
  - Meningomyelocele and encephalocele
  - Craniofacial surgery
  - Vascular anomalies
- Neuroradiology
  - Anesthetic management of neurodiagnostic and neurointerventional procedures
  - Periprocedural neuroradiologic management

### I. INTRACRANIAL PHYSIOLOGY

While the development of the central nervous system (CNS) is incomplete at birth, maturation continues until the end of the first year of life. During this period, dramatic changes in intracranial parameters can occur primarily due to growth in brain tissue, changes in cerebral blood volume (CBV) and cerebrospinal fluid (CSF) production, as well as the closure of skull sutures. CBV is directly determined by cerebral blood flow (CBF), which is usually 100 mL/100 g/minute in children from 3 to 12 years of age. The CBF in children from 6 to 40 months is 90 mL/100 g/minute and in newborns and premature infants, it is approximately 40 to 42 mL/100 g/minute. In the absence of CBF or CBF < 6 mL/100 mg/minute, cell death occurs, while CBF of 15 to 20 mL/100 g/minute is associated with significant neuronal dysfunction. Any

changes in CBF leading to changes in CBV can cause logarithmic changes in intracranial pressure (ICP) secondary to limited skull compliance. As a result, anesthesiologists must constantly be aware of factors that can cause changes in cerebral perfusion.

In stark contrast to autoregulation of CBF in adults, autoregulation limits in infants and children are largely unknown. However, the limits are thought to be lower in value than those in adults and can be easily impaired or abolished. This can lead to varying degrees of intraventricular hemorrhage (IVH) with grave consequences. Studies have demonstrated that hyperventilation restores autoregulation in the neonate and that CBF velocity changes logarithmically and directly with end-tidal carbon dioxide tension ($ETCO_2$) in infants and children. Under normal conditions, ICP depends more on CBF and CBV than on CSF production. All inhalational anesthetics must, therefore, be used with care because they increase CBF and CBV by directly producing vasodilatation. New advances in continuous monitoring of autoregulation are being researched by analyzing spontaneous slow waves of cerebral perfusion pressures (CPPs), the difference between mean arterial pressure (MAP) and intracranial pressure.

## II. PEDIATRIC ANESTHETIC REQUIREMENTS

The anesthetic requirements in pediatric patients vary with age and maturity. Neonates and premature infants have decreased anesthetic requirements relative to older children. The reasons for the lower requirements in babies are the immaturity of the newborn's nervous system, the presence of maternal progesterone, elevated levels of endorphins, and the immaturity of the blood–brain barrier. Research, over the last 20 years, has reinforced the notion that neonates do sense pain and can develop a stress response to surgical stimulation. They, therefore, require adequate levels of anesthesia to blunt the stress response. Secondary to immature organ systems, neonates are sensitive to anesthetic drugs and therefore may benefit more from a narcotic-based anesthetic. While such an anesthetic technique may offer more hemodynamic stability, emergence may be delayed because the liver and kidneys are not fully developed. However, inhalation or intravenous induction of anesthesia in infants is more rapid than that in adults because of the following reasons:

**A.** The ratio of alveolar ventilation to functional residual capacity (FRC) is 5:1 in the infant and 1.5:1 in the adult.

**B.** The neonate has a greater cardiac output per kilogram of body weight than the adult. A neonate's cardiac output can typically range between 200 and 325 mL/kg/minute.

**C.** More of the neonate's cardiac output goes to the vessel-rich group of organs including the brain (up to 25%) and the heart.

**D.** The infant has a lower blood–gas partition coefficient for volatile anesthetics and a lower anesthetic requirement.

1. The rapid induction of anesthesia occurring with most volatile anesthetics may be hazardous in the premature, small for gestational age, or unstable patient.
2. Whatever the choice of anesthetic drugs, sick neonates require resuscitation and normalization of fluid and electrolyte balance before the induction of anesthesia.

The common denominator of neonatal surgery is that the operations are frequently performed emergently. This contributes significantly to the greater than tenfold increase in perioperative morbidity and mortality in neonates as compared to other pediatric age groups. Additional difficulties

can arise because intraoperative hypoxia and hemodynamic instability can be the first indication of previously unrecognized congenital cardiac and pulmonary anomalies. Regression to fetal circulation, leading to increases in pulmonary artery pressures, may also occur intraoperatively in neonates because of hypercarbia, hypoxia, hypothermia, and acidosis. In addition, respiratory complications are not uncommon in neonates owing to the small size of their airway, congenital laryngotracheal lesions, craniofacial anomalies, and acute (e.g., respiratory distress syndrome [RDS], transient tachypnea of the newborn) or chronic (e.g., bronchopulmonary dysplasia) lung disorders.

## III. THE PEDIATRIC AIRWAY AND PULMONARY PHYSIOLOGY

The neonatal period is considered as the first 30 days of extrauterine life and includes the newborn period, defined as the first 24 hours of life. Up to 3 to 5 months of age, the infant is an obligate nose breather in part because of the immaturity in the coordination between respiratory efforts and the oropharyngeal motor and sensory input. As a result of being an obligate nose breather, conditions such as congenital choanal atresia or simple nasal congestion can cause respiratory distress and asphyxia in the infant. Pediatric patients also have anatomically different airways than adults. Along with the cricoid cartilage's being the narrowest part of their trachea, infants have a narrower and angled epiglottis. Additionally, an infant has a larger occiput and a proportionally larger tongue. All of these factors can make the trachea of an infant or child more difficult to intubate.

Furthermore, infants are more prone to rapid deoxygenation. Oxygen consumption in the infant is high—7 to 9 mL/kg as compared to 3 mL/kg in the mature state. Infants also have a high closing volume leading to early alveolar collapse and a high minute ventilation-to-FRC ratio. As a result, pediatric anatomy and pulmonary physiology make airway management more difficult and critical.

## IV. ANESTHETIC CONSIDERATIONS

### A. Preoperative assessment

The preoperative assessment of a pediatric patient who has neurologic dysfunction involves establishing the degree of change in the cerebral compliance. The clinical presentation varies with the age of the patient as well as the rapidity and degree of change in the intracranial contents. Infants might present with a history of irritability, lethargy, and failure to feed. They may have an enlarging head circumference or bulging fontanelle. Older children might present with headaches, nausea, vomiting, or change in the level of alertness. Funduscopic examination may reveal papilledema although this may be a late sign in neonates owing to the presence of an open fontanelle. Some children, especially neonates, might need further evaluation by pediatric cardiologists and other subspecialists because of the presence of congenital cardiopulmonary disorders and other coexisting diseases.

### B. Fluid balance

Any evaluation must also include assessing pre-existing fluid and electrolyte imbalances from lack of oral intake or active vomiting secondary to changes in the ICP. Furthermore, fluid restriction and the combination of hyperosmolar (e.g., mannitol) and diuretic (e.g., furosemide) therapy may result in hemodynamic instability and shock when coupled with intraoperative blood loss. It is, therefore, necessary to establish and maintain normovolemia throughout the perioperative period. While normal saline (or

other non-glucose-containing solutions) may be used as the maintenance fluid because it is slightly hyperosmolar to plasma, enough glucose must also be administered to prevent hypoglycemia. It is imperative to secure excellent intravenous access for fluid and blood replacement and drug delivery before the start of the operation because the opportunities to do so will be limited once the operation is in progress. Two large-bore intravenous catheters, an arterial catheter, and a urinary catheter are necessary for children undergoing craniotomy, craniofacial reconstruction, or extensive spine procedures.

**C. Administration of glucose**

The administration of glucose-containing fluids during neurosurgical procedures is determined by the intraoperative measurement of blood glucose. The automatic addition of glucose to intraoperative maintenance fluid is unnecessary because hypoglycemia may not be a common occurrence in fasting pediatric patients, even in infants < 1 year of age. This is especially true because the stress response to surgery itself results in hyperglycemia from increased sympathoadrenal activity with decreased glucose tolerance, decreased glucose utilization, and increased gluconeogenesis. Furthermore, hyperglycemia, as defined by serum glucose ≥ 200 mg/dL, is associated with higher infection, neuronal loss, and higher mortality rates and is particularly critical in pediatric patients at risk for hypoxic–ischemic insults.

Solutions containing 1% to 2.5% glucose are less likely to cause hyperglycemia than are 5% solutions, especially when administered at a rate of 120 mg/kg/hour (2 to 5 mg/kg/minute). This is sufficient to maintain an acceptable blood glucose level and prevent lipid mobilization in infants and children. The monitoring of intraoperative blood glucose and the continual adjustment of glucose administration may be necessary in certain circumstances (Table 15.1).

The rate of delivery of hyperalimentation may need to be reduced intraoperatively owing to a decrease in the glucose requirement of children receiving hyperalimentation. Alternatively, patients may receive a continuous infusion of dextrose 10% in water (D10W), but will still require intraoperative glucose monitoring.

**D. Premedication**

Sedative premedication should be avoided in all patients suspected of increases in ICP because these drugs may further reduce the respiratory drive, leading to hypercarbia, cerebral vasodilatation, and, ultimately, tonsillar herniation. Patients with normal ICPs scheduled for the repair of vascular lesions may be sedated to control preoperative anxiety and avoid hypertension and rupture of the vascular abnormality.

**TABLE 15.1 Intraoperative Glucose Monitoring and Administration of Glucose**

| | |
|---|---|
| – Long procedures > 3 h | – Prolonged preoperative fasting |
| – Neonates and small infants | – Infants of diabetic mothers |
| – Infants with IUGR | – Children receiving transfusions > 20 mL/kg |
| – Beckwith-Wiedemann syndrome | – Hypopituitary syndrome |
| – Adrenal insufficiency | – Pancreatic islet cell adenoma/carcinoma |
| – Large hepatoma | – Pheochromocytoma |
| – Patients with poor nutrition | |

IUGR, intrauterine growth retardation.

**E. Inhalational and intravenous anesthetics**

Inhalational anesthetics affect mean arterial pressure (MAP), ICP, and CPP in children. At 0.5 and 1 minimum alveolar concentration (MAC), sevoflurane, isoflurane, and desflurane with 60% nitrous oxide ($N_2O$) increase ICP and decrease MAP and CPP in a dose-dependent manner. There is no relationship between the patient's baseline ICP and the ICP elevation after exposure to sevoflurane and isoflurane. Desflurane and isoflurane, however, may increase ICP to a greater extent than halothane or sevoflurane in children whose ICP is elevated preoperatively. The gradual increase in ICP from desflurane may be secondary to an increase in CSF production or a decrease in CSF absorption. Because the effect of a change in MAP on CPP is three to four times greater than the effect of a change in ICP, maintaining MAP is the more important factor in preserving CPP. For children who have a known increase in ICP, intravenous anesthesia may be the better alternative.

With propofol and thiopental administration, there is a dose-dependent decrease in $CMRO_2$, CBF, and ICP until an isoelectric encephalogram (EEG) is achieved. These effects have been noted within 2 minutes after administration and may, thereby, provide a safe alternative to volatile drugs for reducing ICP.

Dexmedetomidine, an alpha-adrenergic agonist similar to clonidine, is also being used with increasing frequency for the sedation of pediatric patients. Its hemodynamically-stable profile and lack of respiratory depression make dexmedetomidine a good choice for children who require ongoing sedation in the perioperative period. While its effects on $CMRO_2$, CBF, and ICP are still being investigated, $CMRO_2$–CBF coupling appears to be preserved.

Opioid analgesics, such as fentanyl and sufentanil, have not been shown to cause an increase in ICP in the setting of controlled ventilation. These specific opioids also have the additional benefit of a short duration of action, thereby allowing for rapid neurologic assessment upon emergence from anesthesia.

Succinylcholine's effect on raising ICP has been extensively documented in the literature and is, in part, due to muscle fasciculations and the resultant increase in intra-abdominal and intrathoracic pressures. This elevation in ICP is seen even in babies, who do not typically fasciculate due to low muscle tone. It is, therefore, contraindicated as a muscle relaxant in the setting of elevated ICP. Conversely, a rapid-sequence induction dose of 1 to 1.2 mg/kg of rocuronium has not been shown to have any deleterious effects on ICP.

**F. Monitoring**

Monitoring depends upon the patient's age and condition and the planned surgical procedure. Routine monitoring includes the use of the precordial stethoscope, electrocardiogram (ECG), oxygen saturation ($SpO_2$) by pulse oximeter, $ETCO_2$, non-invasive blood pressure (NIBP) measurement, temperature probe, and a peripheral nerve stimulator to monitor the degree of neuromuscular blockade. Direct arterial blood pressure monitoring, at least two good peripheral intravenous catheters, and a urinary catheter are recommended for extensive and invasive surgical procedures. Measurement of central venous pressure (CVP) may not reflect intravascular volume accurately, especially in patients in the prone position. As a result, unless a CVP is being inserted for management of intraoperative venous air embolism or for additional intravenous access, the risk of inserting a CVP catheter may exceed the benefits.

**G. Venous air embolism (VAE)**

VAE occurs commonly during craniotomy in infants because of the head position and surgical approach. The head of a small child, particularly the occiput, is large in relation to the rest of the body, causing it to lie above the heart, even in the supine position. In addition, the head of the bed is often elevated to facilitate drainage of blood and CSF during the operative period. Pressure within the superior sagittal sinus decreases as the head is elevated, increasing the likelihood of negative intravenous pressure and entrainment of air, thereby resulting in a VAE. Patients who have a patent ductus arteriosus or foramen ovale are also at risk for paradoxical air embolism through these defects. Consequently, precordial Doppler ultrasonography is used in conjunction with $ETCO_2$ sampling for detecting and assessing the treatment of VAE. The optimal position for the Doppler probe is on the anterior chest just to the right of the sternum in the fourth intercostal rib space. Alternatively, the probe may be positioned on the posterior chest in infants weighing < 6 kg. The anesthesiologist may also elect to monitor for the presence of nitrogen in the end-tidal gas mixture. Due to the fact that VAE has occurred in the sitting, prone, *and* supine positions, the use of $N_2O$ should be avoided to prevent an increase in the size of entrained air bubbles.

**H. Neurophysiologic monitoring**

Monitoring of evoked potentials, electrocorticography, and EEG necessitates low concentrations of inhalational anesthetics. Inhalational anesthetics and $N_2O$ depress somatosensory evoked potentials (SSEPs) for operations on the spine and brain stem; a total intravenous anesthetic (TIVA) technique using narcotics and a propofol infusion may be preferable. The use of electromyography and motor evoked potentials (MEPs) requires that muscle relaxation be reversed and that minimal amounts of volatile inhalational anesthetics are used during electromyography and monitoring of muscle movement.

**I. ICP monitoring**

ICP monitoring has seen increased utilization in the management of pediatric head injury because it facilitates intraoperative and postoperative assessment of a patient's response to therapies. Normal ICP is 0 to 10 mm Hg and can increase due to mass effect, increased CSF, tissue edema, or intracranial bleeding. ICP after traumatic brain injury is controlled by adjusting CPP and the partial pressure of arterial carbon dioxide ($PaCO_2$) via minute ventilation adjustments. Surgeons may also request that steroids, mannitol, and furosemide be administered as a means of decreasing intracranial volume. Microcirculation around contusions is enhanced by maintaining normovolemia and decreasing sympathetic discharge by maintaining adequate levels of anesthesia. This approach has been correlated with an improvement in outcome from traumatic brain injury over the past 10 years.

**J. Temperature regulation**

Hypothermia, an often overlooked issue in infants and small children, usually requires active heating in the operating room by elevating room temperature, using warm-air blankets, radiant warming lights, and humidification of inspired gases, and warming intravenous fluids. However, recent research with pediatric patients suggests that treatment with moderate hypothermia (32°C to 33°C) up to 24 hours after initial injury may decrease mortality.

**K. Positioning**

The extended duration of neurosurgical procedures and the unusual access requirements necessitate paying close attention to the positioning of the patient before placing surgical drapes. This can be achieved

through the use of careful padding of potential pressure points, checking peripheral pulses, and avoiding stretching of peripheral nerves. For patients operated on in the prone position, there must be free movement of the abdominal wall without undue flexion of the head. Excessive neck flexion may cause the endotracheal tube to kink, exert excessive pressure on the tongue, or advance the tube into a mainstem bronchus. The resultant hypoxia and hypercarbia will increase ICP, potentially leading to upper spinal cord and lower brain stem ischemia. Patients who already have posterior fossa abnormalities such as a mass lesion or Arnold-Chiari malformation are especially at risk for this complication. Pediatric patients may also experience flexion-induced swelling of the head and tongue from obstruction of venous and lymphatic drainage. This may result in postextubation obstruction of the airway or croup. Extreme rotation of the head can further limit venous return through the jugular veins, leading to increased ICP, impaired cerebral perfusion, and bleeding from cerebral veins.

**L. Emergence**

The goals for emergence include prompt awakening to aid early assessment of neurologic function, hemodynamic stability, and minimal coughing or straining on the endotracheal tube to avoid intracranial hypertension and bleeding. Patients may receive fentanyl before emergence; arterial hypertension is treated with drugs such as esmolol, labetalol, and hydralazine. Naloxone is avoided because its use has been associated with uncontrolled hypertension and coughing when the endotracheal tube is in place.

The trachea is extubated after the patient responds to commands or when infants and toddlers open their eyes. Alternatively, some anesthesiologists prefer to extubate the trachea when the patient is still deeply anesthetized as long as there are no contraindications (e.g., intraoperative catastrophe, loss of airway reflexes, poor preoperative condition, class III or IV airways). If the patient's awakening is delayed and no anesthetic cause can be determined, the presence of an acute neurologic issue should be ruled out by a computed tomography (CT) scan before tracheal extubation.

**M. Postoperative intubation**

There are several circumstances in which the trachea should remain intubated into the postoperative period. Operations that interfere with cranial nerve nuclei or brain stem function, with resultant impairment of airway reflexes and respiratory drive, require ongoing airway protection and ventilation until these functions can be assessed. The loss of several blood volumes, even with replacement, may necessitate continued maintenance of an artificial airway and protection of the airway reflexes due to fluid shifts and possible laryngeal edema. Also, prolonged operation in the prone position may lead to edema of the face and airway with the possibility of airway obstruction after extubation. If dexmedetomidine has been used in the intraoperative period with an initial loading dose of 1 to 2 mcg/kg over 10 minutes and a continuous infusion of 0.2 to 0.7 mcg/kg/hour, the infusion can be continued at the same rate in the postoperative period for up to 24 hours as a means of maintaining sedation. Of note is the fact that the rapid administration of dexmedetomidine may increase pulmonary artery pressure and pulmonary vascular resistance.

**N. Postoperative care**

Complications in the postoperative period involve a number of organ systems. Respiratory dysfunction in the form of apnea or irregular breathing occurs

frequently after posterior fossa craniectomy leading to prolonged postoperative intubation. There may also be airway obstruction secondary to either edema or cranial nerve injury. Operative injury to either the hypothalamus or the pituitary gland can lead to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) or diabetes insipidus (DI) manifesting as seizures, changes in the level of consciousness, and abnormalities of fluid and electrolyte (especially sodium) balance. When children require sedation for endotracheal intubation postoperatively, the administration of propofol is not recommended for long-term sedation due to reports of children who have developed metabolic acidosis, lactic academia, and bradyarrhythmias after prolonged infusion. Avoidance of propofol infusion syndrome can likely be achieved by limiting infusions to < 48 hours in duration with infusion rates less than approximately 70 mcg/kg/minute and with monitoring for acid/base disturbances.

## V. NEUROANESTHETIC MANAGEMENT FOR SPECIAL PROCEDURES

### A. Hydrocephalus

#### 1. Etiology

Hydrocephalus is caused by the enlargement of the ventricles from increased production of CSF, decreased absorption of CSF by the arachnoid villi, or obstruction of the CSF pathways. It is often manifested as an increase in the head circumference in pediatric patients. Hydrocephalus is typically classified as communicating/non-obstructive or non-communicating/obstructive (see Table 15.2). The causes of increased CSF collection can be congenital or acquired.

#### 2. Preoperative management

The patient should be assessed for any effects of elevated ICP such as nausea or vomiting, changes in the ventilatory pattern, irritability, decreased level of consciousness, bradycardia, or hypertension. Further, obtaining a CT scan may demonstrate increases in the size of the ventricles. Sudden neurologic deterioration in the pediatric patient must be treated quickly with emergent endotracheal intubation, muscle relaxation, hyperventilation with $ETCO_2$ monitoring, and administration of drugs to reduce cerebral metabolic demands (e.g., barbiturates) and diuretics (e.g., mannitol and furosemide) until emergency surgical reduction of the ICP is achieved. In rare circumstances, control of ICP is accomplished by direct needle puncture of the lateral ventricle and aspiration of CSF or by emergency bedside placement of CSF drains.

TABLE 15.2 Causes of Hydrocephalus

| Communicating | Non-communicating |
|---|---|
| – Aqueductal stenosis | – Intraventricular hemorrhage |
| – Myelomeningocele | – Space-occupying lesions |
| – Arnold-Chiari malformation | – Infections (abscess or meningitis) |
| – Spina bifida | |
| – Dandy-Walker syndrome | |
| – Mucopolysaccharidosis (with subarachnoid space obliteration) | |
| – Achondroplasia (with occipital bone overgrowth) | |

3. **Premedication**
   Sedation is relatively contraindicated in patients who have hydrocephalus because the resulting hypoventilation may increase ICP. EMLA cream (a **e**utectic **m**ixture of **l**ocal **a**nesthetics, namely lidocaine and prilocaine) may be safely used whenever possible to achieve intravenous access without causing distress to young patients.
4. **Surgical procedures**
   Surgical management of hydrocephalus can include the placement of ventriculoperitoneal shunts, ventriculoatrial shunts, ventriculopleural shunts, ventriculojugular shunts, or the performance of a ventriculostomy. However, drainage of CSF can be a problem because cardiac arrhythmias may be associated with the rapid removal of CSF. In some circumstances, epidural or subdural hemorrhages can result from a sudden reduction in the ICP. Such a sudden change in ICP from hemorrhaging can cause a rapid change in the level of consciousness of the child even though the shunt may still be functioning adequately.
5. **Anesthetic considerations**
   An inhalation induction is usually not attempted in the setting of hydrocephalus because all inhalational anesthetics are potent cerebral vasodilators and can increase ICP. A modified rapid-sequence intravenous induction (RSI) is the preferred technique to minimize the risk of aspiration from either gastric hypotonia, secondary to the effects of increased ICP, or from a recent meal. In a modified RSI, preoxygenation is followed by intravenous induction with a sedative–hypnotic (e.g., barbiturate or propofol) and a fast-acting non-depolarizing muscle relaxant, such as rocuronium, is administered for ease of intubation. Muscle relaxation is maintained throughout the procedure along with TIVA using propofol and fentanyl or propofol, dexmedetomidine, and fentanyl. Intravenous fluid is given at a maintenance level, and either intravenous ceftriaxone or vancomycin is given (after checking sensitivity) slowly (over 60 minutes) and in a diluted solution (no more than 5 mg/mL) to prevent histamine release and Red Man Syndrome.
6. **Postoperative management**
   At the end of the procedure, the stomach is suctioned and the trachea is extubated when the patient is fully awake. This is usually not a problem as long as the shunt is functioning well. The patient should remain on monitors in the postoperative period with frequent neurologic evaluations looking for signs of elevated ICP.

**B. Craniosynostosis**

1. **Etiology**
   While craniosynostosis is usually a sporadic (i.e., non-genetically transmissable) congenital anomaly resulting from premature fusion of one or more of the six cranial sutures, a genetic defect association with craniosynostosis is currently being researched. In approximately 25% of the cases, craniosynostosis can occur in families due to autosomal dominant or recessive transmission and, in such cases, affects males and females equally. Typically, however, in non-genetic-based craniosynostosis, males are affected twice as frequently as females and the occurrence is in approximately 1 out of 2,000 live births. Since craniosynostosis can also be seen in conjunction with other syndromes such as Apert, Crouzon, and Pfeiffer, a patient's comorbidities must also be investigated. While there are numerous types of craniosynostosis, plagiocephaly, involving premature fusion of the left or right coronal suture, occurs most commonly. Trigonocephaly, involving early fusion of the metopic

(forehead) suture, and scaphocephaly, involving early fusion of the sagittal suture, are also commonly seen. Children will present with an obvious deformity of the face and head but may also present due to difficulty breathing, sleep apnea, and delayed growth, behavior, or speech patterns. Craniosynostosis can cause severe cranial deformity, depending on the involved sutures, and may lead to intracranial hypertension with psychomotor retardation from abnormal brain growth. As infant brain growth is very rapid and because there is no medical treatment for craniosynostosis, surgery is usually performed in the first 6 months of life.

2. **Preoperative management**
   Patients often are otherwise healthy but, in a small percentage of cases, may have underlying comorbidities. As such, assessment for any evidence of increased ICP, congenital cardiac or pulmonary defects, and metabolic derangements may be necessary. Hemoglobin/hematocrit (Hgb/Hct) is determined preoperatively, and blood must be made available prior to surgery in case a blood transfusion needs to be started at the beginning of the surgery. Even though the surgery is not intradural, the surgeons work in close proximity to major venous sinuses, so sudden and massive blood loss is always a concern. Additionally, a significant amount of blood is lost from the scalp and cranial bones and may become larger with an increase in the number of sutures repaired. Anticoagulation studies are not usually obtained unless clinically indicated.
3. **Monitoring**
   Intraoperative monitoring includes ECG, $SpO_2$, $ETCO_2$, NIBP, and esophageal/rectal temperature as well as an arterial catheter for direct blood pressure and arterial blood gas (ABG) measurements. Placement of a precordial Doppler is also recommended due to the increased incidence of VAE noted during craniosynostosis repair. The patient must have at least two good intravenous lines for adequate access and a urinary catheter to monitor urinary output.
4. **Anesthetic considerations**
   Induction of anesthesia can be achieved via either inhalational or intravenous techniques if a catheter is already in place. The endotracheal tube should be well secured so that ventilation is undisturbed with head movements. Anesthesia can be maintained with an inhalational drug, air/oxygen, an intermediate-acting non-depolarizing relaxant, a narcotic (fentanyl or morphine) for analgesia, and/or TIVA (e.g., propofol). Nitrous oxide should, however, be avoided in craniosynostosis repair due to the risk of VAE.
5. **Surgical procedures**
   Intraoperative transfusing of blood has been the norm for craniosynostosis repairs because of blood loss from the scalp and cranium, proximity to venous sinuses, and an infant's physiologic anemia. However, recent advances in surgical techniques (e.g., barrel-stave osteotomies) and the use of hemostatic drugs (e.g., gel foam, Avitene, and thrombin), in addition to the use of bone wax, have dramatically reduced the need for intraoperative blood transfusions. Ongoing studies are underway to evaluate the utility and efficacy of these hemostatic drugs by obtaining serial Hgb/Hct levels in the perioperative period. In addition to obtaining a preoperative Hgb/Hct, these levels should be checked again immediately following the craniotomy during which the greatest amount of blood loss occurs. A final

Hgb/Hct can be obtained as the surgeons are closing the operative site.

A key point in the procedure occurs when the surgeons manipulate the sagittal sutures due to the possibility of VAE. The likelihood of VAE may be decreased by maintaining intravascular blood volume and entrainment of air may be detected by continuous monitoring with Doppler ultrasonography. If evidence of VAE exists, alerting the surgical team enables them to irrigate the entire field with saline, which, along with assumption of the head-down position, prevents further entrainment of intravenous air and enhances hemodynamic stability. If a central venous catheter is in place, the anesthesiologist may also attempt to aspirate air from the central circulation.

6. **Postoperative management**

At the conclusion of the procedure, the patient is first awakened and then the trachea is extubated. Typically, the hematocrit is measured during the recovery period because blood loss continues from the surgical incision, and patients may need either blood or blood products to counteract oozing. However, with newer techniques, patients often do not require intraoperative transfusions and are able to maintain their hematocrit levels in the postoperative period. Ensuring adequate urine output (> 1 mL/kg/hour) throughout the procedure can further indicate the adequacy of intraoperative volume resuscitation and regional organ perfusion.

C. **Intracranial tumors**

1. **Etiology**

Intracranial tumors are the most common solid tumors of childhood and the second most common pediatric cancer after the leukemias. While supratentorial tumors arise from midline structures, the majority of intracranial malignancies are due to infratentorial tumors, two-thirds of which are located in the posterior fossa. The pathologic distribution includes gliomas (30%), medulloblastomas (30%), astrocytomas (30%), ependymomas of the fourth ventricle (7%), and others (3%: acoustic neuromas, meningiomas, etc.). All intracranial tumors increase intracranial volume and, thereby, have a direct effect on ICP. Infratentorial lesions produce signs and symptoms of brain stem compression (e.g., respiratory or cardiac abnormalties, cranial nerve palsies, and ataxia). Additionally, intracranial hypertension from hydrocephalus, secondary to obstruction of flow of CSF, can be seen in lesions near the posterior fossa. Craniopharyngiomas, accounting for 9% of all childhood intracranial tumors, are the most common tumor of the hypothalamic–pituitary area, and may cause disorders of the neuroendocrine system, including DI.

2. **Preoperative management**

Signs and symptoms of increased ICP should be noted as well as the possible need for performing either a ventriculostomy or a shunt before the definitive operation. Patients most commonly present with headaches and vomiting for several days or weeks. Neonates and infants may have a history of poor feeding, irritability, or lethargy. The anterior fontanelle may bulge, eyes may exhibit a "sunset sign," or the cranium may be enlarged. There may be obvious engorgement of the scalp veins, and some patients may show changes in the level of consciousness or focal neurologic deficits, depending on the area of brain compression. Posterior fossa tumors may cause cranial nerve dysfunction, along with signs and symptoms of increased ICP. An endocrine evaluation should

be performed if a craniopharyngioma is suspected along with a plan for steroid replacement to compensate for damage to the hypothalamic-pituitary axis. The hypovolemia and electrolyte imbalance caused by DI are typically corrected before surgery is undertaken.

3. **Monitoring**
   Intraoperative monitoring includes ECG, $SpO_2$, $ETCO_2$, NIBP, and esophageal/rectal temperature. In addition, an arterial catheter for direct hemodynamic monitoring, ABG measurements, and determination of blood chemistry is necessary for pediatric patients undergoing craniotomy. The patient must have at least two good intravenous lines for adequate access and a urinary catheter to monitor urinary output. A central venous catheter is recommended when blood loss is expected, when there is a concern about DI and SIADH, or when the head position and the surgical approach increase the risk of VAE. The femoral vein is recommended for central venous access in small children because of the ease of entry and lack of interference with cerebral venous drainage, as may occur when the jugular veins are cannulated. This location diminishes a central line's utility, however, for treatment of VAE.
4. **Anesthetic considerations**
   a. The history is reviewed and documented to include the presence of seizures and measures taken to control them. A complete physical examination to identify any neurologic deficits is also performed and noted.
   b. The anesthesiologist assesses the patient for signs and symptoms of increased ICP and DI and reviews the results of investigative procedures such as CT scan and magnetic resonance imaging (MRI).
   c. Measures to control ICP, including insertion of either a ventriculostomy or shunt before the definitive operation, are noted. Elevated ICP can also be decreased by the use of dexamethasone (to reduce peritumoral edema), furosemide (which also reduces CSF production), or hypertonic saline. The routine use of mannitol is not advised when the presence of a craniopharyngioma is suspected because it may interfere with the intraoperative identification of DI. The incidence of perioperative DI varies between different publications from 0.5% to 25% of cases.
   d. Patients who have increased ICP may have either altered gastric emptying or dehydration and electrolyte imbalances from poor feeding, vomiting, and SIADH.
   e. The patient's position is discussed with the surgeon, and the head is positioned to avoid any obstruction to venous return. The Mayfield horseshoe headrest is almost exclusively used for prone positioning because pins may cause skull fractures, dural tears, and intracranial hematomas in the pediatric population. Blood is typed and cross-matched and immediately available in the operating room. Although DI is more common in the postoperative period, one must remain vigilant for the presence of intraoperative DI manifested by a sudden increase in dilute urine output. Intraoperative DI may be treated with an infusion of intravenous arginine vasopressin (1 to 10 mU/kg/hour) and administration of intravenous fluids to match the urine output.
   f. Induction is focused on measures to reduce the ICP. The recommended sequence for patients with an existing peripheral catheter is (1) intravenous induction, (2) hyperventilation, and (3) gentle, brief laryngoscopy to secure the airway. The use of bupivacaine 0.25% with

epinephrine 1:200,000 to infiltrate the scalp prior to skin incision confers analgesia and decreases the anesthetic requirement as well as bleeding. Note, however, that limiting the total dose to 1 mL/kg of the bupivacaine 0.25% mixture avoids toxicity.

**g.** Intraoperative concerns include optimal positioning of the head, maintaining body temperature, and adequately replacing fluid and blood loss. The anesthetic technique (air; oxygen; low concentration of inhaled anesthetic; a non-histamine-releasing, non-depolarizing muscle relaxant; and a short-acting narcotic) is designed to avoid oversedation and allow early assessment of neurologic function at the completion of surgery. Positioning and hyperventilation may be used to minimize brain swelling. If necessary, mannitol, 0.25 to 1 g given intravenously, and furosemide may be added, although this negates the use of urine output as an indication of intravascular volume status.

**5. Postoperative management**

A smooth and prompt emergence from anesthesia is desirable. The decision to extubate the trachea of pediatric patients depends not only on the length of the procedure but also on the intraoperative course of events, the extent of the tumor resection, the expected neurologic deficits, and the probability of loss of protective airway reflexes (i.e., gag, cough, and swallow). Additionally, one must consider the possible necessity for continued postsurgical airway protection based upon the possibility of seizures and the degree of need for postoperative control of ICP.

Operation in the posterior fossa may cause either damage to or edema around the brain stem respiratory center or cranial nerves innervating the vocal cords and soft tissues of the upper airway. This may result in apnea, stridor, or postextubation airway obstruction. The administration of drugs, including phenytoin, and the monitoring of ABG, hematocrit, blood chemistry, fluid balance, and neurologic function should be continued in the postoperative period. As previously mentioned, abnormalities in ADH release from the posterior pituitary, manifesting as DI, can be a common postoperative condition. This central form of DI can present with sudden increased urine output, increased serum sodium concentrations, and increased serum osmolarity. Treatment is with fluid replacement to match urine output and with an infusion of vasopressin or intranasal desmopressin (e.g., children 3 months to 12 years of age can receive 0.05 to 0.3 mL or 5 to 30 mcg given as a single dose or divided into two doses a day). The advantage of desmopressin is that it can be administered intranasally twice a day instead of a continuous intravenous infusion as is the case with vasopressin.

## D. Surgery for epilepsy

**1. Etiology**

Epilepsy is a very common neurologic disorder in the pediatric population, with an incidence of almost 1%. While most patients' seizures can be medically managed with anticonvulsants, some patients experience too many medication side effects or may have seizures that are unresponsive to standard medical therapy. Medically unresponsive seizure activity can have deleterious effects on the development of the brain leading to permanent speech, motor, and psychosocial dysfunction. There are also patients who require surgical intervention for intractable seizures owing to congenital disorders, birth trauma, tumors, or vascular malformations.

Perioperative risks arising from status epilepticus include severe hypoxemia and sudden death. The chronic use of large doses of anticonvulsant (e.g., phenytoin and carbamazepine) for the medical management of seizures may alter pharmacologic response because of enzyme induction, liver dysfunction, and jaundice. This may result in rapid metabolism and clearance of anesthetic drugs including narcotics and muscle relaxants. Anesthetic requirements are, therefore, increased, and patients require more frequent administration of anesthetic drugs.

2. **Preoperative management**

Preoperative assessment includes determining the age of onset, type, and frequency of the seizures and any noted deficits in mental status and development. Recent changes in the level of consciousness and a brief neurologic exam must be documented. CBC, electrolytes, and a coagulation profile are obtained preoperatively and, due to the possibility of significant blood loss from the craniotomy, patients should be typed and cross-matched with blood readily available in the operating room.

When targeting important areas of the brain such as the motor cortex and the speech centers, it is preferred that surgery be performed under local anesthesia. For such "awake" procedures, establishing rapport with the patient and explaining the state of dissociation, lack of pain (neuroleptanalgesia), and need for cooperation are essential for the success of the operation. However, young children and those with evidence of anxiety, developmental delay, and psychiatric illness will need general endotracheal anesthesia. Under these circumstances, electrophysiologic monitoring will be required intraoperatively.

No sedatives or anticonvulsants are administered for 48 hours if electrophysiologic studies are to be conducted intraoperatively. Additionally, all patients should receive dexamethasone for 48 hours preoperatively in order to control brain swelling. Ultrashort-acting barbiturates are readily available to control seizure episodes in the perioperative period.

The fluid warmer is used to maintain normothermia. The patient is well padded because these procedures may be lengthy.

3. **Monitoring**

Routine monitors, including a urinary catheter, are employed, and normocapnia is usually maintained during the procedure. Intravenous catheters, arterial catheters, and nerve stimulators are placed on the limbs not being used by the surgeons to observe motor function during the localization of the seizure focus. This is discussed with the surgeons in advance and explained to the patient. Neurophysiologic monitoring is used to guide the actual resection of the epileptogenic focus because it may be in close proximity to areas in the cortex controlling memory, speech, and sensory and motor function. Note that since general inhalational anesthesia can affect the sensitivities of these monitoring modalities, TIVA (e.g., with propofol and narcotics) may be more preferable.

4. **Anesthetic considerations**

While all inhalational anesthetics depress cerebral activity and are typically avoided during EEG studies, the successful use of low concentrations of isoflurane in combination with narcotics has been reported in several centers. Nitrous oxide is avoided for repeat craniotomies, as for removal of electrocorticographic leads or depth electrodes, until the dura is opened because intracranial air may persist for up to 3 weeks after the initial craniotomy. Additionally, $N_2O$ is avoided due to its

interference with neurophysiologic monitoring. Propofol induces dose-dependent changes in the EEG with an increase in beta activity at low infusion rates and an increase in delta activity, followed by burst suppression, at high infusion rates (e.g., > 200 to 300 mcg/kg/minute). Etomidate is not recommended because it produces interictal spiking and might induce clinical seizures in these patients. Ketamine activates epileptogenic foci in epileptic patients and is not recommended. Dexmedetomidine has not been shown to cause any changes in EEGs or SSEPs but can cause significant decreases in MEP amplitudes. A combination of propofol and fentanyl or dexmedetomidine and fentanyl can be used during awake craniotomies. However, propofol or dexmedetomidine should be discontinued approximately 20 minutes before electrophysiologic monitoring is to begin in order to ensure adequate patient feedback.

Non-depolarizing relaxants have no effect on electrical activity. Nevertheless, the dose requirements are higher, due to the interaction with the anticonvulsant drugs. No muscle relaxant is used during the period of direct cortical stimulation so that the surgeons can observe motor activity. This is essential when cortical stimulation of the motor strip is performed under general anesthesia.

5. **Postoperative management**

Careful monitoring of neurologic function is vital during the first 24 hours after the operation. Motor, memory, or speech dysfunction or increased seizure activity may occur in the postoperative period. The hematocrit is monitored because blood loss from a large cranial incision can be considerable. Postoperative pain must also be controlled to avoid episodes of hypertension. Lastly, short-acting barbiturates or propofol should be made readily available in order to treat seizure activity.

**E. Head trauma**

1. **Etiology**

Skull fractures and head injury can occur at all ages as a result of trauma during birth, traffic and playground accidents, domestic negligence, or abuse. Skull fractures may be depressed, open, or basal skull fractures and can increase morbidity and mortality if unrecognized. While traumatic sequelae including epidural, subdural, and intracerebral hematomas are more common in adults, cerebral contusions and edema with signs of intracranial hypertension more commonly occur in pediatric patients as a result of traumatic head injury. Additionally, there is a 5% to 36% incidence of DI following traumatic brain injuries.

a. **Epidural hematomas**

Epidural hematomas account for 25% of all intracranial hematomas and are considered to be true medical emergencies. Most frequently caused by a tear in the middle meningeal artery, epidural hematomas can lead to a decreasing level of consciousness, papillary dilatation, hemiparesis, posturing, or coma. Patients require urgent surgical evacuation of the hematoma and achievement of rapid intracranial hemostasis.

b. **Subdural hematomas**

Subdural hematomas result from parenchymal contusion or blood vessel tears sustained during birth trauma or shaking, as in shaken baby syndrome. Such injuries can cause brain edema and progressive neurologic dysfunction. Treatment consists of ICU monitoring, oxygen therapy, and possible mechanical ventilation. Anticonvulsants and/or surgical intervention may also be required in the event of seizure activity, intracranial bleeding, or traumatic skull fractures.

c. **Skull fractures**
Skull fractures are of concern if they involve major blood vessels and, if depressed, they may require surgical elevation and might be associated with dural lacerations. Signs and symptoms depend on the extent of cortical injury. Basilar fracture might cause periorbital ecchymoses, hemotympanum, changes in the level of consciousness, and seizures.

2. **Preoperative management**
A CT scan is necessary for adequate assessment of the extent of neurologic injury and possible intracranial hypertension. Establishing an airway, maintaining adequate ventilation and circulation, and determining the level of consciousness are of paramount concern. One must also remain vigilant for associated injuries, such as blunt trauma to the abdomen and chest and long-bone fractures, which may cause rapid blood loss, cardiovascular instability, and thermoregulatory problems. Even though cervical spine injury is rare in the pediatric population, the cervical spine should be evaluated and immobilized in all pediatric trauma patients until the presence of a cervical fracture is ruled out. Additionally, renal function must be investigated and the urine analyzed for hematuria. The need for preoperative evaluation of hematocrit, coagulation profile, and acid–base and electrolyte balance depends on the type and extent of injury. However, blood for transfusion must be available and circulating blood volume restored with blood, crystalloid or both.

3. **Monitoring**
Routine monitors and an arterial catheter for direct blood pressure monitoring are essential. Adequate intravenous access is necessary for volume resuscitation as is a urinary catheter.

4. **Anesthetic considerations**
Volume resuscitation precedes the rapid-sequence induction of anesthesia, which is achieved by the administration of thiopental or propofol, a narcotic, and a non-depolarizing muscle relaxant of rapid onset (e.g., rocuronium 1 to 1.2 mg/kg intravenous push). Note, however, that the dose of any sedative or hypnotic should be reduced in hypovolemic patients. The trachea is intubated with the head in "neutral position" using standard, video-assisted, or fiberoptic laryngoscopy to avoid any injury to the cervical spine. Upon successful intubation, ventilation is controlled to avoid increasing ICP. Maintenance of anesthesia with air, oxygen, low-dose inhalational anesthetic, and narcotic allows prompt emergence for early neurologic assessment. Poor preoperative condition and adverse intraoperative events argue against early awakening and extubation.

5. **Postoperative management**
Continued monitoring and control of ICP is vital in the postoperative period. The patient should remain intubated, sedated, and mechanically ventilated in the ICU if there is concern about either neurologic or organ system dysfunction.

F. **Meningomyelocele and encephalocele**

1. **Etiology**
Embryologic neural tube fusion takes place during the first 3 to 4 weeks of gestation. Failure of neural tube fusion leads to herniation of the meninges (meningocele) or elements of the neural tube (myelomeningocele) and can occur at any level of the spinal cord. Abnormalities occurring at the level of the head are referred to as encephaloceles. Such defects, arising at higher levels in the spine, can produce severe bowel, bladder, and lower extremity dysfunction. Most of these patients also have an Arnold-Chiari malformation, which is a downward displacement

of the cerebellar tonsils near or through the foramen magnum, often resulting in hydrocephalus from CSF outflow obstruction. Surgery is performed at the earliest opportunity (usually in the first week of life) to avoid infection of the CNS.

These patients frequently have or may develop latex allergy, either because of repeat exposure (as from frequent catheterization) or because of a genetic propensity and, thereby, need to be treated from birth as if they do have a latex allergy. The incidence of latex sensitivity in spina bifida patients ranges from 34% to 100%. The allergic reactions that may result from exposure to latex range from mild airway involvement (tingling of the lips, facial swelling, wheezing) to severe anaphylaxis with cardiovascular collapse. Severe anaphylaxis should be immediately treated by (1) removal of the inciting latex substance, (2) the administration of fluid, (3) intravenous epinephrine (10 mcg/kg), (4) vasopressors, (5) steroids, (6) diphenhydramine (H1 histamine blocker), and (7) famotidine/ranitidine (H2 histamine blockers). The recommended next steps are to send blood for latex specific IgE (RAST) blood test and to alert the patient's parents of an allergy to latex.

2. **Preoperative management**
   Patients are evaluated for signs and symptoms of hydrocephalus and the presence of any airway problems due to a large encephalocele or thoracic myelomeningocele. There may be considerable evaporative losses with subsequent problems in maintaining body temperature and fluid balance. A hematocrit must be checked preoperatively and blood should be made available for intraoperative transfusion during the repair of large defects. The defect should be well padded in the perioperative period to avoid any complications from compression, CSF leak, bleeding, and infection.
3. **Monitoring**
   Routine monitoring is used. Patients who are expected to experience significant blood loss should have adequate intravenous access for transfusion, an arterial line, and a urinary catheter. Electromyographic monitoring is used to identify functional nerve roots during operation for tethered cord release. The surgical goal is to minimize injury to nerves innervating muscles of the anal sphincter and lower extremities.
4. **Anesthetic considerations**
   Intravenous access should be established before induction. Positioning and airway management may be particularly challenging with a large encephalocele. The patient should be placed in the lateral or supine position with the encephalocele or myelomeningocele padded in a "doughnut" support. Intravenous atropine is given and the trachea may be intubated either awake or after the intravenous administration of a sedative–hypnotic (e.g., thiopental, propofol) and a non-depolarizing muscle relaxant. Additional relaxant should not, however, be given if the surgeon plans to use intraoperative nerve stimulation and electromyographic monitoring. Anesthesia can be maintained with a low concentration of inhalation drug and a narcotic suited to the length of the procedure. Temperature, blood loss, and fluid balance must be monitored closely during the procedure based upon the extent of the defect. The trachea may be extubated after the patient awakens at the end of the procedure and neurologic integrity has been confirmed.
5. **Postoperative management**
   Many infants are at risk for postoperative apnea, including all preterm infants < 50 weeks postconceptual age, patients who have known central or obstructive sleep apnea, and infants who have RDS. These patients

should have $SpO_2$, apnea, and bradycardia monitors in place for overnight observation.

**G. Craniofacial surgery**

**1. Etiology**

Craniofacial deformities (e.g., cleft lip, cleft palate, and hemifacial microsomia) are conditions, much like craniosynostosis deformities, associated with premature closure of the cranial sutures. They are among the most common birth defects in the world occurring in 1 in 1,000 live births. Premature cranial suture closure may be one manifestation of a number of congenital syndromes (e.g., Apert, Goldenhar, Pierre-Robin, Treacher-Collins, or branchial arch syndrome) and is often associated with anomalies involving the heart or other midline organs. Patients may be born prematurely and may have respiratory dysfunction in addition to a difficult airway from the craniofacial deformity.

**2. Preoperative management**

**a.** Detailed evaluation of the etiology of the craniofacial abnormality as well as the presence of associated anomalies is vital. Careful note of any anticipated airway management problems must be made. Previous anesthesia records can be reviewed if the patient has had cardiac or other corrective surgeries in the past.

**b.** The choice of laboratory investigations depends on the specific craniofacial defect and may include an ECG or consultation with a cardiologist.

**c.** Considerations of tracheotomy for airway management in the perioperative period are an important aspect of patient evaluation.

**d.** Significant blood loss is always a concern during these procedures. Therefore, adequate amounts of blood and blood products should be available.

**e.** The ambient temperature in the operating rooms should be increased to facilitate the maintenance of body temperature and airway humidity during what frequently turns out to be a lengthy procedure.

**f.** Fluid warmers are used to warm infusions. Blood replacement is started early and continued in the postoperative period.

**3. Monitoring**

Intraoperative monitoring includes ECG, $SpO_2$, $ETCO_2$, NIBP, and esophageal/rectal temperature. In addition, an arterial catheter for direct hemodynamic monitoring, ABG measurements, and determination of blood chemistry is often necessary for pediatric patients undergoing craniofacial reconstruction. The patient must have at least two good intravenous lines for adequate access and a urinary catheter to monitor urinary output. A central venous catheter is usually not required except when difficult intravenous access is anticipated.

**4. Anesthetic considerations**

**a.** Establishment of good intravenous access is important because these procedures tend to be long and can occasionally involve significant blood loss.

**b.** Every attempt is made to keep the patient warm during surgery by increasing the ambient temperature and using a forced-air warming blanket, heated humidifier, and fluid warmer.

**c.** The successful maintenance of fluid balance is ascertained by hematocrit, urine output, and ABG measurements.

**d.** The coagulation profile should be checked after replacement of one blood volume, especially if continued loss and replacement are expected.

e. Air embolism is always a concern when there is extensive bone dissection.
f. Resuscitation drugs should be available during the procedure.
g. Anesthesia can be induced with either an inhalational anesthetic (e.g., sevoflurane) if airway problems are anticipated or with intravenous drugs if the patient has an intravenous catheter in place and there is no potential problem with the airway. The endotracheal tube must be well secured, especially if the patient is to be operated on in the prone position. Eyes may be lubricated with hypoallergenic ointment and taped securely closed. All pressure points must be well padded particularly in long craniofacial reconstruction procedures. Surgeons may request intravenous steroids and the intraoperative reduction of intracranial volume to help with the retraction of the frontal lobes during dissection of the orbital structures. Maintenance of anesthesia is usually with air, oxygen, a long-acting non-depolarizing muscle relaxant, and a narcotic for analgesia.

5. **Postoperative management**
Intubation of the trachea usually continues into the postoperative period after craniofacial surgery mainly to ensure adequate ventilation. Airway and breathing problems may arise owing to the length of the procedure, expected fluid shifts from massive transfusion, and the use of intraoperative narcotics. Postoperative transfusions might also be required because of continued slow bleeding from the surgical site.

## H. Vascular anomalies

1. **Arteriovenous malformations (AVMs)**
   a. **Etiology**
   AVMs are usually congenital, abnormal connections arising between arteries and veins and can appear in any location along the vascular tree. Most AVMs do not cause any symptoms in patients and are typically incidentally discovered. However, AVMs can be associated with high-output congestive heart failure in infants who may require hemodynamic support. AVMs may also manifest as headaches, seizures, muscle weakness or paralysis, and strokes, in the event of cerebral AVM rupture. Treatment is limited to intravascular embolization (i.e., selective obstruction of blood supply with particulate matter) performed by an interventionalist, radiation for deep AVMs, or surgical excision.
   b. **Preoperative management**
   Because the operation for the ligation of an AVM is associated with considerable blood loss, these patients should have a baseline Hgb/Hct and coagulation profile obtained in the preoperative period. Additionally, these patients should be typed and cross-matched, with blood readily available in the operating room.
   c. **Monitoring**
   Intraoperative monitoring includes ECG, $SpO_2$, $ETCO_2$, NIBP, and esophageal/rectal temperature. In addition, an arterial catheter for direct hemodynamic monitoring and ABG measurements is necessary for pediatric patients undergoing AVM embolization or surgical excision. The patient must have at least two good intravenous lines for adequate access and a urinary catheter to monitor urinary output. A central venous catheter is recommended when blood loss is expected or when inotropic drugs are being used in the setting of infant high-output heart failure secondary to a large AVM.

d. **Anesthetic considerations**
Anesthetic management of this procedure is usually undertaken with a general anesthetic and muscle relaxation. Additionally, these patients receive anticonvulsants as well as moderate hypothermia and hyperventilation in order to improve surgical visualization via vasoconstriction. The anesthesiologist needs to be prepared to treat the sudden hypertension and hyperemic cerebral edema that may develop after ligation of the AVM. In addition to the administration of intravenous narcotics and volatile anesthetic drugs, this treatment includes hyperventilation and the administration of labetalol and/or sodium nitroprusside. One must also be vigilant about the potential of fluid overload in infants with AVMs secondary to high-output cardiac failure and the administration of intraoperative intravenous contrast drugs.

e. **Postoperative management**
The patient should remain sedated and mechanically ventilated in the ICU if there is concern about either neurologic or organ system dysfunction secondary to AVM embolization or excision. Typically, however, the trachea is extubated postoperatively in order to facilitate neurologic examination by the surgeon.

2. **Moyamoya disease**

a. **Etiology**
**Moyamoya disease** is a progressive, chronic vasculo-occlusive disorder limited to the intracranial vasculature, particularly the internal carotid arteries. It is so named because, on angiography, the vessels appear as a "puff of smoke," secondary to tremendous collateralization occurring in the setting of vascular occlusion. This disease can be associated with neurofibromatosis, Down's syndrome, previous intracranial radiation, or hematologic disorders and is more common in pediatric patients with Japanese ancestry. Patients may present with transient ischemic attacks, recurrent strokes, or progressive neurologic defects. Medical management can be achieved with antiplatelet therapy although surgery with redirection of other arteries to the occluded artery is the treatment of choice.

b. **Preoperative management**
Because the operation for treatment of moyamoya can be associated with considerable blood loss, these patients should have a baseline Hgb/Hct. In the setting of antiplatelet therapy, a coagulation profile should be obtained in the preoperative period. These patients should also be typed and crossed, with blood readily available in the operating room. Finally, the physical exam in patients with moyamoya should also focus on symptomatic comorbidities, like those found in neurofibromatosis or Down's syndrome.

c. **Monitoring**
Intraoperative monitoring includes ECG, $SpO_2$, $ETCO_2$, NIBP, and esophageal/rectal temperature. In addition, an arterial catheter for direct hemodynamic monitoring and ABG measurements is necessary for these pediatric patients. The patient must have at least two good intravenous lines for adequate access and a urinary catheter to monitor urinary output. A central venous catheter is usually not necessary in these cases except in the setting of poor intravenous access or anticipation of significant blood loss.

**d. Anesthetic considerations**

Anesthetic management involves the enhancement of cerebral perfusion through adequate preoperative hydration, intraoperative maintenance of the preoperative blood pressure, normothermia, and normocapnia to avoid steal from ischemic areas of the brain. Hyperventilation must be avoided as this may reduce regional blood flow, leading to ischemia and neurologic changes. The combination of air, oxygen, propofol, and narcotic, in addition to muscle relaxation, confers a stable level of anesthesia and permits the use of intraoperative EEG monitoring.

**e. Postoperative management**

Cerebral perfusion is maintained in the postoperative period through optimal intravenous hydration and adequate pain management to avoid cerebral vasoconstriction from hypertension and hyperventilation.

## VI. NEURORADIOLOGY

### A. Anesthetic management of neurodiagnostic and neurointerventional procedures

Most pediatric patients require some level of anesthesia for neuroradiologic diagnostic procedures such as CT scanning, MRI, angiography, and myelography, as well as interventional procedures and radiation therapy. This is usually because of age (infants), anxiety, lack of understanding and cooperation, developmental delay, and an inability to remain still for any length of time. Mild sedation is employed in older, cooperative children undergoing short procedures that do not produce pain and discomfort. Anesthesia is frequently administered in locations remote from the operating suite, which means that the same equipment and level of assistance must be available. In addition, the radiologists and their staff must be educated so that they understand the anesthesiologist's issues and concerns regarding pediatric patients.

**1. Magnetic resonance imaging (MRI)**

MRI makes use of the intense magnetic field emanating from a large static magnet in order to create anatomic tissue images without the use of radiation. Performing anesthesia in a magnetic field with the patient in an MRI tunnel, however, presents unique challenges.

**a.** The patient must be absolutely still and isolated within the tunneled scanning space during the examination. This may cause increased anxiety and induce claustrophobia in pediatric patients.

**b.** All ferromagnetic objects must be removed from the patient because they may induce motion artifact in the magnetic field. Patients must be checked for any metal objects such as aneurysm clips, artificial joints, and cochlear implants. Metal braces frequently present in the oral cavity of pediatric patients pose a particular problem as they are not removable and may cause excessive artifacts. Even medication patches applied to the skin containing trace amounts of metal, such as clonidine or fentanyl patches, can induce heat in these powerful magnetic fields and have been shown to cause burn injuries.

**c.** Ferromagnetic objects should ***never*** be brought into the room housing the magnet. This presents a particular problem to anesthesiologists whose equipment often contains high levels of ferromagnetic material. Anesthesia monitors, ventilators, and laryngoscopes must all be specially designed to be able to function in a magnetic field without containing any ferromagnetic materials.

d. The intravenous infusion of propofol or dexmedetomidine administered by means of an MRI-compatible pump is an effective anesthetic technique for these procedures. Alternatively, inhalation anesthesia may be administered with an MRI-compatible anesthesia machine using a laryngeal mask airway or an endotracheal tube.

2. **Computed tomography (CT) scanning**
   CT scanning is a medical imaging method that, through digital processing, can create a 3D image from a large series of 2D x-ray images. Undergoing a CT scan requires understanding and cooperation on the part of the patient who will need to remain still throughout the procedure in order to secure diagnostic images of high quality. Sedation is often used to enhance patient cooperation even though CT scans are much shorter in duration than MRI scans. Neonates may be scanned without any sedation because they will frequently fall asleep, but infants generally need anesthesia with intravenous or inhalational drugs for the procedure. Sedation is also required in older children who are either uncooperative or developmentally delayed. Healthy children who are older may be scanned without sedation as long as they are assured it will be painless. However, patients undergoing stereotactic-guided radiosurgery require general anesthesia due to the pain associated with the procedure.
3. **Angiography**
   Fluoroscopic angiography is an x-ray based medical imaging technique that is used mainly as an adjunct to diagnostic CT scanning and MRI. Its main indication in the pediatric neurosurgical setting is for the detailed demonstration of AVM's and moyamoya disease, as well as the extent of tumor vascularity. Cerebral angiography is usually performed through the transfemoral route with an injection of non-ionic contrast drugs and requires general anesthesia in small children.

B. **Periprocedural neuroradiologic management**

1. Review the patient's history and any previous diagnostic or surgical procedures and their management.
2. Ensure that the consent form has been signed and that the patient has met standard NPO guidelines (2 hours—clears, 4 hours—breast milk, 6 hours—formula and regular milk, 8 hours—solids).
3. Discuss the procedure with the parent and the older patient and develop rapport with the younger patient.
4. Ensure adequate functioning of the anesthesia machine and suction apparatus and the availability of equipment for difficulty in airway management and resuscitation.
5. Apply all standard monitors routinely used in the operating room: ECG, blood pressure, pulse oximeter, $ETCO_2$, and temperature.
6. Institute controlled ventilation with normocapnia for patients undergoing cerebral angiography to achieve good-quality images after the injection of the intravenous contrast.
7. Because allergic or anaphylactic reactions are always a possibility with the contrast material used during CT scan, MRI, and angiographic procedures, document history of any allergic reactions and be prepared to treat a reaction if one occurs during the procedure.
8. Monitor patients in a recovery area until they are fully awake and stable before discharging them from the unit. Patients who exhibit an

anaphylactic reaction might require intubation, ventilation, and overnight observation because laryngeal edema is a possible sequela of allergic reactions.

9. Monitor patients during transportation from remote locations if they require recovery in the postanesthesia care unit. In addition, procedures that begin in the radiology suite may be continued in the operating room, necessitating that the patients remain anesthetized, stable, and monitored during transportation.

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# 16 Neurosurgery in the Pregnant Patient

**David J. Wlody, Ivan Velickovic, and Lela D. Weems**

## Illustrative Clinical Case

A 30-year-old primigravida at 28 weeks' gestation was scheduled for left parietal craniotomy. She was in her normal state of health and had an uncomplicated pregnancy until 1 month before admission when she developed worsening headaches and weakness in her right upper extremity. Computed tomography (CT) scan revealed an enhancing lesion in the left parietal lobe with minimal midline shift.

The patient was positioned supine on the operating table with 30° left lateral tilt. Aspiration prophylaxis was administered consisting of Bicitra, metoclopramide, and ranitidine. After application of standard monitors, an arterial line was placed and an external fetal heart rate (FHR) monitor was applied. The patient was instructed to hyperventilate. Anesthesia was induced with fentanyl, 5 mcg/kg; propofol, 1.5 mg/kg; and rocuronium, 1.2 mg/kg. The patient was ventilated by mask while cricoid pressure was maintained. The patient's trachea was intubated with a 6.5 mm endotracheal tube. Anesthesia was maintained with sevoflurane 0.5% in air and oxygen and infusions of propofol and remifentanil. Arterial carbon dioxide ($CO_2$) tension was maintained in the range of 28 to 32 mm Hg. Although FHR variability decreased with the induction of anesthesia, the heart rate remained between 120 and 140 beats per minute. At the conclusion of surgery, the patient's trachea was successfully extubated and she was alert and responsive in the immediate postoperative period. Pathologic study revealed a glioblastoma multiforme. The patient was scheduled for a course of external beam radiation.

At 38 weeks' gestation amniocentesis revealed fetal lung maturity and the patient was scheduled for cesarean section. On physical examination, the patient was aphasic and had a dense right hemiparesis. Cesarean section was performed under general anesthesia and a healthy male infant was delivered with Apgar scores of 7 and 9.

The patient continued to deteriorate neurologically and died 3 weeks after delivery.

## Chapter Highlights

- Knowledge of the physiologic changes of pregnancy is essential to the anesthetic management of the pregnant woman undergoing neurosurgery.
- The key to maintenance of fetal wellbeing during surgery is appropriate maternal oxygenation and maintenance of uteroplacental perfusion.
- While many anesthetic drugs pass the placenta, there is little evidence that any of the commonly used anesthetics is teratogenic.
- Whenever possible anesthetic decision making should be based on the best interests of both the mother and her fetus. When these interests conflict, maintenance of maternal wellbeing is paramount.

Neurologic disorders requiring operation during pregnancy are surprisingly common, and most anesthesiologists eventually encounter a pregnant woman who has such a disorder. The anesthetic management of these patients can be complicated by the significant maternal physiologic changes that occur during pregnancy. These changes may require alterations in anesthetic management that are in opposition to the techniques that would be appropriate for a non-pregnant patient who has the same neurosurgical condition.

Additionally, while maternal considerations must remain paramount, it is important to recognize that interventions that benefit the mother might have the potential for causing harm to the fetus. Therefore, the major challenge of neuroanesthesia during pregnancy is to provide an appropriate balance between competing, or even contradictory, clinical goals.

The discussion in this chapter is limited to the anesthetic management of pregnant women undergoing craniotomy for resection of arteriovenous malformations (AVMs) and intracranial neoplasms, aneurysm clipping, and evacuation of spontaneous spinal epidural hematomas (SSEHs). Because the anesthetic management of these procedures is discussed elsewhere in this book, this chapter deals primarily with the ways in which pregnancy alters the anesthetic management.

## I. MATERNAL PHYSIOLOGIC ALTERATIONS DURING PREGNANCY

### A. Neurologic changes

1. **Inhalation anesthetic requirements.** The minimum alveolar concentration (MAC) for inhalation anesthetics decreases by approximately 30% to 40% during pregnancy, a change that occurs as early as the first trimester. This has been postulated to be a result of increased circulating endorphins. Alternatively, an increase in the concentration of progesterone, a hormone with known sedative effects, might account for the diminished anesthetic requirement. As a result of the increased sensitivity to inhalation anesthetics, inspired anesthetic concentrations that would be appropriate in non-pregnant patients can lead to significant cardiopulmonary depression during pregnancy.
2. **Local anesthetic requirements.** Local anesthetic requirements for spinal and epidural anesthesia are decreased by 30% to 40% during pregnancy. This decrease is in part due to the decreased volume of cerebrospinal fluid in the lumbar subarachnoid space secondary to engorgement of the epidural veins. However, the decrease in local anesthetic requirements predates the onset of significant epidural venous engorgement. A progesterone-induced increase in the sensitivity of neurons to the sodium-blocking properties of local anesthetics is thought to be the cause.

### B. Respiratory changes

1. **Upper airway mucosal edema.** The accumulation of extracellular fluid produces soft tissue edema during pregnancy, particularly in the upper airway where marked mucosal friability can develop. Nasotracheal intubation and the insertion of nasogastric tubes should be avoided unless absolutely necessary because of the risk of significant epistaxis. Laryngeal edema can also reduce the size of the glottic aperture, leading to difficult intubation, particularly in pre-eclamptic patients. A 6 to 6.5 mm endotracheal tube is therefore appropriate for most pregnant patients.
2. **Functional residual capacity (FRC).** FRC decreases by as much as 40% by the end of the third trimester while closing capacity (CC) remains unchanged. The FRC decreases further in the supine position, a situation

in which CC commonly exceeds FRC. When CC exceeds FRC, this leads to small airway closure, increased shunt fraction, and an increased potential for arterial desaturation. Additionally, because FRC represents the store of oxygen available during a period of apnea, decreases in FRC can be expected to lead to the more rapid development of hypoxemia when a patient becomes apneic, as occurs during the induction of anesthesia. Because oxygen consumption increases by 20% during pregnancy, significant desaturation can occur even when intubation is performed expeditiously. This mandates at least 4 minutes of preoxygenation and denitrogenation with a tightly fitting facemask before the induction of general anesthesia during pregnancy.

3. **Ventilation**. Significant increases in minute ventilation occur as early as the end of the first trimester. At term, minute ventilation increases by 50% owing to increases in both tidal volume (40%) and respiratory rate (15%). It has been postulated that these increases occur because of a progesterone-induced increase in the ventilatory response to $CO_2$. Because the increase in ventilation exceeds the increase in $CO_2$ production, the normal arterial partial pressure of $CO_2$ ($PaCO_2$) decreases to approximately 32 mm Hg. The increased excretion of renal bicarbonate partially compensates for the hypocarbia so that pH increases only slightly to approximately 7.42 to 7.44.

C. **Cardiovascular changes**

1. **Blood volume**. Blood volume increases by 35% during pregnancy. Because plasma volume increases to a greater extent than red cell mass (50% vs. 20%), a dilutional anemia occurs. Normal hematocrit at term ranges from 30% to 35%.
2. **Cardiac output (CO)**. Significant increases in CO occur as early as the first trimester. Capeless and Clapp demonstrated a 22% increase in CO by 8 weeks' gestation which represents 57% of the total change seen at 24 weeks. CO rises steadily throughout the second trimester. After 24 weeks, it remains stable or increases slightly. Earlier studies demonstrating a decrease in CO in the third trimester reflect measurements made in the supine position with consequent aortocaval compression (see subsequent text).

   Cardiac output can increase by an additional 60% during labor. Part of this increase is caused by the pain and apprehension associated with contractions, an increase that can be blunted with the provision of adequate analgesia. There is a further increase in CO, unaffected by analgesia, from the autotransfusion of 300 to 500 mL of blood from the uterus into the central circulation with each contraction. Finally, CO increases further in the immediate postpartum period by as much as 80% above prelabor values because of the autotransfusion from the rapidly involuting uterus as well as the augmentation of preload secondary to alleviation of the aortocaval compression.
3. **Aortocaval compression.** When pregnant women beyond 20 weeks' gestation assume the supine position, the enlarged uterus can compress the inferior vena cava against the vertebral column. When this occurs, venous return to the heart decreases, sometimes to a marked extent, leading to decreases in CO and blood pressure. This has the potential for decreasing uterine blood flow (UBF) to a level that can impair uteroplacental oxygen delivery. Supine positioning may also produce aortic compression. If this occurs, upper extremity blood pressure might be normal, but distal aortic pressure and therefore uterine artery perfusion pressure both decrease significantly. Because both regional and general

anesthetics reduce venous return, the effects of aortocaval compression are magnified in the anesthetized patient. Therefore, the supine position must be avoided in pregnant patients undergoing anesthesia. Tilting the operating table 30° to the left prevents significant aortocaval compression. Placing a roll under the patient's right hip can also achieve this goal.

**D. Gastrointestinal changes**

1. **Gastric acid production.** The placenta produces ectopic gastrin. This leads to increases in both the volume and the acidity of gastric secretions.
2. **Gastric emptying.** Contrary to common belief, gastric emptying in pregnancy is not significantly altered prior to the onset of labor. With the onset of painful contractions, however, gastric emptying is slowed. Systemic opioids administered during labor have a similar effect.
3. **Gastroesophageal sphincter.** The enlarging uterus causes elevation and rotation of the stomach, which interferes with the pinch-cock mechanism of the gastroesophageal sphincter. This increases the likelihood of gastroesophageal reflux.
4. **Pregnancy and aspiration pneumonia.** The changes described make it more likely that a pregnant patient will regurgitate and aspirate and, if this occurs, the pulmonary injury will be greater because of the increased volume and acidity of the gastric contents. These changes occur by the end of the first trimester if not earlier. Therefore, pregnant patients who have an estimated gestational age of approximately 14 weeks or more are assumed to have a full stomach. They should therefore receive aspiration prophylaxis with either a non-particulate antacid and/or a combination of a hydrogen ($H_2$) blocking drug and metoclopramide. The presence of a full stomach influences anesthetic induction but, as described in the subsequent text, techniques designed to minimize the risk of aspiration might not be ideal for the patient who has an intracranial lesion.

**E. Renal and hepatic changes.** Aldosterone levels increase during pregnancy with a concomitant increase in total body sodium and water. This increase in total body sodium and water can increase edema in an intracranial neoplasm and lead to either worsening signs and symptoms or the onset of symptoms from a previously unrecognized mass lesion. Renal blood flow and glomerular filtration rate increase by approximately 60% at term, paralleling the increase in CO. Therefore, blood urea nitrogen (BUN) and creatinine are usually one-half to two-thirds the values seen in non-pregnant women. What would be considered a normal or only mildly elevated BUN and creatinine in non-pregnant women should be a cause for concern during pregnancy.

Slight increases in alanine aminotransferase, aspartic transaminase, and lactate dehydrogenase are not uncommon during normal pregnancy. Plasma cholinesterase levels decrease, but prolonged neuromuscular blockade does not occur in normal parturients receiving succinylcholine.

**F. Epidural vascular changes**

1. **Epidural venous pressure** is increased mainly by global elevation of intra-abdominal pressure secondary to the pregnant uterus and direct compression of the vena cava. These two factors lead to the diversion of a portion of the venous return from the legs and pelvis into the vertebral venous system with resultant engorgement of the epidural venous plexus. It has been postulated that elevated venous pressure in the epidural space in association with the hemodynamic changes of

pregnancy may predispose the pregnant patient to the rupture of a preexisting pathologic venous wall. Epidural veins are a primitive venous system containing no valves. Therefore, abrupt pressure changes, such as straining and coughing, could be transmitted directly from the abdominal cavity to the epidural veins, causing rupture although this is certainly a rare occurrence.

2. **Epidural arterial vessels** may undergo degenerative structural changes during pregnancy owing to the excess of estrogen and progesterone. The arterial vessels of pregnant women have been shown to demonstrate fragmentation of the reticulin fibers, diminished acid mucopolysaccharides, loss of normal corrugation of elastic fibers, and hypertrophy and hyperplasia of smooth muscle cells. The combination of these structural changes with hemodynamic alterations during pregnancy, particularly in the third trimester, may predispose susceptible patients to the rupture of the epidural arteries.

## II. EFFECTS OF ANESTHETIC INTERVENTIONS ON UBF

**A. Determinants of UBF.** At term, normal UBF is approximately 700 mL/minute which is approximately 10% of total maternal blood flow. The magnitude of UBF is determined by this equation:

$$UBF = (UAP - UVP)/UVR$$

where UAP is the uterine arterial pressure, UVP the uterine venous pressure, and UVR the uterine vascular resistance. Alterations in any of these influences UBF and, therefore, the delivery of oxygen and nutrients to the fetus.

**B. Factors decreasing uterine arterial pressure**

1. Hypovolemia
2. Sympathetic blockade
3. Aortocaval compression
4. Anesthetic overdose
5. Vasodilator overdose
6. Excessive positive pressure ventilation

**C. Factors increasing uterine venous pressure**

1. Vena caval compression
2. Uterine contractions
3. Uterine hypertonus
   a. Oxytocin overstimulation
   b. Alpha-adrenergic stimulation

**D. Factors increasing uterine vascular resistance**

1. Endogenous catecholamines
   a. Untreated pain
   b. Noxious stimulation (laryngoscopy, skin incision)
2. Pre-eclampsia
3. Chronic hypertension
4. Exogenous vasoconstrictors

   **Phenylephrine is now commonly used as the first-line pharmacologic treatment for maternal hypotension.** Although high doses of phenylephrine decrease UBF owing to its vasoconstrictor effects, UBF is well maintained when phenylephrine is given in low doses of 50 to 100 mcg intravenously. In fact, there is growing evidence that phenylephrine maintains fetal acid–base balance better than ephedrine; it has been postulated that transplacental passage of the ephedrine increases fetal metabolism, leading to relative acidemia.

## III. UTEROPLACENTAL DRUG TRANSFER AND TERATOGENESIS

**A. Drug transfer.** A detailed consideration of the various mechanisms (active transport, facilitated diffusion, pinocytosis) by which substances are transported across the placenta is beyond the scope of this chapter. The discussion here concentrates on **passive diffusion**, the mechanism by which most anesthetic drugs administered to the mother reach the fetus. This process does not require the expenditure of energy. Transfer can occur either directly through the lipid membrane or through protein channels that traverse the lipid bilayer.

1. **Determinants of passive diffusion**
   - **a. Concentration gradient** is the primary determinant of the rate of transfer of drugs across the placenta. As an example, the initial rate of transfer of an inhalation anesthetic is quite rapid. As the partial pressure of the drug increases in the fetus, the rate of transfer decreases.
   - **b.** Substances that have a low **molecular weight** cross the placenta more readily than those that have a higher weight.
   - **c.** Drugs that have high **lipid solubility** readily traverse the placenta.
   - **d. Ionization** limits placental transfer.
   - **e. Membrane thickness** can be increased in certain pathologic states, including chronic hypertension and diabetes. The effects of these conditions on drug transfer are of less concern than the resultant limitation of the transportation of oxygen and nutrients. This can lead to intrauterine growth restriction or, in severe cases, fetal demise.
2. **Specific drugs**
   - **a.** The **inhalation anesthetics** cross the placenta freely owing to their low molecular weight and high lipid solubility. The longer the period of fetal exposure to the drug (induction to delivery interval), the more likely the newborn is to be depressed.
   - **b.** The **induction drugs**, thiopental, etomidate, and propofol, are highly lipophilic and unionized at a physiologic pH. Placental transfer is quite rapid. Because most of the blood returning to the fetus from the umbilical vein passes through the fetal liver, extensive first-pass metabolism occurs and neonatal depression after an induction dose of these drugs is uncommon.
   - **c.** Both depolarizing and non-depolarizing **muscle relaxants** are highly ionized at physiologic pH. Placental transfer is minimal.
   - **d.** The **opioids** freely traverse the placenta because of their high lipid solubility and low molecular weight.
   - **e.** The **reversal drugs**, neostigmine and edrophonium, are highly ionized and demonstrate minimal placental transfer.
   - **f.** The **anticholinergic drugs**, atropine and scopolamine, freely pass the placenta. **Glycopyrrolate** is highly ionized and therefore crosses the placenta to a minimal degree.
   - **g.** The commonly-used **anticoagulants**, heparin and warfarin, have remarkably different placental transfer. Heparin, a highly ionized polysaccharide molecule, does not reach the fetus. Warfarin, which is uncharged and has a molecular weight of only 330, readily passes across the placenta. Because warfarin can cause birth defects, its use is contraindicated during the period of organogenesis (see subsequent text).
   - **h. Antihypertensive drugs**. Of the **beta-blocking drugs** that have been studied, all cross the placenta. Labetalol appears to have the least placental transfer of this group of drugs. High-dose infusions of esmolol

have been reported to cause persistent fetal bradycardia lasting up to 30 minutes after the termination of the infusion. The effect of a single dose is not known, but numerous cases of its safe use as a bolus during anesthetic induction have been reported. **Sodium nitroprusside** (SNP) freely passes the placenta and has implications for fetal toxicity (see subsequent text).

**B. Anesthesia during pregnancy and the risk of birth defects**

1. **Principles of teratology.** It is an established principle that any substance, if administered in large enough quantities for a prolonged period of time during critical periods of gestation, can produce fetal injury ranging from growth restriction to major structural anomalies to death. Therefore, it should be a goal of the anesthesiologists caring for pregnant women to minimize the exposure of their fetuses to potentially toxic substances. Nevertheless, fears regarding the potential for injury should be tempered by the following considerations:
   - Most anesthetics are administered for such a brief period of time that the potential for toxicity is minimal.
   - There is **no convincing human evidence** that any of the commonly used anesthetics is dangerous to the fetus.
   - Maternal hypotension and hypoxemia pose a much greater risk to the fetus than do any of the anesthetic drugs.
   - Maternal wellbeing must be our paramount concern. If avoiding a potentially teratogenic drug leads to a poor maternal outcome or maternal death, fetal outcome will be equally compromised.
2. **Evaluation of teratogenic potential**. Because of the ethical and logistical difficulties inherent in large-scale prospective studies of the teratogenic effects of anesthetics in humans, we must rely on more indirect evidence to evaluate the teratogenic potential of these drugs. The principal investigative tools used are small animal studies, retrospective studies of the offspring of women who underwent anesthesia during pregnancy, and, in the case of inhalation anesthetics, studies of operating room personnel who were exposed to low-level waste anesthetic gases during pregnancy. The discussion of specific drugs that follows refers to the studies supporting or opposing their teratogenic potential.
3. **Specific drugs**
   a. Animal studies of the potent **inhalation anesthetics** have demonstrated conflicting results. Reproductive effects appear to be dose related. These effects are more likely to be from the physiologic disturbances (hypothermia, hypoventilation, poor feeding) produced by the anesthetic state rather than the anesthetic drug itself. When animals are exposed to inspired concentrations that do not impair feeding behavior or level of consciousness, reproductive effects are minimal. Neither studies of operating room personnel exposed to trace anesthetics nor of women undergoing surgery during pregnancy support any teratogenic potential for the potent inhaled anesthetics. Fetal loss is increased in women operated during pregnancy, but this is primarily because of the underlying condition requiring surgical intervention and the increased incidence of preterm delivery in women undergoing surgery in close proximity to the uterus.
   b. **Nitrous oxide** has clearly been shown to increase the incidence of structural abnormalities and fetal loss in rats. This was initially thought to be the result of inhibition of the enzyme **methionine synthetase** and a subsequent decrease in the level of methionine and

tetrahydrofolate. This mechanism has been called into question, however, because maximal inhibition of methionine synthetase activity occurs at levels of anesthetic exposure that do not produce teratogenic effects. More recent evidence suggests that the fetal effects of nitrous oxide come from alpha-adrenergic stimulation and a subsequent decrease in UBF, which can be reversed by simultaneously administering a potent inhalation drug. Studies of operating room personnel exposed to trace levels of nitrous oxide and of women receiving nitrous oxide anesthesia fail to show any teratogenic effect.

c. **Muscle relaxants** do not have any teratogenic effect at clinically appropriate doses.
d. **Opioids** have not been shown to be teratogenic in either human or animal studies.
e. Several human studies have suggested that chronic **benzodiazepine** therapy during pregnancy increases the incidence of cleft lip and cleft palate. These studies have been faulted for failure to control for concomitant exposure to other potentially teratogenic substances. There is little evidence to suggest that a single dose of a benzodiazepine during pregnancy poses any risk to the fetus.
f. There is no human evidence suggesting that **local anesthetics** are teratogenic. Chronic **cocaine** abuse has been linked to birth defects.
g. **Coumadin** therapy during pregnancy has been correlated with ophthalmologic, skeletal, and central nervous system abnormalities, presumably from microhemorrhages during organogenesis. Heparin, in both its unfractionated and low-molecular weight forms, does not cross the placenta so that it is the drug of choice in women requiring anticoagulation during pregnancy.

## IV. EPIDEMIOLOGY OF INTRACRANIAL DISEASE IN PREGNANCY AND THE EFFECT OF PREGNANCY ON INTRACRANIAL DISEASE

**A. Subarachnoid hemorrhage (SAH): aneurysm and AVM.** The causes of SAH during pregnancy are numerous, including hypertensive intracerebral hemorrhage, vasculitis, and bacterial endocarditis, but by far the most common are aneurysmal rupture and bleeding from an AVM. The overall incidence of SAH during pregnancy is approximately 1 in 10,000, which is similar to the incidence in the general population. SAH is responsible for approximately 4% to 5% of maternal deaths and has been reported to be the fourth most common non-obstetric cause of death after trauma, malignancy, and cardiac disease.

A review of 154 published cases of SAH during pregnancy demonstrated that the ratio of aneurysms to AVMs was approximately 3:1. There was no link between increasing parity and the incidence of hemorrhage. For both AVMs and aneurysms, there was an increasing incidence of hemorrhage with advancing gestational age, which may be from increases in CO or possibly hormonal influences on vascular integrity. Interestingly, few women bled during labor and delivery, which is consistent with the observation that > 90% of all hemorrhages in non-pregnant patients occur at rest. Of the patients whose rupture occurred during labor and delivery, 34% had hypertension, proteinuria, or both, suggesting that the differentiation between SAH and pre-eclampsia may be difficult on clinical grounds alone.

**B. Neoplastic lesions.** The incidence of intracranial neoplasms does not appear to be appreciably different in pregnant compared with non-pregnant women. However, as mentioned previously, some tumors appear to grow

more rapidly or become symptomatic during pregnancy. This may be because of an increase in either peritumoral edema (secondary to increased sodium and water retention) or blood volume in vascular tumors such as meningiomas.

Considerable evidence indicates that hormonal influences affect the growth of brain tumors, particularly meningiomas. The incidence of meningioma is higher in women than in men but decreases significantly after menopause. Progesterone receptors have been identified in both meningiomas and gliomas. Accelerated tumor growth during pregnancy is likely, owing in part to the high levels of circulating progesterone that occur with gestation.

## V. MANAGEMENT OF ANESTHESIA FOR CRANIOTOMY DURING PREGNANCY

### A. Timing of surgery in relation to delivery

1. **General concerns.** When craniotomy during pregnancy is contemplated, the physicians caring for the pregnant woman must decide whether to allow the pregnancy to proceed to term or whether simultaneous operative delivery will occur. The gestational age of the fetus, with 32 weeks commonly used as the cutoff, determines the decision. While not a hard and fast rule, before 32 weeks, pregnancy is typically allowed to continue; after 32 weeks, cesarean delivery is performed and followed by immediate craniotomy. This determination is not only because viability improves at 32 weeks but also the risks of preterm delivery are believed to become less than the risks to the fetus of such maternal therapies as osmotic diuresis, mechanical hyperventilation, and induced hypotension.
2. **Aneurysm clipping.** A significant improvement in survival for both mother and fetus has been demonstrated when aneurysm clipping was performed after SAH as compared with non-surgical management. Therefore, in patients who are assigned good grades (i.e., are alert with no or minimal neurologic deficit) after SAH, either endovascular coiling or aneurysm clipping should be performed as soon as possible to prevent rebleeding. The clipping of unruptured contralateral aneurysms can be delayed until the postpartum period.
3. **AVM resection.** Resection of unruptured AVMs can be delayed until after delivery with no apparent increase in maternal mortality. Conversely, resection of symptomatic AVMs is usually performed regardless of gestation. The management of women who have a ruptured AVM but are neurologically stable is controversial. Dias and Sekhar showed improved maternal outcome with early operation, but this difference did not reach statistical significance. Trivedi and Kirkpatrick recommend that a conservative approach be followed in patients who have high-risk surgical lesions and that surgical intervention be considered in those lesions in which operative risk is felt to be low. Therefore, the question of early operation for ruptured AVM during pregnancy remains unanswered at this time.
4. **Neoplasm resection.** Resection of a histologically benign neoplasm such as a meningioma can be delayed until after delivery but only if frequent follow-up and careful monitoring for neurologic deterioration can be assured. Surgery for presumed malignant tumors and for those masses producing worsening neurologic deficits should be performed regardless of gestational age.

### B. Anesthetic management

1. Sedative **premedication** may be appropriate in extremely anxious patients, but the risk of hypoventilation, hypercarbia, and subsequent

increases in intracranial pressure (ICP) should be considered and guarded against. It might be more appropriate to defer the administration of sedative medications until the patient arrives in the preoperative holding area where careful observation can be maintained. Because pregnant patients must be considered to be at increased risk for regurgitation and aspiration of gastric contents, medications to decrease the acidity and the volume of the gastric contents should be administered. These include a non-particulate antacid; metoclopramide, 10 mg; and an $H_2$ blocking drug such as ranitidine, 150 mg.

2. Anesthetic **induction** in the pregnant patient who has an intracranial lesion provides the clearest example of the need to reconcile competing clinical goals. A rapid-sequence induction designed to prevent aspiration does little to prevent the hemodynamic response to intubation that can be catastrophic for the patient who has an intracranial aneurysm or increased ICP. At the same time, a slow "neuro induction" with propofol or another intravenous induction drug, an opioid, a non-depolarizing muscle relaxant, and mask ventilation does little to decrease the risk of aspiration. This technique can also be expected to lead to neonatal depression should a cesarean section be performed as part of a combined procedure.

   One acceptable technique for anesthetic induction is described in the Table 16.1; other approaches that accomplish the stated goals are equally acceptable. As described previously, aspiration prophylaxis is mandatory. Cricoid pressure should be maintained from the point at which consciousness is lost until intubation is confirmed by capnography. If cesarean delivery is performed as part of a combined procedure, the physician caring for the newborn should be alerted to the likelihood of neonatal depression and the need to provide ventilatory support.
3. In addition to the standard maternal monitors, **fetal heart rate (FHR) monitoring** can be extremely useful during craniotomy, not because an ominous FHR indicates when cesarean delivery should be performed but because it should lead to a rapid search for potentially reversible causes of decreased uteroplacental perfusion, such as hypotension or hypoxemia. FHR monitoring usually becomes technically feasible at approximately 20 weeks of gestation. Note that decreases in short- and long-term variability, as well as a decreased baseline FHR, are commonly seen even in the healthy, uncompromised fetus whose mother is receiving general anesthesia. The American Society of Anesthesiologists has addressed this issue in its **Statement on Nonobstetric Surgery during Pregnancy.**
4. **Anesthetic maintenance** is not appreciably different between the pregnant and non-pregnant patient undergoing craniotomy (Table 16.2). As is the case during induction of anesthesia, every effort should be made

TABLE 16.1 Anesthetic Induction for Craniotomy

| | |
|---|---|
| Thiopental | 5–7 mg/kg |
| Fentanyl | 3–5 mcg/kg |
| Lidocaine | 75 mg |
| Rocuronium | 0.9–1.2 mg/kg |
| Mask ventilation with cricoid pressure, 100% $O_2$ | |

TABLE 16.2 Anesthetic Maintenance for Craniotomy

| | |
|---|---|
| Fentanyl | 1–2 mcg/kg/h |
| Isoflurane | 0.5%–1% |
| Non-depolarizing muscle relaxant | |
| Thiopental | 5–6 mg/kg/h for "tight brain" |

to maintain hemodynamic stability as well as to avoid increases in cerebral blood volume (CBV) that could interfere with surgical exposure. As stated previously, potentially teratogenic drugs should be avoided, but the commonly-used anesthetics do not appear to fall into this category.

5. **Adjuvants to surgery**
   a. Osmotic diuresis with **mannitol** is commonly used to decrease brain bulk and facilitate exposure during craniotomy. Because mannitol has been demonstrated in both animal and human studies to produce fetal dehydration, some have advised against its use during pregnancy. However, the doses given in these early studies were considerably higher than those currently in clinical use. There is no evidence that mannitol, 0.5 to 1 g/kg, has any significant adverse effect on fetal fluid balance.
   b. **Maternal hyperventilation** can facilitate surgical exposure by decreasing CBV. Severe hypocarbia may impair fetal oxygen delivery, however, by shifting the maternal oxygen–hemoglobin dissociation curve to the left. Hyperventilation can also decrease maternal CO by increasing intrathoracic pressure. Modest hyperventilation to a $PaCO_2$ of 28 to 30 mm Hg should provide adequate surgical conditions without compromising the fetus.
   c. **Controlled hypotension** is becoming less common during aneurysm surgery because of the growing use of temporary clip occlusion of proximal vessels. Some situations, however, make this technique necessary. Because UBF varies directly with perfusion pressure, severe hypotension can lead to fetal asphyxia. Blood pressure should therefore be lowered only to that level deemed necessary for maternal wellbeing and for as brief a period as possible. FHR monitoring might alert the anesthesiologist to the development of fetal hypoxia and lead to the restoration of blood pressure if the need for hypotension is not critical at that time.

      There is an additional concern when **SNP** is used as the hypotensive drug. Because of the limited ability of the fetal liver to metabolize cyanide, it is possible for fetal intoxication to occur in the absence of any signs of maternal toxicity. Although there are several case reports of the safe use of SNP during pregnancy, the duration of administration should be limited to that period deemed essential to maternal wellbeing. The total dose of SNP can also be limited through the administration of adjuvants such as beta-blocking drugs and inhalation anesthetics.
   d. It has been suggested that mild **hypothermia** (33°C to 35°C) has cerebral protective effects. This level of hypothermia has no significant fetal effects. More profound hypothermia, however, can cause fetal arrhythmias and should be avoided.

6. **Emergence.** Before the removal of the endotracheal tube, the pregnant patient should be fully awake and airway reflexes intact to minimize the risk of aspiration. An alert patient also facilitates early neurologic evaluation and eliminates the need for emergent radiologic evaluation of the persistently obtunded patient. At the same time, however, every effort should be made to prevent coughing and straining on the endotracheal tube because this may cause a catastrophic intracranial hemorrhage. Coughing and straining may be prevented through the administration of lidocaine, 75 to 100 mg, and fentanyl, 25 to 50 mcg, at the end of the operation. Because the placement of the head dressing is associated with movement that produces airway stimulation, maintaining neuromuscular blockade until the dressing has been secured is appropriate. These guidelines do not apply to the patient who was obtunded preoperatively or who had a significantly complicated intraoperative course with bleeding, brain swelling, or ischemia. The trachea of such patients should remain intubated until their neurologic status can be evaluated.

**C. Endovascular treatment of intracranial aneurysms**

1. Endovascular treatment of both ruptured and unruptured intracranial aneurysms during pregnancy is utilized increasingly as an alternative to surgical treatment. This approach has a decreased incidence of vasospasm and procedural complications and a similar incidence of obstructive hydrocephalus compared to surgery, although at the price of a somewhat lower success rate of aneurysmal obliteration.
2. Concerns have been raised regarding fetal radiation exposure during coiling procedures, but appropriate shielding will limit fetal radiation exposure to a level comparable to normal background radiation. Heparinization and reversal during the procedure pose no significant risk to the fetus.
3. Intraarterial blood pressure monitoring is indicated to facilitate aggressive blood pressure control, for example, should aneurysmal rupture occur. General endotracheal anesthesia is generally utilized during these procedures; the measures used to blunt the sympathetic response to laryngoscopy and intubation during craniotomy should be utilized in this setting as well. FHR monitoring may provide some guidance regarding the range of blood pressure that provides adequate uteroplacental perfusion and oxygen delivery.

## VI. SSEH DURING PREGNANCY

**A. Epidemiology.** SSEH is a rare cause of spinal cord compression. Only a handful of case reports having a clear etiology for the pregnant and non-pregnant population have been published since 1869. Bidzinski described the earliest case of SSEH in pregnancy in 1966. Spontaneous, or traumatic, spinal epidural hematomas are usually associated with congenital or acquired bleeding disorders, hemorrhagic tumors, spinal AVMs, or instances of increased intrathoracic pressure. Considering the physiologic changes of pregnancy and the inherent hypercoagulable state, very few cases have been reported. To date, the English language literature has reported only six cases. Jea reviewed the cases that involved healthy women in their twenties who were in their second trimester or later. All of the women had profound neurologic deficits, were managed operatively, and exhibited significant neurologic improvement after surgery. Pregnancy was carried to term in three cases, and an emergency cesarean section was performed before evacuation of the spinal epidural hematoma in three cases.

**B. Management of anesthesia for evacuation of SSEH**

1. **Timing of surgery in relation to neurologic symptoms**
   a. **Surgical management.** When the hematoma occurs in the thoracic or lumbar region, initial neurologic symptoms and signs consist of lower extremity radicular pain as well as bladder and bowel dysfunction. Motor and sensory deficits are usually progressive within hours of presentation. The definitive diagnosis is made radiologically, and magnetic resonance imaging appears to be the safest imaging modality during pregnancy. For patients who have profound and progressive neurologic deficits, the treatment of choice is surgical evacuation of the hematoma within 8 hours of the onset of symptoms as recommended in the literature reviewing the cases of pregnant patients. Lawton concluded that neurologic outcome appeared to depend on the length of time that elapsed between the onset of the neurologic deficits and the surgical intervention.
   b. **Conservative management. There are no case reports of the conservative management of pregnant patients who develop SSEH.** However, Duffill reported the successful non-operative management of SSEH in non-pregnant patients. There is some consensus that patients who demonstrate rapid improvement of neurologic symptoms after SSEH may be managed without surgery although these patients must be closely monitored for any renewed deterioration of neurologic status. The decision to manage SSEH conservatively may be influenced by the gestational age of the fetus: being near term may alter the risk considerably.

      **Labor**, vaginal delivery, and the related hemodynamic changes **can precipitate the expansion of the hematoma** and potentially worsen the patient's neurologic status at a time when neurosurgical intervention may be rendered difficult or impossible. Also, cesarean section may be inappropriate during conservative management because there is no way to assess the patient's potentially unstable neurologic status during delivery secondary to the general or regional anesthetic needed for the procedure. If the neurologic status improves dramatically in the pregnant patient who has SSEH and an immature, non-viable fetus (< 24 weeks' gestation), conservative management may be appropriate with close neurologic monitoring for potential deterioration. To date, no case of successful conservative management of SSEH in a pregnant patient has been reported. Therefore, caution is indicated in applying the observations and experience with the non-pregnant population to the pregnant patient.
2. **Timing of delivery in relation to surgery** depends on gestational age. If the fetus is deemed viable (> 32 weeks' gestation) when SSEH is diagnosed, the cesarean section may be performed before neurosurgical evacuation of the hematoma to facilitate optimal neurologic outcome for the patient. If the fetus is determined to be non-viable (at or below 24 weeks' gestation), neurosurgical intervention should be undertaken as soon as possible to improve neurologic outcome with implementation of all the specific considerations for surgery in the pregnant patient.
3. **Anesthetic management of evacuation of SSEH.** The concerns and techniques outlined for anesthetic management of intracranial lesions should be followed for cesarean section and evacuation of hematoma with or without cesarean section, including the recommendations for sedative premedication, anesthetic induction, FHR monitoring, and emergence.

a. **Anesthetic maintenance** is not appreciably different from for that in patients undergoing operation for intracranial lesions except for the need to maintain the mean arterial blood pressure in the high normal range (70 to 85 mm Hg in normotensive patients) to ensure optimal UBF until decompression is completed. To avoid uterine atony, the end-tidal concentration of the volatile anesthetic is maintained at a low concentration (0.3), relying on an opioid-based technique and a non-depolarizing muscle relaxant for maintenance. Alternatively, total intravenous anesthesia (TIVA) with propofol, opioid, and muscle relaxant may be utilized and the volatile drugs avoided altogether.

b. **Positioning considerations** are extremely important in the pregnant patient before thoracic or lumbar laminectomy for hematoma evacuation. Aortocaval compression must be avoided to prevent significant reductions in maternal CO, systemic blood pressure, and UBF in patients for whom prior cesarean section was not performed. Physiologic studies reveal superior relief of uterine compression of the large maternal vessels in the prone position as compared to the sitting or lateral position. The lateral position is actually associated with an increased incidence of aortocaval compression.

   Jea described the use of the four-post Wilson frame with two posts placed just below the clavicles on the chest and the other posts centered on the anterosuperior iliac spines to support the pelvis. With this configuration, the protuberant abdomen hung free of compression between the 4 posts, encouraging the gravid uterus to migrate off the large vessels. Positioning the patient on the Jackson table would similarly reduce aortocaval compression. However, there is a risk of venous air embolus in the prone position as the surgical site is higher than the heart which needs to be borne in mind.

4. **Emergence** is managed as for pregnant patients undergoing surgery for intracranial lesions. Additional precautions must be taken to assess the patient's readiness for extubation after remaining in the prone positioning for surgery because of possible edema of the airway. A leak test should be performed when the patient is fully awake before removing the endotracheal tube.

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# 17 Anesthetic Management of Diagnostic and Therapeutic Interventional Neuroradiolologic Procedures

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## Illustrative Clinical Case

**Introduction**: The last two decades have seen rapid advances in interventional neuroradiologic procedures. The illustrative case (Fig. 17.1) shows how previously untreatable cerebral aneurysms can now be treated by a combination of endovascular interventions. The endovascular procedures have established alternative approaches to conventional surgical treatments of vascular and nonvascular intracranial and spinal diseases. In the case of minimally invasive spine surgery, these advances have blurred the boundary between operations within the confines of the operating room (OR) and those in the angiography suite. This chapter describes procedures conducted in the angiography suite. Interventional neuroradiologic (INR) procedures seem to be technically simple, yet they carry a low but significant morbidity. Approximately 0.2% to 1% of the patients may develop transient or permanent neurologic symptoms after diagnostic cerebral angiography. Compared to diagnostic angiography, therapeutic interventions carry significantly greater risks of neurologic complications.

The **primary goals of anesthesia for INR procedures** are to control the level of sedation in a manner that permits prompt neurologic examination, to render the patient immobile, and to manipulate cerebral hemodynamics. Many INR procedures such as diagnostic angiography, carotid stenting, and embolization of cerebral arteriovenous malformations (AVMs) can be undertaken with **intravenous sedation**. However, a growing number of INR procedures including coiling of intracranial aneurysms, intracranial angioplasty, and embolization of some high-flow AVMs require **general anesthesia**. General anesthesia is also a necessity for diagnostic procedures in children and in uncooperative adults as well as for prolonged procedures such as those on the spinal cord. Often the choice of anesthetic technique is a collaborative decision by the neurointerventionalist and the anesthesiologist, which is based on individual patient assessment.

## Chapter Highlights

- The revised chapter builds on the strength of the previous version. It provides a general description of interventional radiologic procedures and discusses specific applications.
- It reviews all relevant current literature.

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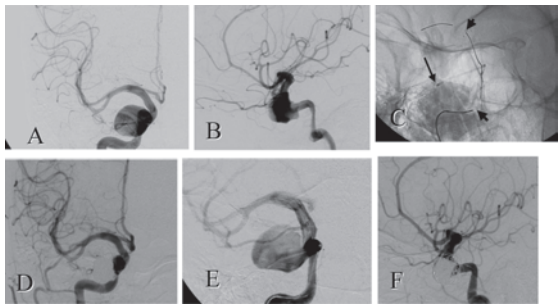


**FIGURE 17.1** Embolization of a giant cavernous aneurysm: Patient presented with severe retro-orbital headache and multiple cranial nerve palsies. **A, B:** Anterioposterior and lateral angiogram. **C:** Stent placement. The short arrows represent the stent markers and long arrow identifies the coiling microcatheter. **D:** Deployment of the stent across the base of the aneurysm. **E, F:** Six-month follow-up angiogram that shows stable and obliterated lesion. Patient had complete resolutions of symptoms.

- It provides a new illustrative case report, figures, and tables.
- It provides an updated review of technical advances and pharmacologic agents and a description of new procedures.
- It describes emerging applications such as thrombolysis, tumor treatment, and vertebroplasty.
- It includes updated information about embolic agents, sedatives, and anticoagulant drugs.

## I. NEUROVASCULAR ACCESS AND METHODS

**A. Vascular access.** INR procedures typically involve **insertion of catheters into the arterial circulation of the head or the neck**, usually through the transfemoral route. As illustrated in Figure 17.2, **transfemoral access** is accomplished by the placement of a large introducer sheath into the femoral artery, usually 5.0 to 7.5 F in size. Through the introducer sheath, a 5.0 to 7.5 F coaxial catheter is positioned by fluoroscopic control into the carotid or vertebral artery. Finally, a 1.5 to 2.8 F superselective microcatheter is introduced into the cerebral circulation that can be used to deliver drugs, embolic substances, or balloons to distal regions of the brain. The transfemoral placement site is usually infiltrated with local anesthetic which can cause a femoral nerve block and temporary weakness of the quadriceps muscle. Transfemoral venous access can be used to reach the dural sinuses and in some cases the arterial side of the AVMs. Direct percutaneous puncture is used to access superficial lesions of the head and neck such as tumors and arteriovenous and venous malformations.

**B. Imaging technology.** Radiologic imaging techniques needed for INR procedures include **high-resolution fluoroscopy** and **high-speed digital subtraction angiography (DSA)** with **road mapping functions** that enable the radiologist to observe the advance of the catheter against the background map of the patient's cerebral vessels "in real time." **DSA** involves the subtraction of images obtained before and after injection of radiocontrast drugs and facilitates visualization of only those vessels that are opacified by contrast injection. Any displacement of the cerebral vessels from movement of the head profoundly degrades DSA images. It is therefore critical that the patient remain immobile during the procedure.

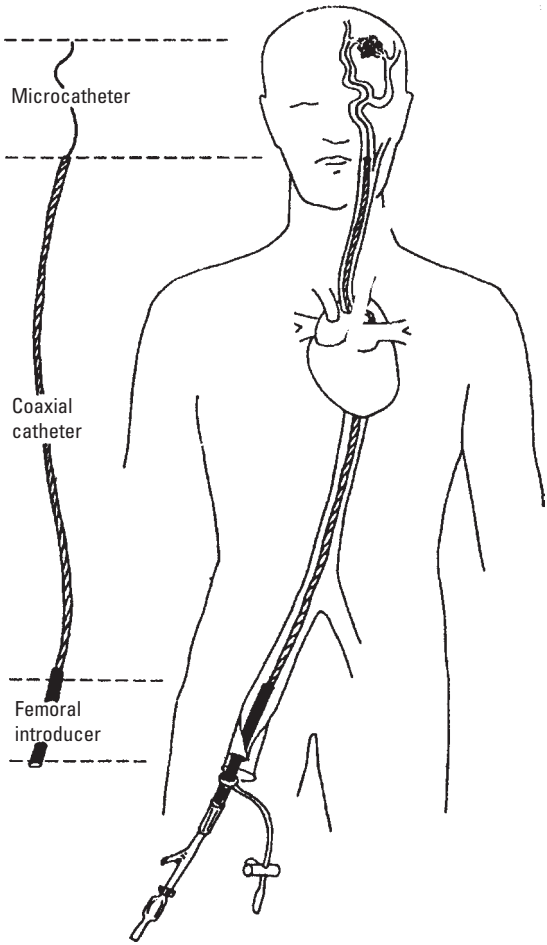


**FIGURE 17.2** Representation of a typical arrangement of the transfemoral coaxial catheter system showing the femoral introducer sheath, the coaxial catheter, and the microcatheter. (From Young WL. *Clinical Neuroscience Lectures*. Munster, IL: Cathenart Publishing, 1999, with permission.)

Prolonged and sometimes repeated INR procedures carry **the risk of radiation exposure** to the patients and staff. Hence, considerable effort is being expended to design fluoroscopes that utilize less radiation and offer superior image quality. To achieve this, better x-ray tubes, x-ray generators, and spectral shaping filter technologies have been developed along with improved logic systems for automated dose rate and image quality control. The newer generation of fluoroscopes combines rotational angiography with computed tomography (CT). Digital images can be manipulated in three dimensions to investigate vascular geometry to optimize treatment.

**C. Materials for embolization and infusion.** Factors affecting the choice of embolic medium include the nature of the disease, the purpose of the embolization, the size and penetration of the emboli and vessels, and the permanency of the occlusion. The ideal choice and the combination of materials remain controversial. **Embolic materials** include balloons, coils, polyvinyl alcohol (PVA) particles, gelatinous embolization spheres, and *n*-butyl cyanoacrylate (NBCA) glue which is available as a liquid monomer that rapidly polymerizes in contact with ionic solutions such as blood and saline. **Onyx** is a non-adhesive liquid embolic system composed of ethylvinyl alcohol dissolved in dimethyl sulfoxide (DMSO). The use of non-adhesive liquid embolic materials decreases the chance of catheter impaction and permits the slower and more controlled delivery of embolic material. The potential systemic toxicity of DMSO can lead to pulmonary edema, bronchospasm, bradycardia, and cardiac arrest. An acute reduction in arterial saturation typically occurs 3 to 7 minutes after Onyx injection in about 10% to 30% of the cases. The desaturation lasts for 20 to 40 minutes and resolves without treatment. Patients may also complain of strong garlic taste during Onyx injection from the DMSO.

**D. Radiation safety.** There are three **sources of radiation** in the INR suite: direct radiation from the x-ray tube, leakage (through the collimator's protective shielding), and scattered radiation (reflected from the patient and the area surrounding the body part to be imaged). The amount of exposure drops off proportionally to the square of the distance from the source of radiation (inverse square law). **DSA delivers considerably more radiation than fluoroscopy.** While working in the INR suite all persons should wear lead aprons, leaded glasses, and thyroid shields and have exposure badges.

## II. ANESTHETIC CONSIDERATIONS

The primary responsibilities of the anesthesiologist in the INR suite are to provide the level of sedation/anesthesia that permits prompt neurologic assessment when needed; to render the patient physiologically stable and immobile; to manipulate the systemic blood pressure (BP) as dictated by the needs of the procedure; and to provide emergent care in the event of catastrophic complications.

**A. Preoperative assessment.** A careful assessment of the **airway** has to be made. A history of snoring may suggest that partial airway obstruction might occur with sedation. Snoring results in movement artifacts that may degrade the quality of images during cerebral angiography. The nature and severity of any **adverse reaction to radiocontrast drugs** need to be carefully assessed. The population of patients who have occlusive cerebrovascular disease may also require optimization of their treatment for **coexisting conditions** such as hypertension, heart failure, or angina. **Preoperative communication with the INR team** is essential to develop a clear strategy for sedation and hemodynamic interventions that might be needed during the procedure.

**B. Preoperative investigations.** Routine guidelines for laboratory investigations before surgery are applicable to INR procedures. Of particular interest is the baseline coagulation screen as anticoagulation will be required for the procedure.

**C. Premedication.** Anxiolytics may be administered depending on the condition of the patient. **Minimal premedication is required for INR procedures.** Oral nimodipine or transdermal nitroglycerin is sometimes used to decrease intraoperative vasospasm. Premedication with steroids and antihistaminics will also be required for patients who have a history of allergic reaction to radiocontrast drugs before exposure.

D. **Room preparation.** The INR suite should be **equipped exactly as for delivering anesthesia in a standard operating room.** Suction, gas evacuation, oxygen, and nitrous oxide should be available from the wall outlets. Ideally, the anesthesia machine should also be able to deliver carbon dioxide for deliberate hypercapnia. An extended anesthetic breathing system is necessary to reach the remotely located patient's airway. Rapid access to all critical equipment should be possible at all times during the procedure. Induction and emergency drugs must be prepared for immediate use.

E. **Patient positioning.** Because INR procedures may last for several hours, it is essential that the patient be made as comfortable as possible before the start of sedation.

F. **Intravenous access.** During INR procedures the patients are often moved cephalad toward the image intensifier and away from the anesthesiologist so that the position of the catheters can be checked. This limits access to potential venipuncture sites and injection ports during the procedure. Therefore, **adequate vascular access** and **sufficient tubing length** should be in place before the start of the procedure. In adults, two **intravenous cannulae** are usually inserted for this purpose, one of which is at least 18 gauge in size. The infusions of anesthetic and vasoactive drugs should be in line before the patient is draped.

G. **Monitoring**

1. **Arterial pressure.** Because of the need to manipulate systemic hemodynamics and at times the emergent need for hemodynamic interventions, it is usually desirable to obtain **direct systemic arterial pressure measurements** during INR procedures. This is most conveniently **achieved by transducing the side arm of the femoral introducer sheath** (Fig. 17.2). If a relatively large coaxial catheter passes through the introducer, however, the arterial pressure trace will be "dampened." Despite dampening, the mean arterial pressure (MAP) will still be reliable. To avoid excessive dampening of the femoral arterial tracing, the introducer sheath should be at least 0.5 F larger than the coaxial catheter. **Radial artery cannulation** may be desirable when systemic BP is to be monitored before insertion of the femoral introducer sheath such as during the induction of general anesthesia for coiling of intracranial aneurysms or when postoperative BP monitoring is necessary.

   For a typical intracranial procedure, two other pressures may be measured in real time in addition to the systemic arterial pressure: the **internal carotid or vertebral artery pressure** through the coaxial catheter and the **distal cerebral arterial pressure** through either the microcatheter or a balloon-tipped catheter. The coaxial catheter pressure is monitored so as to detect any thrombus formation or vasospasm at the catheter tip as evidenced by a dampened arterial trace. High-volume heparinized flush solution is passed continuously through the coaxial tip to discourage thrombus formation. Hence, the arterial pressure reading characteristically increases by 10 to 20 mm Hg when recorded through the coaxial catheter.

   The setup for measuring arterial pressures is shown in Figure 17.3. The pressure transducers and access stopcocks for blood withdrawal and zeroing are mounted, depending on the institutional preference, either on the sterile field or toward the anesthesiologist. Measurement of distal cerebral arterial pressures through the microcatheter is useful during embolization of AVMs (see Therapeutic Embolization of AVMs below). When a balloon catheter is used for internal carotid artery (ICA) occlusion, pressure measurements at the tip of the catheter provide the stump pressure (see Test Occlusion below).

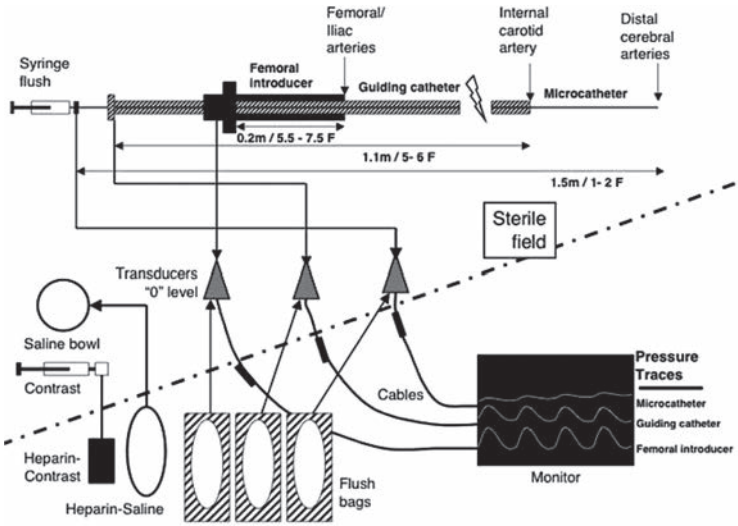


**FIGURE 17.3** Schematic representation of pressure monitoring and the continuous flush systems in the interventional neuroradiology suite.

2. **Other systemic monitoring** includes five-lead electrocardiogram, preferably with ST segment trending and respiratory tracing, automated non-invasive BP, end-tidal carbon dioxide tension, and peripheral temperature monitors. Pulse oximeter probes are placed on the great toes and are useful for qualitatively comparing distal pulses in the lower limbs. Loss of the pulse oximeter tracing on the side of the femoral introducer sheath offers early warning of thromboembolism, vasospasm, or mechanical obstruction.
3. **Central nervous system monitoring.** During many procedures, neurologic examination provides adequate monitoring of central nervous system (CNS) integrity. Adjuncts that are especially useful during general anesthesia or planned proximal occlusion include electroencephalogram (EEG), somatosensory and motor evoked potentials, transcranial Doppler (TCD) ultrasound, and $^{133}$Xe cerebral blood flow (CBF) monitoring.
4. **Urinary output.** Most patients undergoing INR procedures will require bladder catheterization to assist in fluid management and to enhance patient comfort. Diuresis might occur during the procedure from the increase in intravascular volume as a result of continuous flushing of the intravascular catheters and the osmotic load from radiocontrast or mannitol injection. The timing and volume of contrast injected should be monitored, especially during prolonged procedures.
5. **Laboratory tests.** A baseline arterial blood gas (ABG) at the time of arterial puncture is useful to assess the gradient between arterial oxygen tension ($PaO_2$) and arterial oxygen saturation ($SaO_2$) as well as the arterial carbon dioxide tension ($PaCO_2$)-to-end-tidal carbon dioxide tension ($ETCO_2$) gradient. Activated clotting time (ACT) is used to monitor coagulation. The patients receive large quantities of fluid and

radiocontrast and can diurese considerably so that a baseline hematocrit determination is helpful as well.

**H. Anticoagulation.** Careful management of coagulation is required to prevent thromboembolic complications from the presence of foreign bodies (catheters) and endothelial injury from the passage of microcatheters (Table 17.1). After placement of the femoral introducer sheath, a baseline ACT is obtained. Heparin, 2,000 to 5,000 U/70 kg, is given and another ACT obtained approximately 3 to 5 minutes later. The target ACT depends on the clinical needs and could be two to three times the baseline value. Additional heparin may be required throughout the procedure to maintain adequate anticoagulation. On occasion, when the INR procedure is completed, the anticoagulant effect of heparin is reversed with protamine and the femoral artery catheter is removed in the angiography suite. The proliferation of percutaneous closure devices has improved hemostasis at the arteriotomy site particularly in patients receiving thrombolytics and antiplatelet drugs.

## III. DYNAMIC SEDATION

The selection of anesthetic drugs for conscious sedation is guided by the **primary goals of alleviating pain, discomfort, and anxiety and ensuring patient immobility.** At the same time, one must allow for a rapid decrease in the level of sedation when neurologic testing is required. The procedures are not generally painful except for sclerotherapy and chemotherapy. There is an element of pain associated with distention of or traction on the vessels; contrast injection into the carotid artery is frequently described as "burning." Discomfort might result from prolonged periods of immobilization, bladder catheterization, and, to a lesser extent, the femoral puncture site. The

TABLE 17.1 Anticoagulant Therapy

| | Heparin | Low-molecular-weight Heparin | Fondaparinux | Lepirudin |
|---|---|---|---|---|
| Mechanism of action | Inhibits antithrombin | Inhibits antithrombin | Synthetic, specific to the binding region of heparin | Binds to thrombin exosite I |
| Dose | 50–100 units/kg guided by ACT | Acute: 30 mg intravenous; then 1 mg/kg subcutaneous | 2.5–10 mg subcutaneous | 0.1–0.4 mg/kg |
| Half-life | Dose dependent 1–5 h | | 17–21 h | 1.3 h |
| Thrombo cytopenia | Yes | Yes | Yes | No |
| Monitoring | ACT, APTT | PT and APTT insensitive; needs antifactor Xa assay | PT and APTT insensitive, Needs INR | APTT |

ACT, activated clotting time; APTT, activated partial thromboplastin time; PT, prothrombin time; INR, international normalized ratio.

TABLE 17.2 Ramsay Sedation Score

| Sedation Score | Awake or Asleep | State/Response |
|---|---|---|
| 1 | Awake | Restless |
| 2 | Awake | Cooperative |
| 3 | Awake | Responds to verbal commands |
| 4 | Asleep | Response to glabellar tap—brisk |
| 5 | Asleep | Response to glabellar tap—sluggish |
| 6 | Asleep | No response to glabellar tap |

procedure might also be psychologically stressful because of the potential risk of stroke during the procedure. Patient immobility, whether by conscious effort or deep sedation, is essential for INR procedures. Movement can not only degrade the quality of images but can also result in vascular injury. Patients who have impaired communication or dementia, sleep apnea, orthopnea, active congestive heart failure, unstable angina, anxiety, claustrophobia, or poor pain tolerance need to be carefully assessed regarding their suitability as candidates for dynamic sedation.

**A. Sedation scores.** Quantification of the level of sedation during an INR procedure is critical to the control of drug delivery. A variety of sedation scores are available. The Ramsay score that grades sedation at six levels is popular (Table 17.2). Most of the sedation scores require eliciting a response to verbal commands or noxious stimuli. Because of the remote location of the head, communication with and access to the patient may be limited which would make it difficult to elicit a response to the glabellar tap. The surgeons, who are often closer to the patient, could assist in eliciting a verbal response when needed but close observation of the patient for movement and respiratory function remains critical. Monitored respiratory parameters include respiratory rate and $ETCO_2$ by capnography, respiratory excursion by thoracic impedance, and adequacy of oxygen saturation which are especially important when deeper levels of sedation preclude eliciting a verbal response.

**B. Anesthetic drugs.** Our primary approach to the selection of drugs for conscious sedation is to establish a base of anesthesia by the titration of **fentanyl**, 1 to 2 mcg/kg, and **midazolam**, 1 to 2 mg, after intravenous access and monitoring have been established and oxygen administration has begun (Tables 17.3 and 17.4). A small bolus dose of **propofol** can be useful just as the bladder catheter is passed in males. The bolus of propofol also helps the anesthesiologist assess the airway under deep sedation and determine when a nasopharyngeal airway is required. Insertion of the nasopharyngeal airway after anticoagulation can result in troublesome bleeding and is best avoided.

When the patient is in final position, draping is begun and **propofol** is infused initially at a very low dose of 10 to 20 mcg/kg/minute and then increased slowly to render the patient immobile yet breathing spontaneously. The alpha-2 adrenoreceptor agonist, **dexmedetomidine**, offers an alternative to propofol with better airway maintenance. Dexmedetomidine, 0.5 to 1 mcg/kg over 10 to 20 minutes as a loading dose and then an infusion of 0.01 to 1 mcg/kg/hour, permits neurologic examination during awake craniotomy but may reduce the systemic BP. With a number of drugs available for sedation, the choice of anesthetic is based on the experience

TABLE 17.3 Pharmacokinetics of Narcotics

| | Sufentanil | Fentanyl | Alfentanil | Remifentanil |
|---|---|---|---|---|
| Potency relative to fentanyl | 7–10 X | 1 X | 0.1–0.2 X | 0.8 X |
| Vd ss (L) | 98 | 375 | 36 | 35 |
| $T_{1/2\ alpha}$ | 1 min | 3 min | 2 min | 1 min |
| $T_{1/2\ beta}$ | 2.5 h | 4 h | 1.5 h | 5–8 min |
| Cl (L/min) | 0.75 | 1 | 0.3 | 0.3 |
| Octanol:water partition coefficient | 1,800 | 810 | 130 | 18 |
| Sedation dose | 5–8 mcg/kg bolus | 50–100 mcg bolus | 250–500 mcg bolus | 0.03–0.5 mcg/kg/min |

Vd ss, steady state volume of distribution in liters; $T_{1/2\ alpha}$, distribution half life in minutes; $T_{1/2\ beta}$, elimination half life in minutes/hours; Cl, clearance (in liters/minute).

of the practitioner, the needs of the patient, and the requirements of the procedure (Table 17.4).

1. **Dexmedetomidine**, a selective alpha-2 adrenoreceptor agonist, is exceedingly short-acting and has minimal respiratory depression when given in sedative doses. Hemodynamic depression with hypotension and bradycardia can occur so that the drug has to be used with caution in patients who have advanced heart block or severe ventricular dysfunction. Patients sedated with dexmedetomidine tend to have lower BPs in the recovery period. This may not be desirable in patients who are critically dependent on collateral perfusion to maintain adequate cerebral perfusion pressure (CPP, the difference between MAP and ICP). Dexmedetomidine is highly protein bound and can potentially interact with other protein-bound drugs. It is metabolized in the liver by glucuronide formation and by cytochrome P-450. Most of the drug is eliminated in the urine.

TABLE 17.4 Pharmacokinetics of Sedative Hypnotics

| | Dexmedetomidine | Propofol | Midazolam |
|---|---|---|---|
| Commercial name | Precedex | Diprivan | Versed |
| Vd ss (L) | 120 | 250–300 | 80–120 |
| $T_{1/2\ alpha}$ | 6 min | 2–4 min | 6–15 min |
| $T_{1/2\ beta}$ | 2 h | 30–60 min | 100–150 min |
| Protein binding | 94% | 97%–99% | 95% |
| Metabolism | Liver | Liver | Liver |
| Cl (L/min) | | 1.5–2 | 0.5–0.8 |
| Loading dose | 0.5–1 mcg/kg over 10–20 min | Optional for sedation | 10–20 mcg/kg bolus |
| Maintenance dose | 0.2–0.7 mcg/kg/h | 25–100 mcg/kg/min | 0.02 to 0.1 mg/kg/h |

Vd ss, steady state volume of distribution in liters; $T_{1/2\ alpha}$, distribution half life in minutes; $T_{1/2\ beta}$, elimination half life in minutes/hours; Cl, clearance (in liters/minute).

Liver dysfunction affects clearance of dexmedetomidine: mild, moderate, and severe hepatic dysfunction all decrease clearance to 74%, 64%, and 53%, respectively.

2. **Propofol** is a sterile oil-in-water emulsion of 2,6 di-isopropylphenol. Available as a 1% or 2% solution, propofol is a highly lipid soluble and protein-bound compound. Its high initial volume of distribution results in rapid redistribution of the drug after bolus injection. Propofol is principally metabolized in the liver and eliminated in the urine as inactive glucuronide.

   Even in the presence of mild to moderate liver failure, patients still have sufficient hepatic reserve to metabolize propofol, although caution is warranted when there is severe liver failure. Renal failure does not significantly alter the pharmacokinetics of propofol.
3. **Midazolam**, a short-acting benzodiazepine, has an open aqueous soluble ring structure when stored at a pH of 4. After injection the open ring cyclizes at a pH of 7.4 to enhance its lipid solubility. Although midazolam's sedative and anxiolytic properties make it a useful premedicant, it is to be used with caution if memory tests are planned as a part of the diagnostic or therapeutic procedure. Small doses of midazolam, 1 to 2 mg, are unlikely to impair memory if given 20 minutes or more before the test. The use of midazolam for procedures that involve memory tests should be discussed with the surgical team before the procedure.
4. **Narcotics**. As most INR procedures are not associated with ongoing pain, **phenylpiperidine narcotics** have become the mainstay of pain management. Fentanyl, sufentanil, alfentanil, and remifentanil all belong to this class of drugs (Table 17.3). Fentanyl, despite its relatively long duration of action, is the most frequently used narcotic. Remifentanil, however, offers greater titratability because of its exceedingly short elimination half-life as a result of hydrolysis by non-specific esterases in the blood. Respiratory depression, pruritus, and vomiting are some of the side effects relevant to INR procedures. The remote location of the patient's airway mandates that the use of narcotics be judicious. Careful attention has to be paid to respiratory monitoring and the use of narcotics curtailed if the respiratory rate drops below 10 to 12 breaths/minute.

## IV. GENERAL ANESTHESIA WITH ENDOTRACHEAL INTUBATION

General anesthesia with endotracheal intubation in the INR suites is the same as in the OR for both adult and pediatric cases. A theoretical argument can be made for eschewing the use of nitrous oxide because of the possibility of introducing air emboli into the cerebral circulation. The primary reason for employing general anesthesia is **to reduce motion artifact and improve the quality of images**. This is especially pertinent to INR treatment of spinal pathology in which extensive multilevel angiography must sometimes be performed. Because chest excursion during positive pressure ventilation can interfere with road mapping, radiologists frequently request periods of apnea during DSA for certain procedures.

## V. HEMODYNAMIC AND RESPIRATORY MANIPULATION

**A. Deliberate hypotension.** The two primary indications for deliberate hypotension are to decrease the flow through an arteriovenous fistula during injection of glue and to test the cerebrovascular reserve of the patient undergoing carotid occlusion. In most instances, the level of sedation is decreased to permit neurologic examination during deliberate

hypotension. The induction of hypotension in awake or minimally sedated patients can be fairly challenging. Large doses of hypotensive drugs are needed to reduce the BP in minimally-sedated patients. Adrenergic blocking drugs that do not directly affect CBF might be preferable to drugs that are potential cerebral vasodilators. Typically, high doses of esmolol, 1 mg/kg bolus and then an infusion of ≈ 0.5 mg/kg/minute, are required in these patients. Supplemental labetalol might be necessary during the esmolol infusion. Sodium nitroprusside and nitroglycerin may also be used. Hypotension may lead to nausea and vomiting. Additional doses of antiemetic drugs such as ondansetron, 4 mg, and dolasetron, 12.5 mg, may be given before lowering the BP.

**B. Flow arrest**. Transient flow arrest has been used successfully in relatively healthy (ASA I and II) patients for the **treatment of high-flow cerebral AVMs** with NBCA glue embolization. When flow arrest is planned the patient is prepared for **general anesthesia**. In addition to the usual intravenous access, a central venous catheter is inserted for injecting drugs. **Adenosine**, 10 to 90 mg as a bolus, has been used to achieve flow arrest. We recommend conducting a dose response study to determine the optimal dose of adenosine necessary to produce 5 to15 seconds of asystole. A small dose of esmolol or nitroprusside might be necessary to treat rebound hypertension or tachycardia. Transvenous pacing catheters or external pacing pads are placed for treating any persistent arrhythmias. The procedure is generally conducted in two parts. First the target feeding artery is identified and the safety of embolizing the vessel is assessed by conducting a **superselective Wada test** under monitored anesthesia care (MAC) with sedation. Once the catheter is placed in the desired location, general anesthesia is induced.

**C. Deliberate hypertension.** During cerebral arterial occlusion, planned or inadvertent, systemic BP might need to be increased to augment collateral CBF. The level to which the BP is raised depends on the condition of the patient and the nature of the disease. Typically, during deliberate hypertension the systemic BP is raised by 30% to 40% above the baseline or until ischemic symptoms resolve. The electrocardiogram and the ST segments should be inspected for myocardial ischemia. Phenylephrine is the first-line drug for deliberate hypertension. Dopamine might be useful in patients who have a slow heart rate.

**D. Deliberate hypercapnia** to a $PaCO_2$ of 50 to 60 mm Hg may be employed during the treatment of venous malformations of the head and neck. The rationale for employing hypercapnia is to increase cerebral venous outflow relative to extracranial venous drainage and to create a pressure gradient that would divert sclerosing drugs away from the intracranial veins. This is usually achieved by decreasing minute ventilation. Alternatively, carbon dioxide may be added to the inspired gases.

## VI. MANAGEMENT OF PROCEDURAL CATASTROPHES

Complications arising from cerebrovascular instrumentation can be rapid and dramatic and require a multidisciplinary approach. **A catastrophe plan is clearly defined by the anesthesia team in advance of every INR procedure.** Drugs and equipment required for airway maintenance should be immediately available. It is the primary responsibility of the anesthesia team to secure the airway and ensure adequate ventilation. While the airway is being secured, it is essential to communicate with the INR team to determine whether the problem is occlusive or hemorrhagic. Protamine should be at hand for immediate injection if the decision is made to reverse the heparin. Appropriate

neurology and neurosurgical consultants should be contacted as soon as possible.

A. **Vascular occlusive catastrophes** are treated primarily by increasing distal perfusion through BP augmentation, thrombolysis, or a combination of both methods.

B. **Hemorrhagic catastrophes** might be heralded by headache, nausea, vomiting, and vascular pain related to the area of vascular perforation. The proceduralist might see the contrast extravasate seconds before the patient becomes symptomatic. In the case of vessel puncture, heparin reversal before withdrawing the offending wire or the catheter back into the lumen of the vessel will keep the perforation partially occluded until hemostatic function is restored. Immediate reversal of the heparin is indicated as soon as an intracranial hemorrhage is diagnosed. Protamine, 1 mg for every 100 U of heparin, is given without undue regard for the systemic BP. An ACT may be done later to adjust the final dose. With active bleeding the BP should be kept as low as possible. Once bleeding is controlled, the target BP should be discussed with the INR team. If vascular occlusion has been used to control the hemorrhage, the INR team may ask for deliberate hypertension. Allergic reactions to protamine are rare but may occur.

## VII. TRANSPORT AND POSTPROCEDURAL CONSIDERATIONS

A. **Arterial closure devices** permit early ambulation and decrease the chances of postprocedural hemorrhage from the arteriotomy site in high-risk patients who are anticoagulated or morbidly obese or have large-bore femoral sheaths. Manual compression of the groin may be ineffective in such cases, is uncomfortable and operator dependent, and requires postprocedural bed rest for at least 8 hours and observation for 24 hours. A variety of arterial closure devices including Vasoseal, Angioseal, Duett, Perclose, and Starclose have been used to seal the arteriotomy site, decrease the risk of vascular complications, and permit early ambulation. Complications associated with closure devices include hemorrhage, pseudoaneurysm, arteriovenous fistula, proximal arterial occlusion, distal emboli occlusion, and potential infection of the arteriotomy site. Devices like Starclose should not be used in patients who are allergic to metals such as nickel or titanium.

B. **Postprocedural observation** in the intensive care unit (ICU) is indicated for the first 24 hours after intracranial and spinal INR procedures. The groin is monitored for bleeding from the puncture site. In addition, INR procedures have their own inherent potential complications and require neurologic, metabolic, and hemodynamic monitoring. For example, after AVM embolization there might be enough tissue edema to cause some deterioration in the neurologic status during the course of the first evening after the procedure.

## VIII. SPECIFIC PROCEDURES

A. **Superselective anesthesia and functional examination (SAFE) or superselective Wada test** is routinely performed before therapeutic embolizations to minimize the risk of occluding a nutritive vessel to eloquent regions, either in the brain or the spinal cord, which could happen if the microcatheter tip is proximal to the origin of nutritive vessels. However, not all authorities recognize the need for SAFE before embolization. The level of sedation is decreased before testing by discontinuing the propofol infusion. In rare instances it might be necessary to use naloxone or flumazenil to antagonize the sedative drugs. A baseline focused neurologic examination under residual light sedation is performed by the INR team.

**Sodium amobarbital**, 30 mg/mL, or **lidocaine**, 30 mg/mL, mixed with contrast is injected through the superselective catheter and an angiogram of the drug/contrast mixture is obtained. Sodium amobarbital is used for investigating the gray matter. Lidocaine can be used to evaluate the integrity of the white matter tracts, especially in the spinal cord. The injection of lidocaine into cortical areas, especially those close to the motor strip, can cause seizures. Such seizure activity can itself cause transient neurologic deficits so that postictal paralysis may confuse interpretation of the test. For this reason the barbiturate is usually given first, followed by lidocaine. If the amobarbital test is negative, it can protect against seizures but will not interfere with the assessment of lidocaine's effect on white matter tracts.

B. **Superselective angiography and therapeutic embolization of intracranial AVMs.** Typically, patients who present for embolization have large, complex, parenchymatous AVMs, which are composed of several discrete fistulae with multiple feeding arteries. The goal of the therapeutic embolization is to obliterate as many of the fistulae as possible. The procedure can last 4 to 5 hours depending on the complexity of the lesions. A variety of embolic materials have been used to obliterate AVM fistulae including polyvinyl alcohol particles and NBCA glue which has the advantage of more durable results.

1. Although in rare cases INR treatment is aimed at total obliteration, embolization is usually employed as **an adjunct in preparation for surgery or radiotherapy** and can be beneficial in several ways. First, embolization may **facilitate surgery by obliterating deep feeding arteries** that are difficult to approach surgically and thereby reduce the surgical risk. Second, staged obliteration of arteriovenous shunts also theoretically **allows the surrounding brain to accommodate to the alterations in hemodynamics**. Third, obliteration of high-flow feeders can be of benefit in patients who have progressive neurologic deficits or intractable seizures, ostensibly by diminishing steal but more likely by **decreasing mass effect**. Finally, approximately **10% of AVM patients harbor intracranial aneurysms**. Such aneurysms appear to increase the risk of spontaneous hemorrhage from AVMs. The obliteration of intranidal aneurysms during the initial embolization may decrease the rate of recurrent hemorrhage during the course of treatment.
2. **Technique.** When the catheter is in position for potential glue injection, SAFE is performed. If SAFE is positive and focal neurologic deficits develop, then either the catheter is repositioned or embolization of that pedicle is aborted. If the test is negative, glue or other embolic material can be injected. **Controlled deposition of the glue** is necessary to decrease complications from pulmonary embolism or obstruction of the AVM's venous drainage. **Flow arrest** through the fistula is desired during glue injection to permit polymerization and solidification of the glue. Techniques for flow arrest include deliberate hypotension, balloon occlusion of the proximal vessel, and circulatory pause with either adenosine or controlled ventricular fibrillation. In most instances flow arrest can be achieved with deliberate hypotension to a mean systemic BP ≈ 50 mm Hg. Flow arrest is not needed for PVA or Onyx embolization.
3. **Measurement of immediate postembolization pressure** has been suggested as a means of following the course of hemodynamic changes and predicting postprocedure complications. A large increase in feeding artery pressure after embolization may be associated with intracranial hemorrhage. Because AVM feeding arteries supply normal vascular territories to a variable degree, abrupt restoration of normal perfusion pressure to a chronically

hypotensive vascular bed might overwhelm the autoregulatory capacity and result in hemorrhage or swelling, known as normal perfusion pressure breakthrough (NPPB). It is for this reason that the target range for post-treatment BP is at or slightly below the patient's normal systemic pressure. NPPB remains a controversial entity, if it even truly exists.

C. **Embolization of spinal cord lesions** can be used for intramedullary spinal AVMs, dural fistulae, and tumors invading the spinal canal. For cases performed under general anesthesia with endotracheal intubation, an **intraoperative "wake-up test"** may be requested. The wake-up test must be explained to the patient the night before and on the day of surgery. A **nitrous oxide/narcotic anesthetic technique** with concurrent propofol may be employed for the procedure. Neuromuscular blockade, if required, should be readily reversible for the wake-up test. For selected lesions, somatosensory and motor evoked potentials can be helpful in both anesthetized and sedated patients. When motor evoked potentials are monitored the neuromuscular block should be titrated to the monitoring needs.

D. **Treatment of other CNS vascular malformations**

1. **Dural AVMs** induce venous hypertension and, when cortical venous drainage is involved, may cause intracranial hemorrhage. Multiple intracranial and extracranial arteries may feed them so that multi-staged embolization is usually indicated. Superselective anesthesia and functional examination are performed, as in the case of intracranial AVMs. Transarterial embolization of NBCA glue is a commonly utilized technique as well as transvenous coil occlusion of pathologic venous pouches.
2. **Carotid cavernous fistulae.** Trauma to the skull base is the most common etiology of carotid cavernous fistulae. Traumatic fistulae can also occur between the vertebral artery and the paravertebral veins. Such arteriovenous fistulae can lead to chronic hypotension in the surrounding normal vascular territories. Treatment may include transarterial detachable balloon occlusion or transvenous occlusion of the involved cavernous sinus. Obliteration of the fistulae might result in NPPB. Therefore, after obliteration of these lesions the BP should be maintained at 10% to 20% below the patient's normal pressure.
3. **Vein of Galen malformations** are relatively uncommon but complicated lesions that usually present in infancy and childhood. These patients may have congestive heart failure, intractable seizures, hydrocephalus, and mental retardation. Several approaches have been attempted including transarterial and transvenous techniques. The concerns during general anesthesia for INR therapy are the same as for surgical treatment. In the setting of congestive heart failure, pre-existing right-to-left shunts, and pulmonary hypertension, a relatively small glue embolus can be fatal.
4. **Intra-arterial chemotherapy and embolization of tumors.** Preoperative embolization as a means of decreasing blood loss during surgery can be performed for many hypervascular intracranial and spinal tumors. Superselective administration of chemotherapeutic drugs can be used for treating neoplasms refractory to conventional therapy. Paragangliomas can cause catecholamine release from the tumor during embolization so that means for treating hypertensive crises should be at hand.

E. **Carotid artery test occlusion and therapeutic carotid occlusion.** Test occlusion of the carotid artery is undertaken before anticipated sacrifice of the artery or when temporary carotid ligation might be required during surgery. For

the test occlusion, a catheter that has a distal balloon and a lumen is inserted into the ICA. A baseline neurologic examination is performed. **Flow velocity** is measured over the middle cerebral artery (MCA) by TCD ultrasound, if available, and the **CBF** is measured by the intracarotid $^{133}$Xenon injection technique. Baseline femoral and carotid artery pressures are noted. The balloon is then inflated and the pressure in the carotid artery distal to the balloon recorded. Inflation of the balloon might cause headache and at times an increase in the systemic BP. Aggressive treatment of hypertension is probably not warranted as it may decrease collateral perfusion pressure. The anesthesiologist should be prepared to treat bradycardia with atropine. The neurologic examination is repeated a few minutes after occlusion and TCD flow velocity and $^{133}$Xenon CBF measurements are also repeated. After $^{133}$Xenon washout data have been obtained, radioactive tracer for single-photon emission computerized tomography (SPECT) studies may be injected. This provides a snapshot measurement of regional CBF during ICA occlusion. As SPECT tracers usually have a long half-life and bind avidly to cerebral tissues, the imaging part of a SPECT study may be undertaken in the nuclear medicine department after completion of the INR procedure.

1. If the patient does not demonstrate any neurologic impairment during the initial ICA occlusion, **the systemic BP is decreased to assess cerebrovascular reserve**. During the reduction of the systemic BP, neurologic examination is repeated at frequent intervals. The distal ICA (stump) pressure at which neurologic deterioration occurs or whether the patient starts yawning—often a sign of impending cerebral ischemia—is noted along with the corresponding TCD flow velocity. Depending on the clinical condition of the patient, another $^{133}$Xenon measurement is obtained. If overt neurologic symptoms develop, the balloon is immediately deflated, hypotensive drugs are discontinued, and, depending on the clinical situation, vasopressors might be required to increase the BP to normal levels.
2. Although a uniform guideline for interpreting the results of the test occlusion has yet to be formulated, the occurrence of a new neurologic deficit, significant asymmetry on SPECT imaging, or a 25% to 30% reduction in $^{133}$Xenon CBF or TCD flow velocity after occlusion may be considered as relative indications for an extracranial to intracranial bypass procedure before sacrifice of the carotid artery.

**F. Aneurysm ablation.** Many intracranial aneurysms are amenable to endovascular treatment which is increasingly considered to be the primary treatment modality for ruptured and unruptured intracranial aneurysms. The indications for open surgical versus endovascular therapy are currently a topic of vigorous discussion. There are two basic **approaches to endovascular obliteration of intracranial aneurysms**: the **occlusion of the proximal parent artery**, such as the carotid artery which has been discussed above, and **obliteration of the aneurysmal sac**. Endovascular obliteration of the aneurysmal sac is usually accomplished with detachable coils made by a wide variety of vendors. Complicated aneurysms that have wide necks and large sacs may require advanced techniques involving temporary balloon remodeling or intracranial stent placement. These procedures may be prolonged and require **general anesthesia** with endotracheal intubation. In addition the patient may require adequate antiplatelet treatment before stent placement that compounds the risk of hemorrhage during coiling. The anesthesiologist should be prepared for **aneurysmal subarachnoid hemorrhage** (SAH) spontaneously or as a result of intravascular manipulations. **Occlusive complications** may also develop requiring additional maneuvers

to enhance CBF and initiate revascularization. Aneurysm occlusion and thrombosis may continue after intervention so that careful attention to postprocedure BP control remains critical, especially in patients who presented with SAH.

G. **Angioplasty.** Mechanical angioplasty or pharmacologic dilatation may be indicated for vasospasm after SAH and for atherosclerotic cerebrovascular disease.

1. **Angioplasty for cerebral vasospasm** is usually undertaken in patients who continue to have signs and symptoms of cerebral ischemia despite maximal medical therapy. These patients are often in extremis and are therefore frequently mechanically ventilated and receiving vasopressor drugs and have either an external ventricular drain or other intracranial pressure (ICP) monitoring device in place. Angiography is first undertaken to demonstrate that there is a significant degree of spasm in large proximal vessels (anterior, middle, and posterior cerebral arteries). Under fluoroscopic guidance, **a balloon catheter is inserted into the spastic segment and inflated to distend the constricted area mechanically**. If deliberate hypertension has been induced to ameliorate a focal neurologic deficit before angioplasty, the BP should be reduced to the patient's normal range after angiographic demonstration of significant widening of the spastic segment.
2. **Pharmacologic dilatation for cerebral vasospasm** is accomplished **by direct intra-arterial injection of vasodilators under fluoroscopic guidance.** Originally described for papaverine, the armamentarium of vasodilators has now expanded to the more frequent use of calcium channel blocking drugs such as verapamil and nicardipine. The anesthesiologist should monitor for systemic side effects during recirculation including hypotension and bradycardia after the administration of verapamil and nicardipine.
3. **Angioplasty for atherosclerosis.** Recent studies have demonstrated that the **morbidity and mortality from carotid artery stenting are comparable to those from carotid endarterectomy** (CEA). The multicenter Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) revealed a slightly higher stroke rate with stenting and a slightly higher rate of myocardial infarction with CEA. Other studies, such as by Cao et al., have shown somewhat higher stroke rates with stenting as compared to CEA. However, the CREST study also indicated that younger patients were less likely to have a stroke after stenting than older patients. Some people have questioned the routine stenting of asymptomatic patients because of the risk of stroke; others, however, cite the CREST study to justify the procedure in the same subgroup. Besides the patient characteristics, factors such as the skill of the operator may also affect the outcome of these procedures. Further studies and subgroup analysis are necessary to inform the choice between stenting and operative treatment of carotid artery disease. At the moment both procedures seem to carry a similar low overall risk of complications.
   a. **Extracranial angioplasty** is accomplished by balloon dilatation and the placement of a vascular stent. In many cases, a cerebroprotective device may be used to decrease the risk of distal thromboembolism. Angioplasty of the ICA is usually undertaken with **minimal sedation**.
   b. **Intracranial angioplasty** and stenting for atherosclerotic segments of the intracranial arteries have a **higher level of risk** secondary to the inherently more delicate nature of the intracranial vessels which have a thinner media and therefore are more prone to dissection and perforation and may be less effective than maximal medical therapy. **General anesthesia** is required for intracranial angioplasty the

TABLE 17.5 Antiplatelet Drugs

| | Aspirin | Clopidogrel (Plavix TM) | Antiplatelet Antibodies (Abciximab TM) |
|---|---|---|---|
| Mechanism of action | Inhibition of prostaglandin synthesis by cyclooxygenase inhibition | Prevent ADP binding to glycoprotein receptor IIb and IIIa, inhibiting platelet activation | Antibody to glycoprotein receptor IIb and IIIa |
| Dose | 50–325 mg/d | 300 mg loading dose followed by 75 mg/d | 0.15–0.25 mg/kg, followed by an infusion 0.125 mg/kg/min |
| Half-life | 1–2 h | Rapidly metabolized; main metabolite has elimination half-life of 8 h | 10–30 min |
| Correction strategy | Platelet transfusion | Withhold for at least 5–7 d; platelet transfusion | Platelet transfusion |
| Contraindication | Renal and hepatic failure; drug interactions | Allergic reactions | Allergic reactions |

TM, trade mark; ADP, adenosine diphosphate.

considerations for which are the same as for CEA. The selection of anesthetic technique also depends on the patient's medical condition and ability to cooperate during the procedure and whether technical difficulty is anticipated in negotiating the stenotic segment. **Deliberate hypertension** might be required for augmenting collateral blood flow. A variety of antiplatelet drugs are now available to prevent stroke and consolidate the results of endovascular interventions (Table 17.5).

**H. Thrombolysis for acute stroke.** The effectiveness of intravenous thrombolysis in acute thromboembolic stroke **within the first 3 to 4.5 hours of the onset of symptoms** has already been demonstrated in several clinical trials. As compared with intravenous delivery, **superselective intra-arterial delivery** of thrombolytic drugs such as recombinant tissue plasminogen activator (rtPA), streptokinase, and urokinase (Table 17.6) can recanalize the occluded vessel with a higher concentration of thrombolytic drug and less systemic exposure. The disadvantage of intra-arterial thrombolysis is that it is only offered in specialized centers; its administration is often delayed; and it carries a higher potential risk of hemorrhagic transformation which has a high mortality when it occurs. Significant improvement in neurologic outcome has been demonstrated when pharmacologic thrombolysis is completed within 6 hours of the onset of ischemic symptoms (PROACT II, MELT) or when mechanical thrombolysis is performed within 8 hours (MERCI trial).

1. **Mechanical means** of clot retrieval, balloon angioplasty, and ultrasonic and laser ablation are also being developed. These methods can restore arterial flow rapidly in contrast to intra-arterial thrombolysis which

TABLE 17.6 Antithrombolytic Therapy

| | Prourokinase | Tissue Plasminogen Activator (tPA) Alteplase | Reteplase | Streptokinase[a] |
|---|---|---|---|---|
| Mechanism of action (specific features) | Plasminogen activation | Activates fibrin-associated plasminogen (527 amino acids) | Activates fibrin-associated plasminogen (355 amino acids) | Forms activator complex with plasminogen |
| Dose[b] | 4 mg in clot; then 2–8 mg/h | 0.05 mg/kg/h | 5 units; then 0.5–2 units/h infusion | 1–1.5 million units/60 min |
| Half-life | 11–16 min | 4–6 min | 15 min | 10–20 min |
| Antidote | Amicar | Amicar | Amicar | Amicar |
| Contraindication | Allergic reaction | Allergic reaction | Allergic reaction | Allergic reaction |

[a]Not available in the United States.
[b]Doses vary based on route and clinical circumstances.

may require up to 2 hours. In the vertebrobasilar circulation, treatment may be effective even if delayed for as long as 24 hours from the onset of symptoms.

2. **Significant improvement in neurologic outcome** has been demonstrated when pharmacologic thrombolysis is completed within 6 hours of the onset of ischemic symptoms (PROACT II, MELT) or when mechanical thrombolysis is performed within 8 hours (MERCI trial). The current strategies to effect further improvement in outcome after acute thromboembolic stroke include the combination of initial intravenous thrombolysis with subsequent intra-arterial thrombolysis; the use of mechanical clot retrieval devices for removing proximal clot load and then either intravenous or intra-arterial thrombolysis for distal residual clot; and the use of concurrent ultrasound to improve the clot penetration of intravenous and intra-arterial thrombolytic drugs.
3. **Anesthetic considerations** in these patients include those for the elderly and for patients who have widespread arterial disease. Patients are spontaneously hypertensive after acute thromboembolic stroke and, in the face of non-hemorrhagic focal neurologic deficits, should not have their BP aggressively lowered. After clot lysis the BP is maintained in the patients' normal range and ideally titrated to some index of CBF to prevent hyperperfusion injury.

I. **Vertebral compression fracture therapy** with **vertebroplasty** and **kyphoplasty** involves the introduction of acrylic bone cement compounds directly into the vertebral body via a percutaneous, often transpedicular, approach. The characteristics of this patient population who are at once elderly, frail, and osteoporotic and the considerations for prone positioning require extra care during the preparation process. Most of these procedures can fortunately be performed and well tolerated with **mild sedation.** The clinical benefits of vertebroplasty remain to be fully evaluated and could be

improved by proper patient selection, such as including those patients who have better bone densities. Many patients do, however, report significant pain relief after these procedures.

**Conclusions.** INR procedures are now recognized as alternatives to, and are sometime used in conjunction with, conventional surgery for several intracranial and spinal disorders. Their role in the definitive treatment of aneurysms, carotid artery disease, and certain AVMs is well established. These procedures often facilitate conventional surgery for tumors and AVMs by reducing blood loss. For some conditions, such as vertebroplasty, acute stroke, and chemotherapy of tumors, the risk/benefit ratio of INR procedures has yet to be elucidated. Anesthetic management of these procedures, though similar to that for traditional operative approaches, is beset with hazards and requires certain accommodations to ensure safe and successful outcomes.

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# 18 Anesthetic Management of Diagnostic Neuroradiology

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## Illustrative Clinical Case

A 16-year-old, 30-kg patient who has severe developmental delay and scoliosis related to cerebral palsy requires anesthesia for magnetic resonance imaging (MRI) of the spine in preparation for corrective surgery. The patient has had nothing by mouth, has no known drug allergies, and receives a multivitamin daily. He has good range of motion of his neck, a large tongue with prominent incisors, and his airway has been assessed as Mallampati Class II.

Anesthetic (EMLA) cream is applied to the dorsum of his hands 60 minutes before the procedure, and in the MRI suite a 20 gauge intravenous catheter is inserted without incident. Standard American Society of Anesthesiologists monitors compatible with MRI are applied. General anesthesia is induced with propofol, 2 mg/kg, and rocuronium, 40 mg, is administered to facilitate endotracheal intubation with a 6.0 cuffed endotracheal tube. Anesthesia is maintained with isoflurane and nitrous oxide ($N_2O$) while the study proceeds. At the conclusion of the imaging (140 minutes), the neuromuscular relaxation is reversed, the patient is breathing spontaneously, and the trachea is extubated. He is brought to the postanesthesia care unit (PACU), utilizing portable oxygen and a transport monitor.

## Chapter Highlights

- Technical advances in neuroimaging are occurring rapidly. Combination modalities such as single photon emission computed tomography/computed tomography (SPECT/CT) are being used with increasing frequency.
- Anesthesia care must often be provided far from the operating room (OR) and under challenging circumstances.
- Excellent communication between the radiology and anesthesia teams is paramount.
- Anesthesiologists must be aware of potential contrast reactions and appropriate therapy.

The introduction of the first CT scanners in 1975 revolutionized the imaging of neurosurgical lesions. Since that time, the diagnostic armamentarium of the neuroradiologist in terms of neuroimaging has expanded progressively. Diagnostic procedures usually involve limited pain so that the neuroradiologist or a sedation team may administer sedation. The anesthesiologist is involved, however, in cases for which either difficulty with sedation or the need for general anesthesia is anticipated for a myriad of reasons. These include extremes of age, claustrophobia, serious neurologic or systemic illness, and the inability of patients to remain motionless to be able to achieve high-quality images.

Many radiology departments have recently adopted the guidelines for the sedation of children formulated by the American Academy of Pediatrics Workgroup on Sedation. These guidelines address patient selection, dietary precautions, equipment,

monitoring, and discharge criteria. Furthermore, strict selection criteria minimize sedation-related side effects. The screening of patients before the procedure often reveals those who have either anticipated airway difficulties or serious medical conditions for whom the presence of an anesthesiologist becomes advisable. In one study, 13.1% of patients were inadequately sedated for their procedure, resulting in failure of 3.7% of procedures. Older children and those undergoing MRI and CT scans experienced higher failure rates. In addition, Malviya found that 5.5% of children sedated by non-anesthesiologists experienced an untoward respiratory event. These events occurred more commonly in American Society of Anesthesiologists (ASA) status III and IV patients.

## I. GENERAL CONSIDERATIONS

Once involved in the neuroradiologic procedure, the anesthesiologist faces the usual problems of providing anesthesia in an environment foreign to and far from the OR. Non-ferromagnetic equipment and monitoring modalities are required in the MRI suite, and most neuroradiographic procedures require that the anesthesiologist be positioned at a distance from the patient. Additionally, the issue of contrast media with their attendant osmolar effects and potential for toxic and allergic reactions must be considered. Finally, the design of modern medical facilities often requires that patients be either recovered by qualified personnel in an area adjacent to the radiology suite or transported over relatively large distances through the medical center to the regular PACU.

**A. Evaluation.** A thorough preoperative evaluation should be performed for each patient scheduled for a neurodiagnostic procedure. In addition to elucidation of the patient's medical and surgical history, allergies, medications, and experience with previous sedatives and anesthetics, particular attention must be directed to the neurologic examination. Patients are carefully evaluated for signs of increased intracranial pressure (ICP), preexisting neurologic deficits, and, in the case of the emergency head-injured patient, concomitant (and sometimes undiagnosed) injury to the spine and other major organ systems.

**B. Equipment** available in the radiology suite should include compatible anesthesia delivery systems, adequate supplies of medical gases, suction apparatus, age-appropriate drugs and airway equipment, and monitors for oxygen saturation, end-tidal carbon dioxide ($ETCO_2$), electrocardiogram (ECG), and blood pressure (BP) compatible with the imaging modality.

## II. COMPUTED TOMOGRAPHY

**A. Basic considerations.** Ionizing radiation is delivered to the patient during CT scanning. Radiation detectors are permanently fixed all of the way around the CT gantry. For each image, an x-ray tube rotates in a circle within the detector ring emitting a beam of ionizing radiation that passes through the body. The **multiple detectors record the quantity of the x-ray beam that is attenuated or absorbed as it passes through the patient's tissues.** This information from various angles is electronically integrated and the average attenuation value of each point in space is expressed in Hounsfield units.

Attenuation by a substance is directly related to its electronic density. Therefore, structures are hypodense (of lower attenuation), isodense (of similar attenuation), or hyperdense (of higher attenuation) relative to the brain parenchyma. The attenuation of vascular structures is increased by the use of iodinated contrast drugs. While **CT axial images** are displayed initially, high-resolution thin images can be transformed into **coronal and**

**sagittal sections** as well as **3-dimensional representations** through computer reformatting.

CT scanning is relatively insensitive for viewing structures within the posterior fossa because of image degradation by the artifact produced by the interface of bone and brain parenchyma. This modality remains the choice, however, for the **detection of skull fractures and acute subarachnoid hemorrhage** in the emergent setting. The **helical or spiral acquisition CT scan** is also popular because larger anatomic regions can be imaged quickly, which is particularly useful in the trauma situation. For example, visualization from the aortic arch to the circle of Willis can be accomplished in < 1 minute of scan time. With spiral acquisition scanning, unlike conventional CT scans, the patient is moved at a constant speed through the scanning field while the x-ray tube rotates continuously. **CT angiography** utilizes spiral acquisition scanning during the administration of iodinated contrast as an intravenous bolus. Complex intracranial aneurysms < 2 mm in diameter can be visualized with CT angiography.

**B. Management**

1. **Sedation.** With the current rapid CT scanners, very few adults or school-aged children require sedation for CT scanning. Occasionally, either intravenous **midazolam** in titrated doses of 0.5 mg or an infusion of **propofol** at a dose of 25 to 100 mcg/kg/minute may be used for conscious sedation in an anxious adult patient for the brief procedure.
2. **General anesthesia.** If an adult or older child manifests signs and symptoms of **increased ICP or serious airway compromise**, it is better to proceed with general anesthesia rather than attempt sedation. Several suggested techniques for the sedation of small children are listed in Table 18.1 In addition to concerns about equipment, monitoring, and airway management, it must be remembered that the temperature of children within the cold radiology suite environment must be carefully maintained.

   In the clinical situation where increased ICP is a critical factor, the **intravenous induction** of general anesthesia can be accomplished in **children** after the application of EMLA (lidocaine 2.5% and prilocaine 2.5%) cream

TABLE 18.1 Sedation Techniques for Small Children

| Drug | Dose | Route | Onset (min) | Peak Effect (min) |
|---|---|---|---|---|
| Chloral hydrate | 20–100 mg/kg (2 g maximum) | po, pr | 20–30 | 30–90 |
| Dexmedetomidine | 1 mcg/kg loading dose<br>2.5 mcg/kg/h | iv | 1–5 | 5 |
| Midazolam | 0.02–0.15 mg/kg<br>0.3–1.0 mg/kg | iv<br>po, pr | 1–5 (iv) | 20–30 |
| Methohexital | 1–2 mg/kg<br>20–30 mg/kg | iv<br>pr | 5<br>10–15 | <br>45 |
| Pentobarbital sodium | 2–4 mg/kg<br>5–8 mg/kg (120 mg maximum) | iv, im<br>po | 5–10<br>1–5 | 60–90<br>5 |
| Propofol | 150–200 mcg/kg/min | iv | 3–5 | 5 |

po, by mouth; pr, by rectum; iv, intravenous; im, intramuscular.

to the dorsum of the patient's hands and insertion of an intravenous catheter. The issue of undiagnosed muscular dystrophy mitigates against the use of succinylcholine in children. An induction utilizing rocuronium, 0.6 to 1 mg/kg, for relaxation is often indicated. Anesthesia in children is maintained with an intravenous infusion of propofol, 25 to 100 mcg/kg/minute, or low concentrations of inhaled anesthetics.

In **adults**, an intravenous induction utilizing thiopental, 3 to 4 mg/kg, or propofol, 1 to 2 mg/kg, followed by succinylcholine, 1 mg/kg, with the addition of a small dose of narcotic such as fentanyl, 50 to 100 mcg, and lidocaine, 1 mg/kg, to deepen the anesthetic is appropriate for endotracheal intubation. **Rapid awakening** at the end of the procedure is desirable. An infusion of remifentanil, 0.1 to 0.2 mcg/kg/minute, is an alternative in adults and children.

## III. MAGNETIC RESONANCE IMAGING

MRIs are acquired when the protons on water molecules within the patient's body are excited through a combination of a **strong magnetic field** and **intermittent radio frequency (RF) pulses.** Additional magnetic fields are applied to create gradients and excite the protons to different orientations within the basic magnetic field. In the excited state, these **protons gain energy and shift from a low energy state to a high-energy state.** This process is termed **resonance.** When the RF pulse is turned off, the protons lose energy in two ways: T1, the longitudinal relaxation time, and T2, the transverse relaxation time. Fortunately, no ionizing radiation is employed with MRI, but a large, powerful, external magnetic field is necessary.

**Standard MRI sequences** include T1-weighted images, proton density, and T2-weighted images, as well as T1 images with the intravenous administration of gadolinium contrast material. **Fluid attenuated inversion recovery** (FLAIR) utilizes T2 weighting, but suppresses the cerebrospinal fluid (CSF) signal, increasing the visibility of lesions in the cortex, subarachnoid space, and perivertebral region. **Gradient recalled echo** is an additional sequence sensitive to hemoglobin breakdown products such as hemosiderin. This technique allows identification of intraparenchymal hemorrhage in the subacute to chronic phases. **Susceptibility-weighted imaging** provides excellent contrast for gray-white matter, differentiating venous blood vessels and hemoglobin breakdown products. Through constant technologic improvement, the reliability of MRI has increased in difficult clinical scenarios. Currently, the **areas optimally imaged by MRI** include the limbic system, pineal gland region, sella and parasellar structures, cranial nerves, internal auditory canal, cerebellopontine angle, leptomeninges, and posterior fossa.

While **magnetic resonance angiography** provides images of arterial and dural sinus blood flow, **functional MRI** is being utilized with increasing frequency in patient evaluation. Precise 3-dimensional anatomic localization and a contrast effect dependent on the level of blood oxygenation facilitate functional studies of sight and hearing. These permit the accurate identification of the areas responsible for language before epilepsy surgery. **Diffusion-weighted imaging** is useful in the detection of acute cerebral infarctions and is able to identify regions of ischemia within minutes. **Dynamic contrast enhanced MRI** (DCE-MRI) utilizes intravenous gadolinium contrast to augment a diffusion-weighted study to demonstrate the presence of cerebral tissue at risk for further ischemia.

The frequency of **adverse reactions to gadolinium-based contrast** of all types is much lower than the frequency of adverse reactions to iodinated

contrast material. The reactions to gadolinium can, however, range from mild erythema of the skin to severe life-threatening reactions including periorbital edema, respiratory distress, and cardiovascular collapse. In patients who report a previous reaction to gadolinium-based contrast, **pretreatment** with corticosteroids such as ranitidine (Zantac) and diphenhydramine (Benadryl) and substituting a different gadolinium-based contrast can be helpful.

In 2006, nephrogenic systemic fibrosis (NSF) was identified as a rare complication triggered by the administration of gadolinium-based contrast. Patient who have severe chronic kidney disease (glomerular filtration rate < 30 mL/minute) are most susceptible to NSF and the administration of a reduced dose of gadolinium-based contrast (preferably chelated in a cyclic form) is currently the best preventive strategy.

A. **Monitoring.** The MRI suite presents a hostile environment to the anesthesiologist. There are several **important safety considerations.**
   1. **Metallic objects within the patient** can be affected, depending on their metallic properties. Implants (including vascular surgical clips, stents, cochlear implants, and intrauterine devices) are subject to magnetic flux that can induce electrical currents and cause local heating and movement. The function of pacemakers, cardiac catheters, and insulin pumps can be altered with exposure to the magnetic field. The radiologist most commonly assesses the hazards of all metallic implants.
   2. External metal wires, such as the ECG leads and temperature probe, can burn the skin. It is therefore **necessary to use non-ferromagnetic monitoring modalities** especially designed for and compatible with the magnetic resonance (MR) scanner. Pulse oximeters, even non-ferrous and fiberoptically cabled ones, should be placed on a distal extremity as far from the scanner as possible. The occurrence of scan artifacts and local skin irritation and swelling has been reported in patients who have either permanent eye makeup or tattoos that contain ferromagnetic pigments.
   3. Small **loose metal objects can be pulled toward the magnet** and are obviously dangerous. Large objects such as oxygen cylinders can also be pulled into the magnet with considerable force and can be a serious threat to both patients and health care personnel. In general, no metallic objects are allowed in the scanning room.
   4. **Noise** is a problem in the MR scanner. The torque on the loops of wire in which gradient currents are induced during the RF pulses causes vibration and audible noise that can average 95 decibels in a 1.5-T scanner. Newer 3-T machines generate twice the noise, hampering communication and necessitating ear protection for patients regardless of whether they are awake, sedated, or asleep.
   5. RF **heating from induced currents** is a potential problem, particularly in small infants. Periodic assessment of body temperature must be conducted. Infants can also become cold within the magnet because of the low ambient temperature in the scanning room.
   6. Newer, more powerful **3-T MR scanners can induce electric currents** in patients that can stimulate the peripheral nervous system. Paresthesias, cephalgia, and muscle contractions have all been reported. The RF impulse–induced electric currents can also cause burns.
   7. The anesthesiologist must find the point of least distortion by orienting monitors in various positions relative to the magnetic field. Most ECG artifacts cannot be eliminated and **monitors should be MR-compatible** and

have good artifact suppression characteristics. It is important to twist the ECG cables, keeping the electrodes close together, and position the electrodes near the center of the imager with the cables padded to avoid direct contact with the skin, to get the best images and to reduce the possibility of burns.

**Specialized equipment compatible with MRI** is currently available for monitoring BP, $ETCO_2$, Doppler, oxygen saturation, and ECG. Compatible anesthesia machines and ventilators are available as well. Plastic laryngoscopes are also available although the batteries in the handle could still be pulled into the magnetic field. Problems remain in terms of patient accessibility, hypothermia, and the physical limitations of positioning obese patients within the magnet's bore.

**B. Anesthetic management.** Many **sedative techniques** have proven quite reasonable for MR scanning, including the scanning of infants shortly after a meal to take advantage of postprandial drowsiness. The anesthesiologist is called to assist with MRI, however, when a patient is complicated neurologically, manifests serious illness, or has significant airway difficulties. In general, **securing the airway with an endotracheal tube** and then **supplying ventilatory assistance** through hand ventilation, an MRI-compatible ventilator, or a long circuit ensure an optimum combination of monitoring, airway protection, and anesthetic delivery. Certain centers have utilized an intravenous infusion of **propofol**, either with or without a laryngeal mask airway, to achieve the same goals. Whatever the technique, **the ability to maintain adequate control of the airway in the face of limited access remains of paramount importance.**

## IV. POSITRON EMISSION TOMOGRAPHY (PET) AND SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT)

These **nuclear imaging modalities** are used to measure **glucose consumption (PET)** and **regional cerebral blood flow (SPECT),** thereby providing an indirect measurement of tissue metabolism and oxygen utilization.

**A. PET scans** use positron-labeled molecules of which the most common is 2-[$^{18}$F] fluoro-2-deoxy-D-glucose (FDG). The FDG is injected intravenously and taken up into cerebral tissue. Because FDG cannot diffuse out of the brain after phosphorylation, it is well suited for imaging cerebral metabolism. PET scans are used in the **investigation of malignancy** because tumor cells have a much higher glucose metabolism.

As of 2006, major vendors no longer offered PET-only imaging systems. The combination of **PET/CT technology** into a single imaging system allows accurate anatomic localization of functional abnormalities. Whole-body **FDG-PET/CT** examinations are now completed for tumor staging purposes in 10 minutes or less. Research continues in combining PET and MRI imaging and the development of additional $^{18}$F-labeled tracers.

**B. SPECT scans** use radiotracers that emit single photons. Three radiopharmaceutical drugs have been approved by the United States Food and Drug Administration (FDA) for brain perfusion and SPECT scanning. Of the three, Tc-99m hexamethylpropyleneamine oxime ([$^{99m}$Tc]HMPAO) is used most commonly. It reaches maximum uptake 10 minutes after injection but has a constant distribution for hours afterward, which makes scheduling a scan very flexible. **SPECT scans are used to investigate malignancy, cerebral ischemia, neurodegenerative disorders, epilepsy, cortical visual loss, and migraine headaches.** A SPECT scan of the brain takes 20 to 45 minutes. Almost all of the radiopharmaceuticals are cleared through the urinary tract. For both PET and SPECT scans, the radiation exposure for the patient is usually equivalent to a CT scan but may be as high as ten effective dose equivalents.

Recently, SPECT scanning has been combined with CT to differentiate tracer uptake in malignant cells of low-grade tumors from adjacent areas with physiologic tracer uptake with greater accuracy. Several photon emitting tracers, such as thallium-201, [$^{99}$mTc]-MIBI, [$^{99}$mTc]-tetrofosmin and L-3 [$^{123}$I]-iodine-$\alpha$-methyl tyrosine (IMT) have been used to characterize biologic features of brain tumor.

C. **Anesthetic considerations.** Many anesthetic drugs have been shown to alter cerebral blood flow (CBF) and metabolism, but, because of the stability of the tracers after injection, anesthetizing a patient for a scan should not interfere with the results. Anesthetic considerations include the necessity for providing all appropriate monitoring modalities, medical gases, drugs, suction, and airway equipment in a remote location. Unlike MRI, PET and CT scanners do not require non-ferromagnetic monitors, and the visualization of and access to the patient are more easily accomplished. **Combined PET/CT or SPECT/CT scans require no patient movement** so that the images can be easily coregistered.

## V. CEREBRAL ANGIOGRAPHY

A. Cerebral angiography maintains an important position in treatment planning for patients who have subarachnoid hemorrhage and carotid artery disease. The safest and most widely used arterial access is the common femoral artery so that the use of a **transfemoral catheter** has replaced direct puncture of the carotid artery. **Digital subtraction angiography** reduces the volume of intra-arterial contrast required and the overall duration of the procedure. Unfortunately, **neurologic problems** related to the angiography have occurred. In a prospective study of 1,002 angiograms, the overall rate of ischemic events within 0 to 24 hours of the procedure was 1.3% and 2.5% in patients studied for cerebrovascular disease. **Complications from the catheters** include transient global amnesia, cortical blindness, multiple cholesterol emboli syndrome, and vascular complications such as hematoma and pseudoaneurysm at the puncture site. A more recent prospective study documented a lower complication rate of 0.3% when angiography was performed at an academic medical center by a neurointerventionalist.

B. **Anesthetic management.** Although anesthesiologists are asked to participate in diagnostic angiography on rare occasions, they must bear in mind that **contrast media cause vasodilatation and a burning discomfort**. Often the degree of sedation needs to be increased in anticipation of an intra-arterial injection of contrast. As always, there is the possibility that a reaction to the contrast material can occur.

## VI. MYELOGRAPHY

Myelography, a rarely-performed procedure, does offer benefit if MRI is contraindicated. It **defines the contents of the thecal sac and any intrinsic or extrinsic impressions.** The contrast is introduced directly into the subarachnoid space, thereby bypassing the blood–brain barrier. The newest myelographic contrast media are non-ionic, of low osmolarity, and mix well with CSF. The **main complications** related to myelography include headache, contrast-related complications, either subdural or epidural contrast injection, hematoma of the spinal canal, meningitis, seizures, and various forms of neurologic injury. The **incidence of adverse events** is higher in women and increases with cervical versus lumbar puncture and with the use of 22-gauge bevel-tipped versus 24-gauge Sprotte needles. Among the **anesthetic considerations** is the need to position infants and children carefully as the myelogram table is rotated to achieve good flow of the contrast material.

## VII. CONTRAST MATERIAL

**A.** In addition to CT scans, **iodinated contrast** is used for catheter angiography. **High-osmolar contrast media** are ionic monomers at concentrations ranging from 60% to 76% by weight. This material possesses five to eight times the osmolality of human serum (280 mOsm/L $H_2O$). Non-ionic monomers and dimers as well as ionic dimers are considered **low-osmolar contrast agents** (LOCAs) when they have from two to three times the osmolality of human serum. The LOCAs demonstrate more hydrophilia and less tendency to bind to tissue and are therefore more biologically inert. An **iso-osmolar contrast agent** (IOCA) is also available and clinical utilization is increasing.

**B.** **Iodinated contrast materials are nephrotoxic.** Direct toxicity to renal tubular cells may occur and after initial mild vasodilatation, the renal vascular tree undergoes prolonged vasoconstriction. Patients who have pre-existing renal insufficiency, diabetes mellitus, and low cardiac output syndromes are at risk for developing contrast media-induced nephrotoxicity. **Renal insufficiency can be ameliorated or prevented with adequate hydration** and the withholding of any other nephrotoxic medications before the procedure. The use of fenoldopam, *N*-acetylcysteine, and dopamine has consistently failed to preserve renal function more effectively than hydration alone. Patients at risk should receive limited amounts of iodinated contrast media. Diabetic patients who have nephropathy and who receive metformin should be carefully monitored for the development of metformin-induced lactic acidosis after receiving iodinated contrast.

**C.** The **hypertonicity of iodinated contrast media is responsible for the side effects** that occur after injection. These include pain, flushing, nausea, and vomiting. Patients' responses to iodinated contrast material can range from a warm flushing and a metallic taste during contrast injection to an anaphylactoid reaction. Large multi-institutional studies have demonstrated that patients given non-ionic contrast material have a 1 in 10,000 chance of having a severe reaction. **Patients likely to have a problem with contrast** include those who have had previous idiosyncratic contrast reactions, patients who have either asthma or multiple food and medication allergies, and patients who have other illnesses including pre-existing azotemia and cardiac disease. The use of **corticosteroids** such as oral methylprednisolone, 32 mg, both 6 to 24 hours before and 2 hours after the injection of the contrast material, **markedly reduces the chance of a severe reaction to contrast**. Additionally, some centers add antihistamines and $H_2$ receptor blocking drugs to the steroid regimen.

Not infrequently, a few hives about the face, neck, and chest are the **sole reaction** that a patient manifests to contrast. Often the only **therapy** necessary in such cases is reassurance with perhaps a dose of diphenhydramine, 25 to 50 mg. A severe reaction to contrast, as manifest by generalized skin irritation, respiratory difficulties, and hypotension, requires treatment with epinephrine, 100 mcg, and glucagon for refractory hypotension. Equipment must be available in the radiology suite for immediate airway control and the administration of additional adjuncts such as beta 2-agonists including albuterol for treating bronchospasm. Occasionally, large volumes of fluid as well as vasoactive drugs are necessary to support the BP. A prolonged stay in the intensive care unit could be necessary to stabilize the patient.

Delayed reactions can be seen in 1% to 3% of patients receiving x-ray contrast material. These are usually mild and consist of rashes and hives.

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# 19 Parkinson's Disease and Deep Brain Stimulator Insertion

**Alana M. Flexman and Pekka O. Talke**

## Illustrative Clinical Case

A 72-year-old man who has hypertension and gastroesophageal reflux disease presents with a 9-year history of Parkinson's disease (PD). He has a severe resting tremor and progressive bradykinesia, both of which are becoming difficult to control despite the use of increasing doses of levodopa/carbidopa. He is scheduled for bilateral insertion of a deep brain stimulator (DBS) under local anesthesia and sedation.

## Chapter Highlights

- **PARKINSON'S DISEASE**
  - **A.** General
  - **B.** Pathophysiology
  - **C.** Pharmacologic treatment
    - **1.** Dopamine agonists
    - **2.** Non-dopamine agonists
  - **D.** Anesthetic considerations for PD

- **SURGICAL TREATMENT OF PD**
  - **A.** Definitions
  - **B.** Deep brain stimulation (DBS)
  - **C.** Patient selection for DBS in PD
  - **D.** Technique: Stages of DBS insertion

- **ANESTHETIC CONSIDERATIONS FOR DBS INSERTION**

- **Anesthetic options**
  - **A.** Local anesthesia and sedation
  - **B.** General anesthesia

- **ANESTHETIC MANAGEMENT**

- **PERIOPERATIVE COMPLICATIONS**

- **FUTURE DIRECTIONS**
  - **A.** New indications
  - **B.** Neuroprotection
  - **C.** Stem cell transplantation

## I. PARKINSON'S DISEASE

### A. General

1. **Parkinson's disease** (PD) is a progressive neurodegenerative disorder characterized by muscle rigidity, bradykinesia, tremor at rest, and postural instability.
   a. The largest **risk factor for PD is increasing age** with an **incidence of 0.1%** and **prevalence of 1%** in people over 65 years of age. There is a slightly higher incidence in men than women.
   b. **Idiopathic PD** comprises 85% of Parkinsonian syndromes. Secondary causes are rare and include drug-induced (primarily neuroleptic medications), cerebrovascular disease, head trauma, and metabolic causes.
   c. PD causes **non-motor signs and symptoms** in addition to the motor symptoms. These include
      1. Autonomic instability
      2. Sleep disturbance
      3. Sensory abnormalities (e.g., akathisia)
      4. Cognitive impairment
      5. Depression and anxiety

### B. Pathophysiology

1. **Movement** is regulated by complex interactions among the basal ganglia, thalamus, cerebellum, and cerebral cortex.
2. **Loss of dopaminergic cells** in the pars compacta region of the substantia nigra in the basal ganglia results in an imbalance between acetylcholine-induced excitation and dopaminergic inhibition of the striatum. Increased excitation leads to **excessive inhibition of the thalamus and brain stem nuclei**. Suppression of the cortical motor system produces akinisia, rigidity, and tremor while suppression of the brain stem motor areas results in postural instability and gait abnormalities.
3. The **non-motor manifestations** of PD likely result from dopaminergic neurons outside these pathways as well as non-dopaminergic changes elsewhere in the central nervous system (CNS).

### C. Pharmacologic treatment

**Pharmacologic treatment** of PD is targeted at restoring the balance between the neurotransmitters dopamine and acetylcholine in the brain. Over time, however, patients become less responsive to the pharmacologic treatments of PD with progressive impairment in their quality of life.

1. **Dopamine agonists**
   a. **Levodopa**, a dopamine precursor, is converted to dopamine in the CNS. **Carbidopa**, an enzyme that limits conversion of levodopa to dopamine outside the CNS, is commonly coadministered (**Sinemet**). Dopaminergic drugs are effective against all the motor symptoms of PD.
   b. **Apomorphine** is the only parenterally available dopaminergic medication and is generally reserved for use as a rescue therapy. Nausea and vomiting are common side effects, and antiemetics should be coadministered.
2. **Other medications**
   a. **Monoamine oxidase (MAO) inhibitors**. As MAO B degrades dopamine in the CNS, MAO inhibitors are a potential therapy for patients who have PD.
   b. **Amantadine,** an antiviral medication, improves symptoms in mild PD although the mechanism is unknown.
   c. **Anticholinergics** (e.g., benzotropine) may improve tremor and rigidity although are of limited use.

**D. Anesthetic considerations for PD**

1. **Airway complications** such as aspiration, laryngospasm, and inability to manage secretions can result from pharyngeal and laryngeal dysfunction.
2. **Autonomic instability** may be manifest as hypotension, hypovolemia, and arrhythmias.
3. **Respiratory complications** are more common owing to poor cough, recurrent infection, and rigidity-induced restrictive lung disease.
4. **Dementia and depression** are common which may impair intraoperative communication and cooperation. The risk of postoperative delirium is increased.
5. **Difficult monitoring and vascular access** may result from severe tremor and abnormal posturing.
6. **Pharmacologic management** of dopaminergic medications and consideration of their interactions with anesthetic drugs in the perioperative period are paramount.
   a. **Dopaminergic medications should be continued** in the perioperative period to avoid significant motor impairment. The **exception** is in patients undergoing surgical management of PD with DBS insertion for which these medications will typically be held.
   b. **Anticholinergic medications** may worsen the symptoms of PD and **should be avoided**. These include common antiemetics (e.g., metaclopramide, prochlorperazine, phenothiazines) and antipsychotic medications (e.g., haloperidol, loxapine).
7. **Presence of a DBS** has specific anesthetic implications including potential damage or reprogramming by electrocautery or magnetic resonance imaging (MRI). The DBS may also interfere with electrocardiographic (ECG) monitoring.

## II. SURGICAL TREATMENT OF PARKINSON'S DISEASE

**A. Definitions: Pallidotomy** involves permanent lesioning of cells within the globus pallidus internus primarily to alleviate involuntary movements and rigidity. **Thalamotomy** involves permanent lesioning of cells within the thalamus primarily to alleviate tremor.

**B. DBS** involves **high-frequency stimulation** of the deep brain structures **to induce a functional lesioning of the target area**. Targets of DBS are typically the subthalamic nucleus (STN), globus pallidus, and ventralis intermedius nucleus. Stimulation of the STN appears to provide the greatest benefit in PD.

1. DBS offers several **advantages** over surgical lesioning in the treatment of PD and has become the therapy of choice. Advantages include reversibility, programmability, and improved safety profile. In addition, while DBS may be performed bilaterally, bilateral lesioning is considered risky and is contraindicated.
2. DBS **improves quality of life** through reduction in dyskinesia, tremor, and rigidity and improvement in the performance of activities of daily living. While DBS provides symptomatic relief of motor symptoms, it is **not curative** and the disease remains progressive.

**C. Patient selection for DBS in PD**

1. The **optimal timing for DBS is as yet unclear**. Current guidelines recommend waiting a minimum of 5 years to decrease the risk of misdiagnosis and to allow accurate assessment of the response to medications.
2. Patients referred for DBS are typically **uncontrolled medically** and may have severe tremor, rigidity, dyskinesia, and "off" periods.

3. **Exclusions** to DBS are severe depression or cognitive impairment, major behavioral disorder, and major medical comorbidity. While age alone does not exclude DBS, **increasing age is predictive of poorer outcome** and increased perioperative risk.
4. **Levodopa responsiveness** is the strongest predictor of DBS success in PD.
5. **Bilateral stimulators** are used for patients who have bilateral symptoms but may worsen cognitive function in impaired patients. **Unilateral stimulators** are used for patients who have asymmetrical symptoms.

D. **Technique: Stages of DBS process**

1. **Frame application and imaging:** A stereotactic **head frame is applied** to the patient's head using **local anesthesia or scalp nerve blocks and light sedation** (e.g., midazolam). This stage may be accomplished in the preoperative holding area, the operating room (OR), or the imaging suite. The patient **then undergoes either magnetic resonance imaging** (MRI) or computed tomography (CT) imaging with the head frame in place. The STN or other target location is identified on the imaging and the precise coordinates are determined for guidance during lead insertion. The patient is **then brought to the OR** and placed in a semisitting or sitting position after which the head frame is fixed to the OR table.
2. **Burr hole placement:** A small incision is made after **local anesthesia infiltration or scalp nerve blocks**. The creation of the burr hole is accomplished under **moderate to heavy sedation** in addition to the local anesthesia.
3. **Electrode localization:** DBS leads are implanted through the burr hole. This procedure is ideally done with an **awake, cooperative patient**. The electrode lead is advanced through the burr hole toward the thalamus and subthalamic region guided by one or more localization modalities.
   a. **Microelectrode recordings** (MERs) are made as the leads are advanced carefully through the thalamic region in 0.5 to 1 mm increments. Target nuclei are identified through distinctive patterns of spontaneous neuronal firing.
   b. **Intraoperative brain navigation** derived from preoperative MRI or CT imaging helps guide appropriate lead placement and may occasionally be the primary modality used for lead placement. **Real-time fluoroscopy** may be used as an **adjunct to stereotaxis**. Appropriate **radiation safety measures** are indicated to protect the patient and OR personnel.
   c. **Test stimulation** is conducted to identify any undesired responses to stimulation and the effect of stimulation on the patient's symptoms. For example, a severe tremor may be abolished with stimulation.
4. **Electrode internalization and pulse generator insertion:** This stage is often accomplished immediately after lead localization or may be done as a delayed procedure several days later. The head frame is removed and **general anesthesia (GA)** is induced. This stage is done under GA as a period of intense stimulation occurs during tunneling of the leads. The pulse generator is implanted in the chest below the clavicle, and a single generator is sufficient for bilateral DBS. The pulse generator is not turned on for several days or weeks to allow healing.

## III. ANESTHETIC CONSIDERATIONS FOR DBS

A. **Limited airway access** owing to frame placement and/or imaging apparatus
B. **Multiple locations** for provision of anesthesia: OR, MRI suite, CT scanner
C. **Rapid adjustment of anesthetic depth** to facilitate neurologic assessment during electrode placement

D. **Effect of anesthetic drugs on motor evoked responses (MERs)**
E. Anticipation of and **preparation for perioperative complications** of DBS: intracranial hemorrhage, seizure, venous air embolism (VAE), airway obstruction

## IV. ANESTHETIC OPTIONS

A. **Local anesthesia and sedation**: An **awake patient is preferred** during the DBS insertion as the patient's response to test stimulation and adverse effects can be determined. In addition, an awake technique may minimize interference of anesthetic medications with MERs. Typically the patient is **moderately to heavily sedated during the burr hole craniotomy** and then **awake during electrode localization and test stimulation**. Once the electrodes have been localized, the head frame is removed and **general anesthesia is induced for internalization of the electrodes** and implantation of the generator.
B. **General anesthesia (GA)** is occasionally required for pediatric patients and patients who have severe movement disorders or are unable to cooperate. GA, however, has **several disadvantages** as compared with sedation. The effect of GA on intraoperative MERs is not well understood and their interpretation may be difficult. In addition, the patient's response to test stimulation is difficult or impossible to ascertain with GA. There may be a decreased risk of VAE with GA as the patient is in the supine position. A new technique using real-time MRI guidance alone to place electrodes under GA has recently been developed and may provide superior accuracy.

## V. ANESTHETIC MANAGEMENT

A. **Preoperative assessment to determine**
   1. **Comorbid disease** in the elderly patient
   2. Recent **upper respiratory infection** as a cough is a relative contraindication to an awake neurosurgical procedure
   3. **Potential for airway complications** including presence of obstructive sleep apnea (particularly if sedation is planned), difficult airway management, and risk of aspiration from bulbar dysfunction
   4. Patient's **ability to cooperate and emotional stability** if planning an awake procedure
   5. **Medication regimen**. Typically medications taken for motor symptoms will be held overnight and on the morning of surgery.
   6. Baseline **vital signs**
B. **Preoperative investigations** are reviewed.
   1. Recent hemoglobin and hematocrit
   2. Blood group and antibody screen
   3. Preoperative neurologic imaging
   4. Other investigations as dictated by comorbid conditions
C. **Patient preparation and reassurance** are important to ensure cooperation during the procedure if sedation is planned. Ideally, the patient should understand all stages of the procedure and have realistic expectations about the degree of sedation and conduct of the testing.
D. **Preparation of the OR** is important to alleviate the patient's anxiety and discomfort. **Room temperature** should be comfortable with heating blankets available. **Advanced airway equipment** should be readily available with a **plan for emergent airway access** during the procedure already in place with the surgical team. **Access to the airway** may require movement of imaging apparatus, airway adjuncts, and possible urgent removal of the head frame.

E. **Monitoring**
   1. **Hemodynamic monitoring** typically includes a five-lead ECG and non-invasive blood pressure (BP) measurement. Direct arterial BP measurement is not required but may be dictated by patient indications. Monitoring may be difficult due to the tremor and abnormal posturing in PD.
   2. **Respiratory monitoring** is critical to avoid respiratory depression. Non-invasive end-tidal carbon dioxide monitoring is an extremely useful adjunct to continuous pulse oximetry.

F. **Anesthetic drugs**
   1. **Propofol** has been commonly used for sedation of patients during burr hole placement and lead internalization at doses in the range of 20 to 80 mcg/kg/minute. The **advantages** of propofol include a short half-life, the ability to titrate depth of sedation easily, and excellent patient tolerance. While propofol may attenuate MERs if used during GA, baseline recordings return after its discontinuation. Despite this interference, propofol has been used successfully during GA for DBS insertion.
   2. **Opioids**
      a. **Remifentanil** is an **ultra short-acting** opioid that is often used in combination with propofol or dexmedetomidine for sedation during DBS insertion. Remifentanil has a **rapid offset** that facilitates titration of sedation. Care is indicated, however, to avoid respiratory depression.
      b. **Fentanyl** is another opioid commonly used in conjunction with other sedatives. A short redistribution half-life allows **titration of sedation**. The rigidity that occurs with larger doses used under GA may, however, be undesirable in patients who have PD.
   3. **Dexmedetomidine** has many properties that make it a suitable drug for sedation for DBS insertion. Patients receiving dexmedetomidine are **easily roused and cooperative** and may have **less respiratory depression** than with other drugs such as propofol. Dexmedetomidine has been used successfully during MERs at low doses of 0.3 to 0.6 mcg/kg/hour.
   4. **Benzodiazepines** reduce tremor in patients who have PD but can **interfere with MERs**. Their longer half-life may result in **prolonged sedation** and reduced cooperation. They are thus rarely used as the primary sedative for DBS insertion. In contrast, a single dose of a short-acting benzodiazepine such as **midazolam** is a useful adjuvant during frame placement and is not contraindicated.
   5. **Volatile anesthetics** have been used successfully during GA for DBS insertion. However, they **interfere with MERs**. Minimal attenuation is seen when used in low doses of less than 1 minimum alveolar concentration.

## VI. PERIOPERATIVE COMPLICATIONS

A. **Surgical complications**
   1. **Intracranial hemorrhage** may result from surgical misadventure and has a reported incidence of 2% to 4%. The **risk may be increased with intraoperative hypertension**. It may be prudent to target a systolic BP < 140 mm Hg intraoperatively using boluses of intravenous antihypertensive drugs as needed such as labetalol, 5 to 10 mg.
   2. **Seizures** may occur during lead placement and stimulation.
   3. **Venous air embolism** (VAE) is a reported and known risk associated with the semisitting or sitting position. In an awake patient, VAE may present as coughing, chest pain, nausea, shortness of breath, or anxiety. The risk of VAE may be minimized with early fluid loading to avoid hypovolemia and careful surgical technique.

B. **Anesthetic complications**
   1. **Airway obstruction** from loss of airway tone from the effect of sedative medications
   2. **Aspiration**
   3. **Respiratory arrest** from sedative medications
   4. **Hypertension or hypotension** resulting from underlying autonomic dysfunction
   5. **Excessive anxiety or pain**
   6. **Nausea and vomiting**
   7. **Cardiac ischemia** from underlying cardiovascular disease

VII. **FUTURE DIRECTIONS**

A. **New indications** for DBS are emerging. These include
   1. **Psychiatric diseases** such as obsessive–compulsive disorder and depression refractory to standard therapies.
   2. **Dystonia**, a syndrome of abnormal uncontrolled movements and postures. Pallidotomy and/or DBS of the globus pallidus have been used with increasing frequency in the treatment of dystonia although the precise targets for DBS and appropriate patient selection remain unclear.

B. **Neuroprotection** is hypothesized to occur with early insertion of DBS in PD. Through a reduction in glutamate release, DBS may minimize excitotoxic damage although this has not been proven in humans.

C. **Stem cell transplantation** of dopaminergic cells into the basal ganglia is currently being investigated as a potential therapy for PD.

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# 20 Intraoperative Imaging Modalities: Magnetic Resonance, Positron Emission Tomography, Gamma Knife, and Stereotactic Surgery

**Saleh A. Khunein and Pirjo Hellen Manninen**

## Illustrative Clinical Case

A 55-year-old male presented for frameless stereotactic image-guided needle biopsy of a deep left-sided parietal lobe tumor. His symptoms included headaches, speech difficulty, and one seizure. After investigation with computed tomographic (CT) and magnetic resonance imaging (MRI) scans, he was treated with dexamethasone and phenytoin. The surgeon requested that the anesthesiologist assess the patient for management of his anesthetic. The patient was cooperative and willing to undergo this procedure with conscious sedation. Preoperatively, the patient underwent MRI scanning and placement of fiducial markers for precise localization of the lesion. In the operating room, the anesthetic management consisted of non-invasive monitoring, supplement oxygen ($O_2$) via nasal prongs with carbon dioxide ($CO_2$) monitoring capability, and sedation with midazolam and fentanyl. The surgeon then, with the use of local anesthesia, applied a Mayfield head holder and fixed the frame to the operating room table. The patient was supine with his head elevated 30° and turned to his right. The biopsy was performed using an image-guided needle. The initial neurologic assessment was normal. Approximately 10 minutes later, however, while the neurosurgeons waited for the pathology report, it was noted that the patient was very drowsy and not able to communicate. What are the possible causes of this change in neurologic status? How should the patient be managed?

## Chapter Highlights

- Imaging modalities
  - Preoperative evaluation with anatomical and functional imaging techniques
  - Anesthetic considerations for intraoperative imaging
  - Neuronavigation
  - Contrast media
- Stereotactic surgery
  - Frame-based and frameless
  - Anesthetic considerations
- Stereotactic radiosurgery
  - Anesthetic considerations

## SUMMARY

1. The anesthesiologist needs to have an understanding of the various imaging modalities used in the preoperative preparation of patients as well as the anesthetic considerations when these modalities are used in the operating room.

2. Stereotactic surgery, especially frame-based, provides a challenge for the anesthesiologist because of concerns about airway management.
3. Stereotactic radiosurgery, such as gamma knife therapy in children, requires the provision of anesthesia in remote imaging locations and interaction with a multidisciplinary team.

## INTRODUCTION

The imaging of patients who have neurologic disorders plays an important role in their diagnosis, treatment, and outcome. Anatomical imaging with CT and MRI provides structural and pathologic information. Functional imaging with systems such as positron emission tomography (PET) and functional MRI provide neurophysiologic and metabolic information. Preoperative brain imaging and mapping of eloquent function such as speech, motor, and sensory are useful adjuncts in surgical planning. Frame-based and frameless stereotactic surgery and radiosurgery are used for accurate localization and/or safe treatment of deep intracranial structures and lesions. With new developments in imaging technology and computerization, there has been a move to integrate real-time imaging with surgery in the operating room. These systems are proving beneficial as preoperative imaging and mapping may fail to account for brain shifts that can occur during surgery as a result of patient positioning, cerebrospinal fluid drainage, diuretics, and resection.

### I. IMAGING MODALITIES

A. **Computed tomography** provides cross-sectional images of the body using mathematical reconstructions based on x-ray images taken circumferentially around the subject. The images are combined by a computer into a single picture. Contrast dye is used to enhance lesions. CT angiography is used in the diagnosis of abnormalities of the cerebral vasculature thus avoiding direct invasive angiography. Images from CT scanning can also be fused with scans from other modalities, such as PET.

1. **Intraoperative CT** allows for direct imaging during surgery via several different systems.
   a. A **fixed CT unit** is integrated with the operating room table. During surgery, both the patient and the CT unit may be completely covered with sterile drapes, limiting access to the patient.
   b. A **mobile CT scanner** is situated in the operating room and glides on floor rails to the patient when a scan is to be performed.
   c. The **combining of CT with a neuronavigation system** will improve accuracy as the images used for reference can be obtained in the operating room. The navigation can also be updated at any time during surgery.
   d. **Image-guided CT fluoroscopy** provides real-time imaging for specific intraoperative procedures such as localization of the trigeminal nerve for the treatment of neuralgia.
2. **Anesthetic considerations**
   a. During diagnostic CT scanning, patients usually do not need anesthesia or sedation, except in special situations such as an uncooperative or pediatric patient. If required, the principles of anesthesia outside of the operating room must be followed. The anesthetic technique may be either general anesthesia or conscious sedation, depending on the needs of the patient.
   b. All personnel are at risk from **exposure to high levels of radiation** during scanning. Video or remote monitoring of the patient from outside of the CT suite is usually used.

c. In the operating room, the overall anesthetic management is based on the needs of the surgical procedure and patient.
d. Access to the patient, especially the airway, may be limited during the procedure and even more so during imaging. Appropriate placement of monitors and lines is required, especially when a mobile CT unit is used.
e. During CT scanning in the operating room, all personnel should be a safe distance away and must wear proper radiation shielding (lead aprons) and use mobile screens. If possible, one should use video or remote monitoring of the patient outside of the operating room.

B. **Magnetic resonance imaging** is a non-invasive, radiation-free diagnostic procedure that uses a powerful magnetic field and intermittent radiofrequency waves. MRI produces greater contrast between soft tissues, making it is useful for neurologic imaging. Intravenous contrast is frequently given to enhance the appearance of the lesion. MRI angiography is also used to diagnose abnormalities of the cerebral vasculature.
   1. **Intraoperative MRI**: The merger of an operating room and MRI suite has been well accepted and is being used more frequently for neurosurgical procedures. This allows for real-time imaging during surgery (discussed in Chapter 13).
      a. **Anesthetic considerations**
         1. General anesthesia or conscious sedation is administered for diagnostic MRI scanning for patients who are unstable, uncooperative, claustrophobic, and pediatric.
         2. Safety concerns when providing anesthesia in an MRI environment are the same whether it is in a diagnostic suite or an operating room.
         3. A magnetic field is constantly present and extends beyond the magnet. The strong attraction of ferromagnetic objects to the magnetic field can cause them to become projectiles that may harm patients or personnel.
         4. All anesthesia and monitoring equipment must be MRI compatible.
         5. Contraindications to being in the MRI environment for the patient and all personnel must be considered.
         6. The overall anesthetic management including type of anesthetic and requirements for monitoring will depend on the surgical procedure and the patient.

C. **Neuronavigation** is **computer-assisted technology** that is **used in the operating room to localize and visualize intracranial structures and pathology during surgery.** Neuronavigation uses a set of images obtained preoperatively either by CT or MRI.
   1. Before imaging, external fiducial adhesive skin markers are placed on the patient's scalp or a set of marks is located in the reticule of an optical instrument. These markers are then used as points of reference. In the operating room, the orientation of these markers is used to register the computer containing the preoperative images. During the procedure, the imaging can show the relationship of the planned surgical incision or resection of the lesion to the previously obtained images. The **main indications** for neuronavigation are for the targeting of small and deep intracranial lesions, but neuronavigation is widely used now for many neurosurgical procedures. The addition of an intraoperative 3-dimensional ultrasound may also enhance the quality of neuronavigation by adding information about brain shift and tumor remnants.

2. **Anesthetic considerations**: Neuronavigation itself does not impact the actual anesthetic management of the patient, but it **may prolong the duration of the anesthetic**, especially before the initial surgical incision when planning for the procedure is conducted with the aid of navigation. Stimulation is minimal at this time and the anesthetic depth needs to be adjusted accordingly.

D. **Contrast media** are frequently used to improve the visibility of internal structures during imaging. Most contrast drugs are iodine- or barium-based compounds.
   1. **Complications** can occur with the use of intravenous contrast.
      a. Some contrast is hypertonic which can expand the blood volume and promote diuresis.
      b. Vasodilatation may occur causing patients to complain of headache, flushing, and transient burning pain in the face and eyes. Hypotension may also occur.
      c. Contrast nephropathy may develop in patients who have renal insufficiency, dehydration, and a history of congestive heart failure.
      d. The most severe adverse outcome is the development of an anaphylactic reaction. Patients who have had any allergic reaction to dye should be pretreated with steroids (prednisone) and an antihistamine (diphenhydramine).
      e. For MRI scanning, the most common contrast is gadolinium which has a better safety profile than iodinated contrast. Anaphylactic reactions with gadolinium are rare and its use is safer in patients who have renal impairment. The anesthesiologist may be requested to inject the contrast, especially in an intraoperative setting.
   2. **Indocyanine green (ICG)** is a cyanine dye used in medical diagnostics. ICG binds tightly to plasma protein and becomes confined to the vascular system, but is rapidly removed from circulation by the liver.
      a. **Microscope-integrated ICG video angiography** in the operating room is available and safe. It allows for assessment of the blood flow in the cerebral vasculature. After the intravenous injection of ICG dye, arterial, capillary, and venous phases are seen on a video screen and recorded. This provides real-time information to assess the patency of and blood flow in cerebral vessels, as well as residual filling and occlusion of an aneurysm.
      b. **Anesthetic considerations:** The anesthesiologist may be requested to mix and inject the dye.

E. **Functional brain imaging** provides information on the anatomic localization of a variety of brain functions, such as movement, sensation, speech, and memory. Together with conventional imaging methods used to localize the lesion, functional imaging **can be helpful in defining the relationship of the lesion to critical and eloquent brain structures as an aid in operative planning**.
   1. **Functional MRI (fMRI)** is an MRI scan that **measures changes in blood flow in relation to neuronal activity in the brain, thus providing localization of critical functions** such as language and memory. The patient is presented with a stimulus or asked to perform a task that produces an increase in neuronal activity. This results in an increased demand for oxygen that causes changes in the MR signal referred to as a **BOLD (blood–oxygen-level dependent) effect**.
      a. Functional MRI is **non-invasive and safe** and therefore repeatable in a single session and on multiple occasions. Applications of fMRI include the preoperative localization of the primary motor and sensory cortex and the assessment of patients who are unconscious.

b. **Anesthetic considerations**: Most functional MRI procedures are performed without anesthesia. The few exceptions would be pediatric, uncooperative, and claustrophobic patients. If anesthesia is required, the environment of the procedure, including the presence of the magnet, and the needs of the patient are of paramount importance.

2. **Magnetic resonance spectroscopy (MRS)** and **magnetic resonance spectroscopic imaging (MRSI) measure the levels of different metabolites in body tissues**. The MRS signal produces a spectrum of resonances that corresponds to different molecular arrangements of the isotope that is excited. MRSI combines both spectroscopic and imaging methods to produce spatially localized spectra from within the sample or patient. These techniques are **used to diagnose metabolic disorders of the brain**.
3. **MRI perfusion imaging** is a special technique for **evaluation of microscopic blood flow** in cerebral capillaries and venules. For example, the calculated MRI perfusion map of a high-grade brain tumor will demonstrate areas of increased capillary blood volume corresponding to tumor neovascularity.
4. **PET** and **single-photon emission computed tomography (SPECT)** are functional nuclear-imaging modalities that measure metabolism and oxygen utilization by visualizing tracer molecules that preferentially accumulate in specific tissues. With **PET**, used for a wide range of functional brain mapping, the patient is asked to perform a behavioral task. The cerebral blood flow (CBF), as quantified by the tracer, is then measured. **SPECT** scans use single-photon gamma-emitting radioisotopes and rotating cameras to produce 3-dimensional brain images. Both systems **provide imaging of glucose metabolism, oxygen utilization, CBF, transmitter events, and protein synthesis**. They can be used as an isolated imaging tool or as part of multimodality imaging. In **preoperative planning,** they are used to **identify eloquent brain function and for localization of a seizure focus**.
5. **Magnetoencephalography (MEG)** is a non-invasive method of **mapping brain activity by measuring the magnetic fields that accompany neuronal activity**. The magnetic fields are produced by electrical currents, which are seen on the electroencephalogram (EEG).
   a. MEG is **used primarily for mapping the functional cortex and localizing epileptogenic foci in the presurgical evaluation of patients who have epilepsy**. MEG is also used in conjunction with image-guided surgery to aid in the safe resection of lesions adjacent to eloquent areas of the brain.
   b. **Anesthetic considerations**: Most functional MRI procedures are performed without anesthesia. The few exceptions would be some pediatric patients. If anesthesia is required, the environment of the procedure, including the presence of an MRI, and the needs of the patient are to be considered.

## II. TREATMENT MODALITIES

A. **Stereotactic surgery** is a minimally-invasive form of surgical intervention that **uses a system of 3-dimensional coordinates to locate small targets within the brain**. Procedures performed include biopsy, ablation, injection, stimulation, implantation, and resection of intracranial lesions. The term "stereotactic" was coined from Greek and Latin roots meaning "touch in space." Stereotactic surgery requires a planning system that has multimodality imaging and a coordinates calculator in a frame-based or a frameless system.

1. **Frame-based stereotactic surgery** involves the placement of a light-weight head frame with a base that is attached to the cranium with pins. Either CT or MRI imaging, with or without angiography, is used to identify the targeted lesion in relation to the distance from the lesion to the reference points on the external frame. These are measured in 3-dimensions. The surgical apparatus needed for the procedure is attached to the head frame and can be adjusted according to the 3-dimensional coordinates of the target. The surgeon can then approach the target accurately using appropriate surgical instruments.
2. **Frameless stereotactic surgery** uses either external fiducial scalp markers or a set of marks in the reticule of an optical instrument as points of reference. This avoids the invasive attachment of a head frame to the patient's cranium. Images of the same subject produced with two different imaging systems can be correlated by these markers. During the procedure, the imaging will show the relationship of the surgical instruments to the previously imaged brain.
3. **Anesthetic considerations**
   a. The initial step in frame-based surgery is the **placement of the head frame**. In some institutions, this may be performed in a location outside the main operating room as in the radiology suite. After imaging in the CT or MRI suite, the patient is then transported to the operating room for the surgical procedure.
   b. If general anesthesia or sedation is to be administered in a remote location, all anesthesia equipment, monitors, and drugs must be readily available at the site and for transporting the patient.
   c. Anesthetic techniques for frame placement and the surgical procedure include monitored anesthesia care, conscious sedation, or general anesthesia depending on the patient's needs and the type of procedure.
   d. For most adults, **local anesthesia** is used for infiltration of pin sites and for regional scalp blocks. Pediatric patients may require general anesthesia for the entire procedure.
   e. The **management of the airway** needs careful consideration. With general anesthesia, the patient's airway should ideally be secured before the placement of the head frame. The head frame may obscure the patient's mouth and/or nose and prevent extension of the neck because of the posterior parts, making airway manipulation difficult. If intubation is required after frame placement, airway-securing modalities such as the laryngeal mask, video-assisted laryngoscopy, and fiberoptic bronchoscopy will be helpful.
   f. For the procedure, **the stereotactic head frame is attached to the operating room table**. This limits head movement and may seriously compromise the patient's airway. In the awake patient, the anesthesiologist must ensure that the position of the head and neck is comfortable for the patient; mouth opening is good; and there is some access to the patient's airway.
   g. Standard monitors are routine and invasive monitoring is used as indicated. Supplemental oxygen is usually delivered to the awake or sedated patient via nasal prongs or oxygen mask. This allows for continuous monitoring of end-tidal $CO_2$ and respiratory rate.
   h. Frameless stereotactic surgery may also require the use of a pin-fixation frame such as the Mayfield or Suggita. If the patient is awake during placement, local anesthesia will be infiltrated at the pin sites.
4. Continuous vigilance is needed to **diagnosis and treat complications** quickly, especially in the awake or sedated patient.

a. A change in neurologic status or a decrease in the level of consciousness may result from the procedure with attendant intracranial bleeding or neurologic injury.
b. Respiratory depression, desaturation, and a decrease in respiratory rate may be caused by either oversedation or an intracranial event.
c. Acute airway obstruction may be caused by mechanical obstruction if the patient shifts while the head frame is fixed to the operating room table. Treatment is to release the head frame from the operating room table immediately.
d. Cardiovascular events such as hypertension may result from excessive pain or anxiety.
e. Less common are nausea, vomiting, and air embolism.
f. In anesthetized patients, there may also be complications from the anesthetic effects and position-related problems including hypotension and venous air embolism.

5. Postoperative care is in a postanesthesia care unit (PACU) or intensive care unit (ICU) designated and designed specifically for the care of neurosurgical patients. Careful monitoring of the patient's neurologic status is required to diagnose intracranial complications such as bleeding, ischemia, and infarction in a timely fashion.

B. **Stereotactic radiosurgery (SRS)** is a minimally-invasive procedure that delivers therapeutic energy in the form of high-dose radiation to an accurately defined target without an incision. SRS is used to treat a wide variety of conditions including brain tumors, arteriovenous malformations, and pain syndromes such as trigeminal neuralgia. Many different systems are used to deliver the radiation beams including the gamma knife, linear accelerator, and CyberKnife.

1. **Gamma knife** is a device that enables many beams of high-intensity gamma radiation (cobalt 60) to converge on one site. The lesion can usually be treated in one session. A circular array of beams is used and, as each individual beam is of relatively low energy, the radiation has little effect on intervening brain tissue and is concentrated only at the lesion itself. The patient wears a specialized cast-steel helmet that is fixed to a head frame attached to the skull, which enables the target point to remain stationary.
2. **Linear accelerator-based system (linac**) is a type of particle accelerator that greatly increases the velocity of charged subatomic particles or ions by subjecting them to oscillating electric potentials along a linear beamline. The linear accelerator is the device **most commonly used for external-beam radiation treatment**. It delivers a uniform dose of high-energy radiation that can destroy the lesion while sparing the surrounding normal tissue.
3. **Robot-assisted linac radiosurgery** increases the accuracy of imaging and treatment. Robot-assisted SRS involves the use of implanted metallic markers, bony landmarks, or fiducial skin markers to provide reference points for localization and a computerized robotic system for one or more steps of the procedure. This modality has been used in the treatment of intracranial and extracranial tumors, vascular malformations, and neurologic conditions including trigeminal neuralgia and movement disorders.
4. **CyberKnife** is a frameless robotic radiosurgery system that uses the radiation produced from a small linear particle accelerator and a robotic arm. This allows the energy to be directed at any part of the body from any direction with great accuracy. CyberKnife software has the ability to merge MRI and PET images with existing CT images to enhance targeting.

5. **Anesthetic considerations**
   a. Most **SRS procedures in adults are performed without anesthesia**. Anesthesia is frequently required, however, in young children and in some uncooperative adults.
   b. The **administration of anesthesia** requires coordination among the departments of radiology, radiation therapy, and anesthesiology. The overall procedure may be conducted in several steps and at different locations. All appropriate anesthesia equipment, monitors, and drugs must be ready for use at each site and during transportation.
   c. The **anesthetic technique** will depend on the needs of the patient. At many sites, both total intravenous anesthesia (TIVA) and inhalational anesthesia can be used, but TIVA is required during transport from site to site. Radiation therapy units may not be set up for general anesthesia as they may lack gas evacuation, among other requirements, making TIVA the only option.
   d. **Gamma knife radiotherapy in a young child**, for example, is often a whole-day procedure, which requires that the patient remain anesthetized for the duration. The procedure usually begins in the radiology suite with the induction of general endotracheal anesthesia after which the stereotactic head frame is attached to the cranium. The subsequent imaging studies may include CT, MRI, and angiography. If MRI scanning is used, all considerations for anesthesia in the MRI suite must be taken into account from the beginning.

      The radiotherapy team then reviews all the images and plans the course of radiotherapy. This may take considerable time and many children remain anesthetized during the entire period. This requires that they wait in an appropriate location: either a holding area or the PACU where all necessary anesthesia equipment and monitors are available.

      The anesthetized patient is then transported to the gamma knife suite for treatment. The patient's head and airway will be obscured by the head frame and radiation helmet. All personnel leave the suite during treatment as the presence of radiation is very high. The patient is consequently monitored via cameras directed at the patient, monitors, anesthesia machine, and infusion pumps. The video monitors are usually located outside the suite at the control desk. After the therapy session is completed, the patient is transferred to a monitored suite (holding area or PACU) for emergence and postoperative care.

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# 21 Complications in the Postanesthesia Care Unit

**Jean G. Charchaflieh, Samrat H. Worah, and Georges I. Labaze**

## Illustrative Clinical Case

A 52-year-old woman presented to the emergency department (ED) with severe headache. Her head computed tomographic (CT) scan showed a Grade II subarachnoid hemorrhage (SAH) in the right parietal lobe and her cerebral CT angiogram showed a 6-mm berry aneurysm in the right middle cerebral artery. Neurosurgery (NS) and interventional radiology (IR) services were consulted, and it was decided to proceed with aneurysm coiling by the IR service with NS service backup. Her preoperative clinical examination was remarkable for left lower extremity weakness and an elevated blood pressure (BP) of 224/91 mm Hg. She underwent uneventful aneurysm coiling under general anesthesia with direct arterial BP monitoring after which her trachea was extubated in the IR suite and she was transferred to the intensive care unit (ICU) for further monitoring. In the ICU, she was noted to have left lower extremity weakness, which was unchanged from her preoperative examination.

Approximately 2 hours after arrival in the ICU, she complained of a mild headache that progressed rapidly, over a period of 15 minutes, to excruciating pain. Clinical examination revealed an elevated BP of 216/105 mm Hg, left upper and lower extremity weakness, and slurred speech. An infusion of nicardipine was started at 5 mg/kg/h for suspected vasospasm, and the patient was transferred to the radiology suite for an immediate head CT scan that showed an expansion of her SAH. On arrival in the postanesthesia care unit (PACU), her speech became increasingly slurred and she was extremely agitated. The anesthesiologist covering the PACU intubated the patient's trachea for airway protection for which she was sedated and paralyzed. The patient was then transferred to the IR suite for angiography that showed rupture of the coiled aneurysm.

In consultation with the IR service, the NS service decided to proceed with craniotomy and surgical clipping of the aneurysm. After a successful operation, the patient was transported to the ICU in stable condition, her trachea still intubated. In the ICU, she was sedated and mechanically ventilated for 2 days to allow recovery from the brain trauma resulting from bleeding and procedures. Her trachea was extubated on the third postoperative day after meeting extubation criteria. Postextubation, her left-sided weakness was much improved from her precraniotomy examination and her speech was remarkably improved. On

postoperative day 5, she was transferred to the NS step-down unit for further recovery, and on postoperative day 8, she was transferred to the rehabilitation service. She was eventually discharged home on postoperative day 16 with complete return of function.

## Chapter Highlights

Patients undergoing neurosurgical procedures are prone to the development of a variety of postoperative complications. Awareness of these potential complications is essential to early detection, prevention, and treatment.

I. **COMPLICATIONS AFTER OPERATION FOR SUPRATENTORIAL TUMOR**

A. **Increased intracranial pressure (ICP).** The cranial cavity has a limited capacity to accommodate increased intracranial volume without a significant increase in pressure. Increased volume of any one of the three components of the intracranial cavity—brain cells, blood, and cerebrospinal fluid (CSF)—may increase ICP. Increased ICP causes injury to the brain by compression, herniation, and ischemia. Brain ischemia in turn enhances brain edema, propagating a cycle of vascular insufficiency and swelling.

B. **Intracranial hemorrhage, hydrocephalus, and cerebral edema are the most common postoperative causes of increased ICP**. Intracranial hypertension leads to headache, nausea, vomiting, decreased level of consciousness, and neurologic dysfunction. These signs are not specific for increased ICP and are not uncommon postoperatively. Detection of increased ICP relies on clinical signs and symptoms, direct measurement of ICP, and imaging studies such as computed tomography (CT) scanning. Prevention and treatment are aimed at avoiding and alleviating factors that can aggravate intracranial hypertension such as arterial hypertension, impaired cerebral venous drainage, blocked or malfunctioning surgical drains, postoperative pain, respiratory depression, nausea and vomiting, shivering, and seizures.

1. **Cerebral edema** is minimized by intraoperative and postoperative use of dexamethasone, loading dose 10 to 20 mg intravenously; then 4 mg intravenously every 6 hours, and mannitol, loading dose 0.25 to 2 g/kg intravenously over 30 minutes; then every 6 hours as needed, with careful monitoring of fluid intake and output, serum electrolytes and osmolarity, and control of blood pressure (BP) and central venous pressure (CVP).
2. **Venous drainage** is facilitated by head elevation to 30°, BP permitting.
3. **Respiration and oxygenation** should be monitored and supplemental oxygen as well as ventilatory support provided as needed.
4. **Pain** is treated with small doses of fentanyl, 0.5 to 1 mcg/kg intravenously every 1 to 2 hours; morphine, 0.025 to 0.05 mg/kg intravenously every 1 to 2 hours; or hydromorphone, 0.2 to 1 mg intravenously every 2 to 3 hours. Intraoperative scalp infiltration with local anesthetics has been shown to reduce postoperative pain after supratentorial craniotomy.
5. **Postoperative nausea and vomiting** (PONV) are minimized by intraoperative use of dexamethasone (as above Section I.A.1) and 5HT-3 receptor antagonists such as dolasetron, 12.5 mg intravenously in adults and 0.35 mg/kg intravenously in children, or ondansetron, 4 mg intravenously over 4 minutes for adults and children weighing > 40 kg and 0.1 mg/kg intravenously over 4 minute for children weighing < 40 kg. Awake craniotomy for tumor surgery is associated with a reduced incidence of PONV in comparison with general anesthesia.

6. **Postoperative shivering** is treated with gradual rewarming of the patient and small doses of narcotic.
7. **Postoperative seizures** are treated with phenytoin, loading dose 10 to 20 mg/kg intravenously no faster than 50 mg/minute (1,000 mg over 20 minutes in a typical adult); then 5 to 7 mg/kg/day, or fosphenytoin, loading dose "phenytoin equivalent (PE)" 15 to 20 mg/kg intravenously no faster than 100 to 150 mg/minute (1,000 mg PE over 10 minute in typical adult); then 4 to 6 PE mg/kg/day.
8. **Delayed hydrocephalus** may occur after resection of supratentorial malignant gliomas. It should be considered when delayed deterioration follows initial improvement. Shunting of communicating hydrocephalus yields satisfactory results. Multiloculated hydrocephalus requires placement of multiple catheters and is associated with poorer outcome.

## II. COMPLICATIONS AFTER OPERATION FOR INFRATENTORIAL TUMOR

**A. Increased ICP.** The elastance of the infratentorial compartment is greater than that of the supratentorial compartment, which means that it takes smaller increases in volume to produce significant increases in pressure. Furthermore, increased pressure in the posterior fossa is more life threatening because it can compress or herniate the brain stem, which contains the respiratory and vascular control centers. **Brain stem herniation** can occur downward through the foramen magnum or upward through the tentorium, which is most common after resection of tumors of the cervical medullary junction. Signs of **brain stem compression** include a decrease in the patient's level of consciousness and respiratory and cardiovascular abnormalities including collapse. Measures to control ICP should be continued in the postoperative period including head elevation, prevention and treatment of hypertension, pain, nausea, vomiting, and shivering, and maintenance of adequate ventilation and oxygenation (Section I.A.1–7). A decrease in the level of consciousness or the development of respiratory or cardiovascular abnormalities should prompt surgical consultation.

**B. Brain stem injury** can occur intraoperatively. The postoperative signs are failure to regain consciousness or resume spontaneous respiration and cardiovascular abnormalities such as bradycardia and hypertension/hypotension. Pharmacologic causes of such manifestations should be ruled out by ensuring adequate reversal of anesthetic drugs and muscle relaxants. Supportive care in the form of mechanical ventilation and hemodynamic therapy is provided as needed.

**C. Injury to Cranial Nerves IX, X, and XII** may compromise the patient's ability to maintain a patent protected airway due to difficulty in swallowing and clearing secretions. Tracheal extubation should be performed only after the integrity of protective upper airway reflexes is evident. After extubation, respiratory monitoring should continue with readiness to reintubate the trachea and reinstitute mechanical ventilation if the patient fails to maintain adequate ventilation and a patent protected airway. Injury to Cranial Nerve V, the ophthalmic division of the trigeminal nerve, may impair protective reflexes of the cornea and require external protection with an eye patch.

**D. Edema of the mucosa** of the upper airway may occur after prolonged operation, especially in the sitting position. It is more significant in children because of the small diameter of their airways. Tracheal extubation should be performed only after absence of airway edema is ascertained by deflating the cuff of the endotracheal tube and confirming the patient's ability to breathe around the tube. If airway edema is suspected, the trachea should

remain intubated and the patient sedated, if needed, until the edema resolves. Inhaled racemic epinephrine, 0.5 mL of 2% solution in 3 mL saline, decreases localized mucosal edema and might relieve upper airway obstruction. **Macroglossia** may accompany upper airway edema and cause complete airway obstruction. If this occurs, cricothyroidotomy, tracheotomy, or insertion of a laryngeal mask airway may be the fastest means of re-establishing the airway.

E. **Pneumocephalus** occurs after craniectomy, especially in the sitting position, and is usually of little clinical consequence. Tension pneumocephalus, which may decrease the level of consciousness from brain compression, is more common in patients after ventricular shunting and aggressive drainage of CSF, which allow airtrapping in the space surrounding the brain that had been drained of CSF. Pneumocephalus is diagnosed by a CT scan or x-ray of the head and is effectively treated with a burr hole, which can be done under local anesthesia and usually produces rapid recovery of consciousness once the trapped air has been released.

F. Patients who entrain an intraoperative **venous air embolism** may subsequently develop postoperative pulmonary edema requiring mechanical ventilation and diuresis. Extubation is performed after resolution of pulmonary edema as documented by clinical examination, chest x-ray, and arterial blood gases. Patients who have a functionally patent foramen ovale may develop paradoxical air embolism, which causes neurologic deficits, decreased level of consciousness, and cardiac abnormalities postoperatively.

G. **Abnormal regulation of thirst and vasopressin secretion** after operation for craniopharyngioma is associated with a very high incidence (96%) of diabetes insipidus (DI) compared to 30% after procedures for removal of suprasellar pituitary tumors (Section III.A).

## III. COMPLICATIONS AFTER OPERATION FOR PITUITARY TUMOR

A. **Endocrine complications** include adrenocortical insufficiency, hypothyroidism, and DI.

1. All patients receive corticosteroid coverage until testing indicates an intact pituitary–adrenal axis.
2. Thyroid hormone replacement is reserved for patients who were hypothyroid preoperatively.
3. **Diabetes insipidus** occurs in 10% to 20% of patients, usually develops within 12 to 24 hours after surgery, and lasts for a few days. The decreased release of antidiuretic hormone results in the excretion of excessive amounts (4 to 14 L/day) of dilute urine and leads to dehydration, hypernatremia, increased serum osmolality (> 300 mOsm/kg), decreased urine osmolality (< 200 mOsm/kg), and decreased urine specific gravity (< 1.005). An elevated serum sodium (Na) (> 145 mEq/L) within the first 5 days after operation is strongly associated with the development of DI. Signs of **hypernatremia** are non-specific and include decreased level of consciousness, tremulousness, muscle weakness, irritability, ataxia, spasticity, confusion, seizures, coma, and possibly intracranial bleeding from increased serum osmolality.

   **Treatment of DI** consists of hydration and hormonal supplementation. The amount and content of intravenous fluids are guided by urine volume and serum electrolytes and osmolality. Free water ($H_2O$) deficit can be estimated using the following formula:

   Free $H_2O$ deficit (L) = (serum Na − 140) × body weight (kg) × 0.6/140

   If fluid is replaced early, it is not necessary to administer free water ($D_5W$). Rather, a hypotonic solution such as 0.45% sodium chloride (NaCl) or

lactated Ringer's may be given. Insulin and potassium supplementation might be required when dextrose-containing fluids are used, especially if corticosteroids are administered concomitantly. When hormonal replacement is required, 1-deamino-8-D-arginine vasopressin (DDAVP), a synthetic analog of the natural hormone arginine vasopressin, can be given intravenously, subcutaneously, orally, or intranasally. The latter might not be feasible after transnasal trans-sphenoidal pituitary surgery. The usual intravenous or subcutaneous dose is 0.3 mcg/kg/day in two divided doses. The dose of oral medication is 0.05 to 1.2 mg/day at once or divided into two or three doses. The intranasal dose is 10 to 40 mcg/day in one to three doses. The dose is adjusted according to the patient's sleep pattern and water turnover. Once intravascular volume has been restored, persistent hypernatremia may be treated with thiazide diuretics, such as hydrochlorothiazide, 50 to 100 mg/day intravenously.

B. **Rhinorrhea** of CSF may develop after transnasal trans-sphenoidal operations. Spontaneous resolution occurs commonly and clinical observation is sufficient in most cases. If signs of infection develop, antibiotic therapy and surgical repair are indicated.

C. **Airway obstruction** from bleeding and accumulation of blood and secretions in the pharynx sometimes occurs after transnasal trans-sphenoidal procedures. Frequent assessment of the patency of the airway and adequacy of ventilation is mandatory. Excessive bleeding might require tracheal reintubation and surgical consultation.

D. **PONV** might develop due to intraoperative swallowing of blood during trans-sphenoidal resection of pituitary tumors. To minimize the risk of PONV, the pharynx and stomach are suctioned at the conclusion of surgery and 5HT-3 receptor antagonists are administered prophylactically. Drugs include dolasetron, 12.5 mg in adults and 0.35 mg/kg intravenously in children, ondansetron, 4 mg over 4 minute for adults and children weighing > 40 kg and 0.1 mg/kg over 4 minute for children weighing < 40 kg, and granisetron, 0.1 to 1 mg intravenously. The reported incidence of PONV varies from 7.5% to 80%, and the effectiveness of prophylaxis against PONV varies from nil to 30 to 40%.

## IV. COMPLICATIONS AFTER OPERATION FOR HEAD TRAUMA

Systemic sequelae of head trauma frequently become apparent in the postoperative period. These include adult respiratory distress syndrome, neurogenic pulmonary edema (NPE), cardiac arrhythmias, electrocardiographic (ECG) changes, disseminated intravascular coagulation, DI, syndrome of inappropriate antidiuretic hormone secretion (SIADH), hyperglycemia, hyperosmolar non-ketotic (HONK) hyperglycemic coma, and gastrointestinal ulcers and hemorrhage.

A. **Neurogenic pulmonary edema (NPE)** is a fulminant form of pulmonary edema, which can progress rapidly (within hours to days) toward either resolution or death. The pathologic characteristics of NPE are marked pulmonary vascular congestion, pulmonary arteriolar wall rupture, protein-rich edema fluid, and intra-alveolar hemorrhage. The etiology of NPE is a massive transient central sympathetic discharge from an increase in ICP and is particularly associated with hypothalamic lesions. The pathophysiology includes systemic vasoconstriction and left ventricular failure, redistribution of blood from the systemic to the pulmonary vessels, pulmonary venous constriction, and increased pulmonary capillary permeability. Treatment is aimed at reducing ICP, reducing sympathetic hyperactivity, mainly with alpha-adrenergic blockers such as diazoxide, 1 to 3 mg/kg

intravenously every 5 minute, until BP is controlled, up to 150 mg, or phentolamine in 5 mg increments, and providing respiratory supportive care and inotropic therapy as needed.

**B.** The **syndrome of inappropriate antidiuretic hormone secretion** (**SIADH**) causes water retention with continued urinary excretion of Na. This leads to dilutional hyponatremia, decreased serum osmolality, increased urine osmolality, and decreased urinary output. Water retention and serum hypo-osmolality might progress to water intoxication, which leads to non-specific signs such as nausea, vomiting, headache, irritability, disorientation, seizures, and coma.

**Treatment** consists of water restriction, loop diuretics, and hypertonic saline. In mild cases, fluid restriction (1 to 1.5 L/day) is sufficient to correct hyponatremia. Furosemide may be added because it impairs the kidney's ability to concentrate urine. Hypertonic saline is usually reserved for a serum Na < 120 to 125 mEq/L. It is given in small amounts for a short time (1 to 2 mL/kg/hour for 2 to 3 hours) after which serum Na and osmolality are measured. During the acute phase of SIADH, urine output is measured hourly and urine osmolality and specific gravity and serum Na and osmolality are measured every 6 to 8 hours. Serum Na should be increased at a rate of no more than 0.5 mEq/L/hour or 12 mEq/L/day. Faster rates of correction may cause osmotic demyelination, which develops over several days. Osmotic demyelination is associated with non-specific signs such as behavioral changes, movement disorders, seizures, pseudobulbar palsy, quadriparesis, and coma.

**C.** **Spinal cord injury** (SCI) occurring in conjunction with head injury might become apparent only in the postoperative period. Up to 15% of head-injured patients sustain cervical spine injury as well. Precautions to avoid exacerbation of SCI are continued in the postoperative period until cervical spine injury has been ruled out or repaired. Pharmacologic therapy to ameliorate SCI may be given within 8 hours of injury in the form of methylprednisolone, loading dose 30 mg/kg intravenously; then 5.4 mg/kg/hour intravenously for 23 hours. Acute phase spinal shock, which is usually present during the first week from injury, is treated with fluids, inotropes, and pressors. During the chronic phase of spinal injury after the first week, adequate analgesia is provided before somatic or splanchnic stimulation in patients who have injury above T6 to avoid the risk of autonomic hyper-reflexia.

**D.** **Cardiovascular and respiratory monitoring**, in conjunction with the appropriate imaging and laboratory studies, is aimed at detecting extracranial injuries and complications such as pneumothorax, hemothorax, intra-abdominal or retroperitoneal hemorrhage, and fat embolism.

**E.** **Prevention of secondary brain injury** is continued in the postoperative period. Hypotension, hypoxia, hyperthermia, hyperglycemia, hypoglycemia, increased ICP, and any aggravating factors such as pain, nausea, vomiting, seizures, hypertension, hypercarbia, and impaired cerebral venous drainage should all be prevented and treated. Conscious, mechanically ventilated patients are sedated with short-acting drugs, such as propofol, 10 to 30 mcg/kg/minute intravenously, or dexmedetomidine, loading dose 1 mcg/kg intravenously over 10 minute; then 0.2 to 0.7 mcg/kg/hour for < 24 hours, to allow intermittent neurologic assessment. **Pain** from the operative procedure or the primary or associated injury is relieved with opioids such as morphine, 0.05 mg/kg, or fentanyl, 0.5 to 1 mcg/kg. **Nausea and vomiting** are treated with stomach suctioning through the mouth because of the potential for skull base fracture. Pharmacologic therapy includes ondansetron, 4 mg intravenously, dolasetron, 12.5 to 25 mg, or granisetron, 0.1 to 1 mg. **Seizure prophylaxis** after head trauma is somewhat controversial. Phenytoin,

loading dose 15 mg/kg intravenously over 20 minute followed by 5 to 7 mg/kg/day, or fosphenytoin, loading dose "phenytoin equivalent (PE)" 15 to 20 mg/kg intravenously; then 4 to 6 PE mg/kg/day, may be given for 2 weeks after head injury if there have been no seizures or longer if there have.

F. **Clotting** may be impaired because of the release of tissue thromboplastin and a trauma-induced decrease in platelets, prothrombin ( factor II), proaccelerin ( factor V), and plasminogen, and an increase in fibrin degradation products (FDPs).

## V. COMPLICATIONS AFTER OPERATION FOR ANEURYSM

A. **Vasospasm.** Angiographic narrowing of blood vessels occurs in about 30% of patients between days 4 and 14 after subarachnoid hemorrhage (SAH). **Neurologic dysfunction** (disorientation, decreased level of consciousness, focal deficit) occurs in about 50% of patients who have angiographic narrowing. The **risk for developing vasospasm** correlates with the amount of blood around the circle of Willis, the preoperative use of antifibrinolytic therapy, and the postoperative development of the cerebral salt wasting (CSW) syndrome. Pharmacologic **prophylactic therapy** for vasospasm is initiated within 96 hour of SAH and consists of nimodipine, 60 mg by mouth every 4 hour for 21 days or longer. A CT **angiogram** or traditional angiography should be performed to confirm the diagnosis of vasospasm. A CT scan can also rule out other potential etiologies of altered consciousness such as recurrent hemorrhage and hydrocephalus. **"Triple-H" therapy** (hypervolemia, hypertension, and hemodilution) for the treatment of vasospasm after SAH consists of the administration of crystalloid and colloid solutions to achieve a pulmonary capillary wedge pressure of 12 to 16 mm Hg and a hemoglobin of 11 g/dL and the use of inotropes and vasopressors to achieve a mean arterial pressure (MAP) of 120 mm Hg or more. Antidiuretic therapy with vasopressin is sometimes necessary to prevent the diuresis induced by volume loading. Hypotension, heart failure, myocardial ischemia, and pulmonary edema are occasional complications of Triple-H therapy.

B. **Obstructive hydrocephalus** from subarachnoid blood-induced disturbances in CSF circulation may occur after SAH. The resulting increase in ICP may be manifest as a decreased level of consciousness. A CT scan is diagnostic and ventriculostomy with CSF drainage is the effective therapy. Increased ICP, particularly if the ICP does not respond to treatment, is associated with a less favorable outcome.

C. **Hyponatremia** after SAH can be due to the cerebral salt-wasting (CSW) syndrome or, less commonly, to SIADH. The CSW syndrome is caused by increased secretion of atrial natriuretic peptide, brain natriuretic peptide, and C-type natriuretic peptide. These peptides suppress aldosterone synthesis and lead to natriuresis, diuresis, and vasodilatation. Hyponatremia in the CSW syndrome results from increased renal excretion of Na (150 to 200 mEq/L), which is followed by water with resultant hypovolemia. The hyponatremia of SIADH is mainly a result of water retention in conjunction with the renal excretion of Na in a range of 20 to 30 mEq/L.

Treatment of the two forms of hyponatremia is completely different. Patients who have CSW require Na replacement and fluid administration, whereas patients who have SIADH require fluid restriction and diuresis. Fluid restriction and diuresis in a patient who has CSW can be fatal due to the possibility of severe hypovolemia and cerebral infarction. Fluid and salt administered to a patient who has SIADH may lead to osmotic demyelination. Hypertonic saline may be used with close monitoring of serum Na in both cases.

D. **Diabetes insipidus** occurs less frequently than CSW syndrome or SIADH after SAH (see Section III.A). Treatment includes hypotonic fluids in the form of enteral free water or parenteral $D_5W$, $D_5$ 0.2% NaCl, or 0.45% NaCl plus the administration of 1-deamino-8-D-arginine vasopressin, 0.3 mcg/kg/day intravenously or subcutaneously in two divided doses; 0.05 to 1.2 mg/day by mouth; or 10 to 40 mcg/day or three times a day as a nasal spray.

E. **Intracranial hematomas** might develop at the operative site or at the dural bridging veins from overzealous CSF drainage. Manifestations are those of increased ICP, which may be associated with focal deficit. CT scan is diagnostic and treatment with surgical evacuation may be required.

F. **Seizure prophylaxis** is continued in the postoperative period owing to the high risk of seizures after SAH, especially in hypertensive patients. Phenytoin is usually given for 3 to 6 months after SAH. Levetiracetam may be used in patients who have serious adverse reactions to phenytoin.

G. **Neurogenic pulmonary edema** occurs in some patients after SAH because of the sudden increase in ICP, which produces intense sympathetic activation, catecholamine release from the hypothalamus and the medulla, and increased pulmonary vascular pressure and permeability (see Section IV.A). **Diagnosis** depends on the exclusion of other causes of pulmonary edema such as Triple-H therapy and aspiration pneumonia. Treatment includes supplemental oxygen, mechanical ventilation plus positive end-expiratory pressure (PEEP), cardiovascular support, and reduction of ICP.

H. After SAH, patients are at moderate risk for the development of **deep vein thrombosis** (DVT) and **pulmonary embolus**. Mechanical DVT prophylaxis, in the form of graduated stockings or intermittent pneumatic compression of the lower extremities, is instituted in all patients after SAH. Anticoagulation is contraindicated in the acute postoperative phase. Insertion of an inferior vena cava filter may be necessary for the prevention of recurrent pulmonary embolization.

I. **Cardiac complications** are common after SAH. ECG changes of arrhythmia, ischemia, or infarction, which are detected in more than 50% of patients, occur within 48 hours of SAH but may be first noted in the early postoperative period. Evidence of myocardial injury is detected by echocardiography, thallium scintigraphy, and autopsy. These ECG changes may be from hypothalamic injury and high catecholamine levels. **Treatment** depends on the severity of the complications, the hemodynamic stability of the patient, and concomitant vasospasm. Infarcted, stunned, or hibernating myocardium might exclude these patients from Triple-H therapy.

## VI. COMPLICATIONS AFTER ABLATION OF ARTERIOVENOUS MALFORMATION

After operation for the ablation of an arteriovenous malformation (AVM), patients are at risk of developing complications similar to those that occur after aneurysm surgery (vasospasm, hydrocephalus, and seizures). In addition, these patients are at high risk of developing hyperemic complications.

A. The **syndrome of normal perfusion-pressure breakthrough or cerebral hyperperfusion** is a hyperemic state characterized by cerebral edema, swelling, and/or hemorrhage that develops after resection of an AVM. This condition results from the restoration of cerebral blood flow (CBF) to chronically hypoperfused areas or from venous outflow obstruction after AVM ablation. The ensuing cerebral swelling and hemorrhage cause neurologic dysfunction and are a major cause of postoperative morbidity and mortality. Patients who have ischemic rather than hemorrhagic symptoms preoperatively or certain angiographic features such as high or inverse flow in a large, deep, border-zone

AVM are particularly at risk. Staged repair and strict control of blood flow through the AVM may decrease the risk of hyperemic complications. **Treatment** of the manifestations of cerebral hyperemia includes mechanical hyperventilation, osmotic diuresis, and barbiturate coma.

## VII. COMPLICATIONS AFTER NEURORADIOLOGIC PROCEDURES

Endovascular cerebral embolization and coiling procedures may lead to complications such as SAH, intracerebral hemorrhage, cerebral ischemia, cerebral infarction, reperfusion syndrome, seizures, pulmonary embolism, and contrast reactions. The treatment priority in all these complications is to secure a patent and protected airway and maintain adequate cerebral perfusion pressure (CPP), the difference between MAP and ICP, through management of BP and ICP.

**A. Cerebral hemorrhage** may occur immediately from vessel perforation by the catheter or guidewire or aneurysmal rupture or later due to hyperemic complications. Most small perforations can be managed conservatively by observation and follow-up. Alternatively, the catheter itself can be used to tamponade the source of bleeding and occlude the perforation. Other **treatment** measures include reversal of systemic anticoagulation, seizure prophylaxis, analgesic and antiemetic therapy, and insertion of large-bore intravenous catheters for fluid resuscitation and possible blood transfusion. These measures should be instituted in consultation with the attending neuroradiologist or neurosurgeon.

Large perforations with massive bleeding will require emergent surgical intervention. However, the prognosis for this kind of bleeding is grave as most of the patients exsanguinate prior to surgery because of the delay inherent in going from endovascular procedure to craniotomy and vascular repair, especially as most of these vessels are situated deep in the cerebral parenchyma. The introduction of combined endovascular/operative suites may reduce some of this delay.

**B. Cerebral ischemia** may occur from obstruction of venous drainage, unintentional occlusion of surrounding arteries, or local injection of papaverine during the treatment of vasospasm. **Signs** of cerebral ischemia/infarction include hemiplegia, hemiparesis, cranial nerve palsies, aphasia, nausea, vomiting, and seizures. **Treatment** of cerebral ischemia/infarction consists of maintaining adequate CPP through management of BP and ICP, airway protection, and other supportive care as needed. Intravenous thrombolytic therapy is contraindicated in the presence of cerebral ischemia. Interventional endovascular measures to re-establish cerebral perfusion can be attempted.

**C. Seizures** may occur in patients who have a pre-existing seizure disorder or in the absence of such history. The etiology includes cerebral ischemia or infarction from vessel obstruction or trauma (see Section VII.B); localized cerebral edema, which could follow even successful embolization procedures; or the **cerebral hyperperfusion syndrome** (see Section VII.F). Management of seizures involves, in addition to pharmacologic therapy, identification and, when possible, treatment of precipitating factor(s), airway management, and stabilization of hemodynamic parameters. Anticonvulsant therapy includes midazolam, 0.1 to 0.2 mg/kg; lorazepam, 4 to 8 mg; thiopental, 3 to 5 mg/kg; phenytoin, loading dose 10 to 20 mg/kg no faster than 50 mg/minute (1,000 mg over 20 minute in typical adult); then 5 to 7 mg/kg/day; fosphenytoin, loading dose "phenytoin equivalent (PE)" 15 to 20 mg/kg no faster than 100 to 150 mg/minute (1,000 mg PE over 10 minute in typical adult); then 4 to 6 PE mg/kg/day; or levetiracetam, 20 to 60 mg/kg by mouth daily in two equal doses.

D. **Pulmonary embolism** may occur because of the release of embolic materials into the venous circulation from the AVM, especially AVMs that contain large fistulae or those of the vein of Galen, or from vessels accessed en route to the AVM. Depending on the extent and source of the embolization, treatment consists of securing a patent and protected airway, maintenance of adequate oxygenation and ventilation, and, in case of cardiopulmonary collapse, surgical embolectomy.

E. **Contrast media reactions** may be allergic or non-allergic in nature. Signs of allergic reactions include generalized flushing, urticaria, hypotension, and bronchospasm. Treatment consists of supportive measures of airway, breathing, and circulation (ABC) and pharmacologic therapy in the form of epinephrine, 0.5 to 1 mg intravenously or 3 to 5 mL intratracheally of 1:10,000 solution; hydrocortisone, 100 mg intravenously every 6 hours; and diphenhydramine, 25 to 50 mg intravenously every 4 to 6 hours. Non-allergic reactions occur from the sheer volume of the contrast dye, which may lead to CHF in susceptible patients or osmotic diuresis, which may cause fluid and electrolyte imbalances in patients who are already hypovolemic from diuretic therapy and/or restricted salt and water intake.

F. **Cerebral hyperperfusion syndrome** may occur in areas of the brain surrounding large AVMs from diversion of blood flow away from the AVM. These heretofore hypoperfused areas lose their ability to autoregulate blood flow and are usually maximally vasodilated. After embolization, the large amount of blood that had been flowing through the erstwhile AVM is now shunted back to these maximally dilated vessels leading to cerebral hyperemia, edema, and/or hemorrhage. Methods of preventing this sudden increase in blood flow include deliberate hypotension or maintaining a systolic BP < 120 to 140 mm Hg in patients who have had cerebral revascularization; pretreatment with barbiturates; clamping of the cervical carotid artery; and staged embolization of the feeding vessels to allow the surrounding tissues to regain their autoregulatory function. Pharmacologic treatment of cerebral edema includes administration of furosemide, 0.1 to 1 mg/kg, and mannitol, 0.25 to 1 g/kg over 20 minutes.

G. **Complications from the embolic materials. Glues** such as n-butyl cyanoacrylate (NBCA) and iso-butyl 2-cyanoacrylate may cause pulmonary complications including hemoptysis and pleural pain. **Particulate materials** such as polyvinyl alcohol (PVA), silicon beads, silk, steel and platinum microcoils, Gelfoam, and collagen may cause pulmonary or systemic embolism. Also, PVA is known to increase the risk of recanalization of the embolized AVM.

## VIII. COMPLICATIONS AFTER CAROTID ENDARTERECTOMY

A. **Cardiac ischemia and infarction** are the leading cause of mortality after carotid endarterectomy (CEA). Coronary artery disease is common among patients undergoing CEA. Perioperative tachycardia, hypertension, and hypotension increase the risk of perioperative myocardial ischemia and infarction. The alpha agonists, such as phenylephrine, are preferable in the treatment of hypotension in this setting because they raise BP without significantly increasing heart rate. However, the ensuing hypertension may be detrimental. Combined alpha and beta agonists, such as ephedrine, increase heart rate and have been associated with myocardial ischemia and infarction in this setting. CEA is associated with lower stroke rates than carotid stenting in all patients groups: asymptomatic, symptomatic, standard-risk, and high-risk, but carries a higher risk of myocardial infarction.

B. **Occlusion of the operated carotid artery** should be suspected whenever new neurologic signs and symptoms develop postoperatively. This is one cause of postoperative cerebral ischemia that is amenable to surgical intervention. Early diagnosis and treatment significantly alter outcome. A Doppler flow study can detect cessation of flow in the involved vessel, and angiography will confirm vascular occlusion. Surgical re-exploration need not await angiographic confirmation but may be undertaken on the basis of the clinical picture and the ultrasound examination.

C. **Cerebral hyperperfusion syndrome** may develop after CEA from the sudden increase in CBF in a maximally dilated vascular bed that has lost its ability to autoregulate because of long-standing hypoperfusion. This hyperperfusion can lead to cerebral edema or hemorrhage with headache, seizures, decreased level of consciousness, and focal neurologic deficits. Severe carotid stenosis and hypertension contribute to the development of this syndrome. The careful control of BP is essential in preventing hyperperfusion. Preoperative reduced (< 10%) cerebral vasoreactivity is a risk factor for the development of postoperative cerebral hyperperfusion syndrome. In the postoperative period, mild elevation of BP need not be treated, whereas moderate to severe hypertension should be treated to avoid the cerebral hyperperfusion syndrome. A combination of titratable, short-acting drugs such as sodium nitroprusside (SNP), 0.25 to 8 mcg/kg/minute; and esmolol, loading dose 500 mcg/kg over 1 minute followed by 50 to 300 mcg/kg/minute, are preferable in this setting. The beta-blocking effects of esmolol offset the sympathetic hyperactivity from SNP. Labetalol infusion is an alternative therapy but is less amenable to titration due to longer half-life.

D. **Hypotension** is poorly tolerated by hypertensive patients who have a rightward shift in their cerebral autoregulatory curve. Hypotension can lead to cerebral and cardiac hypoperfusion and can increase the risk of thrombus formation in the operated vessel. BP is usually kept at 20% above baseline. Hypotension is treated with volume expansion and infusion of a short-acting alpha agonist such as phenylephrine, 40 to 180 mcg/minute mixed as 20 mg in 250 mL $D_5W$ and infused at 30 to 160 mL/hour.

E. **Treatment of stroke after CEA** consists of BP management, supportive care, and treatment of complications. Intravenous thrombolytic therapy is contraindicated in the postoperative period. Intra-arterial thrombolytic therapy may be considered in institutions that have the expertise. Neuroprotective therapy, still the subject of clinical trials, has not been approved for clinical use.

F. **Airway obstruction** can result from hematoma formation and can be aggravated by laryngeal edema and cranial nerve injury. Re-establishing airway patency might require suture removal and drainage of the hematoma, which is best accomplished by the surgeon, in conjunction with tracheal intubation and racemic epinephrine. If the patient is in extremis, the first person to reach the bedside opens the wound to secure the airway.

## IX. COMPLICATIONS AFTER VERTEBRAL COLUMN PROCEDURES

A. **Anterior cervical discectomy.** The patient's trachea is usually extubated in the operating room after an uncomplicated discectomy. However, tracheal intubation may be maintained postoperatively if upper airway edema is anticipated after a prolonged operation or one associated with infusion of large volumes of fluid. It is important to prevent the patient from coughing and straining while the trachea is intubated. This may cause the newly placed bone graft to dislodge, which can compress the trachea or the

esophagus and require reoperation. After extubation, the patient's voice is evaluated to detect recurrent laryngeal nerve injury, a benign complication that usually resolves over days to weeks.

B. **Cervical corpectomy and stabilization.** These procedures are usually more invasive, more prolonged, associated with more fluid administration, and, therefore, more likely to cause airway edema at the conclusion of surgery. The patient's trachea usually remains intubated until the airway edema resolves, as evidenced by the ability of the patient to breathe around the endotracheal tube after the cuff has been deflated. Sedation is provided as needed while the trachea is intubated.

C. **Transoral resection of the odontoid and occipitocervical fusion.** Operation is usually performed in two steps: anterior transoral resection of the odontoid and posterior occipitocervical fusion. Airway management involves either tracheotomy or an oral endotracheal tube draped out of the surgical field as for tonsillectomy. The procedure is associated with significant posterior pharyngeal swelling, which requires postoperative intubation for several days. The patient is usually awakened at the conclusion of surgery to undergo a neurologic examination and then sedated again. The degree of resolution of the airway edema is evaluated by deflating the cuff of the endotracheal tube and establishing the patient's ability to breathe around the endotracheal tube.

D. **Posterior cervical spine procedures.** Complications are related to the patient's intraoperative position and the degree of airway edema and respiratory dysfunction at the conclusion of the operation.

1. The operative positions include prone, sitting, and three quarters prone. Complications of the prone position include injury at pressure points: eyes, cheeks, lips, breasts, and genitalia. Injury to these structures requires appropriate surgical consultation.
2. **Airway edema** is dependent on the duration of surgery and the amount of blood loss and fluid administration.
3. **Respiratory dysfunction** may exist preoperatively from involvement of C3 to C5 nerve roots or may result from resection of intramedullary spinal cord tumors. These patients are evaluated before extubation to demonstrate the patency of the airway (lack of airway edema) and adequacy of respiratory function (tidal volume, vital capacity, negative inspiratory force). Postoperative intubation and mechanical ventilation might be required until airway edema resolves and respiratory function recovers.

E. **Scoliosis surgery.** These procedures are performed with the patient in the prone or lateral position or a combination of a lateral position operation followed immediately or 1 to 2 weeks later by prone position instrumentation.

1. Complications related to the prone position are those of pressure-point injury, particularly the eyes. **Ischemic optic neuropathy** (ION) is correlated with intraoperative hypotension and ischemia, regardless of position. **Central retinal artery occlusion** can occur during prone-position procedures from improper protection of the eyes. Scoliosis surgery patients are thus particularly vulnerable to ION, which is manifested postoperatively by varying degrees of unilateral or bilateral decrease in visual acuity or defects in the visual field. The decrease in visual acuity may resolve over time, but the defects in the visual field usually persist. Postoperative visual examination is performed routinely in these patients; ophthalmologic consultation is requested if any abnormality is detected.
2. Scoliosis patients may have **respiratory dysfunction** preoperatively due to skeletal deformities, muscular weakness, CNS dysfunction, or a

combination of factors. This respiratory dysfunction might be aggravated postoperatively by the residual effect of anesthetics, inadequate reversal of muscle relaxants in the presence of hypothermia, restrictive effect of pain, and pneumothorax. Airway edema from positioning, prolonged surgery, and administration of a large volume of fluids contributes to the respiratory compromise. Extubation of the trachea is undertaken only after airway patency and adequacy of respiratory function have been established. Pain control is essential for patient comfort and the maintenance of adequate respiratory function.

3. **Postoperative hemorrhage** can continue externally via surgical drains or internally into the operative site. Monitoring of systemic BP, urinary output, CVP, if present, and hemoglobin and hematocrit is necessary. Excessive blood loss is treated with volume expansion, blood transfusion, hemodynamic support, and surgical consultation.
4. **Central and peripheral neurologic function** is monitored postoperatively. Patients might develop spinal cord injury from instrumentation or hematoma formation and CNS dysfunction from pharmacologic or hemodynamic factors. Neurologic dysfunction should prompt a thorough examination of the patient, review of medication, hemodynamic and laboratory workup, surgical consultation, and supportive therapy as needed.

**F. Lateral extracavitary and percutaneous endoscopic procedures.** A factor common to these two operations is the intraoperative use of double-lumen endotracheal tubes or other forms of one-lung ventilation. Pulmonary edema may develop with re-expansion of the lung after one-lung ventilation for > 3 hours, most likely within 1 hour of re-expansion. If mechanical ventilation is to be maintained in the postoperative period, the double-lumen tube is exchanged for a single-lumen tube. Alternatively, a Univent tube, which is a single-lumen tube with a movable endobronchial blocker, may be used intraoperatively and postoperatively during weaning and until extubation.

## X. COMPLICATIONS AFTER SPINAL CORD PROCEDURES

**A. Syringomyelia repair. Respiratory complications** are the main concern. Preoperative respiratory dysfunction is caused by skeletal deformities, autonomic dysfunction, and chronic aspiration and pneumonia from depressed gag reflex and vocal cord paralysis. This may be exacerbated in the postoperative period by airway edema, residual anesthetic effects, and incomplete reversal of muscle relaxants, which could be aggravated by the hypothermia of autonomic dysfunction. Extubation is performed only after the adequacy of respiratory function and airway patency has been established. Respiratory monitoring and support are maintained in the postoperative period as needed.

**B. Resection of spinal cord tumors.** Significant **spinal cord edema** may develop up to 24 hours after resection. The edema-induced respiratory dysfunction associated with resection of upper cervical cord tumors might not become apparent in the immediate postoperative period. Respiratory monitoring of these patients in an intensive care setting for at least 24 hours is recommended.

**C. Spinal cord injury.** Patients who have SCI develop complications related to sympathectomy, skeletal muscle denervation, immobilization, chronic instrumentation, decreased respiratory force, and coexisting injuries involving other organs. About 50% of patients who sustain cervical SCI have concurrent head trauma and about 25% have injuries to the chest, abdomen, or extremities.

1. The severity and mechanism of the initial **spinal shock**, which lasts for 2 to 3 weeks after injury, are related to the level of the injury. With midthoracic lesions (T6–T7), hypotension may not be severe and is mainly a result of vasodilatation. With higher lesions (T4 or above), hypotension may be profound when vasodilatation is added to a decrease in heart rate, contractility, and compliance from loss of cardiac accelerator fibers (T1–T4).
2. Succinylcholine may cause **hyperkalemia** in denervated patients because of the increased number and sensitivity of their neuromuscular cholinergic receptors. These receptor changes start 3 days after the injury and remain for 6 to 8 months. Succinylcholine is therefore avoided in SCI patients from 48 hours to 8 months after the injury.
3. **Autonomic hyper-reflexia** is caused by noxious stimulation below the level of the lesion in a patient whose sympathectomy is **at or above T6**.
   a. The **risk** of autonomic hyper-reflexia is highest during the fourth week after injury but continues thereafter. At this time, while the patient is recovering from the spinal shock phase, which lasts for 2 to 3 weeks after the initial injury, the flaccid paralysis changes to spastic paralysis because of the absence of the effect of central inhibitory pathways. The efferent sympathetic fibers recover from the initial injury but remain unaffected by central inhibitory input from the brain stem and hypothalamus.
   b. The severity and manifestations of autonomic hyper-reflexia are affected by the **level of the sympathectomy**. With midthoracic lesions below the level of cardiac accelerator fibers, hypertension is accompanied by reflex bradycardia transmitted via cardiac accelerator fibers and the vagus nerve. In patients whose sympathectomy is above the level of the thoracic cardiac accelerator fibers, tachycardia may occur because cardiac accelerator fibers become part of the efferent sympathetic activity rather than part of the central inhibitory input from the brain stem and hypothalamus. Arrhythmias and occasionally heart block may accompany changes in heart rate. **Clinical manifestations** of autonomic hyper-reflexia include vasodilatation, decreased sympathetic activity, and increased vagal activity above the level of the lesion including nasal congestion, flushing, headache, dyspnea, nausea, and visceral muscle contraction. Vasoconstriction and increased sympathetic activity below the level of the lesion cause vasoconstrictive pallor, sweating, piloerection, and somatic muscle fasciculation. Patients also develop hypertension with headache, blurred vision, myocardial infarction, and retinal, subarachnoid, and cerebral hemorrhages that can lead to syncope, convulsions, and death.
   c. Autonomic hyper-reflexia may be **prevented or attenuated by regional or deep general anesthesia**, but this is usually impractical in the postanesthesia care unit. **Pharmacologic means** of preventing and treating autonomic hyper-reflexia include alpha blockers such as diazoxide, 1 to 3 mg/kg every 5 minute up to 150 mg, or phentolamine, 5 mg increments; vasodilators such as SNP, 0.25 to 8 mcg/kg/minute; and selective beta-blockers such as esmolol, loading dose 500 mcg/kg followed by 50 to 300 mcg/kg/minute for supraventricular tachycardia.

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# 22 Respiratory Care of the Neurosurgical Patient

**Irene Rozet and Karen B. Domino**

## Illustrative Clinical Case

A 27-year-old male, a restrained driver involved in the motor vehicle accident, was brought to the operating room (OR) for emergency decompressive craniotomy to evacuate a left subdural hematoma causing a 4-mm midline shift. The patient's trachea was intubated with a 7-mm oral endotracheal tube by the paramedic on the scene. The patient was ventilated manually by the respiratory technician using a self-inflating balloon (Ambu bag) with additional oxygen of 5 L/minute. Upon arrival in the emergency department, the Glasgow Coma Scale score was 9, and the patient received morphine, 10 mg, and pancuronium, 10 mg, intravenously. On physical examination in the OR, the left pupil was larger than the right one; the right pupil was reactive to light and corneal reflex was preserved, and the patient was not moving his extremities. Oxygen saturation ($SpO_2$) by pulse oximeter was 93%, blood pressure (BP) 150/90 mm Hg, and heart rate 110 beats per minute. Air entry was diminished over the left lung, compared to the right. No heart murmurs were noted. Other injuries involved left femoral and tibial fractures (in splint) and a possible pelvic fracture. Computed tomography (CT) of the chest revealed a small left pleural effusion, fractures of the sixth and seventh ribs, and no pneumothorax. The surgeon is requesting hyperventilation to maintain the patient's arterial carbon dioxide tension ($PaCO_2$) at 25 mm Hg throughout the case.

*What is your anesthesia plan? What is your plan for the intraoperative monitoring? What are your goals for ventilation of the lung?*

After the patient is positioned, $SpO_2$ decreases to 88% with an end-tidal $CO_2$ of 45 mm Hg. *What is your differential diagnosis? What are your actions? Are you planning to extubate the patient's trachea after the operation is completed?*

## Chapter Highlights

This chapter discusses specific considerations of respiratory pathology and care in neurosurgical patients. Prompt recognition and treatment of respiratory disorders are extremely important in the management of neurosurgical patients in whom the development of respiratory and pulmonary complications worsens neurologic outcome and significantly contributes to mortality.

### I. PATHOPHYSIOLOGY OF RESPIRATORY DISORDERS IN NEUROSURGICAL PATIENTS

**Clinical physiology of ventilation and gas exchange in the lungs.** Inspired gas is mixed with gas in the functional residual capacity (FRC) to make up alveolar gas. Gas exchange in lungs occurs when mixed venous blood in pulmonary capillaries is exposed to the alveolar gas. Both oxygen (moving from alveoli to capillaries) and carbon dioxide (moving from capillaries to alveoli) cross the alveolar–capillary barrier by simple diffusion, driven by the difference in the partial pressures of each gas. Oxygen-enriched blood is distributed to the

systemic circulation as mixed arterial blood. **Any impairment in lung ventilation, perfusion, or gas diffusion inevitably impairs gas exchange** and results in arterial gas abnormalities such as hypercarbia ($PaCO_2$ > 45 mm Hg), hypoxemia (arterial oxygen tension [$PaO_2$] < 60 mm Hg), pH changes, and electrolyte imbalance.

**Arterial hypoxemia**, which eventually causes tissue hypoxia, and **hypercarbia** commonly occur in patients who have central nervous system (CNS) injury. Both arterial hypoxemia and hypercarbia cause cerebral vasodilatation and increase in cerebral blood flow and cerebral blood volume, which could increase the intracranial pressure (ICP) in patients after traumatic brain injury (TBI). Both hypoxemia and hypercarbia in patients who have TBI and spinal cord injury (SCI) are strongly associated with development of secondary brain injury and death.

The **major causes of arterial hypoxemia** are **a decrease in the alveolar oxygen tension ($PAO_2$)** and **an increase in the alveolar–arterial oxygen tension difference ($P[A\text{-}a]O_2$).**

A. **Causes of decreased $PAO_2$.** $PAO_2$, the major driving factor for arterial oxygenation, may be reduced because of either **a decrease in *inspired* oxygen tension** ($PIO_2$) or **diminished alveolar ventilation** from *respiratory depression* (hypoventilation), *increased dead space*, or *mechanical impairment*. $PAO_2$ is determined by the barometric pressure (PB), the fraction of inspired oxygen ($FIO_2$), and the ratio of oxygen consumption ($\dot{V}O_2$) to alveolar ventilation ($\dot{V}A$):

$$PAO_2 = PB \times (FIO_2 - \dot{V}O_2/\dot{V}A) \tag{22.1}$$

As far as $\dot{V}A$ is directly proportional to $CO_2$ production $\left(\dot{V}CO_2\right)$,

$$\dot{V}A = \dot{V}CO_2/PACO_2 \times (k), \text{ and } PACO_2 \sim PaCO_2,$$

Equation 22.1 can be transformed into the alveolar gas Equation 22.2:

$$PAO_2 = FIO_2\,(PB - 47) - (PaCO_2/R_Q) \tag{22.2}$$

where $R_Q$, respiratory quotient; $R_Q = \dot{V}CO_2/\dot{V}O_2$ (0.8 in resting state); and 47, saturated water vapor pressure at the PB in mm Hg.

1. **Respiratory depression (hypoventilation)** can be either ***central*** (from CNS disease such as trauma, tumor, etc., or medications that cause respiratory depression such as narcotics or sedatives) or ***peripheral*** (from airway or chest trauma, neuromuscular disease, or muscle relaxants).
   a. **Central hypoventilation: Voluntary control of ventilation** requires preserved consciousness and cerebral cortex and plays a minimal role in normal breathing. **Involuntary motor control of ventilation is located in the respiratory center in the brain stem** (pons and medulla). After receiving input from the central and peripheral chemoreceptors, baroreceptors (located in the vasculature), and stretch receptors (located in the bronchial tree and lung parenchyma), the respiratory center sends its output to the respiratory muscles via respiratory motor pathways. Input from the peripheral receptors is transferred to the respiratory center via the vagus nerve (Cranial Nerve X) from the aorta and the glossopharyngeus (Cranial Nerve IX) from the carotid arteries.

      **Central chemoreceptors are located in the medulla** and are sensitive to a change of pH in the cerebrospinal fluid (CSF) in response to

changes in the $PaCO_2$. There is an increase in ventilation when the $PaCO_2$ is > 40 mm Hg and/or the arterial pH is < 7.4. Central chemoreceptors are responsible for about 85% of ventilatory effort. **Peripheral chemoreceptors** react to $PaO_2$ with an increase in ventilation when $PaO_2$ is < 60 mm Hg as well as to $PaCO_2$ and pH.

**Variations in both the depth and rate of spontaneous respiration occur in 60% of patients who have an isolated brain injury.** Hypoventilation and hyperventilation are both pathologic respiratory patterns that can lead to hypo- or hypercarbia, hypoxemia, pH disturbances, and electrolyte imbalance. Five respiratory patterns have been described in patients who have TBI or brain tumors (Fig. 22.1). These respiratory patterns are rarely observed in practice, however, because of early endotracheal intubation and mechanical ventilation in the management of patients after CNS injury.

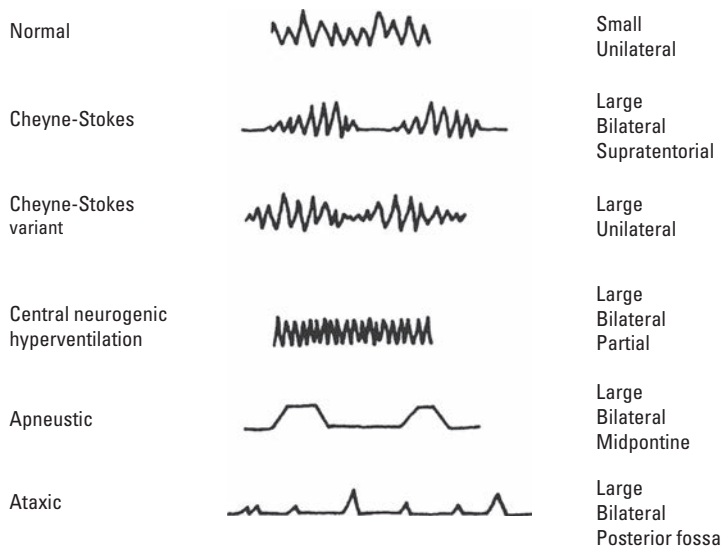


**FIGURE 22.1** Respiratory patterns associated with closed head injury. *Normal breathing* in an awake patient who has a small, unilateral lesion. *Cheyne-Stokes* ventilation is a periodic breathing pattern in which hyperpnea alternates with apnea. The hyperpneic phase lasts longer than the apneic phase. The *Cheyne-Stokes variant* has a shorter apneic phase and is associated with large unilateral injuries. *Central neurogenic hyperventilation* is a sustained, regular, rapid, fairly deep hyperpnea. It occurs with a large pontine lesion, systemic hypoxia, or metabolic acidosis. It is often associated with brain stem tumors, including lymphomas and astrocytomas, and metastatic disease. *Apneustic breathing* occurs with large bilateral midpontine lesions. There is a brief 2- to 3-second pause at the end of inspiration, alternating irregularly with expiratory pauses. It has a very poor prognosis. *Ataxic respiration* is a pattern of irregular breathing in which shallow and deep breaths alternate randomly with irregular pauses. It is associated with medullary compression and has a very poor prognosis. The irregularity distinguishes it from Cheyne-Stokes ventilation. (Reprinted from Plum F, Posner JB. *The Diagnosis of Stupor and Coma*. 2nd ed. Philadelphia, PA: FA Davis Co., 1972 with permission.)

**Commonly used anesthetic medications** such as opioids, gamma aminobutyric acid (GABA)-ergic sedatives, and inhaled anesthetics **inhibit central ventilation.** The alpha-2 agonist **dexmedetomidine** lacks GABA-ergic or central effects. When used in sedative doses (0.2 to 0.6 mcg/kg/hour), dexmedetomidine causes a respiratory phenomenon that resembles natural sleep in which naturally occurring slight hypercarbia leads to hyperventilation with subsequent normalization of arterial $PaCO_2$. As maintaining normocarbia is crucial in the management of patients who have brain and SCI, this unique feature of dexmedetomidine makes it a promising alternative to routinely used sedative medications in the management of neurosurgical patients in both the OR and the intensive care unit (ICU).

b. **Peripheral hypoventilation**

1. High **cervical spinal cord lesions impair ventilation because of** either partial or complete **loss of innervation of the diaphragm (C3–C5),** with loss of the ability to cough. The diaphragm is spared when the injury is below C6–C7. However, **injury at the thoracic level** results in the **loss of intercostal and abdominal muscle function**, which reduces FRC and creates paradoxical ventilation (chest retraction on inspiration and expansion during expiration), loss of cough, and reduced ability to clear secretions. **All lung volumes are markedly decreased** with the exception of residual volume.

   With a **C5–C6 lesion**, ventilation may be inadequate and forced vital capacity (FVC) decreased to 30% of predicted capacity. Improvement of FVC occurs with time because of the strengthening of the accessory muscles (clavicular portion of the pectoralis major and sternocleidomastoid), development of spasticity (which stops the paradoxical chest wall motion), improvement of diaphragmatic function, and decreased use of narcotics and sedatives. At 5 months after injury, FVC reaches 60% of predicted values.

2. **Associated injuries** in multiple trauma patients including *upper and lower airway injuries* such as tracheobronchial fistula or disruption, rupture of the diaphragm, and thoracic trauma with rib fractures can all lead to acute hypoventilation and profound hypoxemia and hypercarbia.

2. **Increased physiologic dead space** is associated with drug administration (such as atropine and sodium nitroprusside for deliberate hypotension), mechanical ventilation with positive end-expiratory pressure (PEEP), hypovolemia, hypotension, hypocapnia, and pulmonary embolism. The Bohr Equation (22.3) can be used in ventilated patients to calculate the physiologic dead space:

$$VD/VT = 1 - \left(PECO_2/PaCO_2\right) \tag{22.3}$$

where VD, volume of the dead space; VT, tidal volume; $PECO_2$, end-tidal $CO_2$ tension in mm Hg, and $PaCO_2$, arterial $CO_2$ tension in mm Hg.

Please note that **VD/VT** represents a fraction of the dead space ventilation, which normally should be about 0.3 (or 30% of tidal volume) in mechanically ventilated patients.

3. **Mechanical impairment. Airway obstruction** from oropharyngeal soft tissue, uncleared secretions, hemoptysis, foreign bodies, bleeding, or bronchospasm can cause mechanical impairment of effective alveolar ventilation.

The restriction of free chest movement from surgical positioning, surgical retraction of the chest and abdomen, traumatic rupture of the diaphragm, pneumothorax, hemothorax, flail chest, and restrictive lung disease can reduce alveolar ventilation significantly. Proper recognition and treatment of traumatic chest injuries are crucial to the successful management of patients after CNS trauma.

**B. Causes of increased $P(A\text{-}a)O_2$.** The $P(A\text{-}a)O_2$ may be increased as the result of both extrapulmonary and pulmonary factors. Decreases in cardiac output and either a respiratory or metabolic alkalosis are important **extrapulmonary factors** that increase $P(A\text{-}a)O_2$ in the presence of lung disease. Dramatic **increases in dead space ventilation**, such as with massive pulmonary embolism, may lead to arterial hypoxemia as well. **Pulmonary disorders** can increase $P(A\text{-}a)O_2$ because of shunting, $\dot{V}A/\dot{Q}$ mismatch, and limitation of diffusion.

1. **Extrapulmonary factors** that commonly contribute to hypoxemia in neurosurgical patients who have pre-existing lung disease are **hyperventilation** to reduce ICP and **excessive depletion of intravascular volume** from fluid restriction and the administration of diuretics.
   a. **Hyperventilation** to induce hypocapnia results in a **respiratory alkalosis** with a **decrease in venous return and cardiac output. Hypocapnia** increases pulmonary shunt, especially in the presence of lung disease. The mechanism is unclear but might be related to hypocapnic bronchoconstriction and inhibition of hypoxic pulmonary vasoconstriction. In addition, the **oxyhemoglobin dissociation curve shifts to the left**, resulting in a lower $PaO_2$ for any given oxygen saturation (Fig. 22.2). This is espe-

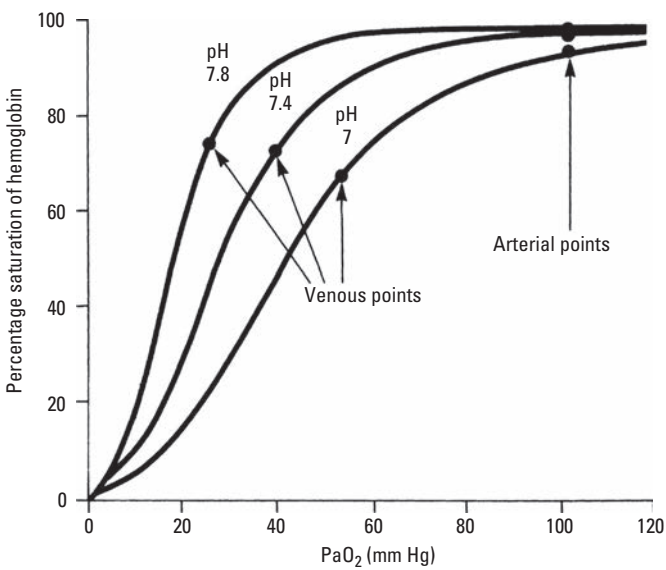


**FIGURE 22.2** Shift in the oxyhemoglobin dissociation curve with change in blood pH.

cially noticeable when the $PaO_2 \leq 70$ mm Hg. Although helpful in reducing ICP because of cerebral vasoconstriction, **hyperventilation should be limited to short periods** with a $PaCO_2$ of 30 to 35 mm Hg. A $PaCO_2 < 25$ mm Hg is avoided because of the potential for worsening cerebral hypoxia and neurologic outcome through excessive vasoconstriction. Hyperventilation also decreases venous return, mixed venous oxygen tension ( $P\bar{V}O_2$ ), and cardiac output.

b. **Hypovolemia and decrease in $P\bar{V}O_2$.** $PaO_2$ is lower when the $P\bar{V}O_2$ is decreased, **as can occur with decreased cardiac output from hypovolemia**, increased oxygen consumption, and severe anemia with increased oxygen extraction. The effect of $P\bar{V}O_2$ can be quite significant, especially when there are areas of low $\dot{V}A/\dot{Q}$ and shunt (Fig. 22.3). For instance, in the presence of $\dot{V}A/\dot{Q}$ mismatch, $PaO_2$ is 80 mm Hg when $P\bar{V}O_2$ is 50 mm Hg. If $P\bar{V}O_2$ is decreased to 20 mm Hg from a decrease in cardiac output, then $PaO_2$ decreases to 40 mm

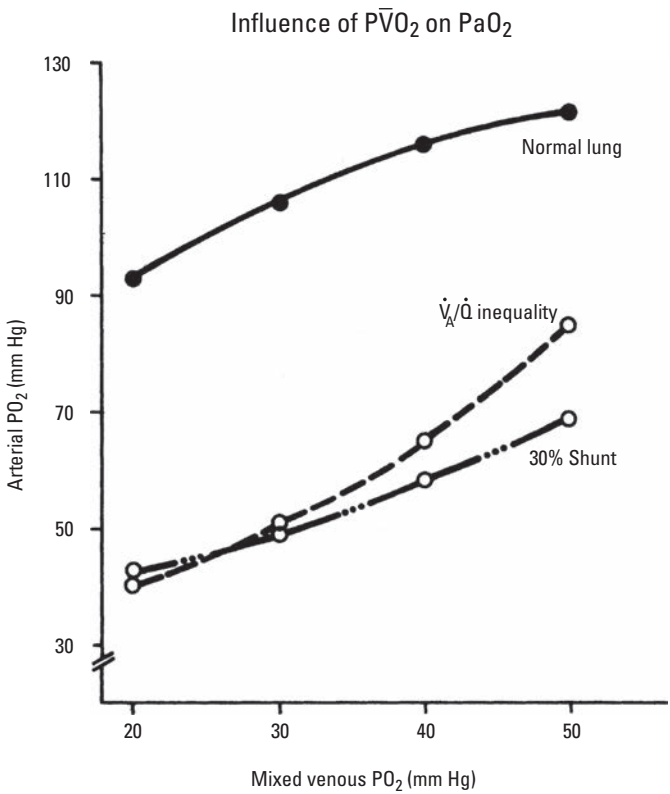


**FIGURE 22.3** Influence of mixed venous oxygen tension on arterial oxygen tension. (Reprinted from Dantzker DR. Ventilation-perfusion inequality in lung disease. *Chest.* 1987;91:749–754 with permission.)

Hg without any change in the degree of $\dot{V}A/\dot{Q}$ inequality or shunt. Therefore, low cardiac output from hypovolemia or myocardial depression increases $P(A\text{-}a)O_2$ and might result in hypoxemia, especially in the presence of pulmonary disease.

2. **Pulmonary factors that increase $P(A\text{-}a)O_2$** in critically ill neurosurgical patients can result from **neurogenic causes** such as neurogenic pulmonary edema (NPE), TBI- and SCI-induced $\dot{V}A/\dot{Q}$ mismatch, and reduction in FRC. **Abnormalities of lung parenchyma** can also cause an increase in $P(A\text{-}a)O_2$.
   a. **Neurogenic causes**
      1. **Neurogenic pulmonary edema** develops in severe CNS injury such as TBI, subarachnoid hemorrhage (SAH), intracranial hemorrhage (ICH), SCI, intracranial surgery, and conditions causing intracranial hypertension (tumor, hematoma, abscess). Of immediate onset, NPE becomes clinically recognizable 2 to 12 hours after injury. The **pathogenesis of NPE** has been suggested recently to involve "triggering" of the posterior hypothalamus and medulla to induce sympathetic stimulation resulting in the massive production of vasoconstrictors, such as norepinephrine, neuropeptide Y, and endothelin as well as proinflammatory mediators and nitric oxide (NO). Subsequently, an **increase in pulmonary capillary pressure** (transmural pressure > 40 mm Hg) causes **endothelial and epithelial damage** resulting in **intra-alveolar leakage**. Release of proinflammatory mediators secondary to disruption of the blood–brain barrier exacerbates endothelial and epithelial damage. Frank NPE is associated with left ventricular overload and arrhythmias.

         **Treatment of NPE** includes control of ICP, mechanical ventilation of the lung with application of PEEP of up to 15 mm Hg, and administration of hypertonic intravenous solutions (mannitol or hypertonic saline) and diuretics. Dobutamine, norepinephrine, and epinephrine may be used to maintain systemic and cerebral perfusion pressure (CPP = mean arterial pressure [MAP] – ICP).
      2. **Reduction of FRC commonly occurs after TBI and SCI** at the cervical and thoracic levels. Head trauma patients might exhibit a reduction in FRC and pulmonary compliance and an increase in pulmonary shunting without evidence of pulmonary disease on the chest radiograph. **$\dot{V}A/\dot{Q}$ mismatch can be seen early on in patients after TBI.** An association between the severity of TBI and the severity of $\dot{V}A/\dot{Q}$ mismatch has been suggested in patients who have acute lung injury (ALI) with $PAO_2/PaO_2 < 300$ being a predictor of poor survival.
   b. **Pulmonary etiologies of increased $P(A\text{-}a)O_2$**
      1. **Atelectasis and lung consolidation** are common in the neurosurgical patient. Hypoventilation from central respiratory depression, pain, sedative medications, cervical and thoracic SCI, altered levels of consciousness, bronchial obstruction from mucous plugs or aspiration of particulate matter, and compression of adjacent lung by traumatic pneumothorax, hemothorax, or pleural effusion all contribute to the formation of atelectasis. **Prevention and treatment of lung collapse** through hyperventilation, recruitment maneuvers (PEEP, inverse-ratio ventilation where inspiration is longer than expiration, "sigh" breaths), and aggressive physiotherapy can prevent the development

of lung infection. As SCI patients are not able to clear secretions adequately, therapeutic bronchoscopy, bed rotation, and turning the patient into the prone position can help clear secretions.

2. **Aspiration of gastric contents** occurs frequently in comatose patients, in trauma patients because of intoxication from alcohol and street drugs, and in abdominal injury. Aspiration of large volumes of fluid with a low pH (< 2.5) or particulate matter results in aspiration pneumonitis and ALI. The aspiration of large foreign bodies, such as gravel, gum, or teeth, might also cause bronchial obstruction, atelectasis, and hypoxemia, and potentially may lead to necrotizing pneumonia. **Treatment of aspiration is primarily supportive.** Prophylactic antibiotics are not indicated.
3. **Nosocomial pneumonia (NP)/Ventilator-associated pneumonia (VAP).** VAP is a NP that develops in patients 48 hours or more after endotracheal intubation. NP is the second most common (after urinary tract infection) and the **most serious in-hospital infection**, particularly in the neurosurgical ICU. About *half* of patients who have isolated TBI and SCI and nearly *two-thirds* of patients after cervical SCI develop NP/VAP, as compared to 5% to 30% in the general ICU population. Pulmonary complications, particularly pneumonia, represent an independent risk factor for death after SCI. **Risk factors for NP/VAP** are presented in Table 22.1.
   a. **Early-onset NP/VAP and late-onset VAP** are distinguished by their respective times of onset and pathogens. In the general ICU population, early-onset NP/VAP develops within the first 5 days of hospitalization while late-onset VAP develops after 5 days. **Early-onset NP/VAP** is characterized by community-acquired microorganisms including gram-positive cocci (*Staphylococcus aureus, Haemophilus influenzae, Streptococcus pneumoniae*), Enterobacteriaceae, and anaerobes. Community-acquired organisms predominate as the causative drugs of pneumonia in critically ill TBI patients, however, in the first 10 days after admission. In **late-onset VAP**, the causative pathogens are hospital-acquired (nosocomial), highly virulent, antibiotic-resistant microorganisms (*Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella*, *methicillin-resistant Staphylococcus aureus* [*MRSA*], *vancomycin-resistant Enterococcus* [*VRE*]). The extreme virulence and the antibiotic resistance of the flora are responsible for the **high mortality rate** of 40% to 60%, which can climb to as high as 80% in late-onset VAP. With comatose patients, VAP develops most frequently between hospital days 4 and 7.
   b. **Pathogenesis of late-onset NP/VAP** in terms of sources of infection includes major aspirations, nasal colonization by *S. aureus*, and microaspiration of colonized oral, upper airway, and gastric secretions, all of which can lead to the development of microabscesses in the lung. Hypoventilation with insufficient alveolar aeration and consequent alveolar collapse and consolidation hastens the onset of infection.
   c. Unfortunately, there is no "gold standard" for the **diagnosis** (Table 22.2) of VAP. Along with clinical criteria, **early bacteriologic detection** of causative microorganisms is important for appropriate antibiotic treatment. If not supported by bacteriologic

TABLE 22.1 Diagnostic Criteria for Nosocomial Pneumonia/Ventilator-associated Pneumonia

| Clinical Criteria | Bacteriologic Criteria | |
|---|---|---|
| I. *"Classic" clinical criteria* (sensitivity and specificity 50%–60%)<br>A. Change in chest x-ray: new and persistent pulmonary infiltrates, or new pleural effusion, *and*<br>B. Two or more findings from the following:<br>1. Fever > 38° C or hypothermia < 36°C<br>2. White blood cell count ($mm^3$) ≥ 12,000 or ≤ 5,000<br>3. Purulent tracheobronchial secretions<br>4. Impaired oxygenation<br>II. *Clinical Pulmonary Infection Score* ≥ 6 (includes scoring system with points for temperature, white blood cell count, tracheal secretions, oxygenation, pulmonary radiography, tracheal aspirate) | I. *Non-invasive techniques*<br>A. Endotracheal tube aspirates<br>1. *Qualitative cultures* (sensitivity 90%, specificity < 50%)<br>2. Quantitative culture ≥ $10^5$–$10^6$ cfu/mL<br>B. Mini-BAL with aspirates from lower respiratory tract with blind protected telescopic catheters (*quantitative cultures*) | I. *Invasive bronchoscopic techniques with quantitative cultures* (sensitivity and specificity 70%–90%)<br>A. BAL: ≥ $10^4$ cfu/mL<br>B. Protected specimen brushing: ≥ $10^3$ cfu/mL<br>C. Gram stain: ≥ 5% infected leukocytes (containing intracellular microorganisms) is optional |

BAL, bronchoalveolar lavage; cfu/mL, colony-forming units per milliliter.

TABLE 22.2 Risk Factors for Nosocomial Pneumonia/Ventilator-associated Pneumonia

| Patient Related | Intervention Related |
|---|---|
| Aspiration | Endotracheal intubation |
| Bacterial colonization of nasopharynx | Mechanical ventilation for > 48 hours |
| Coma, decreased level of consciousness | |
| Atelectasis | Barbiturate use |
| Older age | Traumatic brain injury |
| > 30 in early-onset pneumonia | Histamine type 2 blocking drugs, antacids |
| > 60 in late-onset pneumonia | Muscle relaxants |
| Serum albumin < 2.2 | Excess sedation |
| Adult respiratory distress syndrome | |
| Chronic obstructive pulmonary disease | Frequent ventilator circuit changes |
| Multiorgan dysfunction syndrome | Reintubation/unplanned extubation |
| High gastric pH | Intracranial pressure monitoring |
| Sinusitis | Nasogastric tube/enteral nutrition |
| Uremia | Parenteral nutrition |
| | Patient transport |
| | Length of stay in intensive care unit[a] |

[a]Controversial in long-term intensive care unit survivors.

results, empiric antibiotic treatment is often inadequate. The use of **invasive bronchoscopic techniques** (bronchoalveolar lavage and protective specimen brushing) with **quantitative cultures** of the specimen allows precise adjustment of antibiotic therapy. However, finalizing quantitative cultures takes 2 to 3 days, which inevitably leads to delay in instituting appropriate treatment.

**d.** Choice of **antibiotic treatment** depends on the onset of NP/VAP, risk factors, and severity of the illness. In **early-onset NP/VAP**, monotherapy with amoxicillin clavulinate, a second-generation cephalosporin, or an antipseudomonal third-generation cephalosporin or carbapenem for 5 to 7 days is effective. **Late onset VAP** requires broad coverage of resistant pathogens, and empiric combination therapy with two or three antibiotics should be initiated with an antipseudomonal cephalosporin or carbapenem along with amikacin or quinolone. For **MRSA coverage**, linezolid or vancomycin should be added, although linezolid is more effective than vancomycin. After quantitative cultures have been finalized, **empiric antibiotic coverage should be adjusted** to the particular pathogen and continued for at least 7 to 21 days, depending on the microorganism and the severity of illness.

**e.** **Preventive strategies for VAP** are directed at preventing aerodigestive tract colonization, aspiration, and lung consolidation. **Routine hand washing** with either water and soap or alcohol gel is the most effective strategy for reducing colonization of nosocomial infections. Other modalities include restriction of antibiotic usage, attention to oral hygiene, isolation of patients who have antibiotic-resistant pathogens, and selective digestive decontamination. Semirecumbent positioning, subglottic

drainage, prevention of unexpected extubation, and avoidance of nasal intubation, gastric overdistention, and oversedation can reduce the chance of aspiration.

4. **Acute lung injury/Acute respiratory distress syndrome (ARDS)**
   a. **Definition**. ALI/ARDS is a **clinical syndrome of diffuse lung injury** that results in non-cardiogenic, high-permeability pulmonary edema. ALI/ARDS consists of the following: (1) **acute onset**, (2) **bilateral pulmonary infiltrates** on the chest radiograph, (3) **non-cardiogenic edema**: pulmonary capillary occlusion pressure of < 18 mm Hg, and (4) **hypoxemia**, as defined by a ratio of the $PaO_2$:$FIO_2$ of ≤ 300 in ALI and ≤ 200 in ARDS. The **incidence of ALI/ARDS** in North America and Europe varies from 1.5 to 75 cases/100,000 population. ALI/ARDS is a severe disease with a **significant mortality** of 22% to 32% for ALI and approximately 40% to 70% for ARDS.

      **One-third of ALI cases progress to ARDS in the first week**, particularly in trauma patients. One-third of patients who have isolated TBI develop ALI/ARDS; this increases mortality significantly and worsens neurologic outcome. The **major cause of death** in patients who have ALI/ARDS is sepsis and multiorgan failure. Only about 10% to 20% of patients dying from ARDS die from hypoxemia *per se*.
   b. **Risk factors** (Table 22.3). Primary ARDS is caused by direct lung injury (especially pneumonia) and has a higher mortality rate than secondary ARDS, which is caused by indirect lung injury.
   c. **Pathogenesis and clinical course**. ALI/ARDS usually **develops within the first 72 hours of the initiating event** with 60% to 70% of cases occurring within the first 24 hours. The initial step in the pathogenesis of ALI/ARDS is **endothelial cell activation in the pulmonary microvasculature** by various insulting agents such as microbial products, different cytokines, and histamine. This then leads to microcirculatory distress, microcoagulation, neutrophil activation, imbalance between proinflammatory and anti-inflammatory mediators, **impairment of the alveolar-capillary barrier**, and **influx of protein-rich fluid into the alveoli**. The **alveolar epithelium is damaged**, resulting in the disruption of the epithelial ion- and fluid-transport system, impairment of surfactant production, and loss of the epithelial barrier. **Disorganized epithelial repair leads to fibrosis.**
   d. The **degree of epithelial injury correlates with the severity of illness and outcome**. Significant abnormalities of pulmonary vascular permeability usually persist for 1 week after the onset

TABLE 22.3 Risk Factors for Adult Respiratory Distress Syndrome

| Primary ARDS: Direct Lung Injury | Secondary ARDS: Indirect Lung Injury |
|---|---|
| Pneumonia | Sepsis |
| Aspiration | Trauma with shock |
| Pulmonary contusion | Blood transfusions |
| Fat emboli | Subarachnoid hemorrhage |
| Near drowning | Traumatic brain injury |

ARDS, adult respiratory distress syndrome.

of ARDS. The acute phase may either resolve in the first week or progress to fibrosis with persistent hypoxemia. **Patients who do not improve in the first week have a poor prognosis.** In the late phases, **pulmonary hypertension** can develop as a result of elevated pulmonary vascular resistance, primarily from arteriocapillary obstruction rather than from pulmonary vasoconstriction. **Pulmonary compliance decreases.** The chest CT scan often shows diffuse interstitial thickening and honeycombing. In survivors of ARDS, muscle wasting and weakness are the most prominent extrapulmonary conditions, which persist for a year after recovery.

5. **Ventilator-induced lung injury (VILI)/Ventilator-associated lung injury (VALI)** is an **inflammatory syndrome of diffuse alveolar damage** that **worsens the outcome in patients who have ALI/ ARDS**. Several mechanisms are suggested for the **pathophysiology of VILI**: oxygen toxicity, alveolar overdistension from either high tidal volumes (volutrauma) or high airway pressures (barotrauma), and repeated alveolar opening and collapse during the ventilatory cycle. Because ALI/ARDS is a heterogenous lung disease, positive-pressure ventilation causes uneven distribution of volume and alveolar pressure to the extent that even moderate tidal volumes can overstretch healthy alveoli, leading to inflammatory responses and exacerbation of inflammatory processes. **Positive end-expiratory pressure (PEEP) diminishes VILI** by recruiting alveoli and preventing alveolar collapse.
6. **Cardiogenic pulmonary edema.** Pulmonary edema of cardiogenic etiology can occur in the neurosurgical patient. **Left ventricular dysfunction** may be caused by myocardial ischemia or infarction, adverse drug reactions, tachyarrhythmias, severe hypertension, or fluid overload. Older patients are at greater risk. However, **myocardial ischemia** from severe anemia, hypotension, fluid overload, excessive mannitol administration, and Triple-H therapy can precipitate pulmonary edema in the younger patient, as well. **Treatment** involves diuresis, fluid restriction, and supportive care.
7. **Pulmonary embolism.** Pulmonary emboli are common in neurosurgical patients. In SCI, the incidence of **deep vein thrombosis** (DVT) reaches 100% without prophylaxis and 10% to 25% with prophylaxis. Pulmonary emboli occur in 10% to 20% of SCI patients and usually **originate from venous thrombosis in the lower extremities** and, less commonly, from either the pelvic or prostatic venous plexi or the right ventricle. Pulmonary embolism causes acute pulmonary hypertension, right ventricular failure, and a reduction in cardiac output. The diagnosis of smaller pulmonary emboli should be considered in patients who have unexplained tachypnea and chest pain. The $PaO_2$ is usually normal and the $PaCO_2$ is decreased in the tachypneic patient who has small pulmonary emboli. **Massive pulmonary embolism** causes an **increase in dead-space ventilation** (with a decrease of end-tidal $CO_2$ in the ventilated patient) and **acute cardiorespiratory failure**. The multidetector row spiral CT scan is the first-line diagnostic tool for the diagnosis of pulmonary embolism. If the multidetector row spiral CT scan is not available, pulmonary angiography is indicated. **Treatment** is predominantly supportive and involves anticoagulation. If anticoagulation is contraindicated, an *inferior vena cava filter* should be placed.

C. **Lung-protective strategies for mechanical ventilation** have contributed to the decline in mortality along with the **prevention and treatment of nosocomial infection** such as pneumonia and sepsis, **prophylaxis against upper gastrointestinal bleeding**, and **prevention of thromboembolism**.
   1. **Lung-protective ventilation** is the cornerstone of ALI/ARDS management. Positive-pressure ventilation with a tidal volume of 6 mL/kg of ideal body weight and pressure < 30 cm $H_2O$ significantly decreased mortality as compared with conventional ventilation. PEEP should be adjusted to allow for an $FIO_2$ < 0.6 to prevent oxygen toxicity. The oxygenation goal is either a $PaO_2$ > 60 mm Hg or an SpO2 ≥ 90%.
   2. **Permissive hypercarbia.** Lung-protective ventilation can inevitably lead to hypoventilation. Hypercarbia with a $PaCO_2$ of 60 to 100 mm Hg and a pH of 7.25 can be safely tolerated. However, because $CO_2$ is a potent cerebral vasodilator, permissive hypercarbia is usually contraindicated in neurosurgical patients who have intracranial hypertension, and, if needed, should be applied cautiously in patients who have head injury without increased ICP.
   3. **Prone position.** Turning the patient from the supine to the prone position improves oxygenation through favorable redistribution of ventilation–perfusion matching by **recruitment of collapsed alveoli**. In patients who have subarachnoid hemorrhage (SAH) and normal ICP, the prone position enhances brain tissue oxygenation but can increase ICP slightly. **Risks** of the prone position include accidental extubation, loss of intravenous access, hemodynamic instability, coughing, and late complications such as edema and pressure sores.
   4. **Nitric oxide.** Although not proven to affect survival, inhaled NO **improves oxygenation** and can be administered for life-threatening hypoxemia unresponsive to other maneuvers. The use of NO is safe in patients who have increased ICP and in situations where it is not possible to turn the patient to the prone position.
   5. **Diuresis and fluid restriction.** Regardless of the etiology, diuresis and fluid restriction are beneficial in ALI/ARDS but may be impossible to achieve in patients who have vasospasm after SAH and require hypertensive hypervolemic hemodilution (Triple-H) therapy.
   6. **Glucocorticosteroids.** Although controversial, current data suggest that low to moderate doses of corticosteroids in the early ( first 7 days) and late phase of ARDS may be beneficial in patients who do not have signs of infection. One of the suggested mechanisms is suppression of fibroproliferation in lungs.

## II. RESPIRATORY CARE OF THE NEUROSURGICAL PATIENT

A. **Administration of oxygen and airway management.** All patients who have cerebral injury or cervical SCI are considered hypoxemic until proven otherwise and need to receive supplemental oxygen. A $PaO_2$ > 60 mm Hg or an $SpO_2$ greater than 90% should be maintained in every patient to assure adequate cerebral oxygenation.
   1. **Criteria for endotracheal intubation and mechanical ventilation**
      a. **Impaired consciousness.** Patients who have a **Glasgow Coma Scale score ≤ 8** require endotracheal intubation and ventilation.
      b. **Need for hyperventilation to reduce ICP.** With hyperventilation, the optimal $PaCO_2$ should be from 30 to 35 mm Hg. Although helpful in the short term to reduce ICP, excessive hyperventilation to a $PaCO_2$ < 25 to 30 mm Hg can potentially cause cerebral ischemia and should be avoided.

c. **Need for adequate oxygen delivery** to provide $PaO_2$ greater than 60 mm Hg or $SpO_2$ greater than 90%
d. **Inability to protect the airway** or clear secretions
e. **Hypoventilation** from central or peripheral respiratory depression
f. **Airway compromise**
g. **Hemodynamic instability**

2. **Orotracheal intubation** is preferable for urgent intubation in the presence of increased ICP, hypoxemia, and/or hemodynamic instability. In the hemodynamically stable patient, either thiopental, 3 to 5 mg/kg, or propofol, 2.5 mg/kg, and succinylcholine, 1 to 1.5 mg/kg, can be used to prevent coughing and an increase in ICP. Alternatively, rocuronium, 1 to 1.5 mg/kg, can be used for muscle paralysis. Etomidate, 0.1 to 0.3 mg/kg, and lidocaine, 1 to 1.5 mg/kg, can be used in the less stable patient.

   In trauma patients or patients who have a full stomach, a **modified rapid-sequence induction** with cricoid pressure and ventilation by mask might be used to avoid marked increases in ICP from hypoxemia and hypercarbia. The head and neck are secured by an assistant to achieve **manual inline stabilization** to prevent head movement in the presence of potential cervical SCI. Manual inline stabilization may render a difficult intubation more difficult, however, and also cause movement of unstable neck structures beyond the area of stabilization.

   A variety of **video-assisted laryngoscopes** including the Glidescope have become available recently and are especially helpful in emergency situations and in the management of the difficult airway. The use of the Glidescope, however, does not preclude the application of manual inline stabilization. A "Parker" endotracheal tube with a curved tip and stylet is recommended for endotracheal intubation with the Glidescope.
3. **Nasotracheal intubation** is of minimal use in neurosurgical patients because of the possibility of resultant obstruction of sinus drainage, which increases the risk of sinusitis, pneumonia, and subsequent sepsis and ALI/ARDS. Nasotracheal intubation is absolutely contraindicated in the presence of a basilar skull fracture.
4. **Tracheotomy** is absolutely indicated in the presence of SCI above C5. Emergency tracheotomy or **cricothyrotomy** could be necessary in patients who have TBI and multiple facial fractures rendering bag-and-mask ventilation difficult. Compared with endotracheal intubation, tracheotomy decreases anatomical dead space and the work of breathing slightly, improves access for suctioning, is more comfortable for the patient, and reduces sedation requirements. All of these advantages may be beneficial to patients who have difficulty in weaning from the ventilator.

   **Early tracheotomy** is considered in the first week of admission. Although there is no consensus as to the beneficial effects of early tracheotomy, a **bedside percutaneous dilatational tracheotomy (PDT)** performed on the second or third day after injury significantly reduces the incidence of pneumonia, ICU length of stay, and mortality in patients who were expected to need mechanical ventilation for greater than 14 days. Therefore, early bedside PDT should be considered in patients who have significant neurologic injury, absent gag reflex, inability to protect the airway and clear secretions, or are in a persistent vegetative state. Because of the advantages of bedside PDT, including negation of the need to involve the OR and transport of a critically ill patient, this technique has gained popularity. The procedure requires the participation of two physicians (surgeon, otolaryngologist, intensivist) and consists of cricothyroidotomy and tracheal dilatation using the Seldinger technique with bronchoscopic guidance through the endotracheal tube

by an experienced bronchoscopist. Although complications are rare with a skilled team, the major complication is bleeding and occurs in 1% to 2% of cases.

**B.** The goal of **mechanical ventilation** in the neurosurgical patient is to provide adequate gas exchange in the lungs while minimizing risks for the development of ventilator-induced lung injury. Vital signs should be monitored and arterial blood gases measured 30 minutes after changing ventilator settings. Normocarbia ($PaCO_2$ = 40 mm Hg) and an $SpO_2$ of 91% to 94% are considered optimal in patients who have cerebral injury.

1. **Controlled mechanical ventilation** is used in the OR and occasionally in the neurosurgical ICU in selected patients who have no ventilatory effort owing to neuromuscular blockade, high cervical SCI, absent ventilatory drive, drug overdose, or brain death.
2. For patients in whom spontaneous ventilation is preserved, the preferred **assisted modes of ventilation** are those in which the ventilator delivers a breath triggered by the patient's inspiratory effort. Along with classic **volume-controlled** and **pressure-controlled modes of mechanical ventilation** (assist-controlled, synchronized and non-synchronized intermittent mandatory ventilation, and pressure-support ventilation), modern ventilators provide a variety of new ventilation modes. These modes include **"dual-controlled" mechanical ventilation** with preset tidal volume and inspiratory pressure ("volume-assured pressure support" or "pressure-augmentation" mode), **airway-pressure release ventilation** (pressure-controlled inverse-ratio ventilation mode) that allows for spontaneous breathing, and **proportional-assist ventilation**.
3. **PEEP** increases arterial oxygenation by **alveolar recruitment** and **FRC augmentation,** which **decrease intrapulmonary shunting and $\dot{V}A/\dot{Q}$ mismatching**. The application of PEEP decreases the need to give high, potentially toxic, concentrations of oxygen. On the other hand, **PEEP increases $PaCO_2$** by increasing dead-space ventilation. Hemodynamically, PEEP decreases venous return, cardiac output, and systemic arterial BP. These effects can be partially attenuated by hydration. The varied clinical responses of TBI patients to PEEP might be secondary to PEEP's effect on other hemodynamic and respiratory variables. The use of 10 cm $H_2O$ of PEEP improves oxygenation but can decrease cerebral perfusion from the decrease in cardiac output.

   PEEP usually causes clinically inconsequential increases in ICP in patients who have severe TBI. The influence of PEEP on ICP is less prominent in patients who have stiff lungs (as with ALI/ARDS) and are presumably the ones who need PEEP the most. A PEEP of up to 30 cm $H_2O$ has been used to treat hypoxemia with minimal adverse effect on ICP. However, because significant and potentially serious increases in ICP and clinical deterioration have been observed in some TBI patients after the application of PEEP, **ICP should be monitored when PEEP is used.** Increases in ICP from PEEP can be reduced by elevating the head 30° and concurrently administering mannitol. The abrupt removal of PEEP might also increase ICP.
4. **Non-invasive mechanical ventilation (CPAP, BiPAP, non-invasive mask ventilation) without an endotracheal tube is not routinely utilized** in neurosurgical patients and can be considered only a temporizing measure in extraordinary situations of difficult airway management. Non-invasive ventilation is useful for patients who, in the absence of neurologic deficits, have, for example, an exacerbation of chronic obstructive pulmonary disease or decompensated heart failure.

C. **Monitoring patients receiving mechanical ventilation.** The efficacy and safety of mechanical ventilation in patients is evaluated by monitoring gas exchange, airway pressure, breathing pattern, lung compliance, hemodynamic function, chest radiographs, and chest CT scans, the "gold standard" for diagnosis of lung pathology.

D. **Weaning.** Clinically stable patients are frequently re-evaluated for readiness for a trial of weaning. Weaning should be considered *as early as possible*. A **spontaneous breathing trial (SBT)** is utilized to assess patients' readiness for extubation.

1. ***Clinical criteria*** to be met before attempting to wean include adequate cough, absence of excessive tracheobronchial secretions, resolution of the acute phase of the lung disease, and normal ICP. ***Objective criteria*** include stable hemodynamics (HR < 140 bpm; systolic BP 90 to 160 mm Hg; minimal vasopressors are allowed), stable metabolic status, adequate oxygenation with $SpO_2 > 90\%$ on $FIO_2 \leq 0.4$, PEEP $\leq 8$ cm $H_2O$, and $PaO_2/FIO_2 \geq 150$. However, standard weaning criteria, including normal neurologic status, are not applicable to head-injured patients in whom impaired neurologic status may delay weaning and extubation.
2. A **spontaneous breathing trial** for 30 minutes should be attempted in patients considered candidates for weaning from mechanical ventilation. The trial can be performed with either a T-piece or pressure support $\leq 8$ cm $H_2O$. To pass the trial, the patient must meet the above criteria for weaning and sustain adequate pulmonary function (respiratory rate $\leq 8$ breaths/minute, maximal inspiratory pressure $< -20$ cm $H_2O$, VT > 5 mL/kg, rapid shallow breathing index [respiratory rate/VT in liters] <105 breaths/minute/L) without developing respiratory acidosis.
3. The **rate of reintubation** (failed weaning and extubation) in the neurosurgical ICU patients fluctuates between 8% and 40% when normal neurologic status is not considered necessary for a weaning trial and extubation. The causes of weaning and extubation failures in neurosurgical patients are multifactorial so that the decision to wean is solely a physician-driven one.

## *Suggested Readings*

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# 23 Cardiovascular Therapy

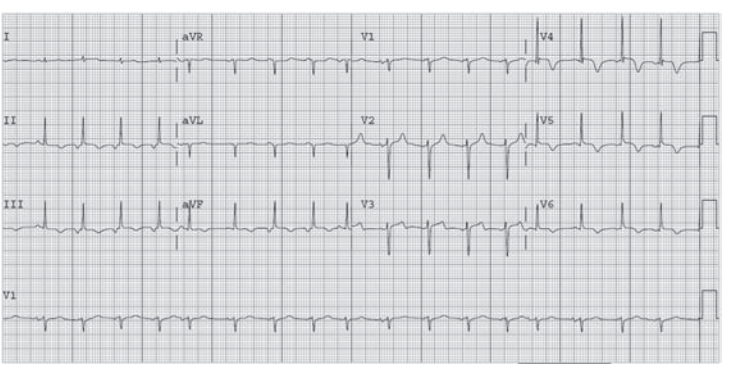
**Sheena M. Howson, John A. Barwise, and Clifford Lee Parmley**

## Illustrative Clinical Case

A 61-year-old white female who has a past medical history of untreated hypertension (HTN), smoking (2PPD for > 40 years), and on no noted home medications presents to an outside hospital 24 hours ago with complaint of the worst headache of her life. Computed tomography (CT) scan revealed subarachnoid hemorrhage (SAH) in the basilar cisterns consistent with rupture of an intracranial aneurysm. She is transferred to your hospital for further care. On arrival, she is a Hunt-Hess grade II but becomes increasingly somnolent; she no longer follows commands and requires endotracheal intubation. The neurosurgical team inserts an external ventricular drain, revealing bloody cerebrospinal fluid (CSF) and an opening intracranial pressure (ICP) of 25 cm $H_2O$. She is taken to the operating room for endovascular coiling of a 9-mm aneurysm of the basilar tip demonstrated on CT angiography.

**What are your hemodynamic goals? How will you calculate her cerebral perfusion pressure (CPP)? What will her target CPP be? Which medications will you use to maintain this CPP? How does her long-standing HTN affect the autoregulation of her cerebral vasculature? What limitations are there in the setting of an unruptured aneurysm?**

The procedure begins without complication. You notice that her central venous pressure (CVP) is elevated at 19 mm Hg; she has become increasingly tachycardic and has developed hypotension that is fairly resistant to fluid boluses and intravenous phenylephrine therapy. Leads II and V5 show marked T-wave inversions on the monitor. The electrocardiogram (ECG) done on admission is found and reveals the following:



The ST changes are new when compared with a prior ECG. You place a pulmonary artery (PA) catheter through an existing introducer in order to assess her cardiac function. Her PA pressures are elevated at 53/37 mm Hg with a cardiac index (CI) of 2.1 L/minute/$m^2$, mixed venous oxygen tension ($SvO_2$) of 60%, pulmonary artery occlusion pressure (PAOP) of 32 mm Hg, and mean arterial pressures (MAPs) in the 50 to 55 mm Hg range. Intraoperative transesophageal echocardiography (TEE) shows an area of marked left ventricular (LV) apical akinesis with severely depressed LV systolic function (ejection fraction [EF] 20% to 30%) and restrictive LV filling.

**What is her differential diagnosis? What are the proposed mechanisms of neurogenic stress cardiomyopathy and Takutsubo cardiomyopathy? How can you differentiate between them? Which medications can you use to improve her cardiac function?**

The neurosurgeon successfully coils the aneurysm, and you have started a dobutamine infusion. Her CI improves to 3.1 L/minute/$m^2$; $SvO_2$ is now 68%; and her MAPs have been stable, giving her an adequate CPP. The neurosurgeon asks about the evolution of neurogenic stress cardiomyopathy and whether it will affect their management if she were to develop vasospasm in the next few days.

**What types of therapies will she receive in the prevention of vasospasm? How will this affect her cardiac function? Which medications can be used to increase her systemic vascular resistance (SVR) in this setting? Is a suspected neurogenic stress cardiomyopathy reversible?**

## Chapter Highlights

- **Oxygen delivery to the brain** is of utmost importance in the perioperative management of neurosurgical patients. Optimization of cerebral perfusion pressure (CPP = mean arterial pressure [MAP] – intracranial pressure [ICP]), cerebral blood flow (normal CBF is 50 mL/100 g/minute), and the various components affecting cardiac output should be the focus of therapy.
- **Hemodynamic goals** for optimizing therapy include: MAP ≥ 80 mm Hg, CPP > 65 to 70 mm Hg, mixed venous saturation ($SvO_2$) ≥ 65%, CI ≥ 2.5 L/minute/$m^2$, and urine output (UOP) > 0.5 mL/kg/hour.
- Vigilant **maintenance of an appropriate MAP** is key. In the absence of significant pre-existing HTN or decreased intracranial compliance, a 20% decline from baseline is usually well tolerated.
- **Vasoactive drugs** are commonly used. Most do not affect cerebral vascular tone directly but can have varied indirect effects on CPP, CBF, and cerebral metabolic rate for oxygen consumption ($CMRO_2$).
- Although **sodium nitroprusside** (SNP) and **nitroglycerin** (NTG) can provide rapid and reliable vasodilatation, the risk of increasing CBF, especially in the setting of elevated ICP, may preclude their use. Calcium-channel blocking drugs such as nicardipine and clevidipine have proven to be safe, effective, and comparably fast acting in such scenarios.
- **Subarachnoid hemorrhage** (**SAH**) and its complications can have varied effects on the cardiovascular system. These include neurogenic stress cardiomyopathy and cerebral vasospasm, along with their hemodynamic sequelae and respective therapies.
- The **management of the cardiovascular complications** of perioperative neurologic disorders, such as autonomic dysfunction and reflexive blood pressure (BP) fluctuations, focuses on tight BP control and maintenance of the hemodynamic goals as mentioned previously. Knowledge of the potential complications specific to each disorder and its treatment is warranted.

## I. BASIC CONSIDERATIONS

The primary goal of cardiovascular therapy in perioperative neurosurgical patients is to provide sufficient metabolic substrate to the threatened central nervous system (CNS). Because glucose is usually not a problem related to cardiovascular therapy, our attention is directed to oxygen delivery. Cardiovascular therapy can affect intracranial volumes and pressures both globally and locally and result in irreversible injury. Therefore, while maintaining oxygen delivery is important, care must be exercised not to compromise intracerebral hemodynamics. The following sections will illustrate the heart-brain paradox, which is an ever-present challenge that deserves much consideration in the realm of neuroanesthesia.

**A. Autoregulation** refers to the interdependence of CBF and mean arterial (blood) pressure (MAP). The range of MAP over which non-hypertensive patients exhibit autoregulation is 50 to 150 mm Hg. Chronically hypertensive patients have altered autoregulation and neither maintain CBF at a MAP in the low end of the normal range nor vasoconstrict adequately when the MAP exceeds 150 mm Hg. A similar alteration of autoregulation occurs with sympathetic activation induced by shock or surgery.

1. When autoregulation is impaired, CBF will become more dependent on the BP; minor swings in MAP might have significant impact on intracranial hemodynamics.
2. Many conditions such as head injury and tumors are associated with either generalized or regional disruption of autoregulation.

**B. Intracranial pressure (ICP)**. The intracranial compartment is essentially a closed space, so ICP is determined by the intracranial volume, which is comprised of cerebrospinal fluid (CSF), cerebral parenchyma, and cerebral blood volume (CBV). Increases in any of these components can contribute to intracranial HTN and result in decreased CPP, the difference between MAP and ICP. Daily CSF production, for example, is fairly constant, as is its volume. Any obstruction to CSF flow or resorption (e.g., tumor, intraventricular hemorrhage, etc.) will result in elevated CSF volumes, and in turn, elevated ICP.

**C. CPP is the difference between MAP and ICP**. In most organs, venous pressure generates the back pressure that determines the pressure drop across an organ. Because venous pressure tends to be negative in the brain, parenchymal pressure (ICP) generates the back pressure for determining CPP. CPP determines CBF both globally and regionally in the CNS. Normal CBF is 50 mL/100 g brain/minute and decreases only if CPP falls from a normal value of approximately 80 mm Hg to below 50 mm Hg unless autoregulation is altered.

## II. CEREBRAL OXYGEN DELIVERY

is a function of CBF and the quantity of oxygen carried in arterial blood ($CaO_2$). CBF is related to CPP, and, because BP is a function of cardiac output (CO) and SVR, CO becomes an important parameter to manipulate to preserve CBF and cerebral oxygen delivery. The normal awake brain consumes 3.3 mL $O_2$/100 g/minute, a value reduced by approximately one-third during the administration of anesthesia.

### A. Cardiac output

1. **Determinants of CO.** The CO is a result of five basic factors: preload; contractility; heart rate (HR); rhythm; and afterload—assuming normal valvular function and the absence of obstructive cardiac pathology.
   a. **Preload** is difficult to monitor but can be best determined by measuring ventricular end-diastolic volume (EDV) by either angiography or echocardiography. Surrogates for preload volume are CVP

as a measure of right atrial preload and PAOP as an estimate of left atrial preload. In addition to PAOP, the volumetric PA catheter monitoring measures right ventricular EDV for preload assessment. Stroke volume variation and pulse pressure variation can be used to assess preload and volume responsiveness when pulse contour cardiac monitoring technology is employed.

b. **Contractility.** The **ejection fraction** measured by either angiography or echocardiography is frequently used to assess contractility, which can also be assessed by evaluating the magnitude of the CO for a given preload condition. Right ventricular EF is available when monitoring is performed with a volumetric PA catheter. CO equals the product of HR and stroke volume. When preload, contractility, or both limit stroke volume, an increase in HR often acts to maintain CO.

c. **Rhythm**. Rhythm disturbances can result in stroke volume variability, and should be treated promptly and appropriately. An adequate and effective stroke volume depends on coordinated contraction of both the atria and ventricles. This variability can negatively affect the accuracy of most monitoring systems, including thermodilution CO and pulse contour analysis techniques.

d. **Afterload**. Afterload is difficult to measure by non-invasive means. Surrogates employed are MAP, which is the afterload against which the left ventricle ejects a stroke volume, and SVR index (SVRI), which can be calculated while using a PA catheter or pulse contour monitoring.

B. **Cardiac failure occurs when CO is insufficient to deliver adequate oxygen**. Typical causes include cardiomyopathies from infarction, ischemia, and chronic HTN; dysrhythmias; increased afterload from arterial HTN; and outflow obstruction from pulmonary embolus. Neurosurgical patients who are critically ill have additional considerations.

1. **Hypovolemia** resulting in insufficient preload can be caused by
   a. **Blood loss** from surgical and traumatic causes including scalp lacerations
   b. **Osmotic diuretic** administration
   c. **Fluid restriction** to minimize cerebral swelling
   d. **Diabetes insipidus** associated with severe traumatic brain injury (TBI) and pituitary surgery
2. **CNS causes**
   a. **Spinal cord injury** and injury to the brain stem vasomotor center can result in hypotension from decreased sympathetic tone.
   b. **Neurogenic stress cardiomyopathy** has been described in patients after they have suffered SAH and acute TBI. The leading theory as to its etiology postulates the massive release of catecholamines at the time of injury. The resulting myocardial wall stress secondary to increasing BP and HR can lead to cardiac injury, and the resultant coronary vasospasm has been suggested as a cause of a reversibly "stunned" myocardium. Takutsubo cardiomyopathy can also present in this fashion, but usually has a more distinct apical distribution to the wall motion abnormalities. Its etiology is similarly linked to a high catecholamine state.

      Patients can have disturbances in cardiac biomarkers, as well as echocardiographic evidence of wall motion abnormalities. The ensuing ECG changes are consistent with ischemia and myocardial dysfunction. The most common changes described include ST-segment abnormalities, deeply inverted T waves, prominent U waves, and prolongation of the QTc interval. Dysrhythmias, especially within the first 48 hours of

injury, can include atrial fibrillation, sinus tachycardia, ventricular tachycardia, ventricular fibrillation, and sinus bradycardia. The frequency and severity of both rhythm disturbances and morphologic ECG changes have been shown to correlate with the severity of neurologic injury. Awareness of these abnormalities, which can commonly occur within the first 72 hours of injury, and recognition of their neurogenic origin and reversibility are integral to the determination of appropriate cardiac management.

3. **Drug induced**. Occasionally, aggressive therapy with calcium-entry blocking drugs or beta-blocking drugs can result in suboptimal myocardial performance.

C. **Blood pressure**

1. MAP = CO × SVR. CO is discussed in the preceding text.
2. Hypotension in the presence of normal intravascular volume and cardiac function occurs because of decreases in SVR.
   a. Hypotension can be secondary to high cervical cord injury.
   b. Brain stem damage involving the vasomotor center results in hypotension. Such an insult is usually lethal.
   c. Fever and sepsis can be associated with hypotension.

## III. PHARMACOLOGY OF CARDIOVASCULAR THERAPY

A. **Guidelines for administration of vasoactive drugs**

1. Use a calibrated pump for all infusions.
2. Inject into the intravenous line as close to vein insertion site as possible.
3. Avoid using systolic blood pressure (SBP) as the primary goal of therapy because this value is prone to fluctuate from a number of causes, not all of which are related to the patient's cardiovascular condition. MAP is a more reliable variable. SBP goals may be used, however, in such settings as an unsecured cerebral aneurysm or hemorrhagic stroke where the concern is more for the sharp systolic upstroke than the mean pressure.
4. Potent vasoactive drugs should be administered in a graded fashion starting with a dose below that thought to be therapeutic. This can prevent large swings in hemodynamics that can be detrimental to surgical hemostasis as well as end-organ perfusion.
5. Consider adrenal insufficiency in patients who are hypotensive and unresponsive to adrenergic therapies.

B. **Adrenergic agonists.** See Table 23.1 for action of adrenergic receptors; see Tables 23.2 and 23.3 for relative adrenergic action and dosing recommendations. Sympathomimetic drugs appear to have little influence on the vascular tone of cerebral vessels. However, raising MAP above the upper threshold of autoregulation increases CBF. Some evidence suggests that beta agonists can increase the $CMRO_2$ and secondarily raise CBF.

1. **Norepinephrine** (Levophed) has some beta activity but is used mainly as an alpha-adrenergic agonist. Its primary use is to treat refractory hypotension.
2. **Epinephrine** (Adrenalin) possesses dose-related alpha and beta properties. Its primary uses are in cardiopulmonary resuscitation, anaphylaxis, and refractory hypotension. The toxicity associated with epinephrine is caused by arrhythmias and the sequelae of vasoconstriction.
3. **Dobutamine** is a synthetic drug that has predominantly beta-1 activity. When compared with other drugs, dobutamine tends to produce less tachycardia and elevation of pulmonary vascular pressure for the same degree of inotropic enhancement. It does not have any dopaminergic agonist action.

TABLE 23.1 Action of Adrenergic Receptors

| Receptor | Site | Action |
|---|---|---|
| $\alpha_1$ | Postsynaptic<br>Vasculature<br>Heart | Vasoconstriction |
| $\alpha_2$ | Presynaptic<br>Peripheral and central nervous system, liver, pancreas, kidney, eye | Vasodilatation |
| $\beta_1$ | Heart | Contractility, chronotropy |
| $\beta_2$ | Heart<br>Vascular and bronchial smooth muscle | Contractility, chronotropy<br>Vasodilatation, smooth muscle relaxation |
| Dopaminergic | Presynaptic<br>Renal and splanchnic circulation, brain stem | Smooth muscle relaxation<br>Nausea and vomiting |

α, alpha; β, beta.

4. **Dopamine** exhibits alpha, beta, and dopaminergic properties in a dose-related fashion. Its primary uses are to treat hypotension and provide inotropic support. Low doses inhibit renal reabsorption of sodium, resulting in a natriuresis. In high doses, dopamine's alpha properties predominate. Evidence suggests that dopamine can produce mild cerebral vasodilatation.
5. **Phenylephrine** is a synthetic drug whose chief characteristic is its relative selectivity for alpha receptors. When used to increase MAP, a baroreceptor-mediated reflex decrease in HR often occurs. Phenylephrine can be the drug of choice when the CI is sufficient but MAP is below the goal.

TABLE 23.2 Adrenergic Agonist and Phosphodiesterase Inhibitor Drugs

| Name | Receptors | Dosage |
|---|---|---|
| Epinephrine | $\beta_2$<br>$\beta_1 + \beta_2$<br>$\alpha$ | 1–2 mcg/min<br>2–10 mcg/min<br>> 10 mcg/min |
| Norepinephrine | $\alpha, \beta_1$ | 4–12 mcg/min |
| Dopamine | Dopaminergic<br>$\beta$<br>$\alpha$ | 0–3 mcg/kg/min<br>3–10 mcg/kg/min<br>> 10 mcg/kg/min |
| Dobutamine | $\beta_1$ | 2.5–10 mcg/kg/min |
| Phenylephrine | $\alpha, \beta_1$ (slight) | 0.1–0.5 mcg/kg/min |
| Ephedrine | $\alpha, \beta_1$ | 5–10 mg |
| Amrinone | Inhibition of phosphodiesterase | 0.75 mg/kg load, then 5–10 mcg/kg/min |
| Milrinone | Inhibition of phosphodiesterase | 50–75 mg/kg load, then 0.5–0.75 mcg/kg/min |

α, alpha; β, beta.

TABLE 23.3 Adrenergic Antagonist Drugs

| Name | Receptor Blocked | Dosage |
|---|---|---|
| Phentolamine | $\alpha$ | 5–10 mg |
| Esmolol | $\beta$ | 0.15–1 mg/kg, then 50–300 mcg/kg/min |
| Labetalol | $\beta > \alpha$ | 5–20 mg, then 2 mg/min |
| Metoprolol | $\beta$ | 2.5–15 mg |
| Propranolol | $\beta$ | 0.25–5 mg |

$\alpha$, alpha; $\beta$, beta.

C. **Adrenergic antagonists** (Table 23.3)
   1. **Esmolol** is an ultrashort-acting (9 to 10 minutes' duration) beta-specific competitive antagonist. Its fast onset and short duration of action render it suitable for rapid intervention in the treatment of tachyarrhythmias in the perioperative period.
   2. **Metoprolol** is a cardioselective beta antagonist whose duration of action is longer than that of esmolol. Metoprolol is most commonly used to treat angina and acute myocardial infarction but can be used intravenously in the perioperative period to control tachycardia. All beta-blocking drugs are capable of inducing bronchospasm, heart failure, or both.
   3. **Labetalol** blocks both alpha and beta receptors with more beta than alpha effects. However, a reduction in MAP usually occurs when the dose is sufficient to decrease HR. Labetalol also has a longer duration of action than either esmolol or propranolol.
   4. **Propranolol** was the original clinically available beta-blocking drug. It is non-selective and has a relatively fast onset, but because the metabolism of the drug in the liver differs widely from patient to patient, dosing is variable. Curiously, propanolol shifts the hemoglobin–oxygen dissociation curve to the right.
   5. **Phentolamine** specifically competes for both alpha 1 and alpha 2 receptors. Because of its duration of action, phentolamine is not frequently used as an antihypertensive in acute perioperative situations.

D. **Phosphodiesterase inhibitors.** (Information is presented in Table 23.2)
   1. **Milrinone** is a non-adrenergic, non-glycosidic compound that enhances contractility and promotes pulmonary and arterial vasodilatation. It is thought to act by inhibiting phosphodiesterase, which increases the intracellular concentrations of cyclic AMP. Milrinone has little potential for causing cardiac arrhythmias but has a long half-life (hours) and can induce thrombocytopenia as well as hypotension.

E. **Vasodilators** (Table 23.4)
   1. **Nicardipine** is a calcium-entry blocking drug that reliably decreases MAP when given as an intravenous infusion. It has low toxicity and a predictable response.
   2. **Clevidipine** is an L-type calcium-channel blocking drug that decreases the MAP by lowering the SVR and lacks any venous effects. It has more rapid onset and is shorter-acting than nicardipine. It, too, can be used as an easily titratable intravenous infusion.
   3. **Sodium nitroprusside (SNP)** is a potent, rapid-onset, short-acting drug that causes more arteriolar than venular vasodilatation via the release of nitric oxide (NO). Administration of SNP is associated with the

TABLE 23.4 Vasodilators

| Name | Dosage |
|---|---|
| Sodium nitroprusside | 0.5–10 mcg/kg/min |
| Nitroglycerin | 5–50 mcg/min |
| Trimethaphan | 1–15 mg/min |
| Hydralazine | 0.1–0.2 mg/kg |
| Nicardipine | 5–15 mg/kg |

activation of the renin–angiotensin system; reflex tachycardia can interfere with BP reduction. Occasionally, patients demonstrate relative resistance to SNP. They are at particular risk for developing cyanide toxicity.

4. **NTG** is a rapid-onset, short-acting drug that induces vasodilatation via NO. Less potent than SNP but with little toxicity, NTG causes more venular than arteriolar vasodilatation.
5. **Adenosine** is an ultrafast-acting vasodilator that decreases MAP and increases CI owing to a decrease in SVR. Heart block is a potential side effect of its use.
6. **Hydralazine** is a vascular smooth muscle relaxant with no effects on contractility or chronotropy. Its use is frequently accompanied by reflex tachycardia.

**F. Other vasoconstrictors**

1. **Vasopressin** (antidiuretic hormone) is a peptide with potent vasoconstricting properties, which can be useful in increasing arterial tone. It is administered as a constant infusion and not titrated up to avoid severe complications of distal ischemia.

## IV. GOAL-DIRECTED PHARMACOLOGIC INTERVENTION FOR CARDIOVASCULAR DYSFUNCTION

The two goals of cardiovascular therapy in neurosurgical patients—adequate CPP and sufficient CO to maintain oxygen delivery—can require different drug regimens. Optimal fluid therapy should be instituted either before or in conjunction with drug therapy.

**A. Increasing MAP** is indicated in a number of clinical settings.

1. **Decreased SVR** from impaired sympathetic tone, sepsis, fever, or anesthetic drugs can be associated with an inadequate MAP. CO can be normal or even high while CPP is too low to optimize cerebral perfusion. Norepinephrine, phenylephrine, and vasopressin are vasoconstrictor drugs that are appropriate in this setting.
2. **Increasing CPP** by raising MAP could be needed to augment cerebral perfusion after carotid endarterectomy and cerebral vasospasm. With intracranial hemorrhage after head injury, it can be desirable to increase MAP to maintain CPP and prevent cerebral hypoperfusion if ICP cannot be controlled.
3. **Anaphylactic reactions.** Hypotension accompanying an allergic reaction is treated with epinephrine.
4. **Cardiopulmonary resuscitation.** Drugs are administered according to the most recent revised advanced cardiac life-support guidelines.
5. **Therapy.** MAP can be increased by administering a drug possessing vasoconstrictive properties that works by direct and/or indirect

adrenergic stimulation (Table 23.2) with varying effects on HR. PA pressure and PAOP also tend to rise, even if no change in intravascular volume has occurred.

6. **Precautions**
   a. **Myocardial risks.** Increasing MAP (afterload) in a patient who has coronary artery disease could increase myocardial oxygen demand sufficiently to outstrip delivery, causing myocardial ischemia and failure.
   b. **Left ventricular (LV) dysfunction.** Increasing MAP could decrease CO if LV dysfunction exists. Therefore, CO monitoring could be indicated during the induction of HTN in patients suspected of having LV dysfunction. TEE assessment of LV function and guidance of therapy in cases of refractory hypotension despite appropriate volume resuscitation and inotropic therapy are indicated.
   c. **Hypovolemia** is treated by augmenting intravascular volume rather than further masking it by the use of adrenergic drugs that only increase the risk of end-organ ischemia. Awareness and management of fluctuations in hematocrit are also warranted, especially in cases of overt blood loss.
   d. **Impaired renal function.** Pharmacologically increasing MAP could cause vasoconstriction of renal vessels and could result in deterioration of renal function if perfusion is marginal.

B. **Increasing CO** is indicated in a number of clinical settings.
   1. **Low CO owing to cardiomyopathy** can be caused by ischemia, viral disease, chemotherapy, or drug overdose. **Goals recommended for inotropic therapy** include the following:
      a. MAP of ≥ 80 mm Hg.
      b. Mixed venous saturation ($SvO_2$) of ≥ 65%.
      c. CI (CO/body surface area) of ≥ 2.5 L/minute/$m^2$.
      d. Evidence of adequate end-organ perfusion. Monitoring UOP can be unreliable after diuretics have been administered.
   2. **Cerebral vasospasm.** Supernormal CO can reduce the risk of permanent neurologic deficit.
   3. **Therapy.** If CO is insufficient after intravascular volume has been optimized, inotropic drugs should be administered.
      a. **Beta agonists** are the first-line drugs because their onset and duration allow rapid titration to effect. Empiric therapy is replaced by goal-directed dosing as soon as appropriate monitoring is available.
      b. **Phosphodiesterase inhibitors.** Milrinone can be used as an adjunct to enhance the increase of CO.
      c. **Digoxin** possesses mild to moderate inotropic activity. It can be given orally or intravenously and can increase CO by 10% to 20% in otherwise stable patients who have chronic heart failure.
      d. **Afterload reduction** can also increase CO in certain circumstances in which forward flow is restricted.
   4. **Precautions**
      a. In doses that are high enough, all adrenergic drugs cause **tachycardia**; patients who have coronary artery disease are at risk for ischemia in this setting. HRs > 120 beats per minute (bpm) should be avoided.
      b. When the dose of an adrenergic drug reaches the range in which alpha activity predominates, **renal perfusion can be compromised**, risking renal failure.
      c. While digoxin is useful in the management of chronic cardiac failure, its onset is not immediate, nor is it easily titratable. Undocumented

previous administration of digoxin, hypokalemia from diuretics, and the onset of renal failure increase the risk of **digoxin toxicity**.

d. Reduction in afterload must be titrated carefully to avoid **inadvertent compromise of end-organ perfusion**.

C. **Lowering MAP** can be indicated in a number of clinical settings.

1. **Hypertension**
   a. **Unclipped aneurysm.** Hypertension in the presence of an unclipped cerebral aneurysm is believed to be a significant risk factor for rebleeding.
   b. **Disrupted cerebral microvascular membrane.** In the presence of the disruption of the blood–brain barrier, HTN can exacerbate the formation of vasogenic edema so that blood pressure control should be considered.
2. **Surgical exposure.** Surgeons can request iatrogenic hypotension to enhance exposure, reduce risk of aneurysmal rupture, or assist with the control of bleeding.
3. **Therapy**
   a. **Analgesics.** Clearly, the control of pain can be sufficient to return the MAP to a more acceptable level.
   b. **Vasodilators.** Although many vasodilator drugs are available, the patient's comorbidities and the urgency of the situation often guide the choice. Regardless, a target MAP should be chosen concomitantly with the start of therapy. In the absence of pre-existing HTN, MAP, measured at the level of the external auditory meatus, can be decreased 20% from the baseline without undue risk.
      1. Rapid control can require the use of vasodilators such as nicardipine, clevidipine, SNP, NTG, or labetalol.
      2. Drugs that have slower onset but fewer drawbacks, such as beta-blocking drugs and hydralazine, can adequately treat less urgent situations.
4. **Precautions**
   a. **Hypovolemia.** Even small doses of vasodilators can cause dramatic hypotension in the presence of hypovolemia.
   b. **Decreased intracranial compliance.** Vasodilators, especially SNP and NTG, have the potential for cerebral vascular relaxation with a resultant increase in CBV. If intracranial compliance is decreased, increases in CBV might raise ICP.

D. **Lowering HR** can be indicated in a number of clinical settings.

1. **Reduced myocardial oxygen consumption.** Tachycardia can increase myocardial oxygen demand and induce ischemia in susceptible patients.
2. **Atrial fibrillation** with a rapid ventricular response can compromise the heart's ability to deliver an adequate CO.
3. **Hypertension.** Although slowing the HR is not usually sufficient to decrease MAP by a significant degree, a smaller dose of an antihypertensive drug is subsequently required owing to the abatement of the reflex tachycardia.
4. **Therapy.** Adenosine and beta-blocking drugs, such as esmolol, metoprolol, propranolol, and labetalol, are often used as first-line drugs owing to their rapid onset and relative safety. Calcium-entry blocking drugs such as verapamil and diltiazem are also used to control ventricular rate, particularly supraventricular tachycardias.
5. **Precautions**
   a. The drugs to decrease HR have negative inotropic and vasodilatory properties that can result in both low CO and hypotension. Particular

caution is necessary when beta-blocking and calcium-entry blocking drugs are combined.

b. Some patients who have bronchospastic disease experience exacerbation of their symptoms when they receive beta-blocking drugs.

## V. MANAGEMENT OF CARDIOVASCULAR COMPLICATIONS OF NEUROLOGIC DISORDERS

### A. Cerebral vasospasm

1. **Pathophysiology.** Vasospasm is a potentially devastating complication of SAH and acute TBI. If extensive, vasospasm can decrease CBF to ischemic levels, causing permanent neurologic deficits or death. Although transcranial Doppler (TCD) is proving to be a useful diagnostic modality, vasospasm is traditionally diagnosed by angiography in which beaded narrowing of the cerebral arteries confirms the diagnosis.
2. **Monitoring.** Angiography is the gold standard for the diagnosis of vasospasm but is impractical for monitoring. TCD has the advantage of being portable, non-invasive, and amenable to regular or even continuous monitoring. TCD detects vasospasm by measuring the velocity of blood flow in a cerebral artery. Because vasospasm narrows a vessel, the velocity of blood traveling through the constriction increases.
3. **Prevention.** A statistical decrease in permanent neurologic deficits in patients at risk has been demonstrated when a cerebral-selective calcium-entry blocking drug is used. This improvement is not associated with an increase in the diameter of the affected vessels.
4. **Triple-H therapy: hypervolemia, hypertension, hemodilution**
   a. **Rationale.** Triple-H therapy seeks to increase blood flow through the narrowed arteries by decreasing the viscosity (hemodilution), increasing the driving pressure (HTN), and expanding the blood volume (hypervolemia). Hyperdynamism is a fourth "H" element in vasospasm prevention that is commonly instituted.
   b. **Invasive monitoring** is usually needed, because the knowledge of intravascular volume and the CO/CI is of central importance. Monitoring CO/CI can be accomplished with PA catheterization, pulse contour analysis technology via arterial catheterization, and TEE. A more rudimentary approach using the Fick principle can prove sufficient and can easily be determined by measuring the arterial and venous oxygen contents:

      $$CO = (O_2 \text{ consumption/arterial} - \text{venous } O_2 \text{ gradient}) \times 100,$$

      where $O_2$ consumption can be assumed to range from 125 mL/minute/$m^2$ at rest to near 200 mL/minute/$m^2$ in a critically ill patient.
   c. **Fluids.** Hypervolemia is accomplished by infusion of isotonic fluids or colloids.
   d. **Vasoactive drugs.** The two hemodynamic goals are to increase MAP and CO. A selective approach is achieved through the use of drugs such as norepinephrine to increase SVR and drugs such as dobutamine to increase contractility.
   e. **Precautions.** Pulmonary edema is the primary concern with Triple-H therapy, even with its conscientious management. Treatment goals must be adjusted after pulmonary edema has been detected.
5. **Cerebral salt wasting** frequently accompanies SAH and other intracranial pathology. Urinary sodium is elevated in the presence of hyponatremia, an electrolyte presentation seen also with the syndrome of inappropriate antidiuretic hormone (SIADH) secretion. With cerebral salt wasting,

unlike SIADH, depletion of intravascular volume develops, which is undesirable when cerebral vasospasm is a risk.

**B. Autonomic hypotension (neurogenic shock)**

1. **Pathophysiology.** Hypotension can occur after spinal cord injury (SCI) at a cervical or high thoracic level. Interruption of the sympathetic nervous system causes vasodilatation from the loss of sympathetic vascular tone and bradycardia because of the involvement of the cardio-accelerator nerves. Young individuals who have a high resting vagal tone, normally balanced by sympathetic activity, could experience bradycardia to the point of asystole.
2. **Treatment.** Care should be taken in managing low BP in patients after they suffer SCI because they lack intact compensatory mechanisms. They tend to tolerate lower BPs without adverse sequelae as compared to neurologically intact patients.
   a. Hypotension without bradycardia can be treated with careful administration of fluids if adequacy of end-organ perfusion is a concern. UOP in the acute phase of SCI is typically low regardless of the CI or intravascular volume status.
   b. If a vasoactive drug is administered, the clinician should remember that denervation hypersensitivity could result in a much larger response than expected.
   c. Bradycardia can be significant enough to require atropine for the first 72 hours after SCI. Bradycardic episodes rarely persist to the point at which a pacemaker is needed.

**C. Autonomic hyper-reflexia: autonomic instability after SCI**

1. **Pathophysiology.** Autonomic hyper-reflexia is an acute syndrome that can occur in up to 85% to 90% of patients who have a high thoracic spinal cord lesion at T6 or above as early as 2 to 3 weeks after the injury. It presents as a lack of autonomic continuity in that an afferent sensory impulse ascends via the spinothalamic tracts/dorsal columns and stimulates the sympathetic ganglia in the thoracolumbar region but stops at the level of the lesion. The normal central inhibitory reflex is not initiated resulting in sympathetic hyperactivity and vasoconstriction below the lesion. The aortic arch and carotid sinus are stimulated causing reflex bradycardia and vasodilatation above the lesion. Common aggravating stimuli include: visceral distention, cutaneous stimulation, and surgical stimulation of the extremities. Urogenital stimulation is the most common initiator of the hyper-reflexia.
2. **Treatment.** Prevention is key. Question the patient as to which stimuli initiate the dysreflexia and avoid them, if possible. Bladder distention is the most common culprit. If a tourniquet is being used, deflation may be required. Sustained hypertensive episodes can be treated with drugs such as labetalol, hydralazine, and nicardipine.

**D. Carotid endarterectomy: postoperative hypotension**

1. **Pathophysiology.** Patients who have atherosclerosis sufficient to require carotid endarterectomy often have cardiovascular disease as well and are prone to instability of BP, HR, and rhythm in the perioperative period. Bradycardia and dysrhythmias occur because of abnormal carotid sinus baroreceptor responses.
2. **Treatment** includes the administration of fluids to correct pre-existing intravascular volume deficits, atropine if carotid sinus stimulation causes bradycardia, and either phenylephrine or dopamine to prevent end-organ compromise if hypotension persists.

**E. Carotid endarterectomy: postoperative hypertension**

1. **Pathophysiology.** Manipulation of the carotid sinus can contribute to postoperative HTN, which is associated with a higher risk of postoperative bleeding, stroke, and death.
2. **Treatment.** Hypertension can be effectively managed by the intravenous administration of labetalol, nicardipine, hydralazine, or, if severe, SNP.

**F. Acute TBI with hypotension**

1. **Pathophysiology.** Hypotension in the patient who survives transport to the hospital after suffering a TBI is most likely the result of blood loss. TBI sufficient to damage the brain stem vasomotor center is almost always fatal.
2. **Treatment** needs to be prompt because the injured brain is particularly vulnerable to low perfusion pressure that may already be compromised by elevated ICP.
   a. As with any trauma victim suspected of having hypovolemia, intravascular volume needs to be expanded.
   b. Positive inotropic drugs or vasoconstrictors can be used for rapid restoration of the MAP to an acceptable level until intravascular volume is expanded.

**G. Acute TBI with hypertension**

1. **Pathophysiology**
   a. Patients are commonly hypertensive after TBI because they secrete excessive catecholamines. This secretion begins within the first 10 days of the traumatic event and can continue for as long as 3 months. Hypertension can be accompanied by tachycardia, tachypnea, restlessness, and diaphoresis limited to the upper body, probably from disinhibition of central sympathetic reflexes.
   b. **Cushing reflex.** MAP could also be elevated as a protective mechanism to maintain CPP if ICP is approaching systemic values. Original descriptions of the Cushing reflex in animals involved bradycardia, whereas tachycardia occurs more commonly in humans.
2. **Treatment.** Hypertension after TBI is typically associated with elevated ICP, and there are two possible etiologies. First, with impaired autoregulation, arterial HTN increases CBF and therefore ICP. Second, elevated ICP induces arterial HTN via the Cushing reflex. Treatment must be cautious with concurrent monitoring of the effect on ICP.
   a. **Sympathetic overactivity.** Hypertension from the post-TBI syndrome is responsive to beta-blocking drugs, but large doses can be necessary to compete with the high levels of endogenous catecholamines. Beta-blocking drugs also have the benefit of improving intracranial compliance and do not cause cerebral vascular relaxation. If beta blockade does not decrease the MAP adequately, then SNP, NTG, or nicardipine can be considered. SNP and NTG can cause cerebral vascular relaxation, increasing CBV and ICP, an effect that can be attenuated by slow infusion of the drug.
   b. **Cushing reflex.** If HTN is thought to occur as a result of the Cushing reflex, attention should be directed to decreasing ICP, because decreasing MAP alone can result in a critical reduction in CPP.

**H. Postoperative hypertension**

1. **Pathophysiology.** Patients who have no prior history of HTN can become hypertensive after a craniotomy. In the absence of intracranial HTN, postcraniotomy HTN should be treated to reduce the risk of cerebral swelling and bleeding in the operative site. However, if ICP is elevated, the treatment of HTN can decrease CPP to ischemic levels.

2. **Treatment.** Hypertension after craniotomy can be treated with analgesics and either labetalol or nicardipine with predictable results. If intracranial HTN is suspected, management should follow that outlined above for TBI.

I. **Intraoperative aneurysmal rupture**

1. **Pathophysiology.** Intraoperative aneurysmal rupture can be devastating and dramatically increases the risk of perioperative morbidity and mortality. Its causes vary, including perturbations in the transmural pressure of the aneurysm, removal of tamponade by surrounding tissues, and operative technique.
2. **Treatment.**
   a. **Surgical**. Presently surgeons can employ various techniques for hemostasis at the time of rupture, including temporary feeding artery occlusion, commonly with EEG burst suppression and induced HTN; double suction technique with concurrent dissection of the aneurysm neck, which can lead to significant blood loss; application of a clip to the dome of the aneurysm; endovascular balloon occlusion with suction decompression; and extracranial carotid occlusion.
   b. **Lowering MAP** as described in the previous section on goal-directed pharmacologic intervention.
   c. **Adenosine.** There has been increasing interest in the use of adenosine-induced hypotension and/or cardiac standstill to facilitate aneurysm clipping after premature rupture. Administration of escalating divided doses of adenosine can be used in coordination with the surgeon to provide a relatively bloodless field for short durations, providing enough time to identify the source of bleeding, to complete the microscopic dissection, or for placement of a temporary and/or permanent clip. Adenosine is also being considered as an adjunct before clipping, even in the absence of premature rupture, as it can facilitate a smooth reduction in aneurysm wall turgor without the mechanical stresses of temporary clipping.

      **Precautions.** Pre-emptive application of external or temporary internal pacing devices is prudent while administering adenosine. Avoid use in patients who have severe reactive airway disease, sick sinus syndrome, severe coronary artery disease, and atrioventricular (AV) conduction blocks. Use caution with concomitant administration of drugs such as methylxanthines, calcium-channel antagonists, digoxin, and carbamazepine; these medications can significantly alter the efficacy of adenosine.

## *Suggested Readings*

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## *Online Resources*

www.pacep.org – hemodynamic monitoring tutorial
www.cvphysiology.com – cardiovascular physiology review website
www.cvpharmacology.com – cardiovascular pharmacology review website
http://www.americanheart.org/presenter.jhtml?identifier = 9181 – the American Heart Association's professional corner with up-to-date guidelines

# 24 Fluid and Electrolyte Management

**Concezione Tommasino, Valentina Picozzi, and Federico Bilotta**

## Illustrative Clinical Case

A 32-year-old man sustained a closed head injury in a motor vehicle accident, and was operated on because of a large subdural hematoma. In the postoperative period, his Glasgow Coma Scale (GCS) score was 14 to 15. Two days later on postoperative day 2 (POD 2), he was noted to have a decreased serum sodium (Na) concentration of 131 mEq/L. Vital signs were normal: BP 130/65 mm Hg, pulse 81 bpm, RR 14, oxygen saturation ($SpO_2$) 99% in air. On POD 4, serum Na concentration decreased to 119 mEq/L and chloride (Cl) concentration to 89 mEq/L. The urine and serum osmolarity showed that urine was hypertonic to the serum. Urinary Na excretion was 78 mEq/L, serum osmolarity 257 mOsm/L, and urine osmolarity 579 mOsm/L. He remained conscious and alert without neurologic deficits.

An appropriate fluid regimen must be selected on the basis of this patient's clinical history.

*Issues to consider:*

1. Water and electrolyte disturbances in patients who have injured brain.
2. Which water and electrolyte disturbances are characterized by serum hyponatremia?
3. How to distinguish between the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting (CSW) syndrome.
4. When treating hyponatremia, what is the best fluid treatment?

## Chapter Highlights

- Intravascular volume and hypovolemia
- Management of cerebral perfusion pressure
- Fluid management and the injured brain
- Intravenous fluid administration
- Implications for patients who have intracranial pathology
- Water and electrolyte disturbances

### INTRODUCTION

Perioperative fluid management in neurosurgical patients is designed to avoid dehydration, maintain an effective circulating blood volume, preserve cerebral perfusion pressure (CPP = mean arterial pressure [MAP] – intracranial pressure [ICP]), and minimize cerebral edema. Cerebral perfusion and hemodynamic stability are essential to the maintenance of neuronal homeostasis. However, there are few useful clinical data to guide the optimal fluid choice for the prevention of secondary brain injury after a neurologic insult.

Cerebral edema, a final common pathway of numerous neurologic diseases, may rapidly become life threatening. Consequently, restrictive fluid management had been the treatment of choice in patients who had brain pathology for fear that

fluid administration would exacerbate cerebral edema and raise ICP. Large volumes of crystalloid used for optimizing cerebral hemodynamics may result in fluid overload and acute cardiac failure and pulmonary edema. Fluid restriction, if pursued to the point of hypovolemia, may result in hypotension that can increase ICP and reduce CPP with devastating consequences.

## I. INTRAVASCULAR VOLUME AND HYPOVOLEMIA

### A. Hypovolemia and hypotension

In neurosurgical patients, and very often in the postoperative period, intravascular volume can be depleted. One of the most common causes of this is the use of diuretics. There is a substantial body of evidence to the effect that systemic hypotension, independently, can increase the morbidity and mortality in patients after traumatic brain injury (TBI). The randomized controlled trial by Clifton on therapeutic hypothermia after TBI showed that low arterial pressure (MAP < 70 mm Hg) and fluid deficit > 600 mL were associated with poor outcome.

Hypotension must therefore be avoided and rapidly corrected, but fluid should always be administered based on clinical assessment.

1. Look at the skin turgor. Is the tongue dry and furry? Is the patient peripherally shut down with cold and clammy skin and prolonged capillary refill time? Is the patient sweating and tachycardic? Usually, a persistently low urine output (< 0.5 mL/kg/hour) may be an indication of inadequate fluid replacement. This requires prompt treatment to ensure sufficient perfusion of all tissues.
2. When diuretics and mannitol are given, urinary output can be misleading, and thirst, an important early warning sign of volume depletion, cannot be evaluated if the patient is drowsy or sedated. The patient can be asymptomatic until the circulating blood volume has decreased by at least 10%. Once the intravascular volume is critically reduced, the perfusion of distal tissues becomes compromised. Hypoperfusion of the brain causes non-specific neurologic symptoms such as confusion and odd behavior.
   a. Confusion is not always a consequence of the neurosurgical procedure.
   b. In taking care of neurosurgical patients, think always of the brain *and* the intravascular volume.
   c. Keep circulating volume as normal as possible and avoid iatrogenic volume depletion.

B. Basic **fluid and electrolyte requirements** should always be considered in the postoperative period. Table 24.1 indicates fluid input and output over 24 hours in a healthy 70 kg adult. To calculate volume replacement, the patient's weight and the suspected blood loss (clinical estimation, see Table 24.2) are needed.

1. Requirements for maintenance fluid are 1.5 to 2 mL/kg/hour (2.5 to 3.5 L in 24 hours for a 70 kg adult). These are independent of the type of surgical procedure. Daily maintenance of sodium (Na) is 1 to 2 mmol/kg/day and potassium (K), 1 mmol/kg/day.
2. For example, consider a 70-kg patient who has lost an estimated 10% of his circulating blood volume. Because 60% of body weight is water, and total water content is around 42 L (70 × 0.6), a 10% volume loss equates to 4.2 L (42 × 0.1), which needs replacement *in addition to* maintenance requirements.
3. In clinical practice, the formula often used to estimate the quantity of fluid needed for replacement is: **Replacement = Resuscitation + Maintenance + Losses**

TABLE 24.1 Normal Fluid Input and Output Over 24 hours in a Healthy 70 kg Adult

| | |
|---|---|
| **In** | |
| Food | 1,000 mL |
| Drink | 1,200 mL |
| Metabolic oxidation | 1,300 mL |
| **Out** | |
| Urine | 1,500 mL |
| Feces | 100 mL |
| Insensible (respiration and sweating) | 900 mL |
| **Total** | |
| In = out | 2,500 mL |

4. A **fluid challenge** (an intravenous bolus of a fixed volume of crystalloid or colloid) can be used both to *assess and treat* volume depletion, particularly at the bedside. Monitoring the central venous pressure (CVP) during this test is often helpful for guiding further fluid administration. For example, if the CVP rises and then falls after a fluid challenge, more fluid is needed.
5. To prescribe rational fluid replacement, it is important to identify which compartment is depleted: specific losses should be replaced with the appropriate fluid.

**C. Blood loss**

1. If blood has been lost and **crystalloid is used for replacement**, the replacement volume is three times that of the estimated blood loss as only a third of that volume remains in the intravascular compartment. The replacement volume is less if colloid is administered. Table 24.3 illustrates the volume effect of different fluids that is defined as the volume of the infused replacement fluid that *remains inside* the vascular space.
2. If a considerable amount of blood has been lost, **replacement with blood** may be appropriate, depending on age, hemodynamic state, and previous

TABLE 24.2 Clinical Assessment of Hypovolemia in a 70 kg Adult Patient

| **Blood Loss (% of Total Volume)** | **500–750 (10–15)** | **750–1,000 (15–20)** | **1,500–2,000 (30–40)** | **≥ 2,000 (≥ 40)** |
|---|---|---|---|---|
| Heart rate (beats/min) | < 100 | > 100 | > 120 | ≥ 140 |
| Blood pressure | Normal | Normal | Reduced | Reduced |
| Pulse pressure | Normal | Reduced | Reduced | Reduced |
| Capillary refill time | Normal (< 2 s) | Prolonged | Prolonged | Prolonged |
| Respiratory rate (breaths/min) | 14–20 | 20–30 | 30–40 | ≥ 35 |
| Urine output (mL/h) | > 30 | 20–30 | 5–15 | Negligible |

s, seconds; h, hour.

TABLE 24.3 Intravascular Volume Effect After Infusion of Replacement Fluid

| Fluid Infused | Intravascular Volume Increase |
|---|---|
| 1 L isotonic crystalloid | ≈250 mL |
| 1 L 5% albumin | ≈500 mL |
| 1 L hetastarch | ≈750 mL |

Volume effect—That amount of infused solution that remains in the intravascular compartment and increases intravascular volume.

illnesses, since acute anemia, both at the time of hospital admission and subsequently, is significantly associated with poorer clinical outcome. However, increased organ dysfunction and poorer patient outcome are associated with "liberal" red blood cell (RBC) transfusion strategies, while a "restrictive" transfusion strategy to maintain the hemoglobin at 7 to 9 g/dL may reduce morbidity and mortality in critically ill patients.

Blood transfusion has also been questioned in the neurosurgical population. While a higher hemoglobin level seems to be associated with improved intermediate outcome after subarachnoid hemorrhage (SAH) and TBI, RBC transfusion during or after surgery in SAH patients has been correlated with a greater risk of vasospasm as well as poorer outcome.

**a.** Physicians should be cautioned against using the "10/30" hemoglobin and hematocrit trigger for administering RBC transfusions *in all patients*, and may need to be more tolerant of normovolemic anemia.

**b.** Unless inadequate tissue oxygenation is part of the patient's underlying disease, a more conservative RBC transfusion strategy may be reasonable for many patients after SAH.

## II. MANAGEMENT OF CEREBRAL PERFUSION PRESSURE

The **clinical use of CPP**, the difference between MAP and ICP, is based on the theoretical consideration that optimal cerebral blood flow (CBF) is necessary to meet the metabolic needs of the injured brain. When cerebral autoregulation is impaired and CPP is below the lower limit of autoregulation, CBF is dependent on CPP. Controversy exists, however, as to the optimal CPP, especially in head trauma patients. Table 24.4 summarizes the main differences among the various approaches to the management of CPP.

**A. CPP-targeted therapy.** The **Rosner approach** is based on the physiologic concept, termed the **vasodilatory cascade**, in which a reduction in CPP from a decrease in MAP and/or an increase in ICP stimulates the cerebral vessels to dilate in order to maintain CBF. This vasodilatation further reduces CPP by increasing cerebral blood volume (CBV) and ICP. Raising the MAP under this circumstance has been reported to break the cycle and reduce the ICP. CPP is maintained at 70 to 80 mm Hg by the use of both systemic vasopressors and fluid therapy with hyperosmolar solutions including mannitol and hypertonic saline. This approach has resulted in outcomes that were superior to an unadjusted control group from the Traumatic Coma Data Bank for which ICP management was the primary therapeutic goal. CPP-targeted therapy is now included as a treatment option in the Head Injury Guidelines.

TABLE 24.4 Strategies for Management of Cerebral Perfusion Pressure: Therapeutic Goals

| Traditional | Rosner | Lund | Robertson |
|---|---|---|---|
| ICP-directed therapy | CPP-targeted therapy | Brain volume regulation | Individualized therapy |
| CPP not considered | CPP > 70–80 mm Hg (above lower limit of autoregulation) | CPP > 50–60 mm Hg (whatever provides adequate perfusion) | (a) hypoperfusion/ ischemia: increase CPP to improve CBF |
| ICP < 20 mm Hg, BP normal | | | (b) adequate perfusion: maintain normal CPP |

BP, blood pressure; CBF, cerebral blood flow; CPP, cerebral perfusion pressure (mean arterial pressure [MAP] – intracranial pressure [ICP]).
Modified from: Robertson C. Management of cerebral perfusion pressure after traumatic brain injury. *Anesthesiology*. 2001;95:1515–1517.

The CPP threshold of 70 mm Hg recommended for intervention has been challenged, however, as there is evidence that elevating the CPP above this threshold by the use of vasopressors and volume expansion may not be beneficial and may actually have detrimental cerebral and systemic effects. CBF-targeted strategy aimed at maintaining the CPP > 70 mm Hg, as compared to conventional ICP-targeted strategy that keeps the CPP > 50 mm Hg, does decrease the time that CPP is < 60 mm Hg and reduces the incidence of secondary cerebral ischemic events. However, this treatment strategy increased the incidence of acute respiratory distress syndrome fivefold and did not improve long-term neurologic outcome.

B. **Brain volume regulation.** The **Lund approach** advocates preserving normal colloid oncotic pressure (COP) and **reducing capillary hydrostatic pressure** through the use of hypotension, venodilatation, and manipulation of the plasma osmolarity. This is accomplished by the infusion of albumin and packed red blood cells and the reduction of MAP with drugs such as metoprolol and clonidine. CBV is decreased by vasoconstricting precapillary resistance vessels with low-dose thiopental or dihydroergotamine. Treatments that increase the transcapillary filtration of fluid are avoided including cerebrospinal fluid (CSF) drainage, high-dose barbiturates, osmotic diuretics, and maintenance of a high CPP. Decompressive craniectomy, which can also increase edema formation, is reserved as a last resort. Proponents of the Lund approach argue that a high CPP increases edema formation and aggravates intracranial hypertension and emphasize instead the reduction of capillary hydrostatic pressure to minimize brain edema.

C. **Individualized therapy.** Because of the heterogeneous nature of brain injury, individualized therapy has been advocated by **Robertson** as the appropriate treatment strategy, matching fluid therapy with the immediate pathophysiologic issue at hand. The pathophysiology of brain damage evolves over time so that treatment deemed appropriate in the first few hours after injury may not be necessarily optimal 2 or 3 days later. A CPP of 60 mm Hg has been shown to provide adequate perfusion for most TBI patients, and higher CPP levels should probably be reserved for those

patients who demonstrate a specific indication for induced hypertension, such as regional or global ischemia.

1. The beneficial effect from the CBF-targeted management in reducing secondary ischemic insult seems to be offset by complications associated with maintaining BP at an increased level.
2. A CPP of 60 mm Hg provides adequate perfusion for most brain injured patients.
3. Higher CPP levels should probably be reserved for those patients who demonstrate a specific reason for induced hypertension such as focal or global ischemia.

## III. FLUID MANAGEMENT AND THE INJURED BRAIN

Few substantial data exist in humans concerning the impact of fluids on the brain that can guide rational fluid management in neurosurgical patients. In addition, the optimal choice of fluid for prevention of secondary brain damage after neurologic insult is unknown. This lack of data makes it difficult to select a best-practice fluid regimen. Fluid selection is most likely institution specific and reflects the personal experience of the physicians. It is possible, however, to examine those factors that influence water movement into the brain and to make some reasonable recommendations.

### A. Physiologic principles

1. **Osmotic pressure** is the hydrostatic force that acts to equalize the concentration of *water* on both sides of a membrane impermeable to substances dissolved in that water. Water will move along its concentration gradient until the osmolalities on both sides of the membrane equalize. Each difference of 1 milliosmole per kilogram of solvent (mOsm/kg) across a semi-permeable membrane generates an osmotic pressure of approximately 19.3 mm Hg. If two solutions of equal concentration are placed on either side of a membrane, there is no driving force.
2. **Osmolarity and osmolality.** *Osmolarity* quantifies the number of particles in a solution, expressed as milliosmoles per liter of solution (mOsm/L). This value is *calculated* by adding the milliequivalent (mEq) concentrations of the various ions in the solution (Table 24.5). *Osmolality*

**TABLE 24.5** How to Calculate the Osmolarities of Crystalloid Solutions

(a) **0.9% NaCl** = 9 g of NaCl (MW 58.43 g/mol) in 1,000 mL of solution
Calculate the molarity: divide 9 g/L by 58.43 g/mol = 0.154 mol/L or 154 mmol/L
Calculate osmolarity: In water NaCl dissociates in Na and Cl ions = multiply 154 ×2 = 308 mOsm/L

(b) **7.5% NaCl** = 75 g of NaCl in 1,000 mL of solution
Calculate the molarity: divide 75 g/L by 58.43 g/mol = 1.283 mol/L or 1,283 mmol/L
Calculate osmolarity: multiply 1,283 × 2 = 2,566 mOsm/L

(c) **20% Mannitol** = 20 g of mannitol (MW 182 g/mol) in 1,000 mL of solution
Calculate the molarity: divide 20 g/L by 182 g/mol = 0.1098 mol/L or 1,098 mmol/L
Calculate the osmolarity: 1,098 mOsm/L

NaCl, sodium chloride; MW, molecular weight.

describes the molar number of osmotically active particles per kilogram of solvent (mOsm/kg). This value is *measured* by determining either the freezing point or the vapor pressure of the solution. For most dilute salt solutions, the osmolality is equal to or slightly less than the osmolarity. Note that the osmotic activity of a solution demands that particles be "independent." As NaCl dissociates into Na and Cl, two osmotically active particles are created. If electrostatic forces act to prevent dissociation of the two charged particles, then osmolality will be reduced.

3. **Colloid oncotic pressure** (COP) or oncotic pressure is the osmotic pressure generated by large molecules such as albumin, hydroxyethyl starch, and dextran. In biologic systems, where vascular membranes are often permeable to small ions but not to large molecules, proteins are the only osmotically active particles. Normal COP is approximately 20 mm Hg (or about 1 mOsm/L).
4. **Fluid movement between capillaries and tissues**
   a. The major **factors that control fluid movement** between the intravascular and extravascular spaces are the transcapillary hydrostatic gradient, the osmotic and oncotic gradients, and the relative permeability of the capillary membranes that separate these spaces. The **Starling equation** describes the forces driving water across the capillary endothelium:

$$\text{FM} = k\,(P_c + \pi_i - P_i - \pi_c)$$

   where FM is fluid movement, $k$ is the filtration coefficient of the capillary wall (i.e., how leaky it is), $P_c$ is the hydrostatic pressure in the capillaries, $P_i$ is the hydrostatic pressure (usually negative) in the interstitial (extravascular) space, and $\pi_i$ and $\pi_c$ are interstitial and capillary oncotic–osmotic pressures, respectively.
   b. **Fluid movement** is thus proportional to the hydrostatic pressure gradient minus the osmotic pressure gradient across a capillary wall. The **magnitude of the osmotic gradient** will depend on the relative permeability of the vessels to solutes. In the **periphery** (muscle, bowel, lung, etc.), the capillary endothelium is freely permeable to small molecules and ions but not to large molecules such as plasma proteins and synthetic colloids. As a result, $\pi$ (osmotic pressure) is defined only by large molecules and the Starling equation can be simplified by saying that (Figs. 24.1 and 24.2):

      Fluid will move into a tissue whenever the hydrostatic gradient increases (either intravascular pressure rises or interstitial pressure falls) or the osmotic gradient decreases.
   c. When the intravascular **COP** is higher than in the interstitium, water is drawn back into the vascular space. If the COP is reduced, such as by the infusion of large volumes of iso-osmolar crystalloid, fluid will begin to accumulate in the interstitium. This is familiar to all anesthesiologists who have seen marked peripheral edema in patients given many liters of crystalloid during surgery or resuscitation.

      By contrast, in the **brain**, where the blood–brain barrier (BBB) is normally impermeable to large molecules (plasma proteins and synthetic colloids) and relatively impermeable to many small polar solutes (Na, K, Cl), osmotic pressure is determined by the *total osmotic gradient*, to which COP contributes only a tiny fraction (COP $\approx$ 20 mm Hg $\approx$ 1 mOsm/L).

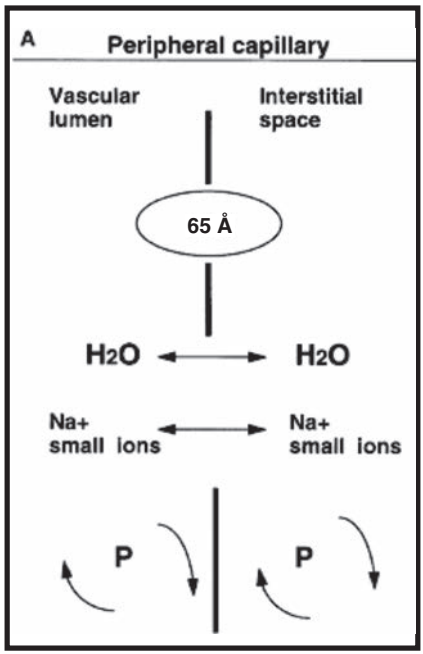


**FIGURE 24.1** Schematic diagram of a peripheral capillary. The capillary endothelium is freely permeable to both water ($H_2O$) and small ions, but not too large molecules, such as proteins or synthetic colloids (P). Å, Angstrom.

Administration of large volumes of iso-osmolar crystalloid will dilute the plasma protein concentration and cause peripheral edema, but will not generally increase brain water content or ICP.

**B. Hemoglobin, hematocrit, and hemodilution**

One common accompaniment of fluid infusion is a reduction in hemoglobin (Hb) and hematocrit (Hct). The **optimal Hb level** for patients who have cerebrovascular disease is unknown, although hemodilution reduces blood viscosity and is typically accompanied by an increase in CBF. In normal brain, the increase in CBF produced by hemodilution is an active compensatory response to the decrease in arterial oxygen content, identical to that seen with hypoxia. It should be stressed that, in the face of brain injury, the normal CBF responses to hypoxia and hemodilution are attenuated, and both changes may contribute to secondary damage. An Hct of 30% to 33% offers the optimal combination of viscosity and oxygen-carrying capacity and may improve neurologic outcome. Marked hemodilution (Hct < 30%) causes a pronounced reduction in oxygen delivering capacity and can exacerbate brain injury.

## IV. INTRAVENOUS FLUID ADMINISTRATION

**A. Crystalloid** is the term commonly applied to solutions that contain water and low molecular weight (MW) solutes that may be charged (e.g., Na, Cl,

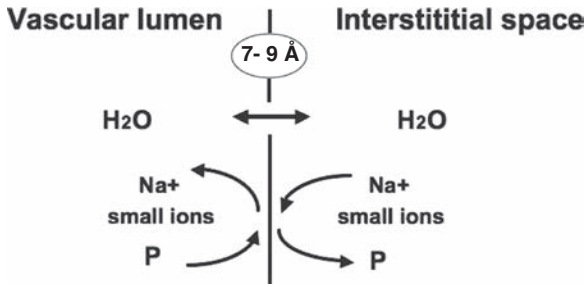


**FIGURE 24.2** Schematic diagram of a cerebral capillary. The blood–brain barrier is impermeable to large molecules (P = plasma proteins and synthetic colloids) and to many polar solutes (Na and small ions). Å, Angstrom.

Mg, K) or uncharged (e.g., glucose or mannitol). Crystalloids are inexpensive, easy to store with a long shelf life, readily available in a variety of formulations (Table 24.6), effective for use as replacement or maintenance fluid, require no special compatibility testing, and have a very low incidence of adverse reactions and no religious objections to their use. Crystalloid solutions have a COP of zero and may be hypo-osmolar, iso-osmolar, or hyperosmolar. They can be made hyperosmolar by the inclusion of electrolytes (e.g., Na and Cl, as in hypertonic saline [HS]) or low MW solutes, such as mannitol (MW 182) or glucose (MW 180).

1. **Hypo-osmolar crystalloids**, when given in large amounts, reduce plasma osmolality, drive water across the BBB, and increase cerebral water content and ICP. Five percent dextrose (D5W) is essentially water (as the sugar is metabolized very quickly), provides "free water" that disperses throughout the intracellular and extracellular compartments, and has little use as a resuscitative fluid. As a consequence, hypo-osmolar crystalloids (0.45% normal saline [NS] or D5W) should be avoided in neurosurgical patients.
2. **Iso-osmolar crystalloids** such as NS and Plasmalyte have an osmolarity ≈ 300 mOsm/L. They neither change plasma osmolality nor increase brain water content. Caution is indicated, however, concerning lactated Ringer's solution (Table 24.6). Its "calculated" osmolarity is ≈ 254 mOsmol/L, which is hypo-osmolar to plasma so that administration of large volumes can reduce plasma osmolality and increase brain water content and ICP. Lactated Ringer's solution and Plasmalyte contain bicarbonate precursors. These anions (e.g., lactate) are the conjugate base to the corresponding acid (e.g., lactic acid) and do not contribute to the development of acidosis as they are administered with Na rather than hydrogen (H) as the cation. The metabolism of lactate in the liver results in the production of an equivalent amount of bicarbonate.
3. **Hyperosmolar crystalloids: Mannitol and hypertonic saline**
   In the presence of a normal BBB, hyperosmolar crystalloid solutions increase the osmotic gradient between the intravascular and cellular/interstitial compartments, leading to a reduction in brain water content, brain volume, and ICP.
   a. **Mannitol** is the primary drug for therapeutic brain dehydration and is effective for control of increased ICP at doses of 0.25 to 1 g/kg. The smallest possible dose is infused over 10 to 15 minutes.

TABLE 24.6 Composition of Commonly Used Intravenous Fluids: Crystalloids

| Fluids | Osmolarity[a] mOsm/L | Na | Cl | K | Ca | Mg | Lactate | Dextrose |
|---|---|---|---|---|---|---|---|---|
| | | mEq/L | | | | | g/L | |
| 5% dextrose in $H_2O$ (D5W) | 278 | | | | | | | 50 |
| 5% dextrose in 0.45% NaCl | 405 | 77 | 77 | | | | | 50 |
| 5% dextrose in 0.9% NaCl | 561 | 154 | 154 | | | | | 50 |
| 5% dextrose in Ringer's solution | 525 | 130 | 109 | 4 | 3 | | | 50 |
| Ringer's solution | 309 | 147 | 156 | 4 | 4–4.5 | | | |
| Lactated Ringer's solution | 275 | 130 | 109 | 4 | 3 | | 28 | |
| 5% Dextrose in Lactated Ringer's solution | 525 | 130 | 109 | 4 | 3 | | 28 | 50 |
| Plasmalyte[b] | 298 | 140 | 98 | 5 | | 3 | | |
| 0.45% NaCl | 154 | 77 | 77 | | | | | |
| 0.9% NaCl | 308 | 154 | 154 | | | | | |
| 3% NaCl | 1,026 | 513 | 513 | | | | | |
| 5.0% NaCl | 1,710 | 855 | 855 | | | | | |
| 7.5% NaCl | 2,566 | 1,283 | 1,283 | | | | | |
| 10% NaCl | 3,424 | 1,712 | 1,712 | | | | | |
| 23.4% NaCl | 8,008 | 4,004 | 4,004 | | | | | |
| 29.2% NaCl | 10,000 | 5,000 | 5,000 | | | | | |
| 20% Mannitol | 1,098 | — | — | | | | | |

[a]Osmolarity = calculated value.
[b]Acetate 27 mEq/L and gluconate 23 mEq/L.
Na, sodium; Cl, chloride; K, potassium; Ca, calcium; Mg, magnesium; $H_2O$, water; D5W, 5% dextrose in water; NaCl, sodium chloride.

Mannitol is recommended as the osmotic drug of choice by both the Brain Trauma Foundation and the European Brain Injury Consortium.

We still do not know exactly how mannitol works. It may have two distinct effects on the brain: a **rheologic effect** (immediate plasma expanding effect that reduces the Hct and blood viscosity and increases CBF and cerebral oxygen delivery) and an **osmotic gradient effect** (established between plasma and cells). Mannitol has several limitations. Hyperosmolality is a common problem, and a serum osmolality > 320 mOsm/kg is associated with adverse renal and CNS effects. The osmotic diuresis may lead to hypotension, especially in hypovolemic patients, and, although controversial, the accumulation of mannitol in cerebral tissue may lead to a rebound phenomenon and increased ICP.

b. **Hypertonic saline (HS)** is a potentially more effective osmotic drug than mannitol because the permeability of the BBB to Na is low and the reflection coefficient (selectivity of the BBB to a particular substance) of NaCl is more than that of mannitol. Thus, HS may be better for reducing elevated ICP in patients after severe TBI. HS also has beneficial effects on vascular tone and may reduce CSF production. In animal models of TBI, HS improves systemic hemodynamics and CBF and may enhance cerebral microcirculation by reducing the adhesion of polymorphonuclear white blood cells and stimulating local release of nitric oxide.
   1. The use of HS for ICP control was discovered from studies on "small volume resuscitation." In patients who had TBI and hemorrhagic shock, HS showed the greatest benefit in terms of survival and hemodynamics. The finding that HS may benefit patients after TBI, while preserving or even improving hemodynamic parameters, stimulated further research in patients who had SAH and stroke.
   2. The principal disadvantage of HS is the danger of **hypernatremia**. During elective supratentorial procedures, equal volumes of 20% mannitol and 7.5% HS reduce brain bulk and CSF pressure to the same extent. However, serum Na increased during the administration of HS and peaked at over 150 mEq/L at the end of the infusion.
   3. HS infusion also bears the risk of **central pontine myelinolysis** in patients who have pre-existing chronic hyponatremia. This has never been reported in conditions of pre-existing normonatremia; magnetic resonance imaging and postmortem studies failed to demonstrate central pontine myelinolysis despite maximum sodium levels of 182 mEq/L. Other adverse effects include the potential for renal failure, rebound increase in ICP, coagulopathies, volume overload, and electrolyte abnormalities.
   4. In patients who have severe TBI and elevated ICP unresponsive to mannitol treatment, 7.5% HS administered as second-tier therapy is associated with a significant increase in brain oxygenation and improved cerebral and systemic hemodynamics. HS can thus reduce ICP while providing rapid volume resuscitation.

B. **Colloids** are solutions that contain high MW molecules and have an oncotic pressure similar to that of plasma (Table 24.7). Colloid solutions used for fluid therapy in clinical practice are divided into the naturally occurring human plasma derivatives (5% and 25% albumin solutions, plasma protein fraction, fresh frozen plasma, and immunoglobulin solutions) and the semi-synthetic colloids (gelatins, dextrans [MW 40 and 70], and hydroxyethyl starches [HES]).
   1. **Human albumin** is currently not considered a suitable choice for acute volume replacement in most countries, mainly for financial reasons. The use of human albumin versus crystalloid for fluid resuscitation did not improve outcome in 6,997 critically ill patients; moreover, in the subgroup of patients who had TBI, it actually increased mortality.
   2. HES products can be divided into three classes by their weight-averaged MW: high MW (450 to 480 kDa), medium MW (approximately 200 kDa), and low MW (70 to 130 kDa). Commercially available starches include 6% high-MW hetastarch in saline (Hespan®), 6% high-MW hetastarch in balanced electrolytes (Hextend®), medium-MW pentastarch in saline

TABLE 24.7 Composition of Commonly Used Intravenous Fluids: Colloids

| Fluid | Na (mEq/L) | Cl (mEq/L) | K (mEq/L) | Ca (mEq/L) | Osmolarity[a] mOsmol/L | Oncotic Pressure mm Hg |
|---|---|---|---|---|---|---|
| Fresh frozen plasma | 168 | 76 | 3.2 | 8.2 | ≈300 | 21 |
| 5% Albumin | | | | | 290 | 19 |
| Dextran (10%) 40 in 0.9% NaCl | 154 | 154 | | | ≈310 | 61 |
| Dextran (6%) 70 in 0.9% NaCl | 154 | 154 | | | ≈310 | 19 |
| Hetastarch (6%) in 0.9% NaCl | 154 | 154 | | | ≈310 | 31 |
| Hetastarch (10%) in 0.9% NaCl | 154 | 154 | | | ≈310 | 82 |

[a]Osmolarity = calculated value.
Na, sodium; Cl, chloride; K, potassium; Ca, calcium; NaCl, sodium chloride; mEq/L, milliequivalent per liter; mOsmol/L, milliosmole per liter; mm Hg, millimeters of mercury; NaCl, sodium chloride.

(Pentaspan®, EloHAES®, HAES-steril®), and low-MW tetrastarch in saline (Voluven®).

Dextran and hetastarch are dissolved in normal saline, so that the osmolarity of the solution is approximately 290 to 310 mOsm/L.

a. **Colloids remain in the intravascular space for longer** and are used for volume expansion and to sustain the BP without associated complications from fluid overload. During active bleeding, more than 90% of the infused iso-oncotic colloids remain in the intravascular compartment. This represents a **volume effect**, defined as that portion of an infused fluid bolus that does not shift into the extravascular space but remains inside the vasculature, of > 90%. The volume effect of colloids is context sensitive in that the effect depends on the "context," that is, the volume and hydration state of the patient. It is reasonable, therefore, to infuse colloids not *before* but *when* relative hypovolemia occurs.

b. The **side effects** of colloid administration range from pruritus to pleiotropic effects on the coagulation system including a reduction in coagulation factors and the number and function of platelets and an increase in fibrinolysis. These effects, however, are clearly related to cumulative dose, mean molecular size, and substitution degree of each preparation. The **substitution degree** refers to the modification of the original substance by the addition of hydroxyethyl groups. The greater the degree of substitution of a colloid, the greater the resistance to degradation and, consequently, the longer it remains in the intravascular space. Small doses of hetastarch of up to 1,000 mL/day do not affect coagulation, and it is recommended that this dose not be exceeded in TBI patients.

c. Intravascular volume replacement with the **third-generation HES** preparation (HES 130/0.4) has been shown to have almost no effect on coagulation and to reduce the inflammatory response in patients undergoing major surgery as compared with crystalloid-based volume

therapy. This has been attributed to an improvement in microcirculation with reduced endothelial activation and less endothelial damage.

**C. Fluid choice and volume expansion**

1. **Crystalloid versus colloid.** Ninety minutes after the administration of 1 L of fluid, crystalloid produces a volume expansion of approximately 0.25 L, whereas dextran and HES preparations produce a volume expansion of 0.7 to 0.8 L (Table 24.3). To obtain significant volume expansion with crystalloid requires infusion of large amounts of solution. This will cause a reduction of the intravascular COP, a significant expansion of the extracellular volume, and tissue edema in the periphery. Large-volume crystalloid resuscitation after major burns is associated with significant tissue edema when compared with colloid resuscitation. Theoretically, this will increase the diffusion distance within tissues with compression of small vessels and capillaries and a resultant compromise of end-organ perfusion and oxygenation. Intestinal edema has been associated with impaired gastrointestinal function, diminished tolerance for enteral nutrition, an increased potential for bacterial translocation, and the development of multiple organ dysfunction syndrome. Evidence suggests that colloid resuscitation may result in less edema and better recovery in the postoperative period.
2. **Hypertonic/hyperoncotic solutions.** Recently, attention has been directed to hypertonic/hyperoncotic solutions in the form of hypertonic hetastarch and dextran solutions. Because of the powerful hemodynamic properties of these fluids in hypovolemic shock, administration to patients after trauma and TBI might be particularly advantageous for the prevention of secondary ischemic brain damage. Small volumes of such solutions can restore normovolemia rapidly without increasing ICP. They have also been used successfully to treat intracranial hypertension in patients after TBI, SAH, and stroke.

## V. IMPLICATIONS FOR TREATMENT OF PATIENTS WITH INTRACRANIAL PATHOLOGY

**A.** Clinically acceptable fluid restriction has little effect on edema formation. The first human study on fluid therapy demonstrated that reducing the "standard" fluid maintenance in neurosurgical patients (2,000 mL/day of 0.45 NS in 5% dextrose) by 50% increases serum osmolality over about a week. Thus the "old concept" of the beneficial effects of fluid restriction was simply a consequence of an increased osmotic gradient over time. The available data indicate that volume replacement and expansion will have no effect on cerebral edema as long as normal serum osmolality is maintained and cerebral hydrostatic pressure is not markedly increased as from true volume overload and elevated right heart pressures. Whether this is achieved with crystalloid or colloid seems irrelevant although the **osmolarity of the selected fluid is crucial.**

Our recommendation is that serum osmolality be checked repeatedly, with the goal being either to maintain the serum osmolality in the normal range or to increase it slightly.

**B. *Calculated* versus *measured* serum osmolality**

1. The reference method to measure serum osmolality is the delta-cryoscopic technique. If the technology is not available, and/or it is not always possible to obtain an emergency measurement, **osmolality can be calculated** from the osmoles that are routinely measured, such as Na (mmol/L), urea (mg/dL), and glucose (mg/dL).

Calculated Serum Osmolality = 2(Na) + urea/2.8 + glucose/18

Be advised that calculation of osmolality introduces a bias, overestimating osmolality in the lower ranges and underestimating it in the higher ranges.

2. The administration of **fluids that reduce osmolality should be avoided**. Small volumes of lactated Ringer's (1 to 3 L) are unlikely to be detrimental and can be safely used. If larger volumes are needed to replace blood loss or other volume depletion, a change to a more isotonic fluid such as NS is probably advisable, taking into consideration that a large and rapid infusion of NS can induce a dose-dependent hyperchloremic metabolic acidosis. Whether this acid–base abnormality is, in fact, harmful remains unclear. While hyperchloremic metabolic acidosis usually does not require treatment, it is important to differentiate it from other causes of metabolic acidosis. One difference is that hyperchloremic metabolic acidosis has a normal anion gap.
3. If **large volumes** are needed, a **combination of isotonic crystalloid and colloid** (Tables 24.6 and 24.7) may be the best choice. Generally, substantially more crystalloid is necessary to effect an equivalent change in hemodynamics. High-volume crystalloid resuscitation reduces oncotic pressure and may predispose to pulmonary and peripheral edema that interferes with tissue oxygen exchange. Hetastarch should be used with caution, however, because of its adverse effect on coagulation although the third-generation HES preparation (HES 130/0.4) seems to be promising. Dextran-40 interferes with normal platelet function and its use is therefore not advisable for patients who have intracranial pathology other than to improve rheology in conditions such as ischemic brain disease.

   These recommendations should not be interpreted as "give all the isotonic fluid you like." Volume overload can have detrimental effects on ICP by increasing CBF or by hydrostatically driven edema formation.
4. **Glucose.** The infusion of salt-free solutions containing glucose (5% glucose) is equivalent to infusing water because the glucose is rapidly metabolized. Thus "free water" is proscribed in patients who have brain pathology to avoid edema formation.
   a. There is solid evidence that **excessive glucose exacerbates neurologic damage** and can worsen outcome from both focal and global ischemia. Glucose metabolism enhances tissue acidosis in ischemic areas. The increase in intracellular lactate can result in neuronal death but it has not yet been completely elucidated why hyperglycemia worsens the outcome. Several clinical studies have indicated a negative relationship between plasma glucose on admission and outcome in patients after cardiac arrest, stroke, SAH, and TBI, and demonstrated that hyperglycemia is an independent predictor of poor outcome, particularly mortality.
   b. Consensus is lacking as to the target range for blood glucose to avoid inducing hypoglycemic episodes, especially in patients who have evolving cerebral damage. Thus, it is prudent to withhold glucose-containing solutions from acutely brain-injured and elective surgical patients. This caveat does not apply to the use of alimentation, perhaps because such hyperglycemic solutions are typically

started several days after the primary insult, and insulin is usually administered concurrently.

c. While several researchers have reported that controlling stress hyperglycemia with intensive insulin therapy improves outcome, a recent multicenter, prospective trial (NICE-SUGAR) suggests that the **aggressive insulin-induced control of hyperglycemia** may **increase mortality in critically ill patients.** For patients admitted to a postoperative neurosurgical intensive care unit (ICU) after brain surgery, strict glycemic control carried a definite risk for hypoglycemia. In SAH patients, intensive glycemic control had no effect on overall in-hospital mortality although it did increase the incidence of hypoglycemia that was significantly associated with mortality.

1. In neurosurgical patients, blood sugar should be controlled carefully, the goal being to avoid both hypo- and hyperglycemia and maintain the serum glucose between 120 and 150 mg/dL.
2. Glucose-containing solutions should be withheld, except in the case of neonates and diabetic patients in whom hypoglycemia can occur very rapidly and be detrimental.

C. **Hemodilution** might be beneficial during and immediately after a focal cerebral ischemic event. Several animal studies have shown that regional oxygen delivery may be increased (or at least better maintained) in the face of modest hemodilution to an Hct of approximately 30% with an improvement in CBF and a reduction in infarction volume. In spite of this, several clinical trials have failed to demonstrate any benefit from hemodilution in stroke patients except in those who were polycythemic to begin with. Moreover, hemodilution has not been demonstrated to improve survival or functional outcome.

In elective neurosurgical patients and patients suffering from TBI, hemodilution to an Hct < 30% to 35% is unlikely to be beneficial. Hemodilution to 30% to 35% might be better tolerated in patients at risk for focal ischemia. Nevertheless, active attempts to lower Hct are probably not advisable at the present time.

D. **Aneurysmal subarachnoid hemorrhage.** When treating SAH patients, two problems should be considered—hyponatremia and hypovolemia. After SAH, patients develop hypovolemia, hemodynamic depression, and increased RBC aggregability. The cause of the relative hypovolemia is multifactorial while hyponatremia results from the increased release of brain natriuretic factor.

1. **"Triple-H" therapy**, a combination of induced hypertension, hypervolemia, and hemodilution, is a strategy widely accepted to prevent/treat cerebral vasospasm after aneurysmal SAH. Hypervolemic hemodilution decreases both the Hct and the RBC aggregability while increasing cardiac output. This type of hyperdynamic management and manipulation of blood viscosity counteracts the reduction in cerebral and circulating blood volume that generally occurs with cerebral vasospasm.
2. Triple-H therapy theoretically **improves CBF to regions of hypoperfusion.** Although this practice has gained widespread acceptance over the past 20 years, it has never been extensively and carefully studied, and it is not clear whether hypertension or hypervolemia is the critical factor. Volume loading is usually performed with colloids and great care is required to avoid reduction in serum osmolality as this will increase brain water content in ischemic as well as normal cerebral regions.

TABLE 24.8 Principal Water and Electrolytes Disorders

| | | DI | SIADH | CSWS |
|---|---|---|---|---|
| Etiology | | Reduced secretion of ADH | Excessive release of ADH | Release of brain natriuretic factor |
| Urine | Output | > 30 mL/kg/h | | |
| | Specific gravity | < 1.002 | | |
| | Sodium | < 15 mEq/L | > 20 mEq/L | > 50 mEq/L |
| | Osmolality vs. serum osmolality | Lower | Higher | Higher |
| Serum | Sodium | Hypernatremia | Hyponatremia | Hyponatremia |
| | Osmolality | Hyperosmolality | Hypo-osmolality | |
| Intravascular volume | | Reduced | Normal or increased | Reduced |

ADH, antidiuretic hormone; CSWS, cerebral salt wasting syndrome; DI, diabetes insipidus; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

## VI. WATER AND ELECTROLYTE DISTURBANCES

Table 24.8 summarizes the principal differences among the commonest water and electrolytes disturbances in patients who have intracranial pathology.

**A. Diabetes insipidus** (DI) is a common sequela of pituitary and hypothalamic lesions, but it can also occur with other cerebral pathology including head trauma, bacterial meningitis, intracranial surgery, phenytoin use, and alcohol intoxication. Patients who have markedly elevated ICP and brain death also commonly develop DI.

1. DI is characterized by the **production of large volumes of dilute urine** in the face of a **normal or elevated plasma osmolality** caused by the decreased secretion of antidiuretic hormone (ADH). This results in failure of the tubular reabsorption of water. Polyuria (more than 30 mL/kg/hour or, in an adult, more than 200 mL/hour), progressive dehydration, and hypernatremia occur subsequently. DI is present when the urine output is excessive, the urine osmolality is inappropriately low relative to serum osmolality (which is above normal because of water loss), and the urine specific gravity is < 1.002.
2. The **management of DI** requires restoration of normal serum Na along with careful balancing of intake and output to avoid fluid overload. The water deficit is replaced over 24 to 48 hours, and the hypernatremia should not be reduced by more than 1 to 2 mEq/L/hour as rapid reduction may cause seizures or cerebral edema. The patient should receive hourly maintenance fluids (Table 24.9) in the form of 0.45% NS and free water with appropriate K supplementation. Serum Na, K, and glucose are checked frequently.
3. If the urine output is > 300 mL/hour for 2 hours, it is now standard practice to administer **aqueous vasopressin,** 5 to 10 IU intramuscularly or subcutaneously, every 6 hours, or the synthetic analog of ADH,

TABLE 24.9 Management of Diabetes Insipidus

- Hourly monitoring of UO
- Maintenance fluids = 75% of the previous hour's UO *or*
- Maintenance fluids = the previous hour's UO – 50 mL
- If UO > 300 mL/hr, give vasopressin or desmopressin

UO, urine output.

**desmopressin acetate,** 0.5 to 2 mcg intravenously every 8 hours or 10 to 20 mcg by nasal instillation.

B. **Syndrome of inappropriate antidiuretic hormone secretion**

1. Various cerebral pathologic processes (especially TBI) can cause excessive release of ADH that leads to the **syndrome of inappropriate antidiuretic hormone secretion (SIADH)** marked by the continued renal excretion of Na (> 20 mEq/L) despite hyponatremia and associated hypo-osmolality. Urine osmolality is therefore high relative to serum osmolality. SIADH can also result from the over administration of free water in patients who cannot excrete free water because of excess ADH.
2. The **mainstay of treatment of SIADH is fluid restriction** to 1,000 mL/24 hours of an iso-osmolar solution. If hyponatremia is severe (< 110 to 115 mEq/L), the administration of HS (3% to 5%) and furosemide might be appropriate. As rapid correction of hyponatremia has been associated with the occurrence of central pontine myelinolysis, it is advisable to restore serum Na at a rate of about 2 mEq/L/hour.
3. The **antagonism of arginine vasopressin** (AVP), also known as ADH, represents a new, more direct strategy for the treatment of SIADH. Two AVP receptor antagonists, conivaptan and tolvaptan, have been recently approved by the Food and Drug Administration. Vaptans (V2 antagonists) block the effects of elevated ADH and promote *aquaresis*, the electrolyte-sparing excretion of water, resulting in the correction of serum Na. Vaptans, however, need to be administered with caution, and serum Na must be carefully monitored during therapy.

C. **Cerebral salt wasting syndrome (CSWS)** is characterized by hyponatremia, volume contraction, and high urine Na concentration (> 50 mEq/L). This syndrome is frequently seen in patients after SAH and the cause seems to be the **increased release of natriuretic factor** from the brain. The **therapy** is to re-establish normovolemia with the administration of Na-containing solutions.

The **distinction between SIADH and CSWS is very important** because treatment of these two syndromes is quite different—fluid restriction versus fluid infusion. In patients who have SAH, in whom normo- to hypervolemia is advocated, fluid restriction (i.e., further volume contraction) might be especially deleterious.

## VII. SUMMARY

As neuroanesthesiologists/intensivists, we should always remember that we treat patients and not just their brains. Thus, with the exception of patients who have SIADH, we need to abandon the old dogma that patients who have intracranial pathology must be "run dry" and replace it with **"run them isovolemic, isotonic, and iso-oncotic."**

- *Movement of water* between the normal brain and the intravascular space is dependent on osmotic gradients.
- Reducing *serum osmolality* by administration of free water or hypotonic crystalloid solutions (0.45% NS) results in edema formation in all tissues, including normal brain tissue.
- Reduction of *colloid oncotic pressure* with maintenance of serum osmolality is associated with increased water content in many tissues, but not in the normal brain. Colloid solutions exert little influence on brain water content and ICP.
- In the setting of *brain injury*, reducing serum osmolality increases edema and ICP. Therefore, the goal of fluid management in neurosurgery is to avoid a reduction of serum osmolality. The reduction of COP, with careful maintenance of osmolality, does not increase edema in the injured brain.
- *Hypertonic solutions:* Mannitol decreases brain water content in normal brain and is commonly used to reduce ICP. HS decreases brain water content and ICP, but can cause hypernatremia.
- *Glucose-containing solutions* should not be used in patients who have brain pathology and are avoided in patients at risk for cerebral ischemia.
- *Fluid restriction* minimally affects cerebral edema and, if over-zealously pursued, can lead to hemodynamic instability that is detrimental in neurosurgical patients.
- To *prescribe rational fluid replacement*, it is important to identify which compartment is depleted: specific losses should be replaced with the appropriate fluid.
- The primary indication for *isotonic crystalloid solutions* is the replacement of urinary output and insensible fluid losses from respiration and perspiration.
- *Isotonic colloids* and the newest tetrastarches are safe regarding coagulation and can be used to restore blood loss and intravascular volume.
- The consequences of the administration of large volumes of fluid, independent of which kind, remain under investigation. Adult respiratory distress syndrome developed five times more frequently in patients who had undergone a hypertensive CBF-targeted protocol than in patients treated with a less stringent ICP-targeted protocol.
- We must use the right kind of fluid in appropriate amounts at the right time to reduce collateral damage. We must carefully distinguish between the different types of losses and replace them accordingly.

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# 25 Nutritional Support in the Critically Ill Patient

**John M. Taylor and Binbin Wang**

## Illustrative Clinical Case

A 44-year-old otherwise healthy woman is admitted to the intensive care unit (ICU) for postoperative monitoring after elective resection of a large meningioma. The patient is mechanically ventilated for 24 hours owing to the possibility of intracranial swelling. No nutrition is administered at this time because of the elective nature of surgery, the patient's good preoperative nutritional status, and the short expected duration of intubation. She has an uneventful extubation on the second postoperative day (POD 2) and begins oral intake. On POD 4, the patient becomes obtunded from intracranial hypertension, aspirates, which necessitates tracheal intubation, and develops aspiration pneumonia. A postpyloric feeding tube is inserted at this time and gradual enteral nutrition is started with full-strength 2 Cal HN at 10 mL/hour.

Although the initial feeds are well tolerated, the patient develops abdominal distention in the setting of adult respiratory distress syndrome (ARDS), sepsis, and severe hypotension requiring multiple vasopressors. An abdominal x-ray shows small bowel distention without obvious obstruction, and she continues to have small liquid bowel movements. The enteral feeds are electively held at this time despite the patient's catabolic state because of severe hypotension and abdominal distention and are restarted slowly 36 hours later after hemodynamic stability has been achieved. The patient's trachea is extubated on POD 10 and she makes a slow but uneventful recovery.

## Chapter Highlights

- Critical illness is a catabolic state and critically ill patients are often malnourished. This chapter begins with a discussion of the pathophysiologic processes of malnutrition.
- Delivery of proper nutrition begins with accurate patient assessment. Nutritional assessment tools for critically ill patients are covered in the chapter.
- To aid in optimal nutritional construction, the estimation of energy requirements, protein requirements, and nitrogen balance is discussed.
- To finish the construction of a nutritional support, the chapter contains a discussion of macronutrients and micronutrients.
- Most efficient nutrition occurs with enteral feeding, when possible. The timing and strategies for initiation of enteral feeding are covered in the chapter.
- For patients who cannot receive enteral nutrition, parenteral feeding strategies, monitoring, and complications are also discussed.

The **goals of nutritional support** are to provide protein and caloric replacement while attenuating a negative nitrogen balance. It is estimated that 50% of

hospitalized patients and 60% to 80% of ICU patients are malnourished. Delays in the initiation of nutritional support may result in muscle atrophy, failure to wean from the ventilator, gastrointestinal (GI) atrophy, heart failure, impaired immunity, increased incidence of sepsis, increased hospital length of stay, and increased morbidity and mortality.

There is no doubt that **effective nutritional support with appropriate monitoring improves patient outcomes**. Since the early 1980s, the importance of nutritional support in the patient who has sustained severe traumatic brain injury has been appreciated, but recent studies have demonstrated the same nutritional and metabolic requirements in patients who have acute ischemic damage and other critical neurologic illnesses. There is also compelling evidence that strict glycemic control in the critically ill patient reduces morbidity and mortality.

## I. PATHOPHYSIOLOGY

The effects of elective operations, trauma, and critical illness activate the neural and endocrine systems. The increase in sympathetic outflow leads to lipolysis, proteolysis, and decreased glucose uptake from the antagonism of insulin by growth hormone and epinephrine. This sympathetic surge acts to increase energy expenditure (EE), tissue catabolism, and mobilization of protein, fat, and carbohydrate. The deleterious effects of augmented sympathetic outflow are exacerbated by immobility and delays in the initiation of nutritional support. Other adverse effects include hyperglycemia, poor wound healing, decreased serum proteins, increased carbon dioxide ($CO_2$) production, release of inflammatory mediators, and depressed immune function

**A. After neurologic injury, the ensuing state of cardiac hyperdynamism increases oxygen consumption and caloric requirements**. Studies using indirect calorimetry demonstrate that severely head-injured patients are hypermetabolic and hypercatabolic. Resting energy expenditure (REE) can increase by as much as 40% to 165%. Patients demonstrate this increase in REE regardless of whether or not they have received steroids. In addition, they can also experience delayed gastric emptying, bacterial translocation, and altered vascular permeability with resultant intestinal edema and malabsorption.

1. Patients who have sustained **head injury** exhibit changes consistent with hypermetabolism, hypercatabolism, hyperglycemia, suppressed immunity, and generalized inflammatory response. Nutritional support should satisfy these physiologic demands.
2. Patients who have suffered a **stroke** also exhibit hypermetabolism. Although it has been suggested that protein supplementation beyond normal nutritional support after stroke may improve outcome, recent trials have not supported this strategy.

**B.** Patients who are **obese,** and recent estimates indicate that approximately 40% of adults in the United States are overweight, are more likely to have comorbid medical conditions including hypertension, coronary artery disease, diabetes mellitus, pulmonary disease, and gout. Critical illness is likely to result in protein malnutrition, inhibition of lipolysis, and preferential use of carbohydrate substrate for gluconeogenesis. It has been suggested that patients who have actual body weights (ABWs) in excess of 125% of ideal body weight (IBW) may benefit from diets that are hypocaloric and high-protein in structure. The goal for obese patients is to provide adequate protein intake to meet and not exceed metabolic demands. Ideally, nutritional supplementation contains enough protein to keep the patient in a positive

nitrogen balance, but a sufficient calorie deficit to encourage net increase in lean body mass (LBM) and loss of total body fat.

## II. NUTRITIONAL ASSESSMENT

The delivery of appropriate metabolic support begins with an assessment of the patient's nutritional status. It is important to identify patients who present with subtle signs of deficiencies in caloric, protein, vitamin, or trace metal intake. These patients should be considered for earlier and more aggressive nutritional support.

**A. Definitions.** The **malnourished state** exists when intake does not meet nutritional demands. When approximately 10% of LBM is lost, moderate protein malnutrition exists. A loss of 20% of LBM indicates severe protein malnutrition and describes a severely underweight patient. When > 35% of LBM is lost, it is likely that irreversible changes leading to death have occurred.

**B. History.** In most cases, a history of decreased spontaneous food intake and unintentional weight loss (5% of LBM in 1 month or 10% of LBM in 6 months) precedes admission to the intensive care unit (ICU). A careful social history may demonstrate vitamin or mineral deficiencies associated with alcoholism or other substance abuse. Patients who have renal failure lose amino acids, vitamins, and trace metals during dialysis. Patients who have cancer may have deficiencies owing either to the underlying disease or to chemotherapy (e.g., methotrexate). Other **risk factors for malnutrition** include age > 75 years, homelessness, nothing by mouth for more than 3 days, major surgery, corticosteroid administration, malabsorption syndromes, and chronic disease states, especially cancer, stroke, and acquired immunodeficiency disease.

**C. Physical examination.** Caloric intake can be assessed by the amount of fat in the extremities, buttocks, and buccal fat pad. The adequacy of protein intake can be evaluated from the bulk of the extremity muscles, grip strength, and the size of the temporal muscle. Vitamin deficiencies may manifest themselves as changes in skin texture and hair quality and texture, cheilosis, glossitis, or loss of vibration and position sense. Examination of the head and neck may reveal xerostomia, malocclusion, odynophagia, dysphagia, esophagitis, or other findings suggestive of difficulty with eating.

**D. Anthropometrics.** Measurements are used to estimate the stores of body fat and protein. Body fat is approximated by the thickness of the triceps skin fold (TSF) and protein status is estimated by the midarm muscle circumference (MAMC).

$$\text{MAMC} = \text{midarm circumference} - \text{fat}$$

$$\text{MAMC} = \text{midarm circumference} - (0.314 \times \text{TSF})$$

These data are then compared with normal values to determine the patient's nutritional status. Two possibly incorrect assumptions are that body fat is uniformly distributed and that population standards apply to patients who are critically ill. In fact, anthropometric measurements are generally invalid in the critically ill owing to anasarca. Adjustments in estimations can be based on IBW calculated from the measurements of height and weight.

**E. Biochemical measurements.** A variety of biochemical and metabolic measurements have been studied as potential indices of nutritional status. Although

many of these tests have significant value in assessing stable patients who are scheduled for elective surgery and those well on the way to recovery, their applicability to critically ill patients has not been demonstrated. The same patient's measurements taken on different days can be compared only if other factors are relatively stable.

1. **Plasma proteins.** The level of plasma protein depends on the synthetic function of the liver and the availability of substrate. Unfortunately, a decrease in plasma protein levels is not specific because the biologic half-life, the catabolic rate, and a variety of non-nutritional factors can alter them. For example, expansion of the extracellular fluid compartment results in a reduction in albumin concentration. In addition, the levels of some serum proteins decrease promptly in response to trauma, sepsis, or severe illness because of fluid shifts, alterations in capillary permeability, and changes in the rates of synthesis and degradation. Liver disease, nephrotic syndrome, eclampsia, and protein-losing enteropathies are additional causes of hypoproteinemia.
   a. **Albumin** has a half-life of approximately 18 days. Its measurement is the most commonly used test to diagnose protein–calorie undernutrition. Depending on measured albumin alone, however, can lead to delays in treating nutritional deficits because plasma levels can be maintained for quite a while owing to the long half-life. In critical illness, albumin may also remain low until the remission of the inflammatory response despite adequate nutritional intake. **Serum albumin levels have been shown to be good predictors of sepsis and major infection in surgical patients**. However, serum albumin levels have not been correlated with either morbidity or mortality in the setting of severe neurologic injury.
   b. **Transferrin** has a half-life of approximately 8 days. Therefore, transferrin levels are a more accurate reflection of acute changes in nutritional status. Low serum transferrin is indicative of protein malnutrition. Iron deficiency, pregnancy, and hypoxia stimulate synthesis of transferrin whereas chronic infection, sepsis, and iron overload decrease transferrin levels.
   c. **Thyroxine-binding prealbumin and retinol-binding protein (RBP)** have a half-life of 2 to 3 days and 8 to 12 hours, respectively. RBP complexes with prealbumin in the circulation. The resultant compounds are much more sensitive to short-term alterations in protein and total calorie intake; low levels can return to normal after only 3 days of adequate nutritional support. While serum levels of the RBP–prealbumin complex reflect acute changes in nutritional status and indicate the adequacy of nutritional supplementation, many non-nutritional factors can affect these levels as well. Infection and trauma depress prealbumin levels. Stress and vitamin A deficiency decrease the concentration of RBP; renal failure can cause erroneous elevation of RBP. The short half-lives and the myriad of factors influencing their serum concentrations have limited the clinical usefulness of these proteins.
2. **Immunologic functions.** Total lymphocyte count and reactivity to skin test antigens are immunologic functions that reflect nutritional status, but they are not routinely used in patients who are critically ill. Any stressful situation, especially any disease process that requires a stay in the ICU, can depress cellular immunity, leading to a non-specific test result.

## III. ESTIMATION OF ENERGY REQUIREMENTS

The previously mentioned tests aid in assessing nutritional status. Different methods are needed, however, to estimate a patient's ongoing nutritional and caloric needs based on his or her individual disease process and body habitus. This is accomplished by using predictive equations or indirect calorimetry.

**A. Predictive equations** can be used to estimate the REE, a patient's energy requirement at rest. More than 200 different equations have been published, many of which are variations of the Harris-Benedict equation.

$$\text{Women: REE (kcal/day)} = 65 + 9.6W + 1.8H - 4.7A$$

$$\text{Men: REE (kcal/day)} = 66 + 13.7W + 5H - 6.8A$$

where W is the ABW in kilograms or IBW in kilograms if the patient is edematous; H is the height in centimeters, and A is the age in years. If the patient is obese, an adjusted IBW should be used as follows:

$$\text{Adjusted IBW} = \text{IBW} + 0.25\,(\text{ABW} - \text{IBW}).$$

Using predictive equations such as the Harris-Benedict equation, which was developed using healthy volunteer subjects, has many limitations and the validity of its application in the critically ill has been questioned. Therefore, some clinicians actually prefer to use a simplified weight-based formula: 25 to 30 kcal/kg/day.

1. **Adjustments to REE.** The EE of patients can vary greatly from the daily REE in active subjects. Hospitalized patients typically require 30 kcal/kg/day in the absence of severe illness or obesity. Fever increases the REE by approximately 10% above baseline for each degree Celsius rise in temperature. Brain injury induces a hyperdynamic state. An elevated EE is also associated with total body surface area burns of 20% to 40%.
2. The estimated REE is adjusted for the state of hypermetabolism that characterizes patients who are critically ill. Table 25.1 shows the usual correction factors that are used.

**B. Indirect calorimetry** provides a more accurate measure of EE than predictive equations, especially in patients who are obese. It relies on the measurement of oxygen consumption ($VO_2$) and the production of carbon dioxide ($VCO_2$). The oxygen consumed in a given period of time is the amount

TABLE 25.1 Correction Factors for the Adjustment of REE for Several Stressors and Disease States

| Stressor or Disease State | Factor |
|---|---|
| Fever | 1.1 × REE (for each 1°C above normal) |
| Minor surgery | 1.1 – 1.3 × REE |
| Minor infection | 1.2 – 1.3 × REE |
| Fracture | 1.2 – 1.4 × REE |
| Major surgery | 1.4 – 1.6 × REE |
| Major trauma | 1.6 – 1.8 × REE |
| Sepsis | 1.7 – 1.9 × REE |
| Severe burns | 1.9 – 2.1 × REE |

required for oxidation of carbohydrate, fat, and protein. Simultaneously, $CO_2$ is produced from the oxidation of carbohydrate, fat, and protein. If the patient inspires a known concentration of $O_2$ and $CO_2$, measurements of $VO_2$ and $VCO_2$ can be made. A metabolic computer can then calculate the REE and the respiratory quotient (RQ). Normal RQ is 0.8. An elevated RQ indicates overfeeding or excess carbohydrate in the diet.

Usually, measurements taken over a minimum period of 20 to 30 minutes generate better baseline values. Indirect calorimetry can be performed only in patients who have fraction of inspired oxygen ($FiO_2$) requirements of 50% or less. To account for sedation, ICU activity, dietary-induced thermogenesis, anabolism, and the work of breathing, an extra percentage is added to the measured EE. Examples of usual correction factors are:

| | |
|---|---|
| Thermogenesis | 5%–10% |
| ICU activity | 10% |
| Anabolism | 5%–10% |
| Sedation | 0%–30% |

1. REE can be calculated using indirect calorimetry:

$$\text{REE (kcal/day)} = \left[3.9 \times (VO_2) + 1.1 \times (VCO_2)\right] \times 1.44$$

**C. The Fick equation and mixed venous oxygen content ($CvO_2$).** The 24-hour EE for an ICU patient is approximately seven times the $VO_2$, calculated using measured arterial oxygen content ($CaO_2$), $CvO_2$, and the cardiac output (CO). The arterial oxygen saturation ($SaO_2$) and mixed venous oxygen saturation ($SvO_2$) should be measured at the same time that CO is measured.

$$CaO_2 - CvO_2 = \text{Hb (g/dL)} \times 1.39 \times (SaO_2 - SvO_2)$$

$$VO_2 \text{ (mL/minute)} = [CaO_2 - CvO_2] \times 10 \times \text{CO (L/minute)}$$

$$\text{24 hour energy expenditure (kcal/day)} = 7 \times VO_2$$

These "spot" measurements should be performed for several days in succession to establish an accurate trend.

## IV. ESTIMATION OF PROTEIN REQUIREMENTS

As with REE, protein requirements can be either estimated using predictive equations or measured. Predictive equations are usually used first and measurements performed later.

**A. Predictive equations.** Protein in the critical care setting is important for the promotion of wound healing, the support of immune function, and the maintenance of LBM. Approximate protein requirements can be estimated on the basis of the patient's weight, degree of illness, and extent of organ system failure. High-dose steroids also increase protein requirements because of catabolism.

| | |
|---|---|
| Normal protein requirement | 0.8–1.0 g protein/kg/day |
| Mild stress requirements | 1.0–1.2 g protein/kg/day |
| Moderate stress requirements | 1.2–1.4 g protein/kg/day |
| Severe stress requirements | 1.4–1.6 g protein/kg/day |
| Patients in renal failure on hemodialysis | 1.2 g protein/kg/day |
| Patients who have encephalopathy | 0.8 g protein/kg/day |

1. Studies of head-injured patients who were receiving 1 to 1.5 g protein/kg/day still reported negative nitrogen balances. The current recommendation is to provide 2 g protein/kg/day if renal function is normal and then reassess the nitrogen balance in a few days.
2. Postsurgical patients typically require 2 g protein/kg/day.

**B. Nitrogen balance** is used to assess the adequacy of caloric and/or protein intake and whether the anabolic state has been achieved as a result of nutritional therapy.

1. Nitrogen balance equals nitrogen intake minus nitrogen output. Total nitrogen output equals urine urea nitrogen from a 24-hour urine collection and 2 to 4 g/day of non-urinary losses. In patients who are critically ill, this may be as much as 6 g/day owing to blood loss, increased mucosal sloughing, and increased fecal nitrogen loss from diarrhea. Because protein is 16% nitrogen, each gram of urinary nitrogen represents 6.25 g of degraded protein.

$$\text{Nitrogen balance} = (\text{protein intake}/6.25) - \left(\text{urine urea nitrogen} + [2 \text{ or } 4]\right)$$

2. Measurements of nitrogen balance may not be reliable in patients who have renal and hepatic failure owing to altered protein synthesis and clearance. For patients who are in renal failure, the creatinine (Cr) clearance must be > 50 mL/minute for results to be considered valid.

## V. MACRONUTRIENTS

**A. Carbohydrates.** As long as adequate energy and protein are provided in the diet, there is no specific requirement for dietary carbohydrate, but the current recommendation is to provide 50% to 60% of the total calories as carbohydrates. Much of this is used by the central nervous system which relies on glucose as its primary source of fuel.

**B. Fat**. The goals of lipid supplementation include providing for essential fatty acids, promoting nitrogen sparing, and offering a balanced approach to fulfilling energy requirements. Increasing dietary fat decreases the incidence of hepatic steatosis and the production of $CO_2$ from a high-carbohydrate diet. Lipid oxidation as an energy source is increased in the critically ill patient. The recommendation is therefore that 30% to 40% of the total calories be provided as lipid. A minimum of 3% of the kilocalories (kcal) delivered as fat should be in the form of linoleic acid to prevent essential fatty acid deficiency.

**C. Protein.** The goal of protein supplementation is to provide substrate for cellular protein synthesis and to maintain LBM. Protein requirements increase if there are excessive losses from the gastrointestinal (GI) tract, skin, or draining wounds. It is often difficult to achieve positive nitrogen balance in critically ill patients, but effort should be made to minimize negative nitrogen balance.

**D. Fluid.** Non-hospitalized patients consume approximately 1 mL of free water/kcal ingested. With a normal diet this is about 30 to 50 mL/kg body weight per day. Hospitalized patients typically require 30 to 35 mL/kg/day. The patient's underlying medical condition and comorbidities must be taken into account when providing replacement fluids. Patients require adequate volume resuscitation before the initiation of parenteral nutrition (PN). When calculating free water replacement in patients receiving enteral nutrition, it is important to remember to subtract the free water in the enteral formula from the total daily free water volume.

TABLE 25.2 Recommended Dietary Allowance of Vitamins for a Healthy 25- to 50-Year-Old Man

| Vitamin | Amount | Vitamin | Amount |
|---|---|---|---|
| Vitamin A | 1,000 mcg | Vitamin D | 5 mcg |
| Vitamin E | 10 mg | Vitamin K | 80 mcg |
| Vitamin C | 60 mg | Thiamine | 1.5 mg |
| Riboflavin | 1.7 mg | Niacin | 19 mg |
| Vitamin $B_6$ | 2 mg | Folate | 200 mcg |
| Vitamin $B_{12}$ | 2 mcg | | |

## VI. MICRONUTRIENTS

Because the response to injury is characterized by greatly increased energy demands and clinical malnutrition, appropriate nutritional support might prevent the multisystem organ failure that often occurs in patients who are critically ill. The gut is an important metabolic organ that has a critical need for certain substrates. In addition to essential vitamins and trace nutrients, immunomodulatory compounds are being increasingly viewed as beneficial in certain subsets of critically ill patients.

**A. Vitamins** are involved in metabolism, wound healing, and immune function. They are essential in that they cannot be synthesized by the body. The 12 essential vitamins that should be supplied daily are divided into fat- and water-soluble categories. Recommended dietary allowances of vitamins are listed in Table 25.2.

**B. Trace nutrients.** Deficiencies in the nine essential trace elements can lead to problems in several organ systems including insulin resistance, myopathy, increased susceptibility to infection, and pancytopenia. Recommended dietary allowances of trace elements are listed in Table 25.3.

For patients who have **renal failure**, zinc and chromium should be either reduced or omitted because they are excreted in the urine. Similarly, in the presence of **biliary tract obstruction**, the intake of copper and manganese is either reduced or omitted because both are excreted primarily in the bile. Decreased serum zinc levels and increased urinary zinc losses have been reported after head injury although the mechanism and clinical significance are unknown. No other specific changes in vitamin and mineral metabolism have been identified after neurologic injury.

**C. Immunomodulators.** Numerous clinical trials have been conducted and are currently ongoing to evaluate diets enriched with immunomodulatory

TABLE 25.3 Recommended Dietary Allowance of Trace Elements for a Healthy 25- to 50-Year-Old Man

| Element | Oral | Intravenous |
|---|---|---|
| Zinc | 10–15 mg | 2.5–4.0 mg |
| Chromium | 50–290 mcg | 10–15 mcg |
| Copper | 1.2–3 mg | 0.5–1.5 mg |
| Manganese | 0.7–5 mg | 0.15–0.8 mg |
| Selenium | 50–200 mcg | 40–120 mcg |
| Molybdenum | | 200 mcg |

components such as glutamine, arginine, and omega-3 fatty acids, and their effects on patients who are critically ill. Evidence shows that patients in the surgical ICU, especially those who have had major elective surgery, trauma, burns, and head/neck cancer, more uniformly exhibit a favorable outcome with the addition of immunomodulators as compared to patients in the medical ICU who did not receive immunomodulators. Meta-analyses have demonstrated a reduction in infectious morbidity and hospital length of stay in the surgical ICU patients. Beneficial effects are currently believed to result from action on myeloid suppressor cells.

1. **Glutamine.** The primary fuel for the intestine, glutamine exerts its many beneficial effects through its antioxidant properties and is important in maintaining intestinal structure and function, preventing mucosal atrophy during starvation, decreasing bacterial translocation, and stimulating the intestinal immune system in sepsis and stress. The administration of glutamine has also been shown to reduce mortality and ICU length of stay significantly in burn patients and to increase protein synthesis in other critically ill patients.
2. **Arginine** improves wound healing, stimulates immune function by increasing the production of natural killer and helper T cells, and enhances intestinal absorption and proliferation. Arginine is also responsible for the synthesis of nitric oxide, which maintains the integrity of the microvascular structure of the gut after injury. The data are conflicting as to whether the arginine-enhanced production of nitric oxide contributes to hemodynamic instability in patients who have severe sepsis. Current evidence suggests, however, that an arginine-containing diet is safe in patients who have mild to moderate sepsis.
3. **Omega-3 fatty acids** are believed to reduce systemic inflammation by displacing omega-6 fatty acids from immune cell membranes, which leads to the production of less active prostaglandins and leukotrienes. The replacement of dietary omega-6 fatty acids with omega-3 fatty acids might therefore down-regulate several aspects of the inflammatory response. There is mounting evidence to suggest that omega-3 fatty acid fortified enteral nutrition may significantly reduce the incidence of organ failure, duration of mechanical ventilation, and mortality in patients who have ARDS, acute lung injury (ALI), and sepsis as compared to standard enteral nutrition. Additional studies are currently underway to elucidate the optimal dose of these fatty acids.
4. **Dietary nucleotides** are important for intestinal structure and function. In animals, the addition of dietary nucleotides to total parenteral nutrition (TPN) diminishes intestinal mucosal atrophy. Ribonucleic acid nucleotides have also been shown to stimulate the immune system by promoting the development of T lymphocytes.

## VII. TIMING AND ROUTE OF FEEDING

Although some patients can safely tolerate protein and calorie deprivation for several days, the initiation of nutritional support should not be delayed in patients who are critically ill and unable to maintain adequate volitional intake. The decision as to whether to use the enteral or parenteral route involves assessing the functional capacity of the gut. It is important to remember that enteral feeding and parenteral feeding are not mutually exclusive. A combination may also be appropriate.

**A. Enteral feeding.** Enteral nutrition (EN) is the **preferred route** of feeding in appropriate critically ill patients. EN helps maintain the structural integrity and immune function of the gut. The **benefits of EN** as compared to PN

include a significant reduction in infectious complications, hospital length of stay, and cost. The patient populations shown to benefit from EN include those whose critical condition is secondary to trauma, burns, head injury, major surgery, and acute pancreatitis. It is important to begin feeding within 24 to 48 hours of ICU admission. Bowel sounds and other evidence of bowel function such as passing flatus or stool are not required for initiation of EN. The absence of these signs may signify altered gut contractility, but the absorptive function and mucosal integrity of the gut may remain intact. **Contraindications** to the use of enteral feeding include severe ileus or intestinal obstruction and the need for total bowel rest. Enteral feedings should be held in hemodynamically unstable patients who require active volume resuscitation or high doses of vasopressors until stability is achieved because of the increased risk of bowel ischemia. EN may be administered to patients receiving low-dose vasopressors but vigilance for signs of feeding intolerance is necessary.

1. **Types of formulas.** The selection of an enteral formula is based on the patient's digestive capacity and specific nutritional needs. Table 25.4 lists some enteral formulas and their nutritional components.
   a. **Polymeric** contains intact nutrients and requires normal digestion and absorption.
   b. **Fiber-enriched** is frequently used in patients who are experiencing diarrhea or constipation.
   c. **Calorically dense** is used in patients who have cardiac, renal, or hepatic failure or when fluid restriction is required.
   d. **Elemental** contains one or more partially digested macronutrients and is used in patients who have compromised GI function.
   e. **Modular** is composed of individual nutrient modules to produce a formula customized to meet a patient's specific needs. These formulations have increased caloric and protein concentrations. They can also be used to modify a pre-existing commercial formula to add to the caloric and/or protein density.
   f. **Immunomodulator nutrients** such as omega-3 fatty acids, branched-chain amino acids, nucleotides, arginine, and glutamine have generated a great deal of interest. There are several commercial formulations of

TABLE 25.4 Enteral Formulas and Their Components

| | | | | Composition Per Liter (g) | | |
|---|---|---|---|---|---|---|
| **Product** | **Formula Type** | **kcal/mL** | **mOsm** | **Protein** | **Fat** | **CHO** |
| Osmolite | Polymeric | 1.06 | 300 | 37 | 38 | 145 |
| Osmolite HN plus | | 1.2 | 360 | 56 | 39 | 158 |
| Jevity | Fiber-enriched | 1.06 | 300 | 44 | 36 | 151 |
| Glucerna | | 1 | 375 | 42 | 56 | 94 |
| Two Cal HN | Calorically dense | 2 | 690 | 84 | 91 | 217 |
| Peptamen | Peptide-based (semi-elemental) | 1 | 270 | 40 | 39 | 127 |
| Paptamen VHP | | 1 | 300 | 62 | 39 | 104 |
| Crucial | | 1.5 | 490 | 94 | 68 | 135 |
| Vivonex Plus | Elemental | 1 | 650 | 45 | 6.7 | 189 |

CHO, carbohydrate; kcal, kilocalorie.

immune-modulating enteral feeds available that vary greatly in the composition and dose of their individual nutrients. The optimal dose and ratio of these nutrients remain controversial.

2. **Routes of enteral feeding**
   a. **Gastric.** Gastric feeding can be established either by the insertion of a feeding tube through the nose to the stomach or by the surgical ("open" or laparoscopic) insertion of a gastrostomy tube. While gastric feeding takes advantage of the reservoir capacity of the stomach, many patients, especially those who have elevated intracranial pressure, might not tolerate this owing to delayed gastric emptying, impaired gag reflex, and/or gastric atony.
   b. **Duodenal**. The proposed advantage of the duodenal route is the reduced risk of reflux and aspiration but, unfortunately, there is no evidence to support this hypothesis. Patients can still aspirate, even with jejunal feeds. Feedings given into the duodenum must be by continuous infusion because large boluses are not tolerated.
   c. **Percutaneous enteral tubes.** Gastric (percutaneous endoscopic gastrostomy [PEG]) and jejunal (percutaneous endoscopic jejunostomy [PEJ]) tubes can be inserted percutaneously under either fluoroscopic or endoscopic guidance. PEG tubes allow enteral feeding of patients who have dysphagia or altered mental status. PEJ tubes allow enteral nutrition with a reduction in gastric residuals. Neither PEG nor PEJ feeding prevents aspiration.
3. **Initiation and advancement.** Before initiating enteral feeding, proper placement of the enteral tube should be ascertained radiographically. An abdominal radiograph is performed to locate the distal-most portion of the enteral tube.
   a. **Isotonic solutions** can be started slowly at full strength and then the rate advanced as tolerated until the goal rate is achieved. **Hypertonic solutions** should be diluted to isotonicity and the concentration advanced to full strength before the infusion rate is increased. These strategies help guard against diarrhea and electrolyte disturbances.
   b. The **volume of enteral feeding** through the stomach (nasogastric or PEG) is typically advanced while monitoring gastric residuals every 6 hours. ICU patients often have delayed gastric emptying and gastric distention which predispose them to aspiration. Enteral feeding may begin at 10 to 15 mL/hour; the rate is increased by 10 to15 mL/hour every 8 hours until a predetermined goal rate is reached. Infusions should be held for residuals > 200 mL.
   c. **Signs of feed intolerance** including emesis, gross abdominal distention with absent bowel sounds, and radiographic evidence of bowel obstruction necessitate alterations in or temporary cessation of feedings.
4. **Complications of enteral feeding**
   a. **Mechanical.** Misplaced nasal feeding tubes might end up in the bronchus or in the brain in patients who have fractures of the cribriform plate. There is also a higher incidence of epistaxis and sinusitis because the tube passes through the nares.
   b. **GI.** Nausea and vomiting might occur from postinjury ileus and gastric atony. Diarrhea can be a problem because of the concentration, osmolarity, or volume of the tube feeds; the presence of lactose, fat, or gluten; low residue; or bacterial contamination. Diarrhea may also be caused by either the lack of fiber or an intestinal obstruction and may lead to either free water deficits or dehydration.

c. **Pulmonary.** Pulmonary aspiration is probably the most common serious, potentially fatal complication of enteral nutrition. The reported incidence is highly variable (0% to 95%) depending on the population of patients studied and the definition of aspiration because chemical evidence of aspiration is more common than clinically diagnosed aspiration pneumonia. Methods used to reduce the risk of aspiration include elevating the head of the bed 30 to 45 degrees, using continuous infusions instead of bolus feedings, and optimizing oral hygiene.

d. **Metabolic.** Serum osmolarity and volume status must be carefully monitored to avoid hyperosmolarity and fluid overload. Electrolyte imbalance (e.g., hyponatremia) is common, especially in head-injured patients who are at risk for the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and diabetes insipidus (DI). Hypophosphatemia, hypokalemia, and hypomagnesemia occur commonly during refeeding.

B. **Parenteral feeding.** TPN should be considered when EN is not appropriate, such as when gut failure is demonstrated. Current guidelines recommend that PN be initiated if patients are malnourished on admission or were previously well nourished before admission but have gone 7 days without adequate EN. Before administering PN, the patient's total energy requirement, total protein requirement, daily fluid requirement, and the proportion of calories to be delivered as fat must be determined.

1. **Parenteral solutions.** There are three elemental nutrients in PN:

a. **Dextrose** is available in concentrations ranging from 10% to 70%. The higher the percentage of dextrose, the higher the osmolarity and the greater the need for central access. Only solutions with < 10% dextrose are considered safe for peripheral intravenous administration because solutions with an osmolarity > 900 mOsm/L can cause sclerosis or phlebitis.

b. **Amino acids** provide the protein requirement.

c. **Fat emulsions** are rich in linoleic acid. The infusions are given over several hours, and the rate of infusion should be adjusted for patients receiving propofol for sedation. Propofol is in a fat emulsion and provides the equivalent of 1.1 kcal/mL of fat calories.

d. **Additives** such as electrolytes, vitamins, and trace elements are added directly to the dextrose and amino acid infusion.

2. **Routes of parenteral feeding.** Intravenous calories can be given peripherally or centrally.

a. **Peripheral access** for administration of TPN should be used only for short-term nutritional support. The hyperosmolarity and low pH of TPN predispose small veins to thrombophlebitis. It is also difficult to provide the necessary caloric requirements by way of this route owing to the limitations imposed by dextrose (maximum 10%) and amino acid concentrations. Long peripheral lines that extend into a central vein can be used as a central line and do not have the same limitations from the dextrose and amino acid concentrations.

b. **Central access** should be used when longer periods of parenteral feeding are necessary or if the patient is seriously ill.

3. **Initiation and advancement.** PN is usually started at a slow rate of infusion and then the rate is advanced every 12 to 24 hours until the goal rate is achieved. When the infusion is discontinued, the rate should be tapered so that hypoglycemia does not result from the increase in insulin production stimulated by the PN.

4. **Complications**
   a. **Mechanical.** Significant venous thrombosis, which can usually be diagnosed by ultrasound or the injection of radiopaque contrast, requires the removal of the catheter and heparinization. Catheter infections must always be suspected. Meticulous catheter care, a high index of suspicion, and a low threshold for removal are essential.
   b. **GI.** Elevated transaminases are common at the beginning of the administration of TPN, but they should not persist for long. Fatty liver might develop from the excess carbohydrates or total calories in the diet. Cholelithiasis or gall bladder sludge might be secondary to changes in bile composition as well as the decreased frequency of gallbladder contractions. These usually resolve after enteral alimentation has been initiated.
   c. **Metabolic.** Elevations in glucose can occur early on from relative insulin resistance and might require an infusion of insulin. Hypercapnia can result from refeeding a malnourished patient who cannot adequately increase minute ventilation. Decreasing the daily caloric intake or replacing dextrose with fat can reduce $CO_2$ production. Any electrolyte abnormality can occur, so daily adjustments must be made in conjunction with the laboratory results. Suggested laboratory monitoring guidelines are listed in Table 25.5. Vitamin K is the most common vitamin deficiency; it is not contained in multivitamin preparations.

C. **Monitoring.** While receiving enteral or PN, the patient must be monitored for changes in body composition, blood chemistry, blood glucose, triglycerides, protein synthesis, and volume status.
   1. Daily weights along with total volume of the patient's intake and output need to be monitored in addition to assessing other markers of hydration and volume status.
   2. Serum electrolytes (Na, K, Cl, Mg, $PO_4$, and Ca), osmolarity, and markers of renal function (blood urea nitrogen and Cr) should be monitored routinely.

TABLE 25.5 Suggested Monitoring Guidelines for Enteral and Parental Nutrition

| Schedule | Enteral | Parenteral |
|---|---|---|
| Baseline | Electrolytes, BUN, Cr, Ca, Mg, $PO_4$, glucose, albumin | Electrolytes, BUN, Cr, Ca, Mg, $PO_4$, glucose, liver function tests, triglycerides, cholesterol, albumin |
| Daily | Intake and output, weight | Intake and output, weight |
| Daily until stable; then 2–3 times/week | Electrolytes, BUN, Cr, glucose | Electrolytes, BUN, Cr, glucose |
| Every other day until stable; then 1–2 times/week | Ca, Mg, $PO_4$ | Ca, Mg, $PO_4$ |
| Every 10–14 days | Albumin | Liver function tests, albumin, triglycerides |

BUN, blood urea nitrogen; PT, prothrombin time; Cr, creatinine; $PO_4$, phosphate; Ca, calcium; Mg, magnesium.

3. Moderate glycemic therapy in patients who are critically ill has been shown to reduce morbidity and mortality. Although there is significant controversy regarding the optimal glycemic range and the patient populations that are most affected, maintaining blood glucose levels < 180 mg/dL in all critically ill patients, regardless of pre-existing diabetes mellitus, most likely reduces morbidity and mortality while avoiding the complications of hypoglycemia. However, numerous studies suggest that, in severely brain-injured patients, tight glycemic control (glucose < 140 mg/dL) significantly improves clinical outcomes.
4. Hypertriglyceridemia is a potential complication of sedation with continuous infusion of propofol because of the lipid carrier solution. Escalating or pre-existing elevated triglyceride levels may predispose patients to pancreatitis and therefore necessitate alternate sedation strategies.

**D. Refeeding syndrome.** Patients who are severely malnourished could have an adverse physiologic response to carbohydrate utilization. During starvation, insulin production decreases in the absence of carbohydrates. Protein and fat are preferentially used to meet metabolic demands. As a result, intracellular electrolytes are depleted, especially phosphate. When carbohydrates are administered, insulin causes electrolyte and fluid shifts. This results in hypokalemia, hypomagnesemia, hypophosphatemia, and fluid retention. Without phosphate, adenosine triphosphate cannot be generated. In the most severe cases, arrhythmias, heart failure, respiratory failure, seizures, or death may occur. Prolonged fasting, prolonged intravenous hydration, chronic malnutrition, chronic alcoholism, and anorexia nervosa are a few of the risk factors for the refeeding syndrome. Closely monitoring electrolytes and vital signs can prevent a potentially fatal complication from refeeding patients who are severely malnourished.

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# 26 Traumatic Brain Injury, Stroke, and Brain Death

**Seth Manoach, Georges I. Labaze, and Jean G. Charchaflieh**

## Illustrative Clinical Case

A 20-year-old woman was brought to the emergency department (ED) of a Level I trauma center after being injured in a car collision as an unrestrained passenger. On primary trauma survey, she had two indications for intubation: (1) significant extensive facial trauma (fractures and swelling) and (2) decreased level of consciousness (Glasgow Coma Scale score of 8). Intubation was performed using rapid sequence induction (RSI) followed by direct laryngoscopy (DL) with manual inline stabilization (MILS) of the neck. RSI consisted of lidocaine 1.5 mg/kg, etomidate 0.2 mg/kg, and succinylcholine 1.5 mg/kg intravenously.

Careful physical exam revealed significant bruising over the left side of the body, strong distal pulses, soft compartments, and no vascular injury that required immediate intervention. A computed tomographic (CT) scan of the head demonstrated traumatic brain injury (TBI) consisting of left occipital subarachnoid hemorrhage (SAH), left frontoparietal subdural hematoma (SDH), a compressed left lateral ventricle, and rightward midline shift. Cervical spine CT scan and chest x-ray were negative. Abdominal–pelvic CT scan showed bilateral pubic rami fractures without significant hematoma. Extremity films showed a left tibial–fibular fracture. None of the extracranial injuries was judged to be hemodynamically significant, and the patient was transferred to the neurosurgical ICU.

The combination of an abnormal head CT scan and a GCS score ≤ 8 constituted an indication for intracranial pressure (ICP) monitoring. Upon arrival in the neurosurgical ICU, a neurosurgeon placed an intraventricular catheter (IVC) in the left lateral ventricle both to measure ICP and drain cerebrospinal fluid (CSF). An orthopedic surgeon reduced and externally stabilized her tibial–fibular fracture pending later definitive repair.

The patient's initial ICP was elevated at 22 mm Hg. First-line treatment for her TBI and increased ICP consisted of elevation of the head of the bed (HOB) to 30°, maintenance of mean arterial pressure (MAP) ≥ 90 mm Hg in order to maintain a cerebral perfusion pressure of 70 mm Hg, diuresis with mannitol, moderate hyperventilation to an arterial carbon dioxide tension ($PaCO_2$) of 35 mm Hg, sedation with propofol, and seizure prophylaxis with phenytoin. Additional therapy included transfusion of packed red blood cells (PRBCs) to an Hb level of ≥ 7 g/dL, transfusion of fresh frozen plasma (FFP) and platelets to correct coagulopathy, empiric broad-spectrum antibiotics and cooling blankets for fever, enteral nutrition via an orogastric tube, stress ulcer prophylaxis with famotidine, and deep vein thrombosis (DVT) prophylaxis with sequential compression stocking to the non-injured leg. When a repeat head CT scan 48 hour later showed no evidence of rebleeding, additional DVT prophylaxis with subcutaneous heparin was provided.

Over a period of 1 week, the patient's ICP decreased from 22 to 10 mm Hg. The neurosurgeon gradually raised the IVC drain transducer from 10 to 15 cm above the level of the lateral ventricle and observed decreased CSF output with no increase in ICP, indicating re-establishment of ICP reabsorption by the subarachnoid granulations.

With the IVC drain closed, a repeat head CT scan showed no evidence of increased ICP and therefore the neurosurgeon removed the IVC drain. Pharmacologic sedation was decreased and the patient was noted to localize to pain. By day 12, the patient was responding purposefully to verbal commands. On day 13, she had a successful trial of spontaneous respiration with pressure support (PS) of 8 cm $H_2O$, positive end-expiratory pressure (PEEP) of 5 cm $H_2O$, and $FiO_2$ of 40%. Her trachea was successfully extubated.

Subsequently, the patient underwent definitive repair of her fractures, and continued her recovery outside the ICU. She was transferred to a TBI rehabilitation center with the goal of enabling her to lead an independent and fully functional life.

## Chapter Highlights

- **TRAUMATIC BRAIN INJURY**
  - **Impact of traumatic brain injury**
  - **Brain Trauma Foundation clinical practice guidelines**
  - **Initial resuscitation**
  - **Critical care management after initial resuscitation**

- **STROKE**
  - **Ischemic stroke**
    1. Pathophysiology
    2. Diagnosis
    3. Treatment
  - **Hemorrhagic stroke and intracerebral hemorrhage**
    1. Pathophysiology
    2. Diagnosis
    3. Treatment

- **BRAIN DEATH AND ORGAN DONATION**
  - **The importance of brain death and organ donation**
  - **Physiology of brain death**
  - **Diagnosis of brain death**
  - **Care of the brain-dead organ donor**
  - **Non-heart-beating donors**

### I. TRAUMATIC BRAIN INJURY

#### A. Impact of traumatic brain injury

Each year in the United States, approximately 52,000 people die and 70,000 to 90,000 suffer permanent disability because of TBI. TBI results from the **primary injury**, or structural damage from the initial transfer of force, and the **secondary injury**, or cerebral ischemia from subsequent systemic and cerebral events. A study based on information from the **Traumatic Coma Data Bank** revealed that, in patients who sustained severe head injury (Glasgow Coma Scale [GCS] score ≤ 8), the presence of hypotension (systolic blood pressure [SBP] < 90 mm Hg) and/or hypoxia (arterial oxygen tension [$PaO_2$] < 60 mm Hg) at the time of arrival at the hospital was associated with increased mortality and worsened outcomes in survivors, independent of the severity of injury. The mortality was 75% when patients had both hypotension and hypoxia.

**Intracranial complications**, such as edema, hemorrhage, and vasospasm, contribute to a reduction in cerebral blood flow (CBF) on post-TBI

day 1 to almost 50% of the pretrauma baseline average of 45 mL/100 g of brain/minute. An estimated CBF ≤ 15 mL/100 g/minute is associated with irreversible cerebral damage. To minimize secondary injury and associated complications, patients who have moderate or severe TBI require treatment in an intensive care unit (ICU).

**B. Brain Trauma Foundation clinical practice guidelines**

The Brain Trauma Foundation (BTF) developed evidence-based clinical practice guidelines (CPGs) that are revised periodically as new data become available. Recent studies suggest that ICU protocols based on BTF guidelines can decrease morbidity, mortality, and cost of care.

**C. Initial resuscitation**

Patients who have TBI should be either treated at a **designated trauma center** that has neurosurgical coverage or transferred to such a center after initial stabilization. Investigators noted a 50% increase in mortality when patients who sustained TBI were initially transported to a non-trauma center. Patients transported to non-trauma centers should be transferred to designated trauma centers as soon as they are stabilized.

The prompt assessment and management of TBI begin with the treatment of associated injuries that may cause hypoxia, hypoventilation, and shock. This is best accomplished using a systemic approach such as the Advanced Trauma Life Support (ATLS) Algorithm, which consists of primary and secondary surveys.

1. **Primary survey**

   To the extent possible, a brief history is obtained according to the **AMPLE mnemonic** (**A**llergies, **M**edications, **P**ast medical history, **L**ast meal, **E**vent). Examination and immediate resuscitation are performed according to the **ABCDE mnemonic** (**A**irway, **B**reathing, **C**irculation, **D**isability, **E**xposure). Plans for initial operative or non-operative management are based on the results of the primary and the secondary surveys.

   a. **Airway:** In the setting of TBI, airway management is performed with particular attention to changes in MAP, ICP, arterial oxygen tension ($PaO_2$), arterial carbon dioxide tension ($PaCO_2$), and **cervical stability**.

      1. **Indications for intubation** include inability to protect the airway, difficulty with oxygenation or ventilation, shock, a GCS score < 9, and rapid neurologic deterioration.
      2. **Manual inline stabilization (MILS)** should be maintained during intubation to minimize the risk of cervical spinal cord injury (SCI) for all patients in whom cervical spine injury has not been ruled out. Although recent work has persuasively questioned the value of MILS, it is still considered to be the standard of care. Modification of this technique should only be made with extreme caution by the most experienced airway managers.
      3. **Rapid sequence induction (RSI)** should be used in patients who require emergent intubation. As with all intubations, airway managers should consider **awake-topical intubation** if they are uncertain about their ability to establish an airway quickly and safely.
      4. For the majority of TBI patients, **direct laryngoscopy** (DL) is still considered to be the fastest and safest way to accomplish intubation in most patients, including those who have possible cervical spine injuries.
      5. **Flexible fiberoptic** (FFO) and **video-laryngoscopy** (VL) techniques provide visualization of the larynx with less force required to establish a line of sight than with DL. **Flexible fiberoptic (FFO)**

**intubation** may be useful in patients who have a difficult airway and unsecured cervical spine fractures. The technique may be limited in unstable or agitated patients and those who have blood in or significant trauma to the airway. **Newer fixed fiberoptic and prism devices**, including the Glidescope, Airtraq, and optical stylets, may offer better-grade views than DL when patients require MILS. These devices vary in their susceptibility to soiling and may fail when there is blood in the airway. Skilled operators who are familiar with these devices may find them helpful when DL views of the larynx are inadequate for safe intubation.

6. **Laryngeal mask airway (LMA) devices**, including the intubating LMA, are useful backup tools for ventilation and intubation. The intubating LMA has been shown in several studies to be a safe and reliable ventilation and intubation conduit in trauma patients. Intubation success is significantly increased when operators employ "up–down movement" and "the two Chandy maneuvers". The up–down movement consists of moving an inserted LMA up about 6 cm and reinserting it down until a potentially folded epiglottis is repositioned. The two Chandy maneuvers are used with the Fastrach LMA (FT-LMA) and consist of (1) sagittal rotation of the FT-LMA to improve ventilation and (2) lifting the metal handle of the FT-LMA to prevent the ETT from impacting the arytenoids.
7. **Surgical airway techniques**, such as cricothyroidotomy and tracheotomy, are also backup methods for intubation and, in rare cases, may be the first line of management.
8. **Lidocaine**, 1.5 mg/kg iv given 1.5 minute before intubation, blunts the increase in ICP that occurs in response to airway manipulation.
9. The induction drugs **propofol and thiopental** decrease ICP, CBF, and cerebral metabolic rate for oxygen consumption ($CMRO_2$). They also have anticonvulsant effects. However, they can also decrease MAP and cerebral perfusion pressure (CPP = MAP – ICP) to an extent that may be harmful in trauma patients. **Etomidate**, 0.3 mg/kg iv, may be a better choice as it produces similar decreases in ICP and $CMRO_2$ without significant decreases in CPP. The importance of etomidate-induced transient adrenal suppression in trauma patients is being debated. Several researchers have reported favorable cerebral and general hemodynamic effects of ketamine and gamma aminobutyric acid (GABA)-agonist combinations in TBI. A recent controlled trial comparing etomidate and ketamine in a group of critically ill patients, including a substantial number of trauma and coma patients, found no difference in clinically important outcomes at any time during treatment. Nonetheless, ketamine remains controversial for TBI because it increases ICP in some patients.
10. Several **neuromuscular-blocking drugs** are appropriate for TBI.
    a. The depolarizing muscle relaxant **succinylcholine** (SCH), 1.5 mg/kg, has the fastest onset of action among the currently available muscle relaxants (30 to 45 seconds). It has been shown in animal studies to increase ICP, but human studies have been inconsistent. In a controlled study in brain-injured patients, SCH's effects on ICP were not significantly different from normal saline. SCH is contraindicated > 24 hours after

TBI associated with spinal, crush, or burn injuries because of the risk of hyperkalemia.

b. High doses of **non-depolarizing neuromuscular-blocking drugs** such as rocuronium, 1 mg/kg, and mivacurium, 0.2 mg/kg, do not increase ICP. They have slower onset, longer duration, and fewer side effects than SCH. At standard doses, the onset of action is slower (60 to 90 seconds), which makes them less suitable for use during a true RSI. Rocuronium at 1.2 mg/kg (twice the standard intubating dose) may produce adequate relaxation in < 1 minute, making this regimen best suited for RSI when SCH is contraindicated.

11. **Endotracheal intubation must be confirmed** by physical examination plus a method for $CO_2$ detection such as colorimetric or continuous capnography.
12. **Chest x-rays** are useful for verification of endotracheal tube position as well as identification of associated chest pathology such as pneumothorax, lung contusion, and pulmonary edema.

b. **Breathing/Ventilation**

1. **Supplemental high-flow oxygen** is provided to all patients before intubation to prevent hypoxia ($PaO_2$ < 90 mm Hg) and provide sufficient apneic time for RSI.
2. **Positive-pressure ventilation** is provided as needed to maintain adequate ventilation and oxygenation.
3. After intubation, the **fraction of inspired oxygen ($FiO_2$) can be adjusted** to minimize oxygen toxicity, but oxygen saturation should be maintained above levels now considered acceptable for patients who have acute respiratory distress syndrome (ARDS). Although we lack high-quality data, it is probably reasonable to **maintain oxygen saturation ($SpO_2$) at or above the mid-90s**. This should be easy to accomplish in patients who do not have pulmonary contusions by keeping the $FiO_2$ between 0.3 and 0.6.
4. A **positive end-expiratory pressure** (PEEP) of 5 to 10 cm $H_2O$ is generally safe in TBI patients. PEEP > 10 to 15 cm $H_2O$ may impair venous return. In hypovolemic patients, any positive-pressure ventilation may decrease cardiac output and, with that, MAP and CPP. Higher PEEP may exaggerate this effect by increasing intrathoracic pressure and interfering with right-sided filling.
5. Many **TBI patients retain cerebrovascular responsiveness to changes in $PaCO_2$**. The $PaCO_2$ should therefore be kept at near-normal levels of 35 to 40 mm Hg to maintain CBF. Patients subjected to hyperventilation demonstrate increased lactate/pyruvate ratios and other markers of cerebral ischemia. In addition, patients who have a $PaCO_2$ < 30 or > 50 mm Hg upon presentation to the ED after intubation in the field are less likely to survive than patients whose $PaCO_2$ is within this range. Hyperventilation is best reserved for brief periods as part of the treatment of refractory intracranial hypertension, particularly when definitive therapy such as surgical decompression is planned.
6. **Sedation and analgesia,** with daily interruption to assess mental status, should be provided to mechanically ventilated patients until they are ready for weaning from mechanical ventilation. The ideal sedative drug in TBI should have rapid onset and offset, anticonvulsant properties, and favorable effects on CPP. Short-acting sedatives, such as **propofol**, 10 to 50 mcg/kg/minute, or **dexmedetomidine**, loading dose

1 mcg/kg over 10 minutes; then 0.2 to 0.7 mcg/kg/hour for < 72 hours, have rapid onset and offset. This allows rapid awakening for neurologic assessment. Both drugs are problematic, however, as they can cause hypotension, and, with dexmedetomidine, this may be complicated by bradycardia. Patients receiving prolonged infusions of propofol may require many hours to awaken sufficiently for reliable neurologic examination.

**Midazolam**, 0.05 mg/kg bolus; then 0.03 to 0.15 mg/kg/hour, is a benzodiazepine that possesses antiseizure properties and is less likely to cause hypotension than propofol. Analgesia and blunting of stimulation associated with the endotracheal tube can be achieved with **opioids** such as **fentanyl**, 0.5 to 1 mcg/kg bolus; then 0.7 to 2 mcg/kg/hour. Patients whose tracheas are not intubated may receive **hydromorphone** for pain provided that close attention is paid to respiratory function. Hydromorphone is free from active metabolites, is available in intravenous, intramuscular, and oral forms, but is 7.5 times more potent than morphine including its respiratory depressant effect. **Morphine** and **meperidine**, even more so, should be avoided in renal failure as their renally excreted metabolites (including seizure-inducing ones) may accumulate and cause respiratory depression and/or seizures.

c. **Circulation:** Life-threatening **hypovolemic or cardiogenic shock** as from tension pneumothorax and cardiac tamponade is identified and either controlled or treated definitively. Systolic BP is maintained at or above 90 mm Hg. Patients may be resuscitated using intravenous fluids and/or blood. In early trauma, all shock is assumed to be hypovolemic or obstructive. Vasoactive drugs are used only after these etiologies are ruled out and less common causes, such as myocardial dysfunction or neurogenic shock, are suspected.

d. **Disability:** When not absolutely contraindicated by the need for immediate endotracheal intubation, the **initial neurologic assessment** should be performed before the administration of sedative or neuromuscular-blocking drugs. Neurologic status is assessed by using the **Glasgow Coma Scale** (GCS) with attention to the signs and symptoms of increased ICP and brain herniation. The GCS defines neurologic impairment in terms of eye opening and verbal and motor responses. In addition, the examiner notes the pupillary response and diameter, presence of lateral deficits, and level of spinal motor and sensory deficits. The GCS scoring system provides a quantitative measure of neurologic status, progress, and prognosis with good interevaluator agreement.

Signs of **transtentorial brain herniation** include unilateral pupillary dilatation, unilateral fixed lateral gaze, sudden neurologic deterioration, contralateral hemiparesis, coma, hypertension, and bradycardia. **Emergency therapy** includes reassessment and treatment of extracranial insults such as hypoxia and shock, elevation of the HOB to 30°, mannitol infusion, brief hyperventilation, and surgical decompression.

e. **Exposure:** The patient is fully undressed and examined for any associated injuries while precautions are taken to avoid hypothermia.

2. **Secondary survey**

a. The secondary survey includes a more complete history and physical examination as well as laboratory and ancillary testing to diagnose the extent of TBI and associated injuries.

b. Commonly requested **investigations** include x-ray examination of the chest and pelvis, complete metabolic panel, complete blood count, clotting parameters (prothrombin time and partial thromboplastin time [PT/PTT]), serum osmolality, urinalysis, ethanol level, urine drug screen, and blood type and screen.
c. Unless contraindicated by need for immediate laparotomy or other procedure to prevent death from shock, all TBI patients should have a **non-contrast computed tomographic (CT) scan of the head and cervical spine** as soon as possible. In addition, a CT scan of the abdomen is often necessary.
d. If immediate craniotomy, laparotomy, thoracotomy, or other interventional procedure is required, the concurrent placement of an **IVC for monitoring and treating ICP** should be discussed with the neurosurgeon. Epidural and subdural hematomas that demonstrate significant mass effect are more amenable to surgical intervention than are other intracranial lesions.

**D. Critical care management after initial resuscitation**

1. **ICP monitoring**
   a. **Indications for placement of an ICP monitor** include an abnormal CT scan and GCS score of 3 to 8 after adequate resuscitation of shock and hypoxia or a normal CT scan and GCS score of 3 to 8 accompanied by 2 or more of the following: age > 40, posturing, or systolic BP (SBP) < 90 mm Hg.
   b. ICP monitoring using an **intraventricular catheter** is preferred because it provides dependable readings and allows therapeutic drainage of CSF.
2. **Treatment to reduce ICP and enhance CPP** should be correlated with the patient's neurologic examination, overall physiologic status, and state of CBF autoregulation. With TBI-induced loss of autoregulation, CBF becomes MAP dependent, which increases the risk of both cerebral ischemia when the MAP decreases and hyperemia (and edema) when the MAP goes up. If an ICP monitor is not in place, treatment aimed at decreasing ICP should be initiated when either neurologic deterioration occurs or signs of brain herniation are present.
   a. **Recommendations for optimizing CPP and ICP vary.** The **"Lund" approach** posits that the integrity of the blood–brain barrier (BBB) for salts is lost after TBI so that the goal of management is to limit the resulting edema and ICP elevation by using colloid with diuretics and maintaining ICP < 20 mm Hg. A CPP of as low as 50 mm Hg is acceptable if necessary to control ICP. The **Rosner approach** is based on the observation that cerebral autoregulation in the injured brain can often be present at a MAP of as high as 100 to 110 mm Hg. As MAP is increased beyond the normal limit of autoregulation, ICP falls and CPP rises. Consequently, the achievement of higher MAP and CPP is emphasized.

      In fact, the **optimization of MAP and CPP is best based on *individual* patient pressure-reactivity curves**. A 2005 study classified patients as having defective or intact autoregulation based on whether ICP rose more than 2 mm Hg in response to a 15 mm Hg increase in MAP (ICP/MAP slope > 0.13). The authors found that the pressure-passive, or **defective, autoregulation patients** (ICP/MAP slope > 0.13) seemed to **benefit from a lower ICP treatment threshold (20 mm Hg) and lower target CPP (50 to 60 mm Hg)**. In contrast, **pressure-active, or intact, autoregulation patients** (ICP/MAP slope < 0.13) appeared to **benefit from a**

**higher ICP treatment threshold (25 to 30 mm Hg) and higher target CPP (> 70 mm Hg)**. Although the BTF recommends maintaining CPP > 70 mm Hg in patients who have suspected loss of autoregulation, a recent study found that **optimizing CPP for individuals** at somewhere between 60 to 100 mm Hg maximized their brain tissue oxygenation ($PbtO_2$). The $PbtO_2$ worsened above or below this range.

b. **Therapy aimed at decreasing ICP** includes elevation of the HOB to 15° to 30°, control of seizure activity, ventilation to low-normal $PaCO_2$ (35 to 40 mm Hg), maintenance of normal body temperature, release of any obstruction to jugular outflow (such as circumferential endotracheal tube tape), assurance of optimal fluid resuscitation and overall physiologic status, and administration of sedatives and neuromuscular-blocking drugs as needed. If these measures fail to decrease ICP, additional therapies are provided in a first- and second-tier stepwise manner.

1. **First-tier therapy**
   a. Incremental **CSF drainage** via an IVC
   b. Diuresis with **mannitol**, 0.25 to 1.5 mg/kg over 10 minutes. Mannitol improves CBF by decreasing blood viscosity and transiently decreases ICP by decreasing brain edema. However, **mannitol-induced diuresis may cause hypotension**, especially in the early resuscitative phase when invasive monitoring is not yet in place and the extent of associated injuries is unknown. Therefore, euvolemia or mild hypervolemia is maintained and serum osmolarity is monitored and maintained < 320 mOsm/L during mannitol therapy. An alternative or supplement to mannitol is **hypertonic saline**, given in various concentrations and doses. Investigators found favorable effects on ICP and $PbtO_2$ when they administered 30 mL of 23.4% saline over 15 minutes to patients who had elevated ICP (> 20 mm Hg for > 20 minutes) despite CSF drainage, sedation, and mild hypocarbia.
   c. **Moderate hyperventilation** ($PaCO_2$ 35 to 40 mm Hg) decreases ICP by decreasing CBF. Therefore, hyperventilation **should be used briefly** to treat either acute neurologic deterioration or increased ICP that is refractory to CSF drainage and mannitol administration.
2. **Second-tier therapy**
   a. Brief periods of **aggressive hyperventilation** ($PaCO_2$ 30 mm Hg) may be required for increased ICP that is refractory to first-tier therapy. This is most appropriate as a bridge to surgical decompression. When aggressive hyperventilation is used, **monitoring of jugular venous oxygen saturation ($SvjO_2$) or $PbtO_2$ is recommended** to assess the effect of the decrease in CBF on $CMRO_2$. **$SvjO_2$** ≤ 55% is consistent with ischemic levels of CBF; $SvjO_2$ of 55% to 60% is consistent with hypoperfusion; and $SvjO_2$ of 60% to 75% is within the normal range. $SvjO_2$ of 75% to 90% is indicative of hyperperfusion or impaired oxygen utilization; and $SvjO_2$ ≥ 90% is indicative of cessation of flow and brain death. For **$PbtO_2$**, normal values are between 25 and 30 mm Hg. $SvjO_2$ and $PbtO_2$ changes in response to therapeutic interventions provide a useful guide to the adequacy and appropriateness of these interventions and the need for alternatives.

b. **High-dose barbiturate therapy** reduces ICP by decreasing CBF in parallel with $CMRO_2$. It is reserved for hemodynamically stable, salvageable patients who have increased ICP that is refractory to first-tier therapy. **Pentobarbital** is typically administered in a loading dose 10 mg/kg over 30 minute followed by boluses of 5 mg/kg/hour for 3 hours and then an infusion of 1 to 3 mg/kg/hour. Complications include myocardial depression and hypotension.

c. **Decompressive craniectomy** has been shown to decrease ICP and may improve outcome in younger patients who deteriorate within 48 hours of injury.

3. **Blood pressure monitoring and treatment**
   a. Insertion of an arterial catheter allows accurate, real-time measurement of MAP and regular arterial blood gas sampling. Severe TBI patients cannot be appropriately managed in an ICU without direct BP measurement. To estimate CPP accurately, the **transducer is placed at the level of the circle of Willis** in line with the external auditory meatus.
   b. Adequate MAP is achieved by infusing isotonic fluids to **maintain euvolemia or mild hypervolemia**. If hypotension persists despite adequate volume resuscitation, vasoactive medications are added. The need for vasoactive drugs should prompt consideration of other critical illness such as ongoing hemorrhage, sepsis, cardiac dysfunction, neurogenic shock, and adrenal insufficiency.
4. **Monitoring intravascular volume status**
   a. Insertion of a central venous catheter allows continuous measurement of **central venous pressure** (CVP), which may help assess intravascular volume status. **Arterial pulse pressure respiratory variation** (PPRV) is more precise in well-sedated, non-dysrhythmic patients receiving at least 8 mL/kg tidal volume. **Ultrasonic assessment of respiratory vena cava change** allows rapid bedside volume assessment.
   b. Insertion of a **urinary catheter** allows precise measurement of urine volume and content. An additional indicator of volume status, measurement of urine output also facilitates the diagnosis of conditions of altered urine production that are associated with TBI such as diabetes insipidus (DI), syndrome of inappropriate antidiuretic hormone (SIADH) secretion, and cerebral salt wasting (CSW) syndrome.
   c. Insertion of a pulmonary artery (PA) catheter is rarely, if ever, indicated for TBI patients.
5. **Seizure prophylaxis** is recommended during the first week after TBI, particularly in high-risk patients including those who have a GCS score < 10; cortical contusion; depressed skull fracture; subdural, epidural, or intracerebral hematoma; penetrating head trauma; or seizure occurring within the first 24 hours after injury. Seizure prophylaxis has reduced the risk of seizures in the first week after injury, but has not been demonstrated to improve outcomes. **Phenytoin** with a loading dose 15 mg/kg over 20 minutes followed by 5 to 7 mg/kg/day or **fosphenytoin** with a "phenytoin equivalent (PE)" loading dose of 15 to 20 mg/kg followed by 4 to 6 PE mg/kg/day is recommended. **Adverse effects** of phenytoin include fever and rash. **Levetiracetam** for early TBI seizure prophylaxis is supported only by a small prospective study that reported improved outcomes for levetiracetam compared to phenytoin-treated patients. This study also reported that 20% more patients died in the

levetiracetam group, but because the study was underpowered, this difference was not statistically significant. Controversy persists about using this drug in TBI patients.

6. **Nutritional support** is required to facilitate recovery and should be initiated as soon as possible. By 1 week after injury, 15% of total calories should come from protein. The BTF recommends **instituting full nutritional replacement by day 7 after the initial injury**. Enteral feeding is preferred, and jejunal placement of the feeding tube protects against aspiration and gastric intolerance. **Stress ulcer prophylaxis** should be provided using $H_2$ antagonists such as famotidine, 20 mg every 12 hours, or proton pump inhibitors such as pantoprazole, 40 mg daily.
7. **Hyperglycemia** has been shown in animal studies to exacerbate neurologic outcome after brain injury. Prospective randomized trials in critically ill patients have produced conflicting results about intensive insulin therapy to maintain glucose levels of 80 to 100 mg/dL. Retrospective data in TBI patients suggest that early hyperglycemia is associated with poor outcomes and that nutritional support does not increase serum glucose concentrations. Hyperglycemia > 200 mg/dL should be avoided, but attempts to achieve euglycemia (80 to 110 mg/dL) may create excess risk for hypoglycemic episodes and possibly early increases in ICP. To balance these risks, maintaining a serum glucose level of between 120 and 160 mg/dL is probably the safest course of action although there is no clear guidance for TBI patients.
8. **Fever** increases ICP and cerebral metabolism and may worsen outcome in TBI patients. Fever should be treated with cooling blankets, acetaminophen, and evaluation for infection and pharmacologic causes (e.g., phenytoin). Studies of the protective effects of hypothermia in TBI have been inconclusive and are ongoing. Cooling may be effective as a second-tier therapy for ICP crisis.
9. **Steroids** do not benefit, and may harm, TBI patients.
10. Trials of drugs intended to reduce oxidative damage, antagonize NMDA receptors, or diminish secondary injury through other mechanisms have yielded uniformly negative results. As of this writing, progesterone is being studied in TBI patients.
11. **Prophylaxis against deep vein thrombosis** (DVT) with pneumatic compression devices should be initiated as soon as possible. Most patients can begin DVT chemoprophylaxis within 48 hours of injury. Intensivists should make the decision to initiate chemoprophylaxis in consultation with neurosurgeons and traumatologists.
12. **Coagulopathy**, whether pharmacologic ( from warfarin or platelet antagonists) or pathologic ( from liver dysfunction), should be corrected.

## II. STROKE

### A. Ischemic stroke

#### 1. Pathophysiology

Ischemic stroke results from cardioembolic, large-vessel atherothrombotic, or small-vessel (lacunar infarct) disease. Lacunar infarcts that occur in the basal ganglia and brain stem may remain subclinical or may produce dementia through multiple repeated events.

#### 2. Diagnosis

The clinical presentation of ischemic stroke consists mainly of **focal neurologic deficits**. Headache and immediately decreased level of consciousness are more likely to accompany hemorrhagic stroke. A **non-contrast CT**

**scan** of the head differentiates between the two. The **differential diagnosis** of stroke includes migraine, postictal deficit, hypoglycemia, metabolic derangements, infection, and, when accompanied by chest or back pain, aortic dissection.

3. **Intravenous thrombolytic therapy** with **recombinant tissue plasminogen activator** (rtPA) has been shown to benefit patients after ischemic stroke. The **randomized, double-blind, placebo-controlled trial** conducted by the National Institute of Neurologic Disorders and Stroke (NINDS) **showed that rtPA administered within 3 hours of symptom onset resulted in a 12% absolute and 32% relative improvement in outcome** with rtPA patients more likely to have minimal or no disability 3 months after stroke. Patients in the treatment group experienced a tenfold greater incidence of symptomatic intracerebral hemorrhage (ICH, 6.4% vs. 0.6%), but there was no significant difference in intergroup mortality. A Cochrane review of this and other thrombolysis trials for ischemic stroke found that **thrombolytic therapy reduced the combined endpoint of death or dependence**, and that rtPA may have advantages over other thrombolytic drugs. The ECASS-III trial extended the rtPA "benefit window" to 4.5 hours. Nonetheless, the earlier rtPA is given, the better the trade-off between benefit and harm. Although initially promising, the reperfusion strategy that uses perfusion/diffusion mismatch on magnetic resonance imaging (MRI) to guide late rtPA treatment remains of unproven benefit.

   In all but the most unusual circumstances, the decision to administer rtPA should be made in consultation with neurologists. When possible, an interventional neuroradiologist should also participate in treatment decisions because certain clinical and imaging features (e.g., late presentation, visualized intra-arterial clot, late diffusion–perfusion mismatch on MRI, etc.) may favor the substitution or addition of an intra-arterial approach to re-establish perfusion. As of this writing, indications for different intra-arterial therapies are being actively investigated.

   a. **rtPA treatment criteria**

      In order to minimize the risk of ICH and other complications, patients who receive rtPA for stroke must meet the stringent criteria derived from NINDS and subsequent trials. Absolute and relative contraindications to rtPA administration must be considered as well.

      1. **Medical history criteria**
         a. The patient **must be > 18 years of age**
         b. The patient **must receive therapy within 4.5 hours of symptom onset**. Patients who cannot precisely recall the onset of symptoms (e.g., those who fell asleep more than 4.5 hours before possible drug administration and awakened with symptoms) are ineligible for rtPA. Some clinicians perform MRI in these patients in order to identify diffusion/perfusion mismatch that may be amenable to later-than-normal intravenous or intra-arterial treatment. Posterior circulation strokes are potentially treatable with intravenous or interventional strategies outside the usual time windows.
      2. **Clinical examination criteria**
         a. Significant, stable (i.e., non-resolving) **deficit**
         b. **SBP < 185 mm Hg and diastolic BP (DBP) < 110 mm Hg**. A trial of nitroglycerin (1 to 2 inches of paste); labetalol, 10 to 20 mg over 1 to 2 minutes repeated once in 10 minutes; nicardipine, 5 to

10 mg; or enalapril, 0.625 to 1.25 mg over 5 minutes, may be attempted to lower the BP. Patients usually should not receive thrombolysis if these measures do not keep the BP below 185/110 mm Hg.

3. **Laboratory criteria**
   a. Platelets must be >100,000/mm$^3$.
   b. Prothrombin time (PT) must be < 15 seconds; international normalized ratio (INR) < 1.7, and partial thromboplastin time (PTT) must be normal.
4. **Radiographic criteria**
   a. **No evidence of ICH or mass lesion on CT scan or MRI**.
   b. Review of NINDS data about patients who developed symptomatic ICH showed that patients who had CT evidence of baseline cerebral edema had double the risk of developing ICH.
5. Because criteria for rtPA administration are so strict, relatively few stroke patients are eligible to receive therapy. **Means of increasing application of this beneficial therapy** include public health campaigns emphasizing the urgency of stroke treatment and comparing stroke to heart attack (i.e., "brain attack") and the creation of organized multidisciplinary stroke teams.

b. **Absolute contraindications**
1. Symptoms suggestive of subarachnoid hemorrhage (SAH)
2. Seizures at the onset of the event as they may mimic stroke
3. Stroke, serious head trauma, intracranial or intraspinal surgery within the past 3 months
4. History of ICH, SAH, or arterial venous malformation (AVM) of the brain
5. Oral anticoagulation with warfarin or heparin within the previous 48 hours or significant coagulation abnormalities
6. Genetically predetermined coagulation disorder (Von Willebrand's disease).

c. **Relative contraindications**
There is some disagreement about the importance of different relative contraindications, so careful weighing of the risks and benefits of rtPA must be made in all cases.
1. Medical: major surgery or trauma within the last 2 weeks; gastrointestinal or genitourinary hemorrhage within the last 3 weeks; arterial puncture at a non-compressible site within the last week; lumbar puncture within the last 3 weeks; postmyocardial infarction (MI) pericarditis
2. Laboratory: serum glucose < 50 mg/dL or > 400 mg/dL. A hypoglycemic etiology of neurologic deficits must be strongly considered, especially if improvement results from administration of glucose.
3. Pregnancy
4. Marked lethargy or coma
5. Clinical or CT evidence suggesting infarction involving more than one-third of the middle cerebral artery (MCA) territory because it increases the risk of ICH

d. **Mode of administration**
1. If indicated, and consent is obtained, **rtPA, 0.9 mg/kg**, is administered intravenously with 10% as a bolus and 90% as an infusion administered over 1 hour.
2. The drug should be administered in the ED if transfer to the ICU will delay therapy.
3. During therapy, patients are monitored for evidence of ICH and neurologic deterioration.

4. After therapy, patients are admitted to the ICU for monitoring of neurologic status and BP over the next 24 to 48 hours.
5. BP is checked every 15 minutes for the first 2 hours and every 30 minutes thereafter.
6. Anticoagulants and antiplatelet drugs are contraindicated for 24 hours after rtPA administration.
7. **SBP > 180 mm Hg or DBP > 110 mm Hg** should be treated with **labetalol**, 10 mg, repeated or doubled every 10 minutes to a total dose of 150 mg followed by an infusion of 1 to 8 mg/minute, if necessary, or **enalapril**, 0.625 to 1.25 mg over 5 minutes.
8. Severe **refractory hypertension** after rtPA (DBP > 140 mm Hg) can be treated with infusions of **nicardipine**, 5 to 15 mg/hour, or **fenoldopam**, 0.1 to 0.3 mg/kg/minute.

4. **Non-thrombolytic therapy**

The **principles of care for patients who are not rtPA candidates** after ischemic stroke emphasize prevention of secondary brain injury, optimization of CBF, prevention of infarct extension and hemorrhagic conversion, prevention of poststroke complications such as pulmonary embolus and aspiration pneumonia, early mobilization and rehabilitation, and attention to psychiatric and social consequences of stroke, including depression and the need for assistance with daily activities.

a. **Medical treatment**

1. Airway management, hemodynamic monitoring, and treatment of increased ICP are provided as outlined above in the section on TBI.
2. **Antihypertensive therapy is generally avoided** because patients tend to have long-term changes in CBF autoregulation after ischemic stroke, which result in optimal CBF at higher MAPs than for healthy, normotensive individuals. As a result, aggressive antihypertensive therapy may exacerbate ischemia by decreasing CBF. A generally **accepted threshold for the administration of antihypertensive therapies** is **SBP > 220 mm Hg**, **DBP > 120 mm Hg**, or **MAP > 130 mm Hg**. The protocol outlined above for treatment of hypertension after rtPA can also be used to control severe hypertension in patients who have not received rtPA.
3. In the absence of hemorrhage on CT scan, **aspirin**, 325 mg followed by 81 to 160 mg/day, is administered by mouth as **antiplatelet therapy**.
4. Multiple studies have failed to show any benefit from heparin administration, although **patients who have atrial fibrillation (A-fib) are usually anticoagulated**.
5. Hyperglycemia worsens neurologic outcome. **Glycemic control should be performed** as recommended above for TBI.
6. **Seizures** are treated with phenytoin, loading dose 15 mg/kg over 20 minute followed by 5 to 7 mg/kg/day, or fosphenytoin, loading dose "phenytoin equivalent (PE)" 15 to 20 mg/kg, then 4 to 6 PE mg/kg/day.
7. **DVT prophylaxis** is provided using pneumatic compression and low molecular weight heparin (LMWH) such as enoxaparin, 0.5 mg/kg

subcutaneously twice a day, or unfractionated heparin, 5,000 units subcutaneously three times a day.

8. **Nutrition** is provided either **by mouth** after evaluation of airway reflexes and adequacy of swallowing or by **feeding tube**, preferably by feeding tube into the jejunum for improved absorption and to decrease the risk of aspiration.
9. Although **the HOB is often elevated** to 30° to facilitate venous drainage and prevent aspiration, there is some evidence that lowering the HOB to 15° in patients who have normal ICP improves CBF and neurologic function.
10. **Rehabilitation and psychiatric evaluation** are essential. Stroke is often complicated by depression. Treatment of depression and other psychiatric comorbidities facilitates rehabilitation and improves functional status.

b. **Neurosurgical consultation for decompressive craniectomy** may be considered, depending upon patient (if known) and family preferences, for life-threatening cerebral edema and herniation resulting from panhemispheric strokes. Treatment of these complications of stroke applies the same principles as those outlined for TBI.

**B. Hemorrhagic stroke**

1. **Pathophysiology**

Hemorrhagic stroke and intracerebral hemorrhage are thought to be **caused primarily by hypertensive cerebrovascular disease** and are most commonly seen in subcortical brain regions. Cortical ICH often results from amyloid angiopathy, which is increasing in incidence as the population ages. Hemorrhagic stroke can be devastating with as few as 30% of patients able to live independently 6 months after the event.

Mass effect has traditionally been thought to play a major role in the pathophysiology of ICH. Recent animal data indicate that the **most important pathophysiologic process** may be **dissection of the hematoma along tissue planes followed by neurotoxicity and cerebral edema resulting from blood proteins and their breakdown products**. Early enlargement of the hematoma and rebleeding occur in about 40% of ICH patients, which can worsen the prognosis significantly.

2. **Diagnosis**

Hemorrhagic stroke typically presents with headache, nausea, vomiting, seizures, and focal neurologic deficits. Larger hemorrhagic strokes cause lethargy, stupor, and coma. A non-contrast CT scan of the head will demonstrate the location and the extent of the intracranial bleeding.

3. **Treatment**

a. **Rapid assessment to detect treatable conditions** that may mimic hemorrhagic stroke is essential in addition to support of the airway, breathing, and circulation; seizure control; reversal of iatrogenic and spontaneous coagulopathy; and general neurointensive care.

b. **Treatable conditions that mimic ICH** include hypoglycemia and other metabolic abnormalities including disorders of sodium and calcium homeostasis; meningitis, encephalitis, sepsis, and shock; toxins, illicit drugs, ethanol, environmental and occupational drugs, and medications prescribed or administered by physicians and nurses. Many of these processes can be detected by simple bedside tests and are easily treated. Hypoglycemic patients should receive glucose, 25 g, and it is reasonable to administer thiamine, 100 mg, and naloxone, 1 mg, to patients who are suspected of ethanol or opiate abuse.

c. **Coagulopathy must be corrected** as rapidly as possible.
   1. **Fresh frozen plasma** (FFP), 15 mL/kg, reverses coagulopathy. As this may require an infusion of a liter or more of FFP, volume status must be carefully monitored.
   2. Most neurologists consider **prothrombin complex concentrates**, 20 units/kg over 20 minute, and **recombinant activated factor VIIa** (rFVIIa) the standard of care for reversal of warfarin-associated ICH.
   3. Long-term correction of coagulopathy is achieved by administering **vitamin K**, 10 mg a day for 3 days. Intravenous administration results in more rapid correction than when given by mouth and the small risk of anaphylaxis is less important than the danger of ongoing CNS bleeding. Patients who have ICH related to rtPA administration may also be treated with FFP although there are no data regarding efficacy to support any specific therapy.
   4. **Reversal of the antiplatelet effects of aspirin**, **clopidogrel**, and other platelet antagonists should be attempted with **DDAVP**, 0.3 mcg/kg over 20 minutes, and the transfusion of either a single pheresis platelet pack or 6 units of matched donor **platelets**. As aspirin binds irreversibly to platelets, it is easier to antagonize with platelet transfusions than clopidogrel that binds platelets as they are infused.

d. **Seizures** are treated with **lorazepam**, 2 mg, **phenytoin**, loading dose 15 mg/kg over 20 minutes followed by 5 to 7 mg/kg/day, or **fosphenytoin**, loading dose "phenytoin equivalent (PE)" 15 to 20 mg/kg followed by 4 to 6 PE mg/kg/day. The American Heart Association (AHA) recommends that seizure prophylaxis with phenytoin be maintained for 1 month in ICH patients.

e. **Euvolemia is maintained** with infusions of isotonic intravenous solutions. Hypotonic fluids may exacerbate cerebral edema, and glucose-containing solutions are avoided unless patients are hypoglycemic.

f. **Treatment of elevated blood pressure** in ICH is the subject of controversy. Concerns about exacerbating hemorrhage must be weighed against the possibility that antihypertensive drugs may reduce CBF and worsen ischemia. As with ischemic stroke patients, many hemorrhagic stroke patients have altered autoregulation and require a higher MAP to maintain CBF. In general, **a MAP cutoff of 130 mm Hg is considered a trigger for treating hypertension**. Patients who have had craniotomies should be maintained at MAP < 100 mm Hg. Labetalol or enalapril may be used as described above to reduce MAP by approximately 10% to 15%.

h. **Normothermia** should be maintained.

i. **Indications for placement of an IVC** for ICP monitoring and therapeutic CSF drainage include intraventricular hemorrhage and hydrocephalus. ICP monitoring may also be instituted for deteriorating or comatose patients who are thought to be salvageable. Prophylactic antibiotics, microbiologic monitoring, and weekly changes have been recommended to decrease the risk of catheter infection.

j. Multiple trials over 45 years have found **no benefit from craniotomy and evacuation of ICH**. Indications for surgery that have traditionally been accepted or may be inferred from recent trials include cerebellar

hematoma > 3 $cm^2$ or accompanied by neurologic deterioration, large and accessible cortical hematomas (< 1 cm from cortical surface), or neurologic deterioration. Younger patients are more likely to benefit from surgery than are older patients.

k. Trials of minimally invasive techniques using **endoscopic evacuation of hematomas** have been inconclusive, although it is possible that refinements in equipment and technique may result in improved outcomes.

l. Pneumatic compressive devices are recommended for **DVT prophylaxis**. Most neurosurgeons begin **chemoprophylaxis** 48 hours after the last bleeding episode or surgery.

m. **Gastric ulcer prophylaxis** is provided by $H_2$ antagonists such as famotidine, 20 mg every 12 hours, or proton-pump inhibitors such pantoprazole, 40 mg daily.

n. **Steroids are contraindicated** in ICH.

o. Critical care issues such as maintenance of CPP, treatment of elevated ICP, the role of barbiturate therapy, and medical complications of ICH are the same as for TBI.

## III. BRAIN DEATH AND ORGAN DONATION

### A. The importance of brain death and organ donation

**Brain death is accepted as a legal definition of death** in the United States and most other countries. The diagnosis of brain death reduces ambiguity for family members, spares medical resources by allowing discontinuation of artificial support of organ function, and facilitates organ donation. **Appropriate counseling of family members** is essential in helping them understand and accept the reality of death despite the maintenance of vital signs through artificial means. **Organ procurement organization (OPO) coordinators assist in this process** by counseling family members, clarifying legal issues, helping to obtain consent, assisting with care for the brain-dead organ donor, and arranging organ harvest. During this process, **the focus of care is shifted from resuscitation to organ preservation** for harvest and transplantation.

### B. Physiology of brain death

Brain death entails cessation of CBF with resultant loss of brain function. The final common pathway for brain death is **loss of cerebral perfusion with cessation of brain stem activity**. The process proceeds in a rostral-to-caudal direction. Loss of blood flow to the medulla is often accompanied by a catecholamine surge that first increases MAP. This is then followed by hemodynamic instability and even frank hypotension. Metabolic derangements ensue, which result from ischemia or infarction of the pituitary gland. The most important consequence of pituitary dysfunction is central diabetes insipidus (DI) which requires replacement of antidiuretic hormone for maintenance of sodium and fluid balance.

### C. Diagnosis of brain death

1. **Clinical signs of brain death** include **complete unresponsiveness, apnea, and loss of brain stem reflexes**. Cessation of cortical function often precedes cessation of brain stem activity, but is not sufficient for diagnosis of brain death. Patients may retain brain stem function indefinitely. **Brain death can only be diagnosed when the cause of coma has been identified** such as TBI, ICH, or SAH **and conditions that mimic brain death have been ruled out clinically**. These conditions include the locked-in syndrome, severe hypothermia, severe intoxication (including anesthetic and neuromuscular-blocking drugs), and Guillian-Barre syndrome with peripheral and

cranial nerve involvement. **Brain death is diagnosed clinically**, and need for confirmation with ancillary tests is based on patient status and age. **Spinal reflexes are often maintained** and do not negate the diagnosis of brain death. **Demonstration of the absence of brain stem reflexes and confirmation of apnea are central to the diagnosis.**

2. The **apnea test** is performed as follows:
   a. The patient is **preoxygenated** with 100% oxygen.
   b. **Apneic oxygenation** is provided at 10 to 15 L/minute through a catheter placed in the endotracheal tube to the level of the carina.
   c. The patient is **disconnected from the ventilator** and **observed for spontaneous ventilation**.
   d. $PaCO_2$ typically rises at 3 mm Hg per minute. In the United States, **apnea in the presence of a rise of $PCO_2$ to 60 mm Hg or an increase of 20 mm Hg from baseline** is **considered confirmatory.** The United Kingdom Code of Practice recommends a 10-minute apnea test.
3. **Confirmatory test results** for brain death include
   a. **Isoelectric EEG**
   b. **Absence of cerebral perfusion** demonstrated by cerebral angiography, technetium-99 scanning, or transcranial Doppler ultrasonography

D. **Care of the brain-dead organ donor** is accomplished in cooperation with the local OPO coordinator.
1. **Exclusion criteria for organ donation** may vary by organ and by geographic region. This should be discussed with the OPO coordinator. **Absolute contraindications** include, but are not limited to, the presence of **human immunodeficiency virus** (HIV) and **prion disease**.
2. **Screening tests** for organ donors include
   a. HIV, hepatitis B, hepatitis C, cytomegalic inclusion virus (CMV), Epstein-Barr virus (EBV), and human T-cell lymphotrophic 1 (HTLV-1) serology
   b. Blood group (ABO) and human leukocyte antigen (HLA) tissue typing
   c. Blood, sputum, and urine cultures
   d. Complete blood count (CBC), metabolic panel, urinalysis, and arterial blood gases
   e. Organ-specific tests as requested by the OPO
3. **Perioperative monitoring** includes ECG, pulse oximetry, temperature, urine output, direct arterial BP, CVP and/or PA pressure. Because the process of organ harvest requires sequential vessel ligation, the arterial catheter is inserted in the left arm and central venous or PA catheterization is performed on the right.
4. **Optimal physiologic goals** for organ donors include
   a. MAP > 65 mm Hg; SBP > 90 mm Hg
   b. CVP 8 to 12 mm Hg; PA occlusion pressure (PAOP) 10 to 15 mm Hg
   c. HR 60 to 100 bpm
   d. Cardiac index > 2.1 L/minute/$m^2$
   e. Urine output 1 to 2 mL/kg/hour; volume replacement = 50 mL/hour more than urine output
   f. Temperature 97 to 100°F or 36 to 37.8°C
5. **Therapeutic maneuvers** include
   a. Antiarrhythmic drugs for the treatment of arrhythmia
   b. Isoproterenol or cardiac pacing for the treatment of severe bradycardia
   c. Isotonic intravenous fluids to maintain adequate perfusion
   d. Vasoactive drugs are used if hypotension persists after achieving CVP of 10 mm Hg.

1. Dopamine, 5 to 15 mcg/kg/minute, if CO is normal or elevated.
2. Dobutamine, 5 to 10 mcg/kg/minute, is added if CO is decreased. For patients who have a decrease in CO and an increase in systemic vascular resistance (SVR), dobutamine is the drug of choice. Dobutamine may, however, cause hypotension through its beta-2-adrenergic agonist effect as well as tachyarrhythmias, especially when combined with dopamine.
3. Phenylephrine, 100 mcg loading dose followed by an infusion of 50 to 150 mcg/minute, may be added to dobutamine to counteract its vasodilating effects.

e. **Diabetes insipidus** is marked by increased urine output (> 7 mL/kg/hour), decreased urine specific gravity (< 1.010), urine osmolarity < serum osmolarity, hypernatremia (>150 mEq/L), and serum hyperosmolarity (> 295 mOsm/L). **Treatment** of DI includes infusion of D5W to replace free water deficits and maintain serum Na < 155 mEq/L. **Vasopressin**, 1 unit loading dose followed by 0.5 to 4 units/hour, or **desmopressin** is given to maintain urine output at 1 to 2 mL/kg/hour.

f. **Insulin infusion**, 2 to 7 units/hour, may be needed to maintain serum glucose between 80 and 160 mg/dL. Potassium replacement may be required in conjunction with the insulin infusion to maintain a serum level > 4 mEq/L.

g. **Triiodothyronine**, 4 mcg intravenously loading dose followed by 3 mcg/hour, is administered to maintain euthyroid status.

h. **Mechanical ventilation** parameters are selected to minimize lung injury.

1. Ventilation rate is set to maintain normocapnia. Triggered breaths can result from cardiac activity and may be confused with spontaneous ventilation.
2. Tidal volume is set at 6 to 8 mL/kg. Pressure-controlled ventilation may be used alternatively to minimize barotrauma. Some OPOs recommend airway pressure release ventilation (APRV).
3. PEEP should be adjusted to minimize oxygen toxicity and plateau airway pressure.
4. $FiO_2$ is reduced to the minimum necessary to maintain $PaO_2$ > 90 mm Hg (target $FiO_2$ < 40%).
5. Hypokalemia, hypophosphatemia, and hypocalcemia are common electrolyte abnormalities that must be monitored and corrected.
6. Packed red blood cells (PRBCs) are transfused to maintain hemoglobin ≥ 9 g/dL.
7. FFP and platelets are transfused to correct coagulopathy and bleeding disorders.
8. Methylprednisolone, 15 mg/kg, and an antibiotic regimen are usually recommended by the OPO coordinator.

E. **Organ harvesting** is typically performed by different teams representing the various potential recipients. The OPO coordinates the process, which is done in steps designed to minimize warm ischemic time for each organ. Muscle relaxants are often used to facilitate organ harvest and prevent reflex movements. After opening the thoracoabdominal cavity, the bowel is retracted, organ attachments are incised, and major vessels are cannulated for infusion of cold organ preservative solution. The aorta is then cross-clamped, preservative solution is infused, and the organs are removed. Mechanical ventilation is terminated after preservative solution is administered and cardioplegia occurs.

F. **Non-heart-beating donors (NHBDs)** are non-brain-dead patients who have irreversible disease processes from whom resuscitative care had been withdrawn because of advanced directives or upon request of the next of kin. **Organ harvesting is initiated immediately after death**. Success rates for renal transplants from NHBD's are similar to those for kidneys harvested from brain-dead donors. Livers and lungs may also be suitable. Corneas, bone, skin, and heart valves are all relatively durable and can be harvested up to 24 hours after death. Because **ethical controversies** surround the issue of NHBDs, physicians should consult with the hospital ethicists, risk management personnel, and local OPO when withdrawal of resuscitative care from a potential NHBD is being considered.

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## *Suggested Internet Sites*

American Stroke Association. Guidelines and other resources for ischemic and traumatic stroke: http://www.strokeassociation.org/presenter.jhtml?identifier=1200037

Eastern Association for the Surgery of Trauma. Updated evidence-based guidelines for trauma management, including TBI: http://www.east.org/Portal/Default.aspx?tabid=57

Emcrit podcast on reversing anticoagulation and antiplatelet agents in TBI and ICH: http://blog.emcrit.org/podcasts/reversal-head-bleeds/

The Brain Trauma Foundation. Evidence-based guidelines and other resources for managing TBI: http://www.braintrauma.org/

# 27 Information Technology: Accessing and Exchanging Information

**Klaus Ulrich Klein and Kristin Engelhard**

## Chapter Highlights

Throughout history, medical education and information have been dominated by the classical textbook. Within the last three decades, however, the World Wide Web has become a parallel bibliographic universe. As the amount of available information increases, it becomes more and more difficult to keep up with the latest developments in medicine. This chapter aims to present hands-on instructions for using the World Wide Web to access, assess, and exchange information in neuroanesthesia.

**I. ASKING QUESTIONS**

Before starting to search, the right questions have to be asked. Clinical questions can be divided into background and foreground questions (Fig. 27.1). Determining the type of question will help to select the best resource for the answer.

**A. Background questions** ask for general information and can be best answered by textbooks, handbooks, and certain databases such as *uptodate.com* and *pharmacopeia.com*. Note that general textbooks, in contrast to the Internet, are very often the best option to find general information. For example, the question "Effects of sevoflurane on cerebral blood flow and metabolism?" is most quickly looked up in a classical textbook. Today many printed books are available as electronic textbooks and may be accessible in academic institutions. *Pubmed.org* can be useful for quickly finding reviews, for example, "pathophysiology of secondary brain damage after traumatic brain injury." Please also access collections of classical papers. The following textbooks are recommended for the search of background questions in neuroanesthesia: (1) Cottrell/Smith: Anesthesia and Neurosurgery; (2) Miller: Miller's Anesthesia, section on Neurosurgical Anesthesia; (3) Cottrell/Young: Cottrell and Young's Neuroanesthesia: Expert Consult; and (4) Gupta/Gelb: Essentials of Neuroanesthesia and Neurointensive Care.

**B. Foreground questions** ask for detailed knowledge aimed at finding relationships among a patient, a condition, an exposure, or an outcome (Fig. 27.2). Practitioners of evidence-based medicine often use the PICO(M) structure

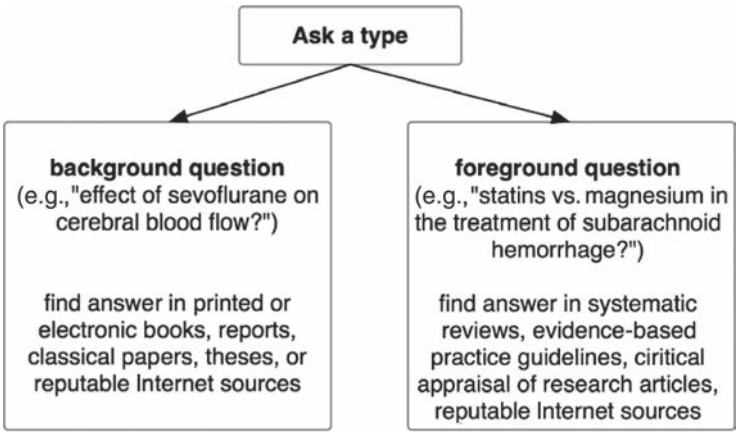


**FIGURE 27.1** Before searching, you have to ask the right question. A background question asks for general knowledge that best can be answered by a classical textbook. In contrast, a foreground question usually requires a specific evidence-based medicine search.

to outline foreground questions where P = patient/population/problem; I = intervention/risk factor/exposure; C = comparison/control; O = outcome; M = method. For example: "Do statins in comparison to magnesium improve the rate of ischemic events in young subjects after traumatic brain injury?" This question may be answered by searching for evidence in prefiltered resources, such as clinical practice guidelines (*guideline.gov*;

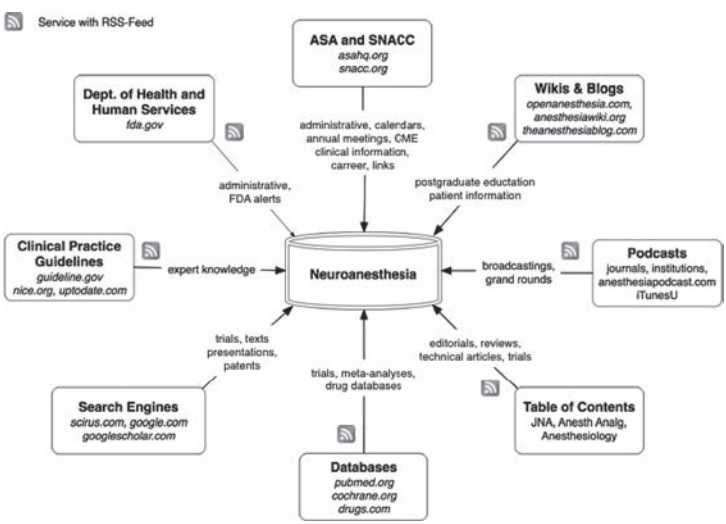


**FIGURE 27.2** Online services for information retrieval. ASA, American Society of Anesthesiologists; SNACC, Society for Neuroscience in Anesthesiology and Critical Care; FDA, Food and Drug Administration.

*tripdatabase.com*) or databases (*thecochranelibrary.com*). Visit the Center for Evidence-Based Medicine (*cebm.net*) for a description of the strength of evidence (systematic reviews or meta-analyses > randomized control trials > cohort studies > cross-sectional studies > case reports or case studies). Often is it very helpful to ask the medical librarian who has the professional expertise to frame and answer extensive foreground questions.

## II. SOCIETIES AND INSTITUTIONS

In addition to other specialty organizations (e.g., American Academy of Neurology, American Association of Neurological Surgeons, Society of Critical Care Medicine), the American Society of Anesthesiologists (ASA) and Society for Neuroscience in Anesthesiology and Critical Care (SNACC) host comprehensive online resources for neuroanesthesiologists and neurointensivists including administrative information, updated bibliographies, continuous medical information, clinical information, career information, links, and more.

## III. MEDICAL SEARCH ENGINES

**A. Google.** Implemented in 1996, Google is by far the most widely used, largest, and fastest free search engine in the world and is an acceptable search engine for common and rare medical conditions. Google provides very global searches and returns articles from the lay press, medical journals, magazines, and organizations. In 2008, Google developed Google Health in response to the fact that 25% of all Internet searches are health related. Successful searching depends on the following general advice: (1) search terms are not case sensitive; (2) enter most important term first; (3) quotation marks define conjoined words; (4) operator * (asterisk) may be used as a placeholder; (5) operators AND or OR specify search; (6) include (+) or exclude (–) terms. Note that Google provides helpful tips on how to search most effectively using their service.

**B. Google Scholar.** This attractive, free, and easy to use offspring searches the full text of peer-reviewed scholarly journal articles and not only the title at publishers' Web sites and abstracts provided by the National Library of Medicine (NLM) through PubMed. Google Scholar is thought to provide increased access to grey literature as it retrieves more than journal articles and includes archives, conference proceedings, and institutional repositories. This service weights the relevance of articles by indicating links to other publications and therefore does not include very recent information. Google Scholar should be used in conjunction with PubMed rather than as a replacement.

**C. PubMed.** One of 23 databases, PubMed is summarized as Entrez in the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM). Searches with regard to genetics, genomics, and proteomics should be performed at Entrez. PubMed's search interface uses the primary database MEDLINE that contains 19 million citations from the 1940s to present. This free service is the primary search engine for physicians who seek information on experimental and clinical research or unusual cases. Bear in mind the following advice: (1) implicitly use Medical Subject Heading (MeSH) terms as searching the correct term makes all the difference; (2) use limit options and Boolean operators (AND, OR, NOR, NOT) to specify your search. Please note the excellent published tutorials explaining how best to search in PubMed. My NCBI provides a valuable storage area for searches of articles you are retrieving, allowing you to set e-mail alerts for new publications in your area of interest.

**D. Scirus** is a free and promising alternative scientific search engine published by Elsevier. Journal sources include BioMed Central, PubMed,

ScienceDirect, Project Euclid, Scitation, SIAM, and special sources, Web pages, courseware, and others. Searches may be specifically filtered to find files such as text files, powerpoint presentations, and patents. Additional alternative search engines are *bing.com*, *clusty.com* (now *yippy.com*), *dogpile.com*, *omni.ac.uk*.

## IV. CLINICAL PRACTICE GUIDELINES (CPG)

A. **National Guideline Clearinghouse.** This excellent compilation of the Department of Health and Human Services (*guideline.gov*) is the most comprehensive CPG resource offering more than 2000 guidelines. There are online and personal digital assistant (PDA) versions of this information service including links to 17 international CPG resource sites.

B. **National Institute for Health and Clinical Excellence (NICE).** This service of the British National Health Service offers more than 100 guidelines. Please also try PubMed for guidelines by adding "practice guideline [ptyp]" to your search term or access alternative services (e.g., United States Preventive Service, Task Force, MD Consult, SUMSearch, InfoRetriever). Washington University provides a collection of cerebrovascular clinical trials (*strokecenter.org/trials*).

## V. EVIDENCE-BASED MEDICINE

A. **Cochrane library** contains high-quality, independent evidence and includes reliable results from Cochrane and other systematic reviews and clinical trials. The service is recognized as the gold standard in evidence-based medicine.

B. **Up to date.** This fee-based service, available since 2006, is the most comprehensive online resource containing original, excellent, peer-reviewed texts embedded with graphics and literature links. Institutional subscriptions are available in many academic centers worldwide.

C. **Alternative online medical resources.** Free resources: *highwirepress.com*, *medicalalgorithms.com*, *medicalpodcasts.com*; sponsored resources: *medscape.com*, *merckmedicus.com*, *amedeo.com*, *e-medicine.com*. Subscription resources: *micromedex.com*, *ovid.com*, *mdconsult.com*, *statref.com*, *essentialevidenceplus.com*, *acpmedicine.com*, *acppier.com*, *firstconsult.com*, *dynamed.com*.

## VI. WEB 2.0 TECHNOLOGIES

A. **Really-Simple-Syndication.** RSS technology is a family of Web feed formats used to publish any kind of frequently updated information. Analogous to a scientific abstract, an RSS feed contains title, author list, summary, and a supplemental link to the original news article. Today all national and international newspapers, scientific journals, publishers, and institutions such as the ASA offer RSS feeds of their current issue (e.g., table of contents) or special compositions (e.g., most cited, most downloaded). RSS feeds may be composed and collectively read utilizing either mobile devices (e.g., mobile phones, PDAs) or RSS readers installed on personal computers or laptops. Today neuroanesthesiologists can collect RSS feeds of interest (e.g., Journal of Neurosurgical Anesthesiology, Anesthesia and Analgesia, Anesthesiology) and receive information tailored to their area of research. Articles of interest may be directly accessed, e-mailed, or twittered to a clinical or research group and colleagues. Online compositions of RSS feeds can be either accessed by using specialized services (e.g., *MedWorm.com*) or installed by using special software (e.g., *Bloglines.com*).

B. **Podcasts.** A podcast is a series of digital media files that are released episodically on the Internet and may contain medical information.

Educational or scientific podcasts are produced by numerous publishers (e.g., Nature, Science, New England Journal of Medicine) and academic institutions (e.g., Harvard University, Massachusetts Institute of Technology, Stanford University, Yale University, Oxford University, Cambridge University).

**C. Wikis**. A wiki is a platform that is created and edited by multiple users (e.g., Encyclopedia Wikipedia). In 2009, two wikis dedicated to anesthesiology (*openanesthesia.org*, *anesthesiawiki.org*) were developed to promote postgraduate education.

**D. Blogs**. The term blog is a contraction of web log. A blog is usually created and edited by a single person and deals with a special topic. Blogs can be used for teaching and updating and sharing links and also provide RSS functionality. For general anesthesia two Web sites are available: *theanesthesiablog.com*, *westmeadanaesthesia.blogspot.com*.

**E. Mobile technology.** Handheld technology has moved from PDAs to smart phones (e.g., PDA phone, BlackBerry, iPhone) with increasing Internet functionality. Many medical schools have integrated these devices into their programs and provide educational materials (e.g., electronic medical textbooks). These technologies have basic organizer functions (e.g., contacts, calendars, memos, tasks) and run multiple medical programs (e.g., document readers, drug databases, medical calculators) that are free, shareware, or fee based. For more information please follow the recommended links at the ASA Web site.

## *Suggested Readings*

Boulos MN, Maramba I, Wheeler S. Wikis, blogs and podcasts: a new generation of Web-based tools for virtual collaborative clinical practice and education. *BMC Med Educ*. 2006;6:41.

Chu LF, Young C, Zamora A, Kurup V, Macario A. Anesthesia 2.0: Internet-based information resources and Web 2.0 applications in anesthesia education. *Curr Opin Anaesthesiol*. 2010;23:218–227.

Ebbert JO, Dupras DM, Erwin PJ. Searching the medical literature using PubMed: a tutorial. *Mayo Clin Proc*. 2003;78:87–91.

Hoyt RE, Sutton M, Yoshihashi A. Medical Informatics - a practical guide for the healthcare professional. Fourth edition 2010. Published by lulu.com. ISBN-13: 978-0-557-60808-9.

Klein KU, Thal SC, Engelhard K, Werner C. Stay tuned in neuroanesthesia using RSS-feeds. *J Neurosurg Anesthesiol*. 2010;22(4):372. PMID: 20622681.

# 28 ASA Practice Guidelines: Prevention of Postoperative Visual Loss and Prevention of Postoperative Neuropathies

**Christine Goepfert, Cynthia M. Monsey, and René Tempelhoff**

## Illustrative Clinical Case

You are the physician responsible for providing the anesthesia for a 55-year-old gentleman who has spinal canal stenosis and is scheduled to undergo an anterior–posterior fusion from T11 to L3. The patient is otherwise well and has good functional status. His long-standing arterial hypertension is well controlled. However, he is morbidly obese with a body mass index of 51 and has recently been diagnosed with type II diabetes for which he is taking oral medication.

After some initial difficulties with achieving the prone position, the total surgery time was a little over 9 hours. The case was uneventful. The total blood loss was 2.5 L; the lowest hematocrit recorded was 27%. Two units of packed red blood cells were transfused. The patient's mean arterial pressure was maintained between 65 and 85 mm Hg with the use of intermittent intravenous injections of phenylephrine. After an unremarkable emergence, the patient was awake enough to follow simple commands and to move all his extremities. His trachea was extubated shortly thereafter and his ventilation was adequate. Soon after arrival in the postanesthesia care unit, he became progressively restless and anxious, trying to rub his eyes and screaming "I can't see! I can't see!" What do you think is going on?

## Chapter Highlights

### Introduction: "Anaesthesia-Paralysis"

"Anaesthesia-paralysis" is the title of a review article published in 1897 by Dr. Henry J. Garrigues, an obstetrician at the New York Maternity Hospital. In this review, he lauds the introduction of surgical anesthesia as "the fairest leaf in the rich wreath of laurels won by American surgery;" however, even early in the history of general anesthesia use in this country, it was recognized that this blessing was not without its own untoward consequences. He writes, "*This blessing to suffering humanity, by which alone the gigantic strides of modern surgery have become possible, is however, not free from danger*." He proceeds to describe a complication of anesthesia: multiple limb paralysis after surgical procedures mostly seen with obstetrical surgery. More than 110 years later, an editorial characterizing perioperative nerve injury as anesthesia's "silent scream" was published in a prominent anesthesiology journal. It addressed the incidence of and damage resulting from intraoperative peripheral nerve injury secondary to a combination of positioning and the anesthesia. These were severe neurologic complications, sometimes resulting in lifelong disability. Modern anesthesia techniques have dramatically improved outcomes after surgery, even for the most dangerous and complex procedures. However, for many reasons, the occurrence of intraoperative nerve injury has not abated.

The modern demands for extreme patient positioning in order to improve surgical access continue to test and tax our ability to position and secure our patients safely on the operating table. These extreme positions can increase the stretch of vulnerable peripheral nerves while efforts to secure the patient safely can lead to increased pressure on nerves. In addition, the advancements in patient monitoring and safety of the anesthetic drugs coupled with the increased technical complexity of the surgical procedures have resulted in prolonged anesthetic times for the patient, increasing the chances of nerve injury. Increasingly, the comorbidities of the surgical patient population have increased and will continue to increase. Lastly, increases in patient size have also made nerve injury more likely for it is a challenge to position patients correctly who have high body mass indices without the proper equipment.

As anesthesiologists, we are all aware of these risks. However, it is often the case that these risks are not explained in detail to the patient. While the risk of dental damage, blood transfusion, or cardiac complications is carefully discussed with the patient, it is rare that a discussion regarding the risk of a severe motor and sensory deficit would take place. Many factors contribute to this lapse. (1) Nerve injuries are perceived as rare complications. (2) It is difficult to predict where the damage might occur. (3) Nerve injuries are considered to pale in terms of gravity when compared to the primary reason for the operation and other complications such as heart attack, stroke, and death. But are intraoperative nerve injuries really too insignificant to discuss preoperatively? Paralysis, blindness, or sympathetic dystrophy (Chronic Regional Pain Syndrome) is a lifelong burden. The ramifications of unexpected postoperative blindness obviously are unfathomable. Even a more "minor" injury such as a persistent ulnar nerve palsy is career ending for anyone who has a job that requires fine motor dexterity such as an artist, musician, or anesthesiologist.

Currently, the estimated incidence of peripheral nerve injury (PNI) associated with an anesthetic is 15% of American Society of Anesthesiologists (ASA) closed claims. The incidence of postoperative visual loss, another type of nerve injury, is approximately 0% to 4.5% worldwide. A proper informed consent process should include the discussion of these risks. Who should be discussing the risk of nerve injury with the patient? Ideally, the responsibility of explaining the risks of unusual positioning should be shared among surgeons, nurses, and anesthesiologists since all have an important role in the positioning of the patient and ultimately the safety of the patient in the operating room. A laissez-faire approach to positioning where the anesthesiology team watches the positioning of the patient by the surgical and nursing teams is not appropriate. When these cases come to court, in the muddy waters of jurisprudence it is often the anesthesiologist's responsibility to help prevent a PNI that is put on trial.

## I. POSTOPERATIVE VISION LOSS

### A. Introduction

#### 1. Definition

Postoperative vision loss (POVL) was first described in the literature in 1948 and as a complication following neurosurgery in 1954. It is a rare and severely debilitating complication of surgery, primarily documented in patients who have undergone either prolonged spine procedures in the prone position or cardiac operations. The vision loss may occur in one or both eyes.

The exact etiology of POVL has yet to be determined, but it has several known manifestations. The most common form is non-arteritic ischemic optic neuropathy (ION). Non-arteritic ION is further

subdivided into posterior (PION) and anterior (AION) forms. PION accounts for the majority of POVL cases. Central retinal artery occlusion (CRAO), cortical blindness (CB), and POVL of unknown origin make up the remainder of the cases.

Of note, outside the operating room (OR) spontaneous non-arteritic ION is well known to ophthalmologists as the most frequent form of acute optic neuropathy resulting in blindness in patients > 50 years of age.

2. **Incidence**

There are conflicting reports about the rising or declining incidence of POVL. Taken as a group, the reports imply a rise in occurrence. Whether this trend is due to the increased awareness of POVL and better reporting or is secondary to the rise in annual spinal operations utilizing complex instrumentation is unclear. Exact numbers are very difficult to determine and, in the current literature, estimates range from 0% to 4.5%. Data primarily come from case reports, case control studies, and retrospective analysis of data sets. Prospective studies have been performed in cardiac surgery where POVL occurs most commonly. These studies are difficult to accomplish in spine and other surgeries because of the rarity of POVL. Adding to the confusion, inclusion criteria and definitions vary vastly among the studies.

The incidence of persistent POVL in all anesthetics ranges from 1:61,000 to 1:118,783 patients. The highest incidence occurs in cardiac surgery, followed by spine surgery, especially spinal fusions. The most recently published 10-year study examined the incidence of POVL related to eight categories of major surgery and confirmed that the highest rate occurred in patients who had cardiac surgery (8.64 in 10,000), followed by spinal fusion (3.09/10,000), and then laminectomy without fusion (0.86/10,000). The majority of cardiac cases exhibited CRAO (77%), whereas in spine surgery, the incidence of ION is higher at 28% with CRAO at 23% and CB at 49%. Surprisingly, in this retrospective study, data showed that spine surgery patients < 18 years of age appeared to have the highest prevalence of POVL (4.37/10,000). These results need to be interpreted with extreme caution as the mode of data acquisition used in this study by "coders" is controversial.

3. **ASA POVL registry**

In order to learn more about POVL, the American Society of Anesthesiologists (ASA) established a task force and registry, the American Society of Anesthesiologists Postoperative Visual Loss Registry, composed of voluntarily submitted cases. Patients who had POVL after prone spine surgery constitute the single largest group (67%). Bilateral disease was present in 66% of the cases with complete visual loss in the affected eye(s) in 58%.

Data in the registry show that among the reported cases of POVL that involved spine surgery the predominant mechanism of blindness was ION (89% of the cases). Of these, 60% involved the posterior optic nerve. Other shared features that appear to be correlated to POVL are blood loss ≥ 1,000 mL (82%) and operative duration *over* 6 hours (94%) (www.asaclosedclaims.org).

**B. The optic canal**

1. **Anatomy**

   a. The **optic nerve** traverses the optic canal in its prechiasma portion. This narrow canal is limited anteriorly by the ocular globe and laterally by bony structures of the frontal and maxillary sinuses. Toward

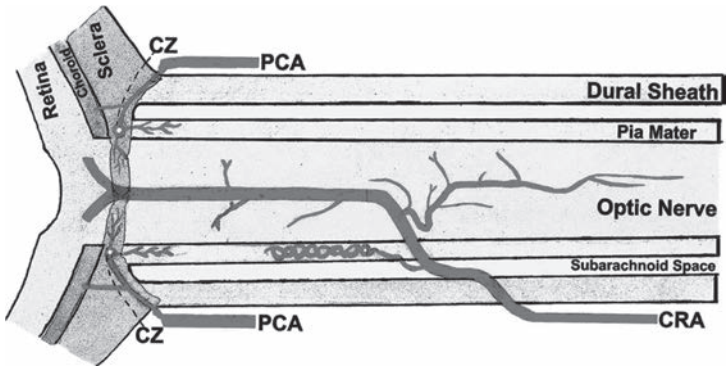


**FIGURE 28.1** Diagram (based on camera lucida drawings) showing one of the intraneural branches of the central retinal artery that runs backward in the axial part of the optic nerve posterior to the central retinal artery. CZ = circle of Zinn and Haller; PCA = posterior ciliary artery; CRA = central retinal artery.

its posterior part, the canal opens within the surrounding cerebral structures. Cerebrospinal fluid (CSF) surrounds the neurovascular bundle up to the globe; the thickness of the CSF layer varies. The space between nerve and bone is 2 to 3 mm wide.

b. **Cup-to-disc ratio**
The optic disc is the anatomical location of the eye's "blind spot," the area where the optic nerve and blood vessels enter the retina. The cup is an apparent space centrally. The usual cup-to-disc ratio is about 0.3. The larger the cup, the larger is the scleral opening at the back of the globe. Of relevance, in some patients, there appears to be the innate existence of a smaller canal from which the optic nerve exits the sclera. This causes a small optic cup-to-disc ratio that may lead to ischemic damage even without the presence of other preconditions. *The diagnosis of POVL depends on which part of the nerve is affected since the anterior and posterior sections have different blood supplies.*

2. **Blood supply and blood flow of the optic nerve**
   a. The optic nerve can be divided into an anterior (optic nerve head) part and a posterior part as determined by the **blood supply** (Figs. 28.1 and 28.2). The interactions of blood supply and blood flow with systemic and local factors contribute to individual susceptibility to optic nerve ischemia. There are individual variations between patients as well as in each optic nerve in the same patient.
      1. The **anterior part** of the optic nerve is supplied mainly by the posterior ciliary artery (PCA) circulation via the peripapillary choroid and short PCA collateral branches. This network is also called the circle of Zinn and Haller. The sectored distribution of these arterial branches is thought to explain segmental vision loss.
      2. The **posterior part** of the optic nerve is supplied by multiple arteries but not by the PCA. The intracanalicular part is supplied anteriorly by the pial vascular plexus constructed of multiple arterial sources and intraneural branches of the CRA and posteriorly

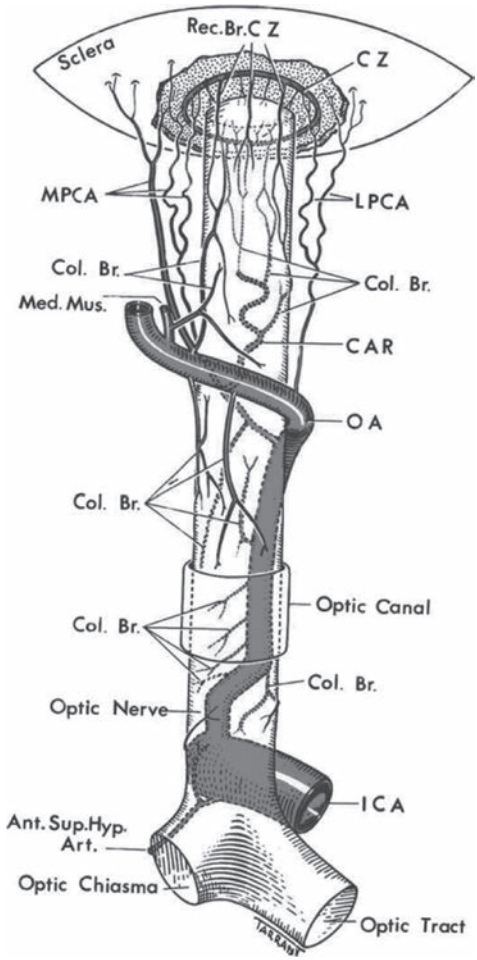


**FIGURE 28.2** Diagrammatic representation of blood supply of the various parts of the optic nerve, and location of the circle of Haller and Zinn (CZ), as seen from above. Blood supply of: (A) the optic nerve head and (B) the optic nerve Abbreviations: A, arachnoid; Ant. Sup. Hyp. Art., anterior superior hypophyseal artery; C, choroid; CAR and CRA, central retinal artery; Col. Br., collateral branches; CRV, central retinal vein; CZ, circle of Zinn and Haller; D, dura; ICA, internal carotid artery; LC, lamina cribrosa; LPCA, lateral posterior ciliary artery; Med. Mus., medial muscular artery; MPCA, medial posterior ciliary artery; NFL, surface nerve fiber layer of the disc; OA, ophthalmic artery; OD, optic disc; ON, optic nerve; P, pia; PCA, posterior ciliary artery; PR and PLR, pre-laminar region; R, retina; RA, retinal arteriole; Rec. Br. CZ, recurrent pial branches from peripapillary choroid/CZ; S, sclera; SAS, subarachnoid space.

mostly by small collateral arteries primarily from the ophthalmic artery (the first branch of the internal carotid artery [ICA]). The intracanalicular part derives its blood supply from fine collateral branches of the ophthalmic artery as well. The intracranial part has only a pial vascular plexus composed of arterioles from the surrounding arteries, mostly the anterior cerebral artery, middle meningeal artery, ophthalmic, and hypophyseal arteries.

Although highly variable, the venous drainage occurs primarily by way of the peripapillary choroidal veins into the central retinal vein and, to a lesser extent, the orbital veins and ultimately into the cavernous sinus.

**b.** There is **substantial anatomical interindividual variability** in the ocular blood supply between patients and even between the two eyes of the same patient. The pattern of PCA circulation can differ with regard to the number of PCA branches, the segmental distribution of the supplied area, and the location of **watershed zones** between the PCAs. The location of the watershed zones determines the vulnerability of the optic nerve head (ONH) to ischemia as in the case of a fall in perfusion pressure. Furthermore, anatomical differences within the PCAs render some PCAs more prone to ischemia during episodes of arterial hypotension.

**c.** **Blood flow to the optic nerve** depends on perfusion pressure, resistance to flow, presence of autoregulation, and rheologic properties of the blood. The resistance to blood flow depends on the autoregulation of ONH blood flow, vascular blood supply, and rheologic properties of the blood.

1. The **perfusion pressure of the orbit** is the mean arterial pressure (MAP) minus intraocular pressure (IOP). MAP represents the major determinant of perfusion pressure of the eye. Animal studies have shown that arterial hypotension can decrease the blood flow to the optic nerve significantly. Oxygen delivery to the optic nerve can be similarly decreased during systemic hypotension alone and even more so when hypotension is associated with anemia and venous congestion.
2. **Autoregulation** of orbital perfusion breaks down at a MAP < 30 mm Hg in patients who have normal vasculature and at higher pressures in patients who have concomitant vascular disease. The posterior portion of the optic nerve derives its main vascular supply from pial vessels that come from branches of the ophthalmic artery. These vessels are incapable of autoregulatory control so that the posterior optic nerve is particularly vulnerable to a fall in perfusion pressure. This part of the nerve is also readily injured by a drop in oxygen availability as from anemia. Clinically, increasing the IOP in the setting of low systemic BP may reduce ocular perfusion pressure (OPP) beyond the point of the autoregulatory mechanism's ability to compensate.

**d.** The normal **IOP** is 10 to 21 mm Hg. An IOP < 5 mm Hg is referred to as ocular hypotony. An IOP > 21 mm Hg is considered abnormally high and is often referred to as ocular hypertension. IOP increases

significantly during surgery in the prone position and rises further as the duration of the operation increases. It may occasionally reach up to three times the patient's baseline pressure, exceeding 21 mm Hg and thus putting susceptible patients at risk for a reduction in perfusion pressure and inadequate ocular perfusion. An increase in arterial carbon dioxide tension ($PaCO_2$) seems to increase the IOP. The clinical significance of this for ocular nerve perfusion during anesthesia is unknown.

**C. What do we know about POVL?**

**1. Signs and symptoms of POVL**

POVL will often appear within the first 24 hours after operation, or sometimes later, as a painless loss of some or all sight. When it is a partial loss, the visual field defects often obey the horizontal midline. These patients may have sluggish pupils or an afferent pupillary defect. All other causes of acute loss of vision must be ruled out. Unfortunately, POVL is frequently bilateral and irreversible at this point in time.

**a. Ischemic optic neuropathy** is an acute ischemic disorder of the optic nerve.

**1.** In **anterior ischemic optic neuropathy** (AION), the fundoscopic examination reveals edema of the optic disc and, occasionally, hemorrhage. An afferent pupillary defect may also be found. Binocular involvement (60%) is more common than monocular involvement (40%). Sixty percent of the patients are female. The 40% of patients who are male are usually middle aged, almost always have undergone lumbar surgery, and have a higher incidence of vascular risk factors, especially coronary artery disease (CAD), diabetes mellitus (DM), and obesity. The onset of AION occurs within 48 hours in 40% of the cases. In about 20%, the onset can be delayed to the ninth postoperative day. In such cases, it is difficult to differentiate spontaneous AION from postoperative AION.

**2.** In **posterior ischemic optic neuropathy** (PION), the optic disc at the time of onset of the visual loss appears normal without edema of the disc. Disc edema may appear several days later as the swelling progresses into the anterior region. Occasionally, there is an afferent pupillary defect and a non-reactive pupil. There are no signs of retinal ischemia (cherry-red spot). As with AION, binocular involvement (53%) is generally more common than monocular involvement (47%). Both eyes are equally affected in approximately 20% to 24% of cases. PION is diagnosed in the majority of cases (59%) upon awakening; an additional 29% are diagnosed within 24 hours. Only 12% occur on postoperative days 2 to 5, but not later.

PION affects more men (70%) and at a younger age with the youngest report at 12 years of age. While PION is more common after lumbar surgery, it can occur after cervical and thoracic operations as well. The operative duration is generally slightly shorter than with AION. Half of the patients have no vascular risk factors; when risk factors are present, the most common is arterial hypertension.

**b. Central retinal artery occlusion** (CRAO) is caused by embolization of the central retinal artery, which results in ischemic necrosis from a loss of blood supply to the inner layer of the retina. The patient has acute and persistent painless visual loss, an afferent pupillary defect, and a pale,

swollen optic nerve with splinter hemorrhages. Occasionally emboli can be seen. Fundoscopic examination within 15 minutes to several hours after the event reveals a pale opacified retina that is yellow white in appearance and a characteristic "cherry-red spot." In the acute situation, CRAO causes edema of the inner layer of the retina and pyknosis of the ganglion cell nuclei. The arterial occlusion usually resolves within 4 to 6 weeks; however, irreversible cell injury can occur in < 90 to100 minutes of total CRAO. Certainly after 24 hours of retinal ischemia, the damage is permanent. Antiplatelet therapy and heparin have been tried with poor results.

c. **Cortical blindness** (CB) is an embolic stroke of the visual cortex in the distribution of the posterior cerebral artery (PCA), the terminal branch of the basilar artery, which leads to unilateral or bilateral visual loss. The visual loss might be accompanied by central nerve palsy and/or signs of a parieto-occipital stroke. CB also occurs with an occlusion of the distal basilar artery. The combination of CB and anosognosia is known as Anton's syndrome. Thrombosis and more rarely dissection of the afferent vessels of the vertebrobasilar circulation can also result in CB. The incidence of CB after cardiac and thoracic surgery is much higher than after spine surgery. CB has also been described following angiography and is associated with the use of radiologic contrast media.

2. **Risk factors**

According to the ASA closed claims database, 81% of postoperative visual loss is diagnosed as ION and the remainder as CRAO and CB. There is some consensus about the fact they may all share certain risk factors.

a. **Factors related to the patient**

The correlation of POVL with age, gender, and comorbidities suggests that some patients may be more susceptible to some types of POVL.

1. **Age.** New data from a retrospective study analyzing more than 5.6 million patient files demonstrated that younger patients (<18 years of age) undergoing spinal surgery experience more POVL, particularly in the form of CB, than older patients. Above the age of 50, ION (and to a lesser extent CRAO) was shown to be the predominant cause of POVL following spine surgery. The significance of this difference is unclear because the results are derived from data of unknown origin.
2. **Gender.** Men are more often affected than women with an odds ratio of 1.3 to 1. This is primarily due to the male predominance of PION, which is the most frequent type of POVL.
3. **Concomitant vascular risk factors.** The paucity of data regarding an association between the known risks for atherosclerosis (DM, obesity, arterial hypertension, hyperlipidemia, smoking) and ION is such that it is impossible to draw any conclusion.
4. **A small cup-to-disk ratio** is correlated with an increased incidence of ION.

b. **Factors related to the surgery**

1. **Type of surgery.** The incidence and odds ratios for POVL are significantly higher after spinal fusion and cardiac surgery as compared with abdominal and other surgery. Among the varieties of spine surgery, patients undergoing lumbar procedures are more likely to develop ION, especially AION, as compared to cervical and thoracic procedures.

2. **Surgical experience and surgical emergency.** The surgical volume as a measurement of operative experience and differentiation between elective and emergency operations do not appear to affect the incidence of POVL.
3. **Length of surgery.** The ASA POVL registry reported that **an operative duration ≥ 6 hours** correlated with 82% to 94% of the reported cases of POVL.
4. **Positioning**. The **posterior approach** in spine surgery with the patient in the prone position is associated with a significantly higher rate of POVL. One explanation is that, during **prone positioning**, the IOP rises substantially and increases further as the length of the procedure increases. If we accept that the perfusion pressure within the orbit, including the canal, is equal to the MAP minus IOP, this increase in IOP could lead to a drop in the perfusion pressure of the ciliary arteries to less than the critical value of 30 mm Hg. The relationship between ION and IOP is not entirely clear, however, as POVL has also developed in patients who were in other positions such as affecting the upper eye in patients in the lateral position. Swelling of the eyelids and periorbital and conjunctival edema occur commonly with prone positioning and have not been associated with POVL.

   A number of **frames** have been designed for surgery in the prone position in an attempt to decrease the intra-abdominal pressure and facilitate venous return while avoiding dangerous pressure-point injuries. Unfortunately, no data are available as to whether they have any effect on the incidence of POVL. Securing the head in a pin head holder eliminates external compression of the eyes but does not seem to reduce the incidence of POVL though it does help to avoid direct trauma to the eyes.
5. **Direct compression** of the eye causes a secondary increase in IOP that leads more often to CRAO than any other form of POVL.
6. **Increased venous pressure** within the eye can cause an increase in IOP. Intraocular venous pressure may be elevated by the perioperative infusion of large quantities of fluid, reduced venous return in the head-down position, or obstruction to venous outflow when the head is turned to the side. Venous congestion in the eye might occur even when the CVP in within normal limit. IOP also rises when there is direct pressure on the abdomen from prone-position malpositioning, which can compress the abdomen and obstruct venous return to the heart.
7. **Blood loss and anemia.** The study of cases in the ASA POVL registry demonstrated a strong correlation between blood loss >1 L and POVL. In spinal surgery, anemia increases the odds ratio for the occurrence of POVL. In surgeries other than spinal surgery, blood transfusions have been associated with POVL although it may not be the fact of the transfusions themselves but rather that they were given after the onset of the ischemic event.

c. **Factors related to anesthesia**

1. **Arterial hypotension.** In the majority of case reports, POVL has been described after significant intraoperative arterial hypotension with prolonged drops in systolic pressure. In retrospective multivariate analysis, however, the correlation between POVL and hypotension did not reach significance.

2. **Vasopressors.** The use of vasopressors to increase or maintain the BP can cause secondary vasoconstriction of small arteries and arterioles that may be involved in POVL. Alpha–beta agonists may be superior to pure alpha agonists, but this remains speculative in the absence of data. The fact that endogenous vasoconstrictors are released in response to blood loss can hypothetically also play a role.

3. **Anesthesia management**
   a. **Preoperative preparation**
      1. **Awareness** of POVL has increased markedly among anesthesiologists and spine surgeons. This may explain in part the increase in reported cases of POVL. There is still some work to be done in terms of educating patients and including a discussion of the risk of POVL in the informed consent.
      2. **Surgery.** As time is of the essence, unnecessary delays during surgery and prolongation of anesthesia time while the patient is in the prone position should be avoided. In surgery that is expected to be > 6 hours in length with some significant blood loss (e.g., the anterior–posterior approach), one may consider a staged approach when it is surgically feasible.
   b. **Intraoperative management.** Contrary to what the early ophthalmology textbooks seemed to imply, anesthetics "per se" do not appear to have any role in the development of POVL except indirectly by their effect on cardiac output and concomitant arterial hypotension. The role of fluids and the negative effect of fluid overload on ocular venous return are a main source of concern in the management of these patients.
      1. **Positioning** is directed toward the prevention of peripheral nerve compression, and also POVL. With the patient in the prone position, every effort must be made to facilitate the venous return from the head and orbits. Abdominal pressure, especially in overweight patients, is probably the main factor in the obstruction of venous return from the upper torso. The operating bed may play a role and should be adapted as closely as possible to the patient's morphology. This includes positioning the patient's head above the body. One study in awake volunteers in the prone position showed that the rise of IOP was limited when the subjects were placed in a 10-degree head-up position.
      2. **Hemodynamics**
         a. **Anemia.** There are no reliable data identifying how much anemia can be tolerated. We can only propose that, if POVL is a concern, a higher transfusion trigger is appropriate. For spine surgery, the hematocrit probably should be maintained at around 30 and the hemoglobin at around 10 mg/L.
         b. **Blood pressure.** Arterial hypotension is avoided through meticulous fluid management and vasopressors if necessary. Even modest hypotension in combination with raised IOP can decrease ocular perfusion and cause optic nerve ischemia. A safe lower limit for the perfusion pressure of the optic nerve remains unknown. As autoregulation of the optic nerve ceases below 30 mm Hg, however, the MAP should be > 30 mm Hg plus the estimated IOP. Analogous to the cerebral perfusion pressure, the intraoperative MAP is maintained for each individual patient according to the preoperative blood pressure and concomitant cardiovascular disease. Furthermore, the vascular tree

in the posterior part of the optic nerve is incapable of autoregulation and is entirely dependent on the MAP.

c. **Fluid management.** Serum hypo-osmolarity from excessive administration of crystalloid that is hypo-osmolar to plasma (e.g., lactated Ringer's solution) should be avoided.

3. **Ventilation** to maintain normocapnia and avoid an increase in $PaCO_2$ might prevent further increases of the IOP.

c. **Postoperative management.** A cursory exam to evaluate gross visual function should be included as part of the immediate postoperative assessment, especially after spinal surgery in the prone position. The postoperative medical team should be aware of the risk of POVL and repeat a simple vision check while patients are in the PACU. Patients need to be questioned closely if they report visual problems. Often, they may have difficulty differentiating between blurry vision that they may consider as "normal" in the postoperative period and a real problem. It is also important to keep in mind that POVL can manifest itself late in the postoperative course. Delayed recognition of the problem and a delay in rapid intervention such as restoration of a reasonable ocular perfusion pressure or acute anemia treatment could worsen the prognosis. Here again, the data are scarce. Patients who have any visual abnormality should have immediate consultation with an ophthalmologist so that intervention, if possible, can be initiated promptly.

3. **Treatment**

a. Treatment for **ION** should be initiated as soon as the diagnosis is suspected. An ophthalmology consultation is requested. Anemia is corrected and the MAP is maintained at or increased to a level above the patient's baseline. Venous drainage is facilitated by elevating the head of the bed. Steroids are usually administered; although this is not evidence-based treatment, most clinicians think it could be useful in case of a vasculitis. Osmotic diuretics can be given if fluid overload is suspected, keeping in mind that the MAP is probably one of the most important factors in the restoration of adequate blood flow to the optic nerve. To prevent aggravation of the ischemic insult, the administration of aspirin or levodopa has been considered.

b. **CRAO and CB** are considered strokes so that neurologists should be involved as soon as possible. The diagnostic and therapeutic procedures follow the recommendations for stroke treatment.

## IN SUMMARY

POVL remains an unpredictable adverse event. As POVL is a rare occurrence, it is difficult to perform controlled prospective studies to dissect the precise etiology. What are available therefore are reports and retrospective studies that are highly contradictory. Animal models do not provide translational information because of major anatomical differences between species.

Risk factors for POVL are not well established. For spinal surgery, however, male patients ≤ 18 and ≥ 65 years of age undergoing a posterior approach to the lumbar spine with a surgical duration of > 6 hours and a blood loss of > 1 L resulting in anemia are at highest risk. The substantial interindividual variation of anatomical structures most likely accounts for the increased susceptibility of some patients for the development of POVL under specific conditions like prone positioning, hypotension, and blood loss/anemia.

## II. PERIOPERATIVE PERIPHERAL NERVE INJURIES IN THE NEUROSURGICAL PATIENT

### A. Introduction

Peripheral nerve injury (PNI) that is unrelated to the operative procedure remains a significant complication in the postoperative period. Anesthesiologists have been documenting perioperative nerve injuries for over a century. Multiple reviews of the ASA Closed Claims Database consistently place PNI as the second or third most frequently settled case at 15% to 16% of closed claims. The most recent review examined cases reported between 1970 and 1995; 670 or 16% of the 4,183 settled cases were for nerve injury claims. Often, patient positioning was thought to play a role in the development of these injuries. However, the scientific data objectively linking a positioning intervention and patient outcome are lacking. This was appreciated by the ASA Task Force on Prevention of Perioperative Peripheral Neuropathies. In 2000, after reviewing 509 positioning studies, the Task Force could only approve a practice advisory for the prevention of perioperative peripheral neuropathies. Only six of the studies reviewed could provide any objective evidence linking a positioning alteration with a change in patient outcome. The ASA published a new advisory in 2011, re-emphasizing the danger of the automatic blood pressure apparatus and the necessity to maintain the anatomic alignment and to consider "when it is appropriate to anticipate if some patients can tolerate the position." The members of the panel agreed on the paucity of the literature regarding this issue. (A practice advisory is a document not supported by scientific literature to the same degree as a practice standard or guideline). In an effort to explain PNI's happening without obvious clinical etiologies, some have suggested that a subclinical insult that would result normally in no injury may become clinically evident when it happens following a pre-existing chronic subclinical injury or by another subclinical injury's happening on the course of one nerve. The authors referred to this phenomenon as the "double crush" syndrome.

Peripheral nerve injuries related to positioning or intraoperative events typically show clinical signs in the immediate postoperative period. The symptoms are restricted to the distribution of the injured nerve or injured portion of a plexus unilaterally. Bilateral injury is rare but not unreported (see Peroneal Nerve Injury). Electromyographic (EMG) evaluation will confirm changes restricted to the muscles innervated by that nerve or portion of a plexus. The diagnosis of brachial plexitis or Parsonage-Turner syndrome, an inflammation of the brachial plexus, must be considered in patients presenting with complaints of PNI in the upper extremities. This poorly understood syndrome goes by many other names. Although of unknown etiology, brachial plexitis is believed to be a reaction in response to the stress of surgery rather than any mechanical injury. It is unpredictable in its occurrence and presents within hours to days with the acute onset of shoulder pain radiating down the arm. The incidence is 1.6 cases per 100,000 annually. EMG will demonstrate changes in the distribution of multiple nerves or plexus elements, differentiating it from PNI from stretch, compression, or other intraoperative events.

### B. Classification of peripheral nerve injuries

Newer methods of classifying nerve injuries have emerged as our understanding of neuronal pathophysiology has improved. One of the earliest classification systems is the **"three-tiered" model** developed by Seddon. Sunderland expanded this model to **"five tiers"** or **degrees of nerve injury.**

1. **Neurapraxia** or first-degree nerve injury by Sunderland: no loss of neural continuity and only minor alterations in the myelin sheath. This injury produces a transient loss of function.
2. **Axonotmesis** or second-degree nerve injury: an interruption of the axon and myelin, but all other tissues such as the endoneurium, epineurium, and perineurium are intact. This surviving tissue framework aids nerve recovery by guiding neuron and axonal regrowth, much like scaffolding on a building guides its final structure.
3. **Third-degree injury**: a class Sunderland places between axonotmesis and neurotmesis, creating a third tier.

   For these injuries, there is still some chance of functional recovery. This class includes damage to the endoneurium plus damage to the axon and myelin sheath. There is still preservation of the epineurium and perineurium.
4. **Neurotmesis or nerve dissection** in which all essential structures have been injured despite the apparent maintenance of structural continuity. Rarely is any degree of recovery possible without surgery.

   Sunderland further breaks down this Seddon class into two tiers of injury:
   a. **Fourth degree**: dissection of the nerve with preservation of the epineurium
   b. **Fifth degree**: dissection of the nerve with a severed epineurium

C. **Mechanisms of nerve injury**: Five *in vivo* mechanisms of injury are currently postulated.
1. Stretch
2. Compression
3. Ischemia
4. Metabolic derangement—inherent to the patient such as diabetes mellitus
5. Surgical laceration—the rarest

   Plus "toxin" exposure as a mechanism of intraoperative neuronal injury.

   In the normal awake patient, extremes of body positioning such as overextension of the elbow or excessive pressure against superficial nerves (pressing on the ulnar nerve as it traverses the cubital tunnel) produce discomfort, prompting spontaneous repositioning of the uncomfortable body part and bringing relief of symptoms. It is unresolved just how much pressure or stretch it takes and for how long it must occur before clinical symptoms appear and spontaneous optimization of position occurs. Once anesthetics and muscle relaxants are introduced, these protective mechanisms are eliminated, which makes the patient more prone to injury. And, in the anesthetized patient, we certainly do not know how much pressure it takes and for how long it can be tolerated before there is nerve injury. Currently, there are no tools that permit non-invasive monitoring of the amount of stretch or compression a nerve is undergoing during positioning and throughout the course of an operation.

D. **Nerve injuries: A continuum of severity**

There is a continuum to the severity of neuronal injuries from stretch or pressure regardless of causation.
1. **Low-grade stretching** of a nerve may cause physical disruption of intraneural blood vessels (*vasa nervorum*), causing patchy areas of nerve ischemia.
2. As **more severe stretching** occurs, the intraneural connective tissue and the intraneuronal blood vessels tear. The resulting intraneural bleeding

can lead to increased intraneuronal pressure and secondary localized nerve necrosis from the pressure as well as the lack of perfusion.

3. Stretching can also cause **focal compression** in the area where a nerve is pulled over a firm fixed prominence such as the ulnar nerve as it goes around the medial epicondyle of the humerus.
   a. **Mild compression** causes a temporary interruption of the blood supply to a nerve. This leads to a transient conduction block that may only require a few minutes of reperfusion to reverse.
   b. **Moderate compression.** As the amount of pressure applied to the nerve increases, an elevation of intraneural venous pressure occurs. Endoneurial edema also develops.
   c. **Severe compression.** As external pressures continue to increase, the intraneural pressures also continue to rise. When the intraneural pressures are high enough, the axoplasmic flow becomes disrupted, inducing a neuropathy that takes much longer to resolve. These neuropathies, lasting hours to weeks, are the clinically symptomatic neuropathies confronting the anesthesiologist in the postoperative period.
   d. **Continued severe pressure**
      1. Eventually, the pressure will lead to Schwann cell and myelin damage. As damage to the myelin progresses, an electromyogram (EMG) will demonstrate slowing and then stopping of the electrical conduction as a result of the ongoing demyelination
      2. Remyelination and recovery may require many weeks.
   e. **Still higher pressures**: Now, the excessive pressure results in total axonal loss, transection, and Wallerian degeneration. The degeneration begins 4 to 10 days after axonal transection. Before degeneration, the distal axon segment may remain electrically excitable. For a complete discussion of Wallerian degeneration with pathologic slides, please see: http://neuromuscular.wustl.edu/pathol/axloss.htm.

**E. Recent Information on PNI in the neurosurgical patient**

Over the last century, our knowledge of the mechanisms of nerve injury and how the injured nerve responds has increased, but our ability to prevent perioperative neuropathies has not kept pace. A prime example is the ulnar nerve. Ulnar neuropathy, first described in 1901, is the most frequent of the postoperative neuropathies. It continues to be so regardless of the amount of padding used to protect the elbow.

Neurosurgical cases have recently been found to have a higher than expected rate of PNI. In a recent 10-year retrospective study of 380,568 patients by Welch, all ages and genders were included. The authors identified 112 cases of PNI that met their inclusion criteria. They examined the incidence of these cases across all surgical fields practiced in the University of Michigan Health System. For each surgical field, the percent occurrence of PNI, the hazard ratio, and the confidence interval for $p = 0.05$ were calculated. Looking specifically at neurosurgery and the closely related specialty of otorhinolaryngology (ENT):

1. Neurosurgery had a total of 13,446 cases of which 13,435 met inclusion criteria. That is 3.5% of the total cases reviewed. Neurosurgery had 10 PNI events of the 112 found in the study or 8.9% of all PNIs. The hazard ratio = 2.7 (CI: 1.4–5.1), $p = 0.05$. This is the highest hazard ratio in the study.
2. Interestingly, ENT had the lowest hazard ratio in the study. ENT accounted for 38,287 included cases (10%) and 3 PNI events (2.7%) for a hazard ratio = 0.2 (CI: 0.1–0.8), $p = 0.05$.

**F. Now what?**

There is no "quick and easy" answer. However, a quick "road trip" around the neurosurgical patient may be useful. Anesthesiologists caring for neurosurgical patients should know which nerves are most frequently injured. This enables us to direct the preoperative evaluation of patients to detect indicators of pre-existing injury and to provide assistance in early detection of injury in the immediate postoperative period when diagnosis and intervention can be most helpful. The following list is not all inclusive or exhaustive. Of note, one of the most excellent and exhaustive reviews of all positioning and possible effects on PNI has been written by Christopher J. Winfree and David G. Kline in 2004. It is almost impossible not to refer to their work when addressing the subject of PNI.

1. **Central nerves**
   - **a.** Cranial Nerve II: See Section on POVL
   - **b.** Cranial Nerve VII
     1. Compression of peripheral branches while using a facemask for ventilation
     2. Compression of branches while in the prone position on donut or horseshoe
     3. Damage to supraorbital branch from goggles used in the prone position
   - **c.** Cranial Nerves IX, X, XII
     1. Damage during infratentorial procedures
     2. Damage during carotid endarterectomy (see below)
     3. Damage will adversely affect airway, swallowing, articulation
   - **d.** Cranial Nerve XII
     1. There are multiple reports of injury (unilateral and bilateral) from the endotracheal tube, oral airway, and supraglottic airway devices such as laryngeal masks.
     2. Cranial nerve XII may be injured, alone or in combination with the lingual nerve and/or recurrent laryngeal nerve. Usually it is a unilateral injury. **Tapia's syndrome**, first described in 1904 by A. G. Tapia, results from extracranial involvement of the hypoglossal nerve and the recurrent laryngeal branch of the vagus nerve. The injury of these nerves is a rare complication of anesthetic airway management. Pressure neuropathy or stretch of both nerves is an accepted cause. Isolated bilateral paralysis of the hypoglossal and recurrent laryngeal nerves (bilateral Tapia's syndrome) after transoral intubation for general anesthesia has been reported.
2. **Mental nerve injury.** Numbness of the lower lip can be related to excessive pressure exerted by the plastic oropharyngeal airway on the mental branch of the inferior alveolar nerve as it enters the mandibular foramen on the inner aspect of the mandibular ramus.
3. **Cervical spine.** There are multiple case reports of cervical lesions with partial or complete ischemia of the cervical cord in the sitting position during which the head was probably overflexed. One has to be aware, however, that the same dramatic complication can happen in the prone position with the head in hyperflexion.
4. **Face and neck**
   - **a.** The patient undergoing carotid endarterectomy (CEA) deserves special attention. CEA has a very high rate of injury to nerves that can impact the patient's ability to breath and handle secretions safely.
   - **b.** Kennmair et al. reviewed 265 carotid endarterectomies in 210 patients (all vein patches in the carotid bifurcation). Altogether

28 (10.5%) cranial nerve injuries were registered. In 6 (2.2%) cases the hypoglossal nerve was injured; in 13 (4.9%) the vagal nerve (N. laryngeal recurrent); and in 9 (3.4%) facial nerve paresis occurred. Cranial Nerves VII and X, which are not directly connected with the surgical site, had significantly more injuries than the hypoglossal nerve ($p < 0.01$), which is located in closer proximity to the carotid artery. The incidence of hypoglossal injury can be related to the experience of the surgeon performing the procedure.

c. Another study looking at nerve complications following CEAs concluded with similar results. In 269 cases, 15 cranial nerve injuries were documented (5.6%). Seven patients (2.6%) had unilateral vocal cord paralysis; nine (3.3%) had hypoglossal palsy; two (0.7%) had glossopharyngeal nerve injury; and one (0.4%) had facial nerve palsy (marginal mandibular nerve). Most cranial nerve injuries are transient and result from trauma during neck dissection, retraction, or carotid clamping.

5. **Upper extremity**
   a. **Brachial plexus** injuries account for 20% of the PNI in the Closed Claims Database. Here is an instance where positioning modifications do help decrease this injury.
      1. Keep the arms abducted less than 90% at the shoulder when the body is supine or prone
      2. Use care when taping the shoulder or clamping to pull the shoulders caudad for better neck exposure. It is possible to overstretch the supraclavicular portions of the plexus.
      3. When in the lateral position, axillary rolls should be placed to suspend the axilla in air. Avoid placing them into the axilla where they will cause direct compression of the neurovascular bundles. If possible, check during the case by placing your hand into the axillary area to verify that the axillary roll is still out of the axilla.
   b. **Radial nerve injury in the upper arm**
      1. Injury can occur to the radial nerve as it crosses the posterior upper arm at the midportion of the humerus. If the arm boards are not at the same height as the bed, the ridge produced by the height differential can compress the radial nerve leading to a postoperative palsy.
      2. Radial nerve injury secondary to placement of an automatically cycled BP cuff has been reported.
   c. **At the elbow, lies a minefield.**
      1. Too much extension can damage the median nerve, so maintain a mild, < 90 degrees amount of flexion.
      2. Flexion
         a. Too much flexion, ≥ 90 degrees, can roll the **ulnar nerve** out of its protective groove in a susceptible patient, increasing risk of injury to this nerve.
         b. Flexion of the elbow (> 90 degrees) can also tighten the arcuate ligament and shrink the cubital tunnel, thereby augmenting the risk of nerve compression in the tunnel.
      3. Elbow padding when arms are at the side has not been definitively shown to reduce the risk of ulnar nerve palsy.
      4. When the arm is outstretched and pronated, the ulnar nerve may become compressed between the operating bed and the bony floor of the cubital tunnel. The message is: Keep hand and forearm supinated.

5. In the lateral decubitus position, the ulnar nerve of the dependent arm may be compressed
6. Beware the distally placed non-invasive BP cuff. As with the radial nerve, the ulnar nerve can also be compressed and damaged.

d. The **wrist** is best maintained in a neutral position. Overextension for prolonged periods (think about arterial line wrist rolls) can cause praxis of the **median nerve** and a carpal tunnel syndrome.

6. **Torso.** There are scattered reports of injuries to the **long thoracic nerve**, **musculocutaneous nerve**, and **axillary nerve**, all possibly due to positioning. The data are too unclear to draw any firm conclusions about cause, effect, or prevention.
7. **Lower extremity**
   a. **Peroneal nerve injury**
      1. Unilateral injury is documented in long cases in the lateral decubitus position. Additional padding between the operating bed surface and the down knee is recommended.
      2. Bilateral nerve injury has been reported after a 14-hour craniotomy in the sitting position.
      3. Overall risk to a neurosurgical patient is < 1%.

   b. **Lateral femoral cutaneous nerve injury.** Compression from prone bolsters causes *meralgia paresthetica*. Bolster size should be tailored to the torso size of the patient, avoiding bolsters that are too long.
   c. **Sciatic nerve injury**, caused by compression between the operating bed and the ischial tuberosity, can occur in the semi-lateral position. Additional padding under the buttocks is recommended.
   d. **Tarsal tunnel syndrome** is caused by improperly protected feet. Keep ankles slightly plantar flexed.
   e. **Sural nerve praxis** is from excessive medial deviation of the foot.

G. **Conclusion**

While PNI is a significant problem when all types of surgery are considered, it remains a relatively rare complication in the neurosurgical patient. The ASA practice advisory for the prevention of perioperative peripheral neuropathies recommends a preoperative assessment to determine whether the position can be tolerated, various considerations for each position, a postoperative assessment to facilitate early recognition of peripheral neuropathies, and better documentation in the anesthesia record of all interventions taken to protect the patient from an intraoperative nerve injury.

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