Chapter

30 CENTRAL NERVOUS SYSTEM DISEASE

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The central nervous system (CNS) deserves special consideration in the perioperative setting for several reasons. First, many CNS diseases, such as intracranial tumors or aneurysms, are amenable to surgical treatment. Second, many patients presenting for non-neurologic procedures have concurrent CNS diseases such as prior stroke or Parkinson disease. Third, the CNS is metabolically active with little oxygen reserve and is therefore sensitive to ischemia and hypoxia even for very brief periods of time. The latter is especially important in patients with increased vulnerability to complications from cerebrovascular insufficiency or other flow-relevant abnormalities. This chapter discusses the relevant knowledge base and clinical care needed when taking care of patients with CNS diseases in the perioperative setting.

NEUROANATOMY

Conceptually, the cranium is divided into supratentorial and infratentorial compartments. The supratentorial compartment contains the cerebral hemispheres and diencephalon (thalamus and hypothalamus), whereas the brainstem and cerebellum make up the infratentorial compartment. In addition, intracranial lesions may be classified as either intra-axial or extra-axial, within or outside the brain parenchyma, respectively. The location of an intracranial lesion has important implications on the anesthetic considerations for that patient and determines the patient's position during surgery. The location of intra-axial mass lesions is particularly relevant, as some lesions may place eloquent areas such as the language centers and motor cortex of the brain at risk. In this case, functional preservation during surgery becomes critically important.

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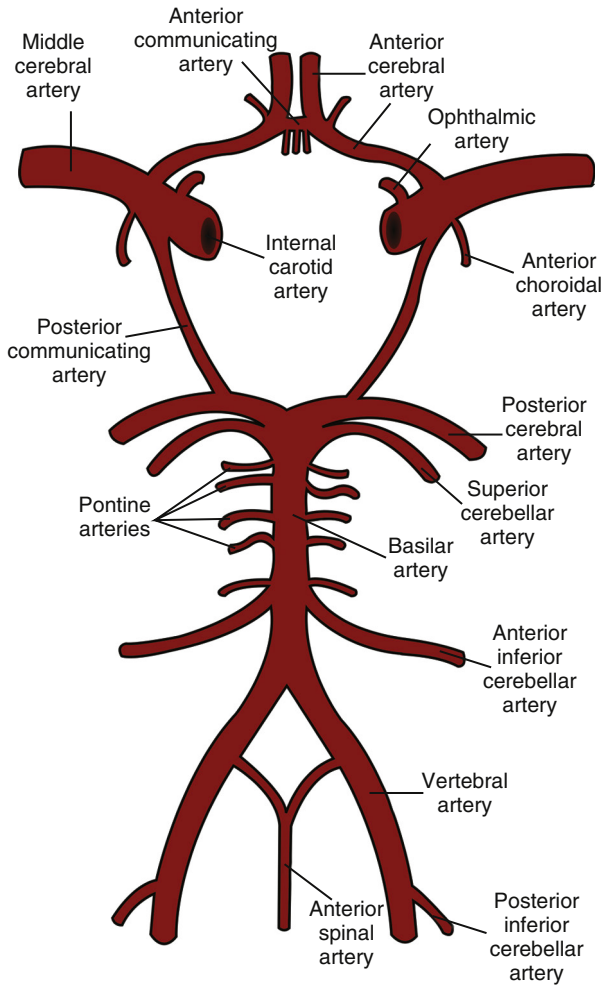

Fig. 30.1 Anatomy of the circle of Willis.

The arterial blood supply to the brain is through the left and right internal carotid arteries (anterior circulation) and the vertebrobasilar system (posterior circulation). Anastomoses between these vessels form the circle of Willis (Fig. 30.1) and create a collateral blood supply to protect against focal ischemia. However, this ring is not complete in all patients; approximately 20% of the population has an abnormal circulation, implying that the collateralization may not be complete. The clinical significance of an abnormal circle of Willis may depend on the pattern of the abnormality and the coexisting cerebrovascular diseases.

There are 12 pairs of intracranial nerves. It is important to understand the distribution and the sensorimotor and autonomic function of each nerve for the following reasons. First, some neurosurgery procedures may jeopardize specific intracranial nerves during surgery; for example, resection of acoustic neuroma may injure the vestibulocochlear nerve. Second, some of the intracranial nerves are monitored intraoperatively to facilitate timely detection of reversible injury and theoretically prevent permanent deficit. Both somatosensory and motor evoked potentials are frequently monitored intraoperatively. The anatomy of the sensorimotor cortex and pathways is also important for the anesthesia provider to understand.

The anatomic and functional integrity of the blood-brain barrier has important clinical implications. The blood-brain barrier is composed of capillary endothelial cells with tight junctions that prevent free passage of macromolecules or proteins. In contrast, lipid-soluble substances (carbon dioxide, oxygen, anesthetic drugs) cross the blood-brain barrier easily. The blood-brain barrier may be disrupted by acute systemic hypertension, trauma, infection, arterial hypoxemia, severe hypercapnia, tumors, or sustained seizure activity. Osmotic pharmacologic therapy for intracranial hypertension or the need for intraprocedural brain relaxation relies on an intact blood-brain barrier in order to move the free water from the brain parenchyma to the intravascular space.

NEUROPHYSIOLOGY

Regulation of Cerebral Blood Flow

Normal cerebral blood flow (CBF) is approximately 50 mL/100 g/min and represents 12% to 15% of total cardiac output. The brain, albeit being 2% of the total body weight, receives a disproportionately large share of cardiac output because of its high metabolic rate and inability to store energy. Some of the important factors or physiologic processes that regulate CBF include (1) cerebral metabolic rate via neurovascular coupling, (2) cerebral perfusion pressure (CPP) via cerebral autoregulation, (3) arterial blood carbon dioxide and oxygen partial pressure ($Paco_2$ and Pao_2, respectively) via cerebrovascular reactivity, (4) sympathetic nervous activity, (5) cardiac output, and (6) some anesthetic drugs. Different regulatory mechanisms may exert distinctive effects on CBF, which are integrated at the level of cerebral resistance arteries/arterioles to determine the CBF.[1,2]

Cerebral Metabolic Rate and Neurovascular Coupling

Cerebral metabolic rate of oxygen ($CMRO_2$) is often used as an index of the cerebral metabolic activity. $CMRO_2$ and CBF are closely related—an increase or decrease in $CMRO_2$ results in a proportional increase or decrease in CBF. This is named neurovascular coupling or cerebral metabolism-flow coupling. In the perioperative setting, $CMRO_2$ can be reduced by hypothermia and most intravenous anesthetic drugs, which produce a coupled reduction in CBF in healthy brains. CBF decreases 7% for every 1° C decrease in body temperature below 37° C.[3] In contrast, $CMRO_2$ and CBF may be dramatically increased by seizure activity.

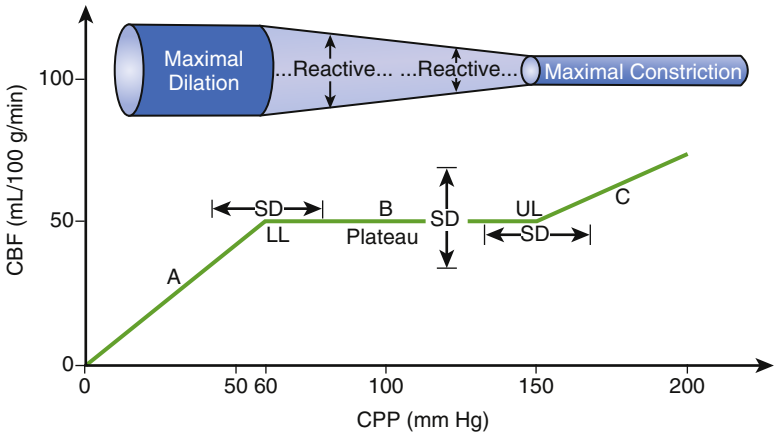

Fig. 30.2 Cerebral autoregulation describes the relationship between cerebral blood flow (CBF) and cerebral perfusion pressure (CPP). The three key elements of an autoregulation curve are the lower limit (LL), the upper limit (UL), and the plateau. The cerebrovascular reactivity is also illustrated. CBF remains stable in the CPP range between the lower and upper limits and is pressure passive outside this range. As described in the text, there is significant variation among individual patients. *SD,* Standard deviation. (From Meng L, Gelb AW. Regulation of cerebral autoregulation by carbon dioxide. *Anesthesiology.* 2015;122:196-205.)

Cerebral Perfusion Pressure and Cerebral Autoregulation

CPP is the difference between mean arterial pressure (MAP) and intracranial pressure (ICP) or central venous pressure. How CPP affects CBF is determined by cerebral autoregulation, which maintains a stable CBF during a fluctuating CPP as a result of cerebral vasoconstriction or vasodilation in response to an increase or decrease in CPP, respectively.[1] That is, the simultaneous and proportionate changes in CPP and cerebrovascular resistance due to cerebrovascular pressure reactivity lead to a stable CBF. However, as static cerebral autoregulation takes minutes to take effect, a rapid increase or decrease in MAP may cause a brief period of cerebral hyperperfusion or hypoperfusion, respectively.[4]

The cerebral autoregulation curve has three portions: the plateau, the lower limit, and the upper limit (Fig. 30.2). The lower limit is the CPP level below which the CBF decreases linearly with a decreasing CPP. In contrast, the upper limit is the CPP level above which the CBF increases linearly with an increasing CPP. The plateau is the CPP range between the lower and upper limits where CBF remains stable (approximately 50 mL/100 g/min). The frequently quoted limits of autoregulation are a lower limit of 60 mm Hg and an upper limit of 150 mm Hg. However, although these numbers may apply to young and healthy humans, they may not apply in patients with various medical and surgical comorbid conditions.[1] For example, chronic uncontrolled hypertension or sympathetic stimulation shifts the autoregulatory curve to the right. If this is the case, then a higher minimum CPP will be required to maintain an adequate CBF.

Cerebral autoregulation may be impaired or even abolished following traumatic brain injury and intracranial surgery. As a result, CBF becomes pressure passive, implying that it no longer remains stable across the autoregulatory CPP range and instead changes linearly with changes in CPP. Severe hypercapnia, often as a result of hypoventilation, can also impair cerebral autoregulation. Higher inhaled anesthetic concentrations are potent cerebral vasodilators and impair autoregulation. In contrast, intravenous anesthetic drugs do not disrupt this regulatory mechanism. In circumstances when cerebral autoregulation is impaired, the CPP should be carefully controlled because a change in CPP also changes CBF owing to the loss of autoregulatory capability.

Cerebrovascular $Paco_2$ and Pao_2 Reactivity

Both $Paco_2$ and Pao_2 are powerful modulators of CBF and can cause a robust cerebrovascular $Paco_2$- and Pao_2-induced reactivity. Changes in $Paco_2$ produce corresponding and same directional changes in CBF when $Paco_2$ is between 20 and 80 mm Hg (Fig. 30.3). CBF increases or decreases approximately 1 mL/100 g/min or 2% for every 1 mm Hg increase or decrease in $Paco_2$ from 40 mm Hg. Such changes in CBF reflect the effect of carbon dioxide–mediated alterations in perivascular pH that leads to cerebral arteriolar dilation or constriction. The $Paco_2$-related change in CBF only lasts for about 6 to 8 hours owing to the compensatory change in bicarbonate (HCO_3^-) concentration. Both extreme hyperventilation and hypoventilation should be avoided as they can cause cerebral hypoperfusion and hyperperfusion, respectively. Prolonged aggressive hyperventilation following traumatic brain injury is associated with poorer neurologic outcome.[5] In contrast, decreases in Pao_2 less than a threshold value of about 50 mm Hg result in an exponential increase in CBF (see Fig. 30.3), likely a compensatory mechanism to maintain cerebral oxygen delivery (cerebral oxygen delivery = arterial blood oxygen content × CBF).

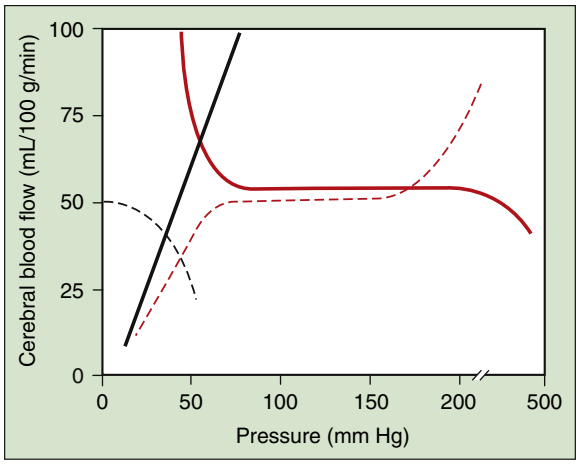

Fig. 30.3 Schematic depiction of the impact of intracranial pressure *(dashed black line)*, Pao_2 *(solid red line)*, $Paco_2$ *(solid black line)*, and cerebral perfusion pressure (mean arterial pressure minus intracranial pressure or central venous pressure, whichever is greater) *(dashed red line)* on cerebral blood flow.

Effects of Anesthetics on Cerebral Blood Flow

Intravenously administered anesthetic drugs such as propofol and thiopental cause simultaneous reductions of $CMRO_2$ and CBF. The effect of intravenous anesthetics on CBF is attributed to neurovascular coupling, that is, the decrease in $CMRO_2$ leads to a corresponding decrease in CBF. The effects of ketamine on cerebrovascular physiology have been variable, which likely reflects different research study conditions.[6] When ketamine is given on its own without control of ventilation, there is an increase in $Paco_2$, CBF, and ICP. However, when ketamine is given in the presence of another sedative or anesthetic drug in patients whose ventilation is controlled, these effects are not noted. Because of this controversy, however, ketamine is usually avoided in patients with known intracranial disease.

Benzodiazepines and opioids decrease $CMRO_2$ and CBF, analogous to propofol and thiopental, although to a lesser extent. However, associated respiratory depression and increase in $Paco_2$ may produce the opposite effect. Opioids should be cautiously given to patients with intracranial disease because of their (1) depressant effects on consciousness, (2) production of miosis, and (3) depression of ventilation with associated increases in ICP from increased $Paco_2$.

α_2-Agonists (clonidine and dexmedetomidine) are unique sedatives in that they do not cause significant respiratory depression. They decrease arterial blood pressure, CPP, and CBF with minimal effects on ICP. α_2-Agonists can be used intraoperatively to reduce the dose of other anesthetic drugs and analgesics, or postoperatively as sedatives and to attenuate postoperative hypertension and tachycardia.

In contrast to intravenous anesthetics, volatile anesthetics are potent cerebral vasodilators. When administered during normocapnia at concentrations higher than 0.5 minimal alveolar concentration (MAC), desflurane, sevoflurane, and isoflurane rapidly produce cerebral vasodilation and result in dose-dependent increases in CBF even though $CMRO_2$ is decreased. Therefore, volatile anesthetics produce divergent changes in $CMRO_2$ and CBF that are distinct from those of intravenous anesthetics. When used in isolation, nitrous oxide increases CBF and possibly $CMRO_2$, however, these effects are attenuated by the coadministration of other anesthetics.

INTRACRANIAL PRESSURE

Determinants of ICP and the Compensation for an Increased ICP

The intracranial compartment normally contains three components: (1) brain matter, (2) cerebrospinal fluid, and (3) blood. Increases in any of these components or the addition of a pathologic lesion (e.g., tumor) can result in an elevated ICP, defined as a sustained increase of ICP higher than 15 mm Hg. Marked increases in ICP can decrease CPP and thereby CBF to the point of causing cerebral ischemia. However, there is a mechanism that restores ICP to normal in the face of an expanding component. This mechanism is accomplished via compensatory reduction of other intracranial components, including the translocation of cerebrospinal fluid from intracranial space to extracranial space. At the moment when this compensatory mechanism is exhausted, ICP starts to increase and cerebral blood vessels are eventually compressed (Fig. 30.4). CBF must be differentiated from cerebral blood volume (CBV) because the former represents flow whereas the latter applies to the intracranial blood volume. These two terms are related but not interchangeable. The treatment of intracranial hypertension is primarily via the reduction of various intracranial components (Box 30.1).

Effect of Anesthetics on Intracranial Pressure

Most intravenously administered anesthetics reduce CBF, which is associated with a decrease in ICP. The effect of ketamine is controversial and has been discussed previously. These drugs should be considered in patients whose ICP is abnormally increased. However, large doses of propofol or thiopental may decrease systemic blood pressure and CPP. An increased frequency of excitatory peaks on the electroencephalogram (EEG) of patients receiving etomidate, as compared with thiopental, suggests etomidate should be administered with caution to patients with a history of epilepsy, especially considering that seizure increases $CMRO_2$, CBF, and ICP as a consequence.[7] Opioids and benzodiazepines reduce ICP

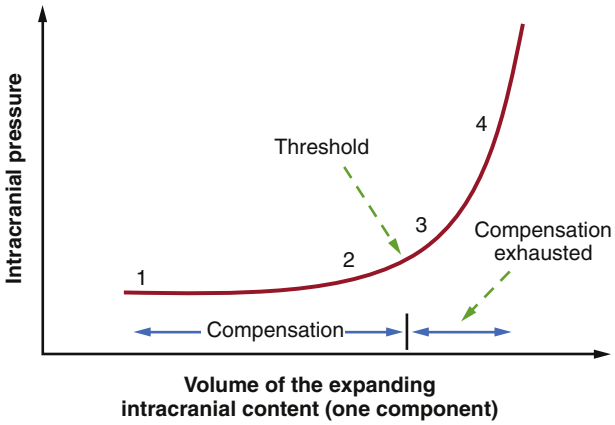

Fig. 30.4 Graph of the effect of an expanding intracranial component on intracranial pressure (ICP). As the volume of an intracranial component increases from point 1 to point 2 on the curve, ICP remains relatively stable owing to the compensatory mechanisms including the translocation of cerebrospinal fluid from the intracranial space into the spinal subarachnoid space. Between points 1 and 2, the volumetric sum of all intracranial components remains relatively constant. Patients with intracranial tumors who are between point 1 and point 2 on the curve are unlikely to manifest clinical symptoms of increased ICP. The compensation ability is exhausted on the rising portion of the curve (point 3) when a small volumetric increase of the expanding intracranial component leads to a noticeable increase of ICP. Clinical signs and symptoms attributable to increased ICP are likely at this stage. Additional increases in intracranial volume at this point, as produced by increased cerebral blood flow secondary to hypercapnia or inhaled anesthesia, can precipitate abrupt further increases in ICP (point 4).

through reductions in $CMRO_2$ and CBF although this benefit will be offset if respiratory depression and an increase in $Paco_2$ occur.

As discussed previously, volatile anesthetic drugs are cerebral vasodilators and produce dose-dependent increases in ICP that parallel the increases in CBF and CBV. Hyperventilation to decrease $Paco_2$ to less than 35 mm Hg attenuates the tendency for volatile anesthetics to increase ICP. In patients undergoing craniotomy for supratentorial tumors with evidence of a midline shift, neither isoflurane nor desflurane significantly affected lumbar CSF pressure when moderate hypocapnia ($Paco_2$ of 30 mm Hg) was maintained.[8] However, these inhaled anesthetics are better avoided in patients with exhausted ICP-compensating mechanisms as evidenced by increased ICP, abnormal mental status, or imaging studies.

Neuromuscular blocking drugs (also see Chapter 11) do not usually affect ICP unless they induce release of histamine or hypotension. Histamine can cause cerebral vasodilation leading to an increase in ICP. Succinylcholine may increase ICP through increases in CBF although this is not well documented.[9] Because CBF is coupled to $CMRO_2$, a decrease in $CMRO_2$ leads to a decrease in CBF and thus facilitates the management of intracranial hypertension. Therefore, in patients refractory to initial treatment of intracranial hypertension, a deep level of anesthesia, such as propofol-induced burst suppression or barbiturate coma, can be an alternative option.

Box 30.1 Methods to Decrease Intracranial Pressure

Cerebral Blood Volume Reduction

Decrease Cerebral Blood Flow

- Intravenous anesthetic drugs are preferred
- Decrease $CMRO_2$ (propofol, barbiturates)
- Employ hyperventilation
- Avoid cerebral vasodilators
- Avoid extreme hypertension

Increase Venous Outflow

- Elevate head
- Avoid constriction at the neck
- Avoid PEEP and excessive airway pressure

Cerebrospinal Fluid Reduction

- External ventricular drain
- Lumbar drain
- Head elevation (translocation of intracranial cerebrospinal fluid)
- Acetazolamide (Diamox)

Cerebral Edema Reduction

- Osmotic therapy (mannitol, hypertonic saline)
- Furosemide (Lasix)
- Prevention of ischemia and secondary edema
- Dexamethasone to reduce peritumoral vasogenic edema

Resection of Space-Occupying Lesions

Decompressive Craniectomy

$CMRO_2$, Cerebral metabolic rate of oxygen; *PEEP*, positive end-expiratory pressure.

NEUROPROTECTION

Many anesthetics have been proposed as neuroprotectants based on their potential to reduce cerebral metabolic rate and excitotoxicity during periods of oxygen deprivation. Many anesthetics, including volatile anesthetics, barbiturates, propofol, and xenon, can provide neuroprotection in animals; convincing human data are lacking. Hypothermia may provide cerebral protection during acute injury. Several animal studies have shown that decreasing body temperature reduces ischemic injury. However, several large prospective, randomized trials of hypothermia in aneurysm surgery and traumatic brain injury have failed to demonstrate such benefit.[3] Yet, cooling patients with return of spontaneous circulation after cardiac arrest improved neurologic outcome in a randomized controlled trial,[10] although a more recent trial contradicted these findings.[11] In contrast, hyperthermia worsens ischemic injury and should be avoided in patients vulnerable to cerebral ischemia.

NEUROPHYSIOLOGIC MONITORING

Neurophysiologic monitoring is employed during various neurologic surgeries with increasing frequency because of minimal risk to patients and the potential to reduce intraprocedural neurologic injuries. An understanding of the effects of anesthetics on various monitoring modalities, including the EEG, somatosensory and motor evoked potentials, and intracranial nerve monitoring, is especially critical in neuroanesthesia. The monitoring techniques can be transcranial, direct cortical, or subcortical in approach. Different monitoring modalities often require different anesthetic regimens to preserve the quality of monitoring. Electrocorticography (ECoG) is frequently used during neurologic surgery (also see Chapter 20) to identify epileptic foci or activity (afterdischarge) during epilepsy surgery or surgery with intraoperative stimulation mapping. ECoG is sensitive to anesthetic drugs that change the seizure threshold (e.g., benzodiazepines, propofol, and volatile anesthetics).

ANESTHESIA FOR NEUROSURGERY

Preoperative Assessment

Patients presenting for neurosurgical procedures can have a wide range of signs and symptoms (also see Chapter 13). Patients with intracranial mass lesions may present with seizures, altered levels of consciousness, headaches, cranial nerve abnormalities, and motor or sensory deficits. Aneurysms and arteriovenous malformations (AVMs) can present with a severe ("thunderclap") headache if ruptured and focal deficits or visual impairment from compression of the optic chiasm when unruptured. Some neurosurgical patients are asymptomatic and present with an incidental finding.

Evidence of increased ICP should be elicited during the preoperative visit. Clinical signs may be consistent with but do not reliably indicate the level of ICP (Box 30.2). Imaging may reveal a midline shift, encroachment of expanding brain on cerebral ventricles, cerebral edema, hydrocephalus, or any combination of these signs. In symptomatic patients, preoperative medications that cause sedation or depression of ventilation are usually avoided. Drug-induced depression of ventilation can lead to increased $Paco_2$ and subsequent increases in CBF and ICP. In alert patients, small doses of benzodiazepines may provide a useful degree of anxiolysis.

Medications the patient takes should be noted, especially antiepileptic drugs (e.g., levetiracetam), drugs used to reduce peritumoral vasogenic edema (e.g., dexamethasone), and drugs used to reduce brain free water (e.g., mannitol, hypertonic saline). In addition, it is important to note antihypertensive drugs, drugs used for blood glucose control, drugs for chronic pain, and anticoagulants. Abnormal laboratory results should be investigated and corrected if clinically indicated. Coagulation profile including platelet count and international normalized ratio (INR) and other studies, such as echocardiography, brain magnetic resonance imaging, computed tomography, and angiography, should be reviewed. The side of the brain lesion, left versus right, should be specifically noted.

Box 30.2 Preoperative Evidence of Increased Intracranial Pressure

- Positional headache
- Nausea and vomiting
- Hypertension and bradycardia
- Altered level of consciousness
- Altered patterns of breathing
- Papilledema

Monitoring

In addition to standard monitors, continuous monitoring of systemic blood pressure via a peripheral arterial catheter is recommended. The advantages of invasive arterial blood pressure monitoring include the ability to continuously assess CPP and intravascular volume via indexes such as systolic pressure variation and pulse pressure variation. In addition, these catheters allow analysis of arterial blood gases especially the $Paco_2$. Central venous catheters are not routinely used; however, exceptions include difficult peripheral venous access and the potential need for massive blood transfusion (also see Chapter 24). Measurement of the exhaled carbon dioxide concentration (capnography) is used to adjust mechanical ventilation or assess spontaneous breathing if the airway is not instrumented. The electrocardiogram (ECG) allows prompt detection of cardiac dysrhythmias caused by surgical stimulation of brainstem or intracranial nerves. Neuromuscular blockade is monitored with a peripheral nerve stimulator (also see Chapter 11). Because of the length of these surgical procedures and the use of diuretics, a bladder catheter is often necessary and helps in guiding intravenous fluid therapy. A continuous monitor of ICP is helpful but rarely used after the bone flap is removed and the dura is opened. There are two types of ICP monitors that are inserted by neurosurgeons. The intraventricular catheter or external ventricular device (EVD) permits direct measurement of ICP and drainage of CSF. The subarachnoid or subdural bolt is placed through a burr hole and can be inserted quickly in an emergency setting, but it does not allow for CSF drainage (also see Chapter 20).

Induction of Anesthesia

The goal of induction of anesthesia is to achieve a sufficient level of anesthesia to blunt the stimulation of direct laryngoscopy and tracheal intubation without

compromising cerebral perfusion by increasing ICP or decreasing MAP. Intravenous induction of anesthesia with propofol, 1.5 to 3 mg/kg, thiopental, 3 to 6 mg/kg, or etomidate, 0.2 to 0.5 mg/kg, produces reliable and prompt onset of unconsciousness and is unlikely to adversely increase ICP. However, the specific dose depends on the patient's age, physical condition, and comorbid conditions in addition to the patient's response to the drug initially administered. Hemodynamic support with sympathomimetic drugs, such as phenylephrine and ephedrine, may be necessary, and such drugs should be readily available, especially in cases in which CPP may already be compromised. A nondepolarizing neuromuscular blocking drug or succinylcholine is used to facilitate tracheal intubation, mechanical ventilation of the lungs, and patient positioning on the operating table (also see Chapters 10 and 19). Increases in ICP may occur after the administration of succinylcholine, but the extent of the increase is usually short-lived and clinically inconsequential.[9] The trachea is intubated ideally after a peripheral nerve stimulator confirms the establishment of skeletal muscle paralysis so that coughing is avoided, which may result in marked increases in ICP. Injection of additional intravenous doses of propofol, thiopental, opioids, or lidocaine 1 to 2 minutes before initiating direct laryngoscopy may be effective in attenuating the increase in systemic blood pressure and ICP that can accompany tracheal intubation.

Positioning

The head of the operating table is frequently turned 90 to 180 degrees away from the anesthesia workstation during intracranial procedures (also see Chapter 19). Typically, the anesthesia provider will have limited access to the patient's head, so the endotracheal tube should be safely secured prior to draping. The breathing circuit, monitor cables, and intravenous and intra-arterial lines should be organized in order to facilitate trouble shooting and avoid cumbersome tangling.

Resection of supratentorial tumors and intracranial vascular lesions is typically accomplished with the patient in supine, semilateral, or lateral position. Resection of posterior fossa/infratentorial tumors frequently requires placement of the patient in prone or sitting position. The sitting position facilitates surgical exposure of posterior fossa tumors, but because of the frequent risk of venous air embolism (>25% incidence), the prone position is often used instead. Other risks associated with the sitting position include upper airway edema as a result of venous obstruction from excessive cervical flexion and quadriplegia from spinal cord compression and ischemia, especially in the presence of preexisting cervical stenosis. An alternative approach is the "park bench position" in which the patient is placed in a lateral position but rolled slightly forward with the head further rotated to "look" at the floor. This position allows the surgeon full access to the posterior fossa and minimizes the risk for venous air embolism (also see Chapter 19).

Extreme rotation, flexion, and extension of the head and neck should be avoided, especially in patients with cervical spine diseases or elderly patients with arthritis or osteoporosis. Twisting, stretching, and compression of the neck vascular structures should also be avoided. A chest roll is frequently used in patients positioned in lateral or in park bench position, but not semilateral. Pressure points should be adequately padded to avoid compression injury. The body weight should be supported at multiple points, not a single point, in an even distribution fashion. Slight flexion of elbows and knees is recommended. The eyelids are closed shut and covered by transparent and waterproof film dressing to avoid scratching and chemical injury to the eyes from preparatory solutions. A soft but effective bite block is recommended to prevent soft tissue injury due to an intraoperative seizure or various motor stimulations due to monitoring. The mechanisms of preventing patients from slipping should be instituted intraoperatively if the operating table is to be tilted at the surgeon's request. A patient's tolerance and ease of airway instrumentation should also be taken into consideration during positioning for any procedure that is to be done under monitored anesthesia care such as deep brain stimulator placement or awake craniotomy.

A special consideration during neurologic surgery is the application of a head frame using three pins (Mayfield head clamp). Caution must be exercised to avoid bucking or movement during the placement and removal of the head frame and while the patient is fixed in the frame to avoid injury to the patient. Additional doses of propofol, or opioids, or both, are frequently administered right before the head frame placement to blunt the hemodynamic fluctuation. Local anesthesia injection at the site of pin insertion will also reduce the painful response to Mayfield head clamp placement.

Maintenance of Anesthesia

After tracheal intubation, measures should be taken to minimize increases in ICP and optimize CPP. Maintenance of anesthesia is often achieved with a combination of opioid (either bolus or infusion), continuous infusion of propofol, and inhalation of a volatile anesthetic with or without nitrous oxide. Volatile anesthetic drugs must be used carefully because of their ability to increase ICP. Nevertheless, at low concentrations, volatile anesthetics (<0.5 MAC) are useful for blunting the increases in systemic blood pressure evoked by surgical stimulation. The choice of anesthetic drugs should also take into account the neurophysiologic monitoring being used because certain drugs (e.g., volatile anesthetics, nitrous oxide, neuromuscular blocking drugs) will impede neurophysiologic monitors such as motor or somatosensory evoked potentials.

Direct-acting vasodilating drugs (hydralazine, nitroprusside, nitroglycerin, calcium channel blockers) may increase CBF and ICP despite causing simultaneous decreases in systemic blood pressure; therefore, use of these drugs, particularly before the dura is open, is not encouraged. On the contrary, sympathomimetic drugs such as phenylephrine or norepinephrine are often infused to maintain an ideal CPP.

Movement, coughing, or reacting to the presence of the tracheal tube during intracranial procedures is avoided because these responses can lead to increases in ICP, bleeding into the operative site, and a brain that bulges into the operative site and makes surgical exposure difficult. Thus, maintenance of an adequate depth of anesthesia is important. Skeletal muscle paralysis is often used to provide added insurance against movement or coughing. However, continuous administration of muscle relaxants is not possible in cases in which motor function monitoring is applied (e.g., either evoked potential, or direct cortical or subcortical stimulation).

Intracranial Pressure Reduction and Brain Relaxation

ICP reduction and brain relaxation are related but distinctive concepts. The former is a pressure concept used in the absence of craniectomy and the latter is more a volume concept used during craniotomy indicating the size relationship between the intracranial components and capacity. Osmotic drugs such as mannitol (0.25 to 1 g/kg intravenously) or 3% hypertonic saline are frequently administered to reduce cerebral water content and decrease ICP before craniectomy, and to improve brain relaxation after craniectomy. The onset of action is 5 to 10 minutes, maximum effects are seen in 20 to 30 minutes, and its effects last for about 2 to 4 hours. However, if administered rapidly, mannitol can also cause peripheral vasodilation (hypotension) and short-term intravascular volume expansion, which could result in increased ICP and intravascular volume overload. Acute mannitol toxicity, as manifested by hyponatremia, high measured serum osmolality, and a gap between the measured and calculated serum osmolality of more than 10 mOsm/kg, can also occur when large doses of the drug (2 to 3 g/kg intravenously) are given. Furosemide (0.5 to 1 mg/kg intravenously) is often used to decrease brain water and ICP and is likely synergistic with mannitol in decreasing ICP. However, hypovolemia secondary to diuresis can decrease the preload and cardiac output that may do more harm than good in terms of tissue perfusion. Intermittent intravenous injections of thiopental or propofol may also be effective in decreasing ICP. When possible, the patient should be in a head-up position to avoid constriction around the neck, which may impair venous drainage. Other useful measures include hyperventilation, discontinuing the administration of volatile anesthetic drugs, and cerebrospinal fluid drainage.

Ventilation Adjustment

After tracheal intubation, ventilation of the lungs is controlled at a rate and tidal volume sufficient to maintain $Paco_2$ between 30 and 35 mm Hg. There is no evidence of additional therapeutic benefit when $Paco_2$ is decreased below this range.

Whether a smaller tidal volume is lung protective during neurologic procedures is not clear. Use of positive end-expiratory pressure (PEEP) is not encouraged because it could impair cerebral venous drainage and increase ICP, but it can usually be counteracted by elevating the head 10 to 15 cm above the level of the chest. Hypoventilation is not indicated because hypercapnia causes cerebral vasodilation, increases CBF and ICP, and impairs cerebral autoregulation.[1] Overall, eucapnia probably should be maintained during intracranial surgery, and relative hyperventilation should be used only as a temporizing measure.

Intravascular Fluid Management

Maintaining euvolemia is recommended. Dextrose solutions are not recommended because they are rapidly distributed throughout body water and, if blood glucose concentrations decrease more rapidly than brain glucose concentrations, water crosses the blood-brain barrier and cerebral edema results. Furthermore, hyperglycemia augments ischemic neuronal cell damage by promoting neuronal lactate production, which worsens cellular injury. Therefore, crystalloid solutions such as normal saline, Plasma-Lyte, and lactated Ringer solution are recommended. Colloids such as 5% albumin are also an acceptable replacement fluid, but no improvement in outcome has been shown (also see Chapter 23).

Postoperative Care

On awakening from anesthesia, coughing or straining by the patient should be avoided because these responses could increase the possibility of intracranial hemorrhage or edema formation (also see Chapter 39). A prior intravenous bolus of lidocaine, opioid, or both may help decrease the likelihood of coughing during tracheal extubation. Low-rate remifentanil infusion can facilitate a smooth emergence. Postoperatively, early and frequent neurologic assessment and adequate analgesia are important. Delayed return of consciousness or neurologic deterioration in the postoperative period should be carefully monitored and evaluated by computed tomography or magnetic resonance imaging. Intracranial hemorrhage and stroke should be detected as soon as possible. Tension pneumocephalus as a cause of neurologic deterioration is a consideration. The postoperative stress response and resulting hyperdynamic events (hypertension, tachycardia) are attenuated with the use of hemodynamically active drugs and opioids. Labetalol is commonly used to treat hypertension based on its ability to reduce MAP without cerebral vasodilation.

Venous Air Embolism

Neurosurgery that requires significant elevation of the head is associated with an increased risk for venous air embolism.[12] Not only is the operative site above the level of the heart but the venous sinuses in the cut edge of bone or dura may not collapse when transected. Air enters the pulmonary circulation and becomes trapped in the small vessels, thereby causing an acute increase in dead space. Massive air embolism may cause air to enter and be trapped in the right ventricle and lead to acute right ventricular failure. Microvascular bubbles may also cause reflex bronchoconstriction and activate the release of endothelial mediators causing pulmonary edema. Death is usually due to cardiovascular collapse and arterial hypoxemia. Air may reach the coronary and cerebral circulations (paradoxic air embolism) by crossing a patent foramen ovale (a probe-patent foramen ovale is present in 20% to 30% of adults) and result in myocardial infarction or stroke. Furthermore, transpulmonary passage of venous air is possible in the absence of a patent foramen ovale.

Transesophageal echocardiography is the most sensitive method to detect air embolism, but it is invasive and cumbersome. A precordial Doppler ultrasound transducer placed over the right side of the heart (over the second or third intercostal space to the right of the sternum to maximize audible signals from the right atrium) is the next most sensitive method (detects amounts of air as small as 0.25 mL) and a practical noninvasive indicator of the presence of intracardiac air. A sudden decrease in end-tidal concentrations of carbon dioxide reflects increased dead space secondary to continued ventilation of alveoli no longer being perfused because of obstruction of their vascular supply by air bubbles. An increased end-tidal nitrogen concentration may reflect nitrogen from venous air embolism if the inspired oxygen concentration is higher than that of room air but this is rarely available. Aspiration of air through a correctly positioned central venous catheter can also be used to diagnose air embolism. In this regard, a right atrial catheter with the tip positioned at the junction of the superior vena cava and the right atrium may provide the most rapid aspiration of air. During controlled ventilation of the lungs, sudden attempts (gasps) by patients to initiate spontaneous breaths may be the first indication of the occurrence of venous air embolism. Hypotension, tachycardia, cardiac dysrhythmias, cyanosis, and a "mill wheel" murmur are late signs of venous air embolism. A pulmonary artery catheter may provide additional evidence that venous air embolism has occurred because of abrupt increases in pulmonary artery pressure. Additional signs in patients who are not receiving general anesthesia include chest pain and coughing.

The surgeon should be notified immediately whenever a venous air embolism is suspected. Venous air embolism is treated by (1) irrigation of the operative site with fluid, as well as the application of occlusive material to all bone edges so that sites of venous air entry are occluded; (2) placement of the patient in a head-down position; (3) gentle compression of the internal jugular veins; (4) provision of 100% of inspired oxygen concentration; and (5) supportive care of hemodynamic derangements. If nitrous oxide is being administered, it should be promptly discontinued to avoid the risk of increasing the size of venous air bubbles because of diffusion of this gas into the air bubbles. Despite the logic of PEEP to decrease entrainment of air, the efficacy of this maneuver has not been confirmed. Furthermore, PEEP could reverse the pressure gradient between the left and right atria and predispose to passage of air across a patent foramen ovale.

COMMON CLINICAL CASES

Intracranial Mass Lesions

Intracranial mass lesions (Box 30.3), especially primary brain tumors, occur most often in patients 40 to 60 years

Box 30.3 Management of Anesthesia for Patients With Intracranial Masses

Preoperative
- Avoid sedatives and opioids if ICP is elevated.
- Standard anxiolytics can be given if ICP is not elevated.

Monitors

Supratentorial Masses
- Standard ASA monitors, arterial line, Foley catheter are used.

Infratentorial Masses—Depending on Positioning
- Prone or park bench position: Standard ASA monitors, arterial line, Foley catheter are adequate.
- Sitting position (associated with frequency of VAE): Standard monitors plus central venous catheter, precordial Doppler, or TEE are required.

Induction
- Deep anesthesia and skeletal muscle paralysis are obtained before direct laryngoscopy/tracheal intubation to avoid increasing ICP while maintaining CPP.

Maintenance
- Minimize ICP and maintain adequate CPP.
- Opioid plus propofol and/or volatile anesthetic with or without nitrous oxide.
- Avoid intraoperative muscle relaxant if motor function is tested/mapped.
- Mannitol (0.25-1 g/kg IV) also can be given.
- Maintain euvolemia.
- Eucapnia if normal ICP; temporary hyperventilation for a tight brain only.

Postoperative
- Avoid coughing, straining, and systemic hypertension during tracheal extubation.
- Rapid awakening allows early neurologic assessment.

ASA, American Society of Anesthesiologists; *CPP*, cerebral perfusion pressure; *ICP*, intracranial pressure; *IV*, intravenous; *TEE*, transesophageal echocardiography; *VAE*, venous air embolism.

of age, and the initial signs and symptoms may or may not reflect increases in ICP. Headache and seizures that appear in a previously asymptomatic adult suggest the presence of an intracranial tumor, and such tumors are usually confirmed by computed tomography or magnetic resonance imaging. Avoidance of abrupt increases in ICP is an important anesthetic goal when managing patients with intracranial tumors.

The sitting position for posterior fossa masses has several additional considerations. The arterial line transducer should be positioned no lower than the external ear canal level in order to facilitate the assessment of CPP. A properly positioned central venous catheter and precordial Doppler should be used given the high incidence of venous air embolism. Adequate hydration is warranted to compensate for the intravascular volume pooling in the lower extremities. Posterior fossa operations have the potential of stimulating or injuring vital brainstem respiratory and circulatory centers and result in intraoperative hemodynamic fluctuations and postoperative ventilation abnormalities. The cranial nerves can also be stimulated or affected, which can lead to intraoperative dysrhythmias and postoperative impairment of protective airway reflexes. Postoperatively, the airway needs to be assessed as to whether the patient will be able to maintain and protect the airway or whether tracheal intubation and ventilation should be continued in the intensive care unit.

Intracranial Aneurysms

Intracranial aneurysms (Box 30.4) are the most common cause of intracranial hemorrhage. They occur in 2% to 4% of the population, with 1% to 2% rupturing per year. Although aneurysms may be found incidentally or appear as a slowly enlarging mass, they are most frequently manifested as hemorrhage together with a sudden, severe headache, nausea, vomiting, focal neurologic signs, and decreased level of consciousness. Major complications of aneurysmal rupture include death, rebleeding, and vasospasm. Definitive treatment may include either endovascular coiling or surgical clipping via craniectomy. Short- to medium-term outcomes are similar in patients treated surgically versus endovascular insertion of platinum coils, although the long-term benefits of one technique over the other continues to be debated.[13] Some patients are unsuitable candidates for endovascular coiling because of the anatomy and location of their aneurysms; in these cases, surgical clipping is needed.

Early treatment is advocated for prevention of rebleeding, but surgery may be associated with more technical difficulty because of a swollen inflamed brain, whereas delaying treatment increases the risk for rebleeding. Cerebral vasospasm is generally manifested clinically 3 to 5 days after subarachnoid hemorrhage (SAH) and is the foremost cause of morbidity and death. Transcranial Doppler and cerebral arteriography can detect cerebral vasospasm before clinical symptoms (worsening headache, neurologic deterioration, loss of consciousness) occur. Treatment of vasospasm often includes "triple H" therapy (hypervolemia, hypertension, hemodilution), which consists of intravenous administration of fluids or inotropic drugs, or both. The intravenous administration of a calcium channel blocker, nimodipine, decreases the morbidity and mortality risks from vasospasm. Other treatment modalities include selective intra-arterial injection of vasodilators and balloon dilation (angioplasty) of the affected arterial segments using interventional radiology approaches.

Other complications of SAH include seizures (10%), acute and chronic hydrocephalus, and intracerebral hematoma. Changes on the ECG (T-wave inversions, U waves, ST-segment depressions, prolonged QT interval, and rarely Q waves) and mild elevation of cardiac enzymes are frequent but do not usually correlate with significant myocardial dysfunction or poor outcome. Hyponatremia is commonly seen after SAH. Significant electrolyte and acid-base abnormalities or hemodynamic derangements should be corrected if present, and a cardiac workup should ensue if Q waves are seen on the ECG.

The anesthetic care for intracranial aneurysm clipping is designed to (1) prevent sudden increases in systemic arterial blood pressure, which would increase the aneurysm's transmural pressure and could result in rupture or

Box 30.4 Anesthetic Management of Patients With Intracranial Aneurysms

Preoperative
- Neurologic evaluation is performed to look for evidence of increased intracranial pressure and vasospasm.
- Electrocardiogram changes are often present.
- HHH therapy is indicated if vasospasm is present.
- Calcium channel blockers.

Induction
- Avoid increases in systemic blood pressure.
- Maintain cerebral perfusion pressure to avoid ischemia.

Maintenance
- Opioid plus propofol and/or volatile anesthetic is recommended regimen.
- Mannitol (0.25-1 g/kg IV) also can be given.
- Maintain normal to increased systemic blood pressure to avoid ischemia during surgical retraction and temporary clipping.
- Maintain euvolemia.
- Maintain eucapnia; avoid unnecessary hyperventilation.
- Burst-suppression and mild hypothermia can be considered.

Postoperative
- Maintain normal to increased systemic blood pressure.
- Early awakening is recommended to facilitate neurologic assessment.
- HHH therapy is given as needed.

HHH, Hypervolemia, hypertension, hemodilution; *IV,* intravenous.

rebleeding, and (2) facilitate surgical exposure and access to the aneurysm (see Box 30.4). Induction and maintenance of anesthesia must be designed to minimize the hypertensive responses evoked by noxious stimulation, such as direct laryngoscopy and placing the patient's head in immobilizing pins. Conversely, CPP must be maintained to prevent ischemia during surgical retraction or temporary vessel occlusion, or as a result of vasospasm.

Hemodynamic control is important during dissection of the aneurysm to prevent intraoperative rupture. Temporary occlusive clips applied to the major feeding artery of the aneurysm can create regional hypotension without the need for systemic hypotension and its inherent risks on multiple organ systems. As a result, normal or even increased systemic arterial blood pressure should be instituted to facilitate perfusion through collateral circulations. In addition to maintaining collateral cerebral circulations via systemic relative hypertension, drugs such as propofol or thiopental may be administered, via either boluses or high-rate infusion to the point of burst-suppression on electroencephalography monitoring, in the hope that they can provide some protection from cerebral ischemia. Occasionally, hypothermic circulatory arrest may be used for very large complex aneurysms. Nonetheless, convincing outcome evidence of these maneuvers is lacking.

The patient's trachea is generally extubated at the completion of surgery unless there is significant neurologic impairment or other intraoperative complications. Measures to prevent vasospasm and seizures while maintaining adequate CPP should be continued during care of these patients postoperatively.

Box 30.5 Management of Anesthesia for Patients With Carotid Stenosis

Preoperative
- Neurologic examination is indicated to look for preoperative deficits.
- Screen for associated CAD.
- Anxiolytics may be useful.

Monitors
- Standard ASA monitors, arterial line, Foley catheter are used.
- Cerebral ischemia monitoring depends on institutional and individual practitioner's preference.

Induction
- Avoid increases in mean arterial pressure or heart rate if CAD is suspected.
- Maintain adequate CPP.

Maintenance
- Maintain adequate CPP (baseline to 20% above) during carotid clamping.
- Opioid plus propofol and/or volatile anesthetic can be used with or without nitrous oxide.
- Close intraoperative monitoring for cerebral ischemia during carotid clamping by keeping the patient awake or based on various monitoring modalities.

Postoperative
- Avoid coughing, straining, and systemic hypertension during tracheal extubation.
- Rapid awakening allows early neurologic assessment.
- Monitor for hyperperfusion syndrome and airway compromise.

ASA, American Society of Anesthesiologists; *CAD*, coronary artery disease; *CPP*, cerebral perfusion pressure.

IV

Arteriovenous Malformations

The incidence of AVMs in the general population and the annual rate of rupture is similar to aneurysms at 2% to 4% and 2%, respectively. Up to 10% of patients diagnosed with an AVM have an associated aneurysm.[14] Risk of hemorrhage is related to the anatomic features of the AVM including size and characteristics of the feeding arteries. These patients may be treated several ways: expectantly, open resection, endovascular embolization, or stereotactic radiosurgery (Gamma Knife). Preoperative embolization is frequently employed to reduce blood loss and facilitate surgical resection.

Anesthesia for resection or embolization of AVMs is similar to that of aneurysms with a few distinct considerations. Because of their flow characteristics (low-pressure, high-flow shunts), AVMs are unlikely to rupture during acute systemic hypertension, such as during laryngoscopy. Despite this, hypertension should still be avoided during induction of anesthesia, given the frequent rate of associated aneurysms. Finally, anesthesia for intracranial AVM resection must include preparation for massive, persistent blood loss and postoperative cerebral swelling.

Carotid Disease

Stroke can result in severe disability and death. Atherosclerotic stenosis of the carotid artery is an important cause of stroke. Despite the technical advancement and increasing adoption of carotid artery stenting (CAS), carotid endarterectomy (CEA) remains the "gold standard" in treating symptomatic carotid disease (Box 30.5).[15] Although the perioperative risk of stroke and death (approximately 4% to 7%) must be taken into account, CEA may be beneficial in asymptomatic patients as well.[16] Data suggest that early CEA (<30 days after symptom onset) is optimal given the presence of unstable atherosclerotic plaque.[17]

Preoperative assessment of patients undergoing CEA should focus on assessment of perioperative risk of cardiac ischemia as these patients typically have atherosclerotic disease. Either general or regional anesthesia (deep and superficial cervical plexus block) may be used for this procedure. Regional anesthesia may permit a more accurate intraoperative assessment of the patient's neurologic status and more stable hemodynamic profile, but it requires a cooperative and motionless patient. Current analysis of the literature suggests that outcomes are

similar whether CEA is performed under regional or general anesthesia.[18]

Goals of anesthesia for CEA include (1) prevention of cerebral ischemia through maintenance of adequate CPP and (2) prevention of myocardial ischemia through avoidance of acute increases in arterial blood pressure and heart rate. Invasive hemodynamic monitoring with an arterial catheter is indicated to ensure adequate CPP. This is especially important during intraoperative clamping of the carotid artery. The anesthesia provider should ensure that the MAP is maintained above the patient's baseline pressure (within 20%) to ensure adequate collateral flow through the circle of Willis. Hypocarbia should be avoided given the risk of cerebral vasoconstriction and ischemia. Many methods have been employed to detect intraoperative cerebral ischemia and need for shunting during clamping including EEG, evoked potentials, transcranial Doppler, cerebral oximetry, and stump pressure, although none has been shown to definitively improve outcome.

Postoperative complications include cardiovascular ischemia and neurologic deficits secondary to intraoperative emboli. Hypertension should be avoided because it may lead to complications such as neck hematoma with airway compromise or hyperperfusion syndrome (ipsilateral headache, seizure, focal neurologic signs in the absence of cerebral ischemia).

QUESTIONS OF THE DAY

1. What is the relationship between cerebral perfusion pressure and cerebral blood flow? How does the relationship change when the cerebral perfusion pressure is above and below the limits of autoregulation? What disease processes can impair normal cerebral autoregulation?
2. How do $Paco_2$ and Pao_2 affect cerebral blood flow? How long do the $Paco_2$-related changes in cerebral blood flow last, and what is the mechanism for this phenomenon?
3. How do different intravenous anesthetics (e.g., benzodiazepines, opioids, propofol, ketamine) and inhaled anesthetics affect cerebral blood flow and cerebral metabolic rate?
4. Draw a diagram of the relationship between intracranial volume and intracranial pressure in the adult. What components of the intracranial compartment can be manipulated to effect a reduction in intracranial pressure?
5. A patient is undergoing craniotomy for removal of brain mass. After craniectomy and dural opening, the surgeon notes "brain swelling" in the operative field. What steps can be taken to promote brain relaxation?
6. What are the goals of anesthesia care for a patient undergoing intracranial aneurysm clipping? What complications of subarachnoid hemorrhage may develop in the perioperative period?
7. What are the manifestations of venous air embolism in a patient undergoing craniotomy during general anesthesia? What are the appropriate steps in management?
8. What are the goals of intraoperative anesthesia management for a patient undergoing carotid endarterectomy? What complications should be anticipated after surgery?

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