

3. *The fluid compartment.* This compartment can be addressed with steroids and osmotic/diuretic agents. The use of these agents is discussed later.
4. *The blood compartment.* This compartment receives the anesthesiologist's greatest attention because it is the most amenable to rapid alteration. The blood compartment should be viewed as having two separate components: venous and arterial.

With respect to the blood compartment, the venous side of the circulation should initially be considered. It is largely a passive compartment and is often overlooked. Despite this passivity, engorgement of this compartment is a common cause of increased ICP or poor conditions in the surgical field (Fig. 57.5). A head-up posture to ensure good venous drainage is the standard in neurosurgical anesthesia and critical care. Obstruction of cerebral venous drainage by extremes of head position or circumferential pressure (cervical collars, endotracheal tube ties) should be avoided. Anything that causes increased intrathoracic pressure can also result in obstruction of cerebral venous drainage. Relevant phenomena include kinking or partial obstruction of endotracheal tubes, tension pneumothorax, coughing or straining against the endotracheal tube, or gas trapping as a result of bronchospasm. Neuromuscular blockade is usually induced during craniotomies unless a contraindication

is present. Such a blockade would prevent a sudden cough that can cause a dramatic herniation of cerebral structures through the craniotomy.

Thereafter, the arterial side of the circulation should be considered. Attention to the effect of anesthetic drugs and techniques on cerebral blood flow (CBF) (see [Chapter 11](#)) is an established part of neuroanesthesia because, in general, increases in CBF are associated with increases in cerebral blood volume (CBV).²⁻⁴ The notable exception to this rule occurs in the context of cerebral ischemia caused by hypotension or vessel occlusion, at which times CBV may increase as the cerebral vasculature dilates in response to a sudden reduction in CBF. However, the relationship generally applies, and attention to the control of CBF is relevant in situations in which intracranial volume compensation mechanisms are exhausted or ICP is already increased. The general approach is to select anesthetics and to control physiologic variables in a manner that avoids unnecessary increases in CBF. The variables that influence CBF are listed in [Box 57.2](#) and are discussed in [Chapter 11](#).

BOX 57.2 Factors that Influence Cerebral Blood Flow

See effects of anesthetics on cerebral blood flow and cerebral metabolic rate in [Chapter 11](#) for detailed discussion.

- PaO_2
- PaCO_2
- Cerebral metabolic rate
 - Arousal/pain
 - Seizures
 - Temperature
 - Anesthetics
- Blood pressure/status of autoregulation
- Vasoactive agents
 - Anesthetics
 - Pressors
 - Inotropes
 - Vasodilators
- Blood viscosity
- Neurogenic pathways (intra- and extra-axial)

TABLE 57.1 Intracranial Compartments and Techniques for Manipulation of Their Volume

Compartment	Volume Control Methods
1. Cells (including neurons, glia, tumors, and extravasated blood)	Surgical removal
2. Fluid (intracellular and extracellular)	Diuretics/osmotic/diuretic agents Steroids (principally tumors)
3. Cerebral spinal fluid	Drainage
4. Blood	
Arterial side	Decrease cerebral blood flow
Venous side	Improve cerebral venous drainage

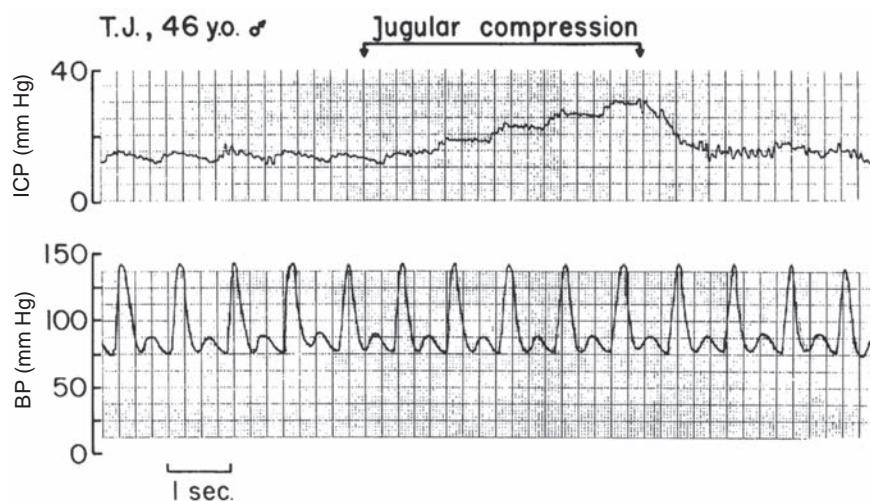


Fig. 57.5 The effect of cerebral venous outflow obstruction on intracranial pressure (ICP) in a patient with an intracerebral hematoma. Bilateral jugular compression was applied briefly to verify the function of a newly placed ventriculostomy. The ICP response illustrates the importance of maintaining unobstructed cerebral venous drainage.

SELECTION OF ANESTHETICS

The question of which anesthetics are appropriate, especially in the context of unstable ICP, arises frequently. [Chapter 11](#) provides relevant information in detail, and only broad generalizations are described here.

In general, intravenous anesthetic, analgesic, and sedative drugs are associated with parallel reductions in CBF and cerebral metabolic rate (CMR) and consequently will not have adverse effects on ICP. Ketamine, given in large doses to patients with a generally normal level of consciousness before anesthesia, is the exception. Autoregulation and carbon dioxide (CO_2) responsiveness are generally preserved during the administration of intravenous anesthetics (see [Chapter 11](#)).

By contrast, all the volatile anesthetics can be, depending on physiologic and pharmacologic circumstances, dose-dependent cerebral vasodilators. The order of vasodilating potency is approximately halothane → enflurane → desflurane → isoflurane → sevoflurane. As noted in [Chapter 11](#), the CBF differences among desflurane, isoflurane, and sevoflurane are unlikely to be clinically significant. The net CBF effect of a volatile anesthetic depends on the interaction of several factors: the concentration of the anesthetic, the extent of previous CMR depression, simultaneous blood pressure changes acting in conjunction with previous or anesthetic-induced autoregulation abnormalities, and simultaneous changes in partial pressure of carbon dioxide in the arterial blood (PaCO_2) acting in conjunction with any disease-related impairment in CO_2 responsiveness.

Nitrous oxide (N_2O) can also be a cerebral vasodilator. The CBF effect of N_2O is greatest when it is administered as a sole anesthetic; least when it is administered against a background of narcotics, propofol, or benzodiazepines; and intermediate when it is administered in conjunction with volatile anesthetics (see [Chapter 11](#)).

Despite the vasodilatory potential of both N_2O and volatile anesthetics, experience dictates that both, with the latter in concentrations less than the minimum alveolar concentration (MAC), can be used in most elective and many emergent neurosurgical procedures when administered as part of a balanced anesthetic technique in combination with opioids. However, there are exceptions. Because both N_2O and volatile anesthetics can be vasodilators in some circumstances, when the compensatory latitude of the intracranial space has been exhausted and physiology is abnormal, omitting them on a just-in-case basis may be prudent. In a somnolent, vomiting patient with papilledema, a large tumor mass, and compressed basal cisterns; or in a traumatic brain injury (TBI) victim with an expanding mass lesion or obliterated cisterns and sulci on CT, a predominantly intravenous technique should be used until the cranium and dura are open. Thereafter, the effect of the anesthetic technique can be assessed by direct observation of the surgical field. Although inhaled anesthetics are entirely acceptable components of most anesthetics for neurosurgery, in circumstances in which ICP is persistently increased or the surgical field is persistently “tight,” N_2O and volatile anesthetics^{5,6} should be replaced by intravenous anesthetics.

Neuromuscular blockers that can release histamine (e.g., atracurium) should be given in small, divided doses. Although succinylcholine can increase ICP, the increases

are small and transient. Moreover, the increases can be blocked by a preceding dose of nondepolarizing neuromuscular blocking drugs and, in at least some instances, are not evident in patients with common emergency neurosurgical conditions (TBI, SAH).^{7,8} Succinylcholine in conjunction with proper management of the airway and MAP can be used when rapid endotracheal intubation is needed.

From the material just presented and from the discussion of cerebral physiology in [Chapter 11](#), a systematic clinical approach should follow easily. A schema for approaching the problem of an acute increase in ICP or acute deterioration in conditions in the surgical field is presented in [Box 57.3](#).

If the problem has not resolved satisfactorily after following the approach in [Box 57.3](#), [Box 57.4](#) presents options for resolution. CSF drainage was discussed earlier. Additional hyperosmolar solutions are frequently used (see the subsequent section Osmotherapy and Diuretics). Barbiturates have long been the most widely used drugs for inducing reduction in CMR, with the objective of causing a coupled

BOX 57.3 High Intracranial Pressure (“Tight Brain”) Checklist

1. Are the relevant pressures controlled?
 - a. Jugular venous pressure
 - i. Extreme head rotation or neck flexion?
 - ii. Direct jugular compression?
 - iii. Head-up posture?
 - b. Airway pressure
 - i. Airway obstruction?
 - ii. Bronchospasm?
 - iii. Straining, coughing; adequately relaxed?
 - iv. Pneumothorax?
 - v. Excessive PEEP or APR ventilation?
 - c. Partial pressure of CO_2 and O_2 (PaCO_2 , PaO_2)
 - d. Arterial pressure
2. Is the metabolic rate controlled?
 - a. Pain/arousal?
 - b. Seizures?
 - c. Febrile?
3. Are any potential vasodilators in use?
 - a. N_2O , volatile agents, nitroprusside, calcium channel blockers?
4. Are there any unrecognized mass lesions?
 - a. Hematoma
 - b. Air \pm N_2O
 - c. CSF (clamped ventricular drain)

APR, Airway pressure release; CSF, cerebrospinal fluid; PEEP, positive end-expiratory pressure.

BOX 57.4 Methods for Rapid Reduction of Intracranial Pressure and Brain Volume (After Review of the Checklist in [Box 57.3](#))

- Further reduction of PaCO_2 (to not $<23-25$ mm Hg)
- CSF drainage (ventriculostomy, brain needle)
- Diuresis (usually mannitol)
- CMR suppression (barbiturates, propofol)
- MAP reduction (if dysautoregulation)
- Surgical control (i.e., lobectomy or removal of bone flap)

CMR, Cerebral metabolic rate; MAP, mean arterial pressure.

reduction in CBF and CBV. Propofol has gained popularity for this application. However, although the use of barbiturates is supported by ICU experience demonstrating efficacy in ICP control¹⁹ (if not outcome), little such evidence has been accumulated for propofol. Furthermore, a frequently fatal syndrome of metabolic acidosis and rhabdomyolysis has been recognized in patients who have received prolonged propofol infusions in the ICU setting.¹⁰⁻¹²

MANAGEMENT OF PaCO₂

The anesthesiologist and the surgeon should agree on the objectives with respect to PaCO₂. Induction of hypocapnia was once a routine part of the management of intracranial neurosurgical procedures. The rationale is principally that the concomitant reduction in CBF (see [Chapter 11](#), Fig. 11.9) and CBV will result in a reduction in ICP, or “brain relaxation.” The rationale is valid.¹³ However, two considerations should influence the clinician’s use of hyperventilation. First, the vasoconstrictive effect of hypocapnia can cause ischemia in certain situations. Second, the CBF-lowering and ICP-lowering effect is not sustained for prolonged time periods.¹⁴

Hypocapnia-Induced Cerebral Ischemia

A normal brain is unlikely to be damaged by the typical clinical use of hyperventilation. However, this may not be the case in certain pathologic conditions.

Normal Brain. Available data¹⁵⁻¹⁹ indicate that in normal subjects, ischemia will not occur at a PaCO₂ greater than 20 mm Hg. However, in one investigation,¹⁸ electroencephalogram (EEG) abnormalities and paresthesia occurred in volunteers hyperventilating to PaCO₂ values less than 20 mm Hg, and these effects were reversed by hyperbaric oxygenation, suggesting that they may truly have been caused by ischemia. Accordingly, given that a PaCO₂ of less than 20 to 25 mm Hg offers very little additional benefit in terms of improvement in intracranial compliance, acute reduction of PaCO₂ should be no more than 22 to 25 mm Hg in previously normocapnic persons.

Injured Brain. Preventing herniation, maintaining ICP less than 20 mm Hg, minimizing retractor pressure, and facilitating surgical access remain priorities that may justify hypocapnia. Yet hyperventilation is potentially deleterious and should not be overused. Hyperventilation can result in ischemia,^{20,21} especially when baseline CBF is low, as is commonly the case in the first 24 hours after injury.²²⁻²⁴ An increased frequency of brain regions with very low CBF has been demonstrated in head-injured patients who were acutely hyperventilated.^{20,21,25} In addition, low levels of jugular venous oxygen saturation (SjvO₂) can be increased by reducing the degree of hyperventilation.²⁶⁻²⁸

The deleterious effect of hyperventilation is difficult to prove. Muizelaar and colleagues²⁹ performed a study that included a near normocapnic group in which PaCO₂ was maintained at approximately 35 mm Hg, and a hypocapnic group in which PaCO₂ was maintained in the vicinity of 25 mm Hg. Outcomes at 3 and 6 months after injury were not different. However, in a subset of patients with the best initial motor scores, outcome was better in the normocapnic

group. These patients with good motor scores probably represented a subgroup in which the severity of injury was such that, although they needed tracheal intubation, hyperventilation was not necessarily required for control of ICP and who therefore had little to gain from hyperventilation. Thus, prophylactic hyperventilation seemed inadvisable. That conclusion has been extrapolated far beyond the circumstances of relatively mild TBI.

Hyperventilation should not be an automatic component of every neuroanesthetic. There should be an indication for its institution (usually increased or uncertain ICP or the need to improve conditions in the surgical field, or both). Hyperventilation has the potential to cause an adverse effect and should be withdrawn as the indication for it subsides. The concern regarding the hazards of hypocapnia, which evolved in the context of TBI, has influenced all of neurosurgery. In particular, it is now widely avoided in the management of SAH because of the low CBF state that is known to occur.^{30,31} In addition, brain tissue beneath retractors can have a similarly reduced CBF.^{32,33} However, hyperventilation, used as briefly as possible, is still very much a component of rescue therapy, when herniation is imminent or in progress, or when conditions in the surgical field are too difficult to allow surgery to proceed.

Duration of Hypocapnia-Induced Reduction in Cerebral Blood Flow

The effect of hypocapnia on CBF is not sustained. [Fig. 57.6](#) is a nonquantitative representation of changes in CBF and CSF pH occurring in association with a sustained period of hyperventilation. With the onset of hyperventilation, the pH of both CSF and the brain’s extracellular fluid space increases, and CBF decreases abruptly. However, the cerebral alkalosis is not sustained. By alterations in function of the enzyme carbonic anhydrase, the concentration of bicarbonate in CSF and the brain’s extracellular fluid space is reduced, and with a time course of 8 to 12 hours, the pH of these compartments returns to normal. Simultaneously,

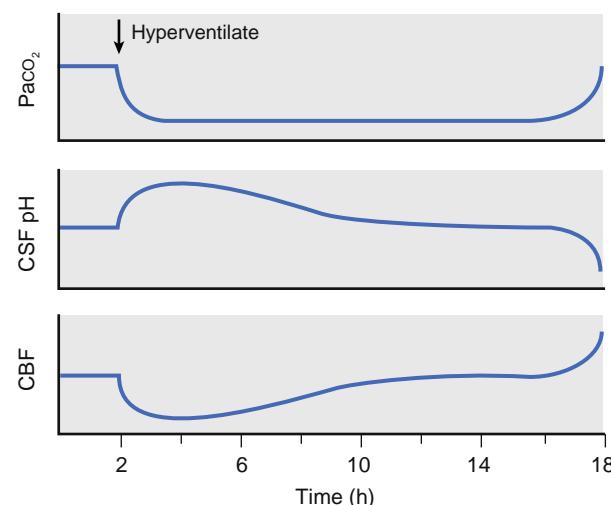


Fig. 57.6 Partial pressure of carbon dioxide in the arterial blood (PaCO₂), cerebral blood flow (CBF), and cerebrospinal fluid (CSF) pH changes with prolonged hyperventilation. Although the decreased arterial PaCO₂ (and the systemic alkalosis) persists for the duration of the period of hyperventilation, the pH of the brain and CBF return toward normal over 8 to 12 hours.

CBF returns toward normal levels.^{34,35} The implications are twofold. First, patients should be hyperventilated for only as long as a reduction in brain volume is required. Prolonged, unnecessary hyperventilation can lead to a circumstance wherein subsequent events call for additional maneuvers to reduce the volume of the intracranial contents, and then incremental hyperventilation is not efficacious. If, after adaptation, PaCO_2 is already in the 23 to 25 mm Hg range, additional hyperventilation may risk pulmonary barotrauma. Second, in a patient who has been hyperventilated for a sustained period (e.g., 2 days in an ICU setting), restoration of PaCO_2 from values in the vicinity of 25 mm Hg to typical normal values (e.g., 40 mm Hg) should ideally be accomplished slowly. A sudden increase in PaCO_2 from 25 to 40 mm Hg in a patient who has been chronically hyperventilated will have the same physiologic effect that a rapid change from 40 to 55 mm Hg would have in a previously normocapnic patient.

If hypocapnia has been required as an adjunct to brain relaxation during craniotomy, PaCO_2 should also be allowed to increase once the retractors are removed (if dural closure requirements permit) to minimize the residual intracranial pneumatocele (see the section on Pneumocephalus).

MANAGEMENT OF ARTERIAL BLOOD PRESSURE

Acceptable arterial blood pressure limits should similarly be agreed on at the beginning of a neurosurgical procedure. One of the prominent themes of contemporary neurosurgery is that CPP should be maintained at normal or even high-normal levels after acute central nervous system insults and during most intracranial neurosurgical procedures. This concept has evolved from the growing appreciation that CBF is frequently very low in some brain regions after acute neurologic insults, in particular TBI and SAH. Two additional factors should be considered. The first is that the autoregulatory response to decreasing blood pressure may not be intact throughout the brain. Fig. 57.7 depicts the ischemic hazard that attends the circumstance of a low resting CBF and absent autoregulation even at blood pressure levels considered safe when autoregulation is intact. In

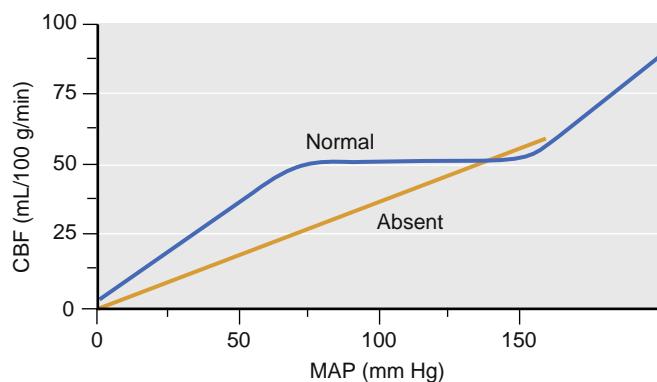


Fig. 57.7 Normal and absent autoregulation curves. The “absent” curve indicates a pressure-passive condition in which cerebral blood flow (CBF) varies in proportion to cerebral perfusion pressure (CPP). This curve is drawn to indicate subnormal CBF values during normotension, as have been shown to occur immediately after head injury²⁶ and subarachnoid hemorrhage.³⁰ The potential for modest hypotension to cause ischemia is apparent. MAP, Mean arterial pressure.

addition, maintenance of arterial pressure is also relevant to brain compressed under retractors³² because the effective perfusion pressure is lowered by increased local tissue pressure.

Although the only supportive data are anecdotal, we believe that an aggressive attitude toward arterial blood pressure support should also be given to patients who have sustained a recent spinal cord injury (SCI). This also applies to a spinal cord that is under compression, at risk for compression or vascular compromise because of a disease process (most commonly cervical spinal stenosis with or without ossification of the posterior longitudinal ligament) or an intended surgical procedure, and to those patients undergoing surgery involving retraction of the spinal cord. We believe that arterial blood pressure during anesthesia in these patients should be maintained as closely as possible to, and certainly within, 10% of average awake values.

STEROIDS

The administration of steroids for the purpose of reducing or limiting the formation of edema has a well-established place in neurosurgery. The efficacy of steroids in reducing edema associated with tumors³⁶⁻³⁹ and radiation-induced necrosis is well confirmed, but not the edema associated with any other intracranial pathology. Although the time course of this effect is relatively rapid, it is too slow for the management of acute intraoperative events. However, administration beginning 48 hours before an elective surgical procedure has the potential to reduce edema formation and improve the clinical condition by the time of craniotomy.⁴⁵ Although clinical improvement occurs within 24 hours,⁴⁰ a reduction in ICP may not occur for 48 to 72 hours after the initiation of therapy.⁴⁹ Steroids somehow improve the viscoelastic properties of the intracranial space before a reduction in edema occurs, although the mechanism remains undefined.⁴¹ The practice of administering steroids to patients with TBI has been abandoned as a result of controlled trials that demonstrated either no benefit or deleterious effects.⁴²

OSMOTHERAPY AND DIURETICS

Hyperosmolar agents and diuretics are used widely in neurosurgery and neurocritical care to reduce the volume of the brain’s intracellular and extracellular fluid compartments. Both osmotic and loop diuretics have been used. Although loop diuretics can be effective,⁴³ hyperosmolar agents are more widely used.

Mannitol

Mannitol is used most commonly intraoperatively because of its long history of rapid and effective reduction of brain volume. The doses vary from 0.25 g/kg to 100 g, with 1.0 g/kg the most common dose. A systematic study in TBI demonstrated that an equivalent initial ICP-reducing effect can be achieved with 0.25 g/kg, although the duration of effect is reduced compared to larger doses.⁴⁴ More recent studies reported better surgical brain relaxation scores with higher doses (1-1.5 g/kg) of mannitol compared to a dose of 0.25 g/kg.⁴⁵ Mannitol should be administered by infusion (e.g., over 10-15 minutes). Sudden exposure of the

cerebral circulation to extreme hyperosmolarity can have a vasodilatory effect, which can produce brain engorgement and increased ICP, both of which do not occur with slower administration.

Mannitol enters the brain and, over a reasonably short time course, appears in the CSF space.⁴⁶ The possibility that the mannitol that gains access to the parenchyma aggravates swelling has resulted in varying degrees of reluctance among clinicians to administer mannitol.⁴⁷ Most clinicians nonetheless find it to be a mainstay of ICP management. There is the concern that it will only be effective when some degree of blood-brain barrier (BBB) integrity is preserved in a significant portion of the brain. Clinicians respond to this concern by making empiric use of this agent; that is, if it is effective in reducing ICP or improving conditions in the surgical field, repeated doses are administered. The use of hyperosmolar agents is theoretically limited by an upper acceptable osmolarity limit of approximately 320 mOsm/L (although the data supporting the validity of that limit are soft⁴⁸). However, in life-threatening situations, the use is frequently empiric, and incremental doses (e.g., 12.5 g of mannitol) are administered until a clinical response is no longer observed.

Hypertonic Saline

In the critical care environment, the use of hypertonic saline (HTS) in place of mannitol is increasing.⁴⁹ Although the initial ICP effects of equiosmolar doses of mannitol and HTS are very similar,⁵⁰⁻⁵³ HTS may have some advantages in the ICU, where repeated administration makes the adverse effects (e.g., diuresis, renal injury) more likely to have clinical significance. In addition, there are anecdotal reports of HTS being effective in patients who were refractory to mannitol.^{54,55} Although there is enthusiasm for HTS,^{54,56,57} supporting data are limited.^{58,59} Furthermore, because of the variations in HTS concentrations (3%, 7.5%, 15%, 23.4%) and osmolar loads in the various studies, it is difficult to make specific recommendations.

Diuretic Combinations

The combination of a loop diuretic (usually furosemide) and an osmotic diuretic is sometimes used. The superficial rationale is that mannitol establishes an osmotic gradient that draws fluid out of brain parenchyma and that the furosemide, by hastening excretion of water from the intravascular space, facilitates the maintenance of that gradient. A second mechanism may add additional justification for the practice of combining the two diuretics. Neurons and glia have homeostatic mechanisms to ensure regulation of cell volume. Neurons and glia that shrink in response to an increased osmolarity in the external environment recover their volume rapidly as a consequence of the accumulation of so-called *idiogenic osmoles*, which serve to minimize the gradient between the internal and external environments. One of those idiogenic osmoles is chloride. Loop diuretics inhibit the chloride channel through which this ion must pass and thereby retard the normal volume-restoring mechanism.^{60,61} These diuretic combinations may cause hypovolemia and electrolyte disturbances.

The normal volume regulatory mechanisms of neurons and glia may also be relevant to the phenomenon of rebound swelling. Rebound is commonly attributed to the

prior use of mannitol and assumed to be a function of the accumulation of mannitol in cerebral tissue. Although possible, the rebound may in fact be hypertonic rebound rather than mannitol rebound. After a sustained period of hyperosmolarity of any etiology, rebound swelling of neurons and glia (which have accumulated idiogenic osmoles) may occur in the event that systemic osmolarity decreases rapidly toward normal levels. Rebound cerebral swelling can certainly occur after an episode of extreme increase in blood glucose concentration. The use of HTS rather than mannitol will not obviate this phenomenon.

ANTICONVULSANTS

The general principle is that any acute irritation of the cortical surface has the potential to result in seizures. This includes acute neurologic events such as TBI and SAH.^{62,63} Cortical incisions and brain surface irritation by retractors may similarly be potential foci. Given the relatively benign nature of contemporary anticonvulsants (e.g., levetiracetam), routine administration to patients undergoing most supratentorial craniotomies seems appropriate in the absence of a contraindication. There is no necessity for rapid administration because the intention is to prevent seizures during the postoperative period.

POSITIONING

The intended surgical position and the necessary positioning aids should be agreed upon at the outset. The commonly used positions and positioning aids and supports are listed in **Box 57.5** (see [Chapter 34](#)).

General Considerations

The prolonged duration of many neurosurgical procedures should be taken into account in all positions. Pressure points should be identified and padded carefully. Pressure and traction on nerves must be avoided. Given the high risk of thromboembolic complications in neurosurgical patients, precautions including graduated compression stockings and sequential compression devices are warranted.⁶⁴ For

BOX 57.5 Common Neurosurgical Positions and Positioning Aids

Positions

- Supine
- Lateral (park bench)
- Semi-lateral (Jannetta)
- Prone
- Sitting

Positioning Aids/Supports

- Pin ("Mayfield") head holder
- Radiolucent pin head holder
- Horseshoe head rest
- Foam head support (e.g., Voss, O.S.I., Prone-View)
- Vacuum mattress ("bean bag")
- Wilson-type frame
- Andrews ("hinder binder")-type frame
- Relton-Hall (four-poster) frame

cranial procedures, some component of head-up posturing (e.g., 15–20 degrees) is used to ensure optimal venous drainage. The conspicuous exception occurs with evacuation of a chronic subdural hemorrhage, after which patients are usually nursed flat to discourage reaccumulation of fluid. Patients are occasionally also maintained flat after CSF shunting to avoid overly rapid collapse of the ventricles.

Supine

The supine position is used with the head neutral or rotated for frontal, temporal, or parietal access. Extremes of head rotation can obstruct the jugular venous drainage, and a shoulder roll can attenuate this problem. The head is usually in a neutral position for bifrontal craniotomies and transsphenoidal approaches to the pituitary. The head-up posture is best accomplished by adjusting the operating table to a chaise longue (lawn chair) position (hip flexion, pillows under the knees, slight reverse Trendelenburg). This orientation, in addition to promoting cerebral venous drainage, decreases back strain.

Semilateral

The semilateral position, also known as the Jannetta position, named after the neurosurgeon who popularized its use for microvascular decompression of the fifth cranial nerve, is used for retromastoid access. It is achieved by lateral tilting of the table 10 to 20 degrees combined with a generous shoulder roll. Again, extreme head rotation, sufficient to cause compression of the contralateral jugular vein by the chin, should be avoided.

Lateral

The lateral position can be used for access to the posterior parietal and occipital lobes and the lateral posterior fossa including tumors at the cerebellopontine angle and aneurysms of the vertebral and basilar arteries. An axillary roll is important for preventing brachial plexus injury.

Prone

The prone position is used for spinal cord, occipital lobe, craniosynostosis, and posterior fossa procedures. For cervical spine and posterior fossa procedures, the final position commonly entails neck flexion, reverse Trendelenburg, and elevation of the legs. This orientation serves to bring the surgical field to a horizontal position. There should be a plan for detaching and reattaching monitors in an orderly manner to prevent an excessive monitoring window. Awake tracheal intubation and prone positioning may be warranted in patients with an unstable cervical spine in whom an unchanged neurologic status should be confirmed before induction of anesthesia in the final surgical position. This approach is also sometimes performed in obese patients.

The head can be secured in a pin head holder (applied before the turn) or positioned on a disposable foam head rest or, less frequently, a horseshoe head rest. A complication of the prone position, which requires constant attention, is retinal ischemia and blindness caused by orbital compression causing central retinal vessel occlusion. It must be intermittently confirmed (e.g., every 15 minutes) and after any surgery-related head or neck movement that pressure has not come to bear on the eye. However, not all postoperative vision loss (POVL) is a result of direct orbital

compression. Ischemic optic neuropathy actually appears to be a more frequent cause of POVL than pressure-causing occlusion of central retinal vessels. The cause-and-effect relationships associated with ischemic optic neuropathy are uncertain, but low arterial pressure, low hematocrit level, lengthy surgical procedures, and large intravascular volume fluid administration are statistically associated with the phenomenon.⁶⁵

Direct pressure can also result in various degrees of pressure necrosis of the forehead, maxillae, and chin, especially with prolonged spinal procedures. Pressure should be distributed as evenly as possible over facial structures. Other pressure points to check include the axillae, breasts, iliac crests, femoral canals, genitalia, knees, and heels. Traction on the brachial plexus must be avoided and can usually be accomplished by not exceeding a “90-90” position (arms abducted not >90 degrees; elbows extended not >90 degrees) with care taken to ensure that the elbow is anterior to the shoulder to prevent wrapping of the brachial plexus around the head of the humerus. An antisialagogue (e.g., glycopyrrolate) and an adhesive (e.g., benzoin) may help reduce loosening of the tape used to secure the endotracheal tube.

An objective during prone positioning, especially for lumbar spine surgery, is the avoidance of compression of the inferior vena cava. Impairment of vena cava return diverts blood to the epidural plexus and increases the potential for bleeding during spinal surgery. Minimizing vena cava pressure is an objective of all spinal surgery frames and is accomplished effectively by the Wilson, Andrews, and Jackson variants. However, this does introduce a risk of air embolism,^{66,67} although severe clinical occurrences have been very infrequent.⁶⁸

Attention should be paid to preventing injury to the tongue in the prone position. With both cervical and posterior fossa procedures, it is frequently necessary to flex the neck substantially to facilitate surgical access. This reduces the anterior-posterior dimension of the oropharynx, and compression ischemia of the base of the tongue (as well as the soft palate and posterior wall of the pharynx) can occur in the presence of foreign bodies (endotracheal tube, esophageal stethoscope, oral airway). The consequence can be macroglossia, caused by accumulation of edema after reperfusion of the ischemic tissue causing airway obstruction of rapid onset after extubation⁶⁹ (discussed later). Accordingly, placing unnecessary adjuncts in the oral cavity and pharynx should be avoided. Omitting the oral airway entirely is unwise because the tongue may then protrude between and be trapped by the teeth as progressive swelling of facial structures occurs during a prolonged prone procedure. A rolled gauze bite block prevents this problem without adding bulk to the oropharynx.

Sitting

There have been several reviews of numerous experiences with the sitting position.⁷⁰⁻⁷⁴ All concluded that the sitting position can be used with acceptable rates of morbidity and mortality. However, these reports were prepared by groups that perform 50 to 100 or more of these procedures per year, and the hazards of the sitting position may be more frequent for teams who have fewer occasions to use it. The sitting position can be avoided by using one of its alternatives (prone,

semilateral, lateral). However, this position will continue to be used because even surgeons who are inclined to use alternative positions may opt for it when access to midline structures (e.g., the quadrigeminal plate, the floor of the fourth ventricle, the pontomedullary junction, and the vermis) is required. Nonetheless, alternative positions for posterior fossa surgery are available and should be considered when contraindications to the sitting position exist.

Achieving the Sitting Position. The properly positioned patient is more commonly in a modified recumbent position as shown in Fig. 57.8 rather than truly sitting. The legs should be kept as high as possible (usually with pillows under the knees) to promote venous return. The head holder should be attached to the back portion of the table (see Fig. 57.8A) rather than to the portions under thighs or legs⁷⁵ (see Fig. 57.8B). This permits lowering of the head and closed chest compressions, if necessary, without the necessity of first taking the patient out of the head holder.

When procedures are performed in the sitting position, the clinician should think in terms of measuring and maintaining perfusion pressure at the level of the surgical field. This is best accomplished by referencing transducers to the level of the external auditory canal. If a manual blood pressure cuff on the arm is used, a correction* to allow for the hydrostatic difference between the arm and the operative field should be applied.

A series of hazards are associated with the sitting position. Circulatory instability, macroglossia, and quadriplegia are discussed in this section. Pneumocephalus is discussed in its own section. Venous air embolism (VAE) and paradoxical air embolism (PAE) are discussed in the section Venous Air Embolism. Several of these hazards are also relevant when cervical spine and posterior fossa procedures are performed in non-sitting positions but occur with greater frequency in the sitting position.

Cardiovascular Effects of the Sitting Position. Hypotension should be avoided. Prepositioning hydration, compressive stockings, and slow, incremental adjustment of table position are appropriate. Intravenous vasopressor administration may be required in some patients. However, in most healthy patients the hemodynamic changes are of a nonthreatening magnitude. In a study of healthy anesthetized adults aged 22 to 64 years old, relatively modest changes were observed.⁷⁶ MAP was relatively unaffected, whereas wedge pressure, stroke volume, and cardiac index decreased—the latter by approximately 15%—although there was some variation with the anesthetics used. The combination of an unchanged MAP (which in general requires the use of a light, high sympathetic tone anesthetic) and a reduced cardiac index implies that systemic vascular resistance (SVR) increased. Their calculations and the observations of other investigators⁷⁷ reveal significant increases in SVR. For patients in whom an abrupt increase in SVR may be poorly tolerated, the sitting position may represent a physiologic threat and alternative positions should be considered.

During procedures performed in the sitting position, MAP should be transduced at or corrected to head level to provide a meaningful index of CPP. Specifically, CPP (MAP – estimated ICP) should be maintained at a minimum value of 60 mm

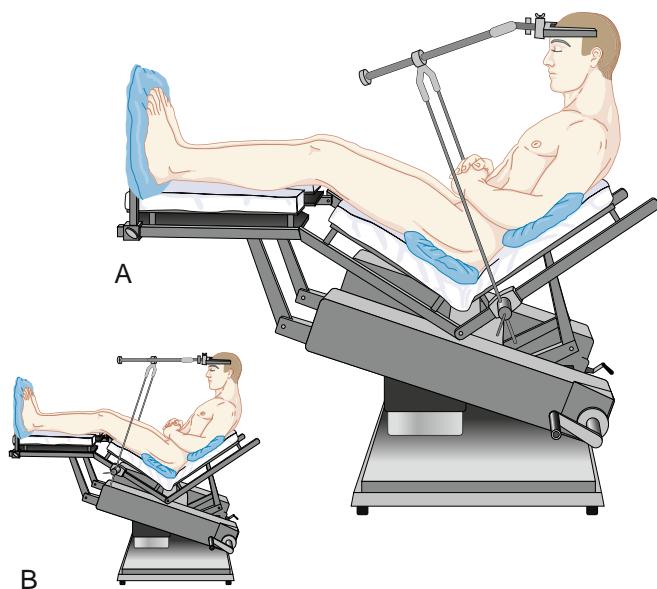


Fig. 57.8 The sitting position. (A) The head-holder support is correctly positioned so that the head can be lowered without the necessity to first detach the head holder. (B) This configuration, with the support attached to the thigh portion of the table, should be avoided. (From Martin JT. *Positioning in Anesthesia and Surgery*. Philadelphia: Saunders; 1988, with permission.)

Hg in healthy patients in whom it is reasonable to assume a normal cerebral vasculature. The safe lower limit should be raised for elderly patients, for those with hypertension or known cerebral vascular disease, or for those with degenerative disease of the cervical spine or cervical spinal stenosis who may be at risk for decreased spinal cord perfusion, and in the event that substantial or sustained retractor pressure must be applied to brain or spinal cord tissue.

Macroglossia. There have been sporadic reports of upper airway obstruction after posterior fossa procedures in which swelling of pharyngeal structures, including the soft palate, posterior pharyngeal wall, and base of the tongue, has been observed.^{39,69,78} These episodes have been attributed to edema formation at the time of reperfusion after trauma or prolonged ischemia, occurring as the result of foreign bodies (usually oral airways) causing pressure on these structures in the circumstances of lengthy procedures with sustained neck flexion (which is usually required to improve access to posterior structures). It is customary to maintain at least two fingerbreadths between the chin/mandible and the sternum/clavicle to prevent excessive reduction of the anterior-posterior diameter of the oropharynx. Consideration of the macroglossia phenomenon may also be relevant as clinicians contemplate the use of transesophageal echocardiography (TEE) in the neurosurgery suite. The centers that routinely use TEE in neurosurgery mostly use pediatric diameter probes to avoid trauma to pharyngeal and perilyngeal structures.

Quadriplegia. The sitting position has been implicated as a cause of rare instances of unexplained postoperative quadriplegia. It has been hypothesized⁷⁹ that neck flexion, a common concomitant of the seated position, may result in stretching or compression of the cervical spinal cord. This possibility may represent a relative contraindication to the

* A column of blood 32 cm high exerts a pressure of 25 mm Hg.

use of this position in patients with significant degenerative disease of the cervical spine, especially when there is evidence of associated cerebral vascular disease. The arterial blood pressure management implications are mentioned in the preceding section on cardiovascular effects. It may also represent a justification for evoked response monitoring during the positioning phase of a sitting procedure for patients perceived to be at high risk (also see [Chapter 39](#)).

PNEUMOCEPHALUS

The issue of pneumocephalus arises most often in connection with posterior fossa craniotomies performed with a head-up posture.^{80,81} During these procedures, air may enter the supratentorial space, much as air enters an inverted pop bottle. Depending on the relationship of the brainstem and temporal lobes to the incisura, the pressure in the air collection may or may not be able to equilibrate with atmospheric pressure. This phenomenon has relevance to the use of N₂O because any N₂O that enters a trapped gas space augments the volume of that space. In those (probably uncommon) intraoperative circumstances where there is, in fact, a completely closed intracranial gas space, the use of N₂O may result in an effect comparable with that of an expanding mass lesion. We do not view N₂O as absolutely contraindicated because, before dural closure, intracranial gas is probably only rarely trapped. Nonetheless, attention to this possibility is important when one is presented with the problem of an increasingly tight brain during a posterior fossa craniotomy.^{82,83}

During a posterior fossa procedure done in a head-up posture, when surgical closure has reached a stage such that the intracranial space has been completely sealed from the atmosphere, N₂O should be omitted because of the possibility of contributing to a tension pneumocephalus. Note that the use of N₂O up to the point of dural closure may actually represent a clinical advantage,⁸⁴ as in rabbits the gas pocket has been shown to shrink more rapidly because of the presence of N₂O (because N₂O diffuses much more quickly than nitrogen). Tension pneumocephalus is often naively viewed as exclusively a function of the use of N₂O. However, tension pneumocephalus can most certainly occur as a complication of intracranial neurosurgery entirely *unrelated* to the use of N₂O.⁸⁵ It is one of the causes of delayed awakening or nonawakening after both posterior fossa and supratentorial procedures ([Fig. 57.9](#)).^{85,86} It occurs because air enters the cranium when the patient is in a head-up position at a time when the volume of the intracranial contents has been reduced because of some combination of hypoxia, good venous drainage, osmotic diuresis, and CSF loss from the operative field. When the cranium is closed and the patient is returned to the near supine position, CSF, venous blood, and extracellular fluid return or reaccumulate and the air pocket becomes an unyielding mass lesion (because of the very slow diffusion of nitrogen). It may cause delayed recovery of consciousness or severe headache. Among supratentorial craniotomies, the largest residual air spaces occur after frontal skull base procedures in which energetic brain relaxation measures are used to facilitate subfrontal access (see [Fig. 57.9](#)). At the end of these procedures, typically done in a supine/brow-up position, the intracranial dead space cannot be filled with normal saline as is commonly done with smaller craniotomy defects, and there may be a large

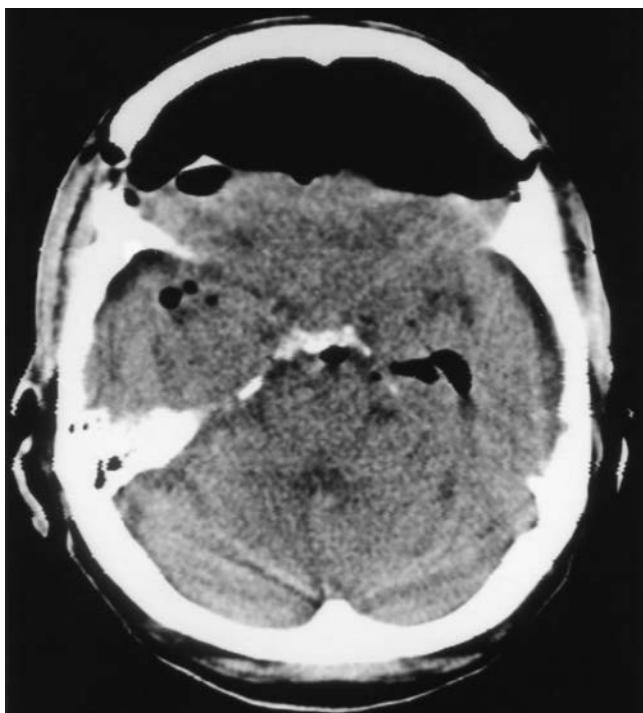


Fig. 57.9 Postoperative computed tomographic scan demonstrating a large pneumocephalus after a subfrontal approach to a suprasellar glioma. Immediately postoperatively, the patient was confused and agitated, and he complained of a severe headache.

residual pneumatocele. We doubt that the possible occurrence of this phenomenon represents a contraindication to N₂O. However, withdrawal of N₂O may be appropriate at the time of scalp closure. The diagnosis of pneumocephalus is established by a brow-up lateral radiography or, more commonly, a CT scan. The treatment is a twist-drill hole followed by needle puncture of the dura.

Residual intracranial air should be considered at the time of repeat anesthesia, both neurosurgical and nonneurosurgical. Air frequently remains evident on CT scan for more than 7 days after a craniotomy.⁸⁷ Pneumocephalus can also develop de novo in the postoperative period in patients who have a residual dural defect and a communication between the nasal sinuses and the intracranial space.⁸⁸

VENOUS AIR EMBOLISM

The incidence of VAE varies according to the procedure, the intraoperative position, and the detection method used. During posterior fossa procedures performed in the sitting position, VAE is detectable by precordial Doppler in approximately 40% of patients and by TEE in as many as 76%.⁸⁹⁻⁹² The incidence of VAE during posterior fossa procedures performed in nonsitting positions is much less (12% using precordial Doppler in the report of Black and colleagues⁷²), and it is probable but unproven that the average volume of air entrained per event is also smaller. The incidence of VAE is apparently lower with cervical laminectomy (25% using TEE in the sitting position versus 76% for posterior fossa procedures⁹¹). Although VAE is principally a hazard of posterior fossa and upper cervical spine procedures, especially when they are performed in the sitting position, it can

occur with supratentorial procedures. The most common situations involve tumors, most often parasagittal or falcine meningiomas, that encroach on the posterior half of the sagittal sinus (Fig. 57.10) and craniosynostosis procedures, typically performed in children.^{93,94} Pin sites can also serve as VAE access sites. Accordingly, pin head holders should be removed after the patient has been taken out of significant degrees of the head-up positioning. Spontaneous ventilation (with the attendant intermittent negative intrathoracic pressure) will increase the risk of air entrainment. A 6% incidence of Doppler-detectable VAE was reported in a series of deep-brain stimulator placement procedures performed in spontaneously breathing patients.⁹⁵

The common sources of critical VAE are the major cerebral venous sinuses, in particular the transverse, the sigmoid, and the posterior half of the sagittal sinus, all of which may be noncollapsible because of their dural attachments. Air entry may also occur via emissary veins, particularly from suboccipital musculature, via the diploic space of the skull (which can be violated by both the craniotomy and pin fixation) and the cervical epidural veins. It is believed (but not confirmed by systematic study) that the VAE risk associated with cervical laminectomy is more likely when the exposure requires dissection of suboccipital muscle with the potential to open emissary veins to the atmosphere at their point of entry into occipital bone. There is also anecdotal evidence⁹⁶ that air under pressure in the ventricles or subdural space can occasionally enter the venous system, perhaps along the normal egress route of the CSF.

Detection of Venous Air Embolism

The monitors used for the detection of VAE should provide (1) a high level of sensitivity, (2) a high level of specificity, (3) a rapid response, (4) a quantitative measure of the VAE event, and (5) an indication of the course of recovery from the VAE event. The combination of a precordial Doppler and expired CO_2 monitoring meets these criteria and is the current practice in many institutions. Doppler placement in a left or right parasternal location between the second and third or third and fourth ribs has a very high detection rate for gas embolization,⁹⁷ and when good heart tones are heard, maneuvers to confirm adequate placement appear to be unnecessary. The TEE is more sensitive than the precordial Doppler (Fig. 57.11) to VAE⁹⁸ and offers the advantage of also identifying right-to-left shunting of air. However, its safety during prolonged use (especially with pronounced neck flexion) is not well established. Expired nitrogen analysis is theoretically attractive. However, the expired nitrogen concentrations involved in anything less than catastrophic VAE are very small and push the available instrumentation to the limits of its sensitivity.⁹⁹

Fig. 57.12 presents the physiologic and monitor response to an air embolic event, and Box 57.6 offers an appropriate management response to such an event.

Which Patients Should Have a Right Heart Catheter?

All patients who undergo sitting posterior fossa procedures should have a right heart catheter placed. Although life-threatening VAE is relatively uncommon, a catheter permits immediate evacuation of an air-filled heart. With

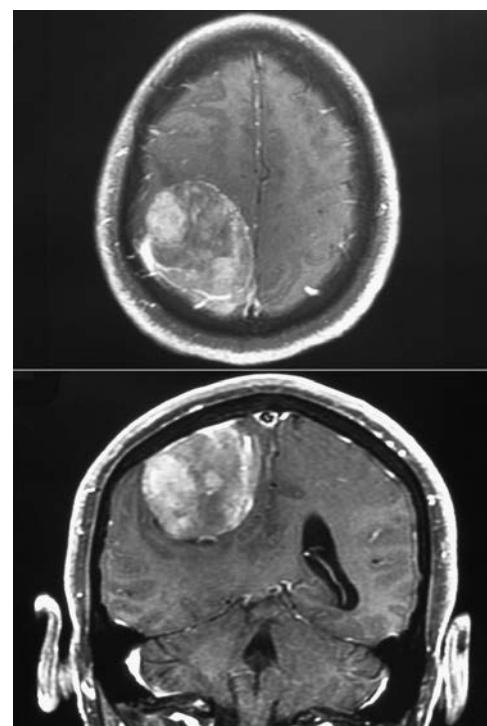


Fig. 57.10 Axial (top) and coronal (bottom) magnetic resonance images of a parasagittal meningioma. Resection of meningiomas arising from the dural reflection overlying the sagittal sinus or from the dura of the adjacent convexity or falk often entails a risk of venous air embolism because of the proximity of the sagittal sinus (the triangular structure at the superior end of the interhemispheric fissure in the bottom panel).

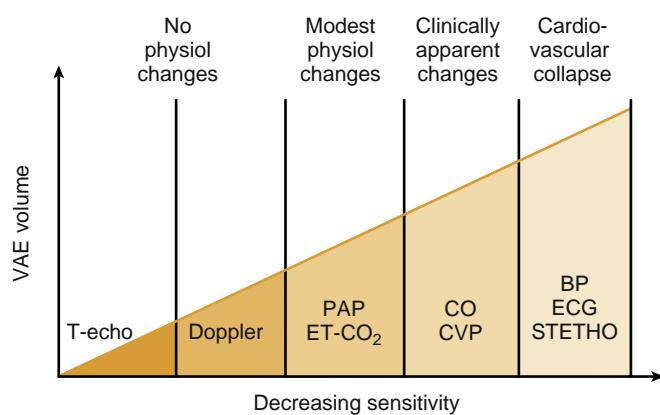


Fig. 57.11 The relative sensitivity of various monitoring techniques to the occurrence of venous air embolism. BP, Blood pressure; CO, cardiac output; CVP, central venous pressure; ECG, electrocardiogram; ET- CO_2 , end-tidal carbon dioxide; PAP, pulmonary artery pressure; Stetho, esophageal stethoscope; T-echo, transesophageal echo; VAE, venous air embolism.

the nonsitting positions, it is frequently appropriate, after a documented discussion with the surgeon, to omit the right heart catheter. The perceived risks of VAE associated with the intended procedure and the patient's physiologic reserve are the variables that contribute to the decision. Microvascular decompression of the fifth or seventh cranial nerves are examples of procedures for which the right heart catheter is usually omitted. The essentially horizontal semi-lateral position and the very limited retromastoid craniectomy that is required have resulted (at our institution) in a

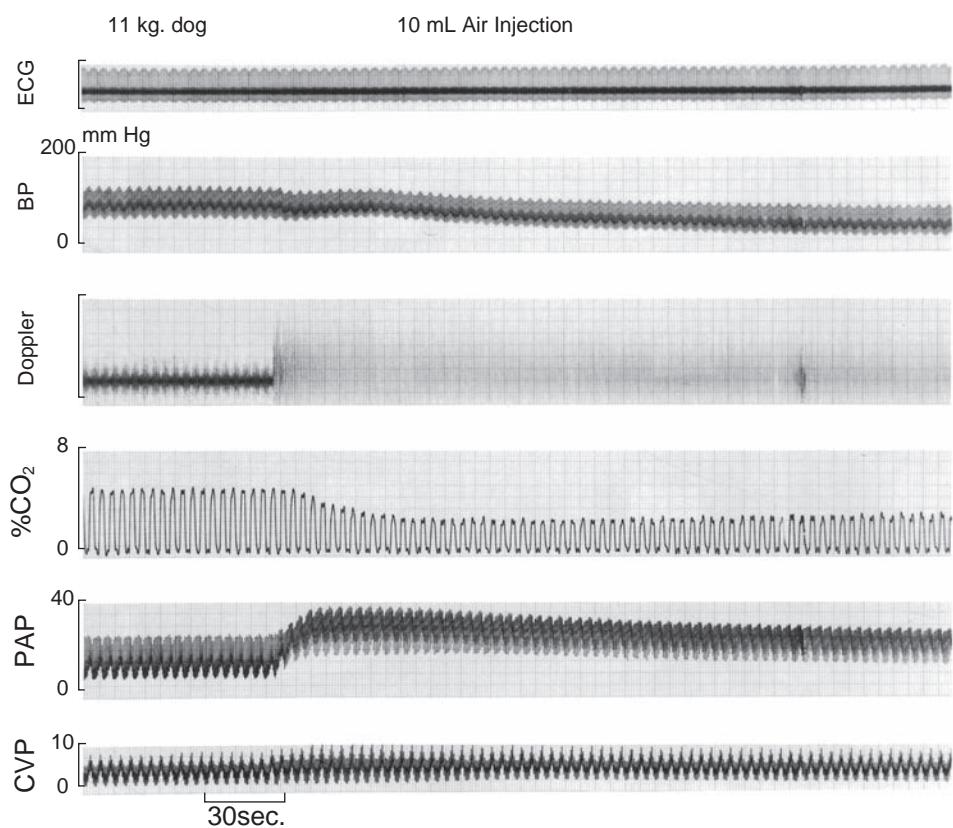


Fig. 57.12 The responses of the electrocardiogram (ECG), arterial pressure, pulmonary artery pressure (PAP), pan-tidal CO₂ concentration, a precordial Doppler and central venous pressure (CVP) to the intravenous administration of 10 mL of air over 30 seconds to an 11-kg dog. BP, Blood pressure.

BOX 57.6 Management of an Acute Air Embolic Event

1. Prevent further air entry
 - Notify surgeon (flood or pack surgical field)
 - Jugular compression
 - Lower the head
2. Treat the intravascular air
 - Aspirate right heart catheter
 - Discontinue N₂O
 - FiO₂: 1.0
 - Pressors, inotropes
 - Chest compression

very low incidence of Doppler-detectable VAE. One should know the local surgical practices, particularly with respect to the degree of head-up posture, before deciding to omit a right atrial catheter. With regard to the Jannetta procedure, the necessary retromastoid craniectomy is performed in the angle between the transverse and sigmoid sinuses, and venous sinusoids and emissary veins in the suboccipital bone are common. If this procedure is performed with any degree of head-up posturing, the risk of VAE may still be substantial.

Which Vein Should Be Used for Right Heart Access?

Although some surgeons may ask that neck veins not be used, a skillfully placed jugular catheter is usually acceptable.

In a very limited number of patients, high ICP may make the head-down posture undesirable. In others, unfavorable anatomy with an increased likelihood of a difficult cannulation and hematoma formation may also encourage the use of alternate access sites.

Positioning the Right Heart Catheter

The investigation by Bunegin and colleagues suggested that a multiorificed catheter should be located with the tip 2 cm below the superior vena caval-atrial junction and a single-orificed catheter with the tip 3 cm above the superior vena caval-atrial junction.¹⁰⁰ Although these small distinctions in location may be relevant for optimal recovery of small volumes of air when cardiac output is well maintained, for the recovery of massive volumes of air in the face of cardiovascular collapse, anywhere in the right atrium should suffice. Confirmation of right heart placement can be accomplished by (1) radiography, (2) intravascular electrocardiography (ECG),¹⁰¹ or (3) TEE.¹⁰² Although there is no literature to support the practice, with catheter access via the right internal jugular vein, a measured placement to the level of the second or third right intercostal space should suffice when the catheter passes readily. The intravascular electrocardiography technique makes use of the fact that an ECG "electrode" placed in the middle of the right atrium will initially "see" an increasing positivity as the developing P-wave vector approaches it (Fig. 57.13), and then an increasing negativity as the wave of atrial depolarization passes and moves away from it. The resultant biphasic P wave is characteristic of an intraatrial electrode position. The technique

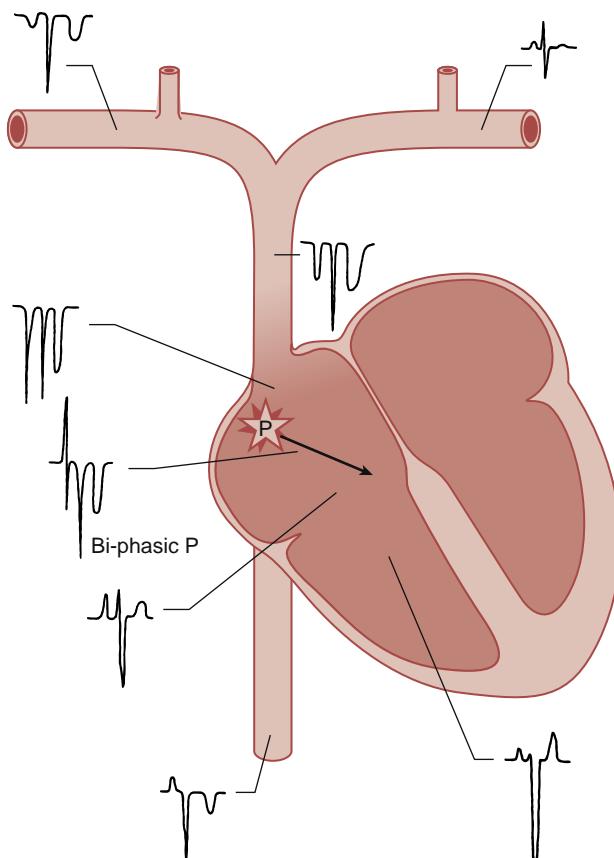


Fig. 57.13 Electrocardiogram (ECG) configurations observed at various locations when a central venous catheter is used as an intravascular ECG electrode. The configurations in the figure will be observed when Lead II is monitored and the positive electrode (the leg electrode) is connected to the catheter. *P* indicates the sinoatrial node. The black arrow indicates the P-wave vector. Note the equi-biphasic P wave when the catheter tip is in the mid-right atrial position.¹⁰¹

requires that the central venous pressure (CVP) catheter become an exploring ECG electrode. This is accomplished by filling the catheter with an electrolyte solution (bicarbonate is best) and attaching an ECG lead (the leg lead if lead II is selected) to the hub of the CVP catheter. Commercial CVP kits with an ECG adapter are available. The ECG configurations that will be observed at various intravascular locations are shown in **Fig. 57.13**. To minimize the microshock hazard, a battery-operated ECG unit is preferable, and any unnecessary electrical apparatus should be detached from the patient during catheter placement.

Paradoxical Air Embolism

The possibility of the passage of air across the interatrial septum via a patent foramen ovale (PFO), which is known to be present in approximately 25% of adults, is a concern.¹⁰³ The risk is major cerebral and coronary morbidity. However, the precise definition of the morbidity that can actually be attributed to PAE is not clear. Although the minimal pressure required to open a probe PFO is not known with certainty, the necessary gradient may be as much as 5 mm Hg. In a clinical investigation, Mammoto and colleagues observed that PAE occurred only in the context of major air embolic events, suggesting that significant increases in right heart pressures are an important predisposing factor

of the occurrence of PAE.¹⁰⁴ Several clinical investigations have examined factors that influence the right atrial pressure (RAP) to left atrial pressure (LAP) gradient. The use of positive end-expiratory pressure (PEEP) increases the incidence of a positive RAP to pulmonary wedge pressure gradient¹⁰⁵ and generous fluid administration (e.g., 2800 mL/patient vs. 1220 mL/control patient¹⁰⁶) reduces it. As a result, the use of PEEP, which was once advocated as a means of preventing air entrainment, was abandoned. Subsequently, the practice of more generous fluid administration for patients undergoing posterior fossa procedures evolved. However, even when mean LAP exceeds mean RAP, PAE can still occur because transient reversal of the interatrial pressure gradient can occur during each cardiac cycle.¹⁰⁷

Some centers have advocated performing bubble studies preoperatively with echocardiography⁹² or transcranial Doppler (TCD),¹⁰⁸ or intraoperatively using TEE prior to positioning¹⁰⁹ to identify patients with a PFO with a view to using alternatives to the sitting position in this subpopulation.^{91,110} Some centers thereafter advocate the use of TEE to identify paradoxical embolization intraoperatively.^{91,111} However, none of these practices has become a community-wide standard of care. Furthermore, because the morbid events attributable to PAE have been relatively infrequent, surgeons who are convinced that the sitting position is optimal for a given procedure⁷⁴ are loath to be dissuaded from using it on the basis of what may seem like the very minor possibility of an injury to the patient occurring by this mechanism.

Transpulmonary Passage of Air

Air can sometimes traverse the pulmonary vascular bed to reach the systemic circulation.¹¹²⁻¹¹⁴ Transpulmonary passage is more likely to occur when large volumes of air are presented to the pulmonary vascular filter.^{115,116} In addition, pulmonary vasodilators, including volatile anesthetics, may decrease the threshold for transpulmonary passage.¹¹⁵⁻¹¹⁷ The magnitude of differences among anesthetics does not appear to mandate any related “tailoring” of anesthetic techniques. However, N₂O should be discontinued promptly after even apparently minor VAE events because of the possibility that air may reach the left-sided circulation either via a PFO or the pulmonary vascular bed.

Box 57.6 presents an approach for responding to an acute VAE event. It includes raising venous pressure by direct compression of the jugular veins. PEEP and the Valsalva maneuver were once advocated. However, both PEEP¹⁰⁵ and the release of a Valsalva maneuver increase the risk of PAE, and the relative superiority of jugular venous compression in raising cerebral venous pressures has been confirmed.^{118,119} Furthermore, the impairment of systemic venous return caused by the sudden application of substantial PEEP may be undesirable in the face of the cardiovascular dysfunction already caused by the VAE event.

It has been recommended that a patient who has sustained a hemodynamically significant VAE should be placed in a lateral position with the right side up. The rationale is that air will remain in the right atrium, where it will not contribute to an air lock in the right ventricle and where it will remain amenable to recovery via a right atrial catheter. The first difficulty is that this repositioning is all but

impossible with a patient in a pin head holder. In addition, the only systematic attempt to examine the efficacy of this maneuver, albeit performed in dogs, failed to identify any hemodynamic benefit.¹²⁰

Nitrous Oxide

Nitrous oxide diffuses into air bubbles trapped in the vascular tree and, accordingly, N₂O should be eliminated after a clinical VAE event to avoid aggravating the cardiovascular impact. As noted earlier, the PAE phenomenon adds an additional reason for eliminating N₂O *after* the occurrence of VAE. When major VAE occurs, no matter how the RAP-LAP gradient was manipulated before the event, RAP increases abruptly with respect to LAP,¹²¹ and major VAE results in an acutely increased risk of PAE in patients with a PFO.¹⁰⁴ Should N₂O be used in patients at risk for VAE? Some clinicians may decide to simply avoid it. However, N₂O can be used with the knowledge that it neither increases the incidence of VAE¹²² nor aggravates the hemodynamic response to VAE provided that it is eliminated when VAE occurs.¹²³

MONITORING

Neurologic monitoring techniques are discussed in [Chapter 39](#). Invasive monitoring is frequently appropriate in neurosurgery. Some of the numerous indications for an arterial catheter are listed in [Box 57.7](#).

Patients with increased ICP may be intolerant of the vascular engorgement associated with sudden hypertension

BOX 57.7 Relative Indications for Intraarterial Pressure Monitoring

- Elevated intracranial pressure
- Ischemia or incipient ischemia of neural tissue
 - Recent subarachnoid hemorrhage
 - Recent head injury
 - Recent spinal cord injury
 - Intended or possible temporary vessel occlusion
- Circulatory instability
 - Trauma
 - Spinal cord injury (spinal shock)
 - Sitting position
 - Possible barbiturate coma
- Possibility of induced hypotension
- Possibility of induced hypertension
- Anticipated or potential major blood loss
 - Aneurysm clipping
 - Arteriovenous malformations
 - Vascular tumors
 - Tumors involving or adjacent to major venous sinuses
 - Craniofacial reconstruction
 - Extensive craniosynostosis procedures
- Anticipated light anesthesia without paralysis
- Brainstem manipulation, compression, dissection
- Anticipated CN manipulation (especially CN V)
- Advantageous for postoperative intensive care
 - Hypervolemic therapy
 - Head injury
 - Diabetes insipidus
- Incidental cardiac disease

CN, Cranial nerve.

occurring as a consequence of light anesthesia. Surgical relief of increased ICP may be associated with sudden hypotension as brainstem compression is relieved. Beat-by-beat arterial pressure monitoring also serves as an important depth of anesthesia monitor and as an early neurologic injury warning system. Much of the brain is insensate. As a consequence, the intradural portion of many neurosurgical procedures is not very stimulating and, to achieve circulatory stability, relatively light anesthesia is often necessary. There should be constant attention to the possibility of sudden arousal (most often associated with cranial nerve traction or irritation). This is especially important when paralysis is precluded by the use of motor-evoked potential monitoring or electromyographic recording from facial muscles to monitor cranial nerve integrity. Blood pressure responses may reveal imminent arousal; they may also serve to warn a surgeon of excessive or unrecognized irritation, traction, or compression of neurologic tissue. These occur most often with posterior fossa procedures involving brainstem or cranial nerves, and abrupt changes should be reported to the surgeon immediately.

The use of right heart catheters for air retrieval is discussed in the section VAE. In the absence of VAE risk and in the presence of good peripheral venous access, we rarely place right heart catheters for neurosurgical procedures. Antecedent cardiac disease may justify a pulmonary arterial catheter. The use of the precordial Doppler is also described in the section VAE.

INTRAVENOUS FLUID MANAGEMENT

The general principles of fluid management for neurosurgical anesthesia are (1) maintain normovolemia and (2) avoid reduction of serum osmolarity. The first principle is a derivative of the concept presented in the section Management of Arterial Blood Pressure, which is that it is generally ideal to maintain a normal MAP in patients undergoing most neurosurgical procedures and neurosurgical critical care. Maintaining normovolemia is simply one element of maintaining a normal MAP. The second principle is a derivative of the observation that lowering serum osmolarity results in edema of both normal and abnormal brain.^{124,125} Administering fluids that provide free water (i.e., fluids that do not have sufficient nonglucose solutes to render them iso-osmolar with respect to blood) lowers serum osmolarity if the amount of free water administered is in excess of that required to maintain ongoing free water loss. Normal saline and balanced salt solutions are the fluids most often used intraoperatively. At 308 mOsm/L, normal saline is slightly hyperosmolar with respect to plasma (295 mOsm/L). It has the disadvantage that large volumes can cause hyperchloremic metabolic acidosis.¹²⁶ The physiologic significance of this acidosis, which involves the extracellular but not the intracellular fluid space, is unclear. At a minimum, it has the potential to confuse the diagnostic picture when acidosis is present. Comparisons between normal saline and balanced crystalloid solutions in the setting of cardiac surgery¹²⁷ and critically ill intensive care patients¹²⁸ did not reveal any adverse events (acute kidney injury, mortality, length of hospital stay) attributable to administration of normal saline. Nonetheless, to avoid hyperchloremic metabolic acidosis, many clinicians use lactated Ringer solution.

Although lactated Ringer solution (273 mOsm/L) is in theory not ideal for replacement of blood and third-space loss or insensible losses, it serves as an entirely reasonable compromise for meeting both needs simultaneously and is very suitable in most instances. It is a hypoosmolar fluid, and in a healthy experimental animal, it is possible to reduce serum osmolarity and produce cerebral edema with a large volume of lactated Ringer solution.¹²⁵ In the setting of large-volume fluid administration (e.g., significant blood loss, multiple trauma), it is the authors' practice to alternate, liter by liter, lactated Ringer solution and normal saline. Alternatively, Plasma-Lyte (Baxter International Inc.; Deerfield, IL), a buffered crystalloid solution (pH 7.4) with physiochemical properties similar to plasma, may be considered, if available.¹²⁹ Plasma-Lyte is considered isotonic with a calculated *in vivo* osmolality range of approximately 270 to 294 mOsmol/kg (depending on the manufacturing country). Although there may be advantages to the use of a physiologically balanced solution such as Plasma-Lyte, there remains insufficient clinical evidence to advocate for one fluid over another at the present time.

The crystalloid versus colloid discussion is a recurrent one. It arises most commonly in the context of the patient with TBI. Although views differ, there has in fact been only a single demonstration that the reduction of colloid oncotic pressure (COP) in the absence of a change of osmolarity can actually contribute to an augmentation of cerebral edema in the setting of experimental head injury.¹³⁰ The transcapillary membrane pressure gradients that can be produced by reduction of COP are in fact very small by comparison of those created by changes in serum osmolarity. Nonetheless, it appears that those small gradients, probably in the setting of an experimental BBB injury of intermediate severity, have the potential to augment edema. A fluid administration pattern should be selected that, in addition to maintaining normal serum osmolarity, prevents substantial reductions in COP. For most elective craniotomies, which entail only modest fluid administration, this does not require the administration of colloid solutions. However, in situations requiring substantial volume administration (e.g., multiple trauma, aneurysm rupture, cerebral venous sinus laceration, filling pressure support during barbiturate coma), a combination of isotonic crystalloid and colloid may be appropriate.

Which Colloid Solutions Should Be Used?

Colloid administration has created increasing concern about not only its efficacy but also its safety. Based on empirical local experience, we view albumin to be a reasonable choice. However, there are conflicting opinions and cross-currents in the literature. An analysis of the subset of patients in the SAFE (Saline vs. Albumin Fluid Evaluation) trial with severe TBI (Glasgow Coma Scale [GCS] score 3-8) revealed increased mortality among those who received albumin.¹³¹ However, there are several reasons to be suspicious of that conclusion. First, SAFE trial patients were not originally randomized on the basis of TBI characteristics and, by chance, there were imbalances in TBI-related characteristics that appear to have placed the albumin group at greater risk.¹³² Second, the 4% albumin solution used was hypoosmolar (274 mOsm/L) and might have been expected to aggravate edema.¹³³ Furthermore, there is no

compelling physiologic explanation for an albumin-specific hazard. The formation of cerebral edema that is more difficult to clear is an inevitable suspicion.¹³⁴ However, if valid, that should be a class effect relevant to all colloids (including fresh frozen plasma and starches) rather than being albumin specific. Furthermore, albumin has been used in TBI by others with no evidence of adverse effects.^{135,136} In contrast to alleged adverse effects in the context of TBI, there are potential beneficial effects in SAH.^{137,138} The ALIAS phase III clinical trial evaluated the use of albumin in acute stroke patients. Although albumin administration was associated with increased rate of symptomatic intracranial hemorrhage (ICH) and congestive heart failure (CHF), no negative impact was detected in the primary outcome measure—the rate of favorable neurologic outcome at 90 days.¹³⁹ At best, the existing literature may justify consideration of limiting albumin volumes in patients with severe head injury. The indications and concerns for colloids, and especially albumin administration, have been recently expressed (see Chapter 47).

The various starch-containing solutions should be used cautiously in neurosurgery because, in addition to a dilutional reduction of coagulation factors, they interfere directly with both platelets and the factor VIII complex.¹⁴⁰ The coagulation effects are proportional to the average molecular weight and the hydroxyethyl group substitution ratio of the starch preparation. There have been several reported instances of bleeding in neurosurgical patients that were attributed to hydroxylethyl starch administration. However, all of those have involved circumstances in which the manufacturer's recommended dosage limit was exceeded¹⁴¹ or in which the starch was administered up to the recommended limit on successive days, probably resulting in an accumulation effect.¹⁴² The latitudes are wider with the subsequent availability of small molecule/lower substitution ratio preparations. These preparations have a record of safety when used in the operating room in general¹⁴³ and have been administered uneventfully to patients with severe TBI.¹⁴⁴ The decision about whether to use these products is frequently a matter of local practice. Although hydroxylethyl starch solutions can be used in neuroanesthesia, clinicians should respect the manufacturers' recommended dose restrictions and should use additional restraint in situations where there are other reasons for impairment of the coagulation mechanism. Recent concern about adverse effects on renal function in patients who have received starches in critical care situations have made some reluctant to use these compounds in any setting. The dextran-containing solutions are generally avoided because of their effects on platelet function.

There is longstanding interest in the use of hypertonic fluids for the resuscitation of polytrauma victims in general, and of patients with TBI in particular. However, there has yet to be a scientifically convincing demonstration of outcome improvement associated with hypertonic solution administration.¹⁴⁵

GLUCOSE MANAGEMENT

There is a widespread notion that increased plasma glucose aggravates a cerebral ischemic insult. This may be true for an acute ischemic event in a previously normal brain, but

that should not be extrapolated to the idea that all “neuro patients” should be submitted to very tight glycemic control. The potential benefits of a lower plasma glucose concentration in the event of an acute ischemic episode (which have not been well confirmed in humans) should be outweighed by the very clear demonstrations that the injured brain (e.g., TBI, SAH) becomes “hypoglycemic” and suffers metabolic distress at plasma glucose levels that are satisfactory for a normal brain.¹⁴⁶⁻¹⁴⁹ This may be because injury can produce a state of hyperglycolysis.^{147,150} Although severe hyperglycemia should be treated to reduce infection rates, patients with acute injuries (e.g., TBI, SAH) should not be submitted to very tight control. As one reviewer said, “extra sweetness [is] required”¹⁵¹ by the injured brain. The authors’ intraoperative intervention threshold is 250 mg/dL (14 mmol/L), the objective being to reduce plasma glucose to less than 200 mg/dL (11 mmol/L). One published guideline recommends an ICU objective of less than 180 mg/dL (10 mmol/L) in patients with cerebral injuries but cautions that plasma glucose not be allowed to decrease to less than 100 mg/dL (5 mmol/L).¹⁵² The NICE-Sugar study’s control group range of 144 to 180 mg/dL (7.8-10 mmol/L)¹⁵³ is probably also a reasonable target. However, control should only be undertaken when processes to prevent hypoglycemia are firmly in place, and the lower the targets, the more comprehensive the hypoglycemia prevention processes must be.

HYPOTHERMIA

The effects of hypothermia on cerebral physiology and its potential cerebral protective mechanisms are presented in [Chapter 11](#). There have been numerous laboratory demonstrations on the efficacy of mild hypothermia (32°C-34°C) in reducing the neurologic injury occurring after standardized cerebral and spinal cord ischemic insults. On that basis, the use of induced hypothermia in the management of cerebral vascular procedures, in particular aneurysms and sometimes AVMs, became widespread. However, an international multicenter trial of mild hypothermia in 1001 relatively good-grade patients undergoing aneurysm surgery revealed no improvement in neurologic outcome.¹⁵⁴ Thus, the routine use of intraoperative hypothermia has inevitably diminished.

Because ischemia is recognized to make a post-insult contribution to neuronal injury after TBI,^{26,155} hypothermia was also studied in laboratory models of TBI.¹⁵⁶ Hypothermia was effective and resulted in a prospective multicenter trial in which hypothermia (33°C) was induced within 8 hours of injury and was maintained for 48 hours. No outcome benefit was evident.¹⁵⁷ Post hoc subgroup analysis indicated that patients younger than 45 years old who arrived at the tertiary care facility with a temperature less than 35°C who were randomly assigned to the cooling limb of the trial did have an improved outcome. A second trial in which more rapid induction of hypothermia was accomplished (35°C by 2.6 hours, 33°C by 4.4 hours) was undertaken. However, the results were similarly negative.¹⁵⁸ Hypothermia has also been evaluated as a neuroprotective strategy in pediatric TBI. The largest randomized controlled trial (RCT) failed to demonstrate improved outcome at 6 months and in fact, demonstrated a trend toward worse outcomes in the hypothermia group.¹⁵⁹

Based on a lack of demonstrated efficacy in humans, routine use of hypothermia in neurosurgery cannot be advocated in a standard textbook. The decision to use it, usually in the context of aneurysm surgery, is local. The authors continue to use mild hypothermia selectively, most commonly in patients perceived to be at an especially high risk of intraoperative ischemia. If hypothermia is used, cardiac dysrhythmia and coagulation dysfunction can occur if body temperatures become too low. Patients should be rewarmed adequately before emergence to avoid shivering, hypertension, or delayed awakening.

By contrast with clinical neurosurgery, the use of hypothermia after cardiac arrest is now practiced widely. Two multicenter trials demonstrated improved neurologic outcome among survivors of witnessed cardiac arrest cooled to 32 to 34°C within 4 hours and maintained at that temperature for 12 to 24 hours.^{160,161} A subsequent randomized trial reported similar outcomes in patients treated with targeted temperature management at either 33°C or 36°C.¹⁶² Widespread clinical application of targeted temperature management has been advocated by an international task force and other groups.^{163,164}

Although mild hypothermia is perceived to convey the hazard of coagulation dysfunction and dysrhythmia, neither has been evident in elective neurosurgery in the temperature ranges typically used (32°C-34°C). The issue of where body temperature should be recorded to best reflect brain temperature has been addressed.¹⁶⁵ It appears that esophageal, tympanic membrane, pulmonary arterial, and jugular bulb temperature are all very similar and provide a reasonable reflection of deep brain temperature, whereas bladder temperature does not. During craniotomies, superficial layers of cortex may be substantially cooler than deep brain and central temperatures.

EMERGENCE FROM ANESTHESIA

Most practitioners of neuroanesthesia feel that there is a premium on a smooth emergence—that is, one free of coughing, straining, and arterial hypertension. The avoidance of arterial hypertension is desired because arterial hypertension can contribute to intracranial bleeding and increased edema formation.¹⁶⁶⁻¹⁷¹ In the face of poor cerebral autoregulation, hypertension also has the potential, through vascular engorgement, to contribute to an increase in ICP. Much of the concern with coughing and straining has a similar basis. The sudden increases in intrathoracic pressure are transmitted to both arteries and veins, producing transient increases in both cerebral arterial and venous pressure, with the same potential consequences: edema formation, bleeding, and elevation of ICP. Coughing is a specific concern with certain individual procedures. In the circumstances of transsphenoidal pituitary surgery in which a surgeon has opened, and subsequently taken pains to close, the arachnoid membrane to prevent CSF leakage, there is a belief that coughing has the potential to disrupt this closure because of the sudden and substantial increases in CSF pressure. Opening a pathway from the intracranial space to the nasal cavity conveys a substantial risk of post-operative meningitis. In other procedures, notably those that have violated the floor of the anterior fossa, air can be driven into the cranium and, in the event of a flap-valve

mechanism, cause a tension pneumocephalus. This latter event can only happen when coughing occurs after the endotracheal tube has been removed.

There is a paucity of systematically obtained clinical data to give a perspective to the actual magnitude of the risks associated with emergences that are not considered smooth. Two retrospective studies have revealed that increased postoperative arterial blood pressure was associated with intracerebral bleeding after craniotomy.^{170,171} However, whether hypertension occurring at emergence causes postoperative intracerebral bleeding is not clear. Also, the relationship between hypertensive transients at emergence and edema formation is unconfirmed. In anesthetized animals, sudden and very substantial increases in arterial pressure can result in a breach of the BBB with extravasation of tracers.¹⁶⁷ However, there are no data to confirm that the pressure transients associated with the typical coughing episode or common emergence are in fact associated with increased edema formation. Nonetheless, it seems reasonable to take measures, to the extent that these measures do not themselves add potential patient morbidity, to prevent these occurrences.

A common method for the management of systemic hypertension during the last stages of a craniotomy is the expectant and/or reactive administration of lidocaine and vasoactive agents, most commonly labetalol and esmolol.¹⁷² Other drugs, including hydralazine, enalapril, diltiazem, nicardipine, and clevidipine have been used to good effect. Administration of dexmedetomidine during the procedure or just prior to its conclusion also reduces the hypertensive response to emergence¹⁷³ and hypertension in the postanesthesia care unit.¹⁷⁴

There are also many approaches to the prevention of coughing and straining. The authors encourage trainees to include in their anesthetic technique as much narcotic as is consistent with spontaneous ventilation at the conclusion of the procedure, as opioids are antitussive and depress airway reflexes. Patients may also emerge more rapidly and smoothly when the last inhaled anesthetic to be withdrawn is nitrous oxide. This can be supplemented, if necessary, with propofol by either bolus increments or infusion at rates in the range of 12.5 to 25 µg/kg/min.

An additional principle relevant to the emergence from neurosurgical procedures is that emergence should be timed to coincide not with the final suture but rather with the conclusion of the application of the head dressing. Many a good anesthetic for neurosurgery has been spoiled by severe coughing and straining that occurs in association with endotracheal tube motion during the application of the head dressing. Another nuance of our practice has been to withhold administration of neuromuscular antagonists as long as possible in the later stages of the procedure. The administration of lidocaine is another apparently effective technique for reducing airway responsiveness and the likelihood of coughing/straining as the depth of anesthesia is reduced in anticipation of emergence. We commonly administer 1.5 mg/kg of intravenous lidocaine just before the head movement associated with applying the dressing.

Because of the premium placed on minimizing coughing and straining and hypertension, there may be a temptation to extubate from the trachea before complete recovery of consciousness. This may be acceptable in some circumstances. However, it should be undertaken with caution

BOX 57.8 Specific Procedures

- Supratentorial tumors
- Aneurysms and arteriovenous malformations
- Traumatic brain injury
- Posterior fossa procedures
- Transsphenoidal surgery
- Awake craniotomy/seizure surgery
- Stereotactic procedures
- Neuroendoscopic procedures
- Neuroradiologic procedures
- Cerebrospinal fluid shunting procedures
- Pediatric neurosurgery
- Spinal surgery

when the circumstances of the surgical procedure make it possible that neurologic events have occurred that will delay recovery of consciousness, or when there may be cranial nerve dysfunction. In these circumstances, it would, in general, be best to wait until the likelihood of the patient's recovery of consciousness is confirmed or until patient cooperation and airway reflexes are likely to have recovered.

Specific Procedures

Many of the considerations relevant to individual neurosurgical procedures are generic ones that have already been presented in the preceding section on Recurrent Issues in Neuroanesthesia. The descriptions that follow will highlight only procedure-specific issues (Box 57.8).

SUPRATENTORIAL TUMORS

Craniotomies for excision or biopsy, or both, of supratentorial tumors are among the most common neurosurgical procedures. Gliomas and meningiomas are among the most frequent tumors. The relevant preoperative considerations include the patient's ICP status, and the location and size of the tumor. Location and size of the tumor give the anesthesiologist an indication of the surgical position, the potential for blood loss, and will sometimes reveal a risk of air embolism. VAE is infrequent for the majority of supratentorial tumors. However, lesions (usually convexity meningiomas) that encroach upon the sagittal sinus may convey a substantial risk of VAE. Full VAE precautions, including a right atrial catheter, are usually reserved for only the supratentorial tumors that lie near the posterior half of the superior sagittal sinus.

Excision of craniopharyngiomas and pituitary tumors with suprasellar extension may entail dissection in and around the hypothalamus (see Fig. 57.18). Irritation of the hypothalamus can elicit sympathetic responses including hypertension. Damage to the hypothalamus can result in a spectrum of physiologic disturbances, notably water balance. Diabetes insipidus is the most likely, although the cerebral salt-wasting syndrome can infrequently occur. The various disturbances of water balance typically have a delayed onset, beginning 12 to 48 hours postoperatively, rather than in the operating room. Postoperative temperature homeostasis may also be disturbed.

Patients who undergo a craniotomy involving a subfrontal approach sometimes manifest a disturbance of consciousness in the immediate postoperative period. Retraction and irritation of the inferior surfaces of the frontal lobes can result in a patient who exhibits either delayed emergence or some degree of disinhibition, or both. The phenomenon is more likely to be evident when there has been bilateral frontal lobe retraction. The anesthetic implication is that the clinician should be more inclined to confirm return of consciousness before extubating the patient rather than to extubate expectantly. A further implication taken by these authors (though not confirmed by any systematic study) is that a less liberal use of intravenous anesthetic drugs (e.g., fentanyl, propofol infusion) may be appropriate when there is to be bilateral subfrontal retraction. This is based on the rationale that low residual concentrations of these anesthetics that are compatible with reasonable recovery of consciousness in most patients may be less well tolerated in this population. Subfrontal approaches are most commonly used in patients with olfactory groove meningiomas and patients with suprasellar tumors including craniopharyngiomas and pituitary tumors with suprasellar extension.

Preoperative Preparation

Patients with a significant tumor-related mass effect, especially if there is tumor-related edema, should receive preoperative steroids. A 48-hour course is ideal (see the previous discussion of steroids), although 24 hours is sufficient for a clinical effect to be evident. Dexamethasone is the most commonly used agent. A regimen such as 10 mg intravenously or orally followed by 10 mg every 6 hours is typical. Because of the concern about producing CO₂ retention in patients whose intracranial compliance is already abnormal, sedative premedication outside of the operating room is usually avoided.

Monitoring

Institutional practices vary; however, we almost invariably place arterial catheters for craniotomies under general anesthesia (GA). Preinduction placement may be appropriate in patients with severe mass effect and little residual compensatory latitude. At a minimum, we achieve intra-arterial monitoring before pin placement. It is the period of induction and pinning during which hypertension, with its attendant risks in a patient with impaired compliance and autoregulation, is most likely to occur. Arterial lines also facilitate careful management of blood pressure during emergence. Procedures with a substantial blood loss potential (e.g., tumors encroaching on the sagittal sinus, large vascular tumors) may also justify central venous catheters when peripheral venous access is limited. If not already present for other indications, ICP monitoring is rarely warranted for induction, given our understanding of the potential impact of anesthetics and associated procedures. Once the cranium is open, observation of conditions in the surgical field provides equivalent information.

Management of Anesthesia

The principles governing the choice of anesthetic drugs are presented in the previous section, Control of Intracranial Pressure and Brain Relaxation.

ANEURYSMS AND ARTERIOVENOUS MALFORMATIONS

Contemporary management and current recommendations regarding ruptured intracranial aneurysms call for intervention as early as feasible to reduce the rate of rebleeding.¹⁷⁵ That intervention may entail either operative clipping or an endovascular approach.¹⁷⁵ The latter is discussed in the subsequent section Neurointerventional Procedures.

Early intervention was originally undertaken only in patients in the better neurologic grades—that is, grades I-III and perhaps IV of the World Federation of Neurosurgeons classification (Table 57.2) or grades I-III of the Hunt-Hess classification (Table 57.3)—but is now recommended for the majority of patients.¹⁷⁵ If early intervention is not feasible and a surgical approach is intended, surgery may be delayed for 10 to 14 days to be safely beyond the period of maximal vasospasm risk (i.e., days 4-10 post-SAH).

The rationale for early intervention is several-fold. The sooner the aneurysm is clipped or obliterated, the less the likelihood of rebleeding (and rebleeding is the principal cause of death for patients hospitalized after SAH¹⁷⁶). Second, the management of the ischemia caused by vasospasm involves fluid resuscitation and induced hypertension. Early occlusion of the aneurysm eliminates the risk of rebleeding associated with this therapy. Prior surgical practices

TABLE 57.2 World Federation of Neurosurgeons Subarachnoid Hemorrhage 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

GCS, Glasgow Coma Scale; WFNS, World Federation of Neurosurgeons.

TABLE 57.3 Hunt-Hess Classification of Neurologic Status After Subarachnoid Hemorrhage

Category	Criteria*
Grade I	Asymptomatic, or minimal headache and slight nuchal rigidity
Grade II	Moderate to severe headache, nuchal rigidity, no deficit other than cranial nerve palsy
Grade III	Drowsiness, confusion, or mild focal deficit
Grade IV	Stupor, moderate to severe hemiparesis, possibly early decerebrate rigidity and vegetative disturbances
Grade V	Deep coma, decerebrate rigidity, moribund appearance

*Serious systemic disease, such as hypertension, diabetes, severe arteriosclerosis, chronic pulmonary disease, and severe vasospasm seen on arteriography, results in placement of the patient in the next less favorable category.

entailed maintaining the patient on bed rest until approximately day 14, when the period of spasm risk had passed. Early aneurysm clipping reduces the period of hospitalization and reduces the incidence of the medical complications (i.e., deep vein thrombosis, atelectasis, pneumonia) associated with a lengthy period of enforced bed rest.

Early intervention makes the surgeon's task more difficult. The brain in the early post-SAH period is likely to be more edematous than after a 2-week delay. Furthermore, some degree of hydrocephalus is very common after blood contaminates the subarachnoid space. In fact, about 9% to 19% of aneurysmal SAH victims eventually require permanent CSF diversion.^{175,177-180} Early intervention may also enhance the risk of intraoperative aneurysmal rupture because of the lesser period of time for a clot to organize over the site of the initial bleed. All this places a substantial premium on techniques designed to reduce the volume of the intracranial contents (see Control of Intracranial Pressure and Brain Relaxation earlier in this chapter) to facilitate exposure and minimize retraction pressures.

Preoperative Evaluation

Many patients scheduled for intracranial aneurysm clipping will come directly from the ICU, and elements of their critical care management may influence their immediate preoperative status.

Intravenous Fluid Management. Some patients develop the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) after SAH and are appropriately managed with fluid restriction. However, hyponatremia after SAH is more likely to be the result of the cerebral salt-wasting syndrome that probably occurs as a result of the release of a natriuretic peptide by the brain.^{181,182} Cerebral salt-wasting syndrome is characterized by the triad of hyponatremia, volume contraction, and high urine sodium concentrations (>50 mmol/L), and its occurrence is correlated with the occurrence of symptomatic vasospasm.¹⁸³ The distinction between cerebral salt-wasting syndrome and SIADH is important. SIADH, which is characterized by normovolemia or mild hypervolemia, is treated by volume restriction. Cerebral salt-wasting syndrome is associated with a contracted intravascular volume. Fluid restriction and further volume contraction may be especially deleterious in the post-SAH patient and should be avoided.¹⁸⁴⁻¹⁸⁶ Although the clinical distinction between these two causes of hyponatremia (SIADH and cerebral salt-wasting syndrome) may be difficult, management of both is relatively simple: administration of isotonic and/or hypertonic fluids using intravascular normovolemia and normonatremia as the end point.

Vasospasm. The anesthesiologist should determine whether vasospasm has occurred and what, if any, therapies for it have been undertaken. Vasospasm is thought to be caused by the breakdown products of the hemoglobin that have accumulated around the vessels of the circle of Willis after SAH. A specific mechanism/mediator has not been identified. Calcium channels are thought to be involved, and there is also suspicion that the nitric oxide and endothelin systems may be contributory.^{186,187}

When there is a clinical suspicion of vasospasm (typically because of a change in sensorium or new neurologic deficit),

surgery is usually deferred and TCD, angiography, or other imaging is performed. Symptomatic vasospasm has historically been treated with "Triple H" therapy (hypervolemia, hypertension, and hemodilution). Current management has shifted toward fluid resuscitation to euolemia (rather than hypervolemia),^{175,188} hypertension, and sometimes balloon angioplasty or intraarterial vasodilators.¹⁸⁹

For patients proceeding to surgery, hypotension should be avoided¹⁷⁵ and CPP should usually be maintained intraoperatively at values near the waking normal range. The association of hypotension with poor outcome,¹⁹⁰ and the potential for hypotension to cause or aggravate cerebral ischemia in patients with some degree of vasospasm, is well recognized.¹⁹¹⁻¹⁹³ This concern should extend even to patients classified as World Federation of Neurosurgeons grade I who may have regions of cerebral ischemia³⁰ that are subclinical when the patient is normotensive.

In the ICU, the regimens used to treat vasospasm usually involve some combination of fluid resuscitation and blood pressure augmentation. The science behind hypervolemic-hypertensive therapy is soft and the efficacy of neither Triple H therapy nor volume expansion in isolation has been proved by prospective study.^{188,194-196} The relative importance of the rheologic and blood pressure effects is undefined, although there is evidence for the relevance of blood pressure elevation in isolation.^{187,196-199} Phenylephrine and dopamine are the most commonly used pressors; exact pressor choice should be primarily governed by systemic cardiovascular considerations. The end point for pressor administration varies. Most commonly, the objective is an increase in MAP of approximately 20 to 30 mm Hg above baseline systolic pressure. However, it has been reported that augmentation of cardiac output with dobutamine, without simultaneous MAP increase, augments CBF in ischemic territories.¹⁹⁶ It is also believed that a hematocrit in the low 30s is optimal for cerebral perfusion, but this is not a therapeutic target that is directly manipulated.

Calcium-Channel Blockers. Calcium-channel blockers are an established part of the management of SAH. Administration of nimodipine decreases the incidence of morbidity caused by cerebral ischemia after SAH,²⁰⁰ although it was not associated with any reduction in the incidence of vasospasm as detected by angiography.²⁰¹ Patients presenting to the operating room after SAH should already be receiving nimodipine. Because nimodipine must be administered orally in North America, nicardipine has been evaluated as an intravenous alternative. The multicenter nicardipine trial^{202,203} revealed a reduced incidence of symptomatic vasospasm but no improvement in outcome. As a consequence, nimodipine remains the standard. Calcium-channel blockers (i.e., verapamil, nicardipine, nimodipine²⁰⁴⁻²⁰⁷) are also used intraarterially as a primary treatment for medically-refractory vasospasm. Milrinone and papaverine are similarly administered.^{206,208}

Other Pharmacologic Therapies. Several other agents/drug classes have been considered for the prevention of vasospasm and delayed ischemic deficits. None of them is approaching the status of standard therapy. A study of the endothelin antagonist clazosentan revealed improved mortality without improvement in the outcome of survivors. After several small trials suggested a beneficial effect of

magnesium, a larger randomized, placebo-controlled trial reported no improvement in outcome among patients in whom magnesium was initiated within 4 days of SAH.²⁰⁹ Several small trials have examined the post-SAH administration of statins. Meta-analysis revealed only nonsignificant trends toward reduced incidence of delayed cerebral ischemia and death.²¹⁰ A subsequent large RCT (STASH) failed to demonstrate either short-term or long-term outcome benefits related to statin administration.²¹¹ The phosphodiesterase inhibitor cilostazol (a platelet inhibitor as well as vasodilator) was reported to reduce symptomatic vasospasm,^{212,213} new cerebral infarctions,²¹³ and improve outcome²¹² following SAH. Although promising, a larger study to confirm the safety and efficacy of cilostazol is anticipated.

Antifibrinolytics. Antifibrinolytics have been administered in an attempt to reduce the incidence of rebleeding. Although they accomplish this end, long courses do so at the cost of an increased incidence of ischemic symptoms and hydrocephalus, with an overall adverse effect on outcome. However, early, brief courses of antifibrinolytics that are continued until the aneurysm is secured may have a net favorable effect on outcome.¹⁷⁵

Subarachnoid Hemorrhage-Associated Myocardial Dysfunction. SAH can result in a largely reversible myocardial “stunning” injury. The severity of the dysfunction correlates best with the severity of the neurologic injury²¹⁴ and is sometimes sufficient to require pressor support.²¹⁵ The mechanism is uncertain but is thought to be catecholamine mediated.²¹⁶ Troponin elevation occurs commonly, though typically reaching levels less than the diagnostic threshold for myocardial infarction.²¹⁷ Peak troponin levels correlate with the severity of both neurologic injury and echocardiographic myocardial dysfunction.^{215,218}

ECG abnormalities are common after SAH. In addition to the classic coved T waves (Fig. 57.14), nonspecific T-wave changes, Q-T prolongation, ST-segment depression, and U waves have been described. There is typically no relationship between the ECG changes and echocardiographic myocardial dysfunction.²¹⁷ ECG abnormalities do not herald evolving or impending cardiac disease.²¹⁹ Accordingly, when ventricular function is adequate and ECG patterns other than those that are typical of myocardial ischemia are observed, no specific interventions or modifications of patient management are warranted, other than attention to the possibility of dysrhythmias. In particular, an increased Q-T interval (>550 ms) occurs frequently after SAH, especially in patients with more severe SAH,²¹⁸ and has been associated with an increased incidence of malignant ventricular rhythms including torsades de pointes.²²⁰

Anesthetic Technique

Important considerations include the following:

1. Absolute avoidance of acute hypertension with its attendant risk of rerupture.
2. Achievement of intraoperative brain relaxation to facilitate surgical access to the aneurysm.
3. Maintenance of a high-normal MAP to prevent critical reduction of CBF in recently insulted and now marginally

perfused areas of brain, or in regions critically dependent on collateral pathways.

4. Preparedness to perform precise manipulations of MAP as the surgeon attempts to clip the aneurysm or to control bleeding from a ruptured aneurysm or during periods of temporary vascular occlusion.

Monitoring

An arterial line is invariably appropriate. A central venous catheter may be appropriate if peripheral access is inadequate.

Anesthetic Selection. Any technique that permits proper control of MAP is acceptable. However, in the face of increased ICP or a tight surgical field, an inhaled anesthetic technique may be less suitable. The prevention of paroxysmal hypertension is the only absolute requirement in patients undergoing aneurysm clipping. The poorly organized clot over the aneurysms of patients undergoing early post-SAH clipping makes them particularly prone to rebleeding. A rebleed at induction is frequently fatal.¹⁷⁶ The escaping arterial blood is more likely to penetrate brain substance because it cannot dissect through the CSF space (filled with clot), and the ICP increase is extreme because of the poor compliance of the intracranial space (swollen brain, hydrocephalus).

Induced Hypotension. The routine use of induced hypotension has essentially vanished (see previous section Management of Arterial Blood Pressure). Nonetheless, the anesthesiologist should be prepared to reduce blood pressure immediately and precisely if called upon to do so. Preparation of an appropriate hypotensive agent must occur before the episode of bleeding. There are theoretical pros and cons for various hypotensive agents. However, the choice should ultimately be made based on which regimen, in the hands of the individual practitioner, results in the most precise control of MAP. There are rare occasions when the anesthesiologist is asked to control MAP in the range of 40 to 50 mm Hg in the face of active arterial bleeding. This can be extremely difficult in a patient who is hypovolemic at the beginning of the bleeding episode. It is our practice to maintain normovolemia.

Induced Hypertension. Relative hypertension may be requested during periods of temporary arterial occlusion (see the later section Temporary Clipping) to augment collateral CBF. In addition, after clipping of the aneurysm, some surgeons will puncture the dome of the aneurysm to confirm adequate clip placement and may request transient elevation of the systolic pressure to 150 mm Hg. Phenylephrine is suitable in either instance.

Hypocapnia. Hypocapnia has traditionally been used as an adjunct to brain relaxation. However, the practice has been questioned on the basis of the concern that it will aggravate ischemia (see the earlier section Management of PaCO₂). It is now generally avoided unless ICP/brain relaxation circumstances demand it.

Lumbar Cerebrospinal Fluid Drainage. CSF drainage has been used to facilitate exposure. However, its use

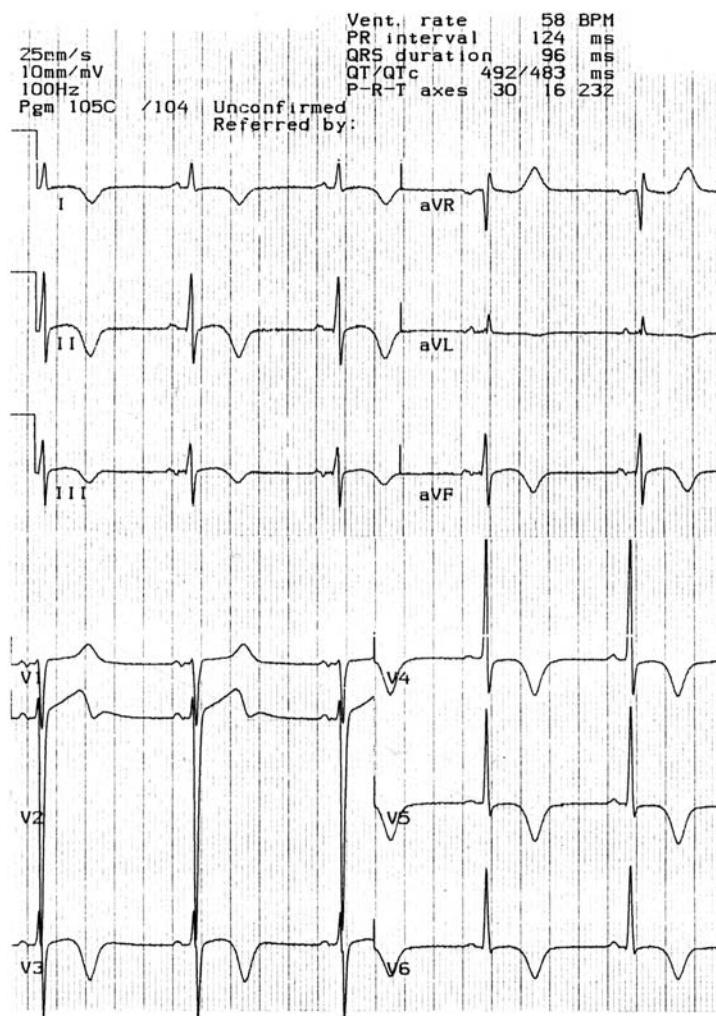


Fig. 57.14 Electrocardiogram abnormalities associated with subarachnoid hemorrhage. The canyon T waves that may be seen after subarachnoid hemorrhage are evident.

appears to be diminishing because surgeons have appreciated that the same brain-relaxing effect can be achieved by release of CSF from the basal cisterns. If a lumbar CSF drain is placed, it is appropriate to avoid excessive loss of CSF. A sudden reduction in the transmural pressure gradient across the dome of the aneurysm (by sudden reduction of ICP consequent upon substantial CSF drainage) should be avoided because of the theoretical concern that this decompression might encourage rebleeding. Having verified the patency of the drainage system, it is usual to leave it closed until the surgeon is opening the dura. The drain is then opened and allowed to drain freely to floor level. Drainage should be discontinued promptly after final withdrawal of the retractors to allow CSF to reaccumulate and to thereby reduce the size of the potential pneumocephalus.

Some surgeons use mannitol relatively aggressively (e.g., 2 g/kg). In part, it is used to facilitate exposure and reduce retractor pressures, but there is evidence that it may have additional benefits. Specifically, there are data derived in both animals and man indicating that mannitol may have a CBF-enhancing effect in regions of moderate CBF reduction.²²¹⁻²²⁴ The mechanism is not defined. Reduction of interstitial tissue pressure around capillaries and/or an

alteration of blood rheology have been proposed as contributors. Typically, mannitol administered in a dose of 1 g/kg just before dural opening provides satisfactory brain relaxation.⁴⁵ Surgeons who believe in its CBF-enhancing effect may request a second 1 g/kg approximately 15 minutes before an anticipated temporary occlusion.

Temporary Clipping. Many surgeons limit inflow to an aneurysm during application of the permanent clip by placing a temporary clip proximally on the feeding vessel. It is occasionally necessary to trap the aneurysm (i.e., to temporarily occlude the vessel on both sides of the aneurysm) to complete the dissection of the neck and apply the clip. This is more common with larger aneurysms. With giant aneurysms in the vicinity of the carotid siphon, the inferior occlusion may be performed at the level of the internal carotid artery via a separate incision in the neck. A clinical survey of the neurologic outcome after temporary occlusion in normothermic, normotensive adults revealed that occlusions of fewer than 14 minutes were invariably tolerated. The likelihood of an ischemic injury increased with longer occlusions and reached 100% with occlusions in excess of 31 minutes.²²⁵ In another institution, the threshold

for ischemic injury was 20 minutes of occlusion.²²⁶ An informal 7-minute rule is sometimes applied to individual periods of temporary occlusion. Typically, MAP should be sustained at high-normal levels during periods of occlusion to facilitate collateral CBF.

Brain Protection. Maintenance of MAP to ensure collateral flow and perfusion under retractors, efficient brain relaxation to facilitate surgical access and reduce retractor pressures, limitation of the duration of episodes of temporary occlusion, and perhaps mild hypothermia are the important brain protection techniques. Specific anesthetic drugs have been promoted as brain protectants, but evidence is limited (see the discussion in [Chapter 11](#)). There have been no convincing laboratory demonstrations that propofol provides any greater tolerance to a standardized ischemic insult than does anesthesia with a volatile anesthetic. Attempts to demonstrate protection by etomidate in an animal model of focal ischemia actually demonstrated an adverse effect of etomidate.²²⁷ Furthermore, a clinical investigation during aneurysm clipping revealed decreases in brain tissue PO₂ in association with administration of etomidate, which contrasted with the brain PO₂ increases that occurred with the introduction of desflurane. During subsequent temporary vessel occlusion, tissue pH decreased alarmingly in patients receiving etomidate and was unchanged with desflurane.²²⁸ Etomidate probably should not be used because of a lack of sufficient data regarding its efficacy. With respect to the volatile anesthetics, attempts in the laboratory to confirm the once proclaimed protective efficacy of isoflurane have demonstrated that there are no differences among the various volatile anesthetics in terms of their influence on outcome after focal or global ischemia in the laboratory.^{227,229-231} Nor has there been any demonstration of greater protective efficacy with concentrations of volatile anesthetics sufficient to cause EEG suppression as opposed to more modest (e.g., 1.0 MAC) levels.^{231,232} Nonetheless, these animal investigations suggest that a standardized experimental ischemic insult is better tolerated, relative to the awake state, by animals receiving a volatile anesthetic.^{230,231,233} In addition, data derived in animals also suggest that there may also be a relative protective advantage to an anesthetic that includes a volatile anesthetic compared with a strict N₂O-narcotic technique. The magnitude of the differences among anesthetics and the absence of proof of relevance in patients precludes advocacy of a particular anesthetic regimen in a standard text. The important anesthetic objectives are precise hemodynamic control and timely wake-up, and those two constraints should dictate the choice of the anesthetic regimen for most aneurysm procedures. Among anesthetics, it is only the barbiturates for which additional protective efficacy has been demonstrated convincingly. Because of their potentially adverse effects on hemodynamics and wake-up, they are not ideal for routine use. They should probably be reserved for situations in which a prolonged vessel occlusion is unavoidable, and in that circumstance, it would be ideal that the ischemic hazard be first confirmed by observation of the EEG response to a temporary occlusion.²³⁴

The patient with, or at substantial risk for, vasospasm probably benefits from a minimum hemoglobin greater

than that which is commonly accepted in stable ICU patients (i.e., >7 g/dL). The best available information suggests a minimal hemoglobin value of 9 g/dL.^{199,235}

Hypothermia. As noted in the previous section Hypothermia, a prospective trial of mild hypothermia in patients undergoing aneurysm surgery revealed no improvement in neurologic outcome.¹⁵⁴ Nonetheless, some neurosurgical teams that were already using mild hypothermia (32°C-34°C) are continuing its use for procedures in which temporary vessel occlusion may occur. The institutions that use the lower temperatures are those in which the team is willing to accept a delay in emergence from anesthesia to achieve sufficient rewarming to avoid the extreme hypertension that can occur when a patient is awakened at low body temperatures.

Neurophysiologic Monitoring. Evoked responses and EEG have been used for monitoring.^{234,236} EEG monitoring can be used as a guide to management during the period of flow interruption or to guide the administration of CMR-reducing anesthetic agents given before occlusion. At some institutions, the surgeon places an electrode strip over the region of cortex at risk during the intended occlusion. However, the more commonly used skin surface frontal-mastoid derivation is probably sufficient to reveal a major ischemic event. In most circumstances, if occlusion is deemed necessary, a temporary occlusion is performed, and the EEG is observed. If the EEG shows significant slowing, the common practice is to raise the MAP and proceed with as brief as possible a period of occlusion or intermittent episodes of temporary occlusion. If the necessity for a sustained period of occlusion seems likely, it may be appropriate to administer barbiturates (discussed earlier) to produce burst suppression. These events are very infrequent (see also [Chapter 39](#)).

Intraoperative Angiography. Intraoperative angiography is an increasingly common component of the management of intracranial aneurysm surgery. It does not have substantial implications for the anesthesiologist except with respect to placement of the radiographic equipment.

Special Considerations for Specific Aneurysms

The most common procedures are performed for aneurysms arising in or close to the circle of Willis. The vessels of origin may be the anterior communicating artery; the middle cerebral artery; the anterior cerebral artery; the ophthalmic artery; the tip of the basilar artery; the posterior communicating artery; and, less frequently, the posterior cerebral artery. These procedures are relatively similar for the anesthesiologist and typically require a supine position with the head turned slightly away from the operative side.

Ophthalmic Artery Aneurysms. Access to the origin of the ophthalmic artery, which is the first intradural branch of the carotid artery, is made difficult by the anterior clinoid process and the optic nerve. As a result, these aneurysms frequently require temporary vascular occlusion. The surgeon commonly first exposes the carotid artery in the neck. When the surgeon reaches the stage of seeking definitive access to the neck of the aneurysm, he or she will occlude

first the carotid artery in the neck and then the intracranial portion of the carotid artery immediately proximal to the origin of the posterior communicating artery. A catheter is placed in the excluded segment and put to suction. Blood loss, which is usually minimal, should be monitored.

Vertebrobasilar Aneurysms. These procedures are typically performed in the lateral position. The exposure may involve a combined middle and posterior fossa approach, with some attendant, although minor, risk of VAE. Cortical or skin surface EEG monitoring is of less relevance with vertebrobasilar aneurysms. Auditory, somatosensory, and motor-evoked responses have been used to monitor for vascular compromise.²³⁷⁻²³⁹ As with any other procedure involving the potential for mechanical or vascular injury to the brainstem, cardiovascular responses should be monitored and sudden changes in response to surgical manipulation should prompt immediate notification to the surgeon.^{240,241}

Vein of Galen Aneurysms. Vein of Galen aneurysms are congenital dural arteriovenous fistulas, usually treated in the neonate using endovascular methods, and share considerations relevant to AVMs. These include anticipation of the possibility of the cerebral dysautoregulation phenomenon and are considered subsequently.

Arteriovenous Malformations

For the majority of intracranial AVMs, the general considerations are similar to those appropriate to aneurysm surgery: avoidance of acute hypertension and the capability to accurately manipulate arterial blood pressure in the event of bleeding. A problem specific to AVMs is the phenomenon of perfusion pressure breakthrough, or cerebral dysautoregulation.^{242,243} It is characterized by an often sudden engorgement and swelling of the brain, sometimes with a relentless cauliflower-like protrusion from the cranium. It tends to occur in the advanced stages of lengthy procedures on large AVMs, or it may be the cause of otherwise unexplained postoperative swelling and hemorrhage. The phenomenon is not entirely understood. An AVM provides a high-volume, low-resistance pathway that chronically diverts blood from adjacent and therefore marginally perfused vascular territories. Perhaps these tissues have long been maximally vasodilated and are incapable of vasoconstricting when exposed to a higher-pressure head after acute obliteration of the AVM. Although this explanation superficially fits the clinical occurrence, experimental data are not entirely consistent with this mechanism.²⁴²⁻²⁴⁵ At least some component of the hyperemia is not passive, and neurogenic or paracrine mechanisms may be involved.

Anesthetic Technique. The management constraints are essentially the same as those relevant to aneurysm surgery, although the risk of intraoperative rupture is much less. Institutional practices will vary. We do not use induced hypotension unless it is necessitated by bleeding. We reason that the effects on the surrounding brain of devascularizing the AVM would be best appreciated if the devascularization occurs at normal pressures. If refractory brain swelling occurs, tight blood pressure control is essential, and reducing MAP may be of use to control swelling. The latter

is based on the notion that CBF through the involved area is pressure-passive and will decrease as MAP is reduced. With severe episodes of swelling, we have used (in addition to hypotension, which we use cautiously because of the associated ischemia risk) hypocapnia, hypothermia, and barbiturates. The latter three techniques probably serve to reduce the bulk of only normal brain tissue, hypocapnia via a direct effect on CBF and barbiturates and hypothermia via the coupled effects of reduction of CMR on CBF. Induced hypothermia is also an adjunct to minimizing the barbiturate doses. In all of neurosurgery, we seek to prevent postoperative hypertension; however, in AVM surgery this should be accomplished with the greatest care because of the concern that the dysautoregulating brain adjacent to the resected AVM will develop edema or hemorrhage if hypertension occurs.

HEAD INJURY

Intubating the Trachea of a Head-Injured Patient

Patients with GCS scores of 7 to 8 (Table 57.4) or less require tracheal intubation and controlled ventilation for ICP or airway control, or both. Patients with less severe TBI may also require intubation because of trauma-related cardiopulmonary dysfunction or, when uncooperative, to facilitate diagnostic procedures. The anesthesiologist, in choosing the intubation technique, may encounter a number of conflicting constraints (Box 57.9). These include: (1) elevated ICP; (2) a full stomach; (3) uncertain cervical spine status; (4) uncertain airway status (e.g., presence of blood, possible laryngotracheal injury, possible skull base fracture); (5) an uncertain volume status; (6) an uncooperative or combative patient; and (7) hypoxemia. The best

TABLE 57.4 The Glasgow Coma Scale

Eyes opening	
Never	1
To speech	2
To pain	3
Spontaneously	4
Best verbal responses	
None	1
Garbled or incomprehensible sounds	2
Inappropriate words	3
Confused but conversant	4
Oriented	5
Best motor responses	
None	1
Extension (decerebrate rigidity)	2
Abnormal flexion (decorticate rigidity)	3
Withdrawal	4
Localizes pain	5
Obey commands	6
Score	3-15

BOX 57.9 Factors That May Be Relevant During Intubation of the Head-Injured Patient

- Full stomach
- Uncertain cervical spine stability
- Uncertain airway
 - Blood
 - Airway injury (larynx, cricoarytenoid cartilage)
 - Skull-base fracture
- Uncertain volume status
- Uncooperative/combative
- Hypoxemia
- Increased intracranial pressure

approach is determined by the relative weight of these various factors along with the degree of urgency. The anesthesiologist must not be distracted by placing an excessive initial emphasis on ICP. The anesthesiologist needs to keep sight of the ABCs of resuscitation: securing the airway, guaranteeing gas exchange, and stabilizing the circulation are higher initial priorities than ICP. Do not risk losing the airway or causing severe hypotension for the sake of preventing coughing on the tube or brief hypertension with intubation.

The Cervical Spine

The possibility of causing or aggravating an injury to the cervical spine is a relevant concern. Approximately 2% of blunt trauma victims who reach a hospital, and 8% to 10% of TBI victims with GCS scores less than 8, have a fracture of the cervical spine.^{246,247} Those incidences suggest that a hypnotic-relaxant-direct laryngoscopy approach for all patients with a closed head injury might convey a measurable risk of injuring the cervical cord. Nonetheless, although the literature contains contradictions, several published series have concluded that rapid-sequence induction does not convey significant risk of neurologic injury.²⁴⁸⁻²⁵¹ However, it is possible that the incidence of intubation-related neurologic injury is underreported. An informal survey²⁵² indicated that there have been more such events than one can infer from the published literature.^{253,254} Nonetheless, the majority of patients with TBI requiring airway control are intubated using a hypnotic-relaxant-laryngoscopy sequence. In our opinion, the possibility of devastating spinal cord injury may be higher with injuries in the atlanto-occipital region, which are also difficult to identify radiologically, and that the anesthesiologist should identify circumstances in which time latitudes allow more detailed examination or radiologic evaluation. When there is any uncertainty regarding the airway or the cervical spine, direct laryngoscopy (with vigorous atlanto-occipital extension) should probably be avoided when the exigencies of the situation do not require an immediate rapid-sequence induction. The nasal route can be considered if the clinical context warrants it, bearing in mind that risk of infection may be increased with skull base fracture and CSF leak. The anesthesiologist should use discretion (e.g., in the presence of an obvious facial injury, the nasal route should be avoided) and be sensitive to unusual resistance in passing the endotracheal tube.

When a hypnotic-relaxant sequence is used (and the exigencies of airway control will frequently demand it), the standard approach includes the use of cricoid pressure and in-line axial stabilization. In-line traction was once favored but has been supplanted by stabilization because of the perceived risk of overdistraction and cord injury in the event of gross instability. The largest of the clinical series that concluded that oral intubation with anesthesia and relaxation is reasonable²⁴⁸ used in-line stabilization with the patient's occiput held firmly on the backboard, limiting the amount of "sniff" that was feasible (Fig. 57.15). There is no question that in-line stabilization, properly performed, makes laryngoscopy somewhat more difficult; however, it serves to decrease the amount of atlanto-occipital extension necessary to achieve visualization of the glottis.²⁵⁵ This is probably because performing the laryngoscopy against the assistant's counterpressure results in greater compression of the soft tissue structures of the tongue and floor of the mouth. Some recommend leaving the back half of the cervical collar in place during laryngoscopy (see Fig. 57.15) because it functions as a strut between the shoulder and the occiput and serves to further limit atlanto-occipital extension.

In a resuscitation situation, before initiating a hypnotic-relaxant sequence, the anesthesiologist should confirm the availability of cricothyrotomy equipment and of someone to make immediate, skilled use of it if necessary. The recently injured brain is very intolerant of hypoxia and hypotension.²⁵⁶ It is inevitable that there is sometimes failed tracheal intubation. In the extensive experience of the Cowley Shock-Trauma Center in Baltimore, the cricothyrotomy/tracheostomy rate is 0.3%.²⁵⁷ As is the case in many other situations, the laryngeal mask may be a very useful device for temporizing in the face of a failed intubation and may also provide access for intubation as an alternative to cricothyrotomy.

As noted in Chapter 11, although succinylcholine can cause ICP increases, these increments are small and probably do not occur in patients with serious cerebral injuries.⁸



Fig. 57.15 Intubating the acute trauma patient with an uncertain cervical spine. A hypnotic and a relaxant have been administered. One assistant maintains in-line axial stabilization with the occiput held firmly to the backboard; a second applies cricoid pressure. The posterior portion of the cervical collar remains in place to limit atlanto-axial extension. (Reproduced with permission from Stene JD. Anesthesia for the critically ill trauma patient. In: Siegel JH, ed. *Trauma: Emergency Surgery and Critical Care*, Melbourne: Churchill Livingstone; 1987:843-862.)

Accordingly, succinylcholine should not be viewed as contraindicated in the TBI victim. If there is an urgent need to secure the airway (to guarantee oxygenation and control CO₂ tension), and if succinylcholine is in other respects the appropriate drug to achieve that end, it should be used. The necessity to use succinylcholine in these circumstances, however, has diminished with the availability of both rocuronium and the reversal agent sugammadex.

What should the anesthesiologist do with the patient whose cervical spine has not been cleared? That situation should arise with decreasing frequency. The once standard plain radiographs (with their inherent difficulties and substantial false-negative rates) have been supplanted by CT scanners that allow rapid, thin-slice evaluation, with sagittal reconstruction. A large meta-analysis concluded that "modern multislice helical CT alone is sufficient to rule out traumatic, unstable cervical spine injuries."²⁵⁸ However, some remain concerned that CT may fail to identify ligamentous injuries that would be evident on magnetic resonance imaging (MRI).²⁵⁹ With respect to a conscious patient who has not yet undergone complete radiologic evaluation, several clinical surveys have confirmed that patients who are alert, not intoxicated, and free of significant distracting injuries invariably have pain, midline tenderness, limitation of voluntary movement, or neurologic signs²⁶⁰⁻²⁶² if they have a cervical spine fracture. Despite the frequency with which an anesthesiologist may encounter patients still wearing their cervical collars because their necks have not yet been cleared, no special precautions appear warranted in the asymptomatic, alert patient.

Anesthetic Technique

Choice of Anesthetic Drugs. Craniotomies are most commonly performed for the evacuation of subdural, epidural, or intracerebral hematomas. The anesthetic approach is similar for all three techniques. The guiding principles have been discussed in the section Control of Intracranial Pressure and Brain Relaxation. In general, anesthetics that are known to be cerebral vasoconstrictors are preferable to those that have the potential to dilate the cerebral circulation. All the intravenous anesthetics, except perhaps ketamine, cause some cerebral vasoconstriction and are reasonable choices, provided they are consistent with hemodynamic stability. All the inhaled anesthetics (N₂O and all the volatile anesthetics) have some cerebral vasoconstrictive effect. Although their administration frequently is consistent with acceptable ICP levels and appropriate conditions in the surgical field, when the ICP is out of control (or unknown), or the surgical field is tight, omitting the inhaled anesthetics in favor of intravenous agents is appropriate. For patients who are likely to remain intubated postoperatively, an anesthetic based primarily on a narcotic, such as fentanyl, and a muscle relaxant usually serves well. Any muscle relaxant is acceptable with the proviso that those that can release histamine (now rarely used) should be titrated in small increments. When immediate tracheal extubation is a possibility (e.g., the patient with an acute epidural hematoma who had a lucid interval before witnessed deterioration), the technique should be modified after the opening of the cranium. Introduction of inhaled anesthetics or the use of shorter-acting intravenous drugs can be undertaken as guided by observation of the surgical

field. If N₂O is contemplated at any time, the anesthesiologist must remember the possibility, in the setting of missile injury or compound skull fracture, of intracranial air.

Monitoring. The anesthesiologist should appreciate that the priority is to open the cranium as rapidly as possible.²⁶³ After achieving intravenous access, the risks and benefits of delaying craniotomy for line placement should be considered carefully. An arterial line, often placed after induction in urgent situations, is appropriate for essentially all acute trauma craniotomies. Peripheral venous access is sufficient in the majority of situations. Sudden hypotension after dural opening with high ICP can occur as brainstem compression is relieved.²⁶⁴ Appropriate intravascular volume resuscitation should mitigate this occurrence. Infrequently, the management of a depressed skull fracture over the sagittal sinus justifies a precordial Doppler and, subject to the surgeon's assessment of VAE risk, a right heart catheter.

Arterial Blood Pressure Management. The concept that the injured brain is extremely vulnerable to what would otherwise be a minor insult (e.g., modest hypotension, moderate hypoxia) has been well confirmed in the laboratory.²⁶⁵ Although clinically the cause-effect relationships are not absolutely confirmed, several surveys demonstrate the association of otherwise minor degrees of hypotension and hypoxia with poor outcome in both adult^{256,266-271} and pediatric patients with TBI.²⁷² This vulnerability to hypotension probably arises because many patients have brain regions with precariously low CBF in the first 2 to 3 days after TBI^{23,26,273-275} and autoregulation is frequently defective.²⁷⁶⁻²⁷⁸ The characteristic behavior of CBF after TBI is an initially low CBF followed by a gradual increase over 48 to 72 hours to normal, or sometimes even slightly hyperemic, levels.^{23,26,273,274,276,279,280} There is considerable evidence that low post-insult CBF values correlate with a poor eventual outcome,^{26,270,275,281-283} and a large percentage of patients who die after TBI have pathologic changes consistent with ischemia.¹⁵⁵ These observations have resulted in a general emphasis among neurosurgeons, neurointensivists, and anesthesiologists on aggressive support of arterial blood pressure in the patient with TBI.

What constitutes an appropriate arterial blood pressure? Systematic studies have revealed that indices of the adequacy of cerebral perfusion derived from SjvO₂ and TCD data begin to deteriorate below a mean CPP of 70 mm Hg,^{270,284,285} and many centers adopted 70 mm Hg as the CPP target. A clinical investigation comparing the ICU management of patients with TBI at CPPs of 70 and 50 mm Hg demonstrated that, although indices of cerebral well-being were improved by the former, there was no outcome advantage, apparently because of the cardiopulmonary morbidity associated with achieving a sustained CPP of 70 mm Hg.²⁸⁶ As a result, many authorities have adopted 60 mm Hg as the minimal CPP management objective.^{279,287-290} The Brain Trauma Foundation has most recently recommended a CPP target range of 60 to 70 mm Hg in adults.⁶² Age-related CPP targets of 40 to 50 mm Hg have been recommended for children.²⁹¹

Maintenance of CPP at 60 to 70 mm Hg in the first 2 to 3 days after TBI is probably reasonable. However, clinicians may encounter other views, including the argument

that a one-size-fits-all approach inevitably denies the heterogeneity of pathophysiology among patients with TBI. It is certainly true that not all patients with TBI have low CBF and not all have absent autoregulation. Although an initially low postinjury CBF is probably the most common clinical occurrence, hyperemia does occur.^{22,24,280,292,293} It tends to occur in patients with mass lesions rather than contusions, although even those patients have an immediate postinjury period of low CBF, with delayed hyperemia peaking at 24 hours or later.^{22,280,282,293,294} Hyperemia may also be more common in children.²⁹⁵ There is evidence that not all patients with TBI benefit from increases in CPP. Patients with TBI and impaired autoregulation, low baseline flows, increased ICP, and low initial GCS score are most likely to benefit.²⁹⁶⁻²⁹⁹ Accordingly, targeted therapy has been advocated.³⁰⁰⁻³⁰⁶ However, techniques to discriminate the various flow states (serial CBF measurement, TCD, SjvO₂) are not universally available. Some institutions, which have the necessary data analysis capacity, take another approach to targeted therapy. They identify a nominal optimal CPP by examining the changes in ICP that occur in response to variations in MAP. The range of MAPs in which the smallest Δ ICP/ Δ MAP occurs is taken to be the range within which autoregulation functions most efficiently and is the target range for that individual patient.^{301,302} This approach is not feasible in most ICUs. As a result, and despite the theoretic attractiveness of targeted therapy, the CPP target of 60 to 70 mm Hg as an objective is more common.

There are at least two alternative approaches to blood pressure management in patients with TBI (Fig. 57.16). The Lund concept is based on the premises that arterial blood pressure causes hydrostatically driven edema accumulation, and that edema formation can be further aggravated by crystalloid administration and subnormal COP.³⁰⁷⁻³⁰⁹ As originally described, the Lund approach in part entailed relative dehydration (furosemide, crystalloid restriction), albumin administration to maintain a normal COP, and the administration of metoprolol and clonidine to lower blood pressure to a CPP target of 50 to 55 mm Hg. At its inception, the approach was controversial because it ran counter to the perceptions of many clinicians of the importance of maintaining a CPP of 70 mm Hg and because of the later demonstration that a negative fluid balance in patients with TBI is deleterious.²⁷¹ Over time (and in parallel with a relaxation of the higher CPP targets by others),^{279,287,288} the Lund proponents have modified their approach. Normovolemia is now the clinical objective, and CPP is 60 to 70 mm Hg in most patients. The latter has made the approach somewhat less controversial. However, CPP may be reduced to 50 to 60 mm Hg when ICP is not well controlled,¹³⁵ and that element remains controversial.³¹⁰ Although the proponents of the Lund approach assert improvements in outcome, those reports invariably entail either no control group or comparisons with nonconcurrent controls.^{136,311-313} The approach has not been adopted in North America.

The second approach, promoted by neurosurgeons at the University of Alabama at Birmingham (sometimes called the “Rosner concept” after its chief proponent), is that induced hypertension can be used as an adjunct to ICP control.^{26,314,315} The underlying concept is that autoregulation is at least partially preserved after TBI and that an increased

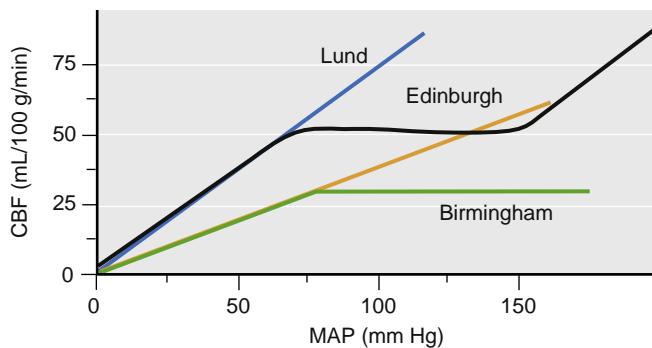


Fig. 57.16 The relationship of cerebral blood flow (CBF) to blood pressure after head injury. There are three cerebral perfusion pressure (CPP) management strategies (see text) driven by differing beliefs about common pathophysiologic derangements. The most commonly held strategy is Edinburgh (so named for the institution of the original proponents); it emphasizes low post-injury CBF, impaired autoregulation, and the necessity to support CPP (mean arterial pressure [MAP]—intracranial pressure [ICP]) to 60 to 70 mm Hg. The Lund concept emphasizes the contribution of hyperemia to the occurrence of elevated ICP. That approach uses antihypertensive agents to reduce blood pressure while maintaining CPP >50 mm Hg.³⁰⁷ That CPP target has increased, in the most recent iteration, to 60 to 70 mm Hg, with allowance for occasional reduction to 50 mm Hg.³⁰⁹ An approach emanating from the University of Alabama, identified as Birmingham, entails pharmacologically induced hypertension. That approach is based on the belief that autoregulation is largely intact and that hypertension will result in cerebral vasoconstriction with concomitantly reduced cerebral blood volume and ICP.^{314,315}

MAP results in autoregulation-mediated vasoconstriction with a concomitant reduction in CBV and, therefore, ICP. These investigators reported a very satisfactory local experience,³¹⁵ but others have reported that induced hypertension was either ineffective or deleterious as a means of reducing increased ICP.^{13,316} The Rosner approach now appears to have few advocates.

What should the anesthesiologist managing the patient with TBI do in the face of these various approaches? Perfusion pressure support of varying degrees is a theme that is common to all of them, and the careful support of CPP at or just above the 60 mm Hg range is probably the most reasonable general approach. When establishing normovolemia alone does not accomplish that objective, phenylephrine, norepinephrine, and dopamine have all been used. With that CPP recommendation offered, it must be acknowledged that convictions vary, and anesthesiologists should come to an understanding with the local traumatologists and neurosurgeons as to CPP targets.

Hyperventilation. The use of hypocapnia has been reviewed in detail in the section Management of PaCO₂. The effectiveness of acute hypocapnia in reducing ICP is well confirmed.¹³ But there is substantial evidence that hyperventilation is potentially deleterious^{20,21,26,29,317,318} and should not be overused. That evidence suggests that hyperventilation and the concomitant vasoconstriction can result in ischemia,^{20,21,25,27,317} especially when baseline CBF is low,²⁷ as is likely to be the case in the first 48 to 72 hours after head injury.^{23,24,26,273} The expert panel convened by the Brain Trauma Foundation specified that “prolonged prophylactic hyperventilation with PaCO₂ of 25 mm Hg or less is not recommended.”⁶² Although they did

not officially carry forward the recommendations from the third edition, they did restate the following recommendations to convey the concern for vasoconstriction-mediated ischemia: (1) “hyperventilation is recommended as a temporizing measure for the reduction of elevated ICP”; (2) “hyperventilation should be avoided during the first 24 hours after injury when CBF is often critically reduced”; and (3) “if hyperventilation is used, $SjvO_2$ or brain tissue PO_2 measurements are recommended to monitor oxygen delivery.”⁶² The totality of available information argues that hyperventilation should be used selectively rather than routinely in the management of patients with TBI. Maintaining ICP less than 20 mm Hg, preventing or reversing herniation, minimizing retractor pressure, and facilitating surgical access are still important objectives in the management of the patient with TBI, and to the extent that these objectives cannot be accomplished by other means, hyperventilation may still be appropriate. Once again, the anesthesiologist should agree on management variables with the surgical team at the outset of all procedures.

Intravenous Fluid Management. Intravenous fluid management of the patient with TBI was addressed earlier in the section Intravenous Fluid Management. The important principles are that fluids should be chosen invariably to prevent reduction of serum osmolarity and should probably be chosen to prevent profound reduction of COP—that is, in the circumstances of a large-volume resuscitation (arbitrarily, greater than half of the circulating volume), using a mix of colloids and crystalloids is probably appropriate. The clinical objective should be the maintenance of intravascular normovolemia, in part as an adjunct to MAP and CPP support. A chronic negative fluid balance, as can occur with the combination of modest fluid restriction and liberal use of osmotic diuretics, has been shown to be deleterious and should be avoided.²⁷¹ The severely injured brain can liberate sufficient thromboplastin into the circulation to result in a consumptive coagulopathy.³¹⁹⁻³²¹ Appropriate laboratory tests and replacement should be performed. The clinician may also find a serum osmolarity determination early in the course of anesthetic management useful in appreciating the cumulative effects of prior administration of mannitol or HTS. The use of hypertonic solutions and the relevant attributes of colloid solutions were discussed in the section Intravenous Fluid Management. Because of the ischemia that can be a component of TBI, the minimal acceptable hemoglobin level should probably be more than that accepted in stable critical care patients (i.e., 7 g/dL). There is relatively little information to provide guidance. However, one investigation, which presented observations of brain tissue PO_2 ($PbtO_2$), suggested 9 g/dL as a hazard threshold in patients with TBI.²³⁵

Monitoring

Jugular Venous Oxygen Saturation. $SjvO_2$ monitoring has been used to guide the management of patients with TBI.^{20,21,27,28,270,285,286,317,322,323} The underlying concept is that a marginal or inadequate CBF results in an increasing oxygen extraction, a widening arteriovenous content difference, and reduction of $SjvO_2$. Normal subjects have $SjvO_2$ values between 60% and 75%. A $SjvO_2$ less than 50% for 5 minutes is commonly accepted as constituting jugular desaturation. There have been numerous reports

of low $SjvO_2$ values improving with interventions including reducing hyperventilation, increasing MAP, or inducing hypervolemia. $SjvO_2$ measurement assesses global oxygen extraction. It might be expected to have limited sensitivity to focal events, and instances in which focal inadequacy of perfusion was not reflected by low $SjvO_2$ have been reported.^{20,21,24,317} An additional limitation inherent to the unilateral placement of the catheter is the observation³²⁴ that there is an average side-to-side difference between simultaneous jugular bulb saturations of $5.3 \pm 5\%$ and that side-to-side differences in hemoglobin saturation of up to 15% are common.³²⁴

Despite the reported successes with $SjvO_2$ monitoring,^{28,325,326} we do not believe that the method is sufficiently well defined to justify advocating widespread intraoperative application. In the ICU, it appears to be potentially useful as a trend monitor that may serve to identify the level of CPP or hyperventilation below which cerebral perfusion begins to be compromised, with the proviso that there is a significant potential for false-negative results.^{20,21,24,317} The technique also has a potential use beyond warning of inadequate perfusion. High $SjvO_2$ values may serve to identify the patient with elevated ICP in whom hyperemia is an important contributing factor and in whom aggressive attempts to decrease CBF (i.e., hyperventilation, barbiturates) may be beneficial.

Brain Tissue PO_2 . $PbtO_2$ has been used to guide the management of both TBI and SAH, and there have been limited reports of improvement in outcomes.^{316,318-331} A $PbtO_2$ equal to or greater than 20 to 25 mm Hg is viewed as normal, and values equal to or less than 10 to 15 mm Hg are assumed to convey a substantial risk of hypoxic injury. One investigation reported that 29% of patients with TBI with GCS scores of 8 or less have brain regions with $PbtO_2$ less than 10 mm Hg, despite meeting CPP and ICP targets of 60 mm Hg or less than 25 mm Hg, respectively.²⁸⁹ This would seem to encourage the use of these monitors. However, $PbtO_2$ monitors suffer from the inverse of the problem that prevails with $SjvO_2$ monitoring: they provide very focal information about the oxygenation status of only small regions of brain surrounding the tip. If they are placed remotely from focal injuries to provide a global measure of oxygenation, they may not see adverse events in at-risk but salvageable perilesional tissue.³³² They may similarly fail to be a useful therapeutic guide if they are within irredeemably injured brain. The use of $PbtO_2$ monitoring is neither standardized nor widespread.

Intracranial Pressure Monitoring for Nonneurologic Surgery in the Brain-Injured Patient. The relevant variables when nonneurologic surgery is considered for the brain-injured patients include:

1. *The level of consciousness.* If there has been a loss of consciousness at any time (or amnesia for the event in the absence of witnesses) or if the GCS score is less than 15, a CT scan should be obtained. If the CT scan reveals compressed basal cisterns (indicative of an exhaustion of supratentorial compensatory latitudes), midline shift, or effaced ventricles, and probably any intracranial lesion (e.g., contusion, small subdural), an ICP monitor should be considered for surgery, with GA performed within 48

hours after TBI. Excessive comfort should not be taken from a good GCS score. Patients with good scores can talk and deteriorate or talk and die after a TBI associated with loss of consciousness. Delayed deterioration has been observed as much as 4 days after the initial injury.^{333,334} Patients with lesions, usually contusions, in the frontal and frontotemporal region, and especially those with medial temporal lesions, are most at risk for this phenomenon. Modest expansion of lesions in this location (i.e., close to the uncus and the incisura where herniation occurs) can result in herniation even at relatively low ICPs (e.g., ≈20 mm Hg). At our institution, neurosurgeons would recommend avoiding an anesthetic in these patients and would certainly advise ICP monitoring if lengthy GA were unavoidable.

2. *Time since injury.* The longer the patient has had to declare his or her clinical course, the less pressing is the need for ICP monitoring. Delayed deterioration has been observed after as much as 48 hours,³³³ and 4.5 days in separate investigations,³³⁴ and a patient with a demonstrable CT lesion and a GCS score less than 15 is a candidate for a monitor during this time frame.
3. *Nature and duration of the intended procedure.* The risks of an untoward ICP event are inevitably greater in a 6-hour spine instrumentation in the prone position than in a 20-minute debridement and suturing of an arm laceration.

Hypothermia

There is clearly an ischemic component to the pathophysiology of TBI, and mild induced hypothermia has been shown to be highly protective in experimental cerebral ischemia. On that basis, the study of hypothermia after experimental TBI was undertaken, and improvements in outcome were demonstrated.¹⁵⁶ Several local, prospective trials of hypothermia after TBI were performed.³³⁵⁻³³⁸ Because those trials appeared to indicate good patient tolerance of sustained mild hypothermia (32°C-34°C) and improvement in ICP and outcome, a multicenter trial was performed. That trial, which required induction of hypothermia within 8 hours of injury, revealed no overall benefit.¹⁵⁷ Because of concern that 8 hours was not sufficiently rapid, a second trial, which achieved the target temperature in 2.5 hours, was performed. It too was negative for benefits.¹⁵⁸ A recent European multicenter trial (EUROTHERM) evaluated hypothermia plus standard care versus standard care alone and failed to demonstrate an outcome benefit of hypothermia.³³⁹ (Also see the section Hypothermia.) As a result, there is no established role for hypothermia in TBI management as of this writing.

POSTERIOR FOSSA PROCEDURES

Most of the topics relevant to posterior fossa procedures (Table 57.5) have been discussed in the section Recurrent Issues in Neuroanesthesia. These include the sitting position and its cardiovascular effects and complications (quadriplegia, macroglossia), pneumocephalus, and VAE and PAE. The use of the sitting position to facilitate surgery in the posterior fossa increases the likelihood of all these phenomena, though they are relevant to nonsitting positions as well. This section reviews the cardiovascular events

TABLE 57.5 Considerations Relevant to Posterior Fossa Procedures and the Location of the Related Discussion in This Chapter

Consideration	Chapter Section, Subsection
Hemodynamic effects of the sitting position	Positioning, Sitting
Venous air embolism	Venous Air Embolism
Paradoxical air embolism	Venous Air Embolism
Hemodynamic effects of brainstem and cranial nerve manipulation	Posterior Fossa Procedures
Macroglossia	Positioning, Sitting
Pneumocephalus	Pneumocephalus
Quadriplegia	Positioning, Sitting

associated with direct stimulation of the brainstem and their possible implications for postoperative management.

Brainstem Stimulation

Irritation of the lower portion of the pons and the upper medulla (Fig. 57.17) and of the extra-axial portion of the fifth cranial nerve can result in a number of cardiovascular responses. The former two areas are most often stimulated during procedures on the floor of the fourth ventricle and the last during surgery at or near the cerebellopontine angle (e.g., acoustic neuromas, microvascular decompression of fifth [tic douloureux], seventh [hemifacial spasm], or ninth [glossopharyngeal neuralgia] cranial nerves). The responses may include bradycardia and hypotension, tachycardia and hypertension, or bradycardia and hypertension, and ventricular dysrhythmias.³⁴⁰ Meticulous attention to the ECG and a directly transduced arterial pressure during manipulation in this region are necessary to provide the surgeon with immediate warning of the risk of damage to the adjacent cranial nerve nuclei and respiratory centers. Pharmacologic treatment of the dysrhythmias that occur may serve to attenuate the very warning signs that should be sought.

Irritation and injury of posterior fossa structures that may have occurred during surgery should be considered in planning extubation and postoperative care. In particular, procedures involving dissection on the floor of the fourth ventricle entail the possibility of injury to cranial nerve nuclei or postoperative swelling in that region, or both. Cranial nerve dysfunction, particularly of nerves IX, X, and XII, can result in loss of control and patency of the upper airway, and swelling of the brainstem can result in impairment of both cranial nerve function and respiratory drive. The posterior fossa is a relatively small space, and its compensatory latitudes are even more limited than those of the supratentorial space. Relatively little swelling can result in disorders of consciousness, respiratory drive, and cardio-motor function. There should be an interaction between the anesthesiologist and the surgeon in deciding whether extubation is appropriate and where postoperative observation should occur (i.e., ICU or non-ICU).

Spontaneous ventilation was once advocated for procedures that entailed a risk of damage to the respiratory centers.³⁴¹ Spontaneous ventilation is now rarely used because

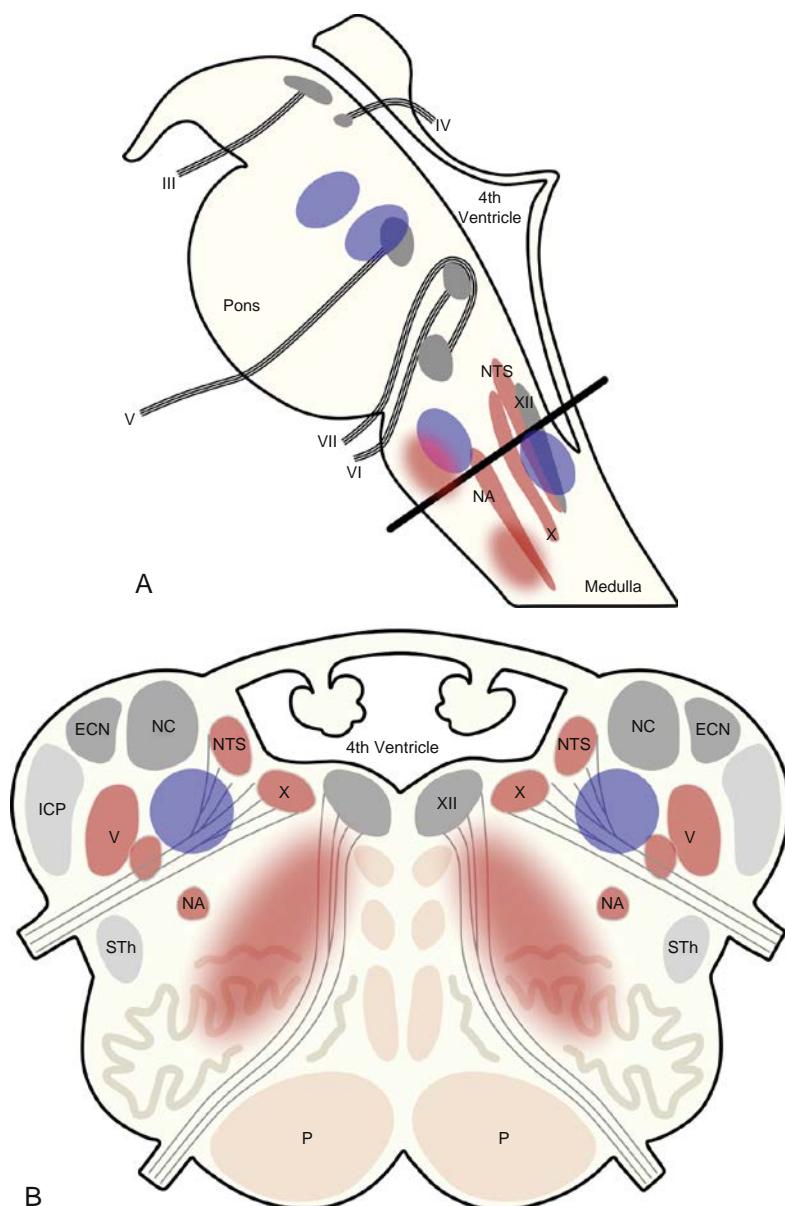


Fig. 57.17 Vasomotor and respiratory centers. Sagittal (A) and axial (B) illustrations of vasomotor centers (red) and respiratory centers (blue) located near the floor of the 4th ventricle. Minor brainstem manipulation resulting in stimulation of structures in red can lead to significant cardiovascular responses including hypertension, hypotension, bradycardia, and tachycardia. ECN, External cuneate nucleus; ICP, inferior cerebellar peduncle; NA, nucleus ambiguus; NC, nucleus cuneatus; NTS, nucleus tractus solitarius; P, pyramid; STH, spinal thalamic tract; V, spinal nucleus and tract of trigeminal nerve; X, dorsal motor nucleus of vagal nerve; XII, hypoglossal nerve nucleus.

the proximity of the cardiovascular and respiratory centers should permit cardiovascular signs to serve as an indicator of impending injury to the latter. Furthermore, electrophysiologic monitoring as a means of detecting brainstem injury has largely supplanted the role of spontaneous ventilation.³⁴¹

Various electrophysiologic monitoring techniques may be used during posterior fossa surgery. These include somatosensory evoked and motor evoked potentials (SSEPs, MEPs), brainstem auditory evoked responses, and electromyographic (EMG) monitoring of lower cranial nerves. MEPs and EMG monitoring require that the patient not be paralyzed or have a constant state of incomplete paralysis. SSEPs and MEPs impose some constraints with

respect to the selection of anesthetics. These are discussed in Chapter 39.

Balloon Compression of the Trigeminal Ganglion

This is another situation in which a dysrhythmia may occur. The procedure attempts to produce a neuropraxia of the fifth cranial nerve by the rapid inflation of a Fogarty-type balloon within Meckel's cave.^{342,343} The balloon is introduced percutaneously through the cheek and beneath the maxilla. The procedure is best accomplished with a general anesthetic because both the entry of the needle into Meckel's cave and the balloon compression (lasting several minutes) are intensely stimulating. A relatively profound, although transient, bradycardia occurs and is sought as confirmation

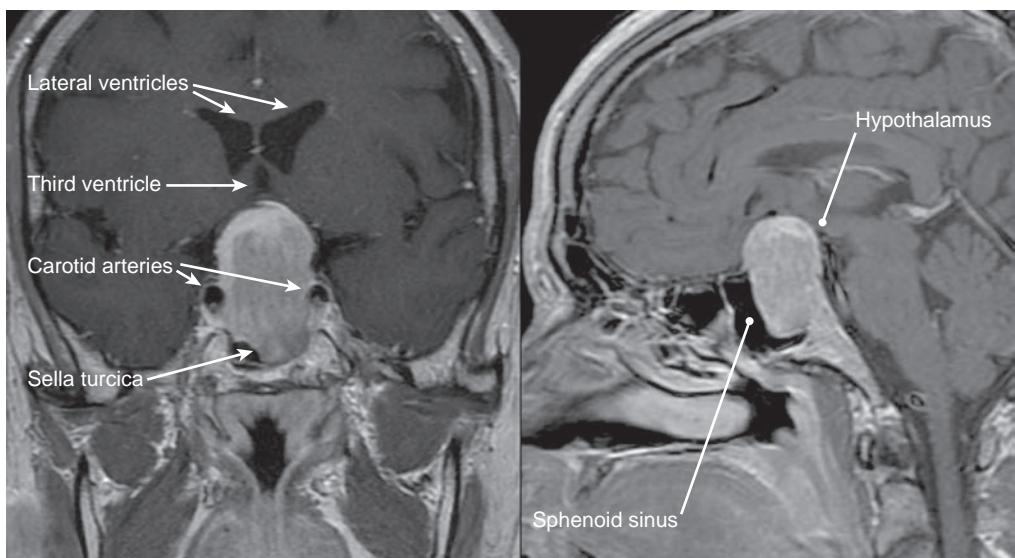


Fig. 57.18 Pituitary tumor with suprasellar extension. The left panel shows the proximity of the tumor to the carotid arteries (which lie within the cavernous sinuses) and the potential for distortion of the ventricular system. The optic chiasm (not seen) lies above the sella in the path of the upwardly expanding tumor. The right panel shows that tumors that lie above the sella (including craniopharyngiomas, which arise in this location) abut and can invade the hypothalamus. The more radio-dense (whiter) cap over the superior and anatomic right lateral aspects of the tumor mass is a normal pituitary gland.

of adequate compression. External pacemaker pads have been advocated but in our experience are unnecessary.

TRANSSPHENOIDAL SURGERY

The transsphenoidal approach to the sella turcica is used for the excision of tumors that lie within the sella or its environs (Fig. 57.18). Most of these lesions are tumors arising from the pituitary gland, and the most common of these are prolactin-secreting microadenomas and nonsecreting macroadenomas. Patients with the former are usually women who present with secondary amenorrhea or galactorrhea, or both. The nonsecreting adenomas tend to manifest with mass effects (headache, visual disturbance, hypopituitarism) and are typically larger at the time of diagnosis. Patients may also present with hypopituitary states as a result of dysfunction of the normal gland caused by compression by the tumor mass. There are three other less common pituitary tumors: growth hormone-secreting lesions, which result in acromegaly; adrenocorticotrophic hormone (ACTH)-secreting tumors, which cause Cushing disease; and a very rare thyroid-stimulating hormone-secreting lesion, which results in hyperthyroidism. A detailed review of the perioperative management of this group of patients is available.³⁴⁴

Preoperative Evaluation

The important preoperative considerations relate to the patient's endocrine and visual status. In general, as a pituitary lesion expands and compresses the pituitary tissue, normal glandular function is compromised. Hormonal function is lost in the following sequence: first, gonadotrophins; second, growth hormone; third, ACTH; and fourth and last, thyroid-stimulating hormone. A decrease in ACTH secretion results in a hypoadrenal state. Attention to this is critical because an Addisonian crisis can ensue, especially under the stress of surgery. Profound hypocortisolism, with

associated hyponatremia, should be corrected preoperatively. Deficiency in thyroid function is uncommon. However, if significant hypothyroidism is present, it should be corrected preoperatively because hypothyroid patients have a diminished tolerance to the cardiovascular depressant effects of anesthetics. Attention to other manifestations of pituitary hypersecretion is also important. Hypertension, diabetes, obstructive sleep apnea (OSA), and central obesity are common concomitants of ACTH-secreting adenomas (Cushing disease). Patients with advanced acromegaly can develop an enlarged tongue and a narrowed glottis, and the airway should be evaluated accordingly. The dermis is thickened, and vascular cannulation can be more difficult. Hypertension, OSA, and a cardiomyopathy may also occur.

Monitoring

Many practitioners place an arterial catheter, and this facilitates monitoring of blood pressure as the nasal mucosa is injected with epinephrine-containing local anesthetic solutions. Access for blood sampling is also a useful adjunct to postoperative care if diabetes insipidus develops. Blood loss is usually modest. However, the cavernous sinuses, through which the carotid arteries pass (see Fig. 57.18), form the lateral boundary of the sella and may be entered during the resection of large tumors. Entry into these structures can lead to catastrophic blood loss. In addition, in some patients there is an extensive venous sinus connecting the two cavernous sinuses that may cover the entire dural lining of the sella, rendering a transsphenoidal approach hazardous. It has, on occasion, actually precluded this approach to the pituitary gland.

Anesthetic Technique

The latitudes are broad with respect to choice of agent, although tumors with suprasellar extension (see Fig. 57.18) can occasionally cause hydrocephalus and add increased ICP constraints to the anesthetic technique. The procedure

is performed in the supine position, usually with some degree of head-up posture to avoid venous engorgement. A pharyngeal pack prevents the accumulation of blood in the stomach (which causes vomiting) or in the glottis (which contributes to coughing at extubation). A right-angle endotracheal (RAE)-type endotracheal tube secured to the lower jaw at the corner of the mouth opposite the surgeon's dominant hand (e.g., the left corner of mouth for a right-handed surgeon) is suitable. A small esophageal stethoscope and temperature probe can lie with the endotracheal tube.

The procedure is commonly performed with a C-arm image intensifier (lateral views), and the head and arms are relatively inaccessible once the patient is draped. It is appropriate to establish the nerve stimulator at a lower extremity site. The surgical approach is via the nasal cavity, usually through an incision made under the upper lip or via the nares. During the approach, the mucosal surfaces within the nose are infiltrated with a local anesthetic and epinephrine solution, and the patient should be observed for the occurrence of dysrhythmias.

Surgical preferences for CO₂ management vary. In some instances, hypocapnia is requested to reduce brain volume and minimize the degree to which the arachnoid bulges into the sella. One of the important surgical considerations is the avoidance, when possible, of opening the arachnoid membrane leading to leakage of CSF. Postoperative CSF leaks can be persistent and are associated with a considerable risk of meningitis. By contrast, when there is suprasellar extension of a tumor, a normal CO₂ level helps deliver the lesion into the sella for excision.³⁴⁵ As an alternative method to accomplish this, some surgeons have resorted to boluses of saline into the lumbar CSF space.³⁴⁶

A smooth emergence (see the section *Emergence from Anesthesia*) from anesthesia is desirable, especially if the CSF space has been opened (and resealed with fibrin glue or by packing the sphenoid sinus with fat or muscle). Repeated intense Valsalva maneuvers, as with coughing or vomiting, may contribute to the reopening of a CSF leak and worsen the risk of subsequent meningitis. The airway should be cleared of debris including formed clots. In situations in which there is concern that a persistent CSF leak may occur, the surgeon may place a lumbar CSF drain to maintain CSF decompression in the early postoperative period.

Diabetes Insipidus

The antidiuretic hormone (ADH) is synthesized in the supraoptic nuclei of the hypothalamus and is transported down the supraoptic-hypophyseal tract to the posterior lobe of the pituitary gland. This portion of the pituitary gland is frequently spared during transsphenoidal tumor excisions. Even when it is excised, water homeostasis commonly normalizes, presumably because the ADH is released from the cut end of the tract. When the pituitary stalk is transected, and sometimes even when the posterior lobe of the pituitary gland is left intact, transient diabetes insipidus may occur. Diabetes insipidus very rarely arises intraoperatively; it usually occurs 12 to 48 hours postoperatively. The clinical picture is one of polyuria in association with a rising serum osmolality. The diagnosis is made by comparison of the osmolality of urine and serum. Hypoosmolar urine in the face of an elevated and rising serum osmolality strongly supports the diagnosis. In the presence of bona fide diabetes

insipidus, urine-specific gravity is low (i.e., ≤ 1.002), though this analysis is now rarely performed.

When the diagnosis of diabetes insipidus is established, the following fluid management regimen is appropriate: hourly maintenance of fluids plus two thirds of the previous hour's urine output. (An acceptable alternative is the previous hour's urine output - 50 mL + maintenance.) The choice of fluid is dictated by the patient's electrolyte levels. In general, the patient is losing fluid that is hypoosmolar and relatively low in sodium. Half-normal saline and 5% dextrose in water are commonly used as replacement fluids. Beware of hyperglycemia when large volumes of 5% dextrose in water are used. If the hourly requirement exceeds 350 to 400 mL, desmopressin acetate is often administered.

AWAKE CRANIOTOMY AND SEIZURE SURGERY

Awake craniotomies are performed when tumors or epileptic foci lie close to cortical areas required for either speech or motor function, or to mesial-temporal structures critical to short-term memory. Many patients have so-called temporal lobe epilepsy. There is commonly a structural lesion visible on MRI. Sometimes there is a history of remote trauma.

Presurgical Evaluation

Before the resection, most patients have undergone a Wada test, video-telemetry, or both.³⁴⁷ More recently, functional testing using MRI or positron emission tomography, or both, has also been introduced to the presurgical evaluation. The Wada test involves selectively anesthetizing the cerebral hemispheres, usually by injection of amobarbital sodium into the carotid artery to localize the hemisphere that controls speech or to confirm that there is bilateral representation for short-term memory, or both. Speech is an issue when the posterolateral portions of the temporal lobe are involved, and memory is the concern when the involvement is mesial.

Anesthesia for Electroencephalogram Electrode Placement

Video-telemetry is performed to permit localization of the seizure focus that is responsible for the clinically problematic events. This usually requires prior placement of either subdural strip electrodes (via burr holes) or a subdural electrode grid (requiring a craniotomy). Electrodes are sometimes placed deep into the parenchyma, usually within the temporal lobe (placed stereotactically via burr holes), or they are positioned to look at the inferior surfaces of the temporal lobe. The latter is commonly accomplished with so-called foramen ovale electrodes. These electrodes are placed using a needle similar to an epidural needle. The point of entry is approximately 2 cm lateral to the angle of the mouth. The needle is passed through soft tissue, under the temporal process of the zygomatic bone and medial to the ramus of the mandible, up to the base of the skull in the vicinity of the foramen ovale. Typically, this procedure is performed with monitored anesthesia care (MAC) only, although small doses of anesthetics, most often propofol, are usually required at the time of stimulation by the needle of the periosteum at the base of the skull. After placement of the relevant electrodes, the patient's seizure medication is discontinued, and the patient remains in an

observation unit with EEG and behavior recorded continuously. In this manner, the EEG events associated with the clinically significant seizure events and their anatomic origin can be identified.

Preanesthetic Evaluation and Preparation

At the preoperative interview, the patient should be educated about the nature and duration of the procedure and the limitations on patient movement. A description of both the aura and the seizures to facilitate recognition of impending events should be obtained, and it should be ascertained whether the patient is subject to having grand mal convulsions. If intraoperative electrocorticography to identify seizure foci is intended, it is common to discontinue or reduce by half the anticonvulsants according to the perceived risk of uncontrolled seizures. Premedicants with an anticonvulsant effect (e.g., benzodiazepines) should not be used because they may interfere with intraoperative EEG localization.

Anesthetic Technique

The objectives of the anesthetic technique are as follows:

1. To minimize patient discomfort associated with the potentially painful portions of the procedure and with the prolonged restriction of movement.
2. To ensure patient responsiveness and compliance during the phases of the procedure that require assessment of speech, memory, or motor/sensory responses to cortical stimulation.
3. To select anesthetic techniques that produce minimal inhibition of spontaneous seizure activity.

There are probably many ways of providing sedation that are consistent with the objectives just cited. The techniques used range from minimal sedation approaches, through deep sedation during which intermittent unresponsiveness is achieved with spontaneous ventilation and an unprotected airway, to asleep-asleep techniques with intermittent airway management with a laryngeal mask airway (LMA) or endotracheal tube, sometimes with positive-pressure ventilation. From the outset, the anesthesiologist should appreciate that the essential element of an anesthetic for an awake craniotomy is the local anesthetic technique. Sedation cannot compensate for inadequate anesthesia of the scalp, as is accomplished by nerve blocks (Fig. 57.19), and pin site infiltration. Although the anesthesiologist can contribute enormously to the patient's comfort and tolerance of the painful components of the procedure and the prolonged immobilization, the anesthesiologist must not get trapped into thinking that it is his or her responsibility to provide a general anesthetic equivalent in a spontaneously breathing patient with an unprotected and all but inaccessible airway.

For sedation, there are many options. Many clinicians (including the authors) use principally propofol,^{348,349} sometimes supplemented with infusion of remifentanil (e.g., 0.02-0.05 µg/kg/min) or dexmedetomidine (e.g., 0.2 µg/kg/h). Other combinations, including propofol with either fentanyl or remifentanil and dexmedetomidine with or without remifentanil, are reasonable.³⁵⁰⁻³⁵² Great care should be taken in administering additional sedative drugs, especially narcotics whose respiratory depressant effects will be synergistic with propofol. This is especially

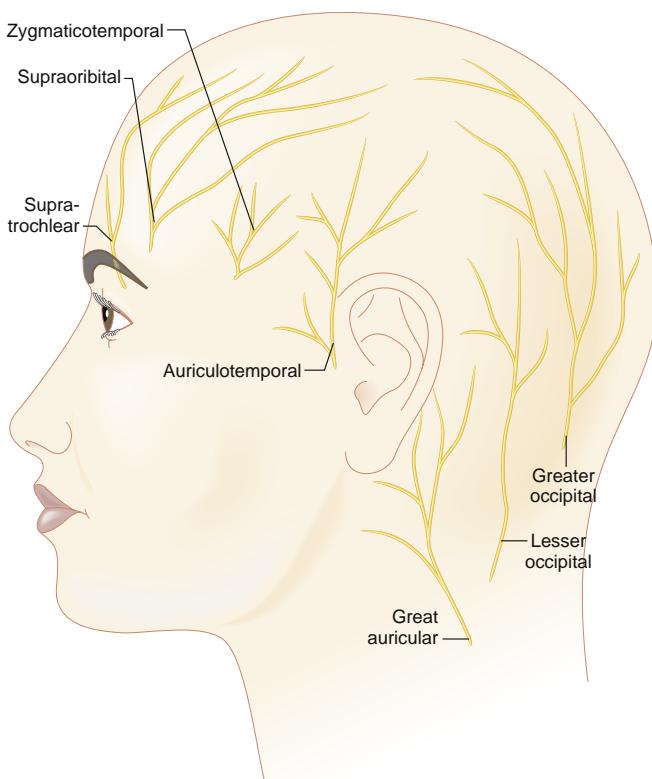


Fig. 57.19 The cutaneous nerves of the scalp.

relevant in the presence of pin fixation, which severely restricts the anesthesiologist's capacity to intervene quickly in the event of excessive respiratory depression or loss of patency of the airway. Propofol should be discontinued at least 15 minutes before EEG recording. Despite prompt awakening, propofol leaves a residual EEG footprint characterized by high-frequency, high-amplitude β activity that can obscure the abnormal activity that is being sought in the cortical surface EEG.³⁴⁸ The use of dexmedetomidine, which in addition to sedation and anxiolysis provides some analgesia with minimal respiratory depression, is increasing.³⁵²⁻³⁵⁶ Satisfactory conditions for functional testing, including brain stimulation for speech mapping and electrocorticography, have been reported with dexmedetomidine infusions ongoing at rates between 0.1 and 0.5 µg/kg/h during the testing.^{352,354,357,358} The occurrence of delays in achieving satisfactory patient responsiveness has also been reported,^{355,359} and using only relatively modest infusion rates (i.e., 0.1-0.2 µg/kg/h) during neurocognitive testing appears advisable.³⁵⁷ Administration of antiemetics (ondansetron or dexamethasone, or both) should probably be routine, especially if narcotics are administered.

Various groups have reported the use of the LMA with either spontaneous or controlled ventilation during the craniotomy, with cessation of sedative administration and LMA removal once the brain surface is exposed.^{353-355,357,360,361} It is obvious that many approaches can be effective, but it should be noted, for the most part, that the LMA techniques have been used in patients who were *not* in pin fixation of the head. An asleep-asleep-awake technique using insertion, removal, and replacement of an endotracheal tube has

been reported, but a customized tube that allows installation of local anesthetic in the glottis and trachea was used.³⁶²

Routine, noninvasive monitors are almost always sufficient. Reliable capnography, to provide breath-by-breath confirmation of airway patency and respiratory drive, is essential if deep sedation is intended for any portion of the procedure. These procedures are often lengthy. Attention to the details of patient comfort (temperature management, padding of pressure areas) improve patient tolerance.

The uncomfortable phases of the procedure are pin head holder placement (not all groups use a pin head holder) and the craniotomy. Many patients also find manipulation of the dura, in particular, traction on subtemporal dura, painful. The actual manipulation of supratentorial brain parenchyma is painless. The volume of local anesthetic used to infiltrate pin sites and perform the scalp nerve blocks can be substantial. It is appropriate for the anesthesiologist to keep track of, and provide advice about, the doses of local anesthetics used.

The anesthesiologist should participate actively at the time of head positioning. The more neck flexion and atlanto-occipital extension that can be achieved before the final lockdown of the head holder, the wider the latitudes will be for sedating the patient, while maintaining spontaneous ventilation and a patent airway. During positioning of the patient, there should also be attention to the need to maintain visual access to the face. A clear line of sight to the face is necessary to present the patient with images to name as part of speech testing and to identify the occurrence of facial motor responses during mapping of the motor strip.

In general, after the dural opening is complete, for seizure-related resections, cortical surface EEG recording is performed to locate the seizure focus. If no seizure activity is observed, provocative maneuvers may be requested.³⁶³ Methohexitol in a dose of approximately 0.3 mg/kg is generally safe and effective. Etomidate, approximately 0.05 to 0.1 mg/kg, has also been used. Localization of seizure focus can also be accomplished during light GA (e.g., N₂O /fentanyl/ low-dose isoflurane). During GA, alfentanil, in a bolus dose of 30 to 50 µg/kg^{364,365}; etomidate in doses of 0.2 to 0.3 mg/kg^{366,367}; and remifentanil, as a bolus of 2.5 µg/kg³⁶⁸ have been reported to be effective in activating seizure foci. Hyperventilation may also help activate seizure foci.³⁶⁹

After localization by EEG (or initially in nonseizure-related resections), functional testing is performed by electrical stimulation of the cortical surface with observation for motor, sensory, or speech interruption effects. During cortical stimulation, the anesthesiologist should be prepared to treat grand mal convulsions. Seizures usually stop with cessation of stimulus or with irrigation of the cortex with cold saline. When they are not self-limited, pharmacologic intervention (e.g., with propofol in increments of 0.5-1.0 mg/kg) may be warranted. However, propofol should be withheld briefly until it is clear that the seizure is not going to terminate spontaneously because it may interfere with subsequent EEG localization for some time.³⁴⁸

STEREOTACTIC PROCEDURES

Stereotactically guided procedures are performed for numerous indications including biopsy of small, deep-seated lesions and placement of deep brain stimulation electrodes.

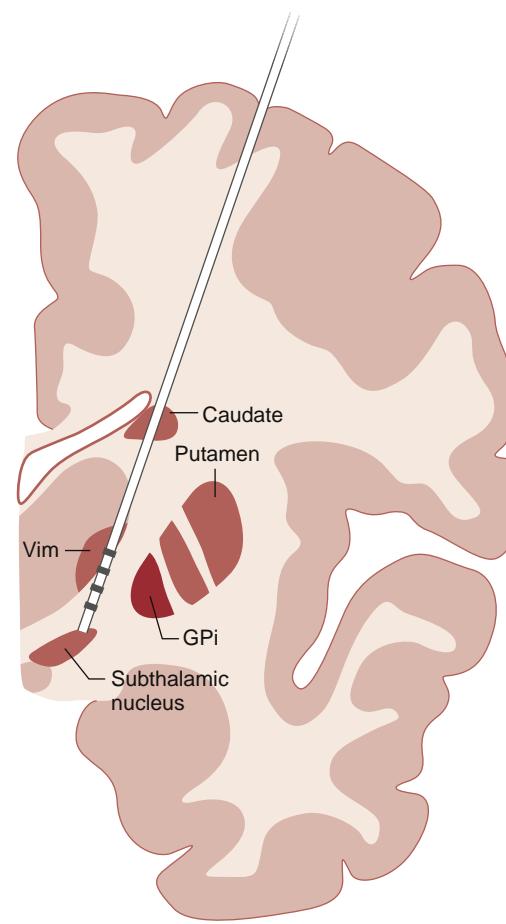


Fig. 57.20 Deep-brain stimulation electrode target sites. The most commonly targeted nuclei for the treatment of movement disorders are the subthalamic nucleus, the ventral intermediate nucleus of thalamus (Vim), and the internal segment of globus pallidus (GPi).

The latter are placed most commonly for the treatment of movement disorders (Parkinson disease, essential tremor, and dystonias)³⁷⁰ and sometimes for a variety of other conditions (Tourette disorder, obsessive-compulsive disorder, and depression). Procedures related to movement disorders most often target the subthalamic nucleus, the internal segment of the globus pallidus, or the ventral intermediate nucleus of the thalamus (Fig. 57.20).³⁷⁰ The mechanism of the beneficial effect of deep brain stimulation is not well understood. A prominent theory is that the abnormal motor patterns are caused by synchronized oscillations in neural circuits involving several basal ganglia nuclei, as well as the cortex, and that high-frequency stimulation of any of several points along the pathway can interfere with the oscillation.³⁷¹

Preoperative evaluation should include ensuring that the coagulation system is intact and that the patient is not taking platelet-inhibiting agents (including herbal medications). There should be careful explanation of the procedure, its likely duration, and the necessary restraints on patient movement.

Several constraints will confront the anesthesiologist including:

1. **Airway access.** Commonly, the stereotactic frame, of which there are many variations, is placed using local anesthetic and the patient undergoes an imaging study

before being brought to the operating room. In some instances, the frame will prevent mask application and ventilation, laryngoscopy, and neck extension. If a general anesthetic is to be used, an awake intubation occasionally may be required. The frame is often anchored to the operating room table. If sedation is to be used, the anesthesiologist should have certain knowledge of how to remove the device rapidly in an urgent situation (including knowledge of the whereabouts of the requisite key or spanner device).

2. *The effect of anesthetics on microelectrode recordings and symptoms.* Localization of deep brain stimulation electrodes typically involves the combination of stereotaxis with fine tuning by identification of the electrophysiologic footprint specific to the targeted nucleus (e.g., the subthalamic nucleus, globus pallidus interna). The sedative agents used must not interfere with that signature. The nature and duration of the effects of anesthetics (which probably vary from nucleus to nucleus) have not been systematically defined. Some surgeons and electrophysiologists may request, on a just-in-case basis, that no sedative agent whatsoever be given. That is likely to be unnecessarily restrictive. Comprehensive reviews are available.³⁷²⁻³⁷⁴ In short, benzodiazepines probably have the greatest potential to interfere and are best avoided. Propofol has been reported to cause severe dyskinesia in patients with movement disorders,³⁷⁵ but has nonetheless been used quite frequently. At a minimum, a substantial interval between propofol administration and recording should be planned. Dexmedetomidine in low doses has been used quite widely without reports of interference with signals.³⁷⁶ Remifentanil, in part because of its rapid clearance, is probably also a reasonable choice, although it too has been reported to suppress Parkinsonian tremor.³⁷⁷ The cessation of the patient's symptoms upon stimulation, without the occurrence of unacceptable side effects, is also an important end point for determining the adequacy of deep brain stimulation position and stimulus parameters. The symptoms must not be suppressed by the sedative agents. This can occur with propofol.³⁷⁸ Satisfactory electrophysiologic recordings and preservation of the tremor have been reported in Parkinsonian patients who received dexmedetomidine in a dose sufficient to maintain a lethargic response to normal speech.^{352,376,379} An additional issue that arises in some patients with movement disorders is the problem of obtaining high-quality radiologic images in the presence of a persistent tremor. Sedation immediately preceding the stereotactic placement may be inevitable. Propofol has been used, but the window between propofol administration and subsequent recording should be as long as possible.
3. *Intracerebral hematoma and prevention of hypertension.* Intracerebral hematoma is a serious, potential intraoperative complication of stereotactic procedures. Prevention and prompt treatment of hypertension are among the anesthesiologist's important objectives. The concern is that, in the face of multiple needle passes through the brain, hypertension will precipitate development of an intracerebral hematoma. In the event of a substantial hematoma, an urgent craniotomy may be required, and the anesthesiologist should be prepared from the outset for this eventuality.

As noted in the section VAE, because of spontaneous ventilation, there is some hazard of VAE during deep brain stimulation placement.⁹⁵

NEUROENDOSCOPIC PROCEDURES

Excision of some intraventricular lesions (e.g., colloid cysts, fenestration of the lamina terminalis or the floor of the third ventricle for treatment of hydrocephalus) can be accomplished endoscopically. Access is usually achieved through burr holes placed over the frontal or occipital horns of the lateral ventricle. The important anesthetic consideration relates to the irrigation fluid (which should be warmed) used to maintain clear visualization, in a manner analogous to orthopedic arthroscopy procedures. Obstruction to the effluent limb produces rapid increases in ICP that are commonly associated with sudden changes in vital signs. An increase in blood pressure and decrease in heart rate (a Cushing-type response) is classic, but the heart rate component is less reliable. Cardiovascular changes may also, but less predictably, represent mechanical irritation of intracranial (e.g., hypothalamic) structures. The surgeon should be notified immediately of any sudden hemodynamic changes. The decision of whether intraarterial monitoring is warranted should be made with the surgeon.

NEUROINTERVENTIONAL PROCEDURES

A wide variety of interventional procedures are performed for the evaluation and treatment of intracranial and extracranial disease. These include: stent-assisted revascularization for atherosclerotic disease; thrombectomy in the setting of acute thromboembolic disease; aneurysm, AVM, tumor, and arteriovenous fistula embolization; and treatment of cerebral vasospasm.³⁸⁰

Much of the management of neurointerventional anesthesia has been discussed previously in the section Recurrent Issues in Neuroanesthesia. Critical components of interventional neuroanesthesia include patient immobility, rapid anesthetic emergence to facilitate neurologic examination, strict hemodynamic manipulation to prevent hyperperfusion and hypoperfusion, and thoughtful PaCO₂ management. Additionally, the anesthesiologist may need to manage (and potentially reverse) anticoagulation. Inherent to neurointerventional procedures is a requisite knowledge of vascular anatomy and appreciation of the underlying pathology. Close communication with the interventionalist throughout the procedure is paramount. Cerebral vascular anatomy, including anatomic vascular distribution is reviewed in Fig. 57.21.

ANESTHETIC TECHNIQUE

GA is widely employed for a variety of reasons: (1) to ensure the immobility that is essential to the technical elements of the procedure; (2) to ensure patient comfort during particularly stimulating procedures; or (3) to control medical comorbidities or neurologic condition of the patient. Protection of the airway and control of ventilation (PaCO₂ manipulation, apnea) may also factor into a decision to employ GA. The potential disadvantages of GA include hemodynamic instability during intubation, extubation, or both;

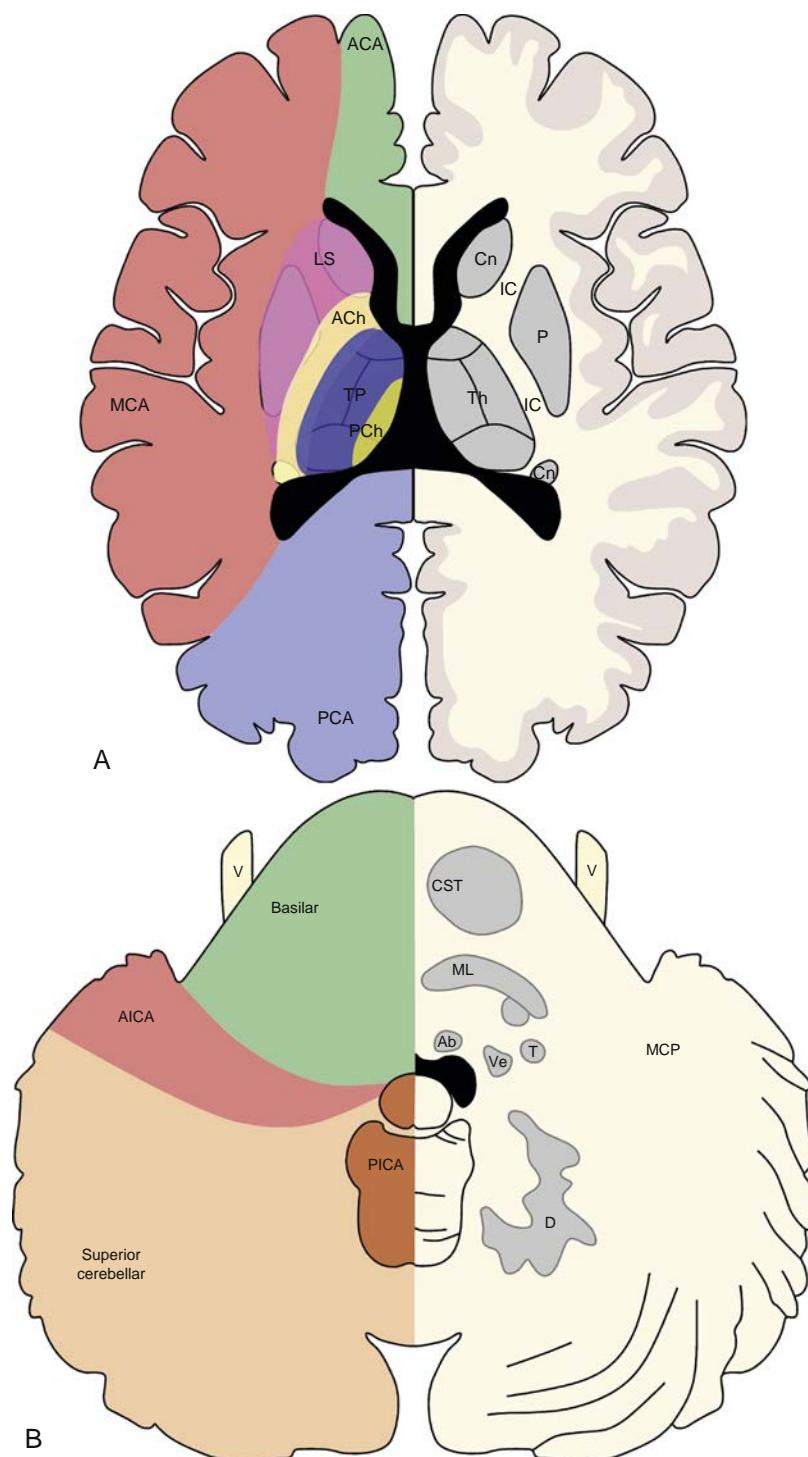


Fig. 57.21 Anatomic cerebral vascular distribution. *Ab*, Abducens nucleus; *ACA*, anterior cerebral artery; *ACh*, anterior choroidal artery; *AICA*, anterior inferior cerebellar artery; *CST*, corticospinal tract; *Cn*, caudate nucleus; *D*, dentate nucleus; *IC*, internal capsule; *LS*, lenticulostriate arteries; *MCA*, middle cerebral artery; *MCP*, middle cerebral peduncle; *ML*, medial lemniscus; *P*, putamen; *PCA*, posterior cerebral artery; *PCh*, posterior choroidal artery; *PICA*, posterior inferior cerebellar artery; *T*, trigeminal nucleus; *Th*, thalamus; *TP*, thalamic perforators; *V*, trigeminal nerve; *Ve*, vestibular nucleus.

anesthetic-induced hypotension causing cerebral hypoperfusion; inability to directly monitor the patient's neurologic status; complications related to coughing and straining during extubation; and delayed emergence or impaired postprocedure neurologic exam due to residual anesthetic drugs.

If GA is employed, there is little evidence to favor specific anesthetic agents over others provided basic neuroanesthetic goals are achieved (strict hemodynamic control,

rapid emergence with minimal residual anesthetic effect on neurologic exam, and smooth emergence/extubation). Some advocate the avoidance of N_2O due to the potential of air bubble introduction into the arterial system during the procedure. Although N_2O could expand such bubbles and potentially increase ischemic risk, local experience of the authors suggests that N_2O is safe provided the interventional technique is meticulous.

MAC with intravenous sedative drugs has been advocated in the interventional radiology suite for various reasons (i.e., better maintenance of CPP, avoidance of hemodynamic lability at induction/emergence, preservation of neurologic exam, expedience). Although these reasons make intuitive sense, it remains unclear whether the anesthetic type truly provides a clear advantage in many of these areas.

ACUTE THROMBECTOMY

The frequency with which anesthesia personnel are enlisted to participate in the care of acute stroke patients having emergent thrombectomy is likely to increase because of the publication of recent studies demonstrating outcome improvement in select patients who undergo thrombectomy as long as 24 hours after the onset of stroke symptoms.^{381,382} There has been some debate in recent years regarding the best anesthetic type (GA vs. MAC) for this procedure. Many retrospective studies found an association between GA and worse neurologic outcome following acute thrombectomy procedures.³⁸³ Inherent in these studies was an obvious selection bias; airway control is generally sought for patients who have significant neurologic deficits and altered level of consciousness that precludes patient cooperation. Subsequent RCTs^{384,385} and a recent meta-analysis³⁸⁶ did not demonstrate an outcome benefit of MAC in this patient population. Although MAC has the potential to hasten vascular access time (imaging to groin puncture time),³⁸³ recent studies have failed to demonstrate an advantage in time to revascularization.³⁸³⁻³⁸⁵ Presumably this is because the small time delay attributed to endotracheal intubation was offset by reduced patient mobility and improved operative conditions. It should be noted that both MAC and GA can cause significant reduction in blood pressure and thereby increase risk of infarct to the ischemic penumbra; however, close attention to, and aggressive treatment of, hypotension by the anesthesiologist appears to negate the potential increased risk of GA-induced hypotension. In select patients (cooperative), MAC may allow for neurologic examination throughout the procedure, which may also serve to provide a therapeutic endpoint during thrombectomy procedures. At the present time, there is insufficient evidence to routinely recommend one anesthetic technique over another. Rather, the technique employed should be based upon a rapid clinical assessment of the patient, comfort level of the anesthesiologist with various techniques, and local practice. When GA is selected, attention must be given to avoid undue delay in endovascular treatment and to the maintenance of cerebral perfusion near awake levels. It is probably also reasonable to maintain normocapnia and to avoid profound hyperoxia.

Tumors and Arteriovenous Malformations

Hyperventilation may be appropriate in an attempt to divert flow away from normal brain and toward a lesion that is intended to receive the occlusive device or material. When the interventionalist is attempting to place glue in high-flow lesions (e.g., AVMs, fistulas), the anesthesiologist may be asked to reduce systemic blood pressure to prevent glue passage into the draining veins or systemic venous

system. The choice of hypotensive agent depends on the anesthesiologist's experience and systemic cardiovascular considerations. Adenosine, which produces temporary flow cessation, is almost certainly the most effective means of accomplishing this objective.³⁸⁷

Intracranial Aneurysms

The International Subarachnoid Aneurysm Trial and subsequent meta-analysis have confirmed the broad applicability of endovascular treatment of aneurysms,^{388,389} and the majority of aneurysms are currently managed by those approaches. Nonetheless, a substantial number of patients continue to undergo operative clipping,³⁹⁰ primarily those with wide-necked aneurysms, diseased or occluded proximal vessels, and otherwise complex anatomy.

Many aneurysm-related procedures, in particular those involving the treatment of vasospasm by selective intraarterial administration of vasodilators (papaverine, calcium-channel blockers) or more commonly by balloon dilatation, can be accomplished without the involvement of an anesthesiologist. The duration of a procedure, individual patient factors, and sometimes the necessity for precise physiologic control may result in requests for MAC or GA. Absolute immobility is commonly needed by the interventionalist and is often the basis for a request for GA. In addition, anesthesiologists may become involved during the resuscitation stage in the event of vascular rupture or of the migration of an intravascular device to an incorrect location. In the event of rupture, the interventionist may request blood pressure reduction while the coil packing of the aneurysm is completed hastily. In addition, immediate reversal of heparinization is required. When detachable devices, such as coils and balloons (the latter now used infrequently), are misplaced and ischemia ensues, fluid loading and pressor administration may be requested to improve collateral CBF while the device is retrieved. A dedicated arterial line is usually warranted. This may or may not be available via a port in the interventionist's vascular access sheath. When these complications do occur, close communication with the interventionalist is essential to ensure appropriate response from the anesthesia team.

Stent-Assisted Revascularization or Stent-Assisted Aneurysm Coil Embolization

Endovascular stent placement typically requires preparation with dual antiplatelet therapy for 5 to 7 days. Aspirin and clopidogrel inhibition assays may be performed on the day of the procedure to confirm patient compliance and physiologic drug response.³⁹¹ Efficacious dual antiplatelet preparation to prevent early in-stent thrombosis may be particularly critical with the use of flow diverting stents (e.g., pipeline embolization device) that possess a larger total metal surface area. Carotid artery stent (CAS) placement may be performed as an alternative to CEA, particularly if the vascular anatomy is unfavorable for CEA or significant concern for coronary artery disease exists. Hypotension and/or bradycardia should be anticipated at the time of stent deployment³⁹² and temporary vasopressor support and/or pharmacologic treatment of bradycardia may be required.

CEREBROSPINAL FLUID SHUNTING PROCEDURES

CSF shunts are inserted for the relief of a variety of hydrocephalic states and pseudotumor cerebri. Hydrocephalus can be communicating or noncommunicating. In a noncommunicating hydrocephalus, CSF egress from the ventricular system is obstructed. This can occur as a result of blood or infection in the ventricular system or tumors in or adjacent to the ventricular system. In communicating hydrocephalus, the CSF escapes from the ventricular system but is not absorbed by the arachnoid villi. This occurs most commonly secondary to infection or blood in the CSF space. Some degree of communicating hydrocephalus is particularly common after SAH.

Placement of a ventriculoperitoneal shunt is the most common procedure. Usually a catheter is inserted via a burr hole into the frontal horn of the lateral ventricle on the nondominant (usually the right) side. A reservoir is placed subcutaneously adjacent to the burr hole and the drainage limb passes via a subcutaneous tunnel to a point near the epigastrium, where it is inserted into the peritoneal space via a very small laparotomy. A moderate degree of muscle relaxation may be helpful. A distended stomach can result in an inadvertent gastrostomy. Sometimes, most commonly in pediatric patients, there may be an obstruction at more than one level in the ventricular system and a so-called double-barreled shunt becomes appropriate. In this instance, there are two proximal ends, usually one in a lateral ventricle and one in the fourth ventricle. This latter procedure is usually performed in the prone position, whereas the majority of ventriculoperitoneal shunts are done supine.

Occasionally, when there is a communicating hydrocephalus, a lumboperitoneal shunt is inserted. The patient is placed in a lateral position and a catheter is put in the lumbar CSF space via a Tuohy-type needle. The catheter is tunneled subcutaneously around to the anterior abdominal wall and inserted into the peritoneal space via a small laparotomy.

Anesthetic Management

Invasive monitoring is generally not required. The anesthetic technique should be chosen to avoid further increases in ICP. Moderate hyperventilation (PaCO_2 25-30 mm Hg) is customary. Because these procedures are not performed in the context of acute injury states, there is less concern about adverse effects of hypocapnia. The target PaCO_2 should be agreed upon at the outset with the surgeon. The procedure is usually performed in the supine position. Blood pressure may decrease abruptly when the ventricle is first cannulated (as brainstem pressure is relieved). Infrequently, brief pressor support is required. Burrowing the subcutaneous tunnel can produce a sudden painful stimulus. There is only minor postoperative discomfort. Unlike the majority of neurosurgical patients, shunt patients are often nursed flat after their procedures in an attempt to prevent an excessively rapid collapse of the ventricular system. Empirically, there is a small incidence of subdural hematoma after shunting, and the tearing of bridging veins at the time of rapid brain shrinkage is a suspected cause.

Pediatric Ventriculoperitoneal Shunts

Shunts are probably more commonly performed in children than in adults. Common indications are hydrocephalus occurring in association with meningocele, neonatal intraventricular hemorrhage, and posterior fossa tumors. Although one can never be casual about the management of these patients, open fontanelles seem to provide some margin for error in younger patients and, in addition, palpation of the fontanelles provides on-line trend monitoring of ICP. Despite its theoretic considerations, inhaled inductions using volatile anesthetics are empirically well tolerated, even in children with closed fontanelles. We avoid the inhaled induction technique in a child who was already stuporous. When an intravenous line is available, a propofol-relaxant induction sequence is preferable. For children in whom cannulation of a peripheral vein cannot be accomplished readily, an inhaled induction with sevoflurane is a common approach, with initiation of controlled ventilation, by bag and mask, as rapidly as possible. After establishing controlled ventilation, an ideal course at this point is to establish an intravenous line and administer a muscle relaxant and perhaps an induction agent, and then intubate the trachea in these optimal circumstances. For children older than 6 months of age who are not stuporous at the outset, we commonly titrate in fentanyl in the belief that this procedure is not entirely pain-free postoperatively, and that a smoother emergence can be accomplished with a narcotic background.

PEDIATRIC NEUROSURGERY

Table 57.6 identifies common pediatric procedures and their anesthetic considerations. The most frequent procedures are probably the placement and revision of CSF shunts (discussed in the preceding section). The majority of pediatric tumors occur in the posterior fossa. Most are near the midline and many are associated with hydrocephalus. For pediatric posterior fossa procedures, VAE risk, monitoring, and treatment are similar for adults and children and have been previously discussed. A Doppler probe and right heart catheters are frequently placed when procedures are done in the sitting position. Craniosynostosis procedures have the potential for substantial blood loss that is roughly proportional to the number of sutures involved. There is a significant VAE risk that justifies the use of a precordial Doppler.⁹³ Children with neuraxial tumors can present for emergent palliative radiotherapy and may have acutely increased ICP or impending herniation. Intractable pain combined with analgesic tolerance, steroid use causing centripetal obesity, and the side effects of other chemotherapeutic agents may be complicating factors.

SPINAL SURGERY

Table 57.7 summarizes the many issues that may arise in the context of spinal cord or spinal column procedures undertaken by neurosurgeons.

Surgery on the spinal column is reviewed in detail in Chapter 66. The relevant electrophysiologic monitoring techniques are described in **Chapter 39**. Prone positioning has previously been discussed.

TABLE 57.6 Pediatric Neurosurgical Disorders and Their Anesthetic Considerations

Age Group	Lesion	Pathogenesis	Anesthetic Considerations
Neonates	Intraventricular hemorrhage	Subependymal vascular rupture	Associated problems of prematurity
	Depressed skull fracture	Forceps injury	Associated cerebral edema
	Meningocele	Out-pouching of meninges through skull defect	Large size creates airway management difficulty
			Prone or lateral position Repair may increase ICP Variable blood loss
	Encephalocele	Out-pouching of meninges and brain through skull	As above
	Meningomyelocele	Protrusion of meninges and nerve roots through spina bifida	Prone or lateral position Respiratory restriction after covering large defects
Infants	Hydrocephalus	Varied	Increased ICP
	Arnold-Chiari malformation	Posterior fossa contents compressed in foramen magnum	Brainstem compression with neck flexion ± Hydrocephalus/Increased ICP; ± Meningomyelocele; Postoperative respiratory depression
	Craniosynostosis	Premature fusion of cranial sutures	Open or endoscopic procedure Substantial blood loss Air embolism Supine or prone
	Craniofacial dysostosis	Developmental abnormality	Lengthy procedures Substantial blood loss Brain retraction Air embolism Endotracheal tube damage
	Vascular malformations	Varied	Congestive heart failure Large blood loss Induced hypotension
	Subdural hematoma	Trauma	Associated injuries
Older pediatrics	Posterior fossa tumors	Ependymoma	Hydrocephalus
		Astrocytoma	Increased ICP
		Medulloblastoma	Prone or sitting position
		Teratoma	Air embolism
		Brainstem glioma	Brainstem compression Postoperative cranial nerve dysfunction or brainstem swelling or compression

ICP, Intracranial pressure.

The physiology of the spinal cord is, in general, similar to that of the brain: CO₂ responsiveness, BBB, autoregulation, high metabolic rate and blood flow (though somewhat less than the brain), and substantial ischemic vulnerability of gray matter. However, measures to reduce spinal cord swelling, analogous to ICP reduction maneuvers, are rarely used. The anesthesiologist should be attentive to situations in which there is significant compression of the spinal cord. This arises most often in the setting of cervical spinal stenosis and should be assumed to be present with fracture dislocation of the spinal column. For these patients, we place arterial catheters and support blood pressure carefully. We believe that in these settings, and in patients with recent spinal cord injury (<7 days), blood pressure should be maintained at a MAP of 85 to 90 mm Hg or waking

baseline level, whichever is higher. Blood pressure support is less important when the issue is nerve root rather than spinal cord compression. The presence of spinal stenosis and chronic cord compression is frequently, but not invariably, associated with lower extremity hyperreflexia and ankle clonus. Awake intubation may be warranted when there is instability of the cervical spinal column and in some instances of severe cervical spinal stenosis in which it is perceived that minor degrees of flexion or extension, or both, might critically aggravate spinal cord compression. Preintubation discussion and agreement with the surgeon is appropriate.



Complete references available online at expertconsult.com.

TABLE 57.7 Anesthetic Considerations and Position Requirements Associated With Various Spinal Surgical Procedures

Spinal Segment and Surgical Condition	Problems and Considerations	Positions Used and Comments
Cervical region: Spinal stenosis, trauma, rheumatoid arthritis, degenerative disk disease	Maintain neutral neck position to avoid cord compression	Supine/anterior approach for most discectomies Posterior approach (prone or sitting) for laminectomy and pedicle screws
	Maintain perfusion pressure near waking normal levels	If existing cord compression, recent cord injury, or if cord retraction is required
	Hypotension (spinal shock)	Occurs with complete cervical cord injury
	Postoperative respiratory insufficiency	Occurs with cervical cord injury
Anterior cervical discectomy	Air embolism	With sitting laminectomies
	Retractor compression of airway Postoperative swelling/airway compression Postoperative cranial nerve dysfunction	Supine Traction may be required for graft insertion endotracheal tube cuff deflation/reinflation after retractor placement
	Awake intubation Awake positioning Manual in-line stabilization for intubation (if awake intubation is not feasible)	Prone or supine
Thoracolumbar region: degenerative disease, spinal stenosis, trauma	Major position change Awake intubation and position	Prone, lateral, or knee-chest If unstable, post trauma and/or major position change required
	Blood loss	Especially with redos, instrumentations, and spinal stenosis; risk of occult aorto- iliac or major venous injury
	Air embolism Postoperative vision loss	Infrequent Etiology unclear; associated with long prone procedures, low hematocrit, large estimated blood loss, and hypotension; patient variables may contribute (see <i>Chapter 34</i>)
	Large blood loss	Prone or anterolateral/retroperitoneal Lung separation for lesions above L1
Vertebral metastasis		
Spinal cord tumors	Maintain perfusion pressure during retraction	Prone
Procedures with major neurologic risk	Wake-up test (now rare)	Rehearse with patient
	Somatosensory evoked responses	Anesthetic agent restrictions
	Motor evoked responses	Anesthetic/relaxant restrictions
	Pedicle screw electromyogram	Relaxant restriction

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GAURAV MALHOTRA and DAVID M. ECKMANN

KEY POINTS

- In the United States more than two out of three people are overweight or obese. Worldwide, more people are obese than are malnourished. Obesity is becoming the largest single preventable cause of death and represents major morbidity and mortality.
- Metabolic syndrome includes abdominal obesity, decreased high-density lipoprotein, insulin resistance, glucose intolerance, and hypertension, and is present in approximately 34% of the adult population in the United States alone.
- The single greatest risk factor for sleep apnea is obesity, with the majority of obese patients having increased oral and pharyngeal tissue. This makes ventilation, intubation, and extubation more challenging.
- Choices for medical management of obesity are limited and efficacious achievement with just medical management is uncommon. Changes in behaviors are important for success.
- Surgery for obesity is recommended at a body mass index (BMI) of 40 kg/m² or BMI over 30 kg/m² with comorbidities expected to respond to weight loss, secondary to surgical therapy, like hypertension, diabetes, and hypercholesterolemia. In clinical trials, long-term survival is better in the surgically treated group over the medically managed.
- Preoperative evaluation should focus on cardiopulmonary issues and securing an airway, along with other concerns such as diabetes, hypertension, and obstructive sleep apnea.
- Anesthetic drugs should be tailored based on lipid solubility and awareness of lingering respiratory depression effects.
- Patient preparation and positioning are keys to successful airway management. Preoperative pressure support ventilation should be used adjunctively if possible.
- Intraoperative ventilation is assisted by complete paralysis, moderate positive end-expiratory pressure, tidal volumes based on ideal body weight, and recruitment maneuvers as needed.
- Common serious postoperative complications are deep vein thrombosis and staple line issues.
- Obese patients presenting for nonweight-loss surgery benefit from anesthetic approaches similar to that used for bariatric surgery.

Obesity as a Disease

Obesity is firmly established as one of the great epidemics of the 21st century.¹ Worldwide, obesity was considered a rarity until the middle of the previous century,² but now there are 1.9 billion overweight adults and over 650 million obese people globally including a significant proportion of the adult population in the United States.³⁻⁵ Obesity is a problem that is affecting the younger population as well since over 340 million children and adolescents aged 5 to 19 were overweight or obese in 2016.⁶ Current estimates are that more than 2 out of 3 of the U.S. adult population are overweight or obese. Of these one in three adults has obesity and 1 in 13 has extreme obesity with a body mass index (BMI) greater than 40.⁷ Among children and adolescents ages 2 to 19, about 1 in 6 are obese, and about 1 in 17 are considered to have extreme obesity.⁸ Obesity and its associated health concerns are now major causes of morbidity and mortality resulting in an enormous impact on healthcare spending. Over 300,000 deaths per annum in the United States and about \$270 billion⁶ in annual

healthcare spending are attributable to obesity, placing it second only to smoking as a preventable cause of death.⁹

Obesity can be defined as a disease since it is a physiologic dysfunction of the human organism with environmental, genetic, and endocrinologic etiologies.⁹ Obesity most frequently develops when food caloric intake exceeds energy expenditure over a sustained period of time. Factors influencing obesity involve either energy intake or energy expenditure, and are influenced by genetic, behavioral, cultural, and socioeconomic factors.¹⁰ For example, there are syndromes that are associated with obesity, including leptin deficiency, Prader-Willi syndrome, and Lawrence-Moon-Biedl syndrome.⁴ Metabolic factors can influence energy regulation, including hormones, peptides, nutrients, uncoupling proteins, and neural regulatory substances emanating from gut, liver, brain, and fat cells, but most of these are not well understood.

The BMI is the most widely applied classification tool used to assess individual weight status.¹¹ The BMI is specifically defined as the patient's weight, measured in kilograms, divided by the square of the patient's height, measured

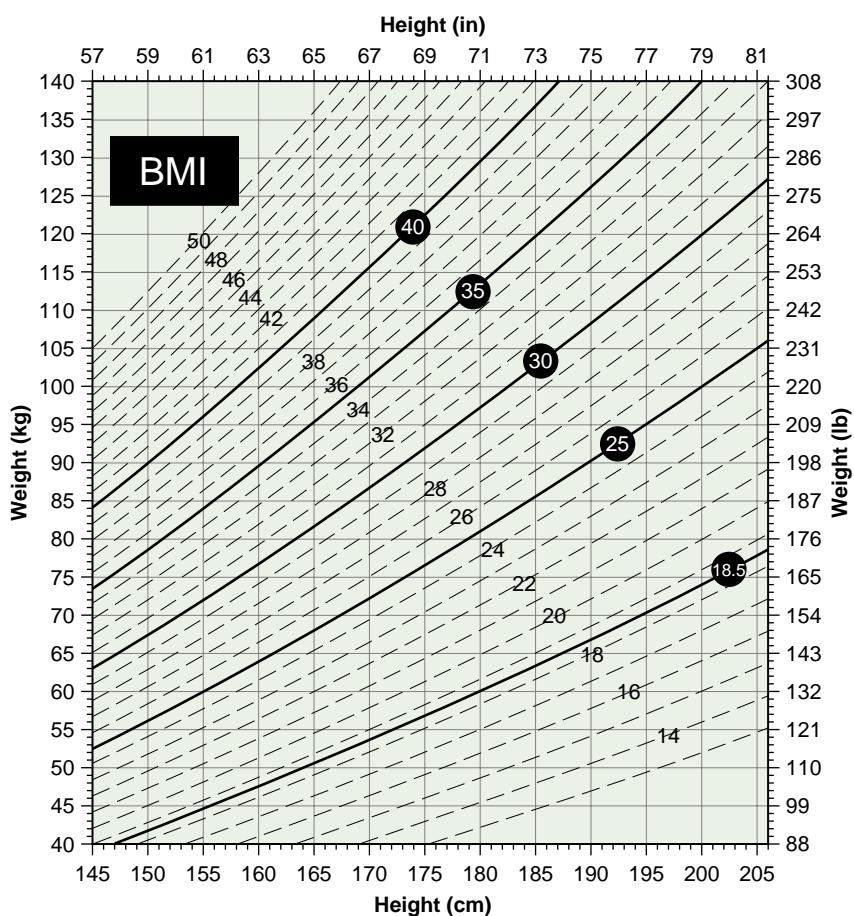


Fig. 58.1 A family of iso-body mass index (BMI) curves for BMI ranging from 13 to 50 and mapped on axes for height (in both centimeters and inches) and weight (in both kilograms and pounds).

in meters, yielding a measurement bearing units of kilograms per square meter (kg/m^2). Fig. 58.1 shows a family of iso-BMI curves for BMI ranging from 13 to 50 kg/m^2 and mapped on axes for height (in both inches and centimeters) and weight (in both pounds and kilograms). Most electronic medical record systems are programmed to indicate patient BMI when height and weight inputs are provided. The National Institutes of Health maintains an online BMI calculator and also provides links for downloadable smartphone BMI applications at https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm. Using this system, patients are classified according to BMI and the associated risk of developing health problems is shown in Table 58.1. Patients are considered to be overweight if they have a BMI between 25 and 29.9 kg/m^2 , and they are classified as obese with a BMI between 30 and 49.9 kg/m^2 . The obese classification is further subdivided into Class 1 (BMI range 30-34.9 kg/m^2), Class 2 (35-39.9 kg/m^2) and Class 3 (40-49.9 kg/m^2). Patients with a BMI of 50 kg/m^2 or greater are classified as superobese. As BMI increases beyond normal weight, the risk of developing serious health problems rises greatly and can be correlated with the individual's waist circumference (Table 58.2). Malnourishment and malnutrition are commonly offered as explanations for the fact that underweight patients are also at increased risk for developing illnesses.

TABLE 58.1 Levels of Risk Associated With Increasing Body Mass Index

Classification	BMI (kg/m^2)	Risk of Developing Health Problems
Underweight	<18.5	Increased
Normal weight	18.5-24.9	Least
Overweight	25.0-29.9	Increased
Obese		
Class 1	30.0-34.9	High
Class 2	35.0-39.9	Very high
Class 3	40.0-49.9	Extremely high
Superobese	≥50	Exceedingly high

BMI, Body mass index.

There are specific diseases commonly associated with obesity, and obesity is often accompanied by multiple, and not single, comorbid states.⁷ These frequently include insulin resistance, type 2 diabetes mellitus, obstructive sleep apnea (OSA), asthma, chronic obstructive pulmonary disease, hypoventilation, cardiovascular disease, hypertension, certain malignancies, and osteoarthritis.^{1,12-22} Virtually every

TABLE 58.2 Waist Circumference and Risk

Waist		BMI (KG/M ²)	
Circumference	Normal Weight	Overweight	Obese Class 1
<102 cm (♂)	Least risk	Increased risk	High risk
<88 cm (♀)			
≥102 cm (♂)	High risk	Very high risk	Increased risk
≥88 cm (♀)			

TABLE 58.3 Health Risks Associated With Increasing Body Mass Index

Metabolic syndrome	30% of middle-aged people in developed countries have features of metabolic syndrome
Type 2 diabetes	90% of type 2 diabetics have a BMI of >23 kg/m ²
HTN	5x risk in obesity 66% of HTN is linked to excess weight 85% of HTN is associated with a BMI >25 kg/m ²
CAD	3.6x risk of CAD for each unit change in BMI
CAD and stroke	Dyslipidemia progressively develops as BMI increases from 21 kg/m ² with rise in small particle low-density lipoprotein 70% of obese women with HTN have left ventricular hypertrophy Obesity is a contributing factor to cardiac failure in >10% of patients Overweight/obesity plus hypertension is associated with increased risk of ischemic stroke
Respiratory effects (e.g., obstructive sleep apnea)	Neck circumference of >43 cm in men and >40.5 cm in women is associated with obstructive sleep apnea, daytime somnolence, and development of pulmonary hypertension
Cancers	20% of all cancer deaths among nonsmokers are related to obesity (30% of endometrial cancers)
Reproductive function	6% of primary infertility in women is attributable to obesity Impotency and infertility are frequently associated with obesity in men
OA	Frequent association in the elderly with increasing body weight—risk of disability attributable to OA equal to heart disease and greater to any other medical disorder of the elderly
Liver and gall bladder disease	Overweight and obesity associated with nonalcoholic fatty liver disease and NASH. 40% of NASH patients are obese; 20% have dyslipidemia 3x risk of gall bladder disease in women with a BMI of >32 kg/m ² 7x risk if BMI of >45 kg/m ²

BMI, Body mass index; CAD, coronary artery disease; HTN, hypertension; NASH, nonalcoholic steatohepatitis; OA, osteoarthritis;

organ system can be included in the extended list of health risks associated with having an abnormally elevated BMI. A listing of the most common specific disease states along with their obesity-associated risk is detailed in Table 58.3. As a result, obesity is also associated with early death.^{11,23}

BOX 58.1 Features Associated With Metabolic Syndrome

Abdominal obesity
Atherogenic dyslipidemia (↑ TGs, ↓ HDL-C, ↑ ApoB, ↑ small LDL particles)
Elevated blood pressure
Insulin resistance ± glucose intolerance
Proinflammatory state (↑ hsCRP)
Prothrombotic state (↑ PAI-1, ↓ FIB)
Other (endothelial dysfunction, microalbuminuria, polycystic ovary syndrome, hypoandrogenism, non-alcoholic fatty liver disease, hyperuricemia)

ApoB, Apolipoprotein-B; FIB, fibrinogen; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; PAI-1, plasminogen activator inhibitor; TG's, triglycerides.

Of all the health risks included in Table 58.3, metabolic syndrome and OSA merit additional attention as they pose special concerns for the anesthetic care of obese patients.

METABOLIC SYNDROME

The clustering of a group of defined metabolic and physical abnormalities is now referred to as the metabolic syndrome.²⁴ Patients with metabolic syndrome commonly have abdominal obesity, reduced levels of high-density lipoprotein (HDL), hyperinsulinemia, glucose intolerance, hypertension, and other characteristic features¹⁵ as listed in Box 58.1. Specific criteria for diagnosing metabolic syndrome are included in Table 58.4. The diagnosis requires that at least three of the following be present: abdominal obesity, elevated fasting glucose, hypertension, low HDLs, and hypertriglyceridemia.²⁵ Weight gain with visceral obesity is a major predictor of the metabolic syndrome. The clinical approach uses waist circumference, rather than BMI, to define the adipose mass component contributing to the metabolic syndrome since BMI has been shown to be a relatively insensitive indicator of the risk for obesity-associated metabolic and cardiovascular diseases. Waist circumference, but not BMI, reflects abdominal subcutaneous adipose tissue as well as abdominal visceral adipose tissue and is therefore a better index of central, or truncal, fat mass.

In the United States, approximately 34% of the adult population have metabolic syndrome.²⁶ Of these, more than 83% meet the criterion of abdominal obesity. The incidence of metabolic syndrome increases with age, with more than 40% of the U.S. population affected by the age of 60 years.²⁴ Men are affected more commonly than women, and Hispanics and South Asians appear to be particularly susceptible. Its frequency is lower in African American men than in Caucasians. Metabolic syndrome may result from use of some commonly prescribed drugs, including corticosteroid, antidepressant, and antipsychotic agents. Protease inhibitors used to treat human immunodeficiency virus (HIV) infection can induce metabolic syndrome secondary to insulin resistance.

Patients with metabolic syndrome have an increased risk for cardiovascular disease events and are at increased risk for all-cause mortality. Metabolic syndrome increases

TABLE 58.4 Clinical Criteria for Diagnosing Metabolic Syndrome

Central obesity	Waist circumference >102 cm in men Waist circumference >88 cm in women
Plus any two of the following:	
Criteria	Defining Value
Triglycerides	150 mg/dL (1.7 mmol/L), or Specific treatment for this lipid abnormality
High-density lipoprotein cholesterol	<40 mg/dL (1.03 mmol/L) in men, or <50 mg/dL (1.29 mmol/L) in women, or Specific treatment for this lipid abnormality
Blood pressure	Systolic blood pressure >130 mm Hg, or Diastolic blood pressure >85 mm Hg, or Treatment of previously diagnosed hypertension
Fasting glucose	110 mg/dL (5.6 mmol/L), or Previously diagnosed type 2 diabetes

the risk of type 2 diabetes, which itself is an important risk factor for atherosclerotic disease and may be considered as a coronary heart disease equivalent.^{17,24} Metabolic syndrome is also associated with a variety of other conditions, such as polycystic ovary syndrome, nonalcoholic fatty liver disease, gallstones, sleep disturbances, sexual impotence, and numerous forms of cancer including breast, endometrial, pancreatic, colon, and liver cancer, as detailed in Table 58.3.²⁷ In multiple trials involving nearly 1900 patients, morbidly obese individuals had much greater weight loss following bariatric surgery than after nonsurgical therapy, with amelioration of most of the diseases associated with morbid obesity in a year's time.²⁸ Metabolic syndrome is resolved by bariatric surgery in over 95% of patients who achieve the expected weight loss,²⁹ making it clear that bariatric surgery is a metabolic intervention and not simply a weight management procedure.³⁰

Inflammatory processes appear to play an important role in the metabolic syndrome.²⁰ Adipose tissue has two major functions: storage and release of energy-rich fatty acids and secretion of proteins required for endocrine and autocrine regulation of energy metabolism. Adipocytes exert their metabolic effects by release of free fatty acids, whose release is enhanced by the presence of catecholamines, release of glucocorticoids, increased beta-receptor agonist activity, and reduction of lipid storage mediated by insulin. Visceral adipose tissue has been identified as an important source of proinflammatory cytokines such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6), as well as antiinflammatory cytokines such as adiponectin. Increased levels of proinflammatory cytokines likely contribute to the etiology of insulin resistance primarily by obstructing insulin signaling and contributing to downregulation of peroxisomal proliferator-activated receptor- γ , which are fundamentally important regulators of adipocyte differentiation and control. Additionally, insulin resistance may promote inflammation through diminution of insulin's antiinflammatory effects.

Lastly, oxidative stress is increased with obesity, primarily as a result of excessive intake of macronutrients and a concomitant increase in metabolic rate. These factors may also contribute to the inflammatory response noted with obesity.²⁰

Native immune responses act aberrantly in obese individuals. Natural killer (NK) cell cytotoxic activity is depressed with obesity, as are plasma levels of cytokines such as IL-12, IL-18, and interferon- γ known to regulate NK cell function.³¹ Other cytokines (primarily IL-6 and TNF- α) and adipokines (leptin, adiponectin, adipose-derived resistin) are two additional major groups of inflammatory proteins produced and released by adipose and adipose-associated tissue.²⁰ Both serum and adipose tissue obtained from obese subjects consistently have elevated levels of IL-6 and TNF- α , and circulating levels of IL-6 are consistently increased in individuals having either type 2 diabetes or impaired glucose tolerance. Proteins such as leptin and adiponectin, which are produced primarily by adipocytes, are classified as adipokines. Although leptin is primarily involved in appetite control, its immunologic effects include protection of T lymphocytes from apoptosis and regulation of T-cell activation and proliferation. Reduced leptin levels may increase appetite and slow metabolism, but may also increase susceptibility to the toxicity of proinflammatory stimuli, such as endotoxin and TNF- α . Elevated leptin levels are proinflammatory, and this likely plays an important role in the progression of heart disease and diabetes, especially in obese patients. Serum levels of adiponectin correlate with insulin sensitivity and do not rise in obesity. Significantly reduced adiponectin levels are found in patients having type 2 diabetes. Adiponectin reduces both TNF- α production and activity. It also inhibits IL-6 production. Resistin, an adipokine that induces insulin resistance, is induced by endotoxin and cytokines. Resistin acts at the cellular level to upregulate production of proinflammatory cytokines, most likely through the nuclear factor κ B (NF κ B) pathway. Resistin appears to present a molecular link among metabolic signaling, inflammatory processes, and the development of cardiovascular disease. Resistin levels have been associated with inflammatory markers apparently independent of BMI in humans.²⁰

An understanding of the role of NF κ B in insulin resistance is required to fully appreciate the links between obesity and inflammation. Both free fatty acids and TNF- α act via intracellular inflammatory cascade pathways to arrest insulin signaling. This process is mediated by activation of transcription factors present within the cell cytoplasm. Following their translocation to the nucleus, they eventually bind to transcription factors regulating the inflammatory process. The cytoplasm also contains NF κ B, another transcription factor whose activation is implicated in a number of diseases, including diabetes. NF κ B is also induced by hypoxia, and it increases production of proinflammatory cytokines TNF- α and IL-6, both of which are frequently increased in patients with OSA syndrome.²⁰ Therefore inflammation provides the common linkage underlying the association between obesity, metabolic syndrome, and OSA.³²

OBSTRUCTIVE SLEEP APNEA—HYPOPNEA SYNDROME

OSA is a condition characterized by recurrent episodes of partial or complete upper airway collapse occurring during

sleep.³³ An obstructive apneic event is defined universally as the complete cessation of airflow during breathing lasting 10 seconds or longer despite maintenance of neuro-muscular ventilatory effort. The definition of an obstructive hypopneic event however may vary depending on the criteria being used for scoring. The Centers for Medicare and Medicaid Services (CMS) defines a hypopneic event as the partial reduction of airflow of 30% or more lasting at least 10 seconds, accompanied by a decrease of at least 4% in the oxygen saturation (SpO_2) as opposed to the American Academy of Sleep Medicine (AASM), which accepts a 3% drop in SpO_2 or a terminal cortical arousal. Additionally, the AASM recommends scoring a third type of respiratory event in which flow limitation is detected and is associated with a cortical arousal. These events are designated respiratory effort related arousals (RERAs).

The diagnosis of OSA can only be made in patients who undergo polysomnography, or a home sleep study.³³ Results of polysomnography are reported as the apnea-hypopnea index (AHI), which is derived from the total number of apneas and hypopneas divided by the total sleep time or the respiratory disturbance index (RDI) which includes RERA. A normal lower limit for AHI has not yet been defined in an epidemiologic study of healthy subjects. Most sleep centers commonly use an AHI between 5 and 10 events per hour as a normal limit. The severity of obstructive sleep apnea/hypopnea syndrome (OSAHS) is arbitrarily defined, but recommendations for disease classification are as follows³³:

Mild Disease: AHI of 5 to 15 events per hour

Moderate Disease: AHI of 15 to 30 events per hour

Severe Disease: AHI of greater than 30 events per hour

Due to the risks of developing systemic and pulmonary hypertension, left ventricular hypertrophy, cardiac arrhythmias, cognitive impairment, persistent daytime somnolence, and other factors, treatment is recommended for patients with either moderate or severe disease. Treatment partly depends on the severity of the sleep-disordered breathing, but the consensus view is that patients with moderate or severe disease should be treated with continuous positive airway pressure (CPAP) during sleep. Other conservative treatment measures may include weight loss, avoidance of alcohol prior to bedtime, and sleeping on one's side.

Numerous studies have confirmed that obesity is the greatest risk factor for OSAHS, with about 70% of patients (up to 80% of males and up to 50% of females) with OSAHS being obese. Severe sleep apnea disease is more common in men until women reach the age of menopause, and a strong negative correlation between the AHI and minimum SpO_2 has been observed. Importantly, the diagnosis of OSAHS may be missed until the patient presents for surgery. In one study of 170 patients presenting for surgery, only 15% had already been diagnosed with sleep apnea, but on pre-operative testing, 76% were found to have OSAHS.³⁴ A STOP-Bang questionnaire (Box 58.2) can be used to screen patients for OSA, with a score of 5 to 8 identifying patients at risk for moderate to severe disease.³⁵ We believe it is important for obese patients presenting for bariatric surgery to undergo preoperative polysomnography testing for OSAHS. Preoperative diagnosis and appropriate interventional

BOX 58.2 STOP-Bang Questionnaire

1. Snoring: Do you snore loudly (loud enough to be heard through closed doors)?
2. Tired: Do you often feel tired, fatigued, or sleepy during daytime?
3. Observed: Has anyone observed you stop breathing during your sleep?
4. Blood pressure: Do you have or are you being treated for high blood pressure?
5. BMI: BMI more than 35 kg/m^2 ?
6. Age: Age over 50 years old?
7. Neck circumference: Neck circumference $>40 \text{ cm}$?
8. Gender: Male?

High risk of OSA: Yes to ≥ 3 questions.

Low risk of OSA: Yes to < 3 questions.

BMI, Body mass index; OSA, obstructive sleep apnea.

management can have the following benefits: less postoperative sleep deprivation, improved response to analgesic and anesthetic drugs, and normalization of cardiovascular disturbances.³⁶

Anatomically, obese patients with OSAHS typically have increased amounts of adipose tissue deposited into oral and pharyngeal tissues including the uvula, tonsils, tonsillar pillars, tongue, aryepiglottic folds, and lateral pharyngeal walls. An inverse relationship exists between the degree of obesity and pharyngeal area. Deposition of fat in the lateral walls decreases the size of the airway and changes the shape of the oropharynx into an ellipse with a short transverse and long anteroposterior axis.³⁷⁻³⁹ This configuration can contribute to both the development and severity of airway obstruction and can also increase the expectation that it will be more difficult to maintain airway patency during mask ventilation and to perform direct laryngoscopy for endotracheal intubation with general anesthesia.⁴⁰⁻⁴¹ Neuromuscular blockade should be fully reversed prior to extubation, and low tidal volumes or lung protective ventilation should be employed.

Additionally, airway obstruction following extubation is likely to be complicated by the use of opiate and sedative drugs needed for postoperative pain management because these drugs tend to decrease pharyngeal dilator tone and increase the likelihood of upper airway collapse.⁴⁰

OSA also plays an important role in inflammation and the metabolic syndrome.^{20,32} The hypopneic and apneic events that occur in OSAHS are part of the cycle of events that involves both arousal from sleep and oxyhemoglobin desaturation. Sympathetic nervous system activation results as patients with untreated OSA undergo cyclic episodes of hypoxia and reoxygenation. This process leads to elevation of proinflammatory cytokines and may also induce oxidative stress of vascular endothelium, thus inducing an even more heightened state of systemic inflammation in obese patients with OSA.³² Levels of many different inflammatory mediators, including IL-6, high-sensitivity C-reactive protein (hs-CRP), leptin, TNF- α , IL-1, reactive oxygen species, and adhesion molecules, such as intracellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), are increased in patients with OSAHS.²⁰ Thus obesity, the metabolic syndrome, and

OSAHS are interrelated diseases that significantly alter a patient's inflammatory disease profile and increase multiple health risks, particularly those of cardiovascular and airway origin. Importantly, surgical intervention to cause weight loss has been shown not only to improve obesity-related respiratory disease,¹⁴ but it also can lead to significant and sustained increases in plasma adiponectin levels while decreasing both IL-6 and hs-CRP levels⁴² as well as improve NK cell function and increase IL-12, IL-18, and interleukin- γ plasma levels.³¹

Nonsurgical Management of Obesity

The primary goals of nonsurgical management of obesity involve weight loss, the treatment of abnormalities associated with metabolic syndrome, and prevention of type 2 diabetes and cardiovascular disease-related events. Treatment of metabolic syndrome needs to follow an aggressive, multi-faceted approach to address multiple underlying metabolic abnormalities and coexistent risk factors simultaneously.²⁴ An appropriate initial treatment of obesity and metabolic syndrome is therapeutic lifestyle change. This includes dietary modification, weight loss, physical activity, and discontinuation of smoking. The treatment aim is improvement in health, and is the primary reason for advocating weight loss. Modification of energy homeostasis is not easily achieved because a strong brain-gastrointestinal axis drives both food intake and satiety. This axis has hormonal components involving endogenous production of ghrelin, an orexigenic peptide that is produced by the foregut of the stomach and that stimulates appetite.⁴³ Therefore it is important to monitor the effects of treatment on risk factors and comorbidities at the systems, organ, cell, and molecular levels. Treatment success should be reflected in the decreasing need to treat other coexisting diseases.

The goal for weight loss in therapeutic lifestyle change is not the achievement of normal or ideal body weight (IBW). Even a modest weight loss, in the range of 5% to 10% from the presentation weight, can result in significant initial improvement in the comorbidities of diabetes, dyslipidemia, and hypertension by lowering total cholesterol and triglyceride levels, raising HDL-cholesterol, lowering arterial blood pressure, and lowering blood glucose values while reducing insulin resistance.^{24,44} Obesity guidelines stress the need for weight reduction using behavioral change to reduce caloric intake and increase physical activity. A decrease in caloric intake is the most important component in achieving weight loss and increased physical activity is critical in maintaining the lost weight.⁴⁵ Reduced-energy diets are more effective and healthier for achieving long-term weight loss. Long-term maintenance of any weight loss achieved is best accomplished with the inclusion of regular exercise as a staple of the weight-reduction regimen. Regular physical exercise improves several risk factors associated with obesity and metabolic syndrome.⁴⁶ The standard exercise recommendation is a daily minimum of 30 minutes of moderate-intensity physical activity that is practical to perform. Larger weight loss goals are more appropriate for the more profoundly obese individuals who are contemplating surgical interventions. Even with surgery, ideal weight is hardly

ever achieved, and after a number of years at a plateau, weight gain often recurs. In some patients, especially in the presence of severe comorbidities, simple prevention of additional weight gain may be the most reasonable goal.

Beyond the beneficial effects of therapeutic lifestyle change, specific intervention may be required to treat the dyslipidemia and hypertension associated with obesity and metabolic syndrome.⁴⁷ Most commonly, patients with metabolic syndrome have elevated triglyceride levels and low HDL cholesterol levels. Many patients receive statin therapy as the treatment of choice when low-density lipoprotein (LDL) cholesterol levels are excessive. Statins reduce cardiovascular disease risk in patients with type 2 diabetes and metabolic syndrome. Ezetimibe, which selectively inhibits intestinal cholesterol absorption, can be combined with statin therapy to further reduce LDL cholesterol by 15% to 20%. Fibrates effectively decrease triglyceride levels while increasing HDL cholesterol. Fibrates lower LDL cholesterol levels mildly, but when combined with statin therapy, fibrates may increase the risk of myopathy. Omega-3 fatty acids decrease triglyceride levels and improve insulin resistance in patients with metabolic syndrome. They are often used in combination therapy with other classes of the hypolipidemic drugs. Nicotinic acid is highly effective in raising HDL cholesterol levels in patients with metabolic syndrome. Nicotinic acid decreases the concentration of small, dense LDL particles and also lowers serum levels of lipoprotein (a).⁴⁷

Dietary salt restriction and therapeutic lifestyle change are the primary means to address hypertension in obesity and metabolic syndrome. According to the 2017 guidelines published by the American College of Cardiology and American Heart Association (ACC/AHA),⁴⁸ patients having arterial blood pressure higher than 130/80 mm Hg may require antihypertensive drug therapy. There is no specific antihypertensive drug that is recommended as a first-line treatment in these patients, and generally the goal of antihypertensive therapy requires that polypharmacy be employed. A considerable element of the risk reduction resulting from antihypertensive therapy is decreasing arterial blood pressure.

The treatment of insulin resistance and hyperglycemia in metabolic syndrome, type 2 diabetes, and obesity is usually achieved with oral hypoglycemic drugs.⁴⁷ A number of different drug groups (and drugs within each group) that work through various mechanisms of action are available to treat hyperglycemia. These include α -glucosidase inhibitors, sulfonylureas, meglitinides, D-phenylalanine derivatives, biguanides, and thiazolidinediones.⁴⁷ Anesthetic implications include the need to assess and treat abnormal blood glucose levels in the perioperative period while being especially careful in the use of insulin in patients who are both insulin resistant and temporarily unable to continue on oral medication. At present, the optimal anesthetic management of patients who are taking metformin is not clear. There is a serious potential for postoperative lactic acidosis that can develop in patients using this drug. This possibility has led some physicians to routinely cancel or delay surgical procedures if metformin has been ingested within 48 hours of the scheduled surgery. Other physicians, however, have their patients continue taking metformin, both before and after surgery, without interruption if possible. Recent evidence indicates that patients taking metformin have a

reduced risk for complications. It appears that metformin may be safely used in the perioperative period.⁴⁹

Patients with metabolic syndrome and obesity may also be prescribed antiplatelet therapy. The AHA recommends that low-dose aspirin be used as a form of primary prevention in patients with metabolic syndrome whose 10-year risk for cardiovascular disease is 10% or greater as determined by Framingham risk scoring.

BEHAVIORAL INTERVENTIONS AND MODIFICATION

Behavioral interventions and behavioral modification are essential for obese patients to change their learned habits related to eating and physical activity in order to produce weight loss and long-term weight reduction.⁴⁷ This applies both for nonsurgical and surgical approaches to weight loss. The key features of typical behavioral programs include self-monitoring, goal setting, nutrition and exercise education, stimulus control, problem solving, cognitive restructuring, and relapse prevention. Patients often benefit from referral to multidisciplinary weight loss programs that incorporate diet, physical activity, and behavioral interventions to achieve their weight loss goals because these combined interventions provide the best weight loss and weight maintenance results without pharmacologic or surgical intervention. However, it is essential to identify and treat patients with eating disorders or major psychiatric disorders who require specialized psychiatric and psychological treatment to achieve meaningful weight loss.

PHARMACOTHERAPY FOR WEIGHT LOSS

Recommendations for pharmacotherapy as a treatment of obesity, first and foremost, stress lifestyle and behavioral modifications as the initial approaches to initiate weight loss.²⁷ Patients who do not reach their established reasonable weight loss goals by a combination of diet and exercise may be directed to pharmacotherapy to increase weight loss. There are weight loss drugs that have been approved by the Food and Drug Administration (FDA) and are currently prescribed for long-term use. These are typically used adjunctively with diet and exercise for patients having a BMI of 30 or greater (≥ 27 for patients with obesity-related risk factors or comorbid diseases). In current practice, there are only two categories of weight loss drugs: appetite suppressants and lipase inhibitors. Three drugs are currently available for the specific indication of weight loss: phentermine, lorcaserin,⁵⁰ and orlistat.⁴⁷ Phentermine, an adrenergic reuptake inhibitor, augments adrenergic signaling within the central nervous system and peripheral tissues. Phentermine decreases appetite and food intake and increases resting metabolic rate to promote weight loss. Its side effects include tachycardia and hypertension. Lorcaserin is a selective 5-HT_{2C} receptor agonist that reduces food intake through the activation of pro-opiomelanocortin. Due to its selectiveness for the 5-HT_{2C} receptor, lorcaserin has a better safety profile than the previous serotonin agonists for weight loss that have since been removed from the U.S. market due to increased risk of stroke and acute coronary syndrome. Lorcaserin should not be used in patients on selective serotonin reuptake inhibitors (SSRIs) or monoamine oxidase

inhibitors (MAOIs) due to the risk of serotonin syndrome, which can be life threatening. Orlistat, a lipase inhibitor, reversibly binds to lipase and prevents both absorption and digestion of certain dietary fats. Because orlistat also interferes with the absorption of fat-soluble vitamins, patients using this drug need to supplement fat-soluble vitamins A, D, E, and K. It has significant gastrointestinal side effects including diarrhea, steatorrhea, flatulence, fecal incontinence, and oily rectal discharge.

ALTERNATIVE PHARMACOLOGIC OPTIONS

Allison and colleagues⁵¹ reviewed the literature on dietary and herbal medications for weight loss. These agents are marketed as "food supplements," thereby escaping the purview of the FDA. Even though these supplements cannot legally claim to treat a disease, they can claim to reduce the risk of a disease. According to the review, claims for weight loss have been made for multiple products such as chitosan, chromium picolinate, conjugated linoleic acid, ephedra alkaloids (*ma huang*),⁵² and *Garcinia cambogia*.⁵¹ Most of the reports involving these compounds are from poor quality studies without any randomization, control groups, or blinding, thereby placing in question both efficacy and safety of these compounds. The only studies involving herbs that have consistently demonstrated weight loss involve combinations of ephedrine and caffeine.⁵³⁻⁵⁴ Pharmacologically, this is expected because ephedrine, an adrenergic agonist, is known to be an appetite suppressant and a thermogenic agent. For this reason, *ma huang*, a natural source of the ephedra alkaloid, is added to most, if not all, dietary supplements marketed for weight loss. The success of ephedrine as a weight loss agent in combination with caffeine and/or aspirin is well established. Unfortunately, multiple cases of cardiac and neurological issues, including hypertension, stroke, seizure, and even death have been reported,⁵⁵ possibly related to the inconsistent doses in the preparations and the lack of medical supervision in people consuming these products for weight loss. Consequently, the National Institutes of Health has banned these products from any recommended weight loss regimen.

IMPLANTED ELECTRICAL STIMULATORS

Implantable gastric stimulators are subcutaneously placed devices that resemble cardiac pacemakers and stimulate along the lesser curvature of the stomach. These gastric stimulators have been tried since the early 2000s and have been found to cause modest weight loss with few side effects.⁵⁶⁻⁵⁷ Numerous clinical trials conducted in the United States and Europe have shown some promising results. Most studies demonstrated weight loss during the first 12 months; however only a few studies had a follow-up period of longer than 1 year.⁵⁸ One study documented a 25% excess weight loss, improved response to oral glucose tolerance test, decreases in arterial blood pressure, and an improvement in symptoms of gastroesophageal reflux disease (GERD), along with an increased parasympathetic drive. No serious side effects were noted in the first 65 patients reported on in this study⁵⁶ or in the 20 patients followed in another.⁵⁷ Ghrelin levels may play a role in the success of these devices.

Surgical Management of Obesity

Adult obesity is clearly rooted in childhood obesity. Unfortunately, pediatric obesity is the most common childhood nutritional disorder in the United States. This is one of the tragedies of the current obesity epidemic: the significant and increasing prevalence of obesity in the young. It has attained a level of controversy that has involved the placement of vending machines in schools and the availability of sweetened snacks and soft drinks in public places as public policy is developed to help control the epidemic of pediatric obesity. The diagnosis of pediatric obesity is commonly defined using criteria developed by the Centers for Disease Control and Prevention (CDC) using BMI-, age-, and sex-specific clinical growth charts.⁵⁹ These percentile curves apply to the ages of 2 to 20 years, and because BMI exhibits nonlinear variation during growth, percentile ranges are utilized. The CDC defines children possessing BMIs in the 5th to 85th percentiles as having “healthy weight.” Children whose BMI is in the 85th to 95th percentile are “at risk for overweight,” while those having a BMI above the 95th percentile are classified as “overweight.” These classifications were previously regarded as “overweight” and “obese,” respectively. This switch in terminology continues to be a source of confusion. Exceeding the 99th percentile is referred to as extreme pediatric obesity.

The National Health and Nutrition Examination Survey 2011–14 data show that the prevalence of obesity in children for age 2 to 5, 6 to 11, and 12 to 19 years are 9.4%, 17.4%, and 20.6%, respectively.⁶⁰ There does not appear to be an influence of gender on the prevalence of obese children above the age of 6 years. While the prevalence of obesity among children of ages 6 to 11 and 12 to 19 has steadily increased since 1988, there has been a slight recent decline in obesity among ages 2 to 5 years. A number of developing countries have childhood prevalence rates higher than that of the United States,⁶¹ indicating that adolescent obesity is becoming pervasive.

Treatment of pediatric obesity is based on the balance of caloric intake and expenditure. These lifestyle changes are most successful with family intervention and support. The three pillars of success in this treatment are: better eating habits, increased physical activity, and decreased sedentary activity.⁶² Success involves more than education of child and family; it incorporates goal setting, self-monitoring, incentives, and stimulus control. Lifestyle interventions remain the treatment of choice in pediatric obesity, but concomitant pharmacotherapy may be beneficial in some patients. Orlistat, which is covered elsewhere in this chapter, should be considered as second-line therapy for pediatric obesity.⁶³

Although in 2000, less than 1% of all bariatric surgery patients in the United States were younger than 20 years of age,⁶⁴ the total number continues to increase. More adolescents are presenting for weight loss surgery, after failing to reduce weight and/or comorbidities in medically supervised and pharmacologically assisted weight loss programs. Even though many adult bariatric surgery programs are well qualified to provide safe and effective perioperative care for these patients, they may not be as well equipped to handle the unique metabolic and psychological needs of teenagers. Because of the shorter duration of obesity and fewer age-related comorbidities, adolescent patients have shorter

length of stay and lower immediate postoperative mortality when compared to adults.⁶⁴

Consent is an important issue in this population. Is parental consent to a semi-elective, relatively high-risk procedure appropriate? Does the child really understand the concept of high risk of death in the month after surgery? These and other such questions of ethics in medicine need to be addressed, but are beyond the scope of this chapter.

The rapid increase in the prevalence of both morbid obesity and superobesity, together with the increased risk of early demise within the obese population, has significantly increased the number of bariatric surgical procedures performed annually. The term bariatric surgery refers to surgical alteration of the small intestine or stomach with a view toward producing weight loss. It is estimated that over 216,000 bariatric surgeries are being performed annually in the United States. Care of obese patients is not limited to obesity surgery, however, as these patients present for all types of operations. Nonetheless, the benefits of surgical treatment of obesity now appear to have clear endocrinologic and cardiovascular value for reversing pathophysiologic effects of metabolic syndrome, type 2 diabetes, and other comorbidities of obesity, in addition to providing a mechanical means of enhancing weight loss.^{65–71} Several alternative procedures in bariatric surgery have evolved from early procedures based on creating malabsorptive gut pathways to newer procedures aimed at altering hormonal regulation of caloric intake drive and satiety.⁷² Primarily the available options can be separated into one of two groups: (1) operative procedures and (2) minimally invasive procedures that combine gastric restriction with induction of nutrient malabsorption.

OPERATIVE PROCEDURES

Surgery for obesity is one of the fastest growing surgeries performed worldwide.⁷³ The operative group can be divided into gastric restrictive procedures and procedures that combine gastric restriction with induction of nutrient malabsorption.^{74–83} These procedures can be performed using an open, laparoscopic, or robot-assisted approach. In general, minimally invasive (laparoscopic, robotic) approaches are preferred over an open procedure as they have a lower complication rate, hospital stay, and morbidity.⁸⁴ The rate of open bariatric procedures has continued to decrease steadily to the extent that nearly 90% of surgical bariatric cases are now performed laparoscopically.⁸⁵

RESTRICTIVE PROCEDURES

The surgical goal of restrictive operative procedures is to reduce and limit the patient’s food intake capacity.⁸⁰ This is most commonly achieved by reducing the stomach’s reservoir capacity. The vertical band gastroplasty was a widely practiced restrictive procedure in the previous three decades, but it was replaced by the minimally invasive laparoscopic gastric band procedure (LGB), which was very popular. However, in recent years, the percentage of bariatric procedures represented by LGB surgery performed has also decreased from 35% in 2011 to approximately 3% in 2016.⁸⁶ This decline in LGB operations is probably secondary to only modest amount of weight loss and high rates of band revisions and adjustments required. Recently, the sleeve gastrectomy (SG) has become

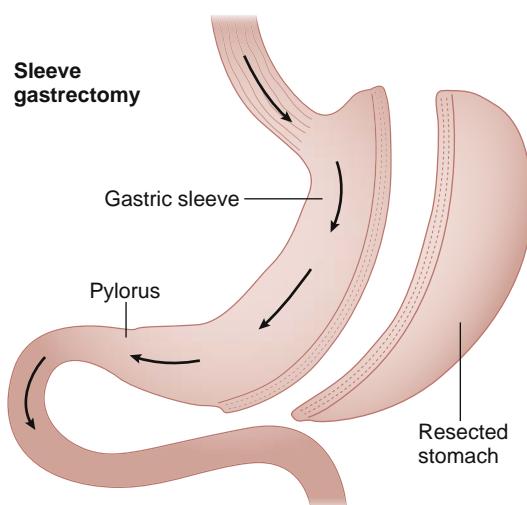


Fig. 58.2 Sleeve gastrectomy: a tubular stomach is created as the fundus and greater curvature of the stomach are removed around a 32F to 40F bougie.

the most commonly performed surgery for obesity. As illustrated in **Fig. 58.2**, in SG surgery, a tubular stomach is created around a 32 to 40 French bougie by removing the greater curvature of the stomach. The SG has been shown to be safe and effective, with a mean excess weight loss of approximately 65%.⁸⁷ The weight loss noted after a SG is not only due to the restrictive stomach, but also due to the decrease in hormonal level of ghrelin that regulates appetite and food intake.⁸⁸

MALABSORPTIVE PROCEDURES

The surgical goal of malabsorptive procedures is to cause weight loss both by gastric restriction and nutrient malabsorption. Historically, early surgical procedures involved creation of a long jejunoileal bypass. Patients achieved significant weight reduction but this was commonly accompanied by an unacceptable incidence of serious vitamin and protein malabsorption, osteoporosis, and hepatic failure.

Today, gastric bypass (GBP), which is illustrated in **Fig. 58.3**, and biliary pancreatic diversion (BPD) are the two most commonly performed malabsorptive operations, and both have achieved success in safety and efficacy.⁸⁹ GBP is more commonly performed than BPD, and it is considered the safer of the two malabsorption procedures. GBP surgery involves the creation of a small gastric pouch by stapling or banding the stomach. This results in an element of gastric restriction. GBP also involves the creation of a Roux-en-Y anastomosis, in which the small gastric pouch is directly connected to the middle portion of the jejunum.⁸⁹ The OrVil device, shown along with nontapered and tapered bougies in **Fig. 58.4**, may be used by the surgeon to assist with creation of the anastomosis. The orogastric portion of the OrVil device is passed through the oropharynx and then pulled through by the surgeon via a gastrostomy, until the anvil portion of the OrVil device reaches the stomach. It is then attached to a stapler to create the anastomosis. The path for food through the gastrointestinal tract subsequently bypasses the gastric remnant and the upper portion of the duodenum. This procedure can be performed with a laparotomy incision or by using laparoscopic techniques.⁹⁰⁻⁹¹

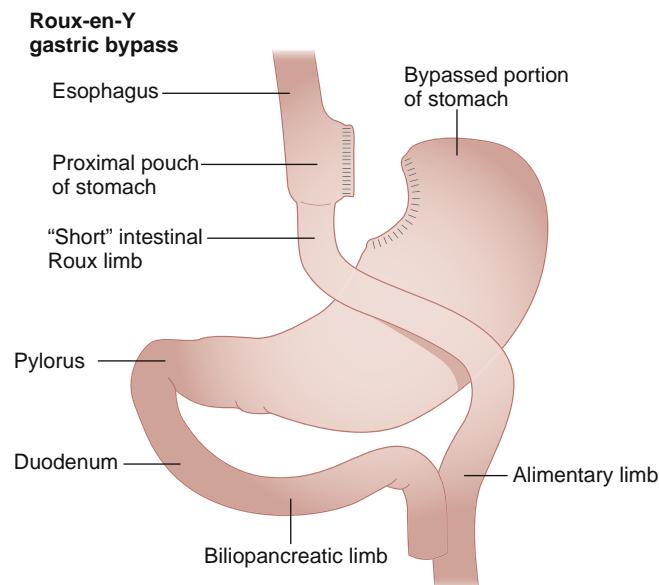


Fig. 58.3 Roux-en-Y gastric bypass: part of the stomach is detached from the rest, creating a small pouch. The pouch is connected to a lower part of the small intestine by a piece of small intestine, resembling a Y. As a result, parts of the stomach and small intestine are bypassed. However, digestive juices (bile acids and pancreatic enzymes) can still mix with the food, enabling the body to absorb vitamins and minerals and reducing the risk of nutritional deficiencies.



Fig. 58.4 32F tapered bougie (top), 40F nontapered bougie (middle), and OrVil device (bottom) commonly used during bariatric surgery.

Although this is considered to be a safe operation, the associated perioperative mortality is higher than that of restrictive procedures.⁷⁷ Additionally, there are some important long-term complications such as vitamin B₁₂ deficiency, anemia, incisional hernia, cholelithiasis, and staple line failure that occur with significant frequency. Often a cholecystectomy is performed concurrently to prevent future cholelithiasis.⁹² BPD is also a form of Roux-en-Y GBP reconstructive alimentary anatomy in which the bypassed intestinal segment includes the portion of duodenum at the point of entry of biliary and pancreatic secretions. This allows the bypassed intestine to be exposed to bile and pancreatic juice. The antrum is removed to avoid peptic ulceration, and food intake is only affected to a limited degree. The essential element of this operation is division of the small intestine about midlength, with the distal end of the alimentary limb being anastomosed to a generous gastric remnant. The more proximal biliopancreatic limb is anastomosed to the alimentary limb about 50 cm from the ileocecal valve. Following either the GBP or BPD form of operation, patients require life-long follow-up and may need micronutrient replacement long term.

MINIMALLY INVASIVE PROCEDURES

There have recently been a few devices approved in the United States for weight loss. One such device is the intragastric balloon that acts in a restrictive manner.⁹³ The intragastric balloon is placed in the patient's stomach endoscopically and is filled with saline to provide a sensation of fullness and satiety. The device can be kept in the patient's stomach for a maximum of 6 months and has been shown to decrease weight by an average of 6.8%. Most common complications of the intragastric balloon are related to gastrointestinal symptoms such as nausea, vomiting, halitosis, GERD, and abdominal discomfort; however serious complications such as balloon rupture, migration, and intestinal obstruction are possible.⁹⁴

Another device that has been approved for use in the United States is an endoscopically placed percutaneous gastrostomy tube to facilitate stomach emptying. The device can be used for draining ingested foods and in preliminary studies has been shown to decrease total body weight (TBW) by approximately 12%.⁹⁵ The most common side effects were abdominal discomfort and peristomal irritation; however serious complications such as abdominal pain requiring hospitalization and peritonitis were noted infrequently.

HEALTH BENEFITS OF BARIATRIC SURGERY

The two most significant outcome measures of bariatric surgical success are weight loss and resolution of comorbidities. Major effects of bariatric operations have been nicely summarized in extensive meta-analyses^{67,96-97} as well as in a major literature review.⁹⁸ Patients undergoing bariatric surgery with either SG or GBP have lost 52% to 68% of their excess weight.⁹⁹⁻¹⁰⁰ This magnitude of weight loss is far greater than what is commonly achievable by nonsurgical methods, and it is considerably closer to patients' desired and expected weight loss. Long-term maintenance of weight loss of this magnitude can also be maintained for well over a decade.

Improvement in obesity-related and metabolic syndrome-related comorbidities have also been evaluated.^{67,97-98,101} One clinical study demonstrated that at 1 year, type 2 diabetes remission rate with bariatric surgery was approximately 40% compared to 12% with medical treatment.¹⁰² Another study showed remission rate at 2 years of approximately 85% compared to 0% with medical treatment.¹⁰³ This benefit seems to persist long-term as well, as at 6 years 62% of surgical patients experienced remission in their type 2 diabetes.¹⁰⁴ Resolution of diabetes following surgery is inversely related to the preoperative duration of the disease and occurs more in those patients having diabetes controlled using oral hypoglycemic agents. This clearly distinguishes surgical treatment of obesity as an important endocrinologic intervention, especially since the modest improvement in diabetes management that is produced by nonsurgical weight loss is accompanied by relapsing disease by nearly 100% of patients within 5 years.

Surgical effects on hypertension and hyperlipidemia are similarly impressive. A study of almost 1900 patients demonstrated that at a 6.5 year follow-up, 32% of surgically treated patients had remission of their hypertension versus 12.5% in medically managed patients.¹⁰⁵ A significant

decrease in triglyceride levels, approximately 30% to 40% postbariatric surgery versus 8% from medical therapy; and increase in HDL cholesterol levels, 30% postsurgery versus 7% from medical therapy, have also been noted at 5 years.¹⁰⁶ Resolution of OSAHS seems to be independent of the specific bariatric surgical procedure employed, with resolution occurring overall in 85.7% of patients.¹⁰⁷ Post-surgical improvement in other comorbidities has also been demonstrated, with improvement in fatty infiltration of the liver, GERD symptoms, in respiratory function and asthmatic symptoms, reversal of the cardiomyopathy of obesity, and improvements in joint pain and mobility all having been reported.^{71,108-112} The reduction in obesity-related comorbidities has been shown to endure with 5-year follow-up.¹¹³ Although bariatric surgery has been shown to provide greater weight loss when compared with nonsurgical lifestyle interventions, comorbidities do resolve and risk factors do improve similarly with successful conservative treatments.¹⁰¹

Anesthetic Management of the Bariatric Surgical Patient

Patients undergoing bariatric surgery are receiving what is now the best long-term treatment for morbid obesity. However, their presurgical state is an agglomeration of abnormal physiologic conditions involving multiple organ systems. For that reason, there are considerable risks of mortality and morbidity associated with all types of bariatric surgery. Preoperative risk stratification can be used to identify patients at highest risk for significant morbid or fatal events when having bariatric surgery¹¹⁴; however detailed planning of the anesthesia care for the perioperative, intraoperative, and postoperative phases must be pursued for purposes of patient safety.

PREOPERATIVE EVALUATION

The preoperative assessment for anesthesia should include consideration of hypertension, diabetes, heart failure, and obesity hypoventilation syndrome. Results of the sleep study that the patient underwent are important. An AHI score greater than 30, implying severe sleep apnea, is a warning sign and a predictor for rapid and severe desaturation at induction. CPAP levels greater than 10 imply a patient with the potential for difficult mask ventilation.

Another useful piece of information in the preoperative evaluation is gleaned by examining the history of prior surgeries, their anesthetic challenges (i.e., ease or difficulty in securing the airway, intravenous access), need for intensive care unit admission, surgical outcomes, and the weight of the patient at that time. This information may either help ease some concerns or allow for better preparation for the upcoming anesthetic care. Recommended preoperative laboratory evaluations include fasting blood glucose, lipid profile, and serum chemistries (evaluating renal and hepatic function), complete blood count, ferritin, vitamin B₁₂, thyrotropin, and 25-hydroxyvitamin D.

If appropriately evaluated, ideally prepared, and optimally managed perioperatively, even patients with well-known

coronary artery disease (CAD) have comparable morbidity and mortality as those without CAD.¹¹⁵ The effect of OSA on perioperative risk remains controversial,¹¹⁶ but most patients are screened for OSA using overnight oximetry or polysomnography, or both, if appropriate. If identified with OSA and recommended for CPAP, then patients are encouraged to initiate therapy at home and it should be continued throughout the perioperative period.

Liver function abnormalities are common in this patient population, especially nonalcoholic fatty liver disease, with the extent of disease a determining factor for perioperative risk and postoperative outcomes. Cirrhotic liver disease with portal hypertension may be considered a contraindication to bariatric surgery.¹¹⁶ Gastrointestinal symptoms of dyspepsia may indicate the presence of *Helicobacter pylori*, which requires treatment by standard medical regimen.

The factors that may be considered contraindications for bariatric surgery include unstable CAD, uncontrolled severe OSA, uncontrolled psychiatric disorder, intellectual disability (IQ <60), inability to understand the surgery, perceived inability to adhere to postoperative restrictions, continued drug abuse, and malignancy with a poor 5-year survival prognosis. In most situations preoperative management of the medical morbidities can help optimize risk and convert high-risk patients to ones of acceptable risk.

The anesthetic care of patients with OSA is complicated by the side effects of anesthetic drugs on an already compromised respiratory system. The commonly presented comorbidities in this patient population only accentuate the problem.¹¹⁷ The change in perioperative risk based on the anesthetic agent utilized is only deduced from anecdotal reports of different cases. There is a paucity of trials to definitively determine an optimal anesthetic regimen. Nevertheless, the American Society of Anesthesiologists and the Society for Anesthesia and Sleep Medicine have both published statements based on existing literature and consensus of expert opinion addressing the perioperative identification and management of patients who carry a formal diagnosis of OSA as well as for those who are at risk for sleep apnea but remain undiagnosed. Additional questions commonly arise and cannot yet be answered on the basis of high-grade scientific evidence: is it safe to perform procedures in patients with sleep apnea and treat them as outpatients or day surgery patients? What procedures pose sufficient risk to the patient to recommend an overnight hospital stay? Does narcotic use impact this decision? Would the increased role of nonsteroidal antiinflammatory drugs (NSAIDs) change these recommendations? Factors such as neck size and open versus laparoscopic surgery are being studied as to their impact on outcomes. Further research on these and other patient safety related questions is continuing.

INTRAOPERATIVE CARE

Obese patients present special intraoperative challenges for the anesthesiologist in airway management, positioning, monitoring, choice of anesthetic technique and anesthetic drugs, pain control, and fluid management. Many of these issues are equally important in their postoperative care. The most significant and best studied are airway management, including endotracheal intubation, pulmonary physiology,

and techniques of maintaining adequate blood oxygenation and lung volume. Specific interventions, techniques, and approaches employed by the anesthesia care team providing anesthesia for obese patients are important determinants of outcomes.

Patient Positioning

Even though there are no evidence-based studies that demonstrate that obese patients have more frequent complications from positioning, it seems fairly intuitive that morbidly obese patients do require extra care in positioning (see also Chapter 34). Even in the supine position, rhabdomyolysis from pressure on gluteal muscles leading to renal failure¹¹⁸ and death¹¹⁹ have been reported. For obese patients placed in the prone position, cushioning gel pads or other weight-bearing rolls may have excessive weight placed on them. Pressure points must be checked carefully, and even though pressure sites may be carefully padded, skin breakdown can still occur. This may cause tissue necrosis and infections, especially in lengthy surgery.¹²⁰ It is difficult to protect the dependent hip from pressure effects with patients placed in lateral decubitus position. Obese patients have excess axillary tissue that may make it impossible or unnecessary to place a traditional axillary roll in this position. In the lithotomy position the challenge may be in supporting the weight of the patient's legs using regular, and not oversized, stirrups. To minimize the risk of tissue compression injury or development of compartment syndrome, the duration during which legs are held in stirrups should be held as short as possible.¹²¹

Airway Management

No positioning issue is more important than that regarding positioning of the obese individual for laryngoscopy and endotracheal intubation. These are often considered to be much more difficult to perform in obese patients than patients having a normal BMI. Difficulty with laryngoscopy and intubation is usually thought to result from the obese patient having a short, thick neck, large tongue, and significant redundant pharyngeal soft tissue. However, the correlation between morbid obesity and difficult laryngoscopy and intubation is not universally observed in clinical practice. This is likely to result from a simple, but important approach to clinical care, with careful attention being paid to patient positioning prior to induction of general anesthesia. Appropriate positioning plays an important role in providing optimal conditions for successful placement of the endotracheal tube under direct vision.

A number of studies have been conducted to determine the incidence of difficult laryngoscopy or intubation in the obese population, with mixed findings. One study found an association between oropharyngeal Mallampati classification and BMI as predictors of difficult laryngoscopy.¹²² During laryngoscopy, the patients' heads were placed in optimum sniffing position, regardless of BMI. In a study conducted exclusively with obese patients, BMI was not found to be associated with intubation difficulties.⁴¹ A high Mallampati score was identified as a predictor of "potential intubation problems," but intubation by direct laryngoscopy was successful in 99 of 100 patients studied. All patients were positioned with pillows or towels under their shoulders, with the head elevated and neck extended.

Another group studied both lean and obese patients and found a Mallampati score of III or IV to be the only independent risk factor for difficult intubation in the obese study group.¹²³ The authors demonstrated that the Mallampati score had low specificity and low positive predictive values (62% and 29%, respectively) for difficult intubation. They concluded that intubation was more difficult in the obese patients. During intubation, patients were placed in a semi-recumbent position (30-degree elevation) with the head in the sniffing position. In another study ultrasound was used to quantify the amount of soft tissue between the skin and the anterior aspect of the trachea at the level of vocal cords.¹²⁴ The authors also assessed the airway by measurement of thyromental distance, mouth opening, degree of neck mobility, Mallampati score, neck circumference, and presence of OSA. Only an abundance of pretracheal soft tissue measured ultrasonically and neck circumferences were found to be positive predictors of difficult intubation with laryngoscopy performed with patients in the sniffing position. A meta-analysis of 35 studies was conducted to determine the diagnostic accuracy of preinduction tests for predicting difficult intubation in patients having no airway pathology.¹²⁵ The incidence of difficult intubation in obese patients was three times the incidence compared to the nonobese population. This may have resulted from suboptimal patient positioning, which was not clearly described in any of the preceding studies, including ramped positioning or elevating the upper body and head of morbidly obese patients to align the ear with the sternum horizontally, as has been shown to improve laryngoscopic view.¹²⁶ In this study, morbidly obese patients were assigned either to be in sniffing position or ramped position for airway management. The study demonstrated a statistically significant difference in laryngeal view, with ramped position providing the superior view. In one study, morbidly obese patients in a ramped position with a Mallampati score of III or IV and male gender were shown to predict possible difficult intubation, while no relationship was noted between difficult direct laryngoscopy and the presence of OSA, patient neck circumference, or BMI.¹²⁷

Based on the evidence from randomized controlled trials and other literature on airway management of obese patients, patients should be readily intubated by direct laryngoscopy if placed carefully in ramped position. This can be achieved using commercially available positioning devices¹²⁸ or by building a ramp from blankets or sheets to achieve the desired placement of the patient's head relative to the thorax.¹²⁹ Obese patients must be examined for the common objective signs of potential difficult intubation, which include small mouth opening, large protuberant teeth, limited neck mobility, and retrognathia. Alternative airway management techniques include the use of a video laryngoscope for intubating obese patients.¹³⁰ Compared to direct laryngoscopy, the use of video laryngoscopy in patients undergoing bariatric surgery has shown to provide a better glottic view and decreased time required to successfully intubate the trachea.¹³¹ Performance of an awake, topicalized direct laryngoscopy with modest sedation can also be utilized to assess laryngoscopic view in deciding whether to proceed with induction of general anesthesia or awake, sedated fiberoptic intubation. Of course, the equipment for emergency airway management including

laryngeal masks and a fiberoptic bronchoscope should be immediately available.

Another area that requires specific attention during the perioperative period is the obese patient's pulmonary physiology. It is especially important to appreciate techniques to maintain oxygenation and lung volume in caring for the obese patient. First, obese patients have multiple pulmonary abnormalities, including decreased vital capacity, inspiratory capacity, expiratory reserve volume, and functional residual capacity. Second, closing capacity in obese individuals is close to or may fall within tidal breathing, particularly in the supine or recumbent position. Moreover, both lung and respiratory system compliance are low with obesity because patients breathe at lung volumes that are abnormally low.¹³² As a result of the underlying physiology, the obese patient is likely to undergo rapid oxygen desaturation, particularly during periods of apnea such as occurs during induction of general anesthesia. However, the presence of OSA by itself does not independently increase the risk of the patient desaturating during induction of general anesthesia as long as appropriate precautions are instituted.¹³³ However, after induction and intubation have occurred, patients may continue to derecruit gas exchange units throughout the anesthetic course.¹³⁴ A variety of maneuvers have been studied to preserve oxygenation and maintain lung volume specifically in the obese population.

In one study of the rate of development of hypoxemia in patients during apnea, patients received 100% oxygen by facemask to achieve denitrogenation before induction of general anesthesia.¹³⁴ The apneic period was continued after induction until the SpO₂ fell to 90%. Obese patients reached the end point in less than 3 minutes, whereas it took 6 minutes in patients having a normal BMI. Efforts to prevent atelectasis formation and desaturation during induction of general anesthesia in obese individuals include application of CPAP during preoxygenation,¹³⁵⁻¹³⁷ and mask application of positive end-expiratory pressure (PEEP), and mechanical ventilation following induction.¹³⁷ Use of 10 cm H₂O CPAP during preoxygenation in the supine position resulted in a higher partial pressure of oxygen (PaO₂) after intubation and decreased the amount of atelectasis that developed.⁸¹ The combination of CPAP during preoxygenation and PEEP/mechanical ventilation after induction significantly increased the nonhypoxic apnea duration from 2 minutes, found in controls not receiving CPAP or PEEP, to 3 minutes. Use of 7.5 cm H₂O CPAP during 3 minutes of preoxygenation while supine, however, did not change the time required for obese patients to desaturate to an SpO₂ of 90%.¹³⁶ Preoxygenation using 25-degree head-up (back inclined) as opposed to supine positioning without positive airway pressure did increase the elapsed time needed for anesthetized, apneic, obese individuals to desaturate to an SpO₂ of 92%.¹³⁸ The patients in head-up position had a significantly higher PaO₂ after preoxygenation, just prior to induction. The obesity-associated gas exchange defect depended on the waist-to-hip ratio, an index of the distribution of adipose tissue surrounding the thorax.¹³⁹ This study further demonstrated that morbidly obese men are more likely to have poorer pulmonary gas exchange than morbidly obese women. In a study conducted to assess the relationship between patient positioning and development of hypoxemia in obese patients during apnea after anesthetic

induction and intubation, patients were ventilated with a 50% oxygen/50% air mixture for 5 minutes before the ventilator circuit was disconnected.¹⁴⁰ Apnea was continued until the SpO₂ fell to 92%, at which time ventilation was resumed. Patients in the supine position reached the end point in 2 minutes, but it took 30 seconds longer if supine position with the back elevated 30-degrees was used and 1 minute longer if 30-degree reverse Trendelenburg position was used. Use of 30-degree reverse Trendelenburg position in obese patients undergoing bariatric surgery was also shown to reduce the alveolar-to-arterial oxygen difference, as well as increase total ventilatory compliance and reduce peak and plateau airway pressures when compared to supine position.¹⁴¹ Vital capacity has also been shown to decrease to a greater extent under general anesthesia in obese patients compared to normal weight patients.¹⁴²

A variety of intraoperative maneuvers to maintain lung volume and oxygenation have also been studied. Increasing tidal volume incrementally from 13 to 22 mL/kg in obese patients ventilated under general anesthesia did not improve the gas exchange defect but did increase airway pressures.¹⁴³ Use of 10 cm H₂O PEEP has been demonstrated to have a greater effect in obese patients compared to normal subjects on improving ventilatory mechanics, increasing PaO₂, and decreasing alveolar-to-arterial oxygen difference during general anesthesia with neuromuscular blockade.¹⁴⁴ In addition to PEEP alone, use of a recruitment maneuver such as sustained lung inflation to 55 cm H₂O for 10 seconds followed by application of PEEP has been demonstrated to prevent atelectasis from developing and to improve oxygenation, whereas neither PEEP nor a recruitment maneuver alone achieved the same degree of maintenance of pulmonary function.¹⁴⁵

Pneumoperitoneum during laparoscopic procedures increases pulmonary resistance and decreases dynamic lung compliance.¹⁴⁶ During pneumoperitoneum, alterations in body position, tidal volume, and respiratory rate had no effect on the alveolar-to-arterial oxygen difference in obese patients.¹⁴⁷ During pneumoperitoneum for laparoscopic bariatric surgery, alveolar recruitment by repeated sustained lung inflation to 50 cm H₂O followed by mechanical ventilation with 12 cm H₂O PEEP has been shown to increase PaO₂ intraoperatively, however at the expense of causing hypotension that required vasopressor use.¹⁴⁸ In an attempt to optimize PEEP in obese patients undergoing laparoscopic surgery, a normal functional residual capacity was maintained with 15 ± 1 cm H₂O PEEP. Infusion of intravascular volume expanders was required to prevent PEEP-induced hemodynamic compromise.¹⁴⁹

In summary, a back-up position with the use of PEEP during preoxygenation at induction of anesthesia and intraoperatively has been shown to decrease the A-a gradient in an obese patient.¹⁵⁰ Furthermore, the application of noninvasive modes of ventilation including pressure support and bi-level delivered by mask for preoxygenation, induction, and maintenance of anesthesia to maintain oxygenation and ventilatory mechanics in obese patients has been shown to be beneficial. Ideal patient positioning, use of PEEP, and special modes of ventilation just prior to emergence and extubation may help maintain pulmonary function and gas exchange postextubation. Currently there are no published guidelines to address the issues of maintenance of

oxygenation and ventilatory mechanics in obese patients undergoing general anesthesia. Considering both the airway management issues detailed previously as well as the oxygenation, lung volume, and ventilatory mechanics issues described above for obese individuals, anesthesia care providers should position patients to achieve the combined goals of providing a superior laryngoscopic view for ease of endotracheal intubation while establishing optimal conditions for oxygenation and preservation of pulmonary mechanical function.

It is the practice at our institution that obese patients are initially placed in a ramped position and then into reverse Trendelenburg, if needed, to achieve a 25- to 30-degree incline of the thorax prior to preoxygenation. Patients are then preoxygenated for 3 to 5 minutes using 100% oxygen delivered under positive pressure. For those patients receiving CPAP at home for OSA, we use CPAP or pressure support ventilation by facemask at a pressure level identical to the patient's home CPAP setting. Otherwise, CPAP of 8 to 10 cm H₂O is appropriate. Following induction, it is reasonable to maintain 8 to 10 cm H₂O PEEP intraoperatively, but care must be taken to treat any hypotension that may occur. Finally, if the patient's position must be changed intraoperatively, one must return the patient to head-up position prior to emergence and extubation.

In preparation for emergence from anesthesia, neuromuscular blockade must be fully reversed before the patient is extubated. Given the advent of a pressure support ventilation mode on many newer models of anesthesia machines, the bariatric patient can be maintained on pressure support during emergence once spontaneous ventilation has resumed. When adequate muscle strength has returned, as demonstrated by sustained tetanus using the nerve stimulator and performance of a 5-second head lift, the awake patient who is following commands can be extubated. Pressure support or CPAP can be delivered immediately by mask applied to the face as is done during preoxygenation prior to induction of anesthesia. The use of PEEP and noninvasive modes of ventilation just after emergence and extubation has been shown to improve pulmonary function in patients up to 24 hours later.¹⁵¹ We utilize CPAP during recovery, especially in those patients already prescribed CPAP for their OSA. The basic premise that must be respected with regard to airway management and its integral relationship to pulmonary function is that morbid obesity incurs significant derangements of lung function and pulmonary mechanics. These factors must be managed carefully in order to minimize intraoperative and postoperative pulmonary complications.^{152,153}

Anesthetic Drugs and Dosing

Anesthetic drugs such as opioids, propofol, and benzodiazepines are all well known to have exaggerated responses in patients with OSA. They may decrease pharyngeal musculature tone, which is essential in maintaining airway patency.^{40,154} In the setting of OSA, volatile agents are known to diminish ventilatory response to carbon dioxide, especially in children with tonsillar hypertrophy. Another pediatric study showed that spontaneously breathing intubated children with a history of OSA have depressed ventilation and half have apnea with 0.5 µg/kg of intravenous fentanyl. Although these data are from the pediatric

literature, it would be prudent to apply the same principles in obese adult patients until proven otherwise. It therefore becomes attractive to use short-acting drugs and nondepressors of ventilation like the α_2 -agonist dexmedetomidine. This should, at least in theory, speed up the return to baseline respiratory function.¹²⁰

Commonly used anesthetic drugs can be dosed on TBW or IBW based on lipid solubility. In the past, IBW was interpreted to mean fat-free weight, implying that it could be used as a substitute for lean body weight or more correctly, lean body mass (LBM), usually approximated as 120% of IBW. LBM is a good weight approximation to use when dosing hydrophilic medications. As expected, volume of distribution (V_D) is changed in obese patients with regard to lipophilic drugs. This is especially true of benzodiazepines and barbiturates, among the commonly used anesthetic drugs. Two exceptions to this rule are procainamide¹⁵⁵ and remifentanil,¹⁵⁶ which even though highly lipophilic, have no relationship between properties of the drug and their V_D .¹⁵⁷ Consequently, commonly used anesthetic drug dosing is based on IBW for propofol, vecuronium, rocuronium, sugammadex, and remifentanil. In contrast, midazolam, succinylcholine, cisatracurium, fentanyl, and sufentanil should be dosed on the basis of TBW. Another caveat to this recommendation is that maintenance doses of propofol should be based on TBW and conversely for sufentanil on IBW.¹⁵⁷ This implies that one can use, based on patient weight, larger amounts of benzodiazepines, fentanyl, or sufentanil, although these are best titrated to desired clinical effect. Conversely, based on real body weight, smaller amounts of propofol are needed to anesthetize the patient.

With vecuronium or rocuronium, the initial dose should be based on IBW with additional doses based on the closely followed state of neuromuscular blockade. Complete blockade in the morbidly obese patient is necessary not just for the surgeon's convenience, but also to facilitate mechanical ventilation. The drug chosen is not as important as the depth of the state of paralysis. The pharmacokinetic profile of sugammadex is similar to that of rocuronium, and its dosing should be based on IBW.¹⁵⁸

Volatile anesthetics are chosen based on physical characteristics of tissue solubility which are expressed as blood-gas partition coefficients and fat-blood partition coefficients. There is some evidence to suggest that desflurane may be the anesthetic of choice based on consistent and rapid recovery profile versus sevoflurane and propofol.^{159,160} Some studies suggest that the differences in immediate recovery between sevoflurane and desflurane are not clinically significant.¹⁶¹

Even though nitrous oxide provides some analgesic effect and is rapidly eliminated, we prefer to avoid it based on the high oxygen demands in the obese. Its entry into air spaces in short intraabdominal surgeries may not be a significant factor, but in bariatric surgery, especially when done laparoscopically or robotically, any increase in bowel gas volume could make a challenging surgical procedure even more difficult for the surgeon.

Induction of Anesthesia

There has been considerable debate regarding obesity, the risk of aspiration of gastric contents, and the need to provide aspiration prophylaxis.¹⁶² Abdominal bloating or fullness and female sex are associated with delayed gastric emptying

of solids and liquids in diabetic patients.¹⁶³ Although many obese patients have type 2 diabetes, separate studies of gastroesophageal reflux during anesthesia have not demonstrated body habitus to be a predictor of reflux rates.¹⁶⁴ Gastric fluid volume and pH have been shown to be the same in obese patients who are fasting or who have oral intake of up to 300 mL of clear liquid 2 hours prior to being anesthetized.¹⁶⁵ Obesity itself does not increase aspiration risk. However, acid aspiration prophylaxis including H₂-receptor agonists or proton pump inhibitors must be considered in patients having identifiable aspiration risks. Rapid sequence induction or awake fiberoptic intubation may also be considered in such patients.⁴⁰

Based on experience from obstetric practice, there is a body of evidence to show that regional anesthesia, especially epidural and spinal, are safe and feasible in patients with large body habitus.¹²⁰ However, regional anesthesia is technically more difficult due to the physical challenge of placing the catheters and the tendency of these catheters to migrate out of the epidural space. Special equipment, including longer needles or special ultrasound probes, may be needed for the correct placement of catheters in these patients. Care should be exercised in dosing these catheters because of the increased cephalad spread of the drug and the block due to the smaller epidural space compared to normal-weight patients.^{166,167} The degree of respiratory compromise suffered by obese patients will also be of a larger magnitude than normal-weight patients with a high regional block.

There is little evidence to suggest that epidural pain management improves overall outcomes. Since the trend of laparoscopic surgery is increasing compared to open laparotomies, this becomes less of an issue. In the morbidly obese patient who is having an open laparotomy, use of a thoracic epidural catheter to control pain has the most important benefit of reducing the attenuation of vital capacity postoperatively.¹⁶⁸

Obesity per se does not require invasive monitoring, so GBP surgery can be performed safely with routine monitoring. The indications for invasive monitoring stem from the comorbidities present in these patients. Since these tend to run together in the patients needing surgery, the incidence of invasive monitoring in these patients thereby increases.¹⁶⁹ Morbidly obese patients having serious comorbidities such as obesity-hypoventilation syndrome, who present with pulmonary hypertension and cor pulmonale, may require a pulmonary artery catheter or intraoperative evaluation utilizing transesophageal echocardiography. The rationale for central venous access may stem from difficulties in peripheral access rather than any other indication. Many patients receive an inferior vena cava filter prophylactically due to the high risk of deep vein thrombosis and pulmonary embolism associated with obesity and bariatric surgery.¹⁷⁰ It is recommended that a central line inserted at the time of surgery should be placed under ultrasound guidance to decrease complications as well as to increase ease of placement. Similarly, difficulty in noninvasive blood pressure measurements, secondary to body habitus-related difficulty in appropriate cuff placement, may be an indication for arterial catheter placement. Obtaining arterial blood gases may help to guide intraoperative ventilation and extubation.

Postoperative pain management in weight loss surgery patients can involve intravenous analgesia employing patient-controlled analgesia (PCA) or thoracic epidural analgesia. There is no clear data proving the superiority of one technique over the other; therefore in many instances, surgical technique, open versus laparoscopic, may help guide that decision. In our practice, we tend to reserve epidural anesthesia for patients undergoing open GBP. Even with these drawbacks, we have approximately an 80% success rate with superobese patients. It may be prudent to test the effectiveness of the epidural prior to induction of anesthesia. An opioid-based PCA with local anesthetic wound infiltration and adjunct non-narcotics is a reasonable alternative approach for most patients. Injection of local anesthetic in the incision site prior to making the incision may result in preemptive analgesia. Adjunct analgesia with non-narcotic medications such as oral and intravenous acetaminophen, NSAIDs, low dose ketamine, and dexmedetomidine, will decrease opioid requirements and thereby opioid-induced side effects as well.

Intraoperatively, utilizing the appropriate operating room table for the patient's weight is critical since the consequences of having a table not rated to the patient's weight can have serious consequences for both patient and the operating room personnel. It may be useful to keep the patient strapped throughout the period of sedation and sleep. Along with a safety strap, it might also be useful to apply a bean bag under the patient to keep the patient from sliding off the operating room table. Thermal management in the operating room is best accomplished by forced-air warmers. Arm boards may need extra padding to keep the patient from having the arm and shoulder out of an anatomical position. If the arms are to be tucked by the side of the patient, then wide, well padded sleds may be useful.

Fluid requirements for the obese patient are larger than predicted for those of normal BMI and even during a relatively short, 2- to 3-hour case these patients may need 3 to 4 L of crystalloid fluid to prevent acute tubular necrosis (ATN) in the kidneys. Hypovolemia, which can cause a protracted prerenal state and contribute to the development of ATN, can be prevented by appropriate hydration. Retrospective data from the University of Pittsburgh Medical Center suggests that primary acute renal failure after weight loss surgery occurs in approximately 2% of patients. Other predisposing factors include BMI greater than 50 kg/m², prolonged surgical time, prior history of renal disease, and intraoperative hypotension.¹⁷¹

POSTOPERATIVE MANAGEMENT

In our practice, we prefer to have the postbariatric surgery patients stay at the same location consistently. This allows skilled nursing and ancillary care to be provided to patients on a consistent basis. These patients are kept on their CPAP or bilevel positive airway pressure machines as much as possible with monitoring of end-tidal carbon dioxide and SpO₂ by pulse oximetry recommended. Monitoring capnometry in the postoperative period is critical for assessing a morbidly obese patient's respiratory function since the administration of supplemental oxygen may delay the diagnosis of hypoventilation. At the Hospital of the University of Pennsylvania, patients identified as having difficult airways

are distinguished with armbands, and with visible signs on their beds, their hospital charts, and on the electronic medical records for the remainder of their hospital stay. Additionally, a note by the attending anesthesiologist explaining the difficulty in intubation as well as the means utilized to secure the airway in the operating room is available in the room. In case of an unexpected emergency intubation, for whatever reason, we feel that this extra information is extremely useful to the resuscitation team.

Postoperative nausea and vomiting (PONV) is a common reason for delayed discharge from the postanesthesia care unit (PACU). Intraabdominal surgery is a known risk factor for PONV.¹⁷² Patients undergoing bariatric surgery have significant manipulation of their stomach, which may increase their risk of PONV. It is recommended to include a multimodal approach to PONV prophylaxis, including ondansetron, dexamethasone, and placement of a scopolamine patch when not contraindicated in order to minimize patient dissatisfaction and serious complications such as aspiration or wound and anastomotic dehiscence.

Enhanced recovery after surgery (ERAS) protocols are being used widely in surgical patients to decrease morbidity and decrease in-hospital stay. One study looking at patients undergoing an SG demonstrated a median hospital stay of 1 day in the ERAS group compared to 2 days in the control group, without any difference in postoperative complications or readmissions.¹⁷³ The ERAS protocol included standardized preoperative patient education, shortened preoperative fasting, multimodal analgesia and antiemetic therapy, avoidance of fluid overload, early ambulation and feeding, and incentive spirometry.

MANAGEMENT OF COMPLICATIONS

Bariatric surgery is considered to be very safe, but not without potential complications, which are increasingly predictable.¹⁷⁴ In-hospital mortality rates for patients undergoing laparoscopic and open bariatric surgery are 0.17% and 0.79%, respectively.¹⁷⁵ Mortality is associated with a need for reoperation during the same hospitalization,¹⁷⁶ with intestinal leakage being a serious complication accounting for a large number of patient deaths.¹⁷⁷ Risk factors also include older age, excessive obesity, poor functional status, and comorbid conditions of congestive heart failure or renal failure.

Morbidity occurring during the immediate postoperative in-hospital period typically falls into one of four categories; wound, gastrointestinal, pulmonary, and cardiovascular complications. The complication rates are significantly lower in each category for patients undergoing laparoscopic rather than open procedures. The American College of Surgeons National Surgical Quality Improvement Program database showed that patients who had an open GBP compared with a laparoscopic GBP had a morbidity rate of 7.4% versus 3.4%, return visits to the operating room rate of 4.9% versus 3.6%, and median postoperative length of stay of 3 versus 2 days, respectively. **Box 58.3** provides a categorical listing of complications of bariatric surgery.

The most common complications requiring reoperation include postoperative intraabdominal bleeding, anastomotic leakage, suture line dehiscence, small bowel obstruction, and deep wound infection,¹⁷⁷⁻¹⁸² all of which may

BOX 58.3 Complications of Bariatric Surgery

Early	Bleeding Infection Dehydration Peritonitis Leak from anastomotic site Bowel obstruction Perforation Pneumonia DVT/PE Death
Late	Anorexia Cholelithiasis/cholecystitis Pouch dilation or stricture Gastroesophageal reflux disease/dysphagia Herniation at surgical site Small bowel obstruction Marginal ulcers Pancreatitis Nutritional issues Fat-soluble vitamin deficiencies, especially vitamin B ₁₂

require a general anesthetic for laparotomy. Despite deep vein thrombosis prophylaxis therapy in the perioperative period, patients can also present postoperatively with deep vein thrombosis or pulmonary embolism and require an anesthetic for placement of an inferior vena cava filter device. As mentioned earlier, prophylactic filters are often placed prior to bariatric surgery.¹⁷⁰ The risk of venous thromboembolism is higher in open bariatric procedures, men, and patients with preexisting lower extremity edema and pulmonary hypertension.¹⁸³

In all cases requiring reoperation shortly after the original bariatric procedure it is prudent to review the anesthesia record. Specific attention should be paid to the documentation of patient position and technique employed for airway management in the prior anesthetic. Patients may be hypovolemic from blood loss, inadequate hydration, vasodilatation, and insensible fluid losses associated with fever and infection. It is especially important to consider additional or new risks of aspiration of gastric contents. This may be due to the presence of a postoperative ileus, small bowel obstruction, and surgical creation of a Roux-en-Y GBP limb that excludes the pylorus as an element of protection from reflux of intestinal contents. Decompression of the gastric pouch in patients going for surgery to relieve a small bowel obstruction can be achieved with careful introduction of a nasogastric or orogastric tube just prior to induction of general anesthesia. Although this may increase the risk of violating a fresh, competent anastomotic suture line, communication between anesthesiologist and surgeon can be pursued to determine the risks and benefits of performing this maneuver. During the ensuing laparotomy, any perforation of a fresh suture line resulting from the attempt to decompress the gastrointestinal tract can be repaired immediately and the nasogastric or orogastric tube can subsequently be left in place for continued postoperative drainage.

Depending on the extent of reoperation, requirement for volume resuscitation, blood transfusion, degree of peritonitis with anastomotic leak, presence of sepsis, or other significant continued risks to health, patients undergoing

reoperation may require prolonged postoperative ventilation. Requirements for postoperative pain management may also be considerably different than those associated with the initial bariatric procedure. In patients who are sufficiently hemodynamically stable immediately prior to reoperation, an epidural catheter can be placed prior to induction for pain management as part of the postoperative care. This is especially valuable in obese patients undergoing laparotomy, as is described elsewhere in this chapter.

There are also a number of potential major complications requiring surgical intervention weeks, months, or even years after a bariatric surgical operation has been performed. Patients may develop anastomotic strictures or ulcers, ventral hernias, gastrogastric fistulae, and severe reflux disorders requiring additional surgery.⁹² Small bowel obstruction may appear weeks after surgery.¹⁸¹ Patients may desire cosmetic operations to remove excess skin or liposuction procedures to sculpt dysmorphic body areas following significant weight loss. Patients may also require adjustment of a gastric band or pursue band removal. The anesthetic considerations for such patients should include a review of the prior anesthetic record to glean information regarding airway and pain management. The degree of weight loss achieved and the resolution of comorbidities including diabetes, hypertension, and OSA may significantly alter the approach used in the bariatric operation.

A fraction of patients develop significant neurologic complications following GBP surgery.¹⁸⁴⁻¹⁸⁶ These are known to include polyneuropathy, polyradiculoneuropathy, myelopathy, encephalopathy, and optic neuropathy. Myelopathy occurs most frequently but does not present until about 10 years after surgery.¹⁸⁴ These patients have demonstrable nutritional deficiencies, but except for the vitamin B₁₂ and copper deficiencies found in patients with myelopathy, no specific nutritional profile has been found to correlate with neurological complications. Although neurologic symptoms accompanying weight loss surgery are not likely to result in additional surgery, they represent new or additional comorbidities that should be fully considered by the anesthesiologist caring for patients having previously undergone bariatric surgery.

The nutritional and metabolic complications of bariatric surgery also include protein and protein-calorie malnutrition. Patients may have excessive weight loss occurring either too rapidly or beyond the predetermined goals, steatorrhea or severe diarrhea, hypoalbuminemia, marasmus, edema, and hyperphagia.^{92,187-189} In cases of severe malnutrition, patients may require enteral or parenteral nutrition therapy. Surgical revision may be required to correct excessive weight loss and hypoalbuminemia. Under such circumstances, an anesthetic regimen accounting for decreased drug binding effects of a low serum albumin must be considered.

Considerations for Management of the Obese Patient Presenting for Nonbariatric Surgery

Few studies have evaluated the importance of morbidity when performing common nonbariatric surgical

procedures on the obese patient. A study by Dindo and coworkers¹⁹⁰ of 6336 patients did not find any difference in the incidence or severity of complications after elective general surgery, except surgical site infections. Other studies have assessed the effect of obesity on wound infections and have shown that they are increased.¹⁹¹⁻¹⁹² Multiple studies have demonstrated that obese patients are at higher risk after gynecological, orthopedic, cardiovascular, urological, and transplantation surgery, while other studies have not shown there to be obesity-related risk differences.¹⁹³⁻¹⁹⁴

From the data of Dindo and associates¹⁹⁰ regarding complications and the type of surgical procedure, operative severity and open surgery were independent risk factors for postoperative complications. They found no differences in the type of postoperative complications in obese and non-obese groups. This study provides data to decrease the prejudice that patients with obesity are implied to have a higher incidence of postoperative complications. This preconception may pertain more to the perception of the medical team as a result of technical difficulties on the anesthetic and surgical end. Surgeries may last longer, about 25% more time for laparoscopic than for open cholecystectomy in the morbidly obese. Significantly, the wound infection rate was much better after laparoscopic than after open surgery, which supports the practice of performing laparoscopic surgery in obese patients rather than the alternative.

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KEY POINTS

- Innervation of the intraabdominal components of the genitourinary system—the kidney and the ureter—is primarily thoracolumbar (T8-L2). The nerve supply of the pelvic organs—the bladder, prostate, seminal vesicles, and urethra—is primarily lumbosacral with some lower thoracic input.
- The spinal level of pain conduction for the external genitourinary organs is S2-4, except for the testes (T10-L1).
- The kidneys receive 15% to 25% of the total cardiac output, with most of this blood directed to the renal cortex. Renal medullary papillae are more vulnerable to ischemic insults. Kidneys successfully autoregulate their blood flow between 60 and 160 mm Hg mean arterial pressures.
- The glomerular filtration rate (GFR) is the best measure of glomerular function. Creatinine clearance is a good measure of the GFR; urine output is not.
- Hypervolemia, acidemia, hyperkalemia, cardiorespiratory dysfunction, anemia, and bleeding disturbances are manifestations of chronic renal failure.
- Serum creatinine, most commonly used as a marker of renal function, has several limitations. Newer biomarkers, such as serum cystatin C, are better and earlier measures of acute kidney injury and the risk of end-stage renal disease, as well as related mortality.
- Although renal transplantation reverses most of the abnormalities in end-stage renal disease, dialysis improves only some and introduces additional complications of its own.
- Newer techniques, such as laser prostatectomy, are making transurethral resection of the prostate (TURP) syndrome a rare event. TURP syndrome is a constellation of symptoms caused by the absorption of hypotonic bladder irrigants. Cardiovascular and neurologic changes are due to hypoosmolality, hyponatremia, hyperglycemia, hyperammonemia, and hypervolemia.
- Regional anesthesia offers several advantages over general anesthesia for standard, but not laser, TURP. Yet, 30-day mortality rates remain unchanged at 0.2% to 0.8%.
- Laparoscopic surgery in urology frequently requires insufflation of carbon dioxide into the retroperitoneal space. In lengthy procedures, pneumomediastinum and subcutaneous emphysema of the head and neck may occur.
- Extracorporeal shock wave lithotripsy (ESWL) historically caused significant physiologic changes related to immersion in a water bath, but newer generations have eliminated the water bath and hence those risks. Shock waves can cause clinically insignificant dysrhythmias. Pregnancy and untreated bleeding disorders are contraindications to ESWL.
- Regarding renal tumors, 5% to 10% extend into the renal vein, inferior vena cava, and right atrium. Complications ranging from circulatory failure to embolization of tumor during surgery may occur. Cardiopulmonary bypass may be necessary for surgery.
- Radical prostatectomy may cause significant blood loss, and intraoperative venous air emboli can occur. Regional anesthesia with spontaneous ventilation is associated with less blood loss than general anesthesia and intermittent positive pressure ventilation. Other advantages of epidural anesthesia include a decreased incidence of deep vein thrombosis and the initiation of preoperative analgesia. Whether outcomes are dependent on the choice of anesthesia is not clear.
- Robotic radical prostatectomy is associated with reduced blood loss and postoperative pain compared with open radical prostatectomy. Anesthetic concerns are related to steep head-down tilt and pneumoperitoneum and include hypercarbia, hypoxemia, increased intraocular and intracranial pressures, decreased perfusion pressure to lower extremities, and positional injuries.
- Anesthetic concerns of robotic-assisted surgery include the length of surgical time, intravenous fluid management, pneumoperitoneum, and positioning. The most frequent reported complications are peripheral neuropathies, corneal abrasions, vascular complications (including compartment syndrome, rhabdomyolysis, and thromboembolic disease), and the effects of edema.
- Postoperative urinary retention should be considered as a source of postoperative pain after urologic surgery. Prompt diagnosis, either clinically or with ultrasound, and bladder catheterization if indicated (postvoid residual >600 mL) is effective and can prevent sequelae.

Patients requiring anesthesia for renal and genitourinary surgery are frequently at the extremes of age. In addition to the physiologic changes of aging in older patients, concomitant cardiovascular and respiratory comorbidity is common. A medical history, physical examination, and appropriate laboratory tests are necessary to evaluate concomitant disease. In pediatric urologic patients, a careful history should exclude other nonurologic congenital lesions.

Urologic procedures are performed mostly on the kidneys, adrenals, ureters, urinary bladder, prostate, urethra, penis, scrotum, testis, and spermatic cord. Because their sensory nerve supply is primarily thoracolumbar and sacral outflow (Table 59.1), these structures are well adapted for regional anesthesia.

Innervation of the Genitourinary System

The parts of the genitourinary system that are in the abdomen receive their nerve supply from the autonomic nervous system by means of sympathetic and parasympathetic pathways. The pelvic urinary organs and genitalia are supplied by somatic and autonomic nerves. Table 59.1 summarizes the pain conduction pathways and spinal levels of the genitourinary system.

KIDNEY AND ABDOMINAL URETER

Sympathetic nerves to the kidney originate as preganglionic fibers from the eighth thoracic through the first lumbar segments and converge at the celiac plexus and aorticorenal ganglia (Fig. 59.1). Postganglionic fibers to the kidney arise mainly from the celiac and aorticorenal ganglia. Some sympathetic fibers may reach the kidney via the splanchnic nerves. Parasympathetic input is from the vagus nerve.¹ Sympathetic fibers to the ureter originate from the tenth thoracic through the second lumbar segments and synapse with postganglionic fibers in the aorticorenal and superior and inferior hypogastric plexuses. Parasympathetic input is from the second through fourth sacral spinal segments.¹ Nociceptive fibers travel along the sympathetics to the same spinal segments. Pain from the kidney and ureter is referred mainly to the somatic distribution of the tenth thoracic through the second lumbar segments—the lower part of the back, flank, ilioinguinal region, and scrotum or labia. Effective neural block of these segments is necessary to provide adequate analgesia or anesthesia.

BLADDER AND URETHRA

Sympathetic nerves to the bladder and urethra originate from the eleventh thoracic to the second lumbar segments, travel through the superior hypogastric plexus, and supply the bladder through the right and the left hypogastric nerves.² Parasympathetic nerves arise from the second through the fourth sacral segments and form the pelvic parasympathetic plexus, which is joined by the hypogastric plexus. Vesical branches proceed toward the bladder base, where they provide the nerve supply to the bladder and proximal part of the urethra (Fig. 59.2). Parasympathetic fibers are the main motor supply to the bladder (with the exception of the trigone) and far outnumber sympathetic fibers in the bladder.²

TABLE 59.1 Pain Conduction Pathways and Spinal Segment Projection of Pain of the Genitourinary System

Organ	Sympathetics, Spinal Segments	Parasympathetics	Spinal Levels of Pain Conduction
Kidney	T8-L1	CN X (vagus)	T10-L1
Ureter	T10-L2	S2-4	T10-L2
Bladder	T11-L2	S2-4	T11-L2 (dome), S2-4 (neck)
Prostate	T11-L2	S2-4	T11-L2, S2-4
Penis	L1 and L2	S2-4	S2-4
Scrotum	NS	NS	S2-4
Testes	T10-L2	NS	T10-L1

NS, Not significant for nociceptive function.

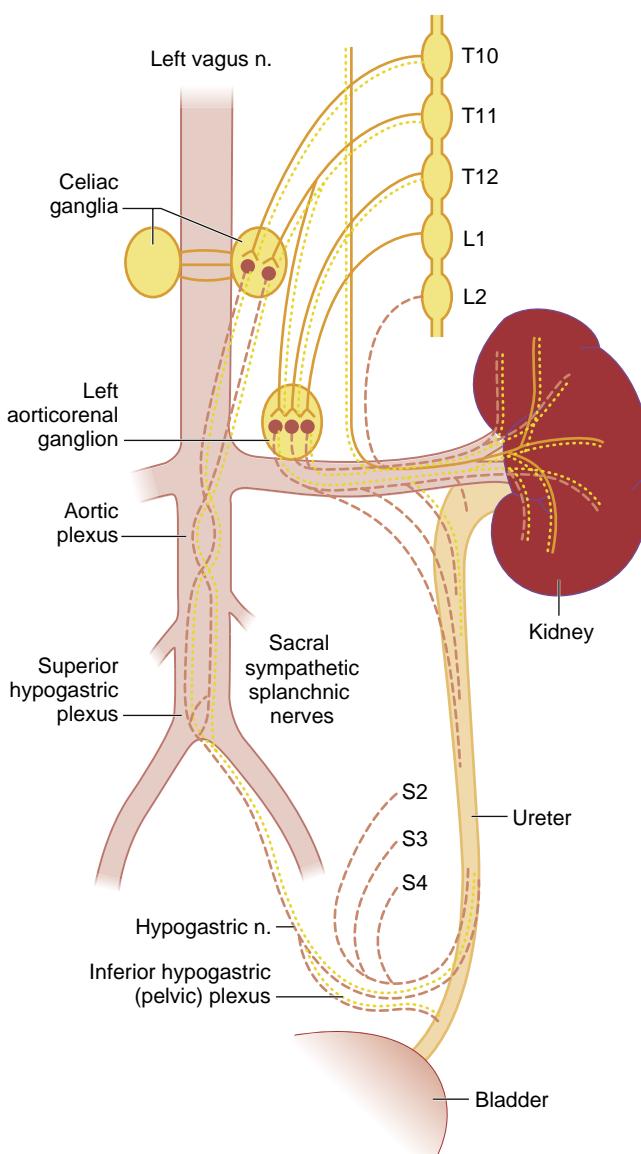


Fig. 59.1 Autonomic and sensory innervation of the kidney and ureters. Solid line indicates preganglionic fibers; dashed line indicates postganglionic fibers; and dotted line indicates sensory fibers. (From Gee WF, Ansell JF. Pelvic and perineal pain of urologic origin. In: Bonica JJ, ed. *The Management of Pain*. 2nd ed. Philadelphia: Lea & Febiger; 1990:1368–1378.)

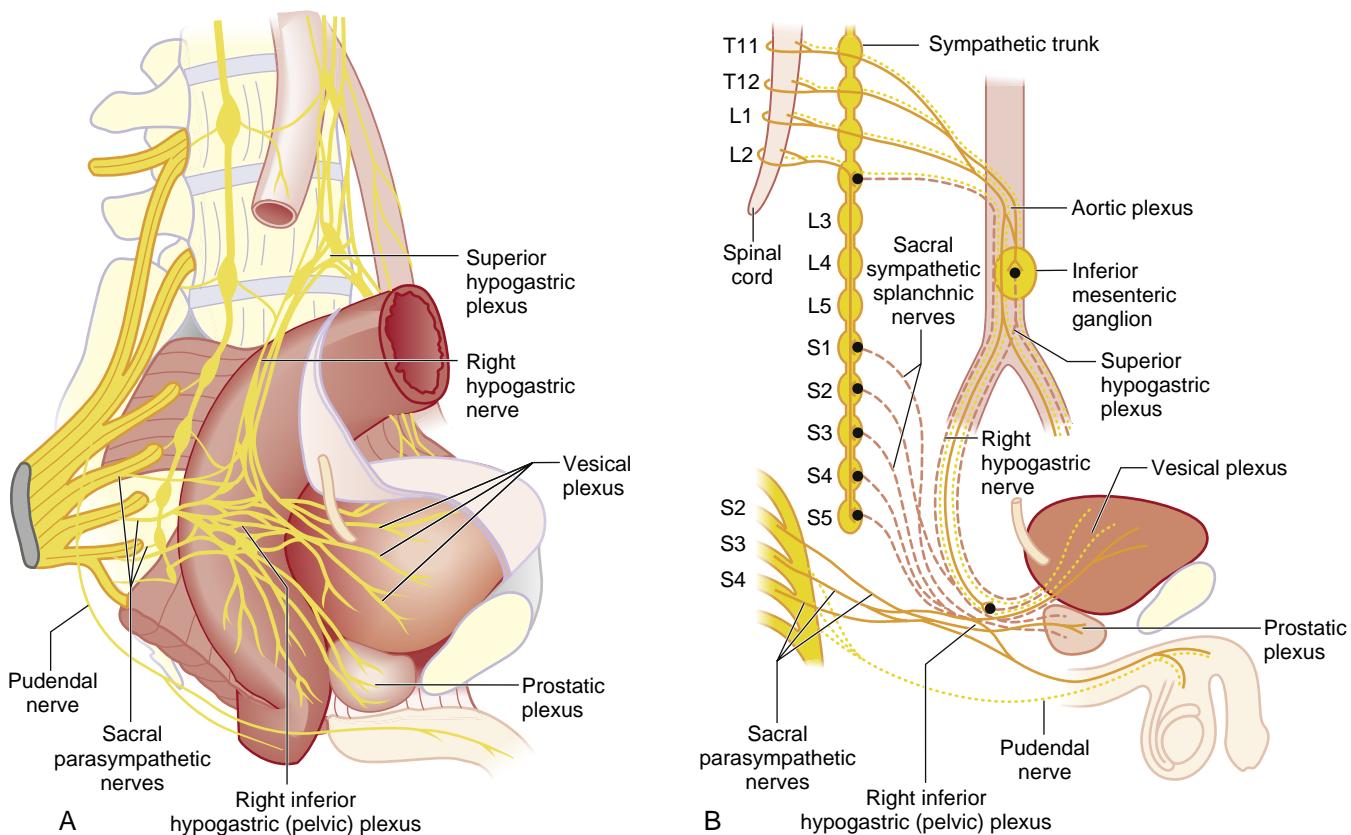


Fig. 59.2 (A) Nerve supply of the urinary bladder and prostate showing the relationship of the various nerve structures to the large intestine and their distribution in the bladder and prostate. (B) Schematic illustration showing the segmental nerve supply to the bladder, penis, and scrotum. *Solid lines* indicate preganglionic fibers; *dashed lines* indicate postganglionic fibers; and *dotted lines* indicate sensory fibers. (From Gee WF, Ansell JF. Pelvic and perineal pain of urologic origin. In: Bonica JJ, ed. *The Management of Pain*. 2nd ed. Philadelphia: Lea & Febiger; 1990:1368-1378.)

The afferents carrying sensations of stretch and fullness of the bladder are parasympathetic, whereas pain, touch, and temperature sensations are carried by sympathetic nerves. Sympathetic fibers are predominantly α -adrenergic in the bladder base and urethra, and β -adrenergic in the bladder dome and lateral wall. Knowledge of these aspects of neuroanatomy is important to appreciate the pharmacologic effects on the urologic system of neural ablation or regional block and drugs with adrenergic or cholinergic effects.²

PROSTATE AND PROSTATIC URETHRA

The prostate and the prostatic urethra receive sympathetic and parasympathetic supply from the prostatic plexus arising from the pelvic parasympathetic plexus, which is joined by the hypogastric plexus. The spinal origin of the nerve supply is primarily lumbosacral (see Fig. 59.2).²

PENIS AND SCROTUM

The autonomic supply to the penile urethra and the cavernous tissue comes from the prostatic plexus. Somatic fibers from the pudendal nerve (S2-4) supply the external sphincter. The dorsal nerve of the penis, the first branch of the pudendal nerve, is its main sensory supply. The scrotum is innervated anteriorly by the ilioinguinal and genitofemoral nerves (L1 and L2) and posteriorly by perineal branches of the pudendal nerve (S2 and S4).²

TESTES

The testes descend from their intraabdominal location to the scrotum during fetal development. Because they share their embryologic origin with the kidney, their nerve supply is similar to that of the kidney and upper part of the ureter and extends up to the T10 spinal segment.²

Renal Blood Flow

The kidneys receive approximately 15% to 25% of total cardiac output, or 1 to 1.25 L/min of blood, through the renal arteries, depending on the state of the body. Most of the blood is received by the renal cortex, with only 5% of cardiac output flowing through the renal medulla, which makes the renal papillae vulnerable to ischemic insults. Renal blood flow is regulated by various mechanisms that control the activity of vascular smooth muscle and alter vascular resistance. Sympathetic tone of renal vessels increases during exercise to shunt renal blood flow to exercising skeletal muscle; similarly, renal blood vessels relax during the resting condition of the body. Sympathetic stimulation resulting from surgery can increase vascular resistance and reduce renal blood flow, whereas anesthetics may reduce renal blood flow by decreasing cardiac output.

Glomerular capillaries separate afferent arterioles from efferent arterioles. Glomerular capillaries are high-pressure systems, whereas peritubular capillaries are low-pressure systems. Consequently, the glomerular capillaries are a

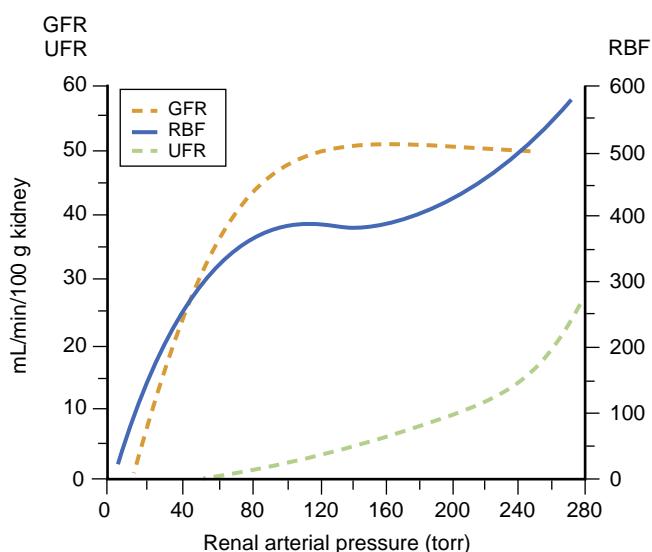


Fig. 59.3 Autoregulation of renal blood flow (RBF) and the glomerular filtration rate (GFR). The relationships between RBF, GFR, and urine flow rate (UFR) and mean renal arterial pressure in dogs are shown as renal arterial pressure is varied from 20 to 280 mm Hg. Autoregulation of RBF and GFR is observed between approximately 80 and 180 mm Hg. (Redrawn from Hemmings HC. Anesthetics, adjuvants and drugs and the kidney. In: Malhotra V, ed. *Anesthesia for Renal and Genitourinary Surgery*. New York: McGraw-Hill; 1996:18.)

fluid-filtering system, whereas the peritubular capillaries are a fluid-absorbing system. The vasa recta, a specialized portion of peritubular capillaries formed from efferent arterioles, are important in the formation of concentrated urine by a countercurrent mechanism. An intrinsic mechanism that causes vasodilation and vasoconstriction of renal afferent arterioles regulates the autoregulation of renal blood flow. A decrease in mean arterial pressure also decreases renal blood flow and eventually affects the glomerular filtration rate (GFR) when the pressure decreases to less than 60 mm Hg. A persistently low mean arterial pressure greater than 60 mm Hg affects renal blood flow but does not affect the GFR because of the intrinsic mechanism of autoregulation (Fig. 59.3). Autoregulation maintains mean arterial pressure between 60 and 160 mm Hg in intact and denervated kidneys.³

Although knowledge of neuroanatomy and renal blood flow is essential to provide adequate anesthesia, a thorough understanding of renal physiology and pharmacology is equally important. Genitourinary surgical patients frequently have mechanical or functional renal disease. Anesthetics and surgery can significantly alter renal function. Conversely, renal dysfunction significantly affects the pharmacokinetics and pharmacodynamics of anesthetics and adjuvant drugs. Evaluation of a patient with renal disease is discussed later.

Anesthesia for Patients With Renal Disease

EVALUATION OF RENAL FUNCTION

Renal disease can be discovered incidentally during a routine medical evaluation, or patients may exhibit evidence of renal dysfunction, such as hypertension, edema, nausea,

TABLE 59.2 Commonly Ordered Renal Function Tests

Test Name	Reference Range	Units
Urea nitrogen	5-25	mg/dL
Creatinine	0.5-1.5	mg/dL
Sodium	133-147	mmol/L
Potassium	3.2-5.2	mmol/L
Chloride	94-110	mmol/L
CO ₂	22-32	mmol/L
Uric acid	2.5-7.5	mg/dL
Calcium	8.5-10.5	mg/dL
Phosphorus	2.2-4.2	mg/dL
Urinalysis, routine		
Color	Straw-amber	
Appearance	Clear-hazy	
Protein	0	mg/dL
Blood	Negative	
Glucose	0	mg/dL
Ketones	0	mg/dL
pH	4.5-8.0	
Specific gravity	1.002-1.030	
Bilirubin	Negative	
Urinalysis, microscopic		
Red blood cells	0-3	per high-power field
White blood cells	0-5	per high-power field
Casts	0-2	per low-power field

From Miller ED Jr. Understanding renal function and its preoperative evaluation. In: Malhotra V, ed. *Anesthesia for Renal and Genitourinary Surgery*. New York: McGraw-Hill; 1996:9.

and hematuria. The initial approach in both situations should be to assess the cause and severity of renal abnormalities. In all cases, this evaluation includes (1) an estimation of disease duration, (2) a careful urinalysis, and (3) an assessment of the GFR. The history and physical examination, although equally important, are variable among renal syndromes; specific symptoms and signs are discussed in sections on each disease entity. Further diagnostic categorization is based on anatomic distribution: prerenal disease, postrenal disease, and intrinsic renal disease. Intrinsic renal disease can be divided further into glomerular, tubular, interstitial, and vascular abnormalities. Laboratory tests useful in evaluating renal function are described next (Table 59.2).

GLOMERULAR FUNCTION

Glomerular Filtration Rate

The GFR is the best measure of glomerular function. Normal GFR is approximately 125 mL/min. However, manifestations of reduced GFR are not seen until the GFR has decreased to 50% of normal. When GFR decreases to 30% of normal, a stage of moderate renal insufficiency ensues.

TABLE 59.3 Clinical Abnormalities in Chronic Renal Failure and Their Response to Dialysis and Erythropoietin Treatment

Improved by Dialysis	Improved by Adding Erythropoietin	Variable Response	Not Improved	Develop After Dialysis Therapy
Volume expansion and contraction	Fatigue	Secondary hyperparathyroidism	Increased lipoprotein level	Adynamic osteomalacia
Hypernatremia and hyponatremia	Impaired mentation	Hyperuricemia	Decreased high-density lipoprotein level	β_2 -Microglobulinemia
Hyperkalemia and hypokalemia	Lethargy	Hypertriglyceridemia	Impaired growth and development	Muscle cramps
Metabolic acidosis	Pallor	Protein-calorie malnutrition	Infertility and sexual dysfunction	Dialysis dysequilibrium syndrome
Hyperphosphatemia	Anemia	Headache	Amenorrhea	Hypotension and arrhythmias
Hypocalcemia	Bleeding diathesis	Peripheral neuropathy	Sleep disorders	Hepatitis
Vitamin D-deficient osteomalacia		Restless legs syndrome	Pruritus	Idiopathic ascites
Carbohydrate intolerance		Paralysis	Lymphocytopenia	Peritonitis
Hypothermia		Seizures	Splenomegaly and hypersplenism	Leukopenia
Asterixis		Myopathy		Hypocomplementemia
Muscular irritability		Arterial hypertension		
Myoclonus		Cardiomyopathy		
Coma		Accelerated atherosclerosis		
Congestive heart failure or pulmonary edema		Vascular calcification		
Pericarditis		Hyperpigmentation		
Uremic lung		Peptic ulcer		
Ecchymoses		Gastrointestinal bleeding		
Uremic frost		Increased susceptibility to infection		
Anorexia				
Nausea and vomiting				
Uremic fetor				
Gastroenteritis				

Patients remain asymptomatic with only biochemical evidence of a decline in GFR (i.e., an increase in serum concentrations of urea and creatinine). Further workup usually reveals other abnormalities, such as nocturia, anemia, loss of energy, decreasing appetite, and abnormalities in calcium and phosphorus metabolism.

As the GFR decreases further, a stage of severe renal insufficiency begins. This stage is characterized by profound clinical manifestations of uremia and biochemical abnormalities, such as acidemia; volume overload; and neurologic, cardiac, and respiratory manifestations. At the stages of mild and moderate renal insufficiency, intercurrent clinical stress may compromise renal function further and induce signs and symptoms of overt uremia. When the GFR is 5% to 10% of normal, it is called end-stage renal disease (ESRD), and continued survival without renal replacement therapy becomes impossible (Table 59.3).

Blood Urea Nitrogen

The blood urea nitrogen (BUN) concentration is not a direct correlate of reduced GFR. BUN is influenced by nonrenal variables, such as exercise, bleeding, steroids, and massive tissue breakdown. The more important factor is that BUN is not elevated in kidney disease until the GFR is reduced to almost 75% of normal.¹

Creatinine and Creatinine Clearance

Measurements of creatinine provide valuable information regarding general kidney function. Creatinine in serum results from turnover of muscle tissue and depends on daily dietary intake of protein. Normal values are 0.5 to 1.5 mg/100 mL; values of 0.5 to 1 mg/100 mL are present during pregnancy. Creatinine is freely filtered at the

glomerulus, and apart from an almost negligible increase in content because of secretion in the distal nephron, it is neither reabsorbed nor secreted. Serum creatinine measurements reflect glomerular function (Fig. 59.4),⁴ and creatinine clearance is a specific measure of GFR. Creatinine clearance can be calculated by the following formula derived by Cockcroft-Gault that accounts for age-related decreases in GFR, body weight, and sex:

$$\text{Creatinine clearance (mL/min)} = \frac{[(140 - \text{Age}) \times \text{Lean body weight (kg)}]}{[\text{Plasma creatinine (mg/dL)} \times 72]}$$

This value should be multiplied by 0.85 for women because a lower fraction of body weight is composed of muscle.

Because there is such a wide range in normal values, a 50% increase in serum creatinine concentration, indicative of a 50% reduction in GFR, may go undetected unless baseline values are known. In addition, excretion of drugs dependent on glomerular filtration may be significantly decreased despite what might seem to be only slightly elevated serum creatinine values (1.5–2.5 mg/100 mL). The serum creatinine concentration and clearance are better indicators of general kidney function and GFR than are similar measurements of urea nitrogen (Box 59.1). However, there are disease states in which even the serum creatinine can be affected independent of the GFR (Table 59.4). The main limitation of current GFR estimates is the greater inaccuracy in populations without known chronic kidney disease than in those with the disease. Nonetheless, current GFR estimates facilitate detection, evaluation, and management of the disease, and they should result in improved patient care and better clinical outcomes.⁵

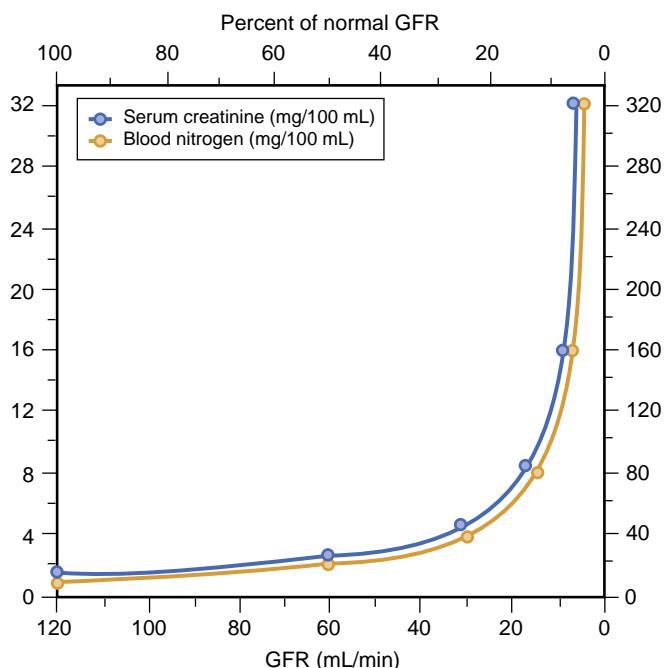


Fig. 59.4 Theoretic relationship between blood urea nitrogen and creatinine versus glomerular filtration rate (GFR). (Redrawn from Kassirer JP. Clinical evaluation of kidney function—glomerular function. *N Engl J Med*. 1971;285:385.)

BOX 59.1 Conditions Affecting Blood Urea Nitrogen Independently of Glomerular Filtration Rate

Increased Blood Urea Nitrogen

- Reduced effective circulating blood volume (prerenal azotemia)
- Catabolic states (gastrointestinal bleeding, corticosteroid use)
- High-protein diets
- Tetracycline

Decreased Blood Urea Nitrogen

- Liver disease
- Malnutrition
- Sickle cell anemia
- Syndrome of inappropriate secretion of antidiuretic hormone

TUBULAR FUNCTION

Concentration

Urinary specific gravity is an index of the kidney's concentrating ability, specifically renal tubular function. Determination of urinary osmolality (i.e., measurement of the number of moles of solute [osmoles] per kilogram of solvent) is a similar, more specific test. Excretion of concentrated urine (specific gravity, 1.030; 1050 mOsm/kg) is indicative of excellent tubular function, whereas a urinary osmolality fixed at that of plasma (specific gravity 1.010; 290 mOsm/kg) indicates renal disease. The urinary dilution mechanism persists after concentrating defects are present, so a urinary osmolality of 50 to 100 mOsm/kg still may be consistent with advanced renal disease.

TABLE 59.4 Conditions Affecting Serum Creatinine Independently of Glomerular Filtration Rate

Condition	Mechanism
CONDITIONS CAUSING ELEVATION	
Ketoacidosis	Noncreatinine chromogen
Cephalothin, cefoxitin	Noncreatinine chromogen
Flucytosine	Noncreatinine chromogen
Other drugs—aspirin, cimetidine, probenecid, trimethoprim	Inhibition of tubular creatinine secretion
CONDITIONS CAUSING DECREASE	
Advanced age	Physiologic decrease in muscle mass
Cachexia	Pathologic decrease in muscle mass
Liver disease	Decreased hepatic creatine synthesis and cachexia

Protein

Patients without renal disease can excrete 150 mg of protein per day; greater amounts may be present after strenuous exercise or after standing for several hours. Massive proteinuria (i.e., >750 mg/day) is always abnormal and usually indicates severe glomerular damage.

Glucose

Glucose is freely filtered at the glomerulus and is subsequently reabsorbed in the proximal tubule. Glycosuria signifies that the ability of the renal tubules to reabsorb glucose has been exceeded by an abnormally heavy glucose load and is usually indicative of diabetes mellitus. Glycosuria also may be present in hospitalized patients without diabetes who are receiving intravenous glucose infusions.

ADDITIONAL DIAGNOSTIC TESTS

Urinalysis and Appearance

Gross and microscopic observations of urine and its sediment, along with determination of urinary pH, specific gravity, protein content, and glucose content, are two of the most readily available, inexpensive, and informative laboratory tests. The gross appearance of urine may indicate the presence of bleeding or infection in the genitourinary tract. Microscopic examination of urinary sediment may reveal casts, bacteria, and various cell forms, supplying diagnostic information in patients with renal disease.

Urine and Serum Electrolytes With Blood Gases

Sodium, potassium, chloride, and bicarbonate concentrations should be determined if impairment in renal function is suspected. However, the results of these tests usually remain normal until frank renal failure is present and hyperkalemia does not occur until patients are uremic. Measuring urinary sodium or chloride excretion is especially useful when attempting to differentiate between causes of hyponatremia, as seen in volume contraction (whether a decrease in total circulatory volume or a decrease in effective arterial blood volume), versus conditions associated with increased salt loss, such as the syndrome of inappropriate secretion of

antidiuretic hormone, salt-losing nephropathy, or adrenal insufficiency.⁶ If significant renal disease is present, patients consuming a diet high in animal protein may develop metabolic acidosis.

Novel Biomarkers of Renal Function. Although serum creatinine is most commonly used as a marker of GFR and hence renal function, it has some limitations in that it is influenced by nonrenal factors such as age, gender, muscle mass and metabolism, diet, and hydration. Furthermore, creatinine levels may take several hours or days to reach a steady state to accurately reflect the GFR as indicator of renal function in acute kidney injury (AKI). Several new markers of renal function have been identified. Serum cystatin C, a ubiquitous protein that is exclusively excreted by glomerular filtration, is less influenced by variations in muscle mass and nutrition than is creatinine. It may better predict risk of death and ESRD across diverse populations.⁷

Other novel biomarkers such as *N*-acetyl- β -D-glucosaminidase, kidney injury molecule-1, interleukin-18, uromodulin, and microRNA are also showing promise at early detection of kidney injury. These biomarkers may have a future role in reducing morbidity and mortality associated with kidney injury in the perioperative setting.⁸

Electrocardiogram. The electrocardiogram reflects the toxic effects of potassium excess more closely than determination of the serum potassium concentration.

Imaging Studies

Renal Ultrasound. Ultrasound is the most frequently used diagnostic examination for the evaluation of the kidneys and urinary tract. It is noninvasive, uses no ionizing radiation, and requires minimal patient preparation. It is the first-line examination in patients with renal dysfunction for assessing kidney size and the presence or absence of hydronephrosis and obstruction. It can be used to assess the vasculature of native and transplanted kidneys. Ultrasound is also used to evaluate renal structure and to characterize renal masses.⁹

Computed Tomography Scan of Kidneys. A stone protocol computed tomography (CT) scan of the kidneys, ureter, and bladder has become the study of choice for the detection of kidney stones because of its ability to detect stones of all kinds, including uric acid stones and nonobstructing stones in the ureter. Even in areas in which ultrasound is the first-line imaging modality, CT offers a complementary and sometimes superior means of imaging. Masses in the kidney can be evaluated using either contrast-enhanced CT or renal ultrasound.⁹

Computed Tomography Angiography. CT angiography is used for the evaluation of renal artery stenosis and is emerging rapidly as a useful diagnostic tool. Although it is comparable with magnetic resonance angiography (MRA) as a noninvasive study, it requires the use of iodinated contrast material, which may cause contrast media-induced nephropathy.⁹

Magnetic Resonance Imaging With Magnetic Resonance Angiography. Magnetic resonance imaging

allows for detailed tissue characterization of the kidney and surrounding structures. It is a good alternative to contrast-enhanced CT, especially in patients who cannot tolerate iodinated contrast material and in patients for whom reduction of radiation exposure is desired, such as pregnant women and children. Gadolinium, a paramagnetic intravenous contrast agent, is used routinely in MRA because it improves lesion detection and diagnostic accuracy. It is generally well tolerated with a good safety profile. However, nephrogenic systemic fibrosis, a rare, multiorgan, fibrosing condition for which there is no known effective treatment, has been recognized to occur in patients with moderate to severe renal disease.⁹

IMPORTANT PATHOPHYSIOLOGIC MANIFESTATIONS OF CHRONIC RENAL FAILURE

Hypervolemia

Total body contents of sodium and water are increased in chronic renal failure (CRF),⁶ although this increase might not be clinically apparent until the GFR is reduced to very low levels. Weight gain is usually associated with volume expansion and is offset by the concomitant loss of lean body mass. The combination of loop diuretics with metolazone, which acts by inhibiting the Na-Cl cotransporter of the distal convoluted tubule, can overcome diuretic resistance.

Acidemia

Although urine can be acidified normally in most patients with CRF, these patients have a reduced ability to produce ammonia. In the early stages, the accompanying organic anions are excreted in urine, and the metabolic acidosis is of the non-anion gap variety. With advanced renal failure, a fairly large "anion gap" can develop (to approximately 20 mmol/L), however, with a reciprocal decrease in plasma bicarbonate ion (HCO_3^-) concentration. This acidemia is usually corrected by hemodialysis. Although acidemia is well compensated in moderate CRF, patients can become acidemic and hyperkalemic¹⁰ in the postoperative period (Table 59.5).

Hyperkalemia

The approximate daily filtered load of potassium (K^+) is 700 mmol. Most of this filtered load is reabsorbed in tubule segments, and most of the K^+ excreted in the final urine reflects events governing K^+ handling at the level of the cortical collecting tubule and beyond. K^+ excretion in the gastrointestinal tract is augmented in patients with CRF. However, hyperkalemia may be precipitated in numerous clinical situations, including protein catabolism, hemolysis, hemorrhage, transfusion of stored red blood cells, metabolic acidosis, and exposure to various medications that inhibit K^+ entry into cells or K^+ secretion in the distal nephron.

Cardiac and Pulmonary Manifestations

Hypertension is a common complication of CRF and ESRD. Because hypervolemia is the major cause of hypertension in uremia, normotension is usually restored by the use of diuretics in predialysis patients or by dialysis in ESRD patients. However, despite therapy, patients remain hypertensive due to activation of the renin-angiotensin system and autonomic factor. Patients generally have left

TABLE 59.5 Metabolic Acidosis in Chronic Renal Failure

	PaCO₂ (mm Hg)	pH	HCO₃⁻ (mEq/L)	K⁺ (mEq/L)
Preoperative	32	7.32	17	5
Intraoperative	40	7.25	18	5.3
Postoperative	44	7.21	19	5.6
	48	7.18	19	5.9

The patient is a 36-year-old man with severe diabetic nephropathy and end-stage renal failure undergoing cadaver renal transplantation. Preoperatively, the patient has a chronic metabolic acidosis (HCO₃⁻, 17 mEq/L) with partial respiratory compensation (PaCO₂, 32 mm Hg; pH 7.32). Potassium is high normal at 5 mEq/L. Intraoperatively, he is given "standard" mechanical minute ventilation, and with "normal" PaCO₂ (40 mm Hg), the metabolic acidosis is unmasked (pH 7.25), and potassium increases to 5.3 mEq/L. His trachea is extubated at the end of the procedure, but graft function is sluggish, and the metabolic acidosis remains unchanged. With residual opioid-induced narcosis, moderate CO₂ retention occurs (PaCO₂, 44 mm Hg and 48 mm Hg), pH decreases further to 7.18, and a dangerous degree of hyperkalemia develops (K⁺, 5.9 mEq/L).

TABLE 59.6 Management Guidelines for Correction of Anemia of Chronic Renal Disease

ERYTHROPOIETIN	
Starting dosage	50-150 U/kg per week IV or SC (once, twice, or three times per week)
Target hemoglobin	11-12 g/dL
Optimal rate of correction	Increase hemoglobin by 1-2 g/dL over 4 wk
DARBEPOETIN ALFA	
Starting dosage	0.45 mg/kg administered as single IV or SC injection once weekly
	0.75 mg/kg administered as a single IV or SC injection once every 2 wk
Target hemoglobin	12 g/dL
Optimal rate of correction	Increase hemoglobin by 1-2 g/dL over 4-wk period
IRON	
Monitor iron stores by TSat and serum ferritin	
If patient is iron-deficient (TSat <20%; serum ferritin <100 g/L), administer iron, 50-100 mg IV twice per week for 5 wk; if iron indices are still low, repeat the same course	
If iron indices are normal but hemoglobin is still inadequate, administer IV iron as outlined above; monitor hemoglobin, TSat, and ferritin.	
Withhold iron therapy when TSat >50% or ferritin >800 ng/mL (>800 g/L)	

IV, Intravenous; SC, subcutaneous; TSat, percent transferrin saturation.

ventricular hypertrophy and accelerated atherosclerosis (disordered glucose and fat metabolism). Pericarditis can be observed in patients with inadequate dialysis unlike patients with CRF who undergo regular dialysis.

Pulmonary edema and restrictive pulmonary dysfunction are a common feature of patients in renal failure. Hypervolemia, heart failure, decreased serum oncotic pressure, and increased pulmonary capillary permeability contribute to the development of pulmonary edema. Diuretic therapy or dialysis can be effectively used to treat pulmonary congestion and edema due to excess intravascular volume.¹¹

Hematologic Manifestations

CRF usually causes a normochromic, normocytic anemia. Anemia is generally observed when the GFR decreases to

less than 30 mL/min and is due to insufficient production of erythropoietin by the diseased kidneys. Other factors are iron deficiency, either related to or independent of blood loss from repeated laboratory testing, blood retention in the dialyzer, or gastrointestinal bleeding.¹² Treatment of anemia with iron, darbepoetin alfa, and human recombinant erythropoietin (Table 59.6) restores a normal hematocrit and avoids repetitive red blood cell transfusions, reduces the requirement for hospitalization, and decreases cardiovascular mortality by approximately 30%.¹³

Prolongation of the bleeding time because of decreased activity of platelet factor 3, abnormal platelet aggregation and adhesiveness, and impaired prothrombin consumption contributes to the clotting defects. The abnormality in platelet factor 3 correlates can be corrected with dialysis, although prolongation of the bleeding time can be observed in well-dialyzed patients. Abnormal bleeding times and coagulopathy in patients with renal failure may be managed with desmopressin, cryoprecipitate, conjugated estrogens, blood transfusions, and erythropoietin use.⁹

EFFECTS OF DRUGS IN PATIENTS WITH REDUCED RENAL FUNCTION

Most anesthetic drugs are weak electrolytes and are lipid soluble in the un-ionized state; they are extensively reabsorbed by renal tubular cells. Termination of their action does not depend on renal excretion; redistribution and metabolism produce this effect. After biotransformation, these drugs are excreted in urine as water-soluble, polar forms of the parent compound. They are usually pharmacologically inactive, and their retention is harmless. Drugs with prominent central and peripheral nervous system activity in this category include most narcotics, barbiturates, phenothiazines, butyrophenone derivatives, benzodiazepines, ketamine, and local anesthetics. However, several drugs are lipid insoluble or are highly ionized in the physiologic pH range and are eliminated unchanged in urine. Their duration of action may be extended in patients with impaired renal function. Drugs in this category include muscle relaxants, cholinesterase inhibitors, thiazide diuretics, digoxin, and many antibiotics (Table 59.7).¹⁴

Opioids

Renal failure has implications of major clinical importance with respect to the metabolism and excretion of morphine

TABLE 59.7 Drugs Used or Encountered in Anesthesia Practice that Significantly Depend on Renal Elimination

Completely Dependent	Partially Dependent
Digoxin, inotropes (used frequently; monitoring of blood levels indicated in chronic renal failure)	Intravenous anesthetics—barbiturates
Others—aminoglycosides, vancomycin, cephalosporins, and penicillins	Muscle relaxants—pancuronium
	Anticholinergics—atropine, glycopyrrolate
	Cholinesterase inhibitors—neostigmine, edrophonium
	Others—milrinone, hydralazine, cycloserine, sulfonamides, and chlorpropamide

and meperidine. For the fentanyl congeners, the clinical importance of renal failure is less marked.¹⁵

Morphine is an opioid with active metabolites that depend on renal clearance mechanisms for elimination. Morphine is principally metabolized by conjugation in the liver, and the water-soluble glucuronides (morphine-3-glucuronide and morphine-6-glucuronide) are excreted via the kidney. The kidney also plays a role in the conjugation of morphine, accounting for nearly 40% of its metabolism.¹⁶ Patients with renal failure can develop high levels of morphine-6-glucuronide and life-threatening respiratory depression. In view of these changes induced by renal failure, alternatives to morphine should be considered in patients with severely altered renal clearance mechanisms.¹⁵

The clinical pharmacology of meperidine is also significantly altered by renal failure. Normeperidine, the chief metabolite, has analgesic and central nervous system (CNS) excitatory effects. Because the active metabolites are subject to renal excretion, this potential CNS toxicity secondary to normeperidine accumulation is especially a concern in patients in renal failure.¹⁷

The clinical pharmacology of the fentanyl congeners is not grossly altered by renal failure, although a decrease in plasma protein binding potentially can alter the free fraction of the fentanyl class of opioids.¹⁵ As with fentanyl, sufentanil pharmacokinetics are not altered in any consistent fashion by renal disease, although greater variability exists in the clearance and elimination half-life of sufentanil when patients have impaired renal function.¹⁸ An increased clinical effect is likely with alfentanil in renal failure because of a decreased initial volume of distribution and an increased free fraction of alfentanil.¹⁹ However, no delay in recovery after alfentanil administration should be expected. Neither the pharmacokinetics nor the pharmacodynamics of remifentanil are altered by impaired renal function.²⁰

Hydromorphone, as the parent drug, does not substantially accumulate in hemodialysis patients. Conversely, an active metabolite, hydromorphone-3-glucuronide, quickly accumulates between dialysis treatments but seems to be effectively removed during hemodialysis.²¹ With careful monitoring, hydromorphone can be used safely in patients who require dialysis. However, it should be used with

caution in patients with a GFR less than 30 mL/min and who have yet to start dialysis or who have withdrawn from dialysis.

Inhaled Anesthetics

All inhaled anesthetics are biotransformed to some extent, with the nonvolatile products of metabolism eliminated almost entirely by the kidney.²² Reversal of the CNS effects of inhaled anesthetics depends on pulmonary excretion; therefore impaired kidney function would not alter the response to these anesthetics. From the viewpoint of selecting an anesthetic that would not be harmful to patients with mild or moderate impairment of renal function, all of the modern potent inhaled vapor anesthetics are acceptable. Fluoride levels after isoflurane increase by only 3 to 5 μ M²³ and by only 1 to 2 μ M after halothane²⁴; therefore these anesthetics have no nephrotoxic potential.

Desflurane and sevoflurane, two newer inhaled anesthetics, are remarkably different from each other with respect to their molecular stability and biotransformation. Desflurane is highly stable and resists degradation by soda lime²⁵ and the liver. The mean inorganic fluoride concentration after 1 minimum alveolar concentration (MAC)-hour exposure to desflurane was less than 1 μ M.²⁶ The safety of desflurane in renal failure patients has been confirmed. In addition, more sensitive indices of renal function—urine retinol-binding protein and β -N-acetylglucosaminidase—showed no evidence of renal damage. Prolonged exposure to desflurane (7 MAC-hours) has been associated with normal renal function.²⁷

Sevoflurane is not very stable. Soda lime causes it to decompose,²⁸ and it is biotransformed by the liver. Plasma inorganic fluoride concentrations approaching nephrotoxic levels (50 μ mol/L)²⁹ have been reported after prolonged inhalation of sevoflurane. However, no evidence of gross changes in renal function has been found in humans.³⁰ Data also suggest that sevoflurane can safely be delivered at fresh gas flows as low as 1 L/min without significant production of a breakdown product named compound A (fluoromethyl-2,2-difluoro-1-[trifluoromethyl] vinyl ether), which is considered potentially nephrotoxic.³¹

Inhaled anesthetics cause a transient reversible depression in renal function. GFR, renal blood flow, urine output, and urinary excretion of sodium are decreased (Table 59.8). Probable mechanisms include loss of renal autoregulation, activation of neurohumoral factors (e.g., antidiuretic hormone, vasopressin, renin), and neuroendocrine responses. Although most inhaled anesthetics have been shown to reduce GFR and urinary excretion of sodium, studies examining their effects on renal blood flow have yielded conflicting results, which can be explained by differences in experimental methodology. Data suggest that renal blood flow is maintained with halothane, isoflurane, and desflurane^{32,33} but that it is decreased with sevoflurane.³⁴

Intravenous Anesthetics

Reversal of CNS effects after the administration of ultra-short-acting barbiturates such as thiopental and methohexitol occurs as a result of redistribution, and hepatic metabolism is the sole route of elimination of these drugs. Thiopental is 75% to 85% bound to albumin,³⁵ the concentration of which may be markedly reduced in uremia.

TABLE 59.8 Effects of Various Anesthetics on Renal Function

	RBF	GFR	Urine Output	Urine Solutes
General anesthesia	↓	↓	↓	↓
Intravenous anesthetics				
Thiopental	↔	↓	↓	↓
Midazolam	↔	↔	↓	↔
Fentanyl (high dose)	↔	↔	↔	↔
Inhaled anesthetics				
Halothane	↔	↓	↓	↓
Isoflurane, Enflurane	↔↓	↓↓	↓↓	↓↓
PEEP Isoflurane	↓↔	↓↓	↓↓	↓↓
Regional anesthesia PEEP	↓	↓	↓	○
Epidural (with epinephrine) Regional anesthesia	↓	↓	↓	○
Epidural (without epinephrine) Epidural (with epinephrine)	↔↓	↔↓	↔↓	○○
Spinal epidural (without epinephrine)	↔↔	↔↔	↔↔	○○
Spinal	↔	↔	↔	○

GFR, Glomerular filtration rate; PEEP, positive end-expiratory pressure; RBF, renal blood flow; ↔, no significant change; ○, significant data; ↓, decrease.

Although conflicting reports of anesthetic effects on RBF have been reported because of different investigative methods, the current literature seems to support these data.

From Hemmings HC Jr. Anesthetics, adjuvant drugs and the kidney. In: Malhotra V, ed. *Anesthesia for Renal and Genitourinary Surgery*, New York: McGraw-Hill; 1996:20.

Because it is a highly bound drug, reduced binding permits a greater proportion of an administered dose of thiopental to reach receptor sites. In addition, thiopental is a weak acid, with its pK_a in the physiologic range; acidosis results in more un-ionized, nonbound, active thiopental. In combination, these changes produce an increase in the free fraction of thiopental from 15% in normal patients to 28% in patients with CRF. With thiopental metabolism essentially unchanged in renal disease, the dose to produce and maintain anesthesia should be reduced.³⁶ The same considerations are true for methohexitol, although metabolism plays a slightly greater part in the termination of its therapeutic effect.³⁷

Propofol does not adversely affect renal function as reflected by measurements of creatinine concentration. Prolonged infusions of propofol may result in the excretion of green urine because of the presence of phenolic metabolites in the urine. This discoloration does not affect renal function. Urate excretion is increased after the administration of propofol and is usually manifested as cloudy urine when urate crystallizes under conditions of low pH and temperature.³⁸

There are no reports of the disposition of narcotics and tranquilizers when used in large dosage for anesthesia in uremic patients. These drugs are extensively metabolized before excretion; therefore they should not have a particularly prolonged effect. The benzodiazepines, especially diazepam,¹⁴ have a long half-life and tend to accumulate. Because of the greater ease of reversibility of the potent inhaled anesthetics versus intravenous drugs, inhaled anesthetics may offer some advantages for the induction of general anesthesia in uremic patients.

Muscle Relaxants and Their Antagonists

Succinylcholine has been used without difficulty in patients with decreased or absent renal function. Its metabolism is catalyzed by pseudocholinesterase to yield the nontoxic end products succinic acid and choline. The metabolic precursor of these two compounds, succinylmonocholine, is excreted by the kidneys. Large doses of succinylcholine, which might result from prolonged infusion, should be avoided in patients with renal failure. Although pseudocholinesterase levels are reduced in uremia,³⁹ these reductions are insufficient and cause a prolonged block. Hemodialysis has been reported to have no effect on cholinesterase levels.⁴⁰

Administration of succinylcholine causes a rapid, transient increase of 0.5 mEq/L in the serum potassium concentration. In traumatized, burned, or neurologically injured patients, the increase may be 5 to 7 mEq/L, probably as a consequence of denervation supersensitivity of the muscle membrane to succinylcholine and to acetylcholine,⁴¹ which can result in cardiovascular collapse. Likewise, an exaggerated increase in serum potassium could be particularly dangerous in uremic patients with hyperkalemia; therefore the use of succinylcholine is inadvisable, unless the patient has undergone dialysis within 24 hours before surgery. If the patient has recently undergone dialysis or has normal serum potassium, the use of succinylcholine is safe in the absence of other contraindications to the medication.

The disposition of nondepolarizing muscle relaxants has been well studied. Renal failure influences the pharmacology of nondepolarizing muscle relaxants by producing either decreased elimination of the drug or its metabolites by the kidney or decreased activity of enzymes that metabolize the drug, such as in the case of mivacurium (Table 59.9).

TABLE 59.9 Pharmacokinetics Data for Nondepolarizing Muscle Relaxants in Normal and Anephric Patients

Drug	Patients Studied	Elimination Half-Life (h)	Clearance (mL/kg/min)	Volume of Distribution (L/kg)
Vecuronium	Normal	0.9	5.3	0.20
	Anephric	1.4	3.1	0.24
Atracurium	Normal	0.3	6.1	0.18
	Anephric	0.4	6.7	0.22
Pancuronium	Normal	1.7	1	0.14
	Anephric	8.2	0.3	0.14
Rocuronium	Normal	0.71	2.9	0.207
	Anephric	0.97	2.9	0.264
Cisatracurium	Normal	—	5.2	0.031
	Anephric	—	—	—
Mivacurium	Normal	0.03	106	0.278
	Anephric	0.06	80	0.478

Consequently, the duration of action of muscle relaxants may be prolonged in patients with renal failure.

Approximately 40% to 50% of a long-acting nondepolarizing muscle relaxant, pancuronium, is excreted in urine. A portion of this excretion occurs after biotransformation to the less active metabolite 3-hydroxypancuronium.⁴² Pancuronium has a prolonged terminal elimination half-life in patients with reduced renal function (see Table 59.9)⁴³; therefore it should be administered cautiously, particularly when several doses are required.

Two nondepolarizing muscle relaxants, atracurium and vecuronium, were introduced into clinical practice during the early 1980s. Atracurium is degraded by enzymatic ester hydrolysis and nonenzymatic alkaline degradation (Hofmann elimination) to inactive products that are not dependent on renal excretion for termination of action.⁴⁴ Predictably, their terminal elimination half-life and indices of neuromuscular blockade (onset, duration, and recovery) are the same in patients with normal and absent renal function.⁴⁵

Approximately 30% of a dose of vecuronium is eliminated by the kidneys. Lynam and colleagues⁴⁶ found that the duration of neuromuscular blockade after the administration of vecuronium was longer in patients with renal failure than in patients with normal renal function (99 vs. 54 minutes) because of a longer elimination half-life (83 vs. 52 minutes) and lower plasma clearance (3.1 mL/kg/min vs. 5.3 mL/kg/min). In a related area, an interaction between the solvent of cyclosporine (Kolliphor EL) with atracurium and vecuronium has been reported, with the action of these muscle relaxants potentiated in cats,⁴⁷ but it is unknown whether such potentiation also occurs in human renal transplant recipients.

Cisatracurium is the single cis isomer of atracurium. Organ-independent mechanisms (Hofmann elimination) account for 77% of the total clearance of cisatracurium. Because renal excretion accounts for only 16% of the elimination of cisatracurium, renal failure should have little effect on its duration of action.⁴⁵

The short-acting drug mivacurium is metabolized by plasma pseudocholinesterase. Its effect has been shown to

be lengthened by 10 to 15 minutes in patients with ESRD, most likely because of a decrease in plasma cholinesterase activity in these patients associated with uremia or hemodialysis^{48,49} and there is a decrease in the mivacurium requirement by infusion in anephric patients.⁴⁹

Rocuronium is an aminosteroid nondepolarizing muscle relaxant. The elimination half-life of rocuronium is increased in renal failure because of an increase in the volume of distribution with no change in clearance. This explanation might account for a longer duration of action in anephric patients, although its clinical significance is uncertain.⁵⁰

Pharmacokinetics data for the cholinesterase inhibitors neostigmine, pyridostigmine, and edrophonium for normal, anephric, and renal transplant patients are presented in Table 59.10; there are no major differences among the three drugs.⁵¹⁻⁵³ Renal excretion is of major importance for the elimination of all three reversal drugs, with approximately 50% of neostigmine and 70% of pyridostigmine and edrophonium excreted in urine. Excretion of all the cholinesterase inhibitors is delayed in patients with impaired renal function to the same or perhaps to a slightly greater extent than is elimination of muscle relaxants. Reappearance of neuromuscular blockade after pharmacologic reversal of neuromuscular blockade in a patient with renal failure is, in most cases, due to some other cause. Table 59.10 contains data indicating that the pharmacokinetics of all the cholinesterase inhibitors is similar in healthy patients and in patients with well-functioning newly transplanted kidneys.

Sugammadex, a newer reversal drug, is a cyclodextrin molecule that inactivates aminosteroidal neuromuscular blockers, such as vecuronium and rocuronium, by selectively binding to them. The resultant sugammadex-neuromuscular blocker complex is excreted by the kidney. In patients with severe renal impairment, these cyclodextrin complexes can accumulate. Although sugammadex can effectively reverse neuromuscular blockade in these patients, the effect of prolonged exposure to sugammadex is unclear. There are insufficient data at this time to recommend the routine administration to patients with severe renal impairment.⁵⁴ There are also data to suggest that

TABLE 59.10 Pharmacokinetics Data for Cholinesterase Inhibitors in Normal, Anephric, and Renal Transplant Patients

Drug	Patients Studied	Elimination Half-Life (h)	Clearance (mL/kg/min)	Volume of Distribution (L/kg)
Neostigmine	Normal	1.3	8.4	0.7
	Anephric	3*	3.9*	0.8
	Renal transplant	1.7	9.4	1.1
Pyridostigmine	Normal	1.9	8.6	1.1
	Anephric	6.3*	2.1*	1
	Renal transplant	1.4	10.8	1
Edrophonium	Normal	1.9	8.2	0.9
	Anephric	3.6*	2.7*	0.7
	Renal transplant	1.4	9.9	0.9

* $P < .05$ vs. normal.

sugammadex complexes can be effectively dialyzed using high-flux hemodialysis.⁵⁵

Vasopressors and Antihypertensive Drugs

Patients with severe renal disease are frequently given antihypertensive and other cardiovascular medications. More than 90% of the thiazides⁵⁶ and 70% of furosemide⁵⁷ are excreted by the kidneys, and they have prolonged durations of action in patients with abnormal or absent renal function. Propranolol is almost completely metabolized in the liver,⁵⁸ and esmolol is biodegraded by esterases in the cytosol of red blood cells⁵⁹; therefore their effects are not prolonged in patients with abnormal or absent renal function. The calcium channel-blocking agents nifedipine, verapamil, and diltiazem are extensively metabolized in the liver to pharmacologically inert products; they can be administered in usual doses to patients with renal insufficiency.⁶⁰ Nitroglycerin can be useful because it is metabolized rapidly, with less than 1% excreted unchanged in urine.⁶¹

Sodium nitroprusside has had a resurgence in use since its initial introduction as a hypotensive drug in the 1920s. Cyanide is an intermediate in the metabolism of sodium nitroprusside, with thiocyanate being the final metabolic product. Although cyanide toxicity as a complication of sodium nitroprusside therapy is well described, it is less well appreciated that thiocyanate is also potentially toxic. The half-life of thiocyanate is normally more than 4 days, and it is prolonged in patients with renal failure. Hypoxia, nausea, tinnitus, muscle spasm, disorientation, and psychosis have been reported when thiocyanate levels are more than 10 mg/100 mL.⁶² Sodium nitroprusside is less desirable for prolonged administration than either trimethaphan or nitroglycerin.

Hydralazine is slower acting than the other three drugs discussed previously. Its action is terminated by hydroxylation and subsequent glucuronidation in the liver, with approximately 15% excreted unchanged in urine.⁶³ The elimination half-life of hydralazine is prolonged in patients with uremia; therefore caution is required when it is administered.⁶⁴ After a single intravenous dose of 0.5 mg/kg of labetalol, the volume of distribution, clearance, and elimination half-life were similar in patients with ESRD and in healthy volunteers.⁶⁵

If administration of a vasopressor is necessary, a direct α -adrenergic-stimulating drug such as phenylephrine would be effective. This type of vasopressor causes the greatest interference with renal circulation. Although β -adrenergic-stimulating drugs such as isoproterenol maintain heart and brain perfusion without renal vasoconstriction, they also increase myocardial irritability. When possible, it is best to substitute simple measures such as blood volume expansion for drug therapy. If these measures are inadequate, β -adrenergic-stimulating drugs or dopamine should be used.

ACUTE KIDNEY INJURY AND HEMODIALYSIS

Although often considered a discrete syndrome, AKI represents a diverse array of pathophysiologic processes of varied severity and cause. These include decreases in GFR as the result of disruption of normal renal perfusion without causing parenchymal injury; partial or complete obstruction to urinary flow; and a spectrum of processes with characteristic patterns of glomerular, interstitial, tubular, or vascular parenchymal injury. AKI-precipitating events are quite often multifactorial and occur in a heterogeneous patient population.⁶⁶ Authors have used terms such as renal insufficiency, renal dysfunction, acute renal failure, and renal failure requiring dialysis somewhat interchangeably. Parameters used to define these terms include (Fig. 59.5) absolute and percentage changes in creatinine values, absolute and percentage changes in estimated GFRs, and reduction in output.⁶⁷ The incidence of AKI depends on the type of surgery and preexisting kidney function (Box 59.2 and Table 59.11).

In cardiac surgery, incidence is between 7.7% and 11.4%⁶⁸ when defined broadly, whereas frequency of AKI requiring dialysis is generally lower, ranging between less than 1% and 5%. In gastric bypass surgery, the incidence is 8.5%,⁶⁹ and after aortic aneurysm surgery, it is approximately 15% to 16%.⁷⁰ Similarly, liver transplant is also associated with a high frequency of AKI. It is reported that 48% to 94%⁷¹ of patients suffer from acute worsening renal function after liver transplantation.

In noncardiac surgery, several independent risk factors for AKI have been identified by Kheterpal and coworkers⁷²:

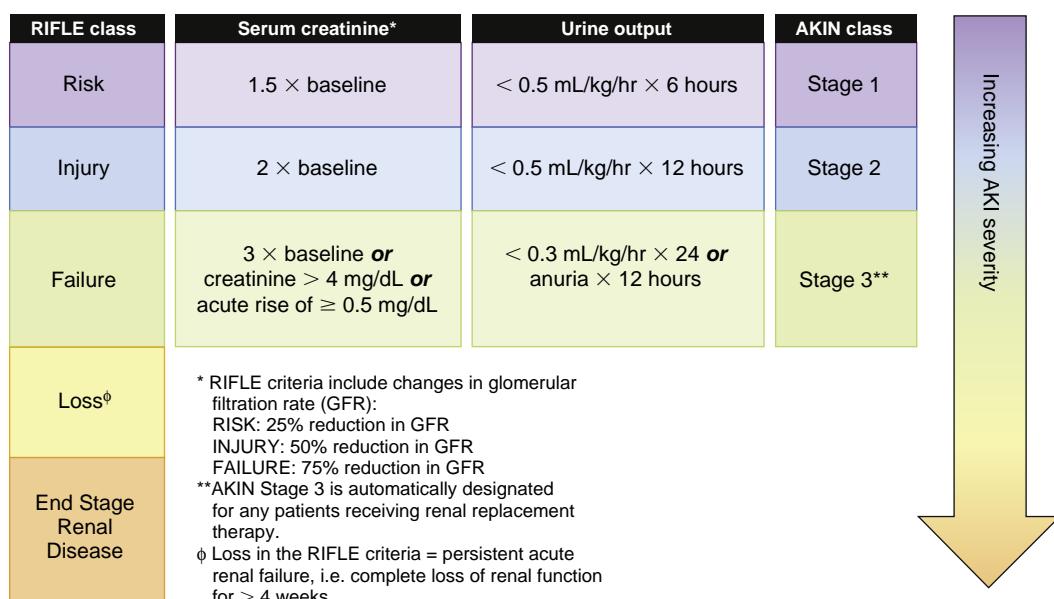


Fig. 59.5 Parameters used to define acute kidney injury (AKI). (From Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in kidney injury. *Crit Care*. 2007;11:R31.)

BOX 59.2 Risk Factors for Development of Postoperative Acute Kidney Injury

Preoperative Factors

- Preoperative renal dysfunction
- Increasing age
- Heart disease (ischemic or congestive)
- Smoking
- Diabetes mellitus
- American Society of Anesthesiologists Physical Status classification 4 or 5

Intraoperative Factors

- Emergency surgery or intraperitoneal, intrathoracic, suprainguinal vascular surgeries
- Erythrocyte transfusion
- Inotrope use
- Aortic cross-clamp time
- Cardiopulmonary bypass: furosemide use, urine output, need for a new pump run

Postoperative Factors

- Erythrocyte transfusion
- Vasoconstrictor use
- Diuretic use
- Antiarrhythmic drug use

Data from Abelha FJ, Botelho M, Fernandes V, et al. Determinants of postoperative acute kidney injury. *Crit Care*. 2009;13:R19; Parolari A, Pesce LL, Pacini D, et al. Risk factors for perioperative acute kidney injury after adult cardiac surgery: role of perioperative management. *Ann Thorac Surg*. 2012;93:584–591.

age, emergent surgery, liver disease, body mass index, high-risk surgery, peripheral vascular disease, and chronic obstructive pulmonary disease (requiring chronic bronchodilator therapy). Based on incremental score, the frequency of renal failure increased, ranging between 0.3% and 4.5%, respectively.

PERIOPERATIVE MANAGEMENT OF PATIENTS WITH ACUTE KIDNEY INJURY

Although many factors have been shown to contribute to AKI in surgical patients, there are few interventions to prevent AKI and no obvious cure for perioperative renal injury. A complete review of such interventions is beyond the scope of this chapter; however, some deserve mention.

Dialysis

Dialysis may not decrease perioperative AKI; however, it can treat the associated acidosis, hyperkalemia, and hypervolemia. For certain surgeries, such as aortic, dialysis actually reduces 30-day mortality rates in patients who develop loss of renal function. As many as 75% of these survivors regain kidney function and become independent of dialysis.⁷³

Nondialytic Management

Optimal therapy for renal dysfunction has not been established, and it is not clear whether interventions such as ACE-I therapy or diuretic therapy prevent decline in kidney function around the time of surgery.⁶⁸

Normal hemodynamic variables probably should be preserved during the operative period in an attempt to prevent AKI. In addition, scavengers of oxygen free radicals such as mannitol and N-acetylcysteine have been given to prevent ischemia-reperfusion injury. However, studies implementing these strategies have failed to show benefit in reduction of AKI in cardiac surgery patients. For years, mannitol was administered before aortic clamping, especially prior to the application of a suprarenal cross-clamp during abdominal aortic aneurysm. Clinical trials thus far have failed to demonstrate that this approach reduces the incidence of renal failure in this population of patients.⁷⁴

Both dopamine and atrial natriuretic peptide initially showed promise in the prevention of AKI because of their vasoactive effects leading to increased renal blood flow.

TABLE 59.11 Common Causes of Postoperative Decreased Urine Output and Acute Kidney Injury

	SITE OF DEFECT		
	Prerenal	Renal	Postrenal
Differential Diagnoses	Hypotension Absolute Relative Hypovolemia Absolute Relative (e.g., IAH)	Acute tubular necrosis Ischemia-reperfusion Radiocontrast Acute interstitial nephritis	Urinary catheter obstruction Catheter kinking Debris Prostatic hypertrophy Bladder spasm Urinary retention

From Chenitz KB, Lane-Fall MB. Postoperative oliguria. *Anesth Clin*. 2012;513–526.

Studies have shown neither dopamine⁷⁵ nor atrial natriuretic peptide⁷⁶ to be associated with improved mortality. Use of fenoldopam, a selective renal dopamine receptor agonist, has been shown to reduce postoperative AKI; however, it has not been associated with a reduction in the need for renal replacement therapy or hospital mortality.⁷⁷

Renal and Genitourinary Procedures

TRANSURETHRAL RESECTION OF THE PROSTATE

Transurethral resection of the prostate (TURP) is associated with a particular set of concerns with anesthetic implications. These issues must be considered when choosing an anesthetic technique, along with the usual considerations, such as the general health of the patient, the length of the procedure, and patient and surgeon preferences.

Pathophysiology of Prostate Hyperplasia

The prostatic gland is often described as a walnut-sized organ at the base of the bladder. There are three major areas—the fibromuscular stroma that surrounds the gland and two glandular zones termed central and peripheral. There is also a smaller, approximately 5% of the normal prostate, glandular region that surrounds the prostatic urethra designated as the transition zone; which is the primary site of benign prostatic hyperplasia (BPH). Nodular expansion of this area causes compression of the urethra along with the associated partial bladder outlet obstruction in men.⁷⁸ The prostate is rich in blood supply with vessels penetrating the prostatic capsule and branching within the gland. There are also large venous sinuses adjacent to the capsule.⁷⁹ The prevalence of BPH increases precipitously from the fourth decade of life, peaking at 88% of men in their 80s.⁸⁰

Surgical Procedures

TURP has long been considered the “gold standard” for the surgical treatment of BPH. Over the past several decades, the number of monopolar TURP (M-TURP) procedures performed annually in the United States has steadily declined secondary to advances in medical management, α -blockers, and 5- α reductase inhibitors; the introduction of newer surgical treatment modalities, bipolar TURP (B-TURP), laser TURP (L-TURP), microwave ablation, and aquablation; and the development of patient care guidelines.⁸¹⁻⁸⁴

The TURP procedure is performed by inserting a resectoscope through the urethra and resecting or vaporizing prostatic tissue in an orderly fashion. This can be accomplished using one of several techniques: M-TURP or B-TURP using an electrically powered cutting-coagulating metal loop, Holmium laser enucleation of the prostate (HoLEP), bipolar plasma vaporization, or laser-vaporization.^{82,85-87} A recently introduced novel technique is aquablation, a minimally invasive water ablation technique combining image guidance and robotics with a high-velocity saline stream for targeted and heat-free removal of prostatic tissue.⁸³ During resection, care must be taken not to violate the prostatic capsule. If the capsule is violated, large amounts of irrigation fluid may be absorbed into the circulation via the periprostatic or retroperitoneal spaces. If perforation is suspected, the procedure should be quickly terminated and hemostasis should be established.⁸⁸

Bleeding during M-TURP is common but is usually easily controlled. Arterial bleeding is controlled by electrocoagulation; however, when large venous sinuses are opened, hemostasis becomes difficult. If bleeding becomes uncontrollable, the procedure should be terminated as quickly as possible, and a Foley catheter should be passed into the bladder and traction applied. Excessive bleeding requiring transfusion occurs in approximately 2.5% of M-TURP procedures.⁸⁹

Irrigation Solutions

Ideally, an irrigation solution for use during TURP should be isotonic, nonhemolytic, electrically inert, transparent, nonmetabolized, nontoxic, rapidly excreted, easily sterilized, and inexpensive.^{90,91} Such a solution does not exist. Initially, the solution of choice for M-TURP was distilled water because it is electrically inert, transparent, and inexpensive, but it is extremely hypotonic. When absorbed into the circulation, it causes massive hemolysis, hyponatremia, renal failure, and CNS symptoms.⁹² Solutions of normal saline or Ringer lactate are isosmotic and are tolerated if absorbed into the circulation but are highly ionized and would cause dispersion of the high-frequency current from the M-TURP resecting loop. These issues led to the use of nearly isotonic irrigation solutions, such as glycine, Cytal (a combination of 2.7% sorbitol and 0.54% mannitol), sorbital, mannitol, glucose, and urea (Table 59.12). These solutions allow for electrocautery and are moderately hypotonic to maintain transparency.^{93,94}

Although these irrigation solutions cause no significant hemolysis, excessive absorption can lead to several

TABLE 59.12 Osmolality of Irrigation Solutions Used for Transurethral Resection of the Prostate

Solution	Osmolality (mOsm/kg)
Glycine, 1.2%	175
Glycine, 1.5%	220
Cytal (see text)	178
Sorbitol, 3.5%	165
Mannitol, 5%	275
Glucose, 2.5%	139
Urea, 1%	167
Distilled water	0

perioperative complications, such as circulatory overload, pulmonary edema, and hyponatremia. In addition, the solutes can have adverse effects: glycine can cause cardiac, neurologic, and retinal effects; mannitol rapidly expands the blood volume and can cause pulmonary edema in cardiac compromised patients; sorbitol is metabolized to fructose and lactate, and may cause hyperglycemia and/or lactic acidosis; and glucose can cause severe hyperglycemia in diabetic patients.

Replacement of distilled water with nearly isosmotic solutions has eliminated hemolysis and its sequelae as a complication of M-TURP. The incidence of severe CNS symptoms associated with severe hyponatremia, such as seizures and coma, has been reduced. However, the other major complication associated with the absorption of large volumes of irrigation solutions, overhydration, still is present. The use of normal saline as the bladder irrigation solution with the newer surgical techniques has eliminated the risks of dilutional hyponatremia and TURP syndrome.

Anesthetic Considerations for Transurethral Resection of the Prostate

Spinal anesthesia is considered the anesthetic technique of choice when traditional M-TURP is performed.⁹⁵ Spinal anesthesia provides adequate anesthesia for the patient with relaxation of the pelvic floor and perineum for the surgeon. Cardiac morbidity and mortality after M-TURP were similar for general or regional⁹⁶; however, spinal anesthesia has the advantage of allowing the patient to remain awake and enables the anesthesiologist to recognize the early signs and symptoms (e.g., mental status changes) of TURP syndrome or the extravasation of irrigating solution. Restlessness and confusion are early signs of hyponatremia and/or serum hypoosmolality and generally not signs of inadequate anesthesia. The continued administration of sedatives or the induction of general anesthesia might mask severe complications of TURP syndrome and even lead to death.⁹⁷

A sensory level of T10 provides satisfactory regional anesthesia for TURP by achieving an anesthetic block level that interrupts sensory transmission from the prostate and bladder neck; in addition, this sensory level eliminates the uncomfortable sensation of bladder distention. Higher sensory levels might mask the symptoms (abdominal or shoulder pain and/or nausea and vomiting) of accidental

perforation of the bladder or prostatic capsule in the awake patient.⁹⁴

Spinal anesthesia has a few advantages over epidural anesthesia for TURP. It is considered to be technically easier to perform in elderly patients. The incomplete block of the sacral nerves, which provide sensory innervation to the prostate, bladder neck, and penis, occasionally occurs with epidural anesthesia and is usually avoided with spinal anesthesia. However, if a regional technique cannot be performed because of technical difficulty, concerns of sacral nerve coverage, coagulation status, and/or patient refusal, then general anesthesia will be required.

Controversy exists on whether regional or general anesthetic techniques influence blood loss during TURP. Some studies have reported decreased bleeding under regional anesthesia,⁹⁸⁻¹⁰⁰ whereas others found no significant difference between the techniques.¹⁰¹⁻¹⁰⁴ Taking into consideration the studies that observed decreased bleeding with regional anesthesia, the authors have postulated that regional anesthesia reduces blood loss not only by decreasing systemic blood loss but also by decreasing central and peripheral venous pressures. However, spinal anesthesia, by reducing central venous pressure (CVP), may allow for greater absorption of irrigating solution compared to general anesthesia.¹⁰⁵ Additional factors that influence blood loss during TURP are the vascularity and size of the gland, the duration of the procedure, the number of sinuses opened during resection, and the presence of infection and prostatic inflammation from repeated or recent catheterizations.^{89,95}

Anesthetic considerations for TURP should also include positioning. TURP is usually performed in the lithotomy position with a slight Trendelenburg tilt. This positioning results in changes in pulmonary blood volume; a decrease in pulmonary compliance; a cephalad shift of the diaphragm; and a decrease in lung volumes such as residual volume, functional residual volume, tidal volume, and vital capacity. Cardiac preload may also increase. Nerve injuries to the common peroneal, sciatic, and femoral nerves may occur.¹⁰⁶

Morbidity and Mortality After Transurethral Resection of the Prostate

Patients presenting for TURP are often elderly and tend to have coexisting diseases. With a reported 30-day mortality rate associated with M-TURP to be between 0.2% and 0.8%, the common causes of death include pulmonary edema, renal failure, and myocardial infarction.^{95,107} Mortality rates are similar in patients receiving regional anesthesia or general anesthesia.¹⁰⁸ In one study the postoperative morbidity rate was noted to be 18%, with increased postoperative morbidity seen in patients with acute urinary retention, gland size greater than 45 g, resection exceeding 90 minutes, and age older than 80 years.⁹⁵

The most concerning complication of M-TURP is TURP syndrome. This syndrome has a multifactorial pathophysiological presentation and is essentially an iatrogenic form of water intoxication caused by a combination of excessive absorption of irrigating solution and the resulting hyponatremia.¹⁰⁹ Large studies have reported an incidence rate of mild to moderate TURP syndrome of between 0.78% and 1.4%.^{110,111} However, a mortality rate as high as 25% has been reported for severe TURP syndrome (serum sodium concentration <120 mEq/L).¹¹²

Another concern, because many of the patients for TURP are elderly, is the incidence of postoperative cognitive dysfunction. In a small prospective study comparing spinal anesthesia with intravenous sedation to general anesthesia in elderly TURP patients, significant reduction in cognitive function was noted in both groups after 6 hours, with no difference in perioperative mental function between the groups at any time or even after 30 days.¹¹³

COMPLICATIONS OF TRANSURETHRAL RESECTION OF THE PROSTATE

Absorption of Irrigating Solution

In almost every TURP procedure, irrigating solution is absorbed through opened prostatic venous sinuses. Several factors govern the amount and rate of absorption: (1) the height of the irrigating solution above the surgical table, which affects hydrostatic pressure; (2) the amount of distension of the bladder; (3) the extent of opened venous sinuses; and (4) the length of surgical resection time.¹¹⁴ On average, 10 to 30 mL of fluid is absorbed per minute of resection time, with the possibility of 6 to 8 L absorbed in procedures lasting up to 2 hours. Whether patients experience complications as a consequence of absorption of irrigating solution depends on the amount and type of fluid absorbed.^{115,116}

Excessive Circulatory Volume, Hyponatremia, and Hypoosmolarity

The rapid volume expansion that occurs with excessive absorption of irrigation fluid leads to circulatory overload. Initially, hypertension and bradycardia may be observed, and in patients with compromised cardiac function, this could progress to pulmonary edema and eventually cardiac arrest.¹¹⁷ After the initial hypertensive stage, a period of prolonged hypotension may follow. One suggested mechanism is the combination of hypertension and hyponatremia, which causes a net water flux along osmotic and hydrostatic pressure gradients out of the intravascular space into the pulmonary interstitium, causing pulmonary edema and hypovolemic shock.¹¹⁸⁻¹²⁰ In addition, the release of endotoxins into the circulation with the associated metabolic acidosis also causes hypotension.^{121,122} Whether symptoms of circulatory overload occur in a given patient depends on the patient's cardiovascular status, the amount and rapidity of absorption of irrigating fluid, and the extent of surgical blood loss.¹¹⁶

The severity of symptoms of hyponatremia correlate with the rate by which serum sodium concentration falls. Acute changes in serum sodium levels are more concerning than chronic hyponatremia.¹²³ In addition, it is often impossible to separate symptoms of cardiovascular compromise caused by hyponatremia from those secondary to circulatory overload. CNS symptoms and cardiovascular effects are observed with acute decreases in serum sodium levels to less than 120 mEq/L. At first, one may observe restlessness and confusion, and with continuing decreases in serum sodium levels this may progress to loss of consciousness and seizures (<110 mEq/L). Hypotension, pulmonary edema, and congestive heart failure may also occur at serum sodium levels of less than 120 mEq/L, along with electrocardiogram changes (widened QRS complexes, ventricular

ectopy, and ST segment increases) observed at levels less than 115 mEq/L. Eventually at levels near 100 mEq/L, respiratory and cardiac arrest may occur.¹²⁴

The classic CNS signs of TURP syndrome are thought to be not caused by hyponatremia itself but are due to the acute serum hypoosmolality that allows the shift of intravascular fluid into the brain and consequent cerebral edema. With the advent of modern nonelectrolyte irrigating solutions, the incidence of severe CNS complications has been reduced; however, CNS disturbances can still occur secondary to severe hyponatremia.^{115,116}

Glycine Toxicity

Glycine is a nonessential amino acid and when absorbed in significant amounts may cause neurologic and cardiac effects. Glycine has been implicated as the probable cause of transient blindness in TURP patients. Centrally acting mechanisms, such as cerebral edema, may also cause visual impairment, but normal pupillary light reflexes are retained. In TURP patients with transient blindness, the pupils are sluggish or nonreactive, suggesting a retinal effect. Glycine is an inhibitory neurotransmitter of the retina, and in one investigation, prolongation of visual evoked potentials along with deterioration of vision was observed after absorption of a few hundred milliliters of 1.5% glycine irrigation.¹²⁵ Glycine has also been shown to have subacute effects on the myocardium with the appearance of T-wave depressions or inversions on electrocardiography; and CK-MB isoenzymes may be elevated in some patients, without meeting criteria for myocardial infarction, for up 24 hours after surgery.¹²⁶

Ammonia Toxicity

Because glycine is metabolized in the liver into ammonia, absorption of glycine may result in CNS toxicity.¹²⁷ The early signs of ammonia toxicity, nausea and vomiting, usually occur within 1 hour after surgery. CNS signs and symptoms are observed when serum concentrations of ammonia are greater than 100 µmol/L.¹²⁸ With higher levels, patients may lapse into a coma lasting from 10 to 12 hours and awaken after levels decrease to less than 150 µmol/L.⁹⁴

Bladder Perforation

Inadvertent perforation of the bladder during TURP is another common complication, with a reported incidence of approximately 1% and with most perforations occurring retroperitoneally.¹²⁹ The usual cause is surgical instrumentation or overextension of the bladder with irrigating solution. An early sign of perforation, often overlooked, is a decrease in the return of irrigating solution. Eventually, a significant volume of fluid accumulates in the abdomen causing distension; conscious patients with a regional anesthetic may complain of abdominal pain and/or experience nausea and vomiting. With intraperitoneal perforations, symptoms are similar and develop sooner, and a patient may complain of severe shoulder pain secondary to diaphragmatic irritation. Intraperitoneal perforations are treated with either open surgical repair or percutaneous drainage of the abdomen.¹³⁰

Transient Bacteremia and Septicemia

The prostate harbors a variety of bacteria, which can be a source of perioperative bacteremia via opened prostatic venous

TABLE 59.13 Signs and Symptoms of Transurethral Resection of the Prostate Syndrome

Cardiovascular and Respiratory	Central Nervous System	Metabolic	Other
Hypertension	Agitation/confusion	Hyponatremia	Hypoosmolality
Bradyarrhythmias, tachyarrhythmias	Seizures	Hyperglycinemia	Hemolysis
Congestive heart failure	Coma	Hyperammonemia	Acute renal failure
Pulmonary edema and hypoxemia	Visual disturbances (blindness)		
Myocardial infarction			
Hypotension			

sinuses. The presence of an indwelling catheter will further increase this risk. Therefore the prophylactic administration of antibiotics in patients is recommended for TURP procedures. The bacteremia is usually transient, symptomless, and easily treated with common antibiotic combinations; however, 6% to 7% of these patients may develop septicemia.⁹⁵

Hypothermia

Using room temperature irrigating solutions may cause shivering and hypothermia in patients undergoing TURP procedures. This may be especially noticeable in older populations who have a reduced thermoregulatory capacity.¹³¹ Warming the irrigation solutions will decrease heat loss and shivering. Concerns that these warmed solutions may cause increased bleeding secondary to vasodilation has not been shown to be clinically significant.^{132,133}

Bleeding and Coagulopathy

Estimates of blood loss during TURP are frequently inaccurate secondary to the mixing of blood with large volumes of irrigating solution. Blood loss during M-TURP has been estimated to range from 2 to 4 mL/min of resection time or 20 to 50 mL/g of resected prostatic tissue⁸⁹; however, these guidelines are rough estimates, and the careful monitoring of the patient's vital signs and serial hematocrits should be used to assess blood loss and the need for transfusion.

Abnormal bleeding after TURP occurs in less than 1% of cases. Possible causes include dilution of platelets (dilutional thrombocytopenia) and coagulation factors secondary to the absorption of large volumes of irrigating solutions, as well as systemic coagulopathy. In these patients, systemic coagulopathy is caused by either primary fibrinolysis or disseminated intravascular coagulopathy. In primary fibrinolysis, the prostate releases a plasminogen activator that converts plasminogen into plasmin, which then increases bleeding via fibrinolysis. If primary fibrinolysis is suspected, treatment is with epsilon aminocaproic acid given intravenously in a dose of 4 to 5 g during the first hour, followed by an infusion of 1 g/h. Some clinicians believe that the systemic absorption of resected prostatic tissue, which is rich in thromboplastin, will trigger the onset of disseminated intravascular coagulopathy.⁸⁹ Treatment is supportive with administration of intravenous fluid and blood products as required.

Treatment of Transurethral Resection of Prostate Syndrome

TURP syndrome may occur as early as a few minutes after the start of the procedure and as late as several hours after

completion. A high index of awareness of the signs and symptoms (Table 59.13) must be present among the surgical team. Initially, based on the patient's symptomatology, supplemental oxygenation, ventilation, and cardiovascular support should be provided; concomitantly, other treatable conditions such as hypercarbia, hypoglycemia and diabetic coma, or drug interactions should be considered.⁹⁰ If TURP syndrome is suspected, blood samples should be drawn for analysis of electrolytes, glucose, and arterial blood gases and a 12-lead electrocardiogram should be obtained. Furthermore, the surgeon should terminate the procedure as rapidly as possible.⁹⁴

Treatment of hyponatremia and volume overload is guided by the severity of the patient's symptoms. If the serum sodium level is greater than 120 mEq/L and the patient's symptoms are mild, then fluid restriction and the administration of a loop diuretic, usually furosemide, will usually return the serum sodium to normal levels.

In severe cases of TURP syndrome accompanied by a serum sodium less than 120 mEq/L, treatment with intravenous hypertonic saline (3% sodium chloride) should be considered. Cerebral edema and central pontine myelinolysis have been associated with rapid correction of hyponatremia with hypertonic saline.^{134,135}

Laser Resection, Plasma Vaporization, Microwave Ablation, and Aquablation of the Prostate

In an effort to reduce perioperative morbidity, the urologic community has developed surgical alternatives to the classic TURP and M-TURP. The main advantage of these newer technologies is the use of physiologic saline instead of hypoosmolar irrigating solutions, such as glycine, which avoids the potential of dilutional hyponatremia and the development of TURP syndrome.¹³⁶ However, the possibility of volume overload is still present. Other advantages observed with these recent surgical modalities are a reduction of intraoperative and postoperative bleeding, less absorption of irrigation fluid, and decreased hospital length of stay. Although spinal anesthesia is the preferred anesthetic for TURP and M-TURP because it allows one to monitor mental status, these newer techniques enable the anesthesiologist to tailor the anesthetic management based upon the patient's medical condition and preference. In addition, patients may be taking anticoagulation medications or have coagulation disorders that may preclude the use of spinal anesthesia or undergoing the classic or M-TURP procedure.¹³⁷⁻¹³⁹

Laser resection of the prostate (L-TURP) has become an increasingly common choice for the treatment of BPH. L-TURP delivers light energy that, depending upon the temperature the prostatic tissue is heated to, will determine whether the tissue is coagulated or vaporized.⁸² HoLEP has been suggested as the new gold standard for surgical treatment of BPH.^{85,140}

Holmium:yttrium-aluminum-garnet laser is a solid-state, high-powered, pulsed laser that emits light at a wavelength of 2140 nm with precise cutting capabilities. Prostatic tissue is vaporized, and the resulting heat dissipation coagulates small to medium blood vessels. This technique allows the retrograde resection of entire prostatic lobes from the capsule, which are then pushed into the bladder and removed with a soft-tissue morcellator. HoLEP can be used safely on patients with larger prostatic glands, greater than 70 to 100 g, with similar outcomes as patients undergoing open prostatectomy.¹⁴¹ When compared with traditional M-TURP, HoLEP is associated with lower transfusion rates, catheterization time, and shorter hospital stays.¹⁴²⁻¹⁴⁵

Another advancement in laser therapy for BPH is the development of the photoselective vaporization of prostate (PVP) technique. The initial 80-watt KTP (potassium-titanyl-phosphate) laser is a high-powered neodymium:yttrium-aluminum-garnet laser that passes a beam through a KTP crystal, which halves the wavelength to 532 nm and doubles the frequency of light. The 532-nm wavelength is selectively absorbed by hemoglobin and blood-rich tissue, poorly absorbed by water, and vaporizes prostatic tissue with minimal dissipation of energy to surrounding tissues. Higher-powered, 120- and 180-watt systems have been introduced that use a lithium triborate crystal that allow for faster vaporization and coagulation of prostatic tissue.^{82,146}

This yields an almost bloodless field, faster hemostatic closure of the venous sinuses, and reduced absorption of irrigation fluid. Several studies have shown that PVP is safe and effective in patients at high risk of discontinuing their anticoagulation therapy for the procedure.¹⁴⁷⁻¹⁴⁹ Potential complications of PVP include capsular perforation, dysuria, and infection (secondary to necrotic tissue that occurs with coagulation). When compared with M-TURP, reoperation rates were higher for PVP for residual adenoma but decreased with the 180-watt powered systems.⁸² This laser modality allows the anesthesiologist to choose an anesthetic technique, including intravenous sedation, based on the patient's medical condition and preference.¹⁵⁰

A recent nonlaser advance in the surgical treatment of BPH is the bipolar plasma vaporization of prostate technique. The design of this bipolar system incorporates both the active and return poles on the same electrode; as a consequence, in contrast to a monopolar system, energy does not transverse the patient's body toward a return electrode pad, but instead it remains at the site of prostate vaporization. The plasma vaporization system produces a plasma corona on the surface of a spherical shaped (described as mushroom- or button-like) tipped bipolar electrode. This electrode generates a thin layer of highly ionized particles as it glides over the prostatic tissue without making direct tissue contact, produces minimal heat, and concomitantly vaporizes and coagulates the tissue. The plasma field vaporizes a limited layer of prostate cells with significantly reduced bleeding.⁸⁷

Transurethral microwave thermotherapy (TUMT) of the prostate is considered an effective alternative to M-TURP that has fewer major complications and can be performed as a minimally invasive office-based procedure under local or sacral block. TUMT heats prostatic tissue via a specialized catheter to a temperature between 45°C and 65°C. Although TUMT is less effective than M-TURP in reducing urinary flow long term, it is an alternative consideration for elderly or high-risk patients.^{86,151}

The newest modality to surgically treat BPH is aquablation, a minimally invasive high-velocity saline ablation technique combining ultrasonic image guidance and robotics for the targeted and heat-free removal of prostatic tissue under general anesthesia. Using the ultrasonic image, the area of the prostate to be resected is mapped and the system generates and adjusts the level of saline pressure for the controlled ablation of the prostate tissue. Directed cautery of the resected area for hemostasis is then performed using either monopolar or bipolar techniques. In initial small studies of this technique, perioperative changes in serum sodium or hematocrit were not significant. Because the resection time is approximately 5 minutes and overall procedure time is 45 minutes, compared with other techniques with longer operative times, this technique may have an improved safety profile. Surgical mapping enables preservation of the bladder neck and tissue surrounding the verumontanum and therefore preservation of normal sexual function. Further clinical studies are needed to validate this new technology.^{83,152}

URETEROSCOPIC LITHOTRIPSY AND PERCUTANEOUS NEPHROLITHOTRIPSY

Nephrolithiasis is a common and costly disease with a reported prevalence of 8.8% in the United States.¹⁵³ Although the majority of patients with renal system stones are conservatively managed, those with more complex calculi will require surgical treatment. The most commonly used surgical modalities are ureteroscopy (URS) and percutaneous nephrolithotomy (PCNL). The choice of treatment is guided by the size and location of the stone within the renal system. URS is recommended in symptomatic patients with smaller non-lower pole renal stones and/or middle or distal ureteral calculi. It has a greater stone-free rate after a single procedure when compared with extracorporeal shock wave lithotripsy (ESWL). In symptomatic (flank pain) patients with a renal stone burden greater than 20 mm or with lower renal pole calculi greater than 10 mm, PCNL should be the treatment of choice. PCNL with higher stone burdens and lower renal pole stones has a higher stone-free rate but carries greater morbidity.¹⁵⁴

The advent of small-diameter, flexible ureteroscopes and the miniaturization of electrohydraulic lithotripsy (EHL) probes, especially laser fibers, have changed the anesthetic concerns associated with this procedure. Initially, URS was performed with larger, rigid instruments requiring ureteral dilation necessitating the patient to undergo a general or regional anesthetic for these procedures. The presumed advantage of these techniques is that they would prevent patient movement, therefore decreasing the risk of ureteral trauma. Although the use of a general or regional anesthetic is still common, studies have shown that URS can be

safely and efficiently performed under local or intravenous sedation.¹⁵⁵⁻¹⁵⁷

EHL uses a flexible probe inserted through the ureteroscope to deliver a high-voltage spark between two electrodes generating a spherical hydraulic shock wave and the formation of a cavitation bubble near the stone to be fragmented. EHL can be performed in a normal saline solution, therefore avoiding the risks of irrigating the urinary track with a hypotonic solution. The major concern of EHL is its ability to damage the ureteral mucosa that could lead to the possibility of ureteral perforation. Laser lithotripsy uses a holmium:YAG flexible laser fiber through the ureteroscope to vaporize the stone via a photothermal mechanism. The holmium laser technique is safer and more efficient than EHL because it can be used in closer proximity to the ureteral wall without causing mucosal harm. In addition, it produces significantly smaller stone fragments.¹⁵⁵

PCNL is the preferred modality for the treatment of large (>20 mm) or complex stones. Contraindications to PCNL include patients with uncorrected coagulopathy and active, untreated urinary tract infections. With the fragmentation of stones, bacteria and bacterial endotoxins may be released, which place the patient at risk for septic complications. To reduce this risk, broad-spectrum antibiotics should be given perioperatively to these patients. Renal access is obtained under fluoroscopic or ultrasonic guidance with the placement of a sheath through which a rigid or flexible nephroscope is inserted. Stone removal then may be achieved by a variety of endoscopic techniques. Commonly PCNL is performed in the prone position under general anesthesia, although regional anesthesia and local anesthesia with sedation have been successfully used.¹⁵⁵ Supine positioning may be used, but results in a smaller surgical field, collapse of the renal collecting system, and increased difficulty in upper pole calyceal puncture.¹⁵⁸ Besides the typical anesthetic concerns, including those related to prone positioning, PCNL has certain additional risks. Pleural injuries, including pneumothorax and hydrothorax; hypothermia secondary to the large amounts of fluid administered to the patient during nephroscopy; and acute anemia from bleeding or dilution may occur. Careful monitoring of the patient's pulmonary status (airway pressures, end-tidal CO₂, and O₂ saturation), hemodynamics, and temperature may alert one to these potential complications.¹⁵⁵

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

ESWL is an alternative treatment for the disintegration of renal stones in the non-lower pole of the kidney and the upper part of the ureter. Although ESWL was considered the treatment of choice for these types of stones, it has been surpassed in the United States by URS.¹⁵⁹ In symptomatic patients with stone burdens smaller than 20 mm, ESWL is still an effective treatment; however, when compared with URS, it is associated with a higher likelihood of repeat procedures. Therefore, to optimize stone-free rates, successful treatment with ESWL depends upon several factors: obesity, skin-to-stone distance, collecting system anatomy, stone composition, and stone density/attenuation.¹⁵⁴ The original first-generation lithotripter (Dornier HM-3) required immersion of the patient into a water bath, which could result in significant effects in the cardiovascular and

BOX 59.3 Changes on Immersion During Lithotripsy

Cardiovascular	Increased Increased Increased	Central blood volume Central venous pressure Pulmonary artery pressure
Respiratory	Increased Decreased Decreased Decreased Increased	Pulmonary blood flow Vital capacity Functional residual capacity Tidal volume Respiratory rate

respiratory systems (Box 59.3). Newer generations of lithotripters use less power and have eliminated the water bath; therefore the efficiency of stone fragmentation is decreased, resulting in higher retreatment rates.¹⁶⁰

Lithotripters generate repetitive high-energy shock waves through the water density of the patient's tissues, which are focused on the stone, causing it to fragment. The original first-generation lithotripter utilized an electro-hydraulic shock wave generated by an electrode (or spark plug) placed in a water bath. This spark caused an explosive vaporization of water resulting in the rapid expansion and collapse of gas bubbles that generate a pressure wave, which is then focused using a metal ellipsoid onto the stone. Newer generations use piezoelectric crystals or electromagnetic generators to produce these shock waves along with water-filled cones or cushions, or silicone membranes and/or gel, for air-free coupling of the generated shock wave to the patient.¹⁶¹

Biomechanical Effects of Shock Wave Therapy

For ESWL shock waves to be effective, there should be no movement of stones during treatment. Otherwise treatment time will be prolonged, while shock wave generation is suspended, until the stone returns or is retargeted to the treatment focal zone; or if shocks are continued, adjoining tissues may become injured from the energy of the shock waves. Using controlled ventilation during a general anesthetic may cause stone excursion to surpass 60 mm. Spontaneous ventilation has been observed to displace stones over 12 mm, whereas in patients with adequate sedation, stone excursion is limited to approximately 5 mm.¹⁶¹

For effective stone disintegration, shock waves should reach the stone unimpeded. The flank area should be kept free of any medium that would provide an interface for the dissipation of shock wave energy. Nephrostomy dressings should be removed, and the nephrostomy catheter should be taped clear of the blast path. Although shock waves pass through most tissues relatively unimpeded, they do cause tissue injury, the extent of which depends on the tissue exposed and the shock wave energy at the tissue level. Skin bruising and flank ecchymoses can occur at the entry site. Painful hematoma in the flank muscles may also occur. Hematuria is almost always present at the end of the procedure and results from shock wave-induced endothelial injury to the kidney and ureter. Adequate hydration is necessary to prevent clot retention.

Shock wave–induced cardiac dysrhythmias were previously reported in 10% to 14% of patients undergoing immersion lithotripsy.^{163,164} Depending on the technology of the newer generations of lithotripters, some authors have observed dysrhythmias in 20% to 59% of patients with piezoelectric source of shock waves versus 1.4% to 9% using electromagnetic lithotripters. These dysrhythmic episodes do not seem to be of any clinical significance.¹⁶² Some of these dysrhythmias may be due to mechanical stress on the conduction system exerted by the shock waves. The intricate grounding system of the lithotripter ensures that any current-induced dysrhythmias are unlikely. Artifacts on the electrocardiogram also are common. Artifacts and dysrhythmias usually disappear when the lithotripsy is stopped.

Anesthetic Choices for Lithotripsy

Historically, anesthetic regimens used successfully for immersion lithotripsy included general anesthesia, epidural anesthesia, spinal anesthesia, flank infiltration with or without intercostal blocks, and analgesia-sedation, including patient-controlled analgesia.^{165–172} With the newer generations of lithotripters, most analgesia-sedation combinations are adequate. Even patient-controlled analgesia with alfentanil and a combination of propofol and alfentanil has been used.^{173,174} Many centers routinely use general anesthesia with short-acting inhaled or intravenous anesthetics and use laryngeal mask airway for ventilation.

Newer Generations of Lithotripters

Newer generations of lithotripters have no water bath, use fluoroscopy and/or ultrasonography to visualize and target the stone, and tend to use multifunctional tables that allow other procedures, such as cystoscopy and stent placement, to be accomplished without moving the patient off the table. The shock waves are tightly focused; therefore, they cause less pain at the entry site, and intravenous analgesia-sedation is the mainstay of anesthesia with these newer lithotripters. Other incidental interventions, such as cystoscopy, stone manipulation, or stent placement, may alter anesthetic requirements. Because these newer lithotripters have a much smaller focal zone for the shock waves, it is essential that adequate analgesia and sedation be provided so that stone excursion with respiration is limited to the focal zone.

Contraindications

Pregnancy, active urinary tract infection, and untreated bleeding disorders are the major contraindications to lithotripsy. Women of childbearing age must have a pregnancy test that is documented to be negative before lithotripsy. Standard tests of coagulation, such as the platelet count, prothrombin time, and partial thromboplastin time, should be obtained as indicated by medical history. Pacemakers, automatic implanted cardioverter-defibrillators (AICDs), abdominal aortic aneurysm, orthopedic prostheses, and obesity are no longer considered contraindications.

Patients with pacemakers can be treated safely if the pacemaker is pectorally placed and the following precautions are observed.^{175–177} Pacemaker programmability should be established before the treatment, and the pacemaker should be switched to a nondemand mode in case the shock waves interfere with pacemaker function. Alternative means of

BOX 59.4 Anesthetic Implications of Radical Nephrectomy for Tumors

- 85%-90% are for renal cell cancer
- 5%-10% extension to the inferior vena cava and right atrium
- Large-bore intravenous access, A-line, internal jugular vein line (preferably on left side if inferior vena cava is involved)
- Paraneoplastic syndrome
- Hypercalcemia, eosinophilia; increased prolactin, erythropoietin, and glucocorticoids
- Occurs more frequently in men than women
- Chronic smoking history usually associated
- Coronary artery disease, chronic obstructive pulmonary disease
- Renal failure

pacing should be available. Although most pacemakers located pectorally are at a safe distance from the blast path, some may be damaged. Weber and coworkers¹⁷⁵ examined 43 different pacemakers and found that three were affected. Dual-chamber pacemakers tend to be more sensitive to interference. Treatment should be started at a low energy level and gradually increased while observing pacemaker function.

Manufacturers of AICDs and lithotripters have considered an AICD a contraindication for lithotripsy; however, patients with AICDs have been treated successfully with lithotripsy.¹⁷⁶ AICD devices should be shut off immediately before lithotripsy, with an alternative means of defibrillating available, and then reactivated immediately after treatment.¹⁷⁸

Patients with small aortic aneurysms have been treated safely, provided that the stone is not close to the aneurysm. Orthopedic prostheses, such as hip prostheses and even Harrington rods, are not a problem if they are not in the blast path, which is usually the case. Positioning of obese patients may be problematic at times. Not only do extremely obese patients present anesthetic challenges related to obesity, but also focusing of the stone may be extremely difficult in the very obese. It is prudent for focusing of the stone to be attempted before administering any anesthetic in this high-risk population.

Open Radical Surgery in Urology

Radical surgery is the excision of a tumor or diseased organ and possibly adjacent structures, along with their blood supply and lymphatic drainage. These procedures are generally performed for patients with malignant rather than benign disease and may be lengthy with sudden and significant blood loss. Although the trend over the past decades has been from open to laparoscopic or robotic-assisted approaches, there are still cases where major open urologic procedures are indicated.

Radical Nephrectomy

The most common malignancy of the kidney is renal cell carcinoma, comprising 80% to 85% of all solid renal masses.¹⁷⁹ Because renal cell carcinoma is refractory to chemotherapy and radiation therapy, surgical resection or ablation can offer curative treatment of localized disease (Box 59.4). The procedure involves removal of the kidney, the ipsilateral adrenal gland, perinephric fat, and the surrounding fascia.

Recently, resection of the ipsilateral adrenal gland has been reserved for patients with large upper-pole lesions or when the adrenal gland is enlarged or appears abnormal.¹⁸⁰ Partial nephrectomy (nephron-sparing surgery) is considered for patients with a solitary functional kidney, small lesions, or bilateral tumors or for patients with increased risk because of other diseases, such as diabetes or hypertension.^{181,182} Nephron-sparing surgery in the treatment of renal cell carcinoma has been shown to have an equal curative potential as radical nephrectomy.¹⁸³

With radical nephrectomy, significant cardiorespiratory changes attendant to the flank position are a concern. Respiratory changes include decreases in thoracic compliance, tidal volume, vital capacity, and functional residual capacity. Dependent atelectasis is common and can lead to hypoxemia. Pneumothorax may occur and can have significant respiratory and hemodynamic consequences intraoperatively. It is common to see a decrease in blood pressure when the kidney rest is raised. This decrease is usually due to compression of the inferior vena cava. In addition, hepatic encroachment on the vena cava and mediastinal shift may reduce venous return and stroke volume further. Cervical plexus, brachial plexus, and common peroneal neuropathies can occur because of stretch or compression of nerves in the lateral position.

In 5% to 10% of patients with renal cell carcinoma, the tumor extends into the renal vein and the inferior vena cava and right atrium. Tumor extension into the inferior vena cava and atrium occurs more frequently with right-sided renal cell carcinoma. Several problems can occur in these patients, ranging from circulatory failure as a result of complete occlusion of the vena cava by tumor to acute pulmonary embolization of tumor fragments during surgery. To operate on these patients safely, the extent of the lesion must be defined preoperatively. Cardiopulmonary bypass may be required. CVP in such cases might not reflect intravascular volume accurately, because venous return through the inferior vena cava can be impaired by thrombus; hence intraoperative transesophageal echocardiography may be of value.¹⁸⁴ A decrease in venous return also predisposes the patient to hypotension during induction of anesthesia. Venous obstruction can lead to dilation of the epidural veins and the development of abdominal wall and retroperitoneal collaterals. The emphasis should center on appropriate preoperative preparation, which is possible only when the full extent of the lesion has been defined.¹⁸⁵

Radical Cystectomy

Bladder cancer is the fourth most common cancer in men and twelfth in women in United States.¹⁸⁶ Radical cystectomy with regional pelvic lymph node dissection is the surgical treatment of choice for the management of nonmetastatic muscle-invasive bladder cancer and the highest-risk nonmuscle-invasive bladder cancer. Radical cystectomy with urinary diversion is considered one of the most complex urologic procedures and involves removal of the entire bladder, the distal ureters, and lymph nodes, as well as the prostate, and seminal vesicles in men or urethra, adjacent vagina, and uterus in women. For urinary diversion, either an orthotopic neobladder or ileal conduit are commonly created.¹⁸⁷ This procedure is associated with significant morbidity and prolonged hospital stays. One

BOX 59.5 Anesthetic Implications of Radical Prostatectomy

- Disease of the elderly
- Coronary artery disease, chronic obstructive pulmonary disease, and renal dysfunction
- Significant blood loss
- Wide-bore intravenous access and invasive monitoring
- Acute normovolemic hemodilution versus autologous blood donation
- Hyperextended position
- Nerve injuries, soft tissue injury, joint dislocations
- Venous air embolism
- Anesthetic management
 - Benefits of regional anesthesia versus general anesthesia debated
 - Not known to influence mortality
 - Epidural anesthesia with spontaneous ventilation decreases blood loss
 - General or combined anesthesia with intermittent positive pressure ventilation increases blood loss

large study looking at a data registry in England of 2537 patients with an open radical cystectomy over a 2-year period (2014-2015) reported a median blood loss of 500 to 1000 mL with a transfusion rate of 21.8%.¹⁸⁸ In the Surveillance, Epidemiology, and End Results-Medicare database of 5207 patients who underwent radical cystectomy between 1991 and 2009 mortality at 30 days in patients older than 65 years old was 5.2%.¹⁸⁹ Complications of this procedure include urinary extravasation, intestinal anastomotic leaks, postoperative ileus, postoperative infections, and venothromboembolism. Enhanced recovery after surgery (ERAS) protocols have shown improved emotional and physical recovery.¹⁹⁰ In addition, patients given alvimopan, a peripherally acting μ -opioid receptor antagonist, showed significantly quicker bowel recovery.¹⁹¹

As with any major operation with the potential for significant blood loss, adequate intravenous access and placement of an arterial line are essential. General endotracheal anesthesia is indicated with consideration of a general/epidural technique for postoperative analgesia and/or the use of ERAS protocols for these procedures. The volume of urinary output cannot be used as a measure of fluid status due to its absence; however, the operative team can observe whether urine flow is noted at the clipped ends of the ureters. Blood lactate levels can be monitored to determine adequate organ perfusion. Placement of a central venous line for resuscitative purposes might be considered when there is anticipation of major blood loss.¹⁹² The implementation of ERAS protocols for open RC with urinary diversion has demonstrated expedited bowel function recovery and shortened hospital stays without an increase in hospital readmission rates.¹⁹³

Radical Prostatectomy

Prostate cancer is the most commonly diagnosed cancer in men and the second leading cause of cancer death of men in the United States.¹⁸⁶ Localized prostate cancer is treated by either radiation therapy or radical prostatectomy (Box 59.5). Radical prostatectomy has become more commonly performed because of routine prostate-specific antigen

testing in men older than 50 years and popularization of the nerve-sparing surgery to reduce the risk of impotence. Although originally described in 1905 via the transperineal approach, the retropubic approach is currently more commonly performed. The prostate, the ejaculatory ducts, the seminal vesicles, and part of the bladder neck are removed along with the pelvic lymph nodes.

Traditionally, the procedure was performed by open laparotomy, but robotic-assisted surgery is replacing that technique with increasing frequency. A potential intraoperative problem with open radical prostatectomy is hemorrhage and rapid blood loss requiring blood transfusion; therefore large bore intravenous access is recommended. Autologous predonation, preoperative recombinant erythropoietin therapy, intraoperative isovolemic hemodilution, and blood cell salvage are commonly practiced to reduce the patient's exposure to allogeneic blood. Early postoperative complications, including deep vein thrombosis, pulmonary embolism, hematoma, seroma, and wound infection, occur in 0.5% to 2% of cases.¹⁹⁴ Late complications include incontinence, impotence, and bladder neck contracture.¹⁹⁵ Patients undergoing radical prostatectomy are placed supine in Trendelenburg position with the back extended, which places the pubis above the head. Air embolism from the prostatic fossa caused by a gravitational gradient between the prostatic veins and the heart has been reported.¹⁹⁶

Comparison of Anesthetic Techniques for Radical Prostatectomy

Epidural anesthesia, spinal anesthesia, general anesthesia, and combined epidural and general anesthesia have been used for this surgery. For the epidural component of combined techniques, a thoracic or a lumbar approach to catheter placement has been used, and spontaneous ventilation or intermittent positive pressure ventilation (IPPV) has been used for the general anesthesia component. Many investigators have reported their findings in comparing the four anesthetic techniques for radical retropubic prostatectomy,¹⁹⁷⁻²⁰⁰ and certain trends emerge.

Intraoperative blood loss is significantly decreased if epidural anesthesia or a combined epidural and general anesthetic with spontaneous ventilation is used. In one study, blood loss in the general anesthesia and the combined anesthesia group with IPPV was significantly more than in the epidural anesthesia group, despite little difference in arterial pressure among the three groups.¹⁹⁷ It was postulated that the increased venous pressure as a result of IPPV was the most likely cause of increased bleeding in the general and the combined anesthesia groups during radical prostatectomy. Previous studies have shown that central and peripheral venous pressures are lower in patients during spontaneous ventilation under epidural anesthesia or combined epidural-general anesthesia than in patients receiving IPPV during general anesthesia.²⁰¹ Epidural anesthesia alone or in combination with a general anesthetic decreases the risk of thromboembolism,²⁰² decreases postoperative pain and analgesic requirements,²⁰³ and speeds recovery of bowel function. The length of stay and the cost of hospitalization can be decreased with the judicious use of epidural anesthesia and adherence to established clinical pathways.^{204,205} In one study, 80% of patients were satisfactorily discharged after 1 day and the mean length of stay was 1.34 days.²⁰⁶

Possible differences in patient outcome with general versus epidural anesthesia are not clear. Local practices are therefore based on the preferences of the urologist, anesthesiologist, and patient.

Robotic and Laparoscopic Surgery in Urology

The advantages of laparoscopic surgery over conventional open surgery, including decreased hospital stay, improved visualization, decreased blood loss, expedited recovery time, reduced postoperative pain, and improved cosmetic outcomes, have been well described. The introduction of robotic-assisted surgery offers further enhancements of control and mobility to the surgeon but with increased cost and controversy over whether there is a clear benefit regarding reduction in morbidity and mortality compared with laparoscopic techniques.²⁰⁷ The use of robots in urologic surgery has been extended to radical prostatectomy, radical cystectomy, pyeloplasty, and renal and adrenal surgery in adults and children.

Anesthetic concerns of robotic-assisted surgery include the length of surgical time, intravenous fluid management, and positioning. The most frequent reported complications are peripheral neuropathies, corneal abrasions, vascular complications including compartment syndrome, rhabdomyolysis, thromboembolic disease, and the effects of edema.²⁰⁸ In addition, significant anesthetic concerns for urologic minimally invasive surgeries surround the physiologic effects of pneumoperitoneum, the use of lateral decubitus, and steep head down tilt (SHDT) positions, as well as restricted access secondary to the robot and the robotic arms and extensions over the patient.

Although all the conventional complications and concerns associated with laparoscopy and robotic-assisted procedures are applicable to urologic procedures, two unique problems are identified. First, because the urogenital system is mainly retroperitoneal, the large retroperitoneal space and its communications with the thorax and subcutaneous tissue are exposed to the insufflated carbon dioxide. Significant subcutaneous emphysema can occur in these patients and may extend all the way up to the head and neck.¹⁹⁵ The upper airway is at risk for compromise in the most severe cases because of pharyngeal swelling secondary to submucosal carbon dioxide. This complication should be kept in mind before extubation of the trachea in these patients. Second, the procedures can be lengthy, allowing for sufficient absorption of carbon dioxide to result in acidemia and marked acidosis.¹⁹⁵ Because of significant increases in intraabdominal and intrathoracic pressure as a result of insufflated carbon dioxide, use of SHDT position in some cases, and the long duration of procedures, general anesthesia with controlled ventilation may be the method of choice. Despite adequate intravascular hydration, intraoperative oliguria may occur and can be followed by diuresis in the immediate postoperative period. Increased perirenal pressure exerted by the insufflated gas in the retroperitoneal space causes an increase in renal vascular resistance with direct compression of the renal parenchyma and renal vein. This causes a release of renin and aldosterone, along with antidiuretic hormone, which temporarily decreases renal blood flow, renal function, and urinary output.²⁰⁹

Ventilatory and respiratory concerns of pneumoperitoneum include decreased compliance, increased airway pressures,

BOX 59.6 Pneumoperitoneum-Related Physiologic Changes

Increased	Decreased
Systemic vascular resistance	Cardiac output
Blood pressure	Functional residual capacity
Peak airway pressure	Lung compliance
Ventilation-perfusion mismatch	Renal blood flow
Intracranial pressure	Glomerular filtration rate
	Splanchnic blood flow

and increased ventilation-perfusion mismatch. Application of positive end-expiratory pressure improves oxygenation in these patients.²¹⁰ Hypercapnia develops within 15 to 30 minutes of carbon dioxide insufflation with resultant hypercarbia, acidosis, tachycardia, dysrhythmias, and other deleterious hemodynamic and CNS effects.²¹¹ Increase in mechanical ventilation can obviate these changes in most patients, and the majority of healthy patients tolerate the changes even though they are clinically significant. Extraperitoneal insufflation of carbon dioxide is associated with larger increases in arterial PCO₂ than in intraperitoneal insufflation.²¹² Hemodynamic changes observed during initiation of pneumoperitoneum (Box 59.6) include increases in systemic vascular resistance and mean arterial pressure. These changes are caused by increased intraabdominal pressure compressing the aorta and increasing afterload.²¹³ Cardiac output has been observed to decrease with insufflation.^{214,215} Variable changes in heart rate have been reported. Reflex bradycardia has been observed to occur with establishment of pneumoperitoneum probably related to peritoneal stretch and vagal stimulation.²¹⁶

Robotic-Assisted Radical Prostatectomy

Robotic-assisted radical prostatectomy (RARP) has become the second most performed robotic-assisted surgical procedure worldwide.²¹⁷ Anesthetic concerns are primarily related to the use of pneumoperitoneum in the steep Trendelenburg position. For RARP the patient is placed in the dorsal lithotomy position, arms tucked at the side of the table, and drapes placed over the patient which limits the anesthesiologist's ability to access the patient. Pneumoperitoneum is initiated, and the patient is then placed in a 30- to 45-degree Trendelenburg position. With limited access to the patient after draping; intravascular lines, monitors, and patient protective devices need to be placed and secured beforehand. Once the robot is positioned over the patient with its arms attached (docked) to the ports; movement of the patient and/or cardiopulmonary resuscitative measures cannot be performed unless the robot is first undocked.²¹⁸ Patient movement during the surgery could result in visceral or vascular injury. Constant assessment of the degree of muscle relaxation intraoperatively is recommended. Because of the limited access and duration of the procedure, careful attention should also be given to pressure areas of the arms and legs to avoid ulnar neuropathy and lateral femoral cutaneous nerve injury.²¹⁴

Physiologic changes resulting from SHDT position include hemodynamic effects such as decreased perfusion pressure of lower extremities, increased mean arterial pressure at the circle of Willis, increased central blood volume, decreased cardiac output, and a decreased perfusion of vital organs in a normovolemic patient. Increased myocardial oxygen consumption, ischemia, dysrhythmias, and decreased oxygen delivery are potential risks in patients with cardiac disease. Despite an observed twofold to threefold increase of right- and left-sided filling pressures in ASA I and II patients during RARP, Lestar and colleagues²¹⁹ observed no significant changes in cardiac performance. Respiratory effects of SHDT including decreased compliance, reduced vital capacity and functional residual capacity, 20% decrease in lung volumes, and ventilation-perfusion mismatch compound the effects of pneumoperitoneum. Pulmonary congestion and edema have been reported in susceptible patients. Facial, pharyngeal, and laryngeal edema may also occur with the SHDT position. Chemosis (conjunctival edema) is common in RARP but is usually self-limiting once the patient is taken out of the steep Trendelenburg position. If facial and/or conjunctival edema is noted at the end of the procedure, the anesthesiologist should have a high index of suspicion for the presence of laryngeal edema. A transient increase in serum creatinine secondary to pneumoperitoneum during robotic prostatectomy has been reported.²²⁰ In the Trendelenburg position, patients with a history of reflux have an increased risk of regurgitation of gastric contents and aspiration.

Other significant effects of SHDT include increased intracranial pressure, increased intraocular pressure (IOP), venous air embolism, brachial plexopathy, arthralgias, compartment syndrome, and finger injuries. Perioperative assessment of the function of a patient with a ventriculoperitoneal shunt scheduled for any laparoscopic procedure is recommended.²²¹ Issues arising from increased intracranial pressure or consequences of a malfunctioning shunt with pneumoperitoneum in SHDT position need to be recognized. Kalmar and associates concluded patients overall clinically tolerated the influence of prolonged SHDT position with CO₂ pneumoperitoneum on cardiovascular, cerebrovascular (including cerebral perfusion pressure and oxygenation), and respiratory homeostasis during robotic prostatectomy.²²²

Significant increases in IOP have been reported in robotic prostatectomy with the steep Trendelenburg position, but the clinical significance is unknown.²²³ However, of concern are patients with primary open angle glaucoma who have decreased outflow through the trabecular network, which causes IOP. Two patients with severe glaucoma were advised against proceeding with a RARP in the steep Trendelenburg position and instead opted for open radical prostatectomies in the supine position.²²⁴ However, another patient with severe glaucoma undergoing RARP was treated intraoperatively with acetazolamide and mannitol to manage the increase in IOP.²²⁵ In addition, there are reports of at least six cases of postoperative visual loss secondary to ischemic optic neuropathy following radical prostatectomy: three open and three robot-assisted prostatectomies.²²⁶ Limiting time in the steep Trendelenburg position and reducing the volume of intravenous fluids administered may decrease the risk of this devastating complication.²²⁷

With the exception of one study, the literature suggests that compared with retropubic radical prostatectomy, RARP is associated with a reduction in blood loss.²²⁸ Mild to moderate pain is expected postoperatively, and low pain scores of 0 to 4 have been reported after retropubic radical prostatectomy and RARP using preemptive analgesia with ketorolac given intraoperatively combined with rescue opiate or nonopiate analgesia.²²⁹ Most patients are discharged home the day after surgery.

Robotic-Assisted Radical Cystectomy With Diversion

The ensuing popularity of robotic-assisted urologic procedures over the past few decades also gave rise to the first robotic-assisted radical cystectomy (RARC) with extracorporeal or intracorporeal neobladder formation as first described in 2003.^{230,231} Since 2003 the use of RARC has increased substantially in the United States and globally, but there is controversy regarding the safety, efficacy, and cost effectiveness of the robotic approach.²³² A meta-analysis of four randomized controlled trials comparing RARC with extracorporeal urinary diversion with open radical cystectomy concluded that blood loss and wound complications were significantly lower in the RARC group; however, operating time was significantly longer with use of the robot. However, there was no significant difference between RARC and open radical cystectomy in perioperative morbidity, length of stay, positive surgical margin, lymph node yield, and positive lymph node status.²³³ In a multicenter, retrospective review comparing RARC with extracorporeal to intracorporeal urinary diversion, the 90-day overall complication rate was not significantly different, but the incidence of gastrointestinal and infectious complications was significantly lower in patients in the intracorporeal group.²³⁴ The intracorporeal technique has several advantages in that the bowel stays inside the abdomen, no hypothermia or loss of fluids via osmosis occurs, and there is decreased bleeding, decreased need for ureteral dissection, and decreased traction on the bowel and ureters.²³⁵ The implementation of ERAS protocols has been shown to reduce the length of stay of patients undergoing RARC with intracorporeal urinary diversion.^{236,237} Although the robotic approach may minimize complications, oncologic outcome has not improved over the past three decades, and surgical technique is unlikely to improve survival outcomes.²³⁸

As in RARP, the anesthetic concerns of RARC include management of SHDT and pneumoperitoneum with the patient in the dorsal lithotomy position, along with limited access to the patient. Epidural analgesia is generally not necessary, because RARC patients have reduced postoperative pain and early mobilization is encouraged. Although the usual intraoperative concerns of preventing hypothermia, hypoxemia, and hypovolemia while avoiding overhydration are present, there is the additional goal of avoiding opioid-based analgesics and their effects on bowel recovery.²³⁹ The implementation of ERAS protocols helps to achieve the goal of limiting the use of postoperative opioids. In one study performed at a medical center with extensive experience in urologic surgery, 100 patients who underwent RARC with urinary diversion experienced operative times ranging from 4 to 12.9 hours, depending on the type

of urinary diversion performed, and with reported blood losses of up to 1400 mL.²³⁷ As a consequence, because these surgeries may be lengthy with the possibility of substantial blood loss, adequate intravenous access along with insertion of an arterial pressure line is recommended. Arterial blood gases may be obtained at regular intervals to assess the presence of either respiratory and/or metabolic acidosis. With long insufflation times of CO₂, respiratory acidosis can occur and should be managed according to end-tidal carbon dioxide values in tandem with PaCO₂. In addition, metabolic acidosis may occur (secondary to fluid restrictions) before and during the procedure and hypothermia, as a result of heat loss due to lengthy operative times or the insufflation of cold CO₂ gas.²⁴⁰

LAPAROSCOPIC NEPHRECTOMY

Laparoscopic nephrectomy is commonly used for radical and living donor nephrectomy. For radical nephrectomy, studies suggest that there are no significant differences in oncologic outcomes between open and laparoscopic procedures, although the laparoscopic technique, as discussed earlier, has the advantages of decreased morbidity, blood loss, postoperative analgesic requirements, and hospital length of stay.^{241,242} In a large retrospective study of 23,753 patients from 2003 to 2015 comparing perioperative outcomes of robotic-assisted to laparoscopic radical nephrectomies for patients with renal masses, there were no differences in the rates of major complications or blood transfusions. However, the use of robotic-assisted nephrectomy increased over the course of the study, from 1.5% to 27% of cases by 2015; and was associated with prolonged operating times and higher hospital costs when compared with laparoscopic surgery.²⁴³

Two laparoscopic approaches are commonly used for nephrectomies: transperitoneal or retroperitoneal. The primary advantage of the transperitoneal laparoscopic approach is the greater working space offered for large renal tumors (≥ 10 cm),²⁴⁴ whereas the retroperitoneal approach avoids transabdominal fatty tissue and allows for limited dissection of the kidney with direct access to the renal hilum.²⁴⁵ The lateral or semilateral decubitus position with some degree of flexion, along with use of a cushioned beanbag, pillows, and axillary roll, is usually used for these procedures. Besides the usual possible complications from laparoscopic surgery (e.g., positioning injuries, subcutaneous emphysema, and CO₂ emboli), the occurrence of rhabdomyolysis is a concern after laparoscopic nephrectomy. Risk factors include prolonged surgical time, high body mass index, volume depletion, and use of the lateral decubitus position. Limiting the amount of flexion has been recommended to decrease the incidence of this complication.²⁴⁶ Anesthetic considerations, other than the previously discussed physiologic effects of pneumoperitoneum, include adequate intravenous access, whereas insertion of an arterial line, CVP catheter, and/or transesophageal echocardiography may be reserved for selected high-risk patients.

Robotic-Assisted Partial Nephrectomy

Partial nephrectomy is the standard for the treatment of small renal masses (< 4 cm) for the reasons previously discussed (see Radical Nephrectomy).²⁴⁷ Surgical excision of

these tumors has progressed from open radical nephrectomy to laparoscopic partial nephrectomy (LPN) and robotic partial nephrectomy (RPN). RPN has become the preferred technique because the learning curve for RPN is estimated to be 25 cases when compared with more than 200 cases for LPN.²⁴⁸ Both LPN and RPN require the temporary clamping of the renal hilum to improve surgical visibility and reduce blood loss; however, to prevent AKI the warm ischemia time related to clamping should not exceed 30 minutes.^{249,250} In a meta-analysis of 23 studies including 2240 patients, RPN when compared with LPN was found to have a lower conversion rate to open or radical surgery, a better postoperative estimated GFR, shorter warm ischemia time, lower estimated blood loss, and shorter length of hospital stay.^{251,252}

Anesthetic concerns for RPN, as in laparoscopic nephrectomy, involve proper positioning and the use of pneumoperitoneum. To allow for unhindered robotic arm movement, the patient is placed in the lateral decubitus position, brought toward the edge of the operating table, and flexed approximately 15 degrees at the kidney.²⁵³ Of concern with partial nephrectomy, there is a decrease in the number of functioning nephrons causing hyperfiltration of the remaining glomeruli. This increase in load to the remaining glomeruli leads to an increase in intraglomerular pressure causing injury to the kidneys in the short and long term. A retrospective study of AKI after partial nephrectomy found that the higher the intraoperative fluid administration, the greater the drop in the GFR postoperatively. RPN was found to be more tolerant of fluid administration than open or LPN. The authors postulated that the precision of the robot allows minimal handling of the remainder of the renal tissue and this may confer protection. Therefore judicious fluid administration is recommended during partial nephrectomy.²⁵⁴

Urogenital Pain Syndromes and Treatment

Pain syndromes of the urogenital system can be divided into those occurring in the immediate postoperative period, acute or chronic nonmalignant pain, and cancer-related pain. Treatment includes medications, neuraxial and regional nerve blocks, and neuromodulation or surgery. Choice of modality in the perioperative period must balance analgesia with side effect profile, particularly as common urologic surgeries become less invasive and focus shifts to fast-track surgeries and ERAS protocols.

POSTOPERATIVE PAIN AND TREATMENT

Inflammatory Pain

Pain after urogenital surgery is similar to other postoperative pain, occurring as a direct result of surgical manipulation and trauma. Acute pain is most commonly inflammatory and related to incision, retraction, and suturing. Mediators of inflammation are local and systemic, including bradykinins, serotonin, prostaglandins, histamine, leukotrienes, and cytokines.²⁵⁵ Pain is worst in the first few days following surgery and generally improves rapidly with tissue healing.

Neuropathic Pain

Neuropathic pain may also exist postoperatively, mediated via neurogenic inflammation²⁵⁶ or due to temporary or sustained pressure, stretch, or direct ligation of nerves. This pain can be immediate or develop over weeks to months as severed nerve endings regrow or are trapped in scar tissue and form neuromas. Pain is described as burning, pins-and-needles, electric, and radiating in a dermatomal or peripheral nerve distribution.

Postoperative Urinary Retention

Particularly with regard to urologic surgery, postoperative urinary retention (POUR) should be considered as a source of postoperative pain. Evaluation may be difficult due to neuraxial or regional block, residual effects of general anesthesia, or the diffuse nature of visceral pain. Risk factors include male gender; duration of surgery; amount of intravenous fluid given; concurrent neurologic disease; perineal surgery; use of anticholinergics, β -blockers, or adrenergic agents; and neuraxial local anesthetic or opioids.²⁵⁷ In addition, high clinical suspicion is merited if pain is accompanied by signs of disparate autonomic changes, such as bradycardia and hypotension. Left untreated, POUR can result in bladder distension and adverse effects on long-term urodynamics. Prompt diagnosis, either clinically or via ultrasound, and bladder catheterization if indicated (postvoid residual >600 mL) can prevent sequelae.

Enhanced Recovery After Surgery

Urologic procedures such as radical cystectomy or radical prostatectomy were traditionally large blood-loss procedures with prolonged recoveries and significant associated postoperative pain. As a result, most pain management algorithms included neuraxial and regional blocks and minimized use of nonsteroidal antiinflammatory drugs (NSAIDs) to decrease bleeding risks. Indeed, various studies have demonstrated the successful use of epidural anesthesia²⁵⁹ or rectal sheath catheters²⁶⁰ in open radical cystectomy. However, with a move toward laparoscopic and robotic-assisted techniques, these procedures have become less invasive and the focus has shifted to early mobilization, recovery, and hospital discharge. These goals are often packaged as part of a perioperative ERAS protocol. From a pain management standpoint, the primary goal of management is use of multimodal analgesia to minimize opioid use and side effects, primarily ileus. Prior to ERAS implementation, postoperative ileus, or lack of gastrointestinal motility, was the most common cause for prolonged hospitalization and readmission, occurring in 12% to 25% of patients after radical cystectomy.²⁶¹

To promote early mobilization, most protocols currently advocate the use of scheduled intravenous or orally administered acetaminophen or paracetamol and of NSAIDs for breakthrough pain, as well as the possible inclusion of gabapentinoids²⁶² and the use of single-shot neuraxial or regional techniques in place of epidural catheters.²⁶³

CHRONIC POSTSURGICAL PAIN

In most cases, postoperative pain resolves quickly, over days to weeks, and can be managed with oral opioid or nonopioid analgesics; however, for some patients, gastrointestinal,

respiratory, or cognitive side effects may prohibit their effective use. Furthermore, a subset of patients develop chronic postsurgical pain (CPSP), defined by the International Association for the Study of Pain as postoperative pain lasting more than 2 months and not explained by preexisting pain or ongoing trauma.²⁶⁴ Risk factors for CPSP are well described across many types of surgery and the incidence can be high, with 20% to 50% of patients reporting persistent chronic pain of any type and 2% to 10% reporting severe disabling pain that ranks from 5 to 10 on the pain intensity numeric rating scale.²⁶⁵ The biggest predictor of CPSP is poorly controlled acute postoperative pain,²⁶⁶ which has led to a focus on the immediate perioperative period.

Perioperative Management Considerations

Specific to renal compromise, meperidine and morphine should be avoided due to accumulation of renal-excreted metabolites including normeperidine and morphine-3-glucuronide, which lower the seizure threshold, and morphine-6-glucuronide, which maintains activity at the μ -opioid receptor and can accumulate to toxic levels if insufficient renal clearance. Opioids, particularly via the neuraxial route, can result in urinary retention. Gabapentinoids, if used, are renally excreted and must be dose adjusted based on creatinine clearance. The antiprostaglandin effect of NSAIDs can decrease renal blood flow or increase bleeding risk in susceptible patients.

ACUTE OR CHRONIC NONMALIGNANT PAIN

Benign Renal Masses

Flank pain is a common symptom in adults with angiomyolipomas, which consist of abnormal growth of blood vessels, smooth muscle, and fat. This benign neoplasm can create a mass effect that affects renal function, and acute worsening of pain should raise suspicion for rupture and hematoma formation. Angiomyolipomas can be associated with tuberous sclerosis but are more commonly found in otherwise healthy individuals. Treatment involves management of symptoms with acetaminophen and antineuropathic agents. Care should be taken with NSAID use, because renal function may be compromised.

Polycystic Kidney Disease

Polycystic kidney disease is most often inherited in an autosomal dominant manner and can lead to massive enlargement of the kidneys with compromised renal function. Renal pain is caused by distention of the cysts and stretching of Gerota fascia. Hemorrhage into the cysts, rupture of the cysts, or infection can produce acute exacerbation of pain. Percutaneous drainage of renal cysts may relieve these symptoms. Opioids can be appropriate in the acute phase.

NEPHROLITHIASIS

Obstruction of the urinary tract causes severe, spasmotic pain in the flank. Pain from the upper third of the ureter may be referred to the lower abdomen and back, pain from the middle third to the iliac fossa, and pain from the lower third to the suprapubic and groin area. Minimal fluid intake and a high concentration of stone-forming salts can predispose

to nephrolithiasis. Renal colic, hematuria, and radioopaque stones (70%–75% of calculi) on radiography or noncontrast CT confirms the diagnosis.²⁶⁷ Opioids and NSAIDs are appropriate for severe, acute symptoms. Despite widespread use, intravenous hydration has not demonstrated benefit.

INFECTIOUS RENAL DISEASE

Infectious renal diseases producing flank pain include pyelonephritis and perinephric abscess. Fever is an important associated finding that suggests the presence of infection. Because the kidneys are retroperitoneal organs, peritoneal signs are generally absent. Differential diagnosis must include inflammatory or infectious disease of surrounding organs, including lower lobe pneumonia, pancreatitis, appendicitis, and cholecystitis. Oral or parenteral opioids are usually effective for pain control in the acute setting. Systemic antibiotics are curative in most cases, although surgical intervention may be warranted and a focal nidus for infection (stone, urethral reflux, recurrent urinary tract infection) should be pursued.

INTERSTITIAL CYSTITIS

Interstitial cystitis is a chronic pain condition marked by suprapubic pain related to bladder filling and symptoms of increased frequency and urgency in the absence of infection or malignancy.²⁶⁸ Pathologic features of interstitial cystitis that may be evident but are not necessary to make the diagnosis include Hunner ulcers (discrete, bleeding areas on the bladder wall) and glomerulations (petechial bleeding after distension). The proposed pathophysiology is thought to be a deficient glycosaminoglycan layer that allows increased permeability of the bladder wall, resulting in inflammation and pain. Options for pain control include pentosan polysulfate (intended to repair the glycosaminoglycan layer), antineuropathics, antihistamines, dimethyl sulfoxide instillation, and sacral nerve stimulators.

NEURALGIAS

Pseudorenal pain syndromes can be caused by entrapment of nerves colocalized with the urinary system in the lower abdomen and groin. Entrapment can occur as the result of trauma or surgical injury or can be idiopathic. Neuralgia of the genitofemoral nerve is common after hernia surgery given its close proximity and variable relation to the spermatic cord. Pain radiates to the inguinal ligament via the femoral branch and to the testicle via the genital branch. Injury to the iliohypogastric or ilioinguinal nerves can occur with lower abdominal incisions or trocar placement for laparoscopy, resulting in neuralgia radiating to the lower abdomen and groin. Pudendal neuralgia can occur with damage to the pudendal nerve along its intrapelvic or extrapelvic course and results in pain of the external genitalia and perineum. Pain sensation is generally neuropathic in these conditions, and dermatomal testing will often reveal sensory deficits. Nerve blocks can be performed under ultrasound guidance²⁶⁹ to help establish the diagnosis, differentiate from urogenital pain, and for therapeutic benefit. Antineuropathic agents can also be of help should nerve injury be confirmed.

CHRONIC PROSTATITIS

Acute prostatitis is usually caused by a bacterial infection and responds to antibiotic therapy. Chronic prostatitis is often referred to as chronic pelvic pain syndrome or chronic abacterial prostatitis to reflect that there is little certainty that inflammation or infection of the prostate is responsible for symptoms.²⁷⁰ Symptoms include genital/pelvic pain and sexual dysfunction, often accompanied by lower urinary tract symptoms. Moderate improvement has been noted with antibiotics, α -blockers, antiandrogens, NSAIDs, and pelvic floor physiotherapy.

PRIAPIST

Priapism is a prolonged erection more than 4 hours in duration and can be ischemic (venoocclusive) or nonischemic (arterial). The former represents an acute emergency, and prompt therapy should be instituted to control pain and prevent subsequent impotence from fibrosis of the corpora cavernosa. Treatment consists of a penile dorsal nerve block performed at the pubic symphysis with needle entry into the subpubic space, performed with local anesthetic without epinephrine, after which aspiration of blood or intercavernosal phenylephrine can be performed.²⁷¹ Nonischemic priapism is most commonly posttraumatic and results from creation of an arteriolar-sinusoidal fistula. This type of priapism is typically not as painful and responds to conservative management. Sickle cell priapism is treated with hydration, alkalinization, and blood transfusion to increase hemoglobin to more than 10 mg/dL.

CHRONIC PELVIC PAIN IN WOMEN

Chronic dysmenorrhea can be addressed with ovulation suppression or use of NSAIDs, which decrease uterine lining thickness and cramping via an antiprostaglandin effect.²⁷² Chronic pelvic pain may also be due to endometriosis, pelvic venous congestion, adhesions, or pelvic inflammatory disease—each of which is most responsive to correction of the underlying disorder for relief of pain. Vulvodynia is a chronic pain condition associated with sexual inactivity or dysfunction due to vulvar pain. Some success with tricyclic antidepressants (TCAs), sitz baths, local estrogen creams, and pudendal nerve blocks has been reported. Vaginismus is associated with increased tone of the muscles of the pelvic floor (pubococcygeus and levator ani) producing spasms and painful sexual dysfunction. Dyspareunia is defined as recurrent and persistent genital pain before or after intercourse not solely explained by infection, trauma, lubrication, or vaginismus. Psychological factors often play a major role and a thorough history should be obtained because there is often a concomitant history of sexual abuse. Treatment involves pelvic floor physiotherapy and desensitization techniques.

TESTICULAR PAIN

Testicular pain can be the result of trauma, torsion, or infection. Trauma or torsion necessitate immediate restoration of blood flow and emergent surgical exploration is the treatment of choice. Orchitis or epididymitis should be suspected

based on a thorough history and if signs of localized or systemic infection accompany pain. Tumors of the testis are most often malignant; however, extratesticular tumors within the scrotum are usually benign. Testicular tumors usually present as a painless testicular mass. Pain is a late sign and is usually described as a dull ache or heaviness due to mass effect.

MEDICATIONS

As with most chronic pain, medication use and risk and benefit must be judiciously weighed. Low-risk, high-yield medications such as topical agents (lidocaine, capsaicin), acetaminophen, and NSAIDs are usually first line treatments, particularly if pain is episodic or infrequent. Antineuropathic agents (gabapentinoids, selective norepinephrine reuptake inhibitors, TCAs) can be useful for prophylaxis, and certain secondary effects can be useful for particular pain conditions (e.g., the anticholinergic effect of a TCA for bladder spasm). Opioids are usually indicated only for acute flares, such as passing of an obstructing stone, and there is little evidence to validate their long-term use.

NERVE BLOCKS AND NEUROMODULATION

When possible, nerves involved with transmission of pain should be identified and treated individually. Treatment can include diagnostic nerve blocks, selective nerve root blocks, therapeutic nerve blocks, pulsed radiofrequency neuromodulation of peripheral nerves, dorsal root ganglia stimulation, cryoablation, radiofrequency ablation, chemoneurolysis, and implantable peripheral field stimulation.²⁷³ Identifying the nerve that is most likely to be injured is the first step in pursuing an interventional approach. Ultrasound guidance offers several advantages that make it highly suited for diagnosing and treating urogenital nerve pain. The machines are portable, there is no radiation exposure, and many of the commonly affected nerves are located superficially. An initial block of the affected nerve using a low volume of local anesthetic can be performed with confirmation of sensory block in the expected distribution. If this block relieves the patient's usual pain, then neuralgia in this distribution is the likely diagnosis.²⁶⁹ Urogenital pain often occurs between the abdomen and thigh, and the nerves supplying the skin and structures in this area are referred to as "border nerves"—the ilioinguinal, iliohypogastric, genitofemoral, and lateral femoral cutaneous nerves arising from the T12-L3 anterior rami as they form the upper lumbar plexus—as well as the pudendal nerve arising from S2-4.

CANCER-RELATED PAIN

Pediatric Tumors

Wilms tumor (nephroblastoma) generally occurs unilaterally and is painless on initial presentation. It may be associated with congenital malformations such as Beckwith-Wiedemann syndrome. Treatment consists of surgical resection most often supplemented by chemotherapy because the tumor is quite responsive to this modality. Perioperative pain may be addressed with epidural anesthesia,

acetaminophen, and opioids. Chemotherapy-induced neuropathy, should it occur, can best be treated with antineuropathic agents.

Renal Cell Carcinoma

Renal cell carcinoma is described as having a classic triad of hematuria, flank pain, and renal mass; however, pain is often a late presentation and may indicate metastatic disease. In cases of metastasis, prognosis is often poor and pain widespread. Early consideration of an intrathecal catheter for continuous delivery of opioids, local anesthetic, or ziconotide can improve patient quality of life. Flank pain may be due to stretching of Gerota fascia, and metastasis is primarily local along the renal vein and inferior vena cava or into the intercostal nerves, which produces segmental neuralgia. In these cases, intercostal nerve blocks and neurolysis can be of use and accomplished under fluoroscopic or ultrasound guidance, most commonly with alcohol or phenol.

Bladder Cancer

The most common urothelial tumor is transitional cell carcinoma of the bladder. Painless hematuria is the most common manifestation, although patients may complain of bladder irritability if there is involvement of the muscular layers. Surgical treatment includes fulguration, transurethral resection, or cystectomy. Pain control is best accomplished with NSAIDs, acetaminophen, opioids, and neuromodulatory agents.

Prostate Cancer

Adenocarcinoma of the prostate is the most common cancer in men and is usually painless, discovered incidentally through routine physical examination. Epidural analgesia can be of use for acute pain control if brachytherapy with seeding is part of treatment. Lumbar or sacral pain with prostatic cancer may be a sign of metastatic disease to bone, which may respond to palliative radiation.

Uterine and Cervical Cancer

Uterine cancer usually presents as irregular bleeding and is associated with increasing age, obesity, nonchildbearing, and hormone therapy. Pain is commonly a late finding, owing to mass effect or invasion into the myometrium. Cervical cancer is generally discovered early through routine vaginal Pap testing, and its incidence has decreased with use of childhood vaccination for specific human papillomavirus strains. However, when present, dyspareunia is a common finding.

Neurolysis

Sympathetic innervation of the uterus and cervix is via the inferior hypogastric plexus, lying within the presacral tissues medial to the foramina sacralia on either side of the rectum, ventral to the S2, S3, and S4 spinal segments. The plexus can be accessed via a transsacral approach,²⁷⁴ and neurolysis can be performed, although particular care is warranted given close proximity to motor nerve roots.

The pelvic viscera in men (the urogenital organs, distal colon, and rectum) are supplied by afferent fibers from the distal lumbar sympathetic chain via the superior hypogastric plexus, a retroperitoneal structure situated along the anterior surface of the L5 and S1 vertebrae. Visceral

innervation follows these fibers, and interruption of these pathways can be achieved with a superior hypogastric plexus block using fluoroscopic or CT guidance and instillation of phenol or ethanol for neurolysis.²⁷⁵

The ganglion impar is another promising target for neurolysis, supplying mixed somatic, autonomic, and visceral fibers to the distal urethra, vulva, perineum, and distal third of the vagina. It can be blocked along the anterior surface of the sacrococcygeal junction, most commonly under fluoroscopic guidance.

Alternatively, peripheral nerve ablation can be performed using a variety of techniques. Ablation should not be performed on any nerves with a significant motor component because weakness will occur. Fortunately, the “border nerves” are primarily sensory; however, neurolysis often creates an area of desensitized skin, which can be bothersome for certain patients and may progress to anesthesia dolorosa, a feared complication manifested by pain in the area despite numbness to stimulation. Nonetheless, these approaches may be of significant benefit in appropriate cases and after full discussion of risks and benefits with the patient. Ablation may be performed with injection of a chemical neurolytic, such as phenol or dehydrated alcohol. Radiofrequency ablation creates a thermal lesion at 80°C along the active needle tip. Cryoablation creates a super-cooled -70°C “ice ball” around the neural sheath, which leads to decreased transmission via wallerian degeneration. Case reports and series have shown promising results with decreased pain and analgesic requirements.

Intrathecal Medications

If intractable pain persists despite optimized oral or intravenous therapy, a single shot or tunneled intrathecal catheter trial can be performed and an implantable drug delivery system should be considered. Continuous intrathecal infusions minimize fluctuation of drug levels in cerebrospinal fluid and allow for significant analgesia and use of spinal adjuncts (local anesthetic, ziconotide) in addition to opioids with significantly lessened dose-limiting side effects.

In summary, perioperative pain syndromes of the urogenital system and those related to pain from malignant or nonmalignant disease require prompt attention, a comprehensive assessment, and consideration of multimodal early intervention including treatment with nonopioid or opioid medications, neuraxial and regional nerve blocks, and neuromodulation or surgery when appropriate.^{276–278}

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