

Chapter 14: Anesthesia for Neurosurgical Procedures

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INTRODUCTION

FOCUS POINTS

1. The cranial vault changes structurally from birth through the first 2 years of life. Eighty percent of the intracranial volume consists of brain and interstitial fluid, with blood and cerebrospinal fluid (CSF) making up the remainder. Intracranial compliance is the change in intracranial pressure (ICP) relative to the volume.
2. The open fontanelles and sutures in infancy results in increased intracranial compliance and allows for slow expansion of contents.
3. The Munro-Kellie hypothesis states that the sum of all intracranial volumes is always a constant. Infants are an exception to this rule because of the increased compliance and pliability of the skull. Mass effect of a slow growing tumor or hemorrhage can thus be masked by this compensation.
4. Acute changes in volume due to hemorrhage or obstruction of the CSF flow are not attenuated and can lead to life-threatening consequences.
5. Cerebral perfusion pressure (CPP), the pressure gradient across the brain, is the difference between mean arterial pressure (MAP) at the entrance to the brain and the mean exit pressure (i.e. central venous pressure), or intracranial pressure (ICP) if elevated. It is a more reliable estimate of cerebral perfusion.
6. In adults, cerebral autoregulation maintains a constant brain perfusion despite moderate changes in MAP or ICP. The lower absolute limits of cerebral autoregulation in infants and children is unclear and the range is believed to be narrower in neonates.
7. Acceptable MAP for a neonate is the gestational age in mmHg. Tight blood pressure control is essential in the management of neonates to minimize both cerebral ischemia with hypotension, and intraventricular hemorrhage with hypertension.

Certain pediatric disease states have specific anesthetic considerations and require tailoring of the intraoperative anesthetic management to the unique disease condition.

The practice of anesthesia for pediatric neurosurgical conditions requires understanding of the distinct differences in children compared to adults, and is made more challenging by the unique management considerations. There are age-related differences in the incidence, anatomy, and pathology of surgical lesions in this population, which translate into the need for an individualized approach to the pediatric neurosurgical patient. Differences in the physiological responses to surgery and anesthesia from adults are what set children apart, and make management decisions different from what is considered the norm of adult neuroanesthetic practice. Over the last couple of decades, the numerous technological advances in neurosurgery coupled with subspecialization, and a better understanding of the postoperative needs of pediatric patients have dramatically improved outcomes in infants and children with neurosurgical lesions.¹

COMMON PEDIATRIC NEUROSURGICAL CONDITIONS

Congenital anomalies and malformations

Tumors

Hydrocephalus

Epilepsy

Craniosynostosis

Vascular anomalies—arteriovenous malformations, vein of Galen, moyamoya syndrome

Neuroimaging and interventional neuroradiological procedures

Neurotrauma

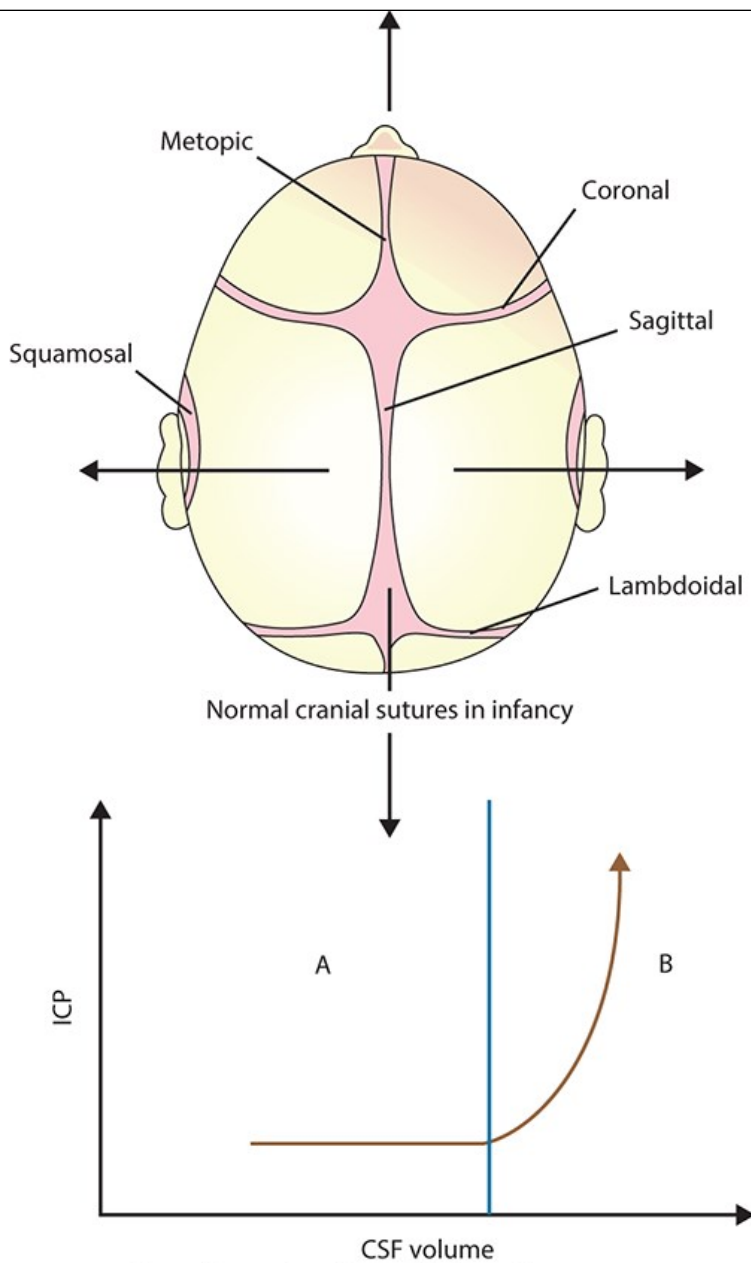
NEUROANATOMY, DEVELOPMENTAL CONSIDERATIONS, AND NEUROPHYSIOLOGY

The infant cranial vault undergoes several structural and physiological changes in the first 2 years of life. The intracranial space is compliant owing to open fontanelles and sutures, allowing for a slow expansion of intracranial volume. The posterior fontanelle is the first to close around 2 to 3 months of age, followed by the sphenoid and mastoid fontanelles, with the anterior fontanelle being the last to close about 2 to 3 years of age. The infant brain triples its weight in the first year after birth. Eighty percent of the intracranial volume consists of brain and interstitial fluid, with blood and cerebrospinal fluid (CSF) making up the remainder. CSF volume is proportionately larger in infants and neonates (4 mL/kg) compared to adults (2 mL/kg), but the rate of production of CSF is similar.

The Munro-Kellie hypothesis states that the sum of all intracranial volumes is always a constant. Infants demonstrate an exception to this hypothesis as the infant skull is pliable up until 2 years of age.² The mass effect of a slow-growing tumor or hemorrhage is thus often masked by compensatory distension of the fontanelle and widening of the cranial sutures. However, acute increases in volume due to massive hemorrhage or an obstructed ventricular system cannot be attenuated by this expansion, and can result in life-threatening increases in intracranial pressure (ICP) or herniation (Figure 14-1).³

Figure 14-1

Cranial sutures and fontanelle in neonates and infants. Initially the compliant skull of the neonate minimizes insidious increases in intracranial volume. However, acute increases in intracranial volume will lead to rapid rises in intracranial pressure. (Reproduced with permission, from Davis P, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. 2011. Copyright © Elsevier. All rights reserved.)

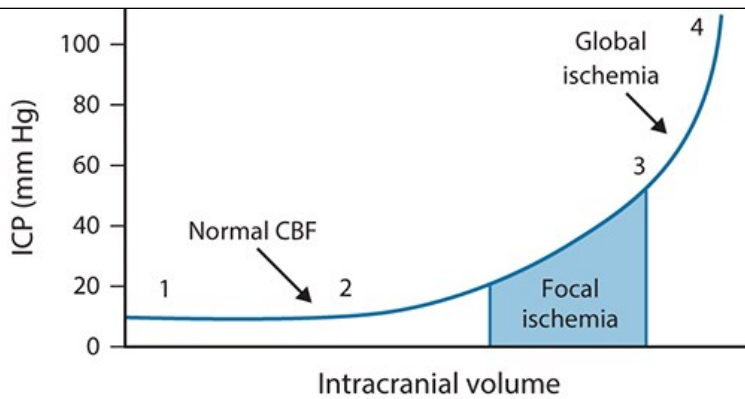


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Intracranial compliance is the change in ICP relative to the intracranial volume. Once the fontanelles and sutures have closed, children have a smaller cranial volume and lower intracranial compliance than adults, putting them at a higher risk for herniation (Figure 14-2).⁴ A higher ratio of brain water content, less CSF volume, and a higher ratio of brain content to intracranial capacity are further contributory factors.

Figure 14-2

Intracranial compliance curve. At normal intracranial volumes (1), ICP is low but compliance is high and remains so despite small increases in volume. As intracranial volume acutely rises (2), the ability to compensate is rapidly overwhelmed, even when the ICP is still within normal limits, but the compliance is low. At higher ICP (3), a threshold is quickly reached where further volume expansion leads to rapid and higher increase in ICP. Maximal intracranial volume and high ICP are shown by the number 4. (Reproduced with permission, from Davis P, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. 2011. Copyright © Elsevier. All rights reserved.)



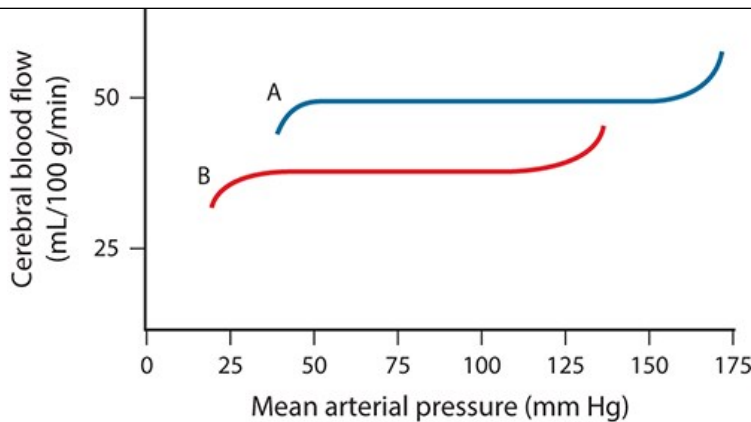
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There are unique differences in cerebrovascular physiology that distinguish children from adults. Cerebral blood flow (CBF) is regulated to meet the brain's metabolic demands. Cerebral metabolic rate for oxygen (CMRO₂) is higher in children at about 5.8 mL/100 g/min compared to adult levels of 3.5 mL/100 g/min. CBF in healthy children is believed to be about 100 mL/100 g/min compared to adults at 50 mL/100 g/min. CBF is tightly coupled to cerebral metabolism and CMRO₂ at global and regional levels. Hypoxemia, hypercarbia, and ischemia cause cerebral vasodilation, which increases CBF. A decrease in brain metabolism similarly reduces CBF. Both CBF and metabolic demand increase immediately after birth and thereafter, the changes mirroring neuroanatomical and psychomotor growth, which in turn reflect cognitive growth. CBF is 10% to 20% of the cardiac output in the first 6 months of life, peaking at 55% between ages 2 and 4 years, settling into adult levels of 15% by 7 to 8 years.⁵

Cerebral perfusion pressure (CPP) is a more practical estimate of the adequacy of cerebral circulation. It is the pressure gradient across the brain, the difference between MAP at the entrance to the brain and the mean exit pressure (ie, central venous pressure), or ICP if elevated. Autoregulation maintains a constant brain perfusion despite moderate changes in mean arterial pressure (MAP) or ICP. In adults, cerebral autoregulation ensures that CBF remains relatively constant within a MAP range of 50 to 150 mm Hg, outside of which CBF becomes pressure dependent. This autoregulation occurs at undefined lower absolute values in infants and children (Figure 14-3). There is data that children as young as 6 months of age autoregulate CBF as well as older children, but the lower limit of autoregulation (LLA) in healthy neonates is unclear. Neonates are believed to be especially vulnerable to cerebral ischemia and intraventricular hemorrhage due to a narrow autoregulatory range. However, previously held beliefs that the LLA is lower in infants than older children have been challenged.⁶ Infants are also likely at increased risk for cerebral ischemia due to lower blood pressure reserve. Analysis of cerebral perfusion in infants and children undergoing cardiopulmonary bypass reveals a wide range in the lower limits of autoregulation suggesting individual variability, and highlights the limitations of currently available monitors to measure and optimize cerebral perfusion.⁷ Diastolic blood pressure might be a better indicator of cerebral perfusion pressure (CPP) in this population.⁸ Cerebral ischemia, heralded by EEG slowing, occurs at CBF values of about 25 to 40 mL/100 g/min and is followed by initially reversible neuronal damage. Rapid cell death occurs at a CBF less than 6 mL/100 g/min. The lower the CBF at ischemic levels, the shorter the duration allowable before irreversible neuronal damage. Tight blood pressure control is, therefore, essential in the management of neonates to minimize both cerebral ischemia with hypotension, and intraventricular hemorrhage with hypertension. A clinically accepted "rule of thumb" is that MAP for a neonate approximates the gestational age.

Figure 14-3

Autoregulation of cerebral circulation in neonates (curve B) and adults (curve A). (Reproduced with permission, from Davis P, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. 2011. Copyright © Elsevier. All rights reserved.)



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Despite these observations, the mechanism of normal cerebral autoregulation in healthy children and adaptations in acute disease are not completely understood. To complicate things further, both anatomical and physiological maturation might play a role in the development of a fully developed autoregulatory response as the child grows.

Vasoreactivity to CO_2 is believed to be higher in children than adults, and is well developed even in healthy preterm infants. Rapid diffusion of arterial CO_2 across the blood-brain barrier (BBB) leads to changes in extracellular pH, which in turn leads to cerebral vasodilation and increased CBF.⁹ The relationship between PaCO_2 and CBF is linear. The mechanism of CO_2R , however, is complex and influenced by a variety of other mediators including nitric oxide, prostaglandin E2, and indomethacin. In comparison, the influence of PaO_2 is of much less clinical significance. There are minimal changes in CBF with changes in PaO_2 above 50 mm Hg. Below a PaO_2 of 50 mm Hg, cerebral vasodilation occurs and increases CBF to maintain adequate cerebral oxygen delivery.¹⁰ This lower threshold of PaO_2 is lower in neonates. Hyperoxia is believed to decrease CBF; however, its influence is controversial.

DRUGS AND THEIR EFFECTS ON NEUROPHYSIOLOGY

The ideal anesthetic agent would be one that decreases ICP and CMRO_2 , and maintains CPP. There is insufficient data on the effects of commonly used anesthetic agents in infants and children. The changes seen in CBF, CPP, ICP, and CMRO_2 as summarized in Tables 14-1 and 14-2 are extrapolated from adult literature and should be used as a guideline.

Table 14-1

IV Anesthetics and their Effects on Cerebral Hemodynamics

	MAP	CBF	CPP	ICP	CMRO_2
Propofol	↓↓↓	↓↓↓	↑↑	↓↓	↓↓↓
Etomidate	0-↓	↓↓↓	↑↑	↓↓↓	↓↓↓
Ketamine	↑↑	↑↑↑	↓	↑↑↑	↑
Benzodiazepines	0-↓	↓↓	↑	0	↓↓
Opioids	0-↓	↓	↓↑	0-↓	↓

Table 14-2

Inhaled Anesthetics and their Effects on Cerebral Hemodynamics

	MAP	CBF	CPP	ICP	CMRO ₂
Isoflurane	↓↓	↑	↓	↑	↓↓↓
Sevoflurane	↓↓	↑	0~↓	0~↑	↓↓↓
Desflurane	↓↓	↑	↓	↑	↓
Nitrous oxide	0~↓	↑~↑↑	↓	↑~↑↑	↓

Intravenous Agents

Propofol

Propofol maintains autoregulation and cerebral responsiveness to changes in PaCO₂, suppresses seizure activity, and may be neuroprotective. In the setting of elevated ICP, propofol may be a superior maintenance anesthetic compared to inhaled halogenated agents.

Opioids

Opioids have very minimal effects on CBF or ICP except in the setting of hypoventilation and elevated PaCO₂. All opioids preserve cerebral autoregulation and CO₂ reactivity, and cause EEG slowing in a dose-dependent manner. Fentanyl has minimal effects, if any, on even the neonatal cerebral circulation and is used extensively. Sufentanil and alfentanil in dose ranges from 10 to 20 mcg/kg reduce both CBF and CMRO₂ by 25% to 30%.¹¹ Remifentanil is an ultra-short-acting opioid that is rapidly metabolized by plasma cholinesterases. It has a very short duration of action, because its context-sensitive half-life is independent of the duration of infusion.¹² This makes it especially suitable for lengthy procedures at the end of which an accurate neurological assessment is mandatory, the one caveat being that because analgesia is very brief after its discontinuation, it is imperative to administer a long-acting opioid analgesic in a timely manner to prevent severe pain and rebound hypertension.

Etomidate

Etomidate is often used in hemodynamically unstable patients as it causes less hypotension than propofol, but it is important to bear in mind that it can cause myoclonus.

Ketamine

Ketamine is unlike other induction agents. It is a potent cerebrovasodilator and increases CBF, with marked increase in ICP that is not prevented by hyperventilation. It is often not an appropriate choice for most neurosurgical patients, unless there is significant hemodynamic compromise.

Dexmedetomidine

Dexmedetomidine is a selective α₂ adrenergic agonist that is being increasingly used in anesthetic practice, either as a supplement to other agents during general anesthesia or as the sole agent for moderate to deep sedation. It was initially found especially useful in awake craniotomies in teenagers, but in recent years its use has encompassed other neurosurgical procedures also.^{13,14} Small-scale studies report that it has a good safety profile.

Volatile Anesthetics

All inhalational agents uncouple CBF and CMRO₂, but to different degrees. They increase CBF and ICP by their vasodilatory effect, while decreasing CMRO₂. They also blunt the autoregulatory response in a dose-dependent manner. It is possible to minimally affect CBF and ICP by employing a balanced anesthetic technique with low concentrations of a volatile agent combined with intravenous agents, and a ventilatory strategy that maintains normocarbida or hypocarbida. Isoflurane and sevoflurane seem to maintain coupling to some degree, significantly decrease CMRO₂, and are often the agents of choice in neuroanesthetic practice.¹⁵ It is worthwhile to note that isoflurane causes an isoelectric EEG at about 2.0 MAC compared to sevoflurane which causes dose-dependent epileptiform activity on EEG.

The use of nitrous oxide is controversial. The increased CBF and resultant increase in ICP can lead to complications especially in the presence of reduced intracranial compliance. Its effects are modified by other agents it is used with, and it is not an adequate anesthetic by itself. Some practitioners prefer to use it for the initial mask induction alone, reinstate it after the dura is opened, and then discontinue it prior to dural closure, as intracranial air can persist for up to 3 weeks after a craniotomy and the rapid expansion of air cavities can cause a tension pneumocephalus. However, it has also been used for entire procedures without detrimental effects and does have a long track record of safety. Most practitioners agree that it should be avoided in the situation where a child has had a recent craniotomy.¹⁶ Its use is not contraindicated in sitting craniotomies; the fact that it might expand a venous air embolism (VAE) might even increase the sensitivity of monitoring for VAE by capnography in these cases.

PREOPERATIVE EVALUATION

A number of pediatric neurosurgical conditions are of an emergent nature. Despite this, a thorough preoperative evaluation and organ system review is essential to identify coexisting morbidities that might increase the likelihood of perioperative complications, and help anticipate physiological derangements. In the setting of emergent surgery, children with a preexisting upper or lower respiratory infection, a full stomach, gastrointestinal reflux, or ongoing emesis are at higher risk and appropriate precautions should be taken to prevent complications. Children presenting with repeated emesis, those who have had prolonged fasting periods, and those with polyuria secondary to diabetes insipidus are at risk for hypovolemia or hypoglycemia, both of which can cause hemodynamic and metabolic perturbations under anesthesia. Many neurosurgical patients have comorbidities that are part of a syndrome, and routinely return to the operating room for repeat procedures. It is useful to inquire about prior anesthetic experiences and issues in the postoperative period. The risk of latex allergy should be considered.

Premature infants are prone to postoperative apneic spells at baseline; this could be amplified by the neurological condition. Intraoperative management and postoperative disposition should take this into account. Craniofacial anomalies can make airway management a challenge; this should be anticipated, and special equipment and techniques utilized as necessary. Congenital heart disease might complicate the perioperative course, especially in the newborn. A thorough evaluation with input from a pediatric cardiologist, and an echocardiogram might be warranted to aid in optimizing cardiac function when the acuity of the condition allows. Children with suprasellar masses might need an endocrinological evaluation. There are certain neurological conditions that warrant special considerations in the preoperative period, as outlined in [Table 14-3](#). Children might present with a vagal nerve stimulator, which might need to be deactivated for the anesthetic as it can cause repetitive vocal cord stimulation.

Table 14-3

Anesthetic Concerns for Pediatric Neurosurgery

Denervation injuries	Hyperkalemia after succinylcholine—use NDPMR Resistance to nondepolarizing muscle relaxants
Chronic exposure to antiseizure medications	Hepatic dysfunction Hematological abnormalities Increased metabolism of anesthetic agents Require increased doses and frequent redosing
Arteriovenous malformations Moyamoya disease	Potential for congestive heart failure Risk of perioperative ischemia
Neuromuscular disease	Malignant hyperthermia Respiratory failure Sudden cardiac death
Arnold-Chiari malformation	Postoperative apnea Aspiration pneumonia Postoperative stridor
Hypothalamic and pituitary lesions	Adrenal insufficiency/excess Thyroid abnormalities Diabetes insipidus/SIADH
Craniofacial abnormalities	Difficult airway Significant blood loss
Neural tube defects (myelomeningocele)	Latex sensitivity, allergy and risk of anaphylaxis

Preoperative physical examination should document the level of consciousness, motor and sensory function, cranial nerves, pupillary reflexes, and signs and symptoms of elevated ICP, which will serve as a baseline for postoperative assessment. The signs of raised ICP vary based on the age of the child, as outlined in [Table 14-4](#). Irritability and altered consciousness are common signs, but papilledema may not be seen even in late stages of intracranial hypertension. Brainstem lesions can present with cranial nerve dysfunction such as impaired gag reflex and swallow, respiratory distress, diplopia, and aspiration. Visual field changes can occur with suprasellar masses. A clinical assessment of volume status is imperative. Preoperative laboratory tests should be tailored to the neurological condition, surgery being performed, anticipated blood loss, and general health of the child. Liver function tests and hematological profile may be necessary in children who are on chronic anticonvulsants. Type and cross-matched blood should be available for surgeries with large volumes of predicted blood loss, such as resection of large tumors, and craniofacial reconstructions. Unanticipated blood loss is a risk with interventional procedures for vascular malformations in the radiology suite. As blood-draws can be challenging in infants, it is reasonable to draw a hematocrit, PT, and PTT soon after induction in the operating room to minimize trauma to the child.

Table 14-4

Signs of Intracranial Hypertension in Infants and Children

Infants	Children	Infants and Children
Irritability	Headache	Decreased consciousness
Full fontanelle	Diplopia	Cranial nerve (III & IV) palsies
Widely separated sutures	Papilledema	Loss of upward gaze (setting sun sign)
Cranial enlargement	Vomiting	Signs of herniation, Cushing's triad, pupillary changes

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Premedication should be utilized judiciously in the pediatric patient requiring neurosurgery. In infants and younger children, it is best to administer this in the preoperative area, to ease separation from parents.^{17,18} Premedication is especially necessary in certain conditions such as moyamoya disease to avoid agitation and crying, or in the case of an arteriovenous malformation that has recently bled. Oral midazolam is usually the drug of choice; it may be administered parenterally if an intravenous catheter is present, and titrated to effect under the direct supervision of a medical provider. The decision to premedicate should be weighed against the risk of oversedation in a neurologically impaired patient in whom hypoventilation might increase the risk of intracranial hypertension.

INTRAOPERATIVE AND POSTOPERATIVE CONSIDERATIONS

Induction technique and choice of induction agent are based on the preoperative status of the patient, a rapid sequence induction being mandatory in the somnolent child with signs of raised intracranial pressure owing to the risk of aspiration. The goal during induction is to minimize further increases in ICP. In general, as discussed earlier, most intravenous drugs decrease CBF, cerebral metabolism, and ICP. It may be necessary to use etomidate or ketamine in the setting of hemodynamic compromise; however, the use of ketamine in traumatic brain injury (TBI) is controversial. In neurologically stable patients, a mask induction with sevoflurane and nitrous oxide can be performed, followed by a muscle relaxant. Manual hyperventilation can be utilized if necessary to decrease ICP. Succinylcholine can result in life-threatening hyperkalemia in patients with denervating processes such as stroke, spinal cord injury, crush injuries, stroke, or muscular dystrophies, and should be avoided.

Positioning requirements vary among neurosurgical cases. Special attention should be paid during positioning to optimize access for both surgeon and anesthesiologist, while ensuring the safety of the patient. Many neurosurgical procedures require prone positioning, with the head of the bed turned 90 to 180 degrees away from the anesthesiologist. All the considerations for prone cases hold true. The head is secured in cranial fixation pins, or a Mayfield frame with the neck flexed or extended to facilitate surgical exposure. Extreme rotation of the head can impede venous return or compromise cerebral perfusion; extreme flexion can cause migration of the endotracheal tube into a mainstem bronchus, or cause brainstem compression in posterior fossa lesions, while extreme extension can lead to unplanned extubation. Sometimes it is required that the head be higher than the torso to facilitate venous and CSF drainage from the surgical site, increasing the risk of venous air embolism (VAE).¹⁹ In infants, VAE can occur even in the lateral, prone, or supine position, as the larger head rests above the heart.^{20,21} The risk is increased in children with intracardiac shunts. Precordial Doppler is the earliest and most sensitive monitor to detect VAE but prone positioning may preclude its use on the anterior chest. In infants weighing less than 6 kg the Doppler could be placed on the posterior thorax between the scapulae. In addition to the characteristic changes in Doppler sounds, a sudden decrease in end-tidal CO₂, dysrhythmias, and ischemic changes on the EKG should alert one to the occurrence of VAE.

Two large peripheral venous catheters are usually sufficient for most cases. Central venous catheters are not routinely used unless needed for difficult access, as the narrow-gauge catheters used in children are often unsuccessful in aspirating air even in the event of a VAE. An arterial line is warranted for major craniotomies owing to the risk of hemodynamic instability from sudden hemorrhage, VAE, herniation, or cranial nerve manipulation. Currently, EEG is considered the most reliable intraoperative monitor for focal cerebral ischemia and is employed for cerebral aneurysm clipping and surgery for moyamoya disease. Near-infrared spectroscopy (NIRS) is increasingly proving useful for early detection of global cerebral ischemia. It

provides a noninvasive assessment of venous oxy-Hb saturation and has been reported to correlate with jugular bulb saturation. EMG is useful in identification and dissection of functional nerve roots in tethered spinal cord syndrome. In surgeries involving the spine, SSEP monitoring is utilized to assess the dorsal sensory pathways of the spinal cord and MEP to monitor the integrity of the corticospinal tracts that transmit motor impulses. Electrocochography (ECoG) is used for cortical stimulation in seizure surgery. Preoperative planning should include a discussion of the type and extent of neurophysiological monitoring to be used, as many anesthetic agents have a depressant effect on some monitors.

Maintenance of anesthesia is optimally achieved with an opioid-based balanced technique that includes low-dose volatile agent and a muscle relaxant. Muscle relaxation should be avoided in cases where intraoperative EMG, MEP, or muscle stimulation is utilized. As discussed, some prefer to avoid nitrous oxide completely while others reserve its use for certain portions of the surgery. Meticulous fluid management is essential and although there is no absolute formula, maintenance of normovolemia is key in most situations. Normal saline or Plasma-Lyte are commonly used as maintenance fluids. The use of colloids in the setting of a disrupted blood-brain barrier is controversial. The decision to transfuse blood is based on the type and duration of surgery, underlying condition of the child, and potential for ongoing blood loss. Brain swelling and raised ICP are managed with a combination of judicious hyperventilation, steroids, and hyperosmolar therapy that may include [mannitol](#) or hypertonic saline, along with furosemide.^{22,23} Hypertonic saline may be associated with natriuresis, central pontine myelinolysis, and rebound increase in ICP, but it is being used increasingly in patients with elevated ICP from TBI.²⁴

The decision to extubate after surgery is based on numerous factors. Airway edema is a concern in prolonged prone cases with significant blood loss requiring large volume replacement. The risk of postoperative apnea and vocal cord paralysis should be considered in surgeries involving the brainstem. If extubation in the operating room is planned, the anesthetic should be tailored to facilitate neurological assessment at or soon after emergence. Emergence and extubation should be smooth to prevent swings in blood pressure and ICP. Postoperative care for the large majority of neurosurgical cases is optimally provided in the intensive care unit for 1 to 3 days after surgery, where close monitoring of neurological status can be achieved. One should be alert to the occurrence of postoperative seizures; although the incidence is low, the effects can be devastating.²⁵ The routine use of prophylactic anticonvulsants for craniotomies is debatable. Levetiracetam is replacing phenytoin in some centers as the anticonvulsant of choice, as monitoring for therapeutic serum levels is not necessary, and risk of toxicity is lower.

CONSIDERATIONS FOR SPECIFIC DISEASE STATES AND SURGERIES

Certain neurological disease states are unique to infants and children. Understanding the natural course goes a long way in providing the optimal anesthetic, while minimizing complications. The general principles of intraoperative management may need to be modified for specific disease states.

Congenital Anomalies

Spinal dysraphism is a midline defect that can be minor involving only the superficial bone and membranous structures, or it may be more extensive involving malformed neural tissue; it can involve the head (encephalocele) or spine. Spina bifida refers to a spectrum of spine defects; a defect containing CSF alone is a meningocele; a defect that also includes neural tissue is a meningomyelocele. These are often associated with hydrocephalus and type II Arnold-Chiari malformations. Primary closure usually is undertaken on the first 1 to 2 days of life. Special attention is to be paid during induction to positioning; if intubation is attempted in the supine position a “donut” ring is used to avoid pressure on the defect. In the case of large defects, intubation in the lateral position may be necessary. This is a field where in utero repair is increasingly being performed as the defect is frequently identified on prenatal ultrasound. These patients are at high risk of developing latex sensitivity and anaphylaxis, as they are repeatedly exposed to latex products, both in surgery for coexisting orthopedic and urological problems, and during routine care as in repeated bladder catheterizations. They may grow to develop a tethered spinal cord that can cause nerve root distortion, progressive neurological deficits, and chronic pain. Intraoperative EMG monitoring can help identify functional nerve roots and avoid inadvertent injury that can lead to fecal or urinary incontinence. Selective dorsal rhizotomy is a procedure performed for severe spasticity associated with cerebral palsy. This involves surgical division of dorsal rootlets to decrease afferent input to motor neurons in the spinal cord. The rootlets are identified by direct stimulation and noting of the corresponding muscle action potential with EMG. These patients have severe somatic pain postoperatively, along with dysesthesia, hyperesthesia, and muscle spasms. A multimodal postoperative pain management strategy is imperative.²⁶

Arnold-Chiari Malformations

These consist of a bony abnormality of the posterior fossa and upper cervical spine, leading to varying degrees of caudad displacement of the

cerebellar vermis and brainstem through the foramen magnum, often accompanied by myelodysplasia. Of the four types, children with type I have milder symptoms, type II often have coexisting hydrocephalus, type III have the most severe symptoms with long-term disability, and type IV is characterized by cerebellar hypoplasia or aplasia. Decompressive suboccipital craniectomy with cervical laminectomies is the surgical treatment. Care should be taken in these patients to avoid extreme head flexion during intubation as it can cause brainstem compression. Abnormal responses to hypoxia and hypercarbia should be anticipated as they have cranial nerve and brainstem dysfunction.

Tumors

Brain tumors are the second most common childhood malignancy, next to leukemias. The majority are infratentorial, occurring in the posterior fossa, and include medulloblastomas, cerebellar astrocytomas, brainstem gliomas, and ependymomas of the fourth ventricle. Infratentorial tumors can obstruct CSF flow early in the course, thereby leading to intracranial hypertension and hydrocephalus, in addition to causing cranial nerve palsies and ataxia. Supratentorial tumors account for 25% to 40% of brain tumors in children and include astrocytomas, oligodendrogliomas, ependymomas, and glioblastomas. Presenting symptom is often a seizure or focal neurological deficit.

Surgery for tumor resection is fraught with anesthetic challenges at every stage. Positioning is often prone or lateral decubitus with the head fixed in pins, and turned 90 to 180 degrees away from the anesthesiologist based on surgeon preference. Skull fractures, intracranial hematomas, and dural tears are risks during pinning. Sinus tears, VAE, and massive blood loss are risks during raising of the bone flap, and require constant vigilance. Elevated ICP is managed by altering ventilation techniques, administering [mannitol](#), or both, or by the insertion of a ventricular or lumbar catheter by the surgeon. Arrhythmias and hemodynamic perturbations are not uncommon during brainstem manipulation. VAE can occur in any position as the head is often elevated to improve venous drainage. Postoperative concerns include apnea and airway obstruction from damage to the respiratory centers and cranial nerves, or airway edema from prolonged prone positioning.

Midbrain tumors seen in children include craniopharyngiomas, pituitary adenomas, optic nerve gliomas, hypothalamic tumors, and papillomas of the choroid plexus. Precocious puberty is often the presentation in hypothalamic tumors. Of the perisellar tumors, craniopharyngiomas are the most common and can be accompanied by endocrine derangements; steroids are often necessary as the hypothalamic-pituitary-adrenal axis is affected. Diabetes insipidus can occur anytime during the perioperative period. Urine output should be closely monitored along with serum electrolytes, and osmolality. The transsphenoidal approach is sometimes used in older children for pituitary adenoma resection; massive bleeding can occur and one should be prepared for urgent conversion to an open craniotomy. Optic nerve gliomas are common in children with neurofibromatosis. They are highly vascular and significant blood loss can occur. Choroid plexus papillomas are less common and usually arise from the lateral ventricle. The increased production of CSF and obstruction to flow can result in early hydrocephalus.

Stereotactic approaches to surgery involve application of a headframe that limits access to the airway, usually applied after induction in the operating room (OR), after which the anesthetized child is transported to the CT scanner, and then back to the OR. Newer thermolaser ablation for inoperable tumors involves transport to the MRI suite where the treatment is delivered with imaging guidance. It is necessary in these cases to have a secure airway, while maintaining TIVA during transport. Hybrid OR-MRI suites have made these procedures more manageable.

Hydrocephalus

Hydrocephalus is a condition of increased CSF volume as a result of mismatched CSF production and absorption, leading to increased intracranial pressure. It is the most common neurosurgical condition in pediatrics, most cases resulting from the obstruction of CSF flow, or an inability to absorb CSF. In neonates, especially premies, intraventricular or subarachnoid hemorrhage is a common cause, as is congenital aqueductal stenosis. Other causes include trauma, infection, and posterior fossa tumors. Hydrocephalus may be nonobstructive (communicating) or obstructive (noncommunicating) based on whether there is unimpeded flow of CSF around the spinal cord. The acuity of presentation depends on the rapidity of development of hydrocephalus and the intracranial compliance. In the infant, the cerebral vault gradually expands to accommodate the increased CSF volume if hydrocephalus develops over time. In older children whose sutures are fused, the risk of herniation is higher as the skull cannot expand. These children present with increasing lethargy and vomiting, can rapidly develop cranial nerve dysfunction and bradycardia, and progress to brain herniation and death. They are definite aspiration risks. Following a rapid sequence induction, hyperventilation is instituted to control the ICP. Definitive treatment is correction of the cause, but immediate treatment involves placement of a ventricular drain or ventriculoperitoneal (VP) shunt with the goal of rapidly relieving the obstruction. VP shunts divert CSF from the ventricles to the peritoneal cavity. When absorption through the peritoneum is compromised, as in peritonitis, the distal end of the shunt is placed in the right atrium or pleural cavity. Shunts may need to be replaced as the child grows or the pathophysiology changes, requiring repeat trips to the operating room. Shunts with programmable valves help minimize this

to some extent. Acute obstruction of a shunt needs to be treated urgently as it can have lethal consequences. Shunt infection is another possible risk; in this situation, the entire shunt system is removed and an external ventricular drain (EVD) established temporarily. A new shunt is placed after treatment of the infection. Transportation and moving of patients with EVDs require special attention to avoid sudden drainage of CSF or dislodgement of the tubing. Excess drainage of CSF can lead to slit ventricle syndrome.²⁷ Fluid overload should be avoided to minimize brain swelling. Endoscopic ventriculostomy is a procedure that creates an alternative route from one area of CSF to another, bypassing an area of obstruction. Common locations for a ventriculostomy are through the septum pellucidum allowing the lateral ventricles to communicate, or through the floor of the third ventricle into the CSF cisterns. Cauterization of the choroid plexus helps to reduce excessive CSF production. Damage to the basilar artery and its branches, or neural injuries are a concern with these procedures and can have dire consequences.

Epilepsy Surgery

Seizures are a common neurological disorder in children, and can be a component of various epilepsy syndromes. Vagal nerve stimulators inhibit seizures at the brainstem/cortical levels. Surgical resection of the seizure focus is undertaken when a child has medically refractory epilepsy that has failed other treatment options, and involves serial craniotomies. The first is for insertion of intracranial grid-and-strip electrodes on the exposed cortex of the brain. During this first anesthetic, it is important to avoid agents that may suppress seizures during and after the procedure, that is, long-acting benzodiazepines. The patient is monitored for seizures in the electrophysiology unit to map the location of the seizure foci; the mapping then serves to guide the neurosurgeon for resection. This may take several days but typically the patient returns to the operating room in 2 to 3 days. Surgical risk and anesthetic concerns are dependent on the location of the seizure focus, its proximity to vital structures, and the age of the patient. Intraoperative neurophysiological monitoring is used to guide the resection; this might include cortical stimulation to identify the motor strip, EEG, and EMG. Advances in neurophysiological monitoring have made these procedures safer and more accurate. The anesthetic technique is tailored to the patient's specific requirements with the goal of not compromising the monitoring, especially when the seizure foci involve functional areas of the brain. A narcotic-based general anesthetic with low levels of volatile agent is optimal. Muscle relaxation is avoided if cortical stimulation of motor cortex or EMG is being used. Upregulation of the hepatic P450 enzymes from chronic use of anticonvulsants can result in rapid metabolism and clearance of neuromuscular blockers and opioids in these patients leading to the need for larger and repeated dosing, but also facilitates monitoring when needed.^{28,29} A major risk during these procedures is harm to the "eloquent cortex," the area of the brain that controls speech, memory, and other vital functions. Awake craniotomies allow the patient to assist in the determination of the limits of safe cortical resection; they are rarely undertaken in children but may be considered in older cooperative teenagers. Anesthesia for an awake craniotomy can range from no sedation with local anesthesia alone to alternating "asleep-awake-asleep" techniques in which general anesthesia is limited to the period before and after functional testing.³⁰ Following induction of general anesthesia, the airway is secured with either an endotracheal tube or a laryngeal mask airway, and the patient is kept asleep for line placement, head pinning, and opening of skull and dura. The anesthetic is then discontinued, and the patient extubated and awakened for the period of functional neurological testing and resection, during which time a psychologist is also often present in the operating room. Once resection is completed, general anesthesia is reinstituted for the closure. This technique allows for the patient to be completely anesthetized for the painful parts of the surgery. A disadvantage is the unpredictability of the patient's emergence with pins in place, and reactions under surgical drapes. Deep sedation with a natural airway, using propofol and dexmedetomidine, combined with an opioid is an alternative. Not all older children are good candidates for an awake craniotomy; patient selection should take into consideration their maturity, psychological preparedness, and ability to cooperate with strangers in an unfamiliar environment. Developmentally delayed children and those with anxiety or other psychiatric disorders are clearly not candidates.

Lobectomy, corpus callostomy, and hemispherectomy are alternative procedures performed when focal resection is not an option. One should be prepared to manage large volumes of blood loss in these cases.

Craniosynostosis

Premature closure of one or more cranial sutures occurs in about 1 in 2000 births; it may be associated with a variety of syndromes, some of which are harbingers of a difficult airway. Uncorrected craniosynostosis can result in increased ICP and brain compression, with neurological sequelae. Correction is usually undertaken in the first 3 to 6 months of life, as brain growth is rapid during this period and the skull bones more malleable. The procedure may be a single strip craniectomy or a complete craniofacial reconstruction. These procedures fall into the purview of plastic surgery, but more extensive cranial exposures involve neurosurgeons. Although extradural, blood loss from the scalp and cranium can be significant, and VAE is a significant risk. Adequate venous access and invasive monitoring are imperative. The use of antifibrinolytics is controversial, but may have some utility. Less invasive neuroendoscopic techniques aim for smaller incisions, minimal dissection and blood loss, and fewer complications, allowing for less

aggressive fluid replacement, less invasive hemodynamic monitoring, and possibly less mortality.^{31,32}

Vascular Malformations

Vascular anomalies in children are rare, most being congenital lesions. Large arteriovenous malformations (AVMs), such as those of the vein of Galen in neonates, are associated with high-output congestive heart failure, with a poor prognosis. Initial treatment often consists of serial embolizations in the interventional radiology suite, followed by craniotomy for surgical excision, or Gamma Knife surgery.^{33,34} Although advances in endovascular treatment have improved outcomes, embolization is still a very high-risk procedure. There are risks associated with the embolic agent, including cerebral hemorrhage or ischemia from total occlusion or extravasation, fluid overload in an infant that is already in high-output cardiac failure, and VAE. Vessel perforation requiring emergent conversion to a craniotomy, and leg ischemia from the femoral puncture site can be devastating. There very often is a need for inotropic support, or antihypertensive treatment with vasodilators during the procedure. Intracranial AVMs may be associated with vascular or lymphatic malformations in the spinal cord, or the face.

Moyamoya disease is a rare condition characterized by chronic progressive steno-occlusion of the arteries of the Circle of Willis, usually the intracranial portion of the internal carotid arteries, with collateral vessel formation at the base of the brain.³⁵ The syndrome can be associated with neurofibromatosis, tuberous sclerosis, Marfan syndrome, Noonan syndrome, homocystinuria, thalassemia, sickle cell disease, congenital heart disease, optic nerve gliomas, basal brain tumors, and chromosomal disorders such as Down, Williams, and Turner syndromes. These children present with frequent transient ischemic attacks or recurrent strokes. These patients require anesthesia for confirmatory angiography, followed by surgery. Surgical treatment aims to increase collateral flow by direct or indirect revascularization procedures, using the external carotid circulation as the donor supply. Indirect procedures are more common in children. In pial synangiosis, an intact superficial temporal artery is fixed to the pial surface with the creation of a wide opening of dura and arachnoid; over time, there is ingrowth of new vessels through the opening to the poorly perfused area of the brain. Perioperative ischemia is a significant risk both during angiography and surgery and thereafter as neovascularization can take several weeks to months; it is imperative to maintain normocapnia, normotension, normovolemia, and normothermia, concepts that are contrary to what is practiced for other neurosurgical cases, and continue them into the perioperative period.^{36,37} Generous preoperative hydration and appropriate sedation to avoid agitation are key. Both hypercapnia and hypocapnia intraoperatively can be detrimental, a cerebral steal phenomenon diverting blood flow away from the compromised ischemic area of the brain. Anesthetic technique should not interfere with EEG monitoring. Measures to optimize cerebral perfusion should be continued into the postoperative period.

Neurotrauma

Traumatic brain injury is the leading cause of death and disability in children over 1 year of age in the United States. Spinal cord injury is often concurrent. Following blunt head trauma, diffuse cerebral edema is more common than intracranial hemorrhage, unlike adults. Most linear skull fractures do not require treatment but depressed skull fractures have a greater potential to harm underlying tissues, and may require urgent intervention. In children, cervical spine fractures can occur without neurological deficit, or present with delayed onset of symptoms; or deficits can occur without a radiological fracture.

Decreased perfusion to the brain and cerebral ischemia occur in the first 6 to 12 hours after a TBI, followed by hyperemia and raised ICP. Outcomes are better in children compared to adults but certain factors such as hypoxia, aggressive hyperventilation, hyperglycemia, hypotension, and intracranial hypertension predict poor outcome. Cerebral autoregulation may be impaired; the CPP threshold required to prevent cerebral hypoperfusion is not well understood. Current recommendation is to avoid CPP <40 mm Hg, although the threshold to prevent ischemia is likely age-dependent with older children requiring a higher CPP.³⁸ A systolic BP higher than normal may be needed to maintain adequate CPP, requiring the use of pressors. Ventricular catheters and fiber-optic transducers help in monitoring of ICP. Children with a GCS score less than 8 to 9 should be intubated for airway protection and management of raised ICP. Nasotracheal intubation should be avoided unless absolutely necessary in those with skull fractures. In the setting of cerebral edema, or when medical measures to decrease elevated ICP fail, decompressive craniectomy is the next option. The goal of surgery is to optimize viable brain recovery by removal of massive hemorrhages or lesions. Anesthetic goals include mild hyperventilation (Paco₂ about 35 mm Hg) to prevent brainstem herniation and intracranial hypertension. Adequate vascular access and invasive monitoring is necessary. Normothermia or mild hypothermia (Temperature 36–37°C) may be protective; hyperthermia should be avoided. There is a high risk of VAE and massive blood loss in craniotomies for evacuation of epidural or subdural hematomas.

Subdural hematomas can result from birth trauma or the occasional “shaken baby syndrome.” When a child presents with a conglomeration of

chronic and acute subdural hematomas, subarachnoid hemorrhage, skull fractures in various stages of healing, with or without other injuries out of proportion to the history, nonaccidental or inflicted trauma should be suspected. Outcomes are usually poor.

Neuroimaging and Interventions in Radiology Suites

Neurosurgical patients go through several imaging studies as part of their workup, including CT, MRI, PET, and nuclear medicine scans, for which younger children require sedation or general anesthesia. Dexmedetomidine has become established as a safe sedative drug for these studies and can be used alone or in conjunction with propofol.³⁹ Stereotactic procedures can start out in the radiology suite where the patient is often anesthetized prior to application of the frame and the anesthetized patient then transported to the operating room. The need for intraoperative MRI for procedures such as laser thermoablation has led to the construction of hybrid suites where imaging and surgery can be performed in a sterile environment. Access to the patient is a challenge in this situation, as is the need for MRI compatible or MRI conditional equipment. Some equipment, specifically Doppler ultrasounds, and fluid warmers are not MRI safe. This is a field that is rapidly evolving and will require the anesthesiologist to be flexible, while remaining vigilant to the need for sudden interventions.

SUMMARY

Pediatric neurosurgical anesthesia covers a wide spectrum of conditions across various age groups. The management of neurosurgical cases presents unique challenges to both surgeon and anesthesiologist, but also offers opportunities for close teamwork and collaboration. Understanding the age-related differences in this population is vital and goes a long way in avoiding complications. Formulating a thoughtful plan, understanding and being prepared for the complexities of the surgery, and maintaining open dialogue with the surgeon at all stages are essential to minimizing perioperative morbidity and mortality.

REFERENCES

1. Chumas P, Kenny T, Stiller C. Subspecialisation in neurosurgery—does size matter? *Acta Neurochir (Wien)*. 2011;153(6):1231–1236. [PubMed: 21547494]
2. Mokri B. The Monro-Kellie hypothesis: applications in CSF volume depletion. *Neurology*. 2001;56(12):1746–1748. [PubMed: 11425944]
3. Shapiro K, Marmarou A, Shulman K. Characterization of clinical CSF dynamics and neural axis compliance using the pressure-volume index: I. The normal pressure-volume index. *Ann Neurol*. 1980;7(6):508–514. [PubMed: 7436357]
4. Vavilala M, Soriano S, Krane E. Anesthesia for neurosurgery. In: Davis P, Cladis FP eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Elsevier; 2017:744–745.
5. Wintermark M, Lepori D, Cotting J et al. Brain perfusion in children: evolution with age assessed by quantitative perfusion computed tomography. *Pediatrics*. 2004;113(6):1642–1652. [PubMed: 15173485]
6. Vavilala MS, Lee LA, Lam AM. The lower limit of cerebral autoregulation in children during sevoflurane anesthesia. *J Neurosurg Anesthesiol*. 2003;15(4):307–312. [PubMed: 14508171]
7. Brady KM, Mytar JO, Lee JK et al. Monitoring cerebral blood flow pressure autoregulation in pediatric patients during cardiac surgery. *Stroke*. 2010;41(9):1957–1962. [PubMed: 20651273]
8. Rhee CJ, Fraser CD, Kibler K et al. The ontogeny of cerebrovascular pressure autoregulation in premature infants. *J Perinatol*. 2014;34(12):926–931. [PubMed: 25010225]
9. Kontos HA, Raper AJ, Patterson JL. Analysis of vasoactivity of local pH, Pco₂ and bicarbonate on pial vessels. *Stroke*. 1977;8(3):358–360. [PubMed: 16363]

10. Ellingsen I, Hauge A, Nicolaysen G, Thoresen M, Walloe L. Changes in human cerebral blood flow due to step changes in $P_{A_{O_2}}$ and $P_{A_{CO_2}}$. *Acta Physiol Scand*. 1987;129(2):157–163. [PubMed: 3554898]
11. Stephan H, Groger P, Weyland A, Hoeft A, Sonntag H. The effect of sufentanil on cerebral blood flow, cerebral metabolism and the CO_2 reactivity of the cerebral vessels in man. *Anaesthesist*. 1991;40(3):153–160. [PubMed: 1827962]
12. Mertens MJ, Engbers FH, Burm AG, Vuyk J. Predictive performance of computer-controlled infusion of remifentanyl during propofol/remifentanyl anaesthesia. *Br J Anaesth*. 2003;90(2):132–141. [PubMed: 12538367]
13. Ard J, Doyle W, Bekker A. Awake craniotomy with dexmedetomidine in pediatric patients. *J Neurosurg Anesthesiol*. 2003;15(3):263–266.
14. Bekker A, Sturaitis MK. Dexmedetomidine for neurological surgery. *Neurosurgery*. 2005;57(1 suppl):1–10; discussion 1–10. [PubMed: 15987564]
15. Wong GT, Luginbuehl I, Karsli C, Bissonnette B. The effect of sevoflurane on cerebral autoregulation in young children as assessed by the transient hyperemic response. *Anesth Analg*. 2006;102(4):1051–1055. [PubMed: 16551897]
16. Reasoner DK, Todd MM, Scamman FL, Warner DS. The incidence of pneumocephalus after supratentorial craniotomy. Observations on the disappearance of intracranial air. *Anesthesiology*. 1994;80(5):1008–1012. [PubMed: 8017640]
17. McCann ME, Kain ZN. The management of preoperative anxiety in children: an update. *Anesth Analg*. 2001;93(1):98–105. [PubMed: 11429348]
18. Kain ZN, Caldwell-Andrews AA, Krivutza DM, Weinberg ME, Wang SM, Gaal D. Trends in the practice of parental presence during induction of anesthesia and the use of preoperative sedative premedication in the United States, 1995–2002: results of a follow-up national survey. *Anesth Analg*. 2004;98(5):1252–1259, table of contents. [PubMed: 15105196]
19. Grady MS, Bedford RF, Park TS. Changes in superior sagittal sinus pressure in children with head elevation, jugular venous compression, and PEEP. *J NeuroSurg*. 1986;65(2):199–202. [PubMed: 3522822]
20. Harris MM, Yemen TA, Davidson A et al. Venous embolism during craniectomy in supine infants. *Anesthesiology*. 1987;67(5):816–819. [PubMed: 3674488]
21. Faberowski LW, Black S, Mickle JP. Incidence of venous air embolism during craniectomy for craniosynostosis repair. *Anesthesiology*. 2000;92(1):20–23. [PubMed: 10638894]
22. Prabhakar H, Singh GP, Anand V, Kalaivani M. Mannitol versus hypertonic saline for brain relaxation in patients undergoing craniotomy. *Cochrane Database Syst Rev*. 2014;(7):CD010026. doi(7):CD010026.
23. Kochanek PM, Carney N, Adelson PD et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. *Pediatr Crit Care Med*. 2012;13(suppl 1):S1–S82. [PubMed: 22217782]
24. Piper BJ, Harrigan PW. Hypertonic saline in paediatric traumatic brain injury: a review of nine years' experience with 23.4% hypertonic saline as standard hyperosmolar therapy. *Anaesth Intensive Care*. 2015;43(2):204–210. [PubMed: 25735686]
25. Hardesty DA, Sanborn MR, Parker WE, Storm PB. Perioperative seizure incidence and risk factors in 223 pediatric brain tumor patients without prior seizures. *J Neurosurg Pediatr*. 2011;7(6):609–615. [PubMed: 21631197]
26. Geiduschek JM, Haberkern CM, McLaughlin JF. Pain management for children following selective dorsal rhizotomy. *Can J Anaesth*. 1997; 41:492–496.
27. Elredge EA, Rockoff MA, Medlock MA, Scott RM, Millis MB. Postoperative cerebral edema occurring in children with slit ventricles. *Pediatrics*. 1997;99:625–630. [PubMed: 9093317]

28. Eldredge A, Soriano SG, Rockoff MA. Neuroanesthesia. *Neurosurg Clin N Am*. 1995;6:505–520. [[PubMed: 7670324](#)]
29. Soriano SG, Martyn JA. Antiepileptic-induced resistance to neuromuscular blockers: mechanisms and clinical significance. *Clin Pharmacokinet*. 2004;43(2):71–81. [[PubMed: 14748617](#)]
30. Sarang A, Dinsmore J. Anaesthesia for awake craniotomy—evolution of a technique that facilitates awake neurological testing. *Br J Anaesth*. 2003;90(2):161–165. [[PubMed: 12538371](#)]
31. Jimenez DF, Barone CM. Endoscopic craniectomy for early surgical correction of sagittal craniosynostosis. *J NeuroSurg*. 1998;88(1):77–81. [[PubMed: 9420076](#)]
32. Jimenez DF, Barone CM, Cartwright CC, Baker L. Early management of craniosynostosis using endoscopic-assisted strip craniectomies and cranial orthotic molding therapy. *Pediatrics*. 2002;110(1 pt 1):97–104. [[PubMed: 12093953](#)]
33. Burrows PE, Robertson RL. Neonatal central nervous system vascular disorders. *Neurosurg Clin N Am*. 1998;9(1):155–180. [[PubMed: 9405772](#)]
34. Ashida Y, Miyahara H, Sawada H, Mitani Y, Maruyama K. Anesthetic management of a neonate with vein of Galen aneurysmal malformations and severe pulmonary hypertension. *Paediatr Anaesth*. 2005;15(6):525–528. [[PubMed: 15910357](#)]
35. Baykan N, Ozgen S, Ustalar ZS, Dagcinar A, Ozek MM. Moyamoya disease and anesthesia. *Paediatr Anaesth*. 2005;15(12):1111–1115. [[PubMed: 16324034](#)]
36. Parray T, Martin TW, Siddiqui S. Moyamoya disease: a review of the disease and anesthetic management. *J Neurosurg Anesthesiol*. 2011;23(2):100–109. [[PubMed: 20924291](#)]
37. Robertson RL, Chavali RV, Robson CD et al. Neurologic complications of cerebral angiography in childhood moyamoya syndrome. *Pediatr Radiol*. 1998;28(11):824–829. [[PubMed: 9799310](#)]
38. Vavilala MS, Kernic MA, Wang J. Acute care clinical indicators associated with discharge outcomes in children with severe traumatic brain injury. Pediatric guideline adherence and outcomes study. *Critical Care Medicine*. 2014;42(10):2258–2266. [[PubMed: 25083982](#)]
39. Sulton C, McCracken C, Simon HK et al. Pediatric procedural sedation using dexmedetomidine: a report from the Pediatric Sedation Research Consortium. *Hosp Pediatr*. 2016;6(9):536–544. [[PubMed: 27516413](#)]