# Anesthesia for the Neonate: Neurosurgery and Ophthalmology

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Both major intracranial and intraocular procedures tend to be avoided wherever possible in neonates due to the technical difficulties of the surgery and high risk of surgical complications. Nevertheless, such surgery is not uncommon and it provides a great challenge for the pediatric anesthesiologist. Lesser procedures, such as examination of the eye, are common and they too can present many challenges to the anesthesiologist.

## Neurosurgery

Neonatal neurosurgery requires an understanding of the general principles of both surgery in a neonate and neurosurgery in general. The anesthesia is particularly challenging due to the paucity of data about normal neurophysiology in the neonate.

## Anatomy and Physiology

### Anatomy of the Cranium

Neuroanatomy and neurophysiology vary with age. At birth, the calvarium or skull cap is composed of ossified plates that cover the dura mater. The plates are separated by fibrous sutures and fontanelles. The posterior fontanelle closes between 2 and 3 months and the anterior fontanelle between 10 and 18 months of age. The dura mater is relatively noncompliant and unable to accommodate an acute increase in intracranial pressure (ICP) even when the fontanelles are open. An acute increase in intracranial volume will therefore cause a rapid increase in ICP that will compress and displace vital CNS tissue and cause cerebral dysfunction. A slow increase in pressure may be accommodated to a limited extent, by expansion of the fontanelles and separation of the fibrous sutures. The fontanelles tend to remain open in the presence of any chronic process that increases the intracranial volume including tumors and hydrocephalus. Intracranial pressure can be monitored clinically in the infant by palpation of open fontanelles or by the application of skin surface pressure transducers [1, 2]. At birth, the brain weighs about 335 g or 10–15 % of the total body weight. It doubles its weight by 6 months of age and weighs 900 g by 1 year. By 12 years of age, the brain reaches adult weight of 1,200–1,400 g. In a meta-analysis of studies, the volume of the brain in infants who are born very premature was very much less than in those born full term and was associated with reduced cognitive function in childhood and adolescence [3]. Such cognitive impairment was exacerbated by the presence of reduced volume of the cerebellum and reduced size of the corpus callosum.

The intracranial space is separated into the supratentorial and infratentorial compartments by a horizontal layer of the dura mater, the tentorium cerebelli. The tentorium is tent shaped and forms a roof over the posterior cranial fossa.

#### The Supratentorial Compartment

This is the largest compartment of the intracranial space and contains the cerebrum and all structures formed from the diencephalon (see below). The cerebrum is separated into 2 hemispheres by the longitudinal cerebral fissure and falx cerebri. Each hemisphere is further divided into frontal, temporal and parieto-occipital lobes. This physical division correlates with the division of function.

The diencephalon is the most rostral part of the brainstem. It is located in the central portion of the supratentorial compartment and consists predominantly of the thalamus

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J. Lerman (ed.), *Neonatal Anesthesia*, DOI 10.1007/978-1-4419-6041-2_11,

together with some epithalamic, subthalamic, and hypothalamic regions. The brainstem is continuous with the spinal cord. It passes through the tentorial notch of the tentorium cerebelli where its anterior surface lies on the body of the sphenoid bone.

If a primary lesion or injury involves gross expansion by hemorrhage or edema, then structures near to the tentorium and the falx become sites of secondary injury. This secondary injury is caused by both direct pressure and shearing forces and by ischemia from anterior cerebral artery compression. If the pressure continues to increase within the supratentorial compartment, the diencephalon, cerebral peduncles, oculomotor nerves, posterior communicating artery and the uncus of the temporal lobe may eventually herniate through the incisura tentorii resulting in contralateral hemiplegia, ipsilateral pupil signs (dilated, irregular, poor reaction to light) and abnormal posturing.

### The Infratentorial Compartment

The infratentorial compartment is located within the posterior cranial fossa and contains the cerebellum, pons and medulla oblongata. The cerebellum is a dorsal expansion of the brainstem with a function that is expressed ipsilaterally and predominantly regulates motor functions. The medulla oblongata lies inferior to the pons and contains the nuclei of the cranial nerves VII to XII as well as the ascending sensory and descending motor pathways.

### The Spinal Canal Compartment

The spinal cord and CSF are contained within the cylindrical vertebral canal. The spinal cord is the continuation of the brainstem. Its caudal tip reaches the intervertebral space of L3 at birth and the adult level of L1–L2 by 8 years of age.

## Vascular Anatomy

In neonates, the brain comprises 2 % of the body weight but receives 15 % of the cardiac output. Cerebral blood flow is supplied by an extensive network of arteries originating from paired internal carotid and vertebral arteries. The vertebral arteries join to form a single midline basilar artery that divides again at the junction of the pons and the midbrain into the paired posterior cerebral and superior cerebellar arteries. The posterior cerebral arteries become interconnected with the vessels originating from the carotid arteries to form the circle of Willis. The communicating arteries are effective anastomoses that reduce the risk of clinical ischemia if a contributing vessel is occluded.

Cerebral veins run in the pia mater and into collecting veins within the subarachnoid layer. They eventually traverse the subdural space and open into venous sinuses that lie between the dura mater and the cranial periosteum. The cerebral venous system is valveless and its walls are thin and lacking smooth muscle. The brain is insensitive to pain but the cerebral dura mater has nociceptive receptors particularly around the venous sinuses.

The superior sagittal sinus is clinically important because it is superficial and midline in location. This makes it vulnerable to damage during surgery. This sinus empties into a confluence of sinuses that drains into bilateral transverse sinuses. The occipital sinus that lies along the foramen magnum also ends in the confluence of sinuses. The cavernous sinus, which surrounds the sella turcica, joins the superior petrosal sinuses and drains into the transverse sinus. The transverse sinuses then course laterally along the attachment line of the tentorium to the occipital bone and become continuous with the sigmoid sinus located within the posterior cranial fossa finally to form the jugular venous bulbs.

### Spinal Cord Vascular Anatomy

The arterial supply to the spinal cord primarily arises from a single anterior spinal artery and 2 posterior spinal arteries both originating from the vertebral arteries. The anterior spinal artery supplies the ventromedial aspect of the spinal cord, which contains the corticospinal tracts and motor neurons. The 2 posterior spinal arteries form a plexus-like network on the posterior cord surface and supply the dorsal and lateral aspects of the spinal cord, which contain the sensory tracts responsible for proprioception and light touch.

The anterior spinal artery does not supply the whole length of the spinal cord. Supplemental blood supply is also received from radicular arteries originating from the spinal branches of the ascending cervical, deep cervical, intercostal, lumbar, and sacral arteries. A large anterior radicular artery called the artery of Adamkiewicz is responsible for supplying blood to as much as the caudal two-thirds of the spinal cord. It arises most commonly between T9 and L5 on the left side, although it may originate beyond these limits. All the other radicular arteries provide important collateral supply to the thoracic and lumbar spinal cord.

The venous drainage of the spinal cord consists of 2 median veins, 2 anterolateral veins, and 2 posterolateral longitudinal veins that empty via the anterior and posterior radicular veins into the internal vertebral venous plexus. This plexus lies between the dura mater and the vertebral periosteum. All the veins are thin walled and valveless. The internal plexus communicates with an external plexus that then drains via the vertebral, intercostal, lumbar, and lateral sacral veins into ascending lumbar, azygous, or hemizygous veins. At the cervical levels, the internal plexus connects to a basivertebral vein, which communicates through the foramen magnum with the occipital and basilar sinuses.

## Physiology

### Cerebral Blood Flow and Cerebral Blood Volume

Global CBF is approximately 15 % lesser in neonates (42 mL/100 g/min) than it is in adults (50 mL/100 g/min). CBF increases during infancy, reaching 90 mL/100 g/min by 6 months postnatal age, and peaks at 100–110 mL/100 g/min by 3–4 years of age. CBF decreases gradually thereafter, reaching 80 mL/100 g/min by 9 years of age. The greater CBF in infants and children reflects the greater energy requirements of the developing brain. As a consequence, cerebral oxygen consumption varies with age. In anesthetized neonates and infants, $CMRO_2$ is 2.3 mL $O_2$/100 g/min. $CMRO_2$ peaks at 5.2 mL $O_2$/100 g/min in children 3–12 years of age and gradually decreases thereafter, reaching 3.5 mL $O_2$/100 g/min in adults. This change again is attributed substantially to the greater energy requirements in the brains of children compared with adults [4].

Cerebral blood flow (CBF) depends on the pressure gradient within the vascular system, known as the cerebral perfusion pressure (CPP). CPP is defined as the mean arterial pressure (MAP) minus either ICP or central venous pressure (CVP), whichever is greater:

$$\mathrm{CPP} = \mathrm{MAP} - \left(\mathrm{ICP\,or\,CVP}\right)$$

While the MAP remains within a specific range, cerebral perfusion is under autoregulatory control. Autoregulation of cerebral blood flow is the intrinsic ability of the cerebral vasculature to maintain constant cerebral blood flow (CBF) despite changes in cerebral perfusion pressure (CPP). In the stressed neonate or preterm infant, loss of autoregulation or perturbations in CBF has been associated with periventricular hemorrhage, hence the importance of understanding cerebral autoregulation and its variables. Myogenic, neurogenic and metabolic factors have been hypothesized as mechanisms responsible for the control of this intrinsic function. If excessive hypotension, hypertension, hypoxia, hypercapnia or cerebral ischemia occurs, these mechanisms may begin to fail, rendering CBF pressure passive. In addition to physiologic variables, pharmacologic therapeutics such as inhalational anesthetic agents may blunt autoregulation via a dose-dependent cerebral vasodilatation (see above).

CBF is autoregulated to maintain oxygen delivery over a wide range of perfusion pressures. Three factors affect CBF: MAP, $CO_2$, and $O_2$. CBF remains constant between MAPs of 50 and 150 mmHg in older children. However, thresholds for autoregulation in infants have not been fully elucidated. Recent concepts in the autoregulation of CBF in stressed neonates have shifted from the notion of "loss of autoregulation" during stress (e.g., hypoxia) to a flattening of the autoregulation curve [5]. In addition, evidence has shown that cerebral autoregulation waxes and wanes with time [6].

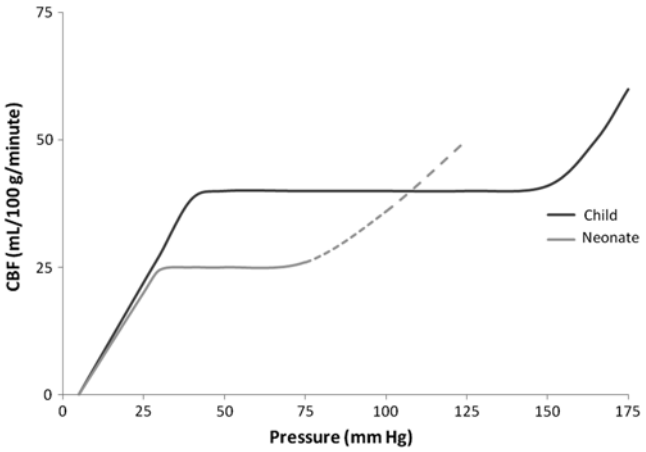


**Fig. 11.1** Cerebral blood flow and cerebral perfusion pressure in a neonate and older child. Note that the relationship between flow and pressure is poorly defined in the neonate especially at higher pressures

Studies in neonatal animals suggest that the limits for autoregulation in this age group lie between 25 and 75 mmHg MAP (Fig. 11.1). Once the limits of autoregulation have been exceeded, CBF changes more passively with MAP [7]. Neonates in severe physiological distress may have blunted autoregulation, demonstrated by a minimal change in CBF in response to varying $PaCO_2$ levels or a direct pressure-passive CBF [8]. The nadir of autoregulation in awake preterm infants 24–34 weeks gestation is 23 mmHg [9, 10]. Studies using more recent technology such as near-infrared spectroscopy have demonstrated that autoregulation is a dynamic phenomenon. For example, CBF is pressure passive 20–50 % of the time in sick preterm infants <1,500 g during the first 5 days after birth [6]. Cerebral autoregulation was maintained despite fluctuations in MAP in normotensive preterm infants weighing ~1,000 g whose lungs were ventilated, although their response to $CO_2$ was blunted. In contrast, cerebral autoregulation to MAP was blunted in hypotensive preterm infants, and their response to $CO_2$ was markedly attenuated or absent [11]. Clinical evidence suggests that fluctuating CBF as in preterm infants with impaired or abolished autoregulation may be at increased risk for IVH [12, 13].

Change in $PaCO_2$ exerts a profound effect on cerebral perfusion. Hypercapnia impairs cerebrovascular autoregulation, while hypocapnia increases vascular tone and hence cerebrovascular resistance, thus decreasing CBF. Changes in ventilation and intrathoracic pressure rather than $PaCO_2$ may be the primary cause of the observed changes in cerebrovascular autoregulation [14]. These observations are in conflict with an understanding of interaction between $PaCO_2$ and cerebrovascular autoregulation but may result from the technique by which cerebral autoregulation was quantified. In adults, CBF decreases 3 % with every 0.75 mmHg (0.1 kPa) decrease in $PaCO_2$ between 20 mmHg (2.7) and 80 mmHg

(10.7 kPa). In contrast, the immature brain is relatively unresponsive to small changes in $PaCO_2$ [15]. In infants and children, cerebral vasoconstriction occurs at a much reduced $PaCO_2$ compared with that in adults [16]. Although hyperventilation minimally increases cerebral vasculature resistance in neonates, a sudden increase in $PaCO_2$ after chronic hyperventilation of more than 24 h may cause cerebral vasodilatation and increased ICP [17]. Mild hypothermia decreases, whereas hyperthermia increases dynamic cerebrovascular autoregulation, although these effects are small. Hemodilution reduces blood viscosity and vascular resistance, thereby increasing CBF [18]. This decrease in vascular resistance can decrease autoregulatory capacity, and the lower limit of autoregulation has been shown to increase with anemia [19].

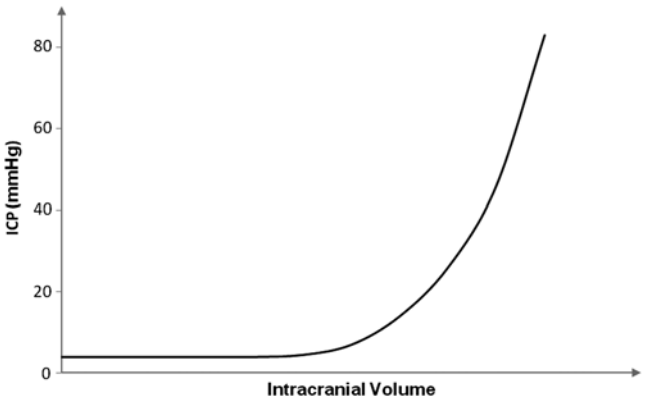


**Fig. 11.2** Idealized intracranial compliance curve in a neonate

## Spinal Cord Blood Flow

Animal data suggest that spinal cord blood flow is influenced by the same factors that influence CBF, although the flow rate is less, reflecting the reduced metabolic rate of the spinal cord. Perfusion of the spinal cord is determined by an equation similar to that for CBF:

$$\text{SCPP} = \text{MAP} - \left(\text{CSF or extrinsic pressure}\right)$$

This highlights the importance of extrinsic pressure on the integrity of the spinal cord, an effect that occurs in the presence of tumors, hematomas, or spinal venous congestion.

## CSF and ICP

Between 50 and 80 % of the cerebrospinal fluid (CSF) surrounding the brain and spinal cord is produced by the choroid plexus, which lines the floor of the lateral ventricles and the roof of the third and fourth ventricles. Up to 30 % of the CSF can be formed in other sites such as ependyma, the brain parenchyma and endothelium of cerebral capillaries. The CSF produced by the choroid plexus flows from the lateral ventricles, through the interventricular foramen of Monro into the third ventricle, then into the cerebral aqueduct of Sylvius to the fourth ventricle. It emerges from the interior of the brain through the two lateral foramina of Luschka and the single medial foramen of Magendie to enter the subarachnoid space. The CSF is absorbed by the arachnoid villi. The mean production rate of CSF in children is about 0.35 mL/min. CBF and CBV are much more important determinants of ICP than is the volume of the CSF.

Controlling ICP is critically important in maintaining CPP. Normal ICP is 8–18 mmHg in adults and 2–4 mmHg in children. The ICP in neonates is positive on the day of birth but then becomes negative, probably because of salt and water loss. Intracerebral volume also acutely and briefly decreases and is matched by a reduction in head size.

Neonates can compensate for slow increases in ICP because their fontanelles and suture lines are open. However, acute changes in intracranial volume are not tolerated because the fibrous connective tissue connecting the fontanelles and sutures is relatively difficult to separate. A small change in volume may result in an insignificant increase in ICP in a neonate with a normal baseline ICP, but once the noncompliant point on the intracranial compliance curve is reached, a small increase in volume causes a greater increase in ICP. Ultimately, the brainstem and cerebellar peduncles may herniate through the foramen magnum (coning), causing coma and death (Fig. 11.2).

## Blood-Brain Barrier

The blood-brain barrier (BBB) is a lipid membrane interface between the endothelial cells of the brain blood vessels and the ECF of the brain. It acts as a barrier to water-soluble drugs. Research from animals suggests that the BBB in the neonate has restrictive properties that are similar to those in the adult. At birth, saturable, carrier-mediated transport mechanisms are present, regulating the entry of glucose, amino acids, organic acids, purines, nucleosides, and choline. No difference in brain uptake of glucose has been observed between adults and neonates in a rabbit model. In contrast to the early suggestion that the BBB in young animals is an immature barrier, studies indicate that the BBB at birth is sophisticated and selective, with carrier systems that have a vital function in regulating the concentrations of metabolites within the neonatal brain [20].

## Embryology and the Pathology of Neural Tube Defects

The CNS is the first organ system to develop in the fetus. Development of the CNS involves the 3 major phases of neurulation, canalization and retrogressive differentiation. Neurulation is the process by which the neural plate, derived from the neuroectodermal layer, folds upon itself to make a groove and then fuses to form the neural tube. Differentiation of the neural tube occurs within the first 60 days after fertilization of the ovum. The nervous system appears in the second week of gestation.

Differentiation of the cortex takes place during the third trimester.

Canalization is the formation of the caudal neural tube including the development of the lower lumbar, sacral and coccygeal segments. Within the neural tube, groups of cells with their corresponding vertebrae proliferate and produce an excess number of segments. These excess segments degenerate in a process called retrogressive differentiation, and the filum terminale and cauda equina remain. The growth of the spinal column brings the conus medullaris to its adult level. Neural tube defects occur during neurulation. Failure of neurulation in early development results in total dysraphism within the brain and spinal cord. Anencephaly occurs only if the brain fails to close. Abnormal neuronal migration results in cortical malformations. Failure of canalization results in spina bifida: a myelocele exposes only neural tissue, a myelomeningocele exposes meninges in addition to neural tissue and a meningocele contains only meninges.

## General Principles of Neuroanesthesia in the Neonate

There are general principles and issues that apply to anesthesia in neonates for any surgical procedure. These have been discussed in other chapters. There are also general principles that apply to anesthesia for all neurosurgical procedures, regardless of age. What follows is a discussion of the latter principles as they apply to the neonate.

### Access and Positioning

Access to the patient is limited during most types of neonatal surgery. Neurosurgery is no exception and indeed access to the airway may be particularly fraught. Great care must be taken that the tracheal tube is well secured and ideally located in the mid-trachea to avoid extubation or migration into a main bronchus. Nasal tubes are easier to firmly secure than oral tubes, particularly for posterior fossa surgery. The anesthesiologist must remain vigilant for the occurrence of dislodged or kinked tracheal tubes throughout the surgery.

Intravenous and arterial lines should also be placed before surgery begins and carefully secured. Attempting to establish new intravenous access during surgery is very difficult in the neonate, so if there is any question regarding the patency of the vascular access, then access must be established before surgery commences. For major neurosurgery, central venous access should be considered in order to provide a secure intravenous line, a line for vasopressor support and a means to measure central venous pressure and hence ensure optimal filling pressures. However, femoral or subclavian access is preferred over jugular venous access to preclude jugular venous obstruction.

ECG and noninvasive blood pressure and temperature monitoring should also be secured before the baby is covered. The eyes should be taped closed to prevent injury. Some neurosurgeons use paraffin and other elaborate means to protect the eyes from pressure and alcoholic skin preparation. Before the drapes cover the neonate, there should be a final check to ensure that pressure areas are well padded, that the tracheal tube is not at risk of being kinked and that all intravenous lines are free of excess tension.

### Temperature

Cooling is neuroprotective and may reduce brain injury, whereas hyperthermia can exacerbate brain injury. Although mild hypothermia may be beneficial in terms of brain protection, it is also associated with cardiovascular instability, apnea, coagulopathy, and reduced immune resistance. If hypothermia is used to reduce potential brain injury, it must be undertaken cautiously with adequate cardiovascular and ventilatory support. Neonates can both lose heat and become overheated very quickly. Hyperthermia must be strictly avoided.

Neurosurgical procedures may involve exposure of relatively large areas as the head is relatively larger in neonates compared with that in adults. Particular care must be taken that heat loss is not excessive during antiseptic skin preparation. A forced air warmer should be used whenever possible and may be complemented with an overhead heating device to maintain thermoneutrality. All neonates need careful temperature monitoring during neurosurgery. Monitoring the temperature via the esophagus or pharynx is preferable to the skin and rectal sites.

### Blood Pressure

Blood pressure control is crucial to maintain an adequate CPP during neurosurgery. With CPP depending on the venous pressure and ICP, the head must be carefully positioned to preclude any obstruction to venous drainage from the brain. Hypotension may lead to underperfusion and ischemia, whereas hypertension may lead to an increased capillary flow, transudation of fluid, and interstitial edema. Evidence suggests that hypotension may impair autoregulation as well as the reactivity to changes in $PaCO_2$. Such edema increases the oxygen gradient between capillaries and neurons, thereby increasing the risk of hypoxic injury. In normal brain and under normal conditions, autoregulation ensures flow matches demand over a range of blood pressures. It reduces the risk of hypertension leading to edema or hypotension leading to ischemia. However, in the injured brain, this autoregulation may be impaired, and thus the range of blood pressures that avoids either excess or insufficient perfusion is much narrower.

Hypotension is poorly defined in both awake and anesthetized neonates and varies with specialists.

In neonates born 26–30 weeks gestation, a MAP <30 mmHg has been associated with IVH. This led to the general principle that the MAP should be ≥gestational age in weeks [21]. Some advocate the use of vasopressors to maintain an adequate MAP, although these have been associated with sequelae. In a survey, the majority of pediatric anesthesiologists defined hypotension in neonates during general anesthesia as a MAP >20–30 % below than awake values [22].

The range of CPP in which autoregulation can be maintained is poorly defined in neonates. In the absence of better data, good practice is to maintain a normal blood pressure for a neonate—though even this is unclear. Certainly excessive hypotension and hypertension must be avoided. To maintain adequate blood pressure, the neonate should be volume replete first, but there should also be a low threshold for vasopressor support. This is best given as an infusion rather than by intermittent boluses as the latter may lead to large fluctuations in blood pressure. To ensure prompt and appropriate responses, blood pressure should be accurately monitored. For critical cases, intra-arterial blood pressure monitoring is ideal.

Many anesthetic drugs also reduce the capacity of autoregulation or lead to a mismatch of flow and demand. All inhalational anesthetics impair autoregulation in a dose-dependent manner, although this effect is limited at concentrations <1 MAC. Nitrous oxide tends to increase flow. Propofol affects autoregulation the least of all drugs, although there are few data describing total intravenous anesthesia dosing regimens for propofol in neonates. Opioids can be used to provide stable hemodynamics and to supplement anesthesia, with limited impact on the autoregulation of CBF. Fentanyl at 5–10 mcg/kg/min may be used, provided there is capacity to continue to provide ventilatory support postoperatively. There is limited experience with remifentanil in neurosurgery in neonates, but it may have a very promising role, given its rapid metabolism and fast recovery. (See section on neuropharmacology below.)

## Ventilation

The primary aim of ventilation is to prevent hypoxia and strive to maintain normocapnia. Hypercapnia increases ICP, possibly causing cerebral edema and making operating conditions difficult. Hypocapnia may lead to hypoperfusion and ischemia. Similarly, hypoxia may exacerbate brain injury. In theory, excessive PEEP increases ICP, although if such a PEEP level optimizes oxygenation and ventilation, then this must take priority. Muscle relaxation may be used to prevent straining and the resultant increase in ICP.

## Fluids, Glucose, and Electrolytes

Extreme fluctuations in blood glucose concentration may exacerbate brain injury. Hypoglycemia may itself lead to brain injury. Hyperglycemia may worsen existing brain injury, although in neonates, there is evidence that this risk is not as great as in older children and adults [23, 24]. Intravenous dextrose should be continued during major neurosurgery in neonates and the blood concentration of glucose checked regularly for extreme shifts in the concentration.

Hyponatremia reduces plasma tonicity, thereby exacerbating cerebral edema. During neurosurgery, isotonic fluids should be administered and the plasma sodium concentration measured regularly. Excessive amounts of sodium chloride may lead to hyperchloremic metabolic acidosis as the immature kidney is unable to excrete the excess chloride. If there is a risk of diabetes insipidus or increased ADH secretion, then the plasma concentration of electrolytes must be checked frequently.

With relatively large heads that receive a disproportionate fraction of the cardiac output, blood loss during neurosurgery in a neonate may be more significant than in older children. A coagulation profile and full blood count should be obtained before all major neurosurgeries. Packed red blood cells should be available for any neurosurgical procedure that may result in bleeding. In neonates, fresh blood is preferable to aged stored blood since rapid transfusion of the latter may lead to acidosis and hyperkalemia, for both of which the neonate has limited buffering capacity. The ideal hematocrit to trigger transfusion in the setting of acute blood loss in neonates is unknown. Not only is it very easy to underestimate ongoing blood loss, but acute losses can occur very rapidly and lead to hemodynamic instability. Therefore, if significant blood loss is occurring, red cells should be given earlier rather than later. During major neurosurgery, platelets and fresh frozen plasma should be available and given early before a coagulopathy develops.

## Analgesia Postoperatively

Neonates have well-developed systems of nociception; they feel and respond to pain as do older children. Furthermore, failure to alleviate pain in neonates can lead to changes in spinal cord morphology and increase postoperative complications. Analgesia should be provided after neurosurgery. Minor procedures may require only simple analgesics such as paracetamol, whereas more involved procedures will require parenteral opioids.

## Neuropharmacology

The effects of anesthetic agents on cerebrovascular autoregulation vary. Inhaled anesthetics exert a dose-dependent uncoupling effect on autoregulation. Sevoflurane, however, impairs cerebrovascular autoregulation the least of all of the inhaled anesthetics. In healthy children, cerebral pressure autoregulation is preserved up to 1.5 MAC of sevoflurane, a finding similar to that in adults [25]. Although regional CBF varies with inhaled anesthetics, global CBF remains unaffected [26]. CBF increases to the greatest extent during

halothane anesthesia, followed by enflurane, isoflurane and then desflurane.

Hypercapnia impairs cerebrovascular autoregulation. Furthermore, this effect of hypercapnia compounds the effects of inhaled anesthetics on the loss of autoregulation. Propofol preserves cerebrovascular autoregulation at $PaCO_2$ values as great as 56 mmHg (7.5 kPa), whereas a similar level of hypercapnia abolishes cerebrovascular autoregulation during sevoflurane anesthesia. Importantly, hypocapnia reverses isoflurane-induced impairment of cerebrovascular autoregulation.

The effects of the non-inhaled anesthetics on cerebral autoregulation vary. Nitrous oxide increases CBF alone and when given with other anesthetic agents. Propofol preserves cerebral autoregulation at both large and small doses in healthy adults. When remifentanil is combined with propofol, it induces a dose-dependent metabolism-coupled reduction in CBF with preserved cerebrovascular autoregulation in adults. Comparable data in neonates are lacking. Opioids have little or no effect on CBF and ICP and cerebral autoregulation remains intact. Benzodiazepines and barbiturates decrease CBF and thus ICP. Barbiturates cause vasoconstriction in the cerebral vasculature and preserve autoregulation. Ketamine may increase CBF by up to 60 % under normocapnia and is therefore contraindicated in patients with increased ICP.

## Neurosurgical Conditions

### Neural Tube Defects

Neural tube defects (NTDs) (also known as spinal dysraphism) include all congenital anomalies that involve failure of the neural tube to close during the fourth week of embryogenesis and can occur anywhere along the formation of the spinal cord, from the brain to the sacrum. The two most common forms of NTDs are spina bifida and anencephaly.

Spina bifida is almost always compatible with survival, although severe physical and cognitive impairments are common. Spina bifida lesions are classified depending on whether or not neural tissue is exposed. Myelomeningocele is the most common and most severe form of spinal dysraphism. It is an open spina bifida lesion in which the spinal cord and meninges protrude through a defect in the vertebral arches and are either uncovered or covered with only a thin membrane. The defect can occur anywhere along the spinal column but is most common in the lumbar region. It can result in marked neurological deficit caudal to the level of the protruding sac.

In contrast to spina bifida, anencephaly is almost always fatal before or soon after birth. In this defect, there is partial or complete absence of the skull bones with only a minimal remnant of a brain.

Occult spinal dysraphism refers to a spina bifida lesion with intact skin covering. This form of dysraphism includes lipomeningocele, meningocele (when the sac contains meninges and cerebrospinal fluid but the spinal cord and spinal root are in their normal position), myelocystocele, dermal sinus, tight filum terminale, and diastematomyelia. With encephalocele, the brain and its covering membranes with CSF protrude through the skull, most often in the occipital region (Fig. 11.3). Spina bifida occulta is a benign and common abnormality in which the spinous processes of the lower lumbar or sacral spine fail to fuse. With these lesions, individuals are asymptomatic. The diagnosis is usually an incidental finding on plain radiographs of the spine/abdomen.

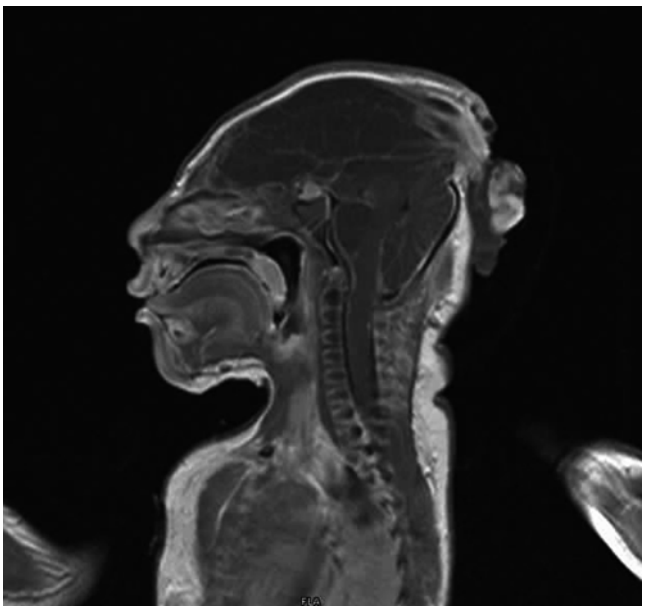

**Fig. 11.3** Sagittal T1 MRI scan of a child with severe cranial dysraphism, with a pronounced brain malformation and encephalocele

The birth frequency of NTDs varies among countries and regions within countries but, in general, is approximately 1 in 1,000. In the UK, the prevalence is around 3 per 1,000 live births compared with 1 in 10,000 in sub-Saharan Africa. Worldwide, the prevalence of NTDs at birth appears to be decreasing. The prevalence in the UK was about 4 per 1,000 in the 1970s and has decreased to 3 per 1,000 live births. There is a significant genetic component to the development of NTDs. If either parent has had an affected child or is affected by the condition, the risk of further offspring having an NTD is approximately 10 %. If 2 affected pregnancies occur, the risk to a further pregnancy is increased by about 20-fold. Nevertheless, at least 90 % of NTDs occur to women without a family history. Since the 1970s, maternal nutrition, particularly regarding folate, has been linked to the occurrence of NTDs. In 1991, a large randomized trial determined that the recurrence risk of NTDs in mothers who consumed folic acid before conception was reduced by 72 % [27]. Two other controlled trials also showed similar reductions in the recurrence risk, with a pooled reduction in risk among those

who were compliant of 87 % [28]. A definitive randomized controlled trial that compared the frequency of NTD in a multivitamin-supplemented group (containing 0.8 mg of folic acid) with a non-supplemented group showed no occurrences in the supplemented group ($n=2,104$ pregnancies) and six in the non-supplemented group ($n=2,052$). It is now recommended that a daily dietary supplement of 5 mg of folic acid before conception will prevent a recurrence of NTD. All women should be advised to take 400 mg of folic acid daily prior to conception to prevent a first occurrence of NTD as well as increasing consumption of folic-rich foods, such as green vegetables and fortified breakfast cereals, until the 12th week of pregnancy. However, because the compliance in taking these supplements is poor, the USA and several other countries instituted folic acid fortification of foods. In 1998, a US policy was drafted to require that enriched grain products be fortified with folic acid. Since this policy was adopted, the frequency of NTDs in the USA has been reduced to about 31 % for spina bifida and 16 % for anencephaly [29]. In addition, infants with spina bifida who were born after the fortification policy had a significantly better first-year survival rate than did those who were born before the policy [30]. However, many countries have not been as willing to embrace fortification. For example, in Finland, mandatory fortification is not permitted over concerns of possibly masking megaloblastic anemia caused by vitamin B12 deficiency in women older than 65 years, a possible small increase in the risk of wheeze and respiratory tract infections in offspring whose mothers took folic acid supplements during pregnancy and a possible increased incidence of lung cancer. However, there is no clear evidence confirming these concerns. The American College of Medical Genetics recommends that all women who are capable of becoming pregnant should strive for an intake of 0.4 mg of folic acid daily, and women who have had a previous NTD-affected pregnancy, who are themselves affected or have a first- or second- degree relative with an NTD, should ingest 4 mg of folic acid, commencing 3 months before conception and continuing throughout the first trimester.

## Myelomeningocele

This is the most common and severe form of spinal dysraphism resulting from a failure of closure of the neural tube around day 21 of development (Fig. 11.4).

Open myelomeningocele is immediately apparent at birth as a defect on the back with a neural placode, which is the open spinal cord. Abnormal nerve roots emerge from it ventrally. It is surrounded by arachnoid adhesions, an incomplete dura and associated paravertebral soft tissues. Antenatal diagnosis is usual. Maternal serum alpha-fetal protein is used to establish the diagnosis, and ultrasound will demonstrate the contents of the lesion as well as other congenital abnormalities. The defect may be covered by a thin epithelial or arachnoid layer, but in some cases, this may have ruptured and CSF can be seen leaking from the defect. Most infants will develop hydrocephalus and a Chiari II malformation (disorganization of brainstem topography, a small posterior fossa, and herniation of the cerebellum through the foramen magnum) is very common. Abnormalities of cerebral gyration, the posterior fossa contents and agenesis of the corpus callosum as well as vertebral anomalies may also be present.

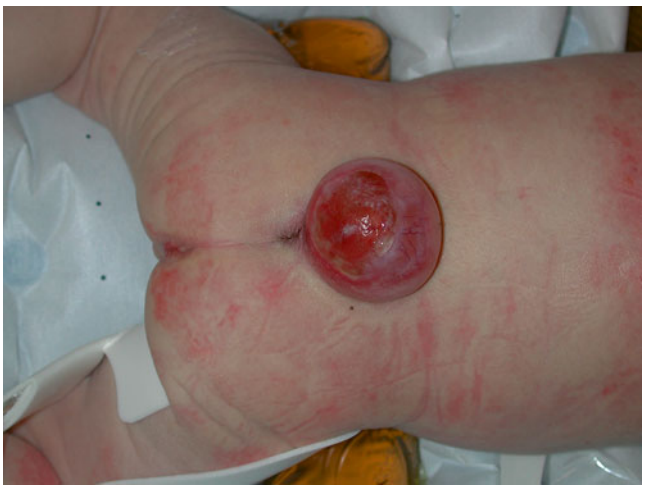

**Fig. 11.4** A child with a lumbar myelomeningocele

The infant with an open myelomeningocele is preferably delivered by Cesarean section to avoid acquiring a CNS infection during passage through the birth canal. The baby should be nursed prone or in the lateral decubitus with a sterile moist dressing covering the defect. Surgery cannot restore neurological function but will protect existing neural structures and prevent infection. Neural tube lesions are investigated with ultrasound, CT and/or MRI scanning. The open myelomeningocele should be closed within 48 h of birth since the risk of infection increases with the more time the defect is exposed.

Two less common forms of dysraphism occur in relation to skull defects. Cephaloceles involve herniation of either meninges (cranial meningocele) or brain and meninges (encephalocele) into the cele. These neural tube defects occur in ~1–3:10,000 live births [31]. Occipital encephaloceles occur two to three times more commonly than nasal (or anterior), parietal, and temporal encephaloceles, with a geographic distribution in which occipital cephaloceles are more common in Western countries, whereas anterior cephaloceles are more common in Asian countries [32, 33]. Occipital cephaloceles more commonly include brain tissue in addition to CSF (which may have to be excised) and are more commonly complicated by hydrocephalus and seizures and thus carry a poorer prognosis than anterior celes [32]. Neurological defects most commonly associated with dysraphism include brainstem hypoplasia, cerebellar dysplasia, Arnold-Chiari

defect, Dandy-Walker syndrome, and lissencephaly (smooth gyri and sulci) [31, 32]. Cephaloceles may also be associated with other congenital defects including cleft lip and palate, syndactyly, ocular defects, and congenital heart defects [31, 34]. Although surgery is usually undertaken in older infants and children, 20–30 % of neonates with cephaloceles undergo surgery in the neonatal period [32, 33].

### Anesthetic Considerations for Neonates with Neural Tube Defects

During the preoperative anesthetic assessment, the presence of any associated congenital anomalies should be excluded and the degree of the neurological deficit confirmed. With cervical encephalocele, the neck is often short and rigid which can make tracheal intubation difficult. These neonates may have feeding difficulties due to the neurological deficit and be volume depleted secondary to evaporative and third space losses from the exposed area. Consequently, preoperative intravenous fluids may be required. Induction of anesthesia may be accomplished using either an inhalational or intravenous induction. In the past, tracheal intubation has been recommended in the left lateral position, but this is not necessary if the spinal defect is first padded to prevent pressure from being applied to the layers covering the spinal cord. The head and body can be raised and supported using foam pads. Surgery is usually performed with the neonate in the prone position. Tracheal intubation is usually accomplished with a reinforced orotracheal tube. However, some anesthesiologists prefer nasotracheal intubation as it may better secure the tube fixation in the prone position because these tubes are less likely to become dislodged by secretions and loose tape than orotracheal tubes. In the case of cephaloceles, tracheal intubation may be difficult. For occipital celes, the airway is often secured with the neonate in the left lateral decubitus position as it is difficult to stabilize the large CSF-filled cephalocele with the neonate supine. With anterior cephaloceles, the child may be positioned supine with the airway secured using orotracheal intubation.

Large-bore intravenous access should be secured, and for cephaloceles that require a craniotomy, an arterial line should also be secured. Blood loss is usually small unless a large skin flap or a craniotomy (in the case of cephaloceles) is planned [32, 34]. However, if brisk blood loss is anticipated (as in the case of cephaloceles), packed red blood cells should be in the operating room at the time of skin incision. Additional monitoring includes core temperature and urine output. In the prone position, particular attention should be paid to the eyes, which should be padded and protected from pressure. Pressure on the abdomen should also be avoided to prevent compression of the IVC and engorgement of the paraspinal vessels as well as to allow free abdominal movement with respiration. This can be achieved by placing "jellies" under the chest and hips. Large lesions may require rotational flaps or tissue expanders to allow skin closure. Analgesia should be multimodal with small doses of intraoperative opioids, intravenous paracetamol, and wound infiltration with local anesthetics. Postoperative analgesia should be paracetamol for smaller defects. Nurse-controlled analgesia using morphine may be required when larger defects are closed. In this case, a high-dependency postoperative bed is needed for the monitoring of respiration and oxygen saturation. Preterm infants are at increased risk of postoperative apnea, especially after neurosurgery [35].

## Hydrocephalus and Shunts

Hydrocephalus occurs as a result of impaired circulation or absorption of CSF. In addition, hydrocephalus can occur as a result of the overproduction of CSF, e.g., in association with choroid plexus papillomas, although these tumors are rare.

Between 70 and 80 % of CSF is produced from the choroid plexus and the remainder of the ependyma and brain parenchyma. Production occurs by filtration across the capillary endothelium and active secretion of sodium by the choroidal epithelium. CSF production is mainly independent of ICP, although production is reduced somewhat in the presence of increased ICP and reduced CPP. CSF absorption is linearly related to ICP. Most CSF is absorbed at the arachnoid villi, which are herniations of arachnoidal tissue into the dural venous sinuses. The precise mechanism of CSF absorption remains unclear.

In adults, CSF is produced at a rate of about 550 mL/day. The total volume of CSF is 100–150 mL, of which 15–25 mL is contained within the ventricular system.

### Etiology and Pathophysiology of Hydrocephalus

An obstruction at any point along the CSF pathway can result in hydrocephalus. Obstructive or noncommunicating hydrocephalus is an obstruction within the ventricular system or at the fourth ventricular outflow. Communicating hydrocephalus is impaired circulation through the subarachnoid spaces or impaired absorption into the venous system.

### Posthemorrhagic Hydrocephalus

Intraventricular hemorrhage is detected in 40–45 % of preterm neonates with a birth weight less than 1,500 g. In this weight range, the hemorrhages often occur in the germinal matrix because the blood vessels there are irregular, have immature connective tissue architecture and lack the ability to autoregulate [12]. About 20 % of neonates who suffer an IVH, which usually occurs within the first few days after birth, require a shunt because of increased ICP. In addition to prematurity, vigorous resuscitation, respiratory distress syndrome, pneumothorax and seizures are associated with an increased risk of IVH [36].

IVHs can be identified using cerebral ultrasound and graded according to the location of the hematoma and its effect on the size of the ventricles. The presence of blood and its breakdown products may lead to hydrocephalus by obstructing the subarachnoid space and arachnoid villi. In addition, it leads to an ependymal reaction with blockage at the aqueduct or outlet foramina of the fourth ventricle. Increasing head circumference and progressive ventricular enlargement require intervention. Preterm, low-birth-weight neonates are at increased risk of shunt infection, and the presence of heavy blood staining or excessive cellular debris in the CSF precludes shunt insertion due to an increased risk of blockage. A shunt can be inserted once the CSF is clear of blood products.

### Hydrocephalus and Myelomeningocele

85–95 % of children with open spina bifida develop hydrocephalus. This is due to the development of the Chiari II malformation which is the disorganization of brainstem topography, a small posterior fossa, and herniation of the cerebellum through the foramen magnum and up through the incisura (Fig. 11.5). This causes obstruction to CSF flow at a number of sites including the cerebral aqueduct and the fourth ventricular outlet, resulting in hydrocephalus.

Other causes of hydrocephalus include aqueduct stenosis, Dandy-Walker syndrome, obstructive hydrocephalus due to tumors and post-meningitic hydrocephalus. Aqueductal stenosis is responsible for about 10 % of cases of childhood hydrocephalus and can present at any time from birth to adulthood. Dandy-Walker syndrome comprises agenesis of the cerebellar vermis with cystic dilatation of the fourth ventricle, enlargement of the posterior fossa and hydrocephalus, which is usually present by 3 months of age. Additional brain malformations are present in over half of the cases, and neurodevelopmental delay is reported in up to 70 %.

Midline tumors, particularly those of the pineal gland and posterior fossa, commonly result in obstructive hydrocephalus, and this is one of the principal ways in which these conditions present. In a case series of posterior fossa tumors with hydrocephalus, 20 % required shunting. Chronic inflammation can produce obstruction to CSF flow especially after bacterial, parasitic, and granulomatous infection.

### Clinical Presentation of Hydrocephalus

Hydrocephalus results in disproportionate head growth before closure of the cranial sutures and fontanelles. Clinical symptoms are often subtle. In the neonate, symptoms include general irritability and poor feeding. Signs include increased head circumference, bulging fontanelles, separation of the cranial sutures, prominence of the scalp veins and sunsetting of the eyes. The presence of bradycardia, hypertension, and irregularities in breathing suggests critically increased ICP and requires urgent treatment. In the neonate, cranial ultrasound scanning is widely used to confirm the diagnosis of hydrocephalus, which can also be investigated by CT and MRI scanning for full evaluation of the ventricular system (Fig. 11.6).

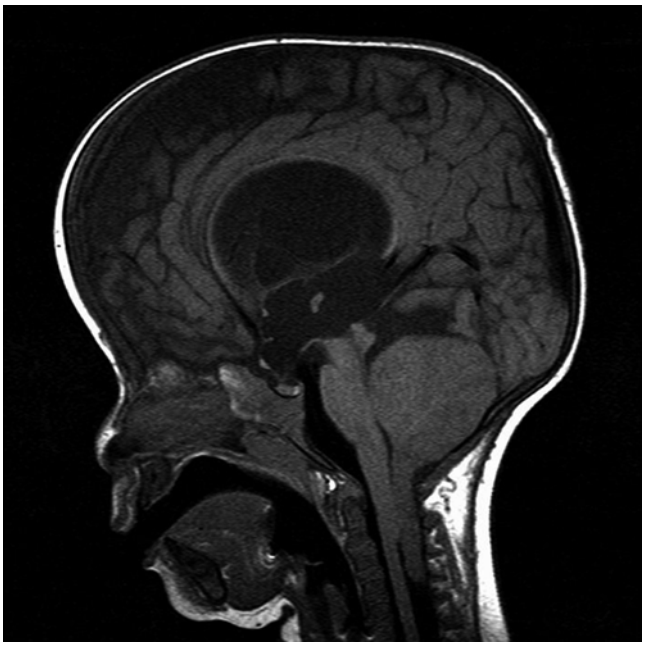

**Fig. 11.5** Sagittal T1 MRI scan of a child with a severe Chiari II malformation and hydrocephalus

### Treatment of Hydrocephalus

The treatment of hydrocephalus involves bypassing the site of obstruction of CSF flow or diversion of CSF from the ventricular cavity to a site where it can be more readily absorbed. This is usually achieved by inserting a ventricular shunt but to a lesser degree also by using neuroendoscopic techniques, such as endoscopic third ventriculostomy. The shunt consists of a proximal catheter, the tip of which is located within the cerebral ventricle, and a distal catheter that drains to an alternative site of CSF absorption, most commonly to the peritoneal cavity but also to the pleural cavity or right atrium. In addition to the tubing that connects the origin of the accumulated CSF with the drainage location, shunts include a valve and reservoir. A variety of valve designs are available. Numerous shunt systems have been devised and marketed over the years, suggesting that the perfect shunt system has yet to be manufactured, although great strides have been made towards perfecting shunt technology.

Some children have a reservoir incorporated into the shunt, e.g., a Rickham reservoir, which is a shunt system reservoir that collects CSF or permits the injection of medications. It is used if frequent collection of CSF is required such as for infection or if injection of medications directly into the CSF is necessary. Its use is uncommon.

If only a brief period of CSF diversion is required, a subgaleal or an external ventricular drain may be used.

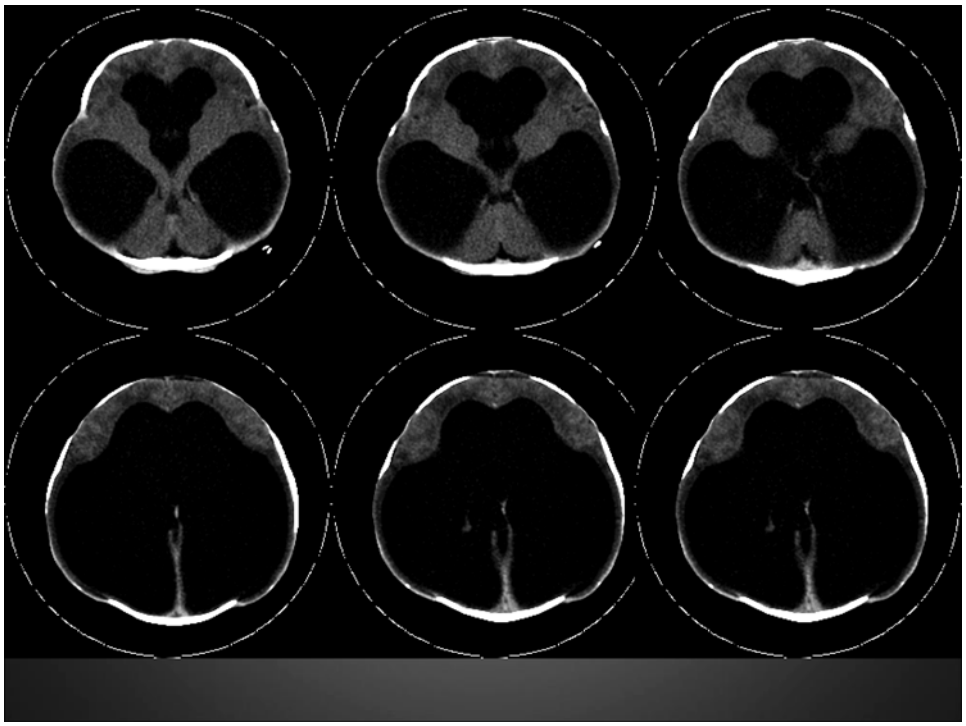

**Fig. 11.6** MRI images of a child with hydrocephalus

The ventriculosubgaleal shunt drains CSF from the ventricles to the space between the skull and the scalp. They are used as a temporizing measure, for weeks to several months in preterm infants [36, 37]. For preterm infants, particularly those <2,000 g, these shunts appear to be most effective to bridge until the infant is large enough for a ventriculoperitoneal shunt. The external ventricular drain consists of a ventricular catheter connected to an external reservoir for the accumulation of drained CSF. They may be placed as a temporary measure, for example, if an infection is present in the CSF, while CSF flow is restored via the normal anatomic pathways or via a peritoneal shunt. Hydrocephalus related to tumor, infection, or hemorrhage may require external drains, at least temporarily.

Insertion of the distal catheter into the peritoneal cavity for a ventriculoperitoneal (VP) shunt is either by mini laparotomy or the use of an abdominal trocar. The VP shunt is the most common surgical CSF shunt procedure offering the advantage of reducing the need for repeated shunt revisions as the child grows. The most common complications are infection and obstruction of the shunt, requiring shunt revision. Mechanical failure and infection account for the majority of shunt complications, although these occur far less frequently today than in the past.

Ventriculoatrial shunts from the lateral ventricle to the right atrium are much less common. The incidence of complications with these shunts including infection, obstruction, pulmonary thromboembolism and air embolism is greater than with VP shunts. Ventriculoatrial shunts require revisions as the child grows. These shunts are generally used when VP shunts are contraindicated, e.g., adhesions or abdominal sepsis. Ventriculopleural shunt, from the lateral ventricle to pleural cavity, is rarely used.

### Anesthetic Considerations

Preoperative assessment should include a general assessment of the infant and a neurological examination for increased intracranial pressure. Any associated conditions should be optimized. Sedative premedication should not be prescribed. Preoperative preparation includes planning for the positioning of the infant, particularly if the head is large (Fig. 11.7). Achieving the optimal position is essential for tracheal intubation, which could otherwise be difficult due to head size.

Induction of anesthesia may be achieved via either the intravenous or inhalational route. Oxygenation and hemodynamic stability should be maintained throughout and acute increases in ICP avoided. The trachea may be intubated with a reinforced or regular uncuffed tracheal tube and/or a nasal tube as the head is heavily draped and access to the airway during surgery is almost impossible. The lungs should be ventilated throughout as spontaneous ventilation is contraindicated when the cranium is open. Bradycardia or other arrhythmias may occur when the ventricular catheter is

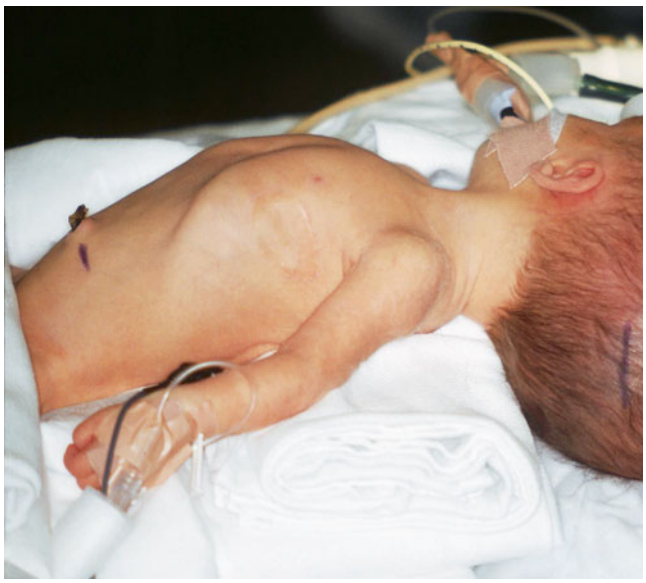

**Fig. 11.7** Position of a neonate with hydrocephalus for a ventriculoperitoneal shunt

inserted. Insertion of the distal end of the VP shunt into the peritoneum requires that a passageway be tunneled under the skin from the head to the abdomen to accommodate the shunt catheter. This is usually a very stimulating maneuvre, requiring small doses of an opioid such as fentanyl. Paracetamol may be used for postoperative analgesia. It is also helpful to infiltrate the abdominal wound with local anesthetic. The abdominal component can be quite painful as access to the peritoneum requires a mini laparotomy.

Thermoregulation can be problematic as a large proportion of the neonate is washed with antiseptic prep and surgery requires a large amount of exposure. To prevent hypothermia, the room must be warmed before the neonate arrives (≥26°C) and a forced air warmer used. Central temperature should be monitored (e.g., esophageal) throughout surgery and the trachea extubated only if the neonate is normothermic.

## Vein of Galen Malformations

Vein of Galen aneurysmal malformation (VGAM) is a rare congenital abnormality (less than 1/25,000 deliveries), in which multiple arteriovenous shunts drain into the median prosencephalic vein of Markowski (not into the vein of Galen itself). Typically, this malformation presents in the neonatal period with high-output cardiac failure and, in severe cases, with brain destruction resulting in serious morbidity and mortality. In the neonatal period, the presentation is usually with high-output cardiac failure, which in the past was often associated with rapid progression to multisystem organ failure (MOF) and death. Endovascular treatment has emerged as the treatment of choice for VGAM presenting in infancy with heart failure. Embolization, both of feeding arteries and draining veins, can substantially reduce aneurysmal blood flow. In many series, however, neonates have not been treated because of perceived poor outcome. A 21-point scale predicts the therapeutic efficacy of endovascular embolization in neonates based on several factors, including cardiac, cerebral, hepatic, respiratory, and renal functions [38]. A score <8 suggests that endovascular therapy would be futile, and thus treatment is not indicated, whereas a score between 8 and 12 suggests emergency embolization is indicated. A score >12 supports medical management until endovascular treatment can be performed when the infant is between 5 and 6 months of age. Although it is desirable to obtain complete occlusion of the lesion in the fewest procedures possible, endovascular treatment often entails multiple sessions.

After birth, with the loss of the low-resistance uteroplacental unit, up to 70 % of cardiac output is directed to the cerebral circulation. Pulmonary arterial pressures remain increased, and the ductus arteriosus remains open, directing right ventricular output through the patent ductus arteriosus and into the descending aorta. The right ventricle becomes distended and noncompliant because of the chronic pressure load. Subsequent right to left shunting at atrial and ductal levels causes arterial hypoxemia and increases the likelihood of ventricular failure. The left ventricle is hyperkinetic with a shortening fraction greater than 40 %. A large shunt through the VGAM occurs during diastole. The increased diastolic flow to the VGAM reduces coronary blood flow and, in combination with increased ventricular pressure, reduces subendocardial perfusion. This may produce myocardial ischemia and potentially exacerbate right heart failure. Stabilization of neonates before neurointervention or neurosurgery is difficult, and the cardiac failure is often resistant to treatment. The use of beta-adrenergic agents (dobutamine, dopamine, or adrenaline) in this setting often worsens cardiac output. Shortening of diastolic coronary filling time induced by tachycardia worsens diastolic dysfunction. The combination of low-dose dopamine and a vasodilator can substantially improve systemic perfusion and reduce the severity of metabolic acidosis [39]. The use of systemic arterial vasodilators or phosphodiesterase inhibitors may be effective in neonates with VGAM who fail to respond to conventional inotropic support since extracranial systemic vascular resistance is increased despite a reduction in total systemic vascular resistance. Arterial vasodilators (especially nitroprusside, glyceryl trinitrate, and milrinone) used to treat severe cardiac failure may reduce neurological injury before, during, and after surgery and are important to stabilize the hemodynamics before intervention. During surgery, they offset rapid changes in systemic vascular resistance induced by coil occlusion of feeding vessels of the AVM. After surgery, they may reduce the incidence of cerebral hyperemia. Prevention of hypertension during and after AVM embolization also

theoretically reduces the incidence of AVM rupture secondary to increased intravascular pressure proximal to the site of occlusion or rerouting of blood flow and pressure away from the AVM.

Effective anesthetic management for AVM interventions involves aggressive cardiovascular monitoring and avoiding hypotension, hypovolemia, and low diastolic blood pressure. Excellent communication and teamwork are required between the interventional neuroradiologist and the anesthetist. Embolization of the aneurysm results in an acute increase in ventricular afterload and may exacerbate cardiac failure. The use of inotropes and vasodilators as discussed above is required to mitigate the effects of increased afterload.

## Tumors

Brain tumors in infants under the age of 1 year are extremely rare. Surgery can be technically challenging, if possible at all, and the sensitivity of the developing nervous system to the side effects of radio- and chemotherapy limits their usefulness. These tumors are often histologically benign, of large dimensions, but are often situated in locations within the brain that preclude surgical intervention and lead to a fatal outcome. In a case series of 250 tumors in the neonatal period, the most common tumors diagnosed in the fetus/neonate were teratomas (29 %), followed by astrocytomas (18 %), primitive neuroectodermal tumors (13 %) and choroid plexus papillomas (13 %) [40, 41].

Brain tumors can be detected on antenatal scans as an intracranial space-occupying lesion, abnormal echogenicity in the head, macrocephaly, and hydrocephalus. The diagnosis can be confirmed and further information gained by performing magnetic resonance imaging. 50–60 % of neonates with tumors present with an isolated increase in head circumference. Tumors can also present with increased intracranial pressure, as evidenced by bulging fontanelle, failure to thrive, apneic episodes, irritability, drowsiness, vomiting, neurological deficits, intraventricular hemorrhage and hydrocephalus. Seizures are present in a minority of cases, 10–15 %. The overall 5-year survival rate of neonatal tumors is in the range of 23–36 %, despite treatment. Postoperative mortality can be as great as 7.3–33 %. The choice of technique and the extent of resection depend on the size, position, histology, and anatomical relationships of the tumor to contiguous structures. Many neonatal and childhood tumors present with hydrocephalus, and it is often this that is immediately life threatening rather than the tumor itself. The neonate may therefore require emergency insertion of a VP shunt or an EVD.

### Anesthetic Considerations for Tumor Resection

Preanesthetic assessment should be as for any neonate undergoing major surgery. Ideally the neonate should have intravenous access and IV fluid hydration preinduction. The site of the craniotomy will depend on the location of the tumor and will determine the position of the neonate during surgery. This should be discussed with the surgeon. Anesthesia can be inhalational or intravenous. Tracheal intubation should be accomplished with either an oral or nasal (reinforced) tracheal tube, depending on the position required during surgery. Craniotomy in a neonate requires invasive monitoring—arterial access is essential and central venous access is desirable. Surgery should not be undertaken without large-bore intravenous access as there is an increased risk of intraoperative bleeding. A urinary catheter should be inserted. Surgery is likely to take place in the prone position as many neonatal tumors are located in the posterior, third ventricle/pineal region. In the prone position, some prefer nasotracheal intubation. After tracheal intubation and before turning the neonate prone, the position of the tip of the tracheal tube is evaluated by maximally flexing the neck to verify that the tip does not impinge on the carina or lodge endobronchially when the surgeon maximally flexes the neck to expose the posterior fossa in the prone position. If the tube is too far down the trachea, then it should be withdrawn and retaped so that it does not cause or trigger airway reflex responses. The usual precautions should be taken when turning the neonate prone with padding. Warming devices should be used. Intraoperative analgesia should be provided with opioids. Blood gases, hemoglobin, and blood sugar as well as urine output should be regularly monitored. This monitoring will give an indication of the condition of the neonate and how long surgery can continue. Again, excellent communication with the surgeon is required in these high-risk procedures. He or she should be informed if the baby's condition is deteriorating so that surgery can be curtailed if necessary. Blood should be present in the operating room before tumor surgery begins in the event sudden and unexpected massive bleeding occurs. Postoperatively, the baby may be extubated, depending on the duration of surgery and the nature of any difficulties encountered. Postoperative care should be in a monitored neurosurgical high dependency or intensive care area. Posterior fossa tumor resections are more painful postoperatively, and analgesia should be with regular paracetamol and IV morphine.

## Hemorrhage and Trauma

In the neonate, surgery is occasionally needed after a trauma or intracranial hemorrhage. The most frequent cause of trauma is birth trauma, and the most frequent complication requiring neurosurgery is evacuation of a subdural hematoma. Intracerebral bleeds may occur due to a rupture of AVMs or in the setting of thrombocytopenia or other form of severe perinatal coagulopathy. Often, attempts are made to treat such hemorrhages conservatively. Neurosurgery for

hemorrhage in the neonate is fraught as the brain is soft and easily damaged during retraction or if the brain herniates through the craniotomy. If surgery is performed, the anesthetist should note that blood loss might have been substantial, and they should check that any preoperative hypovolemia or anemia has been corrected. Similarly, any coagulopathy or thrombocytopenia should be corrected. Intraoperative blood loss may also be substantial. Therefore, large-bore intravenous access is essential and invasive pressure monitoring is preferable. Packed red cells, platelets and plasma must be available and given early in the event of serious bleeding.

## Fetal Neurosurgery

Human prenatal myelomeningocele repair by hysterotomy was first performed in 1997, and by 2003, more than 200 fetuses had undergone the procedure. In studies in animals, prenatal coverage of a spina bifida-like lesion preserved neurological function and improved hindbrain herniation, suggesting the final neurological deficit in spina bifida is a consequence of 2 factors—a failure of neural tube formation as well as spinal cord injury resulting from prolonged exposure of neural elements to the intrauterine environment. The Management of Myelomeningocele Study (MOMS) to compare the safety and efficacy of prenatal repair of myelomeningocele with that of standard postnatal repair has recently been published [42]. In this study, eligible women were randomly assigned to undergo either prenatal surgery before 26 weeks of gestation or standard postnatal repair. Of the 158 women whose children were evaluated at 12 months, shunt placement was required in 40 % of the prenatal surgery group compared with the 82 % of the postnatal surgery group. Prenatal surgery resulted in improvement in the composite score for mental development and motor function at 30 months and improvement in hindbrain herniation by 12 months and ambulation by 30 months. However, prenatal surgery was associated with an increased risk of preterm delivery and uterine dehiscence at delivery. One-third of women who underwent prenatal surgery had an area of dehiscence or a very thin prenatal uterine surgery scar at the time of delivery. Fetuses that were treated prenatally were born at an average gestational age of 34.1 weeks, and 13 % were delivered before 30 weeks of gestation, whereas those in the postnatal surgery group were born at an average of 37.3 weeks of gestation with none delivered before 30 weeks. Thus, although prenatal surgery for myelomeningocele reduced the need for shunting and improved motor outcomes at 30 months, it was associated with maternal and fetal risks.

## Surgery for Craniosynostosis

Craniosynostosis occurs when one or more of the sutures of the skull fuse prematurely (Fig. 11.8a, b). This results in an abnormally shaped skull. If uncorrected, craniosynostosis may lead to hydrocephalus, neurological impairment, and a cosmetic deformity. The most common sutures involved are the sagittal, coronal, and metopic sutures. Craniosynostosis may occur in isolation or in association with a syndrome [43]. Although craniosynostosis may be diagnosed in the

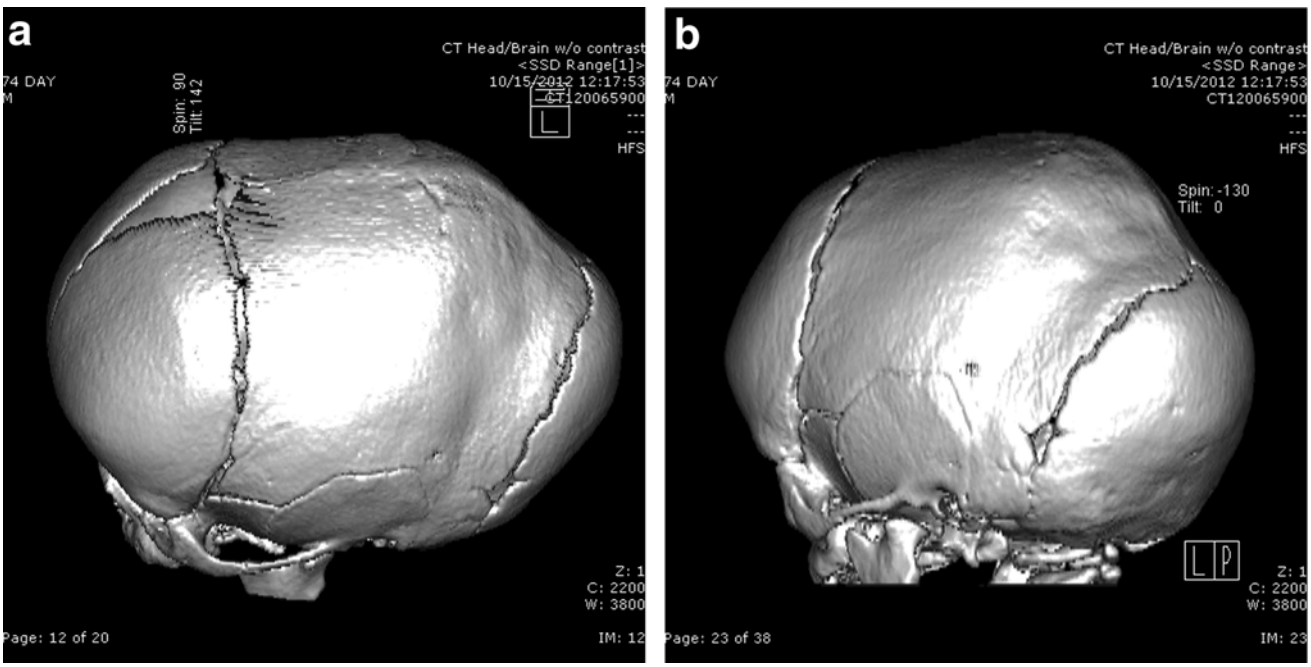


**Fig. 11.8** (**a**, **b**) CT scan of a 2-month-old infant with sagittal synostosis preoperatively

neonatal period and the best results obtained during early correction in infancy, such large procedures are generally not performed in neonates. A variety of procedures have been described for this condition including strip craniectomies, where the fused suture is excised, and larger procedures where extensive areas of the skull are removed, remodeled and replaced [43]. The inner and outer tables may be split to provide more bone areas. These later operations are large procedures that are lengthy and may involve considerable blood loss. If neonatal surgery is undertaken, blood must be available at the time of skin incision to preclude severe hypovolemia and cardiac arrest.

## Ophthalmology

### Introduction

Neonates are subject to ophthalmic conditions such as retinopathy of prematurity (ROP), cataracts, infections, trauma and a variety of developmental conditions. The ophthalmologist has become an integral part of the neonatal intensive care unit, participating in weekly ward rounds to screen for ROP in preterm infants. Optimal anesthesia care is important for surgery in the operating room as well as on the ward and in other offsite locations for the ophthalmic examinations.

### Anatomy, Physiology, and Development

The globe has three layers: the sclera, uveal tract, and retina. The sclera is the fibrous outer covering that maintains the shape of the globe; anteriorly, it is continuous with the cornea, which is transparent and avascular. The uveal tract comprises the iris, ciliary body, and choroid. The iris divides the eye into the anterior and posterior chambers. The ciliary body secretes aqueous humor for the anterior chamber and contains muscles that alter the shape of the lens. The choroid is a highly vascular tissue that supplies blood to the retina. The retina is the thin tissue layer located posteriorly within the globe, where light generates nerve potentials.

At birth, the globe is relatively large, about half the size of that in the adult. The anterior structures are relatively larger at birth compared with those in the adult. The shape of the globe becomes more spherical as the posterior structures grow with age. The sclera is thin at birth and appears translucent with a bluish tinge. The iris is blue in Caucasian neonates with the final adult coloring developing over the first 6 months of age. The eyes appear divergent in as many as 75 % neonates, but this resolves with time.

The eye becomes reactive to light at about 7 months gestation with the full-term neonate capable of following moving targets, albeit slowly. Visual acuity is poor at birth (about 20/400) but this improves rapidly during infancy.

The globe is filled with vitreous humor and aqueous humor. The vitreous humor is the more viscous component. The volume of the vitreous humor remains fairly constant as the neonate matures. The aqueous humor is formed by the ciliary body, flows through the pupil, and is absorbed via the trabecular meshwork (pores of Fontana) and the canal of Schlemm into the venous system in the anterior chamber. Changes in aqueous humor absorption can change intraocular pressure (IOP). IOP increases with increases in venous pressure such as with coughing, vomiting, and valsalva maneuvres as the episcleral veins drain through a valveless system. Hypercapnia and hypoxia also increase IOP; systemic hypertension only increases IOP, about 30 % of the increase in blood pressure.

The oculocardiac reflex is a reflex bradycardia that mediated through the third cranial nerve and the vagus. It occurs after either brisk traction on an extraocular muscle or with direct pressure on the globe. The reflex is enhanced in neonates. Release of the traction by the surgeon immediately resolves the bradycardia. Alternately, atropine (10–20 mcg/kg) or glycopyrrolate (5 mcg/kg) IV can be administered to treat the bradycardia. Both the severity and the incidence of an anticipated bradycardia may be attenuated by pretreatment with an anticholinergic [44]. It remains unclear whether any particular anesthetic regimen significantly affects either the severity or risk of an oculocardiac reflex, although there is some evidence that ketamine may attenuate the bradycardia and propofol may augment the bradycardia [45]. It is important to note that these latter studies were conducted in older children, and little is known about the optimal management of the reflex during anesthesia in neonates. Traction on the muscles and pressure on the globe may also lead to apnea.

### Principles of Ophthalmic Anesthesia

Neonates who require ophthalmic procedures frequently present with other medical conditions such as prematurity, and/or pathological or congenital conditions that might impact the anesthetic care. Careful preoperative assessment is important. Anesthesia in the premature and ex-premature infant is covered in another chapter; however, particular care must be taken to assess the respiratory and cardiac systems. The infant may have chronic lung disease and/or apnea of prematurity. In the case of the latter condition or if the neonate was premature at birth, postoperative admission for 12 h of apnea monitoring should be anticipated and planned before embarking on any anesthetic including sedation. Cardiac diseases such as pulmonary hypertension and cyanotic congenital heart disease should be considered, particularly in the premature infant.

Neonates with syndromes may present with a host of medical issues that warrant our consideration preoperatively.

The incidence of cataracts, glaucoma, and nasolacrimal duct obstruction is greater in neonates with trisomy 21. These infants may also require a smaller-diameter tracheal tube than comparable infants at the same age (due to subglottic airway narrowing, congenital heart defects, and hypothyroidism). Ophthalmic conditions are also associated with Apert and Crouzon syndromes, Goldenhar syndrome, Hunter syndrome, Marfan syndrome, CHARGE syndrome and homocystinuria.

Many of the principles of anesthesia during ophthalmic surgery are similar to those for other operations in the neonate. Access to the infant may be limited, so the airway and intravenous lines must be reliable and secure. Care must be taken to prevent hypothermia or hyperthermia, and glucose and fluids should be given during surgery.

All general anesthetics decrease IOP except ketamine, which may raise IOP although this remains controversial. Succinylcholine causes a transient increase in IOP, but in neonates, this response has not been specifically studied. Brief procedures such as examinations under anesthetic or tear duct probing may be performed with spontaneous ventilation via face mask or with a laryngeal mask airway. Some examinations are performed under sedation. Procedures of greater duration require a tracheal tube. For intraocular surgery, immobility is paramount and hence tracheal tubes and neuromuscular blocking agents are recommended. Some anesthesiologists extubate the trachea during a deep level of anesthesia to avoid coughing. This should only be attempted where the airway is not compromised and staff competent in airway support is in continuous attendance until the infant is fully awake.

## Ophthalmic Conditions in the Neonate

### Retinopathy of Prematurity

In 1988, the landmark multicenter trial of Cryotherapy for Retinopathy of Prematurity ("Cryo-ROP") study was published [46]. Cryo-ROP found that ablative treatment for retinopathy of prematurity almost halved the rate of blindness in severe cases. Before the publication of that study, there was little evidence that treatment for ROP decreased poor visual outcomes, and hence ophthalmic procedures were rarely performed in neonatal units. Infants were sent to ophthalmologists' offices for examinations once they were well enough. Today, the commonest ophthalmic procedure in a neonatal ward is an ROP screening examination.

Severe ROP can lead to a lifetime of blindness. ROP is caused by abnormal neovascularization of the developing retina. Soon after World War II ended, an epidemic of the ROP appeared in the USA, the UK, Australia, and other developed countries. This was due in part to the improved technologies that improved the survival of extremely premature infants (as young as 24 weeks gestation) and allowed the delivery of greater concentrations of inspired oxygen to young infants, particularly those who were premature and who survived to reach childhood and older. It soon became evident that many of the premature infants were blind. In 1952, the landmark Gallinger trial suggested that the administration of excessive concentrations of oxygen was responsible for the blindness [47]. In the subsequent 15 years, the prevalence of ROP decreased from 50–4 % of premature infants, although early neonatal death and cerebral palsy increased dramatically. Currently, approximately 65 % of infants <1,250 g develop ROP [48]. ROP accounts for 13 % of childhood blindness. Although oxygen increases the risk of ROP, reduced oxygen levels have been associated with a greater risk of neonatal death and cerebral palsy. As a result, the dose and delivery of oxygen to premature infants have been debated, resulting in the current position that oxygen saturations should be maintained between 90 and 95 % as saturations >95 % increase the risk of ROP, whereas those <90 % increase the early mortality rate [49, 50].

The notion that gestational age and weight at birth and excessive oxygen levels were the sole determinants of the prevalence and severity of ROP and blindness in premature infants has proven to be oversimplistic. A multitude of factors interact to trigger the retinal vascularization that leads to ROP. Temporally, the pathogenesis and treatment of ROP are regarded in two phases: the first is an avascular phase that results from hyperoxia-induced arrest of retinal vascularization, whereas the second is a proliferative period of neovascularization. The initial trigger for ROP may occur in utero period with a systemic inflammatory response that renders infants susceptible to excess oxygen concentrations. Oxygen modulates the activities of hypoxia-inducing factor 1 and vascular endothelial growth factor, both of which regulate neuroangiogenesis in the retina. A shift in the concentrations of these factors may arrest the initial vascularization of the retina. Additionally, insulin-like growth factor 1 and erythropoietin may modulate the proliferation of retinal angiogenesis. Two further mechanisms may impact on the pathogenesis of ROP. The first is a genetic component that is associated with differential responses to nitric oxide, adenosine, apelin and beta-adrenergic receptors [51]. Indeed, the differential prevalence of ROP in Caucasians and African American infants suggests that single nucleotide polymorphisms in, for example, beta-adrenergic receptors may affect the susceptibility to ROP and its treatment. The second is an inflammatory response that may expose the retina to infectious or inflammatory mediators or to oxidative stress in utero, thereby priming the retina for ROP later [52]. Understanding the relative importance of these mechanisms in the pathogenesis of ROP has led to several innovative therapeutic interventions that may prove to be widely effective [53, 54].

Treatment needs to be a timely evaluation of the vascularity of the neonatal retina to prevent a retinal detachment or dragging of the macula. The macula is the area of the retina devoted to central vision. Any distortion of the macula leads to poor central vision. Several innovative, targeted interventions have been investigated that in the future may hold promise for preventing blindness from developing in these infants [54].

## ROP Screening Procedures

### Pupil Dilation

The use of topical medication to dilate the pupil is crucial to permit examination of the peripheral retina where ROP occurs. Refinements to topical anesthesia regimens have ensured that the pupil can be well dilated, without increasing the risks of drug toxicity to the infants (Table 11.1).

To prevent toxicity from topical ophthalmic medication, the doses should be meticulously calculated a priori. Medications that dilate the pupils are known as mydriatics. Examination of the eyes of infants with possible ROP requires good mydriasis in order to visualize the entire retina, all the way to the ora serrata. Mydriatic drop regimens vary from nursery to nursery. A common combination is cyclopentolate 0.25 % combined with phenylephrine 2.5 %, one drop to each eye, followed by another dose 10–15 min later. The initial dose is given approximately 30–60 min before the examination.

Atropine is also a potent mydriatic. However, like tropicamide, it produces adverse gastrointestinal effects. In the neonate, these effects can be severe. Atropine is an anticholinergic/parasympatholytic (anti-muscarinic) that, in addition to causing tachycardia, flush, and fever, can also cause gastrointestinal effects that minimize bowel sounds. This can imitate necrotizing enterocolitis.

### Analgesia

A screening procedure can be very painful in some situations, e.g., with an inexperienced screener or on an infant with significant periorbital edema from prolonged assisted ventilation. Infants with small palpebral fissures can also be difficult to examine. Steps should be taken to minimize all pain in neonates.

Examination is usually performed under topical anesthesia. Pain can be caused by (a) the bright light of the indirect ophthalmoscope, (b) an eyelid speculum, and (c) the use of an instrument for scleral indenting. Various protocols have been developed to minimize the pain from examination, and each will have been developed for individual nurseries. Topical anesthetic agents are given immediately before an examination. Corneal and conjunctival discomfort is decreased significantly as is the sensitivity to the brightness of the indirect ophthalmoscope's light. Agents including proxymetacaine, tetracaine, oxybuprocaine, and proparacaine are useful topical ophthalmic local anesthetics. However, excessive doses to the eye can weaken the intercellular attachments of the corneal epithelium, which can cause haziness of the cornea or sometimes sloughing of epithelial cells. Some nurseries administer paracetamol or oral sucrose for additional analgesia. However, strong repeated sucking actions by the infant can make the procedure more difficult.

## Anesthesia for Laser Surgery of ROP

During the 1990s, the standard treatment for ROP changed from cryotherapy to laser surgery. Cryotherapy is painful, requiring general anesthesia. Furthermore, postoperative pain after cryotherapy is significant because there is considerable swelling of the conjunctiva. Alternatively, laser surgery causes much less pain and is brief, lasting approximately 30–40 min per eye. Laser burns are applied to the peripheral retina, usually to a full 360°. A lens loupe is used to gently move the eye to the appropriate positions. Occasionally, infants are sensitive to the burns themselves, but more often, the distress from the surgery is associated with physical maneuvring of the globe, the intensity of the light from the indirect ophthalmoscopic delivery system of the laser, the swaddling of the infant and the length of the procedure.

**Table 11.1** Eye drops commonly used in neonates and their possible complications

| Drug | Action | Side effects |
|---|---|---|
| Cyclopentolate | Anticholinergic (similar action to atropine but faster onset of action and shorter half-life) | Grand mal seizure [31–33]; psychotic reactions (in children) [34–37]; gastrointestinal toxicity including death from necrotizing enterocolitis after 6 drops of 1 % (in an infant) [38] |
| Phenylephrine | Sympathomimetic/adrenergic | Increased blood pressure in any age group |
| Tropicamide | Anticholinergic/parasympatholytic | Gastrointestinal (more pronounced in children) [39] |
| Atropine | Anticholinergic/parasympatholytic (anti-muscarinic) | Increased heart rate (in any age group but more pronounced in children) [39]; gastrointestinal [39]; atropine flush/fever (more pronounced in children), acute confusional psychosis |
| Homatropine | Anticholinergic/parasympatholytic similar effects to atropine but weaker | |

The type of anesthesia required for the laser treatment of ROP varies depending on the ophthalmologist and the stability of the infant.

Many ophthalmologists prefer the infants to be paralyzed. This reduces the duration of the procedure as the surgeon can apply the burns more rapidly. Infant eyes can be lasered with sedation (e.g., with chloral hydrate) and a dose of morphine (0.5 mg/kg), but with sicker and smaller infants requiring laser, the risk of oxygen desaturation, apnea, and requirement for emergent intubation during the procedure increases. The heart rate and respiratory rate should be monitored to identify episodes of bradycardia and apnea during the procedure, and this should be communicated to the ophthalmic surgeon.

### Congenital Cataracts

Congenital cataracts may occur in isolation or be associated with many congenital conditions. Cataract surgery is generally delayed until the infant is older than 6 weeks to minimize the risk of aphakic glaucoma. Aphakic glaucoma is a condition that can be catastrophic to vision and has a much greater incidence in infants with cataracts that are extracted before the first month of age. The onset of aphakic glaucoma can occur at any time during childhood.

### Congenital Glaucoma

Congenital glaucoma, as opposed to aphakic glaucoma, sometimes requires surgical treatment in the first few weeks of life to minimize damage from an increased intraocular pressure. Infants with congenital glaucoma may receive antiglaucoma medication as eye drops that could impact on anesthesia. Medication includes

1. Prostaglandin analogues, e.g., latanoprost, travoprost and bimatoprost
2. Beta blockers, e.g., timolol and betaxolol
3. Alpha(2)-adrenoreceptor agonists, e.g., brimonidine and apraclonidine
4. Carbonic anhydrase inhibitors (CAI), e.g., brinzolamide, dorzolamide and acetazolamide

### Beta Blockers

Timolol 0.25 % is widely used. Systemic absorption can lead to side effects relating to beta-adrenergic receptor blockage, including bradycardia and respiratory compromise. Beta-blocking drugs are avoided in premature infants, although on occasion, they may be used in full-term infants with glaucoma.

A new use of beta-blocking agents in ophthalmology in infants and children is to treat capillary hemangiomas [55]. Orbital and periorbital hemangiomas can cause astigmatism and lead to amblyopia. Systemic and topical beta-blocking agents are being used with increasing frequency to treat hemangiomas.

### Alpha(2)-Adrenoreceptor Agonists

Alpha(2)-adrenoreceptor agonists, e.g., brimonidine, are avoided in infants because they may cause drowsiness and CNS depression. Just one drop of topical brimonidine can lead to sleepiness that can be quite prolonged [56].

### Carbonic Anhydrase Inhibitors

Carbonic anhydrase inhibitors such as acetazolamide are used to treat open-angle glaucoma and intracranial hypertension. However, these compounds can lead to significant side effects in neonates, the most serious being metabolic acidosis, dehydration, and renal stones. Paresthesia, which is a problem in adults who ingest acetazolamide, is an uncommon problem in children.

### Tear Duct Obstruction

Neonates may be born with a congenital stenosis or obstruction of the nasolacrimal duct. If the obstruction remains unresolved by the end of the first year, a lacrimal probing may be indicated. During general anesthesia, the duct is dilated with a blunt metal probe passed from either the upper or lower lacrimal punctum. Success is confirmed by the metal probe making contact with another metal probe placed at the inferior meatus in the nose and/or by injecting fluorescein into the punctum and detecting a patent duct by the presence of fluorescein on a pipe cleaner inserted into the nostril. If fluorescein is injected, it may be prudent to place a roll under the infant's shoulders and position the child in slight Trendelenburg. A face mask or laryngeal mask airway may be used; however, if a nasendoscopy is performed, the duration of the procedure may be extended and a tracheal tube required. At the conclusion, it is prudent to suction the oropharynx to remove any blood or fluorescein in the hypopharynx before the infant is awakened.

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