INCREASED INTRACRANIAL PRESSURE

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Increased intracranial pressure (ICP) can occur in a variety of settings in the pediatric population. It is essential that clinicians recognize, understand, and appropriately treat this life- and function-threatening condition when it occurs. This requires knowledge of pertinent neuroanatomy and pathophysiology, which will be reviewed in this chapter with the goal of providing a logical basis for the management of increased ICP.

Intracranial Contents

After closure of the cranial fontanelles and sutures by 2 to 3 years of age, the skull is a rigid container of fixed volume. The intracranial contents constitute the brain bulk (80%), blood volume (10%), and cerebrospinal fluid (CSF) (10%). According to the Monro-Kellie doctrine, intracranial volume is equal to the volume of the brain bulk, blood, CSF, and other mass lesions. Therefore, an increase in the volume of one of these compartments can raise ICP and subsequently reduce cerebral perfusion pressure (which is defined as mean arterial pressure minus ICP) and cerebral blood flow (CBF).

CSF volume appears to be the major compensatory mechanism, with the majority in the subarachnoid spaces of the spine and brain and only 10% in the intracranial ventricular system. This CSF volume compensatory mechanism can be expressed as the volume-pressure intracranial compliance ($\Delta V/\Delta P = \text{compliance}$) or pressure volume index (PVI). The PVI is the volume of fluid injected or withdrawn that would result in a 10-fold change in ICP and is calculated as $PVI = \Delta V / \log P_f / P_o$, where $\Delta V =$ volume of fluid injected or withdrawn, $P_f =$ final ICP, and $P_o =$ initial ICP. The PVI varies in proportion to the estimated neural axis volume. The PVI is 8 mL in an infant and 25 mL in a 14-year-old; therefore, a 10 mL volume added to the neural axis of a 14-year-old may produce a modest elevation in ICP, whereas the same volume can be lethal in an infant (Figure 86-1). However, in infants and young children who have open cranial fontanelles and sutures, the Monro-Kellie doctrine does not apply, because the cranial vault will compensate by expanding.

CSF Dynamics

The CSF is normally secreted from the choroid plexus by active transport, and its rate decreases only when CBF begins to decline. Its absorption occurs passively by a hydrostatic gradient through the arachnoid granulations into the venous circulation. This rate is linearly related to ICP. Therefore, either an increase in CSF formation or a resistance to absorption will lead to an increased ICP. The normal rate of CSF production and total CSF volume during childhood varies as the child matures. It is estimated that the average total CSF volume in a neonate is 40 to 50 mL. In contrast, the average total CSF volume in an adult is 150 mL, with a secretion rate of about 20 mL/h (0.34 mL/min).
Cerebral Edema

Cerebral edema can be classified into five different theoretical types. Each is caused by a different pathophysiologic mechanism on which each specific treatment is based:

1. **Vasogenic edema** results from the physical disruption of brain tissue with impairment of the blood-brain barrier. The pathophysiology of clinically significant vasogenic edema involves: (1) an increase in capillary permeability, (2) an increase in transmural capillary pressure, and (3) retention of the extravasated fluid in the interstitial space.

   First, an increase in capillary permeability may result from damage to endothelial membranes, activation of transendothelial pinocytosis, and disruption of the tight endothelial junctions. Damage to the endothelial membranes by direct injury or secondary edemagenic substances is probably the most likely mechanism.

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   Third, retention of extravasated fluid appears to be mediated by the electrical charge of the protein molecule. For example, albumin, an anionic protein that readily passes through the damaged blood-brain barrier, is subsequently cleared just as readily by pericytes and other cells. In contrast, immunoglobulin G (IgG) fraction, a cationic protein, remains within the interstitial space by adhering to anionic binding sites and, therefore, retains fluid. The complexity of the pathogenesis of vasogenic edema is highlighted by the fact that administration of glucocorticoid steroids improves the edematous process in brain tumors as well as in chronic subdural hematomas. Vasogenic edema occurs adjacent to brain tumors, traumatic lesions, intracerebral hemorrhages, inflammatory foci, and chronic subdural hematomas.

2. **Cytotoxic edema** is primarily caused by impairment of the sodium-potassium-adenosine triphosphatase pump due to the reduction of CBF below critical threshold levels. It is an intracellular process affecting astrocytes and neurons. The resultant ischemic process produces a cascade of biochemical reactions consisting of an increase in potassium in the extracellular space and an intracellular accumulation of calcium, which leads to irreversible cell damage from membrane dysfunction. Cytotoxic edema occurs adjacent to areas of focal or global ischemia and hypoxia, such as a cerebral infarction.

3. **Interstitial edema** is caused by high-pressure obstructive hydrocephalus, whereby CSF infiltrates the periventricular tissues by high hydrostatic pressure within the ventricular system. When this process does occur, the perifocal edema may lead to brain ischemia and neuronal dysfunction. It has been proposed that either the substances in the edema fluid or ischemic cellular cascade products may be responsible for the vascular and neuronal dysfunction that occurs. A representative example is the child with a posterior fossa tumor who presents with high-pressure obstructive hydrocephalus causing neurologic deterioration secondary to hydrocephalus and increasing cerebral interstitial edema.

4. **Hydrostatic edema** is caused by an increase in the transmural vascular pressure (ie, the hydrostatic pressure gradient between the intravascular and extravascular spaces), which leads to an accumulation of extracellular fluid. Loss of cerebral autoregulation may also lead to an abruptly increased transmural pressure at the capillary bed. An example is the formation of diffuse hydrostatic edema of the ipsilateral cerebral hemisphere after an acute subdural hematoma has been evacuated, whereby the sudden reduction in ICP results in an abrupt increase in the cerebral vascular transmural pressure.

5. **Osmotic edema** is a complex process and results from a critical fall in serum osmolality and hyponatremia. Hyponatremia at serum sodium levels < 125 mEq/L may tip the osmotic balance, causing cerebral edema. At a given sodium level, women are more likely than men to suffer brain swelling, presumably due to the differential effects of sex hormones.

**Evaluation**

A rapid and complete history and physical examination as well as neuroimaging studies are crucial to making a definitive diagnosis of increased ICP. Once increased ICP is diagnosed, immediate treatment is essential to prevent...
potentially harmful neurologic sequelae. Children may present with increased ICP from a variety of causes, such as brain tumors, traumatic brain injury, hemorrhage (eg, vascular abnormalities), infarction (eg, stroke), infection (eg, brain abscess or encephalitis), metabolic factors (eg, electrolyte abnormalities), untreated craniosynostosis, and hydrocephalus due to ventricular shunt failure.

Seizures
Children with tumors of the cerebral hemispheres may present with seizures ranging from simple focal seizures to status epilepticus. Immediate management should include (1) control of seizures, (2) maintenance of a patent airway, and (3) maintenance of an adequate blood pressure. Control of seizures may be accomplished by both short-acting anticonvulsants in the acute setting (eg, lorazepam) or long-acting anticonvulsants (eg, phenytoin, carbamazepine, valproate, or phenobarbital). In children who have brain tumors, seizures may have been precipitated by (1) increased surrounding cerebral vasogenic edema, (2) tumor progression, (3) low anticonvulsant drug level, (4) electrolyte disorders, or (5) recent hemorrhage into the tumor. After the child is medically and neurologically stabilized, head computed tomography (CT) or magnetic resonance imaging (MRI), with and without contrast, is indicated to rule out an immediate need for surgical intervention.

Intracranial Hemorrhage
Brain tumors in children may present with intratumoral hemorrhage, leading to increased ICP and neurologic compromise. Examples of these tumors are glioblastoma multiforme, ependymoma, medulloblastoma (primitive neuroectodermal tumor), pontine astrocytoma, oligodendroglioma, and germ cell neoplasms. In addition, intracranial hemorrhages may result from ruptured vascular malformations and aneurysms as well as traumatic injuries. In these cases, emergent measures to stabilize the child medically must be undertaken and should include (1) maintenance of respiratory and circulatory status, (2) ICP management by medical (ie, hyperventilation and diuresis) or surgical (ie, placement of a ventriculostomy drain and hematoma evacuation) treatment, and (3) seizure control, if indicated. If the child is not taking antiepileptic drugs at the time of the cerebral hemorrhage, prophylaxis is also indicated.

Nonshunt-Related Hydrocephalus
Children with posterior fossa, brainstem, optic-chiasm, suprasellar (eg, craniopharyngioma), pineal, or ventricular (eg, choroid plexus papilloma and carcinoma) region tumors may present with acute hydrocephalus associated with neurologic deterioration secondary to hydrocephalus, increasing interstitial edema, or intratumoral hemorrhage. Preoperative unilateral or bilateral ventriculostomy drainage of CSF may therefore be indicated to relieve the hydrocephalus and for monitoring ICP. Although risks such as infection, hemorrhage, parenchymal injury, upward herniation, intratumoral hemorrhage, and porencephalic cavities in infants are associated with placement of a ventriculostomy drain, emergent ventriculostomy placement is essential in this life-threatening situation. Recently, antibiotic-impregnated catheters have shown promise in reducing infections associated with ventriculostomy placement. At the authors’ institutions, obstructive hydrocephalus secondary to a posterior fossa tumor is initially managed with administration of glucocorticoid steroids (ie, dexamethasone) and ventricular drainage if the child is significantly symptomatic. A preoperative ventriculoperitoneal shunt is usually not indicated, as studies have shown that a substantial number of children with posterior fossa tumors will not require a permanent shunt after resection of the tumor.

Shunt Malfunction
A child with a ventriculoperitoneal–atrial–pleural shunt malfunction often presents with signs and symptoms of increased ICP. Infants with a shunt malfunction usually present with irritability, poor feeding, increased occipital-frontal head circumference (OFC), and inappropriate sleepiness. Children with a shunt malfunction usually present with headache, irritability, lethargy, nausea, and vomiting. However, it is important to inquire if the signs and symptoms that the child is presenting with are the same as those during a past shunt malfunction. When a shunt malfunction is suspected, neuroimaging studies consisting of a head CT as well as anteroposterior (AP) and lateral skull, chest, and abdominal radiographs are obtained to evaluate for increased ventricular size and shunt hardware discontinuity. Even though most children with a shunt malfunction present with increased ventricular size on neuroimaging studies, there are those whose ventricular size does not change due to decreased brain compliance (ie, “stiff ventricles”) secondary to scarring of the ventricular lining. In these children and other children with unclear presentations, a sterile shunt tap is indicated to test the proximal and distal shunt flow. Children who are diagnosed with a shunt malfunction must be taken urgently to the operating room for shunt revision.

Diagnosis
When diagnosing a child with increased ICP, initial neurologic documentation is critical to detect signs and symptoms of neurologic deterioration. The initial neurologic examination should assess cranial nerves (eg, examination of pupillary size and reactivity to light) as well as motor, sensory, reflex, and cerebellar functions.
In neonates and infants younger than 6 months of age, it is difficult to measure ICP invasively. Therefore, palpation of the open cranial fontanelles and sutures provides a rough estimation of the degree of increased ICP, on the basis of the fullness or increased tension of the fontanelles as well as the degree of metopic, coronal, sagittal, and lambdoid suture splaying. In addition, increased OFC, decreased level of consciousness, irritability, poor feeding, inappropriate sleepiness, and limited up-gaze or forced down-gaze (ie, sun-setting sign) are signs of increased ICP in neonates and infants. Papilledema is rare in infants.

In children, headache, nausea, vomiting, lethargy, decreased level of consciousness, papilledema, double vision secondary to compression of the abducens cranial nerve, and difficulty concentrating or maintaining attention are signs of increased ICP. Cushing’s triad of bradycardia, hypertension, and an irregular breathing pattern as well as autonomic dysfunction secondary to brainstem compression are also indications of increased ICP in infants and children. Once increased ICP is diagnosed, urgent neuroimaging studies (ie, head CT, ultrasonography, or MRI) are critical to facilitate proper treatment.

If increased ICP is severe enough, herniation of portions of brain from their normal location into other compartments over the dural membranes may occur, leading to compression of adjacent brain structures. Uncal, central transtentorial, and downward herniations are three important brain herniation syndromes. Uncal or unilateral transtentorial herniation results when the uncus is compressed into the tentorial notch, and the midbrain compression leads to an ipsilateral dilated and fixed pupil, decreased consciousness, respiratory and cardiac irregularities, and decerebrate rigidity. Central or bilateral transtentorial herniation results when both cerebral hemispheres compress the diencephalon and midbrain into the tentorial notch, leading to pupillary constriction and then dilation, decreased consciousness, respiratory irregularities, and decerebrate or decorticate rigidity. Downward or cerebellar herniation results when the cerebellum is compressed into the foramen magnum and brainstem compression leads to neck stiffness or head tilt, impaired upward gaze, decreased consciousness, and lower cranial nerve palsies. A lumbar puncture should be carefully considered in any child suspected of having increased ICP, as it may increase the chance of brain herniation.

Treatment

Intracranial Pressure Monitoring

Routine monitoring of ICP is performed in certain clinical situations, as outlined in Table 86-1. Regardless of the method of ICP monitoring, vigilant clinical monitoring to prevent any untoward complications is essential. Invasive devices used to measure ICP in children older than 1 year of age include a fiber-optic intraparenchymal monitor (Camino fiber-optic catheter monitoring system), subarachnoid screw (Richmond bolt), epidural transducer, subdural catheter, and intraventricular catheter. All clinically available invasive ICP monitoring systems have their own recognized advantages and disadvantages. Noninvasive techniques are also available for the measurement of ICP in neonates and infants, in whom it is difficult to measure ICP invasively, including fiber-optic, strain gauge, and transfontanelle pressure transducer measurements.

The most commonly used ICP monitoring systems are the Camino fiber-optic intraparenchymal catheter and the mechanically transduced intraventricular catheter. The ICP monitoring system is routinely placed on the same side as the intracranial pathology, as a pressure differential may exist between the ipsilateral and contralateral sides. ICP monitoring is essential in children with elevated ICP so that appropriate treatment may be tailored to prevent brain herniation and secondary ischemia. Table 86-2 lists the normal ICP of neonates, infants, children, adolescents, and adults. Treatment should be initiated when the ICP is 10 mm Hg greater than the normal range for a specific age for more than 5 minutes.

Intracranial Pressure Treatment

Various treatments are available for the management of elevated ICP and act by (1) decreasing cerebral blood volume, (2) decreasing brain bulk and CSF, and (3) increasing intracranial volume (Table 86-3). Prior to initiating ICP reduction therapy, the respiratory and circulatory systems (ie, airway, breathing, and circulation [ABCs]) must be stabilized to ensure adequate oxygenation. One thing that is commonly overlooked in children with head injuries, who are brought into an emergency setting to be stabilized, is the cervical collar. Sometimes the cervical collar is on too tightly and this can impede venous return, thereby elevating ICP; therefore, it should be one of the first things that is checked.

<table>
<thead>
<tr>
<th>TABLE 86-1. Indications for Intracranial Pressure Monitoring</th>
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<tr>
<td>In a child with Glasgow Coma Scale score &lt; 8 (comatose)</td>
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<td>In a child with rapid deterioration of neurologic examination</td>
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<td>In a child who is chemically paralyzed</td>
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<td>In a child who is heavily sedated</td>
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<td>In a child who is ventilated with high airway pressures or positive end-expiratory pressure</td>
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<tr>
<td>In a child who underwent a small resection or biopsy of a brain tumor, with resultant increasing mass effect and cerebral swelling</td>
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Mannitol, an osmotic diuretic, or furosemide, a loop diuretic, is frequently used for the rapid reduction of ICP. Twenty percent mannitol at a dose of 0.25 to 1.0 g/kg is given as an intravenous infusion, and effective action occurs within 10 to 15 minutes and lasts for up to 8 hours. A decrease in brain tissue volume and CSF formation are two mechanisms that contribute to the rapid action of mannitol. The side effects of mannitol include (1) hemo-
dynamic instability (ie, hypotension followed by hypertension), (2) dehydration and hypovolemia, (3) electrolyte disturbances, (4) hyperosmolarity, and (5) increased rebound ICP phenomena.

The administration of mannitol requires that the child’s serum osmolarity and electrolytes (ie, sodium and potassium) be frequently measured. When serum osmolarity is > 320 mOsm/L, mannitol should be discontinued to avoid the potential complications of hypernatremia, hyperkalemia, low serum bicarbonate, metabolic acidosis, altered mental status, fluid overload, congestive heart failure in children with poor myocardial function, and acute renal failure, which usually occurs 2 to 4 days after mannitol treatment.

Furosemide is also used to reduce ICP by inducing a systemic diuresis and decreasing CSF production without producing significant changes in serum osmolarity. It is initially given as a large intravenous dose (0.5–1.0 mg/kg) alone or at a lower dose (0.15–0.30 mg/kg) in combination with mannitol. It has been demonstrated that the combined treatment with furosemide and mannitol has a synergistic action and prolongs the effect of lower doses of mannitol but may lead to more electrolyte abnormalities and severe dehydration. In a child with impaired cardiac function, furosemide may be preferable to mannitol.

Acetazolamide (Diamox®), a carbonic anhydrase inhibitor, may be used to decrease CSF production both acutely and chronically. It has been shown that acetazolamide can decrease CSF production by 16 to 66% in humans, and the effect of an intravenous dose appears to last for < 2 hours. However, a rapid intravenous dose of acetazolamide may have a cerebral vasodilative effect and, therefore, cause a transient increase in ICP due to tissue

| TABLE 86-2. Normal Intracranial Pressure (ICP) by Age |
| Age | Normal ICP Range (mm Hg) |
| Neonate | <2 |
| Infant (< 1 year) | 1.5–6 |
| Young child | 3–7 |
| Adolescent (> 15 years) | <15 |
| Adult | <15 |

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Cerebral Blood Volume

In most instances, cerebral blood volume (CBV) is the compartment that can be most easily and rapidly altered. Hyperventilation to a PaCO₂ of 25 to 30 mm Hg leads to cerebral arteriolar vasoconstriction and a subsequent reduction in brain and cerebral blood volumes. For immediate reduction in ICP, acute hyperventilation is indicated, but chronic hyperventilation should be avoided. The head should be in the neutral position and elevated 30° above the heart to avoid cerebral venous outflow obstruction and an increased CBV, which will help reduce ICP without a concomitant compromise in cardiac function.

Administration of cerebral vasoconstricting anesthetic agents, such as thiopental, pentobarbital, or propofol, will reduce the cerebral metabolic rate of oxygen and, therefore, decrease CBF and CBV. However, thiopental and pentobarbital may cause significant cardiovascular instability (ie, hypotension). Therefore, it may be necessary to administer vasopressor therapy (ie, phenylephrine or dopamine infusion) in children with poor cardiovascular function. Mannitol may also reduce CBV by reflex compensatory vasoconstriction resulting from the transient increase in CBF.

Administration of analgesic, sedative, and paralytic agents can be used to decrease ICP by decreasing agitation, decreasing somatic stimulation, and preventing breathing against the ventilator. Because hyperthermia increases the rate of brain metabolism and the level of carbon dioxide, the child’s temperature should be monitored closely; if elevated, surface cooling blankets and antipyretics should be used to return the temperature to normal. In experimental studies, hyperthermia has been shown to increase cerebral edema by up to 40%.

Brain Bulk and Cerebrospinal Fluid

Mannitol, an osmotic diuretic, or furosemide, a loop diuretic, is frequently used for the rapid reduction of ICP.

| TABLE 86-3. Treatment to Decrease Intracranial Pressure |
| To decrease cerebral blood volume |
| Hyperventilation |
| 30° head elevation in neutral position |
| Administration of barbiturates |
| Administration of paralytic agents |
| Administration of sedative agents |
| Prevention of hyperthermia |

To decrease brain bulk and cerebrospinal fluid (CSF)

| Osmotic diuretic (mannitol) |
| Loop diuretic (furosemide) |
| Glucocorticoid steroids (dexamethasone) |
| Acetazolamide to decrease CSF production |
| Intraventricular drainage of CSF |
| Surgical resection of a selected cerebral lobe or brain tumor |

To increase intracranial volume

| Surgical decompression of adjacent brain (ie, lobectomy) |
| Extensive decompressive craniectomy and dural expansion to allow for cerebral swelling |

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CO₂ release and a subsequent increase in CBV and CBF. It appears that acetazolamide may be useful as a temporizing measure or as an adjunct to definitive treatment in children with transient alterations in CSF absorption and without acute clinical signs and symptoms of increased ICP, such as clinical situations with slowly progressive hydrocephalus (eg, after resection of a posterior fossa tumor, repair of a myelomeningocele, germinal matrix and intraventricular hemorrhage in a premature infant, or meningitis). Lethargy, poor feeding, tachypnea, diarrhea, and electrolyte imbalances (ie, hyperchloremic metabolic acidosis) are potential side effects of acetazolamide treatment.

ICP can be decreased by glucocorticoid steroid (eg, dexamethasone) administration to decrease cerebral vasogenic edema. Intraventricular drainage of CSF by placement of an external ventriculostomy drain or by inserting a 23-gauge butterfly needle into a shunt reservoir in the presence of a distal catheter shunt malfunction also can decrease ICP (see Table 86-3).

**Conclusion**

Caring for a child with increased ICP must include not only treatment for the child, but also support for the family through frequent and effective communication between the health care team and family members. Early recognition and treatment of increased ICP and attention to detail with regard to all organ systems at all times are essential to effectively manage a child with increased ICP and, ultimately, reduce morbidity and mortality.

**Suggested Readings**


**Practitioner and Patient Resources**

**Brain Injury Association of America (BIAA)**
8201 Greensboro Drive, Suite 611
McLean, VA 22102
Phone: (703) 761-0750 or 800-444-6443
http://www.biausa.org
The mission of the BIAA is to create a better future through brain injury prevention, research, education, and advocacy.

**American Brain Tumor Association (ABTA)**
2720 River Road
Des Plaines, IL 60018
Phone: 800-886-2282
http://www.abta.org
The ABTA exists to eliminate brain tumors through research and to meet the needs of patients and their families.

**Hydrocephalus Association (HA)**
870 Market Street, Suite 705
San Francisco, CA 94102
Phone: (415) 732-7040 or 888-598-3789
http://www.hydroassoc.org
The HA provides support, education, and advocacy for individuals, families, and professionals.