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EMERGENCY MEDICINE PRACTICE
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An Evidence-Based Approach To Severe Traumatic Brain Injury In Children

A four-year-old boy is an unrestrained passenger in a motor vehicle crash and has been brought via EMS to your ED. He was not responsive at the scene, with equal and reactive pupils. Endotracheal intubation was unsuccessful at the scene and he has been receiving bag mask ventilation en route. You look at the monitor and see that his pulse is 80 and his blood pressure is 140/90 with an oxygen saturation of 100%. The resident yells out that his left pupil is 7 mm and minimally reactive and his right pupil is 3 mm and reactive. He extends to painful stimuli on the left and does not move his right side. Several questions run through your mind. How am I going to secure this patient's airway? Do I hyperventilate this patient; if so, how much? What about mannitol? Or should I use hypertonic saline? What is the likelihood of a good outcome?

Traumatic brain injury (TBI) is the leading cause of mortality and severe morbidity in children. Emergency medicine clinicians are the first line hospital responders for children with severe traumatic brain injury. The primary goal in the acute management of the severely head-injured pediatric patient is to prevent or ameliorate factors, such as hypoxemia, hypotension, intracranial hypertension, hypercarbia, hyper- or hypoglycemia, electrolyte abnormalities, enlarging hematomas, coagulopathy, seizures, and hyperthermia, that promote secondary brain injury. It is integral that clinicians recognize the signs and symptoms of severe pediatric TBI, initiate appropriate interventions, and activate the necessary specialty services in a timely manner. An evidence-based review of these

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CME Objectives

Upon completing this article, you should be able to:
1. Describe the pathophysiology of traumatic brain injury.
2. Identify the signs and symptoms of intracranial hypertension and brain herniation syndromes.
3. List appropriate medical therapies for the management of severe pediatric traumatic brain injury.

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considerations will be presented in this issue of *Pediatric Emergency Medicine Practice*.

Abbreviations Used In This Article

AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
APAF-1: Apoptotic-Protease Activating Factor
ATPase: Sodium-Potassium Adenosine Triphosphatase
BVM: Bag-Valve-Mask
cAMP: Cyclic Adenosine 3′,5′-Monophosphate
CBC: Complete Blood Count
CBF: Cerebral Blood Flow
cGMP: Cyclic Guanosine 3′,5′-Monophosphate
CPP: Cerebral Perfusion Pressure
CSF: Cerebral Spinal Fluid
CT: Computed Tomography
DIC: Disseminated Intravascular Coagulation
DTR: Deep Tendon Reflexes
EEG: Electroencephalogram
ETI: Endotracheal Intubation
GCS: Glasgow Coma Scale
ICP: Increased Intracranial Pressure
MAP: Mean Arterial Blood Pressure
MRI: Magnetic Resonance Imaging
NMDA: N-methyl-D-aspartate
TAI: Traumatic Axonal Injury
TBI: Traumatic Brain Injury
TNF: Tumor Necrosis Factor

Critical Appraisal Of The Literature

Literature on the efficacy of specific interventions or comparison between them for treatment of severe pediatric TBI is scant. Part of this can be attributed to lack of attention and funding for research due to the incorrect assumption that the traumatized pediatric brain is "just a traumatized small adult brain." It can also be attributed to the difficult challenges facing clinical trials in pediatric head injury including standardization of treatment, enrollment, consent, and appropriate assessment of outcomes. Until recently, there were no specific consensus or guidelines for the management of the pediatric patient with severe TBI, and clinicians had to rely on adult guidelines.[1] Pediatric patients are not just small adults and there are several key differences between pediatric and adult TBI **(Table 1)**. In 2003, *Pediatric Critical Care Medicine* published "Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents" which is the most extensive review of the literature on management of severe pediatric traumatic brain injury to date.[2] Unfortunately, because the number of pediatric studies was lacking, these authors made many recommendations after reaching a consensus based on published adult guidelines. As a result, clinicians are left to make many clinical decisions based on adult data and clinical experience.

Table 1. Key Differences Between Pediatric And Adult TBI

Causes & Presentation
Nonaccidental trauma may be occult
There may be a delay in presentation to the ED
The first point of contact in falls is likely to be the head
Pathophysiology
The cranium is more compliant
Hypotension is a LATE finding in pediatric shock
Lower lung functional residual capacity
Evaluation
Mental status may be difficult to assess due to developmental milestones
Vague or inaccurate histories are associated with nonaccidental trauma
Management
The narrowest portion of the airway is the subglottic region
Experienced or advanced airway management skills may be needed
Medication dosing and fluid administration should be adjusted based on weight

Epidemiology And Etiology

According to the Centers for Disease Control and Prevention (CDC), approximately 475,000 children under the age of 14 sustain traumatic brain injury annually.[3] Although the majority of these children are treated in the emergency department and released (90%), pediatric TBI results in 47,000 hospitalizations and 2685 deaths each year. Rates of hospitalization and mechanisms of injury vary by age secondary to developmental stages, and it is important for the emergency medicine clinician to be aware of these variations when approaching the head-injured child.[4]

In infants (less than one year of age), inflicted or nonaccidental TBI must always be considered. The median age for inflicted TBI is two to four months and intensive care hospitalization rates have been estimated at approximately 30 per 100,000 children annually.[3,5] Accidental TBI in this age, mainly due to motor vehicle crashes and falls from parents' arms, have intensive care admission rates of 20 per 100,000

children annually. Mortality rates are similar for both groups (six to seven deaths per 100,000 children annually).[5] It must be noted that estimating the accurate incidence of inflicted TBI is challenging due to the fact that many children may not present for treatment or may have an extended interval between injury and presentation for medical care.

By toddler age, children have developed the motor capabilities to encounter more hazards but lack the cognitive ability for avoidance. Inflicted TBI requiring hospitalization is much less common in this age group (four per 100,000 annually), as is non-inflicted TBI (10 per 100,000 annually).[5] Among motor vehicle related injuries in toddlers, pedestrian versus vehicle crashes are more common than motor vehicle occupant injuries, and this difference may be quite striking in the urban environment.[6,7] In school-aged children, falls requiring hospitalization decrease with age, while there is a rise in injuries associated with bicycle crashes. In adolescents, there is a dramatic rise in TBI-related death rates, with violence being an unfortunate common cause (24.3 per 100,000).[3]

Pathophysiology

Traumatic brain injury can be categorized into primary and secondary injury. Primary brain injury results directly from the initial forces generated by impact following trauma. Contact, linear forces are generated when the head is struck by a moving object and generally results in focal injuries (skull fracture, hematomas, and contusions) either localized to the impact site or immediately opposite; these are known as contra-coup lesions. Inertial, angular forces produced by acceleration-deceleration that are severe can produce immediate physical shearing or tearing of axons, termed "primary" axotomy. Following primary brain injury, a cascade of cellular, molecular, and biochemical events occurs in the minutes to hours and days to weeks after the primary brain injury that lead to ongoing or "secondary" traumatic axonal injury (TAI) and neuronal cell damage (secondary brain injury) and, ultimately, neuronal cell death.[8-10] These mechanisms have been the focus of traumatic brain injury research as there is currently no treatment for this type of secondary brain injury. Some of these mechanisms are outlined here.

Cerebrovascular Dysregulation

After TBI, physical damage to cerebral blood vessels and alterations in cerebral blood flow are thought to contribute to secondary brain ischemia. In a study of infants and young children, decreased cerebral blood flow (< 20 mL/100 g/min) in the initial 24-hour period following TBI was associated with poor outcome.[11] Mechanisms that may underlie post-traumatic hypoperfusion include reduced levels of vasodilators, including nitric oxide, cyclic guanosine 3′,5′-monophosphate (cGMP), cyclic adenosine 3′,5′-monophosphate (cAMP), and prostaglandins, which are thought to contribute to decreased cerebral blood flow.[12-14] Similarly, increased levels of vasoconstrictors, such as endothelin-1, are also implicated in cerebral vascular dysregulation.[15]

Excitotoxicity And Apoptosis

Following head trauma, the release of excessive amounts of the excitatory amino acid glutamate (excitotoxicity) is thought to occur; this can lead to neuronal injury in two phases. The first phase is characterized by sodium-dependent neuronal swelling which is then followed by delayed, calcium-dependent neuronal degeneration.[16] These effects are mediated through both metabotropic receptors (which are linked to second-messenger systems) and ionophore-linked receptors, such as *N*-methyl-D-aspartate (NMDA), kainite, and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA). Activation of these receptors allows calcium influx through receptor-gated or voltage-gated channels or through the release of intracellular calcium stores. This increase in intracellular calcium is then associated with numerous processes (such as activation of proteases, lipases, and endonucleases) that can lead to neuronal degeneration and necrotic cell death. Consistent with excitotoxic-mediated neuronal cell death, one research study recently showed that calcium-activated protease (calpains) may participate in neuronal cell loss in the injured cortex following contusive brain trauma in the immature rat.[17]

In contrast to necrotic cell death, which is marked by neuronal cell swelling and dissolution of cell membranes, apoptotic cell death is marked by internucleosomal DNA fragmentation and the formation of apoptotic cell bodies associated with nuclear condensation and neuronal cell shrinkage. Apoptosis requires a cascade of intracellular events for completion of "programmed cell death" and is

initiated by intracellular (intrinsic) or extracellular (extrinsic) signals. Intracellular signals are initiated in the mitochondria as a result of calcium flux, oxidative stress, or depletion of ATP.[18] Mitochondrial dysfunction leads to cytochrome *c* release in the cytosol; in the presence of apoptotic-protease activating factor (APAF-1) and dATP, this activates the initiator protease caspase-9.[19] Caspase-9 then activates the effector protease caspase-3, which cleaves DNA repair and cytoskeletal proteins and endonucleases.[20] Extracellular signaling occurs via tumor necrosis factor (TNF) superfamily of cell surface death receptors, which include TNFR-1 and Fas/Apo1/CD95.[21] Receptor–ligand binding of TNFR-1-TNF-α or Fas-Fas L promotes "death domains" which activates caspase-8, ultimately leading to caspase-3 activation.[22] Because differentiating necrotic versus apoptotic cell death is difficult in TBI, cells that die can be characterized as a morphologic continuum ranging from necrosis to apoptosis.[23]

Animal studies have shown that the developing neuron is more susceptible to excitotoxic injury than the mature neuron, probably because more calcium is transmitted via the NMDA-mediated calcium channel in the immature brain.[24, 25] Although the administration of NMDA antagonists following TBI in immature rats decreased excitotoxic-mediated neuronal death, apoptotic cell death increased.[26] Further research is needed to address the role of excitotoxicity and apoptosis following trauma to the developing brain.

Cerebral Swelling

Diffuse cerebral swelling following pediatric TBI may be a significant contributor to intracranial hypertension that can result in further ischemia and herniation. This swelling is thought to result from blood-brain barrier disruption (vasogenic edema), osmolar changes, and edema at the cellular level (cytotoxic or cellular edema). Furthermore, cerebral swelling is thought to be worsened with hypoxia and hypoperfusion. Osmolar shifts occur primarily in areas of necrosis where osmolar load increases with the degradation of neurons. As reperfusion and recovery occurs, water is drawn into the area secondary to the high osmolar load, and the surrounding neurons become edematous. Cellular swelling independent of osmolar load primarily occurs in astrocyte foot processes and is thought to be brought on by excitotoxicity and uptake of glutamate. Glutamate uptake is coupled to sodium-potassium adenosine triphosphatase (ATPase), with sodium and water being accumulated in astrocytes.[27] Emerging literature suggests that cellular edema, and not hyperemia nor vasogenic edema, may be the primary contributor to cerebral swelling, although further studies need to be done.[28]

Traumatic Axonal Injury

A common pathology observed in infants and young children in both accidental and nonaccidental or inflicted closed-head injuries is traumatic axonal injury (TAI). TAI involves widespread damage to axons in the white matter of the brain. While immediate or "primary" axotomy or immediate physical tearing of the axon can occur following TBI, TAI is thought to primarily occur by a delayed process called "secondary" axotomy. Hypoxic-ischemic injury, calcium and ionic flux dysregulation, and mitochondrial and cytoskeletal dysfunction are thought to play important roles in axonal damage.[29] TAI most commonly occurs in the corpus callosum, basal ganglia, and periventricular white matter.[30] TAI is thought to be a major cause of prolonged coma and morbidity in pediatric TBI.[31] TAI also appears to be common in child-abuse victims.[32] The pediatric population is thought to be at a higher risk for TAI due to the lack of complete myelinization of axons and the higher ratio of head to body mass, which makes children more susceptible to angular forces following TBI.

Future Directions

Despite major advances in the understanding of the mechanisms of TBI in the adult patient, knowledge of the pathophysiology of brain trauma in the pediatric population is inadequate. However, interest in pediatric TBI has increased in recent years with the development of age-appropriate and clinically relevant animal models of closed head injury in the immature species. In addition, a number of recent studies have described the pathology of pediatric TBI patients using sophisticated radiologic techniques and CSF/serum markers. Collectively, these two approaches can be utilized to better understand the molecular and cellular mechanisms underlying neuronal pathology in the brain-injured pediatric patient. Finally, the importance of animal models in the development of age-appropriate treatment strate-

gies to alleviate the chronic "secondary" neurodegenerative problems in the traumatically-injured pediatric brain cannot be overstated.

Furthermore, recent experimental data are showing that there is an "age-dependent response" following TBI, showing evidence that the pediatric brain is simply not a "small adult brain." More importantly, even within the pediatric TBI population, there is evidence to support an "age-at-injury" response.[33-35] For example, following contusive brain injury in post-natal day 11 (neurologically equivalent to an infant) and post-natal day 17 (neurologically equivalent to a toddler) rats, the younger animals sustained more profound long-term cognitive deficits and diffuse brain atrophy, while the older animals exhibited a focal cortical cavity.[36] This parallels what is commonly seen in infants and children following TBI, where the youngest patients (less than four years of age) usually have the worst outcome and commonly suffer chronic brain atrophy.[33, 37]

Differential Diagnosis

The differential diagnosis of the pediatric patient with severe TBI should always focus on the ABC's (Airway, Breathing, Circulation) while recognizing the signs and symptoms of life threatening intracranial hemorrhages and mass occupying lesions that can cause intracranial hypertension.

The differential diagnosis for penetrating head injury mainly differs in that vascular injuries become more common compared to closed head injuries. It is important to note that infants can lose significant portions of their blood volume through intracranial and extracranial bleeding, resulting in circulatory compromise and shock. The following is a summary of the intracranial hemorrhage that the emergency medicine clinician may encounter.

Epidural Hematoma

Epidural hematomas are an accumulation of blood between the inner table of the calvarium and the dura. The leading cause of epidural hematomas in the pediatric population is falls (49%), followed by traffic-related accidents (34%).[38, 39] The main source of epidural bleeding has been historically attributed to the middle meningeal artery but can be the result of injury to the middle meningeal vein, the diploic veins, or the venous sinuses. In a report of 102 pediatric patients, arterial bleeding was found in 18% of epidural hematomas, 32% were associated with venous bleeding, and 31% had no identifiable source.[40] The most frequent locations of epidural hematomas are the temporoparietal and temporal regions.[39, 40]

Subdural Hematoma

Subdural hematomas are an accumulation of blood between the dura and the brain parenchyma, usually the result of injury to the cortical bridging veins. They are more common in infancy and the incidence decreases with age.[41] Acute subdural hematomas are usually the result of high velocity injuries and are associated with primary brain parenchyma injuries such as contusions or TAI.[42] In infants without a clear history or mechanism for accidental trauma or with concurrent interhemispheric bleeding, further evaluation for inflicted trauma must be done.

Subarachnoid Hemorrhage

Subarachnoid hemorrhage occurs after injury to the small vessels traversing the subarachnoid space. It does not typically require emergent intervention unless it causes cerebral spinal fluid (CSF) flow obstruction, but it can be a sign of associated significant brain parenchymal injury.

Intracerebral Hemorrhage

Hemorrhagic contusions are common after pediatric head injury, but large intracerebral lesions are rare.[43] These small lesions are the result of the brain impacting the skull.

Prehospital Care

The focus of prehospital management of the severely head-injured pediatric patient always includes the ABC's with rapid recognition and correction of life-threatening conditions, prevention of secondary brain injury, and transportation to the closest appropriate facility. The biggest challenges and controversies in the prehospital care of the head-injured child are airway management and the role of pediatric trauma centers.

Reversing or minimizing the causes of secondary brain injury, such as hypoxemia and hypotension, are vital components of prehospital care. Episodes of hypoxemia and hypotension can be very detrimental to outcome.[44, 45] A large prospective cohort study of

adults utilizing the Traumatic Coma Data Bank found that TBI patients with hypoxemia in the prehospital environment (defined as cyanosis or apnea) had worse outcomes.[46] Hypoxemia and hypotension are also not uncommon in the pediatric trauma patient.[47,48] Endotracheal intubation of pediatric patients is successful in the most skilled and experienced hands, which may not always be available in prehospital care. Nasotracheal intubation should be avoided in the presence of possible facial or basilar skull fractures due to the rare complication of introducing the nasotracheal tube into the brain. The cervical spine should always be stabilized, as the majority of spinal cord injuries in pediatric patients are in the cervical region due to the relatively large head, weak neck musculature and ligaments, and incomplete ossification of the cervical spine.[49]

There is very limited literature on the management of the airway in severe TBI pediatric patients. A large prospective study of pediatric patients in two urban emergency medical systems comparing endotracheal intubation (ETI) to bag mask ventilation (BVM) found no difference in outcomes.[50] On subgroup analysis, there was no difference in survival or "good" neurologic outcome, although the small numbers in each group must be taken into account. A large retrospective study of 578 cases from the National Pediatric Trauma Registry did not find a difference in mortality between ETI or BVM, but the ETI group had less injury complications to any organ system (58% vs. 71% $P < 0.05$), although the ETI group was older.[51] More recently, a retrospective study of 105 pediatric trauma patients who had an attempted intubation in a rural emergency medical system found that only 9.3% of patients could not be oxygenated or ventilated by BVM, and multiple ETI attempts were associated with transport delays and lower discharge Glasgow Coma Score (GCS).[52] Based on these and other data, the pediatric TBI guidelines published in 2003 concluded that there was "insufficient data to support treatment standards in prehospital airway management," but recommended as a guideline that "hypoxia must be avoided."[2]

Several studies have demonstrated improved outcomes in pediatric trauma patients after implementation of a trauma system;[53-55] the current guidelines recommend that in metropolitan areas, pediatric TBI patients be directly transported to pediatric trauma centers.[2] The more difficult question about what to do in the rural setting - where resources may be scarce and transit times may be long - is difficult to answer and will depend on a multitude of factors unique to each patient; efficient and safe transport to a pediatric trauma center or an adult trauma center with added qualifications to treat children is encouraged.[2]

ED Evaluation

History

When a severely head-injured pediatric patient arrives in the ED, the clinician must quickly gather limited but important information. Details on the timing and mechanism of injury, resuscitative efforts, and therapeutic interventions implemented and attempted from witnesses at the scene as well as from emergency medical personnel are vital. The use of the "AMPLE" mnemonic (allergies, medications currently used, past illnesses, last meal, and events/environment related to the injury) may be helpful for clinicians to quickly acquire the necessary information to improve understanding of the pediatric patient's current physiologic state.[56] Symptoms on presentation have been found to have little or no correlation with injury severity and the clinician must rely on physical examination.[57]

Physical Examination

The emergency medicine clinician must quickly assess the adequacy of the ABC's and the patient's neurological status, while simultaneously evaluating for life-threatening signs and symptoms of intracranial hypertension or impending herniation, such as altered level of consciousness, pupillary dysfunction, lateralizing extremity weakness, Cushing's triad (hypertension, bradycardia, and irregular respirations), or other herniation syndromes **(Table 2)**.

The airway should be quickly assessed for patency. If the patient is intubated, rapid assessment of an esophageal intubation can be done with capnography.[58-60] The patient should have rapid assessment of vital signs including heart rate, respiratory rate, blood pressure, pulse oximetry, and temperature; these vital signs should be regularly re-assessed. The head and spine should be thoroughly examined for any external evidence of injury, such as scalp lacerations and skull depressions, which warrant concern for an underlying skull fracture and severe intracranial injury. In an infant, a bulging fontanelle may be a sign of increased ICP.[9] Mastoid ("Battle's sign") and peri-orbital bruising ("Raccoon eyes") due to

dissection of blood, hemotympanum, and clear rhinorrhea are all signs of possible basilar skull fracture.

It is important that a speedy but detailed and easily reproducible neurological assessment be performed and documented.[57] Pediatric patients with severe head injury will commonly present with an altered level of consciousness or possibly coma. The Glasgow Coma Scale (GCS) for older children and adults is the most widely used method to quantify initial neurological assessment.[61] In younger pediatric patients, the Children's Coma Scale is most often utilized **(Table 3)**.[62] A GCS score of 13-15 is mild, 9-12 is moderate, and 3-8 is severe TBI. It is critical that the GCS be recorded on the initial medical record and repeated regularly to detect changes in GCS over time. For example, a child suffering a head injury may arrive in the ED with an initial GCS of 13 but then rapidly decrease over time secondary to an expanding intracranial hematoma. A coma scale called the FOUR Score has recently been introduced and validated in adults and may provide a better assessment of the intubated neurologically impaired patient.[63] This scoring system eliminates the verbal category but adds an evaluation of brainstem and respirations. The two major disadvantages of this score are that it has not been validated in children and it lacks widespread familiarity and use.

Table 3: Modified Children's Coma Scale

Eye Opening	
Spontaneous	4
To speech	3
To pain	2
None	1
Verbal	
Coos, babbles	5
Irritable	4
Cries to pain	3
Moans to pain	2
None	1
Motor	
Normal spontaneous movements	6
Withdraws to touch	5
Withdraws to pain	4
Abnormal flexion	3
Abnormal extension	2
Flaccid	1

The pupillary examination is vital when assessing the neurological status of the head-injured child. The size, shape, and reactivity to light provide critical insight into the balance of sympathetic and parasympathetic influences. An enlarged unreactive pupil (mydriasis) can be secondary to dysfunction or injury to the oculomotor nerve (cranial nerve III) and can be associated with disorders of oculomotor muscle and ptosis.[9] Transtentorial herniation or a lesion along the course of the oculomotor nerve may cause unilateral mydriasis. Direct trauma to the eye may cause injury to the iris and result in mydriasis without oculomotor dysfunction. Bilateral mydriasis can be the result of ingestions (anticholinergics) or administration of atropine or adrenergic agonists (such as epinephrine) during resuscitation. A small pupil (miosis) is usually secondary to dysfunction of sympathetic innervation. Since the efferent sympathetic fibers travel along the carotid artery, injury to the neck or skull base must also be considered in the pediatric TBI patient.

Evaluation of eye movements and brain stem reflexes are vital and can help localize the intracranial lesion. Dysfunction of all three cranial nerves in eye movement (oculomotor, trochlear, and abducens) can be the result of injury to the ipsilateral cavernous sinus. Cough and gag reflexes detect glossopharyngeal and vagus nerve function. Abnormalities in respiratory pattern may also assist in localizing brain injury and herniation syndromes **(Table 2)**. Deep tendon reflexes (DTR) are typically exaggerated in head-injured patents due to the lack of cortical inhibition.

Table 2. Herniation Syndromes

	Eye Findings	Gross Motor	Respiration
Uncal	Unilateral fixed dilated pupil with unilateral ptosis	Hemiparesis	
Diencephalic	Small midpoint pupils, but reactive to light	Decorticate posturing, hypertonia	Cheyne-Stokes
Midbrain	Midpoint fixed pupils	Decerebrate posturing	Hyperventilation
Medullary	Dilated and fixed pupils	No response to pain	Irregular or gasping

However, decreased DTR may suggest a spinal cord injury. The Babinski response is an abnormal finding in children older than six months of age when the plantar reflex is tested. It is characterized by extension of the great toe and abduction of the remaining toes.

The presence of Cushing's triad (systemic hypertension, bradycardia, and irregular respirations) due to compression of the cardiorespiratory centers in the brainstem is a late and ominous sign for herniation. Patterns of dysfunction utilizing these neurological examination tools can help localize lesions and syndromes. **Table 2** illustrates several different herniation syndromes and the physical findings associated with them.

Diagnostic Studies (Lab, Radiology, ECG, And Point-of-Care Tests)

The mainstay of the diagnostic evaluation of the severely head-injured pediatric patient is radiologic imaging. Prior to transport to computed tomography (CT) scan, the ABC's must always be addressed and appropriate monitoring must be instituted and blood samples sent. For intubated patients, continuous capnometry is vital for titrating treatment of intracranial hypertension. Arterial blood gas to assess pH and correlate $PaCO_2$ with capnometry can be invaluable.

Chemistry panel should be sent to assess electrolyte abnormalities and renal function, especially if hyperosmolar therapy may be instituted.[64] Liver enzymes and pancreatic function should also be evaluated for possible blunt trauma, especially if nonaccidental trauma is suspected. Complete blood count (CBC) evaluating for anemia and thrombocytopenia in the presence of intracranial bleeding is essential. The coagulation profile should also be evaluated for the presence of a coagulopathy, and a type and screen should be sent. In one prospective observational study, 22% of children with severe head injury had laboratory evidence of disseminated intravascular coagulation (DIC).[65] Furthermore, a normal coagulation profile and platelet count on presentation does not rule out the possibility of coagulopathy or thrombocytopenia developing over time.[66] In the adolescent population, where there are increased rates of high impact injuries from motor vehicle crashes, a toxicology screen should also be considered.[67]

Imaging with plain films of the cervical spine should be performed, as well as chest radiographs for intubated patients to evaluate for right mainstem intubations, pneumothoraces, widened mediastinum, and rib fractures. Pelvic radiographs should be considered if pelvic injuries are suspected. Other radiographs should be performed based on the results of the secondary survey. **If there is no clear history or mechanism of accidental trauma, especially in infants and early toddlers, further investigation for other occult injuries, such as abdominal injuries, skeletal injuries, interhemispheric bleeds, or retinal hemorrhages (which are commonly associated with shaken-baby or shaken-impact syndrome) should be sought.**[68] (See "Special Circumstances.") However, this workup should not take precedence over life-threatening issues such as hypoxemia, hypotension, and intracranial hypertension.

There is a large amount of debate in the literature about performing a CT scan on children with mild head injury,[69-73] but this is not the case in severe TBI. In pediatric patients with moderate and severe traumatic brain injury, CT scans are the imaging modality of choice and can rapidly detect skull fractures, intracranial hematomas, intraparenchymal contusions, cerebral edema, and obliteration of the basal cisterns (which is concerning for elevated ICP). CT scan's widespread availability and rapid imaging time make it very useful to the emergency medicine clinician. Obliteration or narrowing of basal cisterns, midline shift, and the presence of subarachnoid hemorrhage in the basal cisterns have been associated with poor outcome.[74-76] The basal cisterns are evaluated at the level of the mid brain; compressed or absent cisterns increase the risk of intracranial hypertension and poor outcome.[76, 77] The presence of midline shift at the Foramen of Monro is also inversely related to prognosis.[74, 76, 77] The presence of traumatic subarachnoid hemorrhage in severe TBI increases mortality, and its presence in the basal cisterns is a predictor of poor outcome.[74, 76, 77] Magnetic resonance imaging (MRI) has demonstrated superiority on detecting traumatic axonal injury and its correlation with long-term outcome; however, due to several factors - including availability, length of time required for image acquisition, and limited physiologic monitoring in the MRI suite - this modality is of limited use in the initial stabilization and evaluation of the pediatric TBI patient.[78-80] In summary, pediatric patients with moderate and severe TBI should have CT imaging as soon as possible, but not before physiologic stabilization has occurred (ABC's)

and appropriate monitoring has been placed (such as end-tidal CO_2).

Treatment

Airway, Breathing, And Circulation ("ABC")

As previously mentioned, hypoxemia and hypotension are to be avoided or treated in the hopes of preventing or minimizing secondary brain injury from hypoxic-ischemic brain damage, which may promote cerebral swelling and elevated ICP. Thus, the first step in treating the head-injured pediatric patient is always to promote adequate oxygenation and ventilation and to prevent or treat shock. This should begin at the scene of injury. These children should be placed on supplemental oxygen. Criteria for tracheal intubation includes hypoxemia not resolved with supplemental oxygen, apnea, hypercarbia ($PaCO_2$ > 45 mmHg), GCS ≤ 8, a decrease in GCS > 3 independent of the initial GCS, anisocoria > 1 mm, cervical spine injury compromising ventilation, loss of pharyngeal reflex, and any clinical evidence of a herniation syndrome or Cushing's triad.[9]

All patients should be assumed to have a full stomach and cervical spine injury, so the intubation should be performed utilizing a cerebroprotective, rapid-sequence induction whenever possible. The airway should be cleared of obstruction due to secretions, emesis, or blood by suction, and an oropharyngeal airway should be used in an unconscious child to relieve airway obstruction from their tongue. Supplemental oxygen (100%) should be delivered by face mask to allow nitrogen washout from the patient's functional residual capacity to allow sufficient oxygenation prior to intubation of the trachea. Bag-valve-mask (BVM) ventilation should not be done unless the patient has signs and symptoms of impending herniation, apnea, or hypoxemia.[81] Vigilant care of the cervical spine is especially advised during BVM ventilation due to an increased risk for cervical spine injury.[82] A second person's sole responsibility is to maintain the child's neck in the neutral position by mild axial traction during airway maneuvers. Cricoid pressure should be performed by a third individual. However, both of these caretakers should not put excess pressure on the soft tissue of the neck as this may lead to inadvertent airway obstruction. As a general rule, the proper tracheal tube size for children beyond six months of age = (inner diameter or ID or mm) = (16 + age [in years])/4. In term infants, a 3.0 or 3.5 mm tracheal tube should be used, while a 4 mm tracheal tube should be used in infants younger than six months of age. However, this "rule" is only a starting estimate; one size smaller and one size larger tracheal tubes should always be available. The depth of insertion of the tracheal tube = (3) X (ID of the tracheal tube); again, this is only a starting estimate. Orotracheal intubation by direct laryngoscopy is the preferred method; as previously discussed, nasotracheal intubation should be avoided due to the possibility of direct intracranial damage in a patient with a basilar skull fracture and also because nasotracheal intubation may require excessive movement of the cervical spine. After successful tracheal intubation, oxygen saturation of 100%, normocarbia (35-39 mmHg) and not hyperventilation (confirmed by arterial blood gas and trended with an end-tidal CO_2), and a chest x-ray showing the tracheal tube in good position above the carina (as right mainstem tracheal intubation is common) should be confirmed.

Unless the patient has signs or symptoms of herniation, prophylactic hyperventilation ($PaCO_2$ < 35 mmHg) should be avoided. Hyperventilation causes cerebral vasoconstriction which decreases cerebral blood flow and subsequent cerebral blood volume; this will lower ICP, but ischemia can also occur.[83] Additionally, respiratory alkalosis caused by hyperventilation shifts the hemoglobin-oxygen curve to the left and makes it more difficult to release oxygen to the brain.

Because endotracheal intubation is a noxious stimulus and can increase ICP, appropriate medications should be used during rapid-sequence induction. The hemodynamic and neurologic status of the patient dictates the choice of drugs used. For the patient in cardiopulmonary arrest, no medications are needed for tracheal intubation. Most other patients should receive lidocaine (1-1.5 mg/kg) intravenously (IV) three minutes before intubation to help blunt the rise in ICP that occurs during direct laryngoscopy.[84] For the hemodynamically unstable patient, the combination of lidocaine, etomidate (0.2-0.6 mg/kg), and neuromuscular blockade with rocuronium (1 mg/kg) or vecuronium (0.3 mg/kg) IV is a popular choice. An alternative is the combination of lidocaine, fentanyl (2-4 micrograms/kg), and rocuronium or vecuronium. In the hemodynamically stable patient, adding a fast-acting benzodiazepine (such as midazolam 0.1-0.2 mg/kg) to either of the above combinations is acceptable. Another

alternative in the hemodynamically stable patient is the combination of thiopental (3-5 mg/kg), lidocaine, and rocuronium or vecuronium. Thiopental and etomidate are ultrafast acting and quickly reduce cerebral metabolism, which ameliorates the increased ICP associated with direct laryngoscopy. In addition, the short-acting narcotic fentanyl, when used with lidocaine, can decrease the catecholamine release associated with direct laryngoscopy.[81] The endotracheal tube should be secured with tape, but the adhesive tape should not pass around the neck as venous return from the brain can be compromised.

Assessment of the patient's circulatory status (central and peripheral pulse quality, capillary refill, heart rate, blood pressure) is critical as hypotension after pediatric TBI is associated with increases in morbidity and mortality rates.[2, 44, 45] The most common cause for compensated or "early" shock (tachycardia with normal blood pressure) and uncompensated or "late" shock (low blood pressure) in the trauma patient is hypovolemic (i.e., hemorrhagic) shock. In severe TBI, rapid intravenous fluid resuscitation is the goal for hypovolemic shock. Isotonic solutions, such as 0.9% NaCl solution and/or packed red blood cells (for hemorrhagic shock), can be administered, but hypotonic fluids should not be used in the initial resuscitation of these patients. Although not yet studied in a clinical trial, resuscitation with hypertonic saline (3% saline) in a severe TBI pediatric patient with initial signs and symptoms of both hypovolemic shock and intracranial hypertension should be considered; (this is discussed further in the "Intracranial Hypertension Management: First-Tier Therapies" section). Special consideration must be given to spinal (neurogenic) shock, especially with suspected cervical-thoracic spine injuries, in addition to hypovolemic or hemorrhagic shock as the etiology of hypotension. These patients may be bradycardic with shock. Both must be treated accordingly with isotonic fluid/blood resuscitation to ensure adequate circulation and prevent further ischemia. In spinal shock, α-adrenergic agonists, such as IV phenylephrine, are also needed to treat the vasodilatation that results from injury to the sympathetic outflow tract.

Prophylactic "brain-specific" interventions (such as hyperventilation and hyperosmolar therapy with mannitol or 3% saline) in the absence of signs and symptoms of herniation or other neurologic deterioration are not currently recommended. However, in the presence of signs and symptoms of herniation, such as Cushing's triad (irregular respirations, bradycardia, systemic hypertension), pupillary dysfunction, lateralizing extremity weakness, or extensor posturing, emergent treatment is needed; this is addressed in the "Herniation" section.

Herniation

While the ABC's are being addressed, signs and symptoms of impending herniation (such as Cushing's triad or one of the herniation syndromes) must also be immediately treated. Early consultation with a neurosurgeon is important. In one study, mass lesions occurred in 30% of children with severe TBI.[85] Hyperventilation with 100% oxygen can be life-saving in the setting of impending herniation, such as a child who has a rapidly expanding epidural hematoma with pupillary dilatation, bradycardia, systemic hypertension, and extensor posturing. Elevating the head to 30° increases venous drainage and lowers ICP.[86] Furthermore, the head should be midline to prevent obstruction of venous return from the brain. If these maneuvers don't relieve the signs and symptoms of herniation, hyperosmolar therapy (mannitol, 3% saline) should be instituted. (See "Intracranial Hypertension Management: First-Tier Therapies.") In addition, intubating doses of short acting medications, such as thiopental or etomidate, as described previously, can be administered emergently in this setting.[9] During this time, the patient usually goes to the CT scanner and/or directly to the OR with the neurosurgeon as the definitive therapy for a rapidly expanding epidural hematoma with herniation symptoms is surgery. Besides expanding mass lesions, diffuse cerebral swelling may also lead to herniation. Diffuse swelling is more common in pediatric than in adult TBI.[87] As a result, secondary causes of brain injury, such as hypoxemia, hypercarbia, hypotension, excessive fluid administration, or seizures, can precipitate herniation and therefore must be prevented or immediately treated.

Intracranial Hypertension Management: First-Tier Therapies

Once the initial resuscitation with the ABC's and herniation and expanding intracranial masses have been medically and surgically addressed, further management is aimed at preventing or treating causes of secondary brain injury (such as hypoxemia, hypotension, intracranial hypertension, hypercarbia, hyper-

or hypo-glycemia, electrolyte abnormalities, enlarging hematomas, coagulopathy, seizures, and hyperthermia).

One of the most important consequences of secondary brain injury is the development of intracranial hypertension. First described in the Monroe-Kellie doctrine, the intracranial vault is a fixed volume of brain, CSF, and blood.[9] An enlarging space occupying lesion, such as an expanding epidural hematoma or worsening cerebral edema, will not initially cause intracranial hypertension because the initial compensatory mechanisms of displacement of CSF to the spinal canal and venous blood to the jugular veins prevents elevated ICP. However, once these compensatory mechanisms are exhausted, even a small increase in the size of the hematoma or cerebral edema will lead to increased intracranial pressure (ICP), which will compromise cerebral perfusion. This will then lead to brain ischemia and further edema and, ultimately, to brain herniation.

Another important concept to understand is cerebral autoregulation and cerebral perfusion pressure (CPP). Under normal conditions, cerebral autoregulation provides constant cerebral blood flow (CBF) over a wide range of cerebral perfusion pressures and is "coupled" to the metabolic demands of the brain. CPP is defined as the difference between mean arterial blood pressure (MAP) and ICP: CPP = MAP - ICP.[9] After TBI, cerebral autoregulation can become "uncoupled" to the metabolic demands of the brain, and alterations in CPP (due to either rising ICP or changing MAP) may result in fluctuations of CBF which can lead to cerebral ischemia or hyperemia. For example, a study utilizing xenon CBF-CT studies in children after TBI demonstrated marked reductions in CBF within the first 24 hours after injury which was associated with poor outcome, while the children with high CBF 24 hours after the injury exhibited improved outcome.[11] However, because this type of study cannot measure minute-to-minute assessment of CBF changes and due to the potential risk of transporting and performing prolonged studies in critically-ill patients, most institutions continuously measure CPP to "estimate CBF."

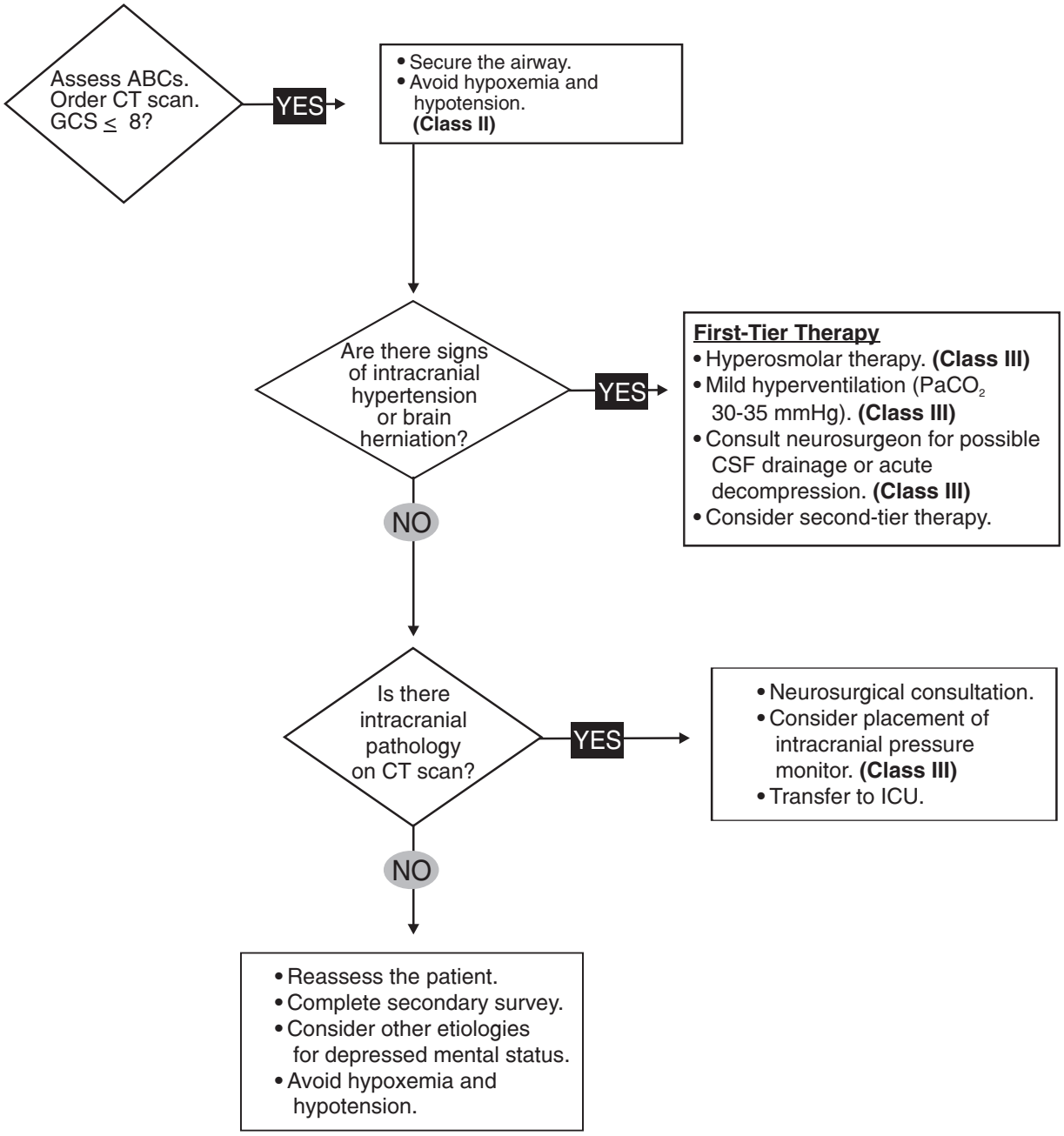
A flow diagram showing a general approach to "first-tier" treatments for established intracranial hypertension in pediatric TBI was provided in the "Guidelines for the acute medical management of severe TBI in infants, children, and adolescents" article **(Figure 1)**.[2] As discussed fully in the following sections, "first-tier" therapies include head position, sedation, analgesia, neuromuscular blockade, ventricular CSF drainage, hyperosmolar therapy, and mild hyperventilation. In general, after initial stabilization and resuscitation for treatment of potential intracranial hypertension, an ICP monitor is placed by the neurosurgeon in children with an initial GCS ≤ 8. If the ventricles are not compressed due to severe cerebral swelling, ICP monitoring by ventricular catheter allows a potential therapeutic option of CSF drainage. Since clinical signs and symptoms of herniation are very late signs of intracranial hypertension, the use of ICP monitors allows early detection of intracranial hypertension before signs and symptoms of herniation are observed.[88] However, ICP monitors can cause hemorrhage and infection. Coagulopathy needs to be corrected before ICP monitor placement; some centers use prophylactic antibiotics.

ICP And CPP

Treatment for intracranial hypertension should begin at an ICP ≥ 20 mmHg, as most pediatric TBI studies show poor outcome with ICP > 20 mmHg, and aggressive treatment of intracranial hypertension is associated with improved outcomes in some studies.[89-92] However, further studies need to be conducted to determine an age-appropriate treatment for intracranial hypertension; in infants and young children, the threshold for treatment may be an ICP lower than 20 mmHg, as the MAP is lower in these patients than in older children and adults. As stated earlier, ICP is used to calculate CPP which represents "the driving pressure for cerebral blood flow." It is currently unknown what the optimal CPP for pediatric TBI is and there is no evidence that targeting a specific CPP improves outcome. However, there are pediatric TBI studies that show a CPP < 40 mmHg to be associated with poor outcome.[93, 94] As a result, the pediatric guidelines recommend the option of maintaining an "age-related continuum" of CPP from 40 to 65 mmHg in infants to adolescents, respectively.[2] Further studies need to be done to determine the "age-appropriate" CPP. In our center, we commonly target CPP greater than 40-50 mmHg in infants and toddlers, 50-60 mmHg in children, and greater than 60 mmHg in adolescents.

According to the formula for CPP, lowering the ICP or raising the MAP will increase CPP. Most treatments are aimed at lowering ICP, maintaining normal MAP, and euvolemia. If the treatments fail to lower ICP, then vasopressors are commonly added to

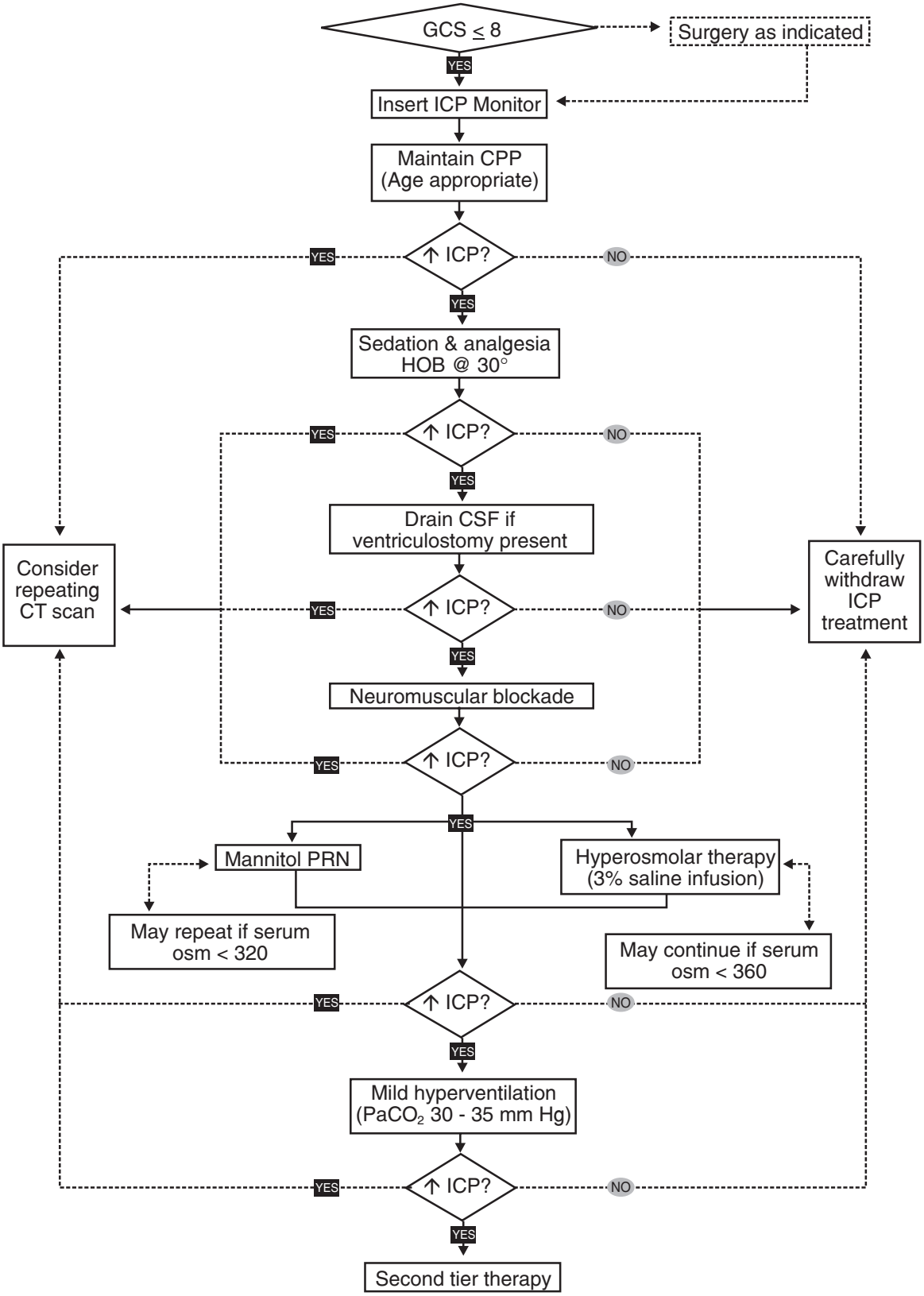
Clinical Pathway: Management Of Children With Severe Traumatic Brain Injury



The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Figure 1. Guidelines For The Acute Medical Management Of Severe TBI In Infants, Children, And Adolescents



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increase the CPP by augmenting the MAP; this mechanism works if autoregulation is intact. Otherwise, as the MAP is increased, the ICP will also increase and there is no net augmentation in CPP. If the child is hypotensive, isotonic fluid boluses and/or vasopressors can be administered to augment the MAP in the hopes of improving CPP.

Head Position

As previously discussed, elevating the head to 30° reduces ICP without decreasing CPP in adults after severe TBI.[86] While no pediatric studies are known, the same degree of head elevation with midline position to promote venous drainage is currently recommended in the pediatric guidelines. In some centers, practitioners avoid placing a central venous catheter in the internal jugular vein to maximize venous drainage from the brain.

Sedation, Analgesia, And Neuromuscular Blockade

If there is continued ICP elevation, sedation, analgesia, and neuromuscular blockade can be administered.

It is well known that anxiety, stress, and pain can increase cerebral metabolic demands which can pathologically increase cerebral blood volume and increase ICP. Narcotics, benzodiazepines, or barbiturates are commonly used. There are virtually no controlled studies of varying the use of sedatives in pediatric patients with severe TBI. As a result, the choice of sedatives is left up to the "treating physician," according to the guidelines.[2] However, the goal should be to use the minimum amount to lower ICP, without causing side effects (such as hypotension). In addition, potentially noxious stimulus (such as endotracheal tube suctioning) should be pre-treated with sedation and/or analgesics, and lidocaine (1 mg/kg IV) should be considered to blunt rises in ICP.

Though controversial, two drugs that are worth mentioning are ketamine and propofol. Ketamine is associated with increasing cerebral blood volume and increasing ICP; it is thought to be contraindicated in patients with increased ICP.[95] A number of non-TBI case reports and one TBI case report have reported metabolic acidosis and death in pediatric patients on prolonged (24 hours) continuous infusion of propofol.[96-99] Based on recommendations of the Food and Drug Administration, "continuous infusion of propofol is not recommended in the treatment of pediatric traumatic brain injury" in the pediatric guidelines.[2]

Neuromuscular blocking agents are thought to reduce ICP by reducing airway and intrathoracic pressure with improved cerebral venous outflow and by preventing shivering, posturing, or ventilator-patient asynchrony.[100] Risks of neuromuscular blockade include hypoxemia and hypercarbia due to inadvertent extubation, masking of seizures, nosocomial pneumonia (shown in adults with severe TBI), immobilization stress due to inadequate sedation and analgesia, increased ICU length, and critical illness myopathy.[100] The loss of clinical examination should be less concerning if ICP monitoring is used, as increases in ICP usually occur before changes in the clinical examination.

Ventricular Cerebrospinal Drainage

By removing CSF, the intracranial volume decreases; this may decrease ICP in a patient with intracranial hypertension. If a child with severe TBI requires ICP monitoring in our center, we encourage the neurosurgeon to place a ventricular ICP monitor, unless contraindications such as coagulopathy or very small ventricles due to diffuse cerebral edema make catheter placement difficult.

Hyperosmolar Therapy

The blood-brain barrier is nearly impermeable to both mannitol and sodium. While mannitol has been traditionally administered, 3% saline is also gaining favor; there is no literature to support the superiority of one over the other in severe pediatric TBI. Mannitol reduces ICP by two mechanisms. It rapidly reduces blood viscosity which promotes reflex vasoconstriction of the arterioles by autoregulation and decreases cerebral blood volume and ICP. This mechanism is rapid but transient, lasting about 75 minutes, and it requires an intact autoregulation.[101, 102] The second mechanism by which mannitol reduces ICP is via an osmotic effect; this increases serum osmolality - causing the shift of water from the brain cell to the intravascular space - and decreases cellular or cytotoxic edema. While this effect is slower in onset (over 15-30 minutes), the osmotic effect lasts up to six hours. This effect also requires an intact blood-brain barrier, and there are concerns that if not intact, mannitol may accumulate in injured brain regions and cause a shift from the intravascular space to the brain parenchyma and worsen ICP. However, this side effect is reported to be more like-

ly when mannitol is present in the circulation for extended periods of time, supporting the use of intermittent boluses.[103, 104] Furthermore, mannitol is a potent osmotic diuretic and may precipitate hypotension and renal failure if the patient becomes hypovolemic and the serum osmolality is > 320 mOsm/L.[105-107] Mannitol is administered in bolus doses of 0.25-1 g/kg IV.[105]

Hypertonic saline has been gaining favor recently for hyperosmolar therapy in pediatric head-injured patients with signs and symptoms of herniation. The main mechanism of action is the osmotic effect similar to mannitol. The main theoretical advantage over mannitol is that hypertonic saline can be administered in a hemodynamically unstable patient with impending herniation, as hypertonic saline is thought to preserve intravascular volume status.[108-111] Hypertonic saline exhibits several other theoretical benefits; these include restoration of normal cellular resting membrane potential and cell volume, inhibition of inflammation, stimulation of atrial natriuretic peptide release, and enhancement of cardiac output.[111-114] Hypertonic saline, as 3% saline, has recently become the most popular concentration used in the setting of TBI. It can be administered as a bolus IV dose; while not well studied, 1-6 mL/kg IV has become a popular bolus dose (unpublished observations). Doses as high as 10 mL/kg IV bolus have been reported in the literature.[115] In our pediatric institution, 2-6 mL/kg as an initial bolus dose is commonly used. Continuous infusions of 0.1-1 mL/kg/hour titrated to maintain ICP < 20 mmHg have also been reported.[116, 117] While the guidelines state that 3% saline will not precipitate renal failure as long as serum osmolality is < 360 mOsm/L,[2] caution should be exercised if the serum osmolality approaches 320 mOsm/L as there may be an increased risk for renal insufficiency.[64] Another potential concern with the use of hypertonic saline is central pontine (demyelination of the pons) or extrapontine myelinosis (demyelination of the thalamus, basal ganglia, and cerebellum) that occurs with hypernatremia and/or its correction,[118] although this has not been clinically reported. Another theoretical concern with the use of hypertonic saline is subarachnoid hemorrhage due to rapid shrinking of the brain associated with mechanical tearing of the bridging vessels; again, this has not been clinically reported. Rebound intracranial hypertension has been described clinically with the use of hypertonic saline bolus administration or after continuous infusion has stopped.[116, 119]

Further studies are needed to compare mannitol administration with hypertonic saline, particularly studies evaluating optimal dosing and evaluating long-term outcome.

Key Points

1. The initial steps in treating the pediatric TBI patient are evaluation and stabilization of airway, breathing, and circulation.
2. Initial management decisions are based largely on GCS and pupillary exam.
3. Avoid hypotension and hypoxemia. Hypotension and hypoxemia exacerbate secondary brain injury and have been shown to lead to worse outcomes.
4. Minimize or prevent conditions which promote or exacerbate secondary brain injury.
5. Mannitol and hypertonic saline are both accepted therapies for controlling intracranial hypertension.
6. Care must be taken to avoid dehydration and hypotension when administering mannitol.
7. Avoid prophylactic hyperventilation. Excessive hyperventilation can lead to decreased CBF and brain ischemia.
8. An evaluation for nonaccidental trauma should always be initiated if the presumed mechanism of injury is not consistent with actual injuries.
9. Cervical spine precautions should always be in place when evaluating and treating the pediatric patient with TBI.
10. The pediatric patient's vitals and neurologic status must be continually re-assessed, as the child may rapidly deteriorate. Hypotension is a very late finding in pediatric shock.

Hyperventilation

As previously discussed, hyperventilation is one of the fastest methods to lower ICP and is the best initial therapy with a child in impending herniation. However, without signs of herniation, mild or prophylactic hyperventilation ($PaCO_2$ < 35 mmHg) in children should be avoided. Mild hyperventilation ($PaCO_2$ 30-35 mmHg) may be considered as a "first-tier" option for longer periods of intracranial hypertension refractory to all the aforementioned measures (sedation, analgesia, neuromuscular blockade, CSF drainage, and hyperosmolar therapy).[2] This rationale is based on studies showing that cerebral blood flow may be decreased early following pediatric TBI and may be associated with poor outcome and that prophylactic hyperventilation may cause further ischemia.[83] However, no studies on the use of hyperventilation and long-term outcomes exist in the pediatric population following TBI.

Risk Management Pitfalls For Severe TBI In Children

1. "My patient's neuro exam was fine 40 minutes ago but the child is now unresponsive."

The child with suspected TBI must continually be re-assessed with frequent neurological examinations. Children may present with a relatively normal GCS after head trauma but deteriorate rapidly after presentation secondary to a rapidly expanding intracranial hematoma.

2. "I was told the endotracheal tube was in good position."

Esophageal intubations and right mainstem intubations in the prehospital setting are not uncommon, especially in the pediatric population. Endotracheal tube placement can be rapidly confirmed by end-tidal CO_2 detection (although false positives are possible if carbonated beverages were recently ingested). Right main stem intubations may not always be apparent by physical examination, and endotracheal tube placement should also be confirmed by chest radiograph as soon as safely possible.

3. "I just got the first blood gas results and the $PaCO_2$ is 20 mmHg."

Prophylactic hyperventilation should be avoided, unless the patient has signs and symptoms of herniation or neurologic deterioration. Titration of hand ventilation with capnography can avoid inadvertent hyperventilation.

4. "The patient is hypotensive and the hemoglobin is 7 gm/dL."

As soon as safely possible, a complete secondary survey should be performed. Unidentified injuries, such as femur fractures, can lead to shock and worsening of secondary brain injury. Infants can lose large blood volumes through both intracranial and extracranial head bleeds.

5. "Why is the patient's sugar 500?"

Do not forget the history as part of the emergency room evaluation. Utilizing the mnemonic "AMPLE," (allergies, medications, past illnesses, last meal, and events/environments) may be helpful. Co-morbidities, such as mental retardation, cerebral palsy, diabetes mellitus, seizure disorder, or bleeding diathesis, may alter the evaluation and management of the child with severe TBI. Also, bolusing pediatric patients with dextrose containing fluids is not recommended (unless hypoglycemia is present) as it can lead to iatrogenic hyperglycemia.

6. "The baby's fontanelle is not full, so ICP must okay."

The anterior fontanelle is an essential part of the examination of an infant with possible TBI, but a flat fontanelle does not preclude the presence of intracranial hypertension. Further diagnostic studies and treatment should not be solely based on the status of the anterior fontanelle.

7. "Intubation in the neutral position is more difficult."

Assume that all pediatric patients with TBI have cervical spine injuries until they have been completely evaluated. For tracheal intubation and bag mask ventilation, the patient's head should be in the neutral position. Tracheal intubation of the child with severe TBI should be performed by the most experienced practitioner available.

8. "The mother said the child hasn't eaten anything in eight hours."

All pediatric patients with TBI should be assumed to have full stomachs and appropriate maneuvers should be performed (cricoid pressure, rapid sequence intubation).

9. "The parent told me the child fell off the bed an hour ago but radiology is reading the CT scan with acute and chronic subdural hematomas."

Children suffering nonaccidental trauma may have delayed presentation to medical care or be found to have injuries of varying ages and stages of healing. The patient should be evaluated for occult injuries - including abdominal injuries - and surgical consultation is warranted.

10."The mannitol brought the ICP down but now the patient is hypotensive."

Mannitol is an effective agent for controlling intracranial hypertension but is an osmotic diuretic. When using mannitol, care must be given to maintaining euvolemia.

Intracranial Hypertension Management: Second-Tier Therapies

Unfortunately, refractory intracranial hypertension occurs in as much as 42% of cases of severe pediatric TBI and is associated with mortality rates between 29% and 100%.[120-123] At this point, a repeat CT scan should be performed to rule out a surgical cause for persistent, refractory intracranial hypertension. If there is no surgical lesion, the guidelines for the acute medical management of severe TBI in infants, children, and adolescents recommend "second-tier" therapies **(Figure 2)**, which include aggressive hyperventilation, barbiturates, hypothermia, decompressive craniectomy, and lumbar CSF drainage.[2] Although there is less data for these therapies compared to "first-tier" therapies, the "second-tier" therapies can be considered in the ultimate hopes of improving outcome for the severe TBI pediatric patient with refractory intracranial hypertension.

Hyperventilation

Aggressive hyperventilation ($PaCO_2$ < 30 mmHg) may be considered as a "second tier" option in the setting of refractory intracranial hypertension. Cerebral blood flow, jugular venous oxygen saturation, or brain tissue oxygen monitoring to help identify cerebral ischemia is suggested.[124, 125]

Barbiturates

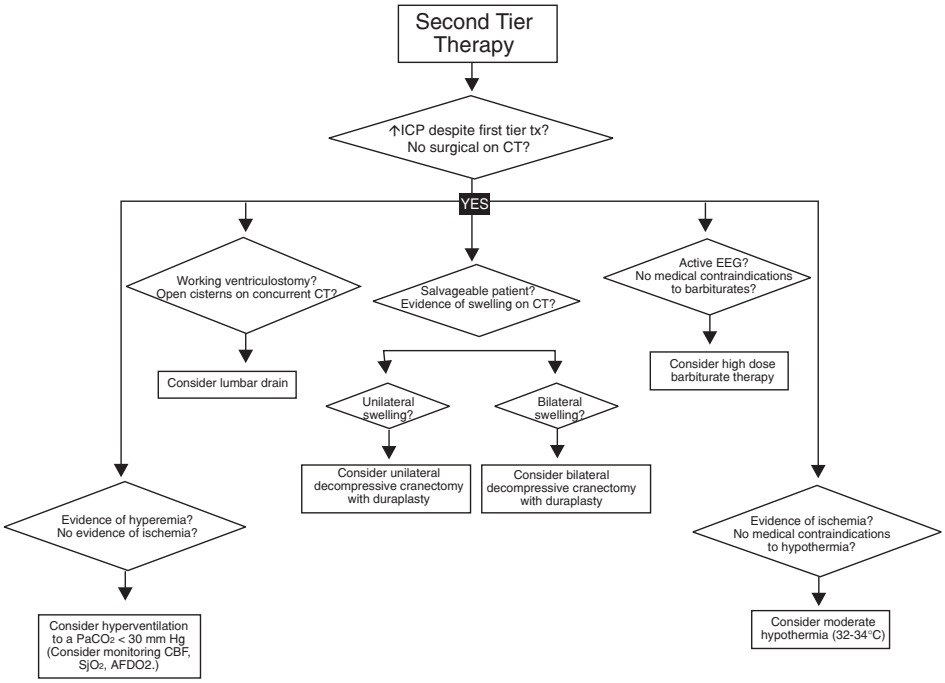
As the use of aggressive hyperventilation for treatment of refractory intracranial hypertension has become less popular, other therapies (such as barbiturates) are being utilized. Barbiturates reduce ICP by decreasing the cerebral metabolic rate.[126-128] An electroencephalogram (EEG) should be used to assess the cerebral metabolic response to barbiturate treatment. Either a continuous infusion or frequent dosing is used. Pentobarbital or thiopental are often administered to achieve burst suppression on the EEG. However, no more than the minimum dose required to achieve that goal should be used as the smaller doses that are associated with EEG activity may still decrease ICP and higher doses can lead to decreased cardiac output, decreased systemic vascular resistance, and hypotension.[121] As a result, if high-dose barbiturate therapy is used to treat refractory intracranial hypertension, then appropriate hemodynamic monitoring and cardiovascular support must be provided.

Further studies need to address optimal dosing to prevent unwanted side effects (such as hypotension) and the long-term effects of barbiturate therapy.

Decompressive Craniectomy

The main goal of decompressive craniectomy is to

Figure 2. Guidelines For The Acute Medical Management Of Severe TBI In Infants, Children, And Adolescents



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control ICP and thus maintain CPP as well as to prevent herniation in the face of refractory cerebral swelling. This surgical option is considered a "second-tier" therapy for pediatric TBI patients with refractory intracranial hypertension and may be particularly appropriate in patients who have a potentially recoverable brain injury. These are patients with no episodes of sustained ICP > 40 mmHg before surgery and exhibited GCS > 3 at some point subsequent to injury. Other indications for decompressive craniectomy include secondary clinical deterioration or evolving cerebral herniation syndrome within 48 hours of injury.[2] Furthermore, decompressive craniectomy should be considered in the treatment of severe TBI and refractory intracranial hypertension in infants and young children with nonaccidental head trauma or shaken-impact syndrome, as these patients had improved survival and neurological outcomes compared to those undergoing medical management alone in one study.[129] However, there are concerns that this procedure may exacerbate hemorrhage and cerebral edema formation, so further studies are clearly warranted on the safety and efficacy of this surgical procedure and the effects on long-term outcome.

Lumbar CSF Drainage

Although not commonly used, lumbar CSF drainage has been shown to be successful in treating refractory intracranial hypertension following pediatric TBI.[130] However, to avoid the risk of herniation, the child must already have a functional ventriculostomy drain as well as open basal cisterns and no mass effect or shift on concurrent CT.

Seizures

Seizures should be aggressively treated as they can cause intracranial hypertension and secondary brain injury. While prophylactic anticonvulsants may be considered a treatment option to prevent early post-traumatic seizures (occurring within seven days following injury) in infants and young children, prophylactic anticonvulsants are not recommended for preventing late post-traumatic seizures (occurring after seven days) as this has not been shown to improve outcome.[131, 132]

Special Circumstances

As discussed earlier, inflicted or nonaccidental pediatric TBI (shaken-baby or shaken-impact syndrome) is a common cause of morbidity and mortality, especially in infants and young children. The emergency medicine clinician must be familiar with the typical features of nonaccidental head trauma and have a low threshold for further investigation.

Nonaccidental head trauma is most common in children under the age of three, with the majority being less than one year of age.[68] In a prospective study of children admitted under two years of age with head injuries, 24% were the result of nonaccidental trauma.[133] Children of young parents, low socioeconomic status, and disability or prematurity have all been found to be at a higher risk for abuse.[134]

Typically, the history is vague or varies over time and consists of a minor blunt impact to the head with a mechanism of injury that is not consistent. Presenting symptoms in the infant can also be vague. Lethargy, irritability, or poor feeding may be the initial complaint for seeking medical attention. Infants may also present with seizures, hyper- or hypotonia, or a full fontanelle. Extracranial findings are not always present but may include bruising or burn marks. Retinal hemorrhages are found in the majority of patients and may be unilateral or bilateral but are not specific for the diagnosis. For instance, vaginally delivered infants may have retinal hemorrhages up to one month after delivery.[135] Non-traumatic causes of retinal hemorrhages include sepsis, coagulopathy, galactosemia, and malignant hypertension which can be difficult to differentiate without considering the entire clinical picture.[136, 137]

As with any children with severe TBI, the first radiologic study of choice is CT scan. Common findings are subarachnoid and subdural hemorrhages. Depending on the timing of the initial scan, diffuse hypodensity of the brain can be observed in nonaccidental trauma patients with severe TBI. Plain films are the modality of choice for the detection of skull fractures. If nonaccidental TBI is suspected, a skeletal survey should also be performed since extracranial abnormalities are detected in a large percentage of cases. In addition, other occult injuries, such as blunt abdominal trauma, should be investigated with laboratory data and/or a CT and surgical consultation. Once there is a concern for possible nonaccidental trauma, social services should be consulted.

Cost-Effective Strategies

Prevention of pediatric head injury is probably the single most cost-effective strategy for severe traumat-

ic brain injury. For example, in the 1980's only approximately 15% of children under the age of 15 wore bicycle helmets.[141] After implementation of bicycle-helmet laws, a Seattle case-controlled study demonstrated risk reduction in head injuries of 85%.[142] Implementation of new prevention strategies requires federal, state, and local initiatives to raise public awareness, to educate, and to enforce these life-saving strategies. *See also the October 2007, Volume 4 Number 10, Pediatric Emergency Medicine Practice article, "Preventing Childhood Injury: The Role Of The Emergency Physician," available at no cost to subscribers at http://ebmedicine.net/redirect/?topic=ped.*

Controversies And Cutting Edge

Hypothermia

Post-traumatic hyperthermia is defined as a core body temperature > 38.5°C (101.3°F), whereas hypothermia is defined as < 35°C (95°F). In animal studies of experimental TBI, hyperthermia has been shown to exacerbate neuronal cell death. However, therapeutic hypothermia was found to be neuroprotective by ameliorating mechanisms of secondary brain injury, such as decreasing cerebral metabolism, inflammation, lipid peroxidation, and excitotoxicity.[138] In one recent study, early hyperthermia (within 24 hours of admission) occurred in 29.9% of pediatric TBI patients and was associated with poor outcome.[139] While most agree that hyperthermia should be avoided in children with severe TBI, the role of hypothermia is unclear. A recent phase II clinical trial showed that 48 hours of moderate hypothermia (32-34°C or 89.6-93.2°F) initiated within 6-24 hours of acute TBI in pediatric patients reduced ICP and was "safe," although there was a higher incidence of arrhythmias (reversed with fluid administration or rewarming) and rebound ICP elevation after rewarming.[140] Until further clinical studies are conducted, moderate hypothermia is reserved for patients with persistent intracranial hypertension refractory to other medical interventions, if no other medical contraindications or evidence of ischemia exist.[2] Potential complications associated with hypothermia include increased bleeding risk, arrhythmias, and increased susceptibility to infection.

Disposition

Pediatric patients with acute severe traumatic brain injury should be admitted to a pediatric intensive care unit with 24 hour neurosurgical capabilities. Intensive care management includes continued treatment of intracranial hypertension with first-tier therapies (**Figure 1** on page 13) and, if needed, second-tier therapies for refractory intracranial hypertension (**Figure 2** on page 17). Nutrition should be initiated within 72 hours of injury and it is recommended that full nutritional support be reached within seven days.[2] Rehabilitation with a comprehensive group of health professionals, such as physiatrists and physical, occupational, and speech therapists, should be initiated as soon as medically possible.

Case Conclusion

You quickly identified that this patient had a GCS of 4. The patient was preoxygenated with 100% supplemental oxygen. You asked the resident to maintain the neck in neutral position and a nurse to provide gentle cricoid pressure. You then performed a modified rapid sequence induction with lidocaine (1.5 mg/kg IV), etomidate (0.3 mg/kg IV), and vecuronium (0.3 mg/kg IV). A 5.0 endotracheal was successfully placed and proper placement confirmed by detection of end-tidal CO_2. Hand ventilation was titrated to maintain end-tidal CO_2 between 30-35 mmHg. A bolus of 3% hypertonic saline (4 mL/kg) was administered for suspected intracranial hypertension.

The resident then observed the pupils becoming equal, and both were reactive. The neurosurgeons were contacted and the patient was transported to radiology for an emergent head CT. On transport, hand ventilation was titrated to maintain end-tidal CO_2 between 30-35 mmHg. CT scan demonstrated a left epidural hematoma with midline shift and uncal herniation. The patient was immediately taken to the operating room for emergent surgical decompression. The patient was extubated on post operative day one with no further episodes of intracranial hypertension.

Summary

Traumatic brain injury is the leading cause of mortality and severe morbidity in children. Initial management of the severely head-injured child is critical to improving outcomes. Avoiding or rapidly correcting hypotension and hypoxemia and other causes of secondary brain injury, such as intracranial hypertension, cannot be overemphasized. Emergency medicine clinicians should be adept at identifying the symptoms of severe TBI, initiating the appropriate

medical therapies, and providing rapid access to specialty services.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available.

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CME Questions

1. Inflicted TBI is most common in:
a. Children less than one year of age
b. Toddlers (two to three years of age)
c. School-aged children
d. Adolescents

2. The highest TBI-related mortality rates are in:
a. Children less than one year of age
b. Toddlers (two to three years of age)
c. School-aged children
d. Adolescents

3. All the following are examples of primary brain injury EXCEPT:
a. Cerebral contusion
b. Cerebral ischemia
c. Parietal skull fracture
d. Epidural hematoma

4. A major cause of prolonged coma and morbidity in pediatric TBI is:
a. Traumatic axonal injury
b. Subdural hematomas
c. Cerebral contusions
d. Intraparenchymal hemorrhages

5. The intracranial vault is a fixed volume containing all of the following EXCEPT:
a. Blood
b. Cerebrospinal fluid
c. Muscle
d. Brain

6. Which of the following causes of secondary brain injury have been demonstrated to worsen outcome?
a. Hyperglycemia
b. Hypoxemia
c. Hyponatremia
d. Coagulopathy

7. Rapid and reliable assessment of an esophageal intubation can be done with:
a. Auscultation
b. Mist in the endotracheal tube
c. Equal chest wall rise
d. Capnography

8. All of the following are signs and symptoms of basilar fracture EXCEPT:
a. Unilateral pupil dilation
b. Battle sign
c. Hemotympanum
d. Clear rhinorrhea

9. Which of the following is not part of Cushing's triad?
a. Hypertension
b. Bradycardia
c. Temperature instability
d. Irregular respiration

10. The imaging modality of choice for pediatric TBI patients is:
a. MRI
b. CT scan
c. Plain skull films
d. Nuclear medicine cerebral blood flow study

11. Indications for endotracheal intubation include all of the following EXCEPT:
a. GCS < 8
b. Hypoxemia
c. Hypotension
d. Loss of gag reflex

12. Hyperventilation lowers ICP by:
a. Reducing cerebral blood volume
b. Decreasing brain edema
c. Reducing CSF production
d. Increasing blood osmolality

13. Agents used for hyperosmolar therapy for intracranial hypertension include:
a. Hypertonic saline
b. Hypotonic saline
c. Packed red blood cells
d. D50W

14. Hypovolemia and shock may be associated with:
a. Vecuronium
b. Mannitol
c. Hypertonic saline
d. Lidocaine

15. Which of the following agents is used to blunt the increase in ICP associated with direct laryngoscopy?
a. Etomidate
b. Rocuronium
c. Ketamine
d. Lidocaine

16. Which type of herniation syndrome is associated with unilateral, fixed pupil dilation?
a. Midbrain
b. Uncal
c. Diencephalic
d. Medullary

Erratum: Volume 4, Number 11: Pediatric Upper Airway Infectious Disease Emergencies

The diagnosis section on page 8, states, "The diagnosis of retropharyngeal cellulitis or abscess is suggested when the retropharyngeal space at the level of C2 is twice the diameter of the vertebral body." This should state: "The diagnosis of retropharyngeal cellulitis or abscess is suggested when the retropharyngeal space at the level of C2 is half the diameter of the vertebral body." We regret any confusion this error may have caused.

Class Of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level Of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case-control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA* 1992;268(16):2289-2295.

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Date of Original Release: December 1, 2007. Date of most recent review: November 1, 2007. Termination date: December 1, 2010.

Accreditation: This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Mount Sinai School of Medicine and *Pediatric Emergency Medicine Practice*. The Mount Sinai School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

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Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals & Objectives: Upon completing this activity, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

Discussion of Investigational Information: As part of the newsletter, faculty may be presenting investigational information about pharmaceutical products that is outside Food and Drug Administration approved labeling. Information presented as part of this activity is intended solely as continuing medical education and is not intended to promote off-label use of any pharmaceutical product. Disclosure of Off-Label Usage: This issue of *Pediatric Emergency Medicine Practice* discusses no off-label use of any pharmaceutical product.

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