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Severe Traumatic Brain Injury In Adults

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Abstract

Traumatic brain injury is the most common cause of death and disability in young people, with an annual financial burden of over $50 billion per year in the United States. Traumatic brain injury is defined by both the initial primary injury and the subsequent secondary injuries. Fundamental to emergency department management is ensuring brain perfusion, oxygenation, and preventing even brief or transient episodes of hypotension, hypoxia, and hypocapnia. Cerebral perfusion pressure is a function of intracranial pressure and systemic blood pressure, and it must be monitored and maintained. Current research is devoted towards the prevention and treatment of secondary injury. The emergency clinician must be vigilant in maintaining homeostasis while coordinating the downstream care of the patient, including the intensive care unit and/or the operating room.

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CME Objectives

Upon completion of this article, you should be able to:

1. Describe the different characteristics and subcategories of severe TBI.
2. Appropriately identify and resuscitate patients with severe TBI.
3. Recognize and implement different treatment pathways for different types of brain injuries.
4. Discuss the limitations and future of treatment options and neuroprotectants for severe TBI, including prevention, primary injury, and secondary injury.

Prior to beginning this activity, see the back page for faculty disclosures and CME accreditation information.

Case Presentations

It is 2 AM on a relatively busy shift on a Saturday night in the ED. EMS arrives with a 27-year-old male involved in a high-speed motor vehicle collision. He was not wearing a seat belt, and he was found ejected from the vehicle. Upon EMS arrival on scene, the paramedics found him unresponsive, with a GCS score of 9 (E2, V3, M4). The patient had been alone in the car, and he did not have identifying information with him. His vital signs included: blood pressure of 110/80 mm Hg, heart rate of 126 beats per minute, shallow respiratory rate of 8 breaths per minute, and oxygen saturation of 96% on room air. The paramedics attempted an oral airway, but it was aborted, because the patient exhibited a gag reflex. Bilateral nasal trumpets were placed, and a nonrebreather facemask with 100% oxygen was administered. He had deformities to his right ankle and left forearm. He smelled of alcohol. The patient was transported on a backboard with a rigid cervical spine collar to maintain immobilization. As you evaluate him on arrival to the ED, his vitals are essentially unchanged; however, you note that his GCS score is now 7 (E2, V2, M3), as he flexes his right arm to painful stimulus. IV access is established, and as you prepare to endotracheally intubate him, you recognize that this patient's survival and ultimate neurologic outcome may depend on your initial management.

Upon successful completion of rapid sequence intubation (without hypoxia or hypotension!) of your first patient, another ambulance presents with an 84-year-old female who fell at home. Her anxious daughter informs you that she tripped on the carpet, fell backwards, and hit her head, but she did not lose consciousness. On your assessment, the patient has a GCS score of 13 (E3, V4, M6) with blood pressure of 174/92 mm Hg, irregular heart rate of 124 beats per minute, respiratory rate of 14 breaths per minute, and oxygen saturation of 100% on the nonrebreather mask placed during transport. As the patient is transferred to the stretcher, she becomes unresponsive, with a GCS score of 5 (E1, V1, M3), with flexion of both arms. You note that her right pupil is now 6 mm and minimally responsive, and her left pupil is 3 mm. You request mannitol (1 g/kg IV) and prepare to emergently intubate her. As her daughter is escorted to the waiting room with the social worker, she hands the nurse a medication list, which includes warfarin. You recall the necessary steps to stabilize and prepare the patient for the operating room, and you wonder if there is more you can provide aside from fresh frozen plasma and mannitol.

Introduction

Traumatic brain injury (TBI) is one of the leading causes of death and disability in the United States. It is a common disease that emergency clinicians care for on a regular basis. TBI is a spectrum of disease, ranging from mild to severe. The military conflicts in Afghanistan and Iraq have highlighted TBI as the signature injury due to blast injuries from explosive devices. In addition, mild TBIs among high-profile athletes in professional and collegiate sports have brought increased attention to this spectrum of the disease. In the United States, 1.36 million cases of TBI are treated in emergency departments (EDs), with 275,000 patients hospitalized and 52,000 deaths each year.[1]

The long-range morbidity of TBI is staggering when one considers the profound and permanent neurologic disabilities and the significant financial and societal impacts. The United States Department of Defense has estimated almost 44,000 TBIs sustained during the Afghanistan and Iraq conflicts between 2003 and 2007, with an estimated $100 million in direct and purchased care and an additional $10.1 million in prescription drug costs.[2] In the United States, direct medical costs and indirect costs (such as lost productivity) of TBI totaled an estimated $60 billion in 2000.[3]

Falls cause the greatest number of TBI-related ED visits and hospitalizations. Motor vehicle accidents are the leading cause of TBI-related mortality, which is highest in adults aged 20 to 24 years.[1] The incidence of TBI is greatest in children aged 0 to 4 years, adolescents/young adults aged 15 to 24 years, and adults aged 65 years and older.[1] Falls cause the majority of TBI in young children and older adults, and child abuse is the leading cause of death from TBI in children < 2 years of age.[1,4]

Nearly half of patients who die from TBI do so in the first 2 hours after injury, highlighting the role of the emergency clinician in the initial diagnosis and management.[5] The pathophysiology of severe TBI can be viewed as a 2-step process that includes: (1) the initial primary injury, occurring at impact, which is irreversible and immediately present; and (2) the secondary injury that occurs after the initial impact, which evolves as a process. Secondary injury is potentially preventable and represents end points for goal-directed resuscitation and research. **(See Table 1.)**

Table 1. Processes That Influence Secondary Injury

Systemic
- Hypoxia
- Hypotension
- Anemia
- Hyperthermia
- Hypercarbia/hypocarbia
- Fluid imbalance
- Sepsis

Central Nervous System
- Hematoma
- Brain edema
  - Cytotoxic
  - Vasogenic
- Brain herniation
- Seizures
- Hydrocephalus
- Ischemia
- Infection

Critical Appraisal Of The Literature

A literature search was conducted using Ovid MEDLINE® and PubMed. Search terms included *craniocerebral trauma* as a MeSH heading and s*evere traumatic brain injury* as the keyword. Results were limited to English language and human publications and were further refined. Over 2500 abstracts were reviewed for inclusion. Emphasis was placed on clinical and randomized trials conducted in the prehospital, ED, and acute settings and those that reported clinical outcomes. The Cochrane Database of Systematic Reviews, National Guideline Clearinghouse (www.guideline.gov), and American College of Emergency Physicians (ACEP) clinical policies were also reviewed and queried using *traumatic brain injury* as the keyword. The Cochrane database yielded 36 results, 18 of which were applicable to this review. There were 63 guidelines found in the National Guideline Clearinghouse, 30 of which are applicable to the prehospital and ED management of patients with severe TBI. There are currently no ACEP clinical policies that apply to severe TBI.

Among the 30 available guidelines, the Brain Trauma Foundation (BTF) produced 27. There are currently 6 sets of BTF guidelines, 3 of which have relevance to TBI. **(See Table 2.)**

High-quality evidence to guide the management of severe TBI is currently lacking.[6,7] Current guidelines, recommendations, and consensus statements are based on Class II (moderate-quality randomized controlled trials or good cohort- or case-controlled trials) and Class III evidence (poor-quality randomized controlled trials, moderate-quality cohort- or case-controlled studies, or case series).

Despite the lack of a single trial demonstrating an effective single therapy or medication for the treatment of severe TBI, it has been shown that compliance with protocols or guidelines that emphasize appropriate monitoring and goal-directed management of cerebral perfusion pressure (CPP) has resulted in a decrease in mortality from 50% to < 25% in the prehospital[10] and inpatient settings while lowering costs and improving cost-effectiveness.[11,12]

Etiology And Pathophysiology

There are several different subcategories of primary injury that encompass the overall disease. One could argue that the different subcategories of TBI are vastly different diseases within themselves, each with different treatment paradigms. The subsequent risk for secondary injury and the different management options further complicate this difficult disease process. For the emergency clinician, the initial management of the different types of TBI is relatively similar, with focus on early airway management, avoidance of hypoxia and hypotension, rapid diagnosis, and consultation/disposition, as appropriate.

Primary injuries are the result of external forces to the head and can be characterized as occurring from direct impact, penetrating objects, or indirect blast waves. Various force vectors such as acceleration, deceleration, and rotational forces further contribute by injuring neurons on a cellular level.[5] It is theorized that brainstem injuries occur more frequently with rotational injuries, given the brainstem's fixed structure within the skull base. The most common primary injuries include subdural hematomas, epidural hematomas, traumatic subarachnoid hemorrhages, cerebral contusions, intraventricular hemorrhage, and diffuse axonal injuries. Each of these injuries is vastly different and often requires different management techniques, yet all are included in the diagnosis of severe TBI.

Subdural Hematoma

Subdural hematoma is most often the result of blunt trauma and the tearing of bridging cortical veins. **(See Figure 1, page 4.)** It is the most common injury, and it accounts for between 12% and 29% of all patients who suffer a severe TBI.[13] In subdural hematoma, blood collects below the dura, directly on the cerebral cortex, giving an appearance on computed tomography (CT) of a concave or crescent shape with irregular borders. In addition to cerebral compression, midline shift, and increased intracranial pressure (ICP), these patients are at increased risk for seizures, delayed cerebral ischemia, and

Table 2. Current Brain Trauma Foundation Guidelines For Severe Traumatic Brain Injury[6-9]

Date	Title	Comment
2008	Guidelines for Prehospital Management of TBI, 2nd edition	Recommendations in 7 topic areas; based mostly on Class III evidence, weak in strength
2007	Guidelines for Management of Severe TBI, 3rd edition	Recommendations for 15 clinical areas, ranking from Level I to Level III; 10 have relevance to ED management Endorsed by principal neurosurgery organizations
2006	Guidelines for the Surgical Management of TBI	Excellent resource for communicating with neurosurgery consultants and advocating for emergency and urgent interventions, when indicated
2000	Early Indicators of Prognosis in Severe TBI	Publication date limits applicability; it is in the process of being updated

Abbreviations: ED, emergency department; TBI, traumatic brain injury.

cerebral vasoconstriction. Concomitant underlying parenchymal injuries can be present with subdural hematomas and are common when the amount of midline shift is greater than the subdural hematoma itself.[14] Surgical management varies based on the patient's neurologic examination and the acuity of the hematoma, but guidelines recommend that acute subdural hematomas > 1 cm in thickness or with 5 mm of midline shift be evacuated, regardless of the patient's Glasgow Coma Scale (GCS) score.

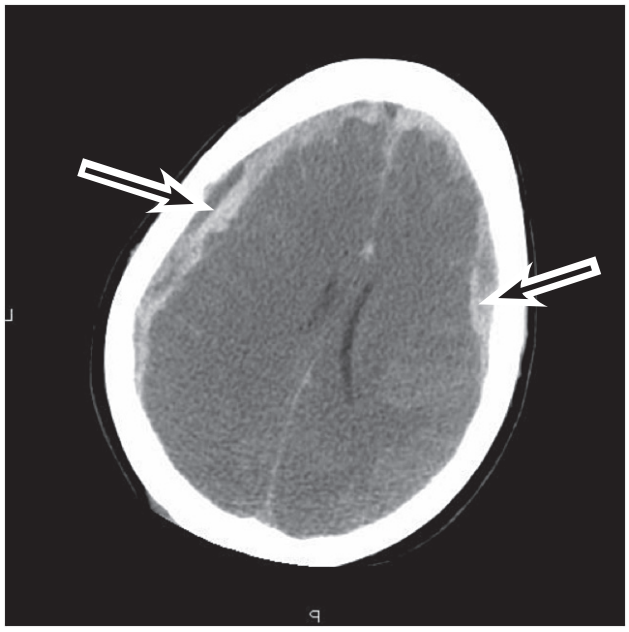
Epidural Hematoma

Epidural hematoma is most often the result of a lateral head impact with resultant skull fracture and laceration of the middle meningeal artery or vein. **(See Figure 2.)** This laceration leads to a rapid accumulation of blood between the dura and the skull and can be immediately life-threatening. The appearance of an epidural hematoma on CT scan is classically smooth, lenticular, or convex in shape, and it can cross the midline. Patients with this injury are candidates for rapid surgical decompression and hematoma removal; if these are accomplished rapidly, these patients have lower rates of mortality than patients with other categories of severe TBI.[15] Epidural hematoma is more common in younger patients; it is present in < 1% of all TBIs.[16]

Traumatic Subarachnoid Hemorrhage

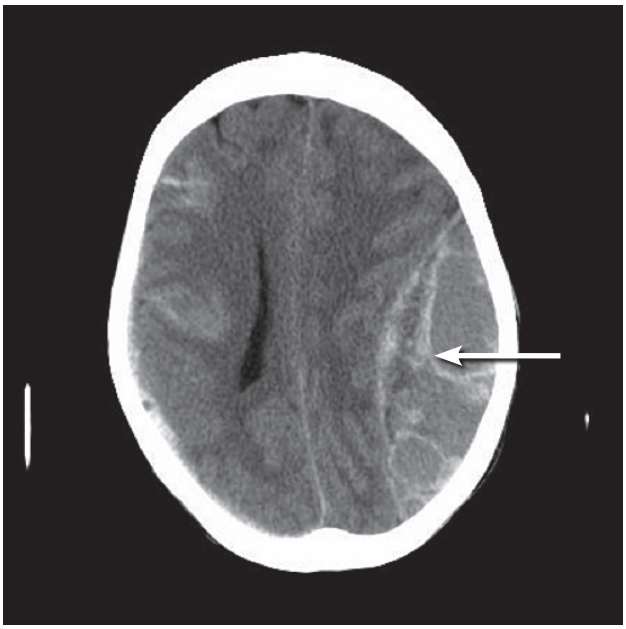
Traumatic subarachnoid hemorrhage is caused by damage to small arteries in the potential space under the arachnoid mater. **(See Figure 3.)** Similar to aneurysmal bleeding, this injury can contribute to a patient's decreased mental status and an elevation in ICP.[17] The amount of blood measured on CT has prognostic significance (ie, whether it is from the

Figure 1. Subdural Hematoma On Computed Tomography



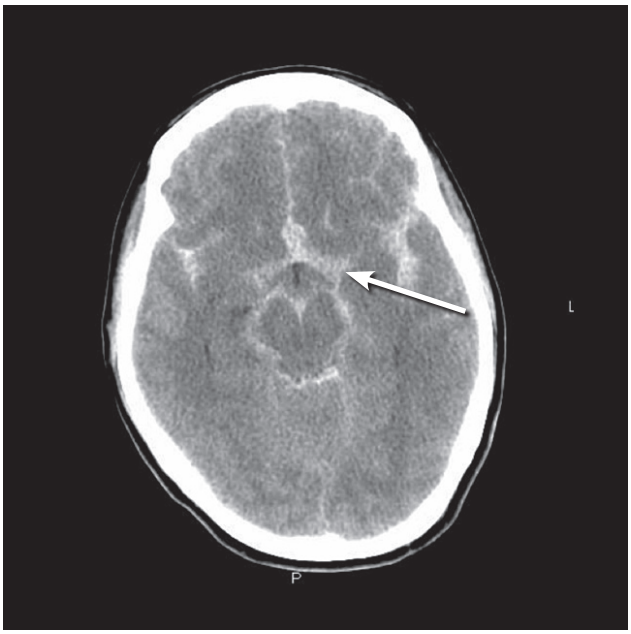
Arrow points to area of subdural hematoma.
Image courtesy of William A. Knight, IV, MD.

Figure 2. Epidural Hematoma On Computed Tomography



Arrow points to area of epidural hematoma.
Image courtesy of William A. Knight, IV, MD.

Figure 3. Traumatic Subarachnoid Hemorrhage On Computed Tomography



Arrow points to area of traumatic subarachnoid hemorrhage.
Image courtesy of William A. Knight, IV, MD.

direct parenchymal injury or the traumatic subarachnoid hemorrhage blood itself).[17] Secondary injuries are common with traumatic subarachnoid hemorrhage, including hydrocephalus (via obstruction of arachnoid villi and increased cerebral venous pressure) and decreased cerebral perfusion. Vasospasm related to traumatic subarachnoid hemorrhage is increasingly recognized as a cause of delayed cerebral infarction.[18]

Cerebral Contusion

Cerebral contusions and/or intraparenchymal hemorrhages are caused by direct injury to the brain parenchyma. **(See Figure 4.)** The equivalent of an ecchymosis to the brain, this injury is an accumulation of blood within the brain tissue and appears hyperdense on CT. Due to the adjacent (and often sharp) bony structures, the most common locations are at the base of the frontal lobes and the temporal lobes. Growth of these hematomas after trauma is common, especially in patients with a history of anticoagulant or antiplatelet use and/or those with alcohol intoxication or abuse. Cerebral contusions are more likely to have associated vasogenic and/or cytotoxic edema, which can contribute to increased ICP, midline shift, worsening mental status, and herniation.[19]

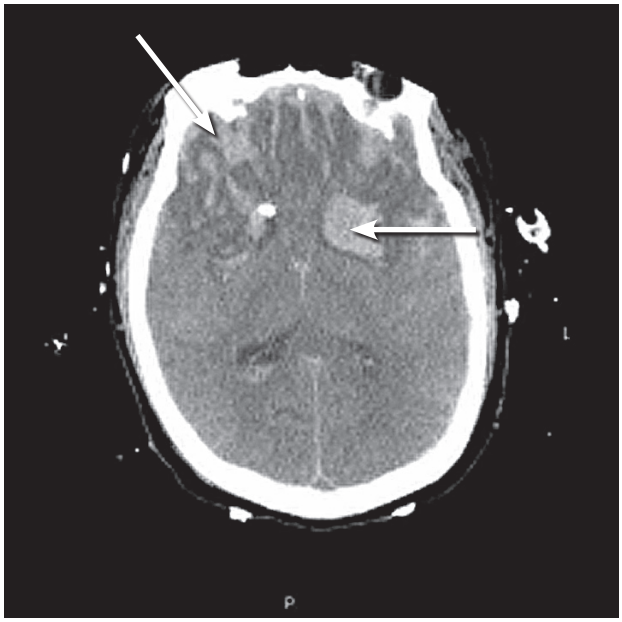
Diffuse Axonal Injury

Diffuse axonal injury often has a benign CT appearance, with small, random areas of punctate hemorrhages that may accompany radiographically inapparent diffuse axonal injury, cerebral edema, or (commonly) a normal CT. **(See Figure 5.)** Diffuse axonal injury can be found in the brainstem, corpus callosum, deep gray matter, and cortical white matter. Diffuse axonal injury is the result of severe acceleration-deceleration and rotational forces, which cause stretching and disruption of axons, leading to a biochemical cascade of events that, ultimately, ends in neuronal death.[20] This damage is widespread, irreversible, and a significant contributor to the morbidity and mortality of severe TBI. Patients with diffuse axonal injury are especially susceptible to secondary injuries from hypotension and hypoxia, given the cellular level of injury of the neurons.[20]

Penetrating Injury

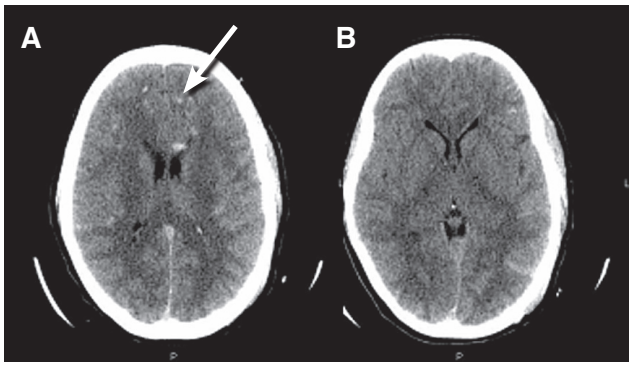
Penetrating TBI is not as common an etiology as blunt TBI, but it accounts for a disproportionate rate of mortality. Gunshot wounds cause the majority of penetrating TBI, followed by stab wounds caused by various objects such as knives and occupational equipment (screwdrivers, drills, and nails).[8] Battlefield-related trauma is complicated by blast injuries from explosive devices, often creating hybrid blunt/penetrating TBIs. The morbidity and mortality from penetrating TBI depends on the characteristics of the weapon or projectile, the trajectory and location of the injury, and the energy of the impact.[21] In addition to the physical damage from the penetrating TBI, a high-velocity missile also has damaging properties such as rotation, pitch, and yaw. These create a shock wave, further stretching or tearing cerebral tissue and leaving cavities larger than the missile itself. Penetrating injuries are also more susceptible to a systemic release of thromboplastin, potentially causing profound coagulopathy and hemorrhagic shock.[22] The most common secondary injury encountered in penetrating TBI is infection.[23] Although the overall outcome of missile-penetrating TBI has historically been poor,

Figure 4. Cerebral Contusions On Computed Tomography



Arrows point to cerebral contusions.
Image courtesy of William A. Knight, IV, MD.

Figure 5. Diffuse Axonal Injury On Computed Tomography



In view A, arrow points to areas of hemorrhage that often accompany diffuse axonal injury. In view B, note that the CT is negative.
Images courtesy of William A. Knight, IV, MD.

patient outcomes from the Iraq and Afghanistan conflicts suggest a possible role for early and aggressive medical and surgical management.[24]

Despite the anatomic and cellular differences of the various primary injuries of severe TBI, there are similar sequelae shared by all. The initial clinical management in the ED is directed at minimizing the damage from the primary injury, recognizing immediate surgical candidates, and preventing secondary injury.

Elevated Intracranial Pressure

ICP is the measure of the pressures within the rigid skull and is determined by the relationships of the volumes of brain tissue, blood in the vascular structures, and cerebrospinal fluid (CSF). This measurement is rarely available during the acute management of severe TBI. ICP can be abnormally elevated in situations where traumatic bleeding, swelling, and hematoma formation lead to additional volume in the cranial vault. The emergency clinician should assume an elevated ICP and be prepared to intervene in the event of an acute herniation syndrome. Herniation is the end result of a malignant, one-way pressure gradient within the rigid skull, often across the dividing tentorial membranes. There are several different herniation syndromes, all of which result in damaging pressures being exerted on cerebral tissue (parenchyma and brainstem) and vasculature. (See the section "Examination Findings Consistent With Deterioration" on page 14.) In addition to autonomic changes and focal cranial nerve changes, a vicious cycle of worsened ischemia and (ultimately) death can occur.

Contrary to the measured pressure of ICP, cerebral perfusion pressure (CPP) is a calculated value. CPP and ICP are intimately related, and CPP is defined as the difference between the mean arterial pressure (MAP) and the ICP. Therefore, CPP = MAP – ICP. In scenarios where the ICP is not available, the emergency clinician should assume an ICP at the upper limit of normal for CPP calculations and management (20 cm H_2O). CPP is a surrogate for cerebral blood flow, and it is critical to maintain it within the normal range to minimize secondary injuries.

The association between hypotension and worsened neurologic morbidity suggests that optimal cerebral perfusion is critical to improving outcomes.[7] Worsened outcomes have been consistently associated with a CPP < 50 mm Hg,[25] with the majority of the data demonstrating an inverse relationship with outcomes at a CPP < 60 mm Hg.[26,27] Earlier studies suggested a benefit with a CPP > 70 mm Hg,[28] though this was subsequently invalidated;[29] in fact, a 5-fold increase in the incidence of acute respiratory distress syndrome occurred.[30] The BTF guidelines currently recommend maintaining a CPP of 50 to 70 mm Hg.[7]

In the patient without brain injury, cerebral autoregulation maintains cerebral blood flow (and therefore ICP) over a wide range of systemic blood pressures; however, when systemic blood pressure is extremely low or high, autoregulation fails to maintain this relationship. Systemic hypertension (MAP > 150 mm Hg) overwhelms the autoregulatory mechanism, resulting in elevated cerebral blood flow and ICP. Interestingly, when systemic hypotension (MAP < 60 mm Hg) occurs, the cerebral vasculature dilates significantly in an attempt to preserve cerebral blood flow, leading to an increase in intracranial blood volume and, therefore, increased ICP.[31] Unfortunately, autoregulation is frequently either globally or regionally impaired in patients with TBI, increasing their vulnerability to derangements in systemic blood pressure. Knowledge of this pathophysiology as well as the data associating improved outcomes with optimized CPP should compel emergency clinician to expeditiously optimize the systemic blood pressure.

Cerebral edema is intimately linked to both ICP and CPP. There are 2 types of edema: vasogenic and cytotoxic. Vasogenic edema is the result of a disruption of the blood-brain barrier, as is often seen with cerebral contusions. Cytotoxic edema is present more often in severe TBI and is the result of neuronal cell death.[5,32,33] Systemic derangements (eg, hypotension, acidemia, hypercapnia, hyperthermia) and central nervous system processes (eg, seizures, inadequate sedation) that cause cerebral vasodilation will increase cerebral blood volume and contribute to increased vasogenic edema and elevated ICP. Decreased blood volume from vasoconstriction (eg, hypertension, alkalemia, hypocapnia) can lead to ischemia and increased cell death, worsening cytotoxic edema and elevated ICP.[5]

The Glasgow Coma Scale Score

The GCS, developed in 1974, scores 3 broad aspects of the patient's neurologic examination: eye opening (E), verbal response (V), and motor response (M).[34] **(See Table 3.)**

The GCS score should be reported as an aggregate score, followed by each individual score, eg, GCS score 8 (E2, V2, M4). This allows clinicians to better understand the complexity of the injury. In order to score a "4" for eye opening, the patient must regard the examiner in order to convey the higher level of cerebral functioning that the score intends. In order to score a "6" for motor response, the patient must follow commands; for a "5," the patient should cross midline to address noxious stimuli. Previously used terms such as "decerebrate" and "decorticate" posturing should be avoided, with focus on functional descriptions such as "flexion," "extension," or "withdrawal." Using these terms

assists with consistency in communication across multiple clinicians. Given limitations with interrater reliability, emergency clinicians should consider emphasizing or relying on communication of the motor score as an isolated value.

The GCS score could have the potential to oversimplify and replace a detailed neurologic examination, but this was not the initial intent. It was designed for evaluation of patients with severe TBIs after 6 hours of maximum resuscitation, although the classification of mild and moderate injuries is often reported with the GCS score.[35] The GCS score is limited by physiologic and pharmacologic parameters such as intoxication, confounding injuries, acidosis, paralysis, and sedation, among others. A single score does not adequately explain the severity of the injury after trauma, and although it is associated with outcomes, it has limited prognostic value.[35,36] Serial scores performed throughout a patient's hospital course are more helpful to correlate with clinical outcomes. After resuscitation, a patient is more likely to have a poor outcome if his low GCS score remains low or if a high GCS score deteriorates. Patients with a low GCS score that improves with resuscitation or begins high and stays high tend to have better outcomes.[36] Emergency clinicians should avoid using the GCS score to help describe other neurologic diseases such as stroke, subarachnoid hemorrhage, and intracerebral hemorrhage, as the GCS score has not been prospectively validated for these disorders.

Differential Diagnosis

Although the diagnosis of severe TBI may be readily apparent based on the history and physical examination, the clinician must maintain an early broad differential. A primary medical event such as stroke, syncope, cardiac arrest, or seizure may have caused the traumatic incident and should be considered as an etiology of the patient's altered mental status. More than 60% of severe TBIs are complicated by alcohol or substance intoxication,[37] and they are more likely to require endotracheal intubation or neurosurgical intervention.[38]

As with most other neurologic disorders, a blood glucose level is one of the first laboratory tests obtained. Hypoglycemia is common and can masquerade as both global and focal neurologic findings. If untreated, it can lead to seizures, permanent neurologic damage, and death.[39] Early recognition and treatment of hypoglycemia is critical in order to address a potentially reversible cause of altered mental status as well as to mitigate secondary injury.

Prehospital Care

Optimizing Perfusion: Crystalloids

Investigators have consistently reported prehospital and ED admission hypotension to be associated with increased mortality in severe TBI. Older publications defined hypotension as a systolic blood pressure (SBP) of < 90 mm Hg,[40] but a recent large retrospective dataset containing over 15,000 patients has called that definition into question by demonstrating that an SBP of < 110 mm Hg on admission to the ED was associated with increased mortality in patients with moderate or severe TBI.[41]

Prehospital studies comparing isotonic solutions are lacking, but researchers have explored the effects of hypertonic solutions on outcomes in 2 large randomized control trials. It was hypothesized that hypertonic solutions would improve CPP by increasing MAP via an expansion of the intravascular volume and decreasing ICP through its osmotic effects on the central nervous system. Enthusiasm for hypertonic solutions in TBI was further fueled by a systematic review and analysis demonstrating an association with improved survival.[41]

The first randomized controlled trial from 2004 included 226 patients and compared 7.5% saline with lactated Ringer's (LR) solution in patients with

Table 3. Glasgow Coma Scale[34]

Eye Opening (E)	Verbal Response (V)	Motor Response (M)
4 – Opens spontaneously*	5 – Alert and oriented	6 – Follows commands
3 – Opens to voice	4 – Disoriented or confused	5 – Localizes to pain†
2 – Opens to pain	3 – Incoherent words	4 – Withdraws from pain
1 – None	2 – Incomprehensible sounds, moaning	3 – Flexion posturing
	1 – None	2 – Extension posturing
	"T" or "I" – if patient is intubated or has tracheostomy	1 – None

* Patient should attend to the examiner in order to score a 4 on the eyes.

† Patient should cross midline to address the noxious stimulus in order to score a 5 on the motor score.

a GCS score < 9 and SBP < 100 mm Hg. The primary outcome (functional status at 6 months after injury) was the same in each group; however, enthusiasm was not extinguished, as there was a nonstatistically significant improvement in 6-month survival (8% absolute difference).[43]

The most recent randomized controlled trial was published in 2010. It compared 7.5% saline/ 6% dextran 70, 7.5% saline, and 0.9% saline in 1331 blunt trauma patients with a GCS score of < 9 and no evidence of hemorrhagic shock. Unfortunately, 6-month functional status was similar among the groups.[44] A criticism of this trial was its inclusion of a large proportion (> 25%) of patients with a GCS score of 3, as their prognosis is poor, making it difficult to achieve large-scale improvements in functional outcome with a single prehospital intervention.

Initial resuscitation of a patient with severe TBI should include isotonic crystalloid (normal saline, LR, etc) with consideration for the use of hypertonic saline (HTS) if there is physiologic evidence for elevated ICP. For more information on the use of HTS in critically ill patients, see the *EM Critical Care* issue Volume 3, Number 1, "Therapeutic Uses Of Hypertonic Saline In The Critically Ill Emergency Department Patient."

Airway Management: Bag And Go Or Stay And Tube?

Hypoxia has been defined as oxygen saturation by pulse oximeter (SpO_2) < 90%. The association between prehospital hypoxia and/or hypotension and increased mortality in severe TBI has been well described.[45,46] The available evidence examining the impact of prehospital intubation on outcomes in severe TBI patients is limited, and results have been mixed. An association with improved outcomes has been reported in some studies,[47] while other studies found intubation to be associated with harm.[48] Prehospital providers have been observed to be successful in establishing an airway,[49] but procedural hypoxia and hyperventilation have been identified as causes for worsened outcomes.[45,50] Benefit has been shown with intubation of the more severely injured TBI patient (no gag reflex and apneic or unconscious with ineffective ventilation),[51] whereas studies with more liberal protocols (GCS score < 9 with an inability to intubate without rapid sequence intubation [RSI]) demonstrated an association with harm.[52]

Favorable 6-month outcomes have been demonstrated when intubation is performed by trained medics and the ground transport time is between 10 and 30 minutes.[53] There may be a benefit to prehospital RSI for severe TBI patients under the following circumstances:

1. When patients are unable to protect their airway or maintain oxygenation
2. During transport by aeromedical providers
3. When ground transport time is > 10 minutes and it can be performed by providers with regular intubation experience and advanced critical care and RSI training

Ventilatory Management

There is an association between prehospital hypercapnia or hypocapnia and poor outcomes in both intubated and nonintubated patients.[45,54,55] Hypercarbia causes cerebral arterial vasodilatation, which initially produces an increase in cerebral blood flow. This leads to an increase in ICP, a subsequent decrease in CPP, and the potential expansion of hemorrhagic lesions.[56] Hypercarbic systemic acidosis may compromise cardiac output as well as coagulation mechanisms, further reducing CPP and promoting the expansion of intracranial hematomas.

End-tidal carbon dioxide ($ETCO_2$) should be used on all ventilated patients, when feasible, to target eucapnia (35-40 mm Hg). If not available, liberal use of blood gases to avoid hypocapnia is recommended. If the patient is well oxygenated, normotensive, and any of the signs of herniation are present, a brief trial of hyperventilation (goal $ETCO_2$ of 30-35 mm Hg) is recommended.[6] Signs of herniation include:

1. Dilated and unreactive pupils (< 1 mm response)
2. Asymmetric pupils (> 1 mm difference)
3. Extensor posturing on motor examination
4. No motor response (not from spinal cord injury)
5. Drop in the GCS score of more than 2 points with a best initial score of < 9

Transport: To Where And By Whom?

TBI patients cared for by providers within organized trauma systems,[57] with advanced training (including physicians),[53] or transported and cared for by aeromedical providers[58] have been demonstrated to have improved outcomes. Regional systems should strive to support logistics that triage providers with a high level of training to the scene, followed by the expeditious transport to a trauma facility with CT scan and neurosurgical capabilities available 24 hours a day, 7 days a week.

Emergency Department Evaluation

Initial Stabilization

ED evaluation begins with a targeted history to elicit information on the patient's preinjury conditions and medications as well as the mechanism of the injury. **(See Table 4.)**

The foundation of early ED resuscitation of the patient with a severe TBI is the stabilization of the airway, breathing, and circulation, while maintaining inline cervical spine immobilization and evaluating for concomitant systemic traumatic injuries. It

is estimated that up to 60% of patients with severe TBI have another traumatic injury.[59] Hypoxia (SpO_2 < 90%) occurs at least once in up to 40% of patients with severe TBI and increases neuronal death and motor deficits and contributes to poor outcomes.[60] Mortality rates double with even 1 episode of hypotension (SBP < 90 mm Hg). Significant morbidity and mortality occur when a patient experiences both hypoxia and hypotension, even when it is merely 1 brief instance of each.[46] Physiologic homeostasis is preferred during the resuscitation of a patient with a severe TBI, with avoidance of supratherapeutic or subtherapeutic vital signs or laboratory test results (ie, sodium, acid/base, coagulation, etc).

Airway

A patient with a severe TBI should be intubated when there is a failure to oxygenate, a failure to ventilate, or a failure to protect the airway or for an anticipated clinical course (eg, air medical transport, operating room, transport to CT, etc). Convention has largely dictated that any patient with a severe TBI (GCS score ≤ 8) warrants RSI. Unfortunately, the GCS score has limitations as the sole predictor regarding airway protection. In 2 studies, up to 27% of patients who were intubated if the GCS score was the sole determinant for definitive airway protection did not have a severe brain injury.[52,61] The GCS score can be particularly misleading in patients who are in shock or intoxicated. In addition, each part of the GCS score is important by itself, and not necessarily just the aggregate score; every patient with a GCS score ≤ 8 is different. Many patients with a GCS score ≤ 8 have adequate oxygenation and ventilation in the ED, further confounding appropriate patient selection for intubation.[61]

The decision regarding the need for endotracheal intubation should be considered on a case-by-case basis. Patients with severe TBI often have occult cervical spine injuries, so inline cervical spine immobilization should be maintained throughout intubation. Fiberoptic or video-assisted intubation should be considered, if available, to minimize or eliminate potential manipulation of the cervical spine.

While providing the positive benefit of definitive airway protection, endotracheal intubation also carries the significant risk of contributing to secondary injury through hypoxia, hypotension, and increased ICP. If pretreatment is utilized, patients should be preoxygenated and appropriate pharmacologic agents that avoid hypotension should be selected. Laryngoscopy, with subsequent laryngeal manipulation and tracheal intubation, can lead to elevated ICP through a reflexive sympathetic response. This response leads to tachycardia and hypertension, which can contribute to pathologic increases in ICP in a patient who has lost cerebral autoregulation due to severe traumatic injury. Once the endotracheal tube is in place, manipulation of the tube can cause a tracheal irritation and direct cough reflex, with resultant ICP spikes.

Pretreatment

Lidocaine

Pretreatment with intravenous (IV) lidocaine prior to endotracheal intubation has been thought to blunt the ICP increase and reduce the catecholamine release. It has been hypothesized that by reducing the catecholamine release during laryngoscopy, cerebral blood flow, cerebral vascular resistance, and cerebral

Table 4. Targeted History

Past Medical History
- Diabetes
- Seizures
- Stroke
- Intracranial masses/lesions

Medications
- Anticoagulants
- Antiplatelet agents

Social History
- Alcohol use
- Illicit or prescription drug use

Accident-Related
- Motor vehicle accident
  - How fast was the vehicle traveling?
  - What were the vectors of force involved in the accident?
  - What caused the accident?
    - Single vehicle, loss of control?
    - Any evidence of a medical cause of the accident?
  - Was the patient wearing a seatbelt?
  - Did the airbags deploy?
  - Was the patient ejected from the vehicle?
    - Was the patient ejected from the passenger compartment?
    - Was there any intrusion into the passenger compartment?
  - Was the windshield "starred" or shattered?
- All-terrain vehicle or cycle
  - How fast was the vehicle travelling?
  - Was the patient wearing a helmet?
    - Was there damage to the helmet? Where?

Fall
- How far (or from what height) did the patient fall?
- Were there any steps? How many?
- Was the patient outside? What were the environmental conditions?

Sports-Related
- Was the patient wearing a helmet?
- What were the circumstances of the injury/hit?

Injury
- Did the patient lose consciousness?
  - If yes, for how long?
- Did the patient return to baseline after the injury?

metabolism are all also reduced, minimizing the ICP elevation recorded with the procedure.[62,63] The best evidence for the use of lidocaine prior to endotracheal intubation is from small studies conducted with patients in intensive care units (ICUs) who were undergoing suctioning or patients intubated under ideal conditions in the operating room with an ICP monitor prior to elective brain tumor resection. Although these studies were not conducted with severe TBI patients in the ED, there has been widespread adoption of pretreatment with lidocaine prior to RSI and endotracheal intubation.[64,65] If lidocaine is utilized as a pretreatment medication, it should be administered at least 3 minutes prior to manipulation with laryngoscopy at a dose of 1.5 mg/kg IV.[65] The dose of lidocaine should mirror the dose of succinylcholine, if used. The best evidence for minimizing secondary injury is avoiding hypotension and hypoxia; therefore, do not sacrifice definitive rapid control of the airway for an unnecessary delay for pretreatment to mitigate ICP elevations.

Fentanyl

Fentanyl, a synthetic opiate, has the advantage of treating pain associated with the initial injuries as well as with laryngoscopy and intubation. It has been shown to decrease associated elevations in heart rate and blood pressure, which may have an effect on blunting the ICP response.[66] If used, fentanyl should be administered at least 3 minutes prior to intubation, at a dose of 3 mcg/kg IV.[66] Fentanyl has the potential to contribute to peri-intubation hypotension, especially in a hypovolemic or underresuscitated patient, which would defeat the purpose of pretreatment to prevent secondary injury.

Vecuronium, Rocuronium, And Pancuronium

Vecuronium, rocuronium, and pancuronium are all nondepolarizing neuromuscular blocking agents. Pretreatment with a smaller dose than required for intubating-condition paralysis theoretically blunts the fasciculation-induced increase in ICP seen with succinylcholine. If used, pretreatment should be administered 3 minutes prior to induction, with vecuronium at a dose of 0.01 mg/kg, rocuronium at a dose of 0.06 mg/kg, or pancuronium at a dose of 0.01 mg/kg. Although these doses should not affect the patient's tidal volumes, close attention should be paid to overall effort, especially when multiple medications are administered concomitantly for pretreatment and induction. One prominent emergency medicine airway management text no longer recommends pretreatment paralytics due to the potential risks and overall lack of evidence of their efficacy.[64,65]

Esmolol

Esmolol is a cardioselective beta$_1$ receptor antagonist with a rapid onset and very short duration of action. The best evidence for esmolol is in cardiac patients undergoing laryngoscopy by anesthesiologists. Esmolol has been shown to be effective in lowering the sympathetic response to manipulation by laryngoscopy. One small study in TBI patients demonstrated that both lidocaine and esmolol did not have significant differences in hemodynamic changes during and immediately following laryngoscopy.[67] Although esmolol is a selective beta$_1$ antagonist with primary chronotropic effects, use caution in volume-depleted or hypotensive patients. If esmolol is selected, it should be administered 3 minutes prior to induction at a dose of 2 mg/kg IV. Although pretreatment with esmolol to modulate ICP increases during intubation may be helpful, the overall evidence is poor, and it should not be used if the patient requires urgent intubation.

Sedation And Induction

There are wide ranges of sedation and induction agents that can be used prior to paralysis for endotracheal intubation. It is critical that patients receive a sedative prior to administration of a paralytic for multiple reasons, including control of ICP, blood pressure, and heart rate as well as for amnesia of the intubation procedure. The most important characteristic of any pharmacologic agent is the emergency clinician's familiarity with its desired effects and potential adverse side effects (such as hypotension). The ideal pharmacologic agent is rapid in onset, provides deep sedation and/or amnesia, and maintains hemodynamic stability. Unfortunately, there is no perfect agent for patients who have sustained a severe brain injury, particularly when one considers the elevated risk of additional systemic injuries.[68] Medication choices and doses selected in the ED may have downstream ramifications in the ICU, especially with medications selected for continuous infusion. **(See Table 5.)**

Paralysis

The final step in RSI is complete skeletal muscle paralysis with neuromuscular blocking agents. The choice to paralyze a patient must be considered carefully, especially in the patient with a suspected difficult airway. In addition to the pain and possible memory of the procedure, paralysis without sedation in even a comatose patient has the potential to elevate the ICP and should be avoided.

The 2 main classes of neuromuscular blocking agents are depolarizing and nondepolarizing. There have been no differences shown in intubation conditions between succinylcholine and rocuronium, but succinylcholine is generally preferred clinically due to its shorter duration of action.[69] Ultimately, the emergency clinician must select an appropriate agent based on the clinical and physical presentation of a particular patient with a severe TBI. Su-

gammadex has been shown to reverse the effects of rocuronium and vecuronium,[70] and it has been in use in Europe since 2008, but the United States Food and Drug Administration (FDA) has not approved its use in the United States due to concerns related to anaphylactic reactions.

Breathing

Hypoxia (arterial oxygen tension [PaO_2] < 60 mm Hg or SpO_2 < 90%) must be avoided at all costs in a patient with a severe TBI.[60] Although most patients will be intubated and mechanically ventilated, supplemental oxygen should be administered for patients who do not require mechanical ventilation or who are being prepared for intubation. Continuous pulse oximetry should be routinely employed. Once a patient is placed on mechanical ventilation, the focus must be on both oxygenation as well as ventilation (partial pressure of carbon dioxide, arterial [$PaCO_2$]), as inappropriate ventilator settings can be lethal. Initial settings should focus on lung-protective ventilation with goal tidal volumes of 6 to 8 cc/kg based on ideal body weight. Studies have demonstrated that high tidal volume ventilation is associated with acute lung injury and acute respiratory distress syndrome in patients with severe TBI; therefore, it should be avoided.[71] The ventilator should be adjusted to maintain plateau airway pressures < 30 cm H_2O. Normal physiologic parameters should be the rule, and the ventilator should be adjusted for a normal PaO_2 (80-120 mm Hg) and $PaCO_2$ (35-45 mm Hg). Once the airway has been secured and the patient has normal oxygenation, the fractionated inspired concentration of oxygen (FiO_2) should be reduced to < 60% while maintaining the saturation > 90% to prevent both pulmonary and cerebral oxygen toxicity.[26]

Continuous $ETCO_2$ monitoring should be used to allow for real-time ventilator adjustments.[73] Prophylactic hyperventilation is associated with increased morbidity and mortality and is not indicated.[74] Cerebral blood flow can be significantly lowered in the first hours after a TBI due to a loss of autoregulation.[75] Hyperventilation causes a reduction of $PaCO_2$, which leads to cerebral vasoconstriction, a reduction in cerebral blood flow, and, ultimately, ICP (by 25%).[7] This can be a valuable short-term maneuver during an acute deterioration or herniation, but it can cause further ischemia and increased morbidity if utilized prophylactically.[32] In addition, the beneficial lowering of elevated ICP during a herniation event is short-lived, and deleterious rebound ICP elevation can be seen as the patient equilibrates. If hyperventilation is used for an acute herniation, it should be a temporizing, life-saving maneuver (goal $PaCO_2$ = 30 mm Hg) until more definitive interventions can be employed (sedation, hyperosmolar therapy, decompressive hemicraniectomy, etc.).[7] It is unclear how the use of temporizing hyperventilation during herniation affects outcome, and its use should be discontinued as soon as the signs and symptoms of herniation improve.

Circulation

A single SBP measurement < 90 mm Hg doubles mortality and worsens neurologic morbidity.[73,76] Much of these data are from the prehospital literature, but late hypotension is seen in up to 30% of patients, with > 60% of hypotensive patients progressing to death or vegetative state compared to 17% of controls.[73] Isotonic crystalloid should be the initial resuscitative fluid of choice if hemorrhagic shock is not present. The utilization of blood products should be guided by local trauma or Advanced Trauma Life Support® (ATLS®) protocols. There is no literature to support the selection of 1 particular crystalloid over another or the administration of blood products for the resuscitation of severe TBI. Although based on a post hoc analysis of a prospective study, a large trial found significantly increased mortality with the use of albumin in severe TBI; therefore, albumin should be avoided.[77] Due to a theoretical risk of negative osmotic fluid shifts, fluids containing dextrose should also be avoided. The use of hyperosmolar agents (discussed in the "Hyperosmolar Therapy" section on page 20) should be reserved for patients with evidence of acute herniation or signs of elevated ICP in the ED.

The ideal blood pressure goals should be to support CPP, which will be difficult to ascertain in the ED without ICP monitoring. If available, CPP should be maintained between 50 and 70 mm Hg and the ICP to < 20 mm Hg.[7] Since invasive monitoring will rarely be available in the ED, the emer-

Table 5. Continuous Infusion Medications For Sedation And Analgesia[64,85,86]

Name	Class	Dosage	Cautions
Midazolam	Benzodiazepine	0.04-0.2 mg/kg/h	Lipid soluble; accumulates
Propofol	$GABA_A$ agonist	10-80 mcg/kg/min	Propofol-related infusion syndrome (lactic acidosis, arrhythmias, cardiovascular collapse)
Fentanyl	Synthetic narcotic	1-3 mcg/kg/h	Hypotension
Remifentanil	Synthetic narcotic	0.1-1 mcg/kg/min	Hypotension

gency clinician should focus on correcting hypovolemia and preventing hypotension (keeping SBP > 90 mm Hg). Fluids and vasopressors are encouraged for the treatment/correction of hypotension,[73] but induced hypertension should be avoided due to the increased risk of acute lung injury and acute respiratory distress syndrome.[71,78] Vasopressors should be used only when the emergency clinician is confident that the patient is euvolemic.

Due to the intrinsic loss of cerebral autoregulation, intrinsic hypertension should not be pharmacologically lowered unless the MAP is > 120 mm Hg. Malignant hypertension may indicate an underlying medical condition that would benefit from treatment, but lowering the blood pressure should be avoided until an ICP monitor is in place. If an elevated blood pressure is going to be treated, short-acting agents are recommended.

Intracranial Pressure Management

ICP should be monitored in all salvageable patients with a severe TBI and an abnormal CT scan. ICP monitoring is indicated in patients with a normal CT scan if 2 of the following features are present: age > 40 years, motor posturing, or hypotension (SBP < 90 mm Hg).[7] The ideal ICP monitor is a ventriculostomy, as it can provide both diagnostic ICP values as well as a therapeutic option (CSF diversion).[79] If ICP monitoring is available, treatment of ICP should be considered when the pressure exceeds 20 mm Hg or with evidence of herniation.

A recent randomized controlled trial investigating the management of severe TBI using ICP monitors versus following serial clinical examinations and head CTs was published in 2012.[80] This study suggested that care focused on maintaining ICP < 20 mm Hg (as measured with an intraparenchymal monitor) was not superior to care based on imaging and clinical examination. This study had many flaws that limit its interpretation and application to the United States (eg, study outcome measures and because it was conducted in South American hospitals where there are differences in prehospital care). Nonetheless, the study raises interesting questions regarding determination of the individual patient ICP threshold for treatment, multimodality treatment, and treatment of patients with severe TBI in centers with limited resources.

The head of the bed should be elevated to 30° to help facilitate cerebral venous drainage and CSF drainage. Reverse Trendelenburg positioning can be used prior to radiographic spine clearance.[81] The head of the bed should not be raised higher than 30°, as doing so can contribute to increased intra-abdominal pressure and a paradoxically increased ICP.

Almost all patients will require cervical spine immobilization until they can be clinically or radiographically cleared per local protocol. Care must be taken that the cervical immobilization collar is sized appropriately to avoid unnecessary pressure on the neck, which can cause jugular venous congestion, decreased venous return, and an elevated ICP.

Sedation and analgesia decrease ICP and optimize CPP.[7] The optimal sedative has a rapid onset and a short duration so that the patient's neurologic status can be examined on a regular basis. Medication-induced hypotension can be avoided by adequate dosing and volume resuscitation. Most of the commonly used sedatives do not have analgesic properties, and an appropriate concomitant analgesic agent is warranted. Sedation and analgesia goals in the ED focus on physiologic targets such as heart rate, blood pressure, respiratory rate, facial grimace, diaphoresis, and motor agitation. Sedation scales are often impractical in the ED environment. Although paralytics may help reduce ICP by eliminating motor posturing, shivering, and ventilator dyssynchrony,[82] their routine use is not recommended in the ED.

Fever is an independent predictor of poor outcome in TBI,[83] and patients should be kept aggressively euthermic. There is no evidence to suggest that any method (endovascular vs surface) is superior to another in maintenance of euthermia or neurologic outcome, and local practice should be guided by consensus protocols. Antipyretics should be administered in the event of fever.[5] Shivering should be controlled, as this can contribute to increased cerebral metabolism and elevated ICP.

The initial management of the patient with a severe TBI is complex and challenging. Traditionally, management of a patient has been a stepwise process with pharmacologic and procedural interventions. Focusing solely on individual parameters such as CPP or ICP is likely not effective and may be harmful. A targeted, goal-directed resuscitation that focuses on global physiologic targets may be more helpful.[84] **(See Figure 6.)**

Diagnostic Studies

Laboratory Tests

Most laboratory tests are not helpful in the initial diagnosis and management of a patient with severe TBI. Local trauma protocols may guide the selection of the initial laboratory evaluation. A point-of-care blood glucose should be performed on every patient who presents with altered mental status, as hypoglycemia is a common and easily reversible condition.[39] A blood alcohol and/or toxicology screen (blood or urine) may assist in identifying contributing causes of altered mental status, but they should not change the clinical management of a patient with a suspected severe TBI. Clinical suspicion (patient history/medication lists) should guide the need for measurements of common anticoagulants, including prothrombin time (PT), partial thromboplastin

time (PTT), international normalized ratio (INR), factor Xa level, and others. Additional tests that are helpful in guiding resuscitation in trauma cases include a complete blood count (CBC), complete metabolic profile, lactic acid level, pregnancy test, blood typing, and profile of the patient's acid/base status (arterial or venous blood gas).[87] If the patient is taking a medication that is monitored with a common laboratory therapeutic profile (digoxin, lithium, phenytoin, valproic acid, etc), those should be monitored as well.

Imaging

In patients with a clinical suspicion of a severe TBI (GCS score ≤ 8), a noncontrast head CT should be obtained. CT images are highly sensitive for traumatic pathology, including acute hemorrhage, hematomas, and bony fractures. They are also sensitive in detecting sequelae of trauma such as mass effect and midline shift, hydrocephalus, and trauma mimics (intracerebral mass, subacute and chronic infarction, primary intracerebral hemorrhage). Some patients with severe TBI have an initially normal CT in the ED due to diffuse axonal injury, and this represents one of the limitations of CT in severe TBI. Findings from the initial CT may have prognostic implications[88] and may help guide neurosurgical intervention (if it becomes necessary).

CT angiography (CTA) may be indicated for patients with certain types of penetrating trauma or skull or cervical spine fractures, especially if the fracture line violates the carotid canal. Emergency clinicians must work closely with their radiology, trauma surgery, and/or neurosurgery colleagues to help guide the appropriate use of this resource. CTA carries the additional risk of a potential nephrotoxic contrast bolus. Most CTAs are indicated after the patient has already received contrast for body imaging to evaluate for other traumatic injuries, so the risks and benefits of an additional contrast load must be taken into consideration.

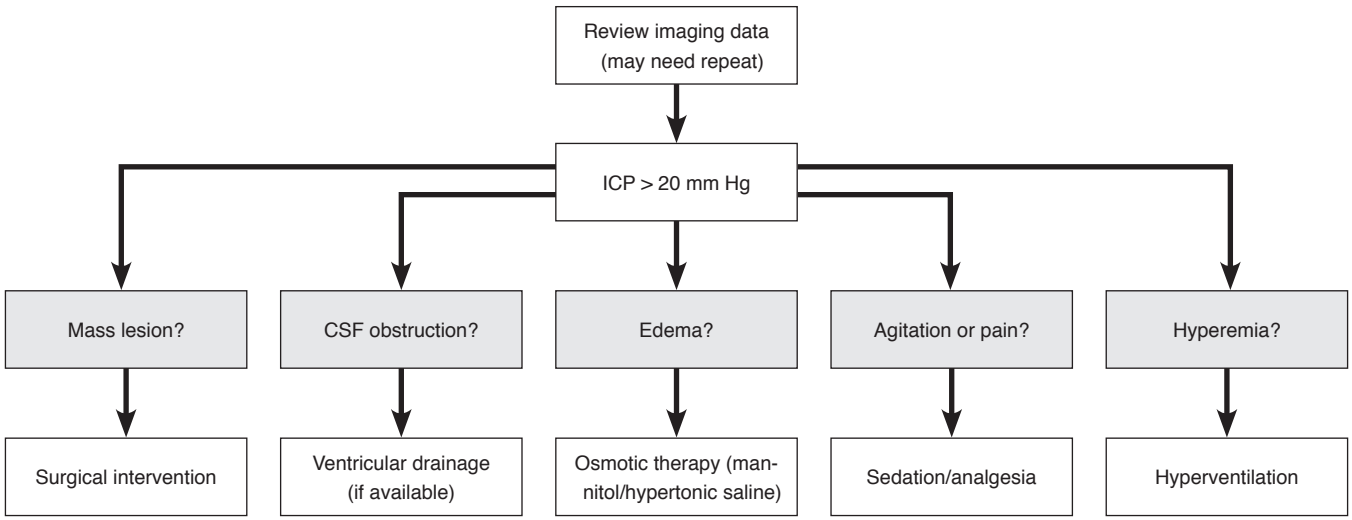
Magnetic resonance imaging (MRI) does not have a role in the initial evaluation of the patient with an acute severe TBI. Not only is CT more sensitive for bony fractures, it is superior for the evaluation of acute hemorrhage.[89] MRI is also not universally available, it takes longer for image acquisition, and there are challenges with monitoring the acutely critically ill patient.[89] MRI has a role in the late management of severe TBI, usually many days later, to help define occult injuries such as diffuse axonal injury and to assist with prognosis.

All patients with severe blunt TBI should have imaging of the cervical spine. These patients are unable to be clinically cleared, and there is a significant percentage of patients with concomitant TBIs and cervical spine fractures.[90] Although plain radiographs have been historically used as the initial test, CT is superior to plain films in detecting bony injury.[91,92] In addition, the patient will already be in the CT scanner for the remainder of the radiographic trauma evaluation. CT does not adequately rule out cervical ligamentous injuries, so emergency clinicians must work with the trauma surgeons and spine surgeons to develop an institutional protocol on how and when to definitively clear cervical spines (eg, long-term immobilization, MRI, flexion-extension plain films).

Management Of Neurologic Deterioration

Preoperative GCS score,[93] preoperative pupillary abnormalities,[94] pupillary abnormalities associ-

Figure 6. Targeted Physiologic Resuscitation



Abbreviations: CSF, cerebrospinal fluid; ICP, intracranial pressure.

Jack Jallow, Christopher M. Loftus, eds. *Neurotrauma and Critical Care of the Brain.* © 2009 Thieme Publishers. (Reprinted with permission)

ated with advanced herniation (ie, mydriasis contralateral to a lesion or bilateral mydriasis),[95] time to surgery,[96] hematoma size,[94,97] time from herniation to surgery,[95,98] and availability of neurosurgical services at the presenting facility[99] are all related to clinical outcomes. Unfortunately, there are no monitoring devices that currently exist for continuous assessment of a patient's neurologic status or intracranial hematoma volume in the ED. Therefore, the emergency clinician must perform frequent and regular neurologic examinations (GCS score and pupillary) to identify deterioration as early as possible so that mitigation measures can be rapidly instituted and neurosurgical services can be expeditiously arranged.

Examination Findings Consistent With Deterioration

When neurologic deterioration occurs, the patient should be assessed for signs and symptoms of elevated ICP and/or a herniation syndrome resulting from compression and displacement of brain tissue. The Cushing triad of bradycardia, hypertension, and irregular respirations is commonly described, but it is present only one-third of the time that ICP is elevated.[16] An ICP increase is the result of expanding intracranial hematomas, progressive cerebral edema, obstruction of venous outflow (eg, from a tight cervical collar[100]), or obstruction of CSF outflow by external compression of the Monro foramen or aqueduct of Sylvius or by blood within the ventricular system.[101] Local increases in hemorrhagic blood volume lead to the compression of neighboring brain tissue. This compression compromises blood flow to the uninjured tissue, causing ischemia and further swelling. This further compresses neighboring tissues, producing a devastating positive feedback loop. This progression often manifests as 1 of 4 herniation syndromes: (1) subfalcine (or cingulate); (2) uncal; (3) central transtentorial; and (4) tonsillar. **(See Figure 7.)**

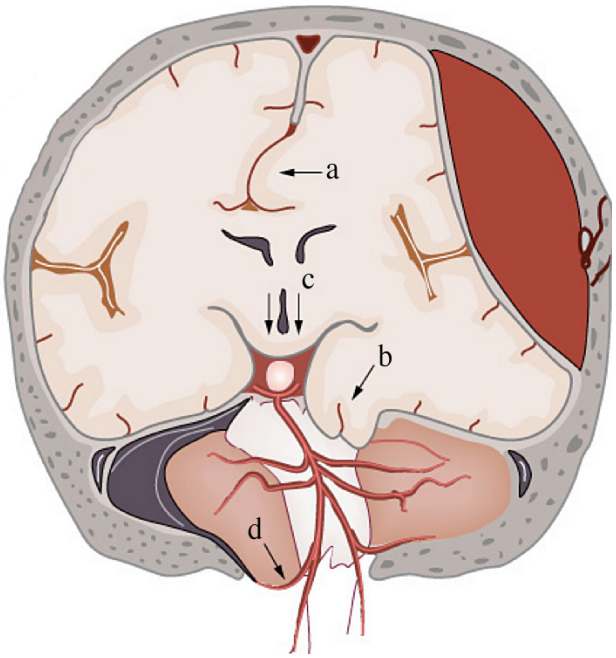
Subfalcine herniation **(seen as "a" in Figure 7)** can be identified on a CT scan and quantified by the amount of midline shift at the pineal gland (or septum pellucidum).[102]

Uncal herniation **(seen as "b" in Figure 7)** often results from an extraaxial hematoma or temporal contusion that displaces the ipsilateral uncus through the tentorium, compressing the midbrain and displacing it laterally against the contralateral tentorium.[103] Ipsilateral pupillary abnormalities caused by stretching of the third cranial nerve are often the initial clinical change.[102] As the ipsilateral midbrain is compressed, contralateral hemiparesis ensues as the motor fibers cross over at the cervical-medullary junction.[103] Finally, as the midbrain is pushed laterally, bilateral extensor posturing is often seen, although flexor posturing can also occur.[102,103] Twenty-five percent of patients experience ipsilateral hemiparesis, misleading the localization of the lesion.[103]

Central transtentorial herniation **(seen as "c" in Figure 7)** is difficult to appreciate clinically. Forces applied caudally onto the midbrain gradually cause the pons and medulla to herniate inferiorly, compressing the posterior cerebral arteries and obstructing the aqueduct of Sylvius.[102] Clinical findings begin with miotic pupils, which progress to being midpoint and fixed. Motor weakness progresses to rigidity, then flexor, and finally extensor posturing. Respirations are irregular and eventually progress to apnea.[103]

Tonsillar herniation **(seen as "d" in Figure 7)** occurs when the cerebellar tonsils herniate caudally through the foramen magnum, usually from cerebellar or posterior fossa hematomas. Compression of the brainstem causes CSF flow obstruction and respiratory and cardiovascular collapse. Pupils become miotic, and the patient develops quadriplegia.[102,103] It is also important to consider physiologic changes that may be contributing to neurologic deterioration. Drops in SBP decrease CPP and, therefore, cerebral blood flow. Areas of the brain with intact autoregulation will vasodilate in an attempt to maintain cerebral blood flow, leading to an increase in intracranial blood volume and, therefore, ICP, which further comprises CPP. Drops in CPP also increase cerebral

Figure 7. Herniation Syndromes



Arrows point to the areas affected by herniation syndromes: a. subfalcine; b. uncal; c. central transtentorial; d. cerebellar tonsillar.
To view the color version of this image, go to: www.ebmedicine.net/E0313Figures.
Adapted from *The Atlas of Emergency Medicine, 3rd Edition*. Kevin Knoop, Lawrence Stack, Alan Storrow, and R. Jason Thurman.

ischemia, further increasing edema and, therefore, ICP. Hypercarbia will directly vasodilate uninjured cerebral vasculature, producing an increase in ICP. It is important to assess changes in the $PaCO_2$ and MAP when addressing neurologic deterioration.

Confounders Of The Neurologic Examination

Interventions performed while stabilizing the ABCs may have an adverse impact on the preservation of the neurologic examination. The most notable are the administration of sedation agents and paralytics for RSI. Due to its short duration of action, succinylcholine is the preferred paralytic (when there are no contraindications to its use). In the event that a nondepolarizing neuromuscular blocking agent is used for RSI, the patient's GCS score will be unobtainable for 60 to 90 minutes, but the pupillary response is largely preserved.[104]

Predictors Of And Factors Associated With Deterioration

Male sex, an initial head CT performed within 2 hours of injury, older age, and an elevated initial PTT have also been associated with hematoma progression.[105] Some authors have demonstrated a relationship between abnormalities in admission PT, PTT, platelet count, or thromboelastogram and delayed deterioration.[106,107] Head CT findings associated with deterioration include a spiral (whirl) sign **(see Figure 8),** temporal epidural hematoma, subdural hematoma, subarachnoid hemorrhage, compressed or absent basal cisterns, posterior fossa lesions, and traumatic lesions > 30 cc.[13,19,97] The use of warfarin has been associated with worse outcomes in patients with traumatic intracranial hemorrhages, presumably due to the greater likelihood of the intracranial hematoma to continue to expand.[107,108] Results have been mixed, however, regarding the impact of preinjury antiplatelet use (ie, aspirin and clopidogrel) on outcomes in TBI,[109,110] although it would be reasonable to maintain a greater degree of vigilance for potential worsening when monitoring these patients.

Response To Deterioration

As soon as neurologic deterioration is identified, the emergency clinician should aggressively optimize CPP and institute ICP-lowering therapies. These include raising the head of the bed to 30° (if not already performed), ensuring adequate sedation and analgesia, hyperventilating to a goal $ETCO_2$ of 30 to 35 mm Hg, and providing hyperosmolar therapy. If the patient is known or suspected to be on anticoagulants, reversal (when possible) should be expeditiously provided, and, ideally, prior to any deterioration.

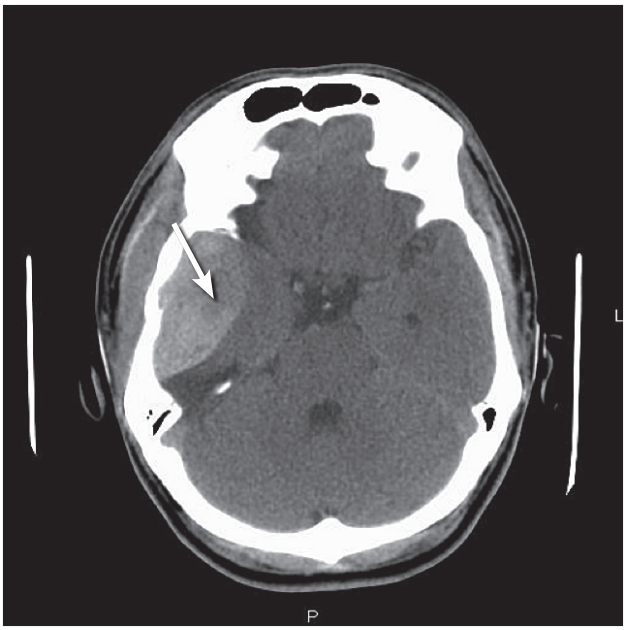
Neurosurgery should be promptly consulted and/or the patient expeditiously transferred to a facility with neurosurgical capabilities. More advanced ICP-lowering therapies such as barbiturates or hypothermia and surgical actions such as ventriculostomy, craniotomy, or craniectomy are best carried out in consultation with neurosurgery, trauma surgery, and/or neurocritical care specialists.

When faced with a patient who is rapidly herniating from a confirmed or suspected expanding epidural or subdural hematoma and there is a delay or inability to transfer the patient to neurosurgical care, skull trephination[111] or burr hole decompression can be considered. This is best performed in communication with neurosurgery. Limited reports suggest that this is a procedure that can be performed by an emergency clinician and may improve patient outcomes.[111]

Controversies And Cutting Edge

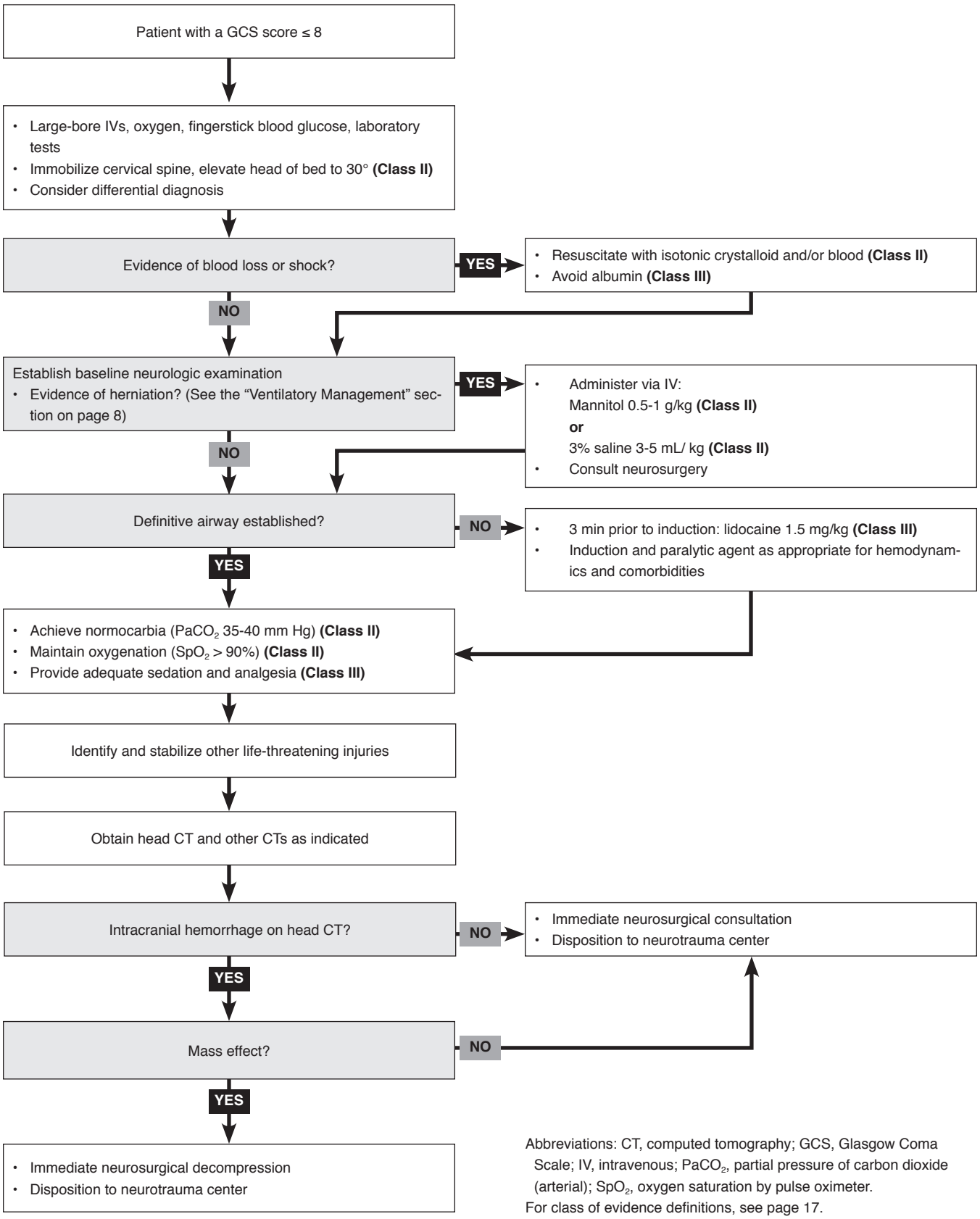
Given the limitations of the current treatment options for the dichotomy of the primary and secondary injuries, most research has been focused on managing primary injury while preventing secondary injury. In addition, the physiologic differences of the different subtypes of TBI contribute to the overall difficulty in demonstrating positive outcomes with neuroprotectant therapy. The heterogeneous mix of pathology within a single disease process limits the effectiveness of potential treatments that may have narrow thera-

Figure 8. Spiral (Whirl) Sign In Epidural Hematoma



Arrow points to a spiral (whirl) sign, which shows different densities within a hemorrhage on CT and is indicative of ongoing bleeding. Image courtesy of William A. Knight IV, MD.

Clinical Pathway For Management Of Severe Traumatic Brain Injury



Abbreviations: CT, computed tomography; GCS, Glasgow Coma Scale; IV, intravenous; $PaCO_2$, partial pressure of carbon dioxide (arterial); SpO_2, oxygen saturation by pulse oximeter.

For class of evidence definitions, see page 17.

peutic targets. Over the past 30 years, only 1 trial has shown a statistically significant outcome in the management of severe TBI. The CRASH (Corticosteroid Randomisation After Significant Head injury) trial clearly demonstrated the harm of steroid therapy for patients with severe TBI.[112] Many agents (including magnesium, dexanabinol, and tirilazad) have been studied that do not definitively cause harm, but none have demonstrated clinical efficacy.

Prophylactic Antiepileptic Medications

Posttraumatic seizures (PTS) are classified as either early (≤ 7 days after injury) or late.[7] It is desirable to prevent both early and late PTS. There is a relatively high incidence of PTS in patients with severe TBI, and there are potential benefits to preventing seizures in this patient population. Animal studies suggest that some antiepileptic drugs may have neuroprotectant effects.[113]

Antiepileptic drugs are effective at preventing early PTS (relative risk, 0.34; number needed to treat = 10), but they do not have an effect on late PTS, functional outcome, or mortality.[114] Phenytoin has demonstrated an absolute reduction in the incidence of early PTS, further establishing a role for antiepileptic drugs in TBI management.[115] Investigators have sought to demonstrate the equivalency of other antiepileptic drugs for early PTS prophylaxis. Valproate has been shown to be similarly effective for seizure prophylaxis, but it was associated with a nonstatistically significant higher mortality rate when compared with phenytoin.[116]

A small single-center randomized trial comparing levetiracetam and phenytoin found an equivalent incidence of early PTS in each group as well as improved long-term outcomes of levetiracetam-treated patients versus phenytoin-treated patients. This was based on improved 6-month Glasgow Outcomes Score-Extended (GOS-E) scores in surviving patients in the levetiracetam group and did not include 10 patients from the levetiracetam group who died due to withdrawal of care (compared to 2 patients in the phenytoin group).[117] Another study compared levetiracetam with phenytoin and found similar rates of early PTS in each group but increased abnormal electroencephalogram findings with the levetiracetam group.[118] Levetiracetam has been found to be significantly more expensive ($480 vs $37.50 for a 7-day course) than phenytoin (including monitoring with free phenytoin levels) for early PTS prophylaxis.[119]

Anticonvulsants are indicated to decrease the incidence of early PTS.[7] Phenytoin can be considered for early PTS prophylaxis. If administered intravenously, care should be taken to avoid causing hypotension, and fosphenytoin is preferred. Valproate and levetiracetam may be considered equivalent agents, but there may be concerns related to their potential association with adverse effects and increased costs.

Corticosteroids

The use of steroids is associated with increased mortality and is contraindicated (Level I recommendation).[7] The CRASH trial was an international multiinstitutional study that enrolled over 10,000 patients with a GCS score ≤ 14.[112] The corticosteroid group was found to have an increase in overall absolute 14-day and 6-month mortality.[120]

Some authors have suggested that a subgroup of severe TBI patients with adrenal insufficiency might benefit from high-dose corticosteroids.[121] The HYPOLYTE (Hydrocortisone Polytraumatise) trial explored the relationship between the administration of 7 days of hydrocortisone and the incidence of hospital-acquired pneumonia. There was a statistically significant decrease in hospital-acquired pneumonia in the patients treated with hydrocortisone

Class Of Evidence Definitions

Each action in the clinical pathways section of *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
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- 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.

that was also present in the TBI subgroup. Mortality was also noted to be higher in the hydrocortisone group but was not statistically significant.[122] A trial of hydrocortisone and fludrocortisone in severe TBI patients with adrenal insufficiency (Corti-TC: Corticosteroid Therapy for Glucocorticoid Insufficiency Related to TBI) is currently enrolling patients.[123]

Progesterone

Progesterone is a naturally occurring steroid hormone found in higher levels in women than in men. Previous studies involving multiple different animal species and laboratory models have demonstrated improved neurologic outcome after TBI in both males and females when exogenous progesterone is administered. It has been shown that progesterone reduces cerebral edema, improves neuronal survival, and enhances behavioral recovery after TBI. Two human pilot trials demonstrated similar positive benefits, while demonstrating overall safety. The current ProTECT III (Progesterone for the Treatment of TBI) trial is a multicenter phase 3 double-blind placebo-controlled randomized clinical trial of adults with moderate to severe TBI. Utilizing exception from informed consent enrollment in the ED, ProTECT III is a rigorous trial with attention to standardizing the clinical management in the hospital. Progesterone (or placebo) is administered as a continuous infusion, initiated in the ED, and continued for 4 days. This trial is currently enrolling and will further contribute valuable information and understanding regarding a potentially promising therapy.[124,125]

Ketamine

Ketamine is a *N*-methyl-D-aspartate (NMDA) receptor antagonist that has been available for clinical use since 1970.[126] It is unique among sedatives and analgesics because it preserves the patient's respiratory drive while maintaining or enhancing cardiovascular hemodynamics.[127] Despite these favorable characteristics, its use in TBI has been discouraged due to concerns that it raises ICP[128] and/or cerebral

Risk Management Pitfalls For Severe Traumatic Brain Injury

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1. **"The patient was in a car crash and had an obvious femur fracture. I didn't think he needed a point-of-care glucose, given the obvious trauma."**
   All patients with altered mental status must have point-of-care blood glucose testing. Hypoglycemia and hyperglycemia can cause altered mental status, and they are easily reversible with treatment. In patients with a severe TBI, hyperglycemia or hypoglycemia may worsen neurologic outcomes if it is not urgently addressed.

2. **"The patient smelled of alcohol and was obviously intoxicated."**
   Over 60% of all severe TBIs are complicated by alcohol or drug intoxication, which may worsen morbidity. Blood alcohol levels and urine toxicology screens may help prove concomitant intoxication, but based on available history and physical examination, a patient should be aggressively resuscitated for severe TBI.

3. **"I assumed her TBI took precedence and didn't realize she also had a cervical spine fracture."**
   All patients with a severe TBI should be assumed to have a concomitant spine injury until proven otherwise, and spinal immobilization should be maintained. A patient with a severe TBI will be clinically unreliable, and the forces to generate a severe TBI should be assumed to have been transmitted to the spine.

4. **"The CT was normal, so I didn't think she had a TBI."**
   Diffuse axonal injury often has a benign CT appearance, and it contributes significantly to the morbidity and mortality of severe TBI. Patients with diffuse axonal injury are especially susceptible to secondary injuries from hypotension and hypoxia and should be resuscitated aggressively, based on available history and the physical examination.

5. **"The patient had a GCS score of 13 when she arrived but then had a 3-minute generalized tonic-clonic seizure. Afterwards, she didn't return to her previous baseline, so I presumed she was just postictal."**
   If a patient does not return to the previous neurologic baseline after a seizure, be concerned about nonconvulsive status epilepticus or a worsening intracerebral process. Repeat a noncontrast head CT and work quickly to arrange electroencephalograph monitoring. The patient should be aggressively treated for potential status epilepticus, and other causes for neurologic deterioration should be investigated.

metabolic demands.[129] The studies demonstrating these effects were performed on either healthy volunteers[130] using lumbar drain pressures[128] or on patients with known CSF outflow tract obstruction.[131]

Clinical trials have since demonstrated that ketamine, when used in combination with another sedative (eg, propofol or benzodiazepines), either has little effect on ICP[132,133] or reduces ICP[134,135] while maintaining or even improving CPP and reducing vasopressor requirements.[132,133] Additionally, ketamine may increase cerebral blood flow more than it increases metabolic demands,[136] implying that it may help salvage ischemic or damaged brain tissue. Furthermore, there is evidence that ketamine has neuroprotective,[137] antiepileptic,[134] and favorable immunomodulatory properties.[137] Unfortunately, there are no human data available to describe the clinical effects of ketamine when it is used as an induction agent for RSI in TBI patients.

Given the harm associated with brief episodes of hypotension and/or low CPP in severe TBI patients, ketamine (with its favorable side-effect profile, including elevated or protected blood pressure/CPP) should be considered for use in combination with propofol or midazolam as an RSI induction agent or sedative in the mechanically ventilated patient with hemorrhagic shock.[127] At this time, there are no known ongoing clinical trials that will help to better elucidate the utility of ketamine in TBI.

Hypothermia

Mild therapeutic hypothermia has proven to be effective in preventing neurologic damage after cardiac arrest.[138] The success of this therapy has drawn attention to its potential application to other neurologic disorders, such as stroke, spinal cord injury, and TBI. There have been several small randomized controlled trials utilizing early hypothermia for severe TBI, but they have failed to demonstrate consistent clinical benefit for improved neurologic recovery or mortality.[139,140] The 2007 BTF guidelines addressed hypothermia therapy and note that the

Risk Management Pitfalls For Severe Traumatic Brain Injury

(continued from page 18)

6. **"The patient had a stable GCS score of 10 an hour ago, but we just discovered he has a blown pupil."**
   TBI is a dynamic process, especially in the first 24 hours. These patients should be monitored closely, and the emergency clinician should anticipate deterioration and be prepared to intervene immediately.

7. **"The patient had a GCS score of 3, and the intern performed the intubation. It went well, but the postintubation blood gas showed a $PaCO_2$ of 20 mm Hg."**
   Care must be taken to avoid routine or prophylactic hyperventilation. Monitor the respiratory rate, especially immediately postintubation when the patient is hand-bagged. The resultant vasoconstriction from lowering the $PaCO_2$ can decrease cerebral blood volume and CPP, worsening secondary injuries.

8. **"The patient's blood pressure kept dropping to 80 mm Hg, and despite 4 L of normal saline, I couldn't keep him normotensive, so I started norepinephrine."**
   Over 60% of patients with a severe TBI have other occult traumatic injuries. A hemodynamically unstable patient should initially be assumed to be in hemorrhagic shock and the source of bleeding investigated. Even a single episode of hypotension can worsen neurologic morbidity and mortality.

9. **"The patient had a GCS score of 9, and the CT didn't look that bad, so I admitted him to our local community medical ICU."**
   Patients with a severe TBI should be managed with early collaboration with trauma surgery and neurosurgery. Special consideration should be given to managing these patients in a neurologic ICU by neurointensivists or intensivists with experience managing neurologic disorders and secondary injury after severe TBI.

10. **"I gave my patient lidocaine as an ICP pretreatment medication prior to intubation, but while I was waiting 3 minutes for it to circulate, her SpO_2 kept dropping below 90% and she seemed to aspirate."**
    Prevention of hypoxia and hypotension are key in avoiding secondary injuries. Given the data on pretreatment to blunt ICP elevations prior to intubation, care should be taken to efficiently intubate the patient without hypoxia or hypotension, even at the expense of a pretreatment agent.

"available pooled data indicated that prophylactic hypothermia is not significantly associated with decreased mortality when compared with normothermic controls."[7] Although not consistent across all trials, hypothermia is associated with higher Glasgow Outcome Scale (GOS) scores compared to normothermia (Level III evidence).[7] Study outcomes involving hypothermia as a neuroprotectant after TBI as they pertain to critical elements such as depth of hypothermia (mild > 33°C vs moderate 30°C-33°C), duration of therapy, and method of hypothermia (surface vs endovascular) have been mixed. Mild hypothermia has been demonstrated to decrease ICP,[139,140] but a well-designed large randomized controlled trial with appropriate outcome measures is needed to define the efficacy of therapeutic hypothermia. At this time, induced hypothermia is not recommended for patients with severe TBI.

Antifibrinolytics: Tranexamic Acid

Tranexamic acid (TXA) blocks the conversion of plasminogen to plasmin. Since its introduction in 1966, it has been used for aneurysmal subarachnoid hemorrhage, upper gastrointestinal bleeding, hemorrhagic stroke, and traumatic hyphema as well as during oral, gynecologic, and orthopedic surgery, cardiopulmonary bypass, and liver transplantation. It is currently FDA approved (as an injection) for hemophiliacs during tooth extraction and as an oral agent for cyclic heavy menstrual bleeding.

A nested cohort of 270 patients with a GCS score ≤ 14 from the 2010 CRASH-2 trial demonstrated a reduction in intracranial hematoma growth, focal cerebral ischemia, and mortality in patients given TXA, although none of the results were statistically significant.[141,142] CRASH-3 will study TXA in trauma patients with a GCS score < 13; it is anticipated to be completed by January 2017.[143]

Hyperosmolar Therapy

Hyperosmolar therapy is commonly used to manage elevated ICP in severe TBI, but the optimal agent remains controversial. Mannitol has the most evidence and clinical experience with its utilization. HTS has shown promise, but it does not have strong evidence to support its routine use and/or recommendation. Regardless of which agent is administered, the use of hyperosmolar therapy in the ED should be reserved for signs of herniation or acute neurologic deterioration (once extracranial causes are ruled out). If intracranial monitoring (ICP, PaO_2, microdialysis, jugular venous saturation, etc) is placed in the ED, the use of hyperosmolar therapy is a part of a more complicated discussion and larger treatment algorithm.

Mannitol is a sugar alcohol that functions as a potent osmotic diuretic. It is filtered by the renal glomeruli but is not resorbed by the renal tubule. This results in an osmotic gradient in the renal tubule and an increased excretion of free water and sodium.[145] Mannitol has a high coefficient of reflection at the blood-brain barrier, and it works by several mechanisms to decrease ICP. Similar to the renal tubule, mannitol causes a shift of free water out of the cerebral tissue and, therefore, a reduction of edema and overall brain mass.[145] Similar fluid shifts occur from the interstitium to the vascular space throughout the body, and an increase in cardiac output is seen (prior to the free water excretion). As a transient plasma volume expander, mannitol indirectly reduces the hematocrit and blood viscosity, which leads to increased cerebral blood flow and oxygen delivery. Mannitol is also known to decrease CSF production, further reducing intracranial contents and decreasing ICP. In patients with a disrupted blood-brain barrier, mannitol can cross into the cerebral tissue and cause a delayed, rebound increased ICP. This negative effect of the osmotic gradient draws free water back into the brain, causing increased edema.[145] Mannitol is dosed at 0.5 to 1 g/kg as a bolus. It can be given every 2 to 8 hours, but it should not be used in a hypovolemic or underresuscitated patient, as hypovolemia, hypotension, and decreased cerebral perfusion can occur.

HTS ranges from 3% to 30% saline, and its use should be guided by clearly defined protocols, as dosing regimens and preferences for use vary widely among practitioners. HTS does not induce diuresis and, instead, functions as a plasma expander. Similar to mannitol, HTS functions with an osmolar gradient to draw free water from the tissues into the vasculature. HTS has a higher coefficient of reflection at the blood-brain barrier than mannitol, and it is more likely to stay in the vasculature and maintain an elevated osmolality, contributing to a robust intravascular resuscitation while minimizing the possibility of a rebound elevation in ICP.[146] HTS has been reported to have vasoregulation, immunologic, and excitotoxic cellular effects, all of which need further study in clinical trials.[147] Several trials have suggested that HTS has similar-to-improved ICP control and brain tissue oxygenation over mannitol, but definitive improvement in mortality and/or neurologic improvement have not been demonstrated.[44]

Although there is not a clear consensus or guideline recommendation for the use of HTS, the emergency clinician must be versed in its use, as it is commonly used in clinical practice.[148] Relatively little is known regarding the risks of mannitol when given in combination with HTS or when used for longer periods of time (> 24 h). Osmotic agents should be reserved for clinical evidence of acute herniation or neurologic deterioration unexplained by any other cause. HTS can be considered for prophylactic use or for continued ICP elevation, although the evidence to support this is not strong. Mannitol

and 3% HTS can be given through a peripheral IV line. Concentrations of ≥ 3% of HTS should be given through central access, except during emergencies. Emergency clinicians should work closely with their neurosurgery and trauma colleagues to review best available evidence and develop protocols that best serve their patient populations.

Reversal Of Anticoagulation

The population is aging, and there is a growing use of oral anticoagulation agents for various medical comorbidities. **(See Table 6.)** In addition to the growing number of patients who require anticoagulation, there is a wide variety of agents available. Several studies have confirmed that patients with a severe TBI who are therapeutically anticoagulated have higher mortality and worse neurologic outcomes.[107,149] There have not been many studies that investigate the benefits of reversing anticoagulation in trauma patients, but others have demonstrated benefit in patients with spontaneous intracranial hemorrhage. Given the current evidence, it is reasonable and logical to attempt to reverse anticoagulation in patients with severe TBI. For more information on the management of coagulopathy, see the January 2011 issue of *Emergency Medicine Practice*, "An Evidence-Based Approach to Managing The Anticoagulated Patient In The Emergency Department" and Volume 2, Number 2 of *EM Critical Care*, "Emergency Management Of Coagulopathy In Acute Intracranial Hemorrhage."

The development and approval of new anticoagulants adds additional medications that can contribute to increased morbidity and mortality with severe TBI. Whereas these agents do not require frequent monitoring and likely have similar (or better) efficacy with less bleeding complications and fewer food and medication interactions, they also do not have readily available and approved reversal agents.[150] Rivaroxaban is an oral, lipophilic, reversible competitive antagonist of activated factor X (Xa), and dabigatran is an oral, lipophilic, direct, reversible competitive antagonist of thrombin (factor IIa). There are currently no reversal agents or antidotes available for rivaroxaban or dabigatran, and their anticoagulant effects will not be reversed by administration of vitamin K or plasma. Dialysis is an effective option for the removal of dabigatran, but due to being highly protein-bound, dialysis has no utility for removal of rivaroxaban. Emergency clinicians can consider dialysis in appropriate patients on dabigatran, taking into account the systems and operational issues associated with dialysis in the critically ill.

Disposition

Patients with a severe TBI should be managed with early collaboration of trauma surgery and neurosur-

Table 6. Reversal Of Anticoagulation

Anticoagulant	Reversal Agent	Dose	Cautions
Warfarin	Vitamin K	10 mg IV	• Requires dilution in at least 50 mL • Must be infused slowly over 30-60 min
	Fresh frozen plasma	15-20 cc/kg	• Intravascular volume • Follow INR
	Factor VIIa	Not recommended for acute resuscitation	• Increased thromboembolic events • May be used intraoperatively, at surgeon's discretion
	Prothrombin complex concentrates	Variable, based on manufacturer	• Markedly expensive • Not widely available • No trials to demonstrate benefit • Contain factors II, VII, IX, and X • Small volume • No need for ABO typing • Rapid administration
• Heparin • LMWH	Protamine	• 0.5-1 mg/100 units heparin • 0.5-1mg/1 mg LMWH • Max 50 mg	• Administer over 10 min to avoid hypotension • Follow factor Xa levels with LMWH (not aPTT)
• Aspirin • Clopidogrel	Platelets	6-8 random donor platelet concentrates	• Platelets likely to be affected by residual antiplatelet activity • Reserve platelets for patients going to the OR or who are actively bleeding, or when guided by consultants or local protocol • Evidence mixed; no clear benefit; can consider
	Desmopressin	0.3 mcg/kg IV	• May shorten prolonged bleeding time • Unable to recommend at this time due to lack of evidence

Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ratio; IV, intravenous; LMWH, low-molecular-weight heparin; NA, not applicable; OR, operating room.

gery colleagues. If consultation is not readily available, the emergency clinician should quickly stabilize the patient and arrange transfer to a facility capable of managing severe TBI. Patients who are operative candidates should not be delayed en route to the operating room. All severe TBI patients should be managed in an ICU by clinicians familiar with current severe TBI management guidelines. Special consideration should be given to managing these patients in a neurologic ICU by neurointensivists or intensivists with experience managing neurologic disorders.

Summary

Severe TBI is the leading cause of death and disability in young people, and it is a complex disease process. Despite years of research and new technology, adjusted mortality rates remain near 25%. The emergency clinician serves a critical role in the early identification and management of these patients. Because the primary injury is irreversible, the prevention and treatment of secondary injuries is paramount to reducing long-term neurologic morbidity and ultimate mortality. The focus of the initial resuscitation should target normal physiologic goals and appropriate disposition to centers with neurologic and critical care expertise in managing these patients. Current research is promising, but, at present, early aggressive care focusing on the basic tenets of resuscitation is the mainstay. Finally, all attempts at neurologic prognosis should be avoided for at least the first 24 hours, even in the face of an apparently devastating injury.

Case Conclusions

The 27-year-old male was successfully intubated after premedication with fentanyl and RSI with etomidate and succinylcholine and was placed on mechanical ventilation, with the tidal volume calculated for 8 cc/kg per ideal body weight. He was monitored with continuous $ETCO_2$ capnography, and his CO_2 target was 40 mm Hg. Sedation and analgesia were administered via continuous infusions of propofol and fentanyl, and he received an initial dose of levetiracetam for seizure prophylaxis. The trauma and neurosurgery teams were activated, and he received a cranial, cervical spine, abdomen, and pelvis CT. His injuries were limited to his head, where he was noted to have diffuse axonal injury, scattered subarachnoid hemorrhage, a frontal intraparenchymal contusion, and a small subdural hematoma. His spine was radiographically cleared of fractures, and the head of the bed was raised to 30°. The neurosurgeon elected to transfer the patient to the neurologic ICU for placement of a ventriculostomy, brain tissue oxygen monitoring, and continuous EEG. The patient ultimately did not require surgical intervention, his ICP was medically managed, and he was ultimately discharged with a tracheostomy and percutaneous enterogastrostomy to a long-term acute care facility after 14 days. After 9 months of intensive physical, occupational, and speech therapy, he was functionally independent and back at work with mild right-leg weakness, short-term memory loss, and occasional word-finding deficits.

The 84-year-old female was successfully intubated and placed on mechanical ventilation with continuous sedation and analgesia infusions with propofol and fentanyl. Her head of bed was maintained at 30°, and she was gently hyperventilated with continuous capnography monitoring for a CO_2 level of 30 mm Hg. You notified the neurosurgeon, and she was transported to the CT scanner. Her INR was 2.8, and her CT demonstrated a large right subdural hematoma. You administered fresh frozen plasma (20 cc/kg) as prothrombin complex concentrate was not available, and administered vitamin K intravenously. After the fresh frozen plasma was complete, the repeat INR was 1.5, and the patient was taken emergently to the OR for evacuation. She was monitored in the ICU and treated for nonconvulsive status epilepticus. After a 10-day ICU stay, she was discharged to a nursing home awake, alert, and confused, with moderate cognitive deficits.

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 will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

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1. What is the leading cause of death in children < 2 years of age?
a. Falls
b. Motor vehicle accidents
c. Nonaccidental trauma
d. Sepsis

2. Which of the following is not a subcategory of severe TBI?
a. Subdural hematoma
b. Epidural hematoma
c. Diffuse axonal injury
d. Depressed skull fracture

3. An 18-year-old male is transported to the ED by EMS after a motor vehicle collision. His eyes are closed but open with painful stimuli. He does not respond when asked questions but moans with painful stimuli. He flexes his right upper extremity, withdraws his left upper extremity, and extends his bilateral lower extremities to pain. What is his GCS score?
a. 6
b. 7
c. 8
d. 9

4. In a patient with a severe TBI who has a fixed and dilated pupil and flexion posturing, what is the target $ETCO_2$ after appropriate ventilator management?
a. 10 mm Hg
b. 20 mm Hg
c. 30 mm Hg
d. 40 mm Hg

5. Which of the following would be the best selection for crystalloid fluid resuscitation of a patient with a severe TBI?
a. D5 normal saline
b. D5 ½ normal saline with 20 meq KCl/L
c. ½ normal saline with 20 meq KCl/L
d. Normal saline

6. In patients with severe TBI, it is most important to prevent which of the following?
a. Heart rate > 120 beats/min
b. Respiratory rate > 20 breaths/min
c. SBP < 90 mm Hg
d. Temperature < 39.2°C

7. ED management of the severely head-injured patient can reverse or prevent all of the following except:
a. Seizures
b. Diffuse axonal injury
c. Cytotoxic cerebral edema
d. Increased ICP

8. Which of the following is an acceptable treatment option for the management of elevated ICP?
a. Surgical intervention
b. Cerebrospinal fluid diversion
c. Osmotic therapy
d. All of the above
e. None of the above

9. Which of the following is contraindicated in the management of a patient with a severe TBI?
a. Dexamethasone
b. Progesterone
c. Ketamine
d. Antiepileptic drugs

10. What is the appropriate dose of fresh frozen plasma for warfarin-related anticoagulation reversal?
a. 5 cc/kg
b. 10 cc/kg
c. 15 cc/kg
d. 25 cc/kg

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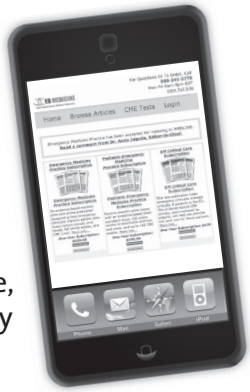

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Physician CME Information

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Accreditation: EB Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. This activity has been planned and implemented in accordance with the Essential Areas and Policies of the ACCME.

Credit Designation: EB Medicine designates this enduring material for a maximum of 4 *AMA PRA Category I Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ACEP Accreditation: *Emergency Medicine Practice* is approved by the American College of Emergency Physicians for 48 hours of ACEP Category I credit per annual subscription.

AAFP Accreditation: This Medical Journal activity, *Emergency Medicine Practice,* has been reviewed and is acceptable for up to 48 Prescribed credits by the American Academy of Family Physicians per year. AAFP accreditation begins July 31, 2012. Term of approval is for one year from this date. Each issue is approved for 4 Prescribed credits. Credit may be claimed for one year from the date of each issue. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AOA Accreditation: *Emergency Medicine Practice* is eligible for up to 48 American Osteopathic Association Category 2A or 2B credit hours per year.

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: Upon completion of this article, 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.

Faculty Disclosure: It is the policy of EB Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. In compliance with all ACCME Essentials, Standards, and Guidelines, all faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Dr. Zammit, Dr. Borczuk, Dr. Legome, and their related parties report no significant financial interest or other relationship with the manufacturer(s) of any commercial product(s) discussed in this educational presentation. Dr. Knight reported a relevant financial interest in Genentech, Inc. in the form of honoraria for lectures, papers, or teaching. Dr. Jagoda reported the following financial interests: Brain Trauma Foundation, advisory board member honoraria and research funding; Banyan Biomarkers, Inc., honoraria; United States Department of Defense, research funding.

Commercial Support: This issue of *Emergency Medicine Practice* did not receive any commercial support.

Method of Participation:

- **Print Semester Program:** Paid subscribers who read all CME articles during each *Emergency Medicine Practice* 6-month testing period, complete the CME Answer and Evaluation Form distributed with the June and December issues, and return it according to the published instructions are eligible for up to 4 hours of CME credit for each issue.
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Hardware/Software Requirements: You will need a Macintosh or PC to access the online archived articles and CME testing.

Additional Policies: For additional policies, including our statement of conflict of interest, source of funding, statement of informed consent, and statement of human and animal rights, visit http://www.ebmedicine.net/policies.

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