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Traumatic brain injury (TBI) is a leading cause of mortality in the United States and represents over half of trauma related deaths.[1,2] Approximately 1.4 million people suffer from a TBI each year.[3] (See Figure 1.) Of these, 1.1 million are evaluated in the emergency department (ED) and subsequently discharged home while another 235,000 are admitted. Of those admitted, approximately 50,000 die annually. Those 14 years and younger accounted for 435,000 ED visits, 37,000 hospitalizations, and more than 2,600 deaths. Males are 1.5 times more likely than females to sustain TBI. Those between the ages of 0–4 years and 15–19 years have the highest TBI-related ED visits, however, adults older than 75 years have the highest rates of TBI-related hospitalization and death.[3] The authors comprehensively review the presentation and management of patients with TBI.

— The Editor

Traumatic Brain Injury

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Introduction

By the year 2030, the number of persons older than age 65 will double relative to 2000, representing almost 20% of the nation's total population.[4] As the population ages, so does the number of elderly people who are admitted to trauma centers with TBI. Older age has been well recognized as an independent predictor of worse outcome after TBI, even with relatively minor head injuries.[6,7]

The Centers for Disease Control and Prevention estimates currently there are at least 5.3 million Americans who have long-term or life-long disability as a result of TBI,[8] with an additional 80,000–90,000 added annually.[3] In 2000, the estimated direct and indirect medical costs including injury-related work loss, disability and lost income from pre-mature death as a result of TBI was $60 billion.[9]

Falls are the leading cause of TBI with motor vehicle collisions (MVC) second. *(See Figure 2.)* However, for those age

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15–19, MVCs are the leading cause of TBI.[3] Overall, MVCs result in the greatest number of all TBI-related hospitalizations, while firearm use is the leading cause of death related to TBI.[3,10]

Pathophysiology

The cranium is a rigid vault that contains three compartments: brain tissue, blood, and cerebrospinal fluid (CSF); the pressure in the skull exerted by these elements is termed intracranial pressure (ICP). According to the Monroe-Kellie doctrine, the intracranial volume is a fixed space and additional collections, such as mass lesions or hemorrhage, must be accompanied by a decrease in another compartment, or ICP will increase. Various intrinsic mechanisms exist to prevent increases in ICP after trauma. These include shunting of the CSF to the spinal subarachnoid space, increasing CSF absorption and shunting venous blood out of the skull.[11] However, eventually this compensation fails and ICP rises.

Cerebral perfusion pressure (CPP) is used as an estimate of cerebral blood flow (CBF), which is difficult to accurately measure clinically. CPP is the difference between the mean arterial pressure (MAP) and the ICP (CPP = MAP - ICP). Normal ICP is 0–10 mmHg, and therefore CPP closely relates to the MAP. Under normal conditions, when CPP is between 50 mmHg and 150 mmHg, the brain has the ability to autoregulate to maintain a constant CBF. However, after TBI, autoregulation fails and the relationship between CPP and CBF becomes linear.[12] This results in increased CBF (and ICP) as CPP increases.

TBI results from both direct and indirect forces. Direct injury is a result of the initial insult and typically occurs at site of impact. Indirect forces are a consequence of the acceleration/deceleration of the brain tissue within the skull and cause injury on the opposite side of impact (coup-contrecoup injury). In addition, this acceleration/deceleration mechanism can cause shearing of neurons, causing diffuse axonal injury (DAI).

TBI may further be classified as primary and secondary injury. Primary injury is a result of the initial trauma, and occurs at the time of injury. These injuries are irreversible, and thus efforts must be aimed at injury prevention. However, after TBI, a cascade of cellular events begins that leads to what is known as "secondary injury." It is the leading cause of in-hospital death after TBI.[13] Most secondary brain injury is the result of cerebral edema with a resultant increase in ICP and decrease in CPP leading to ischemia.[14] As autoregulation fails, CBF and CPP become directly proportional. The increase in ICP lowers the threshold of systemic blood pressure for cerebral ischemia. Secondary injury should be differentiated from secondary insults. The former is a direct result of the primary injury. The latter is a result of discrete, sometimes iatrogenic processes independent of the primary injury.

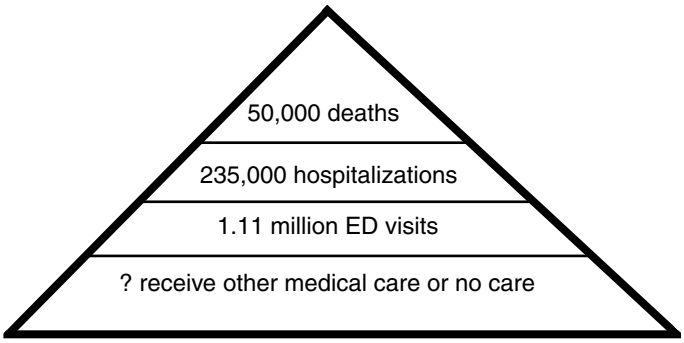
Hypoxia and hypotension are two examples of secondary insult. They often occur in patients with TBI prior to the arrival of pre-hospital providers or arrival to the hospital and are independently associated with significant increases in morbidity and mortality.[15] A single episode of hypotension has been shown to double mortality rates in patients with TBI.[15] Clinical decisions should attempt to minimize secondary insult and improve clinical outcome.

Intracranial Hematomas and Contusions

Subdural Hematoma. Subdural hematoma (SDH) is a result of sudden acceleration/deceleration tearing of the bridging veins. Blood accumulates between the dura matter and the arachnoid, and radiographically it appears as a crescent- or sickle-shaped collection. *(See Figure 3.)* Brain atrophy is common in the elderly and alcoholics, making them more susceptible to SDH. Although the blood accumulates slowly, due to it venous origin, SDH is associ-

Figure 1. TBI in the United States Annually

At least 1.4 million traumatic brain injuries (TBIs) occur in the United States each year:*



*Average annual numbers, 1995-2001.

Source: Langlois JA, Rutland-Brown W, Thomas KE. Traumatic brain injury in the United States: Emergency department visits, hospitalizations, and deaths. Atlanta (GA): Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2004.

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This CME/CNE activity is intended for emergency, family, osteopathic, trauma, surgical, and general practice physicians and nurses who have contact with trauma patients.

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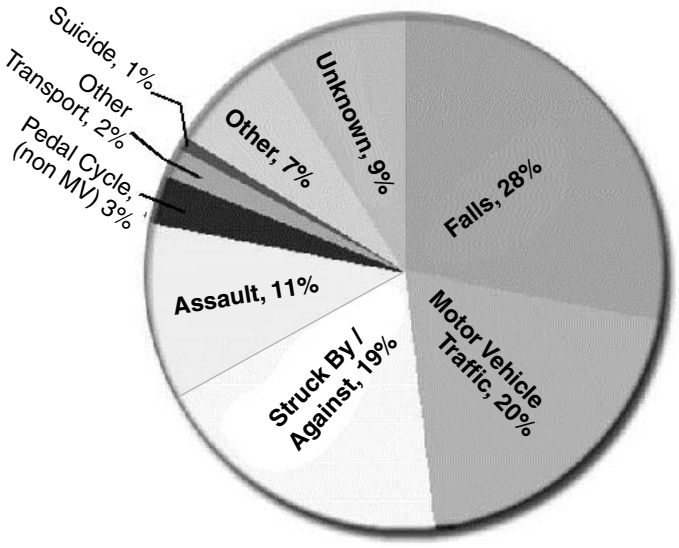
Figure 2. Causes of TBI



Source: Centers for Disease Control and Prevention (CDC), National Center for Injury Prevention and Control. Traumatic brain injury in the United States–A report to Congress. Atlanta (GA): Centers for Disease Control and Prevention; 1999.

ated with more brain parenchymal damage, as opposed to other types of TBI, and thus has worse outcome. However, early surgical evacuation, within four hours of injury, decreases mortality.[16]

SDH accounts for approximately 25%–30% of TBI[17] and can be classified as acute (< 48 hours), subacute (2–14 days) or chronic (> 14 days). Patients with an acute SDH will often present unconscious or with lateralizing signs on exam. (i.e., a unilateral, non reactive, dilated pupil) More chronically, these patients may have a gradual decline in consciousness. Others may have balance issues that will often lead to presentation to the ED. Radiographically acute SDH appear as hyperdense (white) lesions, while subacute and chronic SDH are isodense and hypodense, respectively.

Epidural Hematoma. Epidural hematomas (EDH) typically result from tearing of the middle meningeal artery associated with temporal bone fractures. Blood accumulates between the skull and the dura and gives a biconvex-, lens-, or football-shape collection on CT scan. *(See Figure 4.)* They are more common in younger people and are rare in the elderly and those younger than 2 years of age. In the elderly, the dura is tightly adhered to the skull; thus, blood does not accumulate in this space.

The classic description of a patient with an EDH is someone who loses consciousness immediately after TBI and then awakens to a normal state of consciousness. As the EDH continues to expand, the patient once again loses consciousness. This "lucid interval"' in reality occurs in only 20%–30% of patients.[17] EDHs are not parenchymal injuries, and thus rapid diagnosis and treatment is imperative to prevent herniation and improve outcome.

Subarachnoid Hemorrhage. Traumatic subarachnoid hemorrhage (tSAH) results from injury to arteries surrounding the subarachnoid space. This leads to buildup of blood between pia mater and the arachnoid. On CT scan, blood is seen in the basal cisterns, and hemispheric sulci and fissures. *(See Figure 5.)* The blood is spread diffusely and does not cause a mass effect. Posttraumatic SAH is, however, a marker of severity of injury. Multiple studies have demonstrated those with tSAH on admission CT scan have poorer outcome compared to those who do not have tSAH[18-20]; this is likely related to the initial mechanical damage, as opposed to delayed secondary injury.[19]

Much like aneurysmal SAH, up to 20% patients with tSAH may develop vasospasm.[21] This sometimes leads to hydrocephalus from decreased CSF absorption when the arachnoid villi get obstructed by blood product degradation.[21] Temporary ventriculostomy placement or a permanent ventriculo-peritoneal shunt is sometimes required.[22]

Intracerebral Hematoma/Contusion. Intracerebral contusions result from the brain parenchyma's impact with the skull. *(See Figure 6.)* Typically they are found in the frontal and temporal regions of the brain. Coup contusions occur at the site of impact, where as contrecoup injuries occur at the opposite side of impact. Contusions often evolve over time and increase in size on subsequent CT scans. As they increase in size, the mass effect and cerebral edema worsen and patients often deteriorate.

Diffuse Axonal Injury. Diffuse axonal injury (DAI) is a result of shearing of the axons in the white matter and brainstem during sudden deceleration. These injuries often are not dramatic on the initial CT scan, but clinically the patient has significant neurologic deficits.

Clinical Classification of Traumatic Brain Injury

Glasgow Coma Scale. The Glasgow Coma Scale (GCS) was first described in 1974.[23] The scale was developed to standardize a neurological scoring system and allow reliable inter-observer evaluation of patients with TBI. GCS is best evaluated after resuscitation, as hypoxia, hypotension, hypothermia, or hypoglycemia may cause a decreased mental status unrelated to TBI. The scale is based on three aspects of neurologic function: eye opening, verbal functioning, and motor function. *(See Table 1.)* The best response from each section is added together for a final score ranging from 3 to 15. For those who are intubated, the verbal scale can be replaced with "T," and thus the best response becomes an "11T."

A single score is insufficient to determine the extent of injury, and serial examinations should be performed. Patients who are intubated cannot be assessed for the verbal component, and those chemically paralyzed cannot be assessed for any of the three categories. In addition, those with severe facial trauma may not be physically able to open their eyes due to edema. Patients with a GCS of 13–15 are classified as having mild TBI, 9–12 as moderate, and 3–8 as severe. However, some consider a GCS of 13 to be a moderate TBI.

Mild Traumatic Brain Injury. Mild traumatic brain injury (mTBI), often called a concussion, is one of the most common neurologic disorders and accounts for approximately 80% of TBI. It is defined as an injury to the head from blunt trauma or accelerated/decelerated forces with one or more of the following associated conditions: transient confusion, disorientation or impaired consciousness; memory loss around the time of injury; and/or loss

Figure 3. Subdural Hematoma

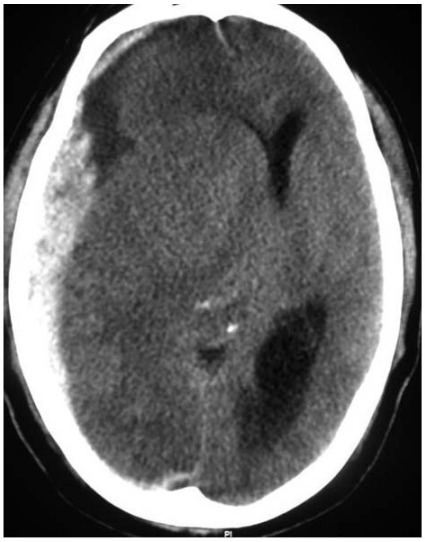


Figure 4. Epidural Hematoma

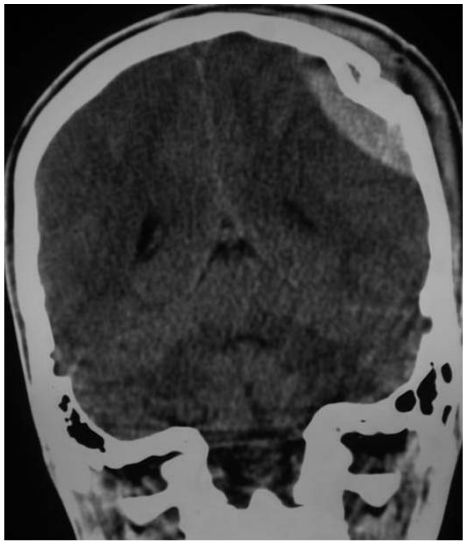


Figure 5. Subarachnoid Hemorrhage

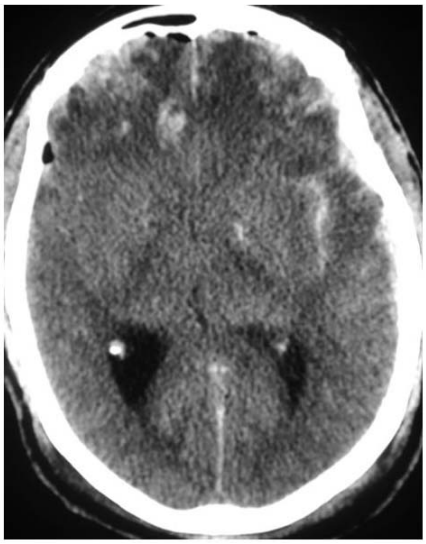
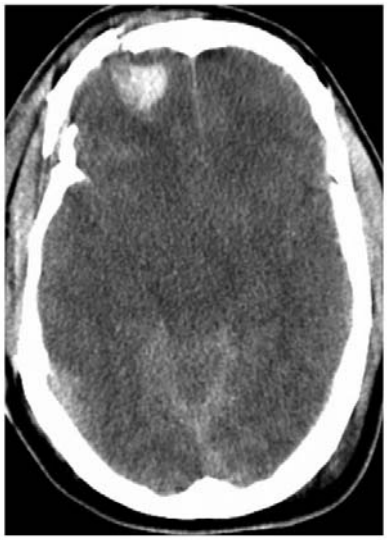


Figure 6. Intracerebral Contusion



of consciousness for less than 30 minutes.[24] Seventy-five percent of all patients with TBI have mTBI, at a cost of nearly $17 billion a year.[25,26] Although most patients with mTBI recover fully, up to 15% of patients may have persistent disabling problems.[27]

Moderate Traumatic Brain Injury. Moderate injuries account for approximately 10% of patients with TBI. Although not often studied, those with moderate TBI often have abnormalities on CT scan and frequently need surgical intervention. In 1982, Rimel and colleagues reported on a series of patients with moderate TBI as defined by GCS.[28] Thirty percent of patients who had a CT scan performed had a mass lesion, and more than 90% of those with a mass lesion had an operative intervention. In 1992, Stein and Ross also demonstrated an increased risk of intracranial lesions and need for operative intervention in a cohort of moderate TBI patients.[29] Thirty percent of their patients with moderate TBI had CT abnormalities; 20% required surgical intervention.

Severe Traumatic Brain Injury. Severe TBI accounts for the remaining 10% of brain injuries. The mortality is considerably higher and the functional recovery is considerably lower in those with severe TBI as compared to those with mild and moderate TBI. The primary management goals for patients with severe TBI center on identifying mass lesions, treating other life-threatening injuries, and preventing secondary brain insult. The remainder of this article will predominantly focus on those with severe traumatic brain injury.

Pre-hospital Care

The pre-hospital management of TBI is critical to maximizing good outcome and the care provided by EMS affects the outcome of a patient with TBI.[30]

Establishing a definitive airway, if necessary; cervical spine immobilization; intravenous access; and controlling hemorrhage

Table 1. Glasgow Coma Scale

SCORE	EYE OPENING	MOTOR	VERBAL
6	—	Follows commands	—
5	—	Localizes (cross midline)	Alert and oriented
4	Spontaneous	Withdraws	Disoriented conversation
3	To voice	Flexes arms (decorticate)	Nonsensical speech
2	To pain	Extends arms (decerebrate)	Moan/unintelligible speech
1	No response	No response	No response

Table 2. Risk Factors for Post-traumatic Seizures

- Glasgow coma score < 10
- Cortical contusion
- Depressed skull fracture
- Subdural hematoma
- Epidural hematoma
- Intracerebral hematoma
- Penetrating head wound
- Seizure within 24 hours of injury

are primary EMS goals. Once a possible TBI is identified, EMS must triage the patient to a facility capable of definitive care. In a large, prospective study, Härtl and colleagues demonstrated a 50% increase in mortality for patients with TBI who were not transported directly to a center that could provide definitive care.[31] Helicopters have been shown to rapidly transport patients over long distances, allowing for earlier definitive care.[32] Davis and colleagues demonstrated that aeromedical response teams appear to improve outcomes in patients with moderate to severe TBI.[33]

Hypoxia at any time will also increase mortality.[15,34] In 2007, The Brain Trauma Foundation (BTF) recommended that any patient with severe TBI who is unable to maintain an adequate airway or pulse oximeter of greater than 90% despite supplemental oxygen should have an airway secured.[35] However, there is very little objective data supporting prehospital airway management. In fact, many studies suggest that outcomes are worse in TBI patients who are intubated prehospital.[36-40] Longer scene times, hyperventilation after intubation, or persistent hypoxia during failed intubations have all been suggested as explanations for worse outcomes. Some authors have suggested a survival benefit from prehospital intubation when performed by more experienced providers, including physicians and flight nurses.[33,41,42]

During initial evaluation and transport by EMS, it is imperative to avoid hypotension. However, the ideal intravenous fluid has not been determined.[43-45] Isotonic fluids are used most commonly. Solutions containing glucose can worsen cerebral edema, and thus should not be used. Hypertonic saline expands intravascular volume, thus stabilizing blood pressure. Smaller volumes of hypertonic saline can be used, thus minimizing potential complications such as extravascular fluid accumulation, cerebral edema, and increased ICP. Although some studies have demonstrated a survival benefit from hypertonic saline in patients with severe TBI in the pre-hospital phase, long-term neurological benefit has yet to be established.[43-45]

ED Evaluation and Management

Upon the patient's arrival at the ED, multiple simultaneous events occur. Beginning with airway, breathing, and circulation, the emergency physician needs to rapidly assess for other life-threatening injuries. For those in a small hospital setting without immediate neurosurgical consultation, steps to facilitate transfer to a tertiary care center should begin early. In addition, the past medical history of the patient, such as anti-platelet or anticoagulation therapy, may elucidate additional risk factors for TBI or other injuries.

Airway. In patients with TBI, hypoxia worsens outcome. Thus, early intubation in the ED seems wise. Those with a GCS of < 9 warrant endotracheal intubation for definitive airway protection. All trauma patients should be considered to have a cervical spine injury until proven otherwise. Thus, cervical spine precautions need to be used during intubation.

During laryngeal manipulation and tracheal intubation, increases in blood pressure and heart rate may cause an increase in ICP. Lidocaine is believed to blunt these increases in ICP during intubation. In addition, lidocaine is thought to reduce cerebral blood flow, cerebral vascular resistance, cerebral metabolism as well as catecholamine release, minimizing ICP elevation during intubation.[46-48] However, a 2001 systematic literature review by Robinson and Clancy failed to demonstrate a reduction in ICP or improved neurological outcome when using lidocaine as a pretreatment during rapid sequence intubation in patients with TBI.[49]

Controversy also exists as to whether lidocaine usage worsens outcome. In a 1990 study by Asfar and Abdulla, the addition of lidocaine to thiopental and succinylcholine caused a significantly lowered blood pressure compared to those who did not receive lidocaine.[50] Others, however, have demonstrated no hemodynamic effects of lidocaine.[46-49] Some authors believe this drop in blood pressure from the lidocaine is related to the co-administration of the thiopental, an agent known to drop mean arterial blood pressure.[51] Lidocaine's ability to blunt the sympathetic response with the use of thiopental may explain the significant drop in blood pressure.[51]

Other pretreatment medications include fentanyl, which not only provides analgesia but is usually not hemodynamically compromising. However, in patients who are not adequately resuscitated, fentanyl may cause hypotension. In addition to fentanyl, defasciculating doses of a non-depolarizing neuromuscular blocking agent, such as rocuronium (0.06 mg/kg), vecuronium (0.01 mg/k), or even pancuronium (0.01 mg/kg) can be used.

Multiple induction agents can be used during intubation. The ideal agent should both blunt increases in ICP and lower mean arterial blood pressure. Etomidate (0.3 mg/kg) has minimal cardiovascular effects and is an ideal choice. However, recent controversy has suggested that etomidate may be associated with adre-

nal suppression.[52,53] A short-acting barbiturate, such as thiopental (3–5 mg/kg) is an alternative choice. If a patient presents hypotensive, a lower dose of thiopental (0.5–1 mg/kg) is recommended. Agents such as ketamine are traditionally not recommended, as they can increase ICP.

Breathing. Traditional management of patients with TBI once included hyperventilation to an arterial $PaCO_2$ < 25 mmHg. Hyperventilation causes cerebral vasoconstriction, thus lowering cerebral blood flow (CBF) and ICP.[54] A 1995 survey indicated that 83% of trauma centers were using hyperventilation as a tool to lower ICP.[55] However, after TBI, patients have 50% less CBF than normal people, and thus, lowering cerebral blood even further can cause cerebral ischemia. Multiple studies have demonstrated that prophylactic hyperventilation increases cerebral ischemia with a resultant worsening of outcome in patients with TBI.[56,57] Currently, the BTF does not recommend prophylactic hyperventilation and further suggest it be used only as a temporizing measure for the reduction of ICP.[58] Currently, common practice is to maintain an arterial $PaCO_2$ at 35 mmHg to 40 mmHg.

Circulation. Delayed resuscitation may improve outcomes in the patient with penetrating trauma.[59] However, this may not be wise after TBI as a single episode of systolic blood pressure below 90 mmHg doubles mortality.[15,60] No literature to date supports an ideal fluid in the ED for the resuscitation of a patient with TBI. In 2007, a post hoc analysis of the SAFE trial demonstrated the use of albumin in patients with TBI was associated with higher mortality rates.[61] The authors suggest that saline is preferable to albumin in the resuscitation of the patient with TBI.

Hypertonic saline provides prompt restoration of volume, and also increases serum osmolarity and decreases cerebral edema, thus lowering ICP.[62,63] As a result, osmotherapy has become an important tool in the management of elevated ICP after TBI.[64] However, there is very limited human data supporting outcome benefits from its use. There are also some side effects with the use of hypertonic saline, including renal failure, osmotic demyelinating syndrome, and rebound increases in ICP.

Mannitol provides an additional option for patients with TBI and elevated ICP. Mannitol is a plasma expander that reduces the hematocrit and subsequent blood viscosity, resulting in increased cerebral blood flow and cerebral oxygen delivery.[65-68] Mannitol also causes a delayed (15–30 minutes), pure osmotic diuretic effect.[65] This can cause hypotension, and so the patient's volume status must be carefully monitored. Currently, the BTF recommends mannitol (0.25 g/kg to 1 g/kg) for the control of elevated ICP. In addition, the panel recommends its use prior to ICP monitoring in patients with signs of transtentorial herniation or neurological deterioration not attributed to extracranial causes.[69]

Neurologic Assessment

It is imperative to obtain an accurate neurologic exam in every trauma patient with suspected TBI. One should attempt an accurate GCS prior to intubation to better communicate with neurosurgical consultants the patient's presenting condition. Hypothermia, hypoglycemia, drugs administered during pre-hospital transport, and other factors can affect GCS.

In addition to GCS, pupil size, reactivity, and anisocoria, as well as motor and brainstem function, must be assessed. Patients with fixed and dilated pupils have a high likelihood of a surgically amenable lesion, usually an ipsilateral hematoma with uncal herniation requiring emergent evacuation. However, previous eye surgery (e.g., cataract), or ocular trauma may also cause pupil dilation. In addition, hypoxia or hypotension should be corrected, as they can also cause pupil abnormalities.

Diagnostic Imaging

CT scanning rapidly identifies life-threatening, space-occupying lesions in need of emergent evacuation. However, rising healthcare costs and concerns for unnecessary exposure to radiation have raised questions about who needs head CTs. Haydel and colleagues evaluated patients with GCS 15 and a history of loss of consciousness or amnesia and concluded that any patient with headache, vomiting, age greater that 60, intoxication, deficit in short-term memory, physical evidence of trauma above the clavicles, or seizure (New Orleans Criteria) warranted a head CT.[70] Absence of all seven predictors had 100% negative predictive value. In 2001, Stiell and colleagues developed a clinical decision rule for those with mTBI that included five high-risk factors: failure to reach GCS of 15 within two hours; suspected open skull fracture; any sign of basal skull fracture; more than two episodes of vomiting; or age greater than 65 years.[71] Two additional medium-risk factors (amnesia before impact > 30 minutes, and dangerous mechanism of injury) were also included. The high-risk factors were associated with 100% sensitivity for predicting the need for surgical intervention and would eliminate 68% of CTs performed. The medium risk factors had a 98.4% sensitivity and 49.6% specificity for predicting clinically important brain injury and would eliminate the need for 46% of CTs. In 2005, the NEXUS II investigators identified eight variables (evidence of skull fracture, scalp hematoma, neurologic deficit, altered level of alertness, abnormal behavior, coagulopathy, persistent vomiting, and age 65 years or older) that were independently and highly associated with intracranial injuries.[72] The decision instrument had a sensitivity of 98.3% and negative predictive value of 99.1%.

Based on a comprehensive literature review, in 2008 the American College of Emergency Physicians' clinical policy on neuroimaging in patients with mTBI recommended that a head CT be obtained in patients with either loss of consciousness or posttraumatic amnesia with one or more of the following: headache, vomiting, age greater than 60 years, drug or alcohol intoxication, deficit in short-term memory, physical evidence of trauma above the clavicles, posttraumatic seizure, GCS less than 15, focal neurologic deficit, or coagulopathy.[73] The committee recommended a head CT in patients with no loss of consciousness or posttraumatic amnesia if there is a focal neurologic deficit, vomiting, severe headache, age ≥ 65 years, sign of a basilar skull fracture, GCS less than 15, coagulopathy, or dangerous mechanism of injury.

Patients with moderate and severe TBI, specifically severe TBI, should have a non-contrast CT scan of the head performed as early as possible. Patients should be adequately resuscitated and life-threatening injuries (e.g., respiratory compromise, active

hemorrhage, tension pneumothorax, open-book pelvis) should be addressed prior to obtaining the CT scan.

Magnetic resonance imaging (MRI) has no role in the initial evaluation of patients with suspected TBI. CT is a superior imaging modality for the evaluation of acute hemorrhage as well as bony abnormalities of the skull associated with TBI. The length of time it takes to obtain an MRI and distance from the ED in many institutions makes it unsuitable during the initial evaluation.

ICP Monitoring: Indications, Methods, and Treatment Threshold

Many patients with moderate or severe head injuries will require ICP monitors after TBI. Although placement of these monitors is beyond the scope of most emergency physicians, knowing the indications allows for more sophisticated communication with consultants or transfer facilities. In addition, longer stays in the ED now require emergency physicians to begin treatment of elevated ICPs.

Current recommendations for ICP monitoring include any patient with severe TBI that has a CT abnormality, including hematoma, contusion, edema, herniation, or compressed basal cistern;[74] and any patient with severe TBI who has a normal CT scan and at least two of the following: age greater than 40 years, unilateral or bilateral posturing, or systolic blood pressure less than 90 mmHg on arrival.

There are a number of monitoring devices available for measuring ICP. The two most commonly used are an intraventricular catheter (IVC) and a parenchymal monitor ("Bolt"). An IVC not only measures ICP, but also provides cerebrospinal fluid drainage to help control elevated ICP. However, the placement of an IVC is a more invasive procedure than the placement of a parenchymal monitor, and complications are more common.

Currently there are no large, randomized trials that determine the optimal ICP threshold. The largest prospective study involved 428 patients and determined that the incidence of morbidity and mortality was strongly related to ICP control when 20 mmHg was used as the treatment threshold.[75] Other studies have suggested 15–25 mmHg represents the optimal treatment threshold.[76-78] The BTF currently recommends beginning treatment of ICP if they are above 20 mmHg[79] with the goal of maintaining CPP between 50 mmHg and 70 mmHg.[80] Furthermore, the BTF recognizes clinical worsening or CT scan findings, such as acute pupillary abnormalities or herniation respectively, can occur with ICPs below the recommended treatment threshold of 20 mmHg and warrant treatment regardless.[79]

Additional Medical Management Therapies

The primary goal of medical management is to control ICP while maintaining CPP, and to ensure adequate oxygenation and hemodynamic stability to minimize secondary insult. While many patients have elevated ICP due to the primary injury, other factors, including agitation, pain, seizure activity, fever, and patient positioning, may also affect ICP.

Sedation. Propofol has become a popular sedative for patients with TBI. Its rapid onset and short half-life allow clinicians to obtain reliable neurologic exams to determine any change in mental status. Propofol decreases cerebral metabolism and oxygen demand, and thus is believed to be neuroprotective. However, little data has demonstrated its benefit in lowering ICP. In addition, complications, including propofol infusion syndrome (PIS), hyperkalemia, metabolic acidosis, and rhabdomyolysis, can occur. Although first identified in children, PIS can occur in adults, as well. Caution must be taken when high doses (> 5 mg/kg/hr) are used for an extended period of time (> 48 hours).[81,82] If not recognized, PIS can lead to cardiovascular collapse and death.

Anticonvulsants. Post traumatic seizures (PTS) have been classified as *early* (within the first seven days after injury) and *late* (after seven days post-injury).[83] PTS increases metabolic demand and ICP, and thus worsens injury; however, early PTS has not been shown to affect outcome. Risk factors have been identified that increase the risk of seizures after TBI. *(See Table 2.)* Early studies suggest that prophylactic phenytoin decreased the incidence of PTS. A 1990 study by Temkin and colleagues confirmed phenytoin's ability to decrease early PTS, but it did not prevent late PTS.[84] Valproate therapy has not been shown to be more effective that phenytoin in preventing early PTS. Nor has it been shown to prevent late PTS more effectively either. Due to a trend towards higher mortality with the use of valproate, its use for preventing PTS over phenytoin cannot be recommended.[85] More recently, levetiracetam has been shown to be as effective as phenytoin in preventing early PTS.[86] Compared to phenytoin, levetiracetam has fewer pharmacokinetic interactions and does not require drug level monitoring.

No studies have demonstrated that prophylactic anticonvulsant therapy will decrease the incidence of late PTS. Currently, anticonvulsant therapy is indicated for the first seven days following injury. In addition, patients who have late PTS should be treated according to standard protocols for those with new-onset seizure.[87]

Positioning. It is common practice to elevate the head above the heart in patients with TBI. Multiple studies have demonstrated lowering of ICP with head elevation.[88-90] Clinicians must rule out lumbar and thoracic spine injuries as well as pelvic fracture prior to raising a patient's head. In the interim, reverse Trendelenburg can be used to elevate the head.

Steroids. Steroids are commonly used to prevent cerebral edema in patients with various types of brain tumors. In the early 1970s, steroids were commonly used in patients with TBI. Early studies demonstrated no significant difference in outcome with use of steroids in patients with TBI.[91,92] However, a 2004 study was terminated early, after more than 10,000 patients were enrolled, because of a significantly increased risk of death in patients treated with steroids after TBI.[93] Thus, based on the current existing literature, steroids should not be used in the setting of TBI.

The Elderly TBI Patient

By the year 2030, the number of persons older than age 65 will double relative to 2000, representing almost 20% of the nation's total population.[4] In persons 65 years and older, TBI is responsible for more than 80,000 ED visits annually.[3] In 2006, more than

$2.8 billion was spent on treating TBI in those older patients.[5] Falls are the leading cause (51%) of TBI in elderly patients, while MVCs are a distant second (9%).[3]

As many as 73% of elderly TBI patients may have at least one co-morbid condition, compared to only 29% of younger patients.[94] Treatment of some of these chronic conditions includes the use of aspirin, clopidogrel, and warfarin, increasing the risk of TBI in the elderly. In a study by Ohm and colleagues, those patients taking either aspirin or clopidogrel or both had two and half times higher mortality rates than those not on antiplatelet therapy.[95] A study by Lavoie et al found that 9% of the older patients with TBI were taking warfarin pre-injury, and it was associated with more severe TBI and a higher rate of mortality.[96] TBI patients on warfarin have demonstrated a five times higher mortality than those similarly injured who were not on warfarin.[97] Others, however, have shown that pre-injury warfarin use in the elderly had no effect on mortality in trauma patients.[98,99]

For patients taking aspirin or clopidogrel, limited options exist to reverse the antiplatelet effects. Aspirin irreversibly inhibits platelet activity for the lifetime of the platelet. However, as aspirin has a relatively short half-life, transfusion of new platelets should be minimally affected by the patient's aspirin consumption. On the other hand, clopidogrel has a long half-life and will affect newly transfused platelets up to seven days after the last dose. Consultation with a neurosurgeon as well as hematology is required for optimal treatment of patients with active bleeds on the CT scan and those going to the operating room

Patients taking warfarin require immediate reversal. Warfarin, a vitamin k antagonist, inactivates clotting factors II, VII, IX, and X. Fresh-frozen plasma (FFP) has traditionally been used to restore these factors. Using a reversal protocol of 2 units of uncrossed FFP and 10 mg of intravenous vitamin K followed by an additional 2 units of cross-matched FFP, Ivascu et al demonstrated decreased time for reversal initiation from 4.3 hours to 1.9 hours, with a subsequent improvement in mortality from 48% to 10%.[100] However, many EDs do not have readily available, prethawed FFP, making rapid reversal difficult. In addition, large volumes of FFP are often required to fully reverse warfarin. In the elderly, this risks pulmonary edema and volume overload.

Alternatives to FFP do exist. Recombinant factor VIIa (rFVIIa) rapidly and effectively treats mild to moderate coagulopathy following injury.[101,102] In addition, rFVIIa decreases the time to neurosurgical intervention (144 vs. 446 minutes) and decreases the use of blood products without increasing the rate of thromboembolic complications.[103] While the initial cost of rFVIIa is high, its use in severely injured patients with TBI can significantly decrease their total charges and costs of hospitalization.[104] Although not considered standard of care, rFVIIa offers a rapid and cost-effective treatment option for patients with TBI and coagulopathy.

Other alternatives include vitamin K, prothrombin complex concentrates (PCC), and cryoprecipitate. The administration of vitamin K may not be helpful in the initial immediate reversal; however, it may help lessen the rebound effect when the FFP or rFVIIa wears off.[100] Limited evidence suggests that intravenous and oral administration of vitamin K are equivalent for warfarin reversal while subcutaneous administration is inferior.[105] PCCs are human plasma derived and undergo viral inactivation. They contain vitamin-K-dependent coagulation factors II, VII, IX, and X. Recent evidence suggests that PCCs may be an effective alternative to FFP for the reversal of warfarin anticoagulation in the acute setting.[106] Currently, PCCs are not commercially available in the United States.

Elderly trauma patients on warfarin with mild TBI and no radiographic evidence of intracranial pathology may be susceptible to delayed hemorrhage and clinical deterioration. Some authors suggest that an initial screening CT of the head as well as interval follow up imaging is unnecessary in this patient population, while others recommend admission and observation for a minimum of 24– 48 hours.[107-109] When clinicians elect not to image or admit patients for close monitoring, they must ensure a strong and reliable social support with 24-hour observation at home. A repeat CT scan should be done for any change in the patient's neurologic exam.

Hypothermia

Hypothermia is the most powerful neuroprotective method in animal models of TBI.[110] Therapeutic hypothermia was common practice in many medical centers in the 1960s and early 1970s however by the late 1970s fell out of favor because of increase rates of infection, especially pneumonia as well as a lack of randomized controlled trials in humans demonstrating efficacy. More recently, a renewed interest in hypothermia for the treatment of severe TBI has emerged. Although studies have demonstrated mild hypothermia's ability to decrease ICP and improve outcome, there is no data demonstrating clear outcome benefit.[111-113]

Serum Markers

Many serum biomarkers have been studied to help predict outcome in patients with TBI. The best studied is S100B. Multiple studies have shown that elevated levels of S100B after TBI are predictive of poor outcome.[114,115] However, a lack of a well-defined cutoff value, as well as the inability in many institutions to obtain timely laboratory results, has precluded widespread use of 100SB. Other markers including neuron-specific enolase and glial fibrillary acidic protein have been studied as possible predictors of outcome after TBI. However, further studies for all biomarkers are needed to help better identify and predict outcome after TBI.

Conclusion

TBI continues to be a leading cause of mortality in the United States. The emergency medicine physician's primary management goals for patients with severe TBI must center on identifying mass lesions, treating life-threatening injury, and preventing secondary brain insult. It is imperative that hypoxia and hypotension be minimized in patients with TBI, as a single episode of either is associated with a statistically significant increase in both morbidity and mortality.

Additionally, as the population ages, so will the number of elderly patients with TBI. Many of these patients are taking either

antiplatelet or anticoagulation medications, or both. Rapid identification of these patients is essential to attempt to reverse the effects of the medications and prevent clinical deterioration. Platelet and FFP transfusions are the traditional treatment options. Alternatives include vitamin K, rFVIIa, and PCC. However, further studies are needed to ensure efficacy and safety.

Finally, research into the benefits of hypothermia in brain injury, as well as serum markers, including S100B and NSE, in predicting outcome after TBI currently are underway.

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CNE/CME Objectives

Upon completing this program, the participants will be able to:

a.) discuss conditions that should increase suspicion for traumatic injuries;
b.) describe the various modalities used to identify different traumatic conditions;
c.) cite methods of quickly stabilizing and managing patients; and
d.) identify possible complications that may occur with traumatic injuries.

CME / CNE Instructions

Physicians and nurses participate in this CME/CNE program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. **After completing this activity, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit.** When your evaluation is received, a letter of credit will be mailed to you.

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CME / CNE Questions

1. Which of the following is an example/are examples of secondary insult?
   A. Hypoxia
   B. Epidural hematoma
   C. Hypotension
   D. Both A and C
   E. All of the above

2. Cerebral perfusion pressure is equal to:
   A. Mean arterial pressure + intracranial pressure
   B. Mean arterial pressure - intracranial pressure
   C. Cerebral blood flow + intracranial pressure
   D. Cerebral blood flow - intracranial pressure
   E. Mean arterial pressure + cerebral blood flow

3. A single episode of hypotension in patients with traumatic brain injury has been shown to:
   A. have no effect on mortality.
   B. double mortality.
   C. triple mortality.
   D. decrease mortality by 10%.
   E. decrease mortality by 25%.

4. The "lucid interval" has classically been associated with:
   A. subdural hematoma.
   B. subarachnoid hemorrhage.
   C. diffuse axonal injury.
   D. epidural hematoma.
   E. None of the above

5. Many studies suggest pre-hospital intubation worsens outcome in patients with traumatic brain injury because of:
   A. longer scene times.
   B. hyperventilation by prehospital providers.
   C. hypoxia due to failed intubations.
   D. All of the above
   E. None of the above

6. Which of the following is *not* associated with lidocaine administration during rapid sequence intubation in patients with traumatic brain injury?
   A. Reduced cerebral blood flow
   B. Reduced cerebral vascular resistance
   C. Reduced cerebral metabolism
   D. Minimized ICP elevation
   E. Increased catecholamine response

7. A single dose of etomidate during rapid sequence intubation has been associated with:
   A. Neutropenia
   B. Thrombocytosis
   C. Adrenal suppression
   D. Thyrotoxicosis
   E. All of the above

8. According to the NEXUS II study, which of the following variables has/have been independently and highly associated with intracranial injuries?
   A. Scalp hematoma
   B. Intermittent vomiting
   C. Age 65 years or older
   D. A and B
   E. A and C

9. All of the following are associated with propofol infusion syndrome *except*:
   A. Hyperkalemia
   B. Metabolic acidosis
   C. Rhabdomyolysis
   D. High-dose infusion
   E. None of the above

10. Which of the following is *not* currently commercially available in the United States for the reversal of warfarin in patients with traumatic brain injury?
   A. Vitamin K
   B. rFVIIa
   C. Fresh-frozen plasma
   D. Prothrombin complex concentrates (PCC)
   E. None of the above

Answers: 1. D; 2. B; 3. B; 4. D; 5. D; 6. E; 7. C; 8. E; 9. E; 10. D

In Future Issues: **Eye Trauma**

Trauma Reports
Evidence-Based Medicine for the ED

TR110109TM

PLEASE NOTE: If your correct name and address do not appear below, please complete the section at right.

Please make label address corrections here or PRINT address information to receive a certificate.

Account #_____

Name: _____

Company: _____

Address:_____

City: _____

State:_____ Zip _____

Fax: _____

Phone: _____

E-mail: _____

CNE/CME Evaluation — Traumatic Brain Injury

Please take a moment to answer the following questions to let us know your thoughts on the CNE/CME program. Fill in the appropriate space and return this page in the envelope provided. **You must return this evaluation to receive your letter of credit. ACEP members — Please see reverse side for option to mail in answers.** Thank you.

CORRECT ● **INCORRECT** ⊘ ✓ ✗ ~~W~~

1. In which program do you participate? ○ CNE ○ CME
2. If you are claiming physician credits, please indicate the appropriate credential: ○ MD ○ DO ○ Other _____
3. If you are claiming nursing contact hours, please indicate your highest credential: ○ RN ○ NP ○ Other _____

After participating in this program, I am able to:	Strongly Disagree	Disagree	Slightly Disagree	Slightly Agree	Agree	Strongly Agree
4. Discuss conditions that should increase suspicion for traumatic injuries.	○	○	○	○	○	○
5. Describe the various modalities used to identify different traumatic conditions.	○	○	○	○	○	○
6. Cite methods of quickly stabilizing and managing patients.	○	○	○	○	○	○
7. Identify possible complications that may occur with traumatic injuries.	○	○	○	○	○	○
8. The test questions were clear and appropriate.	○	○	○	○	○	○
9. I detected no commercial bias in this activity.	○	○	○	○	○	○
10. This activity reaffirmed my clinical practice.	○	○	○	○	○	○
11. This activity has changed my clinical practice.	○	○	○	○	○	○

If so, how? _____

12. How many minutes do you estimate it took you to complete this activity? Please include time for reading, reviewing, answering the questions, and comparing your answers with the correct ones listed. _____ minutes.
13. Do you have any general comments about the effectiveness of this CNE/CME program?

_____

I have completed the requirements for this activity.

Name (printed) _____ **Signature**_____

Nursing license number ***(required for nurses licensed by the state of California)***_____

Optional for ACEP members: In accordance with ACEP requirements, below we provide the option for ACEP members to submit their answers for this CME activity. If you wish to submit answers for this activity, please refer to this issue (Vol. 10, No. 6) and circle the correct responses.

1. A
   B
   C
   D
   E

2. A
   B
   C
   D
   E

3. A
   B
   C
   D
   E

4. A
   B
   C
   D
   E

5. A
   B
   C
   D
   E

6. A
   B
   C
   D
   E

7. A
   B
   C
   D
   E

8. A
   B
   C
   D
   E

9. A
   B
   C
   D
   E

10. A
    B
    C
    D
    E