INTRODUCTION

Traumatic Brain Injury

Traumatic brain injury (TBI) is defined as a disruption in the normal function of the brain or other evidence of brain pathology caused by an external force including a bump, blow, acceleration or deceleration forces, blast, or penetrating injury (1–3). Worldwide, TBI is the leading cause of death and disability in children and young adults and is involved in nearly half of all trauma-related deaths (1).

In the United States, unintentional injury is also the leading cause of death between age 1 and 44 years (4). In 2010, 2.5 million people sustained a TBI (2); of those, an estimated 280,000 were hospitalized, and over 50,000 died. Over the period of 2001 to 2010 in the United States, TBI-related emergency department (ED) visits increased by 70%, although the hospitalization rate only increased by 11%, and death rates decreased by 7% (5). Estimates of the global incidence of hospitalizations due to TBI is highest in Sweden with approximately 450, Brazil with 360, South Africa with 320, the United States with 92, and Pakistan with 50 cases/100,000 people/yr (6). A meta-analysis of reports from 23 European countries reported an incidence of 235 cases/100,000 people/yr (7).

The average TBI-associated mortality rate in Europe is estimated to be 15 deaths/100,000 population/yr (7) compared to 10 in Scandinavia, 20 in India, 30 in the United States, 38 in the Province of Taiwan in China, 81 in South Africa, and 120 in Columbia (8).

Globally, males have at least double the risk of TBI compared to females (1, 9). In the United States in 2010, the rate of TBI-related death was more than two times higher in men than in women (25.4 in males vs. 9.0/100,000 in females). Death rates were highest in persons aged 65 years or older at 45.2/100,000 population (10).

Worldwide, the leading cause of head injury is road traffic accidents, which account for 40% to 50% of hospitalizations due to TBI (1). The World Health Organization (WHO) estimates that 3,000 people die daily and 30,000 people are seriously injured on the roads and nearly half suffer head injury; most are from low- or middle-income countries and are pedestrians, cyclists, motorcyclists, and bus passengers (11). In Australia, India, Northern Europe, and the United States, the leading causes of TBI are due to falls (7, 12). In the United States, falls account for 40.5% of TBI; while 15.5% of TBI are due to “struck by/against” events, which include colliding with a moving or stationary object; 14.3% are from motor vehicle crashes (MVC) and 10.7% from assault; the remainder are not documented (13).

The youngest (age 0–4 years) and oldest (age >65 years) are at highest risk for falls at 72.8% and 81.8% respectively (13). The leading cause of TBI-related death also varies by age. In the United States, falls were the leading cause of death for persons over 65 years, assault for those under 4 years, and MVC for those between 5 and 24 years (13). For mechanism of injury, firearm-inflicted TBI has the highest mortality at 90.4% compared with 10.2% associated with falls (14, 15).

In the military population, mild TBI or concussion is the most common traumatic injury with most occurring in the garrison or home station environment (16). However, during combat, TBI is often due to blast injuries with concussion, contusion, subdural hematoma (SDH), and axonal shear injury as a result (17). During the recent wars, 81% of injuries in Afghanistan and Iraq were explosion related compared to 65% in Vietnam, and 73% during World War II (18).

The economic impact includes the direct cost of hospitalization, outpatient and rehabilitation, and indirect costs for lost productivity both of the patient and caregiver. There are other less tangible social and psychological costs to the patient, family and friends related to death or the reduced quality of life. Over 5.3 million Americans require assistance with activities of daily living (ADL) as a consequence of the long-term effects on cognition and behavior with emotional and physical impairment following TBI (2, 19, 20). In the United States, lifetime costs of TBI, including medical costs and lost productivity, have been estimated at $60 billion annually (21).

Acute Spinal Cord Injury

Acute spinal cord injury (ASCI) represents another form of neurologic injury that can result in significant disability. The incidence of ASCI averages 54 cases/million population/yr, or about 17,000 new cases yearly in the United States (22). The highest incidence has been reported in Mississippi (93 cases/million/yr) (23) Alaska (83 cases/million/yr) (24), and lowest in Kentucky at 29.4 cases/million/yr (25). Approximately half of all injuries occur between the ages of 16 to 30. Previously, the average age was 28.7 years but, currently it is 42.6 years. Over 75% of injuries occur in males, involving alcohol in 38% to 50% of cases (24, 26, 27, 28).

The WHO estimates that every year around the world, between 250,000 and 500,000 people suffer ASCI (27). The annual incidence has been reported to be lowest at 8.0 cases/million in Spain, 12.7 in France, 16.9 in Turkey, 19.5 in Sweden, and the highest in New Zealand at 49.1 (28).

In the United States, 38% of ASCI are related to motor vehicle collisions, followed by falls (30.5%), acts of violence...
such as gunshot wounds (13.5%), and sports injury (9%) (22). Of all patients with ASCI in the 2010 US database, 13.3% were discharged with complete tetraplegia, 45% with incomplete tetraplegia, 20% with complete paraplegia, and 21.3% with incomplete paraplegia; less than 1% had complete neurologic recovery (22). Globally, the most common cause of ASCI is also related to road traffic accidents followed by falls (29). In some countries, such as Malaysia and Bangladesh, 20% of SCIs result from falls while carrying heavy loads, particularly on the head (30).

The level and severity of injury impact mortality and cost. The mortality rate is highest in the first year. In the United States, for those who survive the first 24 hours, if the ASCI is incurred at age 20 years, lifespan is shortened from the normal life expectancy of 79 years by approximately 14 years for a paraplegic, by 19 to 23 years if tetraplegic, and by 33 years if ventilator-dependent at 1 year after injury (22).

The estimated economic burden is reflected in the cost of an estimated Canadian Dollar (CAD) $1.47 million/person with incomplete paraplegia and CAD $3.03 million/person for complete tetraplegia (31). In the United States in 2010, the estimated lifetime cost for a 25 year old at age of injury was $2.3 million with paraplegia and $4.7 million with complete tetraplegia (22). Outcome following both TBI and ASCI is chiefly determined by the severity of the initial injury, age of time to injury, and comorbidities; however, careful attention to prevent complications and prevent secondary central nervous system injury from hypotension, hypoxia, hyperthermia, and hyperglycemia may help decrease morbidity and mortality.

**Prevention**

Given the lack of effective treatments able to reverse injury, primary prevention of TBI and ASCI is paramount. Prevention of neurologic injury includes strategies to increase public awareness to wear seat belts, use child safety seats, wear helmets, avoid driving while intoxicated or distracted such as using a phone with texting or talking, and install window guards and safety gates. To also prevent ASCI, it is recommended never to dive into water that is not clear and the depth is shallow or cannot be assessed.

The mechanism of injury may contain opportunities for prevention. From 2001 to 2009 in the United States, the rate of ED visits for sports or recreation-related brain injury rose 57% in children age 19 or younger (32). The US Centers for Disease Control and Prevention (CDC) has partnered with many national, state, and local organizations to launch a “HEADS UP” campaign to educate children, parents, school professionals, coaches, and sports officials as to the importance of concussion recognition and management (33).

For the elderly, the CDC has a Stopping Elderly Accidents, Deaths and Injuries (STEADI) program that provides tools and educational material based on the American and British Geriatric Societies clinical practice guidelines to screen for fall risk and provide interventions to reduce risk (34). Interventions include exercise programs, minimizing medications, particularly psychoactive medications, and modification of the home environment including appropriate lighting, and handrails (35,36).

Worldwide, road traffic crashes are the leading cause of all injury deaths and the tenth leading cause of all deaths (37); most are due to head injury. The WHO estimated the economic cost to developing countries alone is greater than $100 billion annually and $518 billion globally (38). It predicts that by 2015, the leading cause of premature death and disability for children age 5 and up will be due to road crashes, and that road traffic injuries will become the third largest contributor to the global burden of disease by 2020. In 2009, the United Nations General Assembly, with the sponsorship of more than 90 countries, launched a “Decade of Action for Road Safety 2011–2020” with the goal to decrease road deaths and injuries through road safety management, safer roads, safer vehicles, safer road users, and improved postcrash care (39).

**PATHOPHYSIOLOGY**

**Primary Brain Injury**

Primary focal neurologic injury following TBI includes hemorrhage into the subdural or epidural spaces, intraparenchymal hemorrhage (IPH), and cerebral contusions and lacerations. Primary diffuse injury includes subarachnoid (SAH) and intraventricular hemorrhage (IVH), diffuse axonal injury (DAI), and diffuse edema (40).

**Subdural Hematoma**

SDHs are more common than epidural hematomas (EDHs) and were seen in 25% of patients with severe head injury entered into the Traumatic Coma Data Bank (TCDB) supported by the National Institute of Neurological Disorders and Stroke (NINDS) between 1980 and 1988 (41,42). SDH typically results from tearing of the bridging veins between the brain and the draining venous sinuses. The mechanism usually involves high-velocity acceleration and deceleration forces.

Imaging shows a crescent-shaped hyperdensity that follows the contours of the brain. Hyperacute hemorrhages or SDH in anemic patients are isointense on initial CT and may be overlooked. Acute SDH carries a poor prognosis and is one of the most lethal of all head injuries. Fifty to 60% of patients with SDH die, and only 19% to 38% will achieve functional recovery despite surgical treatment (43,44). Early evacuation within the first 4 hours of injury decreased mortality from 90% to 30% in a single study of 82 consecutive comatose patients. This suggested that preventable secondary injury was the cause of the high mortality; however, multiple studies have not replicated these results. The high mortality following SDH is likely the result of the severity of initial forces from the primary mechanism of injury (45,46).

**Epidural Hematomas**

EDH was found in 9% of 1,030 patients in the TCDB (47). An EDH requires a great impact force and is often associated with a skull fracture that disrupts the middle meningeal artery in the supratentorial space or, if in the posterior fossa, is more likely due to injury of the venous sinuses (48). Classically, patients present awake and alert, a period known as the lucid interval, and quickly lapse into unconsciousness; imaging shows a lenticular-shaped hyperdensity. With rapid evacuation, EDH has a relatively good prognosis, with a mortality rate of 5% to 10% (49). Factors determining mortality and functional outcome include age, best motor response on the Glasgow Coma
come of up to 70% (56). Cisterns carries a positive predictive value of unfavorable outcomes. The presence of tSAH in the basal gyrus, occurring in 21% to 53% of patients with severe TBI, is less likely concentrated in the basal cisterns and is usually found over the hemispheric convexities. The most common areas of contusion are the frontal, temporal lobes and occipital regions. These lesions typically are hyperintense areas within the parenchyma on CT scan and are more diffuse than IPH. As discussed below, secondary injury can result when contusions enlarge, which causes cerebral edema and intracranial hypertension (53). Clinical deterioration or elevation in intracranial pressure (ICP) requires urgent repeat cerebral imaging.

Intraparenchymal Hemorrhage

Intraparenchymal hemorrhage (IPH), similar to a contusion, is hyperintense on CT scan. It is a focal process and less diffuse than a contusion as it is caused by direct vascular injury or by stretching of the vessels with brain shift and distortion. Hemorrhage in the upper brainstem (midbrain and pons), known as Duret hemorrhages, can also occur with rapidly evolving transtentorial herniation and may be due to stretching of the perforating arterioles or from venous thrombosis and infarction. Spontaneous causes of IPH are hypertensive hemorrhagic stroke, or hemorrhaging due to arteriovenous malformation, aneurysm, amyloid angiopathy, or tumor. In the setting of hemorrhage in the basal ganglia, cerebellum, or thalamus, the clinician should consider the differential of spontaneous IPH as a possible cause of the traumatic event, rather than the result.

Subarachnoid Hemorrhage

Trauma is the most common cause of subarachnoid hemorrhage, occurring in 21% to 53% of patients with severe TBI and causes worsened outcome (54,55). In contrast to aneurysmal SAH (aSAH), traumatic SAH (tSAH) is less likely concentrated in the basal cisterns and is usually found over the hemispheric convexities. The presence of tSAH in the basal cisterns carries a positive predictive value of unfavorable outcome of up to 70% (56).

Intraventricular Hemorrhage

IVH in isolation is not commonly seen in TBI. However, like tSAH, it has been associated with worsened outcome (55). Obstructive hydrocephalus may result and may require cerebrospinal fluid (CSF) diversion by external ventricular drainage (EVD).

Diffuse Axonal Injury

DAI occurs in approximately half of patients with severe TBI (57). Sudden acceleration–deceleration impact causes rotational forces and shear injury to axons; the axon may not be entirely transected, but axoplasmic transport is disrupted causing swelling and disconnection (58,59). The result is formation of a retraction ball with the axon undergoing Wallerian degeneration. Since axonal degeneration may be a secondary injury process, pharmacologic strategies to intervene may eventually be developed. Outcome is worsened with severe DAI (60–62). Although microscopic neuronal injury cannot be seen on imaging studies, the diagnosis is best made with MR imaging with gradient echo or susceptibility-weighted sequences that detect blood products from the capillary injury and leak that accompanies DAI (63).

PHYSIOLOGIC PRINCIPLES

The Monro–Kellie hypothesis describes the skull as a semiclosed compartment containing brain and interstitial fluid (80%), CSF (10%), and blood (10%). Compensatory mechanisms to decrease cerebral blood or CSF volume become active in pathologic conditions where intracranial volume and pressure increase. For example, with hemorrhage or edema after TBI, reductions in CSF production and cerebral blood flow (CBF) are seen. Once these compensatory mechanisms are overwhelmed, depending on the compliance (volume/pressure relationship) of the intracranial contents, pressure will increase. Patients with atrophy are able to tolerate larger volumes before the ICP increases. A young patient without much atrophy has low cerebral compliance, which increases the risk for early intracranial hypertension and potential cerebral herniation.

Cerebral perfusion pressure (CPP) is determined as the difference of the mean arterial pressure (MAP) and ICP. When ICP monitoring is used, the CPP supplants MAP goals in the intensive care unit (ICU). Normal ICP is less than 15 mmHg. In a study in which ICP and CPP were closely evaluated with respect to outcome, the most powerful predictor of neurologic worsening was the presence of intracranial hypertension, defined as an ICP of 20 mmHg or greater. As long as CPP was maintained greater than 60 mmHg, CPP did not correlate with neurologic worsening (64). Current Brain Trauma Foundation (BTF) guidelines recommend initiation of treatment of an ICP above 22 mmHg (65) and avoidance of aggressive therapy to maintain CPP above 70 mmHg with fluids and pressors because of an increased risk of acute respiratory distress syndrome (ARDS) (66); recommendations target a CPP between 60 and 70 mmHg and acknowledge that patients with intact pressure autoregulation tolerate higher CPP values. If cerebral autoregulation is not intact, increasing CPP may result in higher ICP and increased edema (67). Prior to placement of an intracranial monitor, recommendations are to maintain a systolic blood pressure (SBP) of 100 mm Hg or greater for patients 50-69 years of age or 110 mm Hg or above for patients 15 to 49 or over 70 years of age to decrease mortality and improve outcomes (68).

DIAGNOSIS

On arrival to the ICU, the initial focus is on respiratory and hemodynamic stability; this will be discussed below. In addition to the usual general examination, in the neurologically injured patient the evaluation includes an examination of the head for scalp lacerations, which can be a major source of bleeding and orbital, facial, and depressed skull fractures. Evidence for basilar skull fractures include periorbital ecchymoses (raccoon eyes) indicative of frontal skull base injury or...
postauricular ecchymosis (the Battle sign) seen with middle fossa or temporal bone fractures. Cervical spine precautions are maintained in these patients and will be discussed later.

During the evaluation and observation of the TBI patient, repeated neurologic monitoring includes the vital signs with special attention to extremes in blood pressure. Hypotension may result in secondary injury, whereas hypertension, not always associated with bradycardia, can be a sign of impending cerebral herniation. If ICP rises, cerebral autoregulation may result in secondary injury, whereas hypertension, not necessarily predictive of failure of nonoperative management (57). Initial contusional or IPH size and effacement of cisterns are strong predictors of progression. Associated tSAH, SDH, and older age are also independent risk factors for progression (54,82,85,86). Other independent risk factors for progression include associated tSAH, SDH, older age, and coagulopathy or alcohol intoxication, deficits in short-term memory, physiologic evidence of trauma above the clavicles, and alcohol level is essential to assist in evaluating for other causes of altered mental status and to determine whether delirium tremens may be a factor in the following days of ICU care. Additional risk factors are early initial imaging within 2 hours of injury (54,78,85,86). Often community standards are to repeat a CT scan within 12 to 24 hours of the initial imaging. Although worsening CT findings does not necessarily require treatment, up to 54% of patients may require neurosurgical intervention including ICP monitoring or craniotomy subsequent to the findings on a repeat scan (53,80–85). A significant risk factor is early initial imaging within 2 hours of injury (54,78,85,86). Often community standards are to repeat a CT scan within 12 to 24 hours of the initial imaging.

Evolving Injury and Repeat Head CT
Progressive intracranial hemorrhage consistent with an evolving contusion is seen in 14% to 38% of patients (57,78,79). Although worsening CT findings does not necessarily require treatment, up to 54% of patients may require neurosurgical intervention including ICP monitoring or craniotomy subsequent to the findings on a repeat scan (53,80–85). A significant risk factor is early initial imaging within 2 hours of injury (54,78,85,86). Often community standards are to repeat a CT scan within 12 to 24 hours of the initial imaging.

In stable patients without clinical neurologic deterioration, the utility of repeat imaging is debated and many believe it is unnecessary since it is unlikely that neurosurgical intervention will be required (54,82,85,86). Other independent risk factors for progression include associated tSAH, SDH, older age, and a large initial contusional or IPH size and effacement of cisterns are strongly predictive of failure of nonoperative management (57).
TREATMENT

Following immediate impact and anatomic damage, secondary damage at the cellular level from inflammation, edema, free radicals, and excitatory neurotransmitters can worsen outcome. Contributing factors include hypoxemia, hypotension, seizures, fever, and intracranial hypertension. Immediate postinjury care focuses on the prevention of these problems.

Hypoxemia and Respiratory Management

Hypoxemia, defined as a PaO₂ less than 60 mmHg or O₂ saturation less than 90%, can independently increase mortality from 27% to 50% and increase poor outcome from 28% to 71% (87,88). Early intubation can prevent aspiration and minimize hypoxic and hypercapnic events (89), and is recommended by the Eastern Association for the Surgery of Trauma (EAST) (90), Advanced Trauma Life Support (ATLS) guidelines from the American College of Surgeons (91), and the Brain Trauma Foundation Traumatic Brain Injury prehospital guidelines (92). A GCS of 8 or less is the usual threshold for endotracheal intubation.

There are caveats to intubation of which the practitioner should be aware. In the prehospital setting, rapid sequence intubation has been associated with increased mortality (93–95). This may be a result of decreased cerebral perfusion due to hyperventilation-induced hypocapnia. Positive pressure ventilation may cause hypotension in a hypovolemic patient if central venous return is impeded by high intrathoracic pressures (96). Intubation is a high-risk procedure which may cause secondary neurologic injury. Sedative/hypnotic medications and bag/mask ventilation with positive pressure ventilation contribute to hypotension and hypercapnia and hypoxemia, respectively, during induction. In addition, direct laryngoscopy causes a marked, transient increase in ICP. Intravenous lidocaine may blunt this ICP response (97,98).

Hyperventilation with resultant hypocapnia causes cerebral vasosconstriction and a reduction in CBF (99–101). Prolonged hypocapnia appears to slow neurologic recovery (102). Prophylactic hyperventilation of PaCO₂ less than 35 mmHg should be avoided, although PaCO₂ as low as 30 mmHg may be necessary for brief periods for immediate treatment of intracranial hypertension. Options to identify cerebral ischemia in the setting of hyperventilation include the use of jugular venous oxygen saturation, arterial jugular venous oxygen content differences, brain tissue oxygen monitoring or CBF monitoring (103).

To achieve adequate ventilation, positive end-expiratory pressure (PEEP) may be necessary. PEEP affects CPP and ICP when the lung is compliant and the chest wall is not. The high lung compliance allows for an increased intrathoracic volume which, in the setting of a low compliant chest wall, increases intrathoracic pressures. The high intrathoracic pressure decreases cerebral venous outflow, which will increase ICP (104,105). Additionally, if intrathoracic pressure is elevated, cardiac venous return is diminished and results in lowered MAP and CPP.

Pulmonary infections were seen in 41% of patients registered in the TCDB and were an independent predictor of unfavorable outcome (106). Bedside management includes adequate pulmonary toilet and strategies such as elevation of the HOB to decrease the risk for ventilator-associated pneumonia (VAP). In patients with intracranial hypertension, during endotracheal suctioning, adequate sedation is necessary to prevent an increase in ICP (107).

Neurogenic Pulmonary Edema

In addition to hypoventilation and aspiration from poor airway protection, a less frequently recognized cause of hypoxemia following TBI is neurogenic pulmonary edema (NPE) (108), resulting from central sympathetic stimulation. Pretreatment with adrenergic-blocking agents prevents experimental NPE (109). Experimental lesions in the hypothalamus (110), bilateral nucleus tractus solitarius (111), and the ventrolateral medulla (112) can produce NPE. TBI causes a sympathetic discharge, which increases systemic and pulmonary vascular pressures; the resultant increase in pulmonary capillary pressure increases the hydrostatic pressure and causes pulmonary capillary injury. This, in turn, causes leakage of fluid and protein and pulmonary hemorrhages (113–115).

Clinical signs include dyspnea, tachypnea, tachycardia, and chest pain if the patient is awake; rales are present on chest auscultation. Laboratory results show hypoxemia and a mild leukocytosis, with chest radiograph showing a bilateral alveolar filling process (116). Pulmonary capillary wedge pressures and pulmonary artery pressures can be elevated or normal. There are two distinct forms of NPE: the classic form appears early, within minutes to a few hours after acute brain injury; a delayed form of NPE slowly progresses over 12 to 72 hours following injury. Treatment is supportive and often requires supplemental oxygen and positive pressure ventilation. Dobutamine may be effective by decreasing cardiac afterload and increasing cardiac contractility (117).

Hypotension

Hypotension, defined as SBP less than 90 mmHg, independently worsens mortality (118,119). The TCDB reports hypotension was present in 29% of patients and doubled mortality from 27% to 55% (106,118). In patients whose SBP were less than 90 mm Hg, mortality was 65% independent of age, admission GCS motor score, hypoxia, or associated severe extracranial trauma. Adequate fluid resuscitation with euvoemia is essential. Independent of ICP, MAP, or CPP, a negative fluid balance of approximately 600 mL was associated with poorer outcome (120). Guidelines recommend adequate fluid resuscitation and have been updated to recommend SBP 100 mm Hg or greater in patients 50 to 69 years old and 110 mm Hg or greater in patients 15 to 49 or greater than 70 years old. Blood pressure support to maintain SBP greater than 90 mmHg (67). Once an ICP monitor is placed, the optimal blood pressure is determined by that required to keep the CPP 60 to 70 mmHg (67).

Contraction Band Necrosis

Following head trauma, SAH, seizures, or stroke, patients may have cardiogenic shock with global hypokinesis associated with transient cardiac dysrhythmias and repolarization changes (121–124). Dysrhythmias may include supraventricular tachycardias, sinus bradycardia, atrioventricular (AV) block, AV dissociation, nodal rhythms, and paroxysmal ventricular tachycardia. These changes are cerebrally mediated and are recognized as myofibrillar degeneration (also known as contraction band necrosis [CBN] or coagulative myocyteolysis). The histologic appearance of CBN contrasts to the coagulation necrosis seen with ischemic injury where there are cytoplasmic...
degenerative changes with cloudy swelling, hyaline droplets, and fatty change. With CBN, the myocardium instead shows loss of definition of the linear arrangement of myofibrils and the appearance of prominent dense eosinophilic transverse bands (contraction bands), and intervening granularity throughout the cytoplasm (125). This injury pattern was first described with pheochromocytoma and has been associated with the administration of catecholamines, including cocaine abuse (126,127). It is postulated that centrally mediated sympathetic or exogenous catecholamine stimulation of the myocardium results in cellular calcium overload and results in the formation of the contraction bands (128). CBN is predominantly located in the subendocardium with the cardiac conducting system, which results in the associated arrhythmias (129).

In CBN, cardiac enzymes are often elevated and may be difficult to differentiate from an acute coronary syndrome. However, the treatment for CBN is vastly different and typically includes observation for dysrhythmias and blood pressure support in contrast to reperfusion therapy with an acute ischemic myocardial infarction. Clinical differentiation typically relies on the recognition of patients with higher risk for coronary artery disease such as older age, hypertension, diabetes, and hyperlipidemia rather than a young patient with massive head injury.

Posttraumatic Vasospasm

Following TBI, posttraumatic vasospasm can occur in as many as 24% to 36% of adults and children (130–132) and causes focal ischemia with lateralizing neurologic deficits such as hemiparesis and aphasia between 2 to 37 days following injury (132–134). In patients with severe TBI, small studies have reported incidences as high as 82% (135). Explosive blast TBI is especially associated with early cerebral edema and cerebral vasospasm (136). Disruption of cerebrovascular tone may be a result of inflammatory and other vascular changes (137). Some mechanisms include an increased expression of an inducible isoform of nitric oxide synthase (138) and a hypercontraction-induced phenotypic switch that potentiates vascular remodeling (139). Transcranial Doppler, while reasonably specific, is not a sensitive test for vasospasm. If vasospasm is suspected, cerebral angiography can confirm the diagnosis. The effectiveness of treatment of posttraumatic vasospasm with modalities used following aSAH (e.g., hypervolemic, hypertensive therapy, or nimodipine) has not been assessed.

Hyperthermia

Hyperthermia accelerates neuronal injury by increasing basal energy requirements (neuronal discharges), excitatory neurotransmitters, free radical production, calcium-dependent protein phosphorylation, ICAM-1 and inflammatory responses, DNA fragmentation, and apoptosis, causing blood-brain barrier changes as seen by extravasation of protein tracers (140,141). Despite this, multiple TBI studies of prophylactic moderate hyperthermia (32°C to 33°C) and their meta-analyses have not shown improved outcome (142–144). This may be due to significant intercenter variability in the management of MAP, CPP, fluids, and vasopressors (145,146).

In the individual patient, therapeutic hyperthermia lowers ICP by reducing the cerebral metabolic rate 7% for each degree Celsius decrease. This treatment can be lifesaving and result in reasonable neurologic recovery (144,147). Pentobarbital coma and/or neuromuscular blockade (NMB) may be necessary to achieve cooling without shivering. Various techniques for intravascular and topical cooling are available. Although complications of hyperthermia can include increased risk of cardiac dysrhythmias, hypotension, bradycardia, thromboocytopenia, and pneumonia, in studies evaluating hyperthermia in cardiac arrest patients, there was no statistical increase in these adverse events (148,149).

Hyperglycemia

Hyperglycemia can cause brain tissue acidosis (150), and early hyperglycemia has been associated with worsened neurologic outcome following TBI (151,152). Persistent hyperglycemia following severe TBI in one study was an independent risk factor of mortality with a 4.9 times increase in risk of death (153). It is not fully understood whether the hyperglycemia is causative or is a marker for severity of injury and subsequent poor outcome; however, control of hyperglycemia following TBI is theoretically reasonable.

In the ICU setting, where glycemic control often uses insulin infusion or injection, patients with acutely altered mental status should be urgently evaluated for hypoglycemia.

Coagulopathy

Brain is rich in tissue thromboplastin and following head injury, increased tissue thromboplastin activity in the frontal, parietal, and temporal lobes activates the coagulation cascade and causes a disseminated intravascular coagulopathy (DIC) (154). The TCDB reported that 19% of patients were coagulopathic (106). In children, the incidence of coagulopathy increased with worsening severity of head injury reflected by the head Abbreviated Injury Scale score and was as high as 40% (155). Although initial evaluation may show thrombocytopenia in 14% and coagulopathy in 21% of TBI patients, in ensuing days, DIC can be seen in 41% to 60% of patients with blunt brain injury (156,157). It is more common in patients with penetrating head trauma (158).

Abnormalities in PT, PTT, or platelet count have been associated with 55% of patients who have progressive intracranial hemorrhage after TBI (159,160). Associated coagulopathy and thrombocytopenia increases mortality in TBI (156,157,160,161). Some centers are using thromboelastometry and portable coagulometers to detect coagulopathy in the ED. Typically, fresh frozen plasma is transfused for an elevated aPTT or a PT international ratio (INR) of 1.5 or more. Current European guidelines for TBI patients recommend transfusion of platelets for values below 100,000 cells/μL or for patients receiving antiplatelet agents (162). Other alternatives such as activated factor VII or prothrombin complex concentrate (PCC) may be effective emergently (158); PCC is recommended in the European guidelines for emergency reversal of vitamin K-dependent and oral antifactor Xa agents such as rivaroxaban, apixaban, or edoxaban (162).

Intracranial Pressure Monitoring and Management

Normal ICP is less than 10 mmHg; the TCDB reports that 72% of patients with severe TBI had ICPs above 20 mmHg (163). Since multiple studies show worsened outcome with
ICP above 20 to 25 mmHg, published guidelines use this as the threshold to treat (65).

Maneuvers for management of ICP begin with those with fewer potential side effects and progress to more invasive treatments with higher complication risk (Fig. 117.1). Elevation of the head of bed to more than 30 to 45 degrees not only decreases the risk of VAP but can facilitate cerebral venous drainage and lower ICP. In orthostatic, hypovolemic patients, however, head of bed elevation can lower MAP; adequate fluid drainage and lower ICP. In orthostatic, hypovolemic patients, this decrease in MAP can enhance cerebral blood flow. Elevation of the head of bed to more than 30 to 45 degrees not only decreases the risk of VAP but can facilitate cerebral venous drainage and lower ICP. If ICP ok CPP > 60–70 mmHg CPP = MAP – ICP

**ICP sustained >25 mmHg 1–12 hrs**

**Surgery options**

**Cooling**

Consider aggressive hypothermia

Temp 34–36°C → 32–33°C

**Drainage**

Surgical options? CSF drainage

External ventricular drain placement (Euvolemia)

If no EVD, if fluid over-loaded, consider furosemide 20 mg (IVP)

**Rescue**

Osmotics: 3% saline solution 250cc or 23.4% 30cc bolus. If hypervolemic: mannitol 0.25–0.5 g/kg (Consider cross of BBB & contribution to mass effect)

**Rescue**

PaCO2 30–35 mm Hg briefly

**Pentobarbital infusion**

For infusion, have

BIS or EEG monitor:

Slow Bolus 20 mg/kg then start infusion 1 mg/kg/hr. Can try low dose titrated to effect but keep SR on EEG or BIS <95%. Can bolus 200 mg if ICP > 20, BIS/EEG SR < 95%

**Paralytic agents**

(Especially if shivering)

Bolus: vecuronium or cisatracurium

If PbtO2 <15

Is PbtO2 catheter working? 100% FiO2 for 5 min. If working (>10 mmHg from baseline), act immediately. If within 4 hrs of insertion, recheck in 1 hr

**Euvolemic?**

I/O, uop, CVP, PCWP?

**Adequate Sedation?**

If CPP <70 Vaspressors eg. norepinephrine

If CPP 70, CI<3, Consider increase O2 delivery with inotropes (e.g., milrinone)

Paralytic Agent?

If anemic

**Premises:**

1) ICP < 22 mmHg

2) CPP > 60–70 mmHg

CPP = MAP – ICP

Intubated

ICP monitor GCS ≤ 8

**Sedation** (consider BIS to 30 ’s)

Benzodiazepines (midazolam infusion)

Propofol (stop if >2 days or barbiturates started)

**BIS/EEG SR < 95%**

Can bolus 1 mg/kg/hr. Can try slow infusion then start infusion

**BIS or EEG monitor:**

For infusion, have

**ICP monitor**

GCS ≤ 8

**TBI: Intracranial hypertension**

ICP > 22 mmHg

CT scan for first time or if sudden >20 & suspect mass lesion

**If not orthostatic, Head of Bed >30°**

Optimize fluids (Euvolemia)

e.g. – CVP ≥ 6 or PCWP ≥ 8

**Normo-Thermia 37°C**

**Pain therapy:**

Opioid infusion, (if fentanyl, watch initially if paradoxical increase ICP)

**Sedation** (consider BIS to 30 ’s)

Benzodiazepines (midazolam infusion)

Propofol (stop if >2 days or barbiturates started)

**If PbtO2 < 15**

Is PbtO2 catheter working? 100% FiO2 for 5 min. If working (>10 mmHg from baseline), act immediately. If within 4 hrs of insertion, recheck in 1 hr

**Euvolemic?**

I/O, uop, CVP, PCWP?

**Adequate Sedation?**

If CPP <70 Vaspressors eg. norepinephrine

If CPP 70, CI<3, Consider increase O2 delivery with inotropes (e.g., milrinone)

Paralytic Agent?

If anemic

**Premises:**

1) ICP < 22 mmHg

2) CPP > 60–70 mmHg

CPP = MAP – ICP

Intubated

ICP monitor GCS ≤ 8

**Sedation** (consider BIS to 30 ’s)

Benzodiazepines (midazolam infusion)

Propofol (stop if >2 days or barbiturates started)

**BIS/EEG SR < 95%**

Can bolus 1 mg/kg/hr. Can try slow infusion then start infusion

**BIS or EEG monitor:**

For infusion, have

**ICP monitor**

GCS ≤ 8

**TBI: Intracranial hypertension**

ICP > 22 mmHg

CT scan for first time or if sudden >20 & suspect mass lesion

**If not orthostatic, Head of Bed >30°**

Optimize fluids (Euvolemia)

e.g. – CVP ≥ 6 or PCWP ≥ 8

**Normo-Thermia 37°C**

**Pain therapy:**

Opioid infusion, (if fentanyl, watch initially if paradoxical increase ICP)
NMB lowers ICP by decreasing muscle tone, especially during shivering. Shivering increases the metabolic rate and generates carbon dioxide. After administering NMB, an ABG analysis should be obtained to ensure that the PaCO₂ has not dropped below 35 mmHg; minute ventilation should be adjusted accordingly. Rapid increases in PaCO₂ may result in rebound vasodilation and ICP elevation. Ventilator manipulation should be performed in small increments when adjusting to increase the PaCO₂. NMB also assists in cooling the patient. As noted above, hypothermia is useful in refractory intracranial hypertension. Temperatures of 32°C to 33°C can be well tolerated. On a cautionary note, the combination of NMB and cooling appears to put the patient at high risk for pneumonia, as they are unable to effectively clear secretions; empiric pulmonary toilet with frequent suctioning is often necessary.

Barbiturate-induced coma, using either thiopental or pentobarbital infusion, lowers the cerebral metabolic rate; this results in lowered cerebral blood volume and ICP. Thiopental in long-term infusion, because of its lipophilicity, may take over a week to clear after the infusion is stopped. For pentobarbital, 20 mg/kg is given as a slow loading dose followed by a maintenance infusion of 1 mg/kg/hr; the loading dose may significantly lower MAP. Often fluids and vasopressor administration may be necessary. Electroencephalography (EEG) is critical to titrating the dose during barbiturate coma. Although the infusion can be titrated to ICP effect, once the EEG is isoelectric, there is little to be gained in the way of ICP control by increasing the infusion; at this point, worsening side effects result from increased drug. These include hypotension from peripheral vasodilation, decreased cardiac inotropy, and ileus; cough reflex is diminished and decreased bronchial activity and slowed leukocyte chemotaxis increase the risk for pneumonia. A benefit of barbiturate coma is a quiescent hypothermia that no longer modulates body temperature. Hypothermia can often be achieved without the need for NMB since shivering is diminished.

Loop diuretics have been used to help manage ICP by decreasing CSF production in the choroids plexus (177). Loop diuretics will decrease volume status, thus unless the patient is hypervolemic, CSF diversion is a more effective method of lowering ICP.

Other therapy for refractory intracranial hypertension requires neurosurgical intervention. Placement of an EVD allows for CSF drainage. Hemicraniectomy may be a life-saving option depending on the patient; case series of 19, 23, and 51 children at three different centers had mortalities of 30% to 31.4%. Favorable outcome with return to school and functional independence was reported in 68% to 81%; 18% to 21% were severely disabled and dependent on caregivers (178–180). In a randomized trial of adults with diffuse brain injury, early bilateral frontotemporoparietal decompresive craniectomy decreased ICP and the ICU length of stay, but was associated with worsened neurologic outcome (181).

**Brain Tissue Oxygenation**

To monitor and help prevent the secondary damage seen with hypoxic brain injury, new modalities to evaluate cerebral oxygenation have been developed. Jugular bulb oximetry (SjvO₂) is a global measure of the balance between oxygen delivery to the brain and oxygen consumption. Local brain tissue partial pressure oxygen (PbO₂) can be measured either by a quenching process by fluorescence or by a polarographic Clark-type microcatheter. An increase in cerebral oxygen delivery is reflected by increases in SjvO₂ and PbO₂. Oxygen delivery to the brain is manipulated by increases in blood pressure, cardiac output, and red blood cell transfusion (182). Normobaric hypoxia has not shown to improve cerebral oxygen metabolism on PET imaging, and the use of 100% oxygen is not supported by the available literature (183). Optimal SjvO₂ is generally accepted as 50% oxygen saturation (103,184). The optimal PbO₂ is not fully established but guidelines currently recommend higher than 15 mmHg (103). Various studies show worsened outcome in patients with mean PbO₂ less than 15 mmHg; other thresholds include 25 mmHg (185–188). Mortality was significantly decreased and functional outcomes improved in one study comparing 25 patients treated by traditional ICP/PET-guided therapy to 28 patients with therapy targeted to a PbO₂ greater than 25 mmHg (189); however, other studies have not shown improvement in outcome (190–192). Cerebral microdialysis evaluating the biochemical byproducts of ischemia such as increased lactate and glutamate and lactate–pyruvate ratio is another potential technology to assist bedside care, but has not yet reached practical clinical use (193).

At the time of this writing, an evaluation of 31 adult neurocritical care units in the United Kingdom managing TBI patients showed that 100% of units followed ICP; 97% monitored CPP with 25 of 31 units using a CPP target of 60 to 70 mmHg; PbO₂ was utilized in 26% of units, cerebral microdialysis in 13%, and SjvO₂ was used in only one unit (194). No unit was using near-infrared spectroscopy, a modality developed to measure cerebral oximetry as a measure of perfusion.

**Antibiotic Prophylaxis**

Fractures of the skull base and severe facial trauma can result in a CSF leak. Various studies report incidences of 2.6% to 4.6% of all patients with basilar or facial fractures (195,196). In one study, otorrhea was three times more common than rhinorrhea (195). Approximately 50% of CSF leaks stop within 5 days (197); the risk of bacterial meningitis is approximately 12% to 21%. Studies conflict as to whether prophylactic antibiotics decrease the risk of infection and meta-analyses suggest no benefit, hence, there are no guidelines or recommendations regarding antibiotics in this setting (197–199); constant surveillance for meningitis is essential.

In the setting of CSF leak, if the spine is stable and blood pressure is adequate, the HOB should be elevated to facilitate leak closure. Stool softeners help avoid vigorous Valsalva maneuvers that may worsen the leak. Neurosurgical intervention with CSF diversion (i.e., lumbar drain or EVD) or surgical closure may be necessary if the leak persists. Following penetrating head trauma, a CSF leak is the primary predictor of intracranial infection. Infection is seen in 38% to 63% of CSF leaks after military-related penetrating cerebral injury (200–202). Current recommendations advise treatment for 5 to 14 days with empiric broad-spectrum antibiotics immediately following penetrating brain injury (202–205).

For clean neurosurgical procedures, such as twist drill craniotomy for EVD or ICP monitor placement, burr holes, or craniotomy, guidelines have been established by the Surgical Infection Prevention and Surgical Care Improvement Projects that recommend an intravenous first-generation cephalosporin within 1 hour prior to surgical incision (206).
Posttraumatic Seizures

Early posttraumatic seizures occur within 7 days of injury; 3% to 6% of patients with closed head injury suffer early posttraumatic seizures, compared to 8% to 10% with penetrating brain injury (207–209). Late posttraumatic seizure by definition manifests at least 7 days postinjury and is seen in 30% of patients with penetrating brain injury; these late posttraumatic seizures may occur up to 5 years after injury. There is adequate evidence to recommend antiseizure medications, for example, phenytoin and carbamazepine, for the first week after closed and penetrating brain injury to prevent early posttraumatic seizures (210–213). Of note, valproate showed no benefit for seizures following brain injury and had a trend to higher mortality (214). Levetiracetam, compared to phenytoin, shows equal efficacy in post-TBI seizure prevention (215,216) and has fewer complications, such as hypotension, and does not require monitoring of therapeutic levels, although dosing should be adjusted in renal failure. There is no evidence that continuing prophylactic antiseizure medications beyond a week prevents late posttraumatic seizures, and it is not recommended for closed or penetrating head injury beyond 7 days of injury (210,213).

Thromboprophylaxis

In the general postoperative neurosurgical population, the risk for deep venous thrombosis (DVT) is 3% to 14% (217–220); following major head injury, the risk for DVT is as high as 54% (221). The BTF recommends the use of graduated compression stockings or intermittent pneumatic compression (IPC) stockings in combination with low–molecular-weight (LMWH) or low-dose unfractionated heparin (LDUH) with the warning that this may result in intracranial hemorrhage expansion; there were no specific recommendations for a preferred agent, dose, or timing of treatment (222). The American College of Chest Physicians (ACCP) 9th edition has similar recommendations for major trauma patients with TBI, ASCI, or spinal surgery for trauma (Grade 2C). The Neurocritical Care Society recommends initiating LMWH or UFH for VTE prophylaxis within 24–48 hours of presentation or 24 hours after craniotomy (223). If LMWH and LDUH are considered contraindicated, mechanical prophylaxis, preferably with IPC devices, should be utilized until the risk of bleeding diminishes and contraindication to chemoprophylaxis resolves (Grade 2C). Inferior vena cava (IVC) filters are not considered acceptable primary prophylaxis in trauma patients (Grade 2C) (220).

Nutrition

Following severe TBI, patients enter a hypermetabolic, catabolic state with rapid weight loss associated with a negative nitrogen balance and protein wasting. In experimental models of TBI, 3 hours after injury morphologic changes are seen in the gut mucosa that include shedding of epithelial cells, fracture of villi, focal ulcers, fusion of adjacent villi, mucosal atrophy, and edema in the villous interstitium and lamina propria. On electron microscopy, there is a loss of tight junctions between enterocytes, damage of mitochondria and endoplasm, and apoptosis of epithelial cells (224). These changes in gut permeability increase bacteria translocation and endotoxin, which increases the risk of the systemic inflammatory response; the amino acids arginine and glutamine modulate gut permeability.

Early parenteral or enteral nutrition within 24 to 72 hours can speed neurologic recovery and decrease disability and mortality (225–228). Early enteral feeding may have benefit over parenteral feeding by protecting against intestinal apoptosis and atrophy (229) and decreasing infection clinically (230). Early enteral nutrition with glutamine and probiotics may decrease the infection rate and length of ICU stay (231,232). There is some theoretical concern that glutamine should not be used in brain injury patients due to the potential increase in cerebral glutamate with neuroexcitatory properties and cell damage, although there are no data to date to support this concern.

Fasted TBI patients lose nitrogen at a rate that reduces weight by 15% per week. Replacement of resting energy expenditure (REE) by 100% to 140%, with 15% to 20% nitrogen calories may reduce nitrogen loss; therefore, BTF guidelines recommend that full (100% REE) nutritional replacement be achieved within 7 days after injury (233). An Institute of Medicine (IOM) report was more aggressive and recommended the provision of early (i.e., within 24 hours of injury) nutrition of more than 50% of total energy expenditure and 1 to 1.5 g/kg protein for the first 2 weeks after injury (232,234).

Stress Gastritis

Stress gastritis was seen in 91% of 44 comatose mechanically ventilated patients within 24 hours of head injury; lesions were most commonly seen in the fundus and body of the stomach (235). Mucosal ulceration is typically prevented by maintaining intraluminal pH above 5 or by H2 receptor blockade (236). In TBI patients, stress ulcer bleeding prophylaxis with proton pump inhibitors or H2 receptor antagonists is recommended. Neither is recommended over the other, but the practitioner should be aware that one retrospective study in neurosurgery patients showed a statistically significant increased incidence of thrombocytopenia of 50 patients on famotidine compared to 98 of those not treated (34% vs. 11.2%) (237).

Prognosis

Survivors of TBI variably suffer from long-term cognitive, motor, sensory, and emotional deficits. These manifest as weakness, incoordination, emotional lability, impulsivity, and difficulty with vision, concentration, memory, judgment, and mood. Nearly 5.3 million in the United States live with disabilities as a result of TBI (14). When the postresuscitation GCS is not complicated by medications or intubation, approximately 20% of patients with GCS 3 will survive and 8% to 10% will have moderate to good recovery such that they are able to live independently (238). Despite this, 34% to 47% of “minor” head injury patients cannot return to work or their previous lifestyle (239,240). Independent predictors of outcome include older age at time of injury, the postresuscitation Glasgow coma score, injury severity score (ISS), pupillary response on admission, and CT scan findings of diffuse edema, rSAH, SDH, partial obliteration of the basal cisterns, or midline shift (241–246). The TCDB reports a postresuscitation mortality rate of severe TBI patients of 76% and 18%, for patients with postresuscitation GCS of 3 and 6 to 8, respectively. Overall mortality was 36% in 746 patients (42). In another study of 1,311 head-injured patients, the highest mortality was associated with spinal cord injury, obstructed airway, difficulty breathing, and
Pathophysiology

Primary spinal cord injury results from cord compression from discs, bone, ligament, or hematoma, or from distractive forces such as flexion, extension, dislocation, or rotation, which cause shearing of the neuronal axons or vasculature with intramedullary hemorrhage. Similar to head injury, the spinal cord undergoes both primary and secondary injury. Secondary injury can result from additional mechanical forces such as flexion, extension, dislocation, or from disc herniation, bone, ligament, or hematoma, or from distraction, which may be a result of hypotension, electrolyte changes, edema, and excitotoxicity.

**ACUTE SPINAL CORD INJURY**

Diagnosis

**Examination**

The physical examination includes a general examination to survey for other injuries; the quality of the patient’s breathing should be assessed to ensure adequate ventilatory effort. The neurologic examination should include a mental status evaluation as concomitant head injury may occur. A complete cranial nerve examination assesses for evidence of cranial neuropathies or nystagmus suggestive of brainstem or cerebellar ischemia that may result from vertebral artery injury. In 1982, the American Spinal Injury Association (ASIA) developed the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) (Fig. 117.2) (251) to improve precision in determining the level and extent of neurologic injury for the National SCI Statistical Center Database (252). These have been updated since that time, have good interrater reliability (253,254), and are recommended as the preferred neurologic examination tool (255). The ASIA Impairment Scale standardizes language used to describe severity SCI (Table 117.2) (251). The single neurologic level of injury is

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defined as the most caudal segment of the cord with intact sensation and antigravity muscle function strength.

**Radiologic Evaluation**

No cervical radiologic evaluation is recommended in an awake, alert, nonintoxicated trauma patient who has no neck pain or tenderness and is neurologically normal unless there are significant associated injuries that would interfere with the history and physical examination. In this setting, cervical immobilization can be discontinued without imaging. However, in patients with neck pain or tenderness, a high-quality cervical spine CT should be performed. The CT scan is better than MRI for evaluating bones; however, for ligamentous injury, dynamic flexion/extension radiographs in an awake patient are preferred. Alternatively, an MRI within 48 hours of injury can also detect ligamentous injury (256). Newer-genera-
tion CT scanners are sensitive, and routine three-view (antero-posterior, lateral, and odontoid) cervical spine radiographs are not recommended unless high-quality CT imaging is not available. In obtunded patients, again, high-quality cervical CT is recommended to rule out clinically significant injury (257). However caution is taken before removing and immobilizing collar since an obtunded patient cannot report pain associated with ligamentous injury and instability. Options to remove the collar include: (1) waiting until the patient is awake and asymptomatic; (2) a normal MRI obtained within 48 hours (3) waiting until the patient is awake and alert, with at least half of key muscles below the motor level on each side with some preservation) ZPP (lowest dermatome or myotome on each side with some preservation)

**TABLE 117.2 American Spinal Injury Association Impairment Scale**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Complete</td>
<td>No motor or sensory function preserved in S4-S5</td>
</tr>
<tr>
<td>B</td>
<td>Incomplete</td>
<td>Sensory but not motor function preserved below neurologic level, including S4-S5</td>
</tr>
<tr>
<td>C</td>
<td>Incomplete</td>
<td>Motor function preserved below neurologic level; ≥50% of key muscles below the neurologic level have muscle grade &lt;3</td>
</tr>
<tr>
<td>D</td>
<td>Incomplete</td>
<td>Motor function preserved below neurologic level; ≥50% of key muscles below the neurologic level have muscle grade ≥3</td>
</tr>
<tr>
<td>E</td>
<td>Normal</td>
<td>Normal motor and sensory function</td>
</tr>
</tbody>
</table>

Data from International Standards for Neurological Classification of Spinal Cord Injury, revised 2011; Atlanta, GA: American Spinal Injury Association; 2015.
limited or conflicting data); (3) at the discretion of the treating physician (236) or 4) more recent guidelines recommend the removal of the collar following a normal high quality CT scan defined as 3 mm slices or less (238).

MRI is recommended for patients with cervical fracture-dislocation injuries if they cannot be examined during closed reduction. An MRI is performed to evaluate for disrupted or herniated intervertebral discs, which are found in up to 33% to 50% of patients with facet subluxation injuries (259). MRI is also recommended for patients with occipital condyle fractures to assess the integrity of the craniocervical ligaments (260).

**Treatment**

**Immobilization**

If the unstable spine is manipulated, 3% to 25% of spinal cord injuries may occur after the initial traumatic event. Additionally, nearly 20% of ASCIs include multiple noncontiguous vertebral levels (261,262). For this reason, early management of patients with SCI includes immediate prehospital immobilization of the entire spine with a rigid cervical collar with supportive blocks for head immobilization on a rigid backboard with straps (263). To prevent decubitus ulcers, it is recommended that the patient be transferred off the hard board as soon as possible; if the patient is awaiting transfer to another institution, they should be removed during the interim and replaced on the board for actual transport. Padded boards or bean bag boards are recommended to reduce pressure to the occiput and sacrum. Current recommendations advise against the use of sandbags and tape (264).

**Hemodynamic Support**

Systemic hypotension, which contributes to secondary spinal cord injury, can result from trauma-related hypovolemia and from neurogenic shock (265–267). Neurogenic shock is defined as the loss of sympathetic innervation that causes loss of peripheral vasoconstriction and cardiac compensatory mechanisms of tachycardia and increased stroke volume and cardiac output. In experimental models, microvascular spasm, thrombosis, and rupture will disrupt spinal cord vascular autoregulation and make the spinal cord more susceptible to systemic hypotension. This worsens spinal cord ischemia several hours after injury (267). MAP augmentation to 85 to 90 mmHg for 5 to 7 days after injury has been shown to reduce morbidity and mortality and shorten length of stay and are recommended by the recent 2013 guidelines (268–272).

Treatment typically includes volume resuscitation with crystalloid or red blood cell transfusion if the patient is anemic. Volume-resistant hypotension is fivefold more common among patients with complete spinal cord injury above the thoracic sympathetic innervation (269); vasoactive medications such as norepinephrine, dopamine, and phenylephrine may be required. In the subset of patients requiring vasopressors and inotropes, central venous catheters and invasive monitoring with arterial catheters should be used.

**Surgical Intervention**

The timing of surgical decompression, reduction of bony structures, and fusion in the treatment of ASCI have been debated. Earlier “practice options” included surgical intervention on patients with incomplete injury with persisting compression from dislocation with bilateral locked facets, burst fracture, or disc rupture, especially in patients with neurologic deterioration (273). Recent data suggest that early surgery, within 24 hours, has a beneficial effect on motor recovery (274) and current guidelines from 2013 are more definitive regarding recommendations with the goal of decompression of the spinal cord with restoration of the spinal canal (275). Recommendations include early (as rapidly as possible after injury) closed reduction of cervical spinal fracture/dislocation injury (259), and early reduction of fracture-dislocation injuries in the setting of acute traumatic central cord syndrome (CCS) with surgical decompression of the compressed spinal cord, particularly if the compression is focal and anterior (276). Overall, early surgery, possibly because of the ability to mobilize the patient earlier, appears to shorten hospital length of stay and reduce pulmonary complications (273,274,277–279).

**Pharmacologic Intervention**

Following ASCI, a cascade of biochemical processes is activated that produces excitatory amino acids, calcium fluxes, free radicals, acidosis, protein phosphorylation, phospholipases, and apoptosis, which can further injure surrounding tissue (267). Pharmacologic agents targeted to interrupt this cascade may provide neuroprotection by preventing secondary injury; however, similar to TBI, no agent has yet shown benefit (280).

Naloxone, GM-1 ganglioside, and methylprednisolone have undergone randomized clinical trials to examine their effects following spinal cord injury. After multiple trials evaluating the use of methylprednisolone (281–284), based on the lack of class I or class II evidence of benefit and inconsistent class III data, current neurosurgical and ATLS guidelines do not recommend the use of methylprednisolone after ASCI (91). Guidelines note that there are class I, II, and III evidence that high-dose steroids are associated with harmful side effects including pneumonia, gastrointestinal hemorrhage, sepsis and result in longer hospital stays, and death (281,285–287).

**Pulmonary Support**

The most common cause of death in patients with spinal cord injury is due to pneumonia, pulmonary emboli, and sepsisemia (22). In patients with tetraplegia, pneumonia and other respiratory complications occur in 40% to 70% of patients (288,289); aggressive pulmonary toilet is, therefore, essential.

Patients with high-level cervical injuries (C3–5) may fatigue over the first few hours to days. Pulmonary compromise can also be seen in patients with lower cervical cord injuries. Although diaphragmatic innervation arises from the cervical levels of three through five (C3–5), an effective cough and deep inspiration requires intercostal musculature and thoracic innervation to split the chest wall while the diaphragm descends. Additionally, patients who are smokers with increased pulmonary secretions or those who have aspirated fluid such as blood, water, or stomach contents may have difficulty clearing their airway and should be monitored closely for failing pulmonary reserve.

Bedside evaluation with deep inspiration will frequently show a “functional flail chest,” wherein, with deep inspiration, the diaphragm descends, the abdomen rises, but the chest wall does not rise, but collapses or is immobile. Of the pulmonary function tests, vital capacity (VC) appears to be the single global measure of ventilatory status that best correlates with other pulmonary function tests (290). Serial measurements of bedside VC can indicate the need for elective endotracheal
intubation if the VC is less than 20 mL/kg or decreasing rapidly. Hypoxia and hypercapnia are late signs of respiratory failure, and intubation should not await these findings.

**Associated Vascular Injury**

Blunt cervical spinal trauma can result in vascular injury and cause cerebral ischemia (291). Incidence varies from 0.03% to 4.8% and likely depends on the screening method (292–294). Mortality ranges from 23% to 28%, while 48% to 58% of survivors have significant neurologic deficits (295). The most common mechanism of blunt cerebrovascular injury (BCVI) is MVC, followed by falls, and pedestrian and motorcycle crashes. Many institutions use modifications of the Denver Screening Criteria for BCVI based on risk factors to determine whom to screen (296). Risk factors include cervical fractures with subluxation or with a fracture through the transverse foramen, displaced or complex midface or mandibular fracture (LeFort II or III), a basilar skull fracture involving the carotid canal or sphenoid sinus, near-hanging resulting in cerebr al hypoxia, and cervical vertebral body fracture or distraction injury, a seatbelt sign or tissue injury of the anterior neck, and massive epistaxis or a cervical hematoma (292). Suspicion should be high if the patient develops a lateralizing neurologic deficit with an initially normal CT scan, or evidence of a recent ischemic stroke on cerebral imaging. CT angiography (CTA) is sensitive for BCVI and has taken the place of conventional cerebral angiography as the recommended screening tool unless CTA is not available or endovascular treatment is anticipated (297–300). In a patient with a vertebral subluxation or complete spinal cord injury, MRI is the recommended diagnostic modality (300).

A grading system of injury has been described by Biffl (301) (Table 117.3). Fifty-seven percentage of grade I injuries heal spontaneously in 10 days independent of therapy (302); therefore, they can be treated with aspirin. Retrospective studies of grade II through IV injuries show no difference between antiplatelet agent or heparin therapy although heparinization increases hemorrhage risk (303,304). Current recommendations suggest individualized therapy dependent on the vascular injury, associated injuries, and the level of hemorrhage. Options include no treatment, antiplatelet therapy, or anticoagulation. No recommendations regarding endovascular therapy can yet be made (300).

**Thromboprophylaxis**

DVT detection with $^{131}$I-fibrinogen scans of patients with ASCI and paralysis ranges as high as 100% (305). Recommended diagnostic tests include: duplex Doppler ultrasound, impedance plethysmography, venous occlusion plethysmography, venography, and the clinical examination (306).

Prophylactic LMWH or LDUFH, in conjunction with mechanical prophylaxis such as pneumatic compression stockings or electrical stimulation, is recommended for patients with ASCI by both the American College of Chest Physicians, the Neurocritical Care Society, and Congress of Neurological Surgeons (221,224). Notably, neurosurgery Level II guidelines recommend that low-dose heparin therapy alone or oral anticoagulation alone is not recommended as a prophylactic treatment strategy. The period of highest risk for DVT is in the first few months following injury. Guidelines recommend early administration within 72 hours of injury and continued for 3 months (306).

By both guidelines, IVC filters are not recommended as primary prophylaxis against pulmonary embolus, but are recommended in patients who fail anticoagulation or who are not candidates for anticoagulation and/or mechanical devices. These may include those with concurrent severe head injury (307). “Quad” coughing is a Heimlich maneuver used for pulmonary toilet to clear secretions in SCI patients with a poor cough; IVC filters have been reported to embolize or perforate with quad coughing (308,309). In one series, the majority of patients with these complications received vigorous pulmonary toilet (46%) including quad coughing. Quad coughing probably should be avoided until the IVC filter is removed. Following trauma, there may be patients who have undergone spinal surgery and require full anticoagulation due to an acute pulmonary embolism, or myocardial ischemia or infarction. There are no prospective randomized studies of the safety of anticoagulation following spinal surgery for ASCI (310). In this setting, an open discussion of the risks and benefits with the patient and his or her decision makers is necessary. If anticoagulation is used, close neurologic checks are essential as early evacuation of an acute EDH can impact neurologic outcome if the injury to the spinal cord is incomplete (311,312).

**Nutritional Support**

As described above, TBI is associated with a hypermetabolic, catabolic state with nitrogen loss. In spinal cord injury victims, indirect calorimetry will be more accurate than the Harris–Benedict equation to determine metabolic needs and is recommended (225,313). Although metabolic needs may be increased, the REE may be lower than expected.

**Autonomic Dysreflexia**

Autonomic dysreflexia is a life-threatening hypertensive emergency that typically occurs in patients with motor-complete SCI above the T6 neurologic level (314,315). Autonomic dysreflexia is typically seen in the rehabilitative phase of SCI; however, it has been recognized as early as 4 days after injury (316). Noxious stimuli including fecal impaction, bladder distention, or pain to the lower extremities increases sympathetic outflow below the injury level. Resultant vasoconstriction of the splanchnic bed forces blood into the systemic circulation and increases blood pressure. Reflex parasympathetic outflow rostral to the injury allows flushing of the skin above the level of the lesion and bradycardia. Recognition of this entity, and detection and removal of the inciting noxious stimulus is
primary. Blood pressure treatment traditionally included ganglionic blockers, although intravenous antihypertensives such as clevidipine, nicardipine or nitroprusside can be effective.

**Prognosis**

Determinants of outcome following ASCI include the level and severity of injury, age, initial motor strength, and MRI findings. The ASIA Spinal Cord Injury Classification is useful for studies and comparison of outcome (317). Incomplete injury has a better prognosis than those that are complete. The ASIA Impairment Scale severity on presentation of injury is one of the strongest predictors for outcome (318,319). Those in group A are unlikely to have significant recovery (319) whereas those in groups C and D recover better than those in B. Most recovery occurs in the first 6 months after injury with the greatest rate of improvement in the first 3 months (22).

MRI shows that complete spinal cord injury is typically associated with more substantial maximum canal compromise, spinal cord compression, increased length of lesion, hemorrhage, and cord edema. Substantial canal compromise, intramedullary hemorrhage, and cord edema at time of presentation can be predictive of a poorer prognosis (320).

Two clinical entities described in ASCI are pertinent to prognosis. The first, spinal shock, is a transient loss of spinal cord sensorimotor function. Patients present with flaccid paralysis and loss of all spinal cord reflexes including the bulbocavernous, cremasteric, and deep tendon reflexes. Priapism can be seen due to local unopposed parasympathetic outflow. If there is no anatomic injury, function returns within hours to days.

The second is the CCS in which the motor deficit in the upper extremities is disproportionately worse than that in the lower extremities, with bowel and bladder dysfunction and variable sensory loss below the level of injury (321,322). Most patients with CCS improve neurologically, although many have significant persistent neurologic deficits. Typically, CCS results from hyperextension injury without a fracture in older patients as a result of a stenotic spondylotic cervical canal (323). It is also seen in a younger population with acute cervical disc herniation or spinal instability which may require early surgical decompression and stabilization (276). Motor recovery is improved when there is a higher motor score at the time of injury (322).

**CONTROVERSIES**

- Current controversies with head injury typically involve imaging and monitoring. Since changes on repeat CT imaging that require clinical intervention are accompanied by changes in the neurologic examination, it would seem that close neurologic monitoring rather than routine repeat imaging should be adopted. It is a costly modality with some risk to the patient including radiation exposure and transport. Yet the possible consequence of a missed injury leads to the practice of unnecessary routine repeat imaging.
- While calculating CPP, there continues to be a lack of standardization of nursing practice of the measurement of MAP with regard to establishing the reference point for the transducer of the invasive arterial monitor. If the patient is being nursed in high Fowler position (HOB elevated) rather than supine, then the MAP relative to the brain will be lower than the MAP when the arterial transducer is zeroed to the heart (i.e., phlebostatic axis at the midaxillary line). When measuring MAP to calculate CPP, the reference point for the arterial transducer should be at the midbrain (i.e., level of the tragus); however, this is rarely the practice. A recent survey noted that of 34 neurocritical care centers, 74% reported using the heart and 16% used the midbrain (324). The same study reviewed 32 articles reporting CPP data. The reference point for MAP was reported in 16 of the studies with 10 using the heart, and 6 using the midbrain. To date, no standardized clinical practice has been achieved (324,325).
- Multimodality monitoring including cerebral blood oximetry, microdialysis, and near-infrared spectroscopy are available commercially. However, it is still unknown as to whether establishing target parameters with aggressive goal-directed therapy improves patient outcome.
- Screening for BCVI can be performed, but if injury is found the evidence base for the most effective and safe therapy especially after traumatic injury does not yet exist. Similarly, if there is an indication for full anticoagulation in a patient, the optimal timing in the setting of intracranial or spinal injury is not yet known.
- Following ASCI, controversies include the timing of surgery. There is no clear definition as to whether “early” surgery translates to 24, 48, or 72 hours or even earlier. The practicability of early surgery can be difficult in many settings and if outcome is poor after surgery, litigious individuals might consider the operative intervention to be causative. For this reason, despite the guidelines for early surgery, surgeons may be extremely conservative as to early operative approach.
- Also, despite guidelines evaluating the existing evidence that recommend that steroids may have more adverse effects than benefit following ASCI, some practitioners still choose to administer steroids in this setting.
- Although advances are being made in the area of the management of neurologically critically ill patients, much more work is needed to improve outcomes for these patients.

**Key Points**

- Primary prevention and avoidance of neurologic injury is essential to decrease neurologic injury. National and global efforts are underway, particularly to improve road traffic safety.
- Head injury: perform a rapid assessment of GCS score to determine severity of injury and need for endotracheal intubation or ICP monitoring.
- Spinal cord injury: early evaluation of the strength of pulmonary mechanics with visual examination of chest excursion with deep breathing and bedside VC measurement to determine need for intubation.
- Initial and serial neurologic bedside examination to assess alteration in mental status, cranial neuropathies, motor and sensory deficits in all patients.
- Emergent CT scan of the brain and spinal column following traumatic injury.
- CTA of the neck and brain to assess for BCVI following trauma in selected patients.
- Recognition of early signs of intracranial hypertension including systemic hypertension.
• To prevent secondary neurologic injury maintain:
  • Adequate oxygenation with PaO₂ above 60 mmHg and O₂ saturation above 90%.
  • Adequate perfusion following head injury with a SBP 100 mm Hg or greater in patients 50 to 69 years old and 110 mm Hg or greater in patients 15 to 49 or greater than 70 years old; or CPP 60 to 70 mmHg, and MAP equal or greater than 85 mm after ASIL.
  • Eurovolemia, euglycemia, and normothermia.
  • ICP monitoring should be performed in patients with GCS of 8 or less.
  • Steroids are not indicated for brain or spinal cord traumatic injury.
  • Age and severity at time of brain or spinal cord injury and level of spinal cord injury are significant determinants of outcome.

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