Chapter 15

TRAUMATIC BRAIN INJURY

LOUIS M. FRENCH, PsyD*; MARIA MOURATIDIS, PsyD†; BRAD DICIANNO, MD§; AND BRADLEY IMPINK, BSE¥

*Director, TBI Program, Departments of Orthopaedics and Rehabilitation, Walter Reed Army Medical Center, Military Advanced Training Center, Building 2A, 6900 Georgia Avenue, NW, Washington, DC 20307; Assistant Professor of Neurology, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, Maryland 20814

†Command Consultant and Subject Matter Expert for Traumatic Brain Injury and Psychological Health, National Naval Medical Center, 8901 Wisconsin Avenue, Bethesda, Maryland 20889

§Assistant Professor, Human Engineering and Research Labs, VA Pittsburgh Healthcare System, 7180 Highland Drive, 151R1-H, Building 4, 2nd Floor East, Pittsburgh, Pennsylvania 15206

‡Predoctoral Fellow, Human Engineering Research Laboratories, VA Pittsburgh Healthcare System, 7180 Highland Drive, 151R1-H, Building 4, 2nd Floor East, Pittsburgh, Pennsylvania 15206; formerly, Graduate Student Researcher, Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania

INTRODUCTION

Traumatic brain injury (TBI) is a global public health issue that is the leading cause of death and disability in young adults in the United States. The Centers for Disease Control and Prevention (CDC) estimates that 1.4 million individuals in the United States sustain TBI annually; 50,000 of those injuries are fatal.[1] Around 80,000 to 90,000 individuals per year sustain permanent disability as a result of TBI. The CDC estimates the monetary cost of TBI to the public to be almost $50 billion annually when treatment costs, lost wages, disability, and death are considered.[2,3]

TBI can significantly impair functioning and may negatively impact an individual's relationships, health, and happiness. Military service, even during peacetime, increases the risk of brain injury. In wartime, combat operations add to that risk. The incidence of TBI in young female service members is similar to that of young adult male civilians, the group with the highest rate of TBI in the civilian population.[4] TBI impacts the military as a whole by compromising the health and well-being of service members and their families and hindering operational readiness.

The survival rate for those injured in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) is much higher than in past wars. The current ratio of wounded to killed in Iraq is over nine to one,[5] compared to a ratio of fewer than three to one in Vietnam and Korea and about two to one in World War II.[6] This rate of survival is related to numerous factors, including advanced in-theater medical care, rapid evacuation, and advanced protective equipment. Concurrent with these survival rates, the military has observed an increased number of those who may have experienced TBI. The most common causes of injury in OEF and OIF are roadside bombs, improvised explosive devices, and explosively formed projectiles. The resultant blast wave from these weapons may cause TBI either through the direct blast effect or the secondary or tertiary effects (impact of an object against a person or a person against an object, respectively). Additionally, many service members deployed in support of OIF and OEF have been exposed to a multitude of blasts. Although a specific injury may be attributed to one of these events, the effect on the brain by cumulative blast exposures has not yet been clearly elucidated. Therefore, it is important that all healthcare providers who work with injured military service members be aware of the potential for existing TBI.

TBI is typically identified soon after injury. However, delayed recognition, especially when the injury is relatively mild, is not uncommon. These "silent injuries," whether occurring in a military or civilian setting, typically resolve without long-term consequences. Under some circumstances though, they have implications for functioning and may significantly impact the recovery and rehabilitation of other, more visible injuries.

As of March 31, 2008, Defense and Veterans Brain Injury Center sites reported 6,602 US service members have sustained TBI related to the global war on terror since January 1, 2003. The majority of those (1,523) were seen at Walter Reed Army Medical Center. Thirty-two percent of those arriving via air from Iraq and Afghanistan were diagnosed with TBI, often in association with another injury. Of all US service members medically evacuated from Iraq or Afghanistan, 25% reportedly sustained injuries to the head or neck.[7] Additionally, military screening of service members returning from deployment (not medically evacuated) have determined 10% to 20% sustained a concussion or mild TBI (MTBI) at some time during their tour.[8]

DEFINITION OF TRAUMATIC BRAIN INJURY

TBI is described as either closed or penetrating injury. A penetrating brain injury occurs when a foreign object or bone penetrates the dura surrounding the brain. In a military setting, this is most commonly a bullet or metal fragment, but it can involve bone from the skull or other foreign bodies, such as stones. Although the dura is not penetrated in a closed TBI, large external forces may act on the head, leading to significant brain damage. Although there is some variability in the definition of TBI, especially with respect to defining milder injuries, most accepted definitions (those advanced by the CDC, American Congress on Rehabilitation Medicine, American Psychological Association, and the World Health Organization) share common elements. The Department of Defense's current definition was drafted in 2007 by a consensus panel of experts (Exhibit 15-1, Table 15-1).

BASIC PATHOPHYSIOLOGY OF TRAUMATIC BRAIN INJURY

The severity of closed TBI is typically characterized by the duration of loss of consciousness; duration of posttraumatic amnesia; and initial, postresuscitation Glasgow Coma Scale score. In addition to these criteria,

EXHIBIT 15-1

DEPARTMENT OF DEFENSE CONSENSUS ON TRAUMATIC BRAIN INJURY DEFINITION

The Department of Defense Consensus on Traumatic Brain Injury (TBI) defines TBI as a traumatically induced structural injury or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs immediately following the event:

- any period of loss of or decreased level of consciousness;
- any loss of memory of events immediately before or after the injury;
- any alteration in mental state at the time of the injury (eg, confusion, disorientation, slowed thinking);
- neurological deficits (eg, weakness, balance disturbance, praxis, paresis/plegia, change in vision, other sensory alterations, aphasia) that may be transient; or
- intracranial abnormalities (eg, contusions, diffuse axonal injury, hemorrhages, aneurysms).

External forces include the following:

- an object striking the head;
- the head striking an object;
- the brain undergoing an acceleration or deceleration movement without direct external trauma to the head;
- a foreign body penetrating the brain;
- forces generated from an event such as a blast or explosion; or
- other forces yet to be defined.

Sequelae of TBI may resolve quickly, within minutes to hours after the neurological event, or they may persist. Some sequelae of TBI may be permanent. Most signs and symptoms will manifest immediately following the event; however, other signs and symptoms may be delayed from days to months (eg, subdural hematoma, seizures, hydrocephalus, and spasticity). Signs and symptoms may occur alone or in varying combinations and may result in functional impairment. The following signs and symptoms are not better explained by preexisting conditions or other medical, neurological, or psychological causes, except in cases of an exacerbation of a preexisting condition:

- cognitive (eg, attention, concentration, memory, speed of processing, new learning, planning, reasoning, judgment, executive control, self-awareness, language, or abstract thinking);
- physical (eg, headache, nausea, vomiting, dizziness, blurred vision, sleep disturbance, weakness, paresis/plegia, sensory loss, spasticity, aphasia, dysphagia, apraxia, balance disorders, coordination disorders, or seizure disorders); and
- emotional/behavioral (eg, depression, anxiety, agitation, irritability, impulsivity, or aggression).

Cognitive, physical, or emotional/behavioral manifestations that cannot be better explained by another process may be casually related to the blast event, even when there is no identifiable evidence of structural brain injury on imaging studies or altered brain function immediately following the event. Further study is needed to determine if an episode of altered brain function at the time of the trauma is required for a diagnosis of TBI resulting from an explosion or blast.

Injury severity is determined at the time of the injury. Although this severity level has some prognostic value, it does not necessarily reflect the patient's ability to function. Serial assessments of the patient's cognitive, emotional/behavioral, and social functioning are required. The patient is classified as mild, moderate, or severe (see Table 15-1).

Data source: US Department of Defense Consensus Traumatic Brain Injury Definition. Developed at: DoD Force Health Protection and Readiness TBI Consensus Meeting; 2007.

neuroimaging results also play a role in injury severity. For example, an individual who loses consciousness or sustains posttraumatic amnesia consistent with MTBI will be classified as having a moderate injury if abnormality is evident on brain images because those individuals have similar outcomes.[9,10] Current definitions and designations of TBI only describe the severity of the brain injury itself, and do not neces-

TABLE 15-1

BRAIN INJURY SEVERITY LEVELS

Level	Structural Imaging	Loss of Consciousness	Alteration of Consciousness	Posttraumatic Amnesia
Mild	Normal	0–30 min	a moment–24 hrs	0–1 day
Moderate	Normal or abnormal	> 30 min–24 hrs	24 hrs; severity based on other criteria	1–7 days
Severe	Normal or abnormal	> 24 hrs	24 hrs; severity based on other criteria	> 7 days

Data source: US Department of Defense Consensus Traumatic Brain Injury Definition. Developed at: DoD Force Health Protection and Readiness TBI Consensus Meeting; 2007.

sarily correlate with resultant symptomatic sequelae, clinical outcomes, or functionality. There is generally a greater chance for persistent problems in those with severe injuries, but it is not uncommon for individuals diagnosed with severe TBI to have a better functional recovery than those diagnosed with MTBI, who may have resultant catastrophic changes in personal, social, and occupational functioning. Fortunately, such poor outcomes are relatively rare and are often mediated by a variety of factors.[11] Further research is required to determine if the typical outcomes seen in a civilian population, especially in the case of recovery from MTBI, are similar to those seen in the combat-injured population. Contextual issues, such as the high rate of comorbid medical, physical, or psychological problems, may also significantly impact TBI recovery in this patient population.

The two most common injury mechanisms associated with TBI are contact and acceleration/deceleration. A third mechanism, blast, has become the subject of increasing debate given the large number of blast casualties returning from OEF and OIF. Blast injuries may have some different characteristics than those resulting from contact or acceleration/deceleration injuries. TBI, regardless of its severity, can result in damage to the structure and function of the brain. Contact injuries can result in focal brain damage, such as lacerations, contusions, skull fractures, penetration wounds, and intracranial hemorrhage. Acceleration/deceleration injuries can result in diffuse brain damage, such as diffuse axonal injury and cerebral edema.[12–16] Immediately following TBI, cerebral blood flow regulation and glucose metabolism are impaired. Cerebral blood flow may decrease significantly, and cerebral ischemia is common.[17–25] Cerebral metabolism is often diminished following TBI, which is related to mitochondrial dysfunction and reduced production of adenosine triphosphate. Reduced cerebral blood flow causes an ischemic-like state wherein anaerobic glycolysis leads to lactic acid accumulation. Anaerobic glycolysis cannot provide sufficient energy for cellular function and, because of adenosine triphosphate depletion, the energy-dependent membrane ion pumps fail. This results in a secondary pathophysiological response, which includes membrane depolarization, excessive neurotransmitter release, and ion flux.[12,26] The primary excitatory neurotransmitter released is glutamate, which over-stimulates ionotropic glutamate receptors, resulting in Ca^{2+}, Na^{+}, and K^{+} fluxes. This leads to a catabolic state, increasing the intracellular concentrations of toxic products, such as free fatty acids and free radicals. Ultimately, the activation of various enzymes (proteases, peroxidases, phospholipases, caspases, translocases, and endonucleases) leads to membrane degradation, blood–brain barrier breakdown, necrosis, and apoptosis. Breakdown of the cerebral-vascular barrier results in increased cell membrane permeability, ultimately resulting in cerebral edema, which may further exacerbate the ischemic state.[27,28] This process is more pronounced as the severity of the trauma increases.[29]

While not considered TBI in itself, secondary brain insults, like systemic hypotension and hypoxia, reportedly worsen outcomes in patients with TBI.[30]

BLAST EFFECTS

In 20th-century military conflicts such as Vietnam, the focus of attention in combat-related brain injuries has been on the penetrating craniocerebral injury.[31] In the current global war on terror, concussive forces

and resultant MTBI have proven challenging. A recent report states that 88% of injuries seen at an echelon II medical unit during OIF were due to explosions.[32] This figure is generally consistent with official reports on mechanism of injury in US troops in Iraq, in which 80% of casualties were due to blast.[33] Sophisticated body armor and protection against penetrating head wounds allow US troops to survive explosive attacks they would not have survived in previous wars. Because of the frequency of TBI and its impact on service members, the military has increased its efforts to screen for MTBI.

Levi and colleagues reported on a series of head-injured patients during the 1982–1985 Lebanese war and found the majority of TBI reported was penetrating.[34,35] One subset (n = 17) of the patients who suffered blast injury were identified. Blast was defined as "a) primary—due to the air blast, b) secondary—due to the impact of blast energized debris (either on the victim or vice versa), and c) tertiary—due to the effects of fire, gases or collapse of a building."[35(p555)] The authors commented on the high frequency of pathology identified by computed tomography, including diffuse brain injury. They concluded that there was a "unique character of head injuries sustained during explosion."[34] In one study of injuries in the Balkan conflicts, 30% of the blast injured had long-term (greater than 1 year) symptoms reflecting central nervous system disorders, as compared to just 4% of the non-blast–injured patients.[36] Building on experience with soldiers, Cernak et al conducted animal studies in the laboratory to examine blast wave effects on the central nervous system. The studies showed structural, biochemical, and cognitive impairments in rat brains after either whole-body or local (chest) overpressure while the head was protected. Both groups of animals showed neuronal injury in the hippocampus. The whole-body–exposed group showed significant decline in performance on a previously learned task that persisted at least 5 days. In the local (chest overpressure) group, there was also a significant drop in performance, but with normalization by 1 day after injury. There was a significant linear relationship between blast injury severity and decline in task performance in each group.[37]

Interest in combat-blast–related injury in the central nervous system dates back to at least World War I and is again discussed in the scientific literature of the World War II era.[38,39] The effects of physical and psychological injuries on soldiers' symptom presentation and functioning was often debated. A more modern understanding fully appreciates the relationship between cognitive functioning and emotional stress; it has been shown that combat exposure puts individuals at higher risk for health-related problems, partly because of potential TBI.[40]

Whether blast-induced brain injury demonstrates a different course of illness and recovery than more traditional causes of TBI is the subject of ongoing investigation, as is whether cognitive and emotional profiles affect outcomes. It has been suggested that differences may result from the effect of the blast wave itself, the added emotional factors associated with military service and combat, and the potential that blasts may cause greater overall extracranial injury. In a study of victims of terror-related activities, Peleg and colleagues showed that gunshot wounds and injuries from explosions differ in the body regions of injury, distribution of severity, hospital length of stay, and length of stay in the intensive care unit.[41] In the blast victims, it was reported that multiple body regions were more often affected. The blast victims also had more critical and fatal injuries compared to the gunshot victims. Traumatic vasospasm has also been reported in a substantial number of patients with severe blast neurotrauma (80.8%–86.7% of those injured). Additionally, it was noted that clinical outcomes were worse for those with this condition.[6] TBI was noted in 56% of patients seen in the Veterans Affairs polytrauma system. Those with blast-related TBI demonstrated unique patterns of injury. Soft tissue, eye, oral and maxillofacial, otologic, and penetrating brain injuries; symptoms of posttraumatic stress disorder (PTSD); and auditory impairments were more common in blast-injured patients than in those with other war-related injuries. Despite these differences in injury profiles, functional outcome was not predicted by the mechanism of the injury.[42]

NEUROBEHAVIORAL SEQUELAE OF TRAUMATIC BRAIN INJURY AND POSTCONCUSSIVE DISORDER

Neurobehavioral changes are a common consequence of TBI. The characteristics, extent, and duration of these changes are dependent on a multitude of factors, including the type and location of injury, genetic predisposition, environment, and psychosocial support system. Psychosocial functioning has also been shown to be affected by TBI. The extent of these functional limitations is related to the demographics of the population injured, existing comorbid injuries, and severity of the head injury itself. As would be expected, more severe head injuries are associated with poorer outcomes, including greater reliance on family and social subsidy systems, greater unemployment, and lower income. The severity of the TBI is also more closely related to objective indices of psychosocial outcome (eg, employment) than to self-perceived

psychosocial limitations.[43]

Cognitive changes are among the most frequently reported difficulties following TBI and can be the most debilitating. In at least one study, physical deficits were not related to the ability to return to employment, but the presence of cognitive, behavioral, and personality changes was significantly related to work failure.[44] The extent of cognitive difficulties is based largely on the nature and extent of damage to the brain, especially the severity of the diffuse axonal injury suffered.[45] Potential cognitive difficulties are wide ranging and encompass disruptions in various aspects of attention, learning and memory, language, and executive functioning (the ability to plan, organize, and self-monitor). These key aspects of executive functioning, which are necessary for the execution of goal-directed activities in daily life, are increasingly disrupted with anterior brain lesions because of the anatomic localization of these critical neural substrates in the anterior forebrain.[46]

In general, MTBI is unlikely to cause persistent, significant cognitive difficulties. In a study of MTBI, Belanger and colleagues conducted a metaanalysis of the relevant literature based on 39 studies involving 1,463 cases of MTBI and 1,191 control cases to determine the impact of MTBI across nine cognitive domains (global cognitive ability, attention, executive functions, fluency, memory acquisition, delayed memory, language, visuospatial skill, and motor functions).[47] The overall effect of MTBI on neuropsychological functioning was moderate, and was found to correlate with patient characteristics, time since injury, and the cognitive domain affected. Acute (less than 3 months after injury) effects of MTBI were greatest for delayed memory and fluency. In unselected or prospective groups of patients, the overall analysis revealed no residual neuropsychological impairment by 3 months after injury. In contrast, clinic-based groups of patients and those groups including participants in litigation were associated with greater cognitive sequelae of MTBI. In another study by the same investigators, a metaanalysis of sports concussion literature from 1970 to 2004 found 21 studies meeting inclusion criteria, leading to a total of 790 cases of MTBI and 2,016 control cases.[48] TBI only modestly effected cognitive functioning, with delayed memory, memory acquisition, and global cognitive functioning showing the greatest effects acutely. No residual effects were found from the group tested over 1 week after injury. Iverson illustrated that moderate and severe TBI have a significant, negative effect on cognition, but, after the acute recovery period, MTBI has essentially no measurable effect.[29] Larger effects were observed in conditions such as depression, bipolar disorder, and attention deficit hyperactivity disorder than from MTBI.

A World Health Organization analysis of MTBI outcomes concluded that although acute symptoms are common, MTBI symptoms resolve in the vast majority of individuals by 3 months after injury, often sooner.[11] However, the authors acknowledge that a subset of those with MTBI continue to manifest persistent symptoms. This has also been clinically observed in both military and civilian settings. In a review article on outcomes from MTBI, Iverson et al report that post-concussion symptoms are common in healthy subjects, including those without history of TBI. These findings have important implications for symptom attribution and recovery.[49] In some cases, without education about recovery and expected course of illness, patients who have suffered MTBI (ie, concussion) may attribute symptoms related to the combat environment or the challenges of everyday life to the effects of a remote brain injury.

The issues surrounding persistent symptoms after MTBI, especially as related to military deployment, has led to debate. The first controversy relates to the scope of the problem itself. Although it has been reported that 10% to 20% of those with MTBI will develop chronic persistent symptoms, it is likely that this figure is closer to 5%.[49] An equally controversial topic is the theoretical cause of persistent symptoms after MTBI. Various authors have attributed MTBI symptoms to different causes, some believing they are related to the type and location of injury, others purporting a multicausal etiology, influenced by premorbid personality characteristics, social-psychological factors, and exaggeration of symptom manifestation (either conscious or unconscious).

TRAUMATIC BRAIN INJURY IN THE AMPUTEE

For those who have sustained limb amputation as a result of combat operations, there is concern about other conditions that may be a consequence of combat exposure, such as TBI, acute stress, and PTSD. Hoge et al surveyed four US combat infantry units either before their deployment to Iraq or 3 to 4 months after their return from combat duty in Iraq or Afghanistan. Those who had been deployed to Iraq reported a high number of combat experiences, with more than 90% reporting being shot at and a high percentage reporting handling dead bodies, knowing someone who was injured or killed, or killing an enemy combatant.[50] Soldiers who served in Afghanistan reported lower but still substantial rates of similar combat experiences.

The percentage of individuals whose responses met the screening criteria for major depression, PTSD, or alcohol misuse was significantly higher among soldiers after deployment than before deployment. Among service members in OIF, the prevalence of PTSD increased with the number of firefights during deployment, reaching 19.3% for those involved in more than five firefights. Additionally within this group, it was found that the rates of PTSD were associated with having been wounded or injured (odds ratio for those deployed to Iraq was 3.27; odds ratio for those deployed to Afghanistan was 2.49). This latter finding is consistent with Koren's study of PTSD rates in injured Israeli war veterans.[51] In that study, findings indicated that bodily injury is a risk factor for PTSD, with odds of developing PTSD following traumatic injury approximately eight times higher than following injury-free emotional trauma.

Although myriad factors influence the overall functional outcome of a service member with a major limb amputation, it is clear that both emotional and cognitive factors play a significant role in recovery. The presence of disorders such as depression or anxiety is associated with greater overall use of healthcare resources.[52] There is limited literature on the predictive value of mental disturbances and cognitive impairments on functional outcome in an amputee population. In general, and representative of the war-injured population, younger men have more difficulties adjusting to amputations, presumably because of concerns over body image, social stigma, or other related factors.[53] These concerns may contribute to the high rates of self-reported sexual problems in those with lower extremity amputations.[54]

In a study of the physical, mental, and social predictors of functional outcome in geriatric, unilateral lower limb amputees, Schoppen et al reported that memory ability was the most important of the mental predictors for functioning after leg amputation,[55] suggesting that good memory may be important for relearning daily tasks. Depression level 2 weeks after amputation was also found to be predictive of outcome at 1 year. In another study of geriatric amputees, records of 2,375 lower extremity amputees treated in Veterans Affairs hospitals were examined to determine which patient factors may influence the prescription of a prosthesis.[56] Those with high cognitive Functional Independence Measure (FIM) scores were 1.67 times more likely to be prescribed a prosthesis than those in the lowest FIM category (the FIM, a widely accepted functional measure in the research community, is an 18-item, 7-level ordinal scale intended to be sensitive to change in an individual over the course of a comprehensive inpatient medical rehabilitation program). Taylor et al investigated the relationship between a variety of preoperative clinical characteristics after major lower limb amputation and postoperative functional outcome.[57] Among other factors, the presence of dementia was significantly associated with failure to maintain independent living status. Because TBI may disrupt cognitive functioning, some aspects of amputee rehabilitation may be complicated, such as learning new tasks, remembering appointments, and regaining independence.

TREATMENT OF TRAUMATIC BRAIN INJURY

Because the majority of TBI that occurs in the civilian and military settings is mild, symptoms can generally be expected to improve over time and, in most cases, completely resolve.[29] MTBI is characterized by immediate physiological changes in the brain, but in the first week after injury, the brain undergoes a dynamic restorative process. This is often seen in athletes, who are typically able to return to preinjury functioning (cognitive and self-report) within 2 weeks after a concussion. Trauma patients usually take longer to return to preinjury functioning because of factors such as preexisting psychiatric or substance abuse problems, poor general health, concurrent orthopaedic injuries, pain, or various psychosocial problems.[29] The clinical team should communicate the expectation of a full recovery with the patient while simultaneously assessing the patient's symptom complex and providing treatment as indicated. The extent of intervention or rehabilitation required will be determined by a patient's comorbid injuries rather than the degree of brain injury.[42]

Symptom treatment for MTBI includes four areas of focus: pharmacological management, educational interventions, rest and return to duty decisions, and targeted therapies. Evidence for the efficiency of various pharmacologic interventions is prolific.[58,59] Pharmacological interventions are often indicated for sleep regulation,[60] headache,[61,62] pain,[63] and depression.[64] Treating these associated conditions improves quality of life and rehabilitation outcomes.

Educational and psychological therapies have also proven effective in treating MTBI. Mittenberg compared two groups of patients with MTBI. Group I (n = 29) participated in a cognitive-behavioral model of symptom maintenance and treatment, learned techniques for reducing symptoms, received printed educational manuals, and met with a therapist prior to hospital discharge to review the nature and

incidence of expected symptoms and instructions for gradual resumption of premorbid activities.[65] The control group (n = 29) received routine hospital treatment and discharge instructions. After 6 months, Group I reported significantly shorter average symptom duration (33 compared to 51 days) and significantly fewer symptoms at follow-up. The conclusion was that brief, early psychological interventions are effective in reducing the incidence of postconcussive symptoms. Ponsford et al have shown similar results.[66] Individuals seen 1 week after injury and given informational material reported fewer symptoms overall and were significantly less stressed at 3 months after the injury than a group that did not receive the same education. A number of educational materials are available from public and private sources, including the Defense and Veterans Brain Injury Center.[67]

ACUTE MEDICAL CARE

Emergency preadmission care is aimed at preventing hypoxia and hypotension, which can lead to secondary neurological injury.[68] When admitting a patient for neurosurgical services, care is geared toward stabilizing the patient, treating infection, and detecting operable lesions that may prevent further neurological deterioration. The role of decompressive craniectomy remains controversial because it does not result in improved outcomes in all cases. Once the patient is stabilized, treatment is focused on creating an environment in which the brain has the best chance of neural recovery; this involves managing temperature, intracranial pressure, and perfusion and oxygenation; glycemic control; and early nutrition.[68,69] Drug-based neuroprotection is one aspect of the acute management of TBI. Medications, such as *N*-methyl-D-aspartate antagonists, are being studied in clinical trials and have shown potential long-term benefit.[69]

The risk of posttraumatic seizures is high in some subpopulations, especially those with war injuries.[70] Steroid therapy has not been shown to have any beneficial effect on seizures.[69] It is also clear from the literature that long-term use of anticonvulsants, such as phenytoin, does not prevent late seizures.[69] Managing early seizures with anticonvulsant therapy remains controversial. One study showed that late-seizure risk factors include brain contusion with subdural hematoma, skull fracture, loss of consciousness or amnesia (lasting > 1 day), and being older than 65 years.[70] However, in another study by four National Institute on Disability and Rehabilitation Research model system sites, bilateral parietal contusion, penetration of the dura, and multiple intracranial operations resulted in the highest risks for late seizures.[71]

Heterotopic ossification (HO), defined as pathologic ectopic bone formation in the soft tissue surrounding the joints, often afflicts patients after TBI, and this can have a significant impact on the rehabilitation and recovery of the amputee. The incidence of HO in TBI varies from approximately 10% to 70%, with a clinically significant incidence reported in the range of 10% to 20%.[72–75] HO typically causes pain and limits range of motion. Larger joints, like the hips, knees, and elbows, are most commonly affected. The pathogenesis of HO is unknown, but several risk factors have been identified, including prolonged coma after TBI, spasticity, immobilization, and increased serum alkaline phosphotase levels. HO is best diagnosed using sonography, three-phase bone scanning, or plain radiography. Range-of-motion therapy is often used to prevent HO. Although there is little evidence to support this theory, some believe active range-of-motion therapy may promote HO, therefore passive range-of-motion therapy is often recommended. Surgical excision, when indicated, is typically delayed until bone fully matures (typically 12–18 months). This waiting period is thought to reduce the risk of reoccurrence, but recent data suggests that early excision may be better and that recurrence is unlikely.[72] Literature concerning HO treatment is generally limited to surgical case studies without control groups.

Preventing and treating deep venous thrombosis (DVT) in patients with TBI can be complicated by concerns for intracranial bleeding. However, many recent studies show that chemical prophylaxis can help prevent DVT in certain populations that are at increased risk of bleeding. The importance of screening for DVT in these populations by ultrasound, computed tomography, and now by D-dimer testing (despite its high false-positive rates) remains critical because the risks of DVT and subsequent fatal pulmonary embolism are high, especially for those with blast injuries.[76] Although there is no consensus on national clinical practice guidelines,[77] Walter Reed Army Medical Center has developed its own guidelines specific to trauma patients.[76]

Diffuse spasticity is a relatively common complication in individuals with severe TBI. Management can often be challenging, but begins with a well-structured and consistent program of stretching and range-of-motion exercises administered by trained therapists. Family members can often be taught how to help facilitate range-of-motion exercises. Oral medications, such as tizanidine[78] or baclofen (which

is more effective at managing lower limb tone),[79] may also be helpful. Unfortunately, oral management may be limited by side effects, such as sedation. For focal spasticity, interventional injections with botulinum toxin can be efficacious.[80] Intrathecal baclofen pumps have also proven to be effective in a number of trials for more diffuse spasticity and may also be useful in managing dysautonomia (the inability to regulate the autonomic nervous system).[69] Dysautonomia can manifest with tachycardia, tachypnea, fever, or hypertension. This process is less well understood, but a collection of case studies suggests that beta blockers, morphine, chlorpromazine, or midazolam may be effective treatments. Caution is needed any time such sedation medications are used in patients with TBI.[69]

REHABILITATION

When discussing TBI rehabilitation, it is important to note that "we have really only recently begun to evaluate the efficacy of approaches being used and the development of alternatives to optimize functional outcomes for TBI."[70] As noted earlier in this chapter, given the heterogeneity of the patient population with TBI and the complexity of the brain, it is difficult to categorize patients with TBI into clear diagnostic groups. Moreover, because recovery is dependent on a multitude of factors (eg, mechanism, location and circumstances surrounding the injury, an individual's premorbid constitution, environmental and psychosocial issues), examining outcomes in this patient population is challenging. These challenges are compounded when trying to evaluate optimal rehabilitation strategies to care for the military service member who sustains TBI in association with other combat-related injuries.

TBI rehabilitation begins with a careful evaluation of an individual's injuries. This evaluation should include a thorough cognitive, neurologic, motor, and extremity examination, as well as a full assessment of any sensory difficulties in vision, hearing, balance, and sense of smell.[81,82] It is also important for all rehabilitation disciplines to perform a thorough functional assessment of the patient, determining areas of function in hygiene, eating, mobility, dressing, toileting, and communication. This thorough, multidisciplinary evaluation facilitates the development and implementation of a comprehensive treatment approach. Assessment and treatment approaches that focus on the entire person, including physical, psychological, cognitive, social, occupational, academic, and spiritual aspects will have the greatest potential for maximizing a patient's functioning and quality of life. A multidisciplinary treatment team is necessary to treat complex patients recovering from polytraumatic injuries, such as those returning from OEF and OIF. Rehabilitation teams may include:

- physiatrists,
- rehabilitation nurses,
- prosthetists,
- neuropsychologists,
- rehabilitation psychologists,
- clinical psychologists,
- health psychologists,
- deployment health psychologists,
- marriage and family therapists,
- psychiatrists,
- neurologists,
- speech pathologists,
- occupational therapists,
- physical therapists,
- rehabilitation engineers,
- rehabilitation counselors,
- vocational rehabilitation therapists,
- clinical social workers,
- nurse case managers,
- substance abuse counselors, and
- chaplains.

In some cases, this team, combined with a patient's community and case managers, will be needed to provide care across the lifespan of the injured individual. In addition to the challenges presented immediately after TBI, symptom complexes may change over time. Symptoms of depression and reduced motor or cognitive function may result from a variety of life factors, such as the development of cardiovascular disease, arthritis, and dementia. Therefore it is important to provide individuals with TBI life-long coordinated health services and access to healthcare to promote the highest quality of life.[83] This is especially relevant for polytrauma patients who have multiple comorbid injuries, such as TBI, traumatic amputation, visual impairment, and psychological illness.[84] Polytrauma patients require an integrated treatment approach whereby patients receive care for all injuries simultaneously, as opposed to sequentially.

The role physical therapists play in assessing and treating TBI-related deficits is wide-ranging.[85] Physical therapy has proven effective in treating pain,[63] balance impairment, and postural instability, which are common symptoms in polytrauma patients with TBI.[86] Physical therapy is also helpful in assessing and treat-

ing motor impairments, especially those associated with severe TBI.[87] Paresis, ataxia, postural instability, tandem gait disturbances, and other motor neuron abnormalities are common and can be addressed through physical therapy interventions.

In addition to helping build independence in activities of daily living, occupational therapy has demonstrated efficacy in improving self-awareness after TBI.[88] Its role as part of a long-term strategy in more severe TBI patients is also well established.[89] Occupational therapists are critical to managing upper limb and hand spasticity positioning and functioning in those with motor deficits. They are also valuable partners to vocational rehabilitation experts, performing work assessments and helping integrate assistive technology to facilitate independence in the workplace.[90]

Evidence suggests that early rehabilitative interventions after TBI improve outcomes.[91,92] Polytrauma patients often have treatment targets in various domains. For example, if an injury was severe enough to require amputation, other areas of the patient's health may also have been affected. Blast-exposed patients may sustain TBI and psychological injuries in addition to the blast injury. Considering all of these factors, a patient's impairments, strengths, and functioning must be assessed to enhance the rehabilitation outcome from a major limb amputation.

Because so many patients undergoing rehabilitation for amputation suffer from brain injury, it is important to explore the particular needs and approaches for treating this dual condition. The presence and severity of TBI can have significant implications on the rehabilitation process. Patients with TBI may have restricted awareness of their injuries or limitations, may process information differently, and are likely to have difficulty participating in treatment at the same pace as amputees without TBI. An undiagnosed TBI or a treatment plan that is not modified based on a patient's cognitive impairment is likely to result in poor treatment response.

A complete neuropsychological evaluation not only reveals if a patient sustained cognitive deficits secondary to blast-related brain injury or other mechanisms, but also identifies the patient's strengths. For the purposes of this discussion, the term "neuropsychological evaluation" means the administration, scoring, and interpretation of empirically validated and normed neuropsychological tests by a neuropsychologist.

Cognitive and psychological function reciprocate and share several mechanisms. Identifying the origin of a symptom will inform the treatment approach. For example, if a patient has poor motivation, it is important to determine if that symptom is primarily due to frontal lobe dysfunction or to depression. In addition, MTBI and PTSD share a similar cognitive dysfunction profile. Trudeau et al have suggested that blast patients may suffer from a complex chronic concussive disorder with overlapping cognitive deficits, depression, and PTSD. Neuropsychological testing can help tease apart these symptoms.[93]

A comprehensive neuropsychological evaluation comprises empirically validated cognitive testing and a complete mental health evaluation. Recommended cognitive testing includes a survey of all major domains of cognitive functioning (Table 15-2). Some caution is warranted when using inventories or questionnaires that have been developed for use in a civilian TBI population. There may be differences in the demographics (eg, education, employment status, etc) or the circumstances of the injury (eg, combat and related emotional factors) in military patients as compared to their civilian counterparts.

The recommended mental health assessment portion of a neuropsychological evaluation includes a review of the patient's personal history, including academic, occupational, military, social, family, medical (especially history of prior TBI or concussion), substance use and family substance abuse, mental health, deployment, and combat history. Patients with amputations may suffer from a number of mental health disorders, not likely limited to PTSD. Among the disorders of concern are depression and possible narcotic dependence secondary to overuse of pain medications. Clinical interviews focus on how amputees and their families are adjusting to daily living, as well as on the patient's strengths and resilience factors. Gathering a thorough history and performing a complete mental health examination is necessary in order to approximate a patient's baseline and to appropriately interpret results from the neuropsychological evaluation.

The results of the neuropsychological evaluation inform the treatment plan, and there are several ways in which the results from a neuropsychological evaluation can be clinically applied. They can be used to modify rehabilitation strategies based on a patient's cognitive abilities, or used to directly treat cognitive dysfunction and psychological injuries. They can also facilitate adjustment to amputation.

In order for many patients to effectively participate in the physical aspects of their rehabilitation, their cognitive deficits must be recognized and addressed. Patients with cognitive deficits often have difficulty participating in "treatment as usual." Many patients are considered "treatment failures" when the expected treatment outcome is not obtained. However, cognitive deficits often interfere with patients' abilities to

TABLE 15-2

DOMAINS OF COGNITIVE FUNCTIONING AND REPRESENTATIVE NEUROPSYCHOLOGICAL TESTS

Cognitive Function	Test
Verbal memory: immediate and delayed	California Verbal Learning Test II
Visual memory: immediate and delayed	Rey-Osterrieth Complex Figure, copy and delayed visual reproduction subtests from the Wechsler Memory Scale III
Executive functioning	Stroop Test, Wisconsin Card Sorting Test, Trail Making Test (part B)
Attention	Conners' Continuous Performance Test, Paced Auditory Serial Addition Test, digit span subtest from the Wechsler Adult Intelligence Scale III
Psychomotor speed	Trail Making Test (part A), finger tapping test, grooved pegboard test
General intellectual functioning	Wechsler Abbreviated Scale of Intelligence
Psychological functioning	Clinical interview, collateral interview, Personality Assessment Inventory, Detailed Assessment of Posttraumatic Stress
Effort/motivation	Test of Memory Malingering, Word Memory Test

understand and follow directions, follow sequences or schedules, practice on their own, remember what they have learned, manage their behavior, maintain sufficient motivation, or work cooperatively with others. Substance abuse, dementia, and stroke literature discuss the value of modifying patients' treatment plans in accordance with their cognitive deficits. Several studies address either comprehensive rehabilitation of patients with cognitive deficits or interventions for specific cognitive deficits.[70] Such approaches also show strong support from the brain injury advocacy community.[94] Treating psychological injuries that occurred with a traumatic event is important for overall clinical improvement. Similarly, as a patient begins to make gains in physical rehabilitation, improvements in mental health symptoms are often observed.

The experience and management of pain also appears to be related to mental health and, more specifically, to PTSD. Patients with depression experience higher subjective pain levels,[95] and pain-related variables have been shown to be significant predictors of PTSD symptom cluster scores in both male and female veterans.[96] These findings suggest that managing pain for the amputee may improve mental health prognosis. Similarly, treating mental health symptoms may improve an amputee's ability to engage in physical rehabilitation because of decreased pain perception. Facilitating patient and family adjustment to TBI and amputation, the rehabilitation process, and return to daily life are integral to patients being able to maintain treatment gains, achieve the highest level of independent functioning, and maximize quality of life.

SUMMARY

In times of peace and during times of active military operations, TBI is a significant and important health issue for US military service members. Even with the best efforts at prevention, a relatively large number of service members can be expected to sustain TBI each year. To optimize treatment and rehabilitation, the complicated interplay between physiologic insult to the brain, the disruption of the mind, and the injury to the body must be better understood. An assessment and appreciation of how these factors act together to ameliorate or hinder an individual's functioning is necessary to maximize outcomes and promote recovery across a patient's lifespan.

REFERENCES

1. Langlois JA, Rutland-Brown W, Thomas KE. Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths. Atlanta, Ga: Department of Health and Human Services, Centers for Disease Control and Prevention; 2004.

2. Lewin ICF. *The Cost of Disorders of the Brain*. Washington, DC: The National Foundation for the Brain; 1992.

3. Thurman DJ. Traumatic Brain Injury in the United States: a Report to Congress. Atlanta, Ga: Centers for Disease Control and Prevention; 2001.

4. Ommaya AK, Ommaya AK, Dannenberg AL, Salazar AM. Causation, incidence, and costs of traumatic brain injury in the U.S. military medical system. *J Trauma.* 1996:40(2):211–217.

5. US Department of Defense. Casualty Update Web page. Available at: http://www.defenselink.mil/news/casualty.pdf. Accessed May 16, 2007.

6. Armonda RA, Bell RS, Vo AH, et al. Wartime traumatic cerebral vasospasm: recent review of combat casualties. *Neurosurgery*. 2006;59(6):1215–1225.

7. Xydakis MS, Fravell MD, Nasser KE, Casler JD. Analysis of battlefield head and neck injuries in Iraq and Afghanistan. *Otolaryngol Head Neck Surg*. 2005;133(4):497–504.

8. US Department of the Army. Traumatic Brain Injury (TBI) Task Force report. Available at: http://www.armymedicine.army.mil/prr/tbitfr.html. Published January 2008. Accessed May 7, 2008.

9. Williams DH, Levin HS, Eisenberg HM. Mild head injury classification. *Neurosurgery.* 1990;27(3):422–428.

10. Hsiang J, Yeung T, Yu AL, Poon WS. High-risk mild head injury. *J Neurosurg.* 1997;87(2):234–238.

11. Carroll LJ, Cassidy JD, Peloso PM, et al. Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*. 2004;43:84–105.

12. Werner C, Engelhard K. Pathophysiology of traumatic brain injury. *Br J Anaesth*. 2007;99:4–9.

13. Baethmann A, Eriskat J, Stoffel M, Chapuis D, Wirth A, Plesnila N. Special aspects of severe head injury: recent developments. *Curr Opin Anaesthesiol*. 1998;11:193–200.

14. Marshall LF. Head injury: recent past, present, and future. *Neurosurgery*. 2000;47:546–561.

15. McIntosh TK, Smith DH, Meaney DF, Kotapka MJ, Gennarelli TA, Graham DI. Neuropathological sequelae of traumatic brain injury: relationship to neurochemical and biochemical mechanisms. *Lab Invest*. 1996;74:315–342.

16. Nortje J, Menon DK. Traumatic brain injury: physiology, mechanisms, and outcome. *Curr Opin Neurol*. 2004;17:711–718.

17. Dietrich WD, Alonso O, Busto R, et al. Posttraumatic cerebral ischemia after fluid percussion brain injury: an autoradiographic and histopathological study in rats. *Neurosurgery*. 1998;43:585–593.

18. Dietrich WD, Alonso O, Busto R, et al. Widespread hemodynamic depression and focal platelet accumulation after fluid percussion brain injury: a double-label autoradiographic study in rats. *J Cereb Blood Flow Metab*. 1996;16:481–489.

19. Bouma GJ, Muizelaar JP, Choi SC, Newlon PG, Young HF. Cerebral circulation and metabolism after severe traumatic brain injury: the elusive role of ischemia. *J Neurosurg*. 1991;75:685–693.

20. von Oettingen G, Bergholt B, Gyldensted C, Astrup J. Blood flow and ischemia within traumatic cerebral contusions. *Neurosurgery*. 2002;50:781.

21. Marion DW, Darby J, Yonas H. Acute regional cerebral blood flow changes caused by severe head injuries. *J Neurosurg*. 1991;74:407–414.

22. Bouma GJ, Muizelaar JP, Stringer WA, Choi SC, Fatouros P, Young HF. Ultra-early evaluation of regional cerebral blood flow in severely head-injured patients using xenon-enhanced computerized tomography. *J Neurosurg*. 1992;77:360–368.

23. Coles JP, Fryer TD, Smielewski P, et al. Defining ischemic burden after traumatic brain injury using ^{15}O PET imaging of cerebral physiology. *J Cereb Blood Flow Metab*. 2004;24:191–201.

24. Inoue Y, Shiozaki T, Tasaki O, et al. Changes in cerebral blood flow from the acute to the chronic phase of severe head injury. *J Neurotrauma*. 2005;22:1411–1418.

25. Overgaard J, Tweed WA. Cerebral circulation after head injury. Part 4: Functional anatomy and boundary-zone flow deprivation in the first week of traumatic coma. *J Neurosurg*. 1983;59:439–446.

26. Madikians A, Giza CC. A clinician's guide to the pathophysiology of traumatic brain injury. *Indian J Neurotrauma*. 2006;3:9–17.

27. Marmarou A, Fatouros PP, Barzó P, et al. Contribution of edema and cerebral blood volume to traumatic brain swelling in head-injured patients. *J Neurosurg*. 2000;93:183–193.

28. Marmarou A, Signoretti S, Fatouros P, Portella G, Aygok GA, Bullock MR. Predominance of cellular edema in traumatic brain swelling in patients with severe head injuries. *J Neurosurg*. 2006;104:720–730.

29. Iverson GL. Outcome from mild traumatic brain injury. *Curr Opin Psychiatry*. 2005;18(3):301–317.

30. Barton CW, Hemphill JC, Morabito D, Manley G. A novel method of evaluating the impact of secondary brain insults on functional outcomes in traumatic brain-injured patients. *Acad Emerg Med*. 2005;12(1):1–6.

31. Salazar AM, Schwab K, Grafman JH. Penetrating injuries in the Vietnam war. Traumatic unconsciousness, epilepsy, and psychosocial outcome. *Neurosurg Clin N Am*. 1995;6(4):715–726.

32. Murray CK, Reynolds JC, Schroeder JM, Harrison MB, Evans OM, Hospenthal DR. Spectrum of care provided at an echelon II medical unit during Operation Iraqi Freedom. *Mil Med*. 2005;170:516–520.

33. Brookings Institution. *Iraq Index: Tracking Reconstruction and Security in Post-Saddam Iraq*. Available at: http://www.brookings.edu/saban/iraq-index.aspx. Accessed September 26, 2008.

34. Levi L, Borovich B, Guilburd JN, et al. Wartime neurosurgical experience in Lebanon, 1982–85. I: Penetrating craniocerebral injuries. *Isr J Med Sci*. 1990;26(10):548–554.

35. Levi L, Borovich B, Guilburd JN, et al. Wartime neurosurgical experience in Lebanon, 1982-85. II: Closed craniocerebral injuries. *Isr J Med Sci*. 1990;26(10):555–558.

36. Cernak I, Savic J, Ignjatovic D, Jevtic M. Blast injury from explosive munitions. *J Trauma*. 1999;47(1):96–104.

37. Cernak I, O'Connor C, Vink R. Activation of cyclo-oxygenase-2 contributes to motor and cognitive dysfunction following diffuse traumatic brain injury in rats. *Clin Exp Pharmacol Physiol*. 2001;28(11):922–925.

38. Mott FW. The effects of high explosives upon the central nervous system. *Lancet*. 1916;4824:331–338.

39. Cohen H, Biskind GR. Pathologic aspects of atmospheric blast injuries in man. *Arch Pathol*. 1946;42:12–34.

40. Bryant RA. Disentangling mild traumatic brain injury and stress reactions. *N Engl J Med*. 2008;358(5):525–527.

41. Peleg K, Aharonson-Daniel L, Michael M, Shapira SC. Patterns of injury in hospitalized terrorist victims. *Am J Emerg Med*. 2003;21(4):258–262.

42. Sayer NA, Chiros CE, Sigford B, et al. Characteristics and rehabilitation outcomes among patients with blast and other injuries sustained during the Global War on Terror. *Arch Phys Med Rehabil*. 2008;89(1):163–170.

43. Dikmen SS, Ross BL, Machamer JE, Temkin NR. One year psychosocial outcome in head injury. *J Int Neuropsychol Soc*. 1995;1(1):67–77.

44. Brooks N, McKinlay W, Symington C, Beattie A, Campsie L. Return to work within the first seven years of severe head injury. *Brain Inj*. 1987;1(1):5–19.

45. Katz DI, Alexander MP. Traumatic brain injury. Predicting course of recovery and outcome for patients admitted to rehabilitation. *Arch Neurol*. 1994;51(7):661–670.

46. Lux WE. A neuropsychiatric perspective on traumatic brain injury. *J Rehabil Res Dev*. 2007;44(7):951–962.

47. Belanger HG, Curtiss G, Demery JA, Lebowitz BK, Vanderploeg RD. Factors moderating neuropsychological outcomes following mild traumatic brain injury: a meta-analysis. *J Int Neuropsychol Soc*. 2005;11(3):215–227.

48. Belanger HG, Vanderploeg RD. The neuropsychological impact of sports-related concussion: a meta-analysis. *J Int Neuropsychol Soc*. 2005;11:345–357.

49. Iverson GL, Zasler N, Lange RT. Post-concussive disorder. In: Zasler ND, Katz DI, Zafonte RD, eds. *Brain Injury Medicine: Principles and Practice.* New York, NY: Demos Medical Publishing; 2006: 373–405.

50. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med*. 2004;351:13–22.

51. Koren D, Norman D, Cohen A, Berman J, Klein EM. Increased PTSD risk with combat-related injury: a matched comparison study of injured and uninjured soldiers experiencing the same combat events. *Am J Psychiatry*. 2005;162:276–282.

52. Simon G, Ormel J, VonKorff M, Barlow W. Health care costs associated with depressive and anxiety disorders in primary care. *Am J Psychiatry*. 1995;152(3):352–357.

53. Rybarczyk B, Nyenhuis DL, Nicholas JJ, Cash SM, Kaiser J. Body image, perceived social stigma, and the prediction of psychosocial adjustment to leg amputation. *Rehabil Psychol*. 1995;40(2):95–110.

54. Bodenheimer C, Kerrigan AJ, Garber SL, Monga TN. Sexuality in persons with lower extremity amputations. *Disabil Rehabil*. 2000;22(9):409–415.

55. Schoppen T, Boonstra A, Groothoff JW, de Vries J, Göeken LN, Eisma WH. Physical, mental, and social predictors of functional outcome in unilateral lower-limb amputees. *Arch Phys Med Rehabil*. 2003;84(6):803–811.

56. Kurichi JE, Kwong PL, Reker DM, Bates BE, Marshall CR, Stineman MG. Clinical factors associated with prescription of a prosthetic limb in elderly veterans. *J Am Geriatr Soc*. 2007;55(6):900–906.

57. Taylor SM, Kalbaugh CA, Blackhurst DW, et al. Preoperative clinical factors predict postoperative functional outcomes after major lower limb amputation: an analysis of 553 consecutive patients. *J Vasc Surg*. 2005;42(2):227–235.

58. Warden DL, Gordon B, McAllister TW, et al. Guidelines for the pharmacologic treatment of neurobehavioral sequelae of traumatic brain injury. *J Neurotrauma*. 2006;23(10):1468–1501.

59. Lee HB, Lyketsos CG, Rao V. Pharmacological management of the psychiatric aspects of traumatic brain injury. *Inter Rev Psychiatry*. 2003;15(4):359–370.

60. Thaxton L, Myers MA. Sleep disturbances and their management in patients with brain injury. *J Head Trauma Rehabil.* 2002;17(4):335–348.

61. Walker WC, Seel RT, Curtiss G, Warden DL. Headache after moderate and severe traumatic brain injury: a longitudinal analysis. *Arch Phys Med Rehabil*. 2005;86(9):1793–1800.

62. Lew HL, Lin PH, Fuh JL, Wang SJ, Clark DJ, Walker WC. Characteristics and treatment of headache after traumatic brain injury: a focused review. *Am J Phys Med Rehabil*. 2006;85(7):619–627.

63. Young JA. Pain and traumatic brain injury. *Phys Med Rehabil Clin N Am*. 2007;18(1):145–163.

64. Alderfer BS, Arciniegas DB, Silver JM. Treatment of depression following traumatic brain injury. *J Head Trauma Rehabil*. 2005;20(6):544–562.

65. Mittenberg W, Tremont G, Zielinski RE, Fichera S, Rayls KR. Cognitive-behavioral prevention of postconcussion syndrome. *Arch Clin Neuropsychol*. 1996;11(2):139–145.

66. Ponsford J, Willmott C, Rothwell A, et al. Impact of early intervention on outcome following mild head injury in adults. *J Neurol Neurosurg Psychiatry.* 2002;73:330–332.

67. Defense and Veterans Brain Injury Center. Traumatic brain injury education Web site. Available at: http://www.dvbic.org/cms.php?p=Education. Accessed October 8, 2008.

68. Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neurol*. 2008;7(8):728–741.

69. Gordon WA, Zafonte R, Cicerone K, et al. Traumatic brain injury rehabilitation: state of the science. *Am J Phys Med Rehabil*. 2006;85(4):343–382.

70. Annegers JF, Hauser WA, Coan SP, Rocca WA. A population-based study of seizures after traumatic brain injuries. *N Engl J Med*. 1998;338(1):20–24.

71. Englander J, Bushnik T, Duong TT, et al. Analyzing risk factors for late posttraumatic seizures: a prospective, multicenter investigation. *Arch Phys Med Rehabil*. 2003;84(3):365–373.

72. Melamed E, Robinson D, Halperin N, Wallach N, Keren O, Groswasser Z. Brain injury-related heterotopic bone formation: treatment strategy and results. *Am J Phys Med Rehabil*. 2002;81(9):670–674.

73. Garland DE. Clinical observations on fractures and heterotopic ossification in the spinal cord and traumatic brain injured populations. *Clin Orthop*. 1996;233:86–101.

74. Garland DE. A clinical perspective on common forms of acquired heterotopic ossification. *Clin Orthop Relat Res*. 1991;263:13–29.

75. Sazbon L, Najenson T, Tartakovsky M, Becker E, Grosswasser Z. Widespread periarticular new-bone formation in long-term comatose patients. *J Bone Joint Surg Br*. 1981;63-B:120–125.

76. Colombo CJ, Mount CA, Popa CA. Critical care medicine at Walter Reed Army Medical Center in support of the global war on terrorism. *Crit Care Med*. 2008;36(7 Suppl):S388–394.

77. Carlile MC, Yablon SA, Mysiw WJ, Frol AB, Lo D, Diaz-Arrastia R. Deep venous thrombosis management following traumatic brain injury: a practice survey of the traumatic brain injury model systems. *J Head Trauma Rehabil*. 2006;21(6):483–490.

78. Meythaler JM, Guin-Renfroe S, Johnson A, Brunner RM. Prospective assessment of tizanidine for spasticity due to acquired brain injury. *Arch Phys Med Rehabil*. 2001;82(9):1155–1163.

79. Meythaler JM, Clayton W, Davis LK, Guin-Renfroe S, Brunner RC. Orally delivered baclofen to control spastic hypertonia in acquired brain injury. *J Head Trauma Rehabil*. 2004;19(2):101–108.

80. Pavesi G, Brianti R, Medici D, Mammi P, Mazzucchi A, Mancia D. Botulinum toxin type A in the treatment of upper limb spasticity among patients with traumatic brain injury. *J Neurol Neurosurg Psychiatry*. 1998;64(3):419–420.

81. Goodrich GL, Kirby J, Cockerham G, Ingalla SP, Lew HL. Visual function in patients of a polytrauma rehabilitation center: a descriptive study. *J Rehabil Res Dev*. 2007;44(7):929–936.

82. Lew HL, Jerger JF, Guillory SB, Henry JA. Auditory dysfunction in traumatic brain injury. *J Rehabil Res Dev*. 2007;44(7):921–928.

83. Lew HL, Poole JH, Guillory SB, Salerno RM, Leskin G, Sigford B. Persistent problems after traumatic brain injury: the need for long-term follow-up and coordinated care. *J Rehabil Res Dev*. 2006;43(2):vii–x.

84. Keel M, Trentz O. Pathophysiology of polytrauma. *Injury*. 2005;36(6):691–709.

85. Hellweg S, Johannes S. Physiotherapy after traumatic brain injury: a systematic review of the literature. *Brain Inj*. 2008;22(5):365–373.

86. Pickett TC, Radfar-Baublitz LS, McDonald SD, Walker WC, Cifu DX. Objectively assessing balance deficits after TBI: role of computerized posturography. *J Rehabil Res Dev*. 2007;44(7):983–990.

87. Walker WC, Pickett TC. Motor impairment after severe traumatic brain injury: a longitudinal multicenter study. *J Rehabil Res Dev*. 2007;44(7):975–982.

88. Goverover Y, Johnston MV, Toglia J, Deluca J. Treatment to improve self-awareness in persons with acquired brain injury. *Brain Inj*. 2007;21(9):913–923.

89. Parish L, Oddy M. Efficacy of rehabilitation for functional skills more than 10 years after extremely severe brain injury. *Neuropsychol Rehabil*. 2007;17(2):230–243.

90. Murphy L, Chamberlain E, Weir J, Berry A, Nathaniel-James D, Agnew R. Effectiveness of vocational rehabilitation following acquired brain injury: preliminary evaluation of a UK specialist rehabilitation programme. *Brain Inj*. 2006;20(11):1119–1129.

91. Mazaux JM, De Sèze M, Joseph PA, Barat M. Early rehabilitation after severe brain injury: a French perspective. *J Rehabil Med*. 2001;33(3):99–109.

92. Wagner AK, Fabio T, Zafonte RD, Goldberg G, Marion DW, Peitzman AB. Physical medicine and rehabilitation consultation: relationships with acute functional outcome, length of stay, and discharge planning after traumatic brain injury. *Am J Phys Med Rehabil*. 2003;82(7):526–536.

93. Trudeau DL, Anderson J, Hansen LM, et al. Findings of mild traumatic brain injury in combat veterans with PTSD and a history of blast concussion. *J Neuropsychiatry Clin Neurosci*. 1998;10(3):308–313.

94. Brain Injury Association of America Web site. Available at: http://www.biausa.org/. Accessed October 8, 2008.

95. Carter LE, McNeil DW, Vowles KE, et al. Effects of emotion on pain reports, tolerance and physiology. *Pain Res Manag*. 2002;7(1):21–30.

96. Asmundson GJ, Wright KD, Stein MB. Pain and PTSD symptoms in female veterans. *Eur J Pain*. 2004;8(4):345–350.