Congenital and Acquired Brain Injury. 3. Spectrum of the Acquired Brain Injury Population

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This self-directed learning module highlights the subpopulations of traumatic brain injury (TBI) that are treated by the rehabilitation practitioner. It is part of the chapter on TBI in the self-directed Physiatric Education Program for practitioners and trainees in physical medicine and rehabilitation. Specifically, this article focuses on the management of patients with mild TBI, children, and individuals with acquired brain injury from other etiologies, such as anoxic events or neoplastic lesions. The clinical spectrum of TBI, from the most severe presentation to the mildest, requires similar clinical skills to evaluate and manage.

Overall Article Objective: To describe the spectrum of brain injury populations based on age, severity, and etiology.

Key Words: Brain concussion; Brain injuries; Brain neoplasm; Hypoxia, brain; Persistent vegetative state; Rehabilitation.

3.1 Clinical Activity: To evaluate a nursing home patient who is reportedly still unresponsive 3 months after her traumatic brain injury.

THE TERM *DISORDERS OF CONSCIOUSNESS* refers to a spectrum of conditions seen after cerebral injury, including coma, vegetative state, and the minimally conscious state.[1] Most patients with severe traumatic brain injury (TBI) transiently pass through a vegetative or minimally conscious state; however, a subset of these patients remains in these states for an extended time. Most of the following discussion applies to disorders of consciousness regardless of etiology. When relevant, differences between traumatic and nontraumatic disorders will be highlighted.

Coma

Understanding the distinction between coma and the other disorders of consciousness rests on appreciating the difference between wakefulness and awareness. Wakefulness refers to the presence of sleep-wake cycles but does not imply awareness of self or environment, the hallmark of consciousness. Coma is characterized by a lack of wakefulness; patients' eyes remain closed, and there is no evidence of sleep-wake cycles on electroencephalogram. In TBI, coma results from damage to the reticular-activating system in the brainstem or its connections to the thalami or hemispheres. In patients who survive, coma usually resolves in 2 to 4 weeks.

Vegetative State

The vegetative state is characterized by the resumption of sleep-wake cycles, but there is still no awareness of self or environment. It is thus also considered a state of unconsciousness. The use of terms such as persistent or permanent is confusing, and it is now recommended that they be avoided and that they be replaced with a description of the etiology and time since onset.[2]

Minimally Conscious State

The minimally conscious state is present when the patient shows minimal but definite evidence of self or exhibits environmental awareness. Signs of consciousness include sustained visual fixation and pursuit, purposeful movements, emotional responses to salient stimuli, command following, and verbalization. These actions suggest that a patient has regained consciousness.[1,2] When the presence of these behaviors is equivocal, it is important to consider the complexity and frequency of these signs and their relation to environmental stimuli. Emergence from the minimally conscious state is characterized by interactive communication or functional use of objects.[1,2]

Differentiating between a vegetative or minimally conscious state has profound implications for prognosis and may even affect the continuation of life-sustaining treatment. Because no pathognomonic imaging or electrophysiologic findings apply, the diagnosis must be made clinically. The rate of misdiagnosis of the vegetative state is 35% to 45%, most likely the result of a lack of familiarity with the diagnostic criteria and the manner in which assessments are often conducted.[2]

The assessment of a patient with a disorder of consciousness involves evaluating whether his/her responses to various forms of stimulation represent true awareness or are merely reflexive or random. Clinicians should be familiar with those behaviors that can be reflexive and thus are not considered unequivocal signs of consciousness (eg, yawning, auditory startle).[1,2] The assessment should reflect what is known about a patient's sensory capacities and what is likely to be within his/her motor repertoire. It is important to vary both the stimuli used (eg, auditory, visual) and the responses that one is attempting to elicit (eg, motor, emotional).

Performance of multiple examinations at different times by various clinicians is critical for detecting subtle or fluctuating signs of consciousness. Observations made by family members should also be collected. They are often well positioned to elicit responses from the patient, even if they sometimes misinterpret the meaning of their observations. All efforts should

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Table 1: Probability of Recovering Consciousness and Function at 12 Months Postinjury Among Adults in Persistent Vegetative State 3 Months After Traumatic or Nontraumatic Injury

Recovery Level	Traumatic Injury (%)	Nontraumatic Injury (%)
Death	35	46
Persistent vegetative state	30	47
Severe disability	19	6
Moderate disability or good recovery	16	1

NOTE. Adapted from the Multi-Society Task Force Report on PVS.[8]

be made to optimize the conditions under which the evaluation is performed by minimizing any potentially sedating factors (eg, medications, hydrocephalus, subclinical seizures) and by maximizing the patient's ability to respond (eg, evaluate patient in an upright position, in a quiet environment).

In ambiguous cases, consider a more systematic assessment such as an individualized quantitative behavioral assessment, which treats the stimuli and the target responses as operations amenable to simple statistical analysis.[3] This type of assessment is not a scale; rather, it is an approach to assessing individual cases. Rehabilitation programs that frequently treat disorders of consciousness should consider adopting a standardized scale as part of the routine assessment of these patients; several are now available and have recently been reviewed.[2,4]

The diagnostic role of ancillary studies such as functional neuroimaging and late event-related potentials is still to be defined.[5,6] These techniques have advanced our understanding of the anatomy and pathophysiology of disorders of consciousness. In particular, functional neuroimaging has shown a greater activation (both in degree and extent) in the minimally conscious state as compared with the vegetative state.[5,6] In the future, these modalities may allow one to detect consciousness in patients who appear to be vegetative[7] or, at least, to identify those patients who are most likely to recover. Currently, however, there are not enough data to recommend the routine clinical use of these modalities for either diagnosis or prognostication.

At this time, prognostication is still based on actuarial-type data derived from large groups such as those reported by the Multi-Society Task Force on Vegetative State[8] (table 1). Several points should be noted about their findings. First, their report only addresses the vegetative state; at this time, not enough data exist on the minimally conscious state to make reliable individual prognoses. Second, the prognosis for a nontraumatic vegetative state is much worse than for traumatic. Third, patients who for 3 months have been in a vegetative state of traumatic origin still have a significant chance of recovering consciousness (35%) and even of attaining higher levels of functional outcome (16%).

Finally, the report probably underestimates the probability of regaining consciousness in people who have been in a traumatic vegetative state for more than 12 months. Although still rare, late recovery after experiencing a prolonged vegetative or minimally conscious state is possible, and several such cases have been reported in the media in the last several years.[9] One of these people, in a minimally conscious state for 19 years, has been studied extensively. A recent report[10] suggested that axonal regeneration may have been a possible mechanism for the late recovery in this person.

For patients who are still in a vegetative or minimally conscious state, treatment has focused on 2 primary objectives. First, there is physical rehabilitation, which optimizes the patient's bodily health to minimize complications that might interfere with function if he/she recovers consciousness. Second, attempts have been made to directly treat the underlying neurologic damage. The rationale is to thereby accelerate neural recovery through treatments such as medications, sensory stimulation, and deep brain stimulation. However, a recent evidence-based review concluded that there was no evidence to recommend the use of either sensory stimulation or conventional deep brain stimulation.[11] Advances in our understanding of the neural substrate of consciousness suggest that more precisely targeted deep brain stimulation might be more successful; this possibility is being actively investigated.[12]

A variety of pharmacologic agents have been reported to be helpful, including dopaminergic agents, other stimulants, and antidepressants.[1,2] Recently, a multicenter observational study[13] found a positive effect of amantadine on outcome. There have also been several intriguing reports of improvement in consciousness with the use of zolpidem.[14] Unfortunately, there are no prospective controlled trials evaluating the use of these medications in chronic disorders of consciousness, so clinicians treating these patients will need to use these agents empirically.

Paralleling the increase in scientific interest in disorders of consciousness, increased attention has been paid to ethical and legal issues.[15] One of the most pressing unsettled questions is whether it is acceptable to withdraw care from a patient who is in a minimally conscious state. This decision is analogous with fairly well-accepted practices for patients in a vegetative state. Our lack of knowledge about prognosis for patients who are in the minimally conscious state complicates our ability to answer this question. Furthermore, more clarification is needed concerning concepts such as quality of life (QOL). What might QOL mean, for instance, for a minimally conscious patient who seems to be in no pain and even appears to experience pleasure? Answering these ethical questions will be as important as advancing our scientific knowledge in enabling us to care for these patients.

3.2 Clinical Activity: To provide a treatment plan for a 43-year-old man with spastic quadriplegia who had a cardiac arrest while playing tennis 3 months ago. The patient was unattended for approximately 5 minutes before basic life support was initiated. He shows posturing and myoclonus, and he inconsistently follows simple commands.

An Overview of Out-of-Hospital Cardiac Arrest

The vast majority of people who sustain an out-of-hospital cardiac arrest succumb to their illness. Herlitz et al[16] reported that between 1980 and 1992, of 3434 patients who suffered an out-of-hospital cardiac arrest, only 704 arrived alive to the hospital. For those who survive, anoxic/hypoxic injury is one of the most devastating injuries that can be sustained.

Cerebral Injury Sustained From Anoxia

Because the hippocampi and cortex are particularly sensitive to decreased oxygen delivery, anoxic injury results in significant cognitive and memory impairments. The basal ganglia and cerebellum are other regions that are sensitive to anoxia. Insufficient oxygen to these areas results in movement disorders, which include parkinsonism, chorea, tics, athetosis, ataxia, various forms of dystonia, and acute or chronic myoclonic syndromes.[17]

Function and Prognostication of Survivors of Cardiac Arrest

The prognosis of anoxic brain injury is far worse than that of TBI, as shown by a study[18] of 51 people who had survived cardiac arrest for at least 2 weeks who were followed for 1 year. Almost a third of them (16/51) died within 90 days of the event, but only 3 died after discharge from the hospital. The researchers found that the majority of recovery occurred by 45 days, and almost all recovery occurred by 3 months. At 1 year postinjury, 43% were dependent in motor performance and 38% in social cognitive tasks.

A recent meta-analysis[19] reviewed the literature between 1966 through 2003 concerning patients who were comatose after cardiac arrest. The reviewers identified 5 early clinical findings that strongly predicted death or poor neurologic recovery: absent corneal reflex at 24 hours, absent pupillary response at 24 hours, absent withdrawal response to pain at 24 hours, and no motor response at 24 and then 72 hours. They found no clinical sign that predicted a good recovery. Their findings noted that 77% had a poor outcome, and a survivor without brainstem reflexes at 24 hours and no motor responses at 72 hours had a very poor prognosis for meaningful neurologic recovery.

Treatment of Cognitive Disorders From Anoxia

Treatment to address the cognitive disorders that result from anoxia differs little from that described for the TBI population discussed elsewhere in this review. In a case series of 5 patients, a limited benefit with levodopa and bromocriptine in the treatment of apathy and motor impairment had been noted, but no benefit was noted in the treatment of memory impairment.[20] The use of cholinergic medications to improve cognition in this population has not yet been well studied.

Posthypoxic Myoclonus

Myoclonus is the term used to describe sudden involuntary action of a muscle or a group of muscles. There are 2 different types of myoclonus that occur after anoxic insult. Acute posthypoxic myoclonus occurs within the first 24 hours after injury, and it consists of severe flexion movements. This acute form occurs in 30% to 40% of cases and is essentially unresponsive to treatment. Chronic posthypoxic myoclonus, also called Lance-Adams syndrome, typically begins within a few days to a few weeks after hypoxic injury.[17] Its incidence is unknown, and there are only 122 documented cases in the literature.[21] The myoclonus primarily affects the limbs when movement is attempted, but it can spread to other muscles. The symptoms disappear with relaxation and tend to be worse when more precise movements are required, greatly complicating performance of activities of daily living. Negative myoclonus, in which uncontrolled relaxation of the limbs occurs, can impair balance and result in falls.

Treatment of myoclonus can be very challenging. Clonazepam, valproate, and piracetam are considered first-line treatments, and some authors report on significant efficacy. The agent 5-hydroxytryptophan has also been suggested as possibly being effective. Other medications reported to be effective in some patients include baclofen, diazepam, ethanol, and methysergide. Several medications (phenytoin, primidone, phenobarbital, tetrabenazine) are reported as not significantly efficacious in any case of chronic posthypoxic myoclonus. Several newer agents that are shown to be effective include levetiracetam and μ-hydroxybutyric acid.[17]

Other Movement Disorders Associated With Anoxia and Hypoxia

Other movement disorders associated with hypoxic injury include akinetic-rigid syndrome and posthypoxic dystonia. Akinetic-rigid syndrome usually is a symmetric condition characterized by combinations of bradykinesia, micrographia, axial and appendicular rigidity, resting or postural tremor, and postural instability. Akinetic-rigid syndrome usually develops within 3 months after injury and is fairly constant. Posthypoxic dystonia can affect the limbs and face and progresses to a symmetric, generalized dystonia. The dystonic syndrome develops over 10 months, with gradual progression. Treatment with parkinsonian medications is of very limited help.[17]

3.3 Clinical Activity: To evaluate a 50-year-old male executive who presents complaining of irritability, headaches, and fatigue after falling off a horse for the third time 2 months ago, reporting he briefly experienced feeling "dazed and confused."

The vast majority of TBIs are classified as mild according to the Glasgow Coma Scale (GCS) (initial score of 13–15). The American Congress of Rehabilitation Medicine defined mild TBI as a traumatically induced alteration in brain function manifested by either loss of consciousness, amnesia for events immediately before or after the event, an alteration in mental state such as feeling dazed or confused, or focal neurologic impairment. It further stipulated that the GCS score measured 30 minutes after trauma be at or above 13, that loss of consciousness not exceed 30 minutes, and that posttraumatic amnesia not exceed 24 hours.[22] The U.S. Centers for Disease Control and Prevention recently suggested a very similar conceptual definition of mild TBI, but they also included signs of neurologic or neuropsychologic dysfunction that are identified soon after an injury. These signs include seizures, headaches, dizziness, irritability, fatigue, and impaired cognitive skills but exclude penetrating injuries.[23]

Most people with mild TBI, often referred to as concussion, recover well, although a significant minority develops postconcussion syndrome (PCS), manifested by a constellation of physical, cognitive, and emotional problems, including headaches, dizziness, fatigue, visual disturbances, light and noise sensitivity, cognitive impairments, depression, anxiety, and irritability. These symptoms are also observed in several non-TBI populations, making it a controversial disorder that many consider to be the result of a combination of both premorbid and injury-related neuropathologic and psychologic factors.[24] Its prevalence is unknown, although impaired performance on cognitive testing shortly after injury identifies people at increased risk.[25] Diagnosis of PCS is often hampered by failure to recognize these symptoms as resulting from mild TBI, associated with the fact that standard neuroimaging studies are typically unremarkable. Newer neuroimaging techniques and serologic tests that better detect evidence of brain injury may offer greater diagnostic sensitivity in the future. Treatment strategies for PCS combine analgesics for pain complaints, antidepressants for mood disturbances, and psychologic interventions that include education, reassurance, and cognitive remediation.[24] Sertraline has been shown to decrease both mild TBI-related depression and irritability related to mild TBI.[26] Other evidence[27] suggests that the provision of both education and coping strategies early postinjury reduces the incidence of persistent PCS.

Mild TBI is among the most common sport-related injuries, with football causing the largest number of concussions because of the large volume of participants.[28] One of the greatest

challenges for sports physicians is determining when a concussed athlete may safely return to play. Data from the National Football League[29] suggest that highly trained professional athletes who sustain a concussion quickly recover both cognitive and physical skills and generally return to play shortly after injury; however, player participation was voluntary, which may have skewed results. Younger amateur athletes show greater individual variability in recovery time[30] with some experiencing a decline in cognitive skills during the first few days after the injury.[31-33] Although the vast majority of younger athletes recover well over time, the potential for both initial cognitive decline and variable recovery rates suggests that early sideline evaluations provide insufficient information to team physicians when deciding when to return athletes to play[32] and that each athlete must be assessed individually over time. Other evidence[34] suggests that younger athletes participating in contact sports may sustain seemingly clinically insignificant multiple mild injuries that, cumulatively, cause subtle cognitive impairments, which is consistent with reports of impaired cognitive performance in boxers who sustain multiple blows to the head. Several guidelines[32] have been developed to assist physicians in their determination of when to permit concussed athletes to return to play, although they are based primarily on expert opinion rather than empirical evidence. However, readiness to return to play based on objective cognitive performance assessed by computer-based serial testing (known as ImPACT) permits comparison of pre- and postinjury cognitive skills; these comparisons help determine when an athlete may safely return to play.[30]

3.4 Clinical Activity: To manage a 12-year-old child who sustained a moderately severe TBI at age 4 with an apparently successful recovery and who is having recent academic difficulties.

The estimated annual incidence of pediatric TBI is 180 per 100,000 in children under the age of 15. Guidelines for the early management of TBI in children now exist, as they do in adults. Although some overlap exists between pediatric and adult guidelines, such as in the use of intracranial pressure monitoring, some differences also exist, such as the use of hypothermia in children to reduce secondary injury.[35] Outcome data in pediatrics have led to the generalization that younger children have worse outcomes than older children. This is probably related to long-term cognitive and behavioral deficits reported in other research.[36]

During the first year after a moderate to severe TBI, a third of children had unmet or unrecognized health care needs. The largest area of need was cognitive service, with the most frequent reason being that it was not recommended by either the physician or the school. A lack of insurance funding and poor family functioning were also contributing factors.[37]

A correlation existed between the severity of injury and performance in neurobehavioral functioning in the areas of intelligence, academic performance, memory, problem solving, and motor performance 1 year after injury. Even though the children who had TBI scored within the normative range, they were substantially below their matched peers.[38] These findings persisted at 3 years after injury. Deficits in behavior and social skills, as rated by parents and caregivers, were also found. Also emerging were deficits in abstract and concept learning, which were not seen at 1 year after injury.[39]

To understand how a static injury to the brain at a particular age can manifest itself with greater symptoms or neurocognitive deficits as one gets older requires study of developmental trajectories. Each person develops cognitive and social skills tempered by his/her previous abilities. The disruption of executive function by damage to the frontal lobes can negatively affect normal cognitive, behavioral, and social development. Deficits, which appear to emerge later, often reflect the interaction between early neurologic weaknesses and failure to develop age-appropriate competencies.[40] Studies clearly identify the need for increased educational support, including special education placement and classroom modifications, for years after TBI. Parents should be counseled regarding later emergence of cognitive and behavioral symptoms.

Specific deficits in executive functions have been widely studied after pediatric TBI. During prospective observation, those children with severe injuries show the most significant impairments in attention, planning, goal setting, problem solving, cognitive flexibility, and abstract reasoning. Although they also showed the greatest recovery over a 2-year period, the severely injured children still had persistent deficits in executive functions.[41] Long-term attentional problems are also observed in 46% of patients with severe TBI in childhood. These are often exacerbations of premorbid attention problems, sometimes significant enough to warrant the diagnosis of attention-deficit and hyperactivity disorder (ADHD). The problems can be defined by parental report by using the Child Behavior Checklist, ADHD rating scales, and neuropsychologic batteries.[42]

Long-term behavioral problems after pediatric TBI have also been studied. Postinjury cognitive function was not a consistent predictor of behavioral problems. Abnormal behaviors in academic and home settings are often measured by the Child Behavior Checklist. Although most children with moderate to severe TBI do not have long-term behavioral difficulties, a small minority may have persistent behavioral issues. It is thought that preinjury behavioral issues and family function may contribute to these problems. It was hypothesized that early psychologic interventions with the patient and family may reduce this prevalence.[43]

Many medications are used clinically to treat cognitive deficits after pediatric TBI. The medications chosen have been extrapolated from those used in adults with TBI and in children with ADHD. Methylphenidate has been studied specifically in children with TBI. When compared with placebo, methylphenidate showed no significant difference in behavior, attention, memory, and processing speed.[44] Case reports also exist for the use of tricyclic antidepressants, amantadine, atomoxetine, and bromocriptine. Practitioners must use neuropharmacologic knowledge to make clinical decisions on a case by case basis. They also must be aware of the risk of extrapolating adult data to children, such as the increased risk of suicide with the use of selective serotonin reuptake inhibitors that is unique to the adolescent population.

3.5 Educational Activity: To justify to an insurance company your plan to admit to your inpatient rehabilitation unit a 50-year-old male patient with a diagnosis of glioblastoma multiforme.

Unlike the far more common acquired brain conditions of stroke and TBI, for which survival rates are high and recovery expected, survival for primary brain malignancies is limited. This consideration emphasizes the importance of providing timely and efficient rehabilitation services to this population. The total incidence rate for primary brain malignancies has slowly declined since 1987, and overall 5-year survival has steadily risen in recent decades to 31% in the year 2001.[45] However, the incidence rate of glioblastoma multiforme, the most common and most malignant primary brain tumor phe-

notype, is 2.8 per 100,000 person-years and appears to be rising. One-year survival rates of 32% have not significantly improved since the 1980s. The median overall survival rate, even after surgical resection and adjuvant radiation and chemotherapy, is 12 to 14 months. But survival appears to be improving after tumor recurrence, with the probability of 5-year survival for those surviving 2 years after diagnosis and treatment estimated to be over 40%.[46,47]

In addition to the direct effects of a mass lesion on brain function, the treatment for primary and secondary brain tumors often leads to significant activity-limiting impairment and restricted social participation. As with other acquired disorders of brain function, this impairment affects all aspects of personal and family life. Coordinated multidisciplinary rehabilitation programs are uniquely suited to address the breadth of their needs. Postsurgical complications, adjunctive radiation, chemotherapy and steroid treatment, and secondary medical risks, including venous thromboembolism and seizures, require close medical attention. Conditions such as sensorimotor and cognitive impairment, communication disorders, and dysphagia require experienced therapists and neuropsychologic evaluation. The frequent need for adaptive equipment and community services requires nursing and social service coordination. Inpatient rehabilitation for patients with malignant brain tumors has commonly focused on basic mobility, self-care skills, and adaptive equipment to allow for timely discharge, maximizing time at home together for the patient and family. Lengths of stay for patients with a brain tumor have been shown to be comparable to or shorter than for patients with stroke or TBI.[48] Patients with a brain tumor also make significant functional gains during inpatient rehabilitation, similar to other acquired brain disorders, with equal or better rates of dismissal home. For patients receiving radiation or chemotherapy during inpatient rehabilitation, timing these treatments after daily therapy sessions maximizes their ability to benefit from the therapeutic intensity of this setting. Both inpatient and outpatient medical rehabilitation settings are effective in managing clinical needs for patients with a brain tumor.[49,50] Furthermore, community-based nursing and therapy services can provide transitional care and promote independence after hospitalization. These comprehensive rehabilitation services are clearly justifiable and should be considered the standard of care for this patient population.

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