Conceptualizing Brain Injury as a Chronic Disease

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HISTORY

Disease is defined in the *Free Online Dictionary* as representing a "deviation from or interruption of the normal structure or function of any body part, organ or system that is manifested by a characteristic set of symptoms and signs and whose etiology, pathology and prognosis may be known or unknown."

In general, the insurance industry uses the term "sickness" rather than disease. Sickness is defined by one medical insurance provider as: "illness, disease of condition of a covered person which first manifests itself after the effective date of the policy and which this policy is in force for such person. Sickness includes any complications of recurrences that relate to such sickness while the policy is in force of the person." (H. Kelso, personal communication, June 30, 2008).

Historically, the medical definition and approach to most, if not all diseases, has evolved over time. Certainly, any student of science has been exposed to the humor theory, which was the most commonly held view of the human body from the age of Hippocrates until the beginning of modern medicine in the nineteenth century. The approach to traumatic brain injury (TBI) has changed as well. In 1927, the Supreme Court of the United States upheld the right of states to sterilize persons with mental disabilities, and yet, only 20 years later, Howard Rusk began providing neurorehabilitation to pilots injured in World War II.

As the TBI continuum of care evolved, acute rehabilitation was hospital-based and followed a strict medical model. The medical model dictated treatment to the patient/family, as most survivors in the acute phase of rehabilitation were incapacitated and unable to participate in decisions made about their treatment. The physicians, nurses, neuropsychologists and allied healthcare professionals were regarded as the experts and very little was negotiable with regard to treatment. As post-acute programs began to develop and carve out a specialty niche in the evolving continuum, there was a push to differentiate post-acute care from acute rehabilitation.

Post-acute rehabilitation defined itself as non-hospital based treatment with an interdependent model of care. Despite the fact that the Latin root of the word means "suffering or sick person," individuals were no longer referred to as patients. Rather, family members and individuals with a TBI, now called clients, (which interestingly has its Latin origin meaning "follower") were seen as experts with regard to the pre-injury history and function of the individual. Treatment at the post-acute level was often provided by non-professionals under the direction of a team of professional consultants (i.e., doctor, nurse, SLP, PT, OT and neuropsychologist). Treatment goals and other aspects of the services delivered were negotiated between the staff delivering the service(s) and the individual receiving the service. The individual and his/her family were considered team members and an important resource for the staff delivering service(s).

Unfortunately, post-acute rehabilitation succeeded in separating itself from the medical model—so much so that it was cut off from most medical funding streams. The science at the post-acute

level was not strong—outcomes not adequately tracked, therapies not evidenced-based, etc. Activities offered to individuals at this level of care were considered to be not much more than therapeutic hand holding by many in the business, and community integration and life satisfaction were not considered covered benefits by most funding sources.

The *American Heritage Dictionary* defines an event as "the final result; the outcome." The *Webster's New World Dictionary* defines an injury as "harm or damage." Traumatic damage to the brain was therefore seen by the industry as an "event." A broken brain was the equivalent of a broken bone—the final outcome to an insult in an isolated body system. Once it was fixed and given some therapy, no further treatment would be necessary in the near or distant future, and certainly, there would be no effect on other organs of the body.

PURPOSE

The purpose of this paper is to encourage the classification of a TBI not as an event, not as the final outcome, but rather as the beginning of a disease process. The paper presents the scientific data supporting the fact that neither an acute TBI nor a chronic TBI is a static process—that a TBI impacts multiple organ systems, is disease causative and disease accelerative, and as such, should be paid for and managed on a par with other diseases.

Despite the fact that patients with a TBI who survive the acute event do not die of their brain injury per se, a TBI is a disease. There are many similar examples in the field of medicine. Chronic kidney disease is an independent risk factor for cardiovascular disease (Sarnak et al., 2003). Patients with chronic kidney disease are more likely to die of cardiovascular disease than end stage renal failure (Sarnak et al., 2003). Patients do not succumb to AIDS. They die from other diseases, such as pneumonia, caused by the AIDS disease. And indeed, diseases can be caused by external forces such as injuries. An individual sustaining a severe chemical burn to the lungs will develop chronic lung disease that may then cause or accelerate cardiac disease. Although the phenomenon is not clearly understood, following chemotherapy, many patients may develop disabling problems with memory, attention, multi-tasking and other domains of cognitive function, known as "chemo brain" (Tannock et al., 2004).

MORTALITY

In a 2004 study on mortality one year post injury among 2,178 individuals with a moderate to severe TBI, it was reported that individuals with a TBI were twice as likely to die as a similar non-brain injured cohort and had a life expectancy reduction of seven years (Harrison-Felix et al., 2006). Follow-up studies on causes of death revealed that individuals surviving *more* than one year with a TBI are 37 times more likely to die from seizures, 12 times more likely to die from septicemia, four times more likely to die from pneumonia and three times more likely to die from other respiratory conditions than a matched cohort from the general population. The greatest proportion of deaths in the study—29 percent—was from circulatory problems. Although this number was not significantly greater than that of the general population, there was still a 34 percent increase over the expected number of circulatory-related deaths (Harrison-Felix

et al., 2006). Shavelle and colleagues found that individuals with a TBI were three times more likely to die of circulatory conditions (Shavelle et al., 2001). Although it is somewhat intuitive that individuals with moderate to severe TBIs would have a higher mortality rate than the normal population, even individuals with mild TBIs have been found to have a small but statistically significant reduction in long-term survival (Brown et al., 2004).

ETIOLOGY

The nature by which a brain injury can impact other organs is not known, but clearly there is an indirect effect. Mirzayan and colleagues (Mirzayan et al., 2008) subjected mice to a controlled brain injury, and sacrificed them at 96 hours. Histopathologic changes were found in the liver and lungs, suggesting that an isolated TBI can lead to the migration of immuno-incompetent cells to the peripheral organs, and thus potentially lead to their dysfunction. Heterotopic ossification (H.O.) is an appropriate disease model for this theory. Ectopic bone formation, most often at the elbows, knees and shoulders occurs in 3-20 percent of TBIs (Mital et al., 1987, Hoffer and Brink, 1975). Generally, the more severe the TBI, the more likely that individual will develop H.O. The immune response is significantly impaired acutely following a TBI ("post-traumatic immune paralysis") and may be associated with the high prevalence of infections in these patients (Kox et al., 2008).

Age is clearly a factor in brain injury disease. Older patients show a greater decline over the first five years following a TBI than younger patients (Marquez de la Plata et al., 2008). Also, the greatest amount of improvement in disability has been noted in the youngest group of survivors.

MORBIDITY

NEUROLOGIC DISORDERS

Epilepsy

Traumatic brain injuries are a major cause of epilepsy, accounting for 5 percent of all epilepsy in the general population (Hauser et al., 1991). Individuals with a TBI are 1.5-17 times (depending on the severity of the TBI) more likely than the general population to develop seizures (Annegers et al., 1998). TBI is the leading cause of epilepsy in the young adult population. Seizures will be observed over a week after a penetrating TBI in 35-65 percent of individuals. In a study of 309 individuals with moderate-severe TBI followed as long as 24 years post injury, 9 percent were being treated for epilepsy (Yasseen et al., 2008). As the time from injury to the time of the first post TBI seizure may be as long as 12 years (Aarabi et al., 2000), there is a need for heightened awareness of the development of epilepsy on the part of the patient, family and treating medical personnel.

Vision

Visual disturbances are common after a TBI, occurring in 30-45 percent of individuals (Sabates et al., 1991). In a review of 254 individuals, two and five years post injury, 42 percent continued to complain of visual difficulties at five years (Olver et al., 1996). Optic atrophy can begin shortly after the brain injury and lead to a marked decreased acuity and blindness. Persistent

visual field deficits also pose a significant safety risk due to the inability to see to the side. High flow carotid cavernous fistulas causing the direct flow from the internal carotid artery system into the cavernous venous sinus may develop weeks after a TBI. If not recognized and treated, permanent visual loss may progressively develop (Atkins et al., 2008).

Sleep

Sleep complaints are common following TBI. Subjective complaints of sleep disturbances have been reported in 70 percent of TBI outpatients (Chesnut et al., 1999, Max et al., 1991, McLean et al., 1984). Disturbed sleep, as measured by polysomnogram, was reported in 45 percent of a group of 71 individuals averaging three years post injury (Masel et al., 2001). Hypersomnia is associated with decreased cognition and decreased productivity, and certainly with a greater risk for accidents. National Highway Traffic Safety Administration data showed that approximately 56,000 auto crashes annually were cited by police officers where driver drowsiness was a factor (Strohl et al., 2005).

Alzheimer's Disease

Alzheimer's disease (AD) is an enormous public health problem in the United States where 5.2 million Americans are living with that disease. The direct and indirect cost of this disease is estimated to be $148 billion annually. (http://www.alz.org/index.asp). Although the cause of Alzheimer's is unknown, numerous studies have shown that a brain injury may well be a risk factor for the development of Alzheimer's disease (Jellinger et al., 2001, Plassman et al., 2000). In a large study of World War II veterans, Plassman and colleagues found that any history of head injury more than doubled the risk of developing AD, as well as the chances of developing non-Alzheimer's dementia. They also found that the worse the head injury, the higher the risk for AD. A moderate head injury was associated with a 2.3 fold increase in the risk, and a severe head injury more than quadrupled that risk (Plassman et al., 2000). In their excellent review on this issue, Lye and Shores (Lye and Shores, 2000) suggested many possible etiologies for this connection: damage to the blood brain barrier causing leakage of plasma proteins into the brain, liberation of free oxygen radicals, loss of brain reserve capacity, as well as the deposition of beta amyloid plaque (present in Alzheimer's disease). Even individuals with no known cognitive impairment after their TBI have a risk of an earlier onset of dementia due to Alzheimer's disease (Schofield et al., 1997).

Chronic Traumatic Encephalopathy (CTE) has recently garnered the attention of both the medical and lay press. At one time referred to as *dementia pugilistica* or "punch drunk," CTE is a distinct neuropathological entity caused by repetitive blows to the head and was at one time deemed to be a disease seen only in old retired professional boxers. CTE is an insidious disease beginning with deterioration in concentration, memory and attention, eventually affecting the pyramidal tract resulting in disturbed gait, coordination, slurred speech and tremors (McCrory et al., 2007). The sporting world has recently been shaken by autopsy-confirmed findings of CTE in retired professional football players (Omalu et al., 2006). As repetitive head injuries occur in a wide variety of contact sports beginning at the high school level, there is a pressing need for further study of this entity.

Neuroendocrine

A TBI is associated with a host of neuroendocrine disorders. Hypopituitarism is found in approximately 30 percent of individuals, over a year post injury, with moderate to severe TBIs (Schneider et al., 2007). Although individuals who develop post-traumatic hypopituitarism acutely may have resolution of that problem over time (Aimaretti et al., 2004), 5 percent of those patients in that study had normal pituitary functioning at three months but developed deficits at one year (Aimaretti et al., 2005).

Growth hormone (GH) deficiency/insufficiency is found in approximately 20 percent of moderate to severe TBIs (Agha and Thompson, 2006). GH deficiency is associated with an increased risk of osteoporosis, hypercholesterolemia and atherosclerosis. These patients have a significant increase in mortality from vascular disease (Rosén and Bengtsson, 1990).

Hypothyroidism is found in approximately 5 percent of individuals post TBI (Agha and Thompson, 2006). Associated signs and symptoms are weight gain, dyspnea, bradycardia and intellectual impairment (Agha and Thompson, 2007). A recent study has shown a connection between hypothyroidism in females and the development of Alzheimer's disease (Tan et al., 2008).

Gonadotropin deficiency is found in approximately 10-15 percent of individuals post TBI (Agha and Thompson, 2006). Adult males will note decreased libido, muscle mass and strength. A correlation has been found between low free testosterone levels and cognitive function, although there is no clear consensus on testosterone supplementation therapy and cognition (Papaliagkas et al., 2008). Hypogonadal women will develop secondary amenorrhea and increased risk for osteopenia.

INCONTINENCE

A TBI frequently affects the cerebral structures that control bladder storage and emptying functions, resulting in a neurogenic bladder. Fox-Orenstein and colleagues reviewed the records of more than 1,000 individuals admitted to rehabilitation centers after a TBI. One-third of the individuals were incontinent of bowel. Twelve percent were incontinent at discharge, but 5 percent were still incontinent at the one year follow-up. In their review of medical complications in 116 individuals with moderate to severe TBI, Safaz and colleagues found that 14 percent had fecal incontinence over one year post injury (Safaz et al., 2008). Fecal incontinence is not only socially devastating, but it will have medical consequences, including skin breakdown, pressure ulcers and skin infections (Foxx-Orenstein et al., 2003).

Urinary incontinence is also an enormous social and medical problem. Chua, et al., (Chua et al., 2003) reviewed the records on 84 patients admitted to a rehabilitation unit within six weeks of injury. Sixty-two percent were incontinent. This improved to 36 percent at discharge; however, 18 percent remained incontinent at six months. Safaz and colleagues found urinary incontinence in 14 percent of their cohort over a year post injury (Safaz et al., 2008). Urinary incontinence is associated with the development of frequent urinary tract infections and decubitus ulcers.

PSYCHIATRIC DISEASE

The impact and cost to society by psychiatric disorders is among the most important healthcare issues of today. Current estimates in the U.S. suggest that the collective cost of psychiatric diseases could be one-third of the total healthcare budget (Voshol et al., 2003). It is critical to note that psychiatric and psychological deficits are among the most disabling consequences of a TBI.

Many individuals with a mild TBI, and the overwhelming majority of those who survive a moderate to severe TBI, are left with significant long-term neurobehavioral sequelae. The costs to society in terms of lost productivity, as well as the costs for medical treatment are enormous. In addition to the aggression, confusion and agitation seen in the acute stages, a TBI is associated with an increased risk of developing numerous psychiatric diseases, including obsessive compulsive disorders, anxiety disorders, psychotic disorders, mood disorders and major depression (Zasler et al., 2007b).

Individuals with a TBI appear to have higher rates of depressive disorders, anxiety disorders and substance abuse or dependence (Hibbard et al., 1998, Holsinger et al., 2002, Koponen et al., 2002, Silver et al., 2001) and often have suicidal plans or suicidal behavior in the context of these illnesses (Kishi et al., 2001). TBI is associated with high rates of suicidal ideation, (Kishi et al., 2001, León-Carrión et al., 2001) suicide, (Silver et al., 2001) and completed suicide (Teasdale and Engberg, 2001). In chronic TBI, the incidence of psychosis is 20 percent. The prevalence of depression is 18-61 percent, mania is 1-22 percent, PTSD is 3-59 percent and post TBI aggression is 20-40 percent (Kim et al., 2007).

Koponen, et al, (Koponen et al., 2002) studied 60 individuals, 30 years post injury. Fifty percent developed a major mental disorder that began *after* their TBI. Another 11 percent developed a major mental disorder later on in their lifetime. Twenty-three percent had developed a personality disorder. In a long-term follow-up study of 254 individuals at two and five years post TBI, it was found that there was a higher incidence of cognitive, behavioral and emotional changes at five years than at two years post TBI. Thirty-two percent of those working at two years were unemployed at five years (Olver et al., 1996). A traumatic brain injury clearly may cause decades long, and possibly permanent, vulnerability to psychiatric illness.

SEXUAL DYSFUNCTION

Sexuality, both physiological and functional, plays an enormous role in our lives. Sexual dysfunction is a large issue in the general population and is a major ongoing problem in the TBI population. Studies have shown 40-60 percent of individuals complain of sexual dysfunction after a TBI (Zasler et al., 2007a). Transient hypogonadism is common acutely following a TBI, yet it persists in 10-17 percent of long-term survivors. Beyond just the fertility and psychosocial issues presented by hypogonadism, muscle weakness and osteoporosis may have a significant impact on long-term function and health with consequences exacerbated by immobility of long durations following a TBI (Agha and Thompson, 2005).

MUSCULOSKELETAL DYSFUNCTION

Muscular dysfunction

Spasticity is characterized by an increase in muscle tone that will result in abnormal motor patterns. This spasticity may well interfere with an individual's general functioning, and limit self care, mobility and independence in the activities of daily living. Spasticity requires life long treatment. Untreated, spasticity will eventually lead to muscle contractures, tissue breakdown and skin ulceration.

Skeletal dysfunction

The incidence of fractures in a TBI is approximately 30 percent. TBI patients with fractures, especially fractures of the long bones, are at risk for heterotopic ossification (HO), which may not develop for as long as three months post injury. HO is defined as "the development of new bone formation in soft tissue planes surrounding neurologically affected joints," and has an incidence of 10-20 percent following a TBI (Colorado, 2006). Safaz and colleagues found HO in 17 percent of their cohort over a year post injury (Safaz et al., 2008). If left untreated, HO will eventually lead to abnormal bony fusions (ankylosis) and subsequent functional limitations.

SUMMARY

Historically, individuals living with a brain injury have been referred to as brain injury *survivors*. No one knows how that term came to be used in this situation. Perhaps the concept of merely staying alive was used because as little as 30 years ago, the majority of individuals with a moderate to severe TBI succumbed soon after their injury. Perhaps it was used to imply that the individual *outlived* their injury and persevered despite the hardship of the trauma.

This term, however, does not address the reality of brain injury. Cancer *survivors* are survivors because it is believed they are cured—and they indeed have outlived their disease. Many individuals who sustain a TBI recover 100 percent. They have truly survived their injury. However, in the U.S. alone, every year, over 125,000 individuals who sustain a TBI become disabled. This paper discusses only a small percentage of the causes of disability and the ongoing and developing medical conditions individuals with TBI face. Presently, more than 3 million individuals in the U.S. are disabled due to the myriad of sequelae of a TBI (Zaloshnja E, Miller T, Langlois JA, Selassie AW. Prevalence of long-term disability from traumatic brain injury in the civilian population of the United States, 2005.*The Journal of Head Trauma Rehabilitation 2008;*23(6):394-400.) Their brain trauma has resulted in a condition that is disease causative and disease accelerative. As a result of their brain trauma, these individuals now have life-long brain injury disease.

Their disease should be reimbursed and managed on a par with all other diseases. Only then will the individuals with this disease get the medical surveillance, support and treatment they deserve. Only then will brain injury research receive the funding it requires. Only then, will we be able to truly talk about a cure.

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The Board of Directors of the Brain Injury Association of America adopted this position paper at its meeting on February 27, 2009, in Washington, D.C. The Association will continue to review the topic of brain injury as a disease as scientific and public policy progress dictates.

Electronic copies of this statement may be obtained from the Brain Injury Association of America's website: http://www.biausa.org.

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