ABSTRACT
“Dings,” “bumps on the noggin,” “seeing stars,” or “knocked out” are terms traditionally used by doctors and the general public to describe concussions, which imply that they are minor, perhaps trivial injuries. While the vast majority of concussions resolve uneventfully, as many as 15% of the 2-4 million persons who sustain a concussion annually have longer-term sequelae. For the past decade research on concussions has enlightened us as to its pathophysiology and risks for and prevention of long-term morbidity. This paper reviews the epidemiology of concussions (mild TBI), biomechanical and neurometabolic factors associated with concussion, risk factors for protracted recovery and guidelines for effective evaluation and management of concussions.

INTRODUCTION
Incidence: Cerebral concussion is frequently viewed by health care professionals and the general public as a minor injury, unworthy of serious concern or attention. Data from The Centers for Disease Control (CDC) indicate that approximately every 22 seconds someone in this country sustains a serious traumatic brain injury (TBI) resulting in 1.4 million deaths, hospitalizations, and emergency department visits annually. Of those, approximately 75% or 1.1 million are seen in emergency rooms and diagnosed with a concussion or another form of mild TBI. An unknown, but an assumed large number of concussions go unrecognized or unreported, with estimates of TBIs related to sports and recreation alone numbering between 1.6 to 3.8 million per year.1 Many individuals who sustain a concussion receive little evaluation, treatment, or guidance following injury, yet there is growing evidence that a concussion or “minor” brain injury is not always so minor or benign.

Over the past several years increased interest in concussion has emerged with commensurate awareness of the potential for significant morbidity. Athletes have become the primary focus of research efforts due to their relatively high likelihood of sustaining concussions and being a captive population in which pre- and post concussion assessments can be performed.

Etiology: Of all brain injuries, falls account for the greatest percentage (28%), followed by motor vehicle accidents (20%), impact by an object (19%), and assaults (11%). Miscellaneous and unknown causes make up the remaining 22%.2 Adolescents aged 15 to 19 years, and children younger than 5 years, have the highest overall incidence of brain injury. The more common causes vary in frequency according to age and social factors. Young children and elderly adults fall, whereas adolescents are prone to head injuries because they take risks, are inexperienced drivers, and more often participate in sports. Preliminary data from Walter Reed Medical Center indicate that 10% of personnel returning from Iraq and Afghanistan have suffered a concussion during their tour.3

PATHOPHYSIOLOGY: BIOMECHANICAL AND NEUROMETABOLIC FACTORS
Concussion involves an alteration of consciousness due to “a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces.”4 Concussion does not necessarily require a direct blow to the head, as it is frequently caused by rapid acceleration/deceleration/rotational forces. Military personnel are of course particularly susceptible to concussive injury. Repetitive exposure to explosive blasts in close proximity that result in waves of over-pressurization can damage internal organs, and the brain is particularly vulnerable. Loss of consciousness (LOC) has long been the clinical hallmark of concussion, but it is not necessary for the diagnosis. Clinical data indicate that only 8-19% of concussions result in LOC.5 (TABLE 1)

The clinical picture of cerebral concussion is attributable to direct injury to neurons and alterations in cell permeability and cerebral blood flow. Compressive, tensile, and rotational forces cause diffuse axonal injury at the gray-white matter interface, corpus collosum, brainstem and basal ganglia. Immediately following the injury there is sudden release of neurotransmitters along with an intracellular efflux of potassium and an influx of calcium. To restore membrane potentials the sodium-potassium
pump works overtime and requires increasing amounts of adenosine triphosphate causing a dramatic jump in glucose metabolism (hyperglycolosis). This occurs against a background of decreased cerebral blood flow, with the disparity between glucose supply and demand resulting in a cellular energy crisis. After this initial period of accelerated glucose utilization, the concussed brain goes into a period of depressed metabolism with continued increases in calcium potentially impairing mitochondrial oxidative metabolism which worsens the energy crisis. Unchecked calcium accumulation can set the stage for cell death, and intra-axonal calcium flux can impair neural connectivity.6 (Figure 1). The American Orthopaedic Society for Sports Medicine released a consensus statement which stated: “Experimental studies have identified metabolic dysfunction as the key post-concussion physiologic event that produces and maintains this state of vulnerability.”

**FACTORS ASSOCIATED WITH PROTRACTED OR INCOMPLETE RECOVERY**

Most individuals recover rapidly and completely from concussion. However, research indicates that up to 15% of patients diagnosed with MTBI may experience persistent disabling problems.7,8 Furthermore, knowledge of post-concussive symptoms among the general public and the medical community is less than optimal. A study out of the United Kingdom found that few of the non-specific symptoms associated with post-concussive syndrome were able to be identified in the absence of prompting by the lay public and general practitioners.9 Consequently there is a reduced likelihood that individuals sustaining MTBI will seek out or be offered help. Specialized psychological intervention has been demonstrated to be effective in reducing social disability and severity of post-concussion symptoms compared with those not receiving treatment.10 The CDC has identified several variables associated with elevated risk of delayed or incomplete recovery: age; gender; a history of prior concussion; a history of headache or postconcussive headache; premorbid developmental disorders; and psychiatric history.

Age: Among athletes, younger age has been found to correlate with a greater incidence of concussion and a slower recovery. The issue does not appear to be simply related to the fact that younger individuals engage in activities that may place them at greater risk. Rather, the younger brain appears to be more vulnerable to sustaining injury and recovery may be more protracted or less complete. The interval to resolution of symptoms is longer in high school athletes than in college or professional athletes.11 One study found that recovery of memory to baseline was 3-4 days slower in high school students than in older athletes.12 (Figure 2) Another study revealed slower

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**TABLE 1. SELECTED SIGNS AND SYMPTOMS OF CONCUSSION.**

<table>
<thead>
<tr>
<th>Somatic</th>
<th>Cognitive</th>
<th>Behavioral/Affective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Confusion</td>
<td>Emotional lability</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Posttraumatic amnesia</td>
<td>Irritability</td>
</tr>
<tr>
<td>Disequilibrium, dizziness</td>
<td>Retrograde amnesia</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Nausea, vomiting</td>
<td>Loss of consciousness</td>
<td>Depression</td>
</tr>
<tr>
<td>Phonophobia</td>
<td>Disorientation</td>
<td>Restlessness</td>
</tr>
<tr>
<td>Visual disturbances</td>
<td>“Fogginess, zoned out”</td>
<td>Impaired sleep</td>
</tr>
<tr>
<td></td>
<td>Impaired attention</td>
<td></td>
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<td></td>
<td>Delayed response</td>
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<tr>
<td></td>
<td>Slurred incoherent speech</td>
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<tr>
<td></td>
<td>Excessive drowsiness</td>
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</tbody>
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**Figure 1:** Neurometabolic cascade following experimental concussion. K⁺, potassium; Ca²⁺, calcium; CMRgluc, oxidative glucose metabolism; CBF, cerebral blood flow.

recovery of high school athletes compared to professionals on measures of verbal and non-verbal memory as well as reaction time and processing speed. Among the factors implicated in this increased susceptibility is a greater vulnerability of the younger brain to cerebral concussion am less complete myelination of the younger brain, a greater head-to-body ratio, and thinner cranial bone density.

It has long been believed that the brain of the infant and child has greater plasticity of function and therefore less vulnerability to persistent sequelae after an injury. Recent animal studies have demonstrated, however, that though the developing brain may respond with greater plasticity to some focal brain injuries, experimentally induced diffuse TBI – such as that occurring in concussion – may have long-term adverse effects. The child’s brain and its neurobehavioral functioning is a process in development that involves emerging skills and a “moving target,” in contrast to an adult’s established and relatively stable skills. Hence, what otherwise might have become the child’s ultimate cognitive capacity, absent of brain injury, is uncertain. There is growing consensus that even mild TBI in children may have significant long term effects, primarily manifested in a slower rate of learning.

In the older population, the neurobehavioral consequence of TBI have been largely ignored, though there are data which indicate that the older adult also appears to be more susceptible to sustaining a concussion following mild TBI, as well as suffering from greater and more persistent cognitive impairment. This increased vulnerability has been attributed to a variety of neuroanatomical factors and to the lesser “cognitive reserve” of the older adult.

Gender: The incidence of concussions in males is 1.5 to 2 times greater than in females, but when men’s higher incidence of risky activities is controlled for, females may actually be more vulnerable to concussion. In a recent epidemiologic study of high school and collegiate athletes playing the same sport, females sustained concussions at a greater rate than male athletes. Among high school soccer players, girls sustained concussions more often than boys by a ratio of 1.7:1 while female concussion rates in high school basketball were almost 3 times higher than among boys. Furthermore, following concussion girls consistently took longer for their symptoms to resolve and to return to play. At 1, 3, and 6 months after a concussion, females have a higher incidence of post-concussive symptoms than men. Women with concussions were 1.7 times more likely to experience cognitive problems, and college women more frequently suffered a subsequent decline in their grade point average. In a meta-analysis of 8 studies with 20 outcome variables, the post concussion scores for women were worse than those for men on 85% of the variables measured.

The reason for this apparent increased vulnerability of females is unclear. Some researchers have speculated that women may be more open about reporting symptoms of concussion to their trainers or physicians, while others have suggested that the smaller head and neck muscles in women predispose them to more injuries from rapid acceleration and deceleration. There has also been speculation about the as yet unknown impact of hormonal factors, but some animal studies have indicated that female hormones have neuroprotective qualities following TBI. More research is being conducted about the role of gender hormones in brain injury.

HISTORY OF PRIOR CONCUSSION: Studies of repeated concussions have led to three principal conclusions:

1. After a prior concussion, an impact of lesser intensity will cause a subsequent concussion;
2. Multiple concussions results in increased risk of cognitive dysfunction;
3. A history of prior concussion is associated with longer recovery time to resolution of symptoms.
Athletes who sustain a concussion were 3 times more likely to sustain another concussion in the same season.\textsuperscript{20} Athletes with 3 or more prior concussions were 8 times more likely to exhibit significant cognitive deficits compared to athletes who sustained their first concussion.\textsuperscript{21} A greater number of concussions is associated with higher symptom number and severity, worse neurobehavioral outcome, and a more protracted course of recovery.\textsuperscript{15, 22} Perhaps of greater concern with respect to multiple concussions is their potential impact on disability later in life. The Center for the Study of Retired Athletes at the University of North Carolina found that 20.2 percent of professional football players who sustained three or more concussions reported suffering from depression, compared with 9.7\% of those sustaining one to two concussions, and 6.6\% of those without identified concussion.\textsuperscript{23} Players with a history of three or more concussions were 3 times more likely to experience memory problems and 5 times more likely to develop earlier onset of Alzheimer’s disease. A 2005 follow up study revealed a connection between concussions, brain impairment, and Alzheimer’s.\textsuperscript{24}

**PRIOR HISTORY OF HEADACHE OR POSTCONCUSSIVE HEADACHE**: A personal and/or family history of headaches, particularly migraines, including post-concussive headaches, is associated with protracted recovery.\textsuperscript{25}

**HISTORY OF DEVELOPMENTAL DISORDERS**: There is evidence to suggest that persons with various developmental disorders such as pre-existing learning disability and attention deficit disorder have longer periods of recovery after TBI due to a detrimentally synergistic effect of these disabilities on recovery, and on the severity of post-concussion impairment.\textsuperscript{26}

**PSYCHIATRIC HISTORY**: There are scattered findings to suggest that a history of psychiatric disorder may be a significant determinant of outcome following mild TBI,\textsuperscript{27} with a particular association between outcome and a prior history of psychological trauma.\textsuperscript{28}

**SECOND IMPACT SYNDROME**
Though rare, second impact syndrome can occur when an individual has not completely recovered from a prior brain injury. A second concussion during this period of increased vulnerability can cause a loss of autoregulation of cerebral blood flow, with consequent vascular engorgement, increased intracranial pressure, and herniation of the brain. Second impact syndrome carries with it a grim prognosis, with significant brain damage and a mortality rate nearing 50\%.

One of the less understood aspects of second impact syndrome is that it can occur even after a relatively minor second blow. At the 2007 National Academy of Neuropsychology conference on mild traumatic brain injury, Micky Collins, Ph.D. of the University of Pittsburgh noted that in second impact syndrome, 1/10 of the force results in 10 times the effect. Interestingly, this syndrome only seems to occur among younger individuals. No cases have been reported in anyone over 18 years of age, perhaps another indication of the increased vulnerability of the younger brain.

**POST CONCUSSIVE SYNDROME**
Post concussive syndrome refers to persistence of concussion symptoms for weeks, months, and occasionally years post injury, resulting in impairment of social or occupational functioning. A significant number of patients (60\%) still experience post-concussive symptoms after one month, and 15\% still do so after one year.\textsuperscript{29} In light of our understanding of the neurometabolic cascade that occurs following a concussion, and the scientific data regarding recovery, we now know that management of the concussed individual’s symptoms is critical to recovery. Both physical and mental exertion increase the risk that post-concussive symptoms will persist beyond the expected recovery time frame. It is hypothesized that exertion increases the metabolic demand of a brain already in crisis, thereby slowing the brain’s ability to recover efficiently and fully.

**EVALUATION AND MANAGEMENT**
As many as 18 systems have been developed for grading the severity of concussions, with guidelines for expected recovery times and return to usual activities. Unfortunately, these guidelines have been found to be unreliable predictors of readiness to resume full activity. Accordingly, in 2004 the 2nd International Conference on Concussion in Sport recommended that “concussion severity can only be determined in retrospect after all concussion symptoms have cleared, the neurologic examination is normal, and the cognitive function has returned to baseline.”\textsuperscript{4}

It has been established that after a concussion, normal cerebral metabolism can be adversely affected in animals for days, and in humans for weeks. These alterations are
present even in head-injured individuals with normal Glasgow Coma scores, indicating the need for in-depth clinical assessment of cognitive and behavioral sequelae. Cognitive and affective symptoms are typically the last to resolve following concussion (Figure 3) and are often quite subtle. Individuals who sustain concussions are often unaware that their cognition is compromised, or they resist reporting symptoms. The cognitive impairment may also be less salient to others, including health care providers. At the recent Vienna and Prague meetings of the Concussion in Sport Group, neuropsychological testing was endorsed as a “cornerstone” of concussion management. Neuropsychological testing is important given the potential unreliability of athlete self-report after injury. Relying only on athletes’ reports of symptoms may result in premature return of athletes to play, potentially exposing them to additional risk. One study demonstrated that neuropsychological assessment increased the likelihood of identifying individuals with persistent concussive symptoms from 65 to 80%.30 Accordingly, neuropsychological assessment has a unique role in identifying the presence of subtle cognitive impairment, and in the management of concussion.

We now know that the post-injury treatment plan is critical to recovery. Routine follow-up and early psychoeducational intervention has been shown to be therapeutic and indicated. Adequate intake of fluids, carbohydrates, and protein to maintain appropriate blood sugar levels is recommended. Exertion, both physical and mental, increases the risk that post-concussive symptoms may worsen or persist beyond the usual recovery time. It is hypothesized that exertion increases the metabolic demand of a brain which is already in crisis, further impeding recovery. Consequently, the three most important recommendations are “rest, rest, and rest.” Rest means “absolute rest,” which is essential for the brain’s recovery following mild traumatic brain injury, and will in the majority of cases result in the best long term outcomes.

After concussion, restrictions in return to school, work, and exercise may aid in the resolution of symptoms. After 2-3 days of rest, concussed patients who are asymptomatic can then resume their usual activities in a graduated manner. If the increase in activity exacerbates post concussion symptoms, return to rest is imperative; resumption of any specific activity should be permitted only if the patient remains free of symptoms during engagement. A premature return increases the risk of incomplete or delayed recovery. Premature return to the responsibilities and demands of normal life may set the stage for increased psychological distress emanating from feelings of decreased efficiency, failure, interpersonal problems, negative feedback from supervisors, poor school performance, etc.

CONCLUSIONS
It should now be apparent that a careful evaluation following concussion is essential to reduce the risk of postconcussion syndrome. Once the medical examination is completed and a concussion has been diagnosed, careful delineation of symptoms and postconcussion risk factors will greatly enhance the likelihood of successful management of the patient’s symptoms.

Fortunately, current research on post-concussion management has taken some of the guesswork out of how much rest a patient requires before returning to work, play, school, or other activities. Recommendations must be tailored to the individual patient based on whether post-concussive symptoms persist with exertion, and should not be based on an arbitrary general time frame that is indiscriminately applied to all patients.

Many in the medical community and society at large continue to need a great deal of education to minimize the potential adverse consequences of concussion. This problem is illustrated by one of our recent patients who had been admitted to another medical facility with a mild TBI. At discharge he was given little information regarding his condition or guidelines for management, other than to search for information on the internet. Upon returning home to his usual activities, he discovered that he was unable to function at his pre-injury level. He
contacted his primary care physician and was admitted to our hospital where he received more detailed evaluation of his history and symptoms. Before discharge, he and his family received information about his mild, but obviously significant brain injury. They were provided with specific detailed instructions regarding management based on the principles discussed above. Upon being seen for follow-up, a dramatic improvement in his status was already evident. He and his family were understandably pleased with his recovery and appreciated the professional attention, education, direction and treatment he received during his hospitalization and subsequent care.

REFERENCES


Neither Dr. Bentz nor any member of his immediate family have any relevant financial relationships with any corporate organizations associated with the manufacture, license, sale, distribution or promotion of a drug or device to disclose.

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