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# Concussion

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**ABSTRACT**

Concussion has been recognized as a clinical entity for more than 1000 years. Throughout the 20th century it was studied extensively in boxers, but it did not pique the interest of the general population because it is the accepted goal of the boxer to inflict such an injury on their opponent. In 2002, however, the possibility that repetitive concussions could result in chronic brain damage and a progressive neurologic disorder was raised by a postmortem evaluation of a retired player in the most popular sports institution in the United States, the National Football League. Since that time concussion has been a frequent topic of conversation in homes, schools, and on television and has become a major focus of sports programs in communities and schools at all levels. Now all 50 states, the District of Columbia, and the National Collegiate Athletic Association have enacted laws and rules to protect the athlete.

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**KEYWORDS:** Chronic traumatic encephalopathy; Concussion; Mild traumatic brain injury; Post-concussion syndrome; Posttraumatic headache

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Concussion has been recognized as a clinical entity for more than 1000 years. Throughout the 20th century it was studied extensively in boxers,[1-3] but it did not pique the interest of the general population because it is the accepted goal of the boxer to inflict such an injury on their opponent. In 2002, however, the possibility that repetitive concussions could result in chronic brain damage and a progressive neurologic disorder was raised by a postmortem evaluation of a retired player in the most popular sports institution in the United States, the National Football League.[4,5] Since that time concussion has been a frequent topic of conversation in homes, schools, and on television and has become a major focus of sports programs in communities and schools at all levels.

In the Unites States, according to the Centers for Disease Control and Prevention, each year 1.7 million people present to a hospital emergency room with a traumatic brain injury (TBI), and 1.365 million are treated and released, indicating that their injuries are not severe. In adults the leading causes of head injury are falls and motor vehicle accidents, but in the 15- to 24-year age group sports are second only to motor vehicle accidents. It has been estimated that 1.6 to 3.8 million sports-related mild TBIs occur in athletes annually, but the exact number is unknown.[6-9] Despite the National Collegiate Athletic Association mandatory concussion education program for student athletes, an anonymous survey of a cohort of college athletes revealed that 43% of athletes who had suffered a concussion deliberately concealed their symptoms, indicating the degree to which underreporting may take place.[10] It is essential that we are able to accurately and expeditiously diagnose a concussion, provide effective treatment, and develop strategies to prevent recurrent injuries.

## DIAGNOSIS

The term "concussion" is derived from the Latin "concussus," which means "to shake violently."[11] Although the first recorded description of concussion has been attributed to Hippocrates approximately 2400 years ago, it was not until the 10th century AD that a Persian physician, Rhazes, made the distinction between concussion as an abnormal physiologic state as opposed to a brain injury. In the 13th century a European physician, Lanfrancus, referred to concussion as "commotio cerebri" in contrast to "contusio cerebri," and that term is still used today in Europe.[12]

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Concussion is often used interchangeably with "mild traumatic brain injury"; however, it is actually a descriptive term for the mildest form. In 2013 the American Academy of Neurology defined concussion as a "clinical syndrome of biomechanically induced alteration of brain function typically affecting memory and orientation, which may involve loss of consciousness."[13] Although this description is accurate, it is not particularly helpful from a clinical diagnostic standpoint. The Zurich Symposium on Concussion in Sport in 2012 placed emphasis on physical signs and symptoms following head trauma; however, the presence of symptoms does not necessarily denote that a brain injury, per se, has occurred.[14] For the clinician making a diagnostic determination after evaluating a patient, in 1997 the American Academy of Neurology provided the most useful definition, describing concussion as a "trauma induced alteration in mental status that may or may not result in loss of consciousness."[15]

## CLINICAL SIGNIFICANCE

- More than 50% of our population participates in sports, and there are approximately 3.8 million concussions per year.
- Concussion is the mildest form of a traumatic brain injury and occurs when a head injury causes a sudden change in mental status.
- Headache and dizziness are the most common post-concussion symptoms.
- Chronic traumatic encephalopathy, a progressive tauopathy, has been attributed to repetitive concussions.

Concussion occurs as a result of direct trauma, rapid acceleration−deceleration of the head such as a "whiplash" injury, or a blast injury commonly seen in military personnel serving in a war zone. With the change in mental status, in its mildest form, the patient is dazed or "sees stars" and may be momentarily confused. Depending on the severity of the injury, loss of consciousness may occur, followed by a brief period of amnesia, but loss of consciousness is seen in less than 10% of patients who suffer a concussion. The loss of consciousness is precipitated by the rotational forces at the junction of the midbrain and thalamus, resulting in a transient disruption of the reticular activating system.[14,16]

Although loss of consciousness does not always predict the outcome of a traumatic brain injury, it does provide incontrovertible evidence that a significant injury has occurred, and prolonged loss of consciousness suggests a severe traumatic brain injury rather than a concussion. The duration of posttraumatic amnesia, both anterograde (an inability to assimilate new memory) and retrograde (memory of events preceding the injury), may be an indication of the severity of the injury; however, amnesia is often difficult to assess because the patient's recollection may reflect what was related to them after the event by witnesses, family, friends, teammates, and coaches.[17-21]

Although the diagnosis of concussion is subjective, based on clinical assessment, there is exciting new research on blood biomarkers associated with astroglial (glial fibrillary acidic protein, S100 calcium binding protein B) and axonal (tau, ubiquitin C-terminal hydrolase 1) injury. The biomarkers have been demonstrated to accurately detect when a TBI has occurred and may be able to predict the severity of an injury.[22-24]

## PATHOPHYSIOLOGY

When head trauma induces an alteration in neurologic function, a series of neurochemical changes develop over hours, as observed in animal studies. There is a sudden release of excitatory neurotransmitters, particularly glutamate binding to *N*-methyl-D-aspartate receptors, causing the sudden release of potassium into the extracellular space, followed by an influx of calcium into the cell. This results in a transient hypermetabolic glycolytic state as membrane pumps become activated to restore homeostasis. Lactate is produced, impairing neuronal function, and there is a reduction of blood flow and diminished glucose utilization. Axonal injury may occur if calcium remains in the mitochondria. Although the average recovery time is 7-10 days, the altered metabolic state and diminished blood flow may last for weeks, and during this period the neural tissue is more susceptible to further injury.[25-27]

The pathophysiologic process that results in cortical spreading depression following head trauma is also observed in migraine and may be the underlying mechanism of the dysfunction that occurs in transient global amnesia.[28-31]

## EVALUATION

When a patient suffers a head injury the initial concern is whether the traumatic insult has caused an epidural or subdural hematoma, parenchymal hemorrhage, or increased intracranial pressure. An accompanying neck injury must be considered, and while the patient is being evaluated the cervical spine should be immobilized. If there is loss of consciousness or a severe injury is suspected then the patient should be taken to the hospital emergency room, and it is of paramount importance to remember that a severe injury can occur without loss of consciousness. A brief generalized tonic clonic seizure may be precipitated by direct brain trauma, and although immediate seizures have a good prognosis they are an indication for an emergent evaluation.[16,32] The Glasgow Coma Scale, which tests eye, verbal, and motor response to stimuli, is useful in the initial assessment of a traumatic brain injury, and patients who have suffered a concussion score 13 to 15 on the 15-point scale.[33,34]

Conventional neuroimaging of the brain with computed tomography (CT) and magnetic resonance imaging scans usually contributes little to the evaluation of concussion because it does not detect microscopic axonal injury. Diffusion tensor imaging is a magnetic resonance imaging technique that assesses white matter microstructural

integrity and has been shown to detect white matter injuries in mild traumatic brain injury, but whether the findings are clinically useful remains controversial.[14,35-37] Indications for a head CT scan in the acute evaluation are listed in Figure 1. A CT scan of the cervical spine should be performed if a spine injury is suspected.

A patient who is evaluated at the emergency room is usually observed for a few hours, and if their examination results are normal and there are no worrisome symptoms they are discharged to home to the care of a responsible party with a written list of instructions, including symptoms that would warrant a re-evaluation at the hospital. After a thorough evaluation has been performed there are no data to support waking the patient up at regular intervals during the night.[16,36]

## POST-CONCUSSION SYNDROME

Headache is the most common post-concussive symptom, followed by dizziness, which is more often a sense of disequilibrium and imbalance than objective vertigo. Patients may report a feeling of mental "fogginess" with mild cognitive difficulty affecting memory and concentration. Common symptoms are listed in Figure 2.[13,14,16,27,36]

Headache following head trauma has been reported to occur in 25%-90% of patients,[38,40-43] with 15%-75% of posttraumatic headaches still present at 3 months and 20% at 4 years. In the pediatric age group the incidence of chronic headache is much lower, and one prospective study reported 6.8% at 6 months.[40,44,45] It is interesting that chronic headaches are more commonly seen following a mild as opposed to a severe traumatic brain injury.[46,47] Post-traumatic headache encompasses 4% of all symptomatic headaches.[48]

Post-concussion syndrome occurs in 30%-80% of patients following a concussion and in 20% will become persistent.[40,42,43,49,50] In the subset of athletes, post-concussion symptoms resolve in 1-2 weeks in 80%-90%.[51,52]

The widely variable statistics are due to the fact that the populations that are studied are not uniform, and we must consider the effects of psychosocial problems, psychiatric disorders, litigation, compensation, and malingering.[50] In Lithuania, where litigation after an accident does not exist, studies have revealed that the incidence of post-concussion symptoms 3 months after a concussion is no different than in a sex- and age-matched control group that did not suffer a head injury.[53,54] Factors that may contribute to the chronicity of the symptoms include comorbid psychiatric disorders, a history of prior concussion, and migraine. Patients who have a high symptom burden immediately after suffering a head injury are more likely to experience persistent symptoms.[44,45,50]

Military personnel deployed in war zones are at risk for concussion, predominantly due to blast injuries, affecting approximately 20% of soldiers during their tour of duty. Headache is the most common symptom and prevents more than 80% from returning to the combat theater.[55,56]

Although the phenotype of posttraumatic headache may resemble many of the primary headache disorders, more than 60% of the headaches meet the International Classification of Headache Disorders-3 criteria for migraine or probable migraine. Trauma to the skull and neck may cause cervicogenic headaches or directly injure the occipital, supraorbital, or infraorbital nerves, resulting in neuralgic pain. A dural tear causing a cerebrospinal fluid leak may result in a postural low-pressure headache, and headaches may be symptomatic of a severe injury resulting in subarachnoid hemorrhage, subdural hematoma, or epidural hematoma.[44,45,55,57]

Abnormal neurologic exam including testing of gait
Progressive headache
Recurrent vomiting
Loss of consciousness > 1 minute
Prolonged anterograde amnesia
Seizure
Skull fracture
Age >60
Alcohol or drug intoxication
Coagulopathy
GCS score of < 12 2 hours post injury

**Figure 1** Indications for neuroimaging after concussion.[14,16,35,39]

**SOMATIC**
Headache
Vertigo/Dizziness
Nausea
Photophobia
Phonophobia
Tinnitus
Difficulty focusing with vision
Postural lightheadedness
Anosmia
Fatigue

**COGNITIVE**
Mental "fogginess"
Memory difficulty
Difficulty concentrating
Word finding difficulty

**BEHAVIORAL**
Mood lability
Irritability
Hypersomnia
Insomnia
Anxiety
Depression
Personality changes

**Figure 2** Post-concussion syndrome.[13,14,27,36,37]

By International Classification of Headache Disorders-3 criteria, an acute headache attributed to traumatic injury to the head must occur within 7 days of the injury. In some patients, however, the headache will begin more than 1 week after the injury, and in one study only 37% of soldiers reported a headache in the 7-day window. Headaches that continue for more than 3 months after the injury are now officially referred to as "persistent headache," attributed to traumatic injury to the head, rather than chronic post-traumatic headache. Medication overuse with rebound must always be considered as a potential cause of persistent headaches.[45,55,58]

## CONCUSSION IN SPORTS

Forty-four million children and 170 million adults participate in sports-related activities, and there are approximately 3.8 million sports-related concussions per year.[6,59] In males the incidence is highest in football, followed by hockey, and in females, soccer. Player to player contact is the most common cause, and as many as 25% are the result of prohibited activity. In football, the risk of concussion is 4 times higher on kickoffs when compared with plays from the line of scrimmage. The majority of concussions occur during competition rather than practice, and only 15% are the result of the head striking the ground. The rate of concussion is higher in females, potentially owing to anatomic, endocrinologic, or physiologic differences, and in athletes who have a history of a prior concussion. Young athletes are also more susceptible to concussion and may have a more prolonged period of recovery.[9,13-15,21,37,60-62]

When a concussion is suspected the athlete must be immediately removed from play for a neurologic examination, including cognitive and balance testing. Standardized sideline tests, such as the Sports Concussion Assessment Tool 3 and Balance Error Scoring System, may be useful, but the reliability, validity, specificity, and sensitivity, without an individual baseline, remain undefined. If the athlete is diagnosed with a concussion they cannot return to play that day and should be managed by a health care practitioner with demonstrated competence in the treatment of concussion. Athletes should be free of symptoms or back to their baseline before they are cleared to begin the 5-day return to play protocol (**Figure 3**).[13-15,27,36,37] Metabolic abnormalities following a concussion usually resolve within 7-10 days, and although the asymptomatic athlete may begin the protocol they should not be subjected to contact until they are 10 days after injury, at the minimum. Case studies of catastrophic brain swelling have been reported in, usually young, athletes who have suffered a second brain injury while still symptomatic from the first injury. This is referred to as second impact syndrome, and although there are no strong scientific data to support this theory the possibility must be respected.[63,64]

Neurocognitive testing, such as the computerized Immediate Post Concussion Assessment and Cognitive Test, can be useful in assessing cognitive function in an athlete who has suffered a concussion. The testing is only helpful when it can be compared with a baseline test completed by the athlete before the injury occurred. The testing is only another parameter to assist in the clinical management of the injured athlete, and test−retest reliability is variable. A diagnosis and recommendations with regard to return to play cannot be made solely according to the results.[65,66]

| STEP - 24 HOUR | REHABILITATION PROGRESSION |
|---|---|
| 1 | Light aerobic exercise |
| 2 | Sports specific exercise |
| 3 | Non- contact training drills |
| 4 | Full Contact practice |
| 5 | Return to play |

**Figure 3** Return to play protocol.[13-15,40,61]

The American Academy of Neurology recommends that each athlete who has suffered a concussion be assessed and managed individually without relying on a grading system. The type of sport and the risk of recurrent head injury should factor into the return to play decision.[13,14]

The use of protective equipment does not reduce the risk of concussion. Helmets, headgear, and mouth guards may prevent serious head, face, and oral injury but do not protect against concussion.[67,68]

## MANAGEMENT OF POST-CONCUSSION SYNDROME

The traditional management of concussion mandated complete physical and cognitive rest. Television, telephone, reading, texting, and video games were to be avoided, and patients were told that all exercise, including exertion with activities of daily living, could be potentially harmful and delay recovery. Recent studies, however, have shown that early physical activity is actually beneficial and that higher levels of exercise after a concussion is associated with lower rates of persistent post-concussive symptoms.[69-71] After 1-2 days of rest patients should be encouraged to exercise as tolerated.

With regard to cognitive rest, the data indicate that maintaining full cognitive activity after a concussion will delay recovery, but moderate cognitive activity is equivalent

to complete cognitive rest in reducing the duration of post-concussive symptoms.[72] For 3-5 days after the injury, patients should be advised to scale down their cognitive activity, then increase as tolerated. Special academic accommodations should be made for student athletes, including extended time to complete assignments, prepare for tests, and take tests.

Unfortunately there is a paucity of evidence from randomized controlled trials to assist the clinician in the treatment of the symptoms of post-concussion symptoms. Simple analgesics, including nonsteroidal anti-inflammatory drugs, are the first-line treatment for posttraumatic headache, and if they are not effective the triptans can be used for headaches with migrainous features. Metoclopramide and prochlorperazine are options both for the headaches and nausea. Narcotic analgesic agents and butalbital compound should be avoided. Care should be taken to avoid rebound and the development of medication overuse headache. For headaches that occur frequently more than 2 weeks after the concussion, a preventative medication should be considered. A tricyclic antidepressant medication, such as nortriptyline or amitriptyline, in low doses before bed, may be effective for both the headaches and insomnia. If the headaches do not respond to the tricyclic agent alone, then propranolol can be added, but the β-blocker can potentially aggravate underlying depression.[73-75] Topiramate can be considered, and evidence suggests that it is more effective than amitriptyline.[75] Topiramate, however, may aggravate the feeling of mental fogginess. For refractory headaches, botulinum toxin A injections, which have been shown to have a very modest effect in reducing the number of headache days each month in patients suffering from chronic migraine, is a potential treatment for patients who conform to the chronic migraine phenotype.[76] However, a randomized, placebo-controlled trial did not find the injections to be effective in the treatment of cervicogenic headache.[77] Controlled trials of spinal manipulation have not demonstrated efficacy in cervicogenic headache or migraine and should not be recommended specifically for the treatment of posttraumatic headache.[78,79] Nerve blocks can be administered for neuralgic pain syndromes, and there are some data that suggest efficacy in cluster, cervicogenic, migraine, and tension-type headache in both adult and pediatric patients.[80-82] For refractory headaches acupuncture can be considered, and a recent Cochrane analysis of randomized trials in the treatment of migraine found it to be effective in reducing the frequency of attacks.[83] There are conflicting data on cognitive behavioral therapy for the treatment of posttraumatic headache, and although it was effective in an open-label study with 20 patients, it was not effective in a randomized, controlled trial of 90 patients with chronic posttraumatic headaches. A systematic review of 10 studies using cognitive behavioral therapy for post-concussion symptoms concluded that there might be a slight benefit.[84-86]

Vertigo and dizziness may occur as the result of an injury to vestibular structures, and the presence of dizziness may portend a longer recovery time. After significant structural causes have been excluded, vestibular rehabilitation therapy should be initiated if symptoms persist for more than 10-14 days.[87,88] Meclizine is effective as a vestibular depressant but will cause a sense of lethargy.

For patients who experience persistent cognitive difficulty after injury, cognitive rehabilitation therapy has demonstrated efficacy and should be considered. Persistent symptoms are often the result of comorbid anxiety and depression and must be managed by a behavioral medicine practitioner.[86,89]

## Chronic Traumatic Encephalopathy

Neuropathologic changes in the brain of a boxer with abnormal results on neurologic examination were well detailed by Harrison Martland, a forensic pathologist, and in 1928 he published the article, "Punch Drunk." He described a progressive neurologic syndrome characterized by ataxia, pyramidal tract dysfunction, cognitive difficulty, dysarthria, tremor, and physical slowing.[1] In 1937 Millspaugh used the term "dementia pugilistica" to describe the disorder, and Critchley in 1949 described the "punch drunk" syndromes as the chronic traumatic encephalopathy of boxers.[90] In 2002 Omalu demonstrated tau deposition in the brain of a football player, Mike Webster, and made the diagnosis of chronic traumatic encephalopathy.[4,5]

Subsequent to Omalu's article, McKee et al demonstrated pathologic changes on the postmortem examination of multiple athletes and military veterans with a history of repetitive concussions, consistent with a progressive tauopathy. The abnormalities were ascribed to chronic traumatic encephalopathy, but in their 2012 analysis of 85 subjects, 65 with pathologic evidence of the tauopathy, 37% had comorbid pathology consistent with Alzheimer's disease, frontotemporal dementia, motor neuron disease, or Lewy body disease.[91-93]

A clinical disorder that is the reflection of the neuropathologic changes is now referred to as "traumatic encephalopathy syndrome." Signs and symptoms begin years after repetitive concussions, are progressive for more than 2 years, and are characterized by cognitive decline, behavioral changes (change in personality, violence, suicide), emotional dysregulation (depression, anxiety, paranoid ideation), and motor disturbance (ataxia, bradykinesia, tremor, dysarthria, rigidity).[94]

Chronic traumatic encephalopathy remains controversial, and the exact incidence and prevalence in retired athletes, military personnel, and the general population at large is unknown. There are no controlled epidemiologic studies to show that retired athletes are at increased risk for developing dementia.[95] Data from the studies on aging (Religious Orders, Memory and Aging Project, Adult Changes in Thought) suggest that a single traumatic brain injury does not increase the risk of developing dementia, although it may increase the risk of Parkinson disease.[96] Studies suggest a connection between recurrent

concussion and clinical depression, and depression in itself may confer an increased risk for developing Alzheimer disease.[97,98] The risk of suicide is actually lower in retired profession football players when compared with the general population.[99]

Multiple head injuries have been implicated as a potential cause of amyotrophic lateral sclerosis, and in a neuropathologic study of 12 athletes with chronic traumatic encephalopathy and evidence of tau deposition in the brain, 3 of whom were also diagnosed with amyotrophic lateral sclerosis, 10 of the 12 had a TDP-43 proteinopathy in the brain that can cause a motor neuron disease phenotype.[100] A more recent study, however, did not find an association between head injury and amyotrophic lateral sclerosis, and in fact the tau pathology of chronic traumatic encephalopathy was evident in amyotrophic lateral sclerosis cases regardless of whether they had suffered a head injury. More rapid progression of the motor neuron disease also did not occur after head injury, and there was no evidence of a specific neuropathologic phenotype.[101]

## CONCLUSION

Concussion has become a major health care concern, and the number of people who are diagnosed with this type of injury has steadily risen. Medical practitioners must be able to diagnose, implement effective treatment, and provide guidance to prevent recurrent injury. The possibility of developing a progressive neurodegenerative disorder from repetitive concussions will factor into the recommendations that we make to our patients.

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