Traumatic Brain Injury 2017

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Traumatic Brain Injury - Overview

- Worldwide major medical problem - marked medical unmet need
- 2.5 million cases / year – US
- Cost to Society: > $80 billion / year
- One million ED evaluations for TBI / year in Europe
- One head injury every 90 seconds in the UK
- Diagnosis in mild cases – subjective; therapy is primarily supportive
A TBI is defined as: a bump, blow, or jolt to the head or a penetrating head injury that disrupts the normal function of the brain; however, blows or jolts to the head do not always result in a TBI.

75% of TBIs are concussions

The severity of the TBI may range from “mild” defined as a “brief change in mental status or unconsciousness” to severe, defined as “an extended period of unconsciousness or amnesia after the injury.”
The term concussion is not a precise term and has been used to describe the mechanism of injury or describe a set of symptoms.

As a clinical diagnosis, concussion is applied to “a state of disordered brain function resulting from and immediately following a head injury…”

All states and the District of Columbia passed laws between 2009-2015 to address TBI; the majority of which enacted legislation targeting youth sports-related concussions.

Uniform questionnaires and treatment protocols continue to evolve.
Negligence – No proximate cause

Although health care providers were found to be negligent when they failed to accurately diagnose a child who suffered a head injury in a fall from a hayloft, treating him for concussion but failing to discover that he had suffered a fractured skull, the court found that their negligence was not a proximate cause of the injuries the child sustained as a result of the fall. Gregory v. Cortland Memorial Hosp., 21 A.D.3d 1305 (N.Y.A.D. 4 Dept Sep 30, 2005).
Causes of Action Involving Concussion Injury

Medical Malpractice – No proximate cause

A patient who brought medical malpractice claims against two doctors, a health center, and a physician’s assistant could not demonstrate that the complications he experienced after he suffered a head injury on the job were the proximate result of the alleged negligent acts of the health care providers. The patient failed to follow instructions for a follow-up visit after his initial examination and treatment at the health center, despite reminders, and failed to keep either an appointment for a CT scan or an appointment for an electroencephalogram. Thomas v. Washington Industrial Medical Center, Incorporated, 187 F.3d 631 (C.A.4 (Md.)) Jul 19, 1999
Causes of Action Involving Concussion Injury

Product Liability – No misrepresentation

Plaintiffs unsuccessfully brought an action against an automobile dealer for misrepresentation, in which they alleged the salesperson had told them that a vehicle with dual air bags was safer for children than a competitor’s vehicle with only a driver’s side air bag, and their child sustained a head injury after the air bag deployed in a collision. The salesperson’s statement was found to be a statement of opinion, rather than a misrepresentation of material fact. Chandler v. Gene Messer Ford, Inc., 81 S.W.3d 493 (Tex.App. Eastland Jul 03, 2002),
Common Defenses – TBI Litigation

- Comparative fault/contributory negligence
- Assumption of risk
- Malingering
- Release
- Immunity

Devices

- Improved helmets that address both direct impact and shear forces

- Lode Shell: Softer shell absorbs impact load by deforming like a car bumper, then bouncing back.
- Form Liner: Waterproof textiles and foams create a form liner that mimics mattress-like memory foam for fit and comfort.
- Core Layer: Inch-and-a-half-thick layer of vertical struts that bend and buckle to slow down impact forces.
- Arch Shell: Hard plastic layer protects against skull.
- Chin Strap: Two of the four snaps fasten to the inner shell to curb energy flowing through the jaw.
Diagnostics

Subjective:

Scat 3 Sport Concussion Assessment Tool (SCAT3)

Sideline assessments

Acute Concussion Evaluation (ACE)

Physicians / Office

Objective:

Evolving battery of blood tests to measure signaling proteins
Subjective: Evolving battery of blood tests to measure signaling proteins

Objective: Diagnostics

Acute Concussion Evaluation

Diagnostics

Physicians / Office

measure signaling proteins

Evolving battery of blood tests to

quire approval by the Concussion in Sport Group.

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tool may be freely copied in its current form for distribution to individuals, teams,

groups and organizations. Any revision or any reproduction in a digital form re-

quires approval by the Concussion in Sport Group.

NOTE: The diagnosis of a concussion is a clinical judgment, ideally made by a

medical professional. The SCAT3 should not be used solely to make, or exclude,

the diagnosis of concussion in the absence of clinical judgment. An athlete may

have a concussion even if their SCAT3 is “normal”.

What is a concussion?

A concussion is a disturbance in brain function caused by a direct or indirect force

to the head. It results in a variety of non-specific signs and/or symptoms (some

examples listed below) and most often does not involve loss of consciousness.

Concussion should be suspected in the presence of any one or more of the

following:

- Symptoms (e.g., headache), or
- Physical signs (e.g., unsteadiness), or
- Impaired brain function (e.g., confusion) or
- Abnormal behavior (e.g., change in personality).

SIDELINE ASSESSMENT

Indications for Emergency Management

NOTE: A hit to the head can sometimes be associated with a more serious brain

injury. Any of the following warrants consideration of activating emergency pro-

cedures and urgent transportation to the nearest hospital:

- Glasgow Coma score less than 15
- Deteriorating mental status
- Potential spinal injury
- Progressive, worsening symptoms or new neurologic signs

Potential signs of concussion?

If any of the following signs are observed after a direct or indirect blow to the

head, the athlete should stop participation, be evaluated by a medical profes-

sional and should not be permitted to return to sport the same day if a

concussion is suspected.

Any loss of consciousness?

“if so, how long?”

Balance or motor incoordination (stumbles, slow/laborious movements, etc.)?

Disorientation or confusion (ability to respond appropriately to questions)?

Loss of memory?

“if so, how long?”

Before or after the injury?

Blank or vacant look:

Visible facial injury in combination with any of the above:

Glasgow Coma Scale (GCS)

Best eye response (E)

Best verbal response (V)

Best motor response (M)

Was your team successful in this game?

Did you score last in this match?

Potential injury?

What are the symptoms?

Maddocks Score

Maddocks score is validated for sideline diagnosis of concussion only and is not used for serial testing.

Any athlete with a suspected concussion

should not be permitted to return to sport the same day if a concussion is suspected.

Notes: Mechanism of Injury (“tell me what happened?”)
Objective:

Subjective:

Diagnostics

Acute Concussion Evaluation

Scat 3 Sport Concussion Assessment Tool

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familiar with the SCAt3, please read through these instructions carefully. this

Specifi  c instructions for use of the SCAT3 are provided on page 3. If you are not

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“Before or after the injury?”

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Visible facial injury in combination with any of the above:

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Any loss of memory:

“if so, how long?”

Deteriorating mental status

Glasgow Coma score less than 15

Potential spinal injury

Deteriorating mental status

Glasgow Coma score less than 15

Progressive, worsening symptoms or new neurologic signs

Glasgow Coma score less than 15


Maddocks Score

“I am going to ask you a few questions, please listen carefully and give your best effort.”

Modified Maddocks questions (1 point for each correct answer)

What venue are we at today?

Which half is it now?

Who scored last in this match?

What team did you play last week/game?

Did your team win the last game?

Maddocks score

Maddocks score is validated for sideline diagnosis of concussion only and is not used for se
The Problem: Steroids were removed from the CNS trauma treatment guidelines in 2004 due to an 18% relative increase in two week mortality.

New Therapeutic in Development

Discovery of the remarkable anti-inflammatory synergy between two safe and effective, well established molecules:

- Levocetirizine: #1 antihistamine in the world
- Montelukast: #1 leukotriene receptor antagonist in the world

The molecules function within the steroid pathway at multiple levels in the immune system; however, without the steroid side effects.
Levocetirizine + Montelukast - Effective Attenuation of Inflammation through Synergy within the Immune Pathway

Trauma
↓↓↓↓

Produces Damaged Associated Molecular Patterns
↓↓↓↓

Recognized by Toll-like receptor family: Pattern Recognition Receptors
↓↓↓↓

Nuclear factor kappa B (NF-kB): family of transcription factors that control inflammation, cell survival, and cell death
NF-κB as a family of transcription factors plays a critical role in mediating responses to a remarkable diversity of external stimuli, inflammation, cell survival, and cell death.

www.bu.edu/nf-kb
Levocetirizine + Montelukast

Millions of patient days of safety / Both pregnancy Category B

Address multiple targets: antihistamine, antileukotriene (leukotrienes are similar to histamine; however 100-1000x more potent on a weight basis than histamine)

Synergistically attenuate eosinophil quantity / migration, neutrophil migration, TNF-α

Can be formulated a ‘first response’ injectable medication
18 year old MVA – rolled his truck over a cement median at high speed / landed upside down in the opposite lane sustaining the following injuries:

- **Severe traumatic brain injury (TBI) with diffuse axonal injury**
  - Bilateral middle meningeal artery bleeding / Neurosurgery that day
  - Skull fractures including a longitudinal temporal bone fracture through the sphenoid

- **Multiple facial fractures** including bilateral cribiform plate fractures

- **Bilateral lung aspiration / contusions**
Severe Polytrauma – Reportable Case

Hospital Day 2

Used by permission from the patient
Severe Polytrauma – Reportable Case
18 year old male

- Fracture of C2
- Fracture of T2
- Liver laceration
- Compound fracture of both femurs
- Fracture of both knees
- Fracture of both feet
- Fracture of the left wrist

- Glasgow Coma Score in the ED: 7-8
- 25-50% mortality from the TBI alone
- 74% chance of a poor neurological outcome
- Day 4 / Temp 102 F, 60% oxygen, PEEP 10
- Clinically deteriorating with bilateral pneumonia
- Initiated dose specific levocetirizine + montelukast
Severe Polytrauma – Reportable Case

Discharged home in 32 days for outpatient rehabilitation

Treated for eight months with the combination therapy – mother informed that following TBI, NF-kB can remain elevated in animal models for one year, leading to neurodegeneration and poor neurological outcomes

Outcome @ 10 months: on NO medications back to work, hiking, etc.

Used by permission from the patient

Video @ six months
Photo @ 10 months post
Independent Research
Montelukast restores Memory in a Mouse Model
October 2015

- Society for Neuroscience
- October 2015, Chicago, Illinois
- Paracelsus Medical University
  Salzburg, Austria
- Montelukast blocks receptors that trigger inflammation

DAILY NEWS 23 October 2015

Old rat brains rejuvenated and new neurons grown by asthma drug
Summary – Traumatic Brain Injury

TBI affects 2.5 million people / year in the United States; #1 US military medical unmet need

Currently there is no FDA approved, safe and effective pharmacotherapeutic agent to actively treat inflammation following TBI

Steroids were removed from the CNS trauma treatment guidelines in 2004 due to an 18% relative increase in two week mortality

Levocetirizine + montelukast are in development as a ‘first response medication’ to safely reduce morbidity and mortality in acute brain and lung injury

Objective diagnostics are also under development to refine existing treatment protocols

Thank you!