Clinical Management of Traumatic Brain Injury

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Epidemiology

- 1.7 million/yr sustain TBI,
- 65K adults 25K children suffer long-term disabilities
- Trimodal age distribution
- 1.4 : 1 males : females suffer TBI
- 10% of children hospitalized GCS of <9
- Estimates of 3 million children suffer MTBI

Blue Book CDC 2006
Estimate annual number of Traumatic Brain Injury per year

- 52,000 deaths
- 275,000 hospitalizations
- 1,365,000 emergency department visits
- ??? Injuries that receive other medical care or no care
Average estimated numbers of external causes of TBI 2002 - 2006

- 35.2% Falls
- 17.6% Motor Vehicle-traffic
- 21% unknown/other
- 16.5% Struck by/against
- 10% Assault
General Care

- **Airway** - intubation - bag mask-NRB C-spine precautions
- **Breathing** - one single episode of desaturation less than 90% increases death and disability in severe TBI
- **Circulation** - avoid hypotension use MAP for age as your perfusion pressure
- **Dextrose/Disability** - no glucose unless hypoglycemic for age reassess GCS
- **Exposure** - similar for all trauma
- **Fluids** - fluid resuscitation with NS
- **Nutrition** - important for all trauma patients
Management - Airway

- TBI is associated with abnormal breathing
  - Central neurogenic hyperventilation
  - Cheyne Stokes
  - Ataxic ventilation
  - Kussmaul breathing
- $\text{PaCO}_2$ relatively normal in most patients.
Airway Management

- **Breathing Patterns**

  - Central neurogenic hyperventilation
  - Ataxic breathing pattern
  - Kussmaul breathing pattern

Chyene Stokes
Management: Airway

- Hypoxemia present in 30% of patients
- Bag Mask or 100% NRB preferred if able to maintain airway
- Endotracheal intubation indications
  - Hypoxia < 90 or hypoventilation
  - Management of increased ICP
- Cervical spine injury present in 1-10% of patients with closed head injury (CHI)
- Cervical collar placed on all trauma patients
- In line traction should be held on all patients requiring intubation.
Airway Management in-line traction

Figure 2
In-line immobilisation during laryngoscopy
Management - circulation

- CPP = MAP - ICP or CVP
- Decreasing ICP or increasing MAP increases CPP
- Maintain MAP at age appropriate levels
- Target CPP
  - > 40mmHg infants
  - > 50 young children
  - > 60 older children
  - > 65 adolescents
- Augmentation of MAP with pure alpha agonist preferable
Management - Dextrose and Fluids

- Avoid hyperglycemia
- Non glucose containing fluids unless glucose drops below age appropriate levels
- Cautious use of insulin
- Normal Saline - initial fluid resuscitation
Interventions: Nutrition

- Full strength full rate feedings within 72 hr
- Attempt gastric or jejunal feedings.
- TPN within 48hr if unable to use enteral route
- Enteral feeds ASAP
- 2-2.3 g protein/Kg/day

- Enteral protein best as small peptides
- Total calories 40%-70% above basal needs
- Lipids 30%-40% of calories
- Lipid source best as MCT oil & ω-6 /ω-3 ratio of 2:1/ 8:1
Mechanism of injury

- **Children’s size** -
  - head to body ratio,
  - thinner cranial bones,
  - less myelinated tissue,
  - greater incidence of axonal and c spine injury
- **Primary insult** - caused by direct injury
- **Secondary insult** - the result of the brain’s response to the primary insult and includes inflammatory and biochemical processes
- **Hypoxia, Hypotension Hyperglycemia Hyperthermia** - further aggravate the secondary insult
Three general patterns of head injury

- Blunt head injury
- Sharp head injury
- Compression head injury
Three general patterns of head injury

- **Blunt head injury**
  - Forcible contact with flat smooth surface
  - Curvature of the skull at point of impact flattens
  - Acceleration/deceleration forces
  - Fractures occur when deformity of skull exceeds the tolerance
Mechanism of Closed Head Injury

Deceleration

Head thrown backward while brain hits front of skull

Acceleration

Head thrown forward while brain hits back of skull
Three general patterns of head injury

- Sharp head injury
  - Impact area and extent of skull distortion - small but explosive
  - Local depression or fragmentation of the skull
  - Laceration of the scalp
  - Tearing of the dura
  - Bruising and laceration of the underlying brain
Three general patterns of head injury

- Compression head injury

- Compression or crush injuries
  - Severe injuries may occur without loss of consciousness
  - Fractures tend to involve the basal foramina producing cranial nerve palsies
  - Internal carotid artery tear producing a fatal hemorrhage
  - Less severe injury can result in dissection and CVA
  - Side to side compression - fracture through the middle fossa through the sella turcica - pituitary is at direct risk
Three main mechanisms of intracranial injury

- Hemorrhage and focal brain tissue effects
- Diffuse traumatic axonal injury
- Secondary injury
Three main mechanisms of intracranial injury

- **Hemorrhage and focal brain tissue effect**
  - Focal injury occurs when the brain impacts against the rigid inner table of the skull resulting in direct cortical contusion
  - Focal brain injury can produce mass effect resulting in herniation
  - Mainly involves cortical grey matter

- **Three main types of focal brain injury**
  - Epidural hematomas
  - Subdural hemorrhages
  - Intraparenchymal hematomas or contusions
Three main types of focal brain injury

- Epidural hematomas

- Complicate 2-3% of all head injury admissions in children more frequent in advancing age with peak age in the second decade
- Infants tend to have venous bleeds in the posterior fossa and have delayed presentations due to the intracranial reserve from unfused sutures
- Older children have arterial bleeds and have a rapid decline LOC due to increasing mass
Three main types of focal brain injury

- Subdural hemorrhages

  - Common in children who suffer inflicted trauma and carries a high mortality
  - Clinical presentation depends on the size and location of hemorrhage
  - The associated brain injury account for the immediate unconsciousness and any focal neurologic deficits
Three main types of focal brain injury

- Intraparenchymal hemotoma or contusion

- Least common form of focal brain injury
- Most commonly involve the white matter of the frontal and temporal lobes
- Seen most frequently in severe brain injury with GCS <8
- Often occult acute white matter changes are present even in the brain regions that appear normal on conventional imaging
- Gray matter loss in the frontal area attributed to focal injury but white matter loss is related to both diffuse and focal injury

Three main types of focal brain injury

- Intraparenchymal hematoma or contusion
Common herniation syndromes.

- Uncal herniation
- Central transtentorial herniation
- Infratentorial herniation
Brain Herniation types

Supratentorial
1. Uncal
2. Central
3. Cingulate
4. Transcalvarial

Infratentorial
5. Upward
6. Tonsillar

openanesthesia.org
Three main mechanisms of intracranial injury

- **Diffuse traumatic axonal injury**

  - Diffuse axonal injury results from shearing forces that act at interfaces of structures with differing integrity
  - The axons that cross multiple brain regions are particularly vulnerable
  - Focal axonal injury or diffuse axonal injury
  - MRI is more sensitive to the white matter changes usually seen in axonal injuries
  - Difficult to determine on autopsy particularly in young children
  - 53 children who died of inflicted TBI - TAI evident in 3 of 53 children despite signs of subscalp bruising or skull fractures concluding diffuse hypoxic brain injury could explain the autopsy findings ¹,²

¹ Geddes et al. Brian 2001
Three main mechanisms of intracranial injury

- Secondary brain insult- Intracranial:
  - Intracranial hypertension
  - Mass lesions
  - Cerebral edema
  - Vasospasm
  - Hydrocephalus
  - Seizures
  - Regional and global cerebral blood flow abnormalities
Pathophysiology

Secondary brain insult - Systemic:

- Hypotension
- Hypoxia
- Anemia
- Hyperthermia
- Hypercapnia / Hypocapnia
- Electrolyte imbalance
- Hyperglycemia / Hypoglycemia
- Acid-base abnormalities
- SIRS/ARDS
Three main mechanisms of secondary injury

- Diffuse cerebral swelling
- Post traumatic ischemia and metabolic derangement
- Hypothalamic - Pituitary pertubations
Three main mechanisms of secondary injury

- Diffuse cerebral swelling
  - Diffuse cerebral swelling can result in unilateral or bilateral cerebral hemispheres and develops over 24-72 hrs
  - Sudural hematomas can produce rapid and fatal unilateral swelling even after evacuation
  - Fifty-three percent of initial head CT demonstrates diffuse cerebral swelling
  - The prognostic significance of this finding is unclear - adults have a 35% mortality and children have a 20% mortality
  - Tissue herniation can occur despite normal global ICP

Cerebral Edema
Pathophysiology

- **Cerebral edema**
  - Water movement from the vasculature to the parenchymal brain tissues increases as plasma oncotic pressure decreases.
  - The brain is isolated from the intravascular space by the BBB.
  - TBI may result in total loss of BBB with leakage of large molecules, partial loss with leakage of small mol weight molecules.
Pathophysiology

- **Vasogenic edema**: blood-brain barrier defect-permeability alterations and extravasation of fluid.
- **Cytotoxic edema**: massive increase in osmolality, breakdown of cellular structures, loss of the cell’s ability to regulate electrolyte gradients.
Three main mechanisms of secondary injury

- **Ischemic and Metabolic Perturbations**
  - Cerebral blood flow is decreased resulting in hypoxemia and hypotension
  - Increased cerebral metabolism accompanies hypoperfusion
  - Relative hyperemia develops following initial hypoperfusion state
  - Two metabolic states
    - Type I classical cerebral ischemia result of overt lack of oxygen and glucose at the mitochondrial level
    - Type II reflects a limited glucose supply and impairment of the glycolytic pathway
Three main mechanisms of secondary injury

- Hypothalamic-Pituitary perturbations

- Direct injury from fracture through the sella turica
- Indirect injury results from vascular ischemia due to tissue swelling and edema
- Autopsy in 106 adults show hypothalamic lesions in almost 43% and pituitary lesions in 28% consistent with infarction or ischemia
  
Critical pathway for treatment of intracranial hypertension in pediatric traumatic brain injury

- General guidelines for GCS <8 First Tier
  - Control body temperature
  - Avoid jugular venous outflow obstruction
  - Maintain adequate arterial oxygenation
  - Initial PaCO2 should be 35mm Hg
  - Maintain age appropriate CPP
  - Head of bed 30°
  - Euglycemia
  - Adequate sedation and analgesia possible muscle relaxation
Critical pathway for treatment of intracranial hypertension in pediatric traumatic brain injury

- First Tier guidelines for GCS < 8
  - ICP drainage
  - Volume status monitored
  - Hyperosmolar therapy
    - Mannitol
    - Hypertonic saline
  - Osmolar limits
    - 320mOsm/L for mannitol
    - 360mOsm/L for hypertonic saline
  - Osmolar therapy ineffective ventilation increased PaCO2 30-35mmHg
<table>
<thead>
<tr>
<th>Criterion</th>
<th>Infant</th>
<th>Child</th>
<th>Score*</th>
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<tbody>
<tr>
<td></td>
<td>Spontaneous</td>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>Eye opening</td>
<td>To verbal stimuli</td>
<td>To verbal stimuli</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>To pain only</td>
<td>To pain only</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>No response</td>
<td>No response</td>
<td>1</td>
</tr>
<tr>
<td>Verbal response</td>
<td>Coos and babbles</td>
<td>Oriented, appropriate</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Irritable cries</td>
<td>Confused</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Cries to pain</td>
<td>Inappropriate words</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Moans to pain</td>
<td>Incomprehensible words or</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>nonspecific sounds</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No response</td>
<td>No response</td>
<td>1</td>
</tr>
<tr>
<td>Motor response†</td>
<td>Moves spontaneously and</td>
<td>Obeys commands</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>purposefully</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Withdraws to touch</td>
<td>Localizes painful stimulus</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Withdraws in response to pain</td>
<td>Withdraws in response to pain</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Decorticate posturing (abnormal</td>
<td>Flexion in response to pain</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>flexion) in response to pain</td>
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<td></td>
</tr>
<tr>
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<td>Decerebrate posturing (abnormal</td>
<td>Extension in response to pain</td>
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<td></td>
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<tr>
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<td>No response</td>
<td>No response</td>
<td>1</td>
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</tbody>
</table>

*Score ≤ 12 suggests a severe head injury. Score < 8 suggests need for intubation and ventilation. Score ≤ 6 suggests need for intracranial pressure monitoring.

†If the patient is intubated, unconscious, or preverbal, the most important part of this scale is motor response. This section should be carefully evaluated.

First tier therapy for intracranial hypertension

Pediatr Crit Care Med, supp 2003
Intracranial Pressure Monitors
Interventions Tier I: Monitoring

- Monitoring goals:
  - ICP < 15 for infants and young children < 20 for older children
  - CPP > 40 for infants > 50 for young children > 60 for older children > 65 for adolescents
  - Ventilation goal: PaCO2 38-40 mm Hg
  - Saturation goals > 90
Interventions Tier I: Osmotheraphy

Mannitol

- Immediate plasma expanding effect
  - Reduces Htc
  - Reduces blood viscosity
  - Increases CBF
  - Increases cerebral O₂ metabolism
- Free radical scavenger
- Osmotic effect- delayed 15-30min
  - Effect begins when gradient >10 mOs
  - Lasts 90min to ~ 2 hrs
Interventions Tier I: Osmotherapy

Mannitol - potential complications

- “Opening” of blood-brain barrier
- Accumulation of Mannitol in the brain
- Risk of renal failure
  - worse with serum osmolarity $\geq 320$
  - compounded by nephrotoxic drugs
  - when sepsis present
  - Chronic renal insufficiency
Interventions Tier I: Osmotherapy

- Hypertonic Saline
  - Penetration across the BBB is low
  - Favorable rheology and osmolar gradient\(^1\)
  - Restoration of normal cellular resting membrane potential\(^2\)
  - Stimulation of atrial natriuretic peptide release\(^3\)
  - Inhibition of inflammation and improvement of cardiac output\(^4\)

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Interventions Tier I: Osmotherapy

- Hypertonic Saline - potential complications

  - Rebound in increase ICP
  - Central pontine myelinolysis
  - Subarachnoid hemorrhage\(^1\)

1 Qureshi et al Crit Care Med 2000
Critical pathway for treatment of intracranial hypertension in pediatric traumatic brain injury

Second tier therapy for refractive intracranial hypertension
Interventions Tier II:

Seizures

- Occur in 2% of all head injured patients
- Occur in 7-9% hospitalized children < 5 yr
- Immediate seizures: within hours
- Early seizures: within 7 days, late: > 7d
  - most are focal, may generalize, may recur
  - Status in 10% adults, 4% children
- Risk factors:
  - Prolonged LOC
  - Depressed skull fracture
  - Hematoma
  - Hemorrhagic contusion
Interventions Tier II:

- **Barbiturates, cautions:**
  - Hemodynamic instability
  - Decrease in CPP
  - Pulmonary complications
  - Depression of leukocyte activation
  - Suppression of leukocyte activity
  - Hypothermia
  - Infection
Interventions Tier II:

- **Hypothermia**
  - Hypothermia reduces the CMRO2
  - Multicenter internationally randomized control trial of 225 children with severe traumatic brain injury
  - Randomized to 32.5° vs 37°
  - Outcome at 6 months severe disability persistent vegetative state or death
  - Results - hypothermia initiated 8hr following severe TBI and continued for 24hrs does not improve neurologic outcome and may increase mortality

Hutchinson et al NEJM 2008
Interventions Tier II: Microdialysis

- A valid method for detecting brain ischemia
- Significant differences in brain neurochemistry in the traumatized brain.
- Elevated LPR in CSF: original marker of brain ischemia or mitochondrial dysfunction
- GFAP, Neuron Specific Enolase (NSE), MBP, S100B
- No specific CPP related to reduction of neuro markers.
- Elevated glutamate below specific CPP threshold.
- Microdialysis markers of impaired metabolism improved by removing mass lesions.

Bloomfield et al. Neurcirt Care 2007
Filippidis et al Neurosurg Focus 2010
Vespa et al. J Neurosurg 1998
The Jugular Bulb Catheter

- Jugular venous O2 sat monitors global cerebral hypoxia and ischemia.
- Reflects the relative balance between O2 requirement and delivery in the brain.
- An increase in cerebral O2 consumption or decrease in delivery may decrease Sjvo2
Interventions Tier II: Monitoring

- Jugular bulb Catheter
  - Normal values
    - $S_jvo_2$ 55%-75%, mean 61.8%
  - Ischemic threshold
    - Anaerobic metabolism in head injury with $S_jvo_2=50\%$
    - Confusion when $S_jvo_2 < 45\%$
    - EEG changes when $S_jvo_2 = 40\%$
    - Unconsciousness when $S_jvo_2 < 25\%$
  - Optimal values after head injury
    - One episode of desaturation ($S_jvo_2 < 50\% \times 10\text{min}$) increases risk of poor outcome from 55% to 75%

Pathophysiology

- Cerebral autoregulation is constant for MAP 60-160 ICP in children 2-4 mm Hg in adults 5-15 mm Hg
- Infants cannot tolerate even small rapid intracranial volume expansion despite open fontanelle and sutures
- In healthy children the metabolic rate for O2 and glucose is higher than in adults.
Brain Autoregulation

Effect of Blood Gases on Cerebral Perfusion

- PaO2
- PaCO2
- CBF
- Blood Pressure
- Partial Pressure
Pathophysicsology

- Release of excitatory neurotransmitters
- Pathologic overexcitation of receptors
  - influx of Na, efflux of K
    - large influx of Ca, may be sustained
    - sustained release of glutamate
      - early intracellular accumulation of Na
      - delayed Ca influx
  - Total brain Na & Ca: up, K, P, Mg & Zn: down
Treatment in evolution

- Antioxidants, free radical scavengers
  - Nonglucocorticoid, 21-amino corticoid
  - Polyethylene glycol-bound superoxide dismutase

- AMPA & NMDA receptor site blockers
  - Glutamate antagonists

- Nerve Growth Factor

- Indomethacin

- Channel Blockers - Ca Mg
Conclusion

- Despite the development of Class III expert opinion pathways for treatment of traumatic brain injury morbidity has not significantly improved
- More randomized controlled trials are needed
- More bench research is needed to understand the pathophysiology of traumatic brain injury to develop new therapies
Glucose disregulation and neurologic biomarkers in critically ill children - Vandhorebeek J Clin Endocrinol Metab 2010

Theory of Mind skills one year after TBI in 6-8 yr old children - Walz et al. J Neurophysic 2010

Classification of Traumatic Brain Injury for targeted therapies - Saatman et al. J Neurotraum 2008

The effect of head injury upon the immune system - Smrcka et al. Bratisk Lek Listy 2007

Hypothermia following Pediatric Traumatic Brain Injury - Adelson J Neurotrauma 2009