Traumatic Brain Injury:
What you need to know

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Objectives

- TBI Primary and Secondary Injury
- Coagulopathy in TBI
- Antiepileptics in TBI
- EVD Indications
- Craniotomy
- Targeted Temperature Management in TBI

Why do we care?

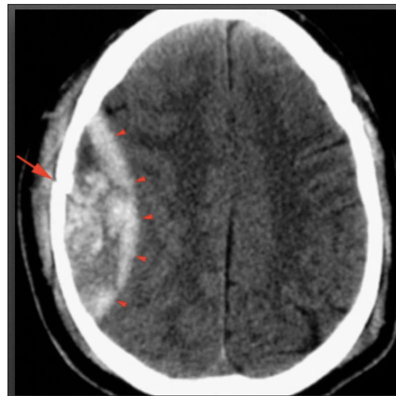
- TBI is the leading cause morbidity and mortality in trauma
- 5.3 million Americans (2% of the U.S. population) live with disabilities resulting from TBI (1)

Epidemiology

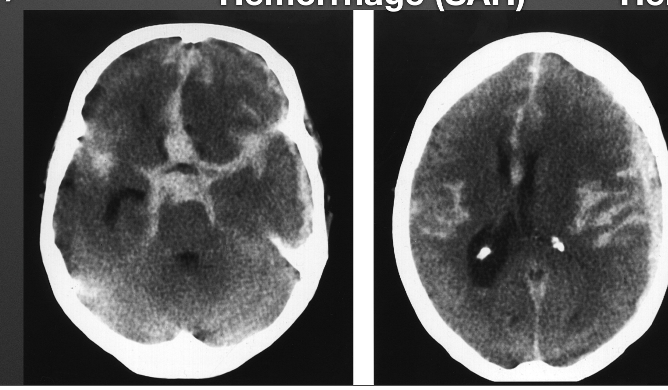
- 1.4 million people suffer from TBI/year (2)
- #1 leading cause death in age <45
- 12% of all hospital admissions are due to TBI

What is Traumatic Brain Injury?

- Primary injury: injury due to external mechanical force, at the time of impact to the brain
- Mechanism: Direct impact, acceleration/deceleration, penetrating
- Intraaxial (contusion, subarachnoid hemorrhage, or diffuse axonal injury)
- Extraaxial (epidural or subdural hematoma)



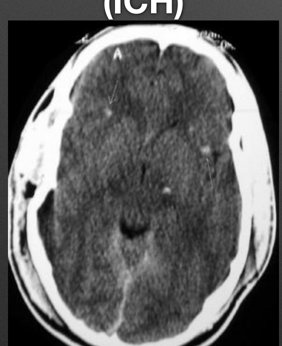
Epidural Hematoma (EDH)



Subarachnoid Hemorrhage (SAH)

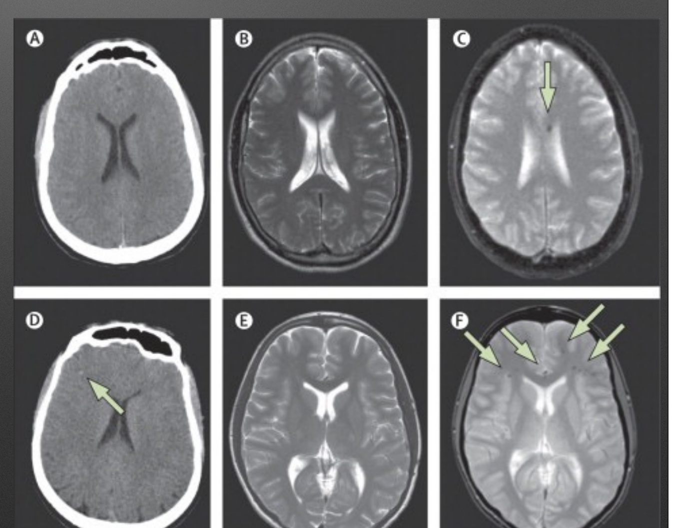
Subdural Hematoma (SDH)

Intracerebral Hematoma (ICH)



Diffuse Axonal Injury (DAI)

DAI on MRI

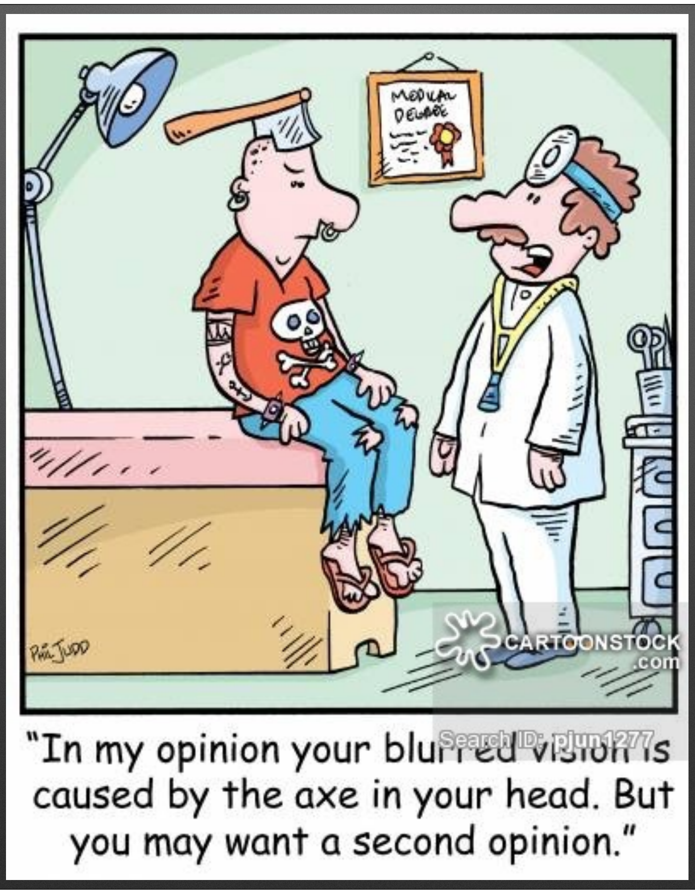


Secondary Injury

- Secondary Injury: preventable injury after primary insult that worsens outcome
- Hypotension
- Hypoxia
- Hyperthermia
- Hyponatremia
- Hypoglycemia/Hyperglycemia
- Hemorrhage
- Edema
- Infection

Secondary Injury

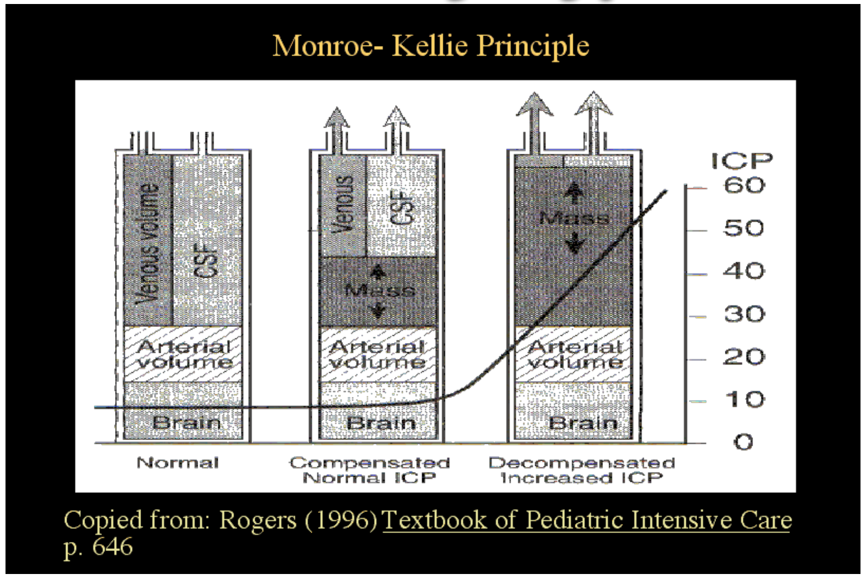
- HYPOTENSION: SBP <90mmHg, a single episode of hypotension increases mortality from 27% to 50% (1)
- Hypoxia: Pa02 < 60mmHg
- Hyperthermia: T >37 degrees C
- Hypoglycemia: BG 80-180



Edema

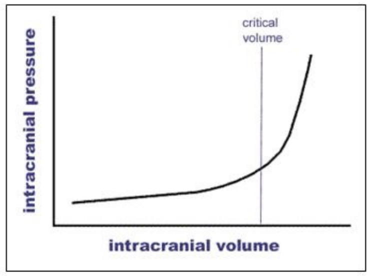
- Vasogenic Edema: blood barrier disrupted
- Cytotoxic Edema: blood brain barrier intact

Monroe-Kelley Hypothesis



- Brain, Blood, CSF
- Brain encased in skull=fixed space
- Intracranial volume can accommodate 100mL then pressure starts to rise

Cerebral Autoregulation



- Monro-Kellie Doctrine
  - Brain + blood + CSF + mass = constant volume
- ICP maintained at constant level
  - …… to a point

- Autoregulation is disturbed in TBI
- Cerebral blood flow reduced in first 72 hrs
- Cerebral blood flow dependent on systemic blood pressure
- Result neuronal ischemia, cytotoxic edema, and increased ICP

Cerebral Blood Flow Autoregulation

- Arterial blood flow and volume controlled by auto regulation process
- Cerebral arteries constrict when SBP elevates, PaC02 decreases, and Pa02 increases
- Cerebral arteries vasodilate when SBP falls, PaC02 increases, and Pa02 decreases
- Brain maintains CBF with MAP between 60-150mmHg

GCS

Eye	Motor	Verbal
4 = Spontaneous	6 = Obedient	5 = Oriented
3 = To Voice	5 = Purposeful	4 = Confused
2 = To pain	4 = Withdrawal	3 = Inappropriate
1 = None	3 = Flexion	2 = Incomprehensible
	2 = Extension	1 = None
	1 = None	

Classification of TBI

- Mild TBI GCS 13-15
- Moderate TBI GCS 9-12
- Severe TBI GCS <8
- Motor score correlates with outcome
- Decreased GCS portends higher mortality in TBI

What Affects GCS?

- Neuromuscular blockade
- Alcohol
- Shock
- Hypoglycemia

Cerebral Perfusion Pressure (CPP)

- MAP-ICP =CPP
- CPP goal 60-70mmHg
- MAP>65mmHg
- CPP>60mmHg associated with reduced mortality, improved quality survival
- May need to induce systemic hypertension, vasopressor and fluids
- CBB=CPP/Cerebrovascular Resistance

Brain Trauma Foundation Guidelines

- HOB > 30 degrees, neck straight to allow venous drainage
- Avoid Hypotension, Hypoxemia, Hyperthermia, Hypoglycemia (8)
- Maintain Normocarbia (Pa02 35-40 mmHg), normal pH 7.4-7.45
- Light sedation
- Seizure Prophylaxis x 7 days (ICH, SDH, No SAH)
- No DVT chemoprophylaxis x 72 hrs due to high risk rebleeding
- INR < 1.5

Antiepileptics in Severe TBI

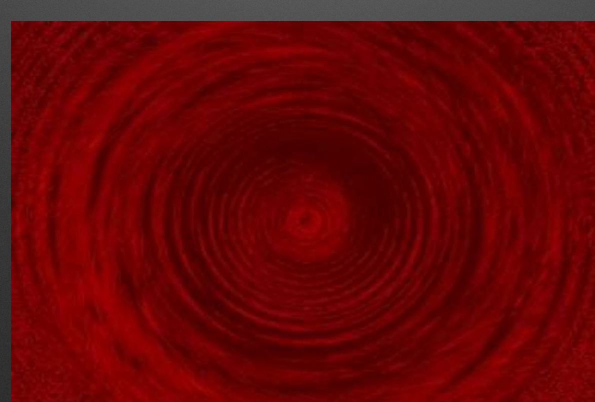
- Post traumatic seizures occur 15% of patients
- Most often within 48hrs
- BTF and American Academy of Neurology (AAN) seizure prophylaxis in severe TBI x7 days post injury
- Phenytoin desired treatment according to BTF, however clinical practice favors Keppra

Phenytoin vs Keppra

- Szaflarski et al. PRCT levetiracetam can be used as an alternative to phenytoin (3)
- Zafar et al. Meta-analysis no particular drug is superior in preventing early post TBI seizures (4)
- Side effect profile favors & lack of drug-drug interaction favors newer anticonvulsants, i.e. levetiracetam

Coagulopathy

- Anti platelet therapy: administer platelets only if abnormal PFA or undergoing surgery
- Renal Failure: DDAVP 0.3micrograms/kg
- Coumadin: INR >1.4, rapid reversal, Vitamin K 10mg (consider redosing), PCC (3 factor or 4) preferred over FFP(5)



NOACs (Factor Xa Inhibitor)

- Rivaroxaban, Apixaban, Epixaban
- Hold offending agents
- Activated Charcoal if administered <2hrs
- Prothrombin Concentrate Complex (PCC), 4 Factor, 3 Factor, or activated 4 Factor if within 3-5 half lives or liver failure
- According to the new NSCCM 2016 Guidelines

NOACs (Direct Thrombin Inhibitors)

- Dabigatraban
- Hold offending agent
- Activated charcoal, if administered <2hrs
- Hemodialysis in setting of overdose or ARF
- Activated PCC or 4 Factor PCC (5)
- Darucizumab (Praxbind): FAB binds to dabigatraban, neutralizes anticoagulant effects (2.5gm IV Q12hrs)

"I don't think it's a concussion ... although the smoke has me a little concerned."

Surgical Intervention in TBI

- EDH: > 30 mL in volume, acute EDH + GCS score ≤8 + pupillary abnormalities (11)
- SDH: > 10 mm in thickness , w/midline shift >5 mm, GCS ≤8 or GCS decreased by ≥2, +/or asymmetric or fixed +dilated pupils, +/or ICP >20 mmHg (12)
- ICH: posterior fossa w/mass effect (distortion, dislocation, obliteration of the fourth ventricle, compression of the basal cisterns, or obstructive hydrocephalus) (13)

Surgical Intervention (cont)

- ICH w/Cerebral Hemispheres: > 50 cm3 in volume, or GCS 6-8 w/frontal or temporal hemorrhage > 20 cm3 w/midline shift >5 mm +/or cisternal compression on CT scan (14)
- Depressed skull fracture: Elevation and debridement for open skull fractures depressed > than thickness of cranium or dural penetration, significant intracranial hematoma, frontal sinus involvement, cosmetic deformity, wound infection or contamination, or pneumocephalus (15)

Decompressive Craniectomy

- Substantial portion skull removed to reduce ICP, alone or in combination with evacuation procedure (16)
- Controversial and its efficacy in TBI is uncertain (17-22)
- Cooper et al, (DECRA), RCT, 155 adults with severe diffuse TBI with elevated ICP refractory, bifrontal decompressive craniectomy vs continued standard care (23)

DECRA Trial

•Surgery decreased ICP, fewer interventions, decreased ventilator days, & decreased ICU stay

•Worse outcome (extended Glasgow outcome scale at six months) & greater risk unfavorable outcome

•Rates of death were similar (23)

Recent Studies (RESCUE ICP TRIAL)

- RESCUE ICP Study: international multicenter randomized control trial 408 patients, >40 centers, 17 countries, diffuse or focal blunt TBI and intracranial hypertension (NEJM 2016)
- Randomized to decompressive craniectomy (unilateral or bilateral) vs optimal medical management (24)
- Dichotomized extended Glascow outcome scale
- Surgery associated with significant less mortality
- “Good outcome” was not significantly different between groups
- “Good outcome” was better in surgical group at 12 months
- Craniectomy associated with 22% reduction in mortality
- Larger percentage of patients in vegetative state, lower severe disability, and upper severe disability
- No difference in rates of moderate disability and good recovery
- Functional outcome not significantly better at 6 months, however significantly better at 12 months

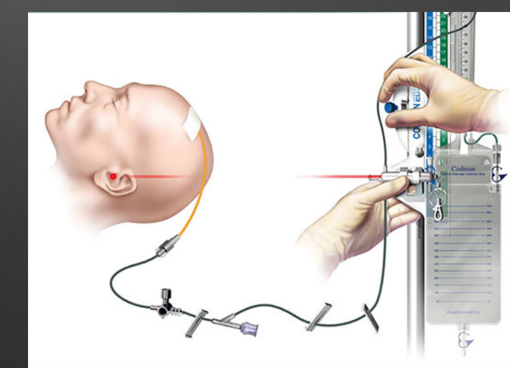
Recent Studies (STITCH Trauma Trial)

- STITCH Trauma Trial: international randomized parallel group trial, traumatic ICH
- Early evacuation by surgeon’s choice within 12 hrs + medical group vs medical treatment + delayed evacuation if necessary (25)

Indications for EVD?

BTF Guidelines:

- moderate -> severe head injury
- cannot assess neurologically
- severe head injury + abnormal CT scan
- severe head injury + normal CT + 2 of the following:
  Age > 40 yrs
  BP < 90 mmHg
  Motor posturing



ICP Monitoring

Chesnut RM, et, al. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med. 2012 Dec 27;367(26):2471-81. doi: 10.1056/NEJMoa1207363. BEST TRIP (26)

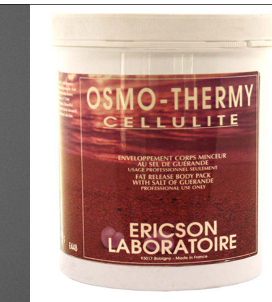
- RCT, 6 sites in Bolivia and Ecuador, 324 patients, severe TBI, or GCS 8 or less, within 48 hours
- ICP monitoring (protocol ICP <20 mmHg) vs clinical exam + CT head only
- No difference in ICU LOS, 6 month mortality, neuropsychological and functional recovery

ICP Monitoring (cont)

Su S-H et al. The Effects of Intracranial Pressure Monitoring in Patients with Traumatic Brain Injury. PLoS ONE 2014; 9: e87432 (27)

- Meta-analysis of 9 studies (n=11,038)
- ICP monitoring no effect on outcome or mortality
- Significant clinical heterogeneity suggests large, RCT needed

Osmotherapy



- Prevent egress of water out of tissue
- Hyperosmolar therapy = bridge to definitive procedure
- Attenuation of ICP
- Serum sodium is a major component of serum osmolality
- GOAL = create an osmotic gradient between the blood and the brain, egress of water into the vascular compartment

Mannitol

- Osmolarity 1100 mOsm/L
- 15-30 minutes to work
- Bolus 0.5-1g/kg
- repeat Q1hr when ICP>20 and sustained
- Endpoint : 320 mOsm/L or osm gap <55mOsm/L
- No independent association between serum osm and renal failure
- Renal Failure RARE when Osm Gap <55 mOsm/L (28, 29, 30)

Mannitol Adverse Effects

- CHF, increase volume, increased CO
- Hypotension
- Renal Failure
- Hyperkalemia
- Pulmonary Edema
- Osmotic Effect
- Promotes vasoconstriction
- Hemolysis
- Metabolic Acidosis

Hypertonic Saline

- The Magic Bullet, 23.4%, always a push
- 3% = 1027 mOsm/L
- 5% = 1711 mOsm/L
- 23.4% = 8000 mOsm/L, Na can increase by 10mEq
- 2-3% gtt @ 50-150 mL/hr
- 250-500 mL bolus (4-6ml/kg ideal body weight)
- Target Na: 145-155, Serum osm: 320 mOsm/L

Hypertonic Saline Adverse Effects

- Hyperchloremic metabolic acidosis
- Phlebitis, regional necrosis, intravascular hemolysis
- No EVIDENCE (31, 32, 33)
- Withholding hypertonic saline due to lack of central line is UNJUSTIFIED

Mannitol vs the Others

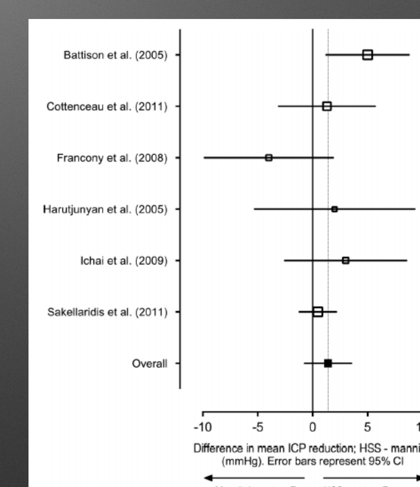
Wakai A et al. Mannitol for acute traumatic brain injury. *Cochrane Database Syst Rev.* 2013; 8: CD001049 (34)

- 4 RCT using mannitol in TBI (n=197)
- Mannitol vs “standard of care”, pentobarbital, HTS, and placebo
- Mannitol may decrease mortality compared to pentobarbital
- Mannitol may have detrimental effect compared to HTS
- ICP-targeted treatment shows small benefit compared to neurologic and physiologic indicators
- Insufficient reliable evidence

HTS vs Mannitol

Rickard AC et al. Salt or sugar for your injured brain? A meta-analysis of randomised controlled trials of mannitol versus hypertonic sodium solutions to manage raised intracranial pressure in traumatic brain injury. *Emerg Med J* 2014; 31: 679-83 (35)

- Six studies (n=171)
- Variety of solutions
- Primary outcome: mean reduction ICP
- ICP difference 1.34 mmHg
- Both agents effectively lower ICP
- Trend toward HTS
- More work needed….



Normothermia

- Puccio et al. efficacy of induced normothermia with intravascular cooling catheter, reduced ICP compared to control group (36)
- Suehiro et al. TTM is significantly effective for TBI management comparing to no temperature management (37)
- Several studies hyperthermia associated with increase ICU LOS, lower GCS on discharge from ICU, and lower neurological function 6 months (38, 39)

Temperature Targeted Management (TTM)

- Basic science research: TTM and therapeutic hypothermia (TH) promise for neuroprotective treatment (40, 41)
- Clear evidences in TBI not yet proven in RCTs
- TTM for TBI optional recommendation (level 3 in BTF guideline) (42)

Hypothermia

- Clifton et al. 2001: normothermia vs surface cooling hypothermia, no efficacy of hypothermia in TBI (43)
- Clifton et al. 2016: early hypothermia, no change mortality and morbidity (44)
- Maekawa et al. 2015: prolonged mild hypothermia (32-34 degrees C) vs fever control, no differences in the likelihood of poor neurological outcome or mortality (45)
- HOPE Trial (ongoing study): rapid hypothermia prior to emergent craniotomy for SDH and outcome (46)

Refractory ICP and TTM

- Aggressive treatment of elevated ICP reduces mortality and improves outcome BTF (47,48)
- TTM promising for controlling intracranial pressure in TBI (49,50)
- EUROTHERM 3235 on going trial, refractory ICP TH vs standard treatment no TTM (51)
- Preliminary data: efficacy of TTM controlling refractory ICP (52)

Conclusions

- Avoid secondary injury
- PaC02 35-40mmHg, Pa02 >80mmHg, Na 145-155 mEq/L, INR <1.4, SBP >90mmHg, MAP >65mmHg, ICP<20 mmHg, HOB >30 degrees (BTF)
- Reverse coagulopathy
- Antiepileptics Keppra/Phenytoin both effective preventing seizure post TBI
- Aggressive lowering ICP improves outcome
- Decompressive Craniectomy doesn't change outcome
- Hypertonic/Mannitol both effective lowering ICP
- Target Normothermia
- WHAT YOU DO MATTERS

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