MANAGEMENT OF SEVERE PEDIATRIC TRAUMATIC BRAIN INJURY – an EBM approach

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INTRODUCTION

• Head injury is the most common cause of death and disability in children.

• Approximately 7000 children die from head injuries in the US every year.

• In younger children, they are usually pedestrians struck by vehicles, or from falls.

• In older children, the most common cause is from passenger or driver MVAs. In certain areas, penetrating injuries are more common.

Severe pediatric traumatic brain injury

Pediatric is defined as <18 yrs of age

Severe TBI is defined as GCS score of 3-8 after cardiopulmonary resuscitation
### Classification of Evidence

- **Class I evidence**: RCTs > gold standard. However, not all RCTs are class I evidence.

- **Class II evidence**: Clinical studies in which data was collected prospectively OR retrospective analysis that was based on clearly reliable data.

- **Class III evidence**: most studies based on retrospectively collected data.

### Degrees of Certainty

- **Standards**: Accepted principles of patient management that reflect a high degree of clinical certainty.

- **Guidelines**: A particular strategy or range of management strategies that reflect a moderate clinical certainty.

- **Options**: The remaining strategies for patient management for which there is unclear clinical certainty.
TALK OVERVIEW

- Indications for ICP monitoring
- Threshold for treatment of intra-cranial hypertension
- Cerebral Perfusion Pressure (CPP)
- Sedation and neuromuscular blockade
- Role of CSF drainage
- Hyperosmolar therapy

- Hyperventilation
- Barbiturates
- Hypothermia
- Decompressive craniectomy
- Corticosteroids
- Anti-seizure prophylaxis

TREATMENT ALGORITHM
INITIAL RESUSCITATION

- Management of patients with severe head injuries follows ATLS guidelines.

*Airway*

- Stabilize the cervical spine and start 100% O₂
- Intubation to minimize secondary brain injury from hypoxia and to prevent aspiration
- Proceed with rapid sequence induction assuming full stomach
INITIAL RESUSCITATION

Breathing

- Hypoxia should be avoided with the goal of normocarbia.

Circulation

- Treat shock aggressively. Presence of hypotension doubles the mortality associated with severe head injury.
- Correct volume losses. Transfusions should not be delayed; hemoglobin and hematocrit should be kept >10 mg.dL and 30% respectively
Intracranial pressure (ICP)
**OVERVIEW**

Benefits of maintaining ICP within normal range

- Maintain adequate cerebral perfusion pressure (CPP)
- Maintain oxygenation and metabolic substrate delivery
- Avoid cerebral herniation events

Why use physiologic ICP monitoring in severe TBI?

- Clinical signs of raised ICP:
  1. change in level of consciousness
  2. cerebral herniation

Two lines of evidence support the use of ICP monitoring in severe TBI

- Intracranial HTN (ICH) associated with poor neurological outcome
- Aggressive treatment for ICH associated with best reported clinical outcomes
Indications for ICP monitoring in severe TBI

(key elements from the adult guidelines)

Severely head-injured patients are at high risk for intracranial hypertension, even with a normal admission CT scan, intracranial hypertension may be present.

The combination of severe head injury and an abnormal CT scan suggests a high likelihood of raised ICP.


Indications for ICP monitoring in adults:

Severe head injury (GCS<8) + abnormal CT

OR

Severe head injury + normal CT + 2 of the following:

Motor posturing
Systemic hypotension
Age >40
### Evidence table
>60 relevant studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Description of Study</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfenninger et al.</td>
<td>Retrospective study.</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>Treatment threshold: ICP&gt;20-25 for &gt;3 mins</td>
<td></td>
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<tr>
<td></td>
<td><strong>ICP&gt;40 associated with death. ICP&lt;20 with good outcome.</strong></td>
<td></td>
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<tr>
<td>Esparza et al.</td>
<td>Retrospective study.</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>Treatment threshold: ICP&gt;20</td>
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<tr>
<td></td>
<td>ICP&gt;40: Mortality rate 100%. ICP 20-40: 28 %. ICP&lt;20: 0%</td>
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<tr>
<td></td>
<td><strong>ICP&gt; 20 is a valid treatment threshold.</strong></td>
<td></td>
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</tbody>
</table>
**Recommendations**

<table>
<thead>
<tr>
<th>Standards</th>
<th>Options</th>
<th>Guidelines</th>
<th>Insufficient data</th>
</tr>
</thead>
</table>

The critical value of ICP and its interaction with other cerebral physiologic variables are major unanswered questions.
Cerebral perfusion pressure (CPP)
OVERVIEW

CPP = MAP – ICP

Defines the pressure gradient behind cerebral blood flow
  Related to metabolic delivery of essential substrates to brain tissue

Posttraumatic brain has a significant incidence of vasospasm
  Increases cerebral vascular resistance
  Decreases CPP > Ischemic brain

Regional CBF may be even more reduced in the vicinity of intracranial hematomas and contusions

What is the optimal CPP in severe pediatric TBI patients?
### Evidence table

>50 relevant studies

<table>
<thead>
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</table>
### Recommendations

<table>
<thead>
<tr>
<th>Standards</th>
<th>Guideline</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled, prospective, randomized studies are needed to determine optimal CPP levels in various pediatric age groups.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insufficient data</td>
<td>Stand</td>
<td>Treatment continuum threshold</td>
</tr>
</tbody>
</table>

**A CPP between 40 and 65 probably represents an age-related continuum for the optimal treatment threshold.**

**Options**

A CPP > 40 mm Hg in children with TBI should be maintained.
Dog bites
Life-threatening dog attacks: A devastating combination of penetrating and blunt injuries

August 2001, Pages 1115-1117

- Depressed cranial fractures should be irrigated, debrided, and elevated.
- Dural tears should be repaired.
- Expedient management is necessary to prevent meningitis and its associated sequelae.
- Evaluate for blunt trauma
Sedation, analgesia and neuromuscular blockade
OVERVIEW

Proposed benefits of sedation and analgesia

- Facilitate general aspects of patient care
- Mitigate aspects of secondary damage
- Anticonvulsant and anti-emetic actions

Sedative induced reductions in arterial BP can lead to cerebral vasodilation and exacerbate increases in cerebral blood volume and ICP

Evidence Table

Less than 10 studies addressed the use of sedatives and/or analgesics in severe pediatric TBI

None of these studies reached the level of class III data
OVERVIEW

Proposed benefits of neuromuscular blocking agents

- Reduction of ICP
- Reduction of metabolic demands

Risks of neuromuscular blockade

- Nosocomial pneumonia
- Cardiovascular side effects – myopathy
- Immobilization stress
- Masking seizures

Evidence Table

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<thead>
<tr>
<th>Reference</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Vernon et al.</td>
<td>Prospective, unblinded crossover study of the effect of neuromuscular blockade on total body oxygen consumption</td>
<td>II</td>
</tr>
<tr>
<td>Crit Care Med 1</td>
<td>NMB reduced oxygen consumption and energy expenditure by 8.7 and 10.3 %</td>
<td></td>
</tr>
</tbody>
</table>
Recommendations

In the absence of outcome data, the choice of sedatives, analgesics and neuromuscular blocking agents should be left to the treating physician.

Options

Insufficient data

Guidelines

Insufficient data

Standards

Based on FDA recommendations, continuous infusion of propofol is not recommended in the treatment of pediatric TBI.
Propofol is not indicated for pediatric ICU sedation as safety has not been established.


CSF drainage
OVERVIEW

Ventricular CSF drainage is often employed to reduce ICP in ICU setting

Ventricles are often small in TBI
30% of compliance of CSF system is in spinal axis

What about lumbar CSF drainage in addition to ventricular drainage??

Evidence Table

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<tr>
<td>Pediatr Neurosurg</td>
<td></td>
<td></td>
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<tr>
<td>1991-2; 17:115-120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levy et al.</td>
<td>Retrospective study N = 16 children with severe TBI; lumbar drains with</td>
<td>III</td>
</tr>
<tr>
<td>J Neurosurg 1995;</td>
<td></td>
<td></td>
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<tr>
<td>83:452-460</td>
<td></td>
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</tbody>
</table>

3/5 patients survived with favorable neurologic outcome
14/16 patients survived; 11 with favorable neurologic outcome
### Recommendations

<table>
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<tr>
<td>CSF drainage, in the setting of refractory intracranial hypertension, can be accomplished via EVD alone or in combination with a lumbar drain</td>
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The addition of LD should be considered as an option only in the case of refractory ICP with:

1. A functioning ventriculostomy
2. Open basal cisterns
3. No mass lesion or shift
Hyperosmolar therapy
OVERVIEW

IV administration of hyperosmolar agents shown to reduce ICP

Mannitol
Urea
Glycerol

Mechanisms of action for Mannitol

Viscosity autoregulation of CBF
Osmotic effect

Limitations of Mannitol

ATN with serum osm >320
Injured BBB – reverse osmotic shift

Hypertonic Saline

Osmolar effect
Level of 360 mOsm/L tolerated
Central pontine myelinolysis
<table>
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<tr>
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<td>James HE. Acta Neurochir 1980; 51:161-172</td>
<td>Retrospective study. N = 60 patients treated with 0.5g/kg mannitol bolus.</td>
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<tr>
<td>Fisher et al. J Neurosurg Anesthes 1992; 4:4-10</td>
<td>Double blind crossover study comparing 3% saline and 0.9% saline. N = 18 children with severe TBI. Serum sodium concentration increased ~ 7 mEq/L over 2 hrs.</td>
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**Evidence table**

>45 relevant studies

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Mannitol causes ICP reduction of >10% after 116/120 boluses

Hypertonic saline group required fewer interventions for ICP control

Hypertonic saline associated with lower ICP

Successful reduction in ICP and an increase in CPP

Hypertonic saline appears safe for purposes of ICP reduction
### Recommendations

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<tr>
<td></td>
<td>Insufficient data</td>
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</tr>
<tr>
<td></td>
<td>Choice of mannitol or hypertonic saline as a first-line hyperosmolar agent should be left to the treating physician</td>
<td>Limited clinical experience, stronger evidence vs. hypertonic saline</td>
</tr>
</tbody>
</table>
Harpoon
“The principles of management for penetrating injuries of this kind remain very similar to those followed in gunshot wound treatment. They consist in debridement and removal of the projectile and of all accessible bone fragments, followed by excision of necrotic tissue and surrounding clots, together with meticulous hemostasis, and dural closure to avoid CSF fistulas.”
Hyperventilation
OVERVIEW

Hyperventilation reduces ICP by inducing hypocapnia

Associated with a risk of iatrogenic ischemia

Chronic hyperventilation depletes brain tissue interstitial bicarb buffer

Respiratory alkalosis from hyperventilation causes left shift of the hemoglobin-oxygen dissociation curve > impaired oxygen delivery to tissues

Cerebral vasoconstriction
Reduction in CBF
Reduction of CBV > dec ICP

Evidence table
20 relevant studies

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<thead>
<tr>
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<tbody>
<tr>
<td>Skippen et al.</td>
<td>Prospective cohort study. N = 23 children with isolated severe TBI, GCS&lt;8</td>
<td>II</td>
</tr>
<tr>
<td>Crit Care Med 1997:</td>
<td>Hypocarbia increased frequency of cerebral ischemia from 28.9% to 73.1%</td>
<td>II</td>
</tr>
<tr>
<td>25:1353</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stringer et al.</td>
<td>Nonrandomized selected series of case studies. N = 12. Cerebral ischemia demonstrated by Xenon-enhanced CT</td>
<td>II</td>
</tr>
<tr>
<td>AJNR 1993:</td>
<td>Hyperventilation induced ischemia affects both injured and intact brain tissue</td>
<td>II</td>
</tr>
<tr>
<td>14:475-484</td>
<td></td>
<td></td>
</tr>
<tr>
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Stringer et al. AJNR 1993: 14:475-484
**Recommendations**

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<th>Standards</th>
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<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild or prophylactic hyperventilation in children should be avoided.</td>
<td>Insufficient data</td>
<td>Aggressive hyperventilation may be used for brief periods in cases of cerebral herniation or acute neurologic deterioration</td>
</tr>
<tr>
<td>Aggressive hyperventilation may be considered as a second tier option for refractory ICP</td>
<td>Insufficient data</td>
<td></td>
</tr>
</tbody>
</table>
Barbiturates
OVERVIEW

Barbiturates lower ICP through metabolic suppression

Neuroprotective effects

- Inhibition of free radical-medicated lipid peroxidation
- Membrane stabilization
- Effects independent of ICP lowering properties

Limitations of barbiturates

- Myocardial depression
- Increased risk of hypotension - pressors
- Need for invasive homodynamic monitoring

Management approaches

- Prophylactic administration early after injury
- Use in the treatment of refractory ICP
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Eisenberg et al.</td>
<td>Multiple-center randomized control trial. N = 73 patients (15-50yrs) ▪ High dose pentobarb an effective adjunctive therapy ▪ 4:1 when stratified by prerandomization cardiac complications</td>
<td>II</td>
</tr>
<tr>
<td>J Neurosurg 1988; 69:15-23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatr Neurosci 1988; 14:241-249</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pittman et al.</td>
<td>Case series. N = 27 children with severe TBI; pentobarb for ICP&gt;30 ▪ Inconclusive ▪ Fourteen (52%) achieved ICP&lt;20. Seven with sustained ICP elevation – 3/7 recover. Total of six deaths.</td>
<td>III</td>
</tr>
<tr>
<td>Standards</td>
<td>Options</td>
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<tr>
<td>High-dose barbiturates are effective in lowering refractory ICP in children with severe TBI</td>
<td>High-dose barbiturate therapy may be considered in hemodynamically stable patients with refractory ICP</td>
<td></td>
</tr>
</tbody>
</table>
Hypothermia
OVERVIEW

Posttraumatic hyperthermia >38.5 C

Effect of hyperthermia on mechanisms of secondary brain injury
  
  Increased cerebral metabolism
  Increased inflammation
  Increased lipid peroxidation
  Increased excitotoxicity and cell death

Posttraumatic hypothermia <35 C

Adverse affects of hypothermia

  Increased SVR, decreased CI
  Impaired immune system – nosocomial pneumonia
  Metabolic acidosis
  Electrolyte imbalances (decreased K, Mg, Phos)
  Coagulation impaired – increased bleeding time
### Evidence Table

**28 relevant studies**

<table>
<thead>
<tr>
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<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hendrick EB: AMA Arch Surg 1959; 17-20</td>
<td>Uncontrolled retrospective case series, $N = 18$ children with severe TBI who presented with decerebrate posturing, cooled to 32-33°C. Ten long-term survivors.</td>
<td>III</td>
</tr>
</tbody>
</table>

**Potential for improved outcome in severe TBI**

**No difference in outcome with addition of steroids to hypothermia**
**Recommendations**

<table>
<thead>
<tr>
<th>Standards</th>
<th>Insufficient data in children. Extrapolated from adult data, hypothermia may be considered in the setting of refractory ICP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guidelines</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>Options</td>
<td>There is presently NO published support for temperature control or therapeutic hypothermia in pediatric TBI.</td>
</tr>
</tbody>
</table>
Close range GSWs
Gunshot wounds are the eighth leading cause of unintentional injury deaths among persons in all age groups in the United States and the third leading cause of such deaths among children and teenagers aged 10-19 years.

For males aged 10-19 years, the death rate was 10 times that for females.

Children and teenagers living in the South were at greatest risk for dying from an unintentional gunshot wound; those living in the Northeast were at lowest risk.
Nearly a million people worldwide die by suicide annually. While completed suicides are higher in men, women have higher rates for suicide attempts.

People die by suicide more often during spring and summer. The idea that suicide is more common during the winter holidays is a common misconception.

Decompressive craniectomy
OVERVIEW

Main objective of decompressive craniectomy is to control ICP, maintain CPP and cerebral oxygenation, as well as prevent herniation.

Is decompressive craniectomy successful in controlling ICP?

Does decompressive craniectomy improve clinical outcomes?

Which patients are appropriate candidates for decompressive craniectomy?
## Evidence table

>20 relevant studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Description of Study</th>
<th>Class</th>
</tr>
</thead>
</table>
| Polin et al.       | Single-center, case controlled study  
N: 35 pediatric/adult patients underwent bifrontal cranies  
Outcome measurement: Glasgow Outcome Scale | III   |
| Cho et al.         | Single-center, case controlled study  
N = 23 children <2 year old with non-accidental trauma  
Outcome measurement: Child Outcome Score | III   |
| Taylor et al.      | Single-center, prospective RCT  
N = 27 children randomized to bitemporal craniectomy vs. no surgery  
Outcome measurement: Child Outcome Score | III   |

- Significantly higher rate of favorable outcome in pediatric patients
- Surgical group with improved survival and neurological outcomes
- Marginally non-significant trend towards improved clinical outcome @ 6 months
**Recommendations**

<table>
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<tbody>
<tr>
<td><strong>Options</strong></td>
<td><strong>Decompressive craniectomy for severe TBI and med refractory intracranial hypertension lowers ICP and may improve outcome</strong></td>
</tr>
</tbody>
</table>

- Diffuse cerebral edema on CT
- Within 48 hrs of injury
- No episodes of sustained ICP > 40 before surgery
- GCS > 3 at some point subsequent to injury
- Evolving cerebral herniation syndrome
Corticosteroids
OVERVIEW

Corticosteroids have been commonly used in children for a wide range of neurologic disorders

- Infection
- Gastrointestinal hemorrhage

Complications

- Reducing cerebral edema
- Attenuation of free radical production

Evidence table

45 relevant studies

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<tr>
<td>Kloti et al. Childs Nerv Syst 1987; 3:103-105</td>
<td>Prospective, RCT. N = 24. Group 1: dexamethasone (1mg/kg/day); Group 2: None. Steroids made no difference in long term outcome.</td>
<td>II</td>
</tr>
<tr>
<td>Fanconi et al. Intensive Care Med 1988; 14:163-166</td>
<td>Prospective, RCT. N = 25. Group 1: dexamethasone (1mg/kg/day x 3 days). No difference in ICP, CPP or outcome. Increased infection rate.</td>
<td>II</td>
</tr>
</tbody>
</table>
**Recommendations**

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<tr>
<td>Use of steroids not recommended for improving outcome or reducing ICP in traumatic brain injury</td>
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Despite two class II studies failing to show efficacy, the small sample sizes preclude support for a treatment guideline for this topic.
Anti-seizure prophylaxis
OVERVIEW

Posttraumatic seizure (PTS) classification – early vs. late

Infants/children have lower seizure thresholds

Clinical detection often difficult

Single drug therapy usually not effective

Seizures: neurologic sequelae

Anticonvulsants: adverse side effects

- Increase brain metabolic demand
- Increase intracranial pressure
- Secondary brain injury

- Impaired learning/neurobehavioral side effects
- Rashes, Steven Johnson syndrome
- Hematoc abnormalities
- Ataxia

Children < 2 with 3 times greater risk for early PTS
Rate for early PTS varies from 20-39% in children
Rate for late PTS ranges from 7-12%
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Young et al. Childs Brain 1983; 10:185-192</td>
<td>Prospective, randomised, double-blind, placebo controlled. Phenytoin vrs placebo for late PTS, N = 41</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>Showed no reduction in late PTS</td>
<td></td>
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<tr>
<td></td>
<td>Showed reduction in early PTS: 53% vs. 15%</td>
<td></td>
</tr>
<tr>
<td>Tilford et al. Crit Care Med 2001; 29:1056-1061</td>
<td>Retrospective cohort study. Compared outcomes and therapies. AED use linked to improved survival, odds ratio 0.17</td>
<td>III</td>
</tr>
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Recommendations

Prophylactic anticonvulsant therapy is NOT recommended to prevent late posttraumatic seizures in children.
Treatment algorithm
This critical pathway is a committee consensus and, therefore, must be viewed as class III ("expert opinion") evidence.
GCS ≤ 8
CT scan (+): Lesion, diffuse or focal swelling

Insert EVD or ICP monitor
Maintain CPP > 50 – 60 mmHg (age dependent)

Elevated ICP

Intracranial Hypertension?

Low/normal ICP

FIRST TIER INTERVENTIONS
1. CSF diversion; EVD at 0 - 3 cm above tragus
2. Sedation and/or paralysis
3. HOB at 30°
4. PaCO2 maintained at 35 to 38 mmHg
5. O2 saturation maintained ≥ 92%

Low/normal ICP:
Carefully withdraw ICP treatment.
Withhold one intervention at a time.
Elevated ICP → Repeat CT scan

SECOND TIER INTERVENTIONS
1. Mild hyperventilation (Pa CO2 30 to 35 mmHg)
2. Mannitol (0.25 – 1.0 g/kg/IV q 4 – 6 h) with serum osmolarity < 320
3. Hyperosmolar therapy (3% saline boluses or slow infusion) with serum osmolarity < 370
4. Barbiturates (low dose [5 mg/kg IV q 6h] with escalation to burst suppressed, barbiturate coma)

Elevated ICP → Repeat CT scan

THIRD TIER INTERVENTIONS
1. Decompressive craniectomy or temporal lobectomy
2. Moderate hypothermia (32 - 33 °C)
3. Hyperventilation to PaCO2 < 30 mmHg (use transiently)

Low/normal ICP
Go Jefferson!!!