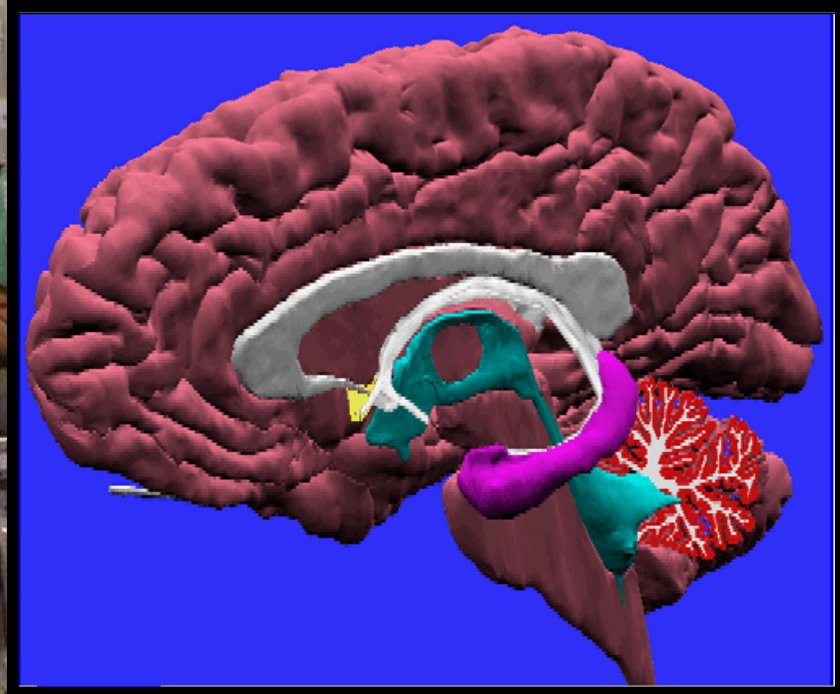


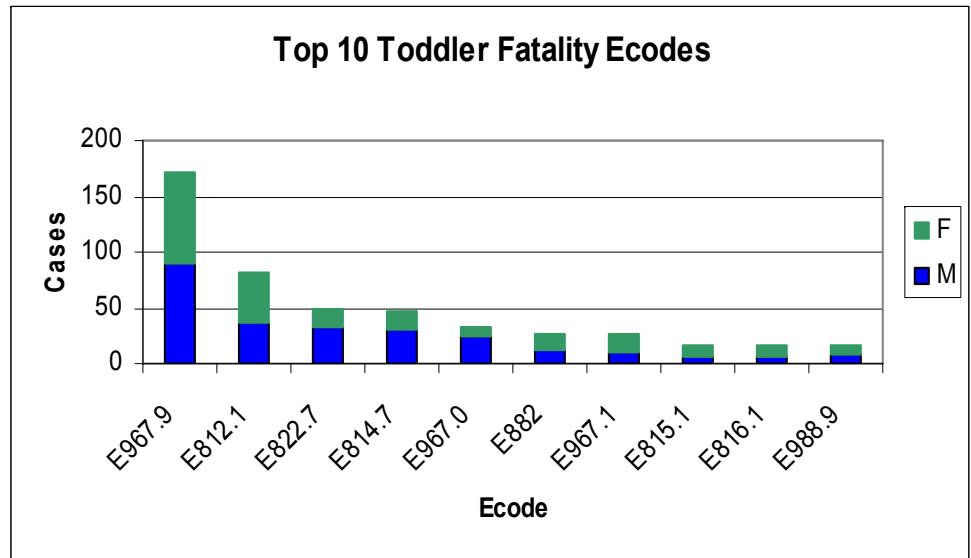
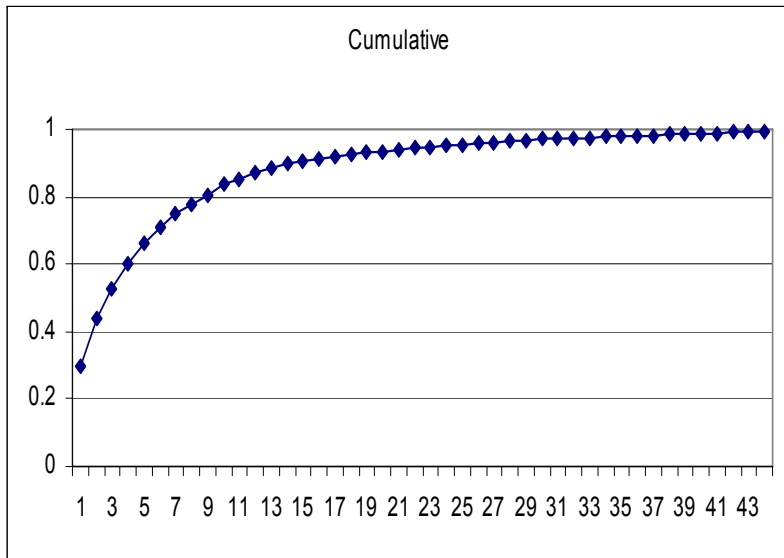


Our Agenda

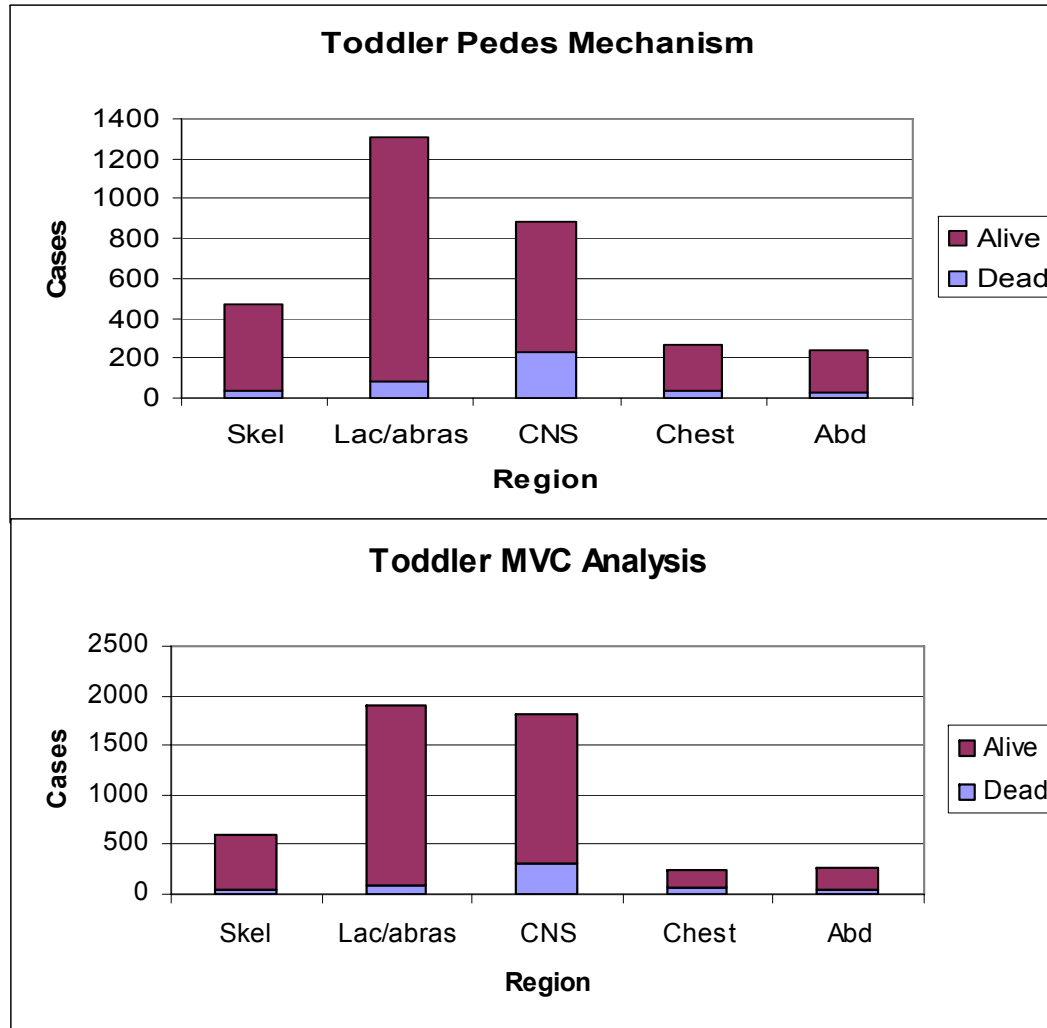


Discharge Disposition

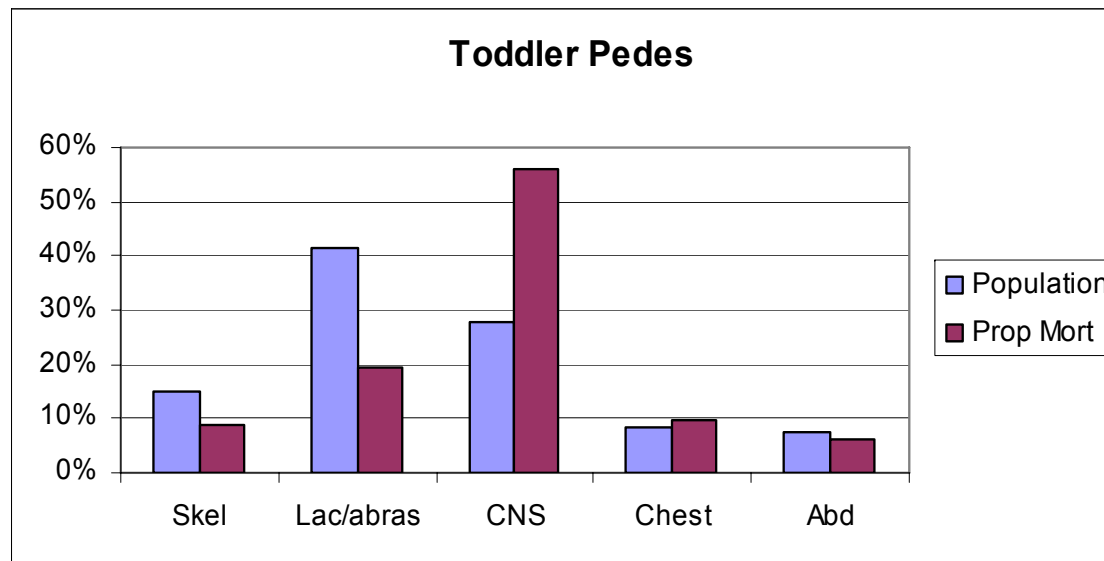
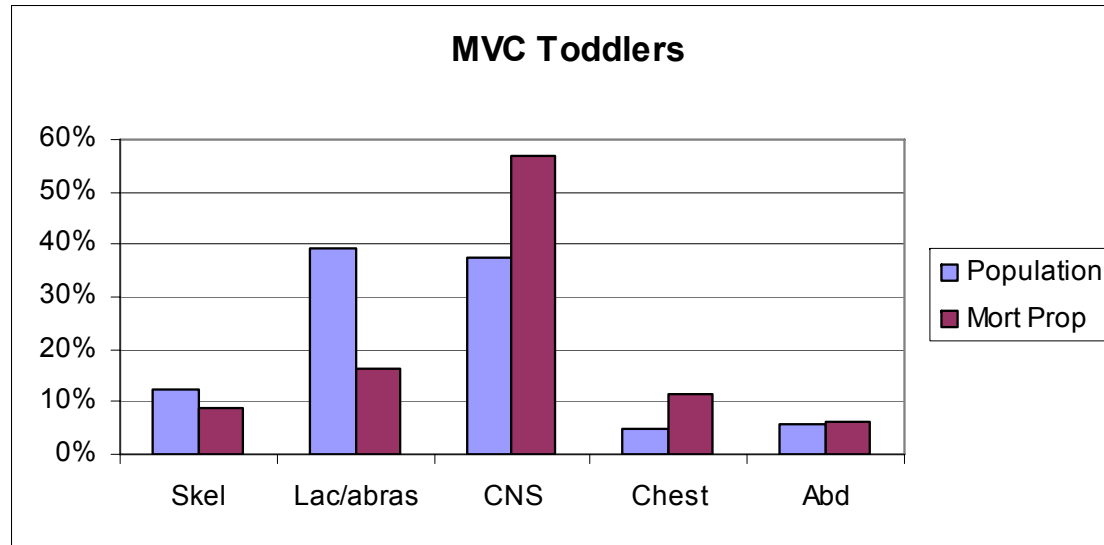
Sex	Alive	Dead	Total	%Mort
F 41%	5126	277	5403	5.1%
M 59%	7435	296	7731	3.8%
Grand Total	12561	573	13134	



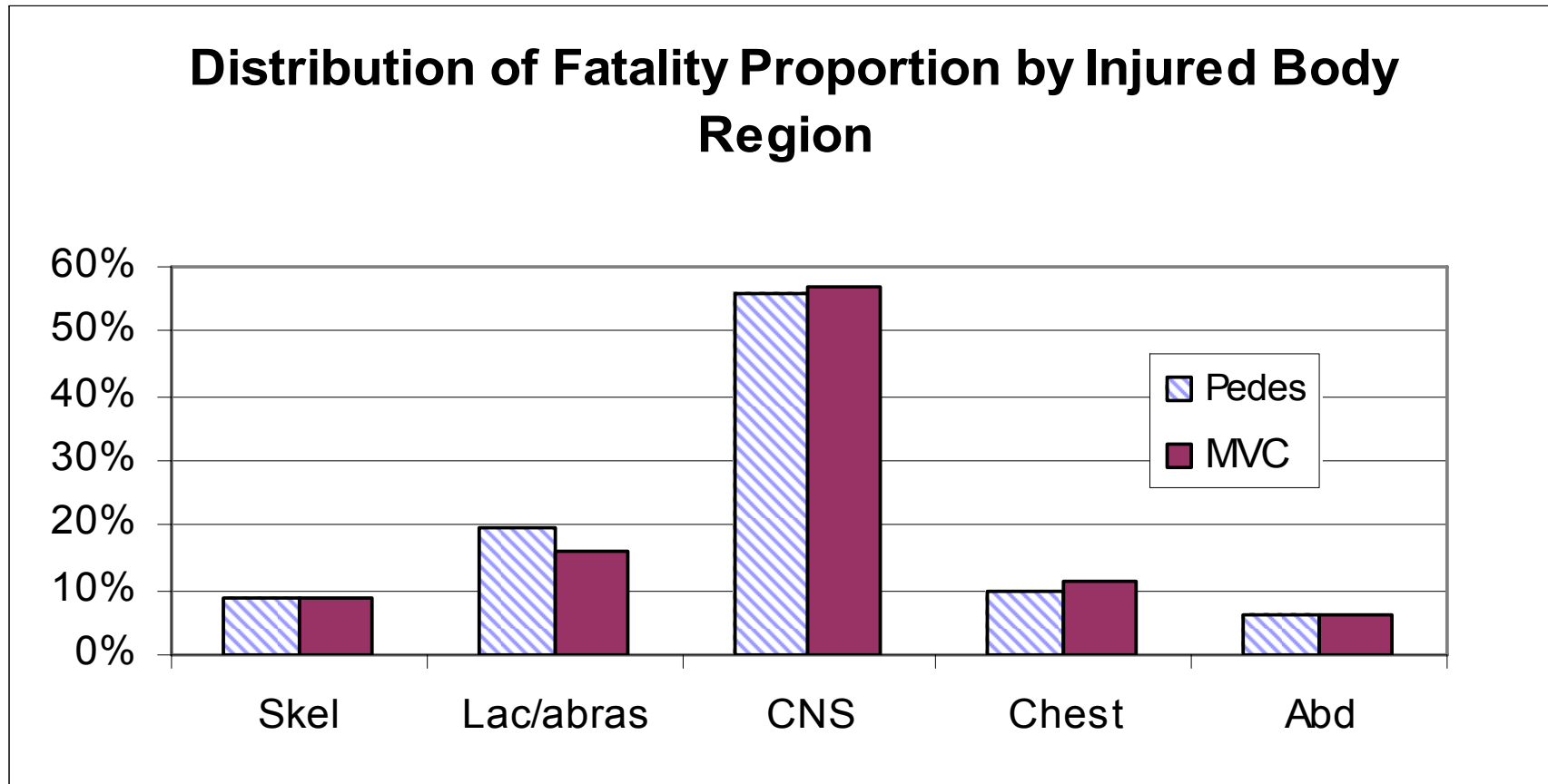
Organ System Injury by Common Mechanisms



HIT BY or HURT IN CARS

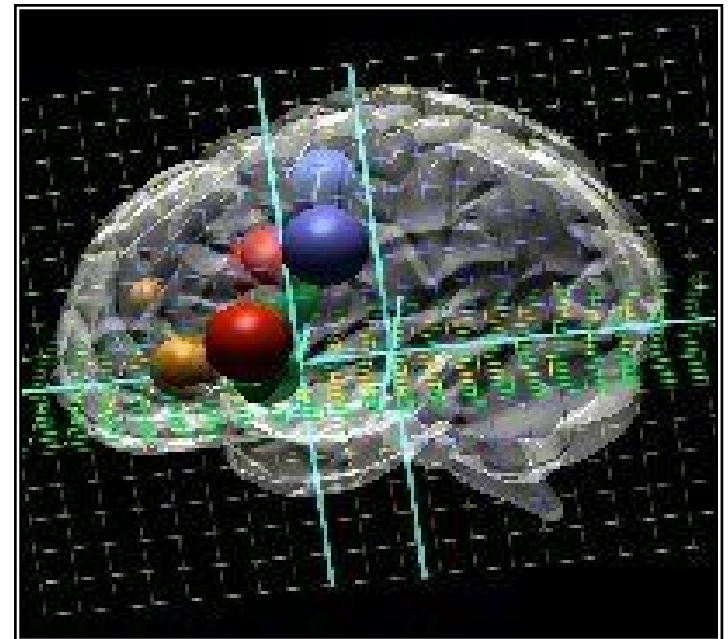


The Primacy of TBI



Traumatic Brain Injury

- **Incidence: 200/100,000 population**
- **Severe TBI: 50,000 cases/year**
- **Mortality: 30% (1 person every 30 minutes)**
- **Many survivors demonstrate long term disability**

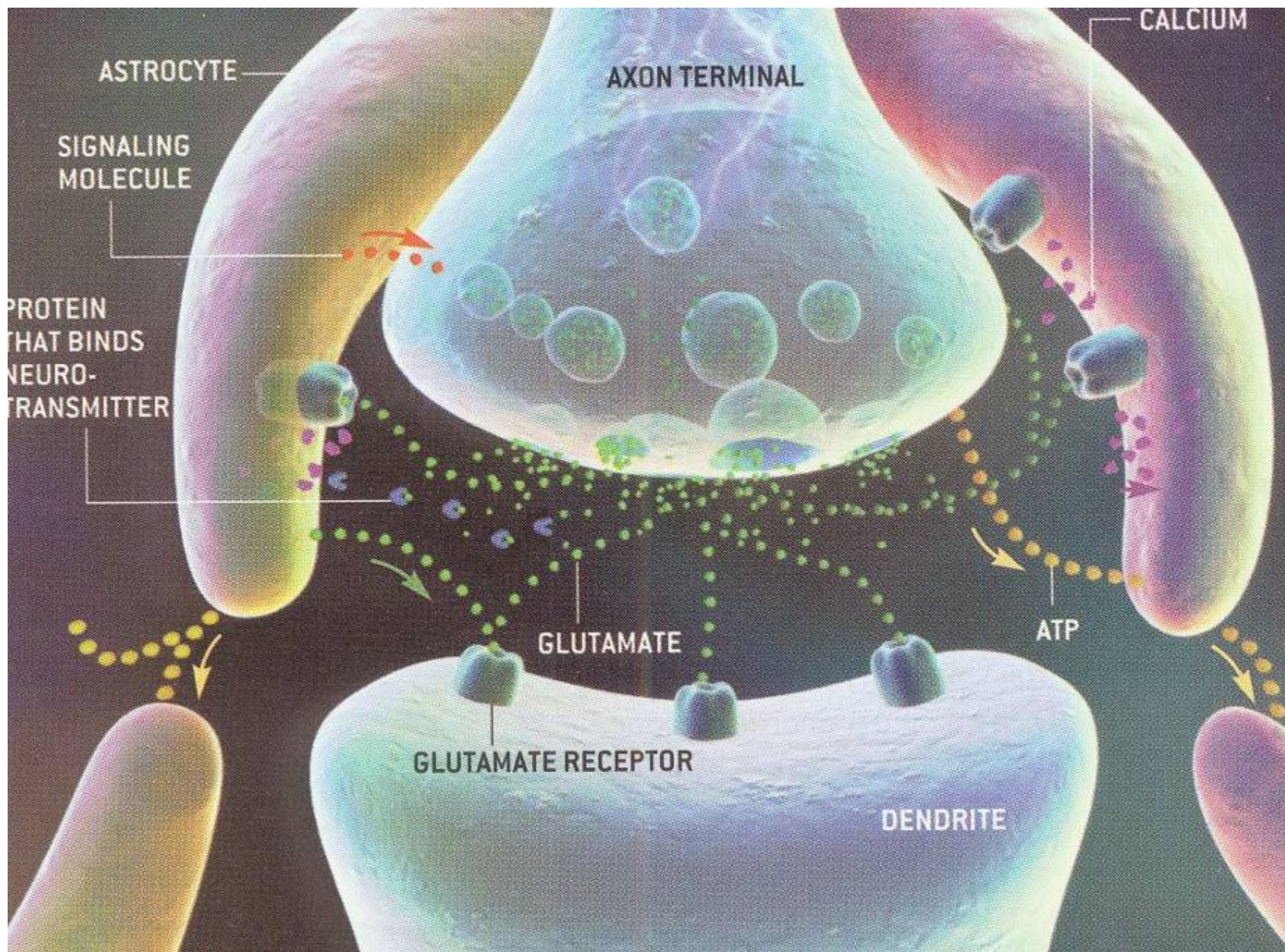


Narayan, 2002

CNS Checklist

- **Brain development and the effect of injury**
- **Brain injury**
 - Excitatory stimuli
 - Perfusion
 - Cytokine cascade
 - Necrosis
- **ICP/ CPP**
 - The ideal?
 - How to manage
- **Sodium/chloride/magnesium and phosphate**
- **Glucose homeostasis**
- **Nutrition**
- **Imaging**
 - How many CT's are enough?
 - Dangerous road trips
- **The future**
 - Biomarkers





The Primacy of Brain Injury



SHOCK

6% of cases

18% dead

34% of all deaths

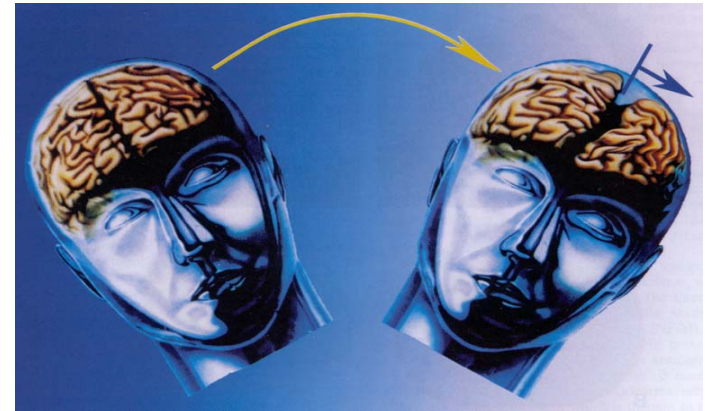
NO SHOCK

94% of cases

2% dead

66% of all deaths

Traumatic Brain Injury



- ***Excitatory Imbalance***
 - ***Immediate receptor blockade***
- ***Perfusion Anomaly***
 - ***ICP/ CPP***
 - ***BBB permeability - autoregulation***
- ***Pro-inflammatory Cytokine Cascade***
 - ***Pre-emptive management of S.I.R.S.***

The Surgical Sides Of Injury Control.

In Practical Terms:

Understanding the global stress response

Orchestrating multiple disciplines

Optimizing recovery:

Aggressive neurocare

Precise fluid management

Effective ventilator care

Adequate nutritional care



Paralytic

Analgesic

Sedation

Seizure Prophylaxis

Abx

Steroid

Pressor/Pent

Ulcer Prophylaxis

Diuretics

The Surgical Sides Of Injury Control.



In Practical Terms:

1. Understanding the global stress response
2. Orchestrating multiple disciplines
3. Optimizing recovery:
 - ***Aggressive neurocare***
 - Precise fluid management
 - Effective ventilator care
 - Adequate nutritional care



ICP/ CPP

**The ideal?
How to manage**

Hagen - Poiseuille

Flow:

Directly related to

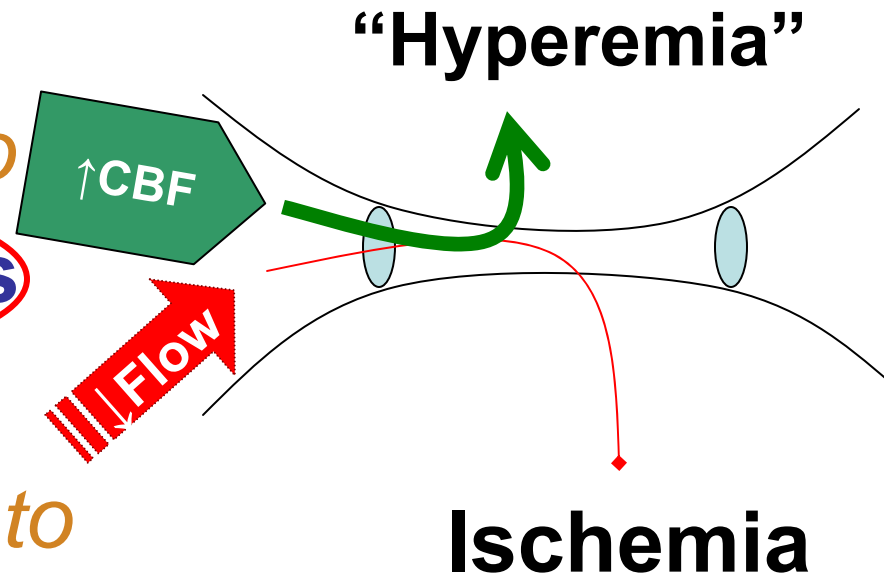
Vessel radius

Pressure

Indirectly related to

Viscosity

Vessel length



DO₂
Uncoupling
Autoregulation

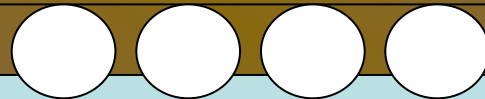
Mort 47% > 8%
PVS 11% > 13%

NEURON

Arteriolo



Venule



**'NUTHER
NEURON!'**

**Clonidine
Metoprolol**

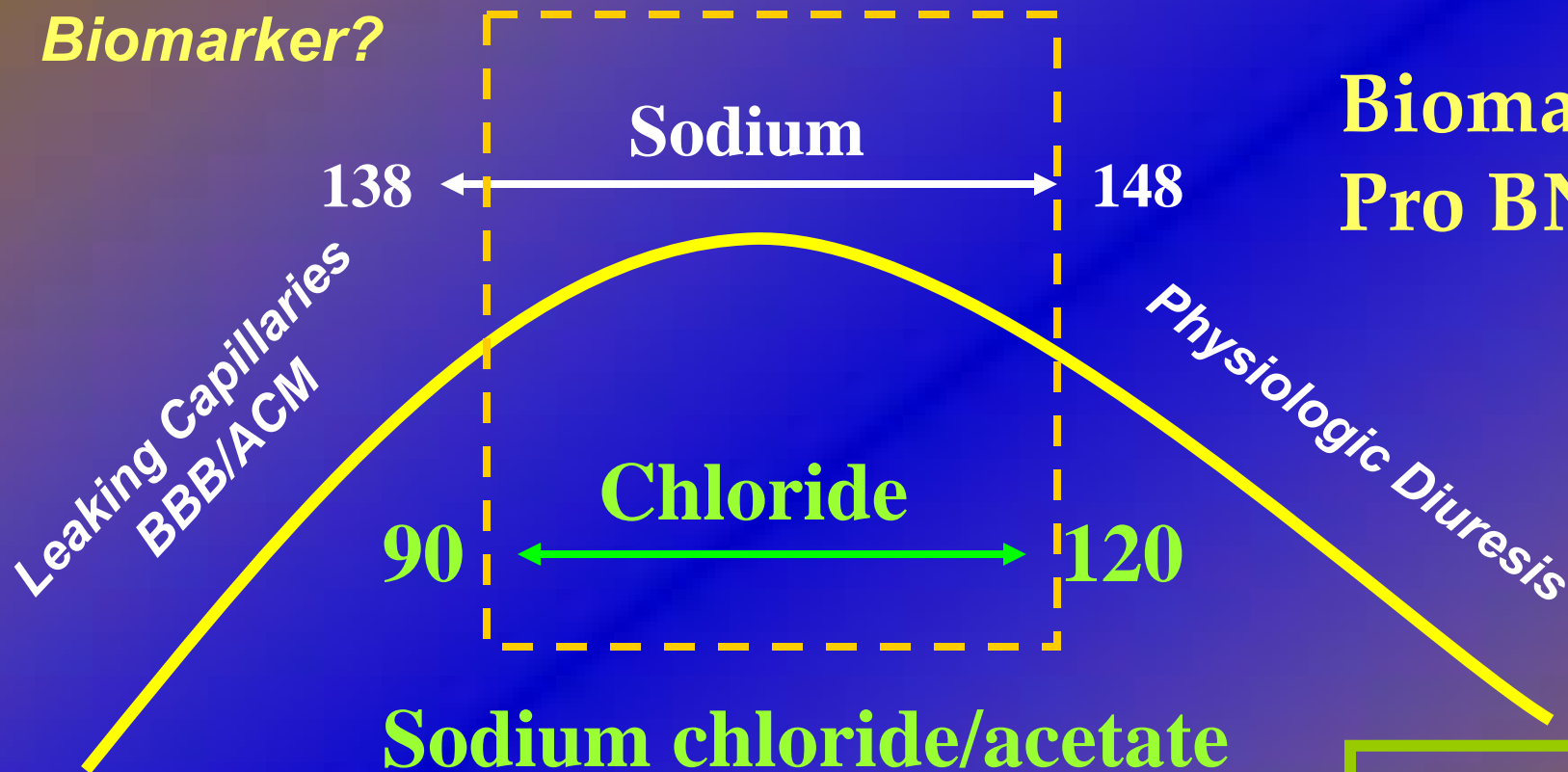
Ergotomine

“LUND” Protocol

*CCM 26(11)
1881-1886*

FLUID MANAGEMENT = NS

Biomarker?

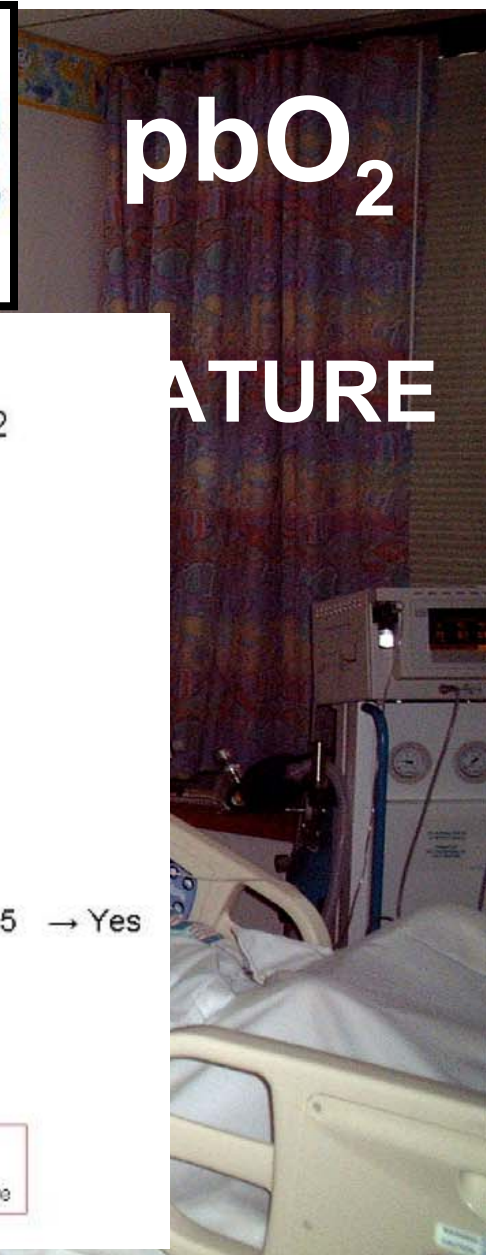
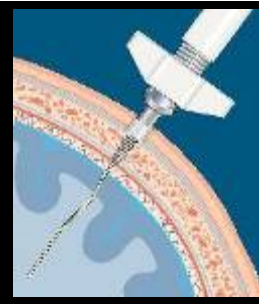


**Biomarker:
Pro BNP**

**Sodium chloride/acetate
Base deficit**

**Beware
Of
Drips!**

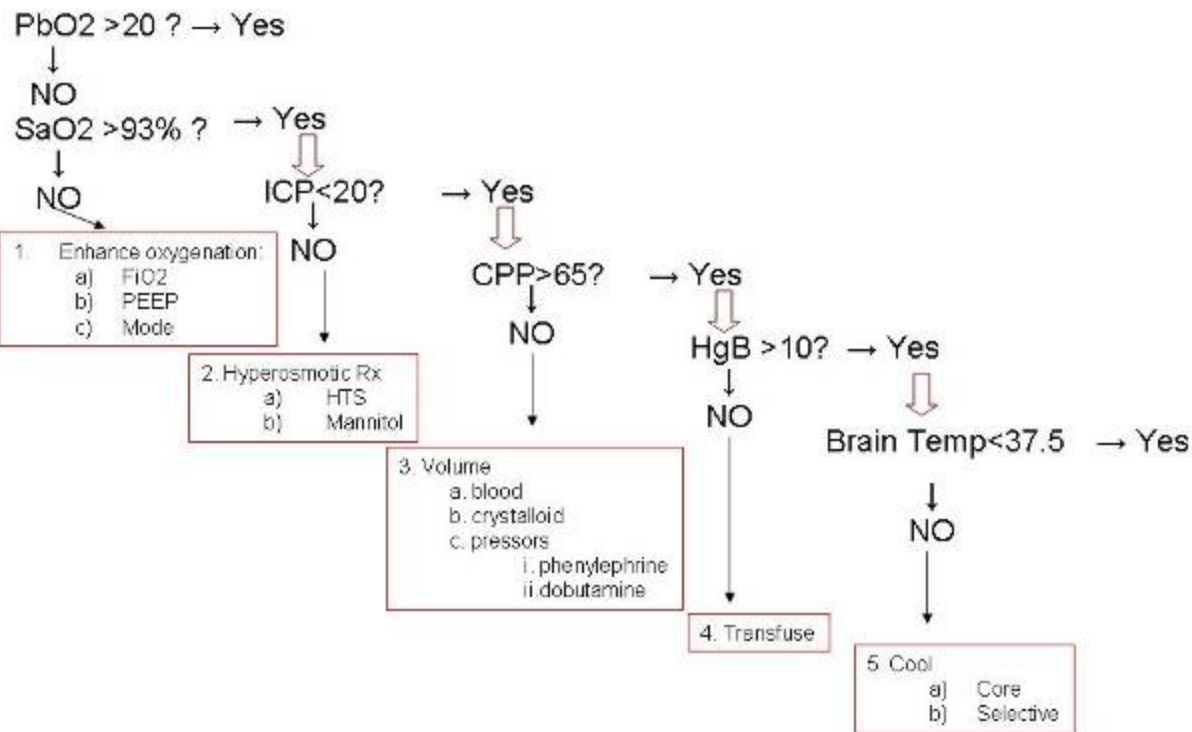
Advanced Neuromonitoring



pbO₂

TEMPERATURE

Management Protocol For Low PbO₂



Trophic Agents

Glycemia Control:

HLA-DR monocyte receptor and sepsis

Insulin

CHO: 110 – 180

Constitutive vs Acute phase protein

Insulin: Anti-inflam. molecule

Improves organ function by signal transcription

Decreases IL1,6,8

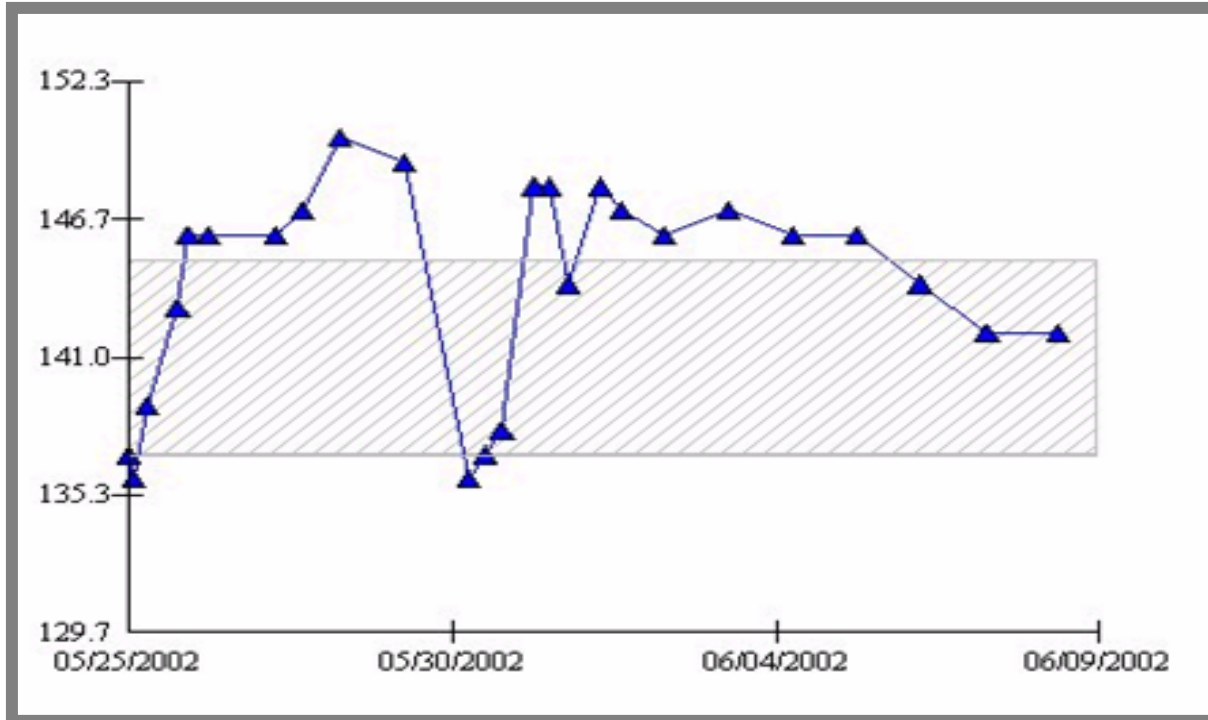
Increases IL10

EPO

Hematopoiesis

GI trophic effect

Optimize means Normalize!



D.I.

CSWS

NA: 140-150
Reflection Coeff=1
Improves rCBF
Restore cell resting potential
Stimulates ANP
Reduces PMN endo-adhesion

23.4 %HYPERTONIC SALINE

- *Hemodynamic*
- *Vasoregulatory*
- *Decreases Neutrophil Activation*
- *Stimulates Lymphocyte Proliferation*
- *Macrophages/ Monocytes:*

Inhibits Pro-inflammatory Cytokines

Stimulates Anti-inflammatory Cytokines

Monocyte

CD14⁺⁺/CD16⁻ (90%)

CD14⁺/CD16⁺⁺ (10%)

Pharmacologic treatment of intracranial hypertension

Requires: Na < 150 meq/l; Measured Osm < 310

Dose = BW x .75 in cc over 30 min in CVL

Delta Na = 5 → 5x.6BW = amount of Na meq

23.4% HS → 4 Meq /cc approximates .75BW!

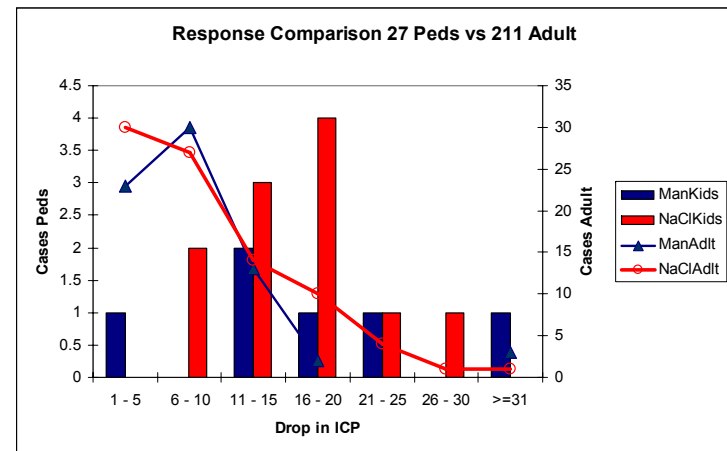
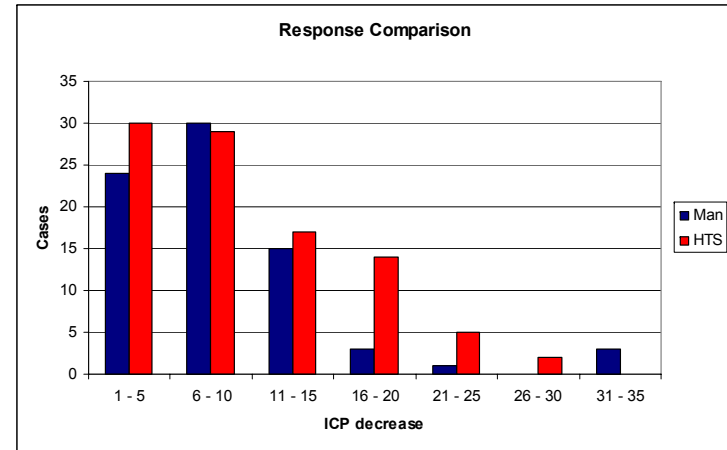
HTS Data

240 doses in 22 patients with severe TBI (within 96 hours of injury)

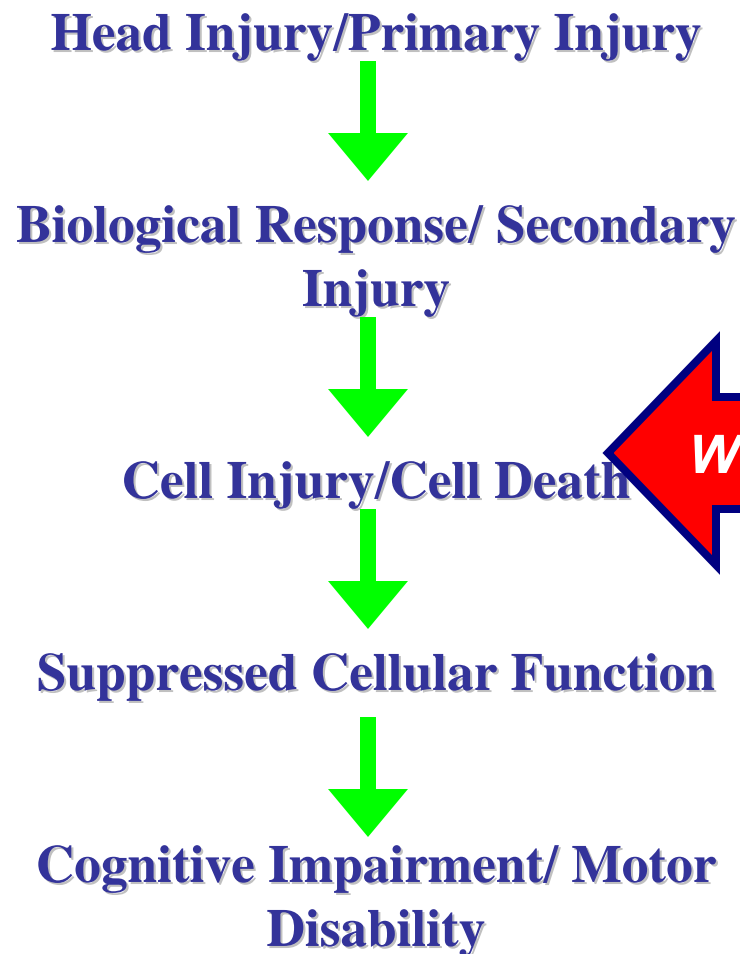
Mannitol
N = 118

23.4% HTS
N=120

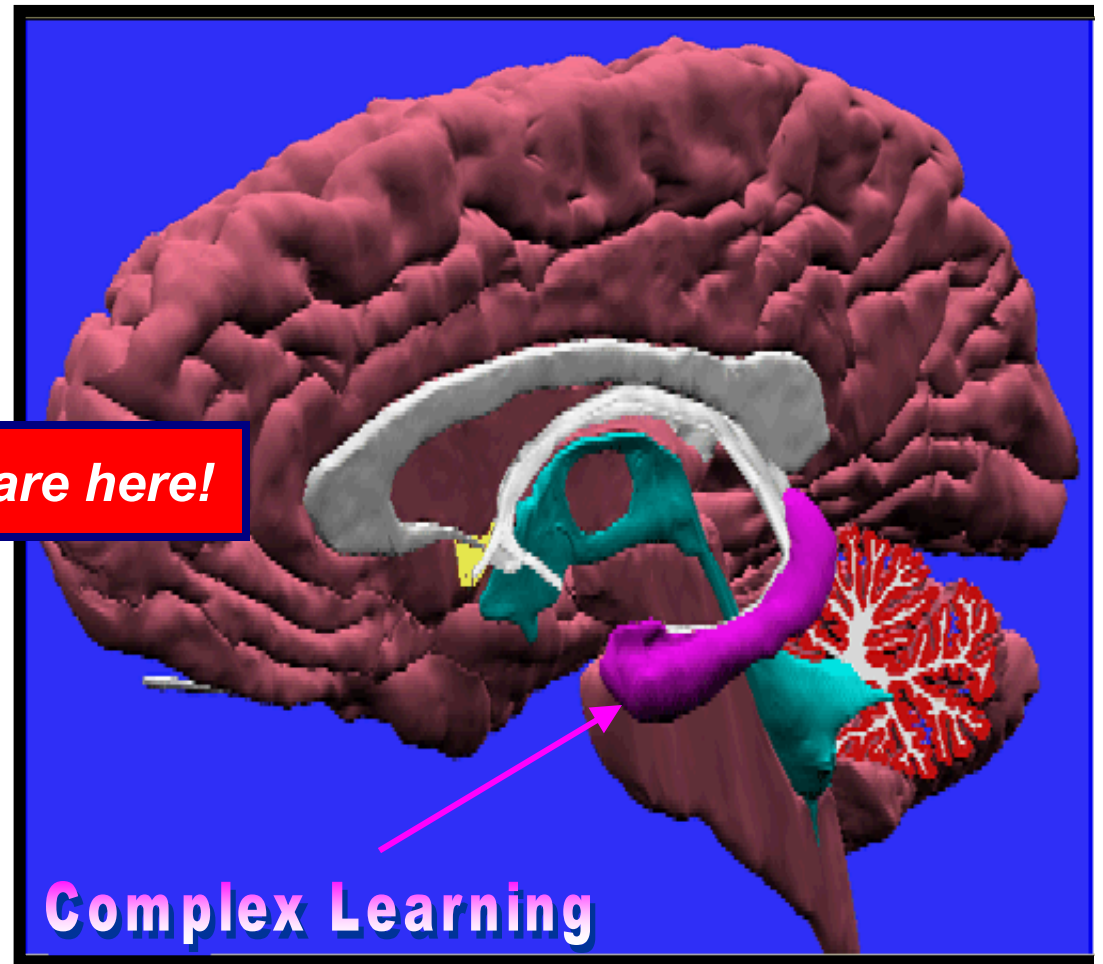
41 (35%)	No Response	22 (18%)
6.2 ± 8.2	Mean Decrease	8.3 ± 7.5



What happens to the brain cells after TBI?



We are here!



Inflammatory Biocascade



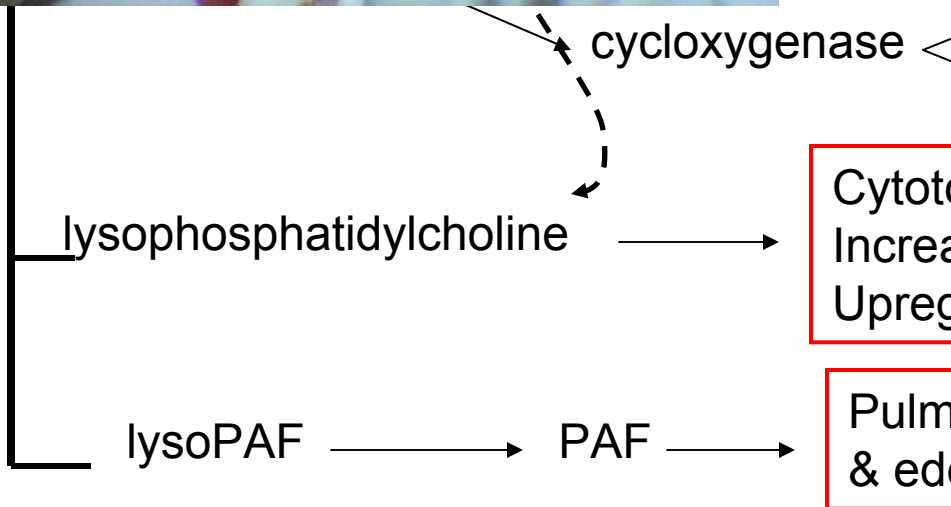
...s at *sn*-2 position by sPLA₂
 (secretory phospholipase A₂)-which
 hydrolyzes surfactant! - - -

...ase — leukotrienes

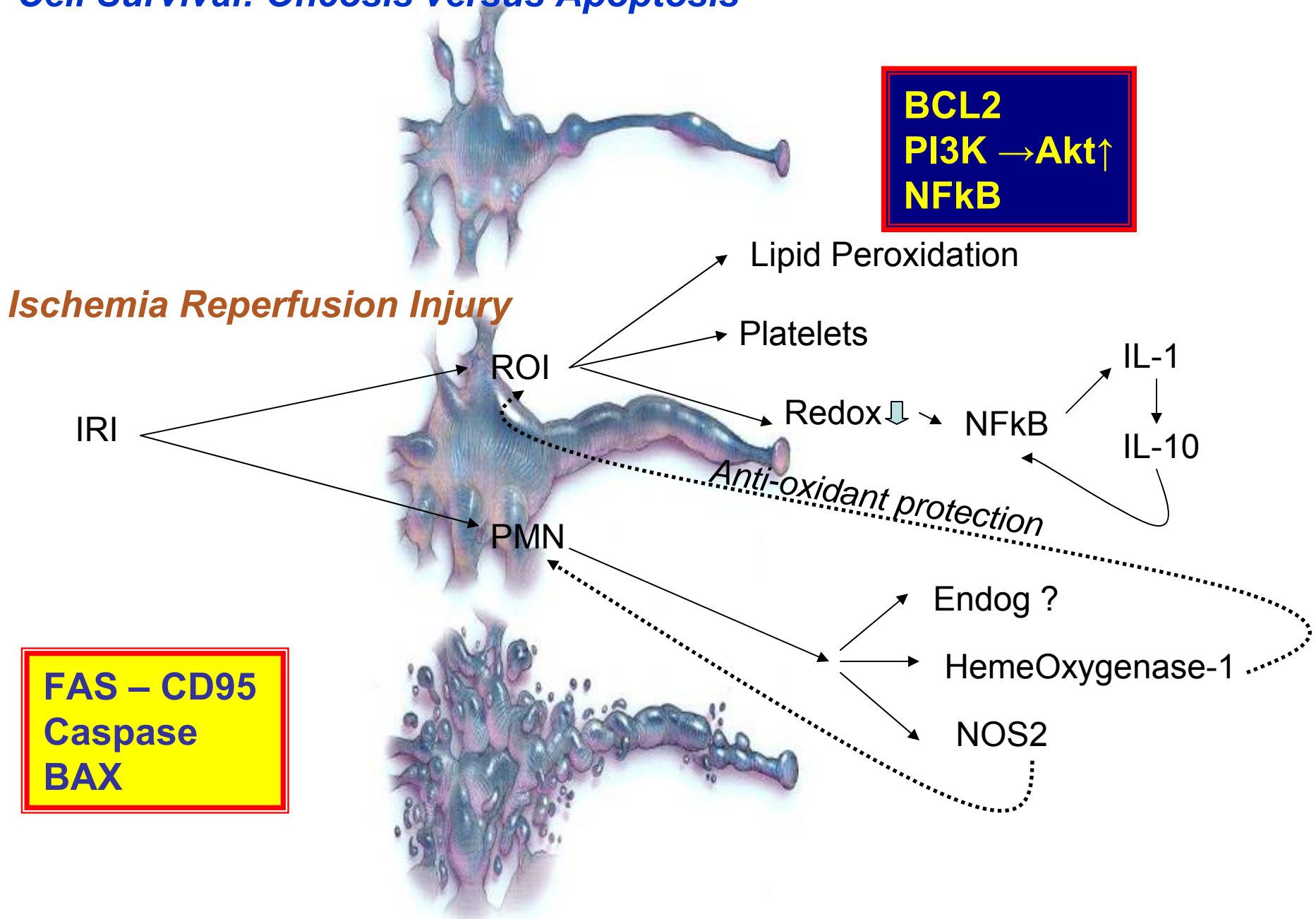
Potentiate pulm.

...en.

ly



Cell Survival: Oncosis versus Apoptosis



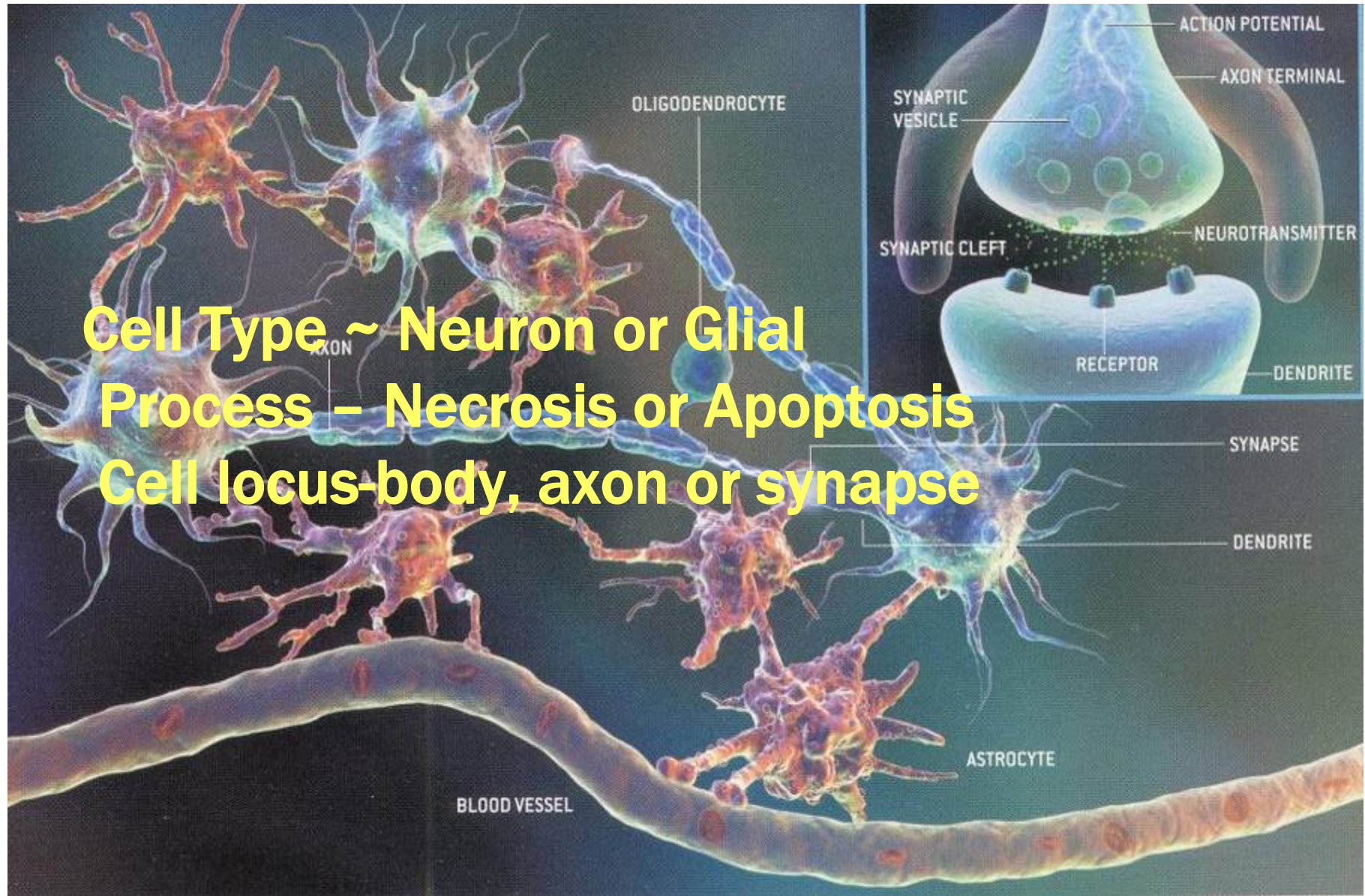
OIF-OEF



5 Determinants of Prognosis

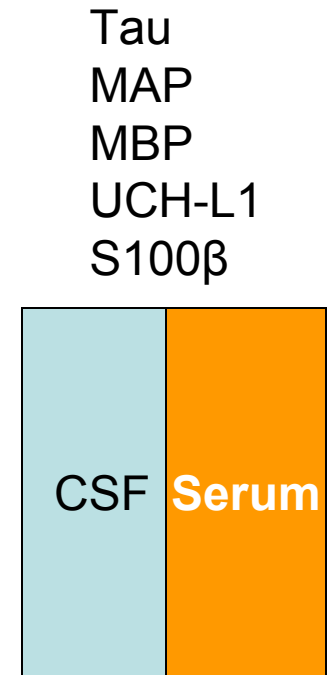
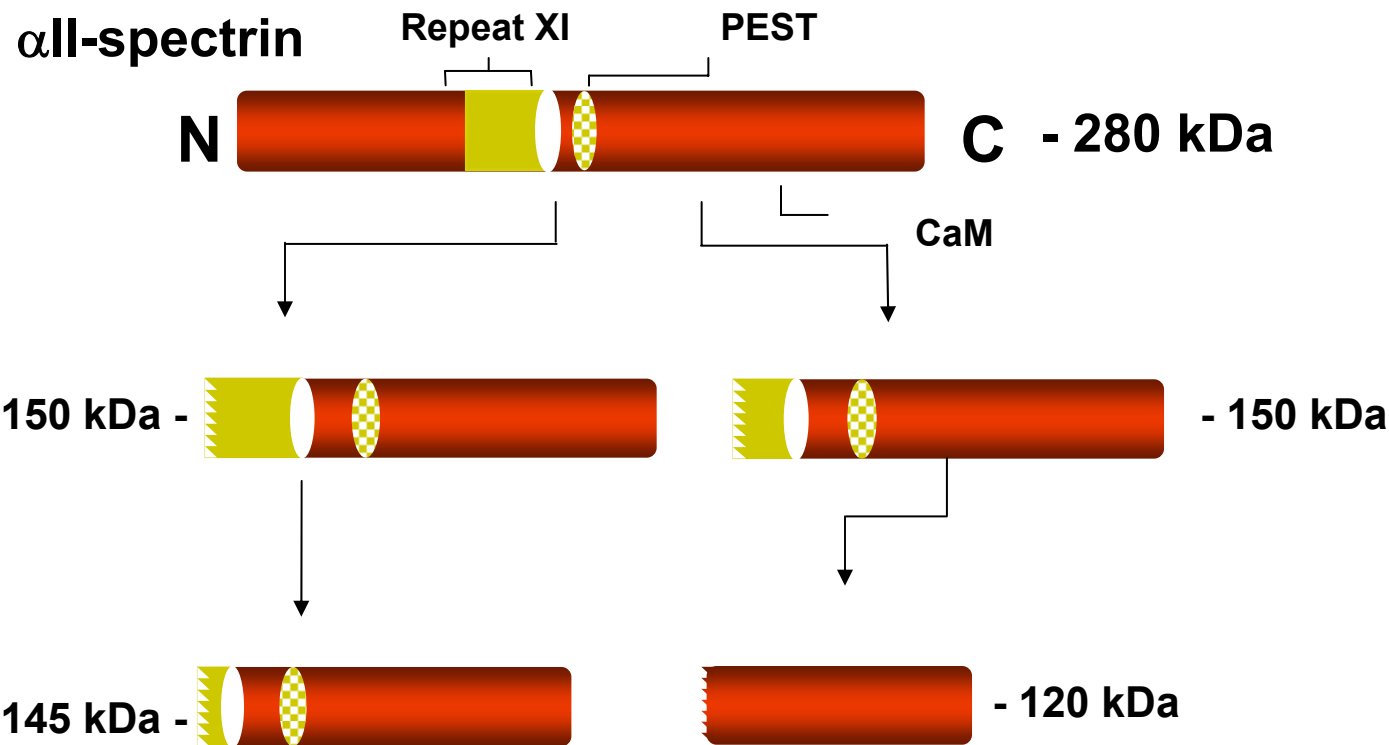
- **BP < 90**
- **Hgb < 12**
- **Hypothermia < 35°C**
- **BD < 6**
- **INR > 1.5**

Biomarker Mapping



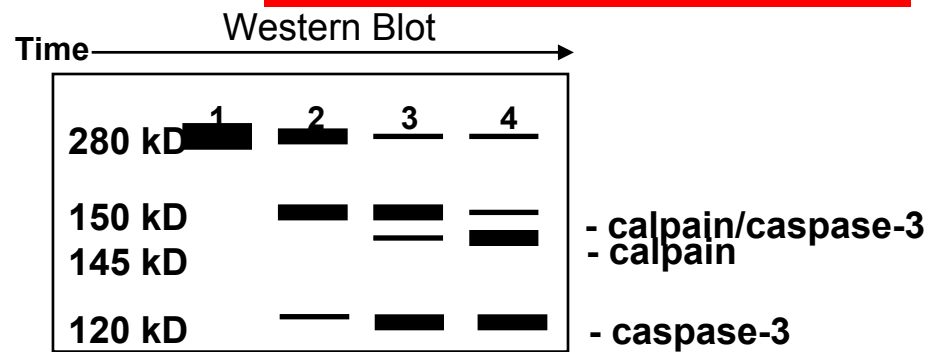
Cell Type ~ Neuron or Glial
Process – Necrosis or Apoptosis
Cell locus-body, axon or synapse

α II-Spectrin is a part of the TBI degradome

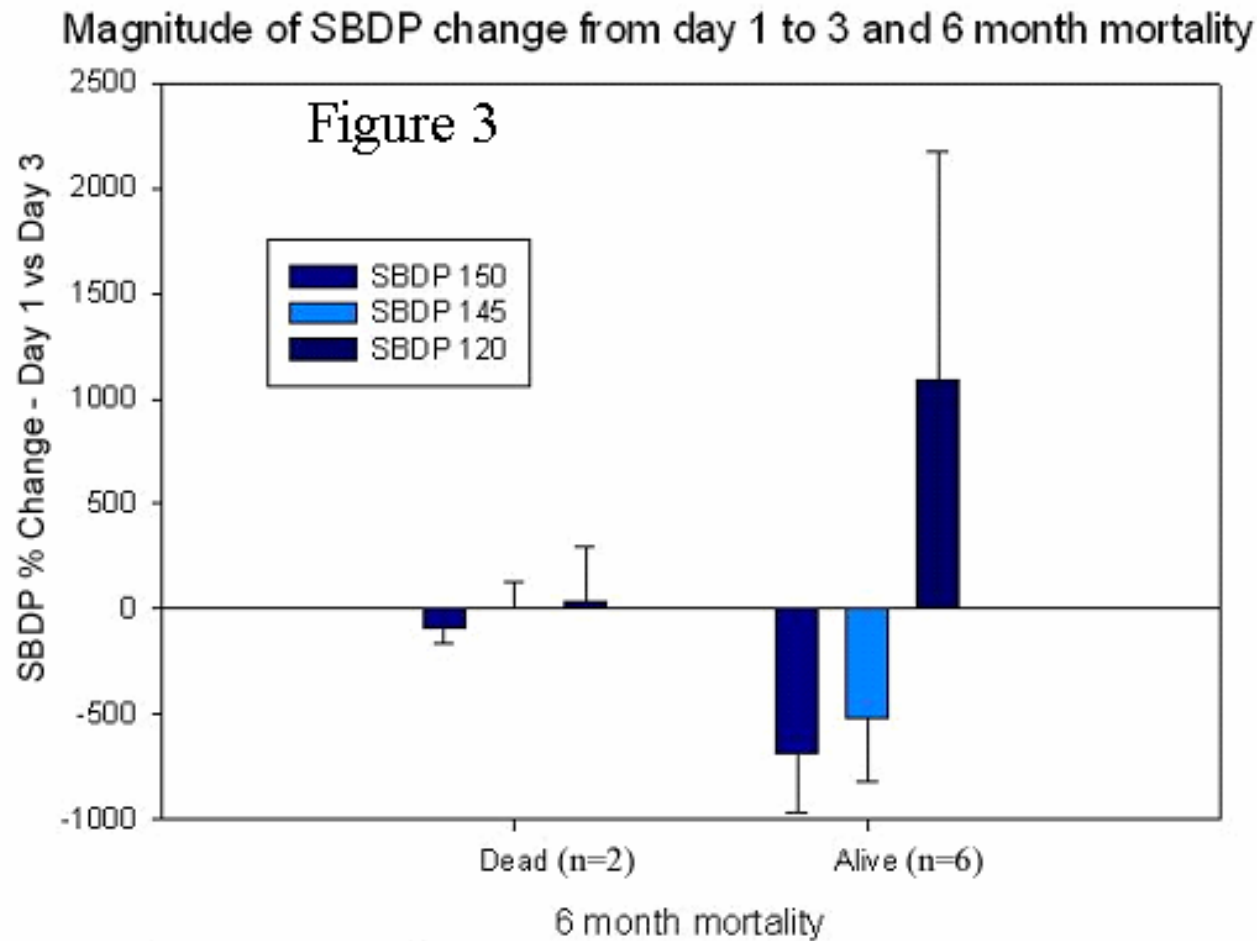


Calpain-specific SBDPs

Caspase-3-specific SBDPs



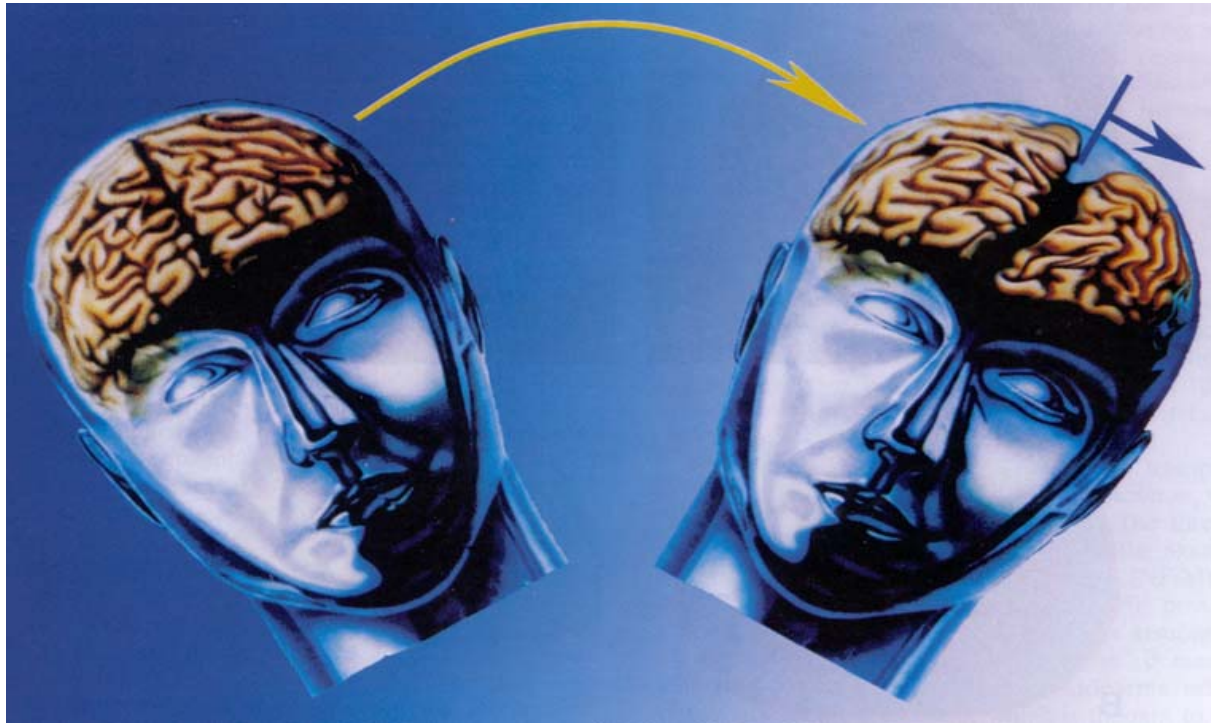
PRELIMINARY RESULTS





*We all must understand the nature and therapy
of the disease of injury,
so that we can know the joy of giving
a fully recovered child back to its parents.*

In Summary



- ***Excitatory Imbalance***
- ***Perfusion Anomaly***
- ***Pro-inflammatory Cytokine Cascade***