# Pre-Hospital Mannitol for Traumatic Brain Injury (TBI)


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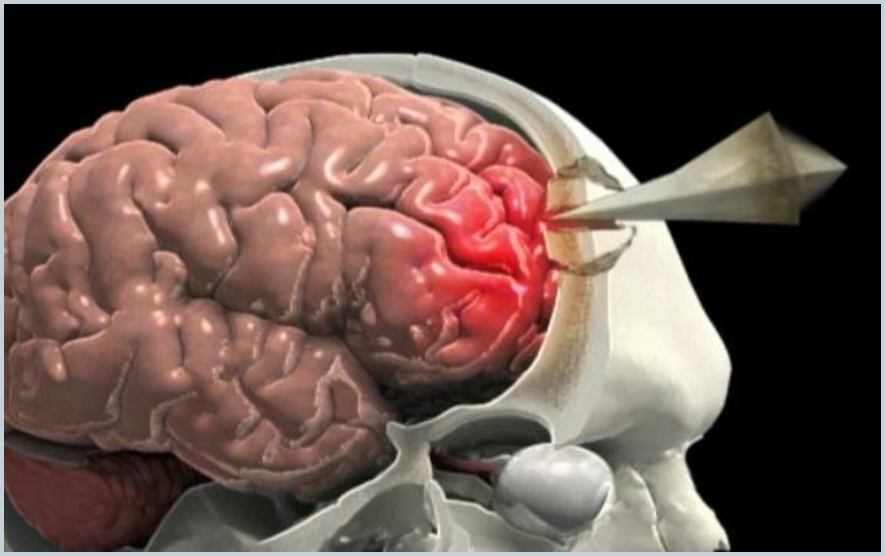
# Defination

- **TBI is defined as an alteration in brain function, or other evidence of brain pathology, caused by an external force.**



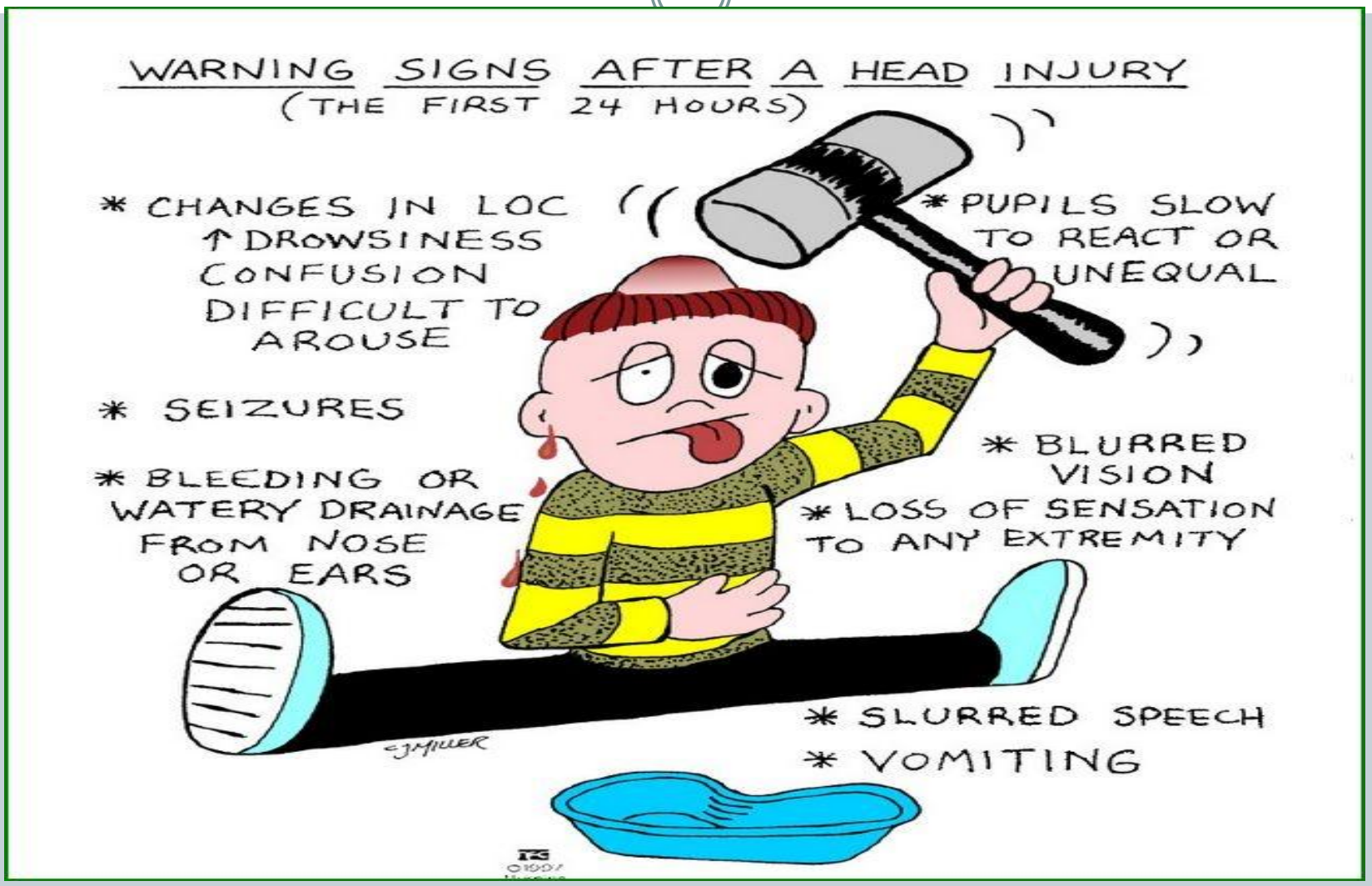
## CLASSIFICATION OF BRAIN INJURY

| | | | |
|---|---|---|---|
| **Mild** | LOC less than 30 minutes | **GCS 13-15** | PTA less than 24 hours |
| **Moderate** | LOC greater than 30 minutes, but less than 24 hours | **GCS 9-12** | PTA 24 hours to 7 days |
| **Severe** | LOC greater than 24 hours | **GCS 8 or less** | PTA more than 7 days |

Clinical signs and symptoms that suggest increased ICP include:

2) Headache
3) Nausea/vomiting
4) Blurre vision
5) Papilledema
6) Somnolence alter level of consciousness
7) Pupillary dilatation
8) Cushing triad

- Bradycardia
- Hypertension
- Irregular respiration


WARNING SIGNS AFTER A HEAD INJURY
(THE FIRST 24 HOURS)
* CHANGES IN LOC
↑ DROWSINESS
CONFUSION
DIFFICULT TO AROUSE
* SEIZURES
* BLEEDING OR WATERY DRAINAGE FROM NOSE OR EARS
* PUPILS SLOW TO REACT OR UNEQUAL
* BLURRED VISION
* LOSS OF SENSATION TO ANY EXTREMITY
* SLURRED SPEECH
* VOMITING
C.J. MILLER

# Types of brain insults

- **<u>Primary insult</u>: Due to trauma; irreversible**

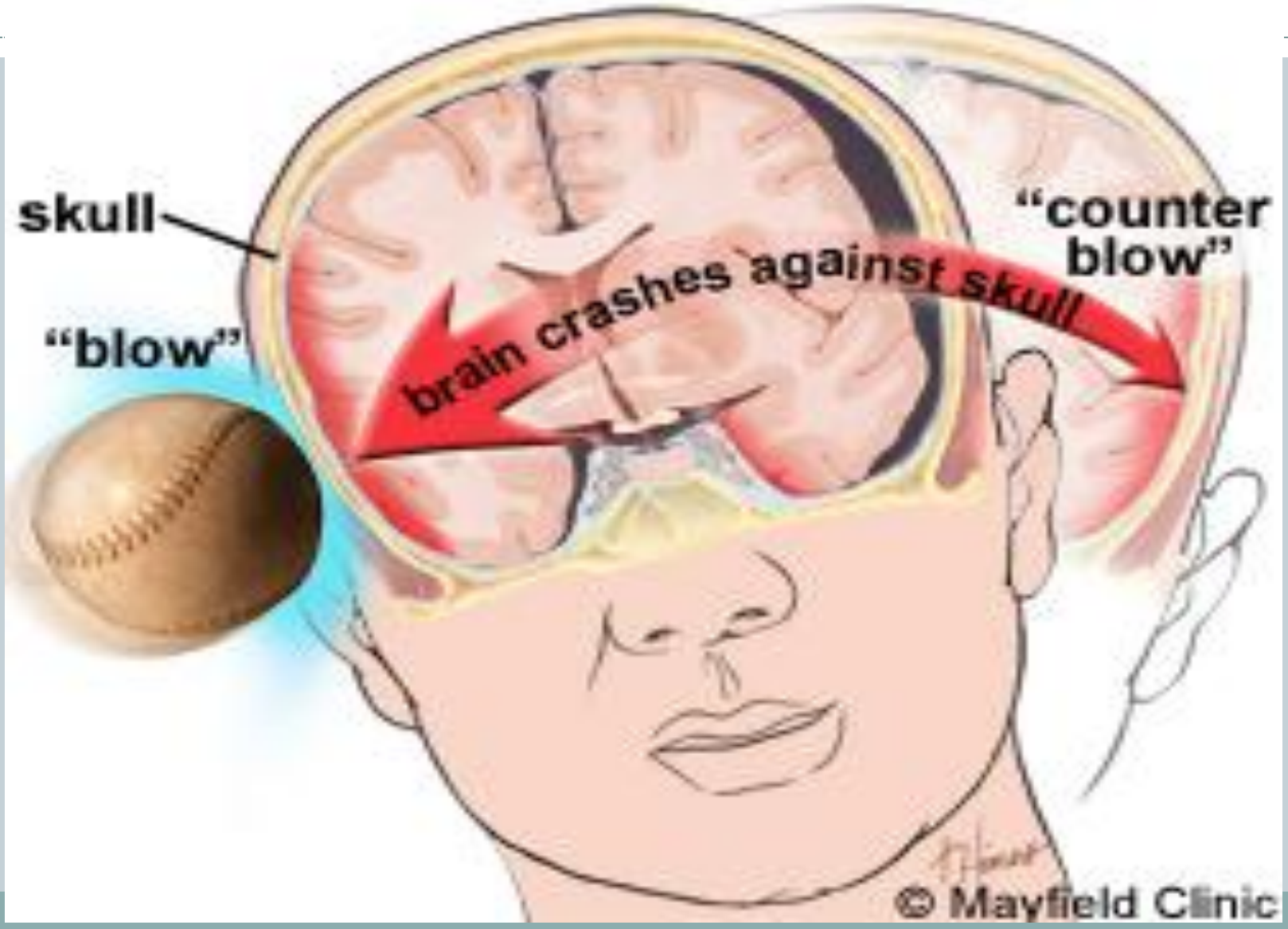
**<u>Secondary insult</u>: Worsening ischemia due to intracranial pressure (ICP), edema,or hypoxia**

**Secondary brain injury is the leading cause of in-hospital deaths after traumatic brain injury**

# PREHOSPITAL CARE

- **Early appropriate management can have a profound impact on the patient's final outcome.**

- **For patients with moderate to severe head injury, provide stabilization and rapid transport to a facility with experience in the management of brain injury.**


skull
"blow"
brain crashes against skull
"counter blow"
© Mayfield Clinic

# PREHOSPITAL CARE

- **Issues related to treating these victims in the field or at the place of injury have lagged behind pre-hospital advancements in medical and general trauma management.**

# PREHOSPITAL CARE

- **In the last 30 years, dedicated trauma programs have demonstrated that aggressive prehospital programs reduce morbidity and death from TBI**

# PREHOSPITAL CARE

- **Improved outcomes following aggressive treatment of mass lesions, hypoxia, hypotension, and fluid and electrolyte abnormalities have shown that secondary events following TBI are preventable and treatable.**


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

# Mannitol

- **Mannitol as a treatment following head trauma was first described in the literature in 1961 (Wise and Chater)**

- **Mannitol is an osmotic diuretic ($C_6H_8(OH)_6$)**

# Mannitol


500 mL
20% MANNITOL I.V.
MANNITOL INJECTION, USP (20 g/100 mL)


%20
MANNİTOL
ENJEKTABL SOLÜSYONU

# Mannitol

- **Mannitol has two main mechanisms of action.**
- **Immediately after bolus administration it expands circulating volume, decreases blood viscosity and therefore increases cerebral blood flow and cerebral oxygen delivery.**
- **Its osmotic properties take effect in 15-30 minutes when it sets up an osmotic gradient and draws water out of neurons.**
-

# Dosage Forms

**injectable solution**

- **5%**
- **10%**
- **15%**
- **20%**
- **25%**

# Therapeutic Use

- **Promotion of diuresis in the prevention or treatment of the oliguric phase of acute renal failure before irreversible renal failure becomes established.**
- **Reduction of intracranial pressure and brain mass.**
- **Reduction of high intraocular pressure when the pressure cannot be lowered by other means.**
- **Promotion of urinary excretion of toxic materials.**

# Adverse Effects

- **Angina-like chest pains**
- **CHF**
- **Hypotension**
- **Phlebitis**
- **Convulsions**
- **Chills**
- **Dizziness**
- **Headache**
- **Acidosis**
- **Fluid/electrolyte imbalances**
- **Thirst**
- **Nausea**
- **Vomiting**
- **Blurred vision**
- **Urinary retention**

# Contraindications

- **Well established anuria due to severe renal disease.**
- **Severe pulmonary congestion or frank pulmonary edema.**
- **Active intracranial bleeding except during craniotomy.**
- **Severe dehydration.**
- **Progressive renal damage or dysfunction after institution of mannitol therapy, including increasing oliguria and azotemia.**
- **Progressive heart failure or pulmonary congestion after institution of mannitol therapy.**
- **Do not administer to patients with a known hypersensitivity to mannitol.**

# Pre-hospital mannitol

- **When to actually give mannitol in victims of head trauma has been a source of great discussion and controversy.**

- **In contrast to the hospital environment,the dilemma in the pre-hospital environment is the inability to look at a CT scan and characterize the injury**

# Pre-hospital mannitol

- **If the patient has active intracranial bleeding say from an epidural hematoma, the argument has been that administration of mannitol wil increase the bleeding and increase the mass lesions (blood collection).**
- **This has led to the recommendation that without the presence of a CT scan, the patient should have lateralizing signs to be considered for the administration of mannitol.**

- **However after prolonged administration (continuous infusion) mannitol molecules move across into the cerebral interstitial space and may exacerbate cerebral oedema and raise ICP.**

- **Mannitol is therefore best used by bolus administration where an acute reduction in ICP is necessary.**

# Mannitol

**Cerebral Edema dosage**

- **1.5-2 g/kg IV infused over 30-60 minutes**

- Pregnancy Category: C

# *Mannitol in Head Trauma: The Controversy*

- **There are insufficient data on the effectiveness of pre-hospital administration of mannitol**

# The Uncertainity over use of mannitol

- **All guidelines acknowledge that this is an area of considerable clinical uncertainity.**
- **There is uncertainity over the optimal treatment regimen ,**
- **over the effectiveness of mannitol as compared to other ICP lowering agents and**
- **over the usefulness of mannitol given at other stages following head injury, (i.e. in the pre-hospital setting)**

# Pre hospital use of mannitol.

REVIEW ARTICLES

# REVIEW ARTICLE

- Kou Kou, *et al* ***Current pre-hospital traumatic brain injury management in China*** *World J Emerg Med. 2014; 5(4): 245–254.*

# REVIEW ARTICLE

- **A literature search was conducted in January 2014 using the China National Knowledge Infrastructure (CNKI).**
- **Articles on the assessment and treatment of TBI in pre-hospital settings practiced by Chinese doctors were identified.**

# REVIEW ARTICLE

- **The information on the assessment and treatment of hypoxemia, hypotension, and brain herniation was extracted from the identified articles.**

- **62% of the papers claimed that their pre-hospital doctors assessed TBI patients' neurologic status in pre-hospital settings.**

# REVIEW ARTICLE

- **Most of the papers showed clinical signs of brain herniation by observing the patients' pupils and levels of consciousness**

- **Interventions to control elevated intracranial pressure (ICP) were documented by 92% of the identified papers.**

# REVIEW ARTICLE

- **45% of the papers documented that agents had been administered to control ICP for all TBI patients.**

- **The most common medications used to control ICP in Chinese pre-hospital settings were mannitol, furosemide, and corticosteroid**

# REVIEW ARTICLE

- ***Murthy et al Prehospital Care of Traumatic Brain Injury. Indian J Anaesth 2008 ;52:258***

**Concluded that:**

- **Mannitol is effective in reducing intracranial pressure and is recommended for control of ICP .**
- **There is however no data to support its use in patients without signs of cerebral herniation and without ICP monitoring.**

Cochrane Library

Cochrane Database of Systematic Reviews

# Mannitol for acute traumatic brain injury (Review)

Wakai A, McCabe A, Roberts I, Schierhout G.

Mannitol for acute traumatic brain injury.

*Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No.: CD001049.
DOI: 10.1002/14651858.CD001049.pub5.

**www.cochranelibrary.com**



WILEY

# REVIEW ARTICLE

- *Wakai A, McCabe A, Roberts I, Schierhout G.*

*Mannitol for acute traumatic brain injury.*

*Cochrane Database of Systematic Reviews 2013, Issue 8.*

# REVIEW ARTICLE

## Objectives

- **To assess the effects of : different mannitol therapy regimens, mannitol compared to other intracranial pressure (ICP) lowering agents, and**

- **to quantify the effectiveness of mannitol administration given at other stages following acute traumatic brain injury.**

# REVIEW ARTICLE

***Search methods***

- *searched the Cochrane Injuries Group Specialised Register, CENTRAL (The Cochrane Library), MEDLINE (OvidSP), EMBASE (OvidSP), ISI Web of Science (SCI-EXPANDED & CPCI-S) and PubMed.*

- **They found four randomized controlled trials**

## REVIEW ARTICLE

1. One trial compared ICP-directed therapy to 'standard care'
2. One trial compared mannitol to pentobarbital
3. One trial compared mannitol to hypertonic saline
4. One trial tested the effectiveness of pre-hospital administration of mannitol against placebo

# conclusions

- **Mannitol therapy for raised ICP may have a beneficial effect on mortality when compared to pentobarbital treatment,**

- **but may have a detrimental effect on mortality when compared to hypertonic saline.**

# conclusions

- **ICP-directed treatment shows a small beneficial effect compared to treatment directed by neurological signs and physiological indicators.**

- **There are insufficient data on the effectiveness of pre-hospital administration of mannitol.**

REVIEW ARTICLE

# Out-of-hospital administration of mannitol vs placebo

Sayre et al, *Academic Emergency Medicine* (1996)

# REVIEW ARTICLE

- **Sayre compared pre-hospital administration of mannitol with placebo.**

- **They included patients of head injury with GCS 11 or less and the patients were either administered 20% mannitol 5 ml/Kg over five minutes or placebo (0.9% saline) in equal amounts.**

- **This the only single prospective study thus far conducted on prehospital use of mannitol for the treatment of increased ICP.**
- **But it did not produce clinically improved outcomes,**
- **Mainly because this study was significantly underpowered, with only 20 participants**

- **Furthermore, no long term outcome data was reported, as patients were only followed for two hours after mannitol administration**

# REVIEW ARTICLE

- **Evaluation of the Impact of Implementing the Emergency Medical Services Traumatic Brain Injury Guidelines in Arizona: The Excellence in Prehospital Injury Care (EPIC) Study Methodology**

- *Academic Emergency Medicine 2014;21:818–830 © 2014 by the Society for Academic Emergency Medicine*

**The review stated that:**

- **An ideal therapeutic agent for ICP reduction should reduce ICP while maintaining cerebral perfusion (pressure).**

- **While mannitol can cause dehydration over time, HTS helps maintain normovolemia and cerebral perfusion, a finding that has led to a large amount of pilot data being published on the benefits of HTS, albeit in small cohorts.**

- **Prophylactic therapy is not recommended with mannitol, although it may be beneficial with HTS**

- **The review found that treatment with mannitol for increased intracranial pressure reduced the likelihood of death when compared to treatment with pentobarbital.**

- **In contrast, it found that treatment with mannitol may increase the likelihood of death when compared to treatment with hypertonic saline.**

- **The review also found a small benefit when mannitol treatment is directed by measurement of intracranial pressure compared to ‘standard treatment.’**

- **The review found insufficient data on the effectiveness of pre-hospital administration of mannitol**


# Guidelines for the Management of Severe Traumatic Brain Injury

## 4th Edition

- **The Brain Trauma Foundation's Guidelines for the Management of Severe Traumatic Brain Injury 4th Edition (2016)**

- **Mannitol is effective for control of raised intracranial pressure (ICP) at doses of 0.25 g/kg to 1 g/kg body weight. Arterial hypotension (systolic blood pressure 90mmhg should be avoided.**

## The Brain Trauma Foundation's Guidelines for the Management of Severe Traumatic Brain Injury 4th Edition (2016)

- **Restrict mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurological deterioration not attributable to extracranial causes.**

## The Brain Trauma Foundation's Guidelines for the Management of Severe Traumatic Brain Injury 4th Edition (2016)

- **The Committee is universal in its belief that hyperosmolar agents are useful in the care of patients with severe TBI.**

- **However, the literature does not currently support recommendations that meet the strict criteria for contemporary evidenced-based medicine approaches for guideline development.**

## The Brain Trauma Foundation's Guidelines for the Management of Severe Traumatic Brain Injury 4th Edition (2016)

- **The recommendations in the 3rd Edition of these guidelines about administration of hyperosmolar agents were based on**
- **one Class 2 study and nine Class 3 studies.**

# Summary

- **For patients with moderate to severe head injury,provide stabilization and rapid transport to a facility with experience in the management of brain injury.**

- **The goals of care during prehospital triage, stabilization, and transport are to recognize life-threatening raised intracranial pressure and to circumvent cerebral herniation**

# Summmary

- **Mannitol for reduction of ICP in TBI has been used since 1961**
- **Most of trials and publication have concentrated on the hospital environment**
- **Very few trails for the pre-hospital administration of mannitol**
- **There are no class I trials only class II & III trials**

# Summary

- **For pre- hospital administration of mannitol use The Brain Trauma Foundation's Guidelines for the Management of Severe Traumatic Brain Injury 4th Edition.**

- **Mannitol is effective for control of raised intracranial pressure (ICP) at doses of 0.25 g/kg to 1 g/kg body weight. Arterial hypotension (systolic blood pressure 90mmhg should be avoided.**

# Summary

- **Restrict mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurological deterioration not attributable to extracranial causes.**

- **If transport times are short, do not give mannitol or hypertonic saline for elevated ICP.**

# Summary

- **Prolonged administration (continuous infusion) mannitol may exacerbate cerebral oedema and raise ICP.**

- **Mannitol is therefore best used by bolus administration where an acute reduction in ICP is necessary.**

# Finally

**"Half of what you'll learn in medical school will be shown to be either dead wrong or out of date within five years of your graduation; the trouble is that nobody can tell you which half -- so the most important thing to learn is how to learn on your own..."**

*-Dr. David Sackett, evidence-based medicine pioneer*

- THANK YOU FOR YOU PATIENCE