



PHARMACY PEARLS: OSMOTHERAPY

PHIL TOBIAS, PHARMD, BCCCP

CLINICAL PHARMACIST – NEUROSURGERY

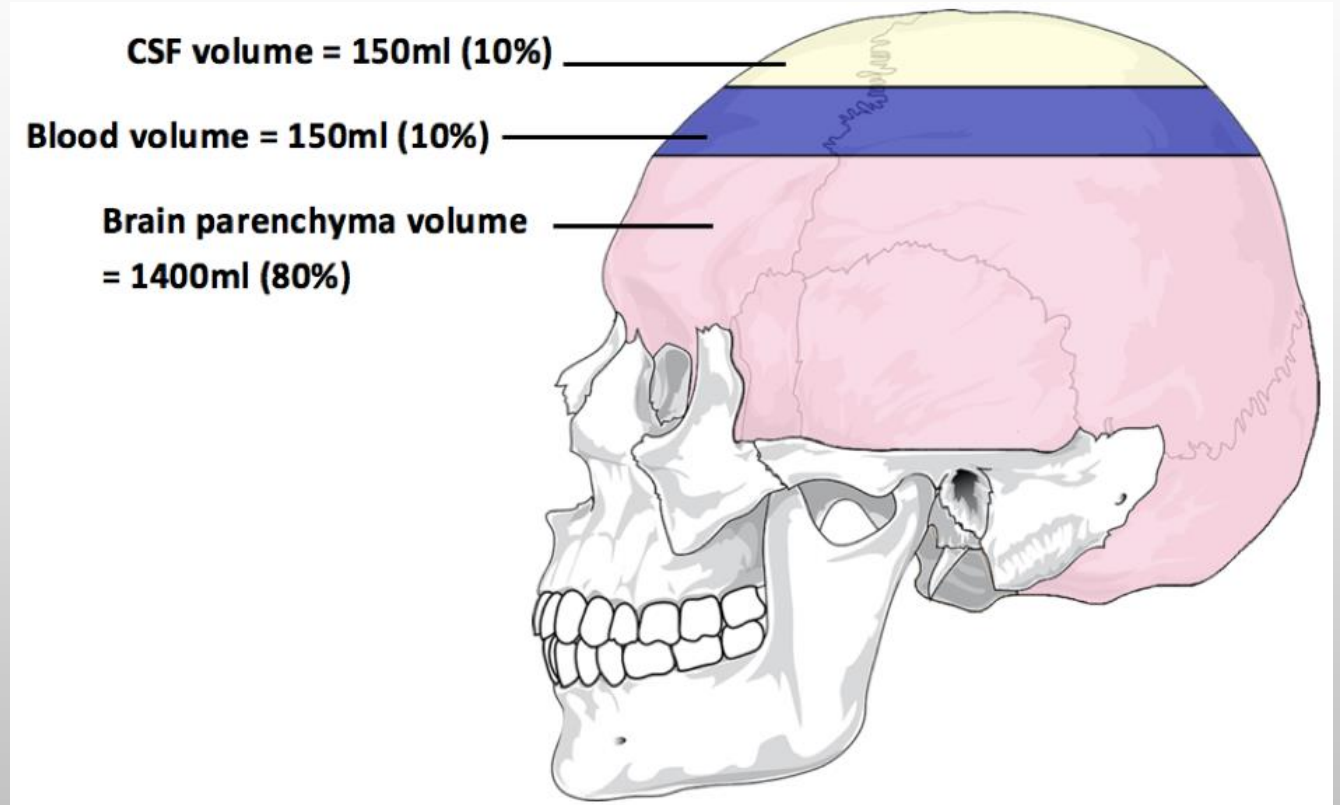
DENVER HEALTH

OBJECTIVES

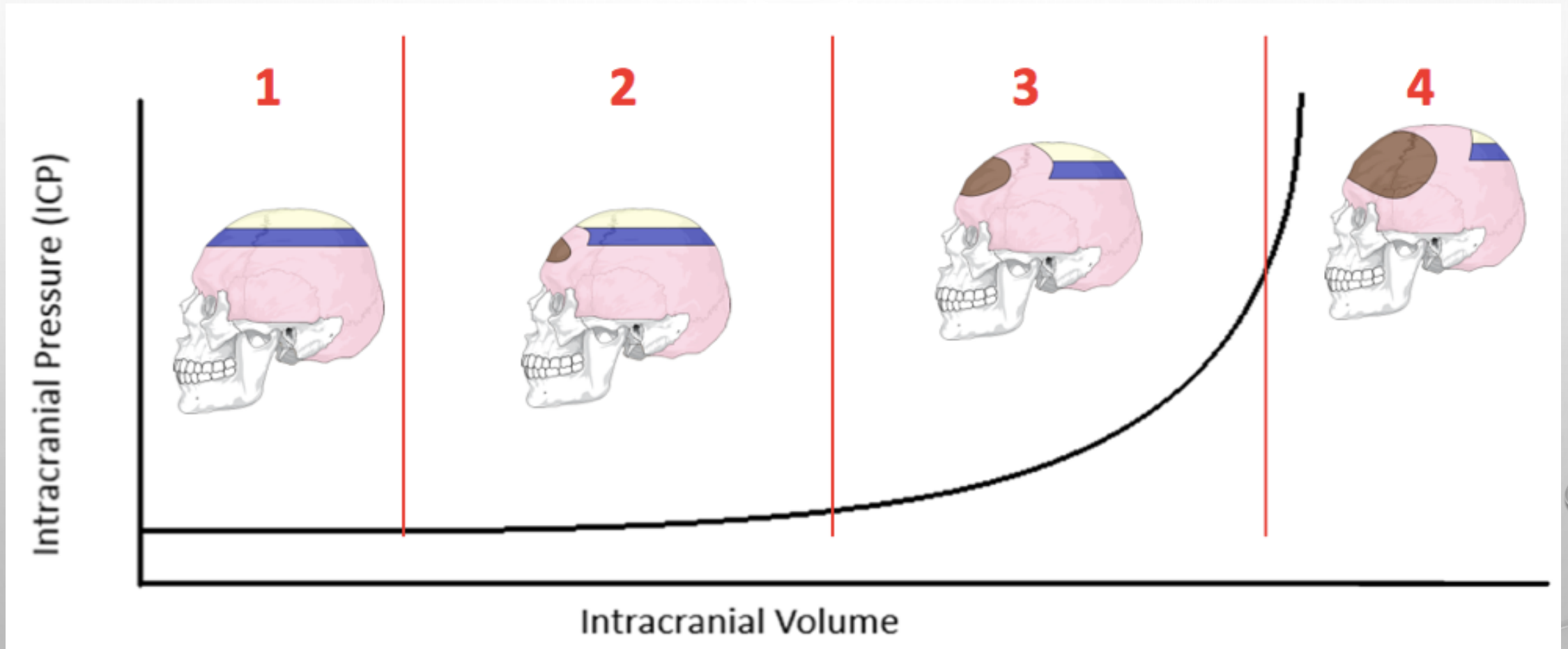
- UNDERSTAND THE TREATMENT GOALS AND TARGETS IN MANAGEMENT OF ELEVATED INTRACRANIAL PRESSURE
- COMPARE HYPERTONIC SALINE AND MANNITOL IN REGARDS TO DOSING, ADMINISTRATION AND ADVERSE EFFECTS

CRANIAL VAULT

- RIGID COMPARTMENT THAT CONTAINS BLOOD, BRAIN AND CSF
- IN NORMAL CRANIAL PHYSIOLOGY, THESE THREE COMPONENTS EXIST IN EQUILIBRIUM
- IF THE VOLUME OF ONE COMPONENT INCREASES, THE VOLUME OF ANOTHER MUST DECREASE



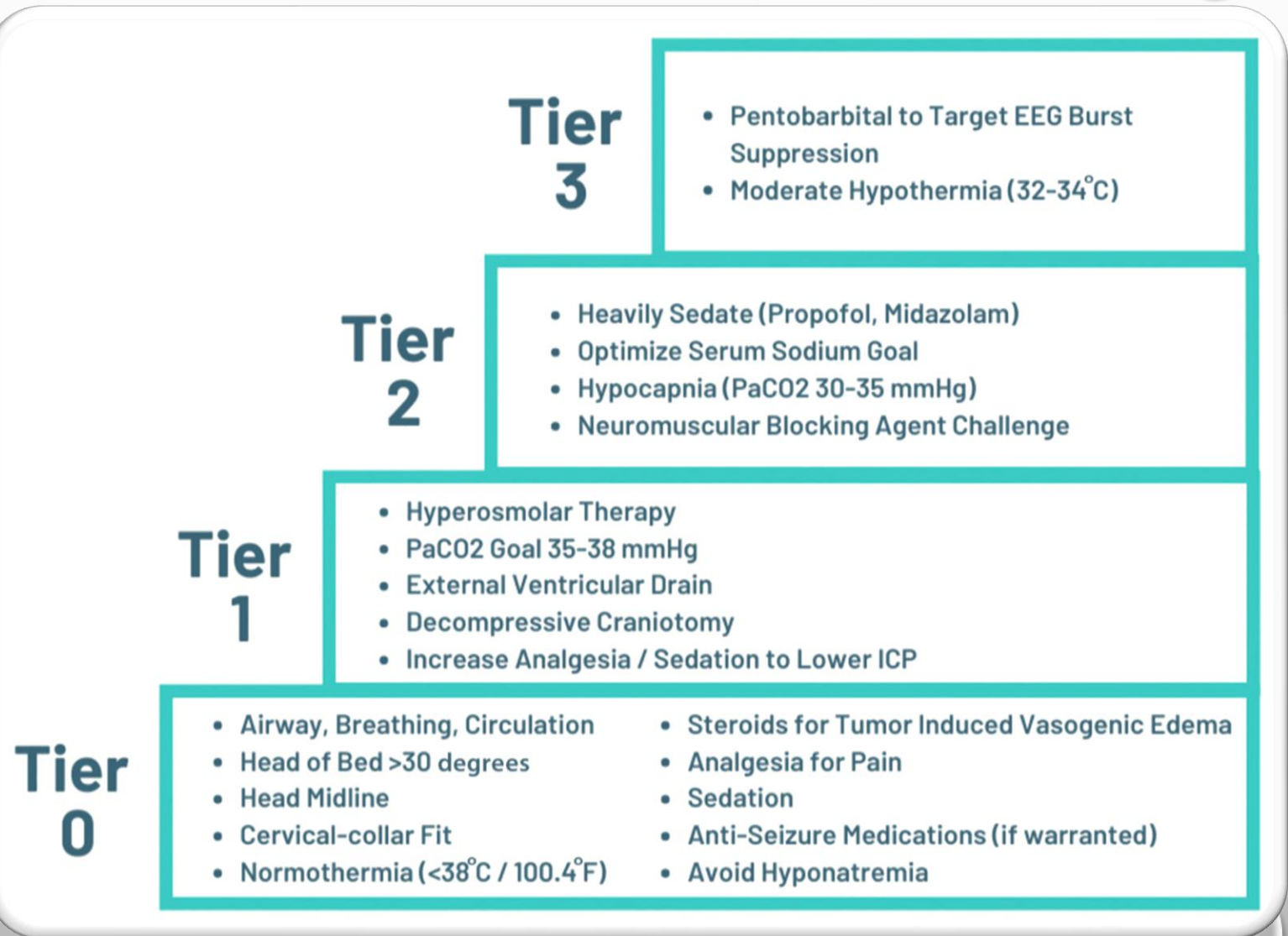
MONRO-KELLIE HYPOTHESIS



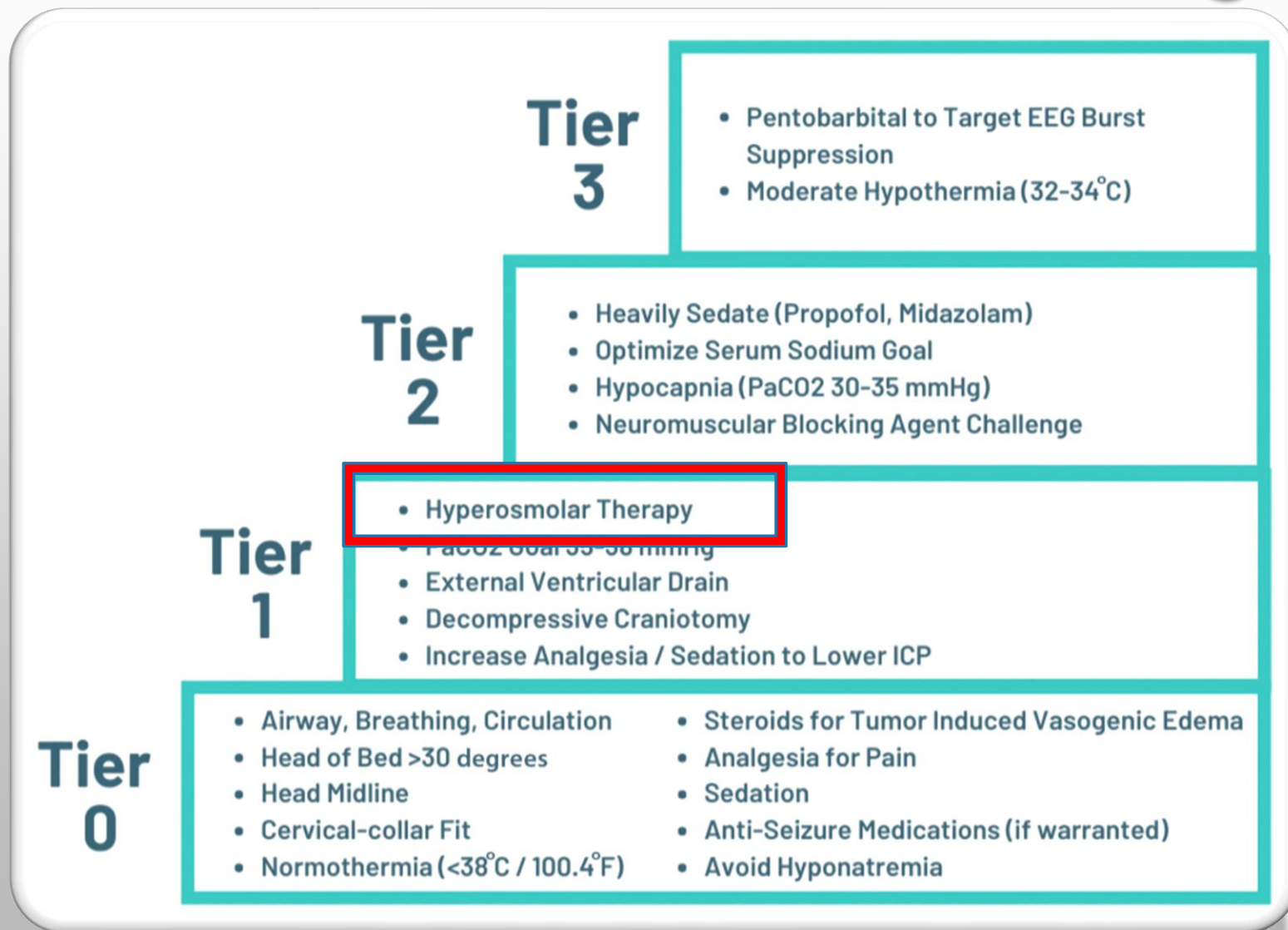
INTRACRANIAL PRESSURE

- PATHOGENESIS OF ELEVATED INTRACRANIAL PRESSURE (ICP) VARIES DEPENDING ON THE INITIAL INSULT
- GOALS OF ICP MANAGEMENT:
 - MAINTAIN ADEQUATE BRAIN OXYGEN DELIVERY
 - AVOID FURTHER INJURY
 - PREVENT HERNIATION
- TARGETS:
 - ICP < 22 MMHG
 - CEREBRAL PERFUSION PRESSURE (CPP): 60 – 70 MMHG

ICP TREATMENT OPTIONS



ICP TREATMENT OPTIONS



OSMOTHERAPY

Osmotic therapy uses agents to create an osmotic gradient across the blood-brain barrier that draws water from the brain into the vascular space

Agents:

- Mannitol
- Hypertonic saline (HTS)

Regardless of the cause of elevated ICP, osmotherapy is considered a mainstay of medical therapy, and should be administered as soon as possible

OSMOTHERAPY

MANNITOL

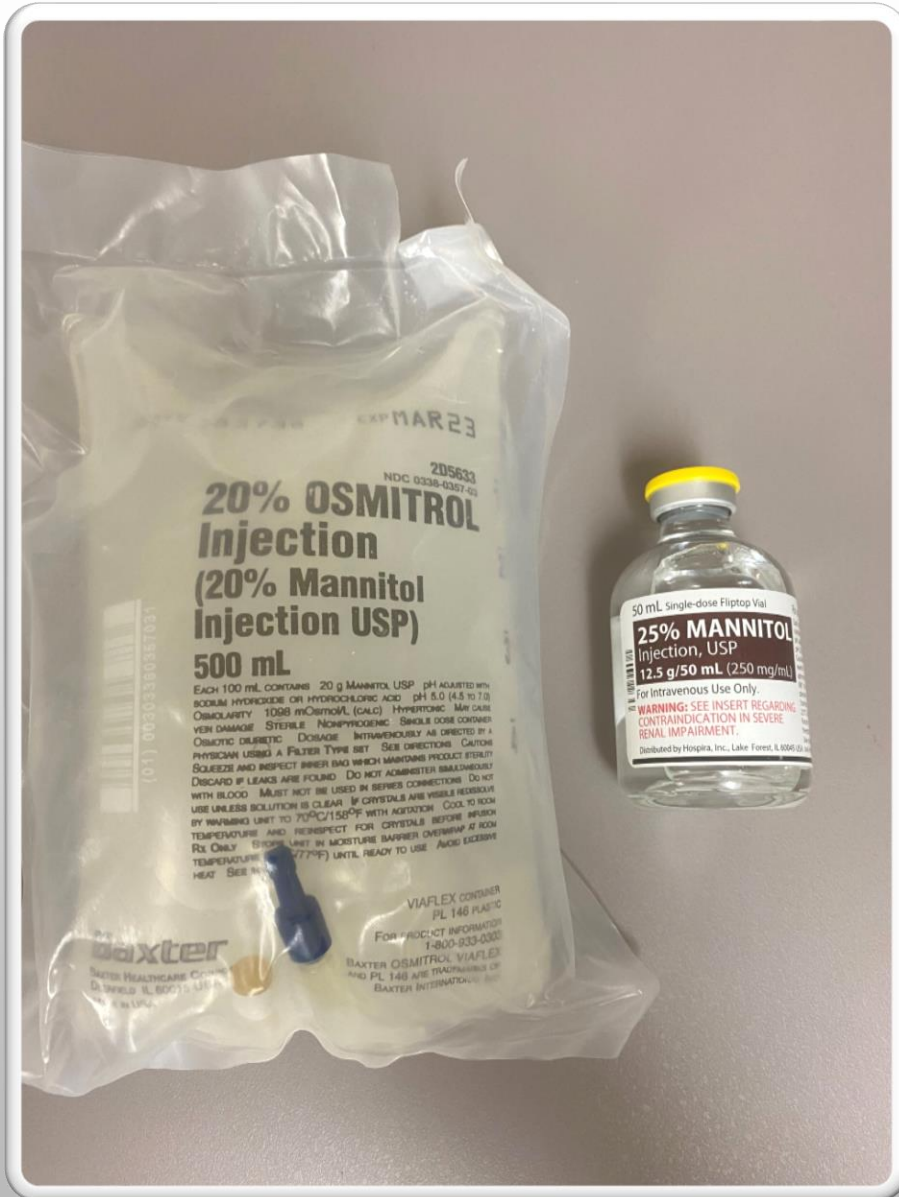
- DOSE: 0.25 – 1 G/KG
- ADMINISTRATION: CENTRAL OR PERIPHERAL
 - 0.22-MICRON INLINE FILTER REQUIRED
- ADVERSE EFFECTS:
 - ACUTE KIDNEY INJURY
 - ELECTROLYTE ABNORMALITIES
 - HYPOTENSION

HYPERTONIC SALINE (HTS)

- DOSE/ADMINISTRATION: DEPENDS ON SODIUM COMPOSITION
- ADVERSE EFFECTS:
 - ACUTE KIDNEY INJURY
 - OSMOTIC DEMYELINATION SYNDROME
 - ELECTROLYTE ABNORMALITIES

OSMOTHERAPY

	20% Mannitol	3% HTS	23.4% HTS	8.4% Sodium Bicarbonate
Equiosmolar Dose	0.5 g/kg	2.5 mL/kg	30 mL	1 mL/kg
Osmolality (mOsm/L)	1098	1027	8008	2000
Infusion Site	Central or PIV	Central, PIV or IO	Central	Central or PIV



MANNITOL DOSING

- 20% MANNITOL
- 20 GRAMS/100 ML
- 100 KG PATIENT:
- DOSE: 1 GRAM/KG
- 100 GRAMS = 500 ML



MANNITOL ADMINISTRATION

- CRYSTALLIZATION CAN OCCUR AT LOW TEMPERATURES
 - SHOULD NOT BE ADMINISTERED IF CRYSTALS PRESENT
 - 0.22-MICRON INLINE FILTER REQUIRED
- ADMINISTERED OVER 10 – 20 MINUTES TO AVOID TRANSIENT HYPOTENSION

MANNITOL ADVERSE EFFECTS

- ACUTE KIDNEY INJURY
 - INCIDENCE: 6 – 12%
 - USUALLY TRANSIENT AND REVERSIBLE WITH CESSATION OF ADMINISTRATION
- ELECTROLYTE ABNORMALITIES
 - HYPER/HYPONATREMIA
- HYPOTENSION
 - AVOID IN HYPOTENSIVE (SBP < 90 MMHG) PATIENTS

HYPERTONIC SALINE

- DOSING OF HTS DEPENDS ON CLINICAL SCENARIO AND WHAT IS AVAILABLE
 - BOLUS VS CONTINUOUS INFUSION
- ADMINISTRATION RATE CAN VARY
 - 3% - CAN BOLUS 250 ML OVER 15 – 30 MINUTES
 - CAN ADMINISTER 30 ML/HR VIA PERIPHERAL LINE X 48 HOURS
 - 23.4% - CAN BOLUS 30 ML OVER 15 – 30 MINS OR IVP OVER 2 – 5 MINS BY PROVIDER
 - REQUIRES CENTRAL LINE
- RAPID ADMINISTRATION CAN LEAD TO TRANSIENT HYPOTENSION

HYPERTONIC SALINE ADVERSE EFFECTS

- ACUTE KIDNEY INJURY
 - INCREASED RISK WHEN SODIUM LEVELS GREATER THAN 160 MEQ
- OSMOTIC DEMYELINATION SYNDROME
 - CAUSED BY RAPID INCREASES IN SODIUM (GREATER THAN 8-12 MEQ/L WITHIN 24 HOURS)
 - INCREASED RISK IN PATIENTS WITH CHRONIC HYPONATREMIA
- ELECTROLYTE ABNORMALITIES
 - HYPERNATREMIA
 - HYPERCHLOREMIA
 - HYPOKALEMIA

PHARMACOKINETIC EFFECTS

	20% MANNITOL	HYPERTONIC SALINE
Onset	5 – 10 mins	Rapid
Peak effect	15 mins	10 – 15 mins
Duration	2 – 5 hours	2 – 6 hours

MANNITOL VS. HYPERTONIC SALINE

- BRAIN TRAUMA FOUNDATION TBI GUIDELINES, 4TH EDITION:
 - “ALTHOUGH HYPEROSMOLAR THERAPY MAY LOWER INTRACRANIAL PRESSURE, THERE IS INSUFFICIENT EVIDENCE ABOUT EFFECTS ON CLINICAL OUTCOMES TO SUPPORT A SPECIFIC RECOMMENDATION, OR TO SUPPORT USE OF ANY SPECIFIC HYPEROSMOLAR AGENT, FOR PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY”
- NEUROCRITICAL CARE SOCIETY GUIDELINES FOR ACUTE TREATMENT OF CEREBRAL EDEMA:
 - “WE SUGGEST USING HYPERTONIC SALINE SOLUTIONS OVER MANNITOL FOR THE INITIAL MANAGEMENT OF ELEVATED ICP OR CEREBRAL EDEMA IN PATIENTS WITH TBI.”

OSMOTHERAPY TAKE AWAY POINTS

- THERE ARE RISKS & BENEFITS ASSOCIATED WITH BOTH MANNITOL AND HYPERTONIC SALINE, SO USE PATIENT SPECIFIC FACTORS TO GUIDE THERAPY
- TIME IS BRAIN: UTILIZE WHICHEVER AGENT THAT CAN BE QUICKLY ADMINISTERED
- HTS ADMIN: $30 \text{ ML } 23.4\% = 250 \text{ ML } 3\%$



PHARMACY PEARLS: OSMOTHERAPY

PHIL TOBIAS, PHARMD, BCCCP

CLINICAL PHARMACIST – NEUROSURGERY

DENVER HEALTH