Cerebral Edema

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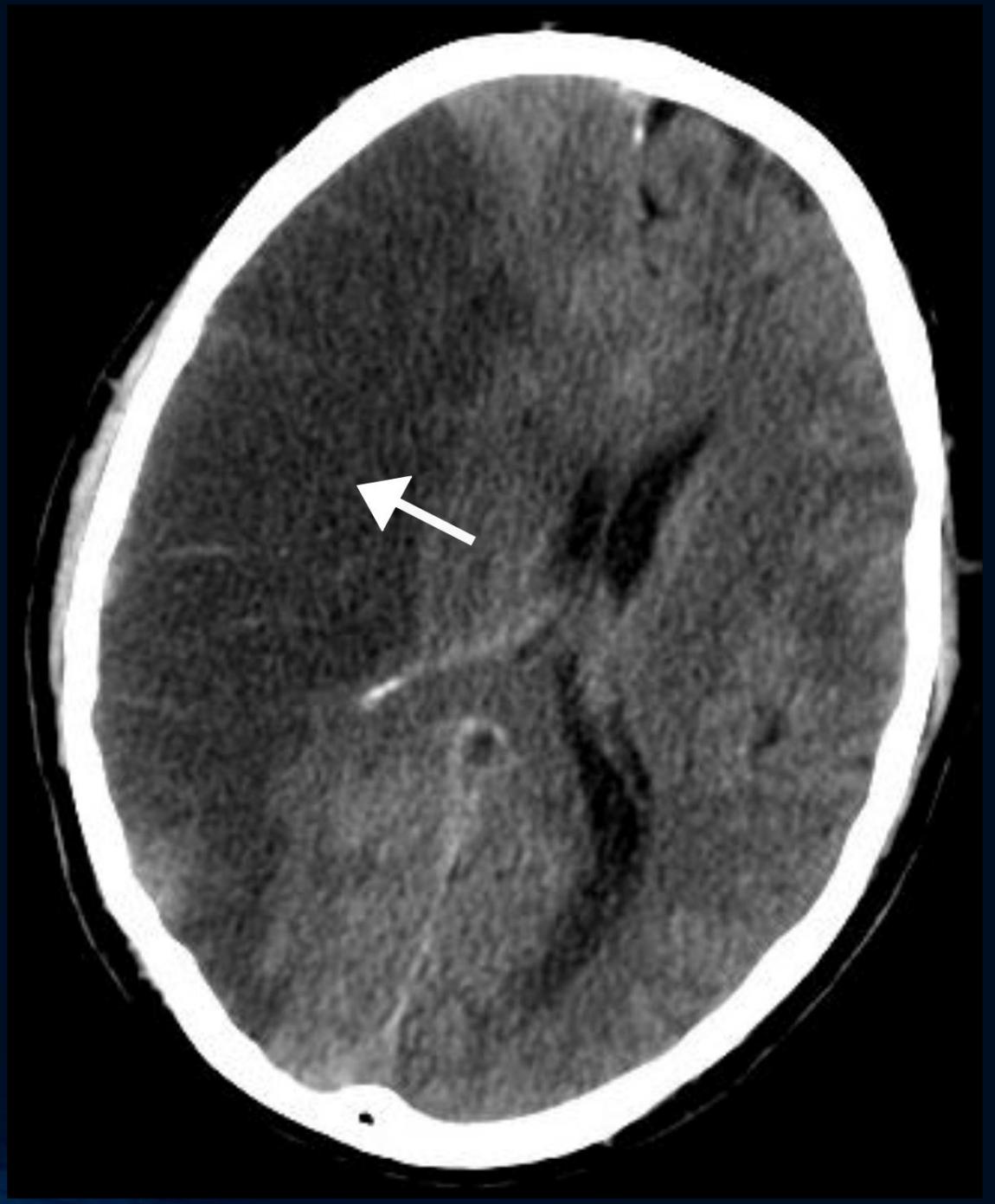
Objectives

- Define cerebral edema
- Identify causes for cerebral edema
- Describe the presentation of cerebral edema
- Summarize treatment options for cerebral edema

What is cerebral edema?

Cerebral edema is a non-specific pathological swelling of the brain that may develop in a focal or diffuse pattern after any type of neurological injury



Common Causes

- Traumatic brain injury (TBI)
- Stroke/ Vascular ischemia
- Subarachnoid hemorrhage (SAH)
- Subdural, epidural, intracerebral hematoma
- Tumor
- Infection
- Hepatic encephalopathy
- Hyponatremia
- Acute hypertension

Clinical Presentation

- Can be asymptomatic
- Altered mental status/ Coma
- Bradycardic
- Hypertensive
- Anisocoria

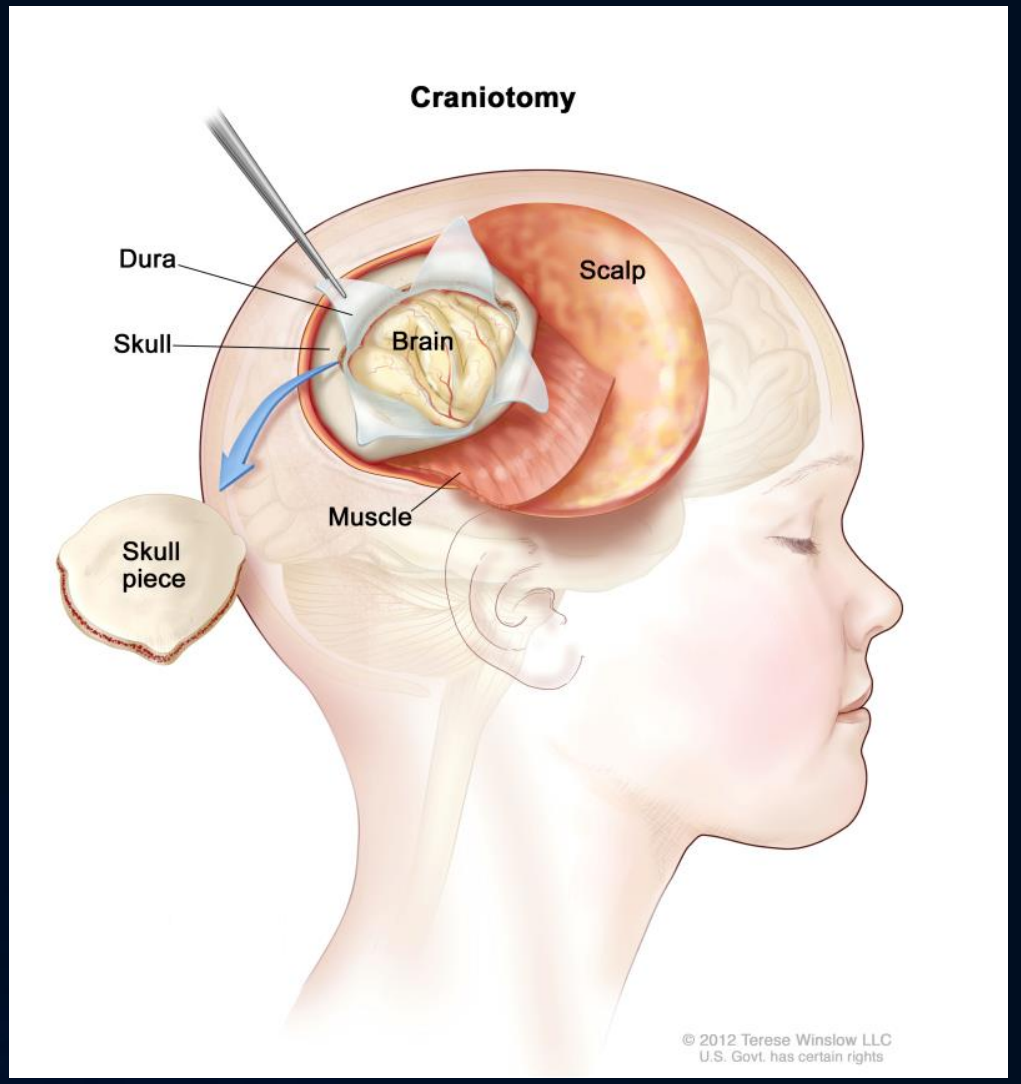
Diagnosis and Monitoring

- Diagnosis
  - CT
  - MRI
  - CT angiography (CTA)

- Monitoring
  - Serial neuroimaging
  - Intracranial pressure (ICP)
  - Level of consciousness/ worsening focal deficits

Non-Pharmacological Treatment Options

- Elevate head of bed
- Brief episodes of hyperventilation
- External Ventricular Drain (EVD)
- Craniotomy



Pharmacological Treatment- Hyperosmotic therapy

- Hypertonic saline (HTS)
  - 3% and 23.4% are the most common strengths
  - 23.4% reserved for refractory ICP
  - MOA: exact mechanism unknown. Most common theory is the creation of an osmotic shift of fluid from the intracellular space to the interstitial and intravascular space
  - Warnings/ precautions:
    - Vesicant, must be administered via large vein
    - Sodium toxicity
    - Avoid hypernatremia/ hyperchloremia during treatment with HTS to avoid AKI/ acidosis
      - Na goal: 145-155 mEq/L

Pharmacological Treatment- Hyperosmotic therapy

- Hypertonic saline (cont.)
  - Dosing:
    - 3% NaCl
      - Continuous IV
      - Max rates
        - Peripheral line: 30 mL/hr
        - Central line: 70 mL/ hr
    - 23.4%
      - One time bolus
      - To be administered through central line. Emergent short-term administration via peripheral line while central access is obtained.
      - Rate
        - 15-60 mL over 10-20 minutes
        - Typically will see 30 mL
      - This should NEVER have a standing order

Pharmacological Treatment- Hyperosmotic therapy

- Mannitol
  - MOA: exact mechanism unknown. Thought to withdraw water from the brain parenchyma and excrete in urine
  - IV Lasix 0.5-1 mg/kg may be used to potentiate effect
  - Warnings/ precautions:
    - Vesicant
    - Nephrotoxic
    - MUST be filtered
    - Should be inspected for crystals prior to administration. If crystals are present, re-dissolve by warming solution

Pharmacological Treatment- Hyperosmotic therapy

- Mannitol (cont.)
  - Dosing:
    - 0.25- 1 mg/kg/ dose over 20 minutes; May repeat every 6-8 hours as needed
    - Vials
      - 25% solution (12.5 g/50 mL)
      - Use a 0.22 micron filter
    - Bags
      - 20% solution (100 g/ 500 mL)
      - More readily available
      - Can use up to a 5 micron filter
      - CHI uses 1.2 micron filters, which are packaged with the bags in Pyxis

Pharmacologic Treatment- Hyperosmotic therapy

- Subarachnoid Hemorrhage
  - Symptom based dosing rather than goal based dosing in management of ICP or cerebral edema
  - Do not have dosing recommendations for neurological outcomes

  - Nimodipine
    - Benefit: improvement of neurological outcomes by reducing incidence and severity of ischemic deficits
    - MOA: exact mechanism unknown. Proposed mechanism include dilation of small arteries, reduction of dependent excitotoxicity, diminished platelet aggregation, and inhibition of ischemia triggered by red blood cell products
    - Dosing
      - 60 mg every 4 hours for 21 days
      - Oral administration only!
      - Must be started within 96 hours of the onset of subarachnoid hemorrhage
    - Hepatically metabolized, dose reduce to 30 mg q 4 hours in patients with cirrhosis

Pharmacologic Treatment- Hyperosmotic therapy

- Traumatic Brain Injury
  - Recommend using HTS over mannitol
  - HTS was at least as safe and effective but fluid resuscitation was better
  - Suggest against the use of mannitol and HTS in pre-hospital setting just for improving neurological outcomes
- Acute ischemic stroke
  - No specific recommendation regarding using one agent over another
  - Recommend not using prophylactic mannitol as some studies have shown that it can cause harm---increased risk of death and/or functional dependency
- Intracerebral hemorrhage
  - Recommend using HTS over mannitol
  - Using either symptom or target driven dosing
  - Recommend against corticosteroids to improve neurological outcomes due to increased risk of infection/mortality
- Bacterial meningitis
  - Dexamethasone 10 mg IV Q 6 h for 4 days to reduce neurological sequelae
    - Administer before or with first dose of abx
  - Insufficient evidence to determine if HTS or mannitol is more effective in reducing ICP
- Hepatic encephalopathy
  - No specific recommendation regarding using one agent over another

HTS vs Mannitol Controversy

- Hypertonic saline was proven to be more effective than Mannitol in combined burden of intracranial hypertension and associated hypoperfusion
- HTS does not carry as high of a risk of nephrotoxicity as mannitol
  - However, does carry risk of hypernatremia
- Both HTS and mannitol effectively reduce ICP, but HTS has a more sustained effect on ICP and can effectively increase cerebral perfusion pressure (CPP)

Pharmacologic Treatment (specific to spontaneous ICH)

- Blood pressure control
  - Options include:
    - Nicardipine
      - Continuous IV infusion
      - Initiate at 5 mg/hr; titrate by 2.5 mg/hr at 5-15 minute intervals
      - Max dose: 15 mg/hr
      - Conc: 25 mg/250 mL (D5W or NS)
    - Labetalol
      - IV push
      - Initial dose: 5-20 mg over 2 minutes
      - Can follow with 20-80 mg every 10-15 minutes until target BP achieved
      - Vial size: 5 mg/ mL

  - Patient's presenting with SBP between 150-220 mmHg and without any contraindications to acute blood pressure treatment, acute lowering of SBP to 140 is safe and can be effective for improving functional outcomes

  - Patient's presenting with SBP >220 mmHg, it may be reasonable to consider aggressive reduction of blood pressure

Pharmacologic Treatment- Miscellaneous

- Seizure prophylaxis
  - Guidelines do not make clear recommendations for or against
  - Levetiracetam most common antiepileptic drug used
- Anticoagulant reversal
  - Warfarin
    - PCC (1500-2000 units)
    - Vitamin K (5-10 mg IV)
    - FFP
  - DOAC
    - PCC (50 u/kg)
  - Heparin
    - Protamine (1 mg for every 100 mg)
  - Pradaxa
    - Praxbind (5 g x 1)

Pharmacologic Treatment- Surgery

- Remifentanil
  - Indications
    - Analgesic agent during induction and maintenance of general anesthesia
    - Continuation as an analgesic agent into immediate post op
  - MOA: Potent μ-opiate receptor agonist
  - Dosing:
    - Can be given as bolus or continuous infusion
    - Induction: 0.5 mcg/kg/min
    - Maintenance: 0.25-0.4 mcg/kg/min
    - Continuation: 0.1 mcg/kg/min
  - Restricted at CHI to:
    - Anesthesia providers
    - Craniotomies with very low associated post-op pain
    - Awake fiberoptic intubations

Pharmacologic Treatment- Surgery

- Gleolan (aminolevulinic acid (ALA)
  - Indication: Optical imaging agent used in patients with glioma as an adjunct for the visualization of malignant tissue during surgery
  - MOA: Causes accumulation of the ALA metabolite PpIX in tumor cells. Used in conjunction with a blue emitting light source, allowing tumor tissue to be visualized.
  - Dosing:
    - 20 mg/kg administered 3 hours prior to start of anesthesia
  - Phototoxicity
    - Avoid concomitant use of phototoxic medications 24 hours during the perioperative period
    - Protect patient from light up to 48 hours after administration

Pharmacist's role

- Be familiar with common medications
- Understand each individual medication's role in the larger picture
- Provide recommendations and resources to physicians when appropriate

Questions?