Cerebral Edema

ETIOPATHOPHYSIOLOGY

BRAIN EDEMA - brain volume↑ due to increase in extravascular brain water.
- it is general reaction to insults.

N.B. differentiate from BRAIN ENGORGEMENT - brain volume↑ due to increase in intravascular volume (e.g. obstruction of cerebral veins, arterial vasodilatation).

### Etiopathophysiology

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**Vasogenic Edema** - increased capillary permeability to macromolecules = BBB disruption (widening of tight junctions + increase in pinocytotic vesicles).
- etiology (most common type of edema!):
  1) tumor
  2) abscess, meningitis, encephalitis
  3) stroke (ischemia, infarction, hemorrhage)
  4) trauma (diffuse BBB disruption up to several hours after trauma - window of opportunity to administer cerebral protective drugs that would not penetrate intact BBB)
  5) lead encephalopathy.
- accumulates preferentially in white matter and can become very widespread.
  - exception is corpus callosum (so tightly bundled that there is little extracellular space - edema does not spread readily).
- paucity of brain lymphatics impairs resorption of excess fluid.
- eventually resolves (edema fluid is reabsorbed into vascular space or ventricular system).
- BBB disruption causes CT/MRI contrast enhancement, CSF protein↑.

**Cytotoxic Edema** - swelling of cells (neurons, glia, endothelial) due to membrane pump failure.
- etiology:
a) **decreased energy supply** to brain cells (e.g. ischemia, hypoxia, trauma) → increased intracellular osmoles (Na\(^+\), lactate, H\(^+\)) → rapid water entry into cells.
   - even after short ischemia, brain may respond to reperfusion with severe brain edema.

b) **plasma osmolality↓:**
   1) **osmotic disequilibrium syndromes** (in hemodialysis, diabetic ketoacidosis) - excessive intracellular solutes (organic acids in uremia; glucose & ketone bodies in diabetic ketoacidosis) result in excessive cellular hydration when plasma osmolality is rapidly reduced with therapy.
   2) acute dilutional hyponatremia
   3) inappropriate secretion of ADH

c) acute **hepatic encephalopathy, Reye's syndrome.**
   - accumulates in white & grey matter.
   - extracellular fluid volume is compensatory reduced!

**Conditions associated with generalized edema have elements of both **vasogenic** and **cytotoxic** edema.
   - both **vasogenic** and **cytotoxic** edema occur in setting of **trauma**!
   - acute **hypoxia** causes **cytotoxic** edema, which is followed by **vasogenic** edema as infarction develops.

**INTERSTITIAL (S. HYDROCEPHALIC) EDEMA** (best characterized in obstructive hydrocephalus) - **CSF movement across ventricular walls.**
   - accumulates in periventricular white matter (esp. at angles of lateral ventricles).
   - volume of periventricular white matter is reduced! (after successful CSF shunting, edema is reduced, and thickness of mantle is restored)

**MECHANISMS by which edema alters neuronal function:**
1. ICP↑
2. Increased distances for nutrient diffusion (e.g. O\(_2\)).
3. Lipid peroxidation in membranes

**PATHOLOGY**
- edematous brain is softer and appears to "overfill" cranial vault.
- gyri are flattened, intervening sulci are narrowed.
- ventricular cavities are compressed.
- as brain expands, herniation may occur. see p. S54 >>
Multiple small metastases causing cerebral edema seen at right which obscures structures:

**CLINICAL FEATURES**

- **intracranial hypertension:**
  1. **Generalized brain dysfunction** (disturbances of consciousness, etc) – due to DIFFUSE edema.
  2. **Focal neurologic deficits** – due to FOCAL edema, brain herniation.
     
     N.B. in brain tumor, clinical signs are often caused more by surrounding edema than by tumor mass itself (so deficits maybe reversible with steroids)!

- *rate of edema formation* is directly proportional to *severity of neurologic deficits.*
- in chronic hydrocephalus **interstitial edema** manifestations are usually minor (in advanced cases - **dementia** and **gait disorder** become prominent) - CSF accumulation in extracellular space is much better tolerated than is presence of plasma in extracellular space (as in vasogenic edema).
Cerebral Edema (MRI better than CT):

1) **decreased density** of brain parenchyma (water content↑) – T1-MRI and CT signal↓, T2-MRI signal↑.
   - blurring or loss of visible distinction between gray matter and white matter.
   - N.B. vasogenic edema spreads along white matter tracts - no grey matter involvement with preserved grey-white junction (vs. cytotoxic edema)

2) **mass effect**:
   - a) **diffuse edema**: loss of definition of cortical sulci → bilateral compromise of ventricles → effacement of basal cisterns.
   - b) **focal edema** - focal mass effect.

- **MRI / CT with contrast** → brain parenchymal enhancement in vasogenic edema (BBB disruption!); no enhancement in cytotoxic edema.

**CSF - protein↑ in vasogenic edema** (BBB disruption!); normal in cytotoxic edema.

**EEG**:
- a) vasogenic edema – slowing.
- b) interstitial edema – normal.

### Treatment

1. **Intensive care** - patent airway, avoidance of hypoxia, maintenance of BP.
   - N.B. avoid salt-free fluids IV!

2. **Surgery** - excision / decompression of intracranial mass lesions, shunting procedures.

3. **Pathogenetic treatment**:

   - **Cytotoxic edema** - augment CPP + increase intravascular osmolality.
   - **Vasogenic edema** – decrease hydrostatic pressure in capillaries + decrease BBB permeability.

1) **Glucocorticoids** (**Dexamethasone** 10 mg IV or IM loading → 4 mg q6h maintenance; pediatric dose 1-2 mg/kg loading → 0.25 mg/kg qid maintenance) - direct effect on endothelial cell function – decreased BBB permeability – for vasogenic edema (around tumor, abscess, radiotherapy field).

   - **Glucocorticoids dramatically and rapidly (in hours) reduce focal and general signs of brain edema around tumors!**

   - usual complications of steroid therapy are expected (esp. **gastric hemorrhage** - all patients receiving steroids for more than few hours should receive RANITIDINE OR PPI!).
   - not useful in cytotoxic edema (e.g. no efficacy in TBI, stroke).
   - conflicting reports about efficacy in acute bacterial or tuberculous meningitis (e.g. steroids reduce deafness in infants with bacterial meningitis).

2) **Osmotherapy** (**Mannitol**) – for cytotoxic edema.

   - effect is short-lived (solute reaches equilibrium concentration in brain after delay of only few hours).
   - parts of brain most likely to “shrink” are normal areas (e.g. regions of vasogenic edema with increased capillary permeability do not shrink*).
*even develop rebound edema following mannitol use because solute accumulates in edematous tissue.

- no rationale for long-term use - brain adapts to hyperosmolality with increase in intracellular osmolality.

3) **DRUGS THAT REDUCE CSF FORMATION** *(ACETAZOLAMIDE, FUROSEMIDE)* – for interstitial edema.

**BIBLIOGRAPHY** see p. S50 >>