Cerebral Edema

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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).

	Cerebral Edema		
	Vasogenic	**Cytotoxic**	**Hydrocephalic (s. interstitial)**
Pathogenesis	Capillary permeability↑	Cellular swelling	Intraventricular fluid↑
Location	White matter	Gray & white matter	Ventricular, white matter (periventricular)
Edema fluid	Plasma filtrate	Intracellular H_2O & Na	CSF
Extracellular fluid volume	↑	↓	↑
Contrast enhancement	+	-	-

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***.

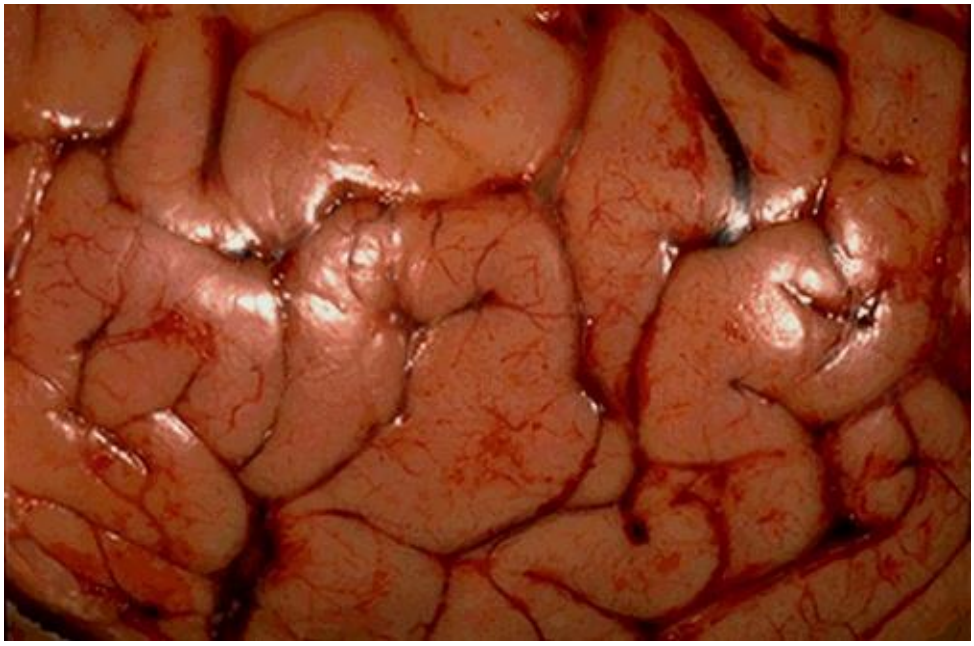
- accumulates in **periventricular white matter** (esp. at angles of lateral ventricles).
- volume of periventricular white matter is reduced! (after successful CSF shunting, edema is reduced, and thickness of mantle is restored)

MECHANISMS by which edema alters neuronal function:

1. ICP↑
2. Increased distances for nutrient diffusion (e.g. O_2).
3. Lipid peroxidation in membranes

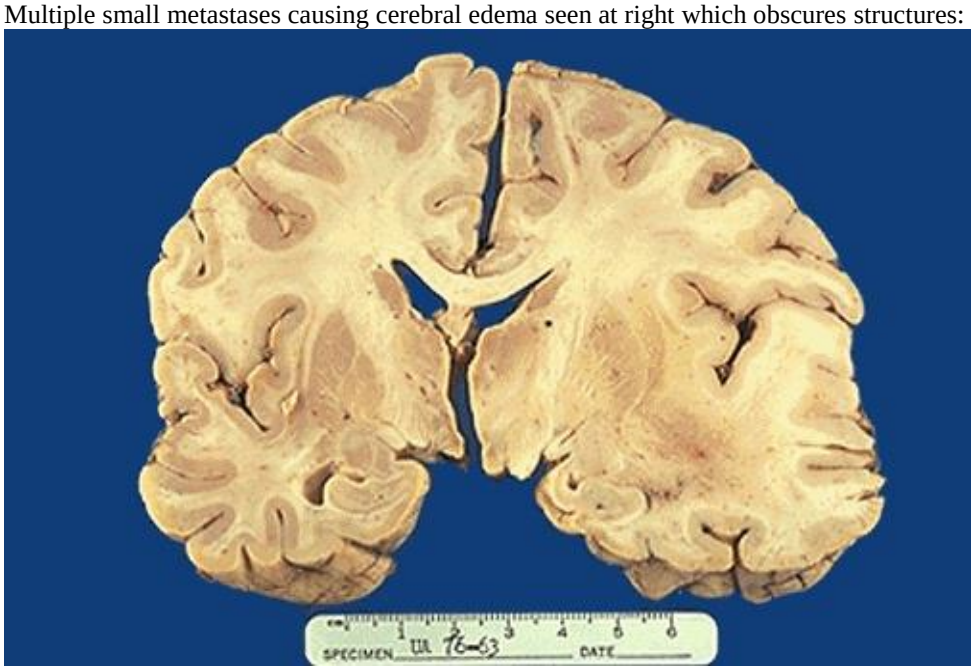
PATHOLOGY

- 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 >>



Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

Multiple small metastases causing cerebral edema seen at right which obscures structures:



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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).

DIAGNOSIS

Neuroimaging (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 >>