Introduction to Neuropathology

- The CNS can only respond to injury in a limited # of ways
- Distribution of injury is different for each disease
- **Remember that consequence is site dependent, not size dependent**
- Basic responses can be subcategorized according to the constituents of the CNS
  1. Neurons
  2. Glia
     - astrocytes
     - oligodendroglia
     - ependyma
     - microglia
  3. Meninges and their constituents
  4. Blood vessels and their constituents

BASIC RESPONSES TO INJURY OF CNS CONSTITUENTS

Neurons

- **Central chromatolysis**
  - Nissl substance and nucleus displaced to periphery of the neuronal cytoplasm
  - response to axonal transection or damage
  - result of axonal reaction
- **Eosinophilic neurons**
  - coagulative necrosis of neurons
  - results from hypoxic or ischemic injury
  - neurons – triangular, eosinophilic, loss of nuclear detail, cytoplasmic blebbing
- **Axonal spheroids**
  - occur as a result of membrane injury and axonal transection
  - axonal cytoplasm becomes dilated and engorged w/ eosinophilic granular material
- **Neuronoghagia**
  - Macs surrounding neuron; phagocytosis
- **Intraneuronal deposits**
  - lipofuscin
  - metabolic substrates
  - viral inclusions – eosinophilic bodies (Negri bodies) in cytoplasm – Rabies
  - byproducts of neurodegenerative disorders – Ex. neurofibrillary tangles of Alzheimer's
- **Atrophy**
  - neuronal loss **and accompanying astrogliosis**
  - mild cell loss is hard to assess; Brain wt. Decreased

Glia (oligodendroglia, ependyma, astrocytes)

- **Astrocytes**
  - **astrogliosis**
    1. reactive response of astrocytes to many form of insult or injury
    2. proliferate and hypertrophy in response to almost any challenge to the CNS
    3. Hypertrophic astrocytes produce **GFAP (glial fibrillary acidic protein)** – makes them eosinophilic
    4. these cells are the scar tissue of the CNS
    5. can be due to normal aging
  - **Rosenthal fibers (MUST KNOW FOR BOARDS!!)**
    1. found in areas of brain with longstanding astrogliosis and edema
    2. Brightly eosinophilic due to GFAP
    3. located within astrocytic processes and consist of α-B-crystallin surrounded by GFAP
    4. serves as barrier function
    5. also found in Juvenile pilocytic astrocytomas and in the white matter of patients with Alexander's disease.

- **corpora amylacea**
  1. end feet of astrocytes
  2. predominate in a perivascular, subependymal, and subpial dist.
  3. glycogen or polyglucosan polymers
  4. basophilic, round, concentrically lamellated bodies
- **Alzheimer type 2 astrocytes**
  1. seen in hepatic encephalopathy and Wilson's disease
  2. large vesicular nuclei which contain an eccentric nucleolus and no discernible cytoplasm by L.M.

- **Oligodendrocytes**
  - produce and maintain myelin in the white matter
  - develop viral inclusions in progressive multifocal leukoencephalopathy
- **Ependyma**
  - glia beneath the ependyma proliferate if the lining is destroyed or separated
  - the glial proliferation is termed **ependymal granulations**
  - ependyma can also be infected with CMV
- **Microglia**
  - CNS macrophages
  - bone-marrow derived
  - proliferate and cluster together (nodule formation) in response to injury

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CEREBRAL EDEMA

- cerebral edema⇒ increased intracranial pressure (ICP)
- most common causes of ICP is tumor, hematoma, and abscesses

REMEMBER!!!

- at some point the ICP increases to equal the perfusion pressure (PP) which results in Cerebral Blood flow (CBF) = 0.
- **CBF = PP – ICP**
- Never want ICP and PP the same.

Normal CBF = 55mL/100gm/minute
- lower than 15 mL/100gm/min results in cell death

Intracranial pressure values
- Normal < 15 mmHg
- Ischemia – 40 mmHg
- No autoregulation – 60 mmHg
- recommended to keep at 15-20 mmHg or below

Autoregulation
- compensation for ↓ perfusion by arteriolar dilatation
- pCO_2 regulated
- results from hypoTN or ↑ ICP

- if significant reduction in CBF is prolonged, the brain tissue will become ischemic and undergo *'intravitum autolysis'* with decomposition
- results in – diffuse gray discoloration, sofening, swelling – "respirator brain"

Types of Cerebral Edema

Vasogenic edema

- results from increases vascular permeability
- results in deposition of plasma in white matter
- alteration in BBB results in vasogenic edema (remember the junctions between capillary endothelial cells)
- Histologically seen as: **VACUOLATION OF THE WHITE MATTER**
- Causes of vasogenic edema
  1. adjacent to a mass lesion (abscess, tumor, hematoma)
  2. infarction and ischemia
  3. trauma
  4. hemorrhage
  5. lead encephalopathy
  6. HTN encephalopathy
  7. Purulent meningitis

Cytotoxic edema

- results from damage to cell membrane
- swelling of endothelial, glial, and neuronal cells from influx of H_2O and Na into the cell cytoplasm
- Micro: swelling and vacuolation of the cytoplasm
- **PREDOMINATES IN THE GRAY MATTER**
- no alteration in permeability to plasma proteins
- no method of radiologic detection
- Associated with the following
  1. Hypoxia/ischemia
  2. hypoosmolality from H_2O intox.
  3. Reye's syndrome

Interstitial edema

- results from too much CSF in the ventricles
- transudation of CSF out of ventricles past ependymal cells into surrounding **white matter**
- similar radiologically to vasogenic edema, except surrounds ventricles
- Results from severe hydrocephalus

Gross appearance of cerebral edema

- gyral flattening
- sulcal narrowing
- generalized softening, vascular congestion, and dusky discoloration

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HYDROCEPHALUS

- Definition: enlargement of the ventricles with an associated increase in the volume of CSF.
- **CSF is produced at a rate of 20 mL/Hr or 500mL/day**
- Average volume of the ventricles and Subarachnoid Space (SAS) is 150 mL
- Assume CSF turnover 3 X per day
- CSF produced by choroid plexus⇒ foramen of L & M⇒ SAS ⇒ arachnoid villi ⇒ superior sagittal sinus
- any obstruction can produce hydrocephalus

<u>Types of Hydrocephalus</u>

Communicating Hydrocephalus

- obstruction is along the subarachnoid flow of CSF distal to the outlet of the foramen of L & M
- usually occurs at the level of the basal cistern
- Clinical disorders where this is seen:
  1. post-meningitis fibrosis of the SAS and AV
  2. organizing subarachnoid hemorrhage
  3. meningeal tumor
  4. arnold-chiari malformation
  5. **Non-obstructive communicating hydrocephalus**
     - choroid plexus papilloma
       - ➢ overproduction of CSF may result
       - ➢ arachnoid villi are saturated

Non-communicating hydrocephalus

- obstruction is intraventricular
- most common site
  1. foramen of Monro
  2. 4^{th} ventricle
  3. cerebral aqueduct
- most commonly seen in:
  1. CNS tumors – by far most common
  2. Cysts
  3. Large cerebral artery aneurysms
  4. Hemorrhage
  5. malformations

Normal pressure Hydrocephalus

- syndrome of slow growing hydrocephalus
- triad of clinical features – dementia, urinary incontinence, and ataxia

Hydrocephalus ex vacuo (compensatory Hydrocephalus)

- occurs with atrophy and loss of brain substance
- compensatory expansion of the ventricular system

HERNIATIONS (4 TYPES)

Subfalcine or cingulate

- herniation of the cingulate gyrus beneath the falx cerebri
- results from mass lesion medially displacing the cerebral hemisphere
- Anterior cerebral arteries can be compressed

Transtentorial (uncal)

- temporal lobe herniation over the free edge of the tentorium cerebelli
- herniated brain compressed the adjacent cerebral peduncle and posterior cerebral artery
- important implications
  1. cranial nerve III compression – ophthalmoplegia and pupillary dilatation
  2. ipsilateral hemiparesis – from cerebral peduncle compression against the tentorial edge
  3. **Kernohan's notch –** hemorrhage and notching of the lateral peduncle
  4. midbrain compression by the uncus – altered consciuosness
  5. **infarction of the visual cortex and temporal hemispheres – due to compression of the PCA**
  6. cerebral aqueduct compression
  7. **Duret's hemorrhages** – tearing and shearing of the penetrating vessels of the midbrain and pons with these hemorrhages

Tonsillar

- cerebellar tonsils are caudally displaced into the foramen magnum
- due to pressurized supratentorial or posterior fossa contents
- Compression of the medulla- alteration in respiratory pattern leading to respiratory arrest

Fungus cerebri

- herniation of edematous brain through skull defect

REMEMBER!!!

- All brain-herniation syndromes are LIFE THREATENING
- Emergency measures taken to treat herniation
  1. airway maintenance
  2. respiratory and pressor support
  3. alleviation of pressure by:
     - osmotic agents (mannitol) and diuresis
     - surgical debulking
     - hyperventilation to decrease pCO_2 and **constrict** vasculature
     - drainage of CSF by shunt
     - fenestration of septum pellucidum to allow for lateral ventricle communication
     - "burr hole"