Pathology of Cerebrovascular Disease

- Cerebrovascular disease – 3rd most common cause of death – most common of all CNS diseases
- Stroke = sudden and dramatic development of a focal neurological dificit due to a vascular impairment
    - 10% of all deaths in the U.S.
    - 500,000 new victims each year
    - mainly results from HTN, cerebral atherosclerosis, or both
- SYMPTOMS OF STROKE
    1. sudden weakness or numbness of the face, arm, or leg on one side of the body
    2. loss of speech, or difficulty in speaking or understanding speech
    3. dimness or loss of vision, in one eye
    4. unexplained dizziness

- TIAs = reversible focal neurological symptoms secondary to ischemia which last from several seconds to 24 hrs

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ARTERIAL INFARCTION

Pathophysiology

- Chief causes: embolism and thrombosis
- Factors contributing to infarction
    1. Decreased O_2 in blood
        - reduced hemoglobin in blood
        - hypoxemia
    2. Decreased perfusion
        - cardiac arrest, hypoTN, shock, pulmonary embolism
        - venous stasis, CHF, Increased ICP
    3. Altered composition of blood
        - polycythemia, thrombotic thrombocytopenic purpura
        - macroglobulinemia
        - oral contraceptives, pregnancy, and puerperium
- Misc. causes of infarction
    1. Hypoglycemia
    2. Vasculitis
    3. Infection with local thrombosis or endarteritis obliterans
    4. Compression of vessels by tumors, aneurysm
- Major sources of emboli
    1. atria, valve, and mural
    2. aorta and Neck + vessels – Ex. atheroma
    3. Peripheral vessels – rare because of entry into right side of heart first.

Remember topographical features are determined by artery of supply

- Size and extent of infarcts influenced by:
    1. Site of the occlusion (the more proximal, the more extensive)
    2. presence and efficacy of collateral circulation
    3. rapidity of occlusion (the more rapid, the more extensive)
- Two main types of infarcts
    1. infarcts of end-arterial zones
    2. boundary zones (water-shed) infarcts

Classification of Infarcts

I. According to type
    - anemic (Pale)
    - Hemorrhagic (red)

II. According to site of involvement
   - cortical and subcortical
   - Cortical only
     - laminar necrosis
     - granular atrophy
   - White matter only – HTN etiology
   - Basal Ganglia

Remember

- Know distribution of Arteries!!
- MCA
  - has greatest volume of distribution
  - most common vessel thrombosed/occluded/embolized
- The larger the wedge-shaped infarcted area, the more proximal the emboli/thrombosis is.

EVOLUTION OF CEREBRAL INFARCTS

1 – 2 days	swelling, pallor, gray-white matter edema	**manifests as Coagulation necrosis** eosinophilic degeneration of neurons swelling of myelin and axons degradation of glia **influx of neutrophils**
3 – 5 days	**MAXIMAL SWELLING**, mushy and friable	influx of monocytes macs phagocytose necrotic tissue lipid-laden macs (**Gitter cells**) prominent capillaries (4-6 days) **INCREASED ICP** **herniation common**
2 weeks	liquefaction begins; necrotic debris begins to disappear	disintegration of necrotic tissue numerous Gitter cells meshwork of richly cellular C.T. many thickened capillaries **hypertrophy and hyperplasia of astrocytes** **BARRIER FUNCTION**
3 weeks	Hole forms (cavitation)	fewer Gitter cells in center prominent reactive changes at egde
Few months	Fluid-filled cavity	Fewer vessels dense glial scar at edge

Main stages in the evolution of Cerebral infarcts are:

Stage I: Coagulative necrosis (with edema)

- Ischemic cell change (eosinophilic neurons)
  1. nuclear pyknosis with cytoplasmic eosinophilia – eosinophilic neurons
  2. pallor of nuclear and cytoplasmic nucleic acids – ghost neurons
  3. shrinkage and condensation of the perikaryon – dark neurons
  4. precipitation of formaldehyde pigment on the neuronal perikaryon – incrustation
  5. neuronal scalloping
  6. neurorial vacuolation
  7. development of a perineuronal halo
- MICRO: molecular and sub-molecular layer intact

Stage II: Liquefaction (and phagocytosis)

Stage III: Cavitation (and shrinkage)

- cavitation probably results because astrocytes can't grow on a dead substrate

SELECTIVE VULNERABILITY TO ISCHEMIA

- various components of the brain react in different ways to the same ischemic injury

Following HypoTN or Cardiac Arrest the most vulnerable sites are:

1. distal arterial territories ("water-shed")
   - major and abrupt fall in systemic BP – arterial-border-zone pattern of injury
   - slow onset HypoTN for a prolonged duration – generalized and continuous ribbon of cortical necrosis – **Laminar necrosis**
2. hippocampus
3. cerebellar cortex
4. Cortical layers 3,5,6 are more susceptible than 1,2, & 4.
5. laminar necrosis occurs in zones 2-6 (1 is spared)

Neurons are more vulnerable to ischemia than oligodendrocytes
Oligodendrocytes are more vulnerable to ischemia than astrocytes

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OTHER ISCHEMIC LESIONS

Spinal Cord Infarction

- T4 and L1 are the most vulnerable spinal cord areas
  - ➢ are arterial border zones
- Causes
  1. aortic atherosclerosis
  2. chronic HypoTN (elderly patients)
  3. dissecting aneurysms
  4. after surgical repair of aortic aneurysms

CEREBRAL AND/OR MENINGEAL HEMORRHAGE

3 main non-traumatic causes: *HTN, Vascular malformation, Blood dyscrasias*

Hypertension

- causes vascular changes
- most important etiological factor in infarction and hemorrhage
- accentuates atherosclerosis of the large arteries
- alters the wall of the arterioles in the following ways:
  1. Hyaline degeneration
  2. Fibrinoid necrosis
  3. **Charcot-Bouchard aneurysm**
     - ➢ most frequently found in the small arteries of the basal ganglia
     - ➢ changes lead to hemorrhage
  4. Thrombotic obliteration of altered vessels
- **5 Sites of HTN hemorrhage**
  1. Putamen
  2. cerebral hemispheric white matter
  3. thalamus
  4. pons
  5. cerebellar white matter
     - ➢ the location and relative incidence of HTN hemorrhages is in accord with the distribution of Charcot-Brouchard aneurysms
- Complications of HTN: rupture into ventricles or through cortex into leptomeninges

Other HTN lesions

Lacunar Infarcts

- defined by their size
- caused by rupture of Charcot-Bouchard aneurysms
- most frequent in basal ganglia and basal pons

Binwanger's disease (subcortical arteriosclerotic encephalopathy)

- clinical picture
  - persistent HTN
  - systemic vascular disease
  - history of acute strokes
  - multifocal neurological symptoms
  - long latent periods
  - lengthy clinical course
  - dementia
  - ventricular dilatation
- Pathological findings
  - diffuse degenration of white matter associated with multiple infarcts
- **Numerous white matter lesions seen on the MRI of a demented patient w/ HTN should suggest Binswanger's disease**
- due to resetting of the pressure monitor

Hypertensive encephalopathy

- presents with alterations of cansciousness and severe headaches
- Pathological findings
  - fibrinoid necrosis of arterioles
  - edema
- Failure of vascular autoregulation and forced opening of the BBB by sudden or prolonged HTN
- Remember: autoregulation is maintained from 45-170 mmHg normally

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Hemorrhages due to vascular malformations

Intracranial arterial aneurysms

Saccular or "berry" aneurysms

- clinically most relevant
- Pathogenesis
  - medial muscular defect (congenital)
  - degeneration due to hemodynamic stress
- Rupture in 65% with subarachnoid and intracerebral hemorrhage
- "**The worst headache of my life!**"
- **MAY FORM MASS – DON'T BIOPSY**
- may be further complicates by arterial spasm – which may lead to thrombotic infarction
- treat these patients with Ca^{2+} CHANNEL BLOCKERS prophalactically
- most common locations of saccular aneurysms
  1. anterior communicating artery (30%)
  2. middle cerebral artery (30%)
  3. internal carotid artery and its branches (35%)
  4. basilar artery bifurcation and vertebral artery (5%)

Other types of arterial aneurysms include: atherosclerotic, Charcot-Bouchard, infectious, posttraumatic, neoplastic, and dissecting

Arteriovenous Malformation (AVM)

- large vascular spaces with intervening brain
- most common of all the vascular congenital abnormalities in neurosurgical specimens
- clinical manifestations
  1. hemorrhagic stroke
  2. convulsions
- more than 90% supratentorial
- 10% of subarachnoid hemorrhages are caused by AVMs

Venous Angiomas

Cavernous angiomas

- veins are back-to-back
- no intervening brain
- slower flow of blood and become calcified and thrombosed

Capillary talangiectases

PERINATAL CEREBROVASCULAR DISEASES

Germinal Matrix Hemorrhage

- thin-walled capillaries in the germinal matrix rupture and extend into the lateral ventricles
- Graded radiologically (ultrasound) on a four grade system
  - Grade 1: rupture into the germinal matrix, no extension into the ventricles – CERBRAL PALSY
  - Grade 2: extension into the ventricle, no cast formation of the ventricle – CERBRAL PALSY
  - Grade 3: extension into the ventricle, ventricular cast formation – hydrocephalus and death
  - Grade 4: Grade 3 + extension into the white matter – hydrocephalus and death
- occurs in the perinatal period
- usually with: concurrent prematurity, acidosis, increased ICP, or hypoxemia.