CEREBROVASCULAR DISEASES

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Cerebrovascular diseases

• Brain disorders caused by pathologic processes involving **blood vessels**

• 3 pathogenic mechanisms
  (1) thrombotic occlusion,
  (2) embolic occlusion,
  (3) vascular rupture/Hemorrhage
• **Stroke:**

is the clinical term for acute-onset neurologic deficits resulting from hemorrhagic or obstructive vascular lesions.

transient ischemic attack (TIA) ????
Hypoxia, Ischemia, and Infarction

- The brain may be deprived of oxygen by two general mechanisms:

  **Functional hypoxia:**
  - low partial pressure of oxygen (e.g., high altitude),
  - impaired oxygen-carrying capacity (e.g., severe anemia, carbon monoxide poisoning),
  - inhibition of oxygen use by tissue (e.g., cyanide poisoning)

  **Ischemia:**
  - Hypoperfusion ----- hypotension, vascular obstruction
  - transient or permanent
Global Cerebral Ischemia

• occur in the setting of severe **systemic hypotension**, usually when systolic pressures fall below 50 mm Hg, as in **cardiac arrest**, **shock**, and **severe hypotension**.

• Neurons are more susceptible to hypoxic injury than are glial cells
• The most susceptible neurons (**vulnerable areas**) are:
  - The pyramidal cells of the hippocampus and neocortex
  - Purkinje cells of the cerebellum

- In severe global cerebral ischemia, widespread neuronal death occurs irrespective of regional vulnerability
• MORPHOLOGY:
the brain is swollen, wide gyri, narrowed sulci. The cut surface shows poor demarcation between gray and white matter
• Irreversible ischemic injury---- infarction

**Early changes** (12 to 24 hours):
- acute neuronal cell change
- the reaction to tissue damage begins with infiltration by neutrophils

**Subacute changes** (24 hours to 2 weeks)
- necrosis of tissue
- influx of macrophages
- vascular proliferation,
- reactive gliosis

**Repair** (after 2 weeks)
- removal of all necrotic tissue
- Loss of organized CNS structure
- gliosis
• The distribution of neuronal loss and gliosis in the neocortex typically is uneven with preservation of some layers and devastation of others—a pattern termed pseudolaminar necrosis.
• Border zone ("*watershed*") infarcts:
  - wedge shaped
  - regions of the brain and spinal cord that lie at the most distal portions of arterial territories.
  - In the cerebral hemispheres, the border zone between the anterior and the middle cerebral artery distributions is at greatest risk.
• The clinical outcome varies with the severity and duration of the insult:

**Mild insult** ---- only a transient postischemic confusional state, with eventual complete recovery

**Severe insult** ---- vegetative state, brain death---mechanical ventilation----brain autolysis
Focal Cerebral Ischemia

• Cerebral arterial occlusion ----- focal ischemia ---- infarction in the distribution of the compromised vessel.

• modified by collateral blood flow ------- the circle of Willis or cortical-leptomeningeal anastomoses
Collateral Circulation

- Collateral circulation
  - develops in later age
  - arteries grow to make a natural bypass towards an area of reduced blood flow
• By contrast, there is little if any collateral flow to structures such as the thalamus, basal ganglia, and deep white matter, which are supplied by deep penetrating vessels.
• Causes:

- Emboli  more common
- Thrombosis
• **Emboli:**
  - Cardiac mural thrombi (myocardial dysfunction, valvular disease, and atrial fibrillation)
  - Arterial thromboemboli (atheromatous plaques within the carotid arteries or aortic arch)
  - Venous emboli/paradoxical embolism (thromboemboli from deep leg veins and fat emboli)
• The territory of the middle cerebral artery, a direct extension of the internal carotid artery, is most frequently affected by embolic infarction.

• Emboli tend to lodge where vessels branch or in areas of stenosis, usually caused by atherosclerosis.
• **Thrombosis:**
  - Thrombotic occlusions usually are superimposed on atherosclerotic plaques

- common sites are:
  
The carotid bifurcation,

  The origin of the middle cerebral artery,

  At either end of the basilar artery.
• Infarcts can be divided into two broad groups: 

**Nonhemorrhagic infarcts**---

**Hemorrhagic infarcts**--- result from reperfusion of ischemic tissue, either through collaterals or after dissolution of emboli ---- multiple, petechial hemorrhages

Thrombolytic therapies????
• MORPHOLOGY:
Macroscopic appearance of a nonhemorrhagic infarct:
first 6 hours---no change
48 hours---tissue is pale, soft, and swollen
days 2 to 10---the brain turns gelatinous and friable, and the boundary between normal and abnormal tissue becomes more distinct as edema resolves in the adjacent viable tissue.
day 10 to week 3---the tissue liquefies, eventually leaving a fluid-filled cavity lined by dark gray tissue, which gradually expands as dead tissue is resorbed
• Microscopically:

**After the first 12 hours:**
- ischemic neuronal change (red neurons)
- cytotoxic and vasogenic edema. Endothelial and glial cells, mainly astrocytes, swell
- myelinated fibers begin to disintegrate.

**Up to 48 hours:** neutrophilic emigration

**2 to 3 weeks:**
- Macrophages
- astrocytes at the edges of the lesion progressively enlarge, divide, and develop a prominent network of cytoplasmic extensions

**After several months:**
- the striking astrocytic nuclear and cytoplasmic enlargement regresses
- dense feltwork of glial fibers admixed with new capillaries lining the cavity wall
• Hemorrhagic infarction:
  + blood extravasation
Intracranial Hemorrhage

- intracerebral hemorrhage (intraventricular, intraparenchymal)
- subarachnoid hemorrhage
- epidural hemorrhage
- subdural hemorrhage
Primary Brain Parenchymal Hemorrhage

• Spontaneous ----- nontraumatic

• peak incidence at about 60 years of age

• rupture of a small intraparenchymal vessels
- Hypertension is the leading underlying cause

- Hypertensive intraparenchymal hemorrhages typically occur in the basal ganglia, thalamus, pons, cerebellum
• it can affect small regions and be clinically silent

• can be clinically devastating when it affects large portions of the brain or extends into the ventricular system
MORPHOLOGY:
extravasated blood
cavity with a brown, discolored rim

Anoxic neuronal and glial changes
Edema
pigment- and lipid-laden macrophages
reactive astrocytes
Cerebral Amyloid Angiopathy

• is a disease in which amyloidogenic peptides (beta amyloid), typically the same ones found in Alzheimer disease, deposit in the walls of medium- and small-caliber meningeal and cortical vessels.

• Amyloid deposition weakens vessel walls and increases the risk of hemorrhages
• CAA-associated hemorrhages often occur in the lobes of the cerebral cortex (lobar hemorrhages) ----- Primary intraparenchymal hemorrhages
Hypertensive Cerebrovascular Disease

• Hypertension --- **hyaline arteriolar sclerosis** --- weakened wall---- vulnerable to rupture

• arteries and arterioles that supply:
  - the basal ganglia,
  - the hemispheric white matter,
  and the brain stem
• In some instances, minute aneurysms (Charcot-Bouchard microaneurysms) form in vessels less than 300 μm in diameter.
• Pathologic brain processes are related to hypertension:
  - Intracerebral hemorrhage
  - Lacunar infarcts
  - slit hemorrhage
  - Acute hypertensive encephalopathy
• Lacunar infarcts:
  - are small cavitary infarcts
  - found most commonly in:
  deep gray matter (basal ganglia and thalamus),
  the deep white matter,
  the pons
  - caused by occlusion of a single penetrating branch of a large cerebral artery
Lacunar Infarct in pons
• **Slit hemorrhage:**
  - Rupture of the small-caliber penetrating vessels
  - Hemorrhages resorb, leaving behind a slitlike cavity
• Acute hypertensive encephalopathy:
  - sudden sustained rises in diastolic blood pressure to greater than 130 mm Hg
  - increased intracranial pressure
  - global cerebral dysfunction
  - headaches, confusion, vomiting, convulsions, coma
  - brain edema,
  - transtentorial or tonsillar herniation
  - Petechiae and fibrinoid necrosis of arterioles in the gray and white matter may be seen microscopically
Vasculitis

• cause cerebral infarction

• Infectious

• systemic forms of vasculitis

• Primary angiitis of the CNS