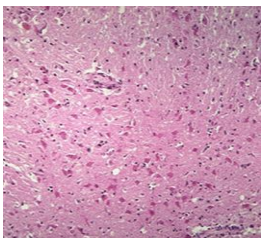
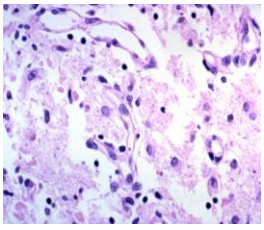
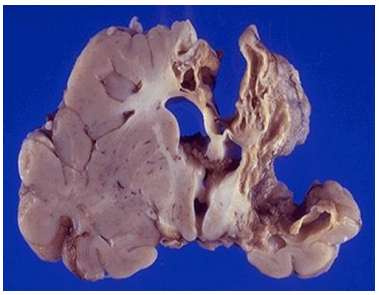
Unit VIII – Problem 4 – Pathology: Crebrovascular diseases

- **The brain needs a constant supply of oxygen and glucose. It is consuming 15% of the energy produced by the body. Note that the brain has no storage of energy and it is totally depending on the blood supply.**
- **Hypoxic-ischemic encephalopathy**: is a term describing the resultant condition due to a deficit in oxygen supply to the brain.
- **Cerebrovascular diseases:**
  - **There are 2 types of cerebrovascular accidents:**
    - ✓ Hemorrhage: intracerebral space occupying lesion with increased intracranial pressure.
    - ✓ Infarction: pathological changes depend on post-infarcted day:
      - ❖ *Early infarction*: shows insignificant changes.
      - ❖ *72 hours after infarction*: cavity and cyst formation.

      Note: cerebral thrombosis with infarction is responsible for 90% of cerebrovascular accidents.
- **Ischemic injury:**
  - **There are 2 types of acute ischemic injury:**
    - ✓ Global cerebral ischemia:
      - ❖ It is involving wide areas of the brain.
      - ❖ *Occurring due to:*
        - Cardiac arrest.
        - Shock.
        - Severe hypotension.
      - ❖ *Outcome: varying with severity of insult:*
        - In mild cases: transient confusion and reversible tissue damage (although irreversible damage might occur).
        - Selective vulnerability: neurons are the most sensitive cells and in different regions they show great variability in the susceptibility to ischemia. Notice that hippocampal cells are first to be affected followed by pyramidal cells and purkinje cells of cerebellum (these are the most vulnerable cells due to their overproduction of glutamate which is toxic). Degree of sensitivity: cerebral cortex > thalamus > brainstem (the spinal cord is resistant to damage).
        - In severe cases: widespread infarction with brain death!
      - ❖ *Morphology:*
        - Gross: brain is swollen – gyri are widened – sulci are narrowed.
        - Microscopic:
          - ➢ Early changes (12-24 hours): presence of red neurons (dead neurons: red coloration is due to degradation of the nucleus and loss of Nissl bodies) and infiltration with neutrophils.
          - ➢ Subacute changes (24 hours – 2 weeks): tissue necrosis, influx of macrophages, vascular proliferation and reactive gliosis.
          - ➢ Repair (after 2 weeks): removal of necrotic tissue, loss of normal structure, gliosis and cyst formation.

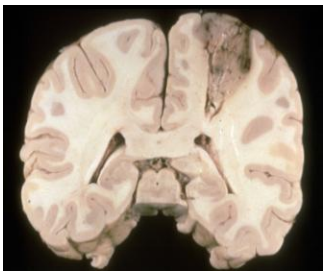




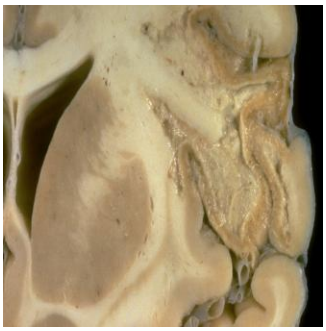


large remote cerebral infarction. Resolution of the infarction has left a huge cyctic space ecompassing much of the cerebral hemisphere in this neonate.

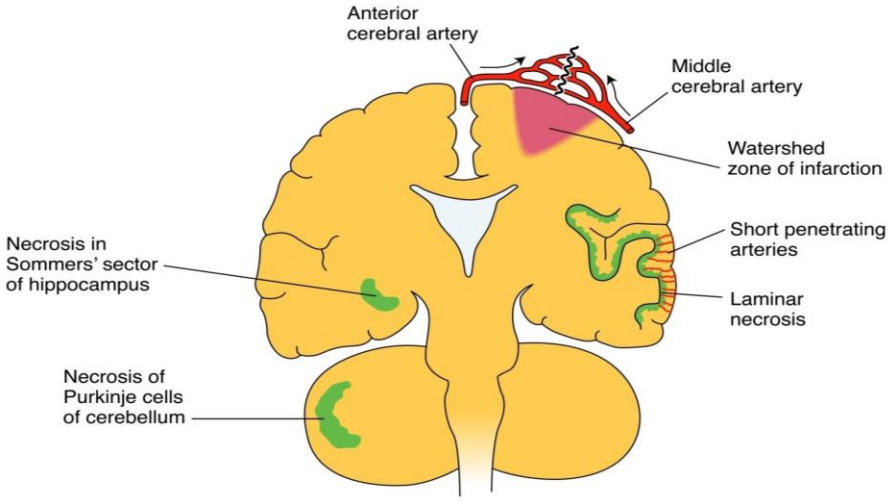
- *Watershed infarcts (border zone infarcts):*
  - Wedge-shaped area of infarction.
  - Caused by: systemic hypotension or myocardial infarction (MI).
  - Areas affected: regions of the brain that are sensitive to diminished blood flow (area perfused by the distal ends of 2 arteries: mostly the region between anterior and middle cerebral arteries).



- *Laminar necrosis:*
  - It is a localized lesion.
  - Areas affected: deeper zones of the brain receiving blood from short penetrating arteries entering the cortex from the surface pial vessels. They branch and form rich plexus of capillaries deep in the grey mater, notably in 4^{th} to 6^{th} neuronal cell layers. Note that abrupt loss of circulatory pressure diminishes flow through this terminal capillary plexus.



- *The image below is summerizing consequences of global cerebral ischemia:*



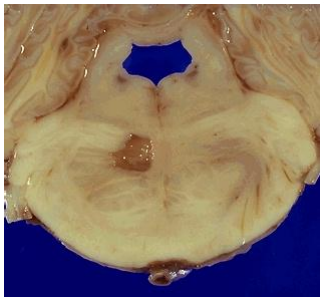
✓ <u>Focal cerebral ischemia:</u>

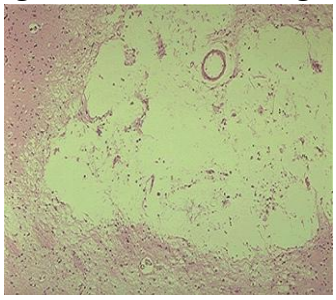
- Reduction of blood flow to a localized area in the brain.
- *Occurring due to:*
  - Thrombosis.
  - Embolism (emboli might be composed of fat or air).

- Vasculitis or arteriosclerotic lesion due to hypertension.
- Atherosclerosis (see the image below: atherosclerosis of cerebral vasculature).

❖ *Lacunar infarcts:*

- Caused by: occlusion of a single, deep penetrating artery arising directly from vessels of:
  - Circle of Willis.
  - Cerebellar arteries.
  - Basilar artery.
- Areas affected**:** Deep nuclei of the brain:
  - Putamen: 37%
  - Thalamus: 14%
  - Caudate: 10%
  - Pons (16%).
  - Posterior limb of internal capsule (10%).
- **Risk factors:**
  - Advanced age.
  - Chronic hypertension.
  - Smoking.
  - Diabetes mellitus.
- **Proposed mechanisms are:**
  - Microatheroma.
  - Hypoperfusion.
  - Embolism.
- **Morphology:**
  - Gross: arteriolar sclerosis resulting from chronic hypertension leads to small lacunar infarcts (< 15mm), one of which is seen in the pons in the image below.
  - Microscopic: cystic space from the resolved lequifactive necrosis surrounded by gliosis. There can be hemosiderin pigment from hemorrhage as well.



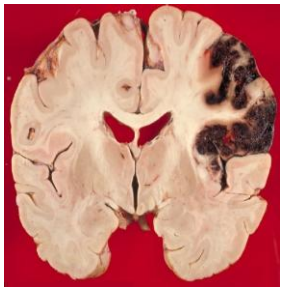


❖ *Hemorrhagic infarct:*

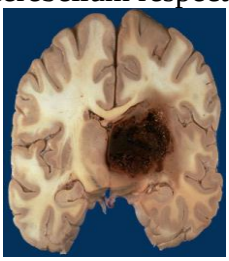
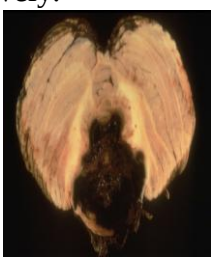
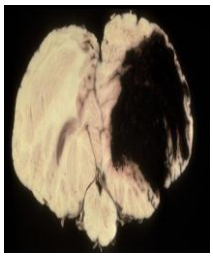
- **Caused by**: occlusion of veins or an artery occlusion of an organ with dual circulation. This occlusion is associated with embolism.
- Use of anticoagulants may convert a bland infarct into a hemorrhagic one (blood leaks from collateral vessels or

through necrotic capillaries when the occluding thrombus or embolus breaks up and the infracted area is reperfused).

- **Morphology:**
  - Gross: infarct stippled (مُنَقَّط) with petechiae or showing confluent larger hemorrhages.
  - Microscopic: RBCs are dispersed and finely mixed with the intervening nectrotic tissue unlike in intracranial hemorrhage where there are large aggregates or clots of RBCs within the tissue.



- **Cerebral hemorrhage:**
  - It is spontaneous, occurring without trauma.
  - **The 3 major causes are:**
    - ✓ Hypertension (hypertensive intracerebral hemorrhage):
      - ❖ *Occurring in:*
        - Basal ganglia-thalamus (65%).
        - Pons (15%).
        - Cerebellum (8%).
      - ❖ Chronic hypertension forming small areas of vessel distention (microaneurysms) in small arteries which arise from larger vessels. Further rise in blood pressure will lead to rupture of those microaneurysms resulting in intracerebral hemorrhage.
      - ❖ *Morphology:*
        - Gross: hemorrhage involving basal ganglia (putamen in particular) tend to be non-traumatic and caused by hypertension which damages and weakens the small penetrating arteries. A mass effect with midline shift, often with secondary edema, may lead to herniation. Note: middle and right images showing spontaneous hemorrhages in pons and cerebellum respectively.

    - ✓ Rupture of an arterial aneurysm (Berry aneurysm):
    - ✓ Arteriovenous malformations: