Central Nervous System pathology-1

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12/9/2024

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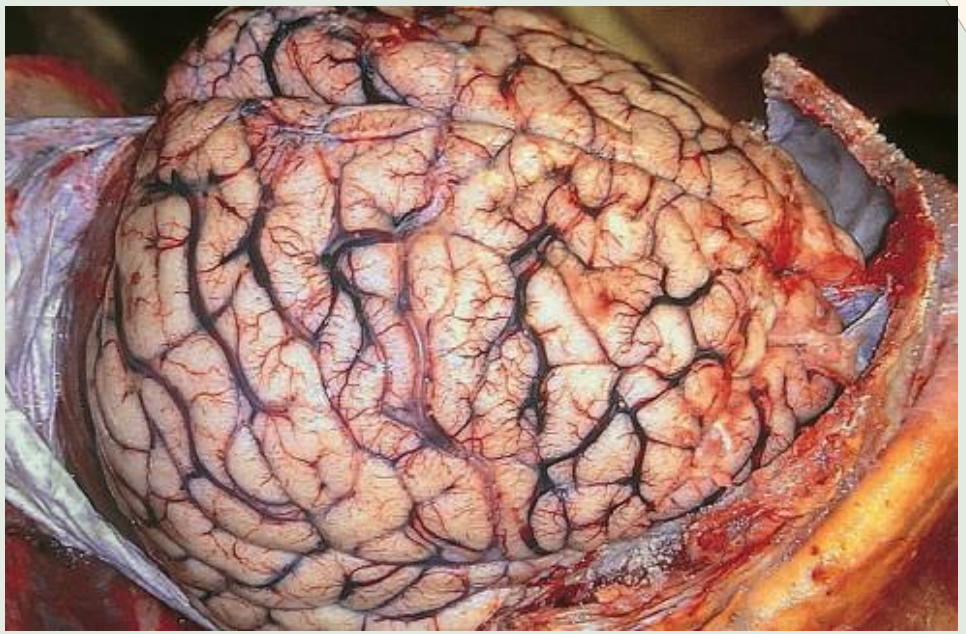
Cerebral Edema

The accumulation of excess fluid within the brain parenchyma.
There are two types, which often occur together, particularly after generalized injury.

• Vasogenic edema occurs when the integrity of the normal blood-brain barrier is disrupted, allowing fluid to shift from the vascular compartment into the extracellular spaces of the brain.
Vasogenic edema can be localized (e.g., the result of increased vascular permeability due to inflammation or in tumors) or generalized.

• Cytotoxic edema is an increase in intracellular fluid secondary to neuronal and glial cell injury, as might follow generalized hypoxic or ischemic insult or exposure to certain toxins.

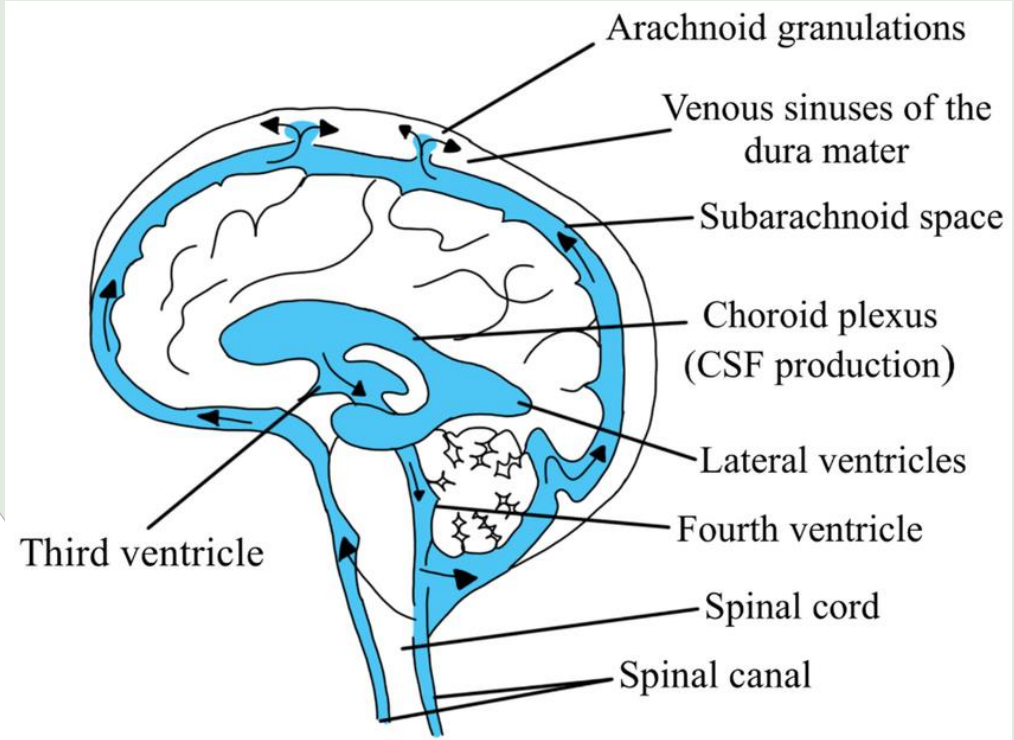


The edematous brain is softer than normal and often appears to “overfill” the cranial vault. In generalized edema, the gyri are flattened, the intervening sulci are narrowed, and the ventricular cavities are compressed

The surfaces of the gyri are flattened as a result of compression of the expanding brain by the dura mater and inner surface of the skull..

Hydrocephalus

- CSF: produced by the choroid plexus in ventricles→ circulates through the ventricular system → flows through the foramina of Luschka and Magendie into the subarachnoid space → absorbed by arachnoid granulations.→ venus sinuses
- The balance between rates of generationand resorption regulates CSF volume.
- **Hydrocephalus** an increase in the volume of the CSF within the ventricular system.
- A disorder most often is a consequence of impaired flow or decreased resorption of CSF

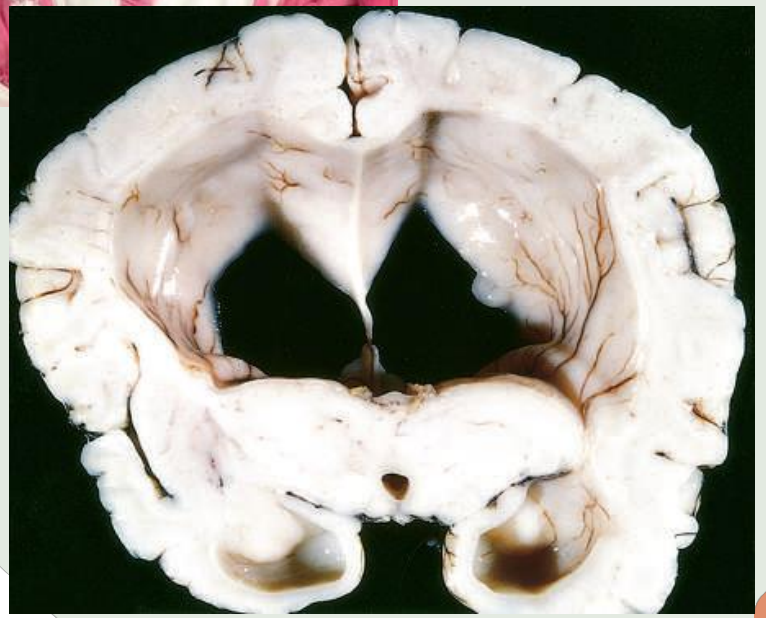


DOI: 10.3390/biomedicines11051461

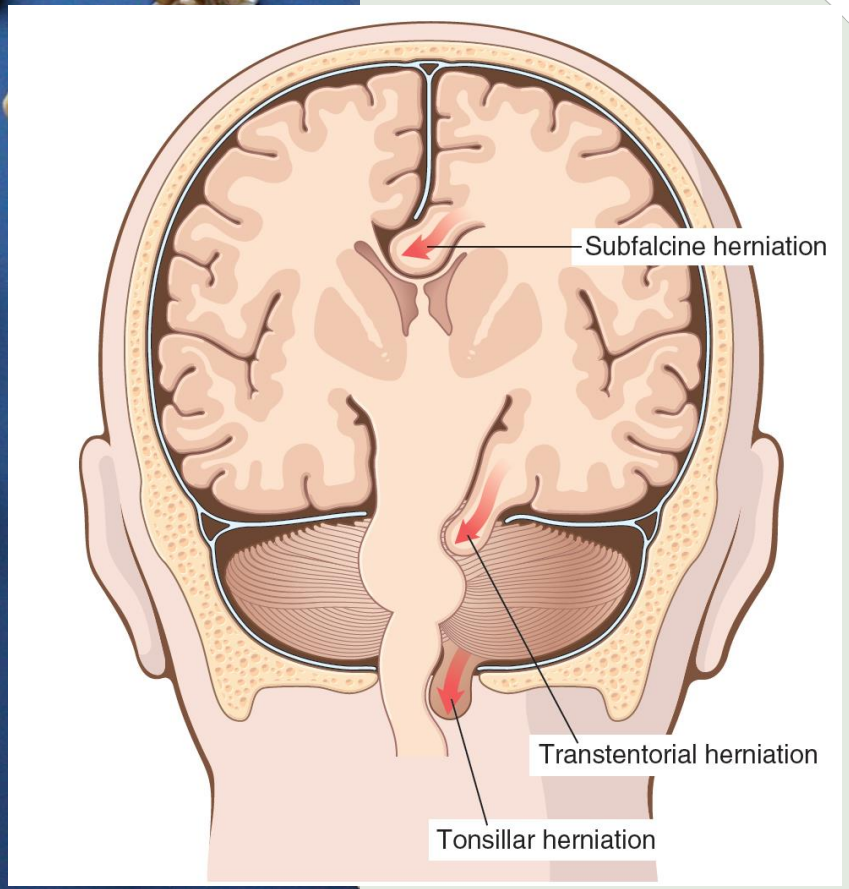
Hydrocephalus

- Noncommunicating hydrocephalus: caused by a localized obstacle to CSF flow within the ventricular system, then a portion of the ventricles enlarges while the remainder does not.
- Most commonly is caused by masses obstructing the foramen of Monro or compressing the cerebral aqueduct.
- Communicating hydrocephalus: the entire ventricular system is enlarged; it is usually caused by reduced CSF resorption (subarachnoid hemorrhage, infection, trauma, tumor, surgery etc)

- If Hydrocephalus developing in infancy before closure of cranial sutures, the head enlarges.
- Once the sutures fuse, hydrocephalus causes ventricular expansion & increased intracranial pressure, but no change in head circumference.

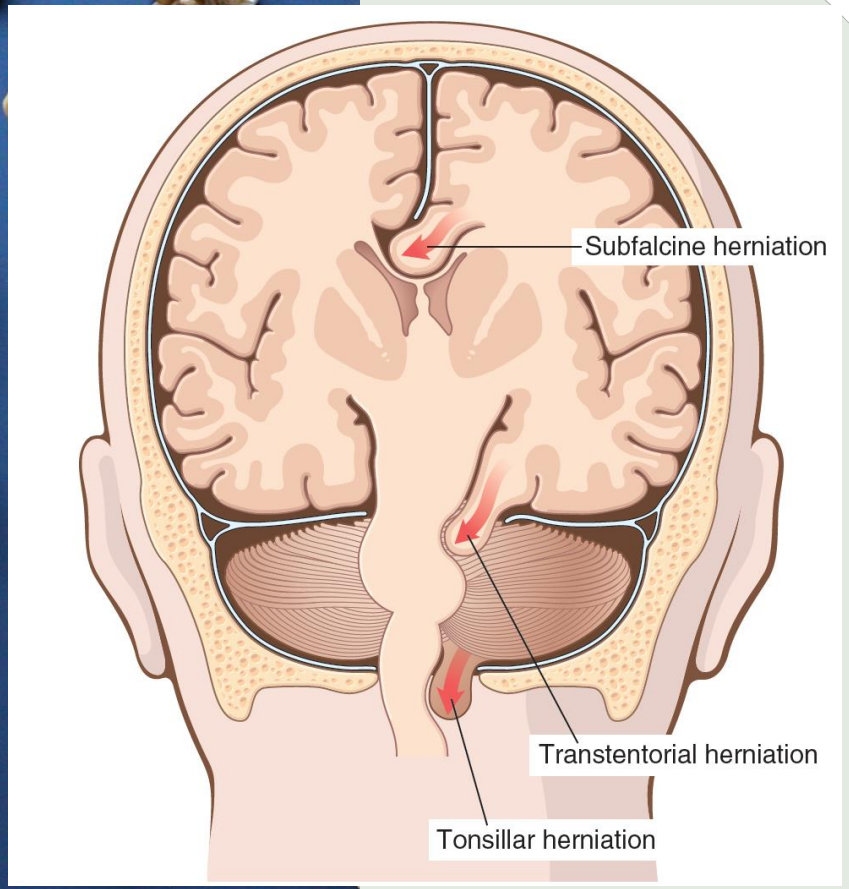


Herniation



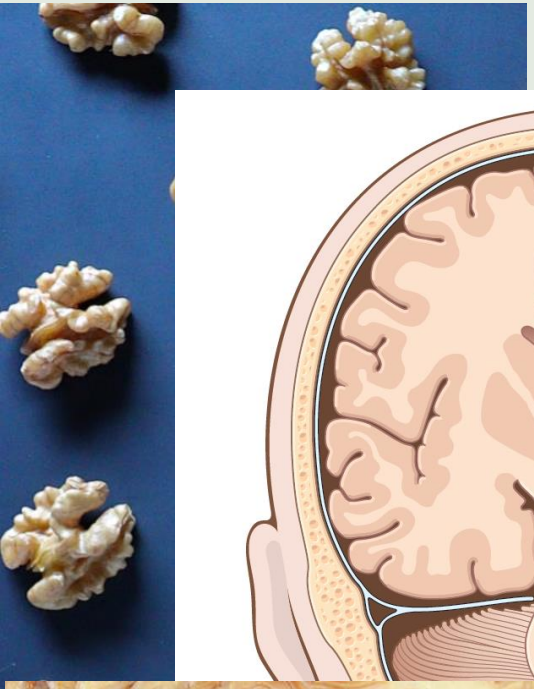
- **Herniation** is the displacement of brain tissue from one compartment to another in response to increased intracranial pressure.
- The intra-cranial compartment is divided by rigid dural folds (falx and tentorium).
- If the pressure is sufficiently high, portions of the brain are displaced across these rigid structures.
- Herniation often leads to compromise of the blood supply to compressed tissue, producing infarction, additional swelling, and further herniation.

Herniation



• *Subfalcine (cingulate) herniation:* a unilateral or asymmetric expansion of a cerebral hemisphere displaces the cingulate gyrus under the edge of the falx.
This may compress the anterior cerebral artery.

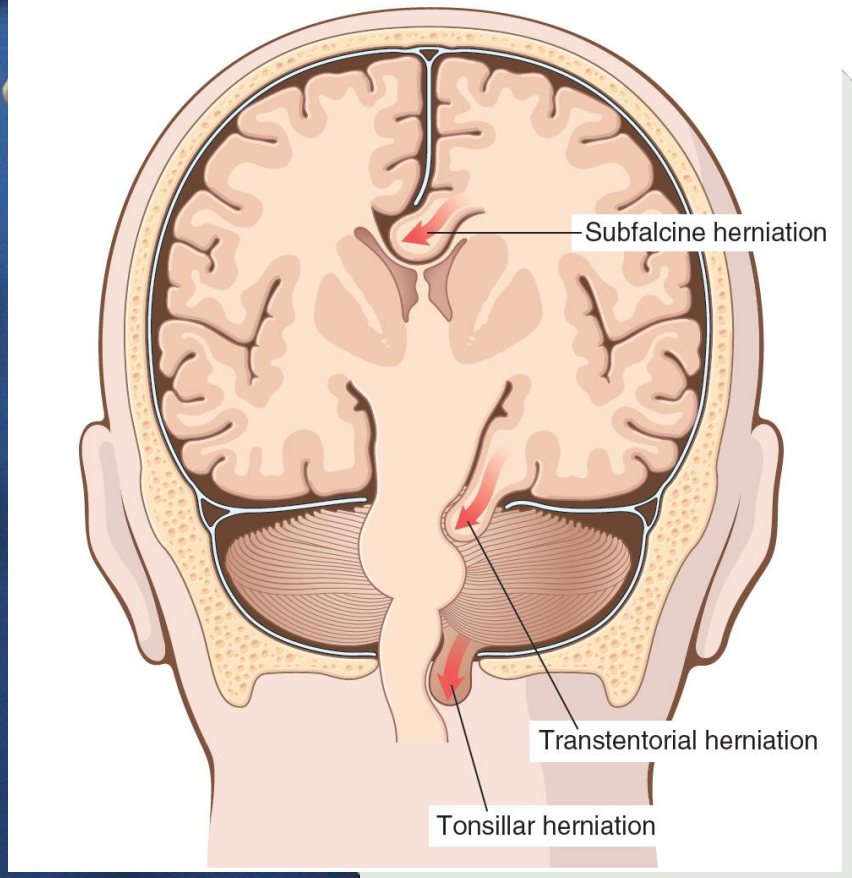
Herniation



• *Transtentorial (uncinate) herniation:* the medial aspect of the temporal lobe is compressed against the free margin of the tentorium. As the temporal lobe is displaced.

- 3rd cranial nerve is compromised → pupillary dilation & impaired ocular movements on the side of the lesion.
- Posterior cerebral artery may be compressed→ ischemic injury to primary visual cortex.
- Further displacement of temporal lobe, pressure on the midbrain→ compress the contralateral cerebral peduncle against the tentorium → hemiparesis ipsilateral side of the herniation.
- Compression of the midbrain and the ascending reticular activating system → depressed consciousness.
- Progression of herniation → tearing of penetrating veins & arteries supplying the upper brain stem → linear or flame-shaped hemorrhages in the midbrain and pons, termed **Duret hemorrhage**

Herniation



• *Tonsillar herniation* refers to displacement of the cerebellar tonsils through the foramen magnum. This type of herniation causes brain stem compression and compromises vital respiratory and cardiac centers in the medulla and **is often fatal.**

CEREBROVASCULAR DISEASES

Brain disorders caused by pathologic processes involving blood vessels.
A major cause of death in the developed world and are the most prevalent cause of neurologic morbidity.

three main mechanisms:
(1) thrombotic Occlusion
(2) embolic occlusion
(3) vascular rupture

Stroke is the clinical designation applied to all of these conditions when symptoms begin **acutely**

A. Thrombosis and embolism have similar consequences → Hypoxia, ischemia and infarction
B. vascular rupture → Hemorrhage → direct tissue damage as well as secondary ischemic injury

Hypoxia, Ischemia, and Infarction

- The brain is a highly oxygen-dependent tissue that requires a continual supply of glucose and oxygen from the blood.
- Receives 15% of the resting cardiac output & responsible for 20% of total body oxygen consumption.
- Cerebral blood flow normally remains stable over a wide range of blood pressure and intracranial pressure because of autoregulation of vascular resistance.
- The brain may be deprived of oxygen by two general mechanisms:

1. **Functional hypoxia**, caused by a low partial pressure of oxygen (e.g., high altitude), impaired oxygen-carrying capacity (e.g., severe anemia, carbon monoxide poisoning), or toxins that interfere with oxygen use (e.g.,cyanide poisoning)
2. **Ischemia, either transient or permanent**, due to tissue hypoperfusion, which can be caused by hypotension, vascular obstruction, or both.

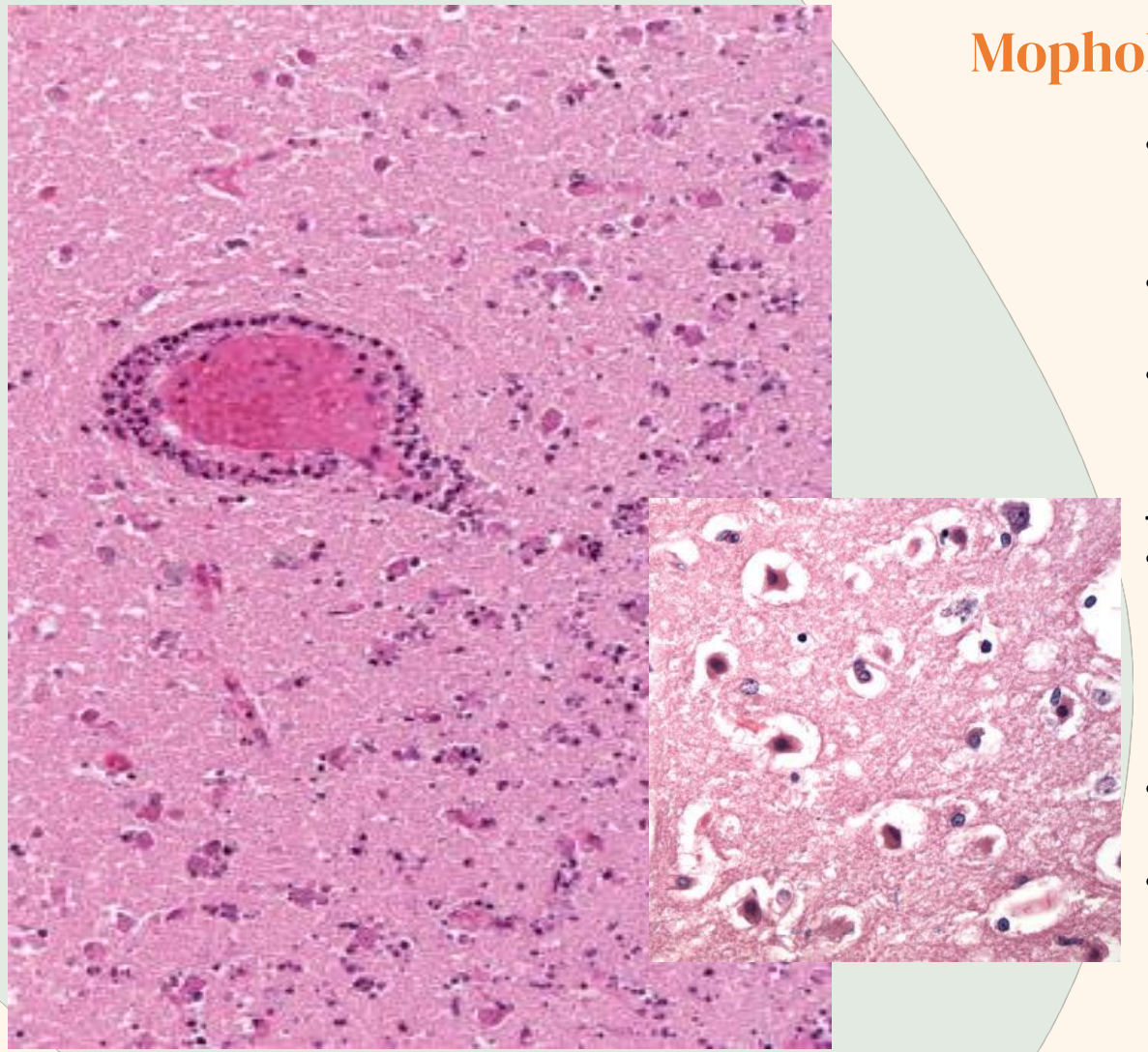
Global Cerebral Ischemia

- Widespread ischemic-hypoxic injury can occur in the setting of severe systemic hypotension, usually when systolic pressures fall below 50 mm Hg, as in cardiac arrest and shock.
- The clinical outcome varies with the severity and duration of the insult.
- **When the insult is mild**, there may be only a transient postischemic confusional state, with eventual complete recovery.

Neurons are more susceptible to hypoxic injury than are glial cell, the most susceptible neurons are:
- the pyramidal cells of the hippocampus and neocortex.
- Purkinje cells of the cerebellum.
- in some individuals, even mild or transient global ischemic insults may cause damage to these vulnerable areas.

Global Cerebral Ischemia

- In severe global cerebral ischemia, widespread neuronal death occurs irrespective of regional vulnerability.
- Patients who survive often remain severely impaired neurologically and in a persistent vegetative state.
- Other patients meet the clinical criteria for so-called “brain death,” in which all voluntary and reflex brain and brain stem function is absent including respiratory drive.
- When patients with this form of irreversible injury are maintained on mechanical ventilation,the brain gradually undergoes autolysis



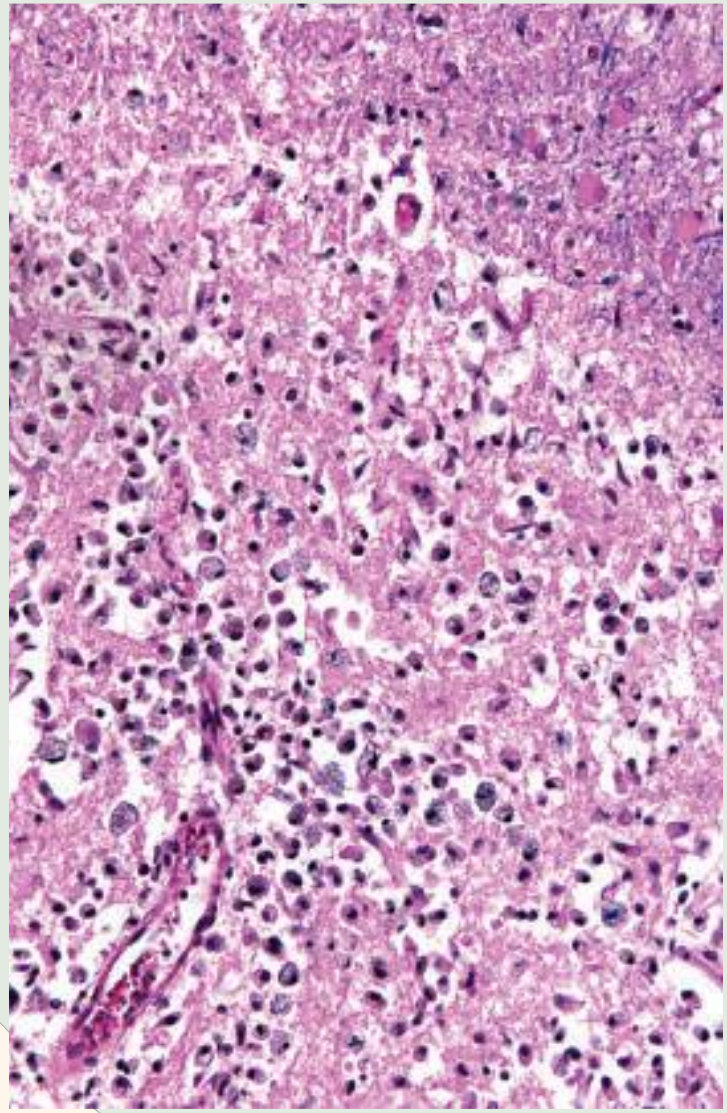
Mophology:

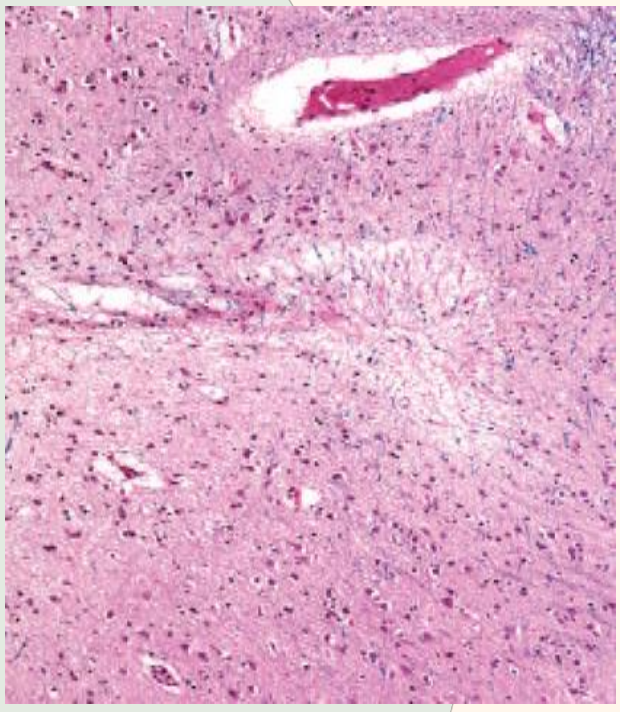
- Gross: In the setting of global ischemia, the brain is swollen, with wide gyri and narrowed sulci.
- Cut surface shows poor demarcation between gray matter & white matter.
- Microscopic changes in irreversible ischemic injury (infarction) are grouped into three categories:

- Early changes, 12 to 24 Hrs after insult:

- acute neuronal cell change (red neurons) characterized initially by microvacuolation → cytoplasmic eosinophilia, and later nuclear pyknosis and karyorrhexis.
- Similar changes occur somewhat later in astrocytes and oligodendroglia.
- After this, reaction to tissue damage begins with infiltration of neutrophils

Mophology:

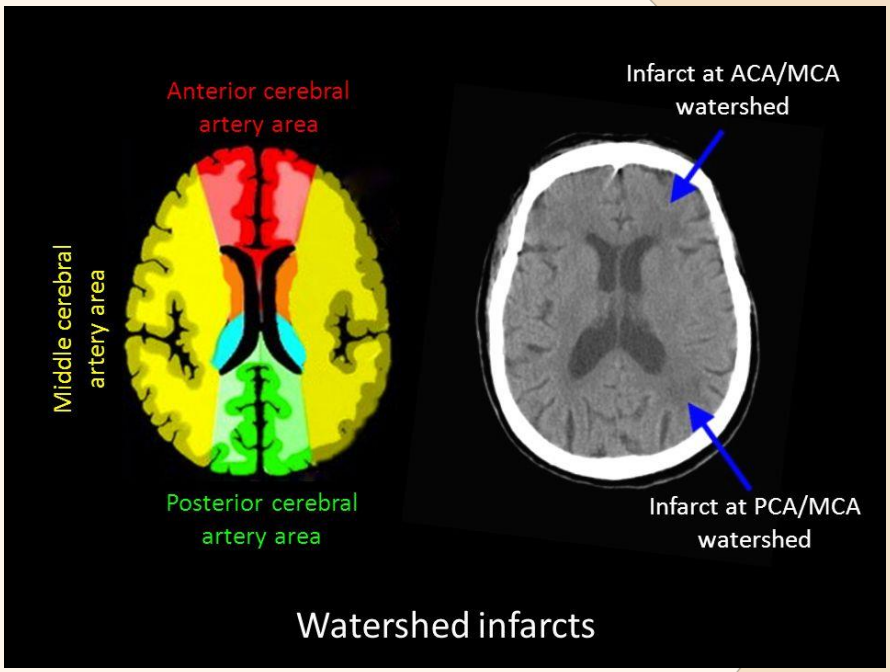




- **Subacute changes,** 24 Hrs – 2 weeks, include necrosis of tissue, influx of macrophages, vascular proliferation, and reactive gliosis.
- **Repair,** seen after 2 weeks,a is characterized by removal of necrotic tissue & Gliosis.

Border zone ("watershed") infarcts

- Border zone (“watershed”) infarcts occur in regions of the brain and spinal cord that lie at the most distal portions of arterial territories.
- They are usually seen after hypotensive episodes.
- In the cerebral hemispheres, the border zone between the anterior and the middle cerebral artery distributions is at greatest risk.
- Damage to this region produces a wedge-shaped band of necrosis over the cerebral convexity a few centimeters lateral to the interhemispheric fissure.



Focal Cerebral Ischemia

- Cerebral arterial occlusion leads first to focal ischemia and then to infarction in the distribution of the compromised vessel.
- The size, location, and shape of the infarct and the extent of tissue damage that results may be modified by collateral blood flow. Specifically, collateral flow through :
- The circle of Willis or cortical-leptomeningeal anastomoses can limit damage in some regions.
- By contrast, there is little if any collateral blood flow to structures such as the thalamus, basal ganglia, and deep white matter, which are supplied by deep penetrating vessels

Embolic infarctions

- More common than infarctions due to thrombosis.
- Cardiac mural thrombi are a frequent source of emboli.

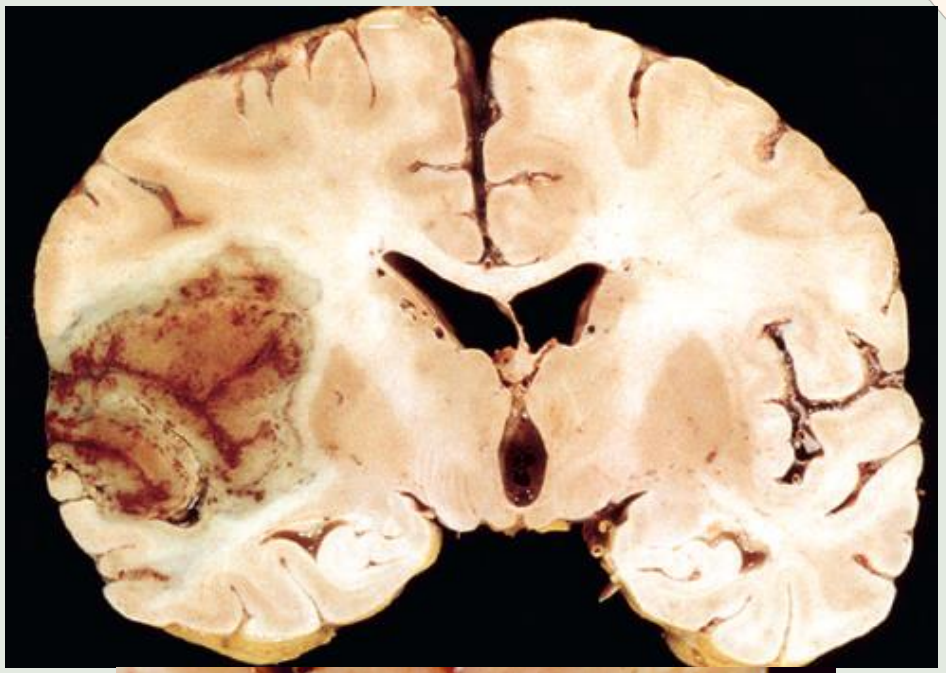
- Myocardial dysfunction, valvular disease,and atrial fibrillation are important predisposing factors.

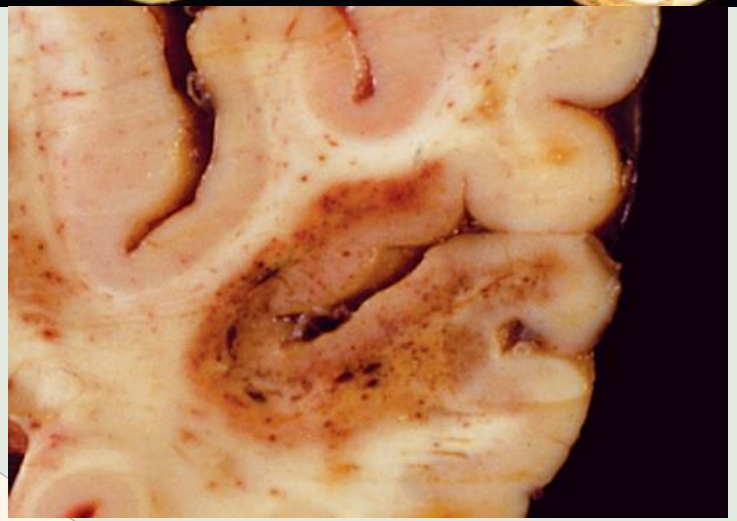
- Thromboemboli also arise in arteries, most often from atheromatous plaques in the carotid arteries or aortic arch.
- The territory of the middle cerebral artery, a direct extension of the internal carotid artery, **is most frequently affected by embolic infarction**.
- Emboli tend to lodge where vessels branch or in areas of stenosis, usually caused by atherosclerosis.

Thrombotic occlusions

- Thrombotic occlusions causing cerebral infarctions usually are superimposed on atherosclerotic plaques.
- **Common sites are the carotid bifurcation, the origin of the middle cerebral artery, and either end of the basilar artery.**
- These occlusions may be accompanied by anterograde extension, as well as thrombus fragmentation and distal embolization.
- Thrombotic occlusions causing small infarcts of only a few millimeters in diameter, so-called “lacunar infarcts,”

- occur when small penetrating arteries occlude due to chronic damage, usually from long-standing hypertension

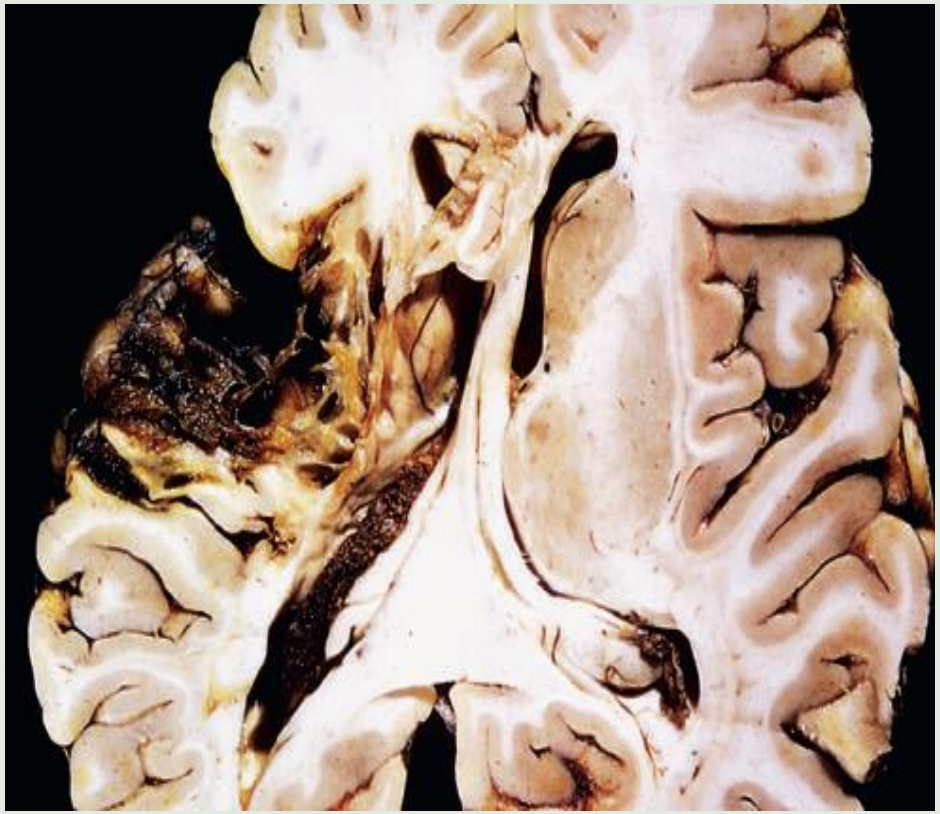




Infarcts can be divided into two broad groups .

1. Nonhemorrhagic infarcts: result from acute vascular occlusions
2. Hemorrhagic infarcts: There is reperfusion of ischemic tissue, either through collaterals or after dissolution of emboli

- Hemorrhagic infarcts usually manifest as multiple, sometimes confluent, petechial
- The microscopic picture & evolution of hemorrhagic infarction parallel those of ischemic infarction, with the addition of blood extravasation & resorption.



The macroscopic appearance of a nonhemorrhagic infarct evolves over time:

- During the first 6 hours, the tissue is unchanged.
- By 48 hours, the tissue becomes pale, soft, & swollen.
- From days 2 to 10, the injured brain turns gelatinous & friable, and the boundary between normal and abnormal tissue becomes more distinct as edema resolves in the adjacent viable tissue.
- From day 10 to week 3, the tissue liquefies, eventually leaving a fluid-filled cavity, which gradually expands as dead tissue is resorbed

Intracranial Hemorrhage

Hemorrhages within the brain are caused by:
(1) Hypertension & other diseases leading to vascular wall injury.
(2) structural lesions such as arteriovenous and cavernous malformations
(3) tumors.

- Subarachnoid hemorrhages most commonly are the result of ruptured aneurysms but also occur with other vascular malformations.
- Subdural or epidural hemorrhages usually are associated with trauma.

Primary Brain Parenchymal Hemorrhage

- Spontaneous (nontraumatic) intraparenchymal hemorrhages are most common in mid to late adult life.
- Most are due to the rupture of a small intraparenchymal vessel.
- Hypertension is the leading underlying cause, and brain hemorrhage accounts for roughly 15% of deaths among individuals with chronic hypertension.
- Intracerebral hemorrhage can be clinically devastating when it affects large portions of the brain or extends into the ventricular system.
- Alternatively, it can affect small regions and be clinically silent.
- Hypertensive intraparenchymal hemorrhages typically occur in the basal ganglia, thalamus, pons, and cerebellum

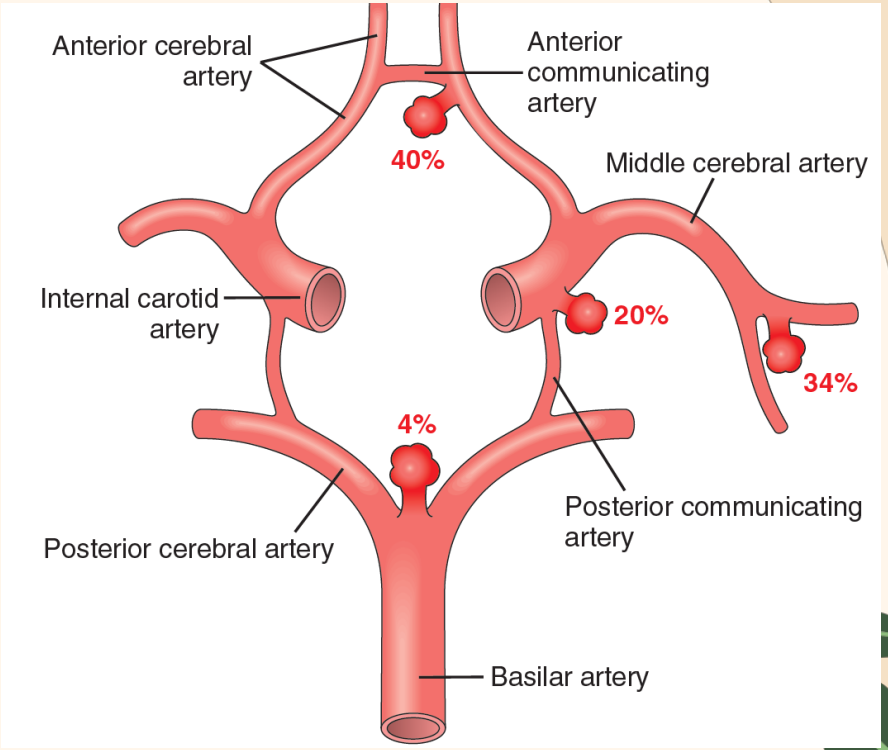
Primary Brain Parenchymal Hemorrhage

Subarachnoid Hemorrhage and Saccular Aneurysms

- The most frequent cause of clinically significant non-traumatic subarachnoid hemorrhage is rupture of a saccular(berry) aneurysm.
- Hemorrhage into the subarachnoid space also may result from vascular malformation, trauma, rupture of an intracerebral hemorrhage into the ventricular system, coagulopathies, and tumors.
- In about one-third of cases, rupture of a saccular aneurysm occurs at the time of an acute increase in intracranial pressure.
- Blood under arterial pressure is forced into the subarachnoid space, and the patient is stricken with sudden, excruciating headache (known as a thunderclap headache, often described as “the worst headache I’ve ever had”) and rapidly loses consciousness.
- Between 25% and 50% of affected individuals die from the first bleed, and recurrent bleeds are common in survivor

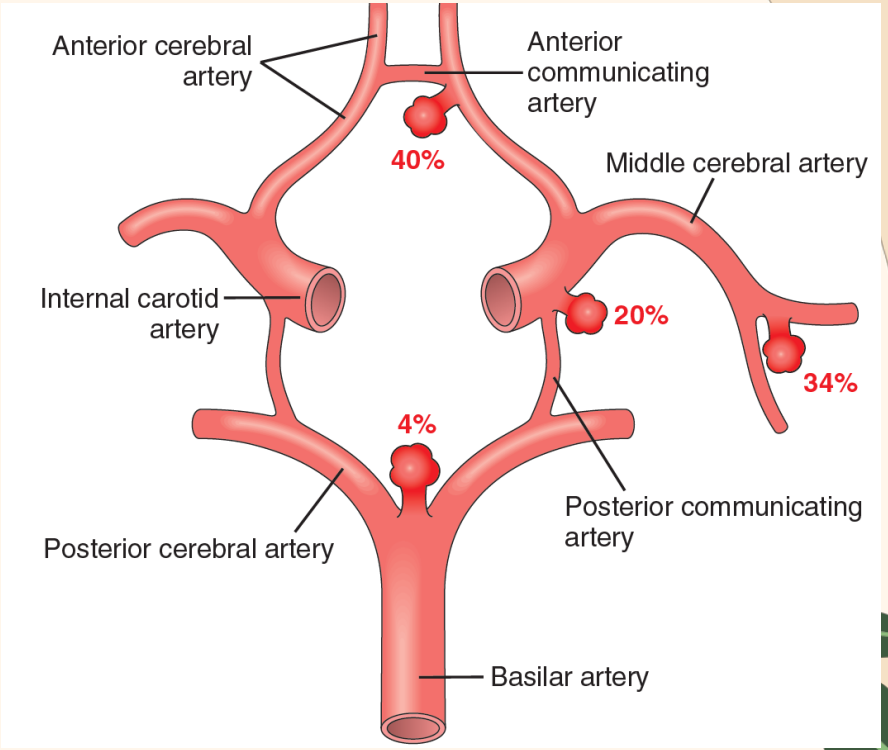
Subarachnoid Hemorrhage and Saccular Aneurysms

- ~ 90% of saccular aneurysms occur in the anterior circulation near major arterial branch points. Multiple aneurysms exist in 20% to 30% of cases.
- The aneurysms are not present at birth but develop over time because of underlying defects in the vessel media.
- Increased risk for aneurysms in patients with autosomal dominant polycystic kidney disease &genetic disorders of extracellular matrix proteins (e.g., Ehler-Danlos syndrome).



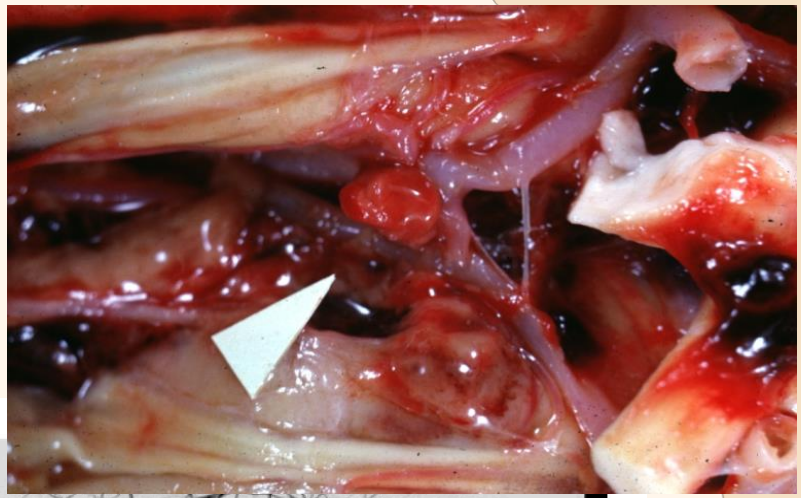
Subarachnoid Hemorrhage and Saccular Aneurysms

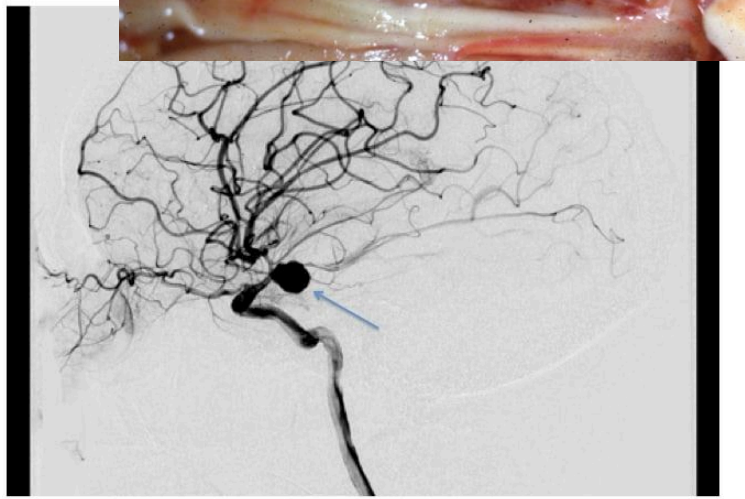
- Overall, roughly 1.3% of aneurysms bleed per year, with the probability of rupture increasing with size; larger than 1 cm in diameter have a roughly 50% risk for bleeding per year.
- In the early period after a subarachnoid hemorrhage, there is an additional risk for ischemic injury from vasospasm of other vessels.
- Healing andthe attendant meningeal fibrosis and scarring sometimes obstruct CSF flow or disrupt CSF resorption, leading to hydrocephalus.



Subarachnoid Hemorrhage and Saccular Aneurysms

- A saccular aneurysm is a thin-walled outpouching of an artery beyond the neck of the aneurysm, the muscular wall and intimal elastic lamina are absent, such that the aneurysm sacis lined only by thickened hyalinized intima.
- The adventitia covering the sac is continuous with that of the parent artery.
- Rupture usually occurs at the apex of the sac, releasing blood into the subarachnoid space, the substance of the brain, or both.





Questions?
thanks

EaTemp