Vascular Diseases of the central Nervous System I

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CEREBROVASCULAR DISEASES

- Cerebrovascular diseases denote brain disorders caused by pathologic processes involving the blood vessels
- They are a major cause of death in the developed world and are the most prevalent cause of neurologic morbidity.

- The three main pathogenic mechanisms are:
  1. Thrombotic occlusion of vessels
  2. Embolic occlusion of vessels
  3. Vascular rupture.

- From the standpoint of the pathophysiology and pathologic anatomy, cerebrovascular diseases are divided into two main processes:
  A. Hypoxia, ischemia and infarction
  B. Hemorrhage

CEREBROVASCULAR DISEASES

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

- Thrombosis and embolism have similar consequences for the brain: loss of oxygen and metabolic substrates, resulting in infarction or ischemic injury of regions supplied by the affected vessel.

- Similar injury occurs globally when there is complete loss of perfusion, severe hypoxemia (e.g., hypovolemic shock), or profound hypoglycemia.

- Hemorrhage accompanies rupture of vessels and leads to direct tissue damage as well as secondary ischemic injury.

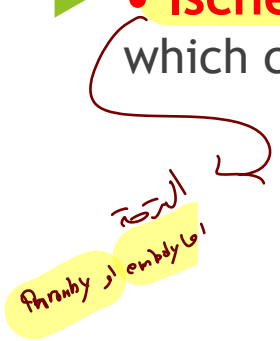
Hypoxia, Ischemia, and Infarction

- The brain is a highly oxygen-dependent tissue that requires a continual supply of glucose and oxygen from the blood.
- Although it constitutes no more than 2% of body weight, the brain receives 15% of the resting cardiac output and is 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.

Hypoxia, Ischemia, and Infarction

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

- • **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)
- • **Ischemia**, either transient or permanent, due to tissue hypoperfusion, which can be caused by hypotension,vascular obstruction, or both



Clinically

1. Stroke :

Is the clinical designation applied to:

a. Abrupt onset of focal or global neurological Symptoms.

b. Ischemia or hemorrhage.

c. The symptoms must continue for more than 24 hours.

d. There should be permanent damage to the brain.

2. Transient ischemic attack(TIA):

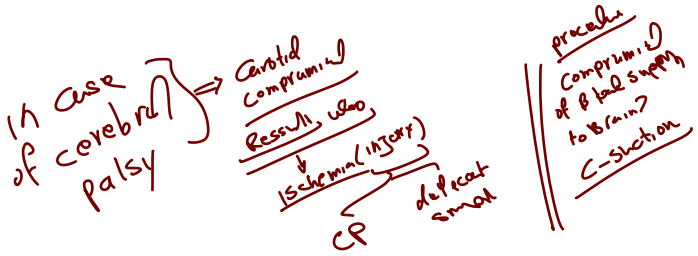
a. The neurologic symptoms resolve within 24 hours

b. No irreversible tissue damage

c. The cause is small emboli from the carotids or vertebrobasilar circulation that resolve before causing irreversible injury

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.



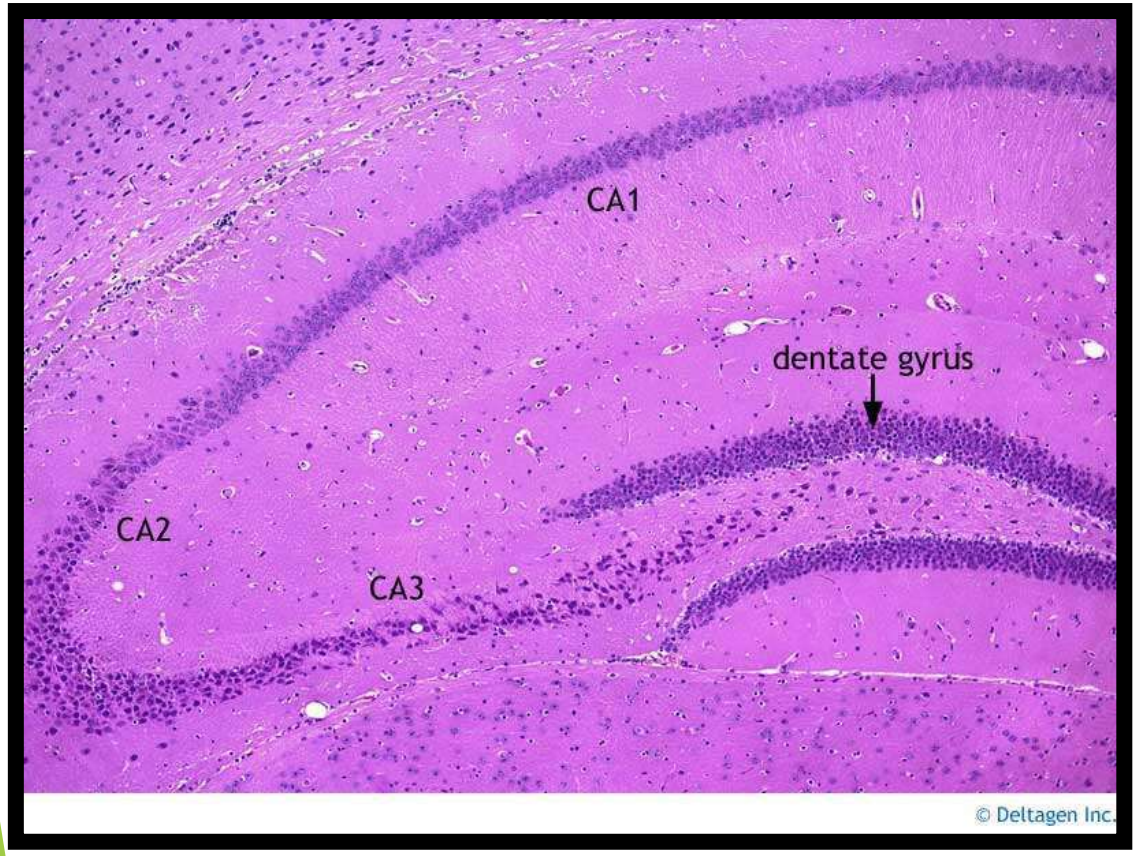
- The most sensitive neurons to transient global ischemia are;

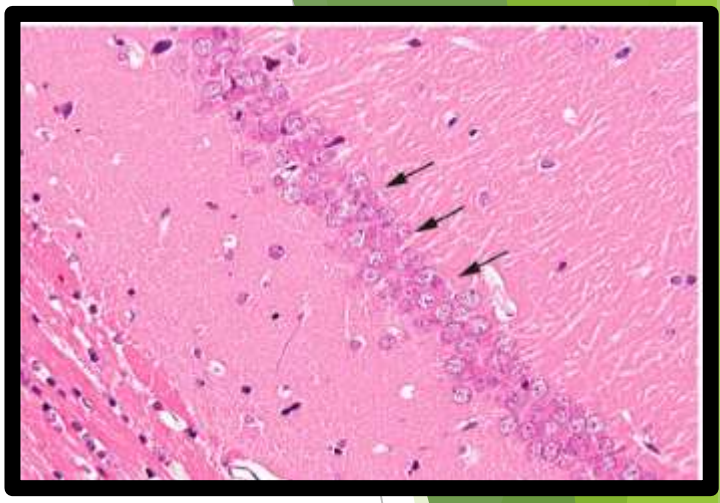
i. The pyramidal cells of the hippocampus (especially) CA1 neurons.

ii. Cerebellar purkinji cells.

iii. Pyramidal neurons in the cerebral cortex produces a pattern called pseudolaminar Necrosis.

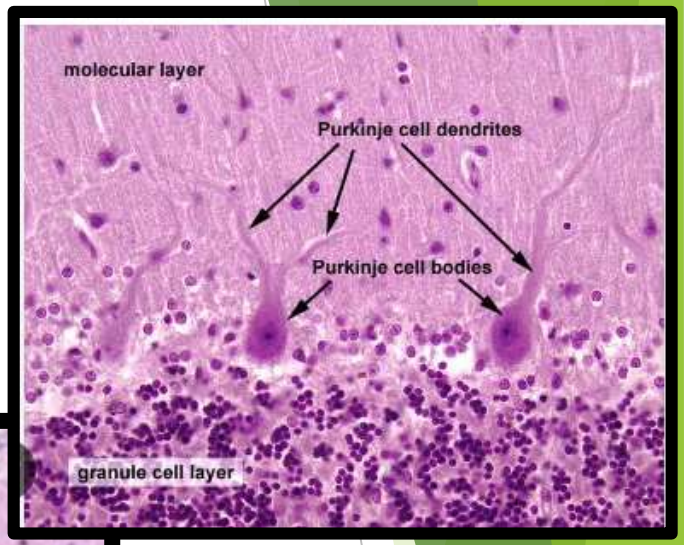
Hippocampus

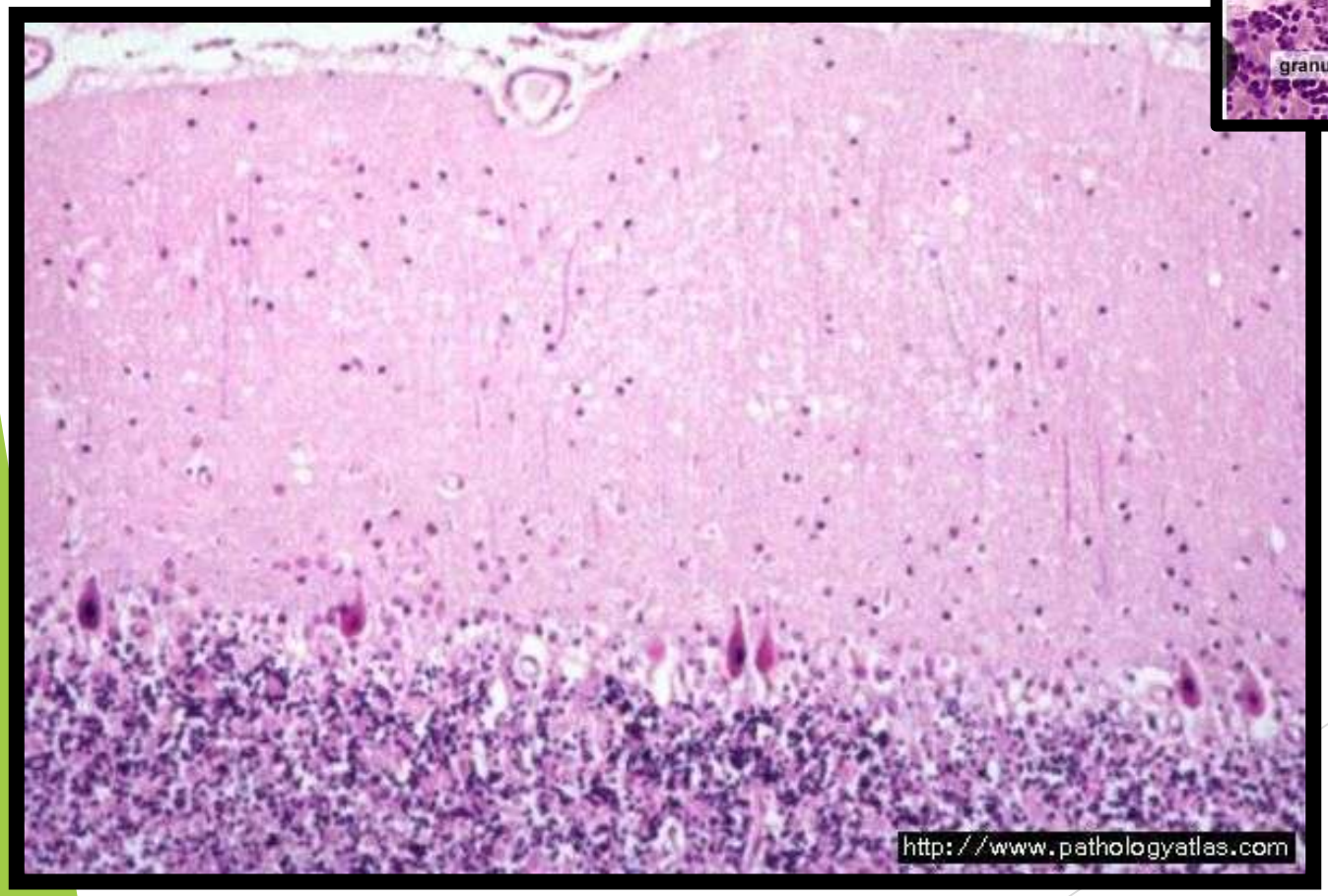




The pyramidal cells

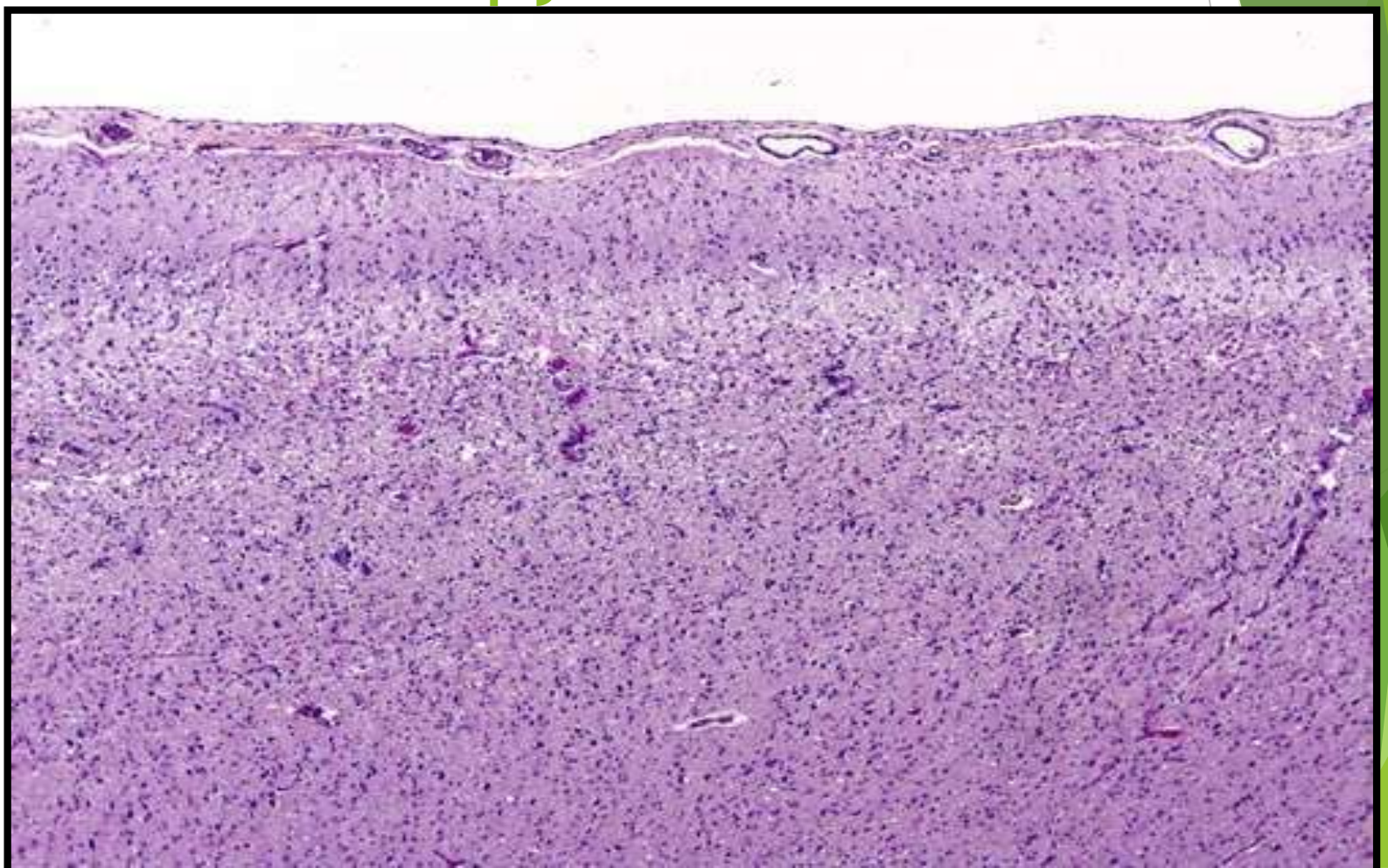
Death of purkinjii cells





Pseudolaminar necrosis

necrosis of pyramidal cells



ii. Brain death

Refractory drugs for BP

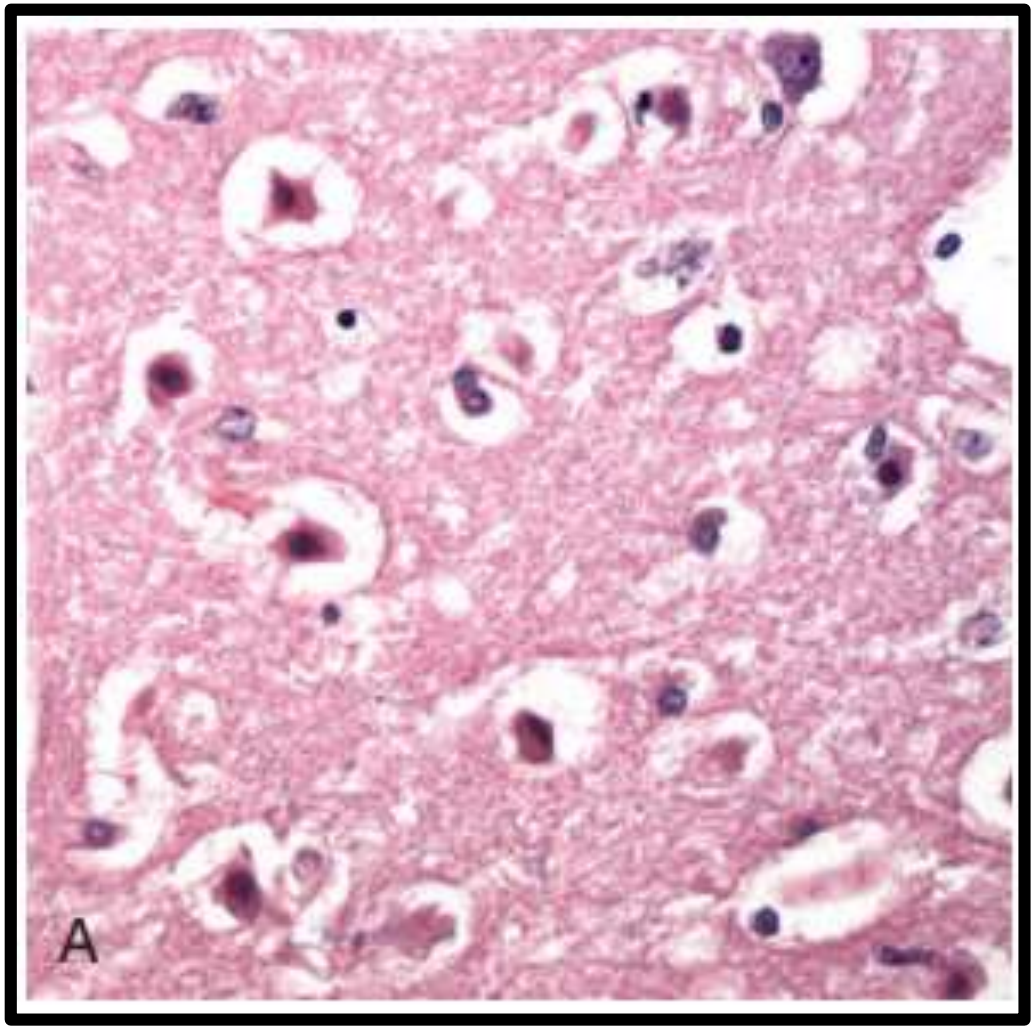
- Other patients meet the clinical criteria for "brain death," including:

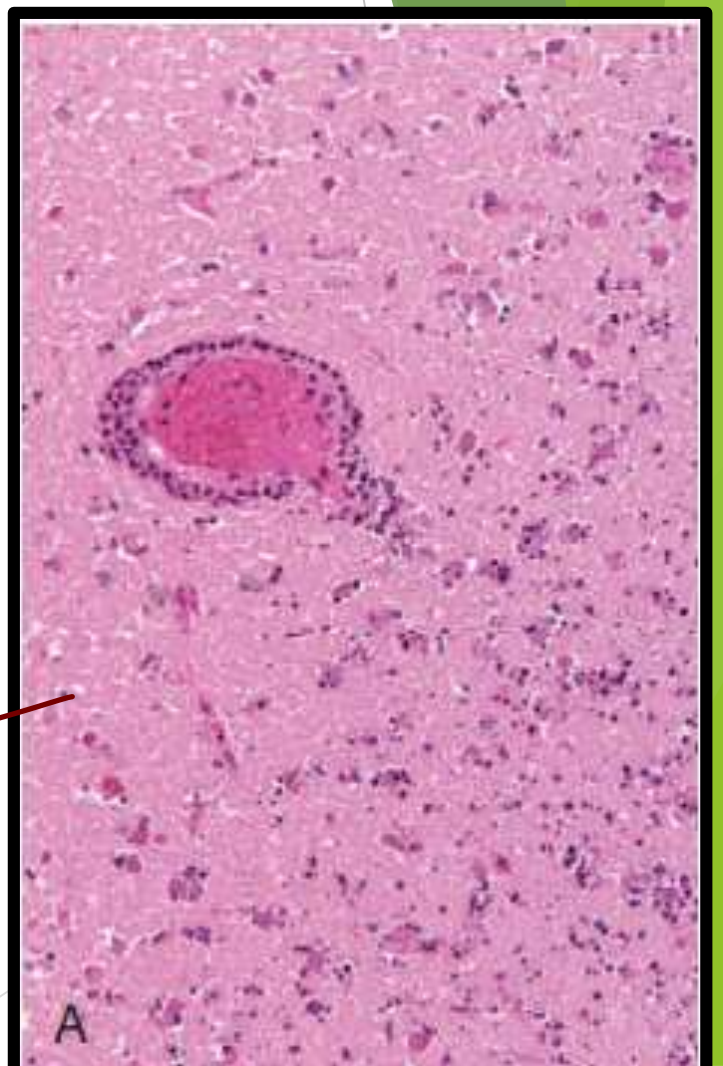
1. Evidence of diffuse cortical injury.(isoelectric, or "flat," electroencephalogram (EEG)

2. And brain stem damage, including absent reflexes and respiratory drive.

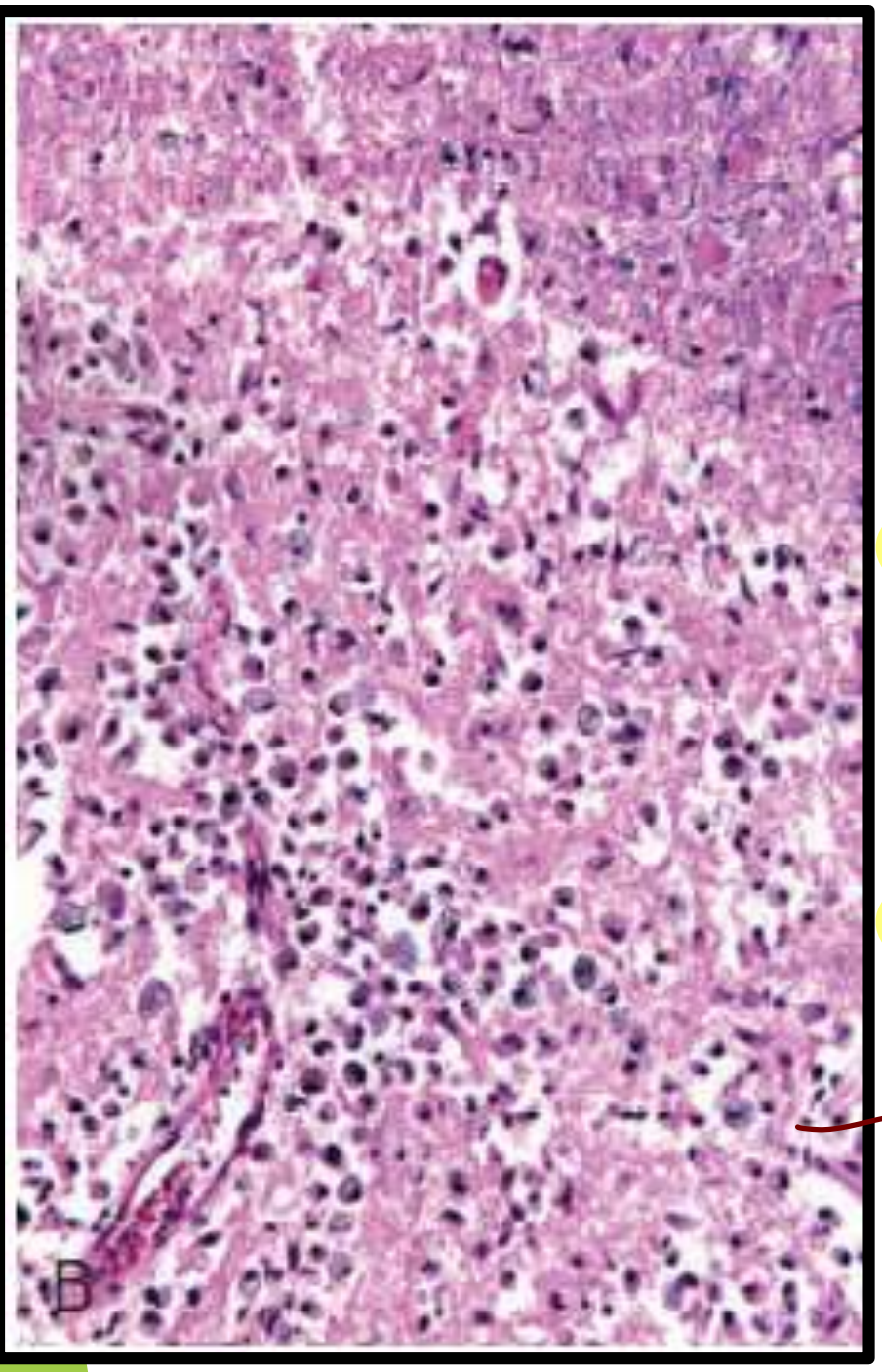
Morphology

- In the setting of global ischemia, the brain is swollen, with wide gyri and narrowed sulci.
- The cut surface shows poor demarcation between gray matter and white matter.
- The histopathologic changes that accompany irreversible ischemic injury (infarction) are grouped into three categories.
- **Early changes**, occurring 12 to 24 hours after the insult, include acute neuronal cell change (red neurons) characterized initially by microvacuolation, followed by cytoplasmic eosinophilia, and later nuclear pyknosis and karyorrhexis.
- Similar changes occur somewhat later in astrocytes and oligodendroglia.
- After this, the reaction to tissue damage begins with infiltration of neutrophils

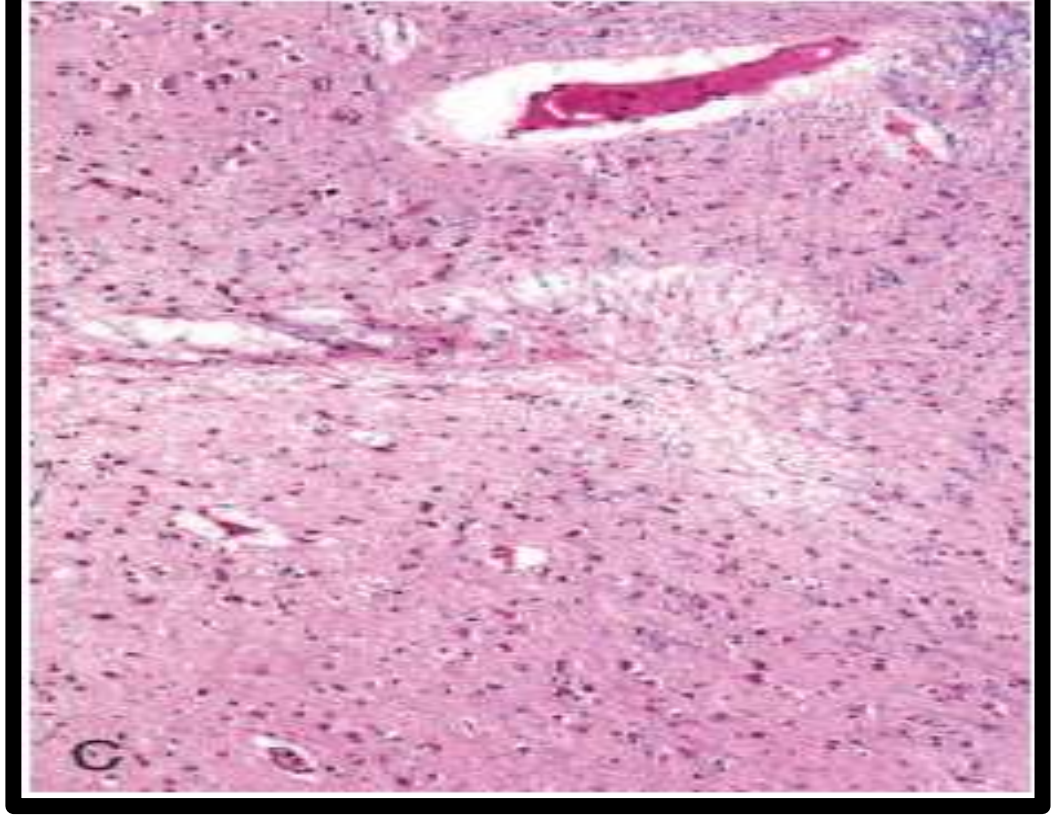




- margination of neutrophils
- to make leukocytes



Subacute changes, occurring at 24 hours to 2 weeks, include necrosis of tissue, influx of macrophages, vascular proliferation, and reactive gliosis).

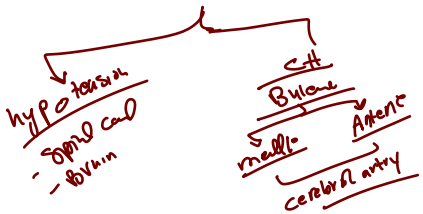


- **Repair,** seen after 2 weeks, is characterized by removal of necrotic tissue and gliosis

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

- 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.
- Deep leg veins and fat emboli, usually following bone trauma.
- Emboli tend to lodge where vessels branch or in areas of stenosis, usually caused by atherosclerosis

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.

- 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

Thrombotic occlusions

- Infarcts can be divided into two broad groups .

1. **Nonhemorrhagic infarcts** result from acute vascular occlusions and may evolve into

2. **Hemorrhagic infarcts :**

There is reperfusion of ischemic tissue, either through collaterals or after dissolution of emboli

Morphology

Hemorrhagic infarcts

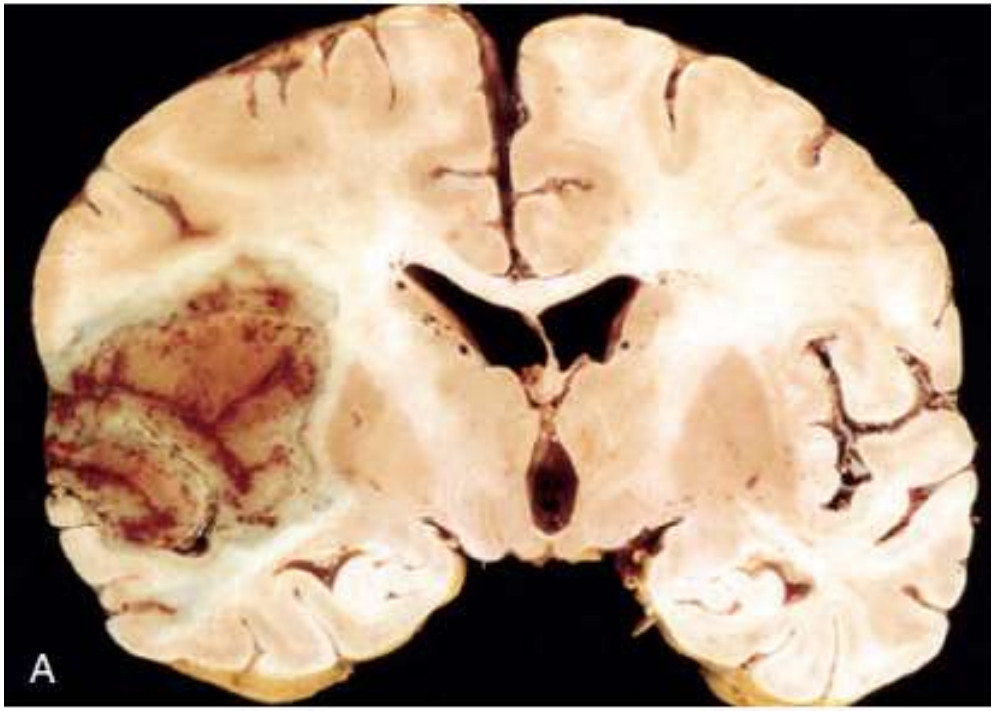
- Usually manifest as multiple,sometimes confluent, petechial hemorrhages .

- The microscopic picture and evolution of hemorrhagic infarction parallel those of ischemic infarction, with the addition of blood extravasation and resorption.

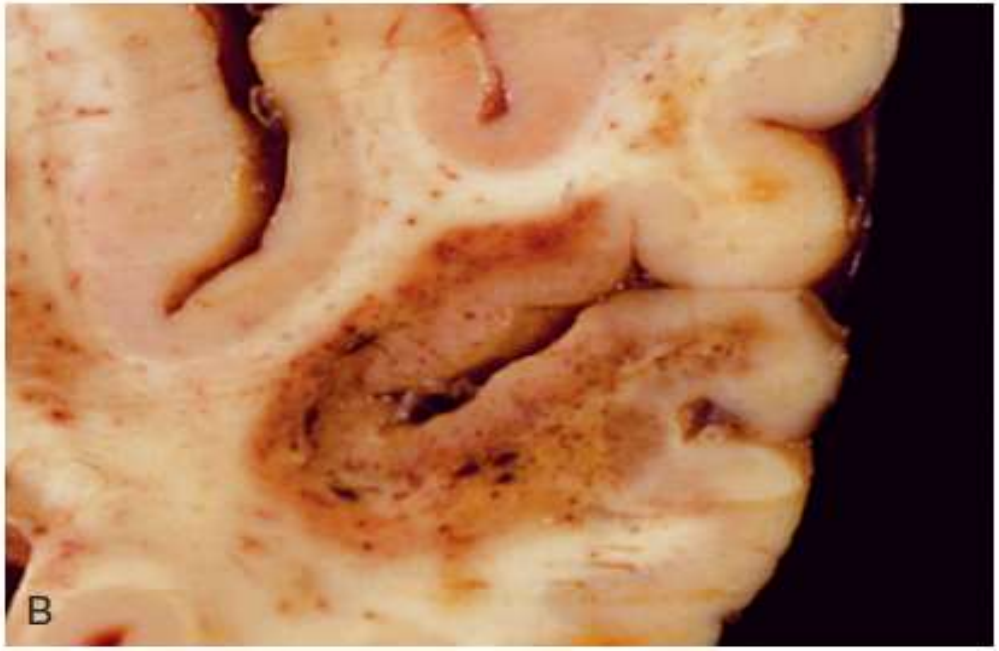
- In individuals with coagulopathies, hemorrhagic infarcts may be associated with extensive intracerebral hematomas.

Morphology
Non-Hemorrhagic infarcts

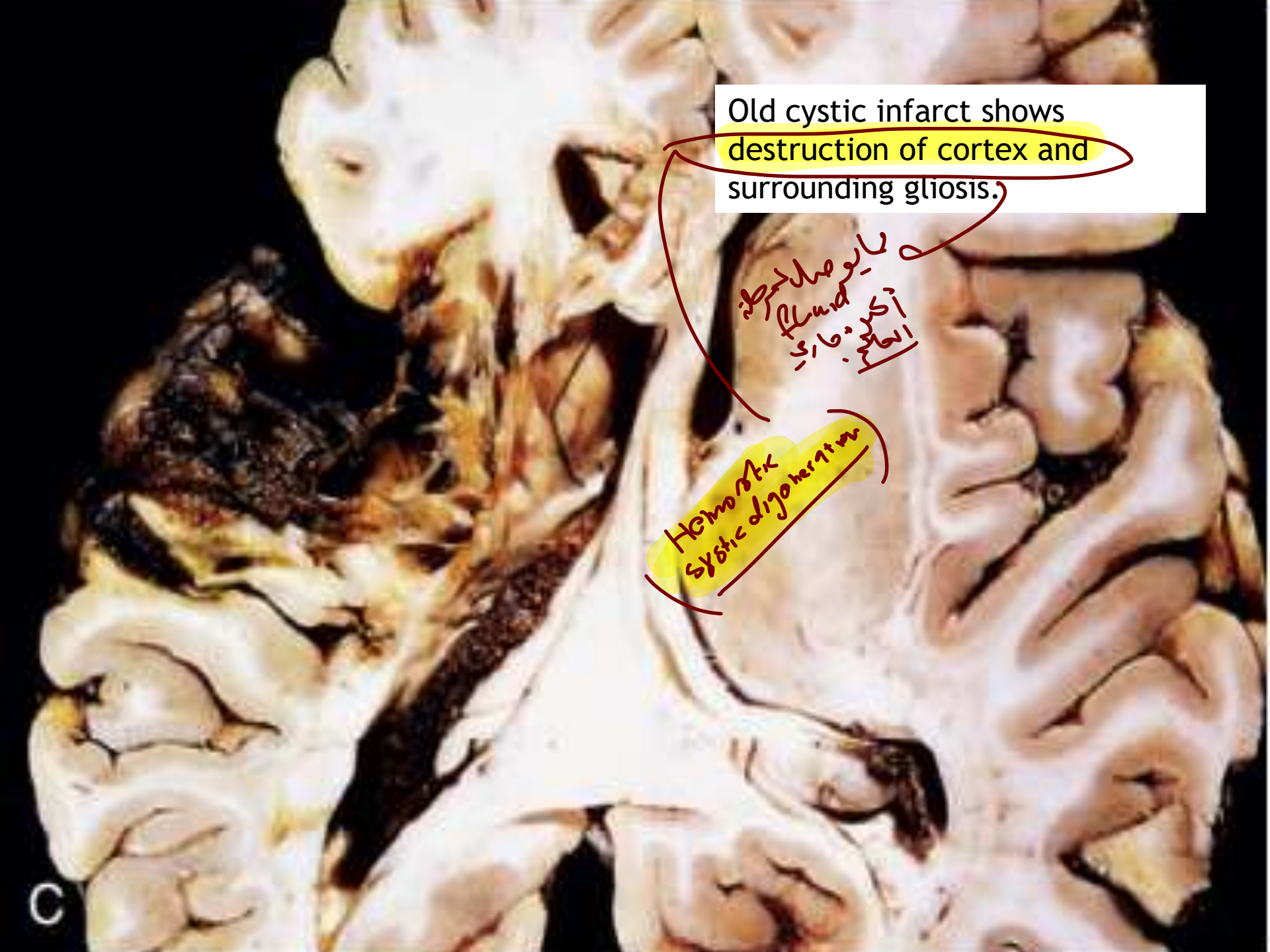
- The macroscopic appearance of a nonhemorrhagic infarct evolves overtime.
- During the first 6 hours, the tissue is unchanged in appearance, but by 48 hours, the tissue becomes pale,soft, and swollen.
- From days 2 to 10, the injured brain turns gelatinous and friable, and the boundary between normal 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



(A) Section of the brain showing a large,discolored, focally hemorrhagic region in the left middle cerebral artery distribution (hemorrhagic, or red, infarction).

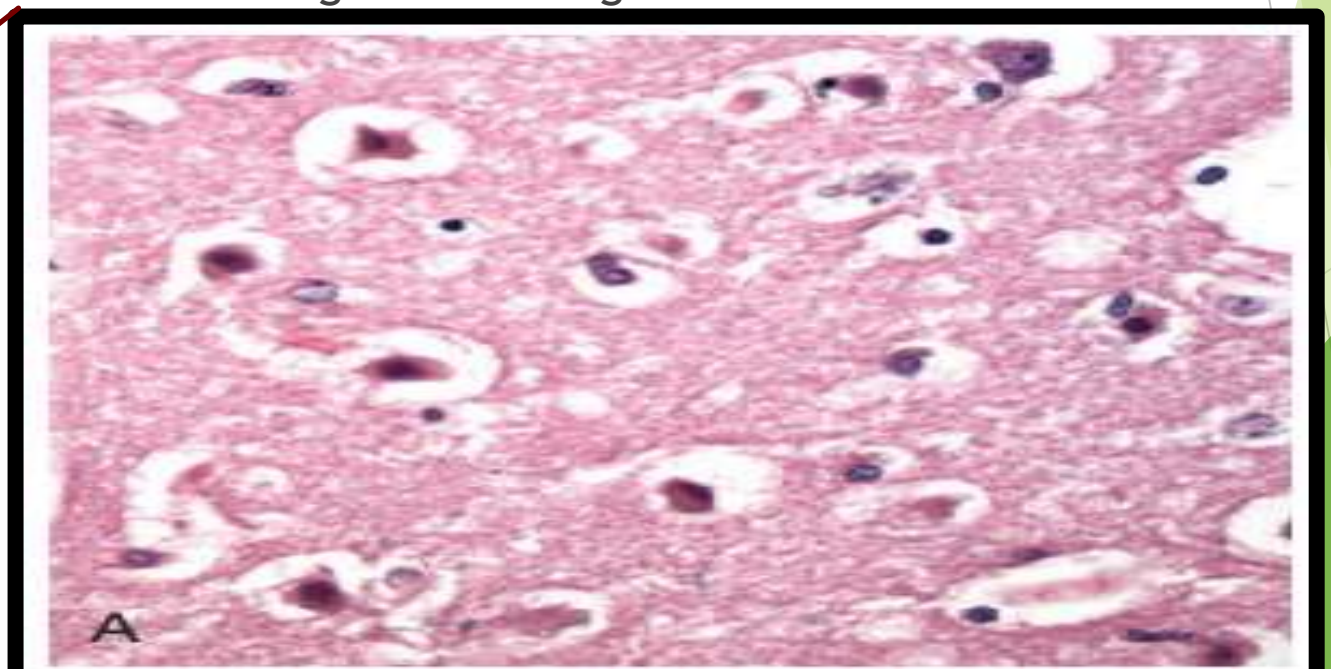


(B) An infarct with punctate hemorrhages, consistent with ischemia-reperfusion injury, is present in the temporal lobe. (


Old cystic infarct shows destruction of cortex and surrounding gliosis.
Hemorrhagic cystic oligodendroglioma
C

Morphology Microscopically

- The tissue reaction follows a characteristic sequence. After the first 12 hours, ischemic neuronal change (red neurons)) and cytotoxic and vasogenic edema appear.
- Endothelial and glial cells, mainly astrocytes, swell, and myelinated fibers begin to disintegrate.



Morphology Microscopically

- During the first several days neutrophils infiltrate the area of injury, but these are replaced over the next 2–3 weeks by macrophages.

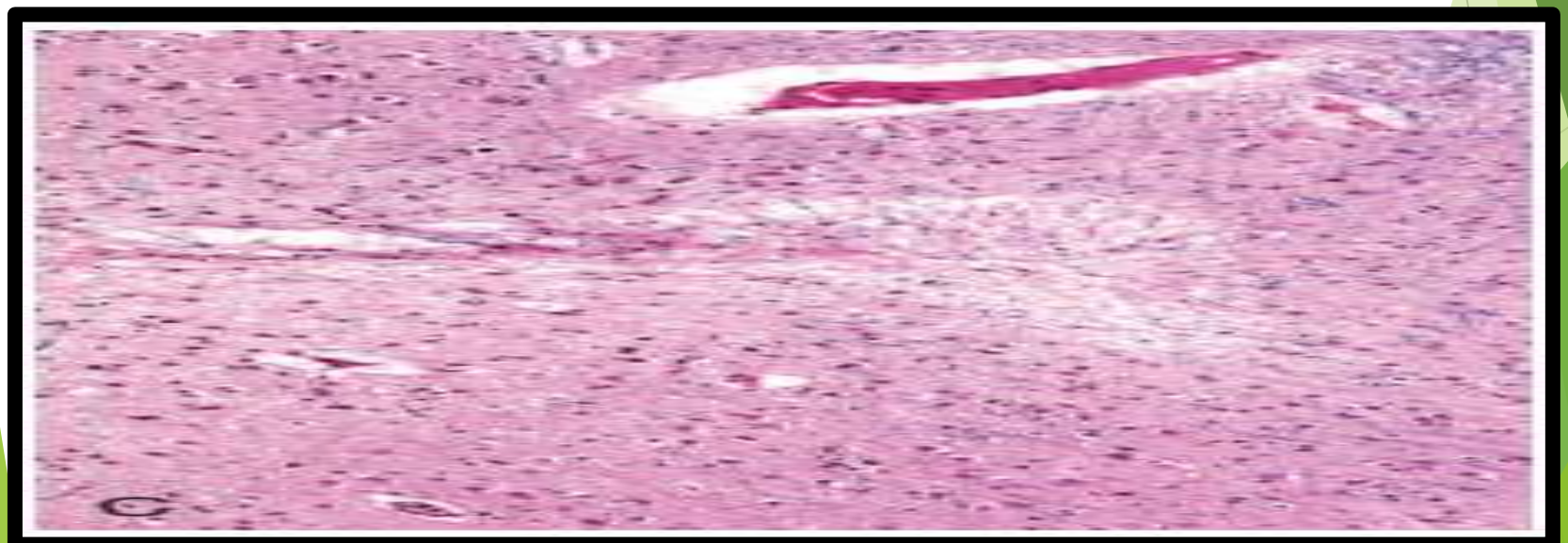
- Macrophages containing myelin or red blood cell breakdown products may persist in the lesion for months to years.

- As the process of phagocytosis and liquefaction proceeds, astrocytes at the edges of the lesion progressively enlarge, divide, and develop a prominent network of cytoplasmic extensions.

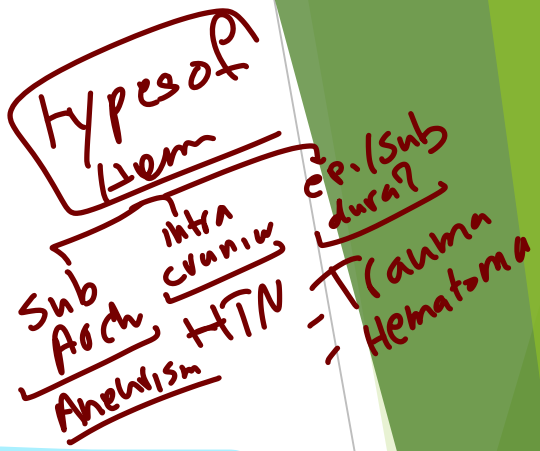
Morphology Microscopically

- After several months, the striking astrocytic nuclear and cytoplasmic enlargement regresses.

- In the wall of the cavity, astrocyte processes form a dense feltwork of glial fibers admixed with new capillaries and a few perivascular connective tissue fibers



Intracranial Hemorrhage



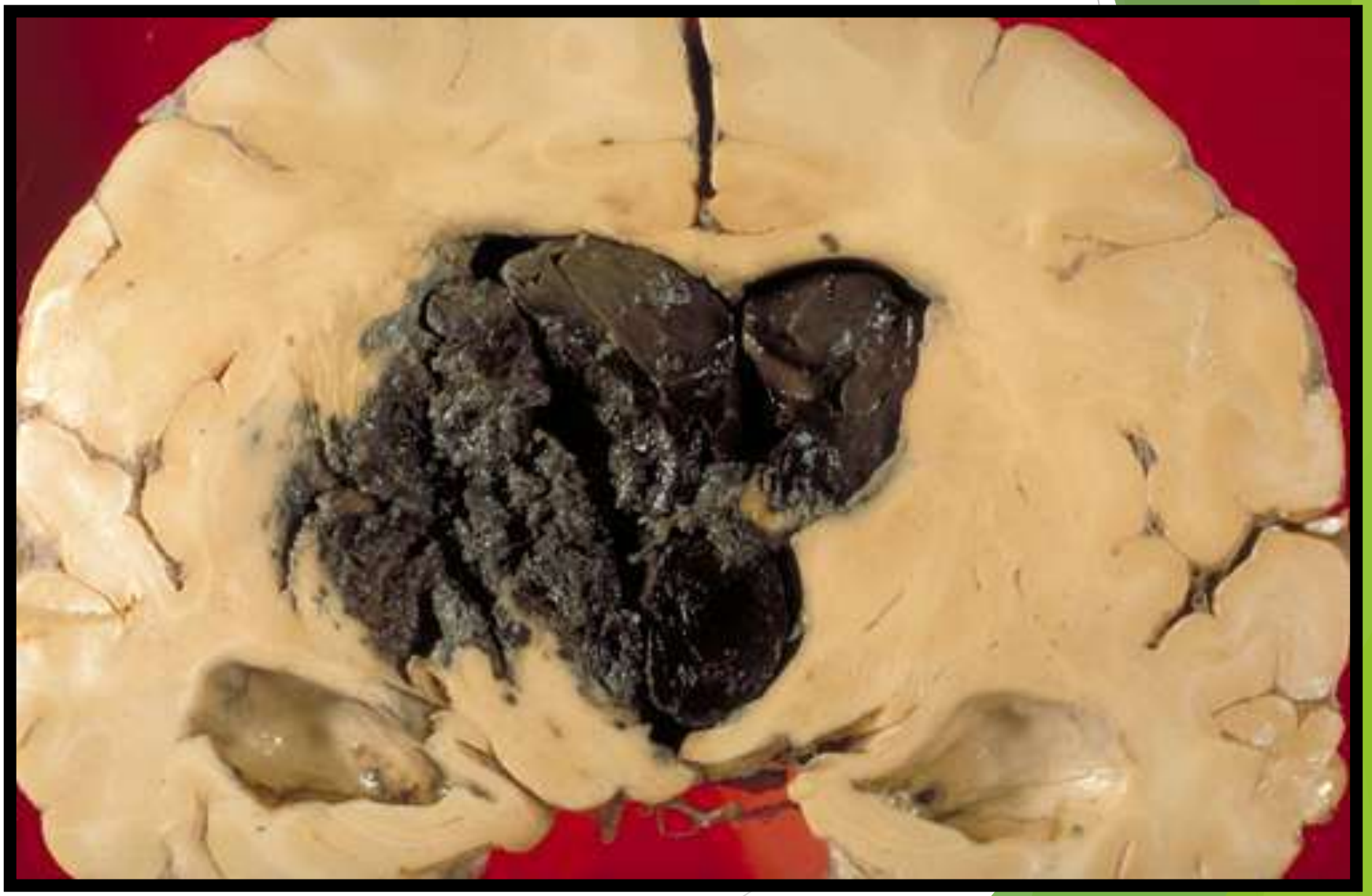
- Hemorrhages within the brain are caused by
- (1) Hypertension and other diseases leading to vascular wall injury,
- (2) Structural lesions such as arteriovenous and cavernous malformations
- (3) Tumors.
- **Subarachnoid hemorrhages** most commonly are the result of ruptured aneurysms but also occur with other vascular malformations. (Hemangioma)
- **Subdural or epidural hemorrhages** usually are associated with trauma.

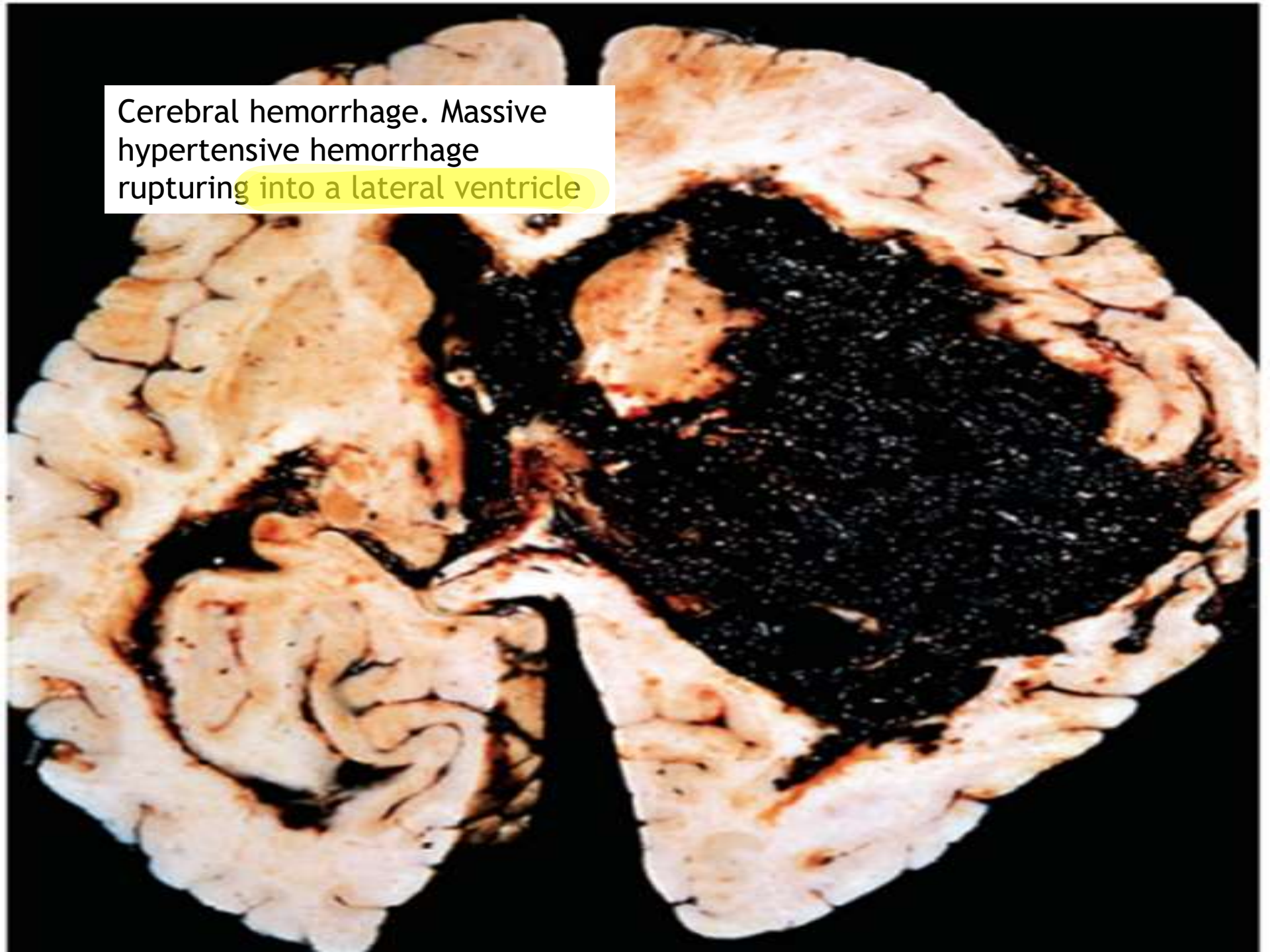
Cheyer-dowlur synd
cause life Qut Bleeding
as result of
opening the BVs

Intracranial Hemorrhage

- Spontaneous (nontraumatic) intraparenchymal hemorrhages are most common in mid to late adult life, with a peak incidence at about 60 years of age.
- 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.
- 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

Basal ganglia hemorrhage




Cerebral hemorrhage. Massive hypertensive hemorrhage rupturing into a lateral ventricle

Cerebral Amyloid Angiopathy

- Disease in which the same amyloidogenic peptides as those found in Alzheimer disease deposit in the walls of medium- and small-caliber meningeal and cortical vessels.
- The amyloid confers a rigid, pipe-like appearance and stains with Congo red.
- Amyloid deposition weakens vessel walls and increases the risk for hemorrhages, which differ in distribution from those associated with hypertension.
- CAA-associated hemorrhages often occur in the lobes of the cerebral cortex (lobar hemorrhages).
- In addition to these symptomatic hemorrhages, CAA also results in small (<1 mm) cortical hemorrhages (microhemorrhages)

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.

Saccular Aneurysms

- 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 survivors.

Saccular Aneurysms

- About 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.

- There is an increased risk for aneurysms in patients with autosomal dominant polycystic kidney disease and genetic disorders of extracellular matrix proteins (e.g., Ehler-Danlos syndrome).

Brain Aneurysms

- Other types of aneurysms include:
- 1. Atherosclerotic aneurysm , mostly of the basilar artery
- 2. Mycotic aneurysms
- 3. Traumatic aneurysms
- 4. Dissecting aneurysms

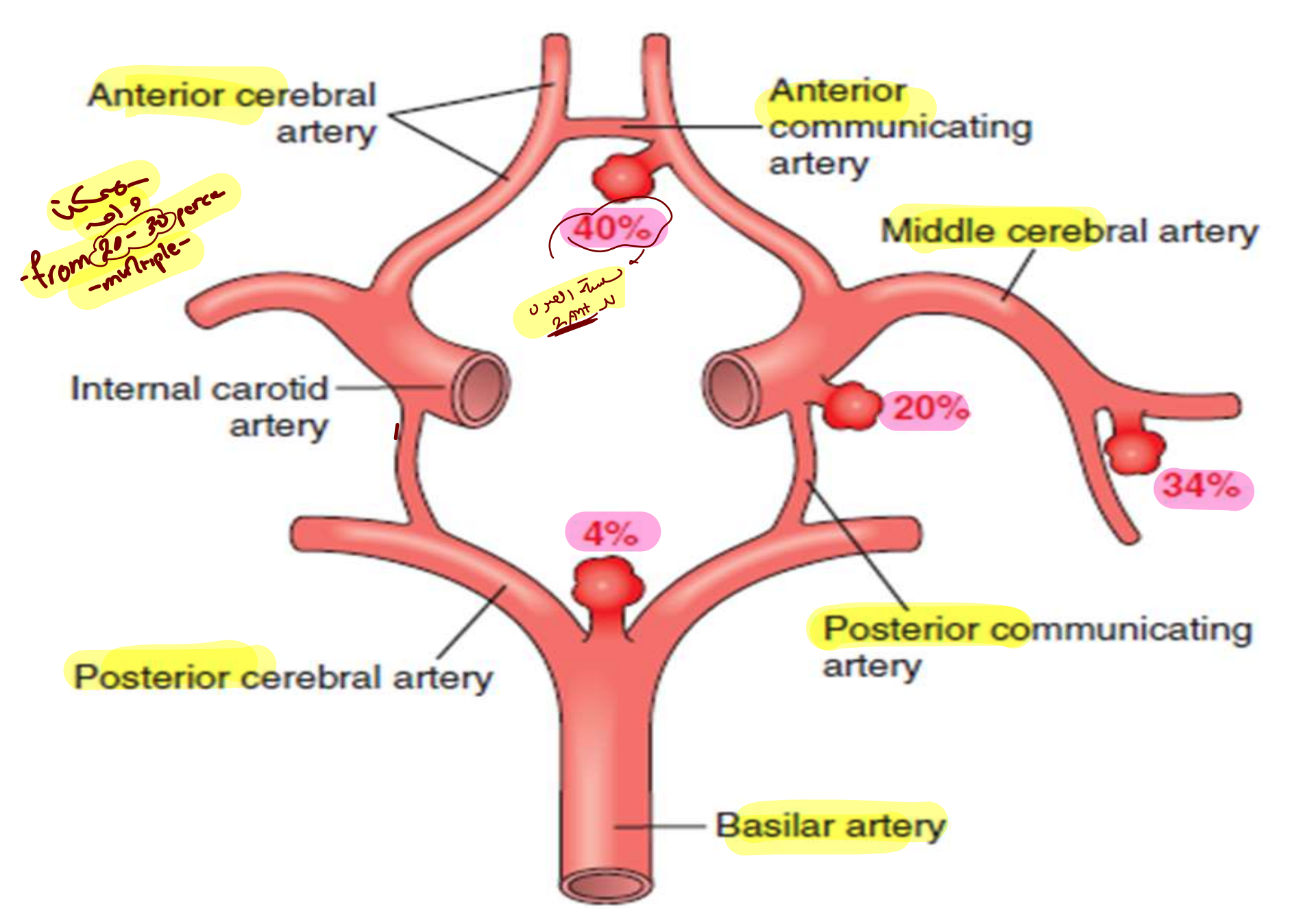


Figure 22–9 Common sites of saccular aneurysms.

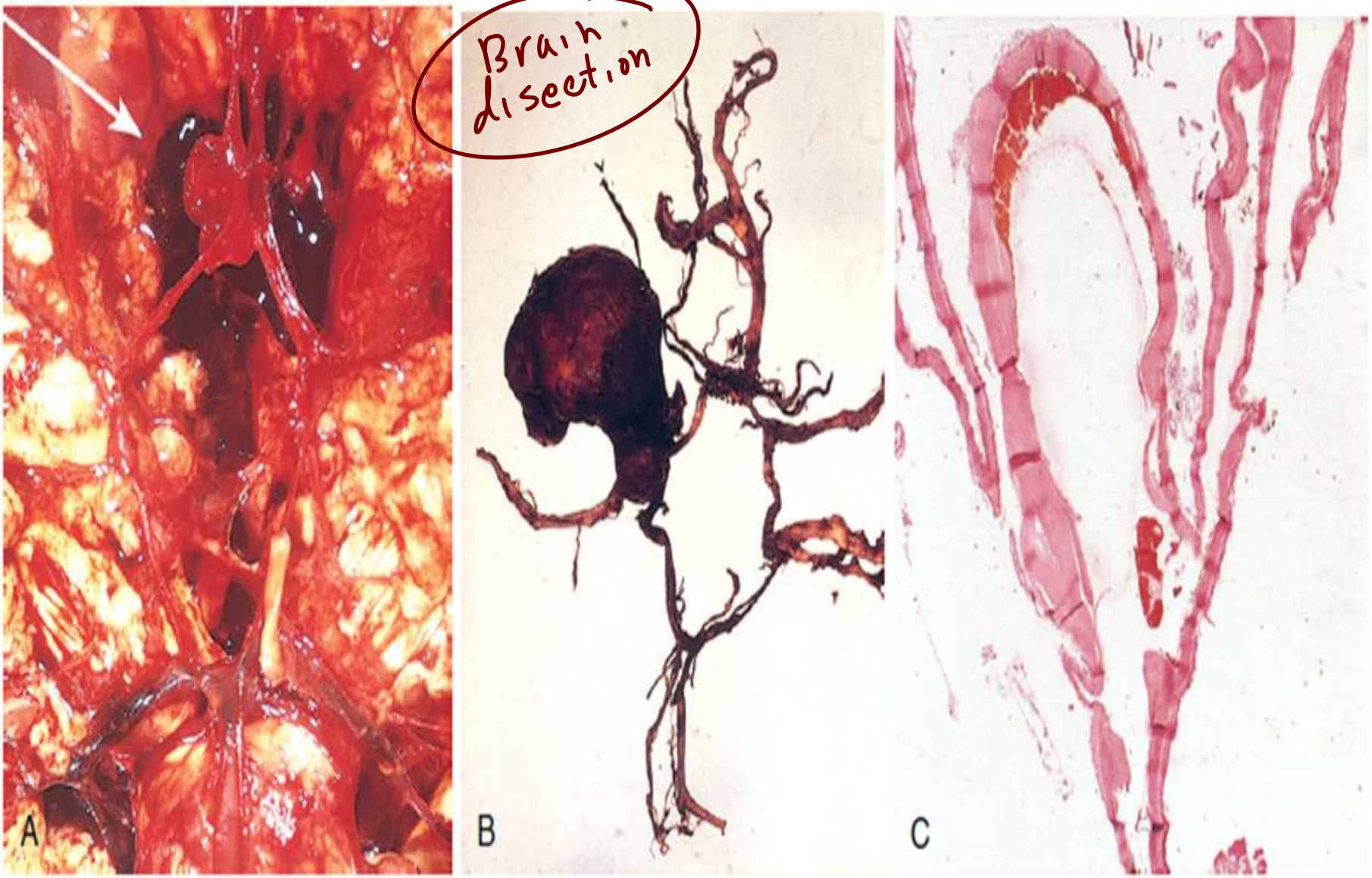


Figure 22–10 Saccular aneurysms. **A,** View of the base of the brain, dissected to show the circle of Willis with an aneurysm of the anterior cerebral artery *(arrow)*. **B,** Circle of Willis dissected to show large aneurysm. **C,** Section through a saccular aneurysm showing the hyalinized fibrous vessel wall. Hematoxylin-eosin stain.

Hypertensive cerebrovascular diseases

- Hypertension causes hyaline arteriolar sclerosis of the deep penetrating arteries and arterioles that supply the basal ganglia, the hemispheric white matter, and the brain stem.

- Affected arteriolar walls are weakened and are more vulnerable to rupture.

- In some instances, minute aneurysms (Charcot-Bouchard microaneurysms) form in vessels less than 300 μm in diameter.

Hypertensive cerebrovascular diseases

- Effect of hypertension on the brain(other than Massive hypertensive intraparenchymal hemorrhage) include:

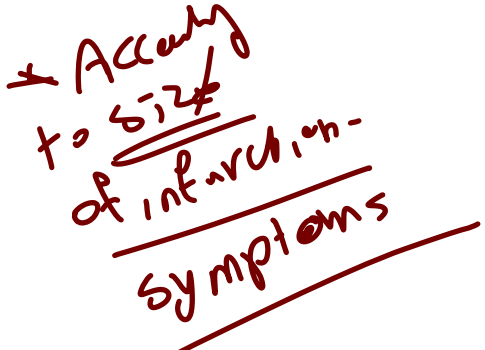
1. Lacunar infarcts
2. Slit hemorrhages
3. Acute hypertensive encephalopathy

1. Lacunes or lacunar infarcts :

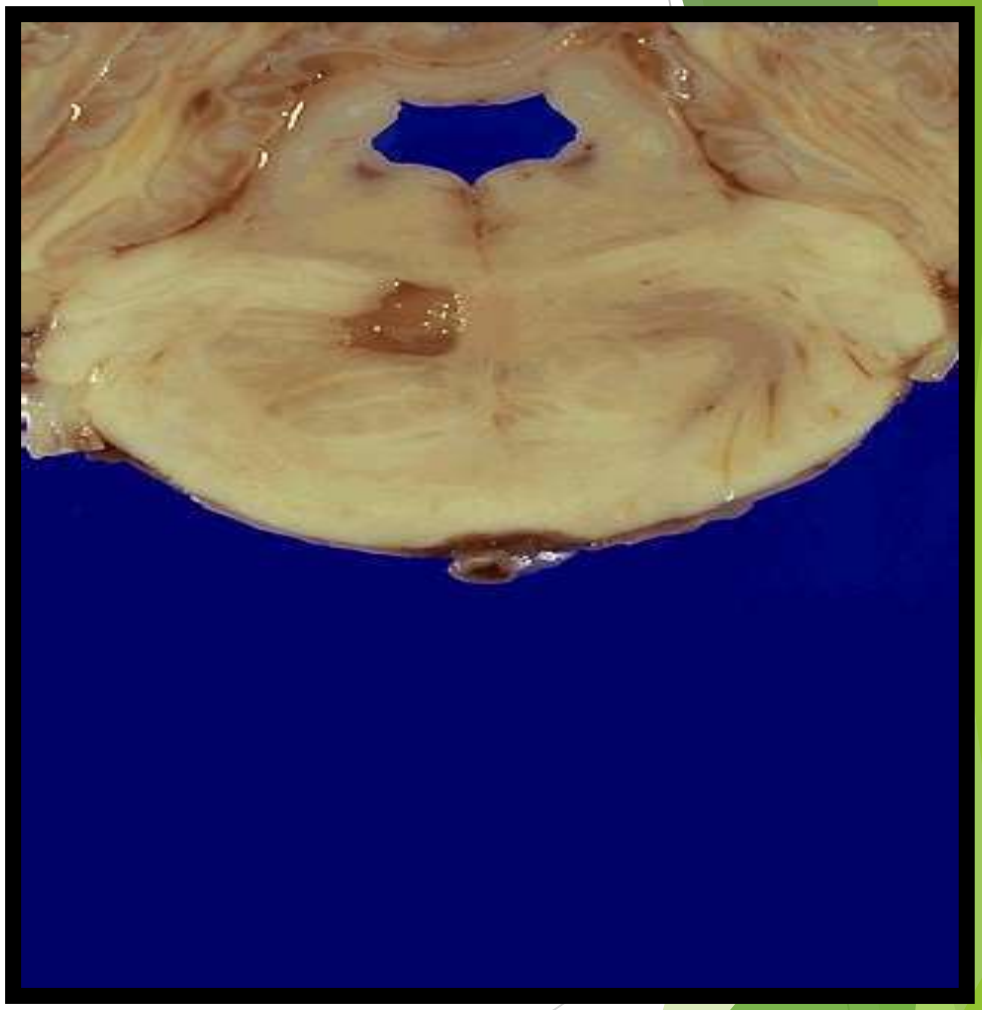
- Small cavitary infarcts, just a few millimeters in size, that are found most commonly in the deep gray matter (basal ganglia and thalamus), the internal capsule, the deep white matter, and the pons.

- They are caused by occlusion of a single penetrating branch of a large cerebral artery.

- Depending on their location, lacunes can be silent clinically or cause significant neurologic impairment.



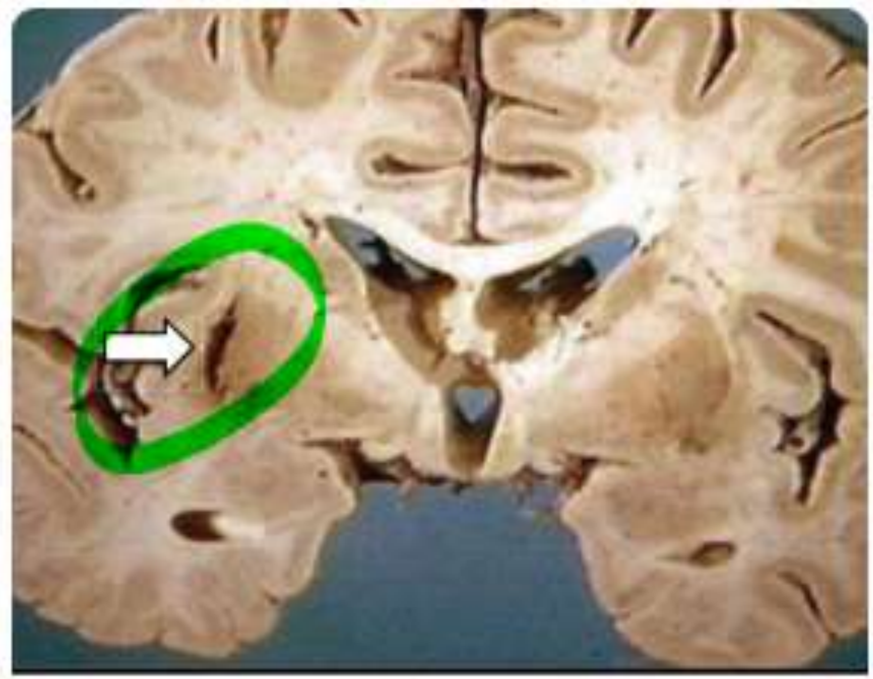
Lacunar infarct in the Pons



2. Slit hemorrhages;

- Hypertension can lead to rupture of the small caliber blood vessels and lead to development of small hemorrhages.

- With time these hemorrhages resorb leaving behind a slit-like spaces called slit hemorrhages.



Slit Hemorrhage

Microscopically characterized by:

i. Focal tissue destruction

ii. Pigment-laden macrophages

iii. Gliosis

3. Hypertensive encephalopathy

- Is a clinicopathologic syndrome arising in the setting of malignant hypertension.

- Most often is associated with sudden sustained rises in diastolic blood pressure to greater than 130 mm Hg and characterized:

A. By increased intracranial pressure due to loss of autoregulation and forcefull overdistention of blood vessels, leading to fluid extravasation (hydrostatic edema).

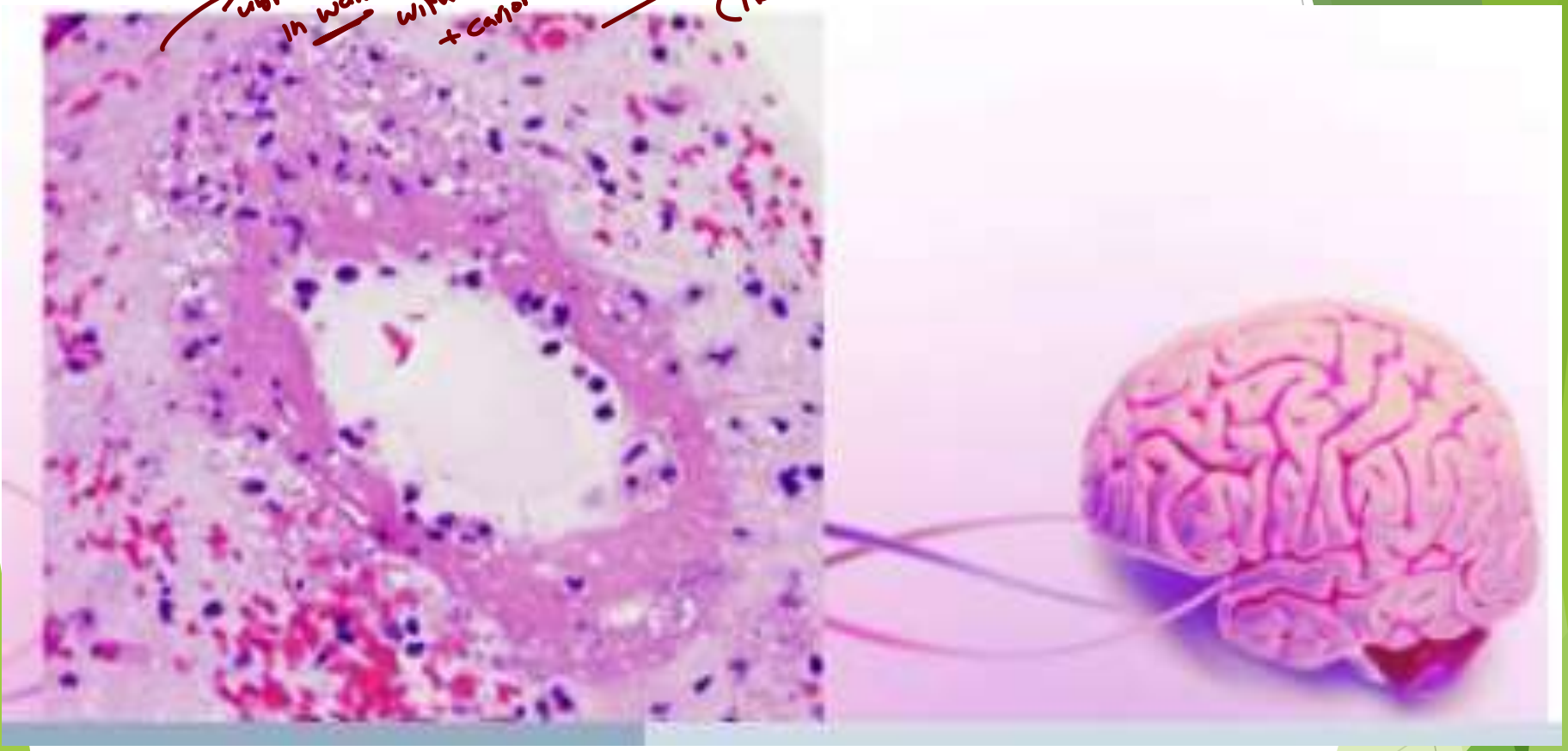
B. Global cerebral dysfunction, manifesting as headaches, confusion, vomiting, convulsions, and sometimes coma.

- Rapid therapeutic intervention to reduce the intracranial pressure is essential, because this syndrome does not remit spontaneously.

MICROSCOPICAL AND MACROSCOPICAL FEATURES

- Postmorteum examination shows edematous brain with or without trantentorial or tonsillar Herniations.

- Microscopic examination shows Fibrinoid necrosis and thrombosis of arterioles and capillaries ASSCOITAED with microinfarcts and microhemorrhages


fibrinoid
abnormal material
in wall - amyloid
with neutrophils
+ caseous
Amyloid
(Acellular, Homogenious
material)

Inflammatory processes that involve blood vessels (vasculitis)

A. Infectious vasculitis is common in the setting of immunosuppression and in opportunistic infection such as aspergillosis and CMV encephalitis.

B. Primary angiitis of the CNS:

- Is an inflammatory disorder that involves multiple small to medium-sized parenchymal and subarachnoid vessels.

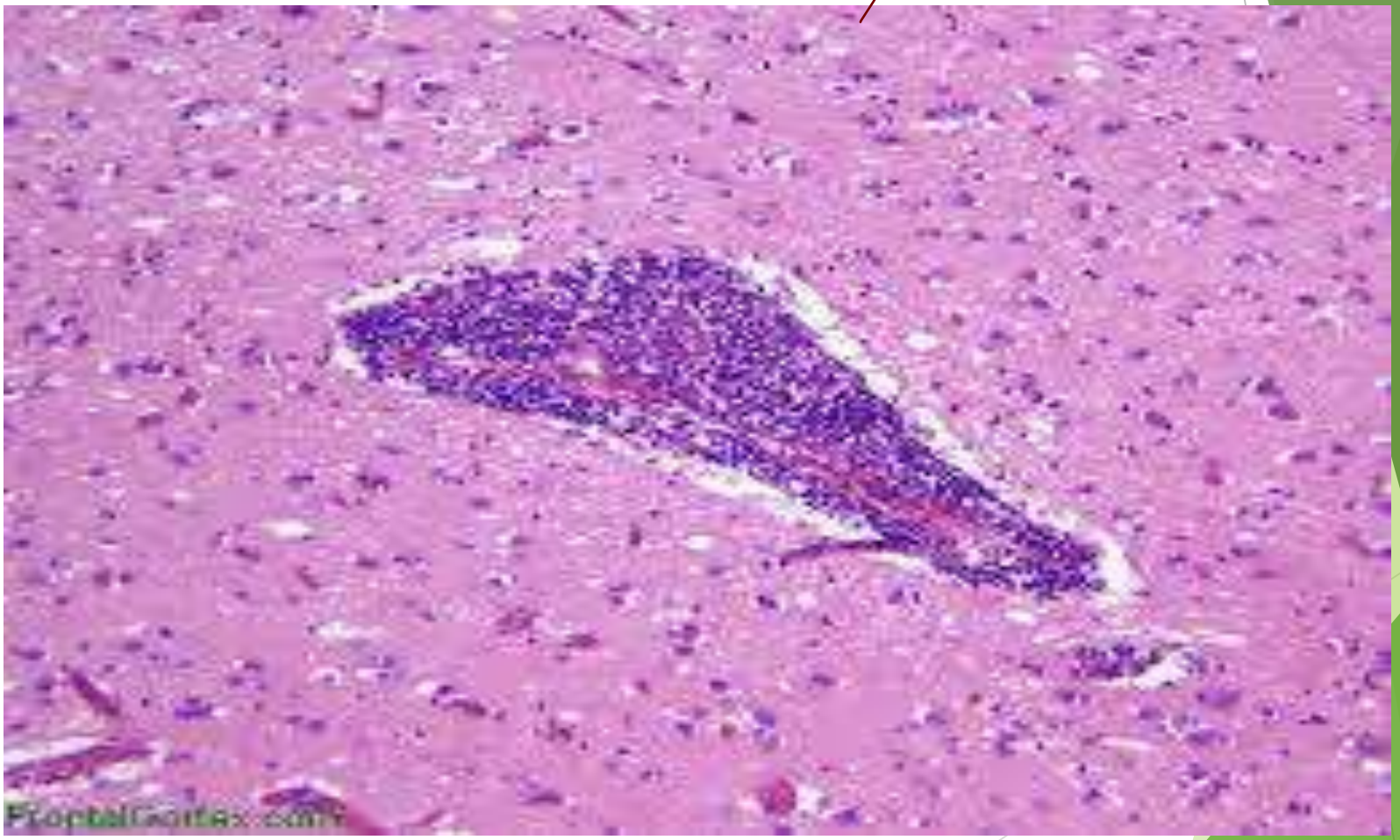
- Characterized by chronic inflammation, multinucleated giant cells and destruction of the vessel wall.

C. Granulomas if present it called granulomatous angiitis of the central nervous system.

- Affected individuals may present with diffuse encephalopathy or multifocal clinical picture often with cognitive dysfunction.

- Patients improve with steroids or immunosuppressive therapy

Primary angiitis of CNS



The End

Good Luck