CNS PATHOLOGY

Lecture I

CEREBROVASCULAR DISEASE

Cerebrovascular disease

- Ischemic or hemorrhagic etiologies
- Ultimately infarction → Tissue necrosis
- Stroke versus TIE → Transient ischemic attack → Cerebrovascular disease of CNS if last < 24 h
- The 3rd leading cause of death → After cardiovascular diseases and cancer
- Ischemia/hypoxia → Deficiency of blood supply; → Deficiency of O_2 only
  - Global or focal → Global: if the entire CNS is affected; focal: only portions
  - ✓ Manifestation related to the region affected
  - ✓ Embolism more common than thrombosis

Cerebrovascular disease of CNS if last > 24 h → This will result in neurologic findings

Ischemia → Deficiency of blood supply → O_2 deficiency + nutrients deficiency + deficient waste products removal → It's more hazard than hypoxia

Cerebrovascular disease

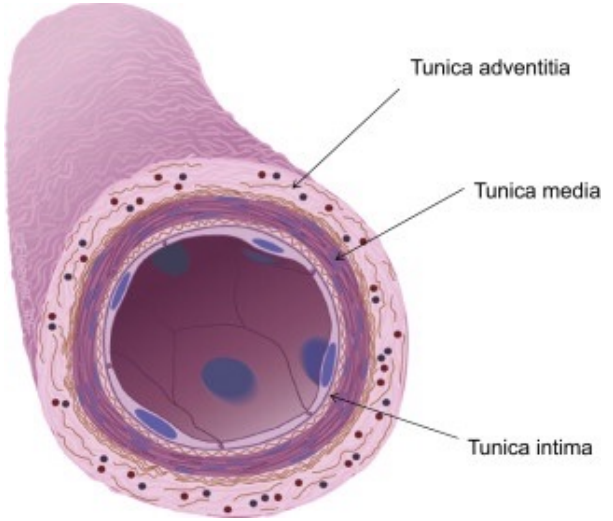
- Hemorrhage
  - Due to hypertension and vascular anomalies (aneurysm and malformation)

خاصة لما يكون malignant HTN → > 200/120 mmHg

aneurysm ↓

Brain aneurysms & Congenital aneurysms characterized by loss of Tunica media

وبالتالي بصير عبارة عن wall بالشريان T. intima & T. adventitia Cannot stand high BP وبالتالي



Hypoxia and ischemia

- 20% of O2 consumption
- Autoregulation of blood flow
- Strictly dependent on aerobic metabolism

Although the CNS constitutes only 2% of body mass!

So it is very susceptible to ischemia

Hypoxia and ischemia

- The size of the lesion determined by
  - Duration
  - Magnitude and rapidity of the reduction
  - Collaterals
    - From C. of Willis/external carotid/ophthalmic
    - Cortical/leptomeningeal
    - Deep parts lack collaterals → So more susceptible to infarctions

If gradually developed (through months, years..) there's a chance for collateral circulations

Small BV will induce less lesions comparable to the lesions that will result from large BV

Hypoxia and ischemia

- Excitotoxicity
  - Release of glutamate NT → very toxic
  - Damage neurons by excessive influx of Ca++
- Penumbra → Partial ischemia
  - Area of "at risk" brain tissue
  - Can be rescued by antiapoptotic interventions

دلوقتي أي neuron بيتعرض لـ hypoxia أو ischemia بيحصل Release of glutamate

لما يحصل occlusion لـ artery معين بيحصل infarction في المنطقة اللي بتغذيها بس في مناطق متكونش جوا المنطقة دي بيحصل نقصان لـ blood بس مش بشكل كامل وهي دي الـ Penumbra

Ischemia is potent inducer of cell death 'Apoptosis' وبالتالي لو استهدفنا الـ apoptotic mechanisms هنقدر نقلل الـ death من neuron

Focal cerebral ischemia

- Embolism
  - Sources
    - Most commonly cardiac thrombi
    - Atheroma plaque within the carotid → affected الشرايين الدماغية بال Atherosclerosis وخاصة عند الـ Bifurcation into ICA & ECA
    - Paradoxical
    - Cardiac surgery
    - Tumor, Fat, and air → After trauma
  - Most frequently the middle cerebral artery → Continuation لشريان الـ Common Carotid artery

In general, the most common cause of embolisms are DVTs
↓
في الـ DVT الهدف عادة بيكون الجهة اليمين (RV) يعني embolism into the lung
بخف انه يرجع على الجهة الشمال (يعني الـ LV) ومن ثم إلى CNS أو أي مكان تاني عادة ما بصير إلا إذا في Heart defect (e.g. interventricular septum defect)

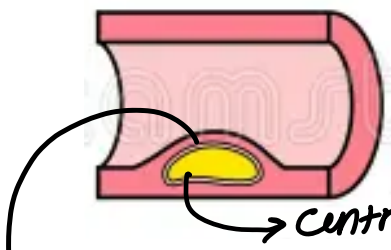
Focal cerebral ischemia

- Thrombotic occlusion
  - Most commonly acute plaque changes in the bifurcation
- Inflammatory process
  - Syphilis and TB
  - Vasculitis

very rare

Disruption of the plaque → Rupture → Ulceration

↳ Bcs of slowing of BF (Turbulence)



central fat 'lipid-laden macrophages'

C.T. wall 'endothelial cells'

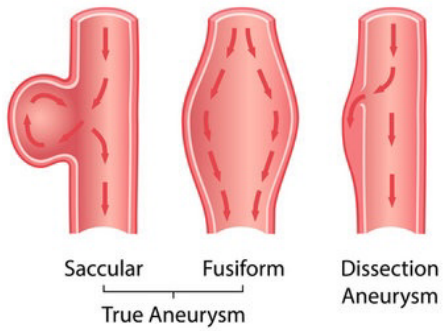
↳ If disrupted → exit of collagens 'become exposed to blood'

↓

Collagen is strong inducer of coagulation → Thrombus formation

Focal cerebral ischemia

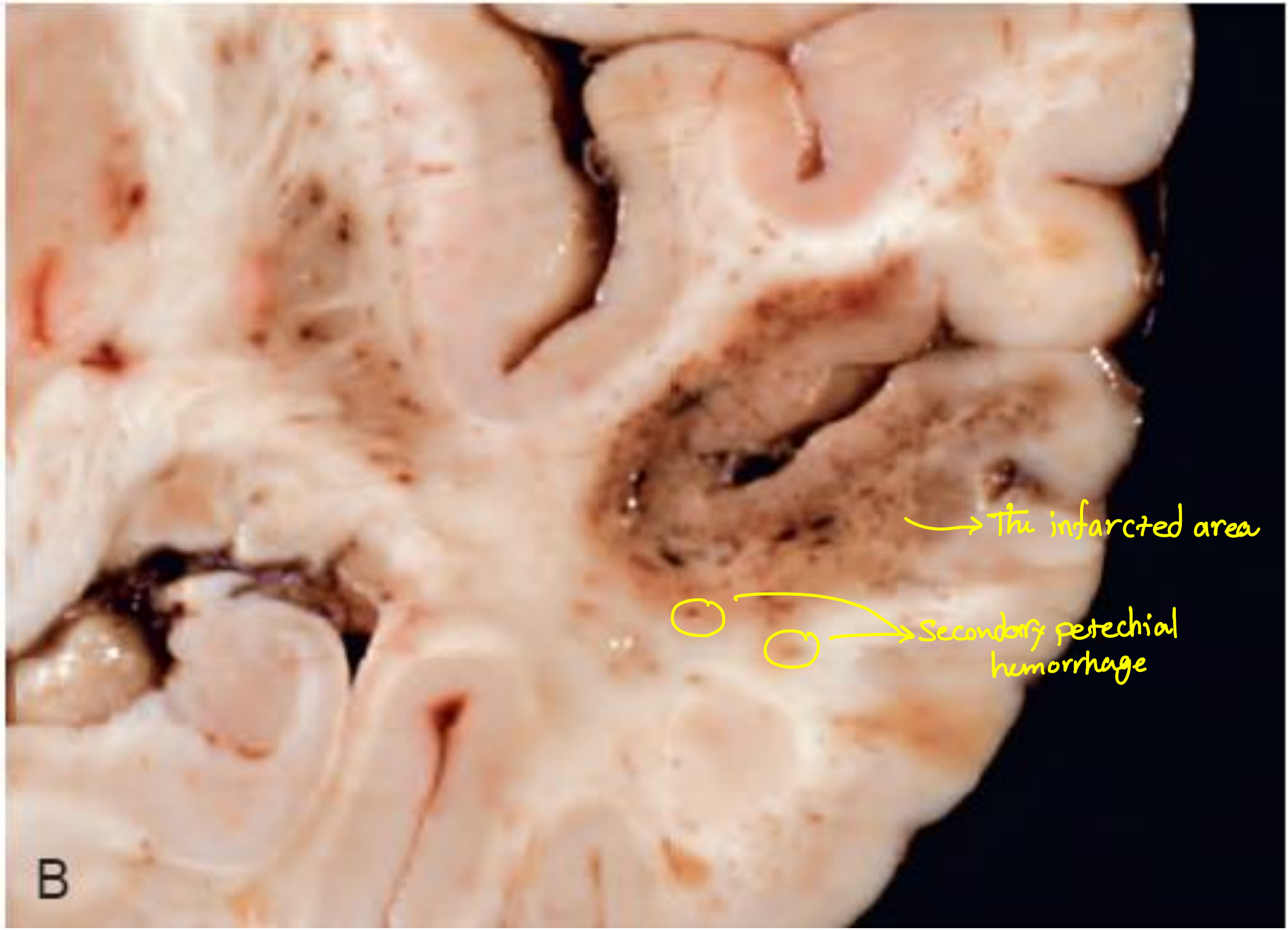
- Other
  - Hypercoagulability
  - Dissecting aneurysm
  - Drug abuse



Focal cerebral ischemia

- Starts as nonhemorrhagic (pale/anemic)
- Secondary hemorrhage
  - Due to reperfusion → Reperfusion injury → لما منطقة تكون ischemic ورجع عليها الـ blood فجأة هتتحمل كمية الـ O_2 وبالتالي هتكون free radicals كمية كبيرة من
  - Leading to hemorrhagic infarct
  - Petechial morphology
  - Cautions with thrombolytic treatment ✓✓

Secondary hemorrhage due to ischemia and reperfusion injury
هيكون على شكل نقاط بيكن لما آجي injury من reperfusion تكون هيكون hemorrhagic كمية hematoma


→ The infarcted area
→ Secondary petechial hemorrhage
B

Focal cerebral ischemia

- Gross morphology
  - First 6 hours
    - Little change
  - By 48 hours
    - Pale, soft swollen, indistinct gray-white matter
  - 2-10 days
    - Gelatinous, friable, distinct normal/infarcted area
  - 10 days-3 week
    - Liquefaction, fluid filled cavity

Discrimination btw white and gray matter will be lost

The infarcted area become well demarcated from the surrounding healthy area

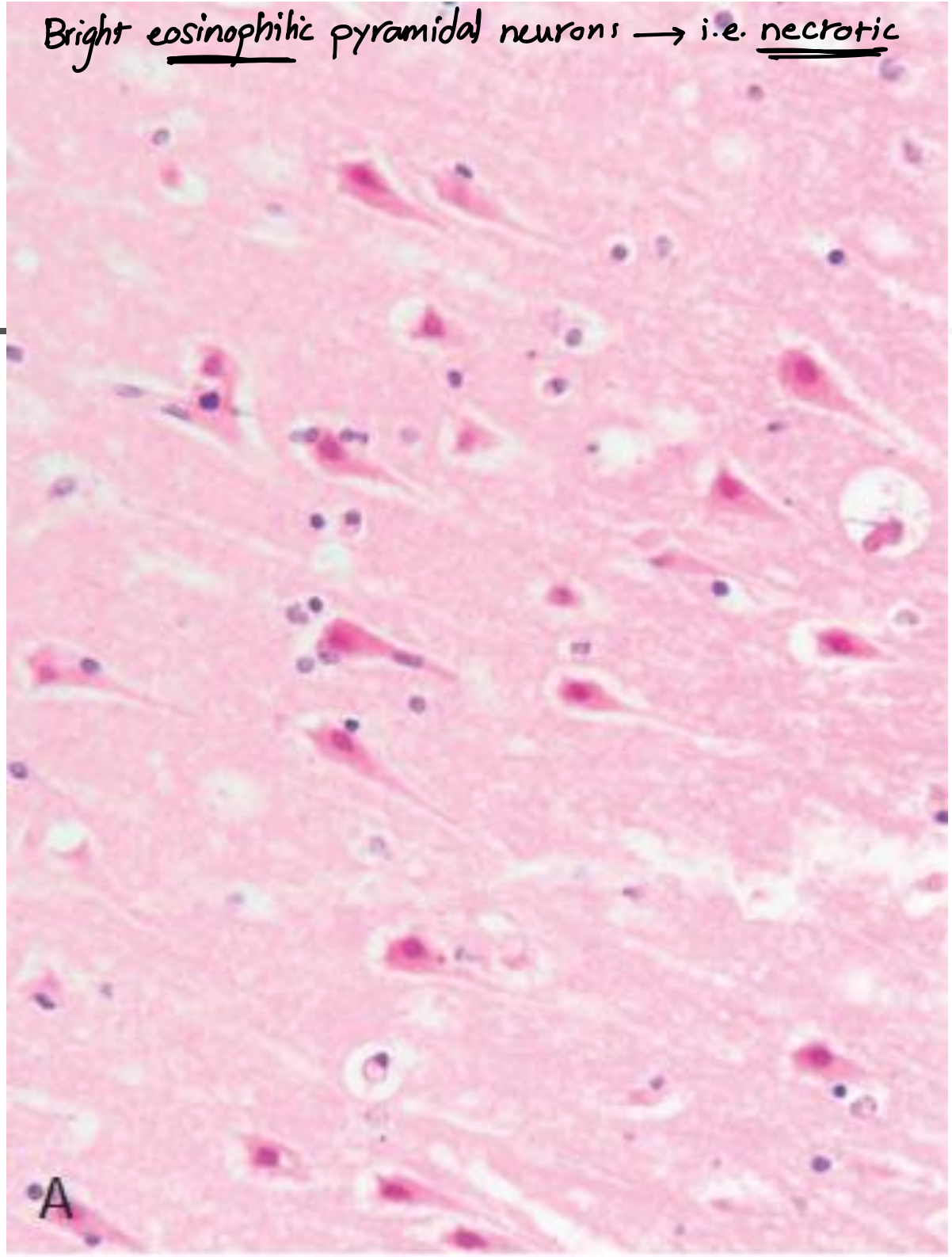
Type of necrosis

Focal cerebral ischemia

- Microscopic
  - Acute infarct
    - 6-12 hours
      - Eosinophilic neuronal necrosis
      - Edema
      - Indistinct gray/white matter
      - Disintegration of the glial cells, fibers and endothelium
    - 48 hours
      - Neutrophilic emigration ✓

Due to disintegration of genetic materials (DNA & RNA) which are stained with blue (Basophilic)

↳ So when disintegrated, the acidophilic components well constitute the largest portion of the cells


Bright eosinophilic pyramidal neurons → i.e. necrotic
A

Focal cerebral ischemia

- Microscopic
  - Subacute (evolving) infarct
    - 48-72 hours
      - Phagocytes and microglia
      - Reactive astrocytes
      - New blood vessels (as early as 1 week after the insult)
        - Astrocytes at the edge develop a network of cytoplasmic extensions

Then

Then

عشان كدا الـ outer areas بيصيروا لها Repair قبل deep areas

Start from outside toward the center

Granulation tissue formation لحد

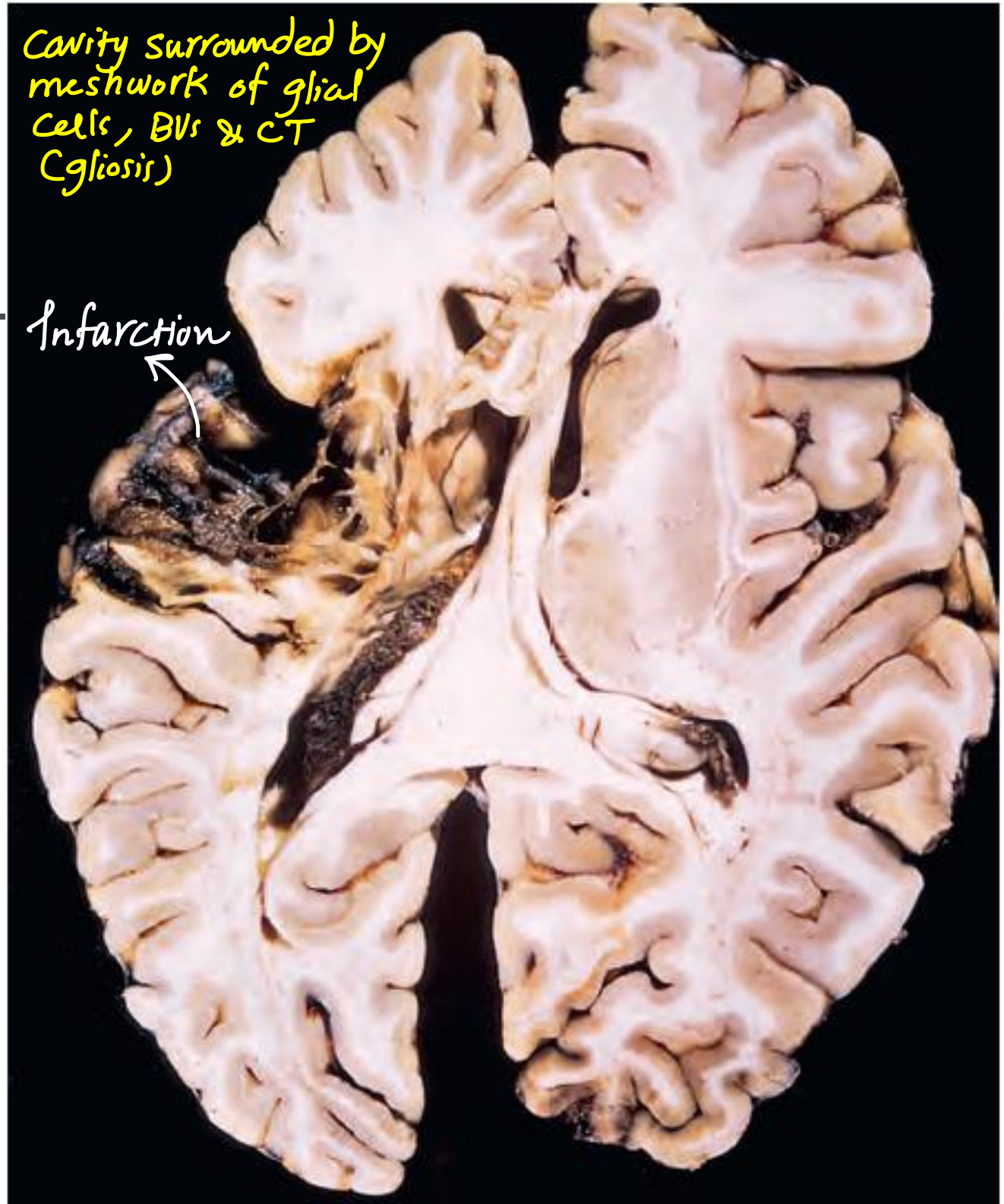
Almost completely occupied by inflammatory cells
(mainly macrophages)
neutrophils & others
leukocytes
new blood vessels
B

Focal cerebral ischemia

- Microscopic
  - Healed infarct (after several months)
    - Dense meshwork of glial fibers → This will completely replace the infarcted area
    - New capillaries
    - Perivascular connective tissue
    - Chronologic morphologic changes
  - Hemorrhagic infarction → نفس خطوات الـ ischemic infarction بس بتضاف إليها blood extravasation
    - The same with blood extravasation added
    - Extensive if under anticoagulant
    - Venous infarction
      - Thrombosis of the sinuses

"Zonation" نوع من يعني المنطقة الأقرب لـ Periphery هتكون قطعت شوط أكبر في عملية الـ Repair

كل اللي تحدثنا عنه فوق بيخص الـ Arterial infarction لكن ممكن يحصل نتيجة Venous


Cavity surrounded by meshwork of glial cells, BVs & CT (gliosis)
Infarction

Lacunar infarcts

Small infarcts due to occlusion of small BVs

- Occlusion of small vessels as a result of arteriolosclerosis/hypertension
- Less than 15 mm
- Single or multiple
- Involves, putamen, globus pallidus, thalamus. Internal capsule, deep white matter, caudate nucleus and pons

الكبر مناطقه inner بتأثر هي areas (Basal ganglia)

- Tissue loss surrounded by gliosis

Arteriosclerosis
- Arteriolosclerosis
  - Hyaline
  - Proliferative
- Atherosclerosis
- Mönckeberg sclerosis (calcinosis)

Global cerebral hypoxia/ischemia

- Cardiac arrest, shock, and severe hypotension
- CO poisoning
- Transient postischemic confusional state with complete recovery
- Or irreversible damage; "diffuse hypoxic/ischemic encephalopathy

يصحى ماخوم وشش oriented يكون بعدها بعيني المصنوع بدرجة طبيعي

Global cerebral hypoxia/ischemia

- Border zone (watershed) infarcts
  - Border between arterial territories
  - Result in wedge shaped infarct
  - With secondary hemorrhage
  - Often bilateral
  - Commonly after cardiac arrest resuscitation

مناطق بين البنيين، بتاخد من هنا شوية Blood ومن هناك شوية

نلاحظ انه الـ hemorrhage على شكل
Petechial hemorrhage نقاط (يعني
Ischumic وبالتالي ناتج من
hemorrhagic infarct وليس

Global cerebral hypoxia/ischemia

- Morphology
  - Edematous and swollen brain
  - Poor gray white demarcation
  - Irreversible injury
    - 6-12 hours; dead red neuron
    - 24 h-2 weeks, Subacute changes; necrosis, macrophages, vascular proliferation and gliosis
    - After 2 weeks; removal of necrotic tissue and gliosis

تقريباً نفس ← focal

Intracranial hemorrhage

- Epidural and subdural; mostly trauma related ①
- Subarachnoid and intraparenchymal; related to ② cerebrovascular disease

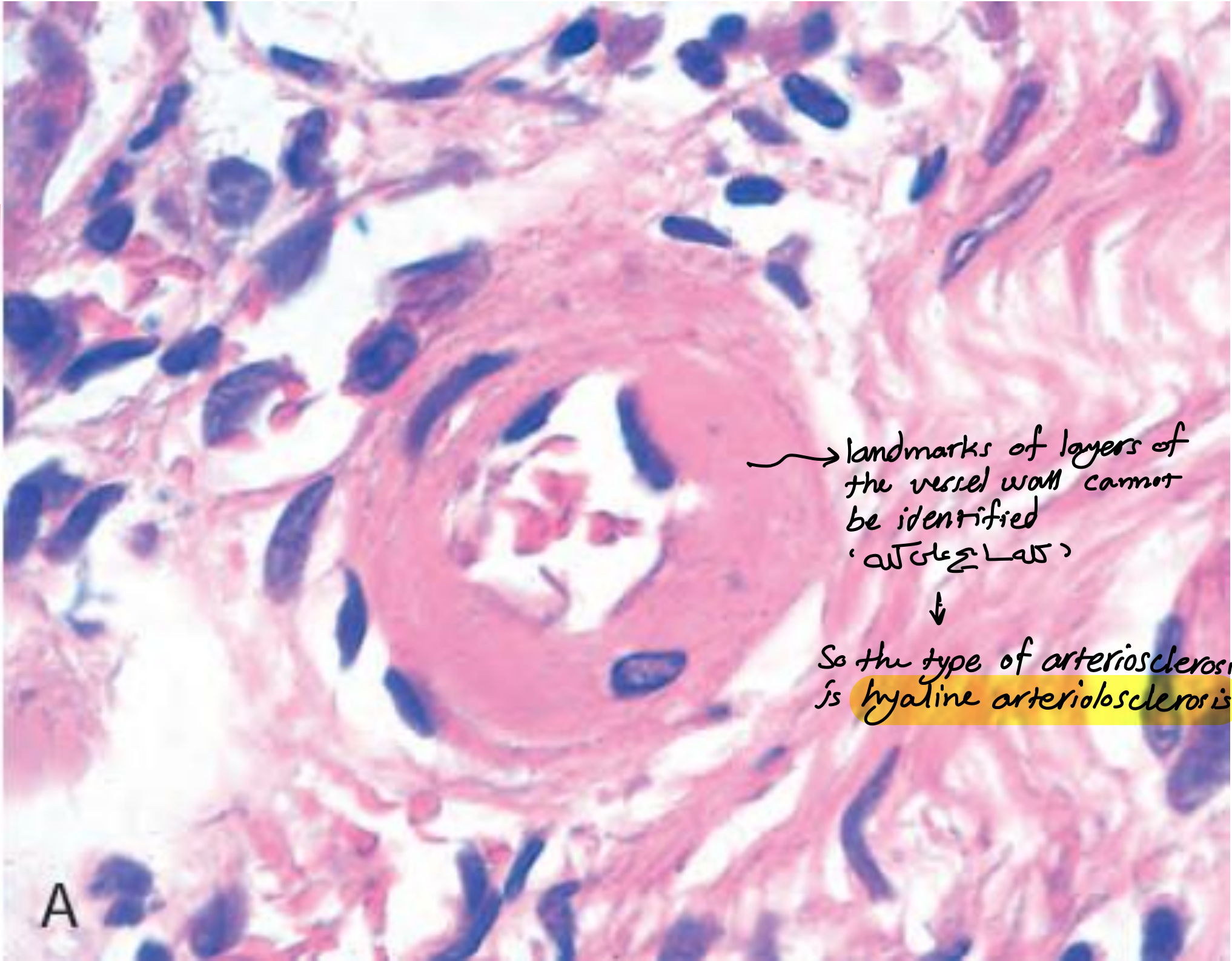
Intraparenchymal hemorrhage

- Sudden onset of symptoms
- Versus secondary hemorrhage
- Middle/late adult life
- Ganglionic versus lobar hemorrhage
  - from Basal ganglia
  - from lobe 'outer surface (gray matter) of the cortex
- Hypertension is the most commonly associated factor with ganglionic intraparenchymal hemorrhage
  - 50-60% Putamen

Proliferated arteriolosclerosis → malignant HTN
Hyaline arteriolosclerosis → HTN within the normal range

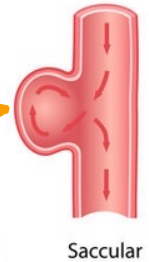
Intraparenchymal hemorrhage

- Effects of HT on blood vessels
- Cerebral amyloid angiopathy is the risk factor most commonly associated with lobar hemorrhage
- Morphology → Hematoma and blood collection


landmarks of layers of the vessel wall cannot be identified
So the type of arteriosclerosis is hyaline arteriolosclerosis
A

Subarachnoidal hemorrhage

- The most common cause is rupture of saccular "berry" aneurysm in a cerebral artery
  - Saccular aneurysm
    - 2% of the population
    - 90% found near major arterial branch points in the anterior circulation



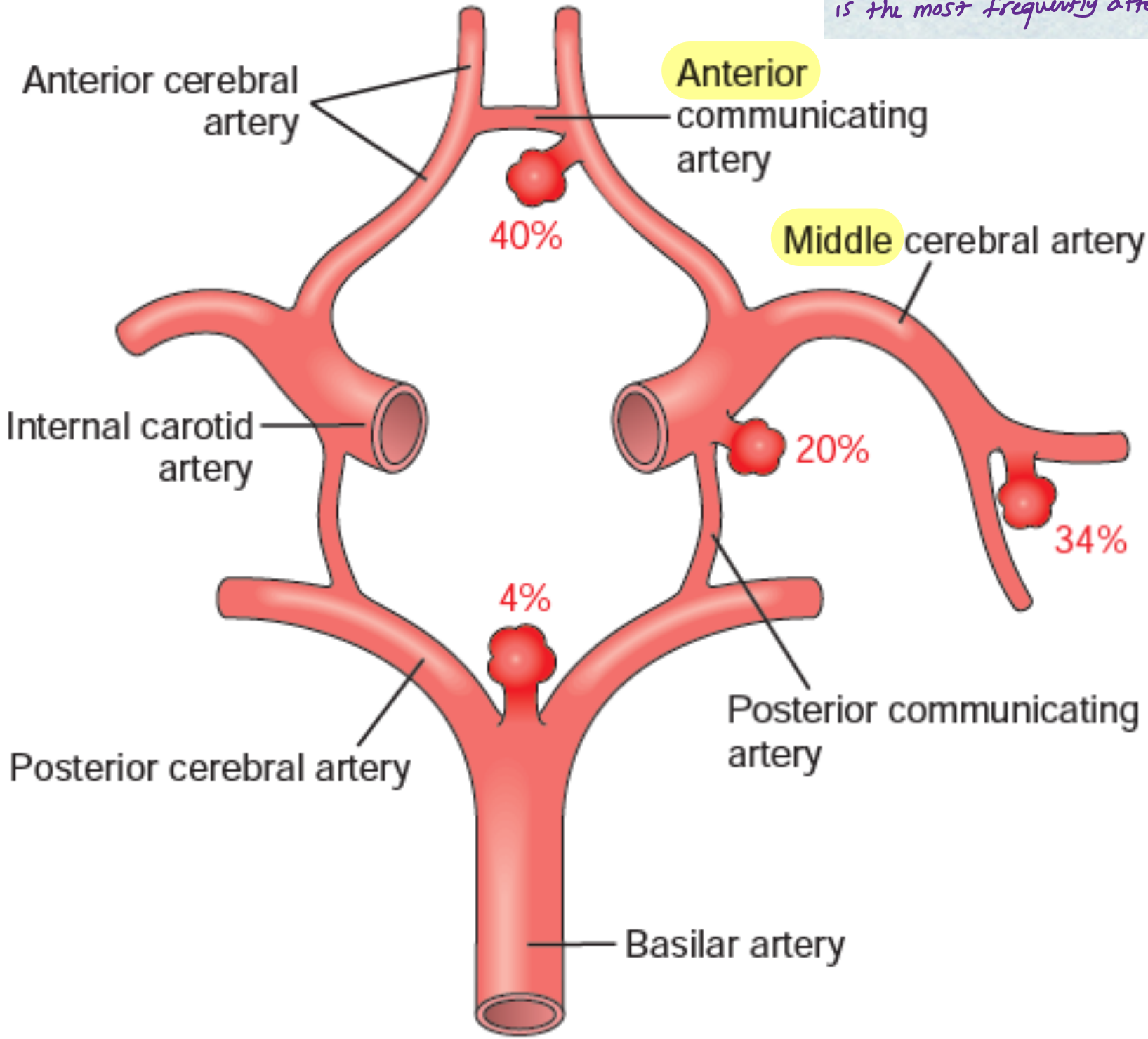
C. of willis خاصة في
where the arteries are branching

شكل التركيب:

عدد كبير نوعاً ما

الناس اللي بيموتوا فجأة بيكون عمرهم صغير وارد جداً أنه يكون بسبب الموضوع aneurysm

The anterior circulation is the most frequently affected



Subarachnoidal hemorrhage

- Pathogenesis
  - A developmental anomaly
  - Absence of smooth muscle and elastic lamina
  - The majority are sporadic
    - Cigarette and HT
  - Genetic factors

Subarachnoidal hemorrhage

- Morphology
  - Shape and size — Saccular; mms to Cms
  - Atheroma, thrombus — Due to turbulence and slowing of the blood in the dilated part
  - Prior hemorrhage — طالتعل لشخص بتلاقي autopsy signs of prior hemorrhage
  - Bleeding into the subarachnoid or brain substance
  - Absence of smooth muscle and elastic lamina
    - Thickened hyalinized intima and a covering of adventitia ✓

i.e. T. media

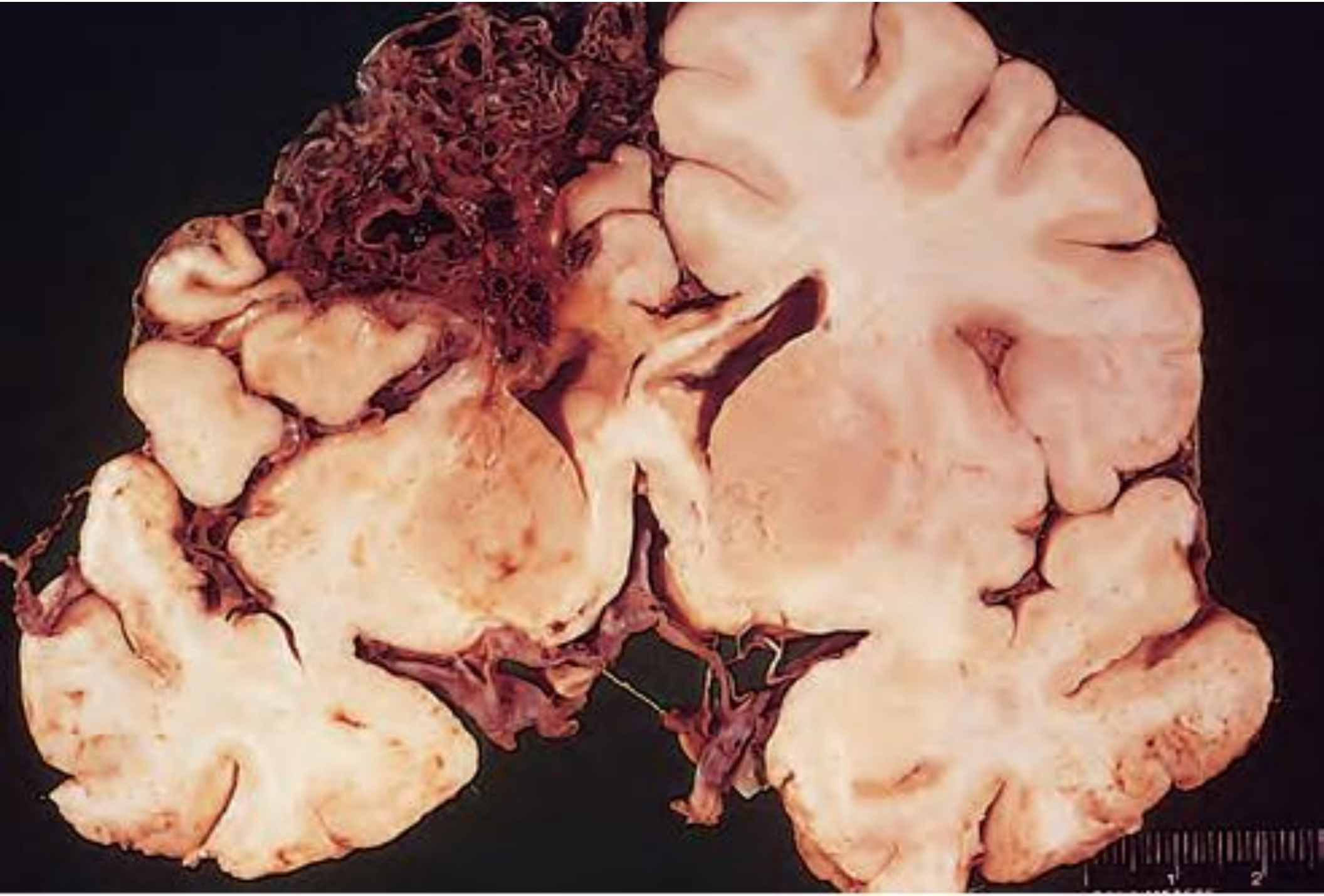
Vascular malformations

- 4 groups
  - AV malformations → Abnormal connection btw the artery and vein
    - Risk of hemorrhage
    - KRAS mutation → Maybe a type of neoplasm ??
  - Cavernous malformations ← congenital ← extremely dilated BVs
    - Risk of hemorrhage
  - Capillary telangiectasias
  - Venous angiomas

Vascular malformations

- Morphology
  - AV malformations → Serious problem as it a significant cause of intracranial hemorrhage
    - Warm like
    - Pulsatile shunting ← artery نابضة أحمر vein داكن جوا Pulsation فيكون في
    - Subarachnoid or brain
    - Prior hemorrhage → Dark brown due to hemosiderin accumulation
    - Duplication and fragmentation of elastic lamina
    - Thickening and replacement of media by hyalinized CT
    - Separated by gliosis

تخليه معرض لـ hemorrhage



Vascular malformations

- Morphology
  - Cavernous malformation
    - No brain parenchyma
    - Most often cerebellum, and pons
    - Low flow → non-pulsatile
    - Old hemorrhage

Vascular dementia

الخَرَف

Dementia بشكل عام هي loss of brain material بتيجي للناس الي أعمارهم كبيرة

- Multiple infarcts over years
- Dementia, gait abnormality → Disorientation... loss of motor function...
  مشية غير طبيعية
- Caused by
  - Atherosclerosis
  - Thrombosis/embolus from the carotid or heart
  - Arteriolosclerosis from chronic HT