Circulatory Diseases of the CNS

APPROVED

86 slides... but very straightforward lecture

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- **I have no financial interests or relationships to disclose**

- **Reference:**
  - **Robbins and Cotran Pathologic Basis of Disease 8th Edition**

He just read these objectives. A lot of material to cover in 50 mins!

Learning Objectives

- **Introduce the basic concepts and mechanisms associated with cerebrovascular disease**
- **Describe the gross and microscopic pathology of ischemic brain injury (stroke)**
- **Classify cerebral hemorrhage according to location and list the causes and contributing factors**
- **Describe and differentiate the various types of CNS vascular malformations**
- **Identify and explain the etiologies of embolic infarcts and arterial dissection**

Cerebrovascular Disease (CVD)

Leading causes of death in the USA:

- **Heart disease**
- **Cancer**
- **Cerebrovascular disease**

#3 leading cause of death

CVD is the leading neurological disorder in terms of morbidity and mortality

summary: CVD is very common

What is CVD?

Cerebrovascular Disease

- **CVD is an abnormality of the brain caused by a pathologic process of blood vessels**

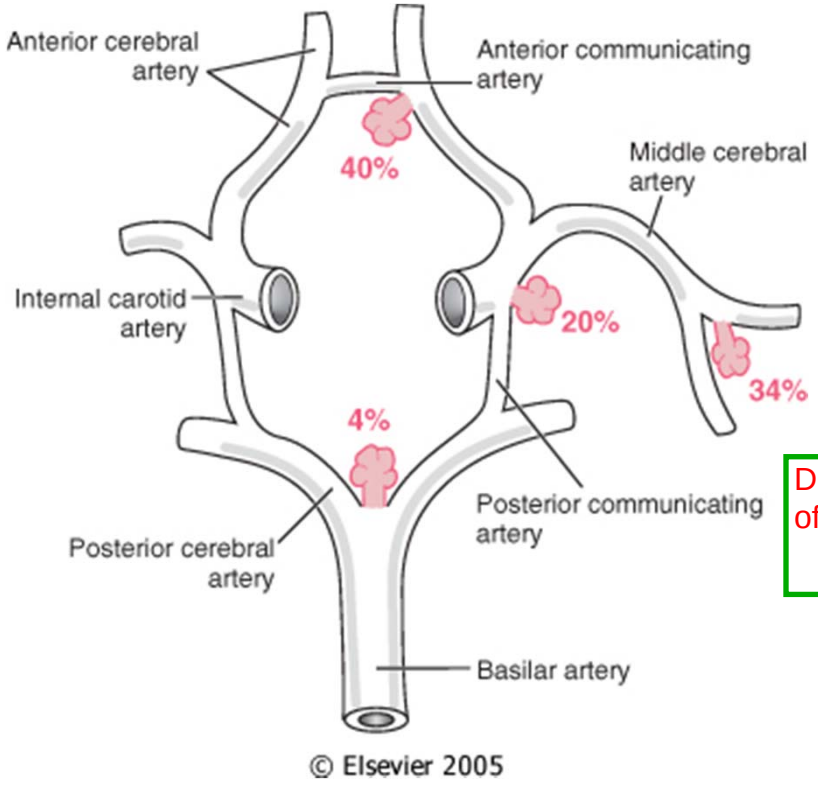


Diagram showing Circle of Willis

Summary:
Basic mechanisms of CVD
1. ischemia and hypoxia
-blood supply or oxygenation of CNS is impaired
2. Hemorrhage
-due to hypertension, aneurysm, vascular malformation

Mechanisms of Cerebrovascular Disease

- **Ischemia // Hypoxia**
  - **Impairment of blood supply and // or oxygenation of CNS tissue**
- **Hemorrhage**
  - **Hypertension**
  - **Aneurysm**
  - **Vascular Malformation**

Summary:
Brain needs constant supply of oxygen.
Oxygen deprivation can be due to
1. functional issue: problem with oxygen
2. ischemic issue: problem with getting oxygen to the brain via the blood supply

Oxygen Deprivation

- **Functional hypoxia (an oxygen issue):**
  - **Low partial pressure of oxygen** — within blood
  - **Impaired oxygen carrying capacity of the blood** — ex) problem with Hb molecule
  - **Inhibition of oxygen use by the tissue** — tissue can't adequately utilize oxygen provided
- **Ischemia (a blood issue):** — Not enough blood is going to the brain
  - **Interruption of the circulation**
  - **Hypotension**
  - **Vessel obstruction**

2 types of ischemic injury
1. Global
2. Focal

Ischemic Injury

- **Global**
  - **Generalized reduction of cerebral perfusion**
  - **Cardiac arrest, shock, severe hypotension**

- **Focal**
  - **Local reduction or cessation of blood flow**
  - **Atherosclerosis, thrombosis, emboli**

ex) thrombus in middle cerebral artery

ex) emboli of tumor

In an unfortunate event where you have reduced blood flow or ischemic event, what determines brain tissue survival?

Cerebral Ischemia

- **Brain tissue survival is influenced by:**
  - **Duration of ischemia**
  - **Availability of collateral circulation**
  - **Magnitude and rapidity of the reduction in flow**

is it brief or prolonged?

Certain cells in brain are more vulnerable to ischemia than others

Cerebral Ischemia

- **Selective Vulnerability:**
  - **Certain neurons and glial cells (glial cells = astrocytes, oligodendrocytes, and ependyma) are more vulnerable to ischemia than others**

- **Vulnerable Neurons**
  - **Purkinje cells -cerebellum**
  - **Hippocampus - CA 1,3,4 Ammon's horn**
  - **Cerebral cortex**

- **Vulnerable Glia**
  - **Oligodendrocytes**
  - **Astrocytes**

Oligodendrocytes and astrocytes are more vulnerable than ependyma to ischemia

Generally speaking, we are more worried about ischemic events on neurons than glial cells

Summary Points

Summary of what he talked about so far

- **The major mechanisms of cerebrovascular disease are ischemia, hypoxia, and hemorrhage**
- **The brain can be deprived of oxygen from deficiencies in the oxygen, the blood, or from interruption of the circulation**
- **Ischemia can affect the brain focally or globally**
- **Some neurons and glial cells are more susceptible than others to ischemia**

Cerebrovascular Accident

- **Stroke is the clinical description of a CVA**
- **Think of strokes as:**
  - **Ischemic**
  - **Hemorrhagic**
  - **Combined (delayed bleed into an ischemic site**

You have ischemic event then you hemorrhage into an ischemic site. This can happen in any organ in the body.

- **Acute therapeutic intervention with thrombolytic agents led to promotion of the term “brain attack”**

In last decade, there was large push to treat acute stroke with thrombolytic agents and that had promoted use of the term "brain attack" like "heart attack".

In old days, no treatment was available for stroke patients. Today, there is a lot can be done if you get to ER on time and have certain lesions in treatable locations.

The "Brain Attack" promotions have come out of favor although it used to be big thing. Here is an example !

Brain Attack, Like a Heart Attack, Is a Medical Emergency!

Remember the three "R's"...

Reduce Risk of Stroke!

- Check blood *pressure.*
- *Don't smoke.*
- Recognize and treat *diabetes.*
- Consult your doctor about drinking *alcohol.*
- Eat a *healthful diet.*
- Be physically *active.*
- Get regular medical *checkups.*

Recognize Signs of Stroke!

- Sudden *weakness* on one side.
- Sudden *dimness* or loss of *vision.*
- *Trouble talking* or understanding speech.
- Sudden severe unexplained *headaches.*
- Sudden *dizziness* or falls, especially with any of the previous symptoms.

Respond Immediately to Stroke!

- Call the *emergency* medical service system. This may be 911 or another number.
- If the *fastest way* to get the person to the hospital is to drive them, then do so. Go to the *nearest* medical facility with 24-hour emergency care.

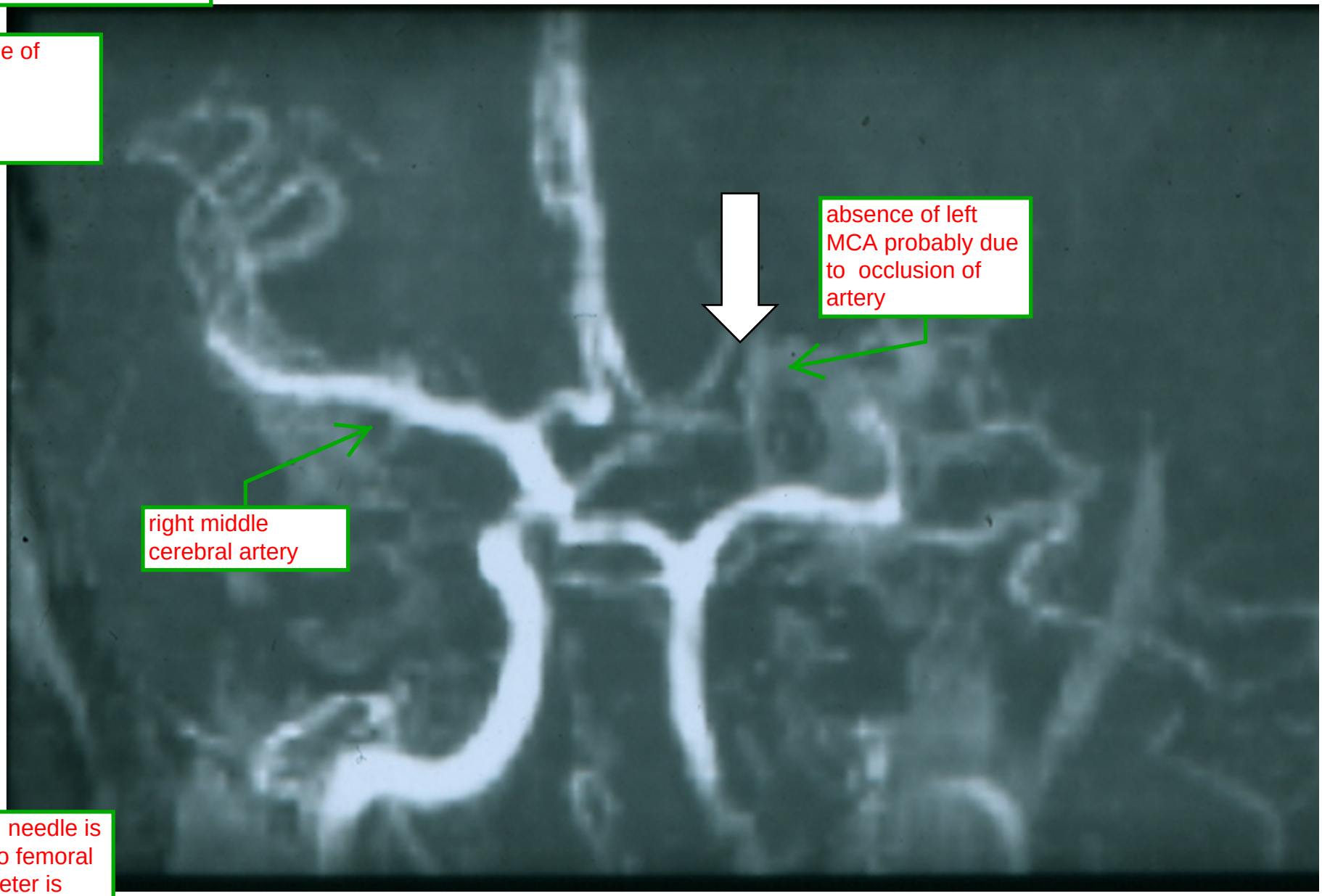
If you or someone you know has experienced a stroke, or is at risk of a brain attack, call Stroke Connection.

1-800-553-6321

Stroke Connection

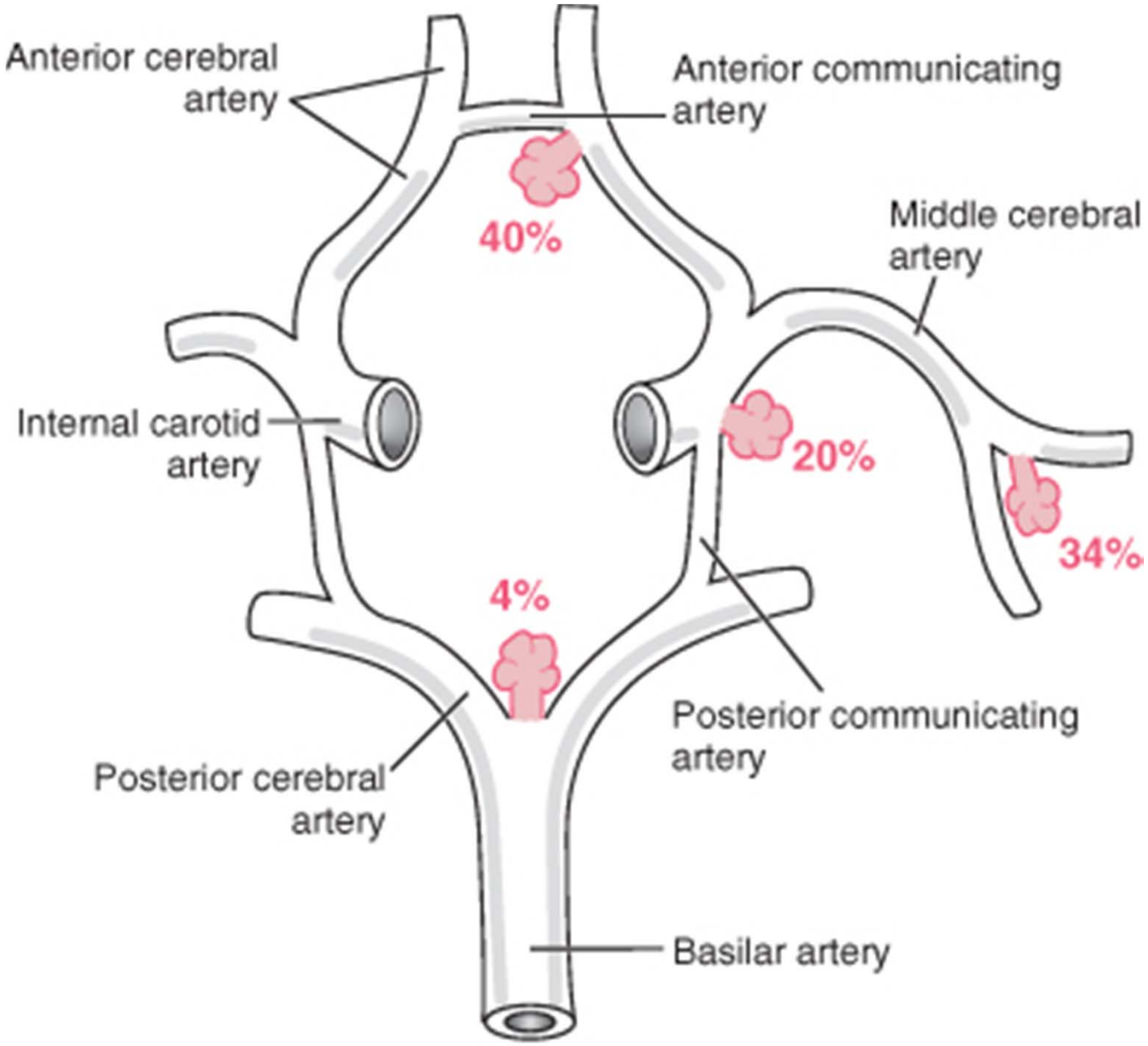
When you look at any image of brain, you are looking for something asymmetrical.

This is Circle of Willis..



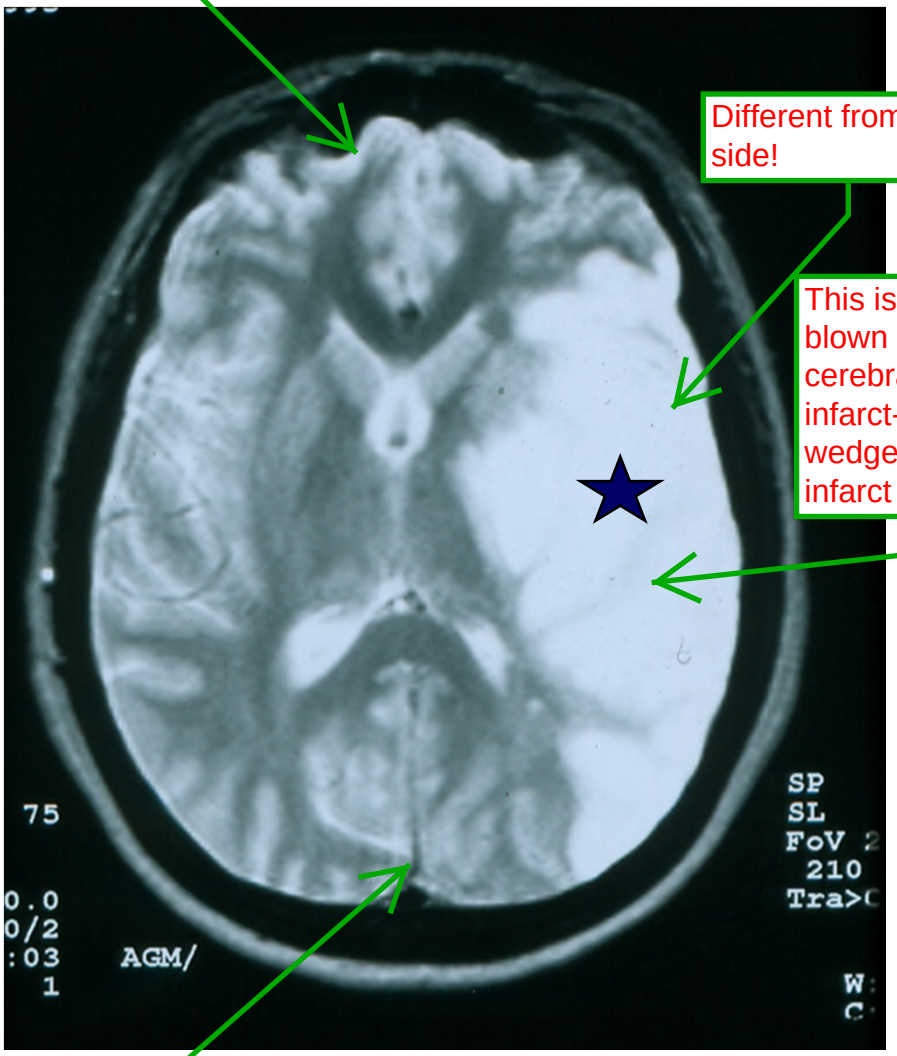
Angiogram: needle is inserted into femoral artery, catheter is inserted, dye is injected and travels to brain, picture of brain vasculature is taken.

Angiogram, Circle of Willis, occluded left MCA



Again, you are looking for any asymmetry in the brain

T2-weighted MRI of the brain: Infarct involving the left middle cerebral artery (MCA) territory ★



Anterior cerebral artery domain is more anterior part of the brain

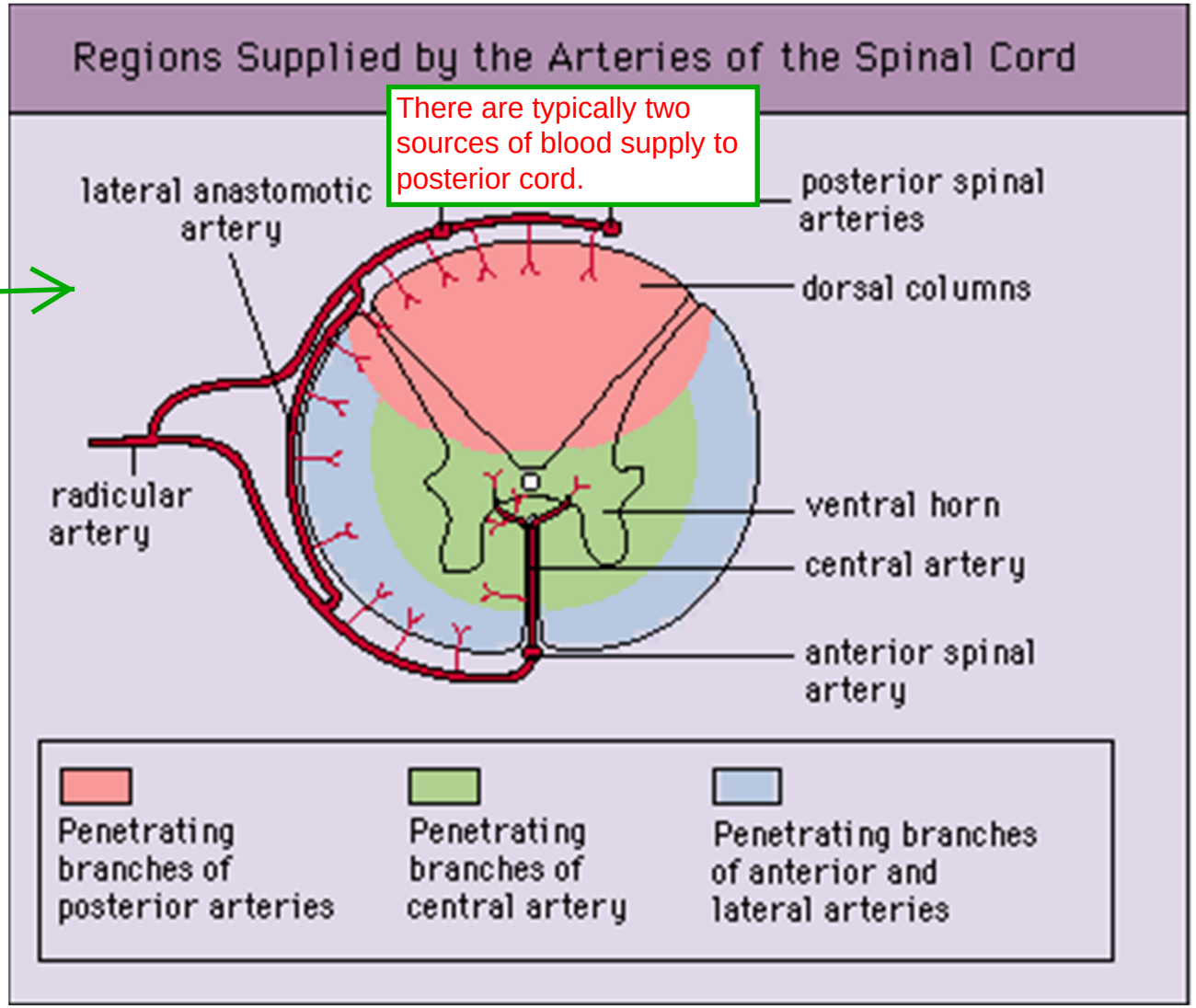
Different from right side!

This is classic full-blown middle cerebral artery infarct- classic wedge-shaped infarct

Posterior cerebral artery is more in the back of brain

Infarcts do occur in the spinal cord.

Infarcts also occur in the spinal cord



Remember the blood supply of spinal cord from brain&behavior? Reduced blood flow to spinal cord results in infarct.

These descriptions are important for figuring out what exactly happened to pt and when exactly infarct happened

Pathology of Infarcts

Two levels of pathology

- Gross
- Microscopic

Infarcts can be described as

- Acute (12 hours – 3 days)
- Subacute (3 days – 2 weeks)
- Chronic (weeks, months, years, decades)

Chronic infarcts will always be there.

Gross descriptions of acute infarct (<3days old)

Acute Infarct
Gross Pathology

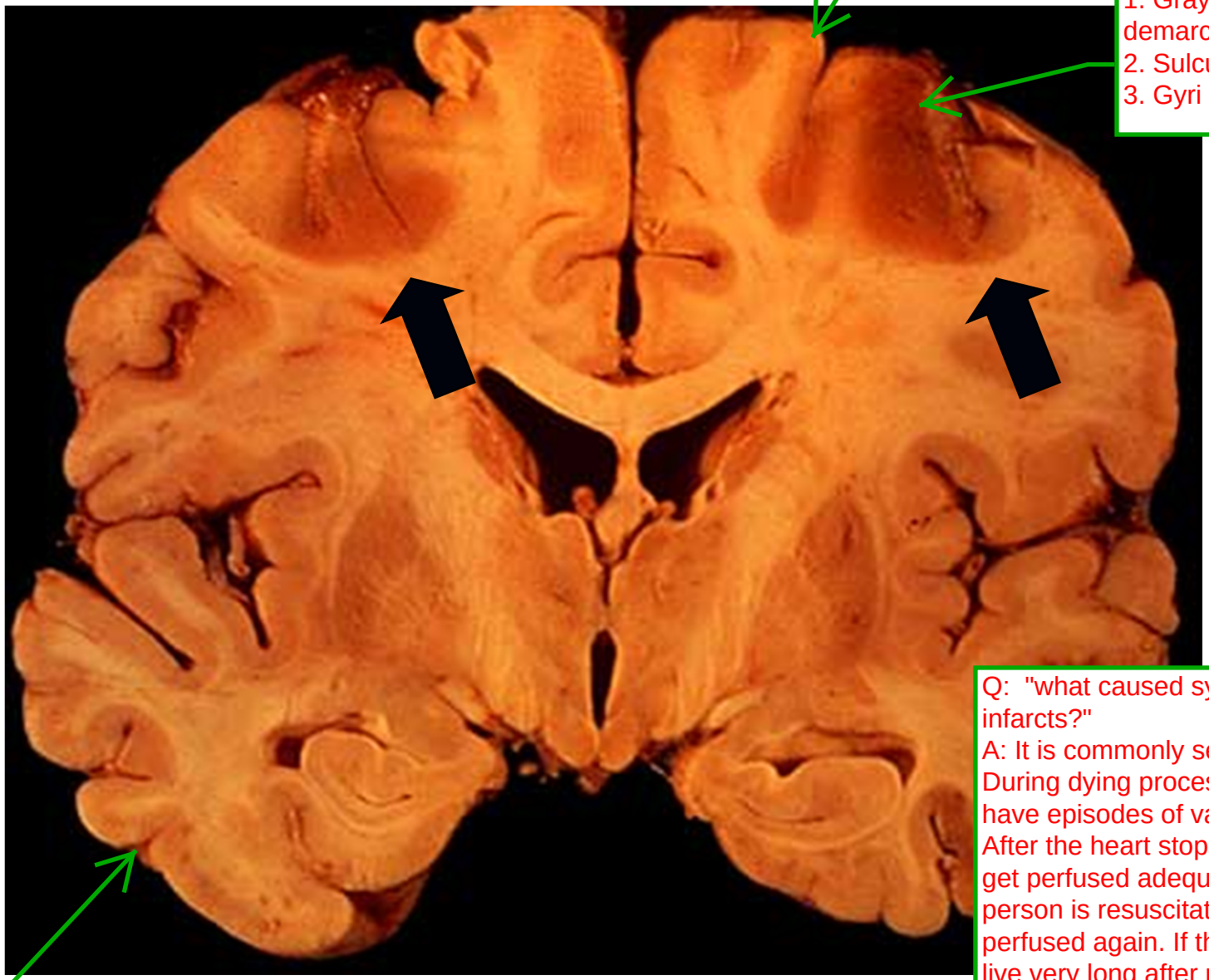
- **Brain swelling**
- **Gyri are widened**
- **Sulci are narrowed**
- **Gray-white junction poorly demarcated**

border zone

Acute infarct
1. Gray-white matter is poorly demarcated.
2. Sulcus is thin.
3. Gyri are widened.

We're looking at coronal section of brain

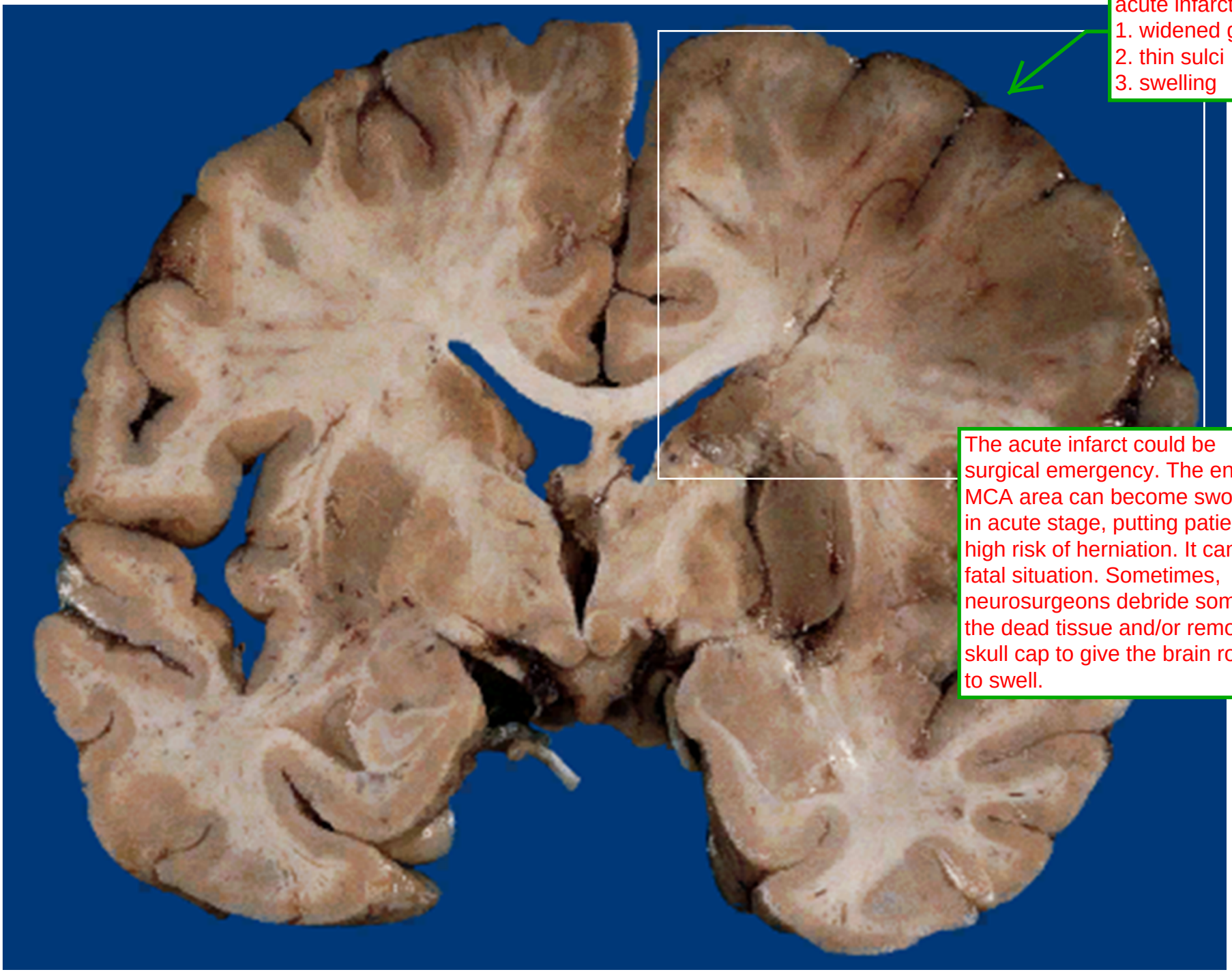
Arrows are where the infarcts are. Infarcts often occur at watershed areas or border zones. where ACA and MCA meet or MCA and PCA.



Watershed area infarct // Border zone of AC

Normal brain tissue
1.Normal gray/white junction
2.Normal size of gyrus and sulcus

Q: "what caused symmetrical infarcts?"
A: It is commonly seen during autopsy. During dying process, you frequently have episodes of vascular collapse. After the heart stops, the brain doesn't get perfused adequately. When the person is resuscitated, brain is perfused again. If the person doesn't live very long after resuscitation, you will see this kind of infarct at autopsy. Main point: the symmetrical kind of pathology is more commonly seen during dying process. Something bilateral implies a global event.


Another picture of acute infarct
1. widened gyri
2. thin sulci
3. swelling
The acute infarct could be surgical emergency. The entire MCA area can become swollen in acute stage, putting patient at high risk of herniation. It can be fatal situation. Sometimes, neurosurgeons debride some of the dead tissue and/or remove skull cap to give the brain room to swell.

The histological descriptions could make great exam questions !!

Acute Infarct Histology

- Neutrophils
- Red (eosinophilic) neurons

Neurons are usually blue/ purple color. In acute infarct, they turn red.

- Nuclear pyknosis and karyorrexis

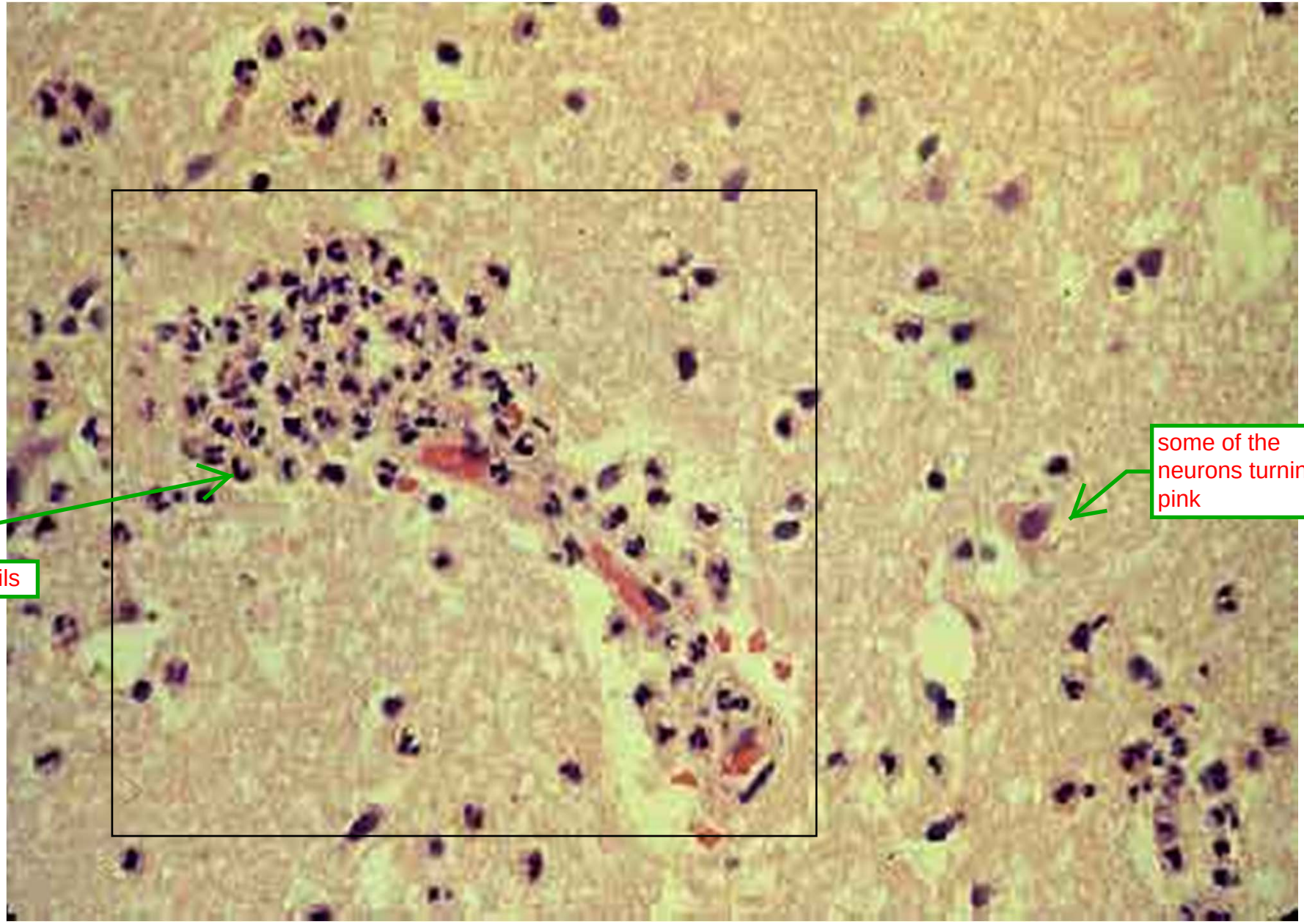
Nucleus begin to shrink and disintegrate.

- Vacuolation of the neuropil (edema)

substance in the parenchyma of brain

what acute infarct would look like histologically

Neutrophils



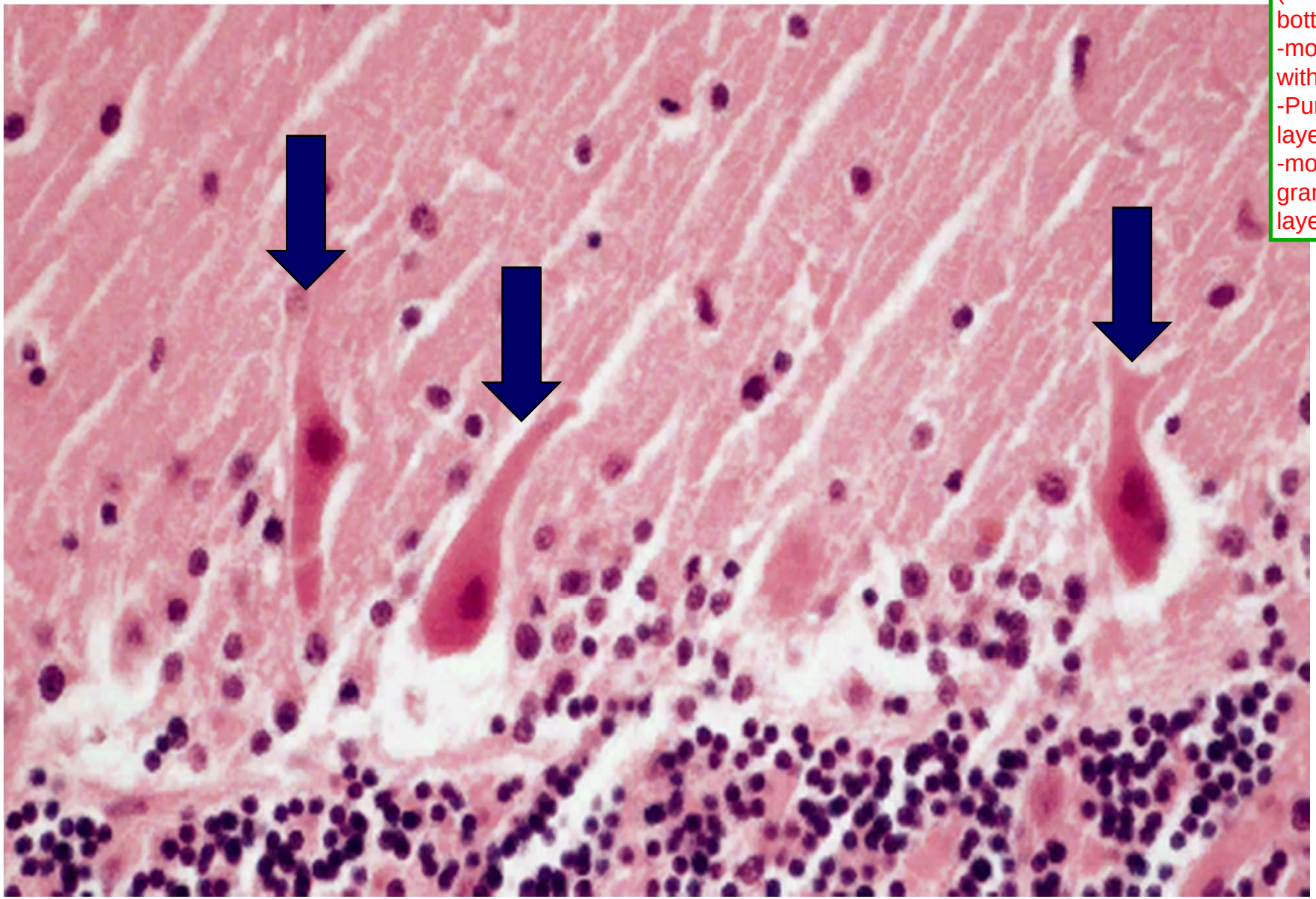
lots of neutrophils

some of the neurons turning pink

Main point: Neurons in acute infarct are bright red, eosinophilic looking.

Red Neurons: Purkinje neurons, cerebellum

How do you know it's cerebellum? (from top to bottom)
-molecular layer with glial cells
-Purkinje neuron layer
-molecular layer/ granular neuron layer



Subacute Infarct Pathology

after 3-4 days

- **Gross:**
  - **Brain softening**

still edematous looking

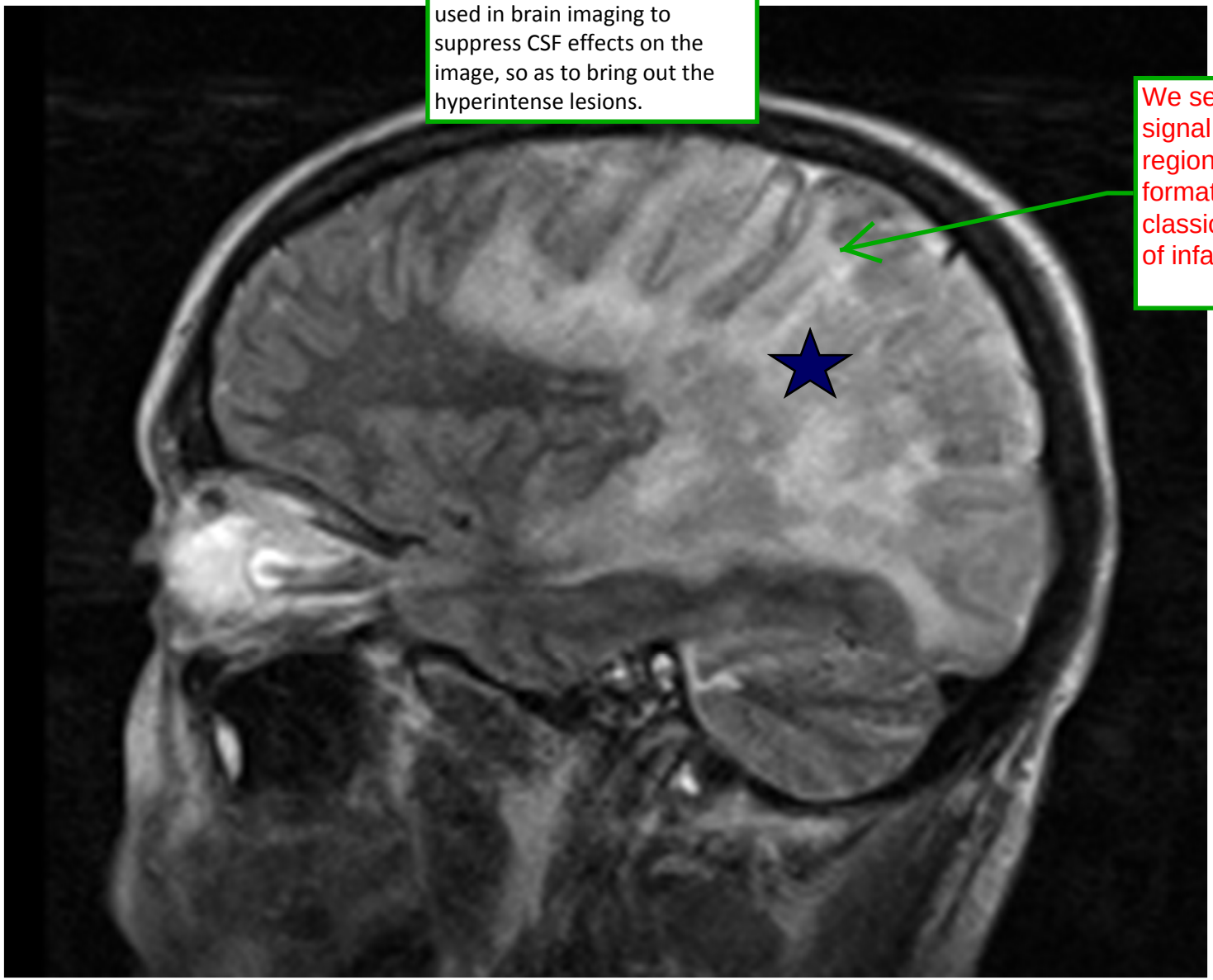
- **Histology:**
  - **Macrophage infiltrate**
  - **Capillary proliferation**
  - **Gliosis (reactive astrocytes)**
  - **Necrosis**

Neutrophils have left and macrophages have come. So if you see macrophages, you know its at least subacute or chronic stage.

You can often detect infarct with MRI.

Sagittal FLAIR subacute infarct

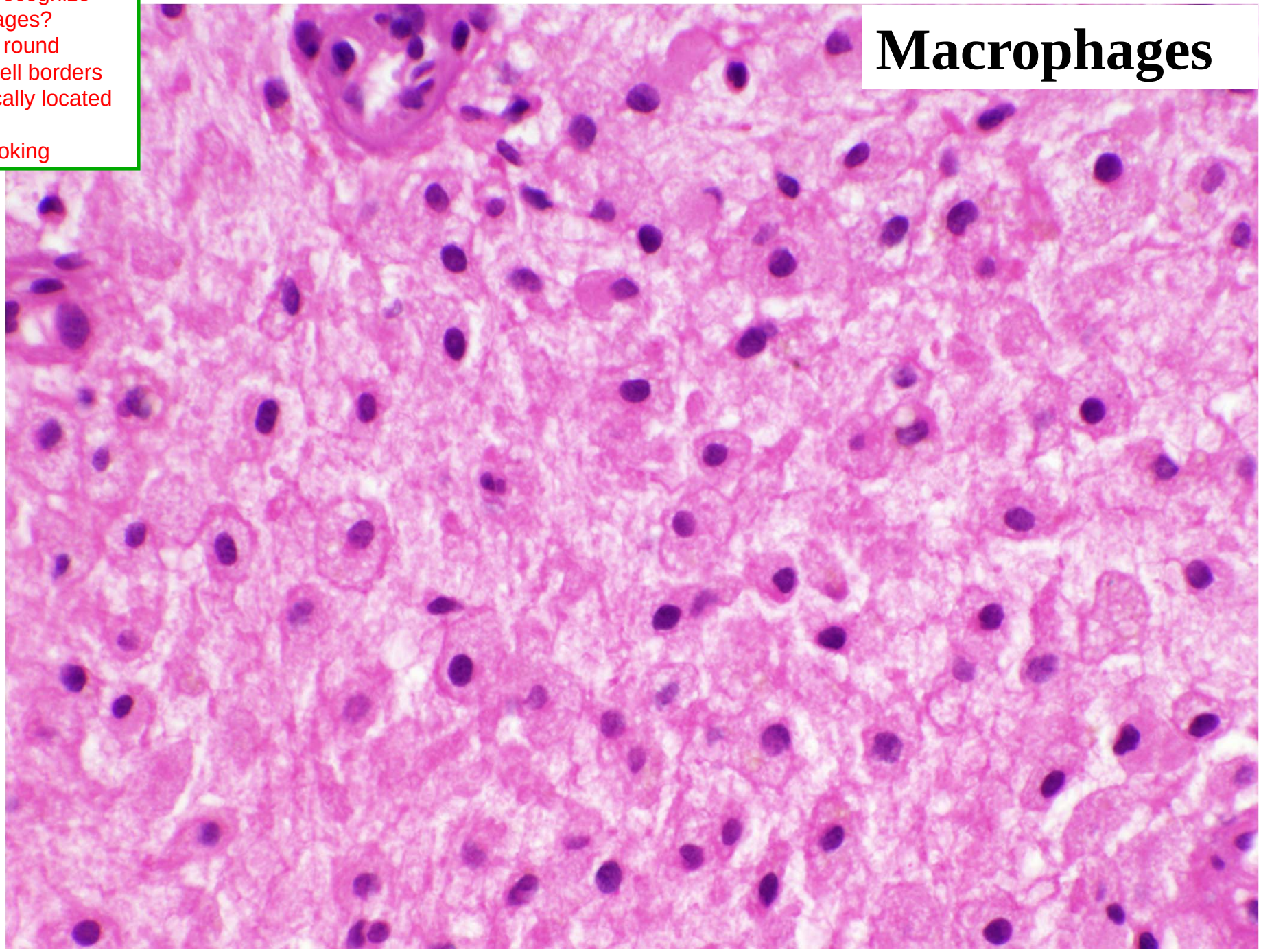
Fluid attenuated inversion recovery (FLAIR) is a pulse sequence used in magnetic resonance imaging. The pulse sequence is an inversion recovery technique that nulls fluids. For example, it can be used in brain imaging to suppress CSF effects on the image, so as to bring out the hyperintense lesions.



We see bright high signal in MCA region and gyral formation. This is classic appearance of infarct on MRI.

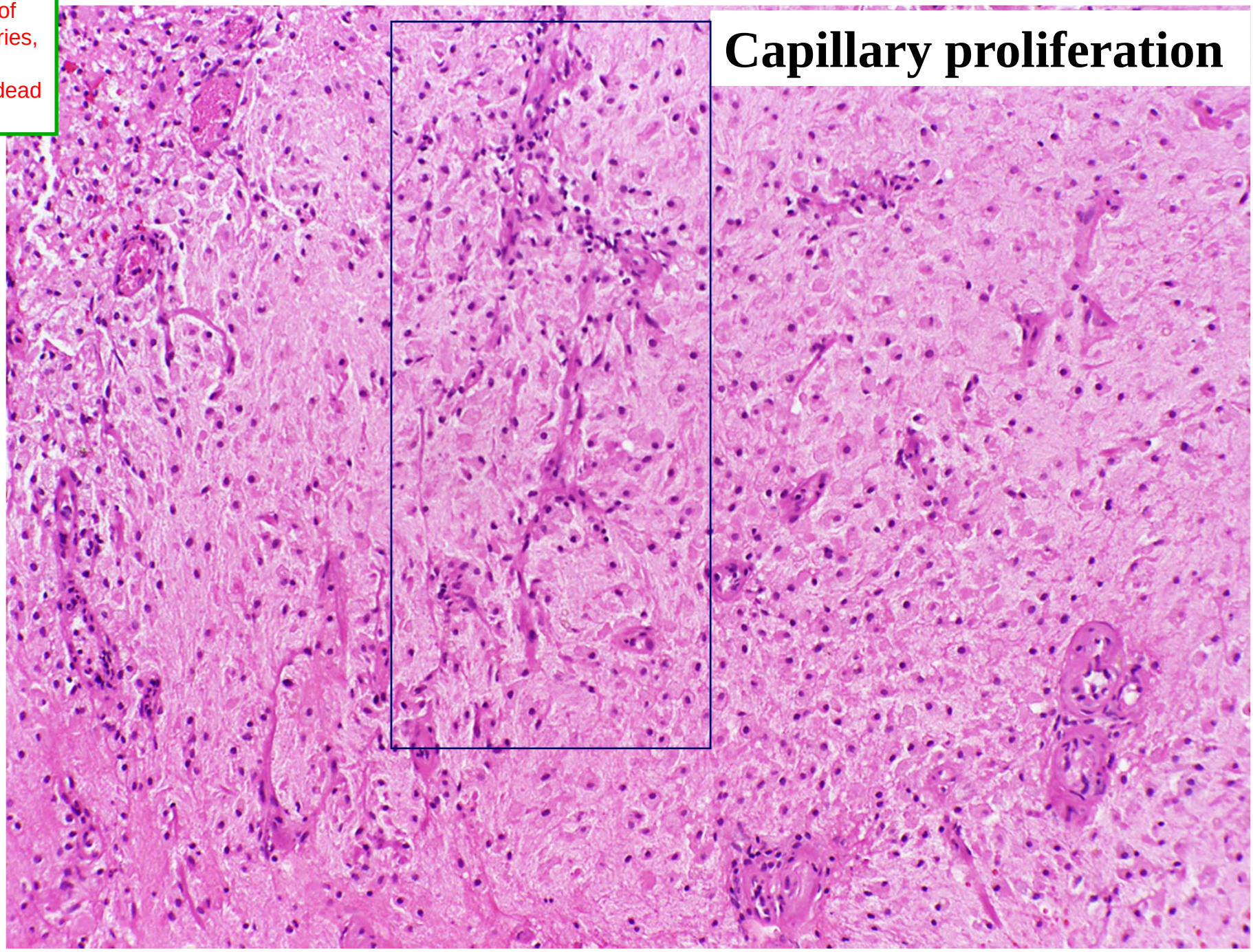
Can you recognize macrophages?
-perfectly round
-distinct cell borders
-eccentrically located nuclei
-foamy looking

Macrophages



You see proliferation of small capillaries, trying to re-vascularize dead tissue.

Capillary proliferation



Chronic Infarct Pathology

- **Gross:**
  - **After removal of the necrotic tissue, a cystic fluid-filled cavity remains; this is known as encephalomalacia**

Dead tissue is taken away with macrophages.

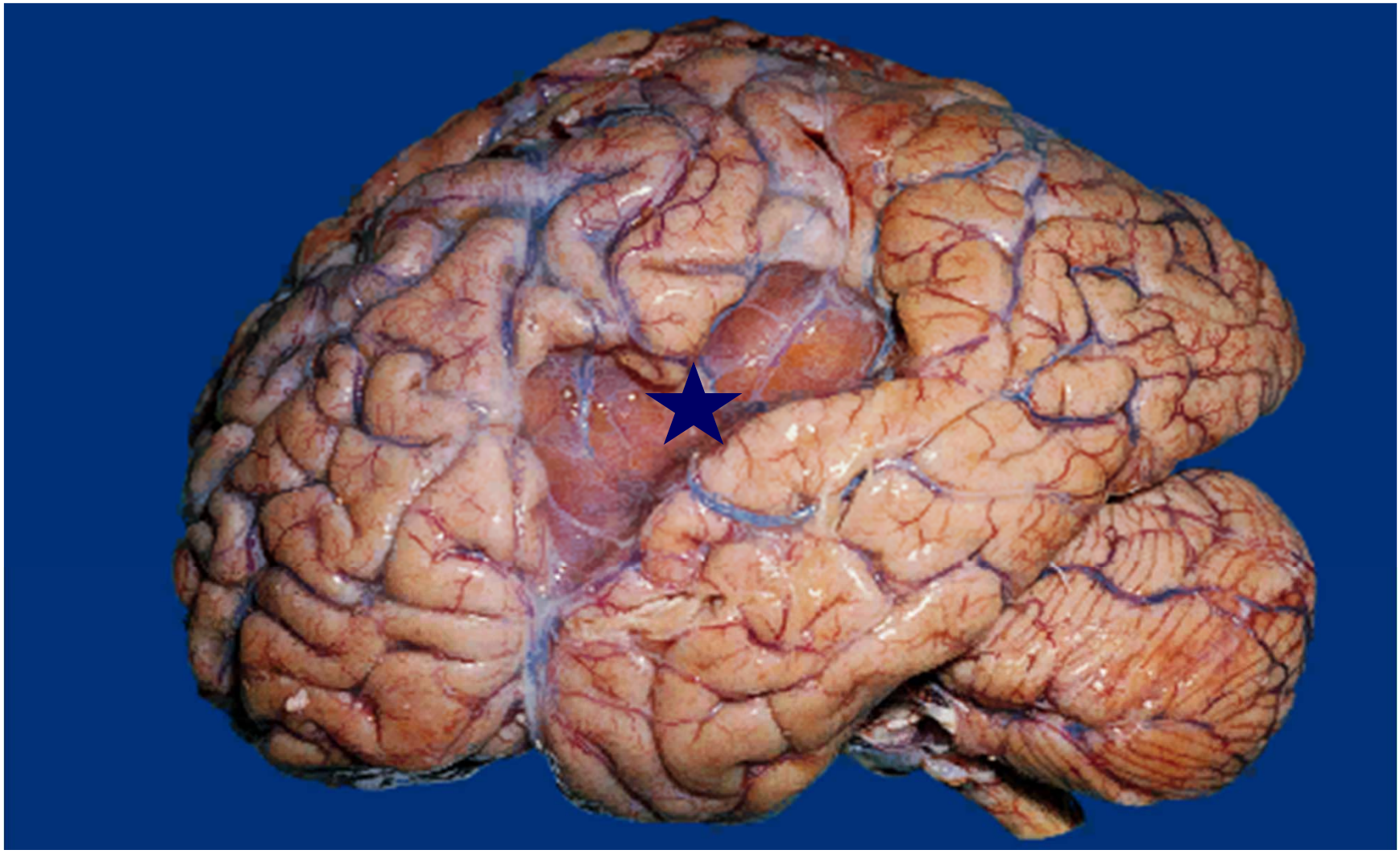
"bad brain"
-malacia: meaning bad
-encephalo: meaning brain

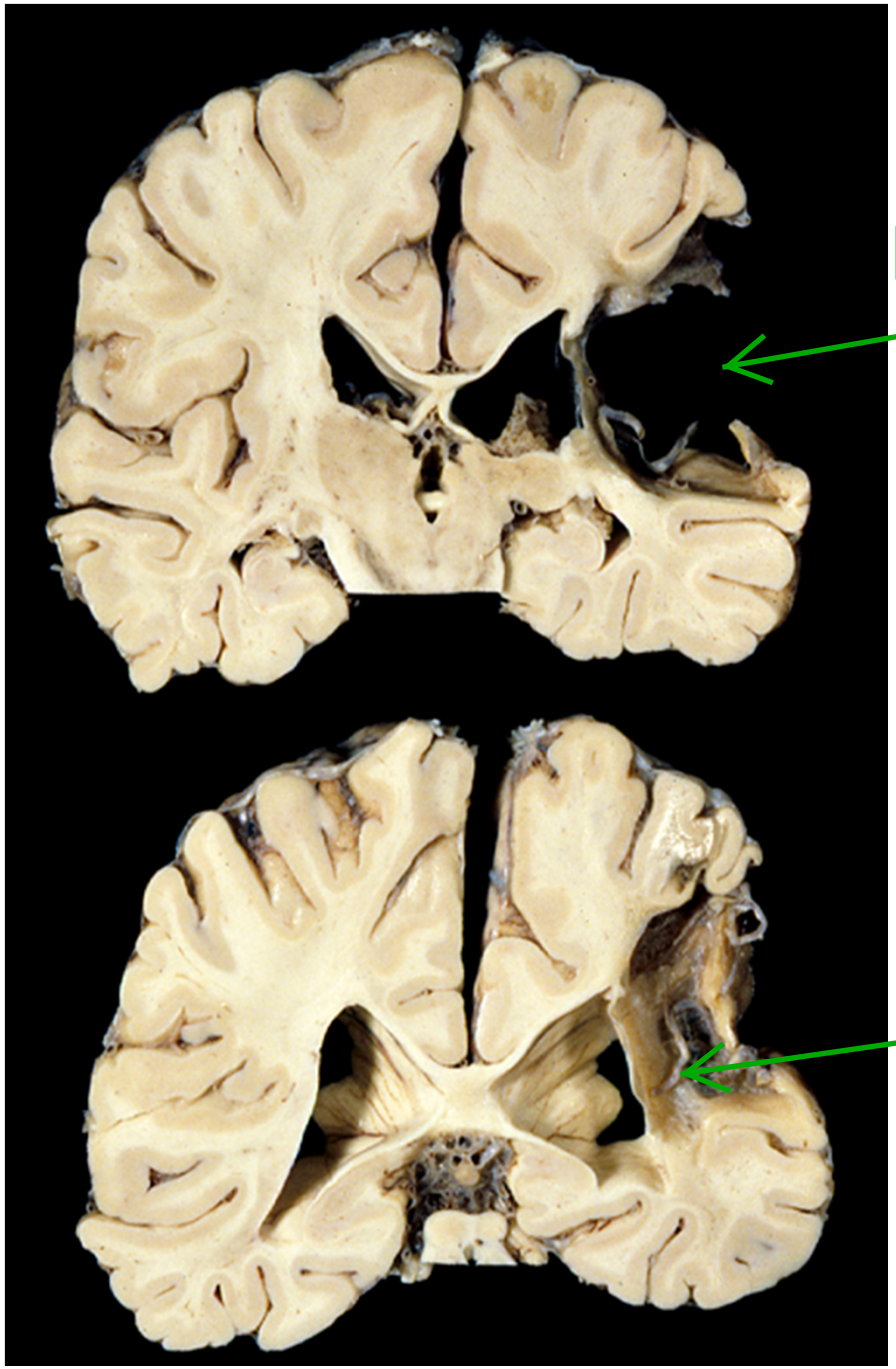
Brain does not repair itself as other organs do. The differences are
1. There is limited space for brain to swell.
2. No scar tissue is formed. Cavity is filled with CSF.

- **Histology:**
  - **Gliosis, hemosiderin, and macrophages remain indefinitely**

blood breakdown product, typically seen inside the infarct

Chronic Infarct





Chronic Infarct: Encephalomalacia

Big cyst
Histologically, it would be contain macrophages, reactive astrocytes and some blood products mostly at the edges of the injury. The dead tissue has been reabsorbed.

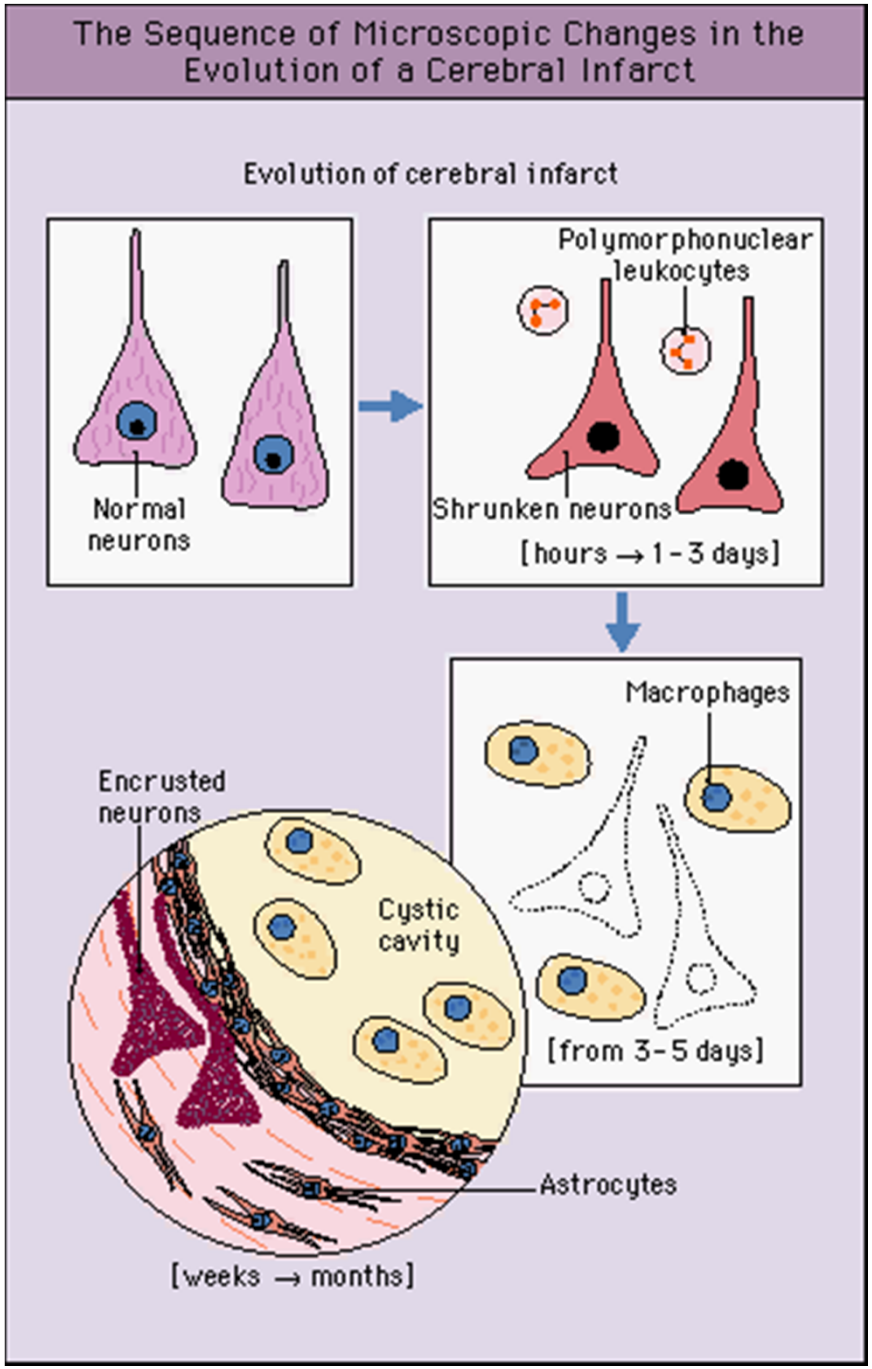
Take Home Points

- **Clinical examination and neuroimaging can determine where the lesion is and what vascular distribution is responsible**

- **Gross and microscopic findings can determine the age of a stroke**
  - **Acute**
  - **Subacute**
  - **Chronic**

Acute: pink neurons, shrunken nuclei, leukocytes
Subaucte: dead neurons, macrophages
Chronic: encrusted neurons, cyst cavity filled with macrophages and reactive astrocytes

Infarct Histology Summary



CNS hemorrhage classified by location

CNS Hemorrhage

can be classified by etiology and location

Classification // Location

- **Parenchymal**
  - **Basal ganglia (hypertension)**
  - **Lobar (congophilic amyloid angiopathy)**

present typically in elderly pt

meaning parenchyma of frontal, temporal, occipital lobe

- **Subarachnoid**
  - **Aneurysm rupture (Circle of Willis)**
  - **Trauma (convexity)**

- **Other types of hemorrhage not covered in this lecture:**
  - **Epidural – trauma**
  - **Subdural – trauma**
  - **Intraventricular: often secondary event**
  - **Combined**

Hemorrhagic Stroke
Mechanisms

3 main mechanisms

- **Hypertension**
- **Congophilic amyloid angiopathy**
- **Aneurysms // Vascular malformations**

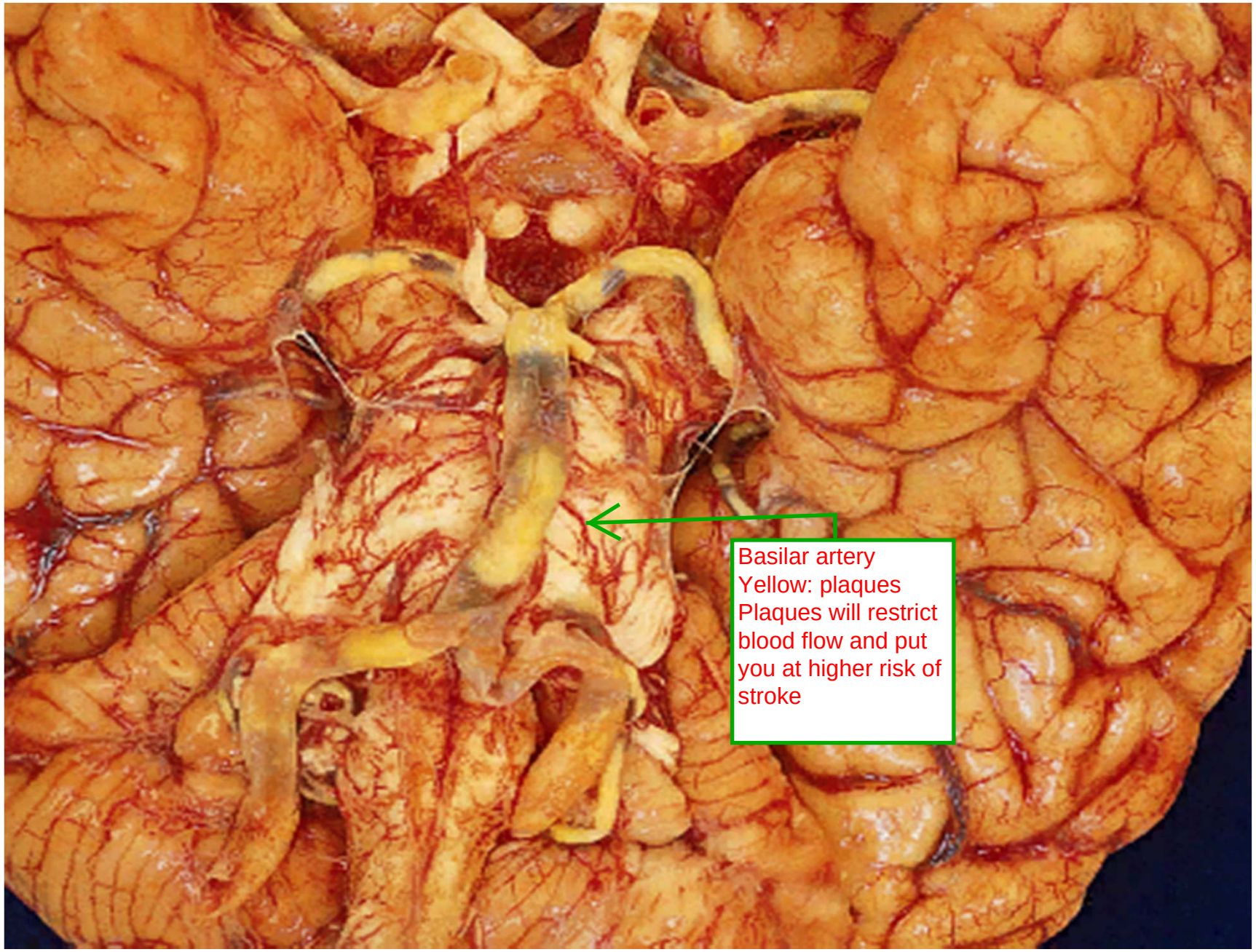
- **Other mechanisms not covered in this lecture:**
  - **Bleeding diathesis**
  - **Trauma**
  - **Neoplasm**

Hypertensive Cerebrovascular Disease

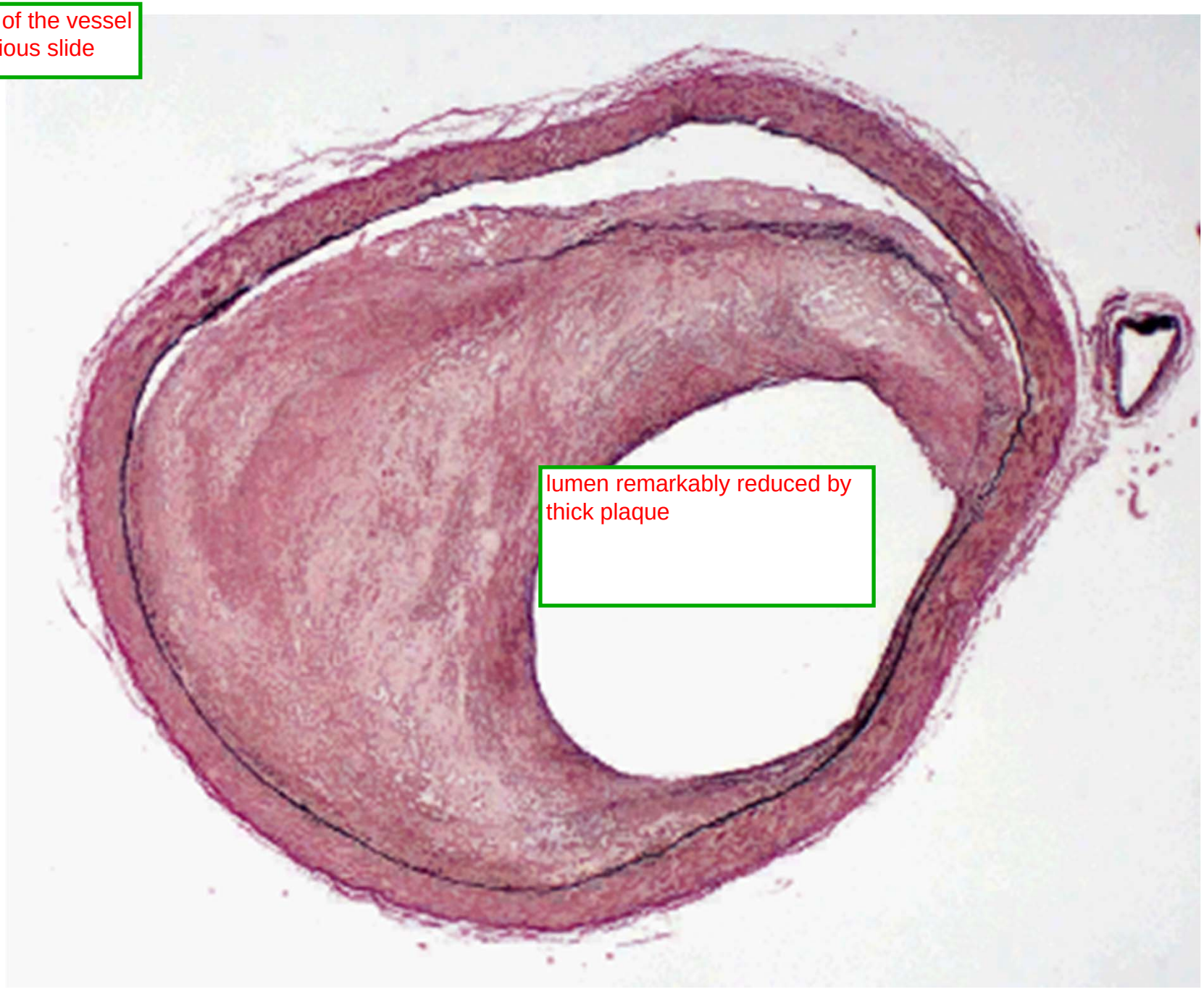
- **Hypertensive hemorrhage**
- **Lacunar infarcts**
- **Hypertensive encephalopathy**

malignant hypertension -> blood vessels in the brain become leaky, causing headaches

- **Frequent associations:**
  - **Atherosclerosis**
  - **Diabetes mellitus**


Basilar artery
Yellow: plaques
Plaques will restrict blood flow and put you at higher risk of stroke

A section of the vessel from previous slide

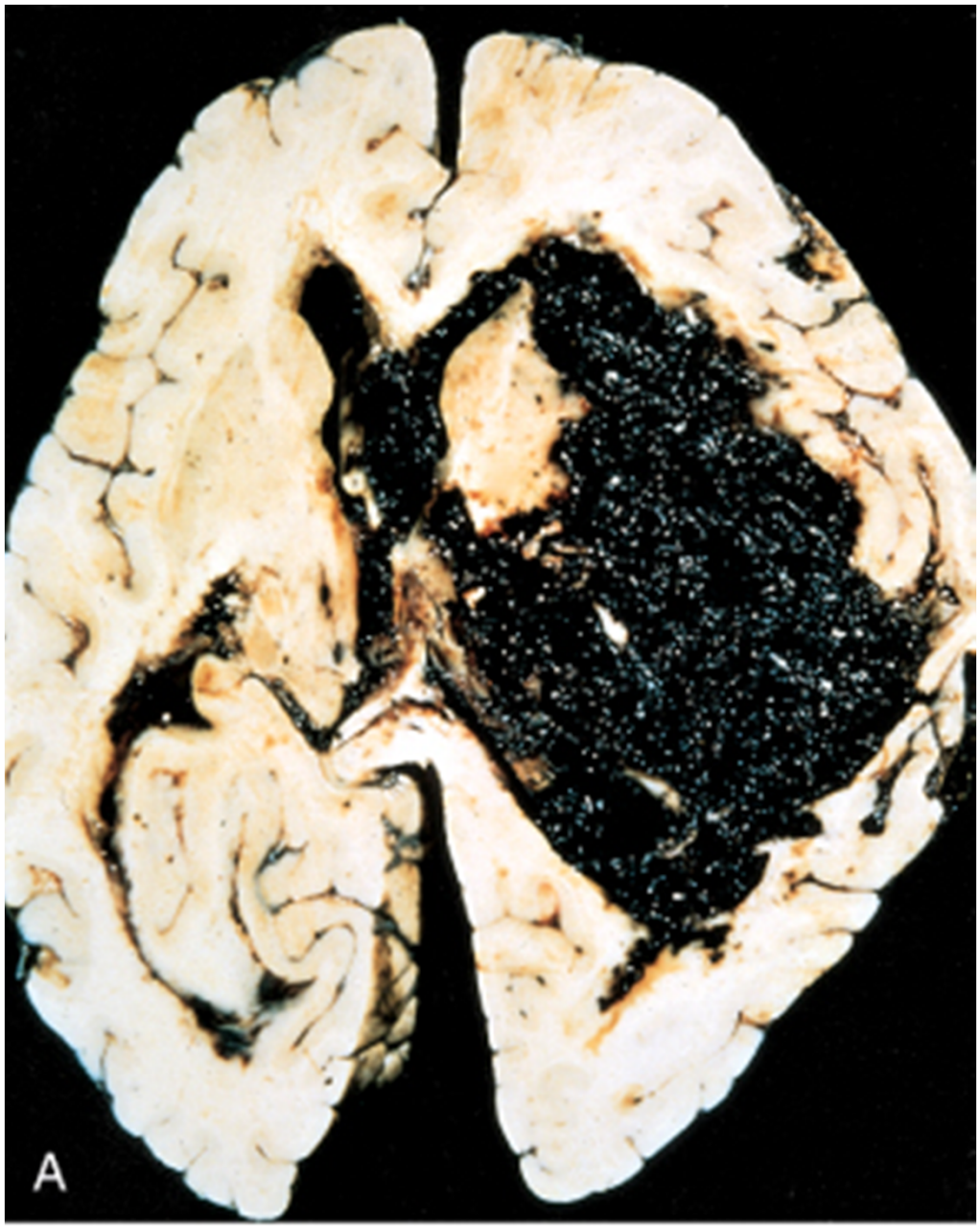


Main locations of hypertensive hemorrhage:
basal ganglia (thalamus, putamen, caudate nucleus), pons, cerebellum

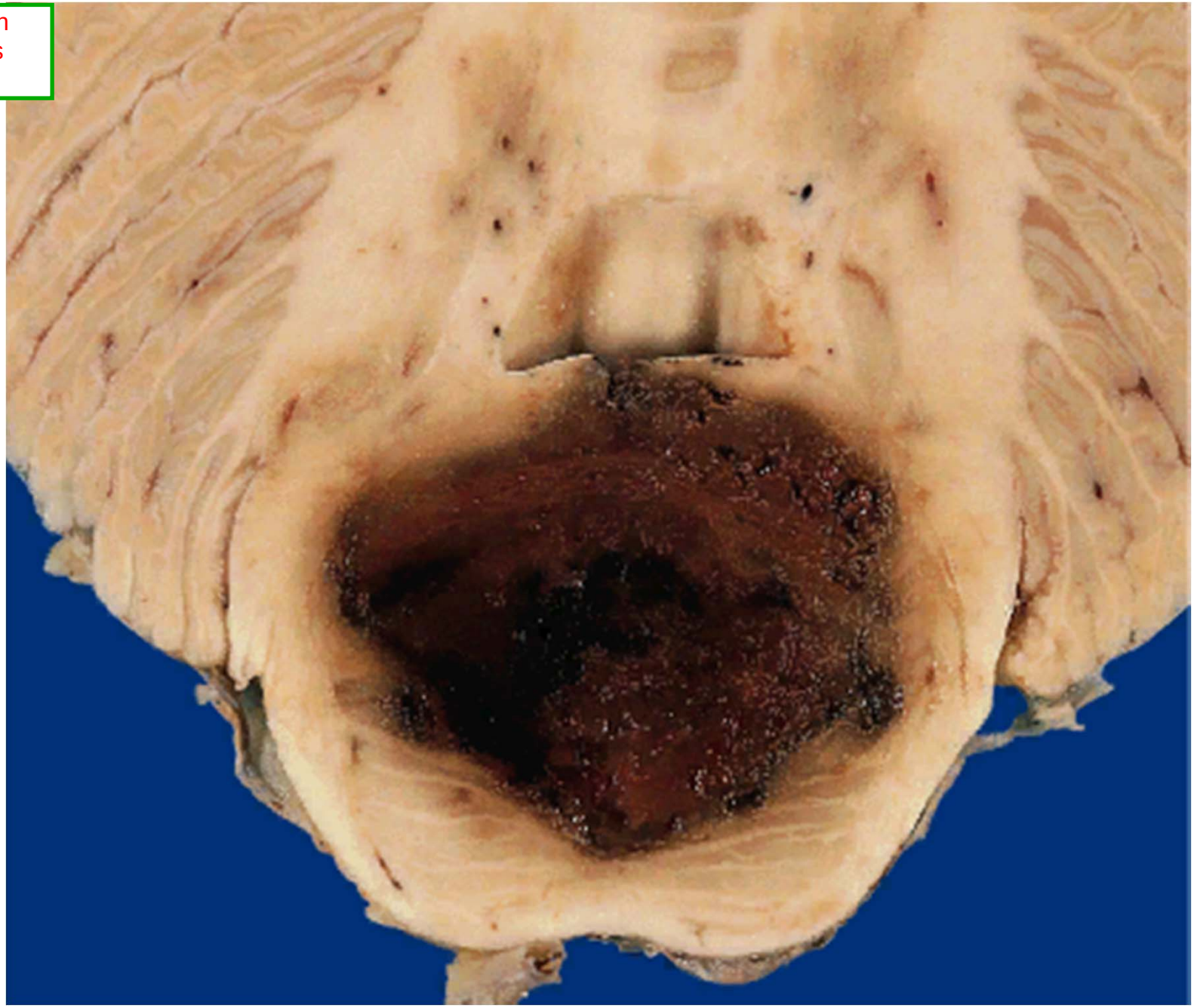
Hemorrhage

- **Hypertensive hemorrhage**
  - **Usually occur in region of basal ganglia**
  - **Other sites are mid-pons and cerebellum**

A picture of basal ganglia hemorrhage with secondary intraventricular hemorrhage



Hemorrhage within middle of the pons



Lacunar infarcts

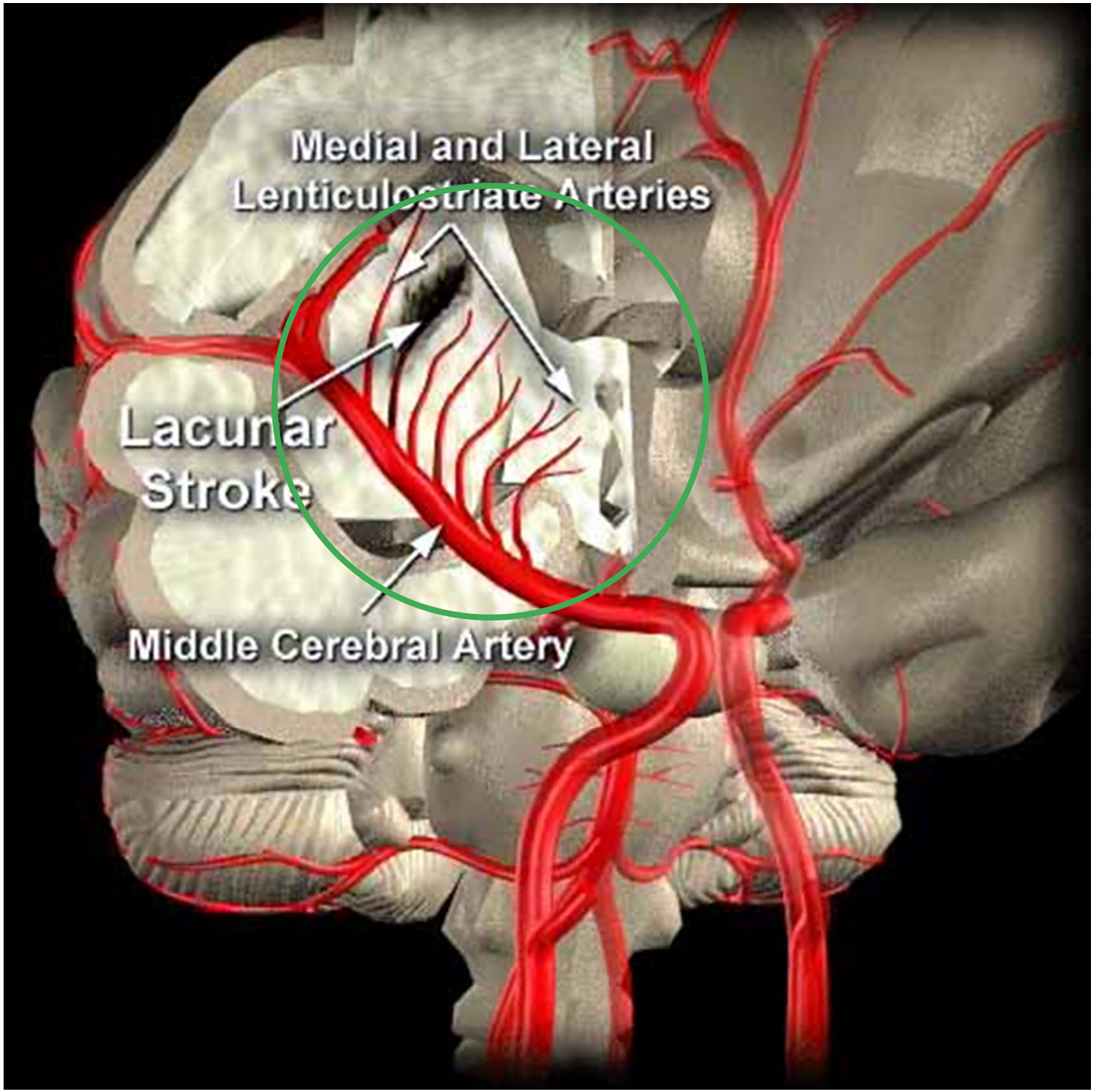
- **Hypertension, arteriolar sclerosis**
- **Medial and lateral lenticulostriate arteries**
  - **Lenticular nucleus, thalamus, internal capsule, deep white matter, caudate nucleus, pons**
- **Single or multiple; < 15 mm diameter**

They are tiny.

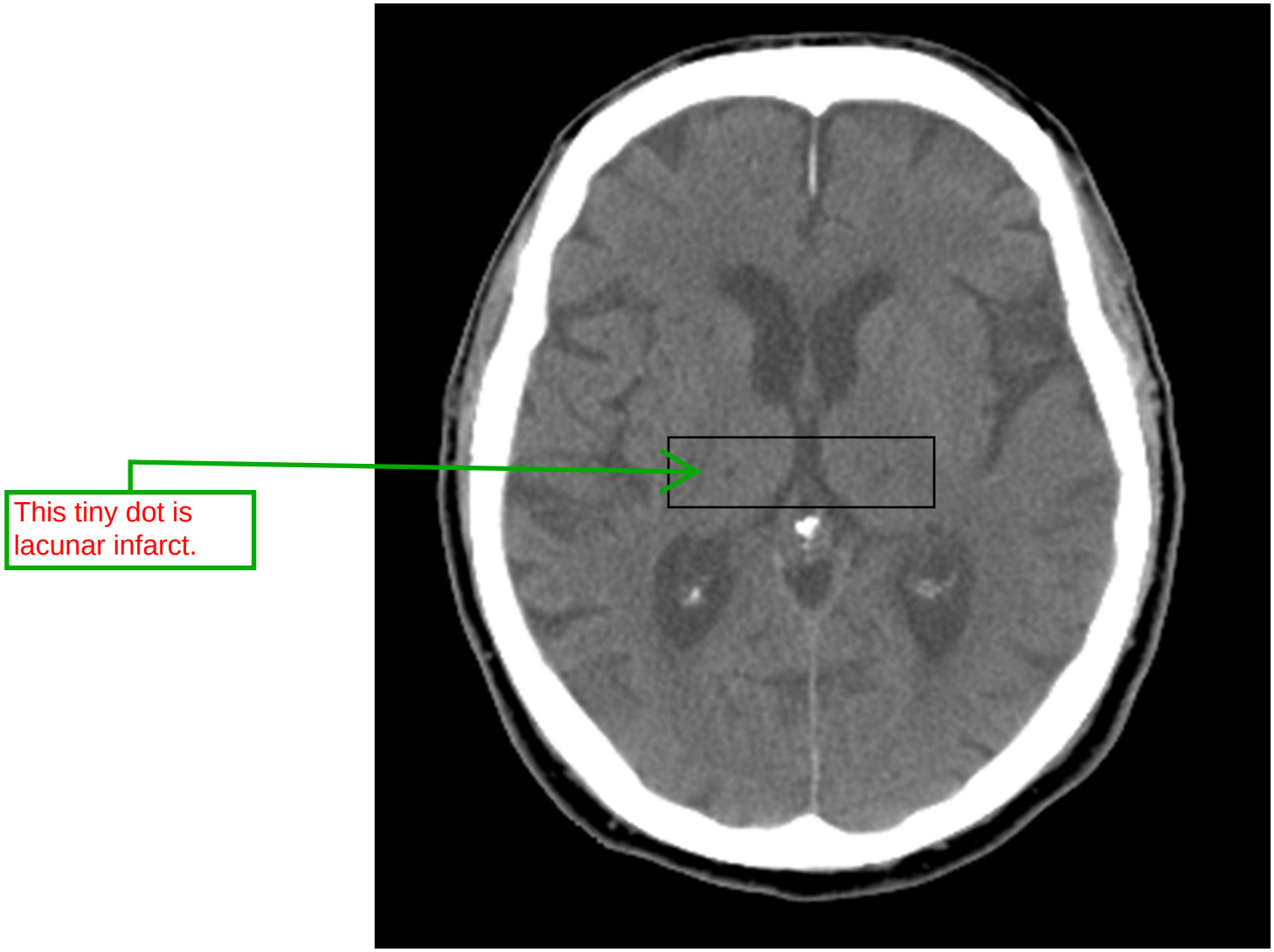
- **Clinically silent or devastating complications**

A lot of pathology and sequelae of neurological disease is highly dependent on location. Likewise, lacunar infarcts can be silent or devastating depending on its location.

See the arrows. That's where lacunar stroke occurs.



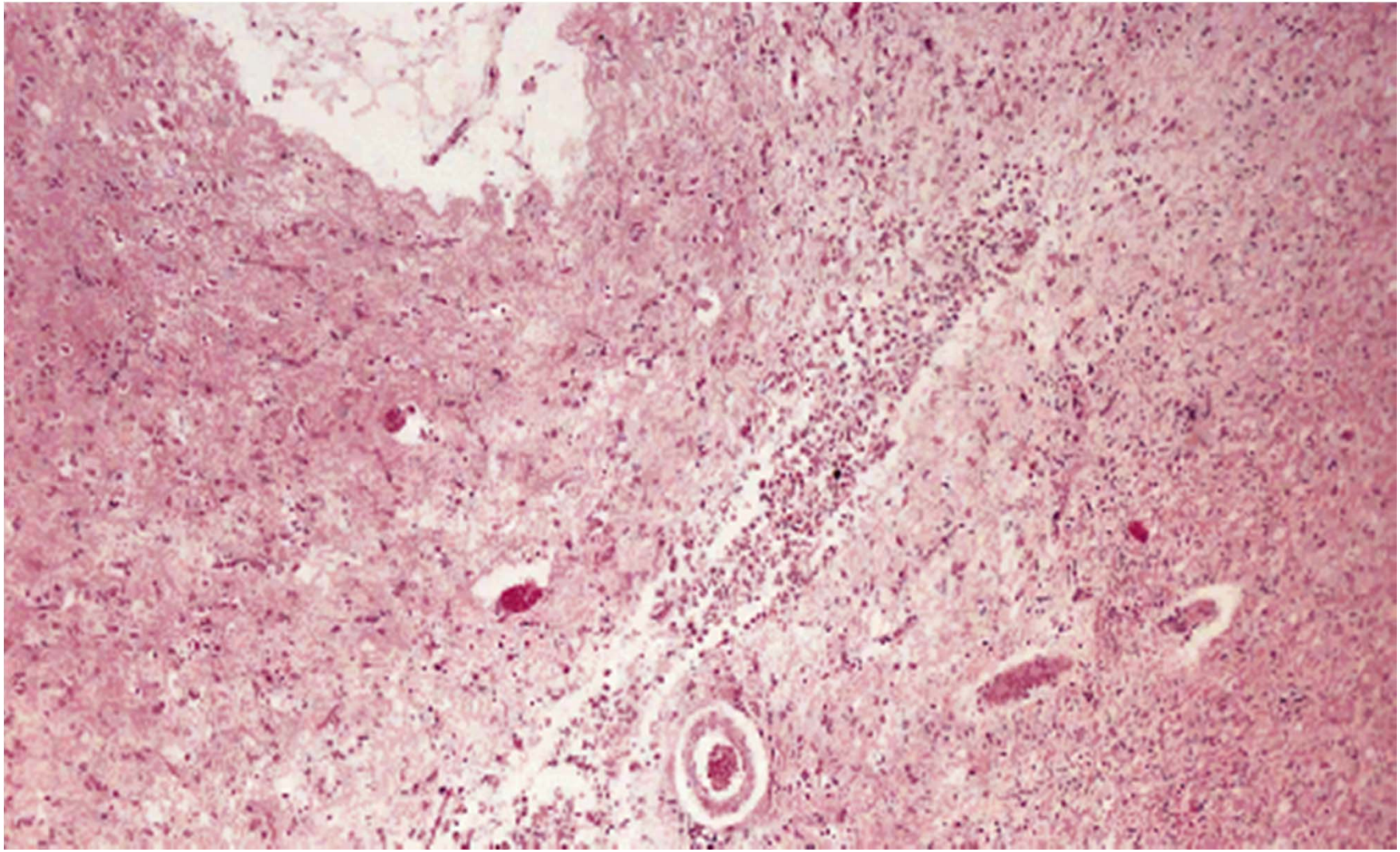
CT Brain: Lacunar infarcts



Lacunar infarcts, caudate, putamen

Histology is the same.
-capillary proliferation
-macrophages
-necrotic dead tissue.

Infarct



We're talking about systole BP at least 180 or 200

Hypertensive Encephalopathy

- **Acute:**
  - **Headaches, confusion, coma**
- **Chronic:**
  - **Vascular (multi-infarct) dementia**
  - **White matter (Binswanger disease)**
  - **Gray matter**

Congophilic Amyloid Angiopathy

- Usually occurs in 7^{th} - 8^{th} decades
- Parenchymal "lobar" hemorrhage
- Amyloid deposits in vessel walls
- "Lead-pipe" appearance of vessels
- Congo Red histochemical stain for amyloid

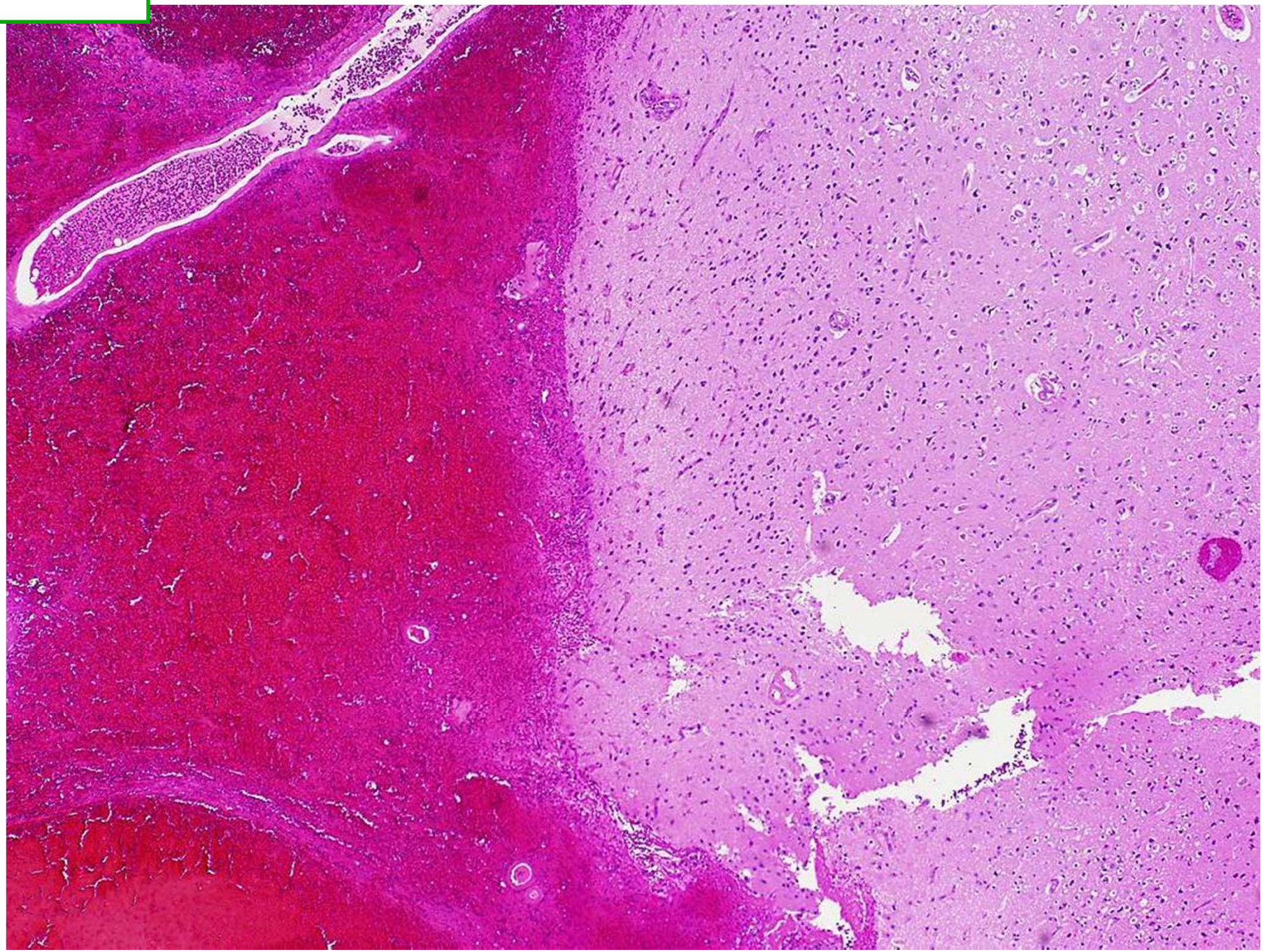
older population

Amyloid is a material that be deposited anywhere in the body.

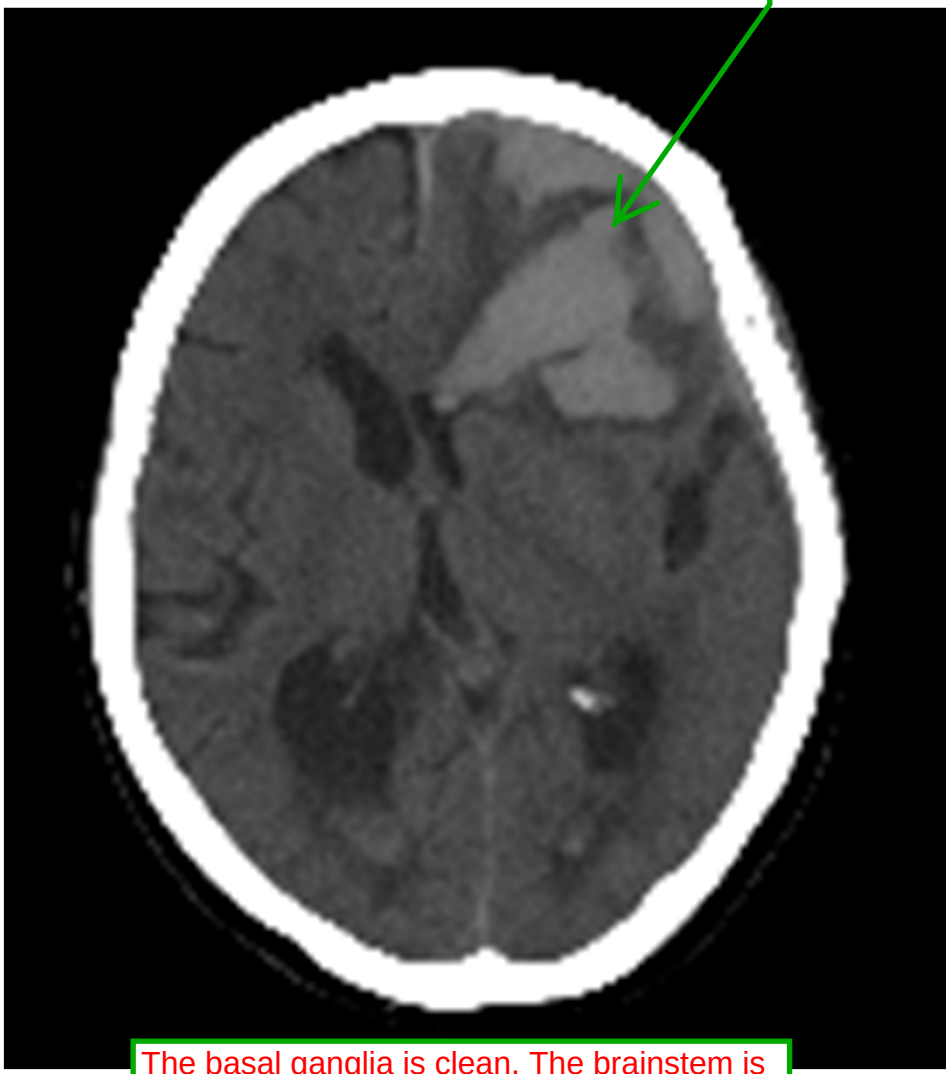
very round, rigid looking

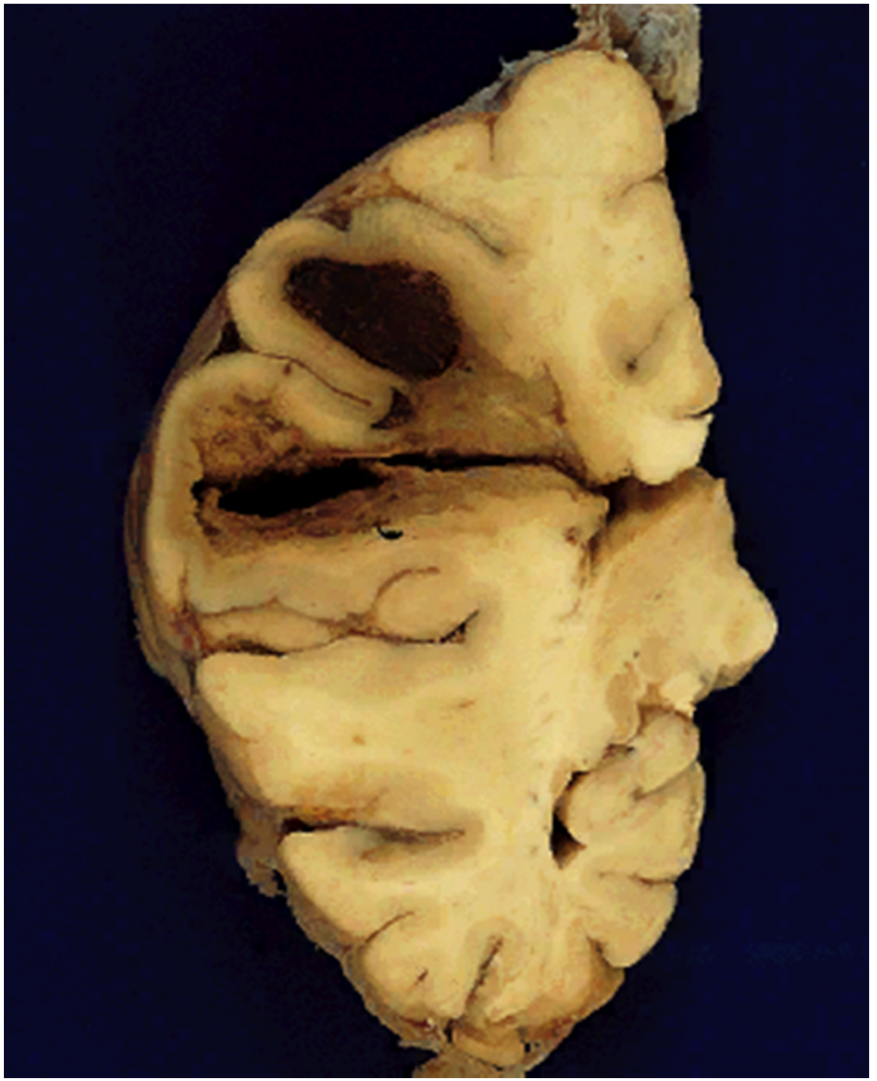
stain for amyloid

unremarkable at this level



massive hemorrhage in frontal lobe

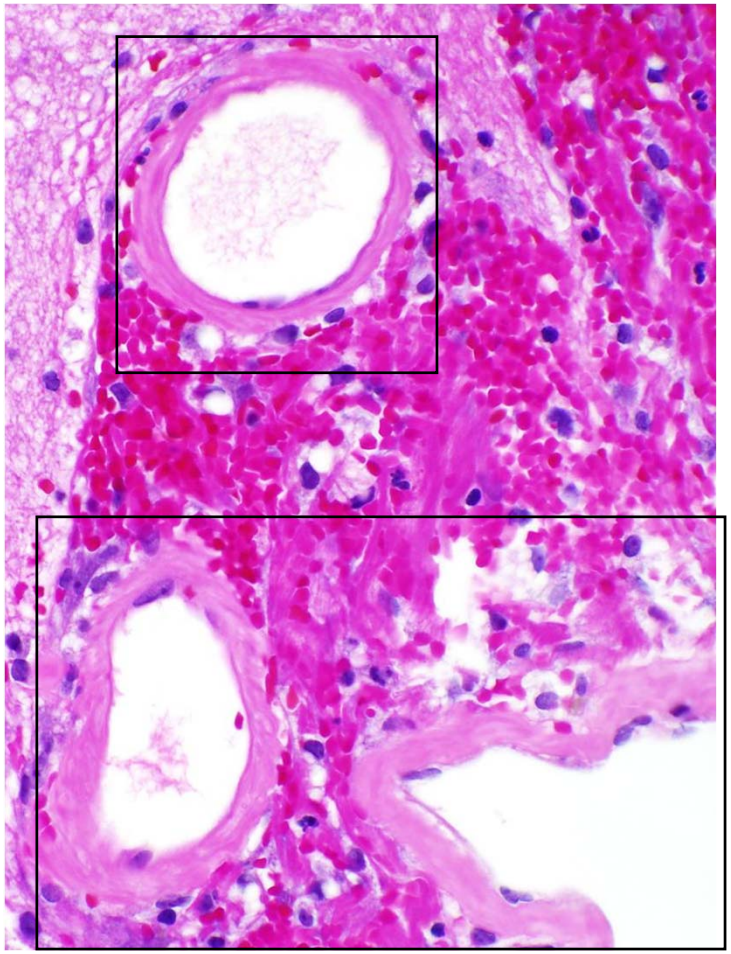




The basal ganglia is clean. The brainstem is clean. The ventricles are clean. Hemorrhage is restricted to frontal lobe. This is a good clue for 70 or 80 yrs old that the cause of this is congophilic amyloid angiopathy.

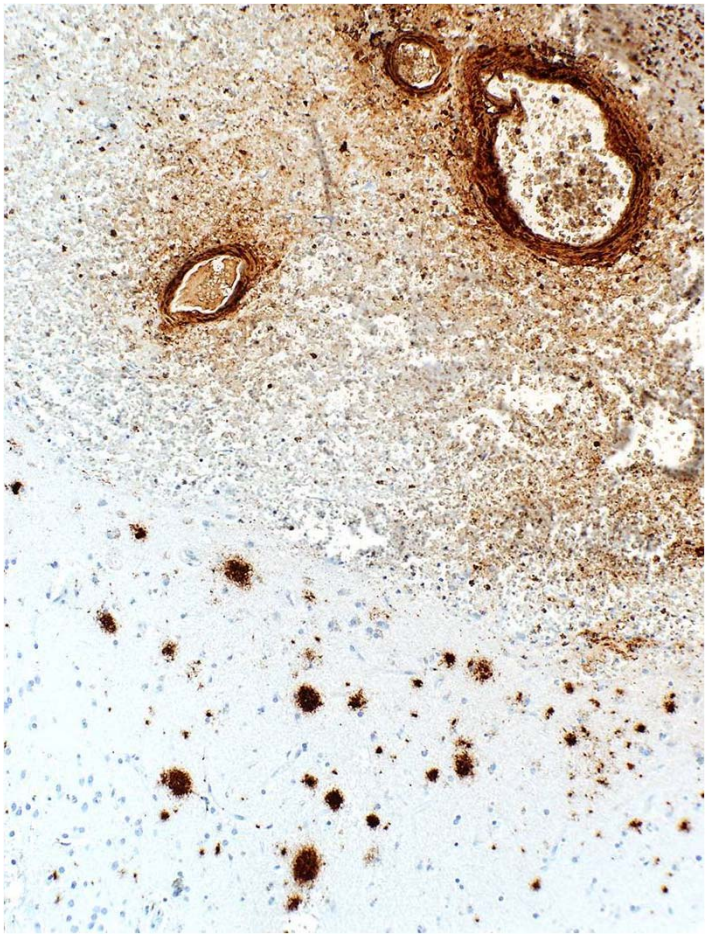
Blood vessels are lined by bright, red material.

H & E (amyloid pink in vessel walls)

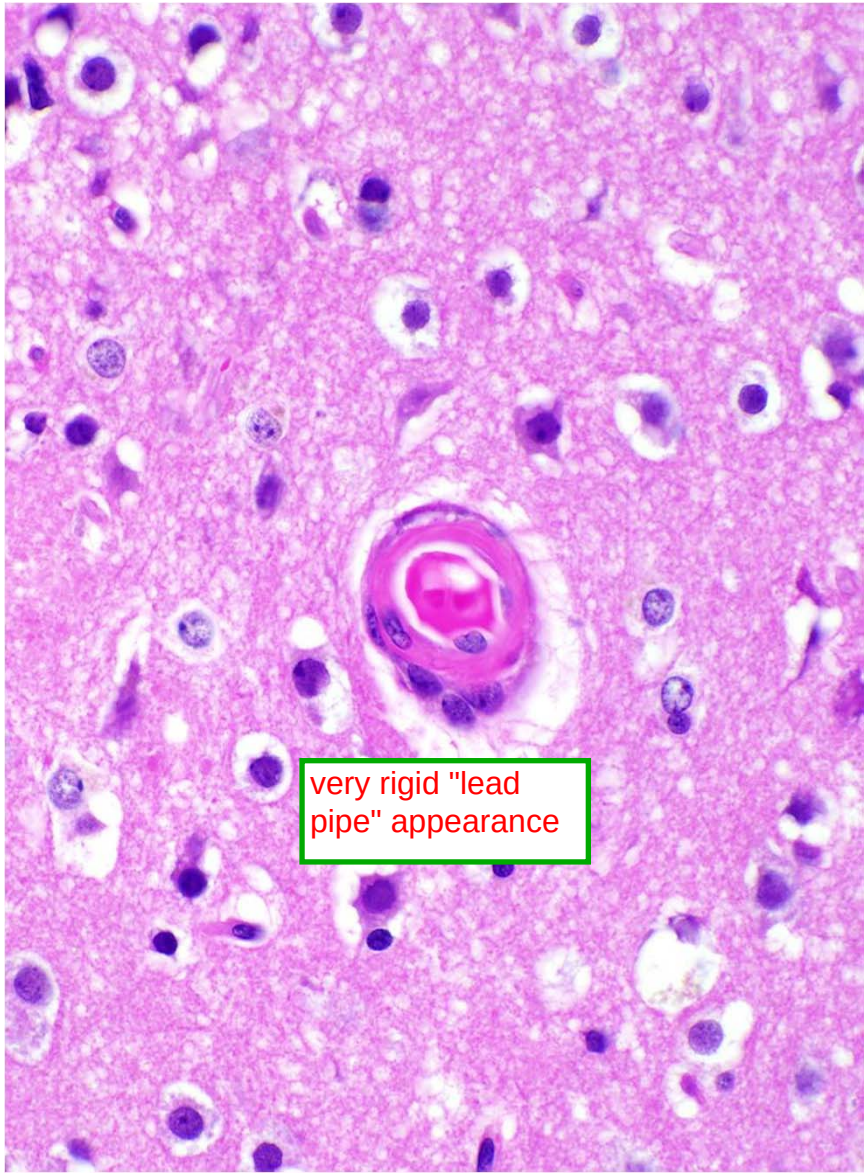


Congo stain, staining amyloid

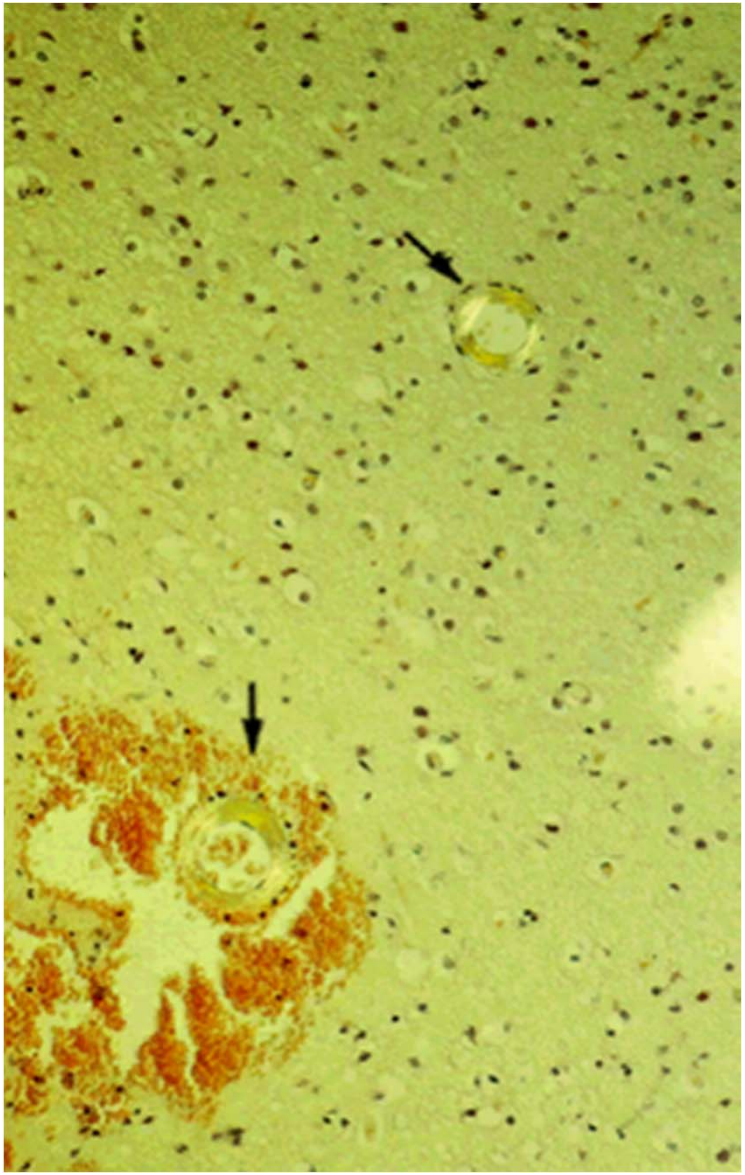
Amyloid immunostain (amyloid stains brown)



H & E



Congo red



Summary of CNS hemorrhage

Take Home Points

- **Hypertension:**
  - **Hemorrhagic stroke**
  - **Ischemic (lacunar) strokes (basal ganglia, pons, cerebellum)**
  - **Encephalopathy**

- **Amyloid angiopathy**
  - **Hemorrhages are parenchymal, lobar**
  - **Patients usually in 7^{th} - 8^{th} decades**

2 types

CNS Vascular Malformations

- **Aneurysms**
- **Vascular malformations**

Intracranial Aneurysms

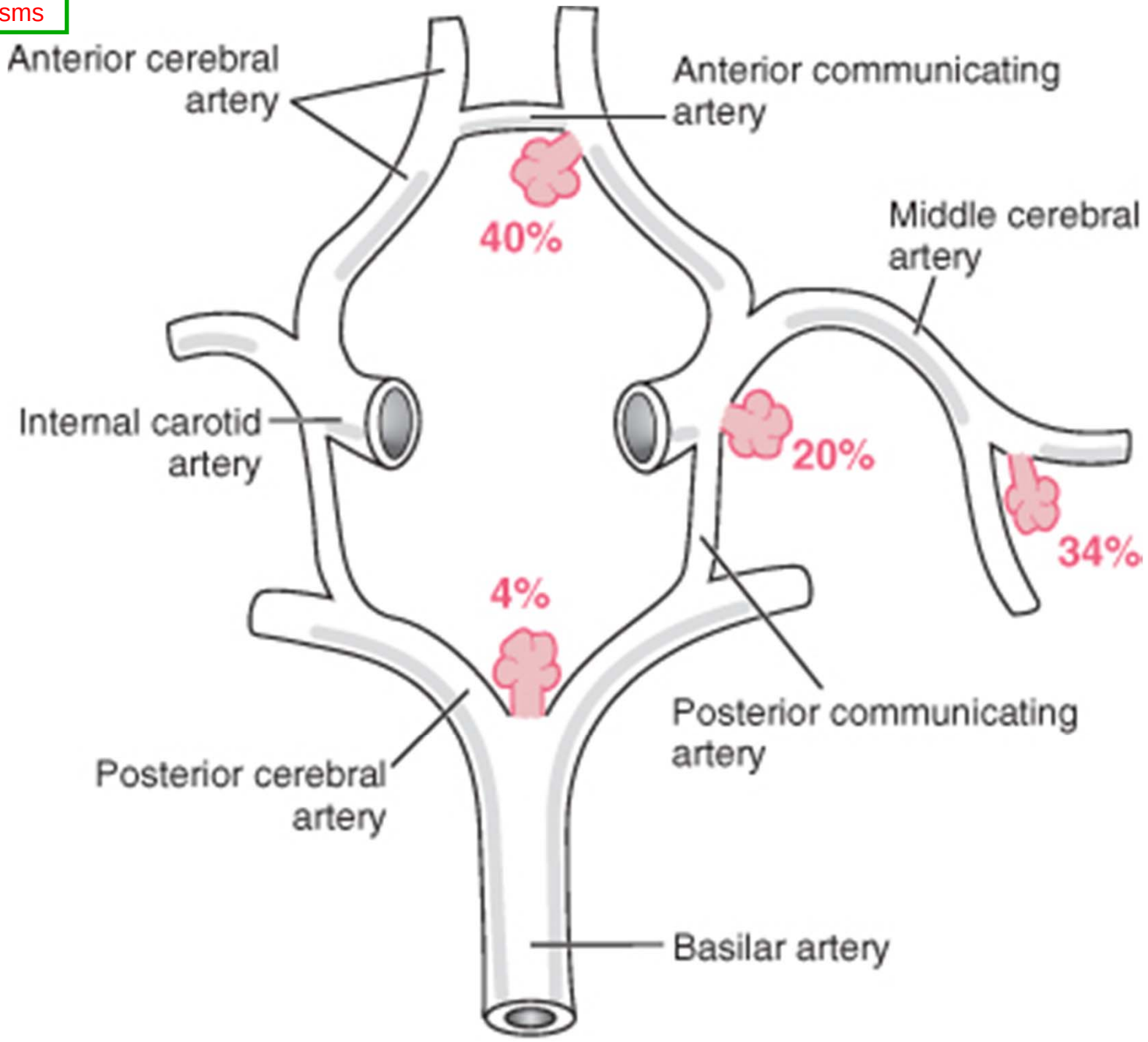
- **Usually present in 4th and 5th decades**
- **75% occur in three sites (MCA, ACA, PCA), often at site of vessel bifurcation**
- **Rupture causes subarachnoid hemorrhage**

b/c blood flow is turbulent here

pts usually give very graphic description of their pain for subarachnoid hemorrhage

There are lot of sensitive nerve fibers in subarachnoid space so its very painful.

Diagram showing incidence of aneurysms



Intracranial Aneurysms

- **Congenital defect in media**

- **Sometimes associated with:**
  - **Coarctation of the aorta**
  - **Adult polycystic kidney disease**

Important Point:
You should evaluate these two things for pt with intracranial aneurysm. Usually, it's the other way around. Patients present with polycystic kidney disease are evaluated for intracranial aneurysm.

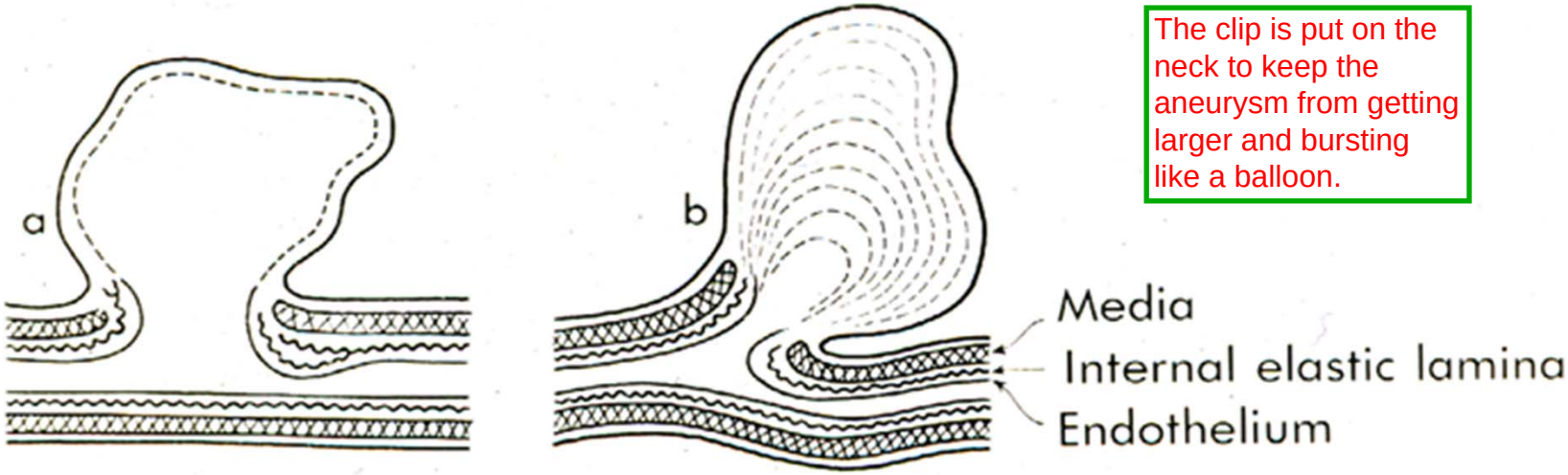
Types of Aneurysms

- **Saccular (congenital, defect in media)**
- **Fusiform (often atherosclerotic)**
- **Mycotic (infectious // inflammatory)**

Saccular is the most common type.

Medial defect aneurysm

- **Most common** intracranial aneurysm
- "Congenital" though not usually present at birth
- Media defective in wall
- **"Neck"** often amenable to surgical clipping



The clip is put on the neck to keep the aneurysm from getting larger and bursting like a balloon.

Mycotic Aneurysm

- Occur from septic emboli or local infection
- They are “pseudoaneurysms”
  - Walled off inflammatory reaction after the vessel ruptures
  - Not treated with surgical clipping: there is not a ‘neck’ like in a saccular aneurysm

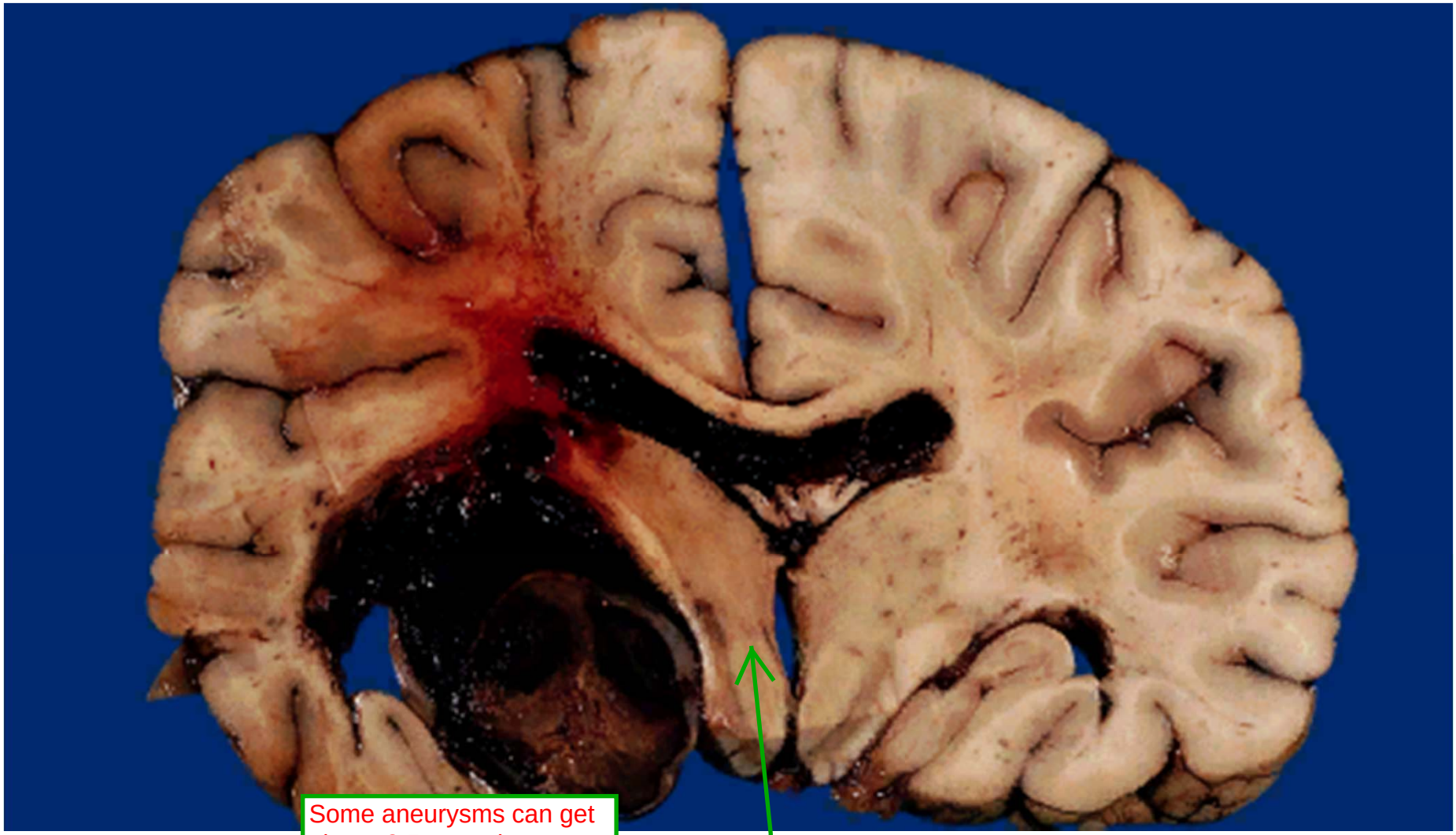
Atherosclerotic Aneurysm

This cannot be clipped. The only way to treat this is to trap it and do bypass.

- **Fusiform**
- **Occur in vertebro-basilar system**
- **Cause symptoms by brainstem compression, obstruction of penetrating branches, and rarely hemorrhage**


clip trapping
aneurysm

Giant MCA aneurysm, temporal lobe



Vascular Malformations

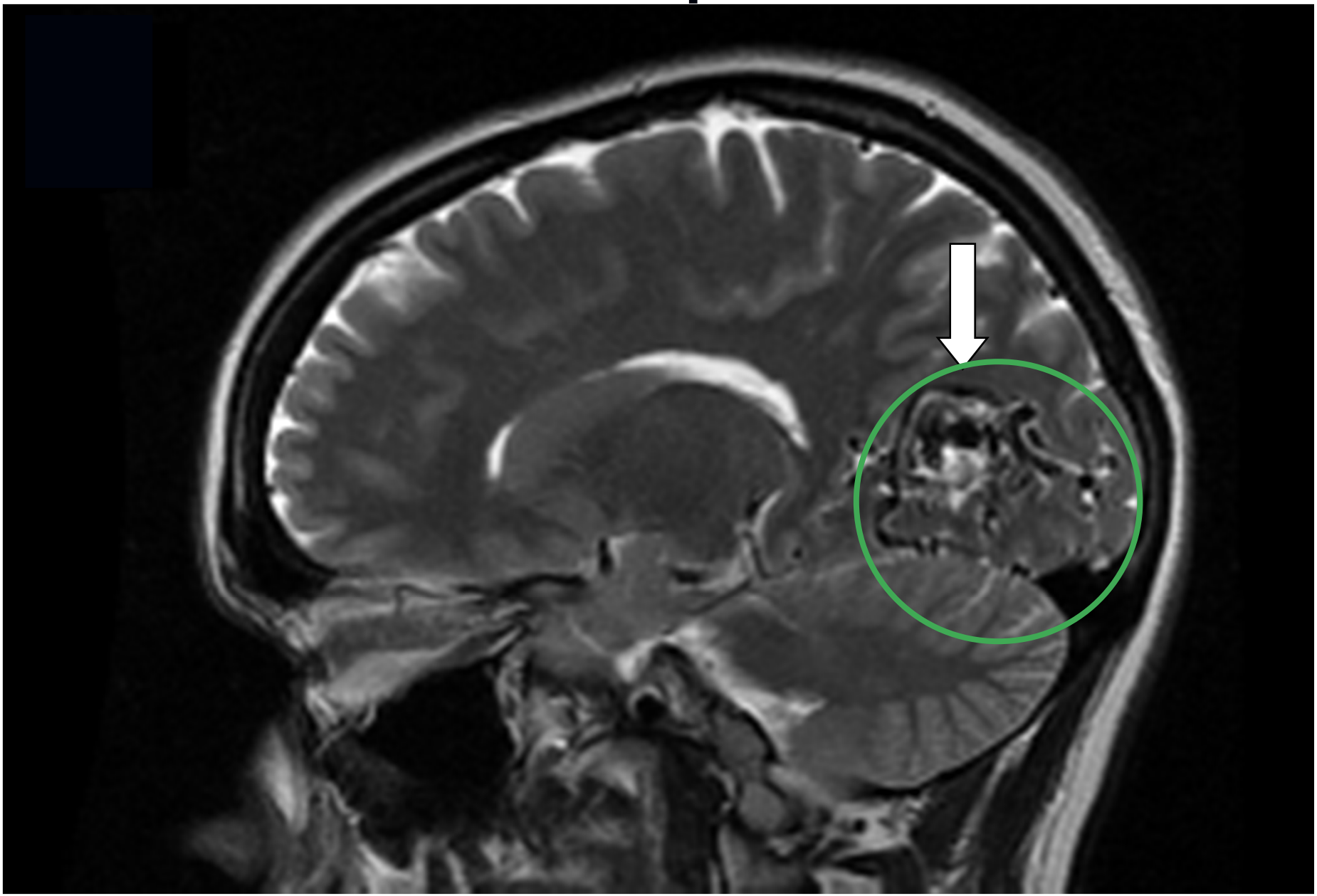
- **Arteriovenous malformation (AVM)**
- **Cavernous angioma (cavernoma)**
- **Capillary telangiectasia**
- **Venous angioma (varix)**

Vascular Malformations

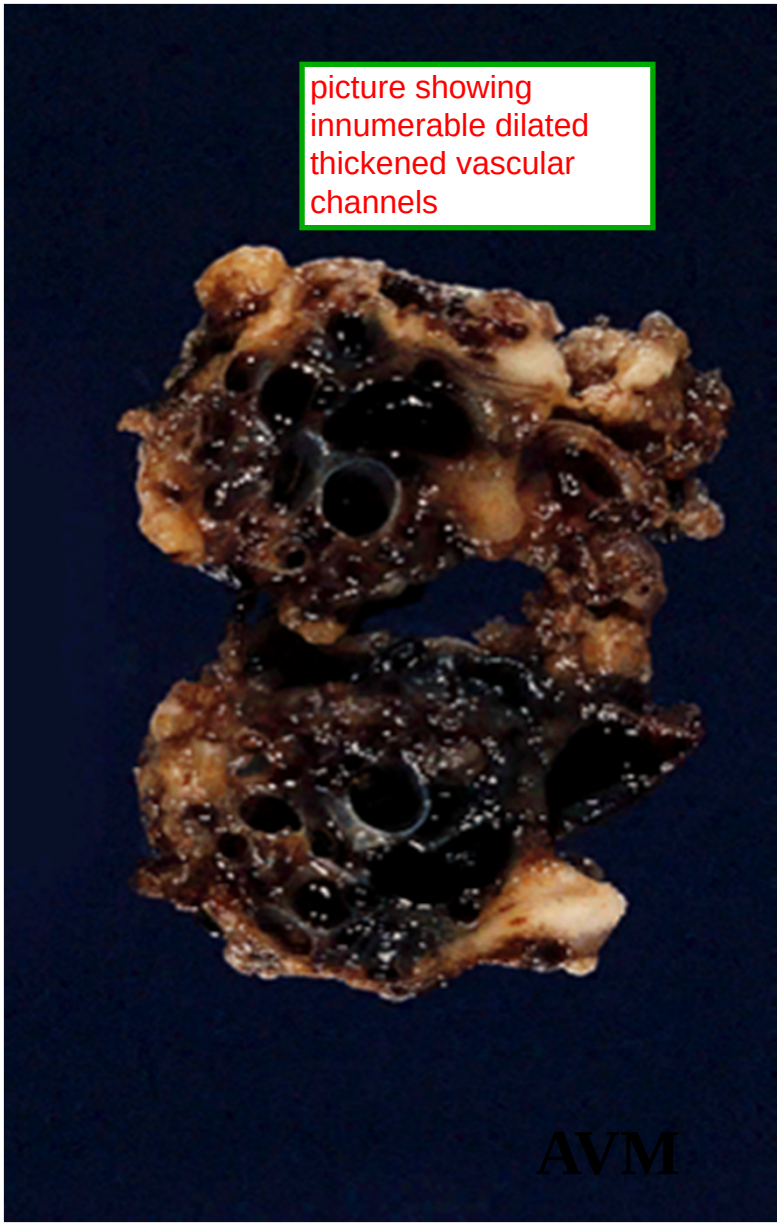
- **Arteriovenous malformation (AVM)**
  - **Lacks a capillary shunt between the arterial and venous systems**
  - **Potentially devastating hemorrhage**

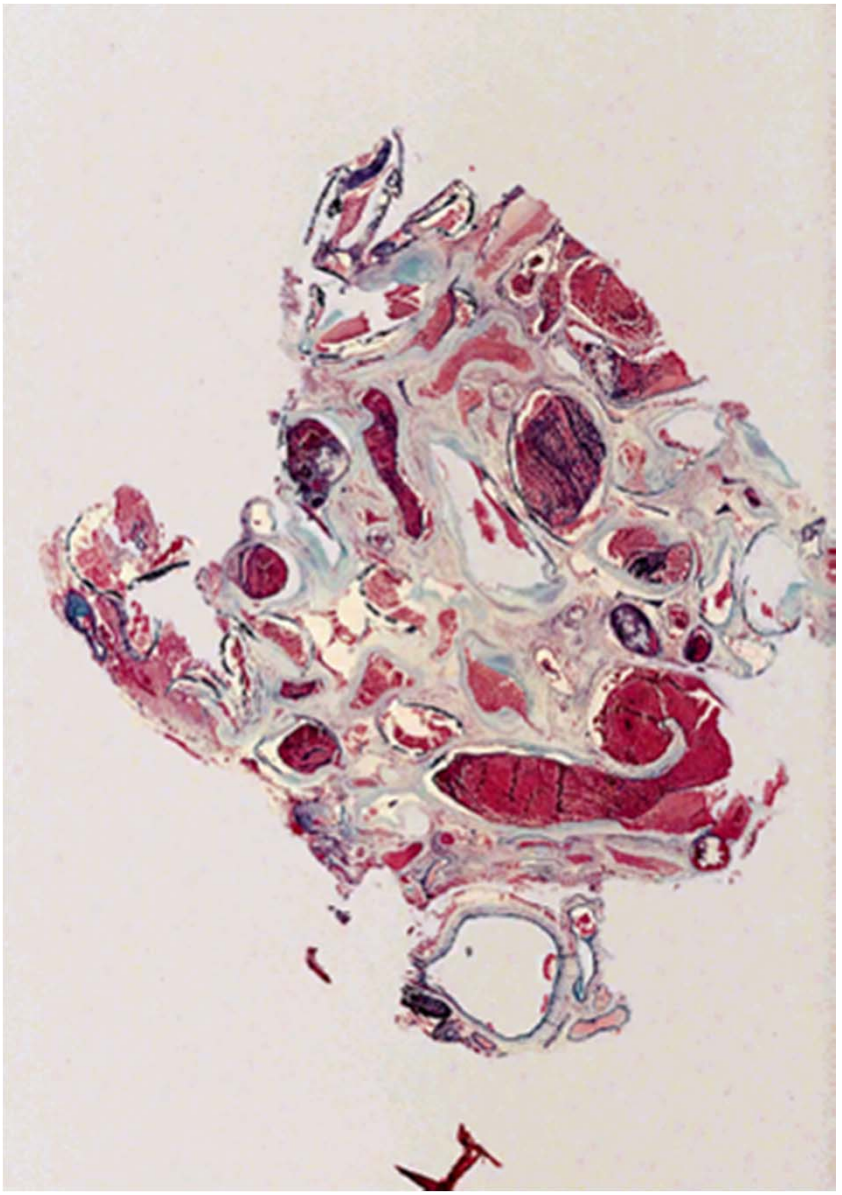
The pressure in AVM is whatever your systolic and diastolic BP is.

AVM occipital lobe

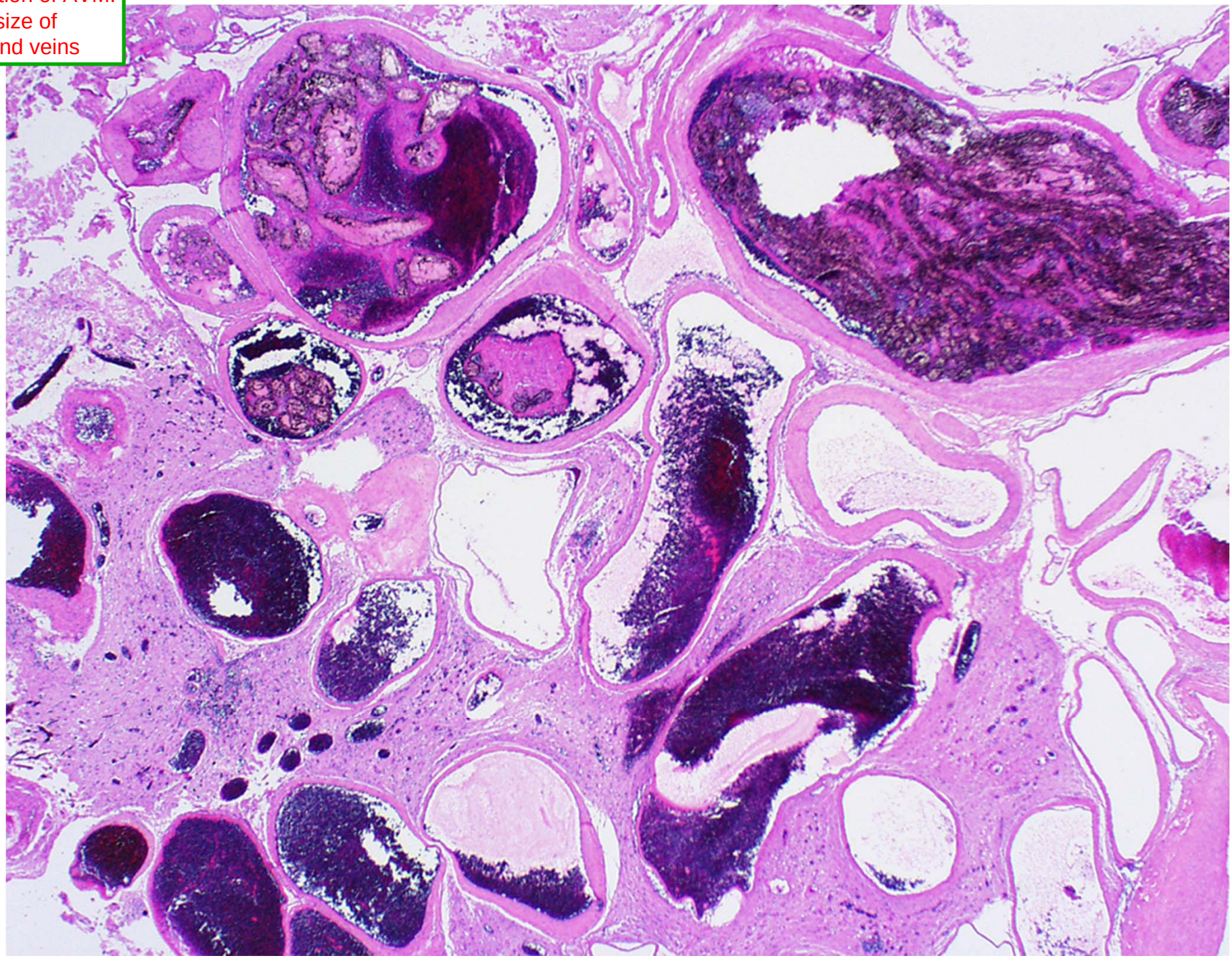


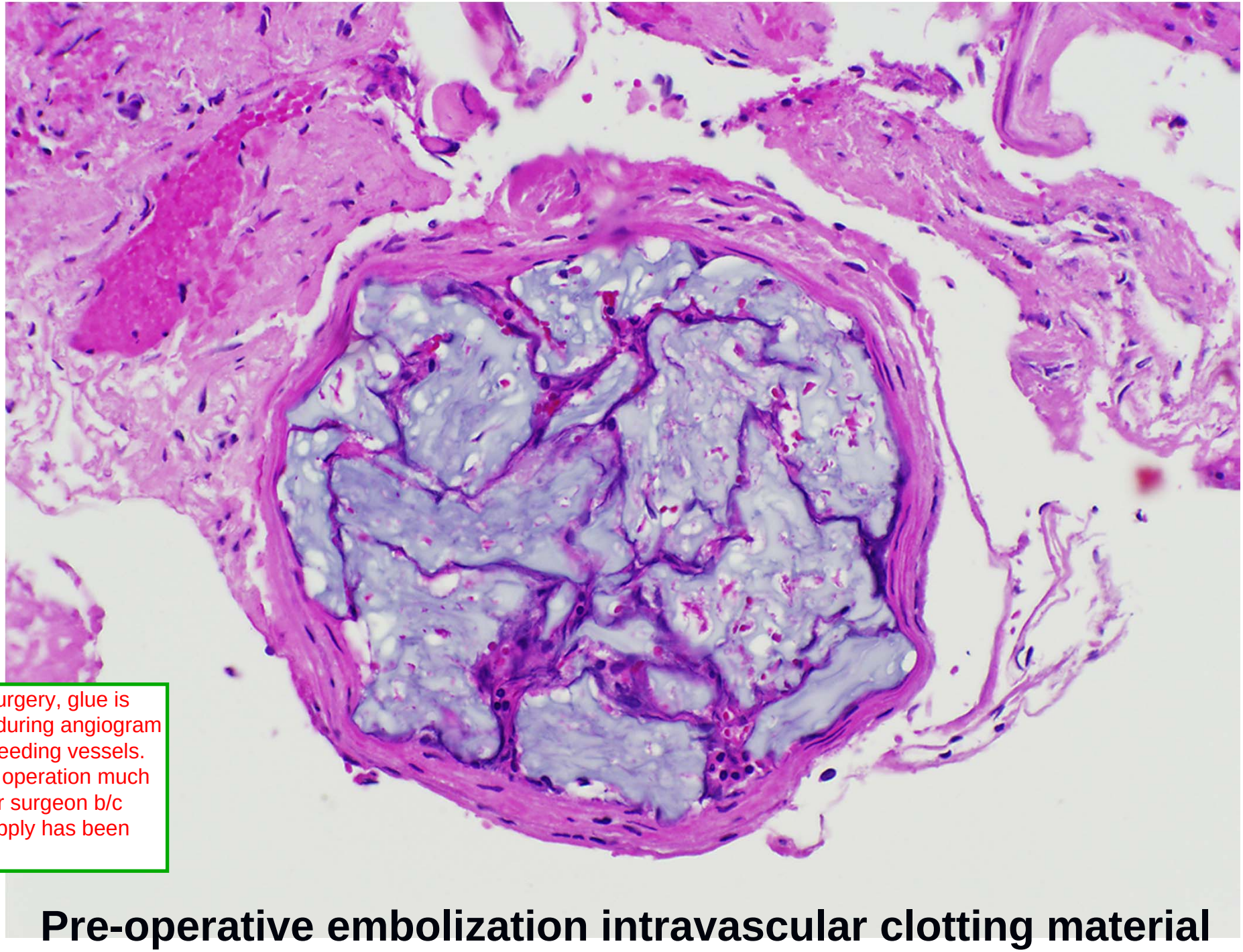
AVM, gross and microscopic





Histo section of AVM:
Variable size of
arteries and veins





Before surgery, glue is injected during angiogram into the feeding vessels. It makes operation much easier for surgeon b/c blood supply has been cut off.

Pre-operative embolization intravascular clotting material

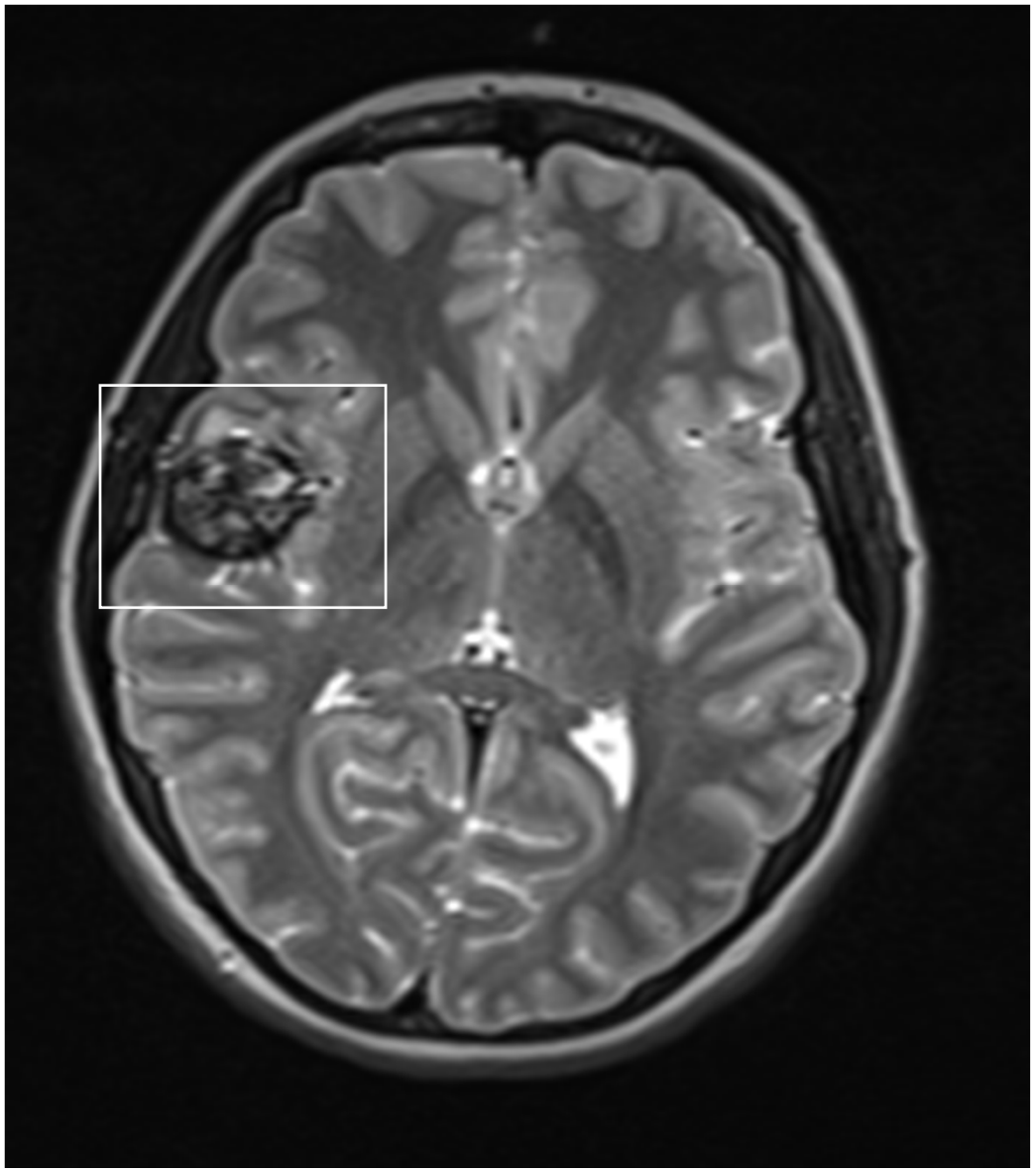
Vascular Malformations

- **Cavernous angioma (cavernoma)**
  - **dilated mass of vessels usually of capillary or venous “low-flow” origin**
  - **local hemorrhage common**

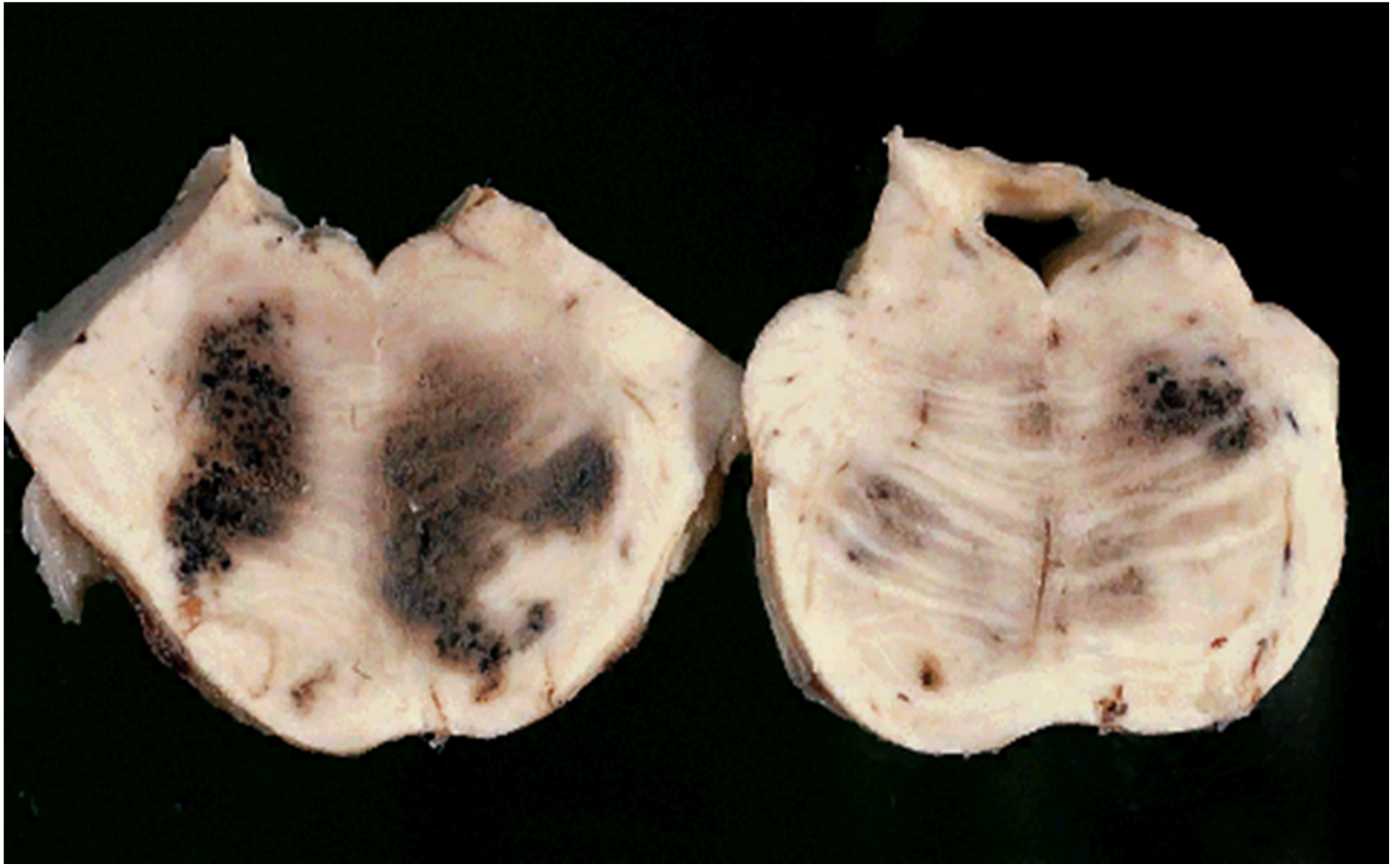
not fatal

MRI: Cavernous angioma

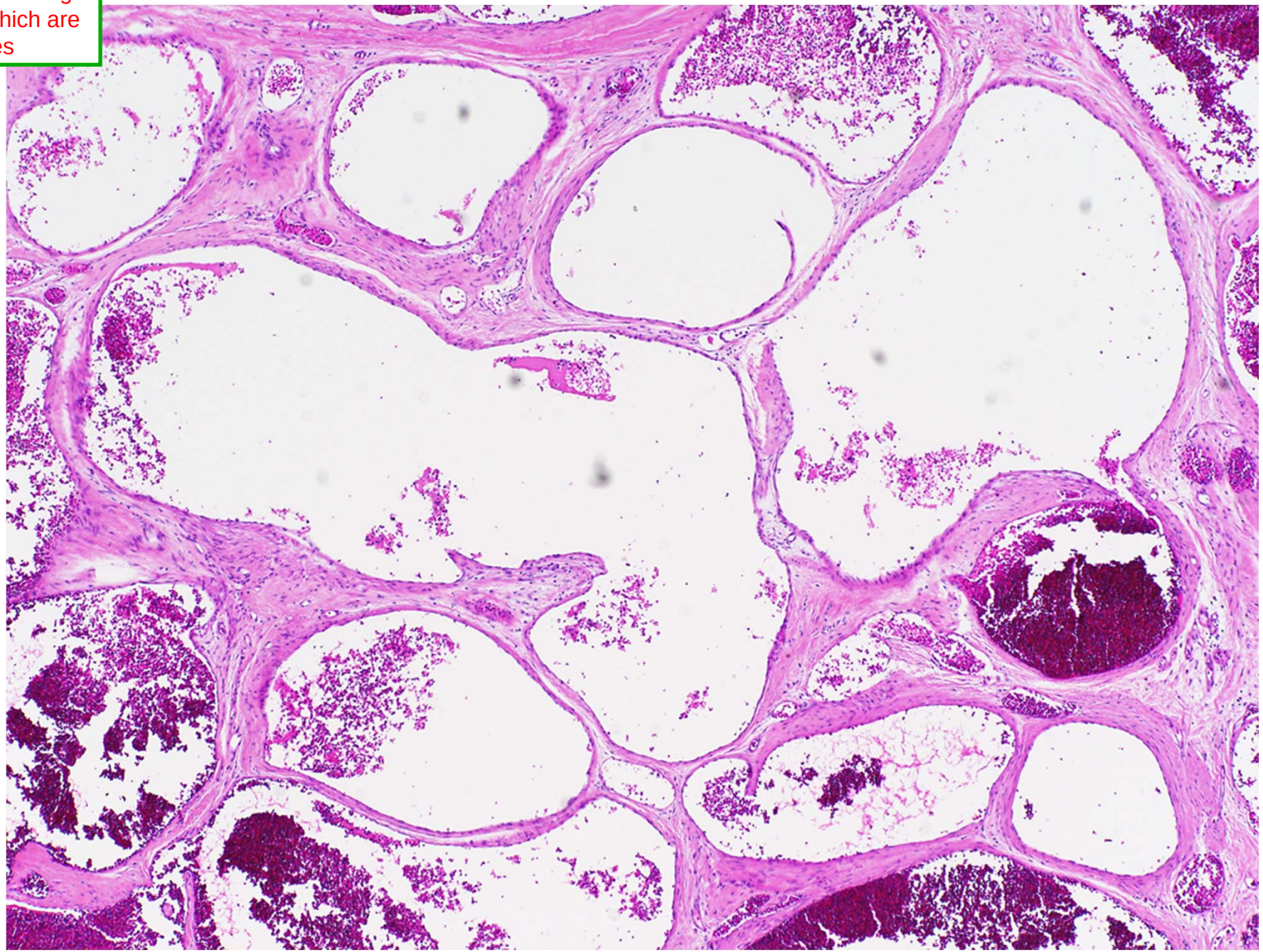
It has characteristic look on MRI. He didn't describe it.



Cavernous angioma

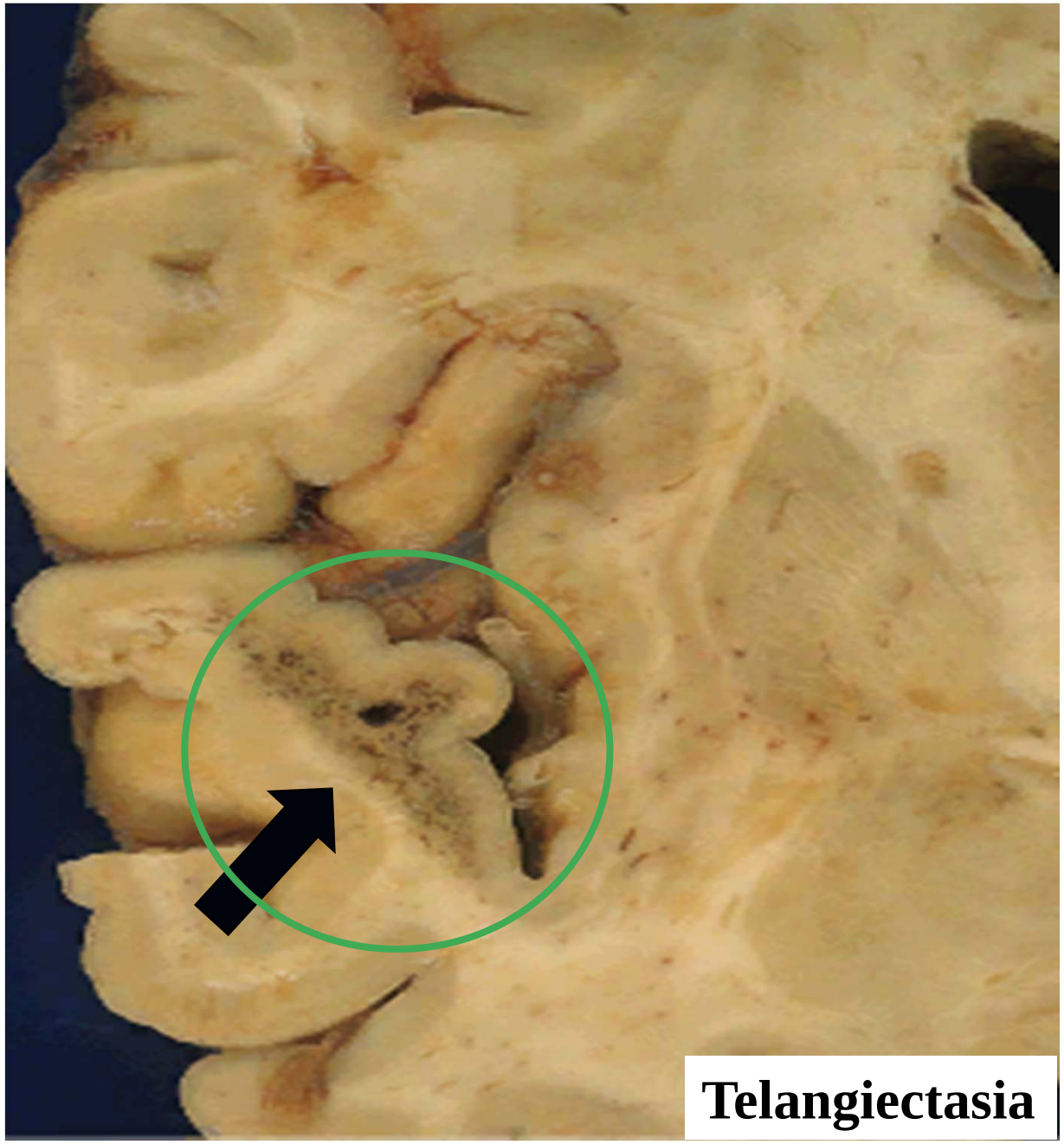


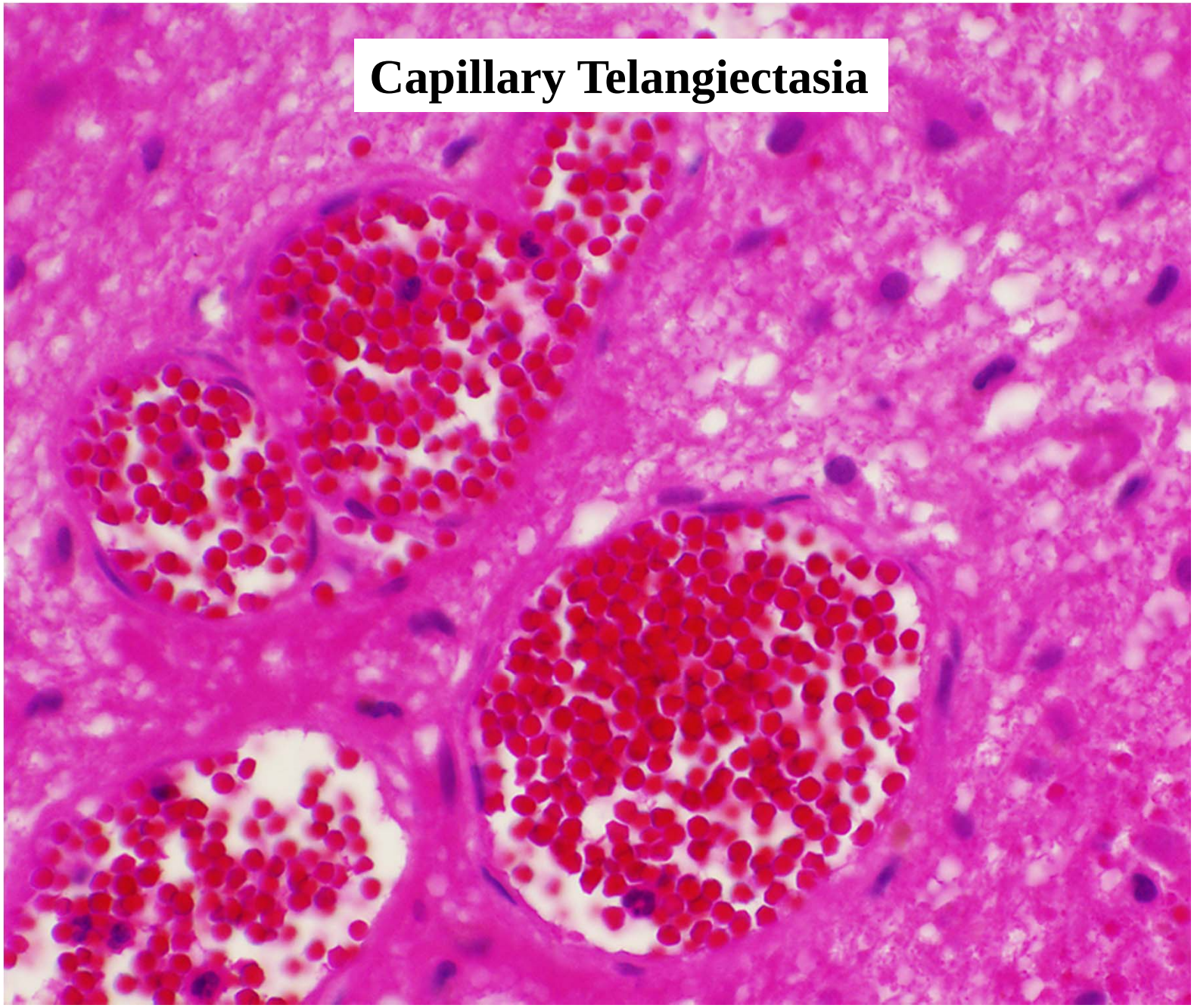
cavernous dilated back to back large vessels which are not arteries



Vascular Malformations

- **Capillary telangiectasia**
  - **brainstem**
  - **usually incidental finding at autopsy**
- **Venous angioma**


Telangiectasia


Capillary Telangiectasia

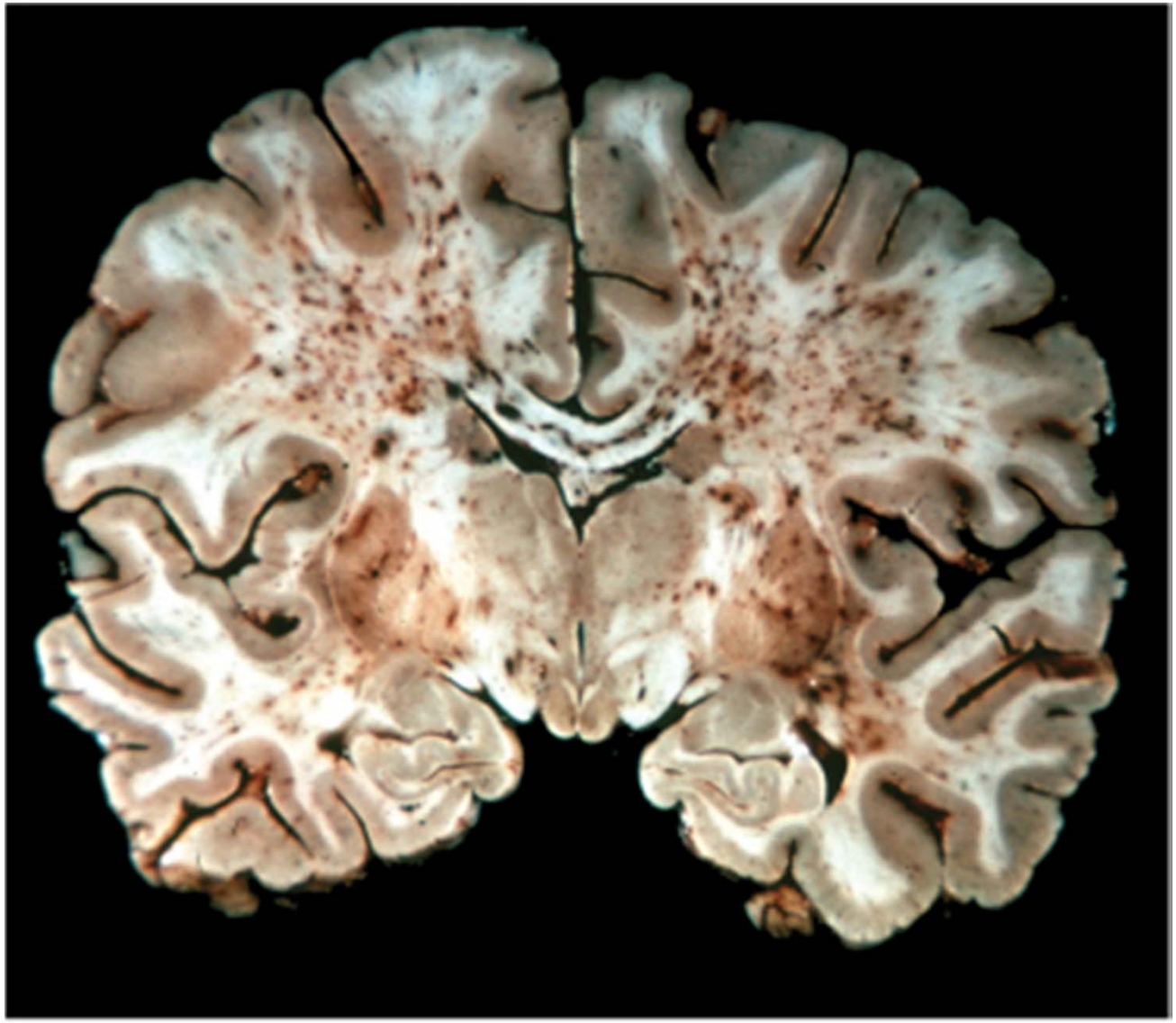
Take Home Points

- **CNS vascular malformations:**
  - **Aneurysms**
  - **Saccular, fusiform, mycotic**
  - **Name 2 systemic associations**
  - **Arteriovenous malformation**
  - **Cavernous angioma**
  - **Capillary telangiectasia**

Embolic Infarcts

- **Cardiac mural thrombi** from heart attack or cardiac arrhythmia
- **Atheromatous plaque: carotid artery**
- **Fat: traumatic long bone fracture**
- **Air: neurosurgical procedure**
- **Intervertebral disc tissue**
- **Tumor**

Bone marrow embolization



Arterial Dissection

- **Young adults**
- **Carotid or vertebral artery**
- **Intimal tear, media or subendothelial hematoma, vessel occlusion, infarction**

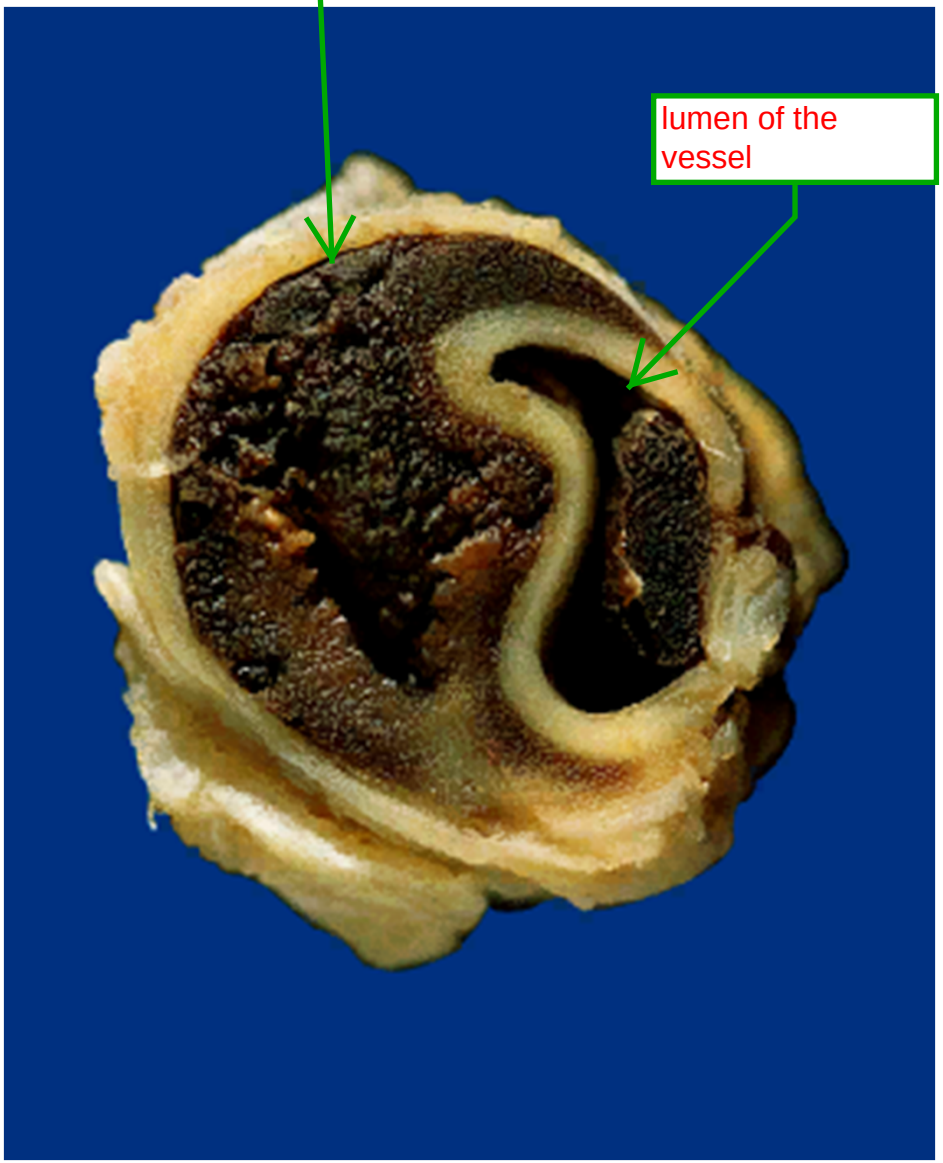
- **Etiologies:**
  - **Spontaneous**
  - **Mild trauma**
  - **Fibromuscular dysplasia**

more often in women

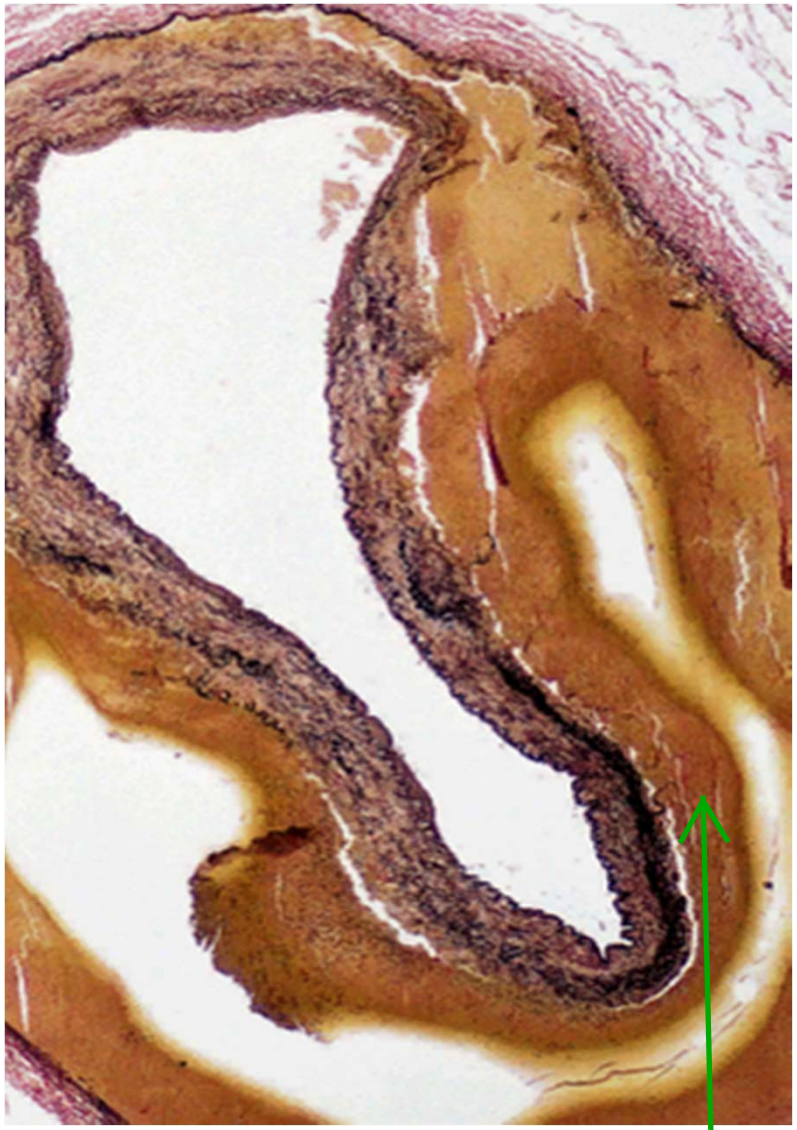
Blood flows thru media

blood flows in the media

lumen of the vessel



For young patients, it can be treated by aspirin.



blood flow is within media.

The End