Neuropathology lecture series

Cerebrovascular Disease

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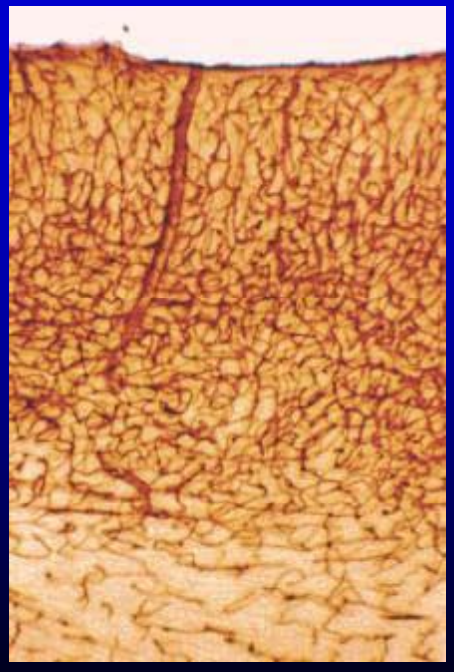
Physiology of cerebral blood flow

Brain makes up only 2% of body weight

Percentage of cardiac output: 15-20%
Percentage of O_2 consumption (resting): 15%
Distribution of circulation:

- **anterior circulation > posterior circulation**
  (70%) (30%)
- **gray matter > white matter**

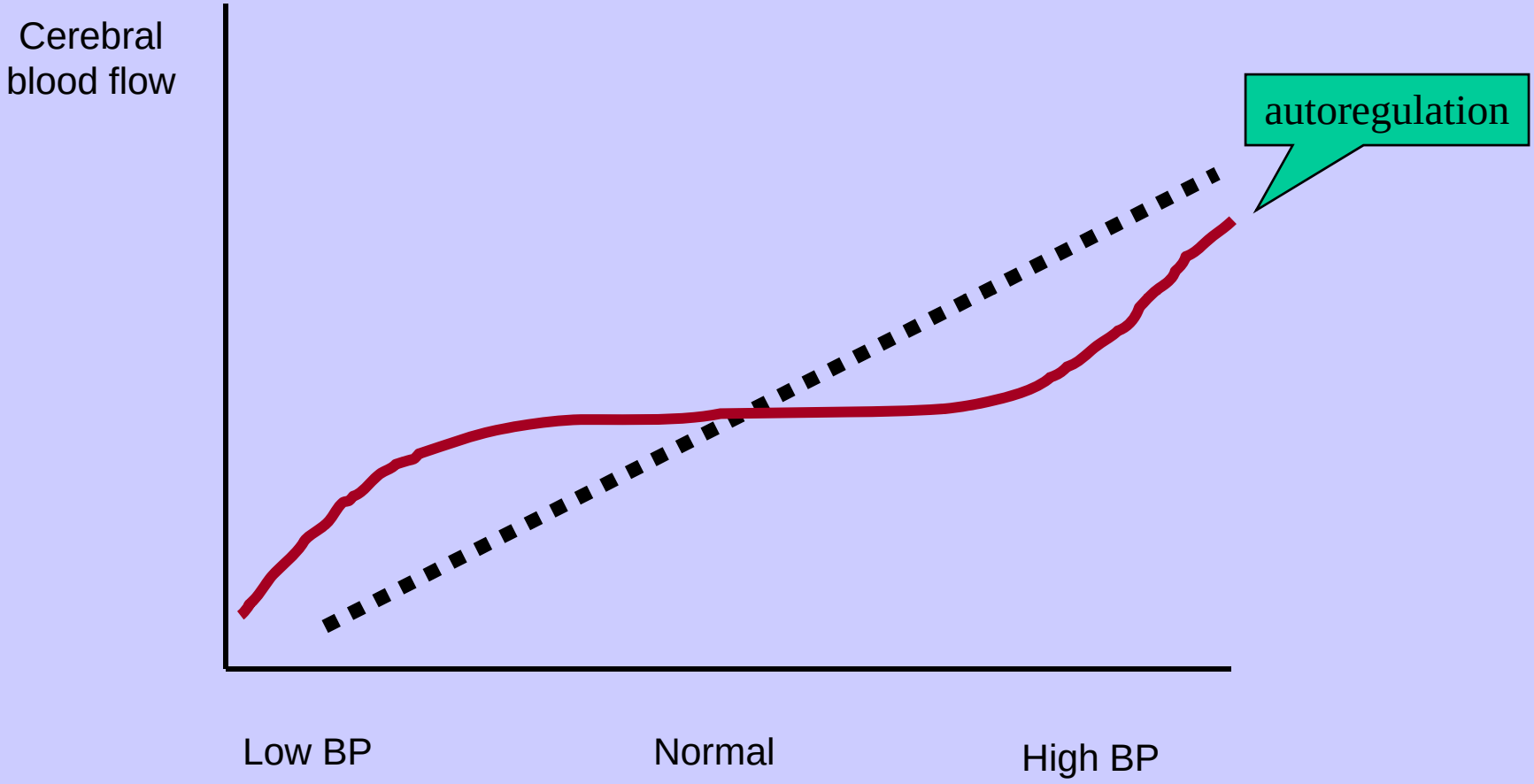


Blood flow is a fraction of:

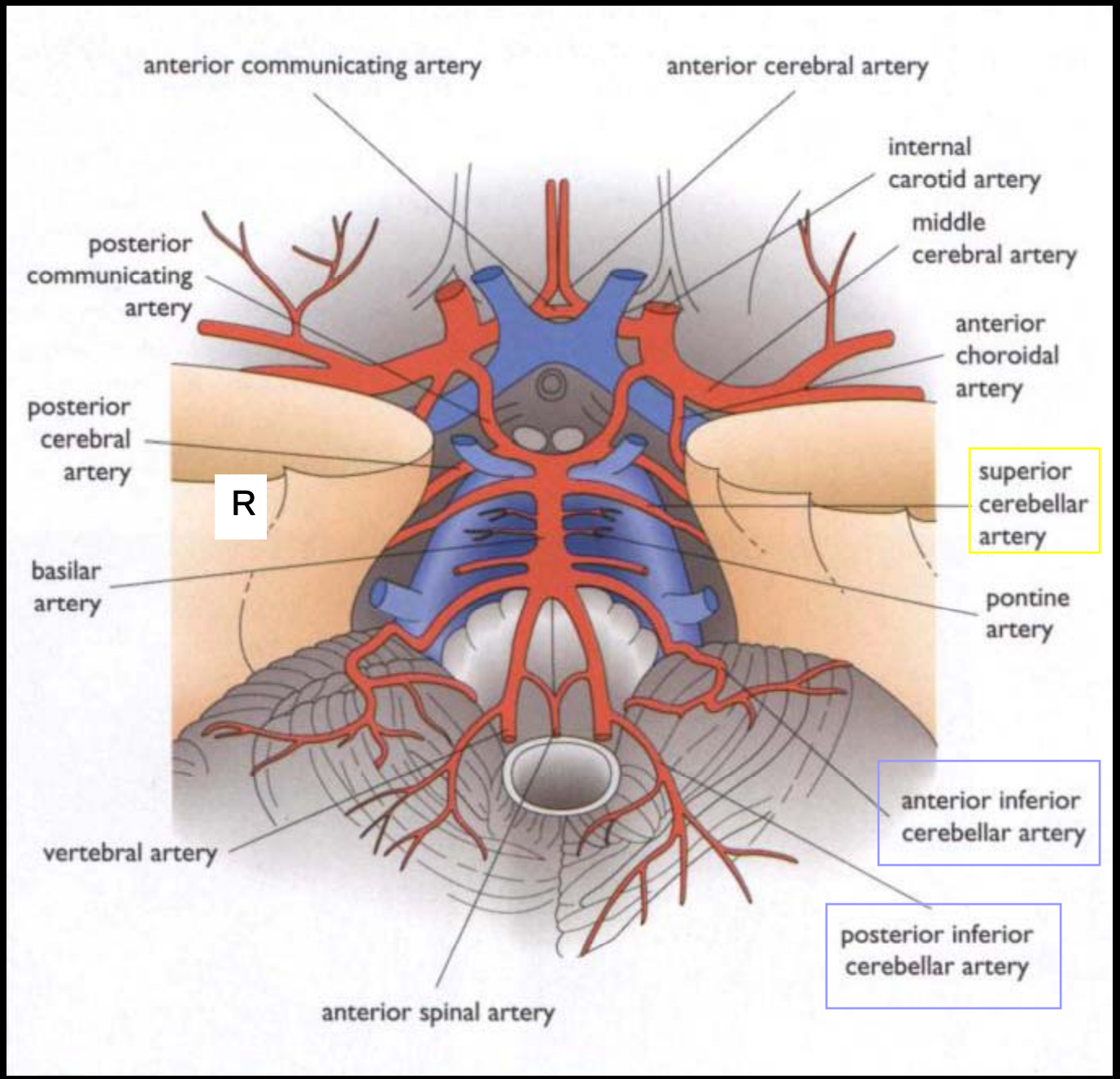
- perfusion pressure
- resistance of vascular bed as modified by:
  - arterial pressure
  - pCO_2, pH, and oxygen
  - intracranial pressure
  - blood viscosity
  - neurotransmitters???

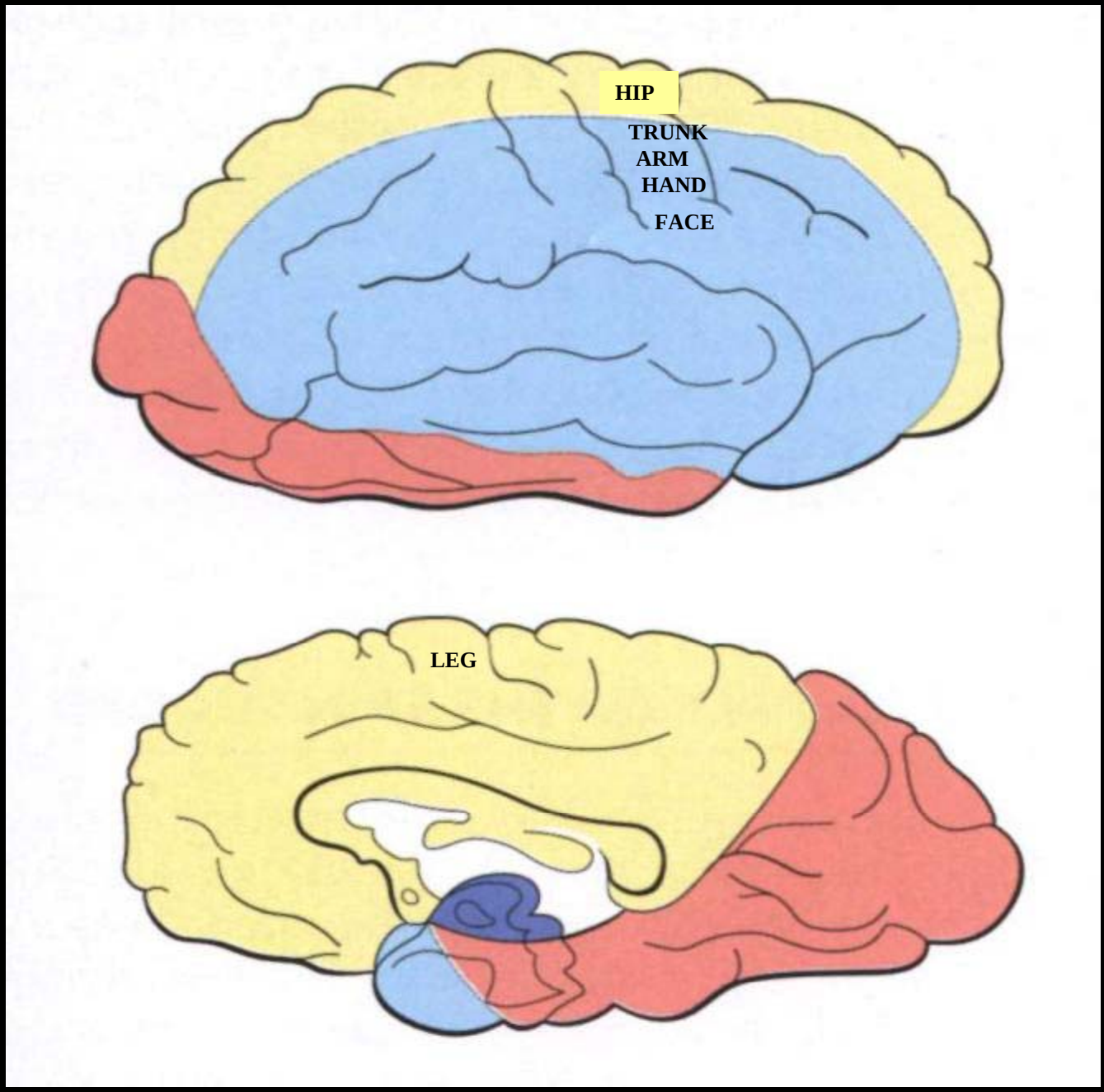
Relatively constant blood flow primarily governed by autoregulatory mechanism

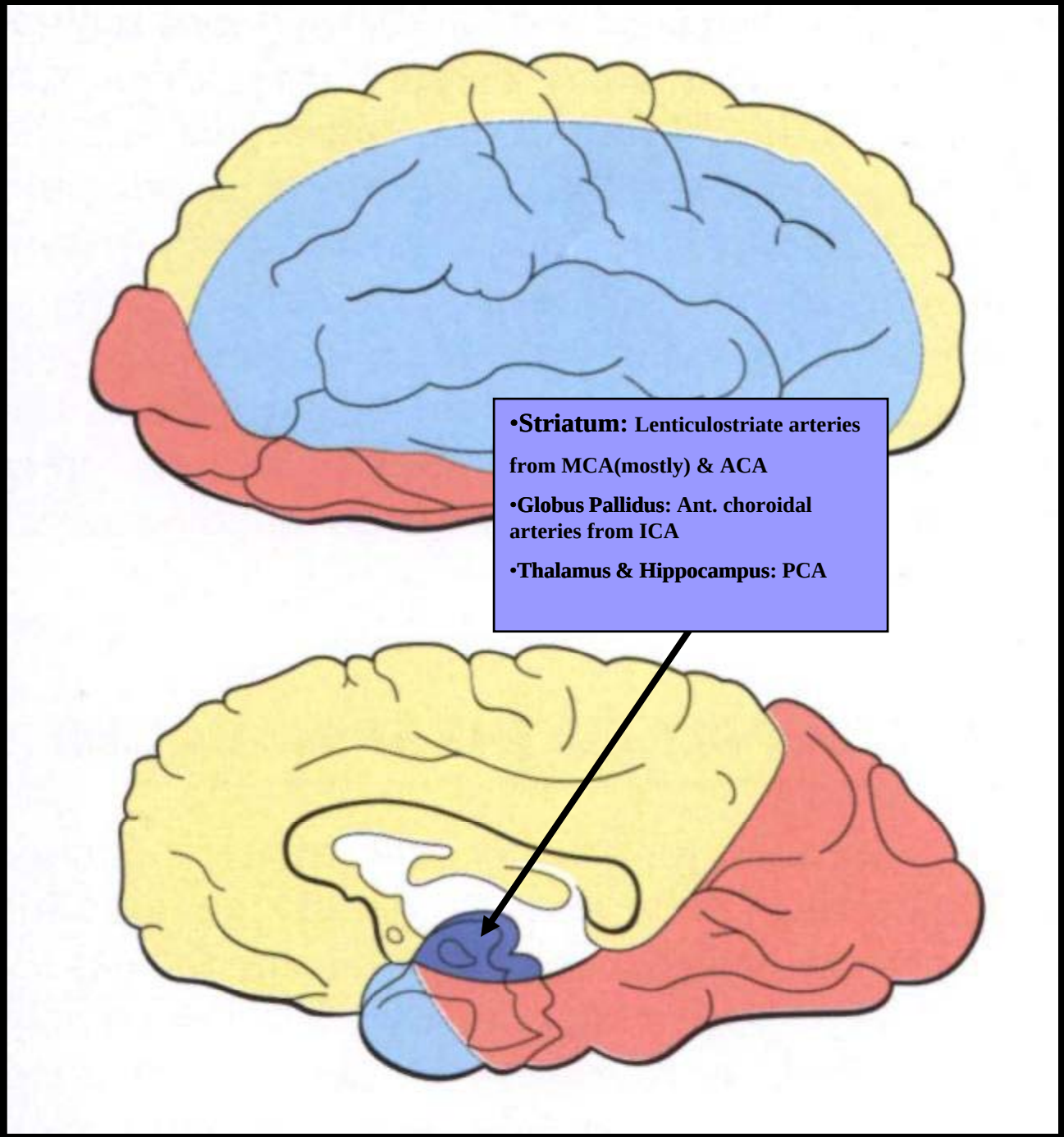
Effects of cerebral perfusion pressure on cerebral blood flow



Mendolow AD et al. Br J Surg 1983


anterior communicating artery
anterior cerebral artery
internal carotid artery
middle cerebral artery
posterior communicating artery
anterior choroidal artery
posterior cerebral artery
R
superior cerebellar artery
basilar artery
pontine artery
anterior inferior cerebellar artery
vertebral artery
posterior inferior cerebellar artery
anterior spinal artery

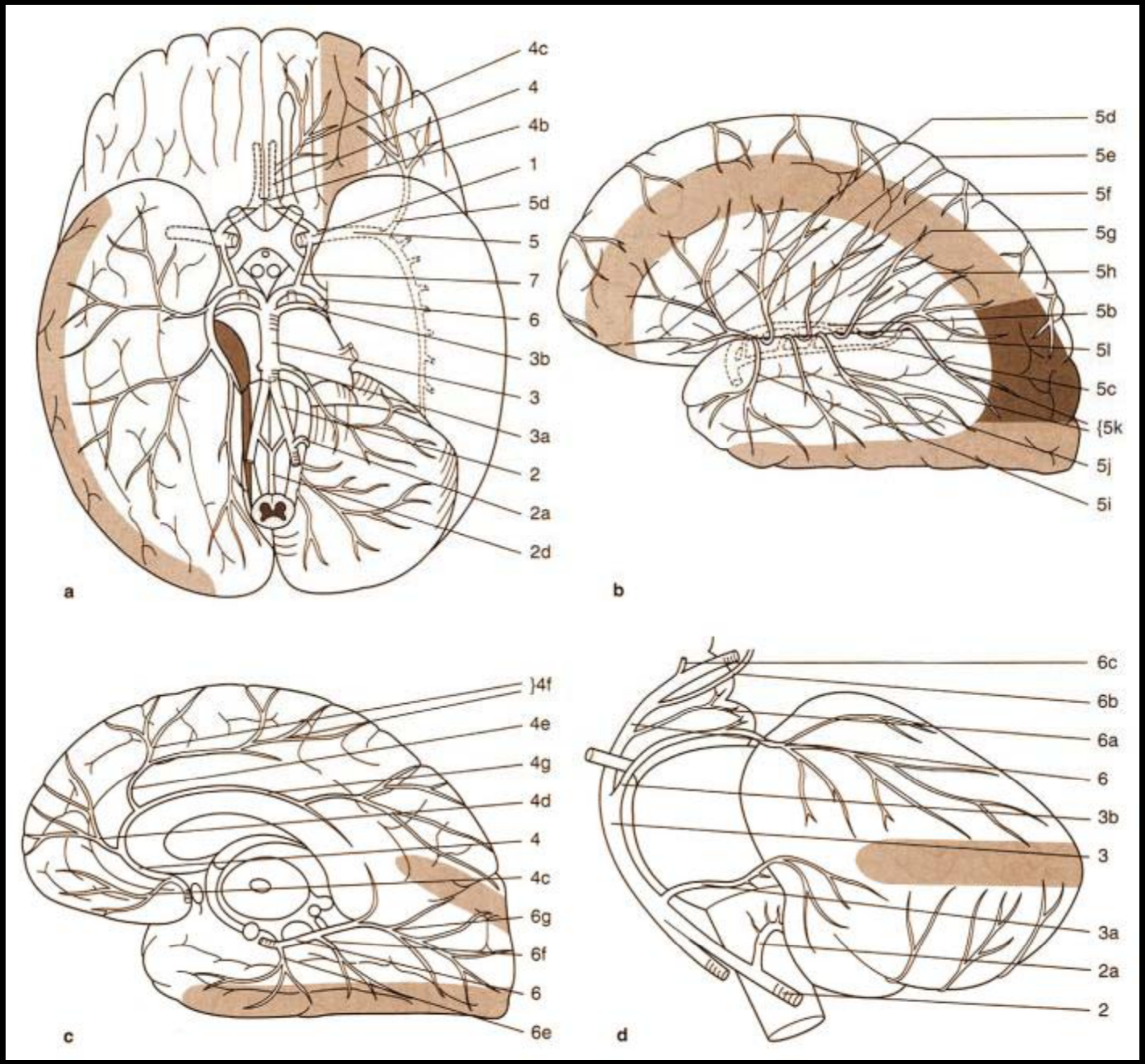

HIP
TRUNK
ARM
HAND
FACE
LEG

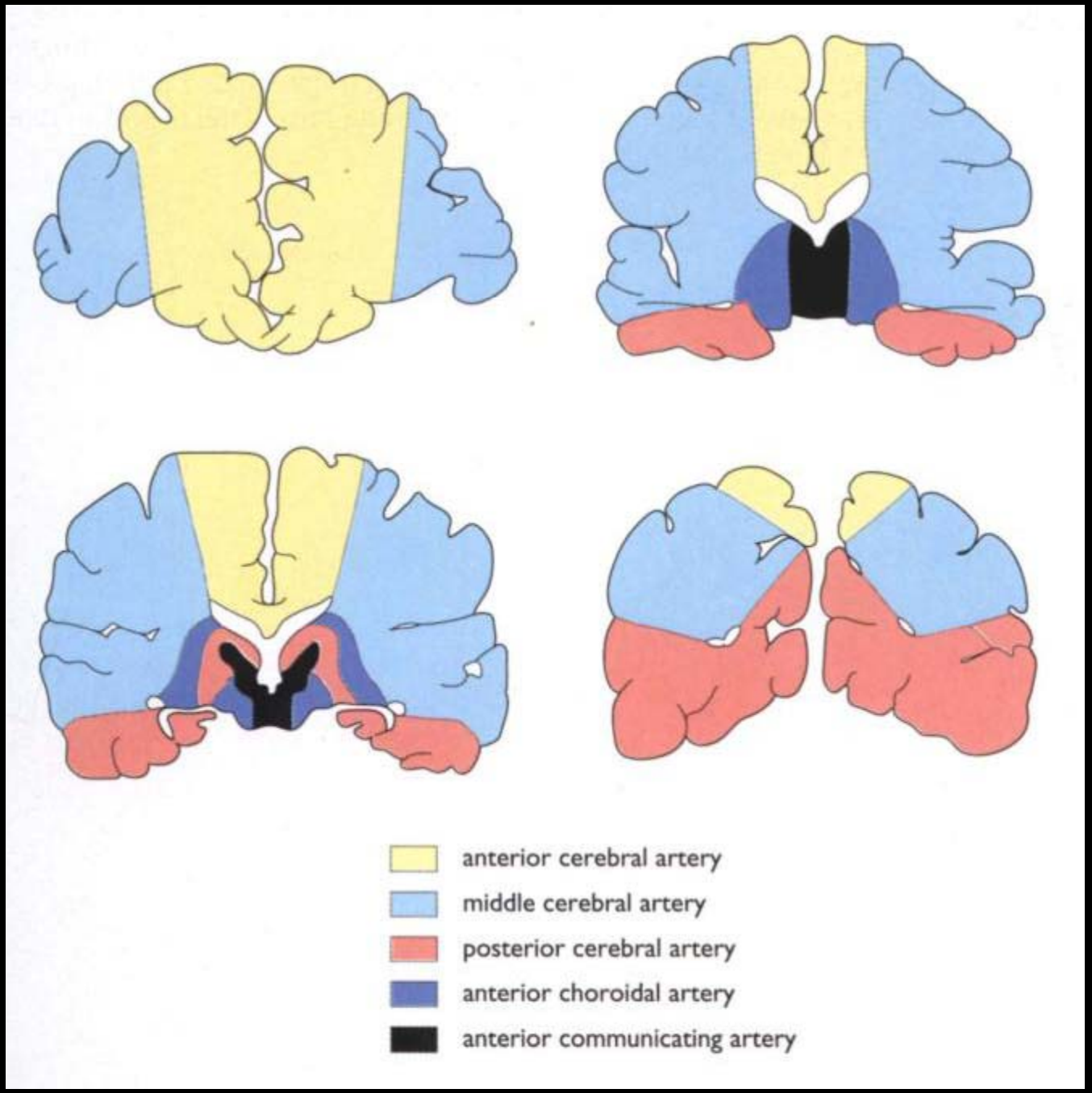

•Striatum: Lenticulostriate arteries from MCA(mostly) & ACA
•Globus Pallidus: Ant. choroidal arteries from ICA
•Thalamus & Hippocampus: PCA

Boundery zone

(watershed)

most distal part of arterial irrigation




anterior cerebral artery
middle cerebral artery
posterior cerebral artery
anterior choroidal artery
anterior communicating artery

Epidemiology of stroke

- **Almost 750,000 new or recurrent strokes per year in the U.S.**

- **Third leading cause of death in the U.S.; second worldwide**

- **Almost 4 million Americans are living with neurologic deficits due to stroke**

- **Prevention, prevention, and prevention** (Only 1-2% of ischemic stroke patients nationally are treated with Tissue Plasminogen Activator.)

Stroke

Classical definitions (WHO 1980):

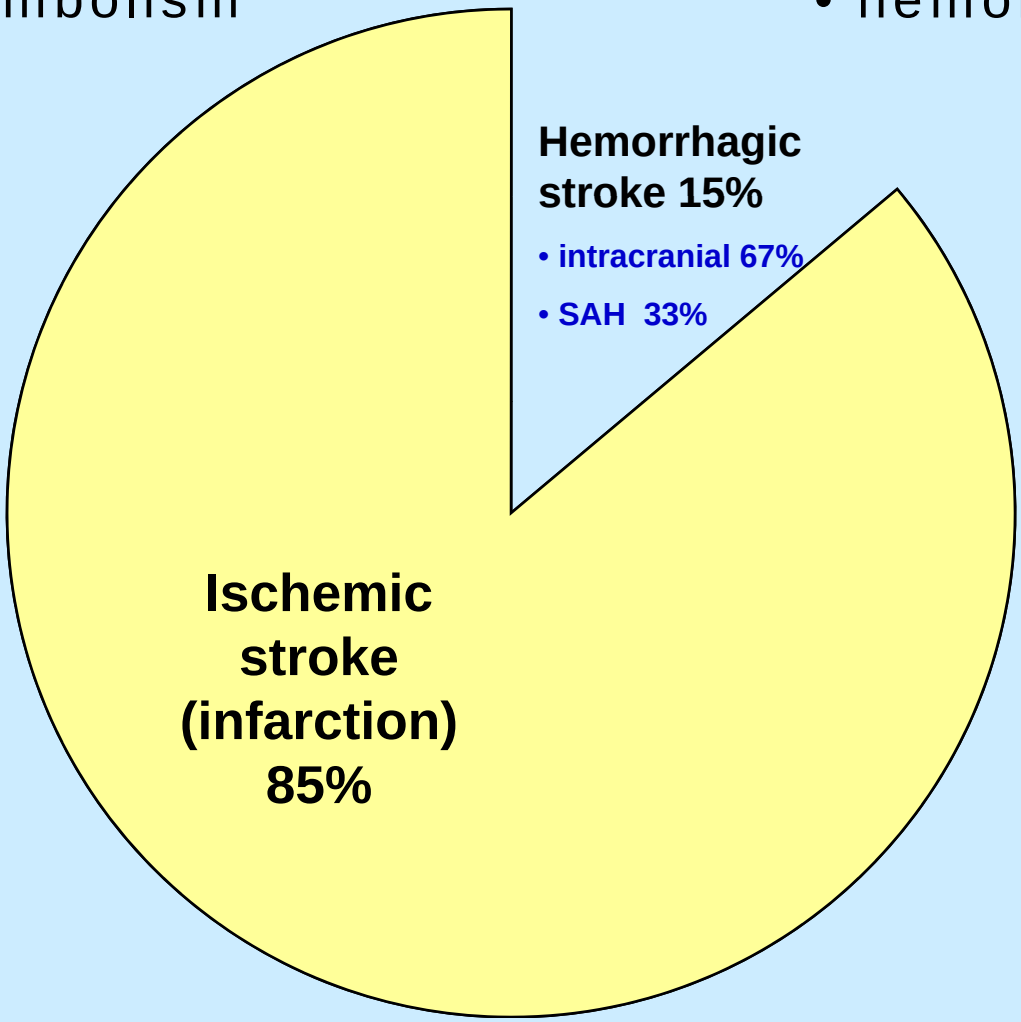
"Rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin."

If symptoms resolve within 24 hours the episode is called a transient ischemic attack – **TIA***.

* Total risk 25% for stroke in 90 days

Types of stroke

- thromboembolism
- hemorrhage



Types of stroke vary in the world.

Determinants of stroke

Nonmodifiable risk factors

- Age
- Gender
- Ethnicity
- Heredity

Modifiable risk factors

- Hypertension
- Diabetes
- Cardiac disease (atrial fibrillation)
- Hypercholesterolemia
- Cigarette smoking
- Alcohol abuse
- Physical inactivity

Cerebral infarction

Morphologic Evolution

Sequence of microscopic changes in brain infarcts

> 1 hour	**Microvacuoles within neurons (swollen mitochondria)** **Perineuronal vacuolation (swollen astrocytic processes)**

Sequence of microscopic changes in brain infarcts

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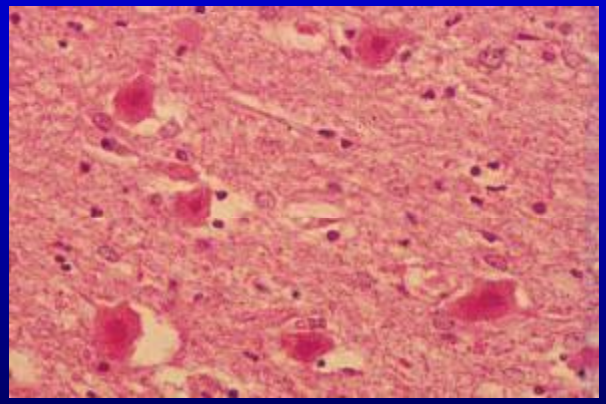
4-12 hours	**Neuronal cytoplasmic eosinophilia** **Disappearance of Nissl bodies** **Pyknotic nuclei** **Leakage of blood-brain barrier**



Sequence of microscopic changes in brain infarcts

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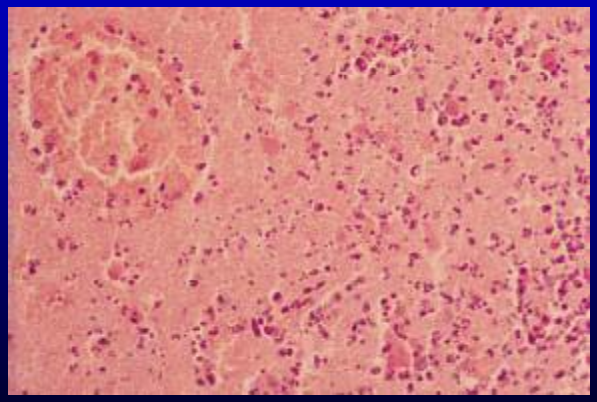
15-24 hours	Neutrophil infiltration begins



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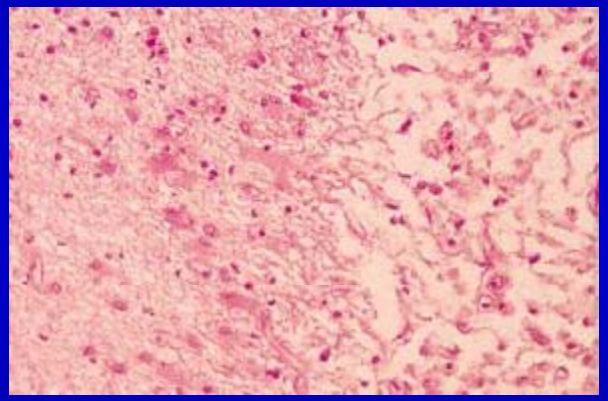	Neuronal cytoplasmic eosinophilia Disappearance of Nissl bodies Pyknotic nuclei Leakage of blood-brain barrier
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5 days	Neutrophilic infiltration ceases
~ 1 week	Proliferation of astrocytes around core infarct

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Topographic features – size & extent of infarct

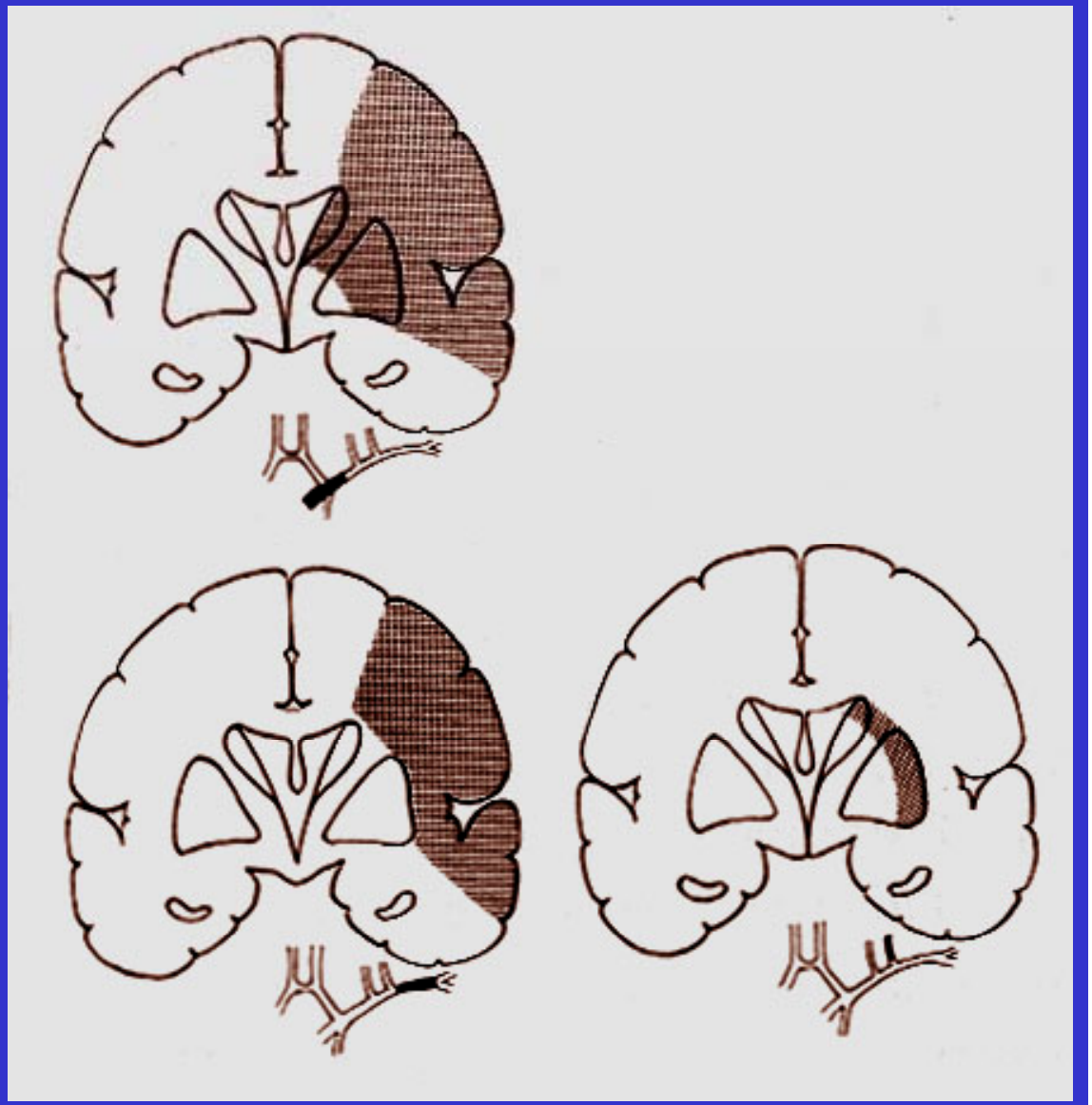
Site of occlusion

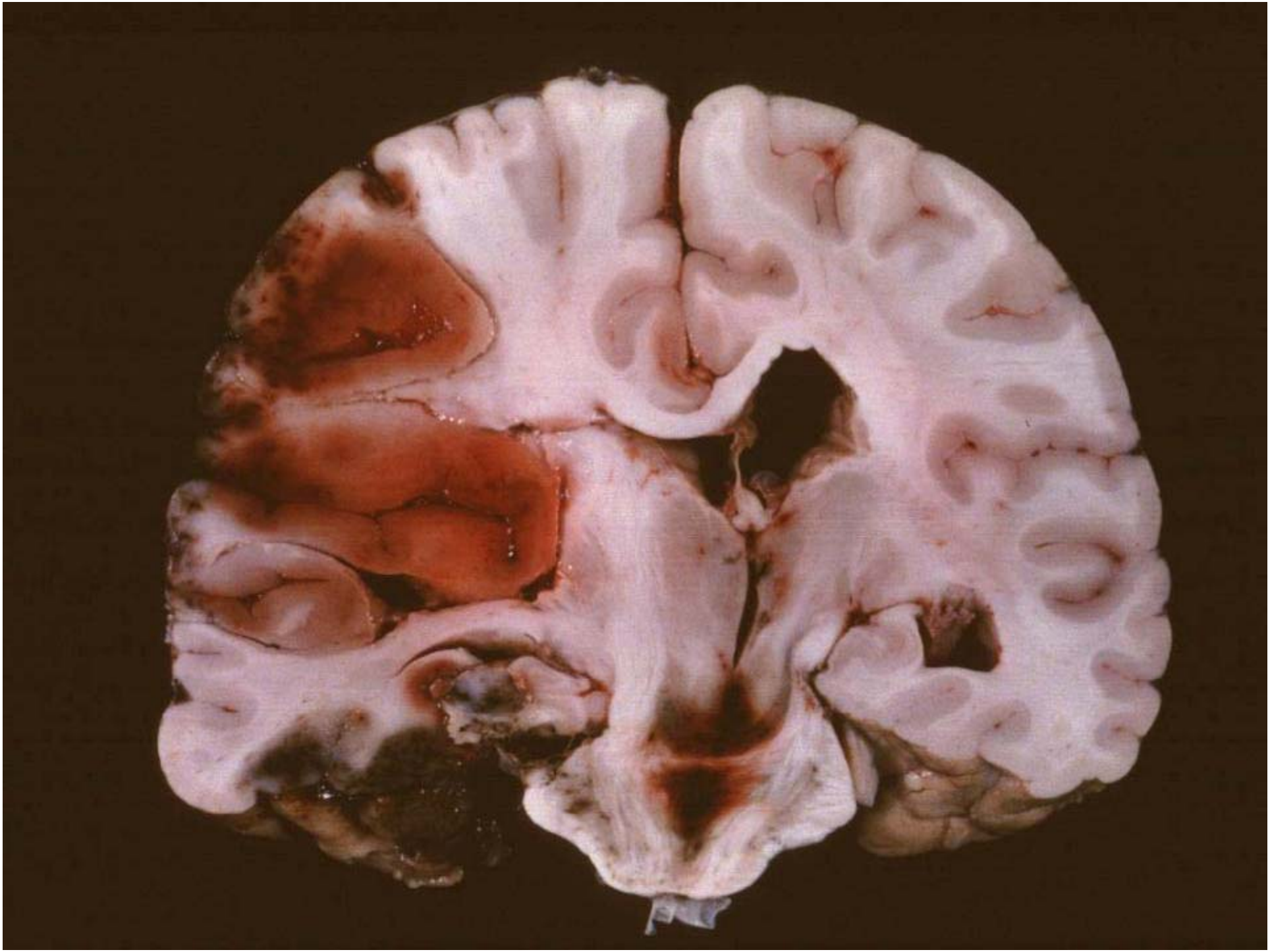
Presence/absence of anastomosis

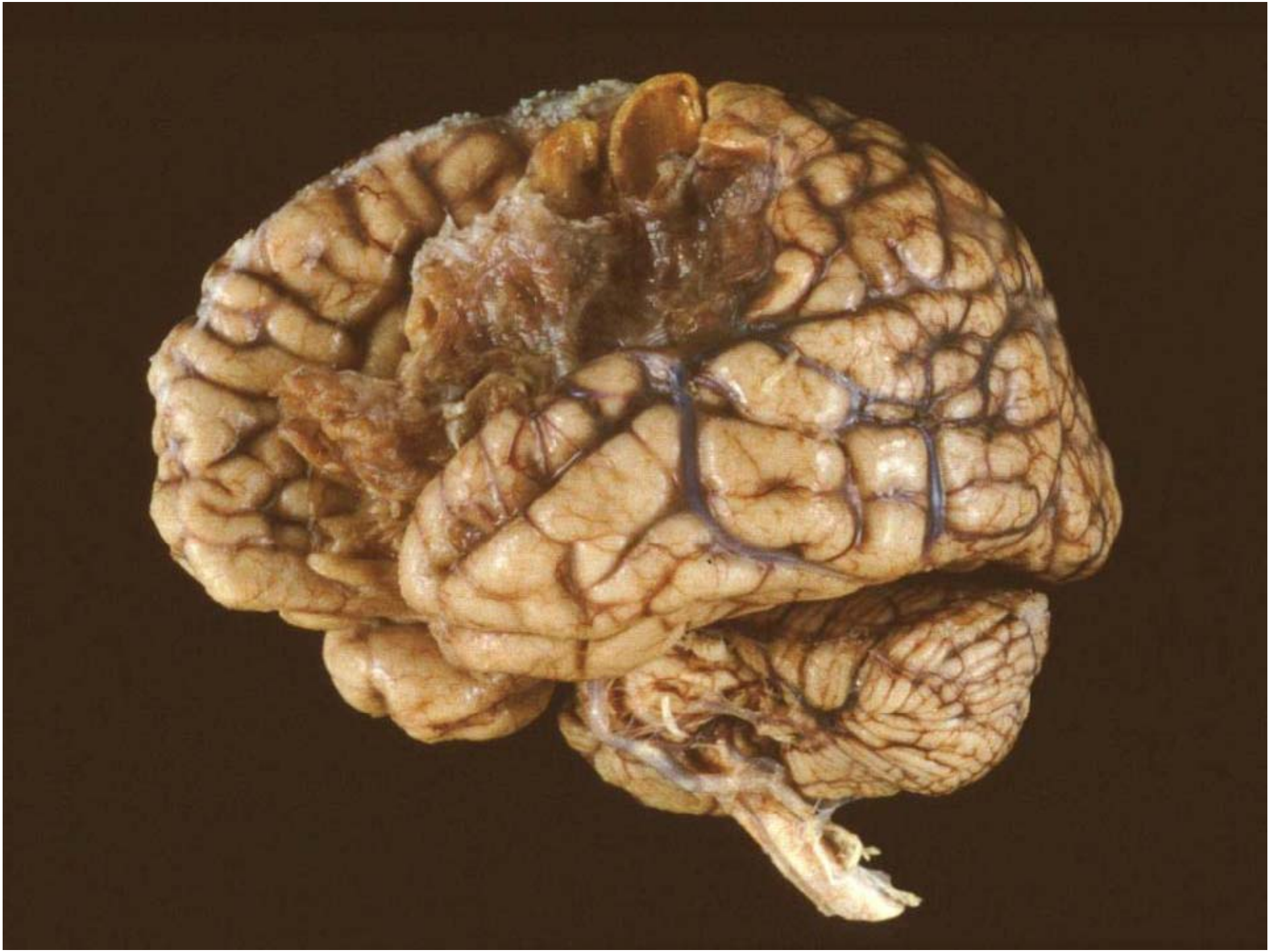
Ophthalmic artery (EC-IC)

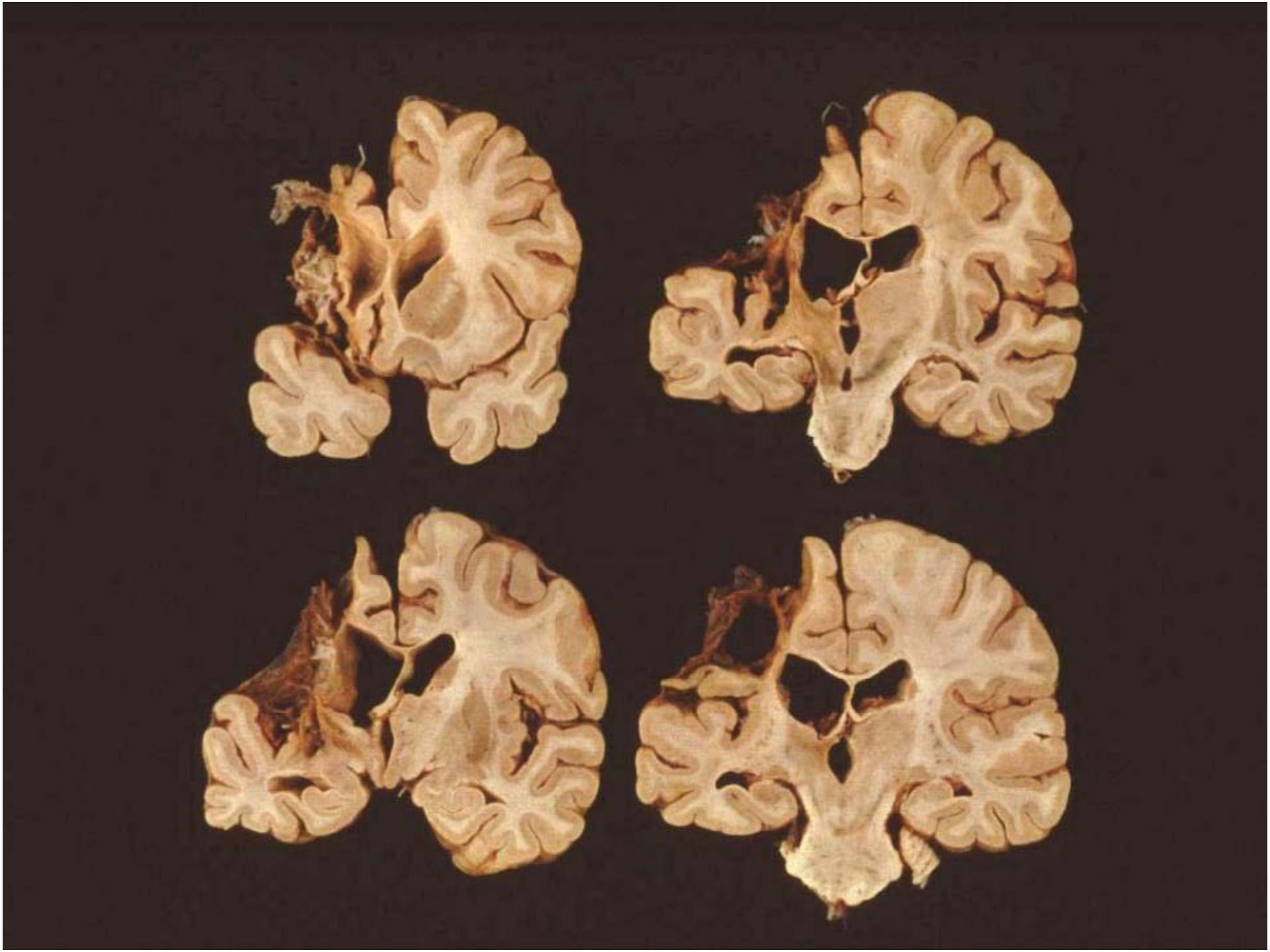
The circle of Willis

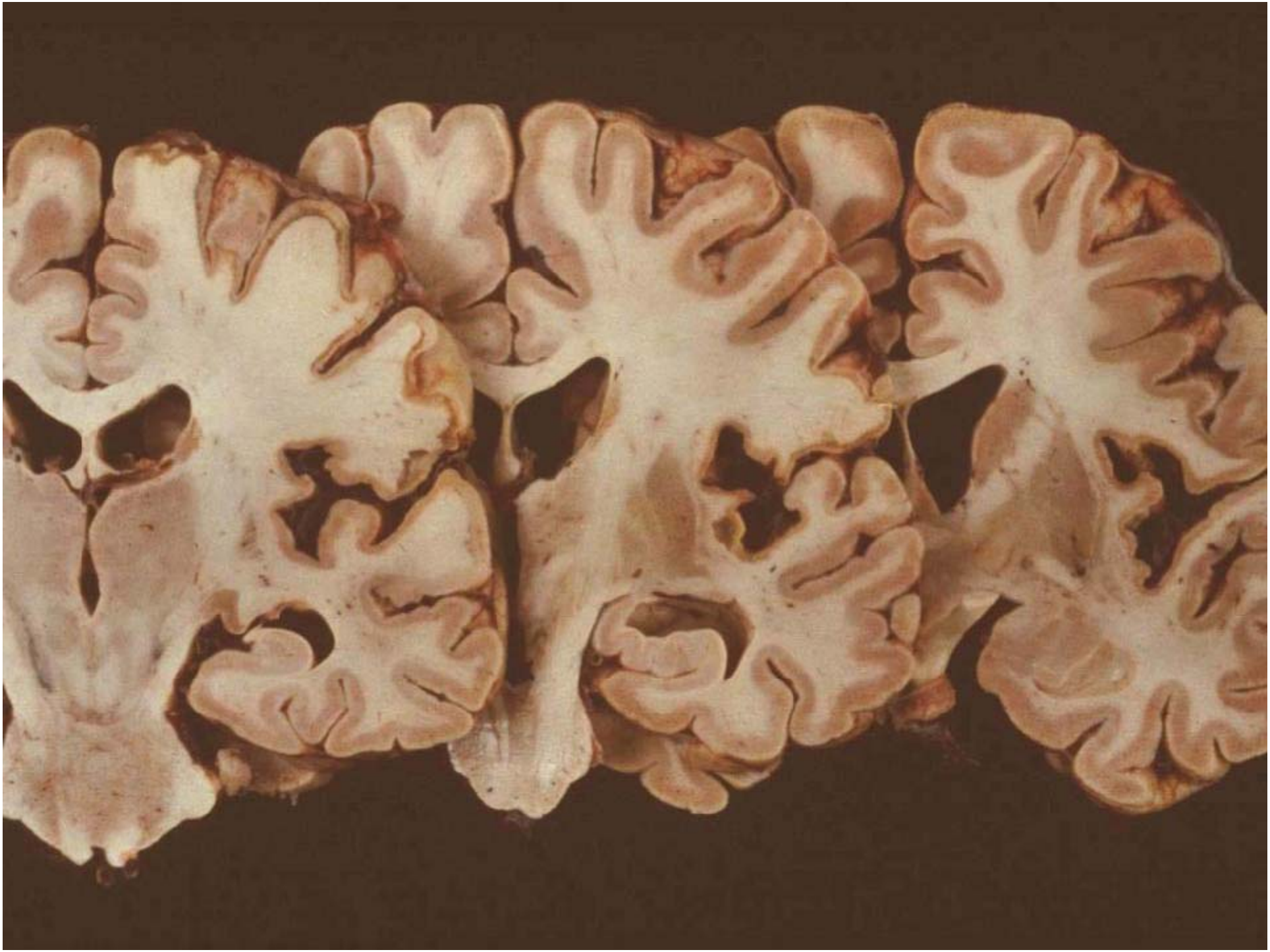
Leptomeningial anastomosis





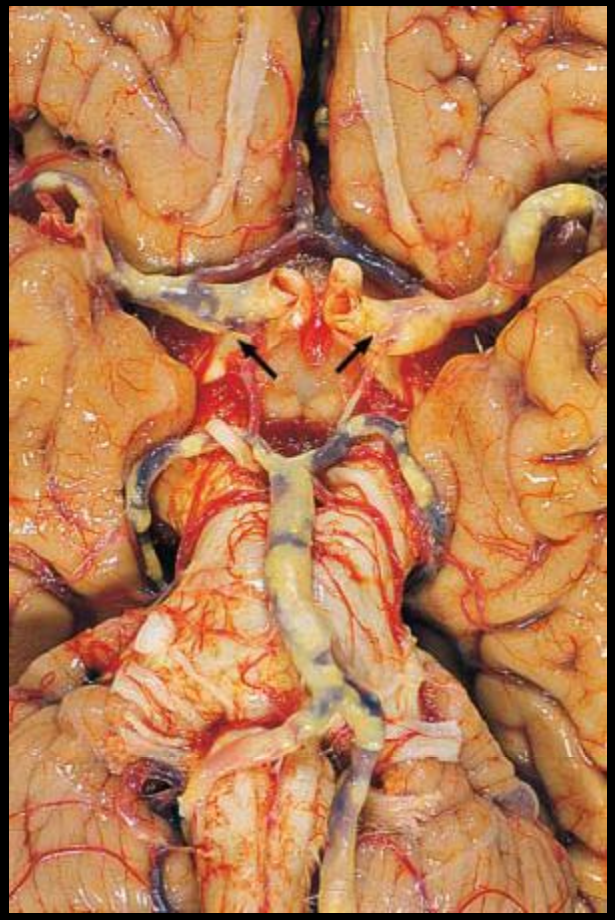


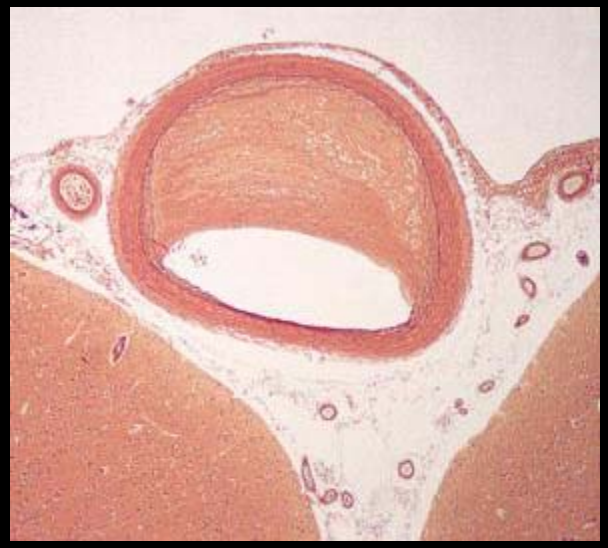


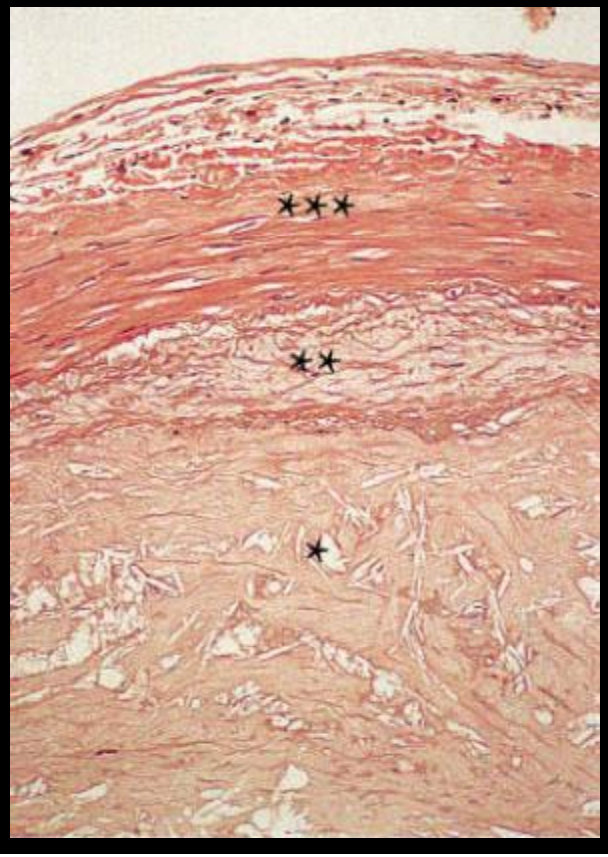


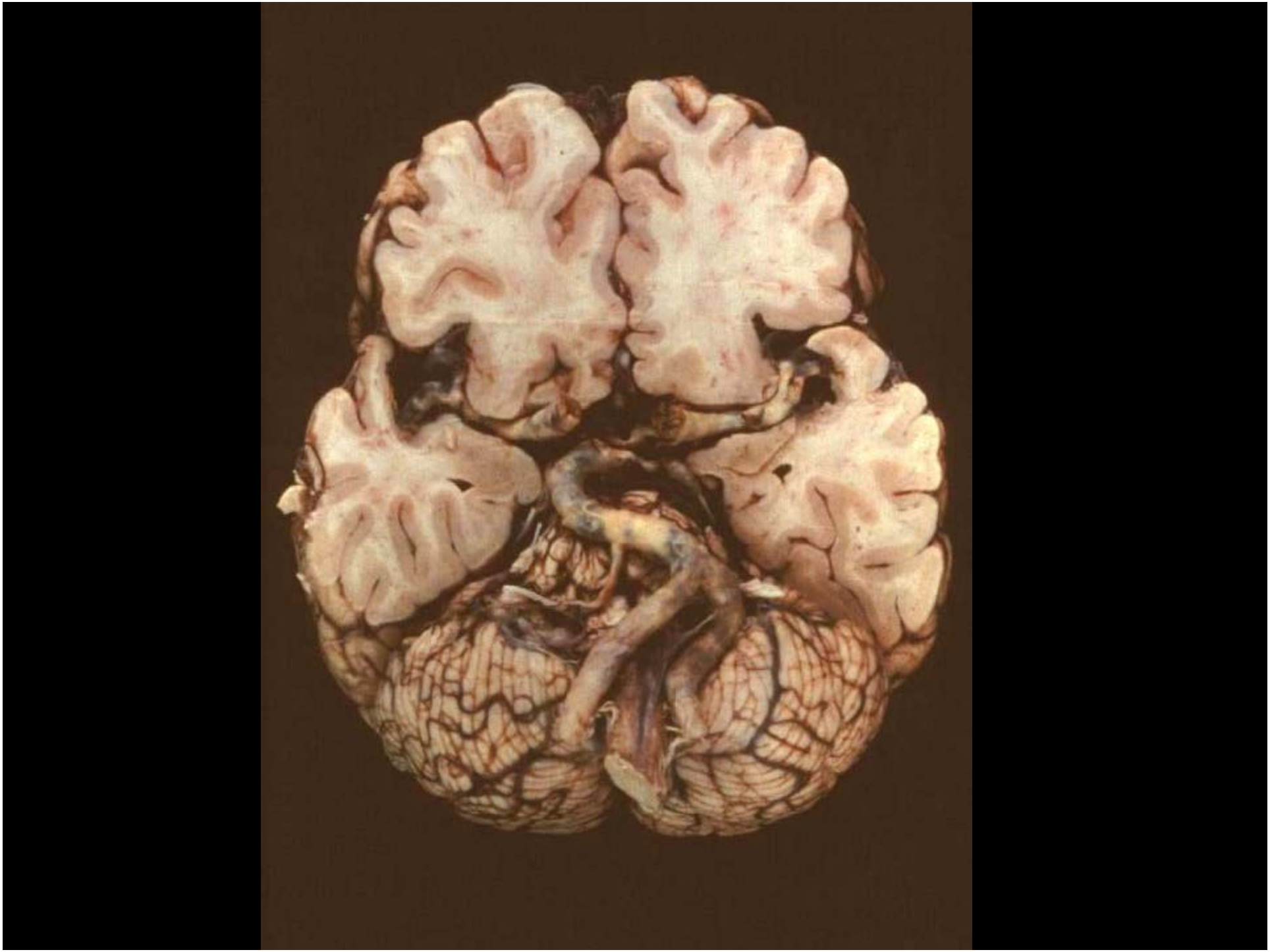
Underlying conditions of infarction

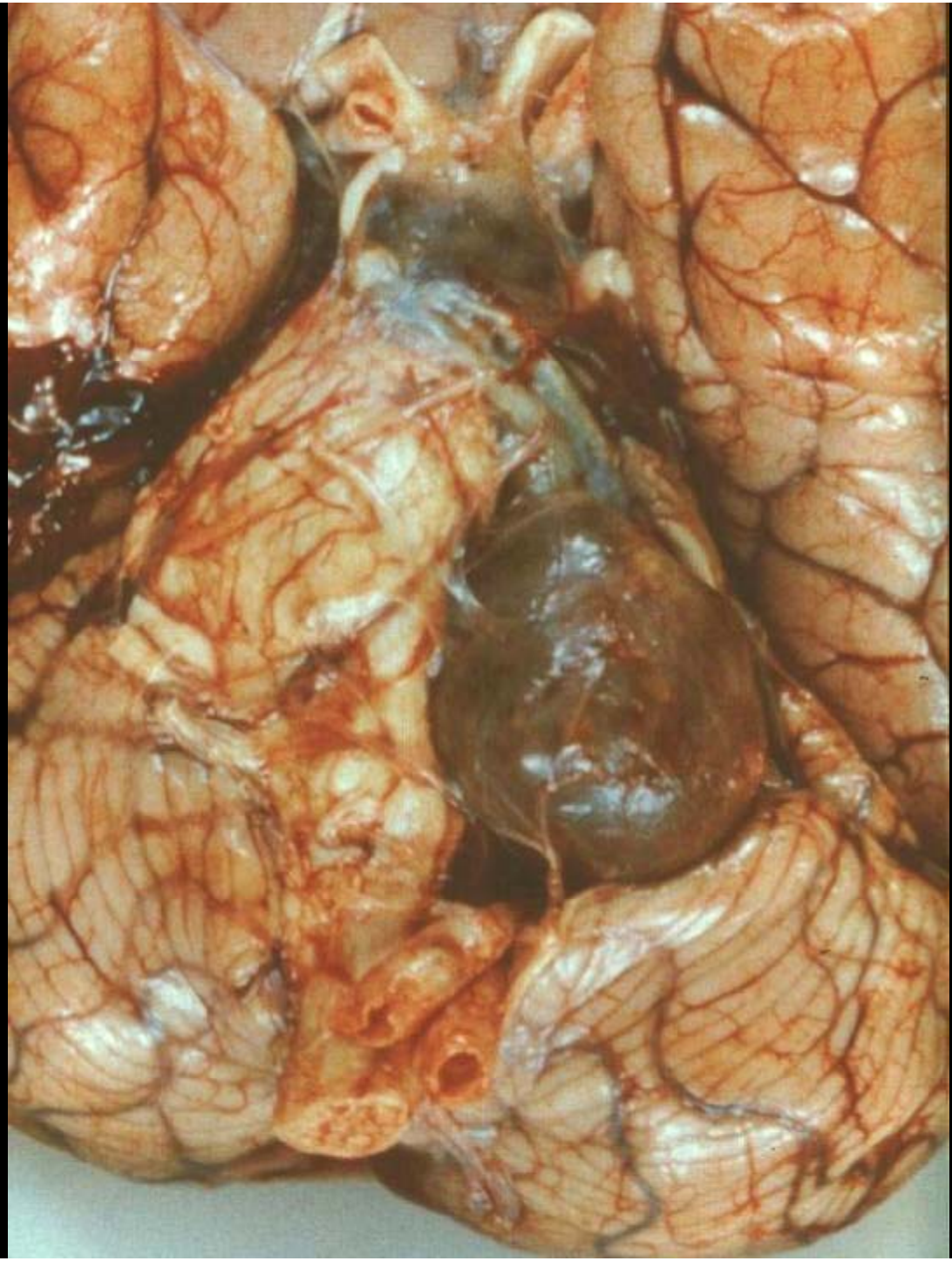
I. Atherosclerosis

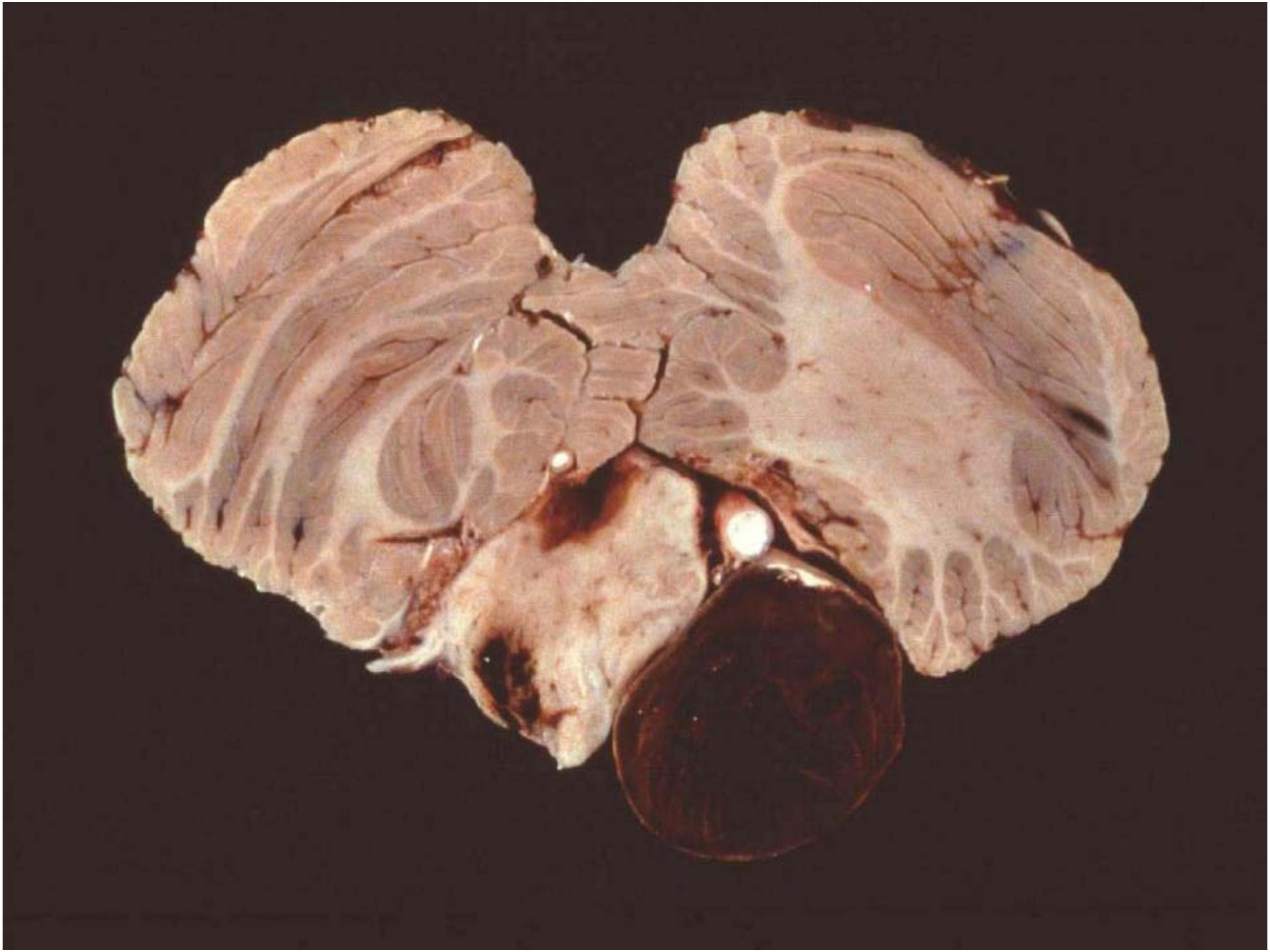


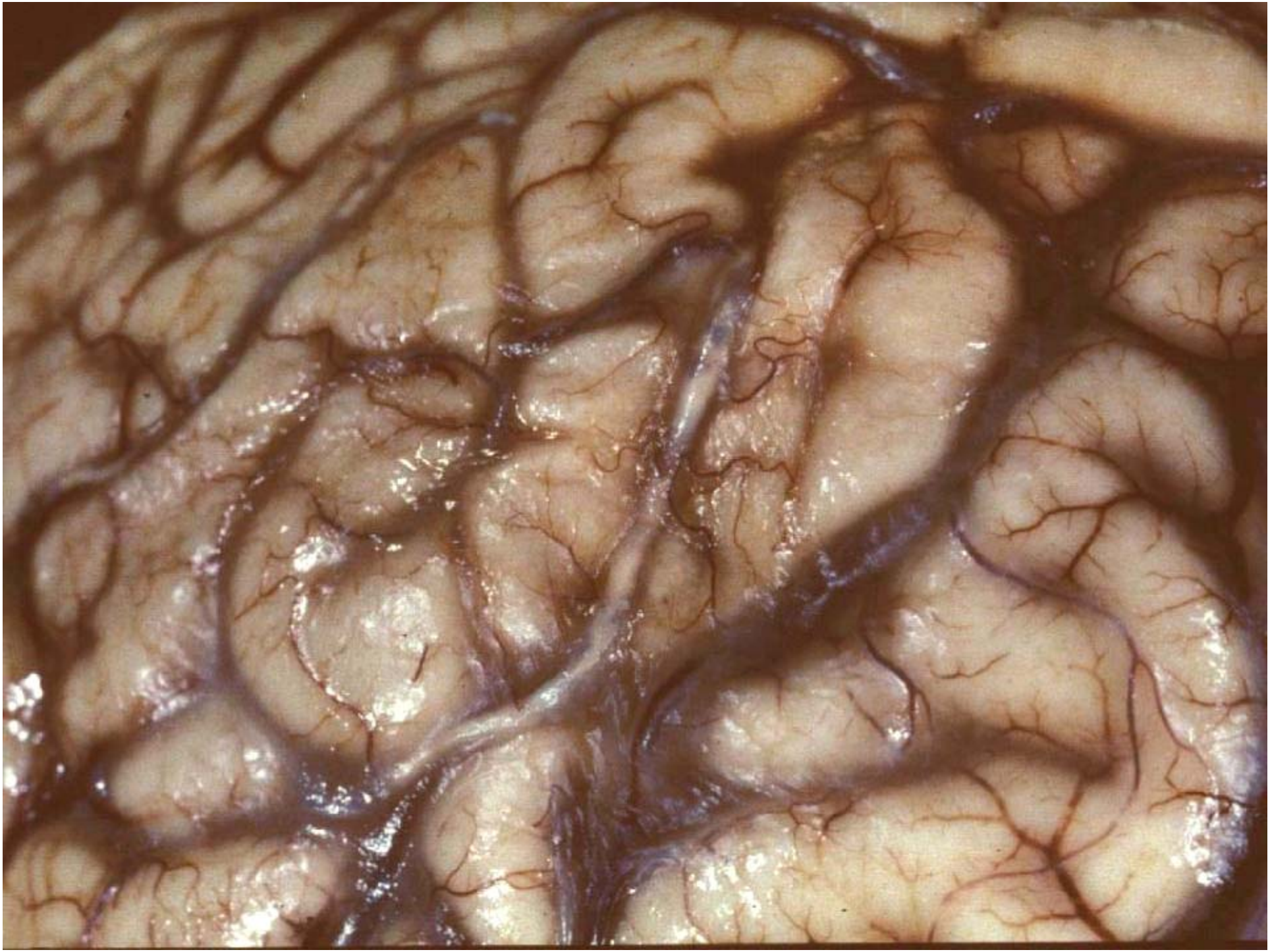








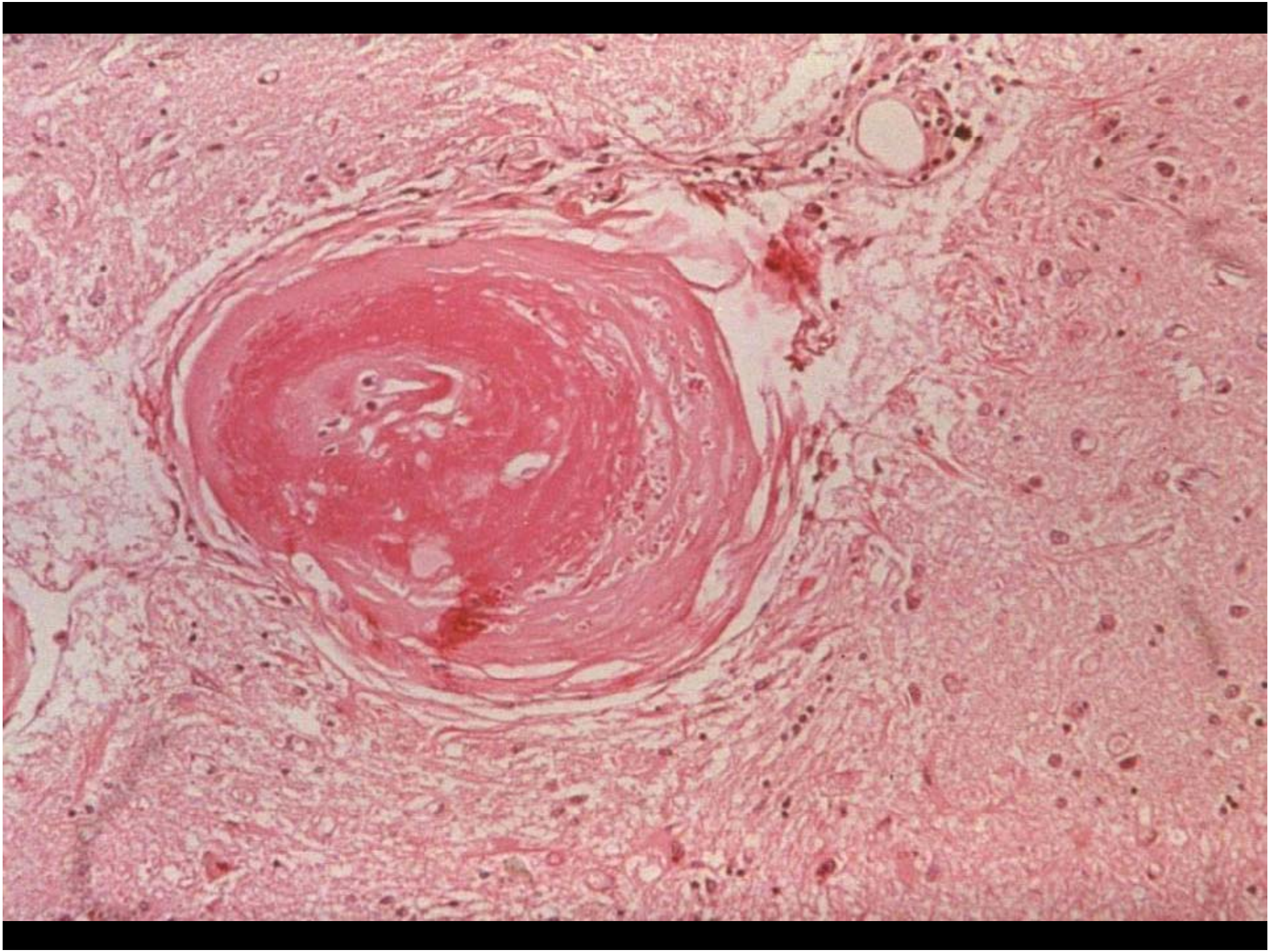


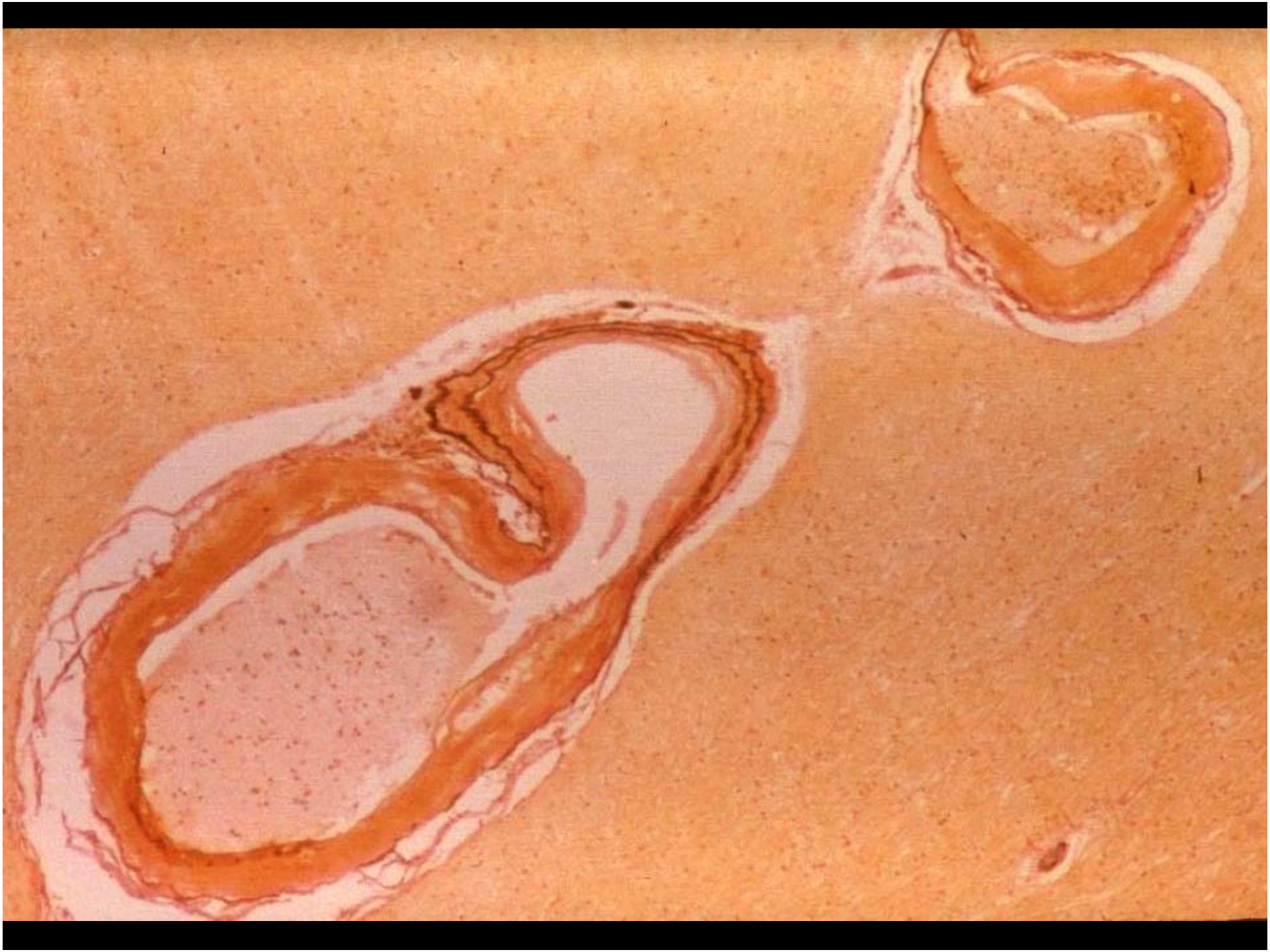


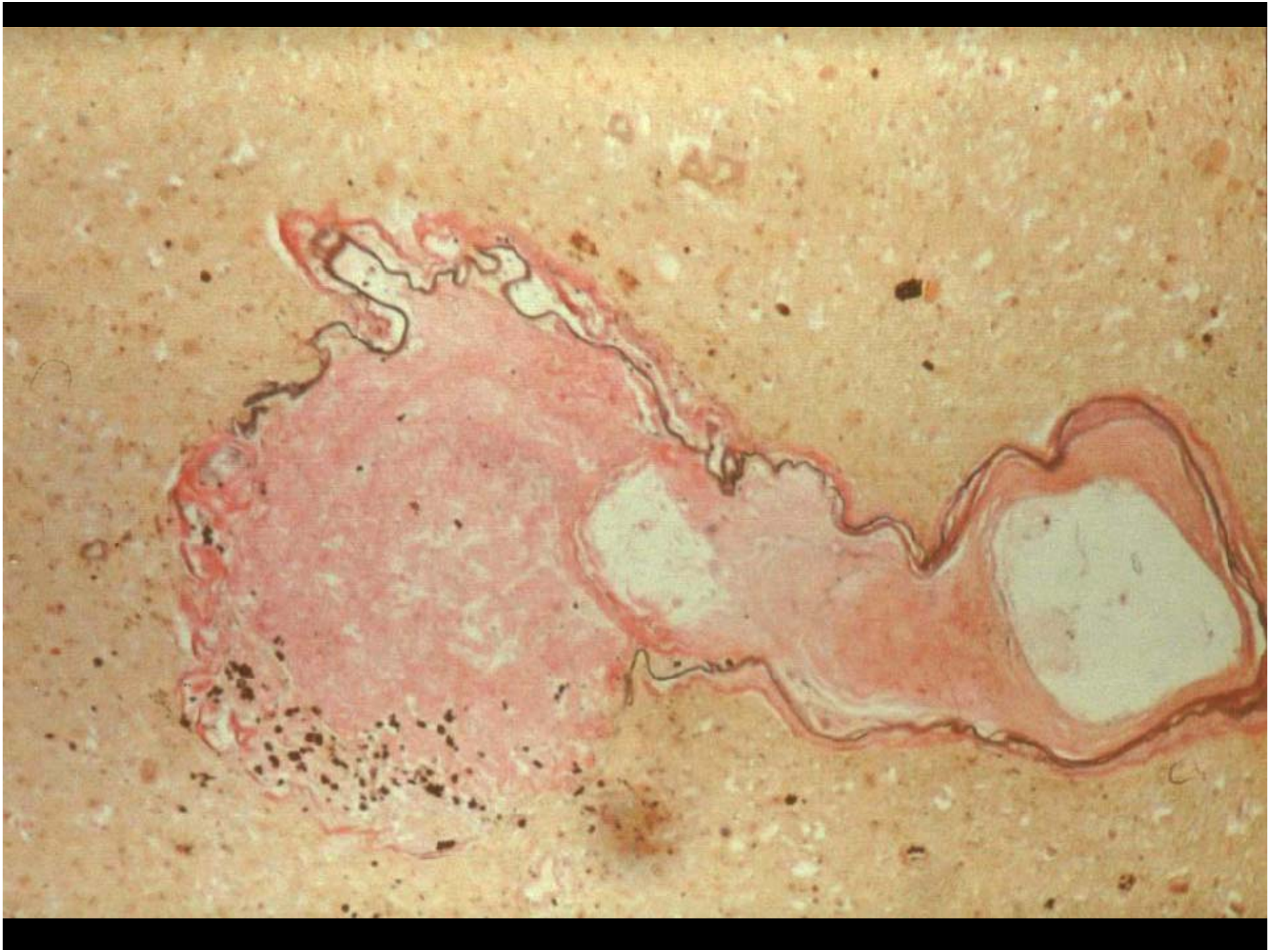
Underlying conditions of infarction

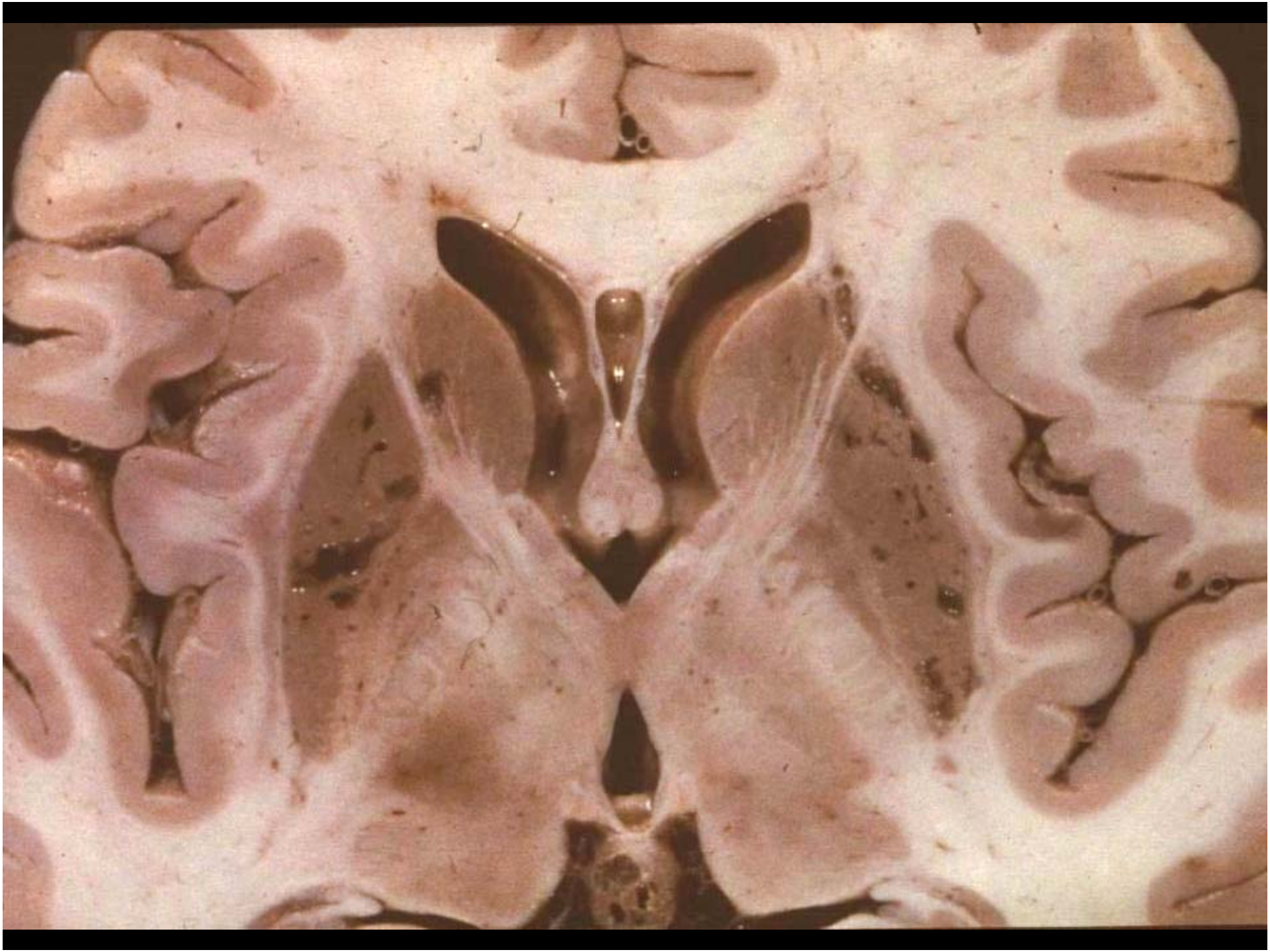
II. Arteriolar sclerosis (small vessel disease)

- aging
- **sustained systemic hypertension**
- **diabetes mellitus**









Underlying conditions of infarction

III. Cerebral embolism

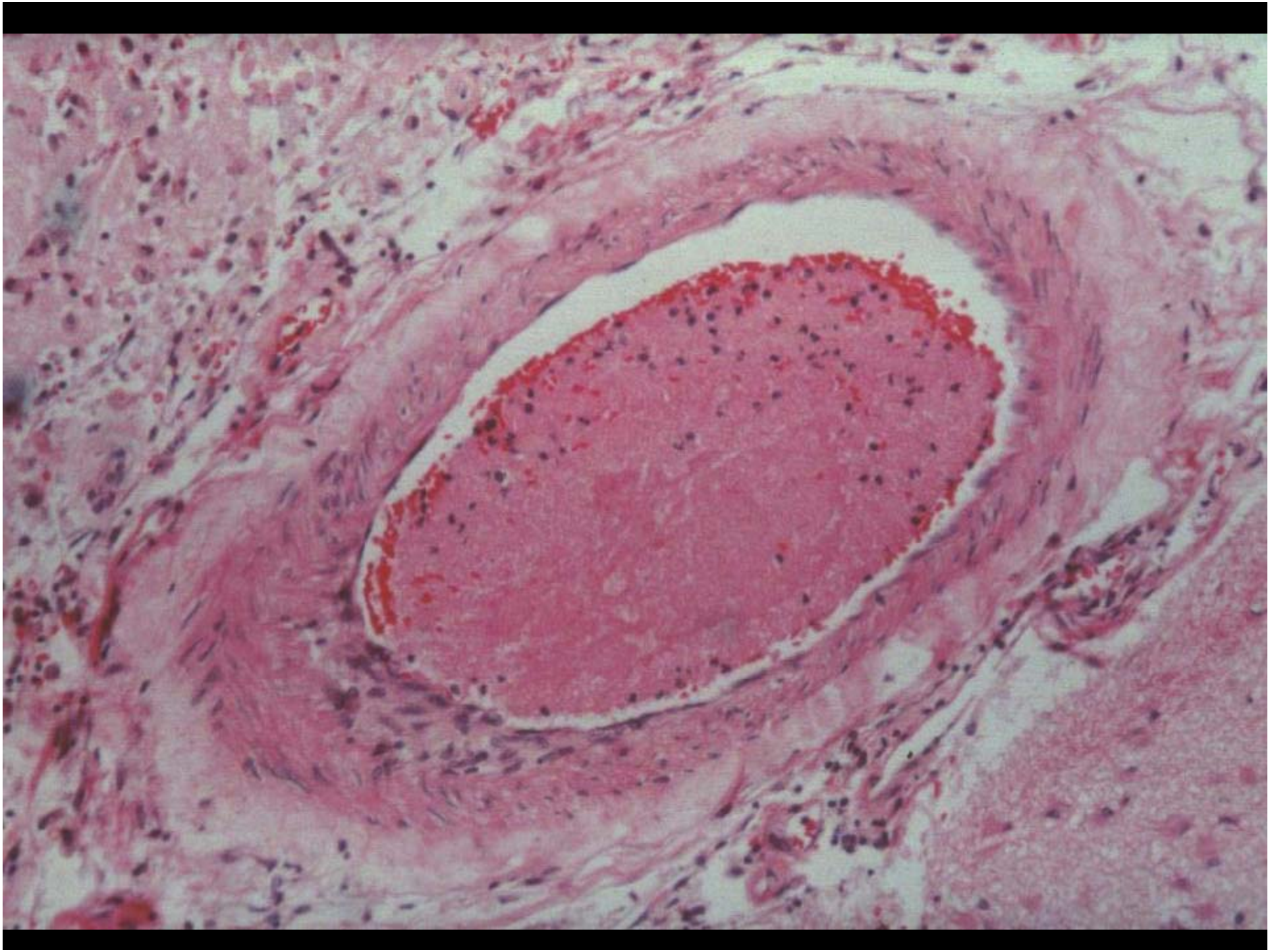
Some causes of cerebral embolism

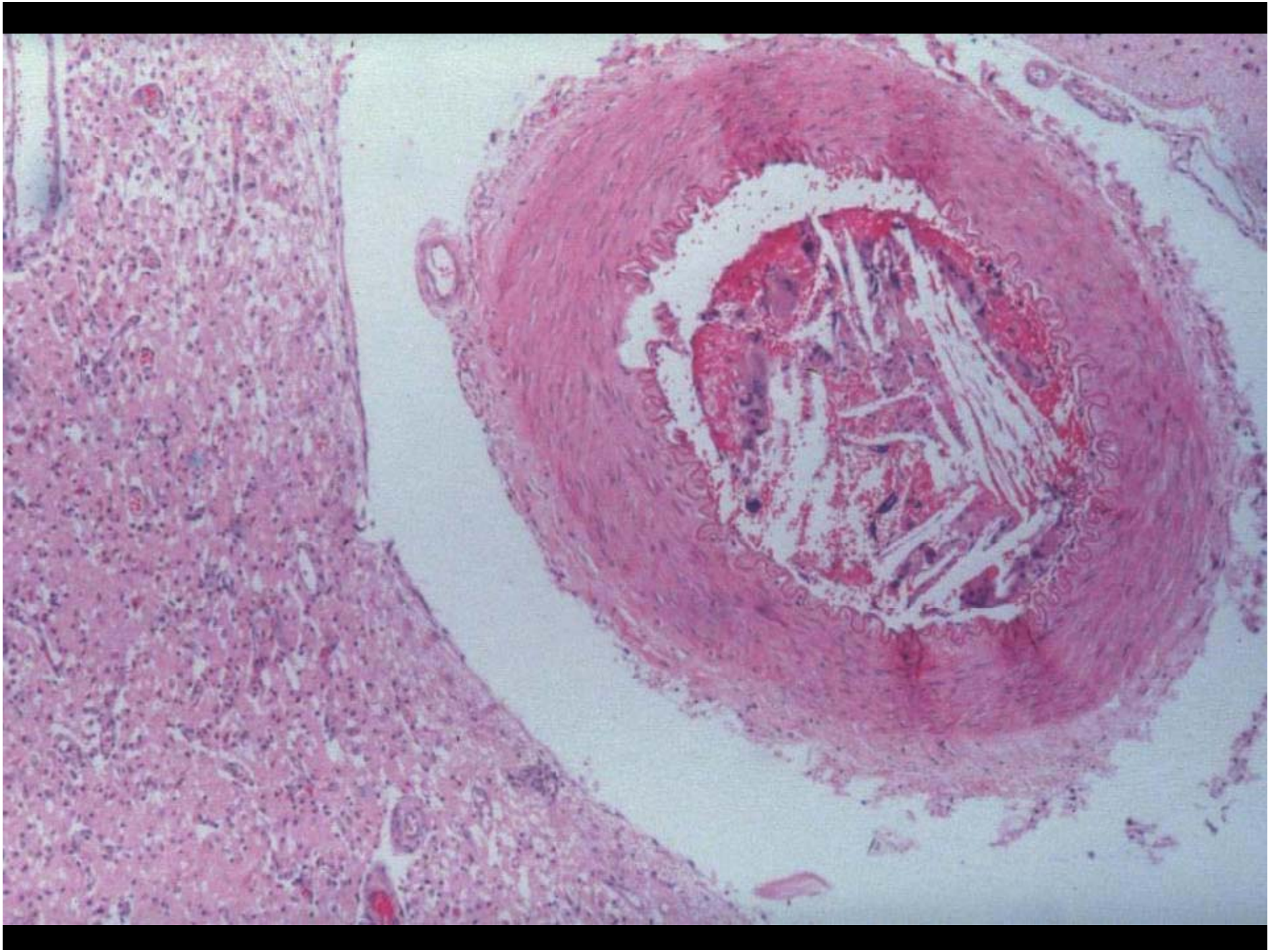
Large or small emboli:

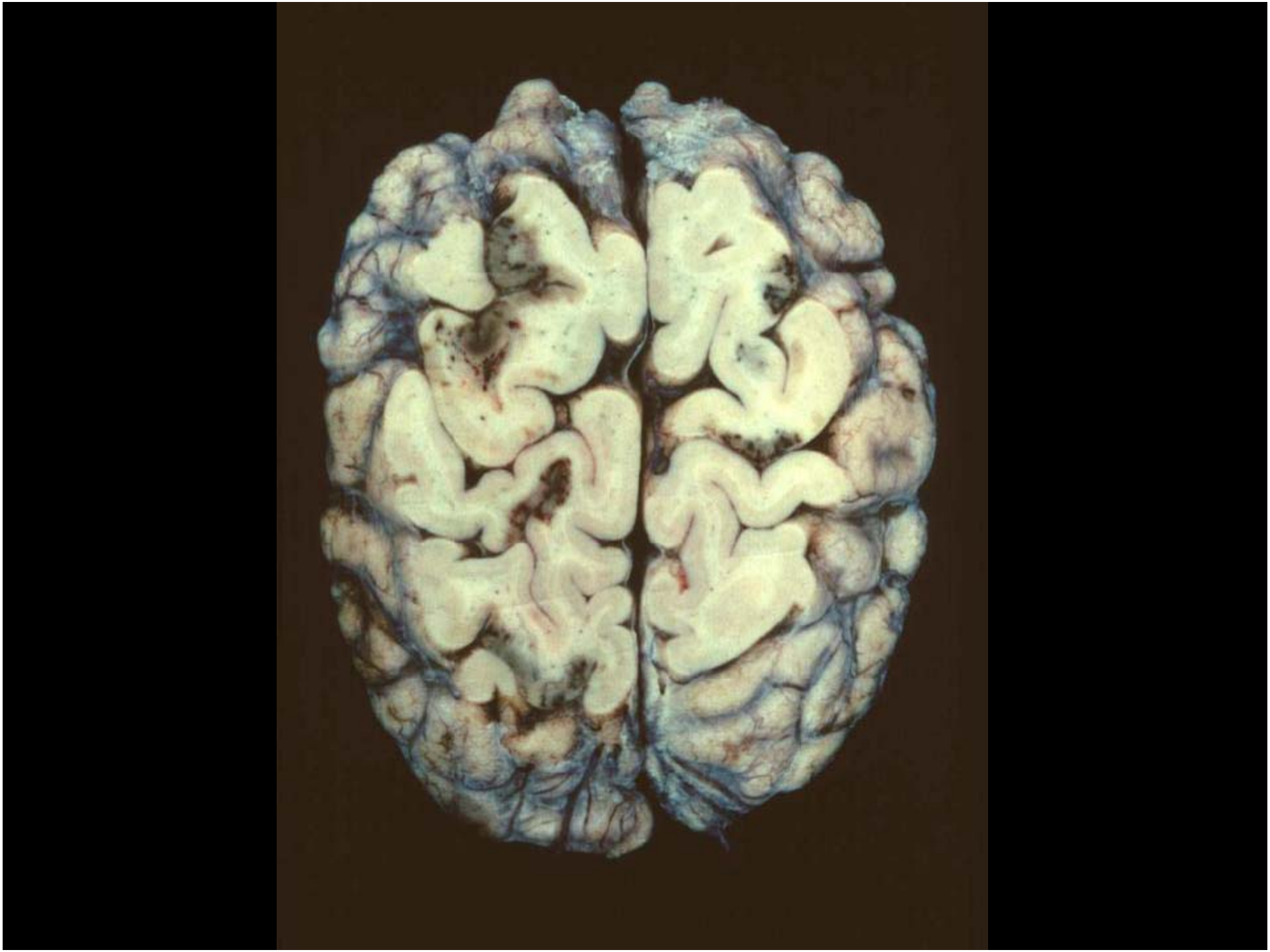
- atrial fibrillation
- myocardial infarction
- bacterial endocarditis
- rheumatic endocarditis
- nonbacterial endocarditis
- cardiac surgery
- arterial thrombosis

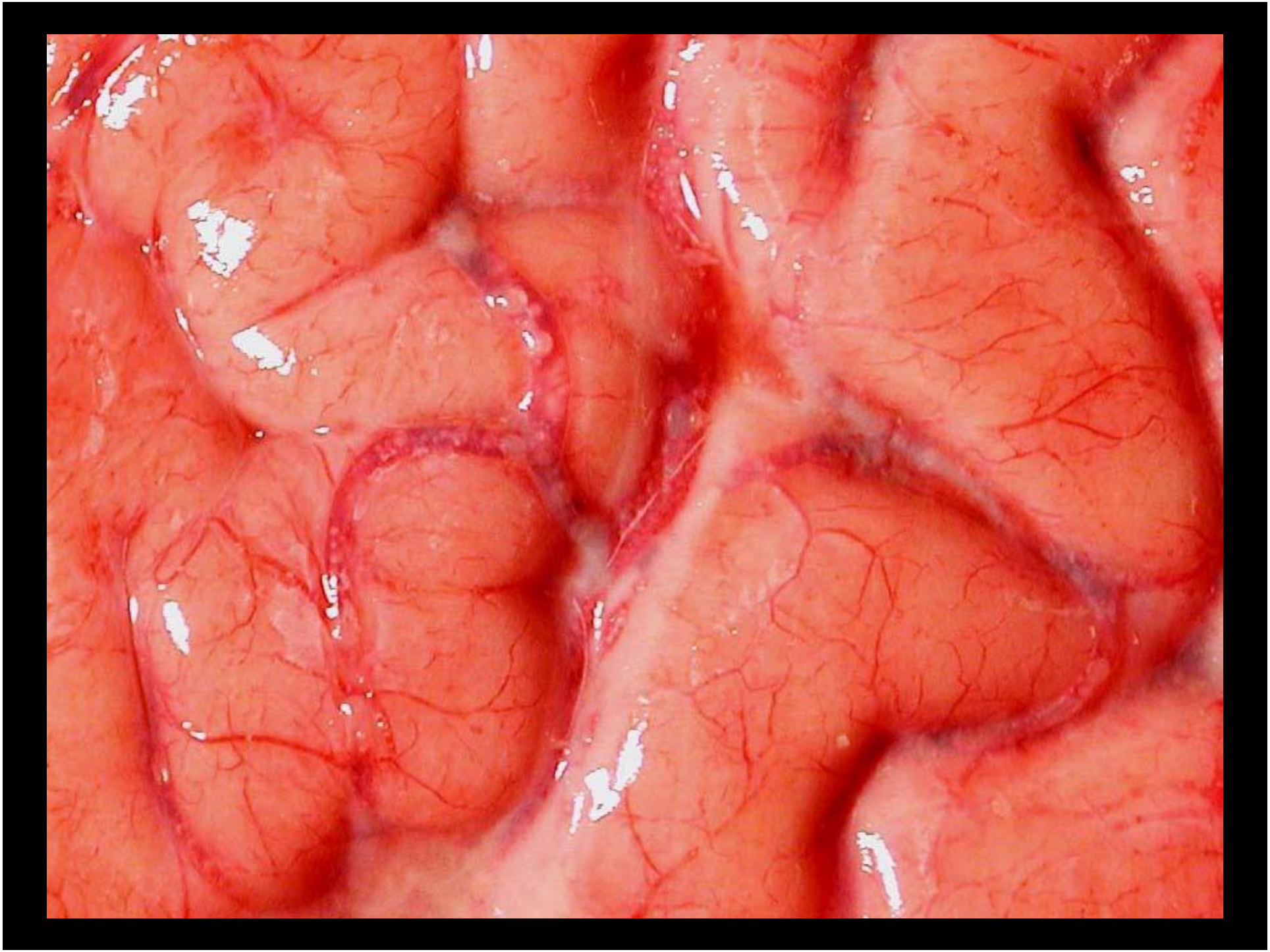
Small emboli:

- ulcerated atheroma
- trauma (fat emboli)









Underlying conditions of infarction

IV. Vasculitis/vasculitides

Inflammatory CNS vascular diseases

Non-infectious vasculitides

Primary cranial and/or cerebral inflammations

- Takayasu's arteritis
- giant cell or temporal arteritis
- primary angiitis of the CNS (granulomatous angiitis)

Manifestations of systemic diseases

- systemic lupus erythematosus
- polyarteritis nodosa
- Wegener's granulomatosis
- Churg-Strauss syndrome
- Behcet's syndrome
- malignancy related

Drug induced vasculitis

Infectious vasculitis

Cerebral hemorrhage

- **intracerebral**
- **subarachnoid**

- epidural /subdural (trauma)

I. Intracerebral hemorrhage

Incidence:

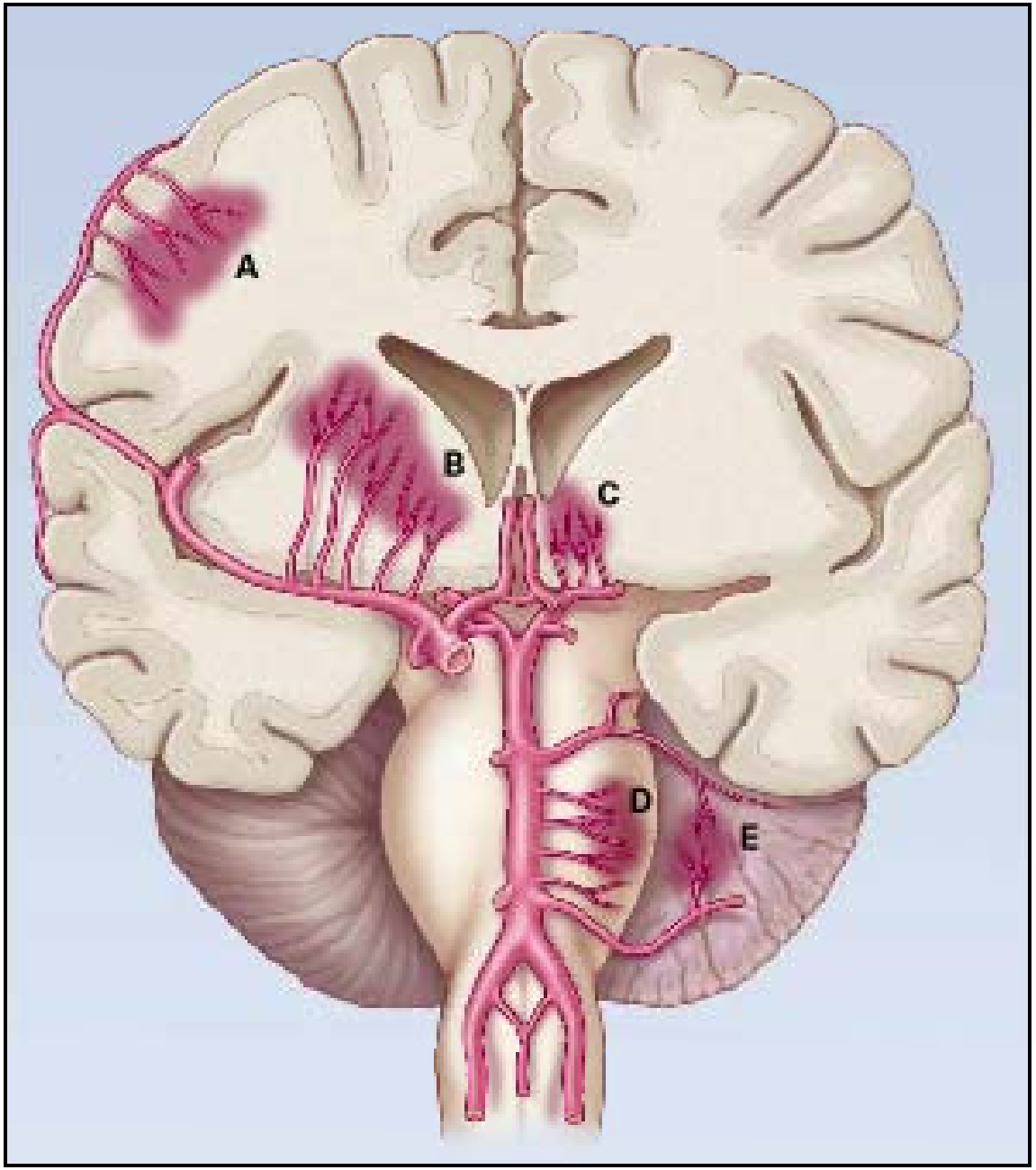
Asians > African Americans > Caucasians

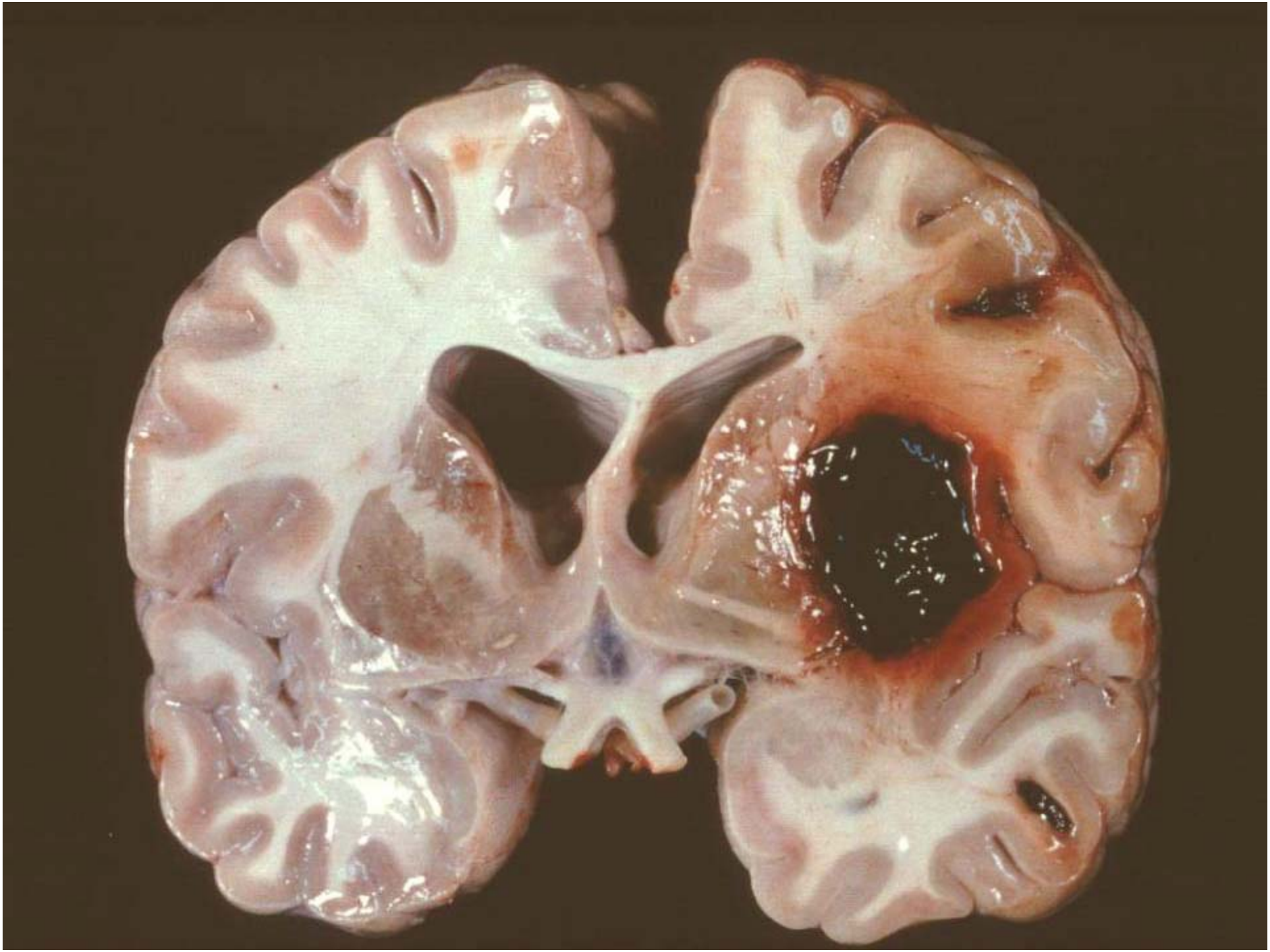
Causes of non-traumatic ICH:

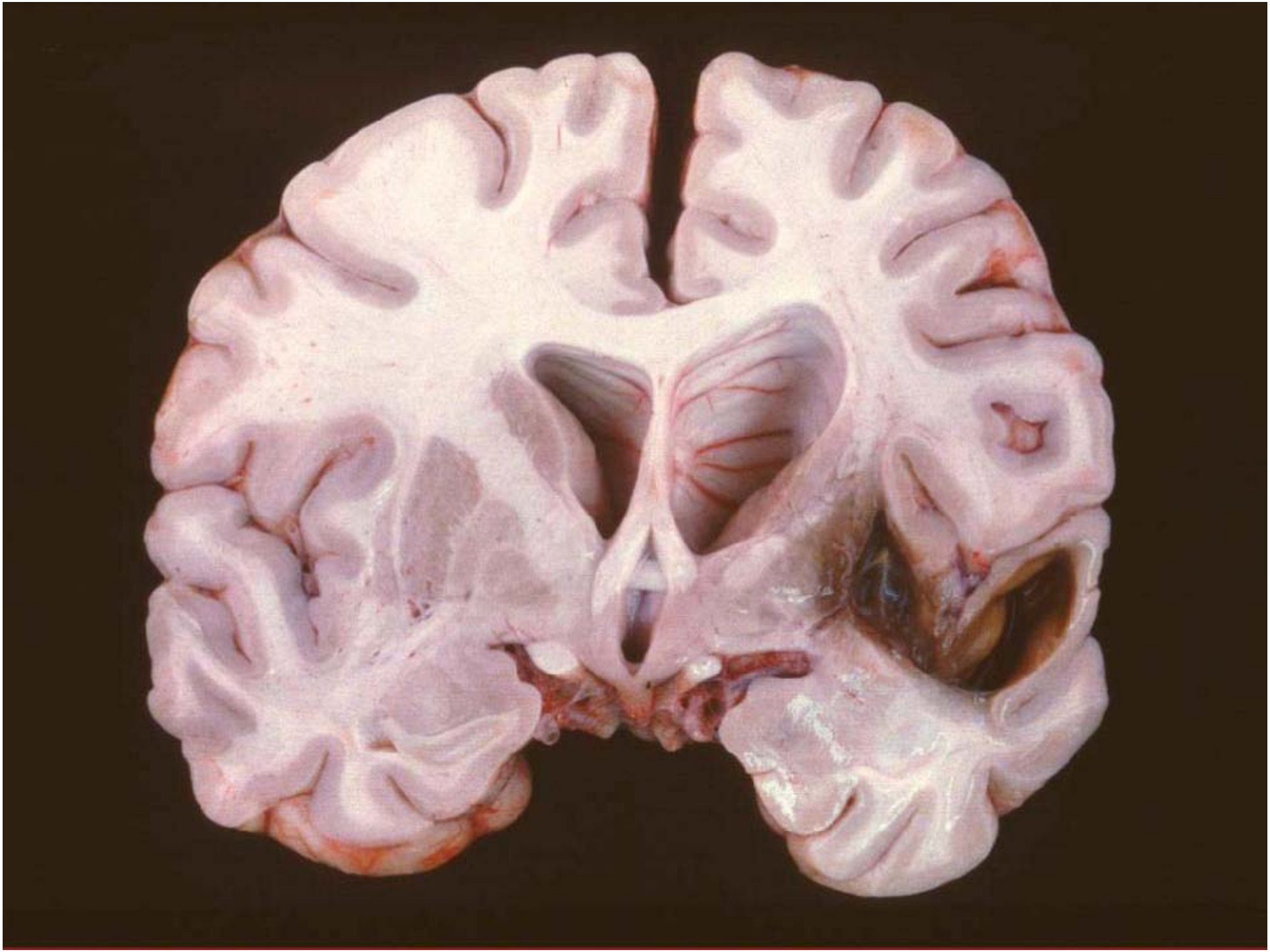
hypertension	50%
cerebral amyloid angiopathy	12%
anticoagulants	10%
tumors	8%
illicit and licit drugs	6%
arteriovenous malformations and aneurysms	5%
miscellaneous	9%

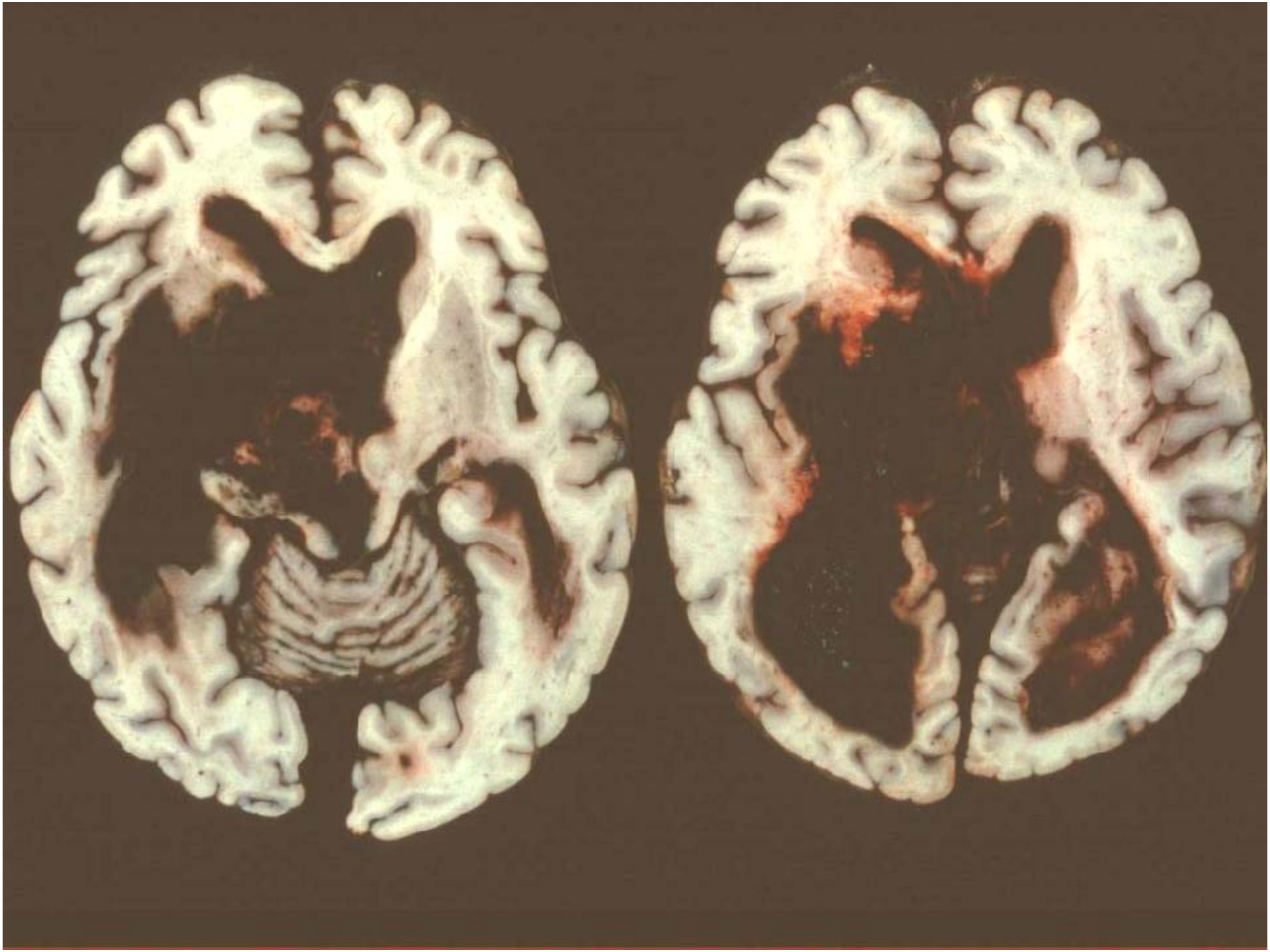
Hypertensive hemorrhage

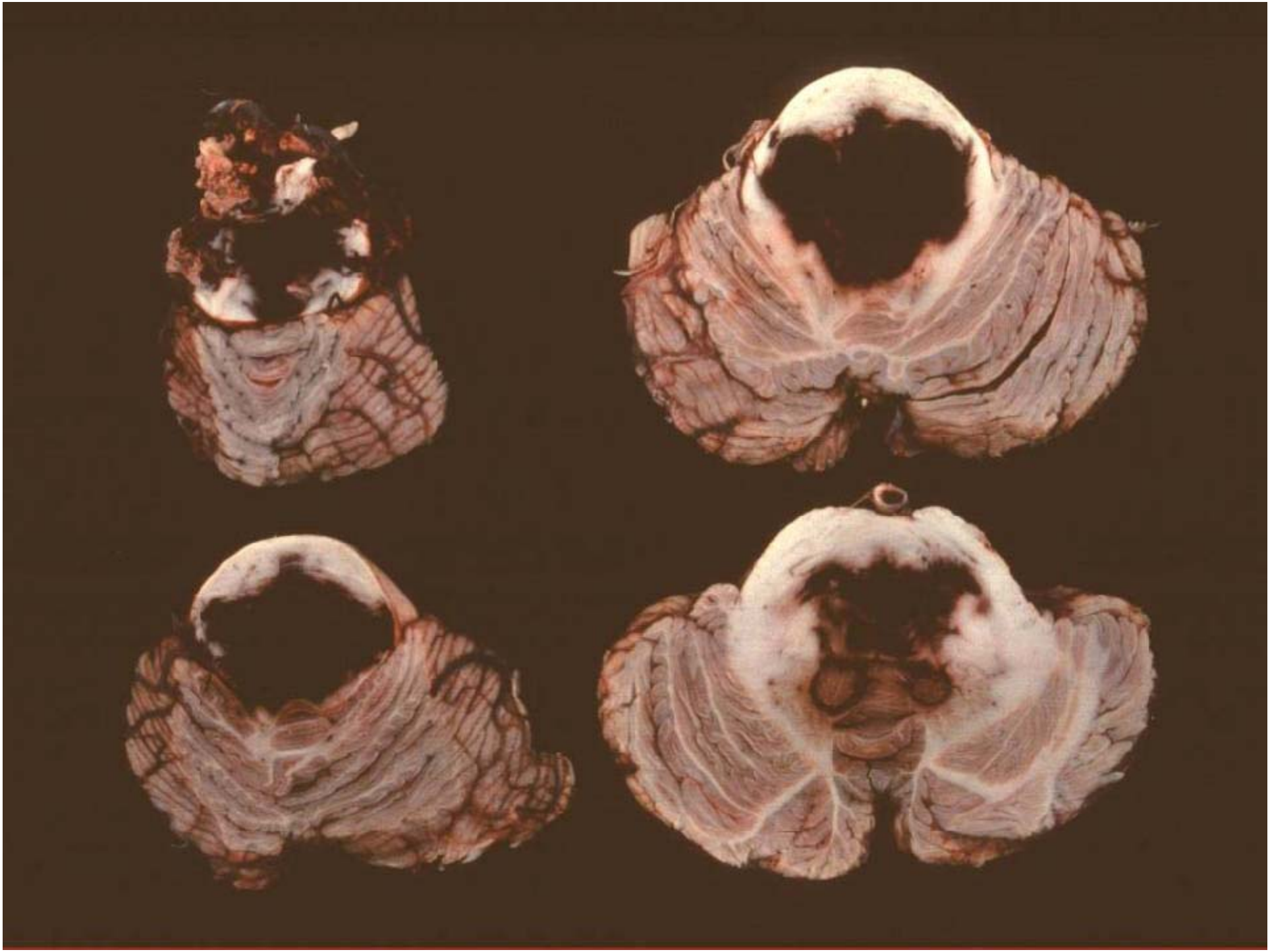
Frequent sites of involvement

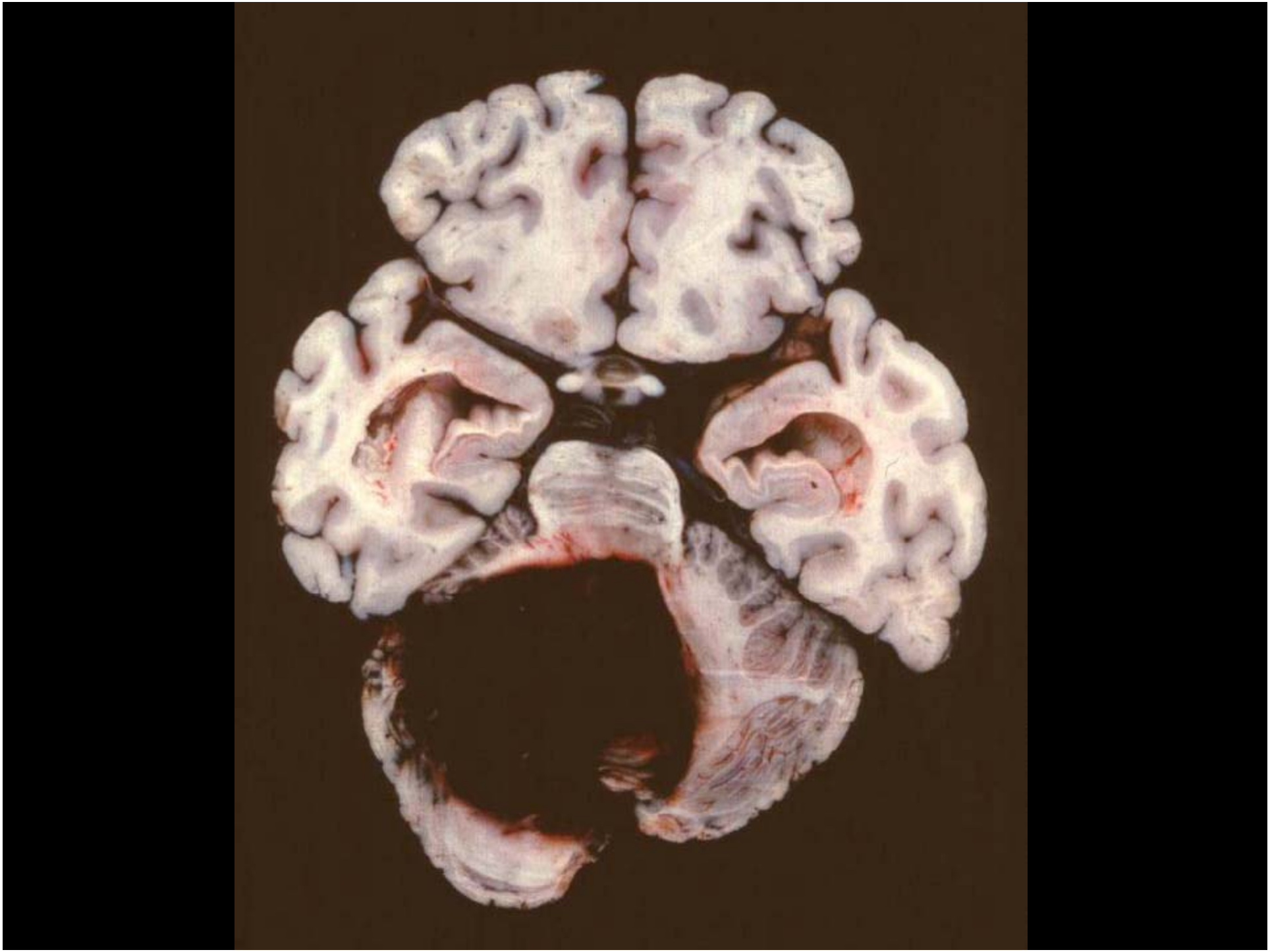












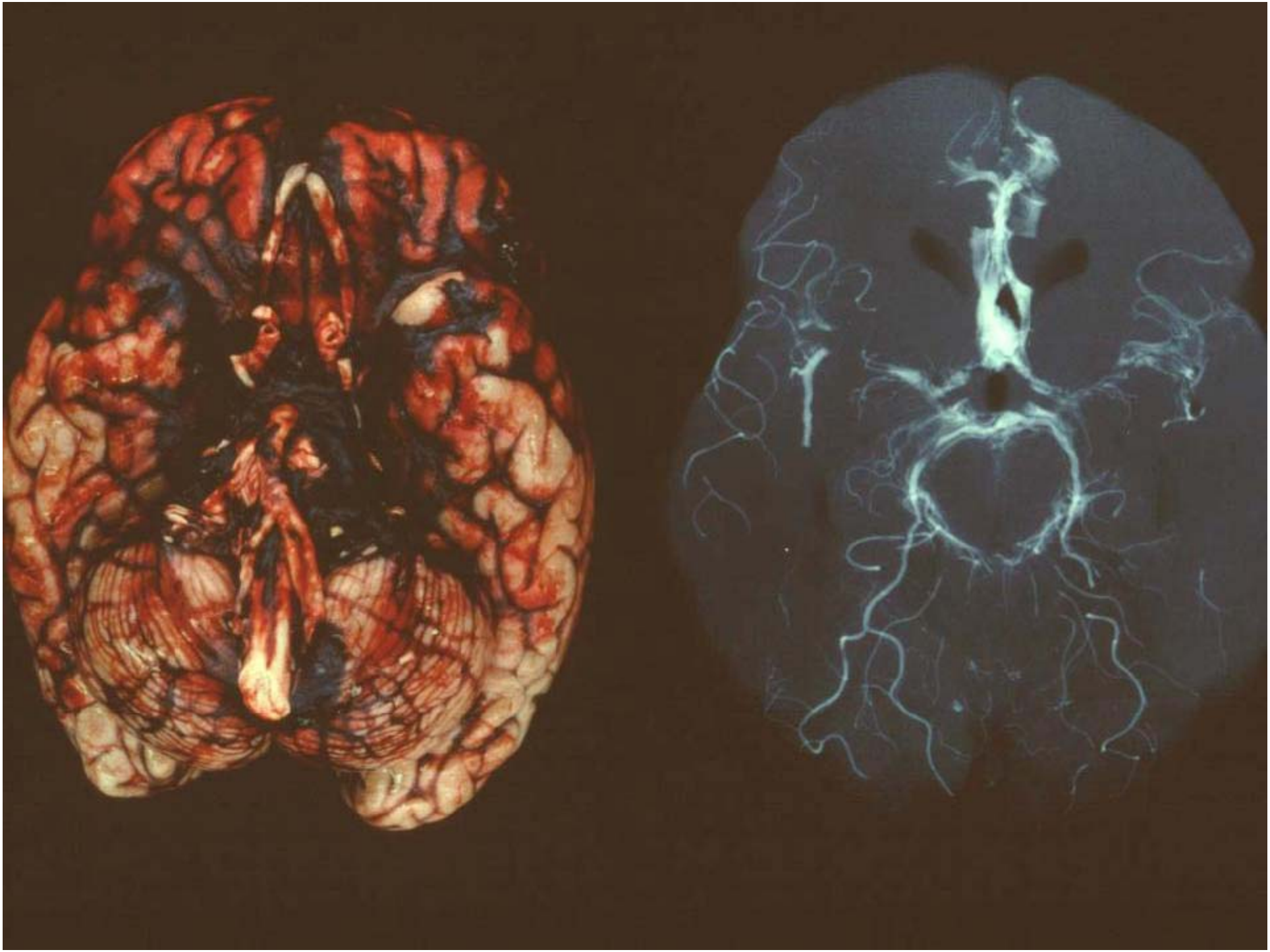
Cerebral hemorrhage

II. SAH subarachnodial hemorrhage

Frequency: Approx. 5% of all strokes

Reported annual incidence: 10-11 / 100,000

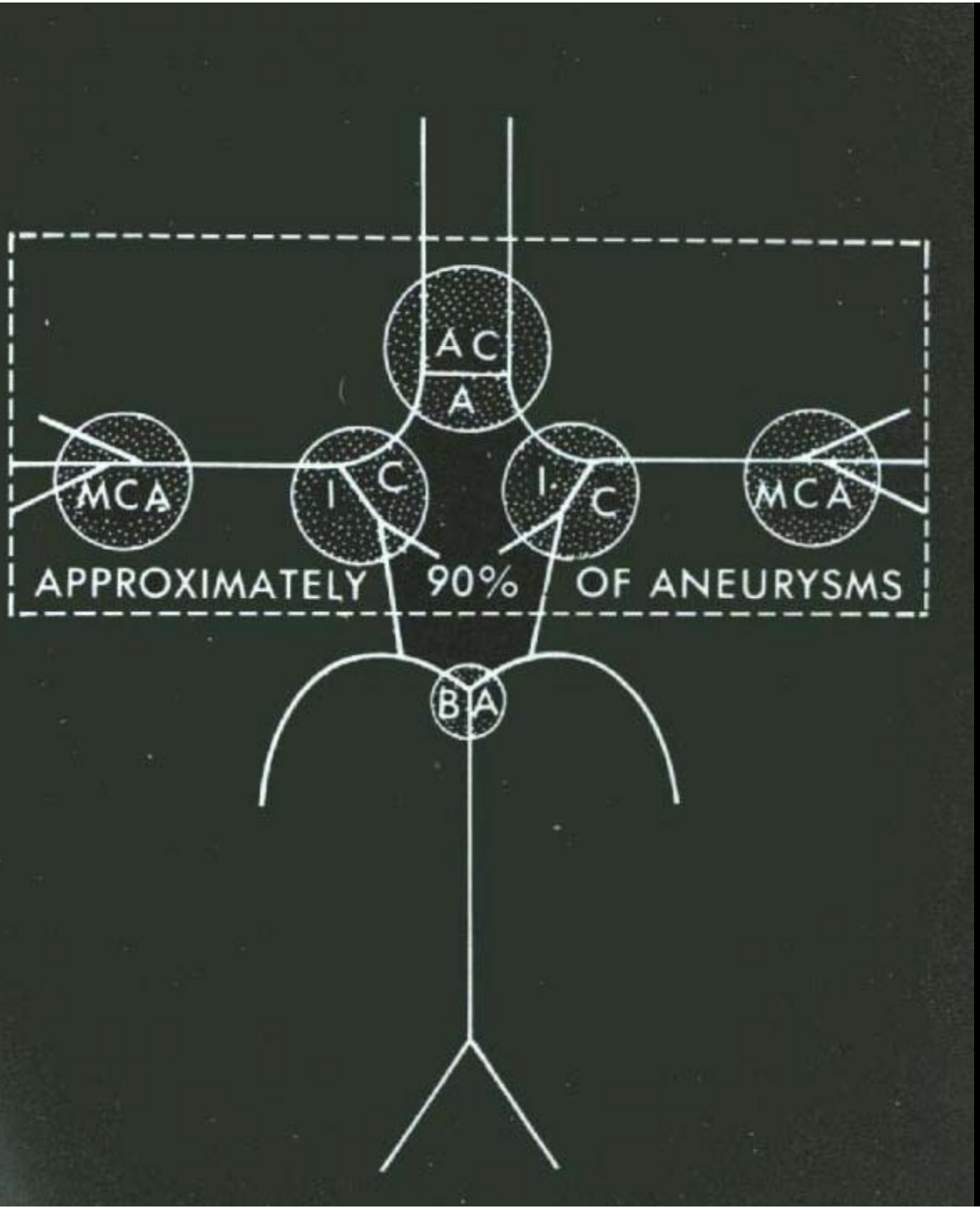
- **Non-traumatic conditions**
  - rupture of aneurysm* 80%
  - arteriovenous malformations** 5-10%
  - unidentified cause 10-15%
- **Traumatic**

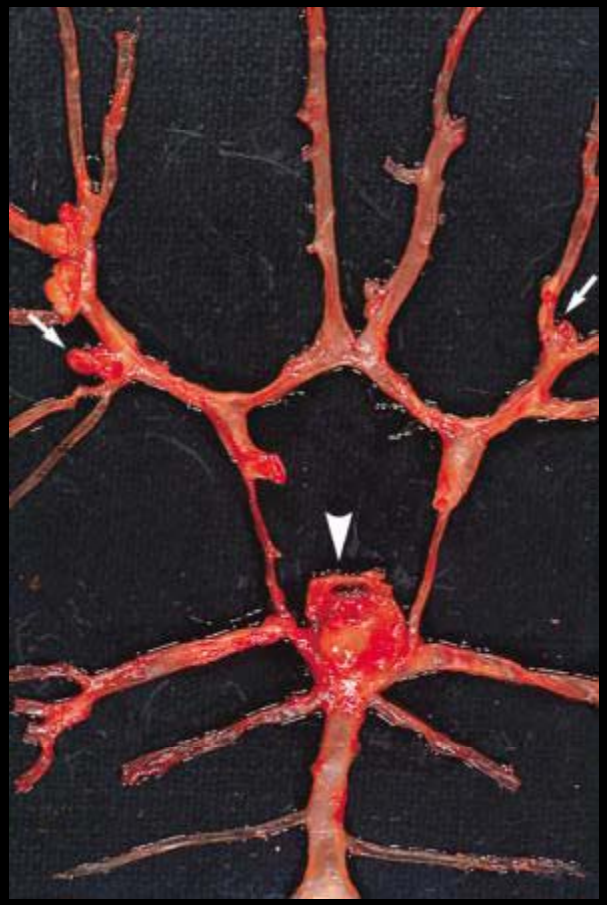


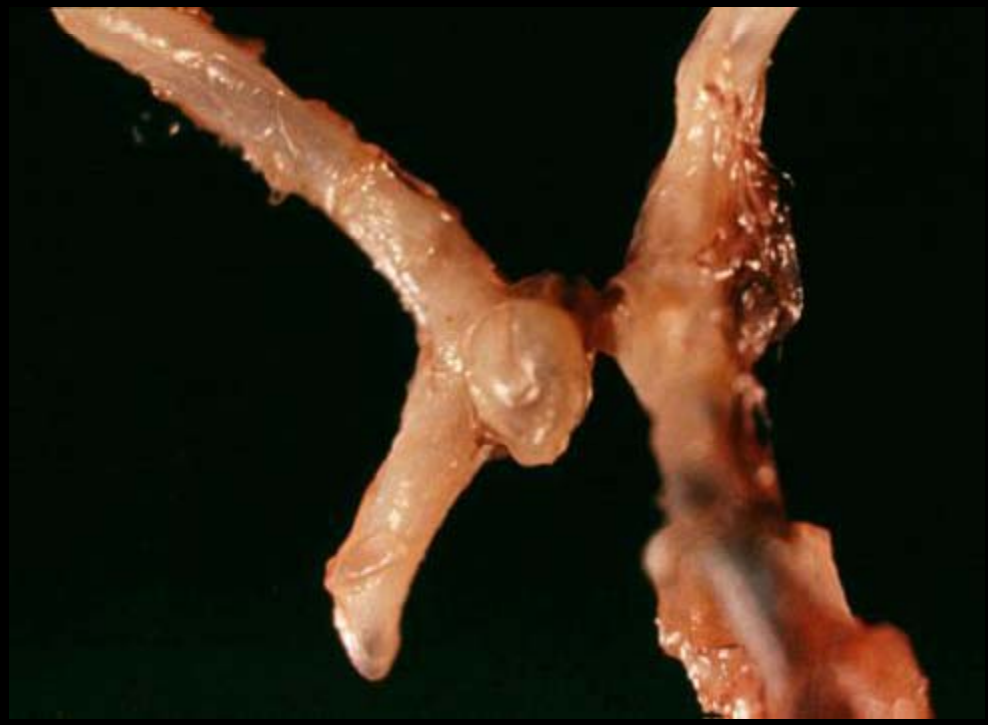
Underlying conditions of SAH

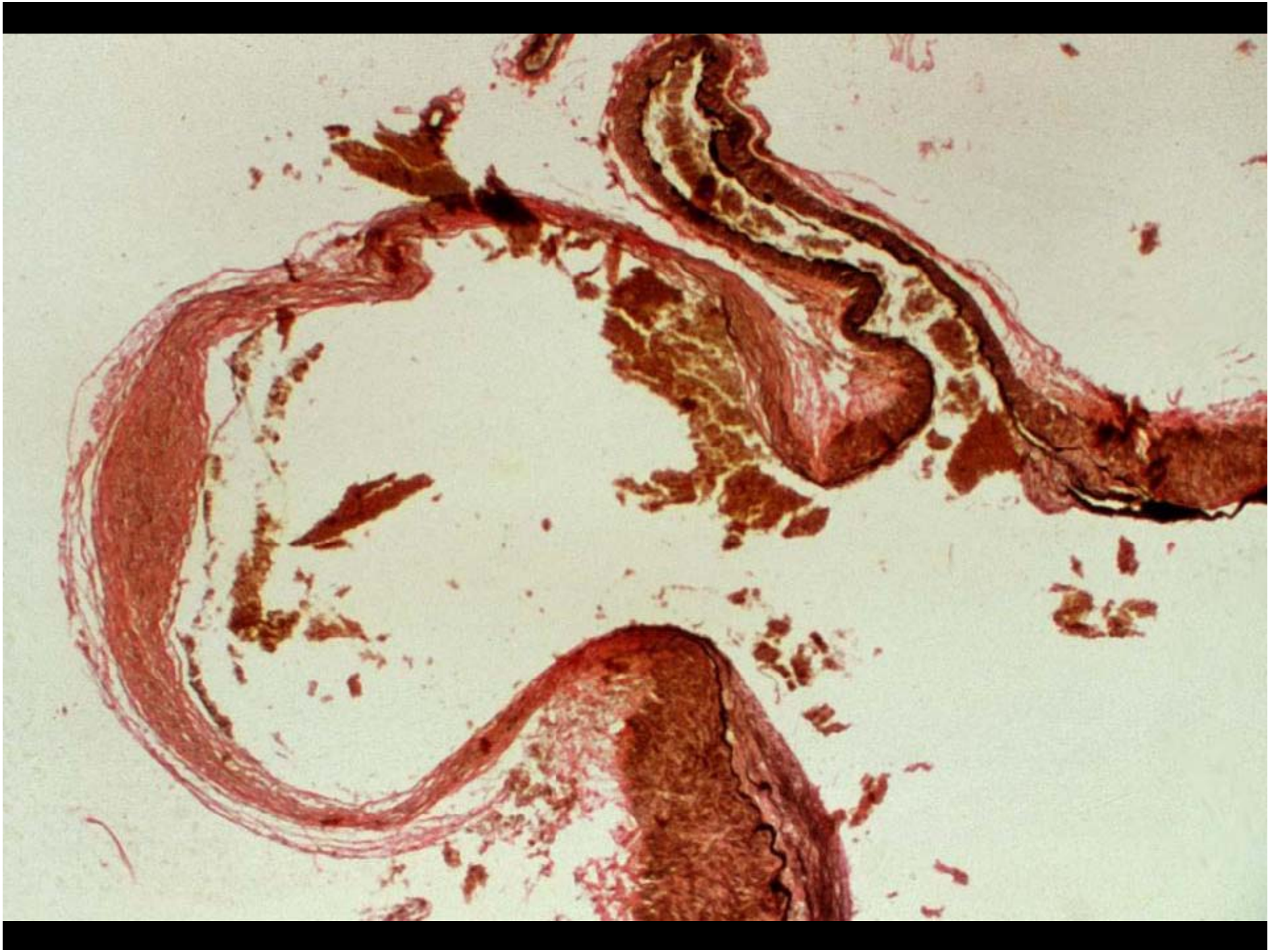
a. Saccular (berry) aneurysms

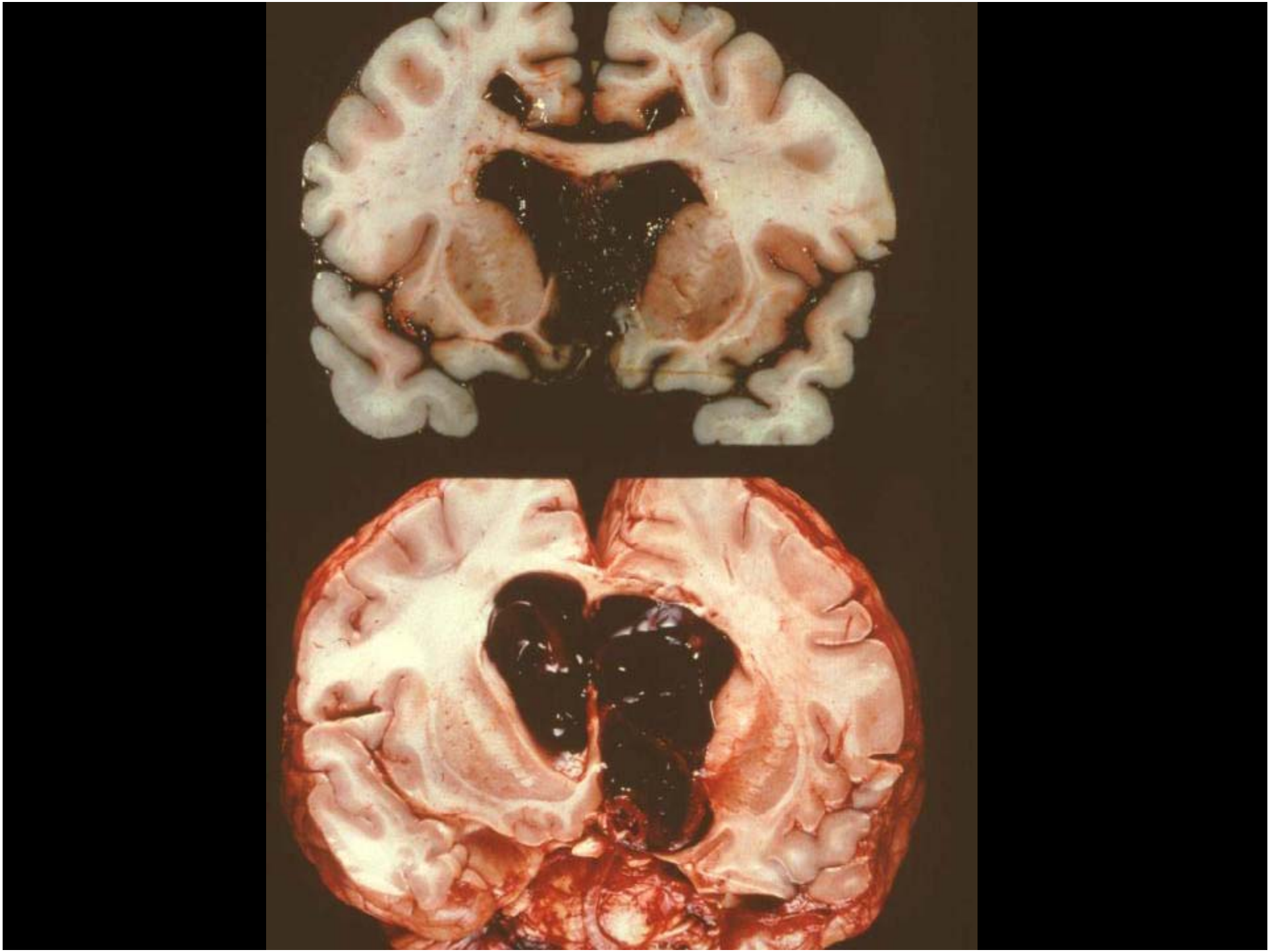
Frequency at autopsy:	**1 to 6%**
Age at autopsy:	**30 - 70 yrs**
Sex ratio:	**F:M = 3:2**
Associated hypertension:	**50%**
Familial:	**Rare**
Location:	**Anterior circulation > 80%**
	Posterior circulation < 20%
Multiple:	**20%**
Ruptured aneurysms:	**Size > 0.5 cm**
Mortality:	**60%**


AC
A
MCA
I C
I C
MCA
APPROXIMATELY 90% OF ANEURYSMS
B A









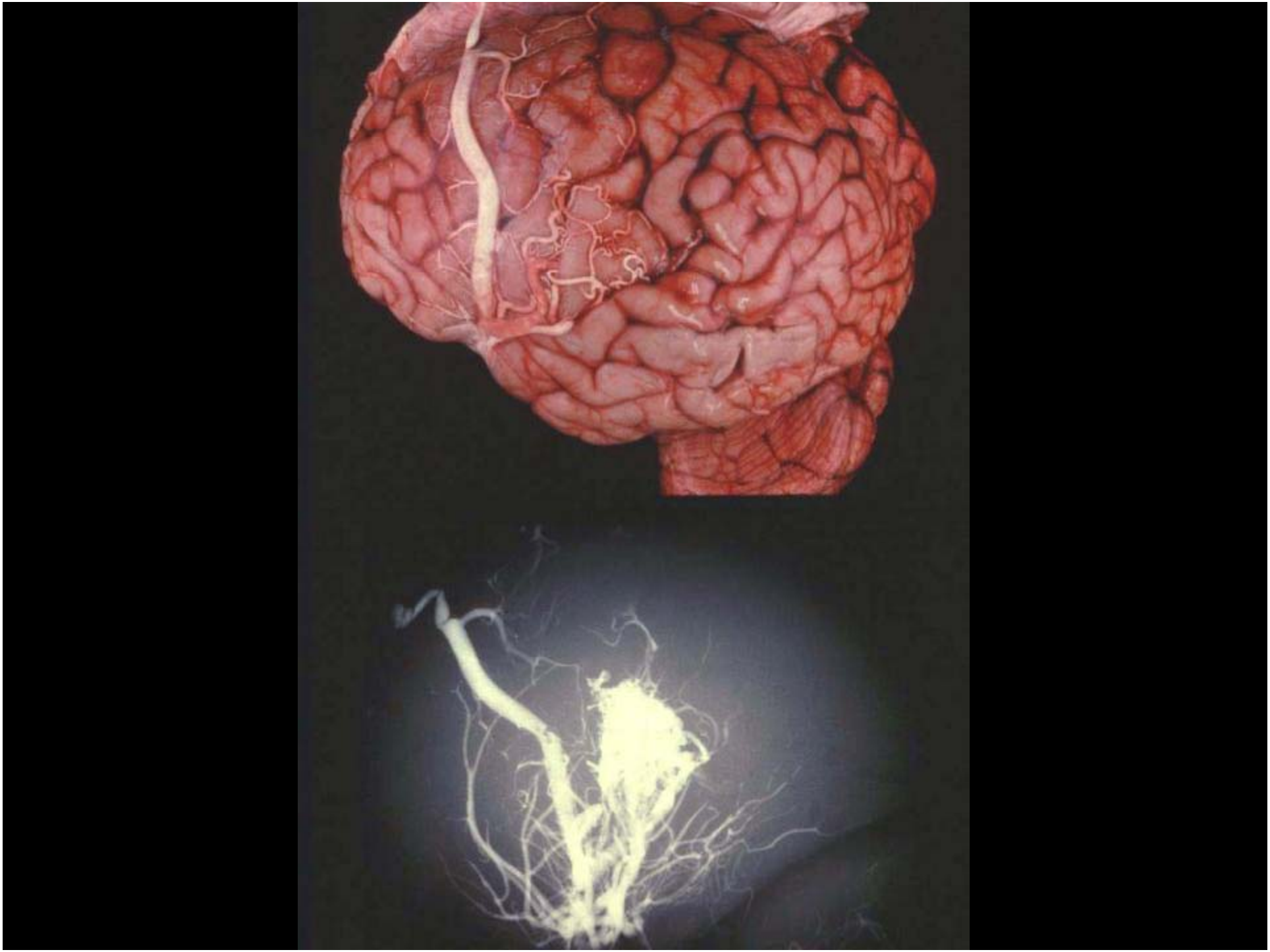
Cerebral hemorrhage

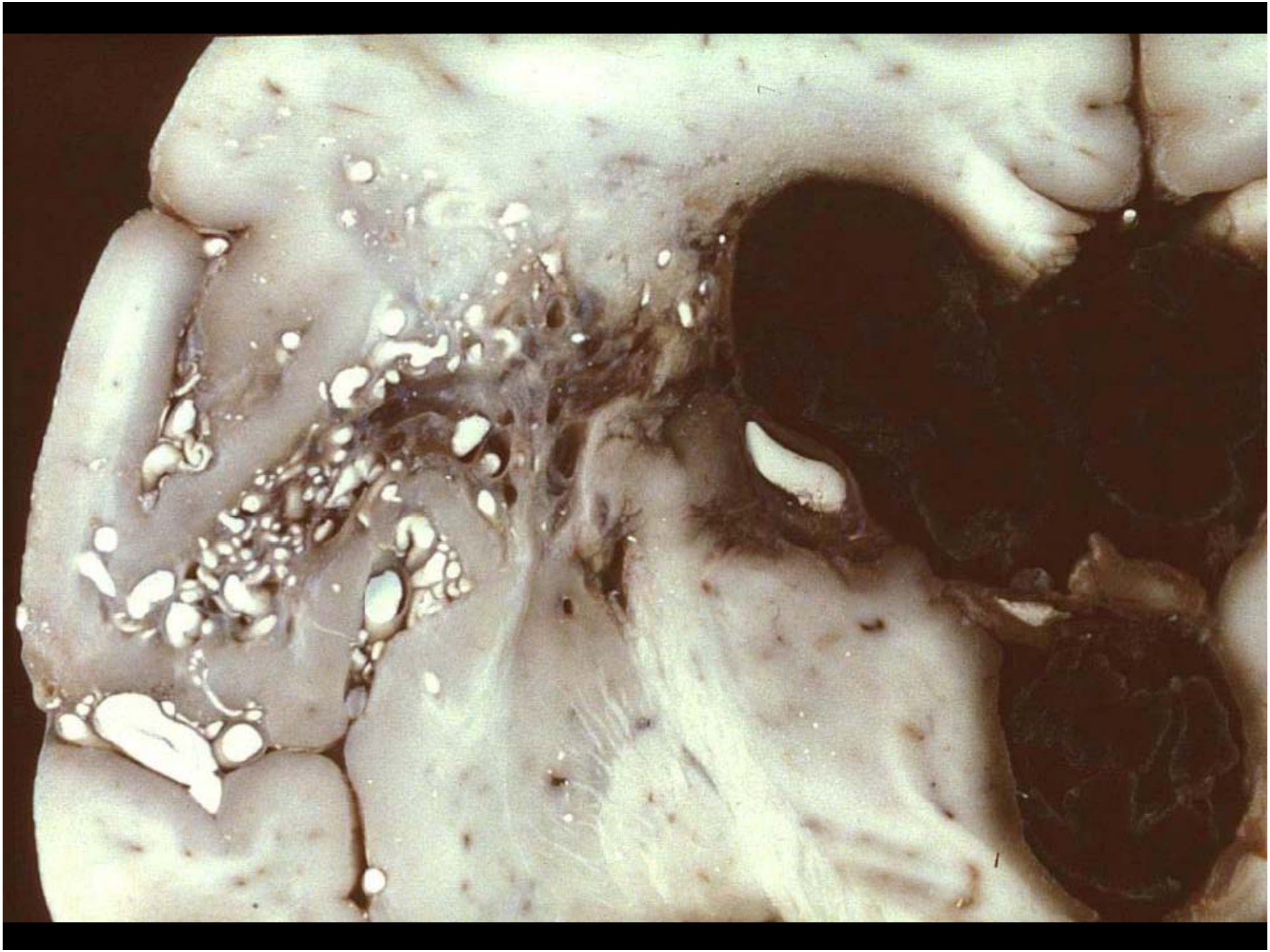
2. Arteriovenous malformation

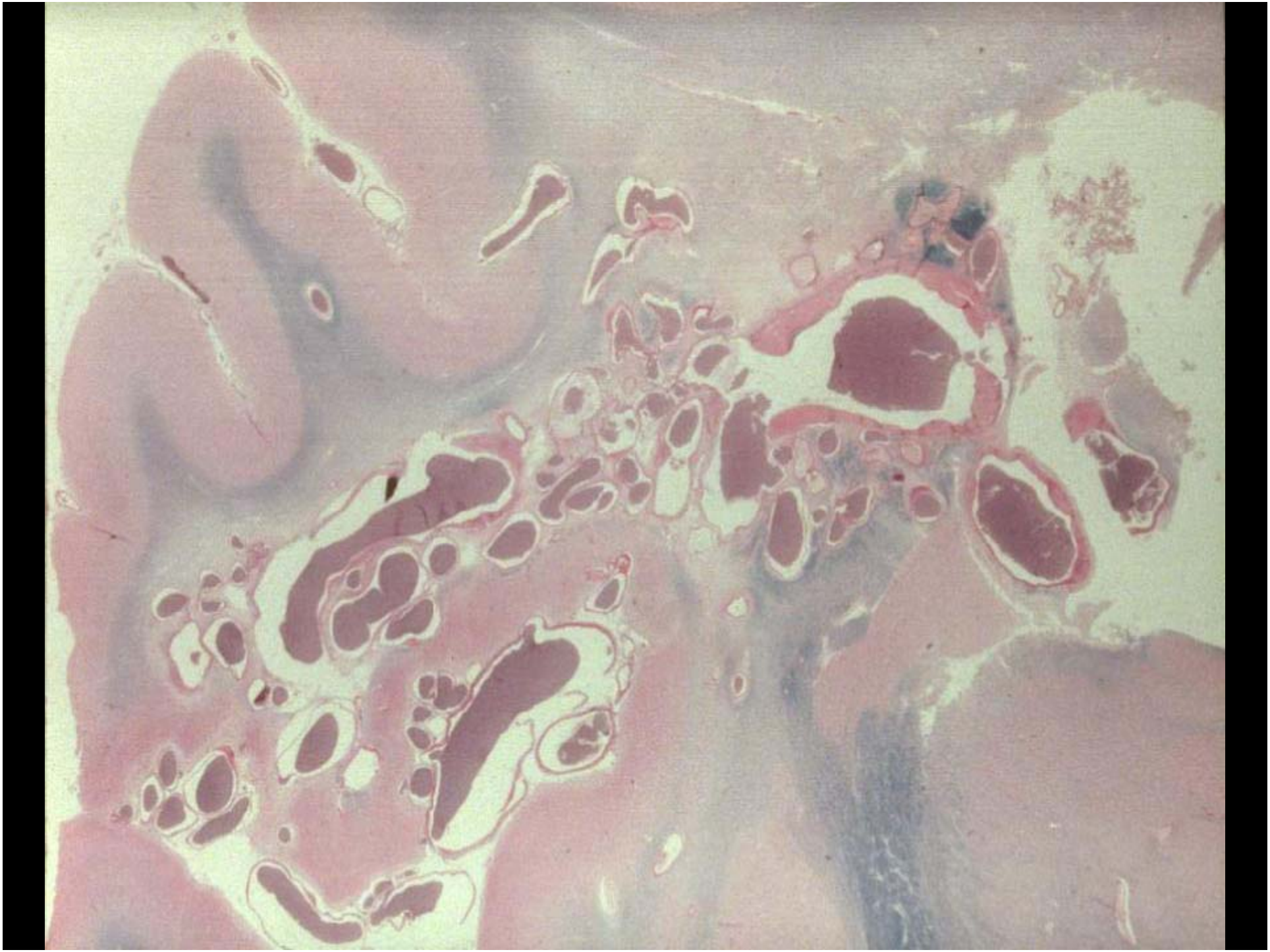
IPH / SAH

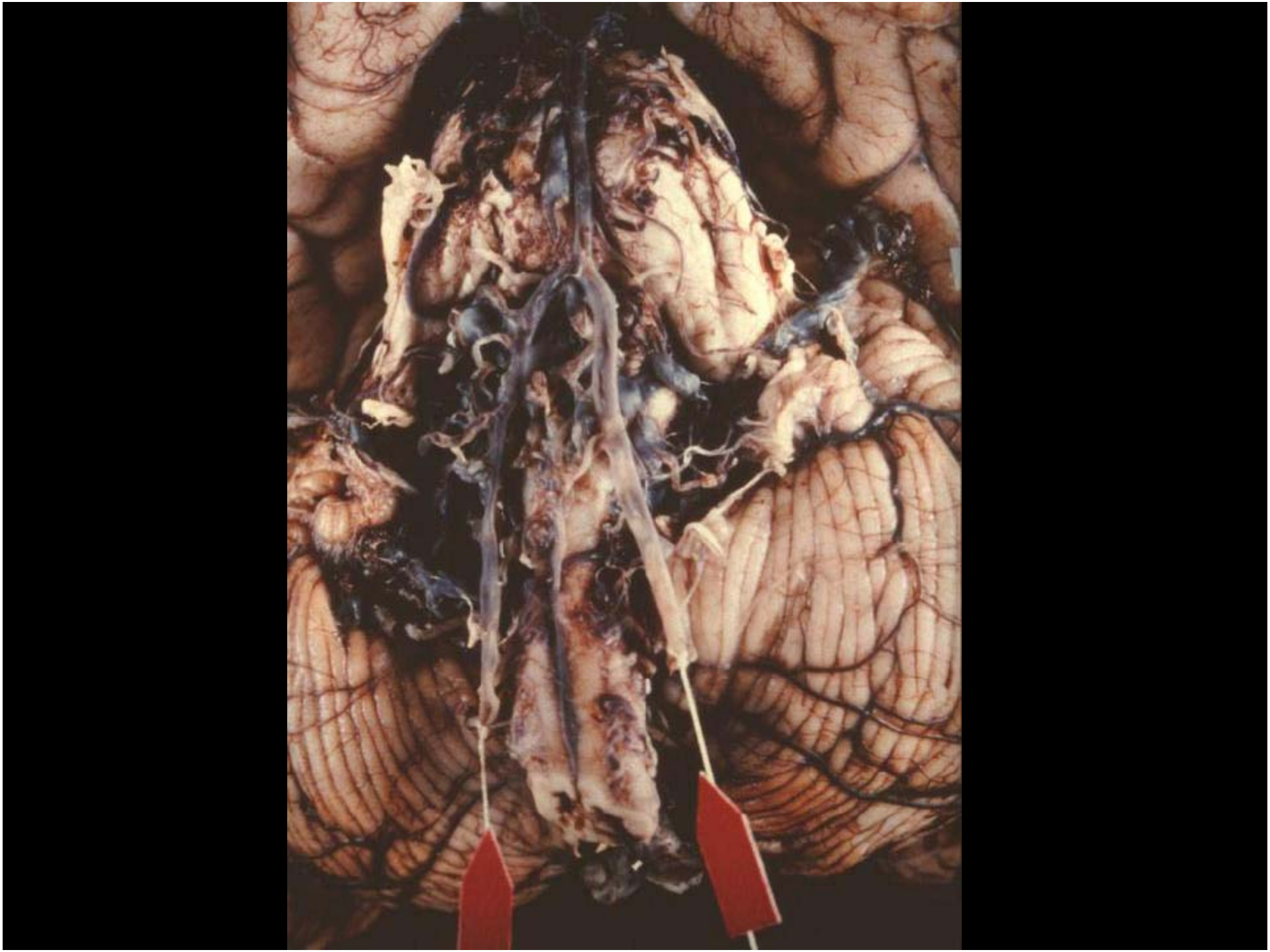
Arteriovenous malformations

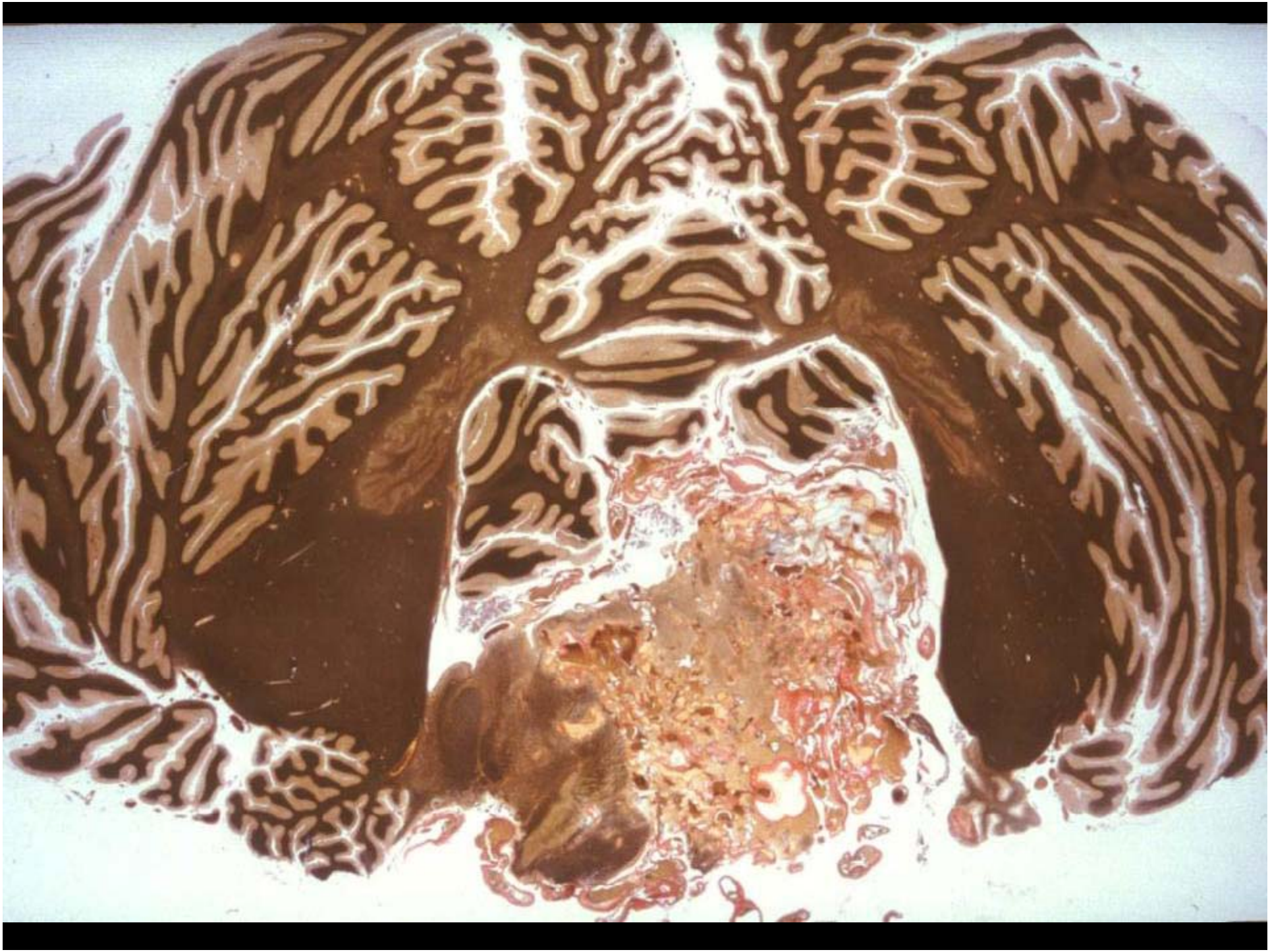
Clinical onset:	**Age 10 to 40**
Sex ratio:	**M:F = 2:1**
Location:	**Usually supratentorial**
Clinical presentation:	**Headache, seizures, focal neurologic deficit, hemorrhage**
Angiography:	**Evidence of arteriovenous shunt and abnormal blood vessels**
Mortality after hemorrhage:	**20%**











Genetics and Stroke

Genetic cardiovascular disorders leading to thromboemboli in CNS

Arterial dissection, Cardiomyopathies, Neuromuscular diseases, Metabolic conditions

(e.g. Homocysteinuria, Coagulopathies, Dyslipidaemia)

Genetic metabolic disorders prone to obstruct CNS vessels (e.g. Fabry's disease)

CADASIL (AD arteriopathy with subcortical infarcts and leukoencephalopathy)

notch 3

MELAS (Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes)

mitochondrial DNA mutations

The End

ENJOY small group study!