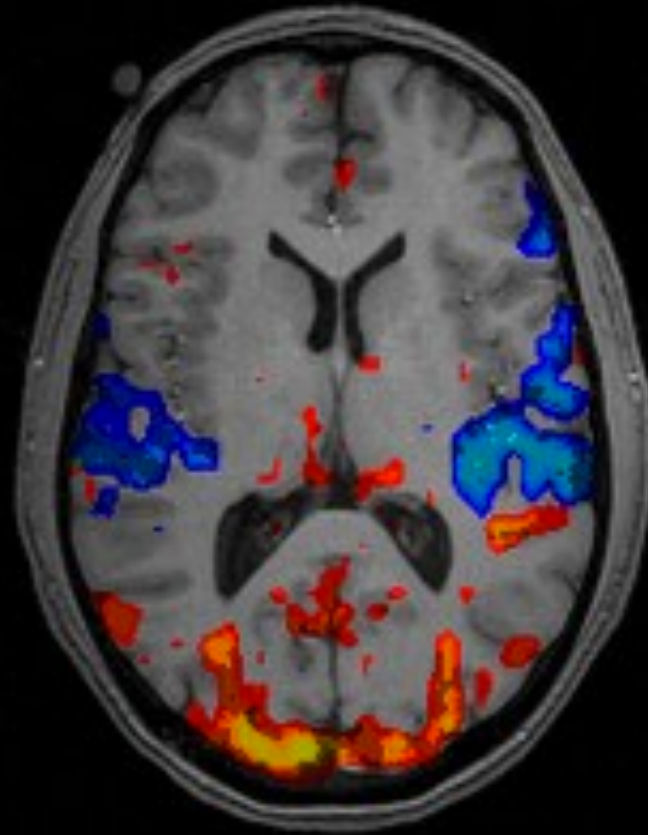


ASHI691:

Why We Fall Apart:
The Neuroscience and
Neurophysiology of Aging

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Lecture 6:
STROKE



Age-related changes in the circulatory system

Blood

no major changes

total volume begins to diminish >80

hemoglobin diminish >65

plasma proteins tend to decrease

red marrow replaced by yellow marrow, therefore
new blood cell formation rate may decrease

Age-related changes in the circulatory system

Heart

slight reduction in size

general decrease in size and number of
myocardial cells, with some loss of strength

increased fat deposition on heart surface

Age-related changes in the circulatory system

Heart

increase in elastic and reticular fibers, and fat,
within cells of conduction system

blood pressure increases

maximum oxygen consumption value begins to fall
at 30; may be 40% reduction at 65

heart rate decreases

cardiac output decreases

Age-related changes in the circulatory system

Blood vessels

loss of arterial elasticity (50% reduction >70)

increased collagen in walls of arterioles

narrowing of vessel internal diameters by gradual accumulation of lipid

venous walls thicken and calcify in spots

peripheral resistance gradually increases as a result of vessel changes

Selected leading causes of death, by sex

	1997				
	<u>Number</u>	<u>%</u>	<u>Total</u>	<u>Males</u>	<u>Females</u>
			Rate ¹		
All causes	215,669	100.0	658.7	844.0	521.6
Cancers	58,703	27.2	181.5	229.7	148.5
Diseases of the heart	57,417	26.6	173.0	230.8	129.7
Cerebrovascular diseases	16,051	7.4	47.8	52.8	43.9
Chronic obstructive pulmonary diseases and allied conditions	9,618	4.5	29.0	44.5	20.1
Unintentional injuries	8,626	4.0	27.6	37.8	17.9
Pneumonia and influenza	8,032	3.7	23.7	31.5	19.2
Diabetes mellitus	5,699	2.6	17.4	20.6	14.8
Hereditary and degenerative diseases of the central nervous system	5,049	2.3	15.0	16.7	13.9
Diseases of arteries, arterioles and capillaries	4,767	2.2	14.3	19.5	10.6
Psychoses	4,645	2.2	13.6	13.3	13.4
Suicide	3,681	1.7	12.0	19.5	4.9
Nephritis, nephrotic syndrome and nephrosis	2,654	1.2	8.0	11.0	6.1
Chronic liver diseases and cirrhosis	2,030	0.9	6.4	8.9	4.2
Neurotic disorders, personality disorders and other nonpsychotic mental disorders	1,163	0.5	3.5	4.8	2.5
HIV infection	626	0.3	2.0	3.6	0.5
1 Age-standardized mortality rate per 100,000 population.					
Source: Statistics Canada, Health Statistics Division.					

Leading Cause of Death in Canada:

Cardiovascular disease: 36% of all deaths
(37% among women, 35% among men)
about 80,000 people per year

Men are more likely to develop heart disease early in life; women tend to "catch up" around menopause. Women experiencing heart disease or stroke are often under-diagnosed or managed differently than men

More than 450,000 Canadians were hospitalized for cardiovascular disease in 2000
(almost 15% of the population)

Cardiovascular disease is the most costly disease affecting Canadians. In 1998, it was responsible for \$18.8 billion in expenditures, 11.8% of the total cost of all illness in Canada. Of this, \$7 billion was in direct costs, particularly for hospital care, and \$11.8 billion was in indirect costs, most of it due to premature death

The most common heart problems are coronary artery disease, arrhythmias, valve disorders and heart muscle disease, including congestive heart failure.

It is estimated that one in four Canadians, or eight million people, has some form of heart disease, disease of the blood vessels, or is at risk for stroke

Coronary Artery Disease:

arteries to the heart (the coronary arteries) become hardened and narrowed due to buildup of plaque (atherosclerosis)

as plaque increases in size, insides of coronary arteries get narrower and less blood flows through them.

blood flow to heart is reduced – heart does not receive oxygen it needs

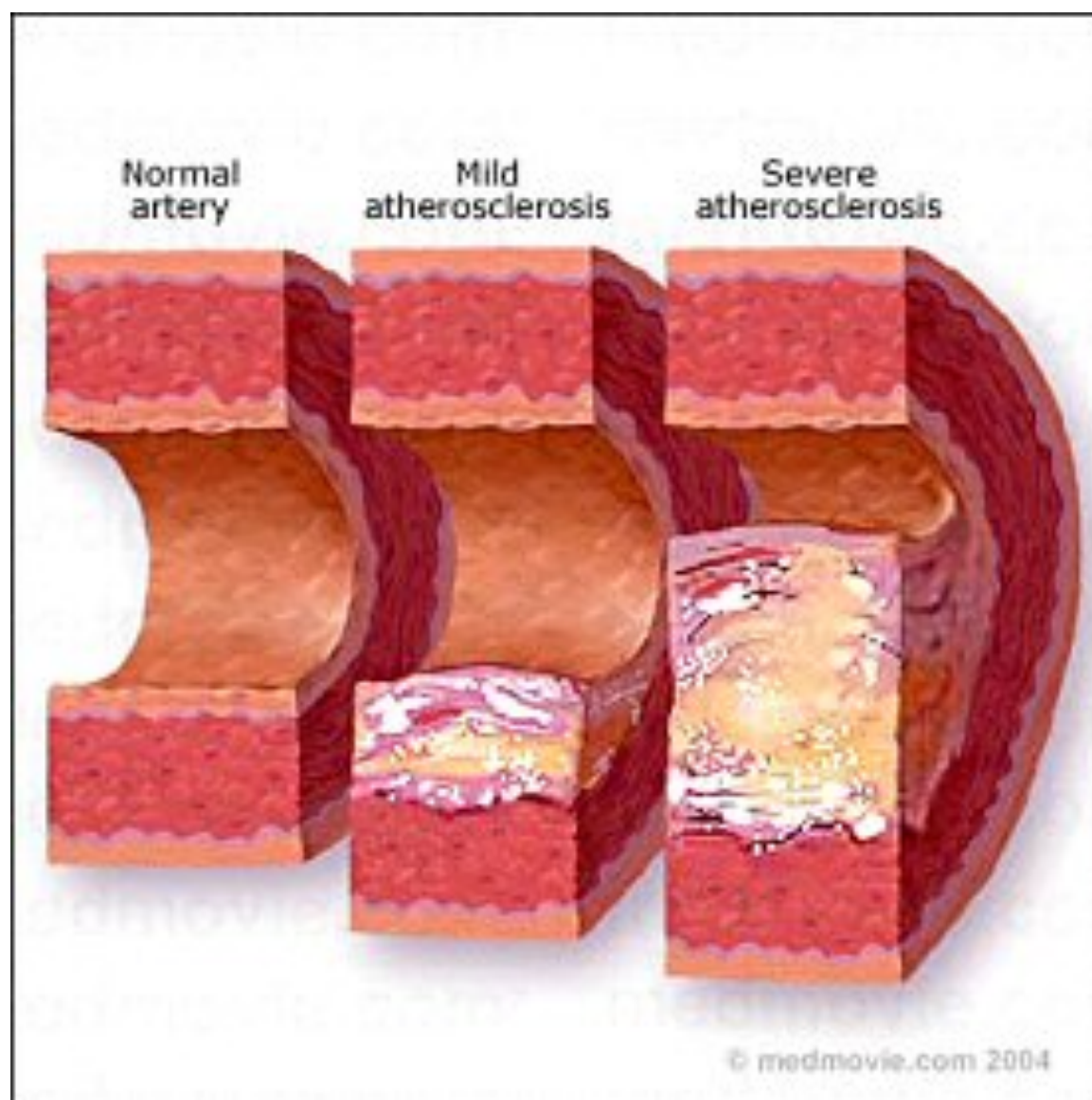
can result in:

angina (chest pain)

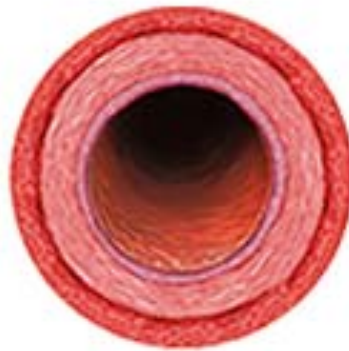
heart attack (clot blocks blood flow, massive cell death)

heart failure (blood not being pumped properly)

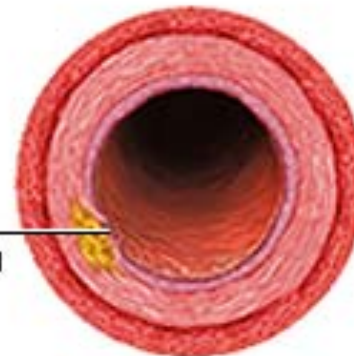
arrhythmias (irregular beating)



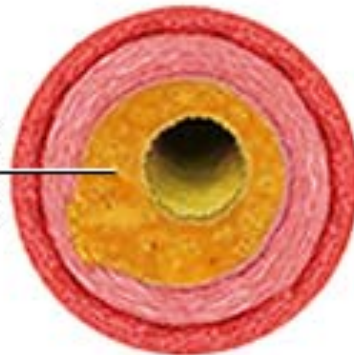
Normal cut-section of artery



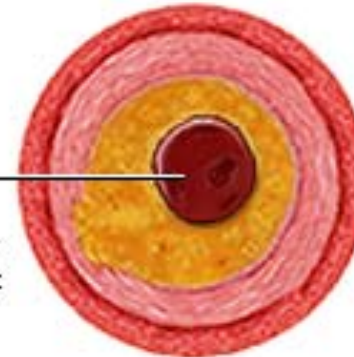
Tear in artery wall

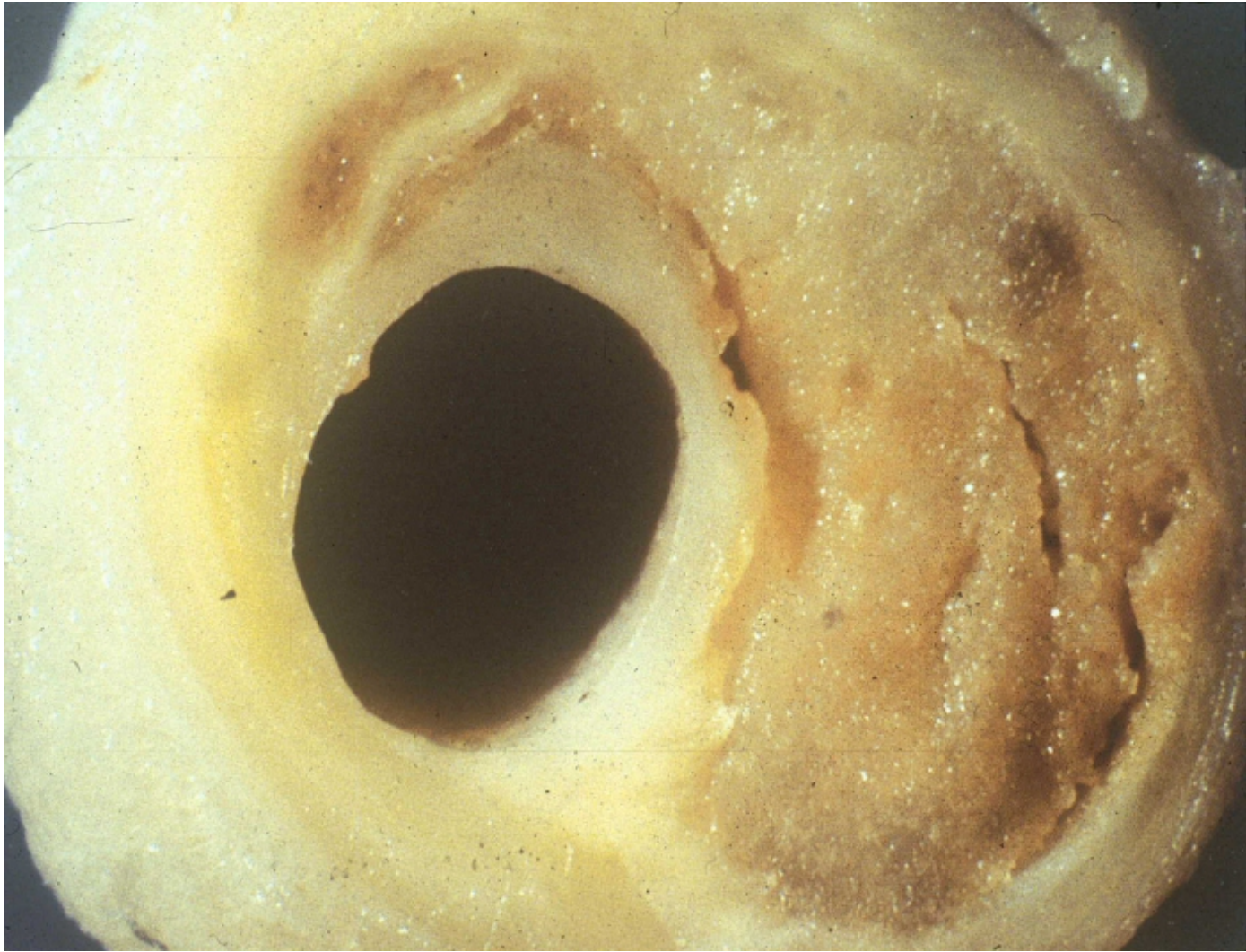


Fatty material is deposited in vessel wall



Narrowed artery becomes blocked by a blood clot





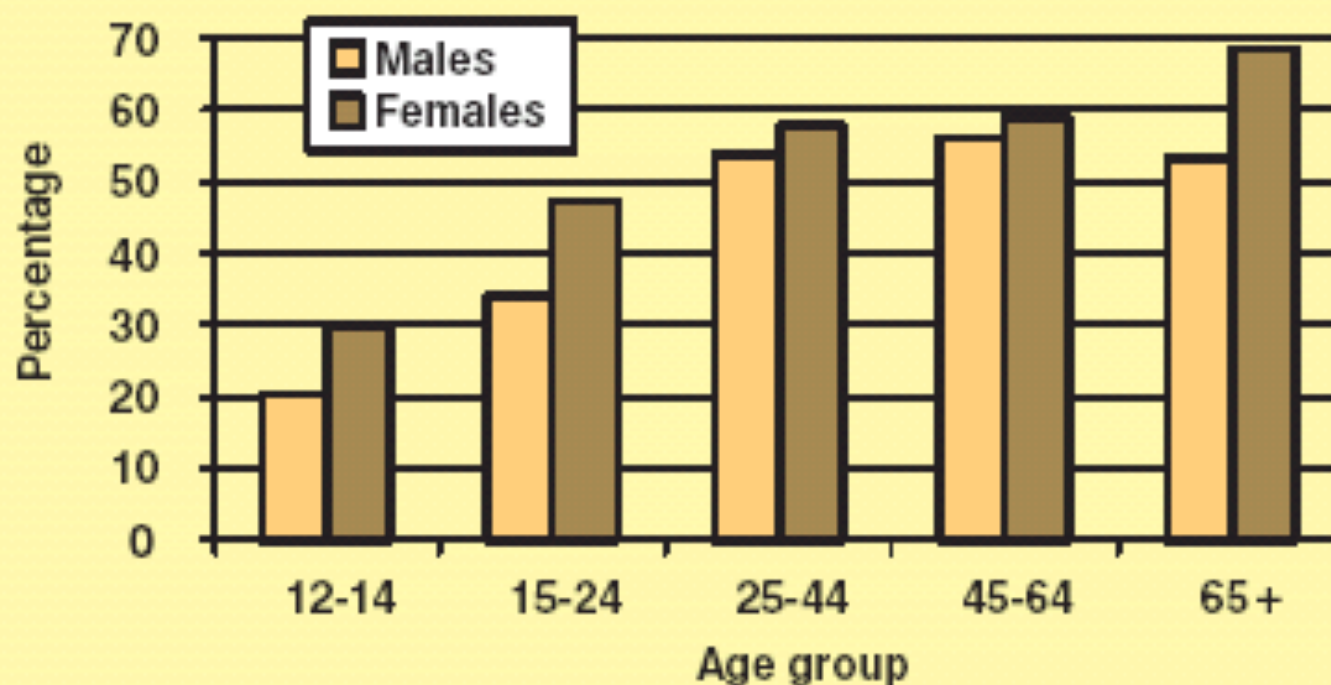
Heart Disease Risk Factors

- High blood pressure
- Family history
- Cigarette smoking
- High cholesterol levels
- Physical inactivity
- Diabetes
- Obesity
- Stress

Why high blood pressure a risk factor?

- Heart has to work harder.
- Since heart muscle is working harder, it can become enlarged.
- Wear and tear on the arterial wall can increase the likelihood of lipid and calcium deposits adhering to the arterial wall. This leads to hardening of the arteries.

Physical Inactivity, by Age and Sex, Canada, 2000/01



Source: Canadian Community Health Survey, 2000/01

Mechanisms by Which Exercise May Reduce Resting Blood Pressure

1. Decreases resting heart rate
2. Decreases resting cardiac output
3. Decreases total peripheral resistance
4. Decreases plasma norepinephrine levels
5. Decreases peripheral sympathetic nervous system stimulation
6. Alters renal function, which lowers blood pressure
7. Decreases body weight and body fat

From American College of Sports Medicine (1993).

Benefits of Regular Exercise on Cardiovascular Risk Factors

Increase in exercise tolerance

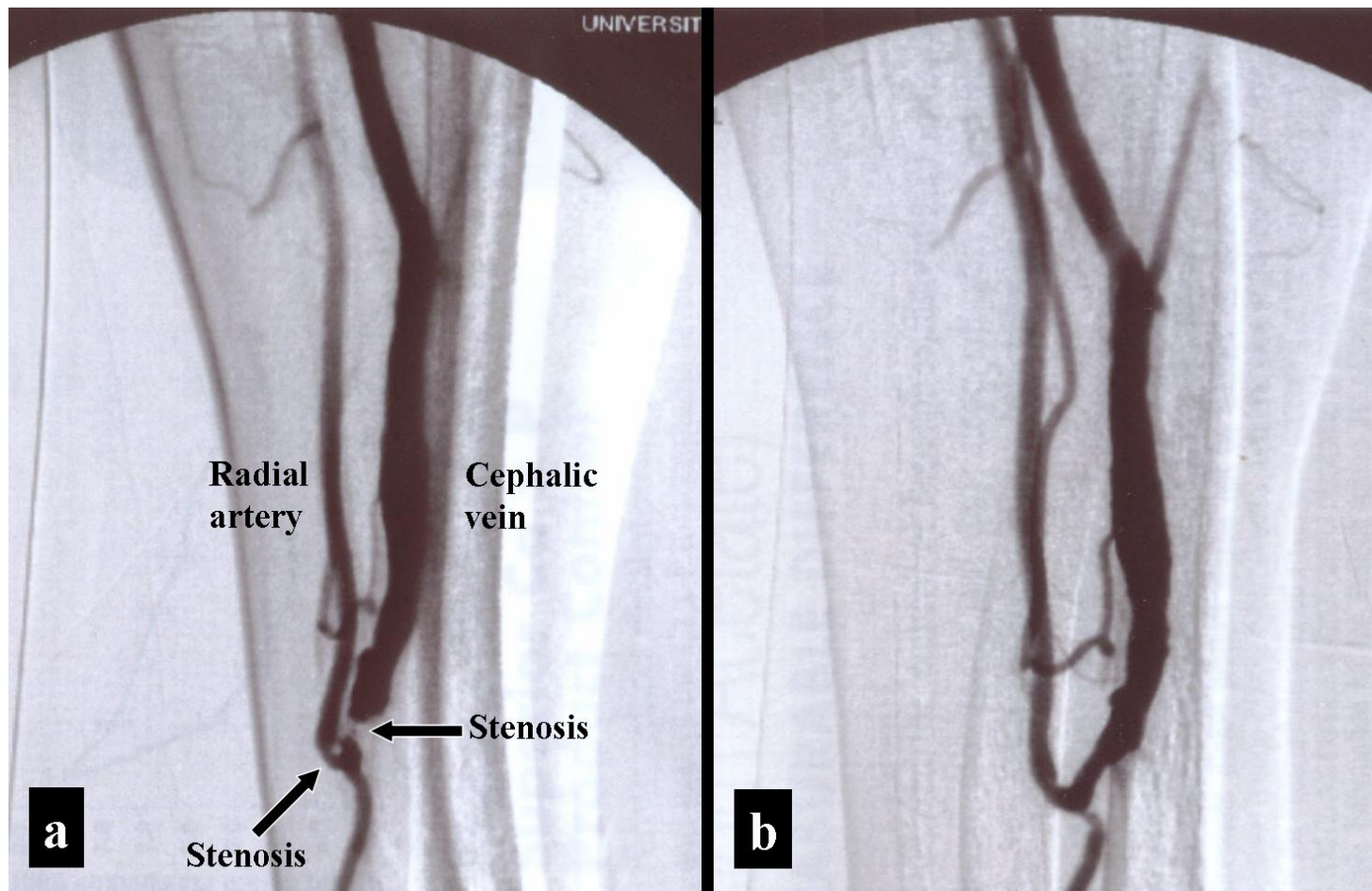
Reduction in body weight

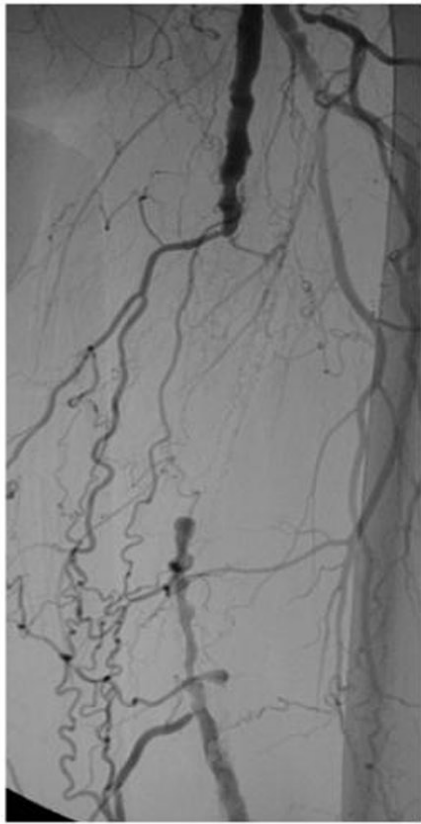
Reduction in blood pressure

Reduction in bad and total cholesterol

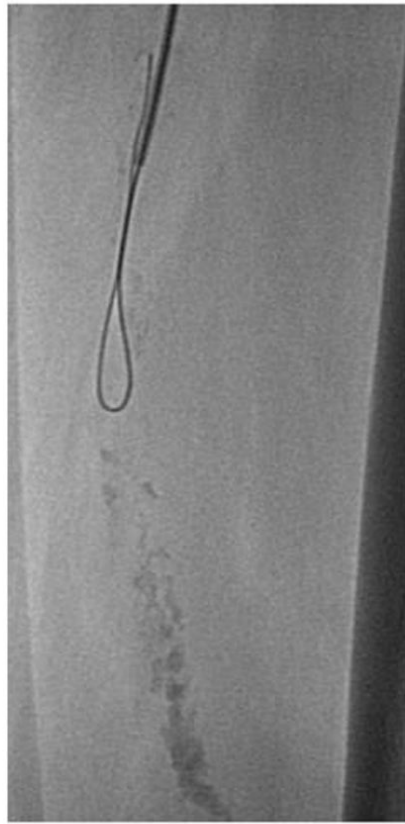
Increase in good HDL cholesterol

Increase in insulin sensitivity

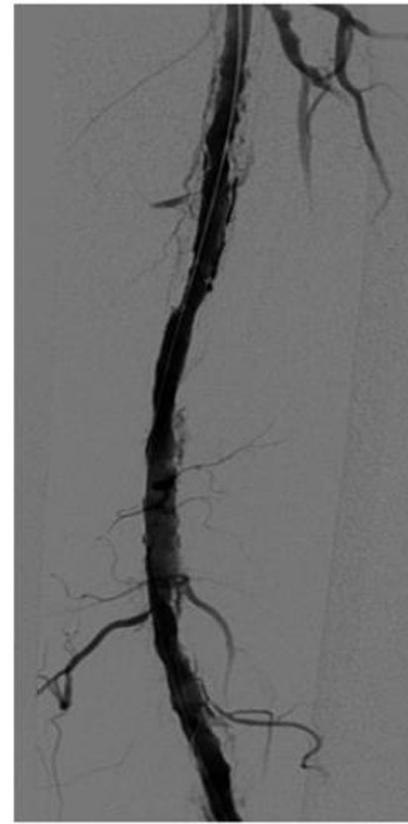




(A)

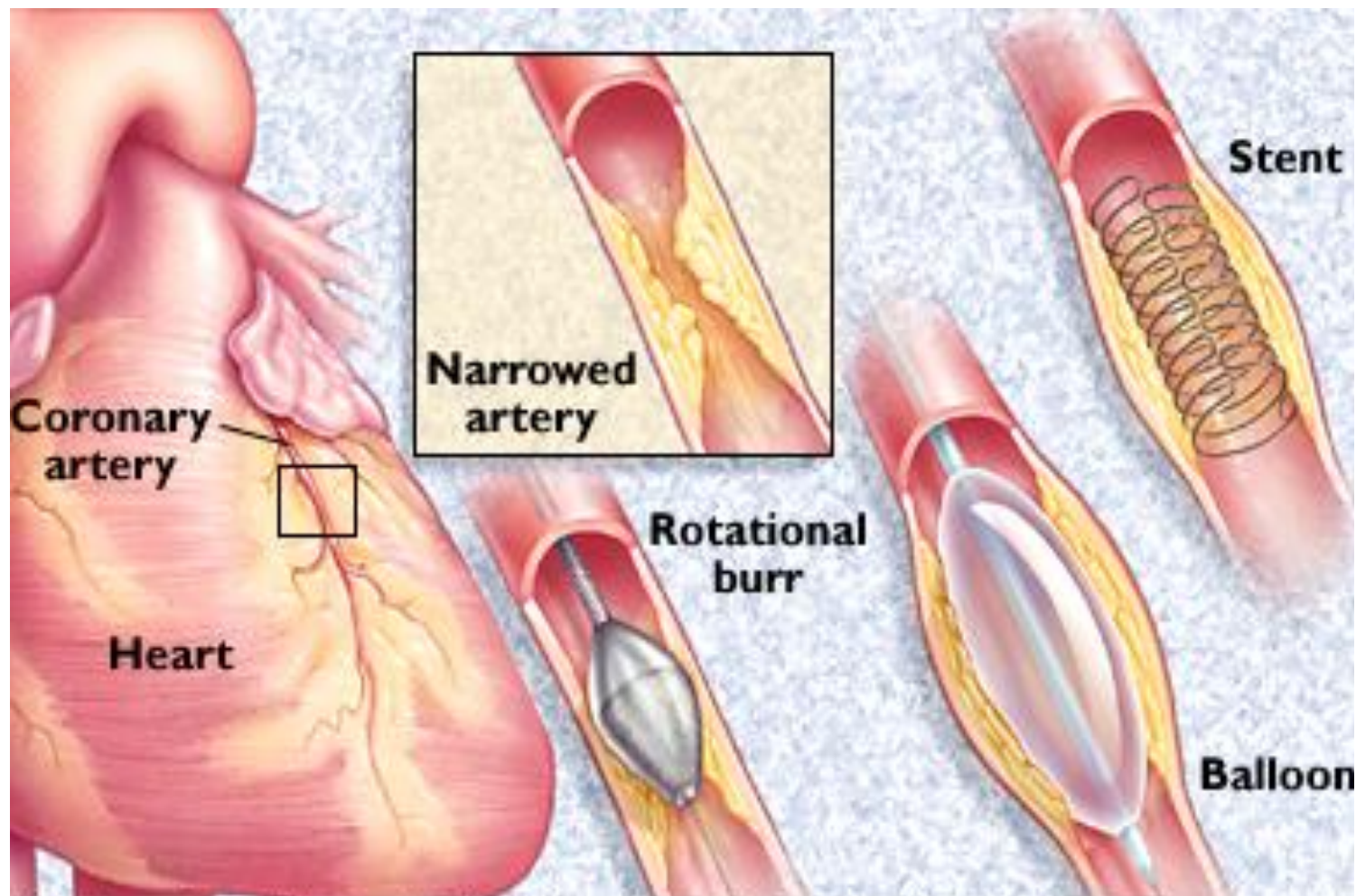


(B)



(C)

Figure 1. Subintimal angioplasty of a superficial femoral artery occlusion.
(A) Angiogram demonstrating level of occlusion. (B) Subintimal guidewire advanced in "wide loop" configuration toward distal end.
(C) Post-procedural angiogram demonstrates restoration of flow.



Cerebrovascular Disease

Cerebrovascular Disease

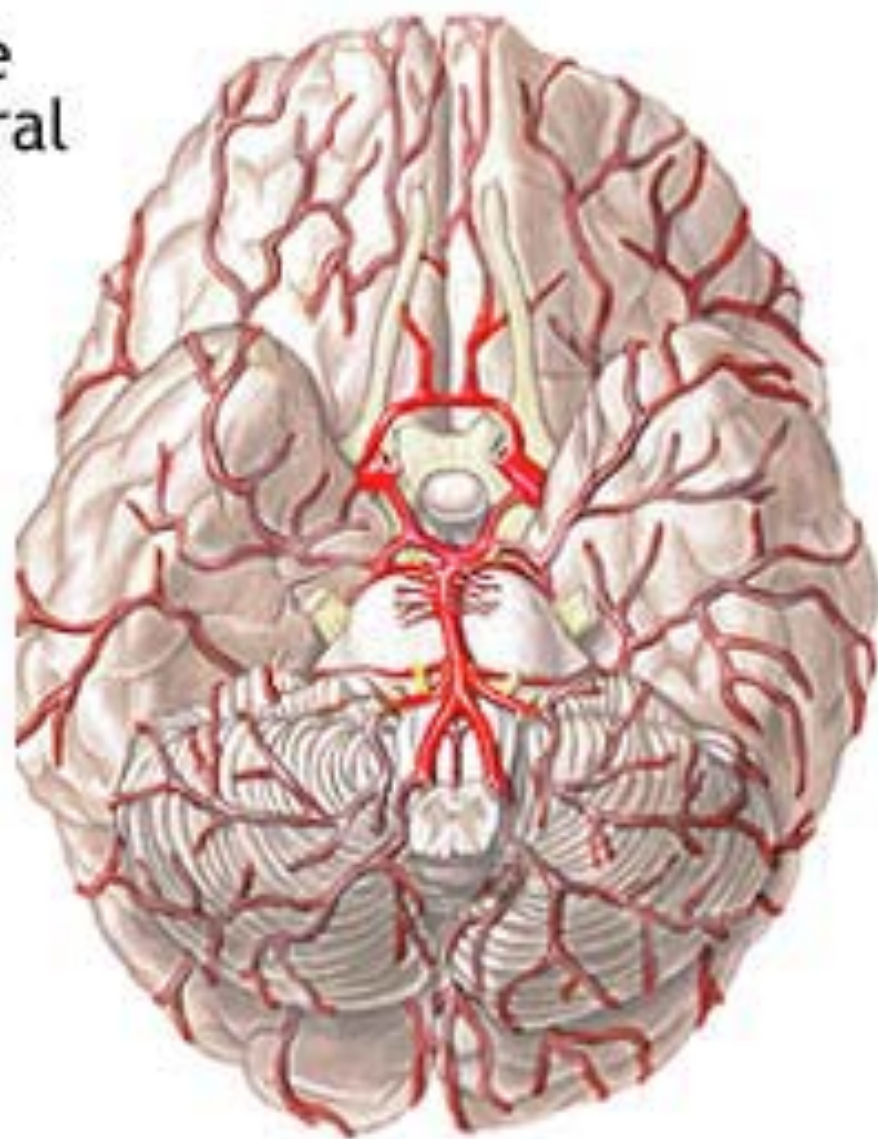
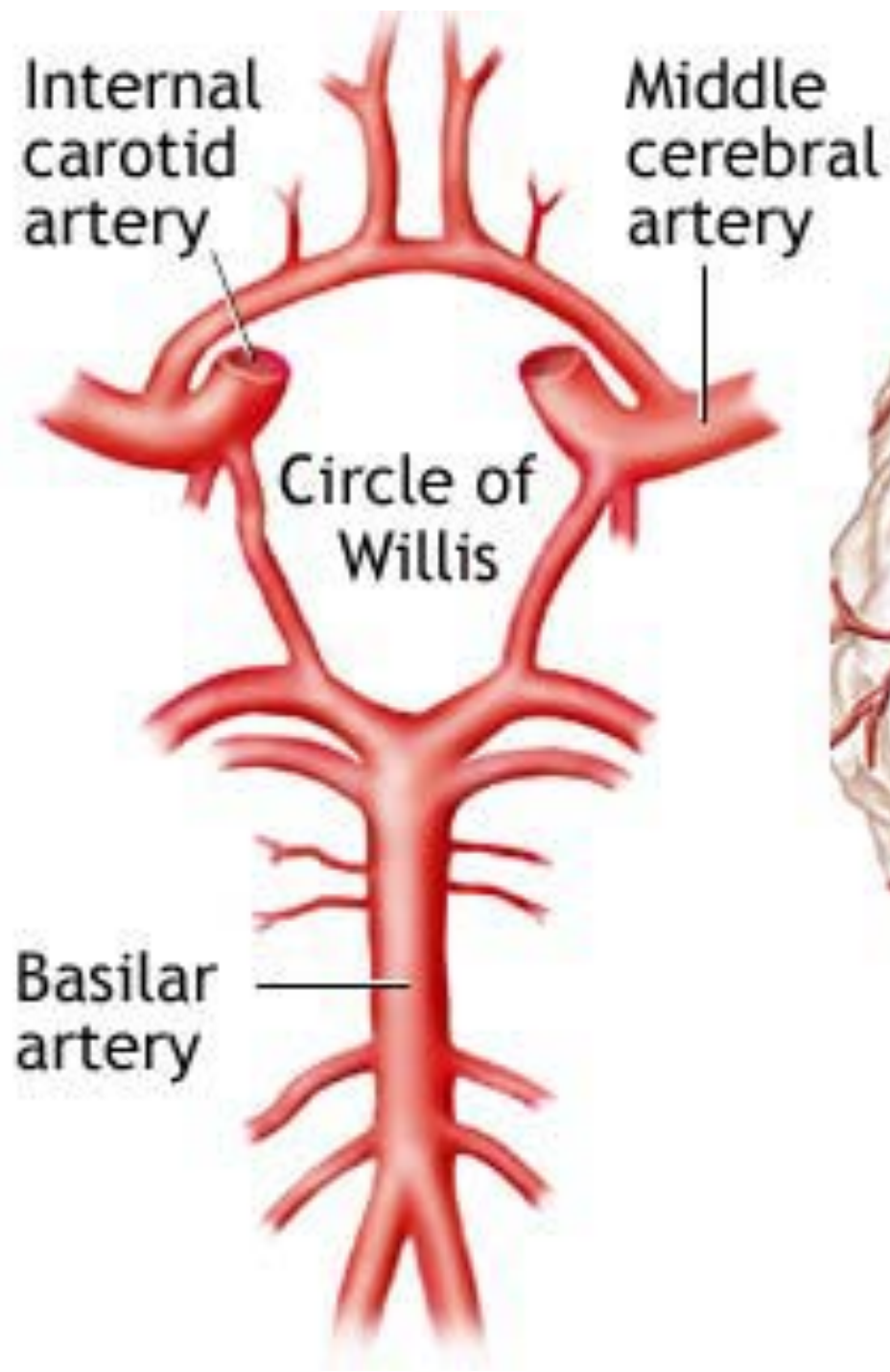
- 3 main underlying causes:
 - 1. Atherosclerosis of large arteries at bifurcation of common carotid artery or in vertebral artery
 - 2. Heart Disease
 - 3. Hypertension leads to intracerebral hemorrhage or lacunar infarcts

Blood supply to brain

- Blood Supply of the Brain
 - - internal carotid and vertebral arteries supply brain
 - -superficial and deep veins drain the brain

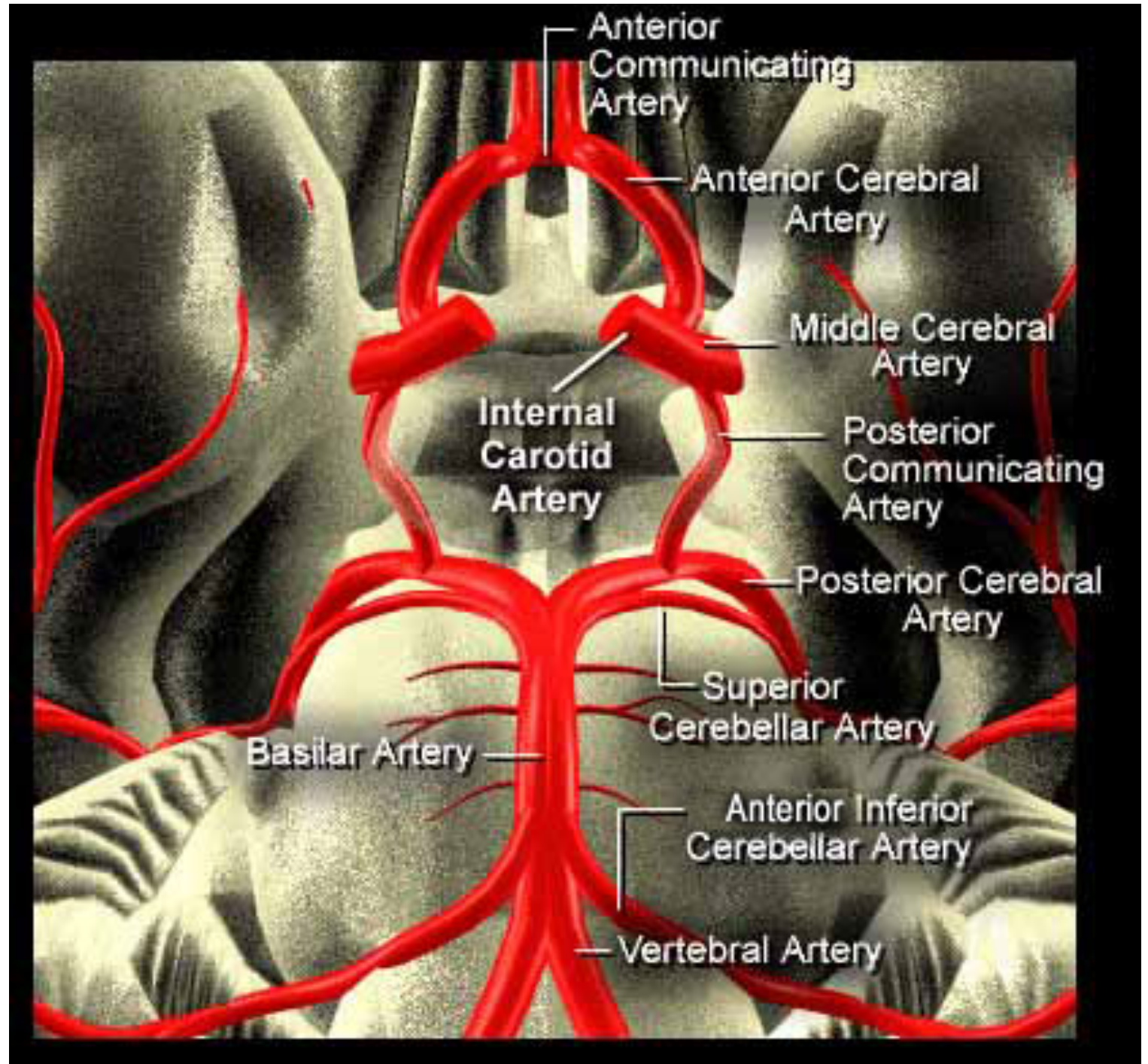
Arterial supply

- Brain – 2% body weight, 20% body's oxygen use
- Internal carotid divides into Anterior(ACA) & Middle cerebral(MCA) after giving off Ophthalmic artery; posterior communicating branch joins Posterior cerebral to form Circle of Willis (Anterior communicating joins ACA's)
- Primary motor & sensory areas – dorso-medial part ACA, remainder MCA blood supply
- Internal capsule – anterior limb & genu – ACA; remainder, penetrating branches of Int. carotid and MCA.

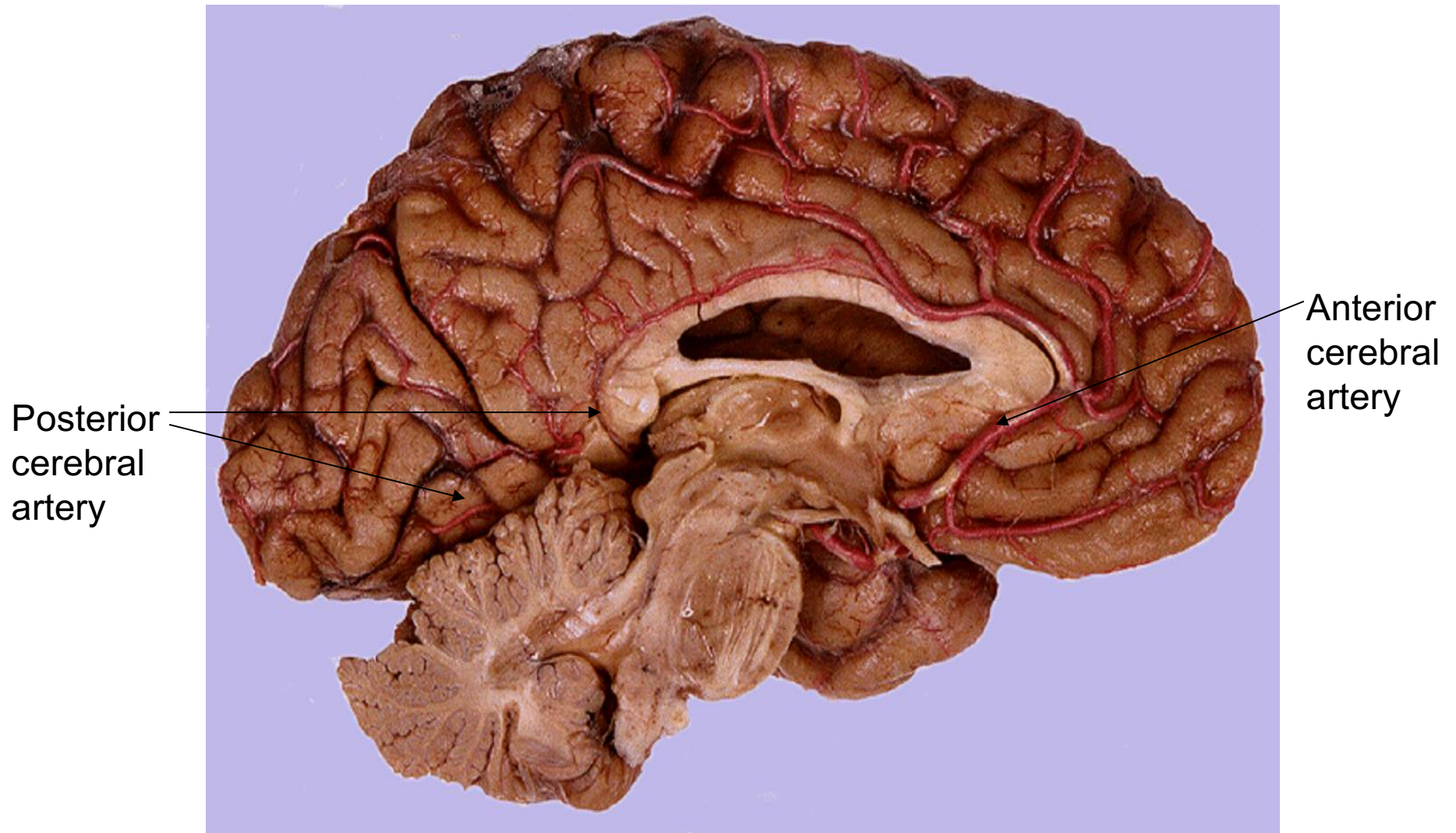


Bottom view of brain

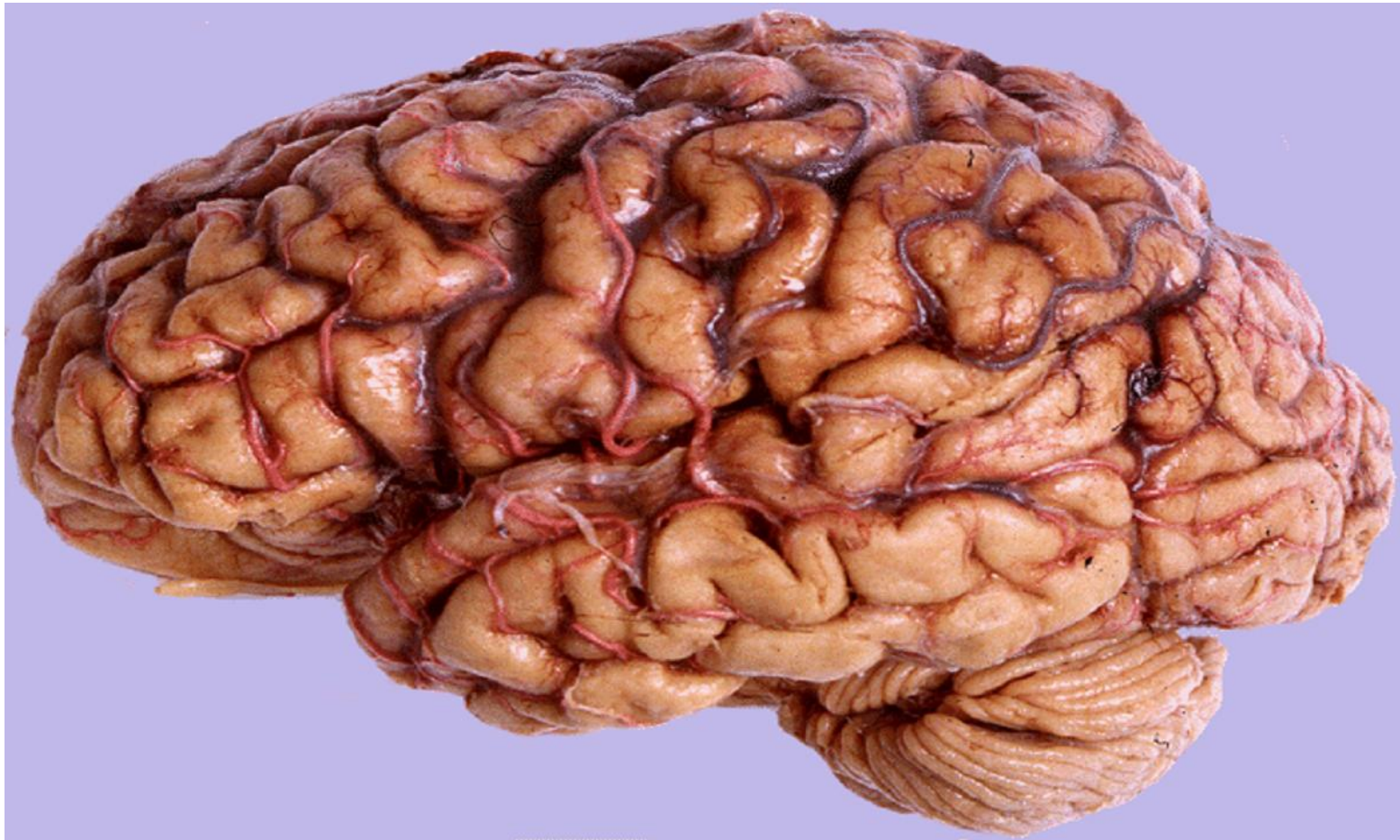
Blood supply to brain and the Circle of Willis



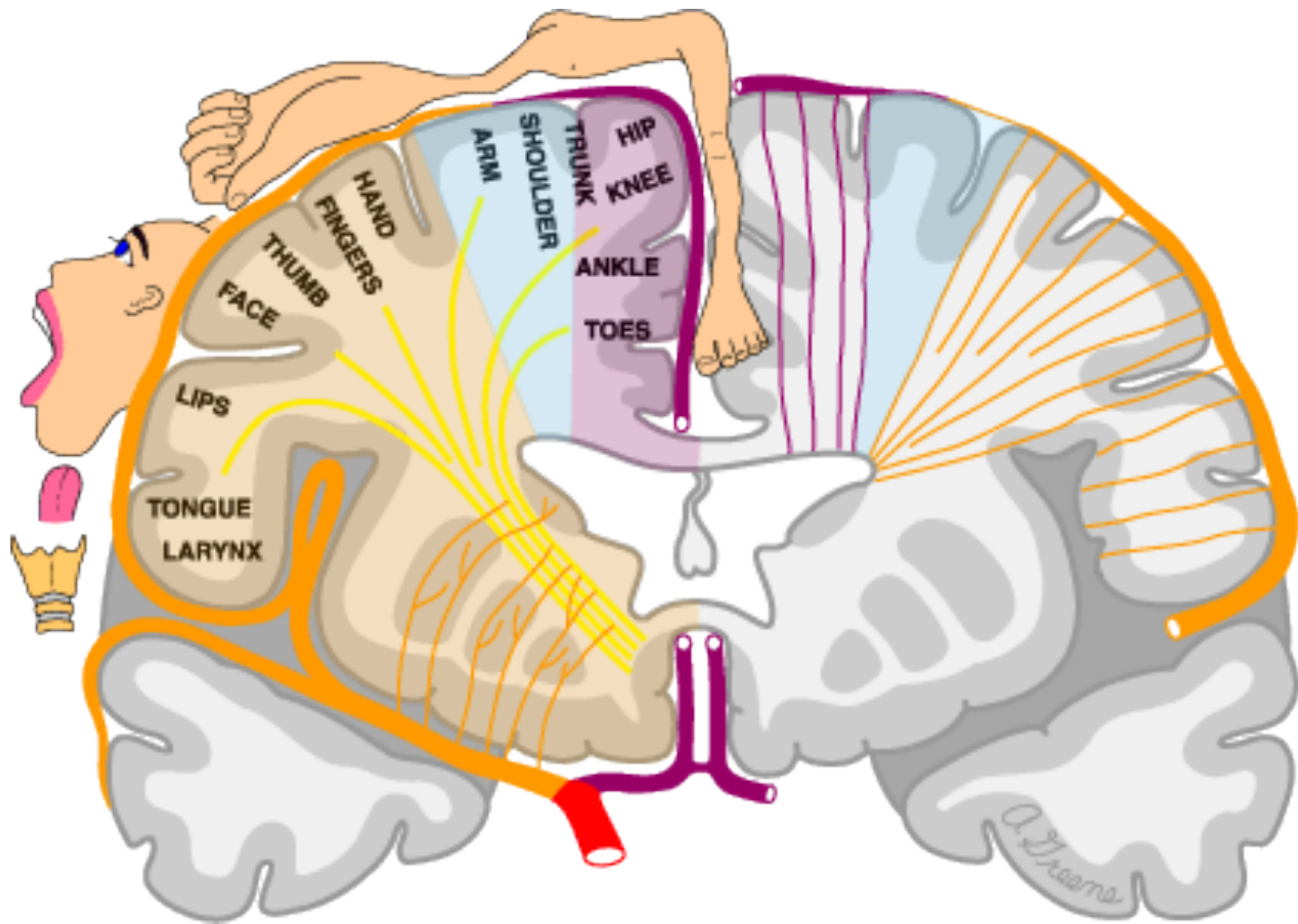
Medial view of blood supply



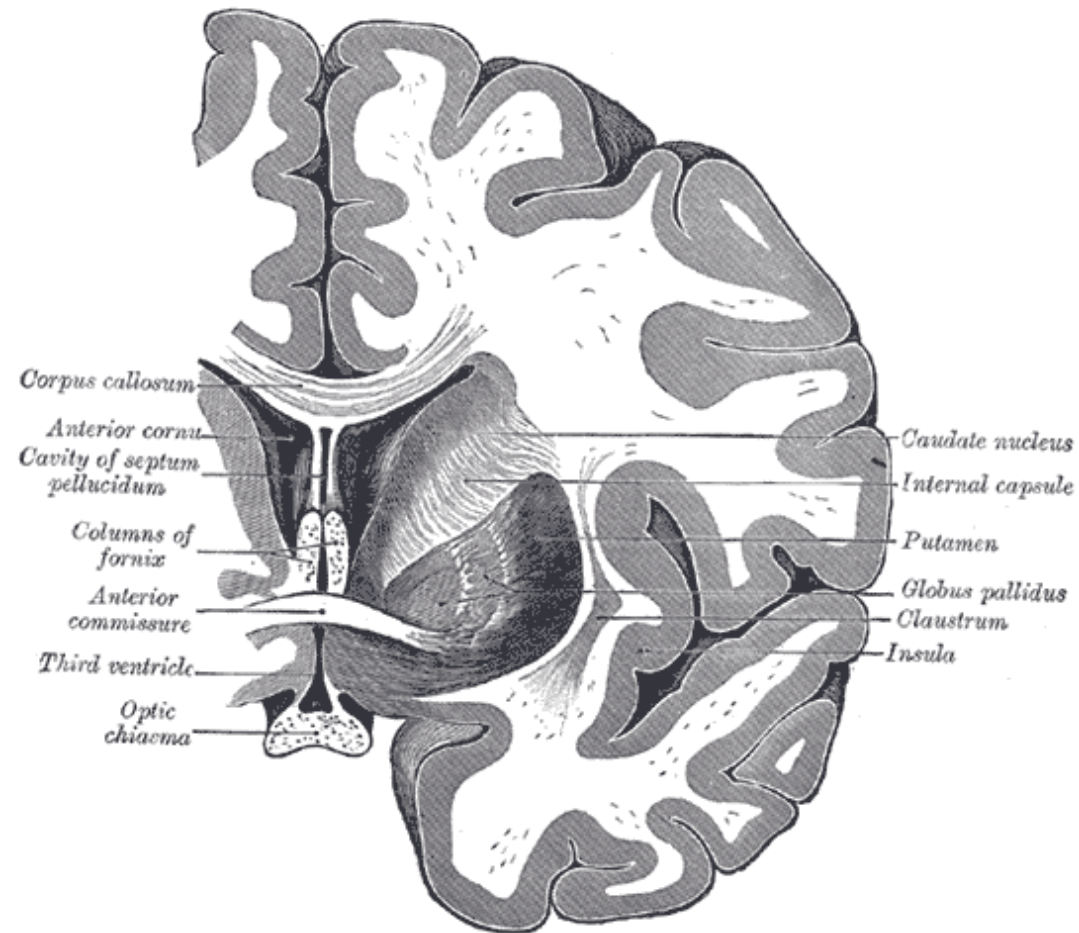
Lateral view of blood supply-
mostly from middle cerebral artery



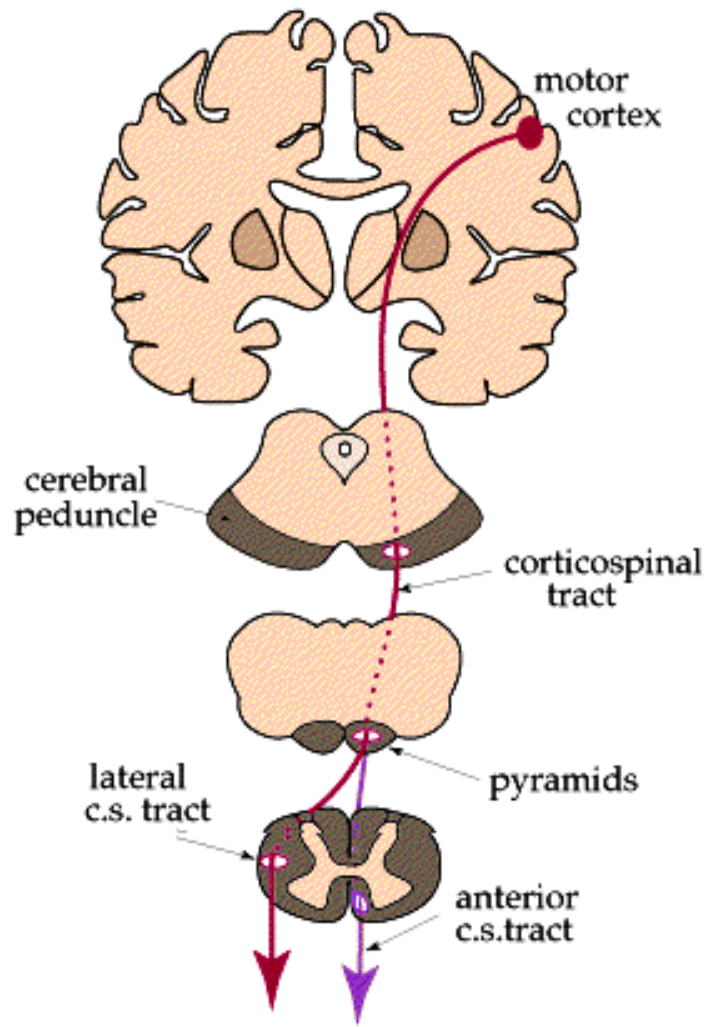
Motor Homunculus



The internal capsule is an area of white matter in the brain that separates the caudate nucleus and the thalamus from the lenticular nucleus.



Internal Capsule



- **Most of the internal capsule is supplied by the middle cerebral artery via lenticulostriate (lateral striate) artery!**

What is a stroke?

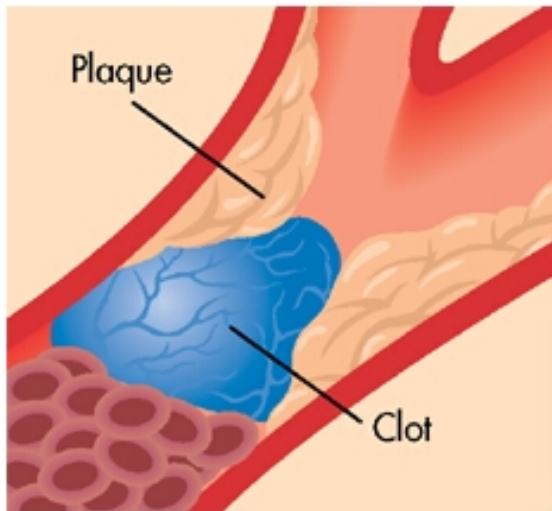
- Tissue damage to area of the brain due to disruption in blood supply, depriving that area of the brain of oxygen.

Strokes- Cerebrovascular accident

- Defn: Focal neurological deficit of vascular origin lasting more than 24 hrs
- Most strokes originate in middle cerebral artery territory because it receives 80% of blood supply
- Chief causes of stroke:
 - Atherosclerosis
 - Heart Disease
 - Hypertension
 - Ruptured Berry aneurysm-10%
- Ischemic strokes commonest- thrombus (blood clot) or embolus (blockage by foreign object)
- Leads to infarcts that vary from lacunar (small artery) to massive (neural region)

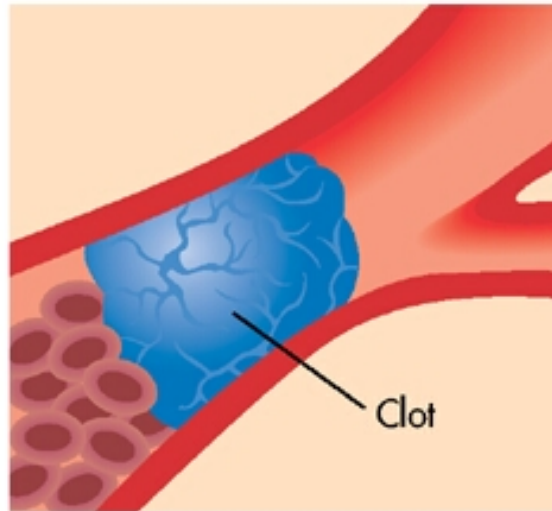
Major Types of Stroke

A



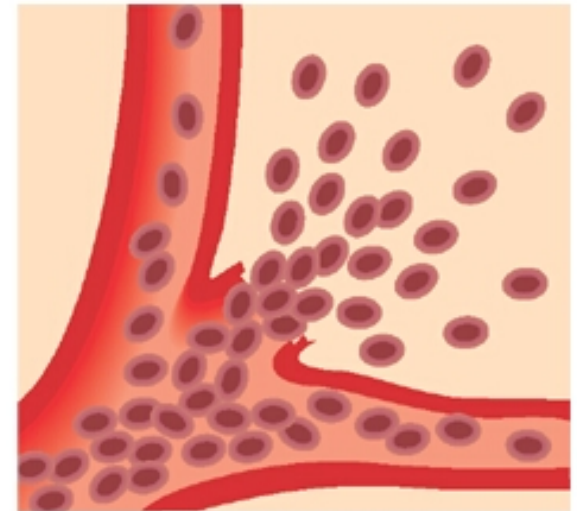
Thrombotic stroke. Cerebral thrombosis is a narrowing of the artery by fatty deposits called *plaque*. Plaque can cause a clot to form, which blocks the passage of blood through the artery.

B



Embolic stroke. An embolus is a blood clot or other debris circulating in the blood. When it reaches an artery in the brain that is too narrow to pass through, it lodges there and blocks the flow of blood.

C



Hemorrhagic stroke. A burst blood vessel may allow blood to seep into and damage brain tissues until clotting shuts off the leak.

Ischemic Stroke

- Result of inadequate blood flow to brain due to partial or complete occlusion of an artery
- Constitute 85% of all strokes
- Most patients with ischemic stroke do not have a decreased level of consciousness in the first 24 hours
- Symptoms often worsen during first 72 hours d/t cerebral edema

Ischemic Stroke

- Thrombotic stroke
 - Thrombosis occurs in relation to injury to a blood vessel wall → blood clot
 - Result of thrombosis or narrowing of the blood vessel
 - Most common cause of stroke

Ischemic Stroke

- Thrombotic stroke
 - Two-thirds are associated with HTN and diabetes
 - Often preceded by a TIA

Ischemic Stroke

- Embolic stroke
 - Embolus lodges in and occludes a cerebral artery
 - Results in infarction and edema of the area supplied by the vessel
 - Second most common cause of stroke

Ischemic Stroke

- Embolic stroke
 - Majority of emboli originate in heart, with plaque breaking off from the endocardium and entering circulation
 - Associated with sudden, rapid occurrence of severe clinical symptoms

Ischemic Stroke

- Embolic stroke
 - Patient usually remains conscious although may have a headache
 - Recurrence is common unless the underlying cause is aggressively treated

Hemorrhagic Stroke

- Account for approximately 15% of all strokes
- Result from bleeding into the brain tissue itself or into the subarachnoid space or ventricles

Hemorrhagic Stroke

- Intracerebral hemorrhage
 - Bleeding within the brain caused by a rupture of a vessel
 - Hypertension is the most important cause
 - Commonly occurs during activity

Hemorrhagic Stroke

- Intracerebral hemorrhage
 - Often a sudden onset of symptoms that progress over minutes to hours b/c of ongoing bleeding
 - Manifestations include neurologic deficits, headache, N & V, decreased levels of consciousness, and HTN

Hemorrhagic Stroke

- Subarachnoid hemorrhage
 - Bleeding into cerebrospinal space between the arachnoid and pia mater
 - Commonly caused by rupture of a cerebral aneurysm

Causes of Strokes

1. Infarction – blockage in cerebral artery that cuts off or reduces blood supply
 - a) Thrombosis – blood clot
 - b) Embolus – piece of plaque becomes lodged in the artery.
2. Hemorrhage – happens suddenly. Less frequent than infarction but more damaging and more likely to cause death.

Possible Symptoms (Acute Onset)

- Hemiparesis or quadriparesis (latter in basilar occlusion)
- Facial weakness
- Aphasia
- Dysarthria
- Limb/truncal/gait ataxia +/- nausea & vomiting
- Vertigo, tinnitus, hearing deficit (posterior circ.)
- Impairment of vision in homonymous visual field defect
- Monocular impairment of vision (amaurosis fugax)
- Diplopia
- Impairment or loss of consciousness or confusion
- Hemineglect (visual or sensory)
- Headache (non-specific symptom)
- New onset seizure (3-4%) or acute new movement abnormality

Stroke Risk Factors

- Rare up to age 55, then risk increases sharply with age (doubling with each decade).
- More common in men but women more likely to die from them.
- Rates highest among blacks and lowest among Asians.
- Family history

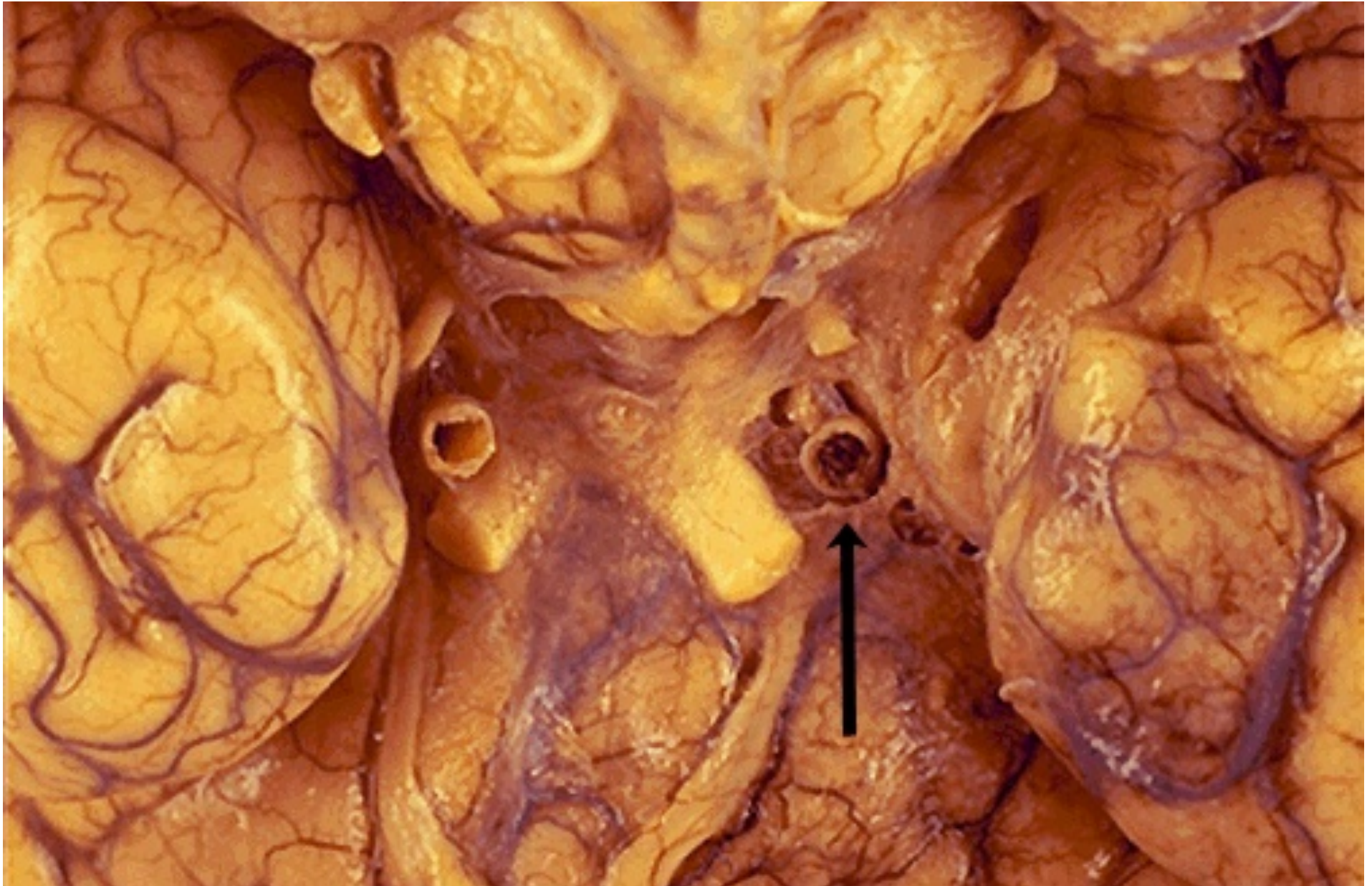
Stroke Risk Factors

- High blood pressure
- Cigarette smoking
- Heart disease, diabetes, and their risk factors such as obesity and physical inactivity.
- High red blood cell count (making the blood thicker and likelier to clot).
- Mini-strokes – transient ischemic attacks (TIA)

Carotid
angiogram
showing
stenosis of
origin of
internal
carotid
artery



Thrombosis of left internal carotid artery



Complete occlusion right internal carotid



Middle cerebral artery infarct



Older infarct with early cystic change- anterior cerebral artery territory



Effects of a Stroke

- Some motor, sensory, cognitive, or speech impairment usually occurs
- Limitations may be permanent but lessen in severity over time.
- Younger patients recover better
- Impairments caused by hemorrhages more easily overcome than those caused by infarctions.

Effects of Stroke

- Motor impairments often due to paralysis on one side of the body (side opposite to brain damage).
 - After about 6 weeks of rehab about 50% of patients can perform independently (many with cane or walker).
- Language, learning, memory, and perception problems depend on location of the injury.

Effects of Stroke

- Left-hemisphere damage more commonly associated with language problems called aphasia.
 - Receptive aphasia – difficulty understanding verbal information.
 - Expressive aphasia – difficulty producing and using language.
- Damage to right side of brain often associated with difficulties in visual processing and emotions.

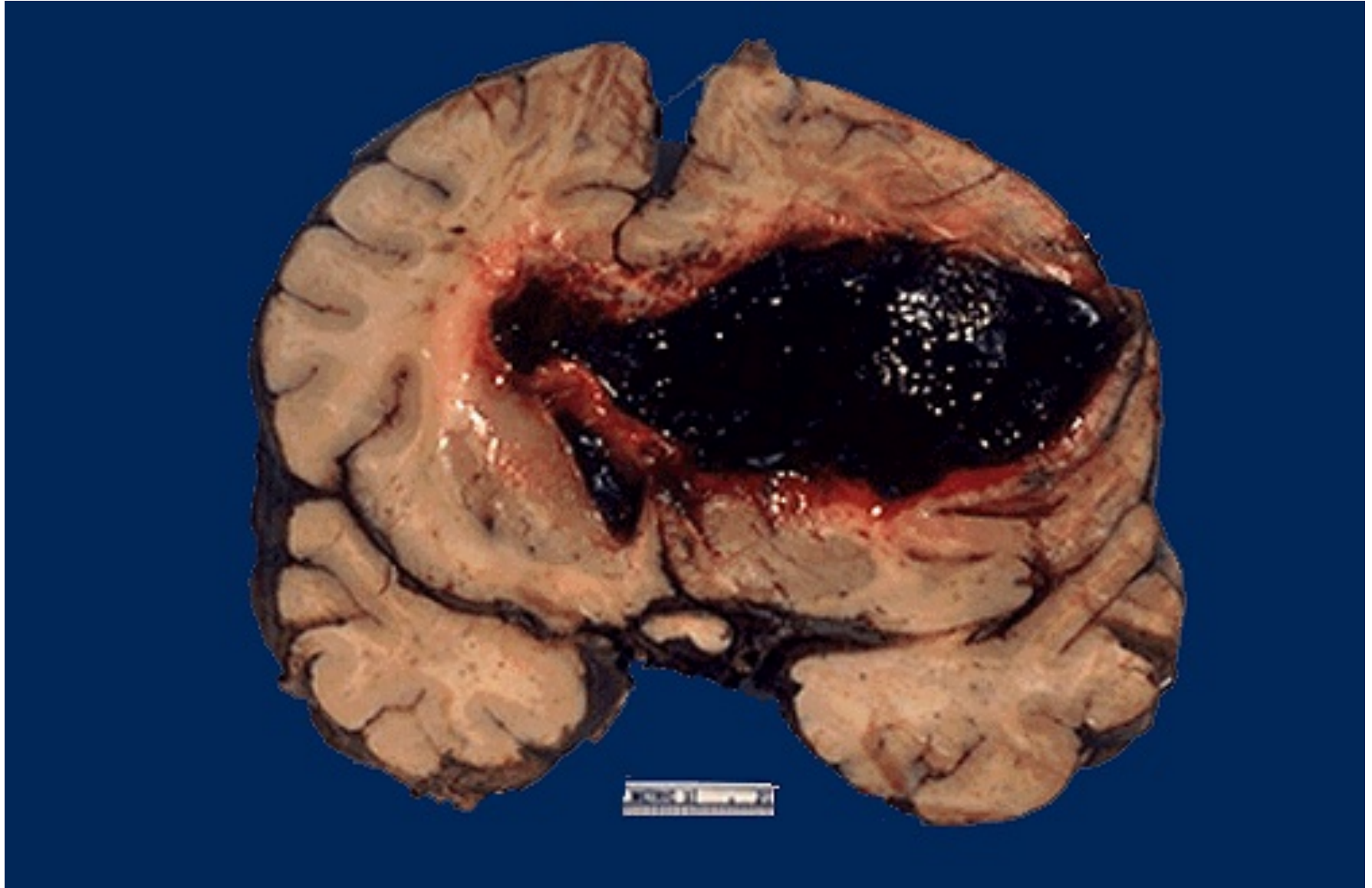
Psychosocial Aspects of Stroke

- Denial is common
 - Unclear whether psychological or physiological basis.
 - This ambiguity also applies to depression when it occurs after a stroke.
- Less than 1/2 of the patients return to work following a stroke.

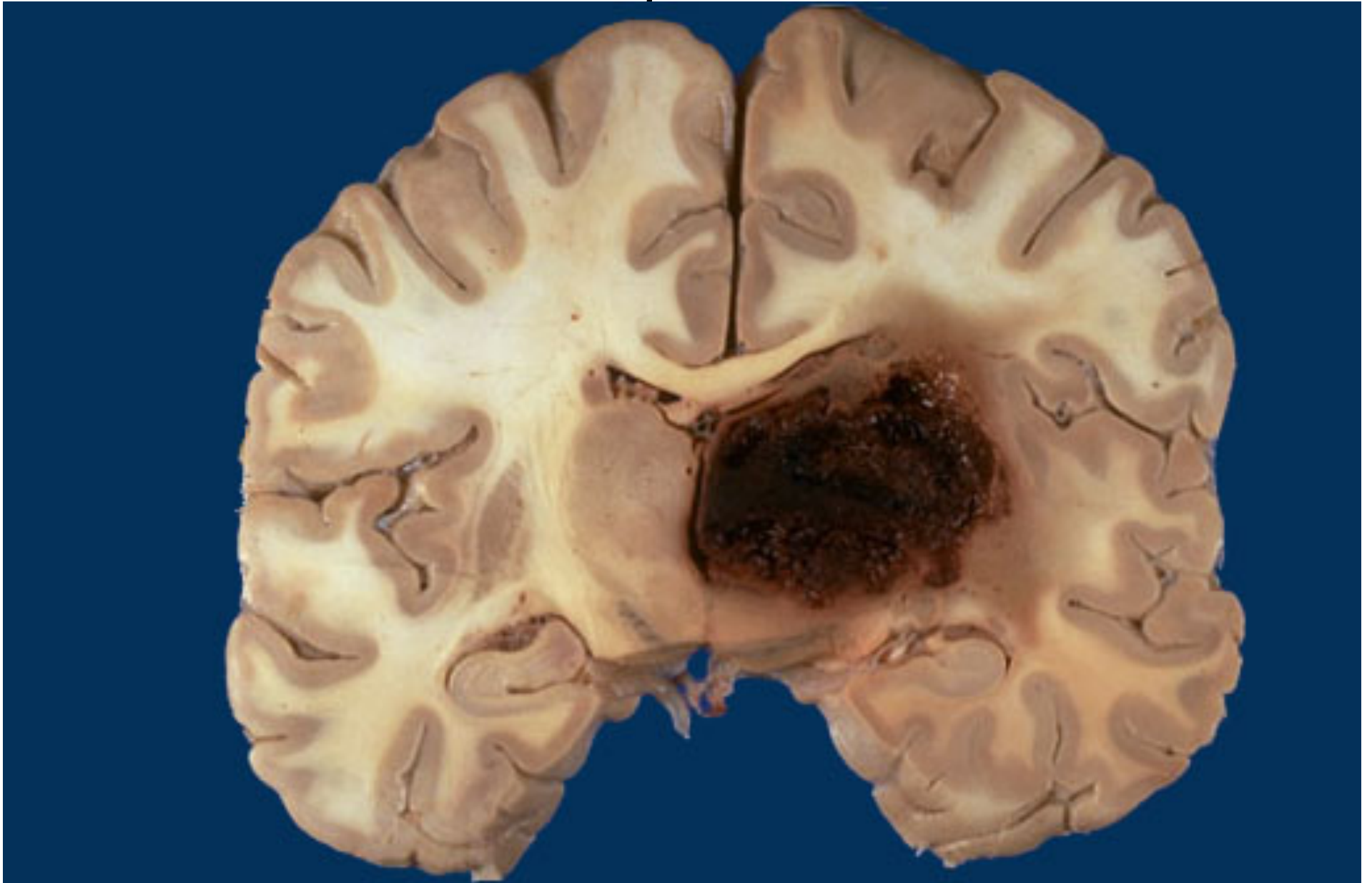
Intracerebral hemorrhage

- Different to ischemic stroke
- Due to hypertension or vascular abnormality

Intracerebral hemorrhage from hypertension



Intracerebral hemorrhage from hypertension leading to stroke



Cerebral Arteriography



Circle of Willis

Berry
aneurysm



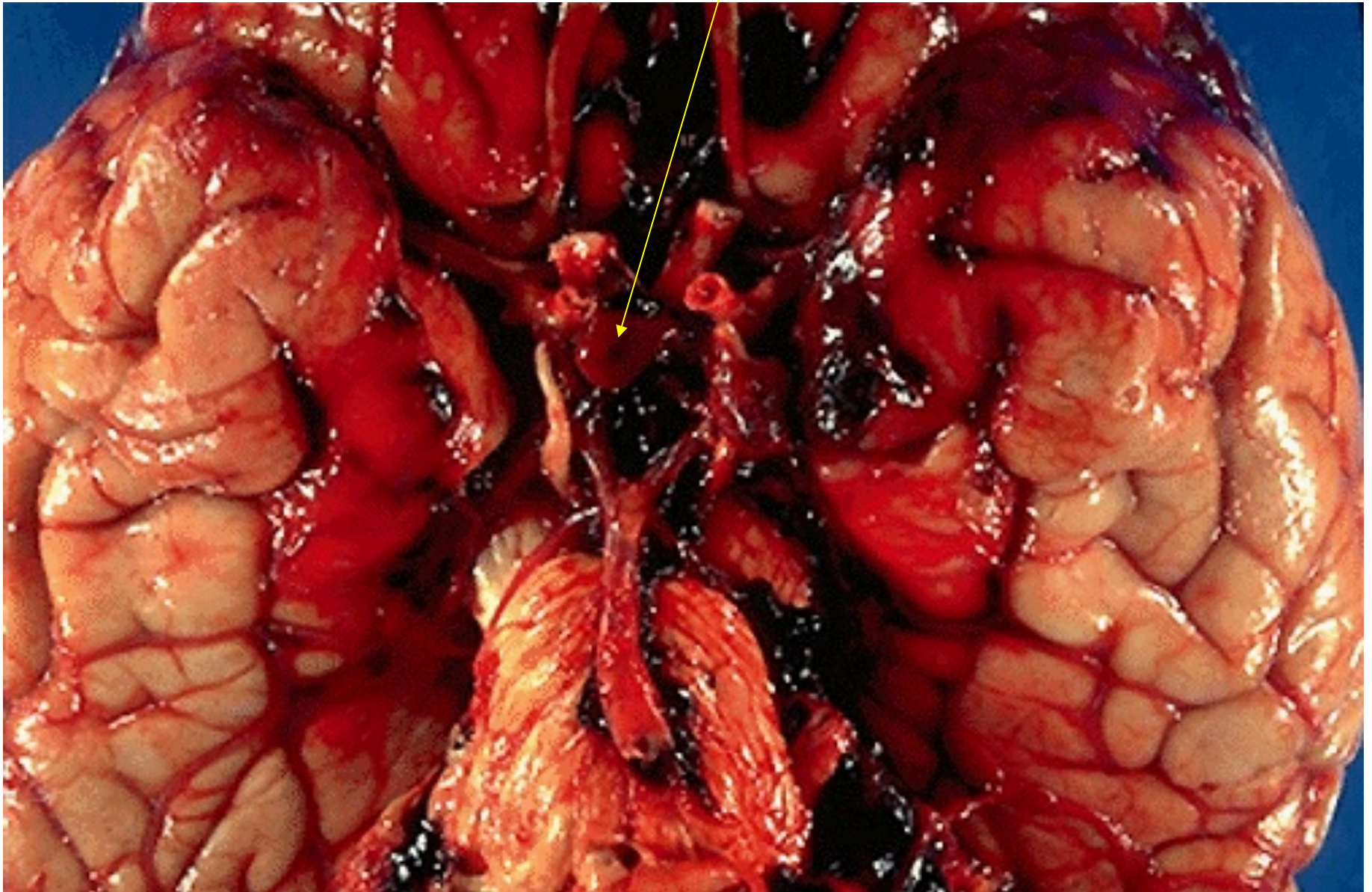
Multiple berry aneurysms



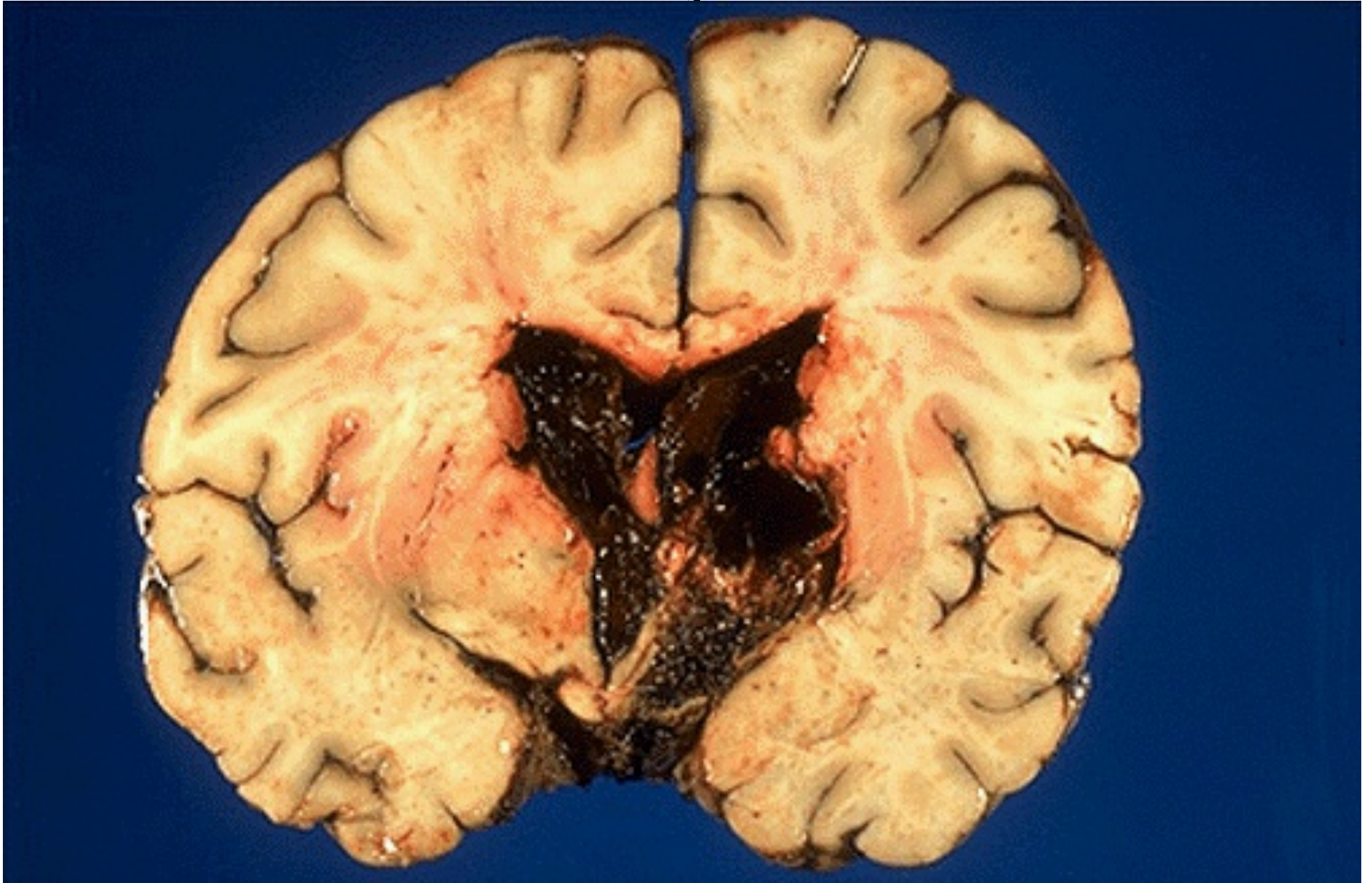
The white arrow on the black card marks the site of a ruptured berry aneurysm in the circle of Willis. This is a major cause for subarachnoid hemorrhage.



Ruptured berry aneurysm with subarachnoid hemorrhage



Intracerebral and intraventricular hemorrhage secondary to AVM



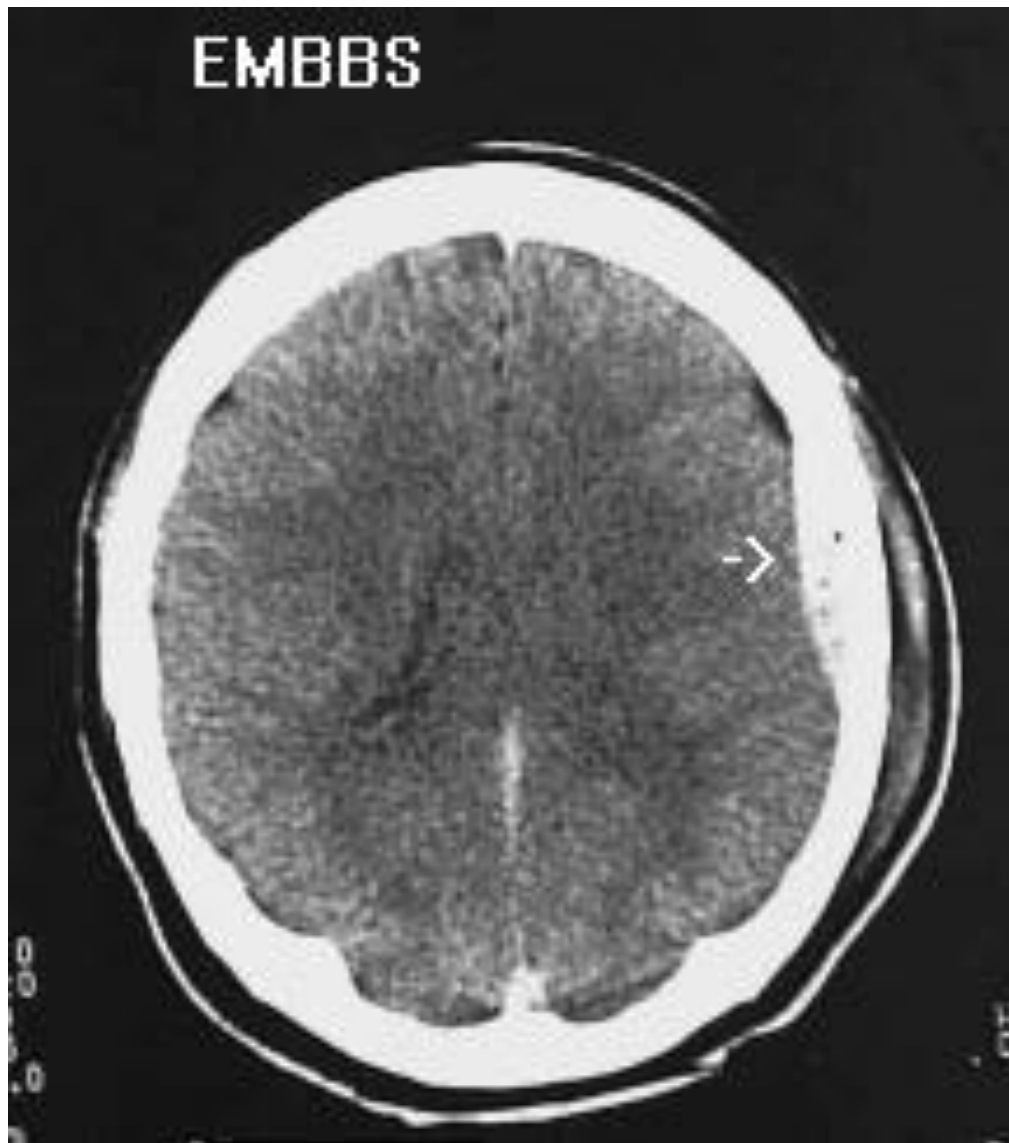
Transient Ischemic attacks (TIA's)

- Defn: Episode of vascular insufficiency that causes a temporary loss of brain function with total recovery within 24 hrs.
- Most last for less than half an hour with no residual signs so diagnosis relies on a good history
- Due to small atheroemboli that subsequently dissolve
-

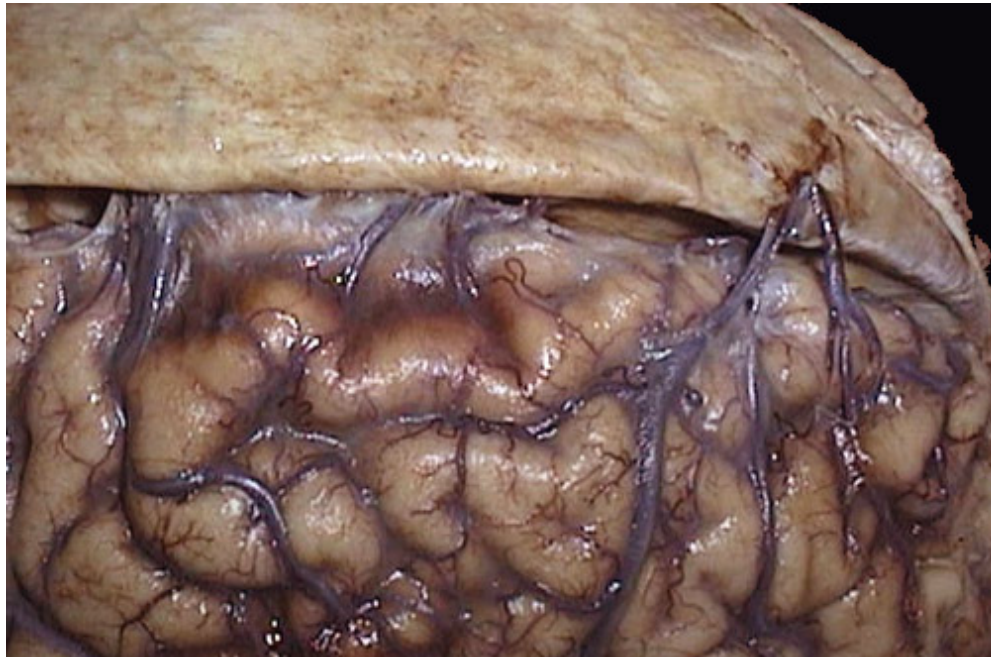
Pseudolaminar
necrosis (cell death)
of cerebral cortex in
persistent vegetative
state
eg Terry Schiavo –
paper thin cerebral
cortex



Acute Extra-Dural hematoma

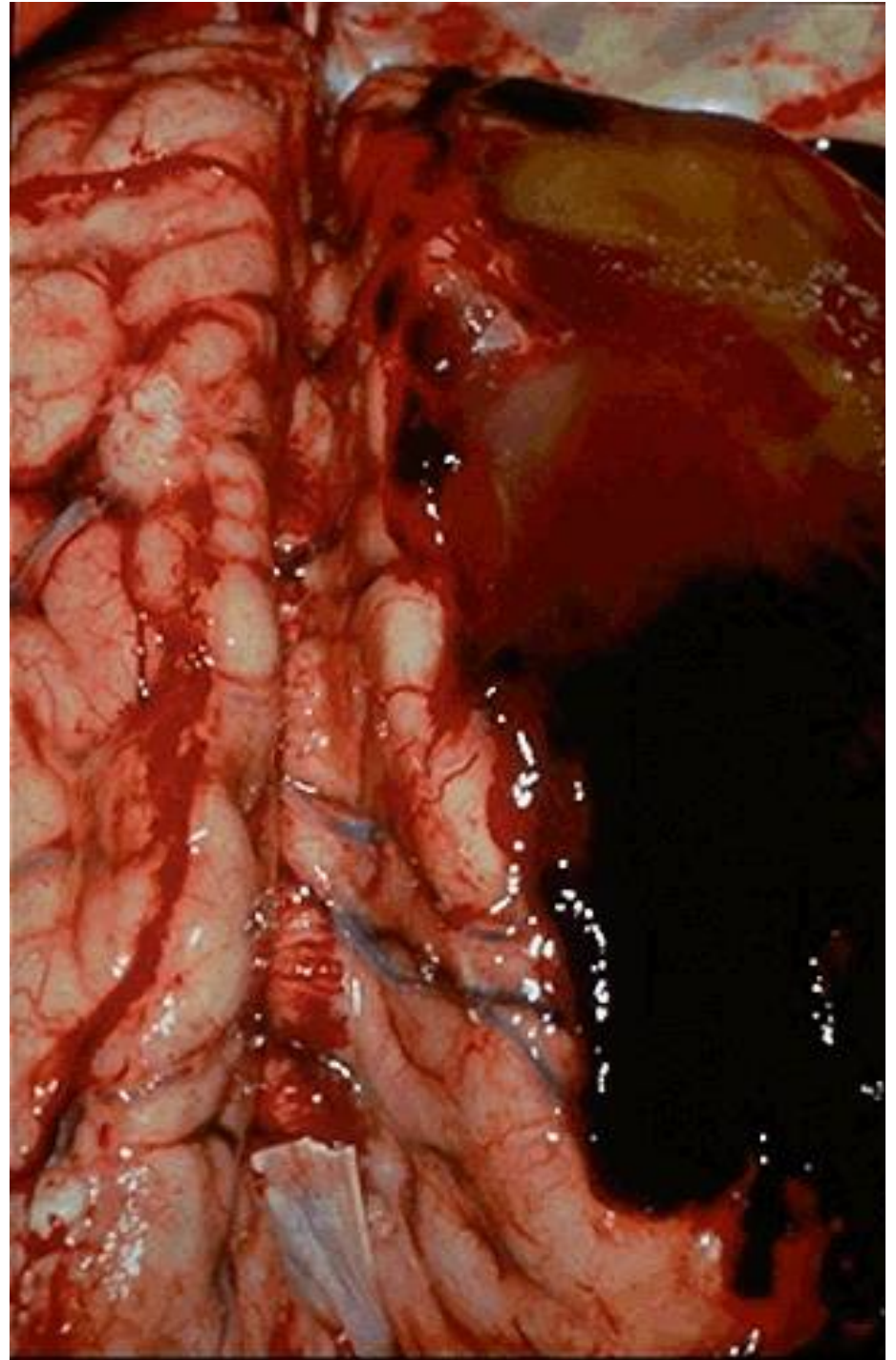


Bridging veins that tear and lead to subdural hematoma



Subdural hematoma

- Tearing of veins that lie between inner surface of the Dura and the Arachnoid mater due to trauma - results in a lower pressure venous leak and accumulation of blood in the subdural space; may be acute or chronic.



Large Subdural hematoma



Post-traumatic
subarachnoid
hemorrhage
and cortical
contusions-
contracoup type



Cortical contusions due to contracoup injury



Evaluation & Treatment

Initial Evaluation and Management

- Urgent transport to the nearest stroke receiving hospital via 911 system
- Notification of the destination ED
- Alert ED of the need for urgent CT

Code Stroke

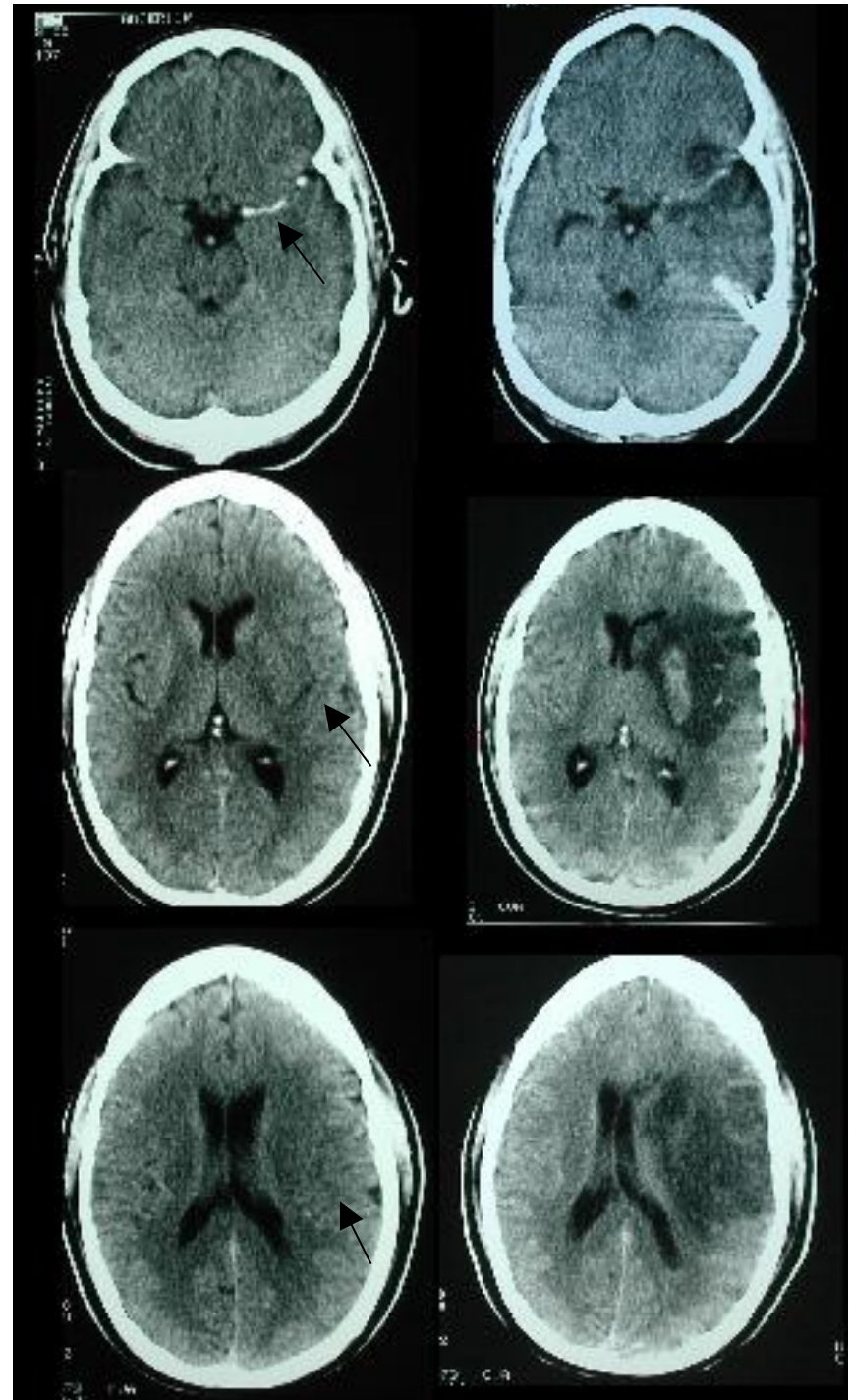
Medical “Code” to Signal Priority Treatment

Initial Evaluation

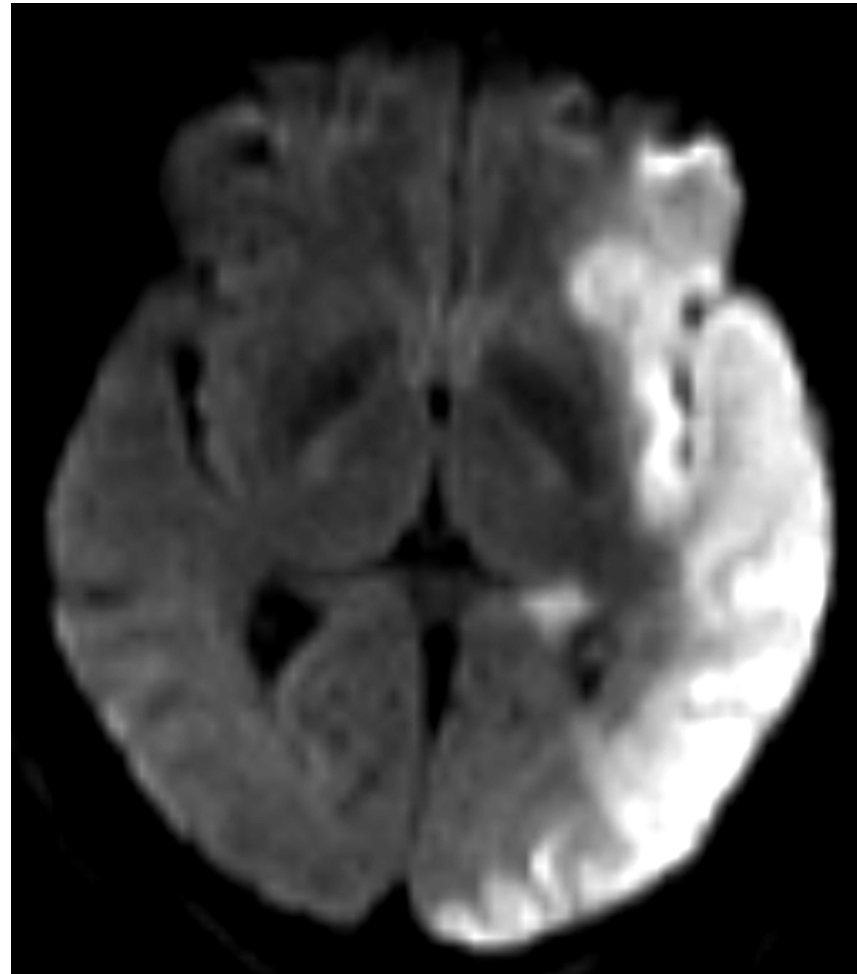
- Cardiac monitoring, pulse-ox, ECG
- Stat CT brain
- xray
- CBC, Platelet, PT, PTT
- Accucheck & blood glucose, serum electrolytes
- Cardiac markers, ABG's
- Blood alcohol level, Toxicology screen, Pregnancy test

CT Brain

CT Patterns



MRI Brain



Acute Therapy

- NINDS Stroke Study group: randomized placebo controlled clinical trial (N Engl J Med 1995)
- Intravenous recombinant tissue Plasminogen Activator (IV t-PA) given within 3 hour of symptoms onset in acute ischemic strokes
- N=624 patients (IV t-PA or placebo):dose 0.9mg/kg, 10% IV bolus, then the remainder is IV drip over 1 hour

NINDS Stroke Study

- Patients in the t-PA arm were at least 30% more likely to have minimal or no disability at 3 months
- Symptomatic Intracranial Hemorrhage was 6.4% in the t-PA group versus 0.6% in the placebo arm
- Mortality at 3 months was not statistically different between t-PA and placebo
- The benefit of IV t-PA was sustained at one year follow up
- The earlier the treatment the better the outcome

Poor Outcome Predictors in Ischemic Stroke

- Age
- Elevated blood sugar
- Initial NIHSS score which is a measure of the patient's initial deficit
- Cerebral infarction changes on CT brain

Is Stroke Preventable??

Prevention

- Primary prevention
- Secondary prevention

Primary Prevention

- Primary prevention starts at the level of the physician playing the role of the primary care and occasionally at the level of the cardiologist and the stroke neurologist
- Key is identification of underlying risk factors and modification and treatment of modifiable risk factors

Primary Prevention Elements

- Establishing good medical history and family history
- Identifying the patient's vascular risks including medical illnesses, habits such as smoking and substance use and genetic predisposition through review of significant family history for cardiovascular risk factors and stroke
- Exam elements which are key: **pulse** (rate and establishing how regular), blood pressure, carotid auscultation (**bruits**), cardiac auscultation (**murmurs** and abnormal **rhythm**), symmetry and detection of pulses, diabetic peripheral changes

Identification of Risk Factors for Stroke

- Non-modifiable risk factors
- Modifiable risk factors

Modifiable Risk Factors

Risk factors that can be controlled
by life style changes or by
medications or surgery

Non-modifiable Risk Factors

- Age: the risk of stroke doubles with every decade after the age of 55 years
- Sex: lifetime risk in Male>Female but risk in F>M after age of 80 years
- Race and ethnicity:
 - Stroke incidence and subtypes: higher in African Americans and Hispanics >Caucasians
 - Stroke related mortality is higher in African American population
 - Asian population has an increased risk of hemorrhagic stroke subtype compared to Caucasians

Well Documented Modifiable Risk Factors

- **Hypertension**
- Smoking
- Diabetes Mellitus
- Carotid disease
- Cardiac disease: [Atrial Fibrillation](#), Myocardial infarction secondary to coronary artery disease
- Dyslipidemia or hyperlipidemia (high cholesterol, high LDL, low HDL)
- Migraine with aura in women
- Obstructive sleep apnea

Less-Documented Potentially Modifiable Risk Factors

- Obesity
- Lack of exercise
- Poor diet
- Alcohol abuse
- Hyperhomocysteinemia
- Illicit drug abuse
- Hypercoagulopathy
- Sickle cell disease
- Estrogen/HR hormonal therapy
- Inflammation
- Infection