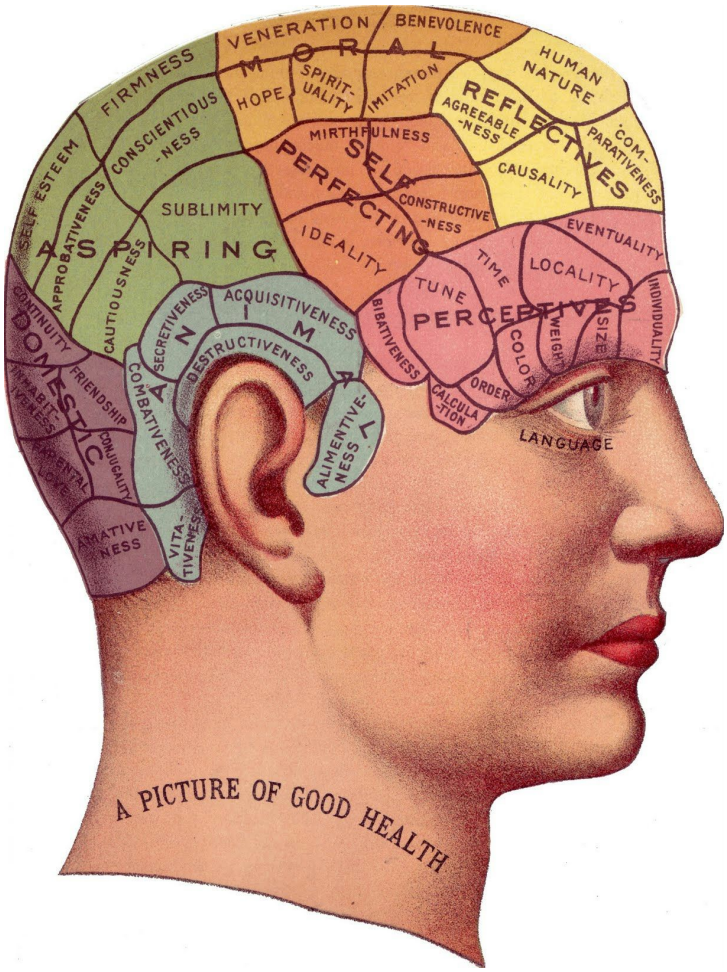
Cerebrovascular accidents

Robbins page 814



Objectives:

- Explain the concepts of brain "Hypoxia", "Ischemia" and "Infarction".
- Understand the pathogenesis of thrombotic and embolic stroke and be able to identify clinical risk factors.
- Identify the causes and consequences of subarachnoid and intracerebral hemorrhage.
- Build a list of the different causes that can lead to cerebrovascular accident.

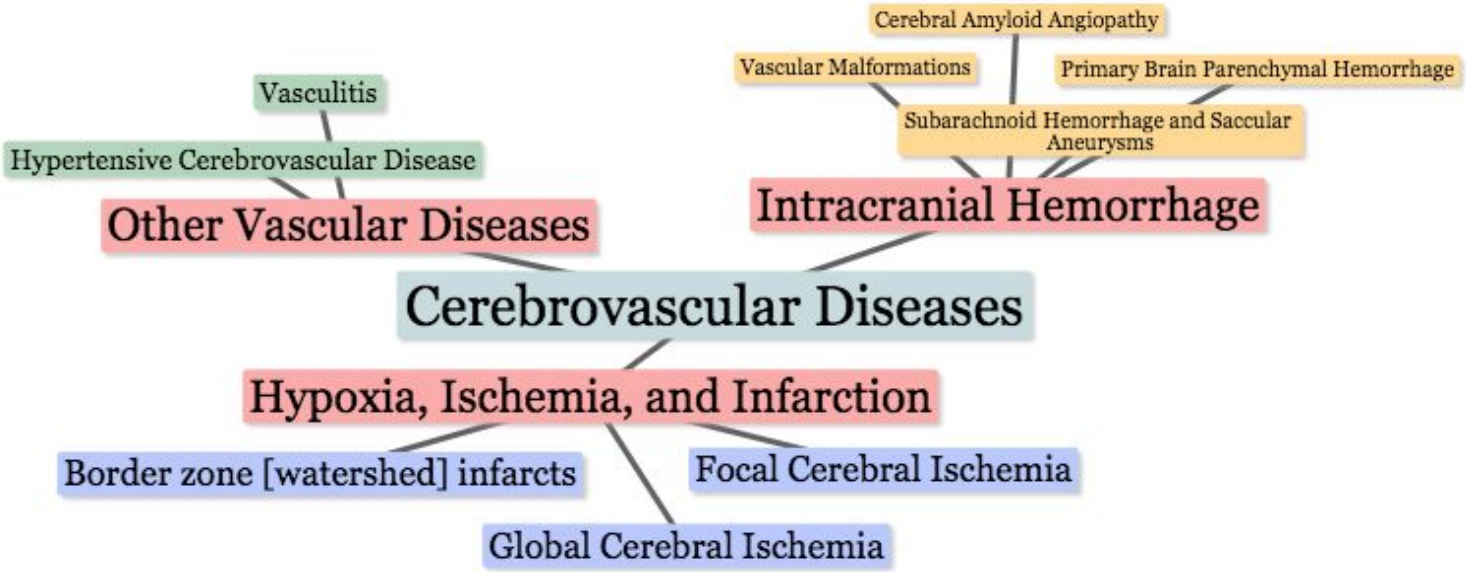
Important note: **Please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: Pathology Edit**

Red: Important
Grey: Extra notes

Introduction

Cerebrovascular disease is the **third** leading cause of death (after heart disease and cancer) in the United States. It is also the most prevalent neurological disorder in terms of both morbidity and mortality.

Contents of lecture (not all of them are included)**:**



Recall..

- **Hypoxia:** Deficiency in the amount of oxygen reaching the tissues.
- **Ischemia:** An inadequate blood supply to an organ or part of the body.
- **Infarction:** Obstruction of the blood supply to an organ or region of tissue, causing local death of the tissue.

The brain may be deprived from oxygen by several mechanisms:

1. Functional hypoxia.

- Low partial pressure of oxygen (e.g., high altitude).
- Impaired oxygen-carrying capacity (e.g., severe anemia, carbon monoxide poisoning).
- Inhibition of oxygen use by tissue (e.g., cyanide poisoning).

2. Ischemia.

Either *transient* (in short duration) or *permanent* due to tissue hypoperfusion, which can be caused by **hypotension** (due to hemorrhage or surgery), or **vascular obstruction**, or *both*.

Stroke.

Acute onset of a neurologic deficit as the result of vascular lesions due to:

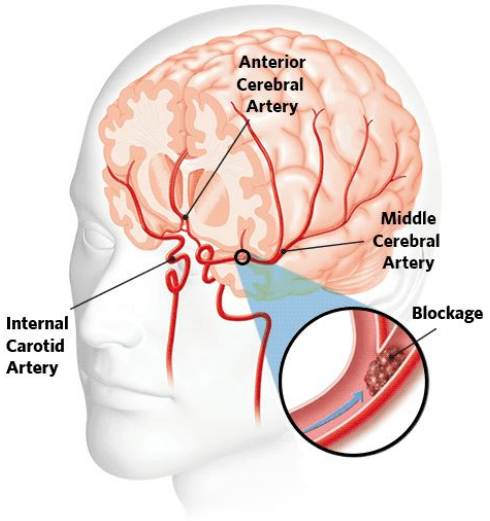
1. Hemorrhage (15%)
2. Loss of blood supply - embolic or thrombotic - (85%)

Thrombosis Vs. Embolism.

- **Thrombosis:** Formation of blood clot (thrombus) inside a blood vessel, obstructing the flow of blood.
- **Embolism:** Intravascular solid, liquid, or gaseous[1] mass that is carried by the blood to a site distant from its point of origin.

Embolic stroke.

Embolic infarctions are more common than thrombosis. Usually involve **middle cerebral arteries.** **WHY?** due to the size and the direct blood flow from *internal carotid artery* into the middle cerebral artery.



Sources of emboli include:

a- Cardiac mural thrombi[2] (more frequent):

- Myocardial infarct.
- Valvular disease.
- Atrial fibrillation.

b- Arteries, (often atheromatous plaques within the carotid arteries or aortic arch)

c- Paradoxical emboli[3], particularly in children with cardiac anomalies. (Paradoxical means that the formation of the embolus was in abnormal situation)

d- Emboli associated with cardiac surgery.

e- Emboli of other material (tumor, fat, or air).

Thrombotic stroke.

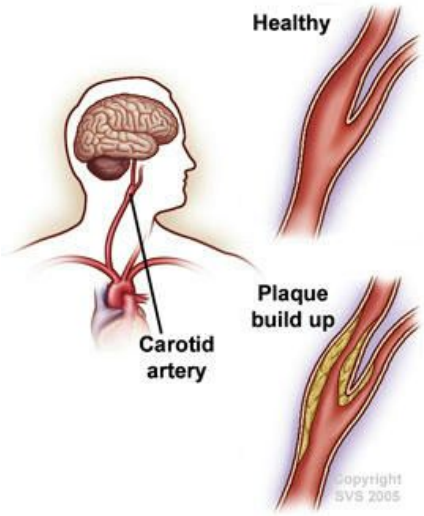
Thrombotic occlusions causing cerebral infarctions are due to **atherosclerosis**. (rupture of atherosclerotic plaques)

The most common sites of primary thrombosis:

a- The carotid bifurcation

b- The origin of the middle cerebral artery

c- At either end of the basilar artery



Atherosclerotic stenosis can develop on top of a superimposed thrombosis[4], accompanied by anterograde extension, fragmentation, and distal embolization.

[1] gas

[2] Mural thrombi are thrombi that adhere to the wall of a blood vessel and occur in large vessels.

[3] Passage of a clot from a vein to an artery through a septal defect or patent foramen ovale.

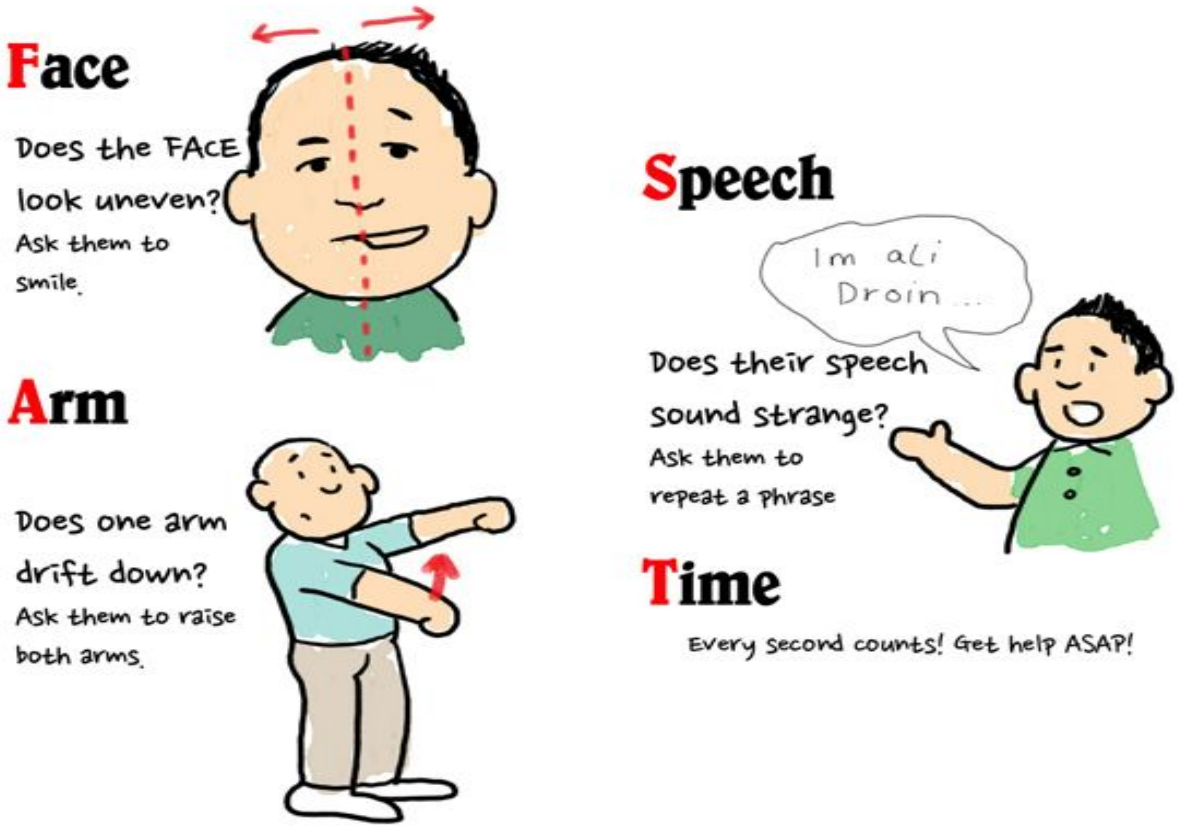
[4] The process by which a thrombus will be formed on top of an existing pathology, for example, thrombosis on top of atherosclerosis.

Clinical presentation of stroke:

Depends on which part of the brain is injured, and how severely it is injured. It is very important to recognize the warning signs of a stroke:

- Sudden.
- Sometimes people have a *headache*, but stroke can also be completely *painless*.
- The most common is *weakness or paralysis of one side of the body* with partial or complete loss of voluntary movement or sensation in a leg or an arm.
- *Speech problems* and weak face muscles, causing drooling.
- Numbness or tingling is very common.
- Can affect balance, vision, swallowing, breathing and even unconsciousness. (involving the base of the brain)
- May be deep coma, paralysis of one side of the body, and loss of speech, followed by death or permanent neurological disturbances after recovery. (In cases of severe brain damage there)

Remember signs of stroke (FAST).



Global Cerebral Ischemia.

Widespread ischemic/hypoxic injury occurs (the whole brain suffers from it). When there is a generalized reduction of cerebral perfusion, usually below *systolic pressures* of less than 50 mmHg.

Majors etiologies:

- Low perfusion **(atherosclerosis)**
- Acute decrease in blood flow (severe hypotension or shock and cardiac arrest).
- Chronic hypoxia.
- Repeated hypoglycemia (insulinoma[5]).

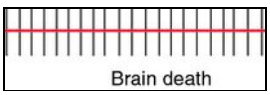
The clinical outcome.. varies with the severity of the insult:

1- Mild:

- Only a transient post-ischemic confusional state.
- Eventual complete recovery.

2- Severe:

- Widespread neuronal death, irrespective of regional vulnerability, occurs. If the patient survives, he could suffer from one of the points in the table:

1. Persistent vegetative state (Disorders of consciousness)	**2. Respirator brain**
Impaired neurologically and deeply comatose[6].	"**brain death**," including evidence of: a. Diffuse cortical injury (isoelectric, or "flat," EEG). b. Brain stem damage, including absent reflexes and respiratory drive. 
	When this patient is maintained on mechanical ventilation, the brain gradually undergoes an **autolytic process.**

Sensitivity to ischemia:

Neurons are much more sensitive to hypoxia than glial cells. The most susceptible to ischemia of short duration are:

1. **Pyramidal cells** of the **Sommer sector (CA1)**[7] of the hippocampus.
2. **Purkinje cells** of the cerebellum.
3. **Pyramidal neurons** in the neocortex.

[5] Presence of insulin in blood.
[6] Being in a state of a coma, or being unconscious
[7] Sommer's sector is region CA1 of the hippocampus, it's one of the vulnerable areas in Global Cerebral Ischemia.

Gross pathology:

- The brain is swollen, with wide gyri and narrowed sulci.
- The cut surface shows poor demarcation between gray and white matter.

Microscopically, infarction shows:		
Early changes	**Subacute changes**	**Repair**
12 to 24 hours after the insult	24 hours to 2 weeks	after 2 weeks
Red neurons, characterized initially by microvacuolization, cytoplasmic eosinophilia, and later nuclear pyknosis and karyorrhexis.	- Necrosis of tissue, influx of macrophages, vascular proliferation and reactive gliosis - The reaction to tissue damage begins with infiltration by neutrophils.	Removal of all necrotic tissue, loss of organized CNS structure and gliosis.

Focal Cerebral Ischemia.

Cerebral arterial occlusion → **focal ischemia** → **infarction** of distribution of the **compromised vessel**.

The size, location, and shape of the infarct and the extent of tissue damage **is modified by adequacy of collateral flow such as:**

- **The major source of collateral flow is the circle of Willis.**
- **Cortical-leptomeningeal anastomoses.**

These can **limit damage in some regions.**

In contrast, there is little if any collateral flow for the deep penetrating vessels supplying structures such as:

- **Thalamus**
- **Basal ganglia**
- **Deep white matter**

Gross pathology (Non-hemorrhagic infarct).

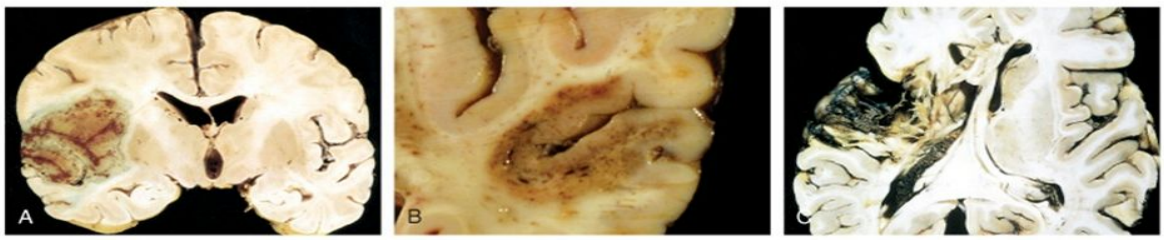
First 6 hours	After 48 hours	2 to 10 days	10 days to 3 weeks
irreversible injury, little can be observed	tissue becomes pale, soft, and swollen, and the corticomedullary junction becomes indistinct.	brain becomes gelatinous and friable, & boundary between normal and abnormal tissue becomes more distinct as edema resolves in the adjacent tissue that has survived.	tissue liquefies, eventually leaving a fluid-filled cavity lined by dark gray tissue, which gradually expands as dead tissue is removed.

Microscopic appearance (Non-hemorrhagic infarct).

First 12 hours	Until 48 hours	2 to 3 weeks	After several months
● Red neurons and both cytotoxic and vasogenic edema predominate. ● Loss of the usual of white and gray matter structures. ● Endothelial and glial cells, mainly astrocytes, swell, and myelinated fibers begin to disintegrate.	There is some neutrophil emigration.	● Macrophages containing myelin breakdown products or blood 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 protoplasmic extensions.	● Striking astrocytic nuclear and cytoplasmic enlargement regress in cortex. ● The pia and arachnoid are not affected and do not contribute to the healing process.

Microscopic appearance (hemorrhagic infarct).

- Parallel ischemic infarction.
- Blood extravasation and resorption.
- If the person is receiving anticoagulant treatment, may be associated with extensive intracerebral hematomas.



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

Border zone ("watershed[8]") infarcts.

Border zone "watershed" infarcts are **wedge-shaped areas** of infarction occur in those regions of the brain and spinal cord that lie at the most distal portions of arterial perfusion ..

- In the cerebral hemispheres, the border zone between the **anterior** and the **middle cerebral artery** distributions are at **greatest risk.**
- **Damage to this region produces a** *band of necrosis over the cerebral convexity* a few centimeters lateral to the interhemispheric fissure.
- Border zone infarcts are usually seen after **hypotensive episodes**.

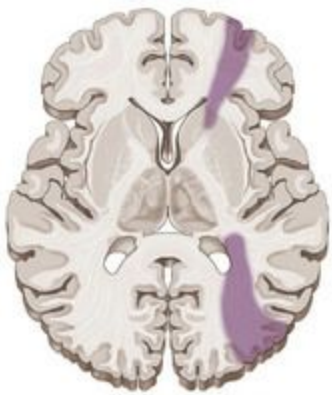


Figure – Purple areas are watershed territories between ACA-MCA and MCA-PCA distributions.

[8] regions of the body that receive dual blood supply

Intracerebral hemorrhage.

Hemorrhages within the brain (intracerebral) can occur secondary to:

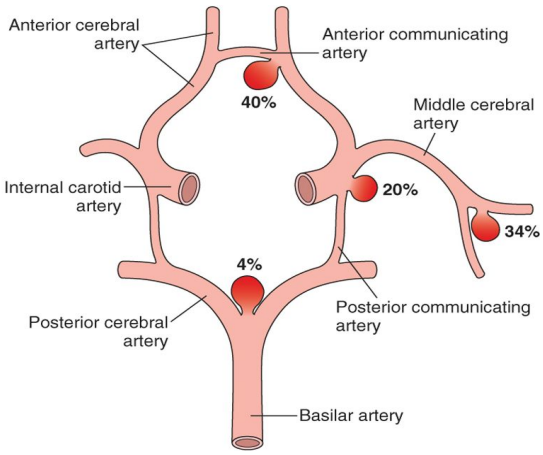
- **Hypertension and diseases lead vascular wall injury** (e.g. vasculitis).
- **Sturecal lesion such as Arteriovenous malformation** and cavernous malformation.
- **Intraparenchymal tumor.**

Hemorrhages associated with the dura (in either subdural or epidural spaces) associated with trauma.

Symptoms: Nausea, Severe headache, vomiting and eventual coma - most common in mid to late adult (60 years old) -.

Subarachnoid Hemorrhage.

Between 25% and 50% of individuals die with the first bleed, although those who survive typically improve and recover consciousness in minutes. Recurrent bleeding is common in survivors; (it is currently not possible to predict which individuals will have recurrences of bleeding). The prognosis worsens with each episode of bleeding.



Causes:

- **Rupture of a saccular (berry) aneurysm** (The most frequent).
  - The figure shows common sites of saccular (berry) aneurysm.
- **Vascular malformation.**
- **Trauma** (it is usually associated with other signs of the injury).
- **Rupture of an intracerebral hemorrhage into the ventricular system.**
- **Hematologic disturbances.**
- **Tumors.**

Rupture can occur at any time, but in about **one-third of cases** it is associated with **acute increases in intracranial pressure**, such as with **straining at stool** or **sexual orgasm.** Blood under arterial pressure is forced into the subarachnoid space, which lead to:

- Sudden excruciating headache (classically described as "the worst headache I've ever had").
- Rapidly lose consciousness.

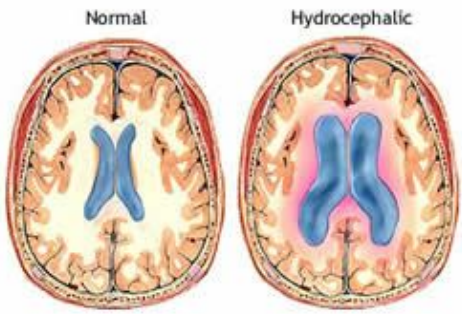
About 90% of **saccular aneurysms** occur in the anterior circulation near major arterial branch points. **Multiple aneurysms** exist in 20% to 30% of cases. (sometimes referred to as congenital, they are not present at birth but develop over time because of underlying defects in the vessel media)

- The probability of **aneurysm rupture increases with the size of the lesion** (e.g. aneurysms greater than 10 mm have a roughly 50% risk of bleeding per year) There is an increased risk of aneurysms in patients with autosomal dominant polycystic kidney disease, as well as those with genetic disorders of extracellular matrix proteins.
- Early period after a **subarachnoid hemorrhage** have risk to → **vasospasm**[9] **involving other vessels** (**additional ischemic injury from**).

In the healing phase of subarachnoid hemorrhage, shows:

- Meningeal fibrosis
- Scarring

These sometimes leading to **obstruction of CSF flow as** or **distribution of CSF resorption** lead to **Hydrocephalus.**

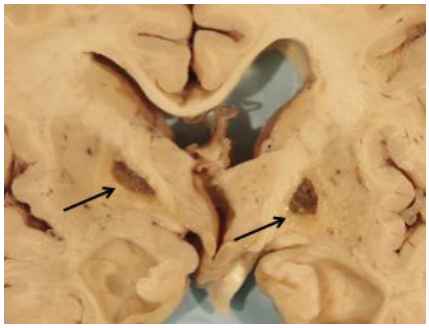


[9] sudden constriction of a blood vessel, reducing its diameter and flow rate.

Hypertensive Cerebrovascular Disease.

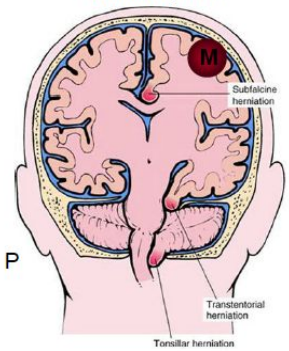
Hypertension causes several changes, including:

- ***hyaline arteriolar sclerosis* in arterioles** (weaker than normal vessels and become more vulnerable to rupture.)
- chronic hypertension is associated with the development of **minute aneurysms(*Charcot-Bouchard microaneurysms)*** in vessels that are less than 300 μm in diameter , which may rupture.
- Hypertension affects the **deep penetrating arteries** and **arterioles** that supply the **basal ganglia and hemispheric white matter and the brain stem**



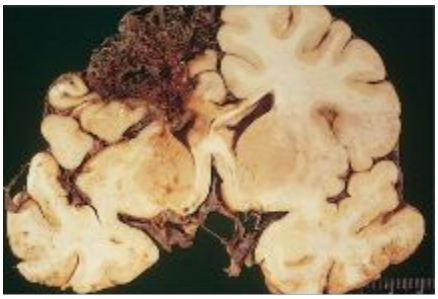
The most important effects of **hypertension on the brain** include:

- **Lacunar infarcts**
- **Slit hemorrhages**
- **Hypertensive encephalopathy**
- **Massive hypertensive intracerebral hemorrhage**



Lacunar infarcts	**Lacunes or Lacunar infarcts are:** ● Small cavitary infarcts ● Most commonly in deep gray matter (basal ganglia and thalamus), internal capsule, deep white matter, and pons. ● Consist of cavities formed by degeneration of brain tissue with scattered *lipid-laden macrophages* surrounding gliosis. ● Depending on their location in the CNS, lacunes can either be silent or cause significant neurologic impairment
Slit hemorrhage	● Rupture of the small-caliber penetrating vessels lead to development of small hemorrhages. ● In time, these hemorrhages resorb, leaving behind a slitlike cavity surrounded by brownish discoloration (iron from blood)
Acute hypertensive encephalopathy	● A clinicopathologic syndrome:defined as diffuse cerebral dysfunction including headaches, confusion, vomiting, and convulsions, sometimes leading to coma ● May be associated with an edematous brain, with or without transtentorial or tonsillar herniation.(see pic above) ● **Microscopically**: Petechiae and fibrinoid necrosis of arterioles in the gray and white matter
Massive hypertensive intracerebral hemorrhage	(discussed earlier, most important)

Vasculitis.



Arteriovenous malformation

It is infectious arteritis of small and large vessels:

- Previously in association with syphilis and tuberculosis
- Now more commonly occurs in the setting of immunosuppression and opportunistic infection (such as toxoplasmosis, aspergillosis, and CMV encephalitis)

- Systemic forms of vasculitis, such as polyarteritis nodosa, may involve cerebral vessels and cause single or multiple infarcts throughout the brain

Primary angiitis of the CNS:

- An inflammatory disorder that involves multiple small to medium-sized parenchymal and subarachnoid vessels
- Affected individuals manifest a diffuse encephalopathic clinical picture, often with cognitive dysfunction
- Improvement occurs with steroid and immunosuppressive treatment

So what can cause or contribute to a stroke ?

- **Hypertension**
- **Atherosclerosis**
- Thrombophilia, e.g. Sickle cell anemia
- **Embolic diseases**
- Systemic hypoperfusion, Global hypoxia, e.g. shock
- Vascular malformations
- **Vasculitis**
- Tumors
- Venous thrombosis
- **Amyloid angiopathy (leptomeningeal and cortical vessels)**
- **Heart diseases**

Did you know? Brain tissue ceases to function if deprived of oxygen for more than 60 to 90 seconds & after approximately three hours, will suffer irreversible injury possibly leading to death of the tissue.

Homework.

Q1/What are the risk factors of stroke?

- **Age**
- **Hypertension**
- **High cholesterol**
- Male more than women in adult
- Obesity
- Smoking

Q2/Define: Transient ischemic attack.

Is like a stroke, producing similar symptoms, but usually lasting only a few minutes and causing no permanent damage.

SUMMARY

Cerebrovascular Diseases

- *Stroke* is the clinical term for acute-onset neurologic deficits resulting from hemorrhagic or obstructive vascular lesions.
- Cerebral infarction follows loss of blood supply and can be widespread or focal, or affect regions with the least robust vascular supply ("watershed" infarcts).
- Focal cerebral infarcts are most commonly embolic; with subsequent dissolution of an embolism and reperfusion, a nonhemorrhagic infarct can become hemorrhagic.
- Primary intraparenchymal hemorrhages typically are due to either hypertension (most commonly in white matter, deep gray matter, or posterior fossa contents) or cerebral amyloid angiopathy.
- Spontaneous subarachnoid hemorrhage usually is caused by a structural vascular abnormality, such as an aneurysm or arteriovenous malformation.

MCQ's. * 9 & 10 are questions from USMLE site.

1- What is a stroke?

a- Blood clot stops the flow of blood in a limb.
b- The heart slows and nearly stop functioning.
c- Blood flow to the brain is interrupted, or a blood vessel in the brain bursts.
d- It is the clinical term for a disease with acute onset of a neurologic deficit as the result of vascular lesions.
Answer: D

2- Which of the following is not a common site of primary thrombosis in the brain:

a- The carotid bifurcation.
b- The anterior cerebral artery.
c- The origin of the middle cerebral artery.
d- At either end of the basilar artery.
Answer

3- Regarding subacute changes, which of the following is not present in histopathological slide examination:

a- Neutrophils infiltration
b- Reactive Gliosis
c- Red neurons
d- Necrosis
Answer: C

4- Which of the following is considered as the major source of collateral blood flow to the brain :

a- Internal carotid artery
b- External carotid
c- Vertebral artery
d- circle of Willis
Answer: C

5- which of the following best describes the watershed zone :

a- It is the area in the brain which has high blood perfusion because it is supplied by middle and anterior cerebral arteries.
b- It is the area in the brain which has a low blood perfusion because it is supplied by posterior and middle cerebral arteries.
c- It is the area in the brain which has a low blood perfusion because it is supplied by anterior and middle cerebral arteries.
d- It is the area in the brain which has the least liable to have ischemia.
Answer: c

6- Which of the following triggers a Subarachnoid Hemorrhage with the highest clinical significance:

a- Hematologic disturbance
b- Tumors.
c- Hypertension.
d- rupture of a saccular aneurysm
answer: D

7- which of the following is true regarding subarachnoid hemorrhage:

a- Recurring bleeding isn't common.
b- The prognosis enhances with each episode of bleeding
c- It is possible to predict recurrence attacks
d- Subarachnoid hemorrhage increases the risk of ischemic injuries
Answer: d

8- An autopsy was applied on a body was suffering of malignant hypertension what do you expect to see as a microscopic findings: (choose the best answer):

a- hyaline arteriolar sclerosis in arterioles
b- liqufative necrosis
c- gliosis
d- new vascularization
Answer: A

9- As a resident physician you are viewing an angiogram, which illustrates the occlusion of the Anterior Cerebral Artery supplying the right hemisphere. Because of this information, you know that the patient will have a deficit in which of the following?

a- Motor and sensory function in the right lower limb
b- Motor and sensory function in the left lower limb
c- Motor and sensory function in the right upper limb
d- Motor and sensory function in the left upper limb
e- Motor and sensory function in the upper and lower limbs

Answer: B

10- A 64 year old lady has the worst headache of her life. She is brought to the hospital with photophobia and vomiting as well. On examination she has positive Kernig's and Brudzinski's signs and bilateral extension on plantar reflex. Lumbar puncture shows blood, thoroughly mixed with CSF.

a- Glioblastoma of parietal lobe
b- Medulloblastoma
c- Ruptured berry aneurysm
d- Meningitis
e- Encephalitis

Answer: C

SAQ's.

1- **Describe the difference between transient and permanent ischemia.**

Transient ischemia is a temporary reduction in blood perfusion to a particular area in the brain causing attacks by a many triggers (the symptoms depend on the area has been affected. However these attacks doesn't cause infarction.

Permanent ischemia: indicates that there is a tissue necrosis. (Infarction).

2- **Explain why there are many differences in the clinical presentation of the stroke?**

The symptoms vary between simple and serious disabilities depending on which part of the brain is injured and how severely it is injured.

3- **Mention the CNS cells that are more susceptible to ischemia.**

- pyramidal cells of the Sommer sector (CA1) of the hippocampus
- Purkinje cells of the cerebellum
- pyramidal neurons in the neocortex

4- **what are the Lacunar infarcts ?**

Small infarcts consisting of cavities of tissue loss with scattered lipid-laden macrophages and surrounding gliosis

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For any suggestions or questions please don't hesitate to contact us on: Pathology434@gmail.com

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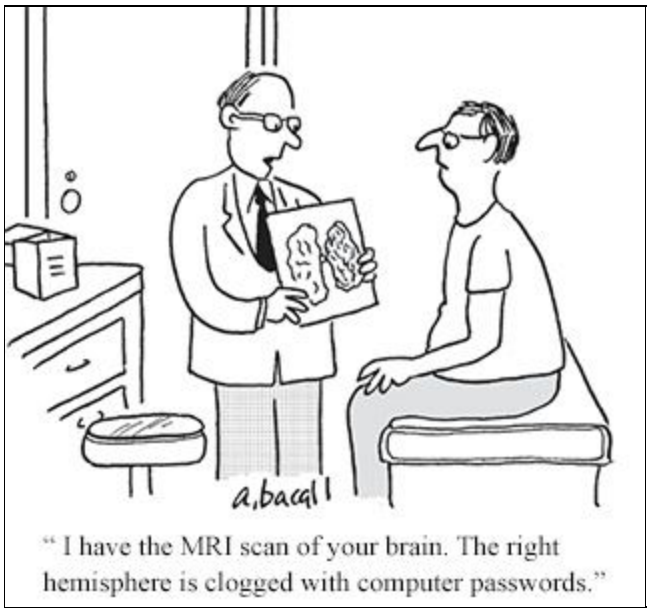
Ask us: www.ask.fm/Pathology434

Good Luck! :)



" I have the MRI scan of your brain. The right hemisphere is clogged with computer passwords."

مها الربيعة
سارة محمد الجاسر
ريما الناصر
ريما الرشيد
سارة الحسيني
ريم لبني

حسين الكاف
سامي القرني
سعد الخريجي
عبدالعزيز الطويل
أحمد الصالح
محمد المحمود