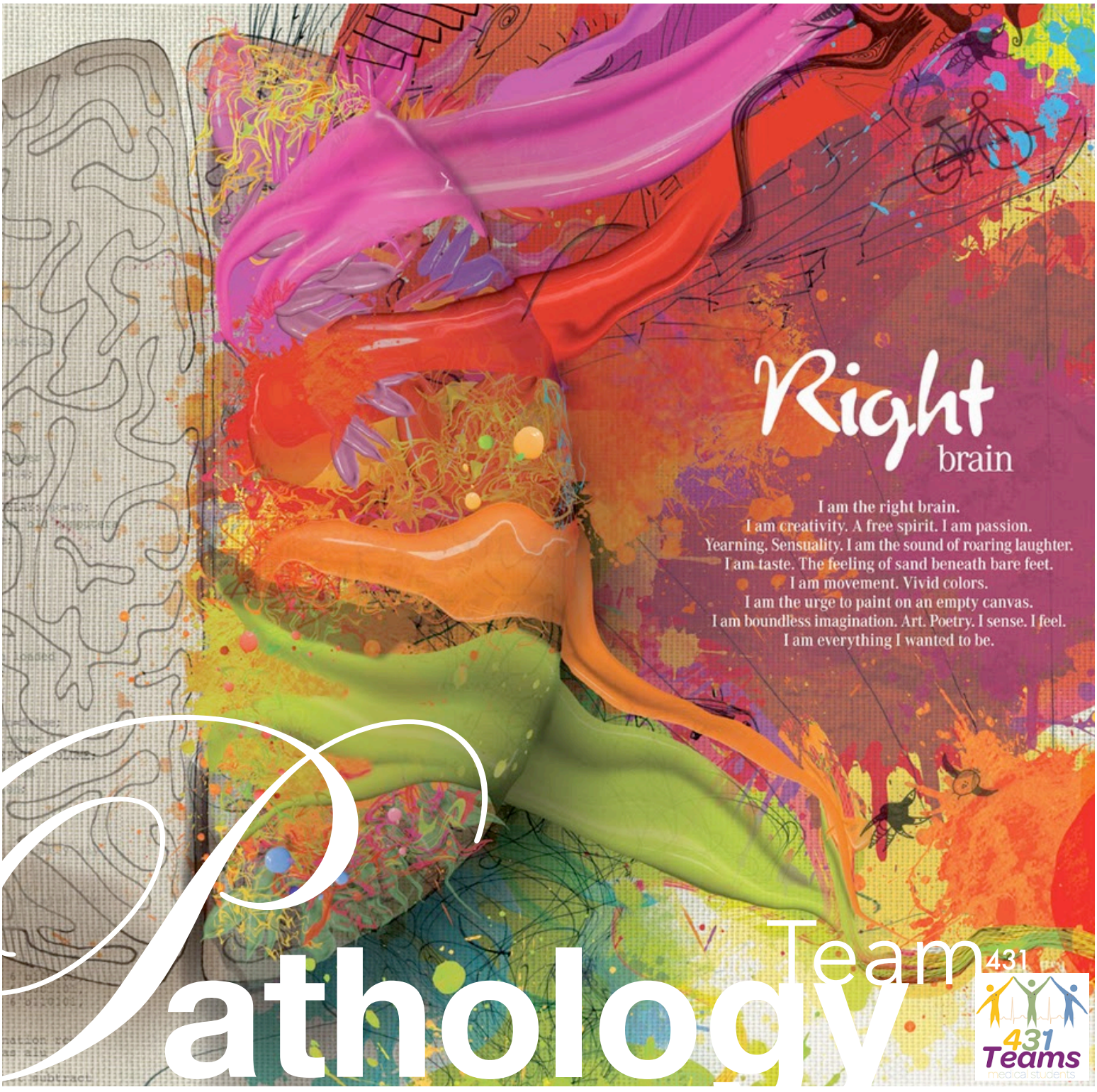

Pathology

Team 431

431 Teams medical students

5 /9

CNS Block

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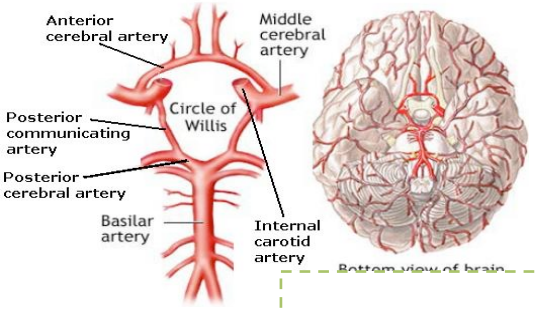
Focal cerebral ischemia:

• Cerebral arterial occlusion ⟶ focal ischemia
• The size, location, and shape of the infarct and the extent of tissue damage that results are determined by modifying variables, most importantly the <u>adequacy of collateral flow</u>:

• The major source of collateral flow is the **circle of Willis** (so it's rare to have focal ischemia in this region)

Collateral flow: circulation in an area of tissue or an organ with a number of different pathways for blood to reach it



• Partial collateralization: provided over the surface of the brain through **cortical-leptomeningeal anastomosis**

<u>Leptomeninges</u>: The two innermost layers of tissues that cover the brain and spinal cord, the arachnoid mater and pia mater

• In contrast, there is little of any collateral flow for the deep penetrating vessels supplying structures such as: (areas lack collateral flow so they are more susceptible to focal ischemia)

- Thalamus
- Basal ganglia
- Deep white matter

The cortex has many collaterals so the effect will be more in deep structures

<u>1)Nonhemorrhagic infarction:</u>

It's important to know the time required for each change .

Gross pathology:

1-**<u>The first 6 hours</u>** of irreversible injury, little can be observed

2-**<u>By 48 hours</u>**: 1.tissue becomes pale, soft, and swollen
2.corticomedullary junction becomes indistinct

3-**<u>From 2 to 10 days</u>**:1.the brain becomes gelatinous and friable
2.the previously ill-defined boundary between normal and abnormal tissue becomes more distinct as edema resolves in the adjacent tissue that has survived.(we can't distinguish between the normal and the abnormal tissue)

4-**From 10 days to 3 weeks**: the tissue liquefies (Liquefactive necrosis) eventually leaving a fluid-filled cavity lined by dark gray tissue, which gradually expands as dead tissue is removed.

Microscopically:

The tissue reaction follows a characteristic sequence:

• After the first 12 hours:

- Red neurons and both cytotoxic and vasogenic edema Predominate.

Just for you to understand: Vasogenic edema (regular edema) occurs when the normal blood-brain barrier is disrupted. With increased vascular permeability, fluid shifts from the vascular compartment into the intercellular spaces of the brain. It is a result of increased permeability due to inflammation or tumors. Cytotoxic edema is an increase of intracellular fluid from neuronal, glial, or insult or with exposure to some toxins. hypoxic/ischemicendothelial cell membrane injury as in

- There is loss of the usual characteristics of white and gray matter structures
- Endothelial and glial cells, mainly astrocytes, swell, and myelinated fibers begin to disintegrate

In the glioblastoma there was endothelial proliferation ,While in the focal ischemic infarction it is endothelial swelling

• Until 48 hours:

There is some neutronphilic emigration followed by mononuclear phagocytic cells in the ensuing

•2 to 3 weeks:

•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 extension

• **After several months:**

• the striking astrocytic nuclear and cytoplasmic enlargement recedes (stops)

• In the wall of the cavity, astrocyte processes form a dense feltwork of glial fibers admixed with new capillaries and a few perivascular connective tissue fibers. (There are new capillaries but there is no endothelial proliferation)

• In the cerebral cortex the cavity is delimited from the meninges and subarachnoid space by a gliotic layer of tissue, derived from the molecular layer of cortex

Remember no granulation tissue only gliosis

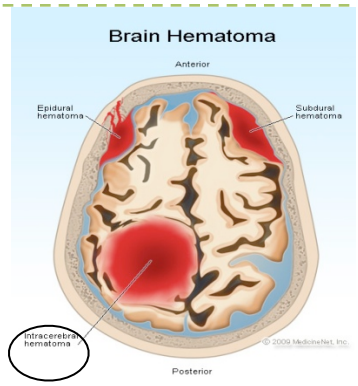
• The pia and arachnoid are not affected and do not contribute to the healing process

2)Hemorrhagic infarction:

- The microscopic picture and evolution of hemorrhagic infarction parallel (similar to) ischemic infarction, with the addition of blood extravasation and resorption

Extravasation: a discharge or escape of blood from a vessel into the tissue.
resorption the action or process of reabsorbing something
grossly: we see blood , microscopic:RBCs

- In persons receiving anticoagulant treatment, hemorrhagic infarcts may be associated with extensive intracerebral hematomas (intracerebral hematomas: Bleeding within the brain)



Border zone ("watershed") infarcts:

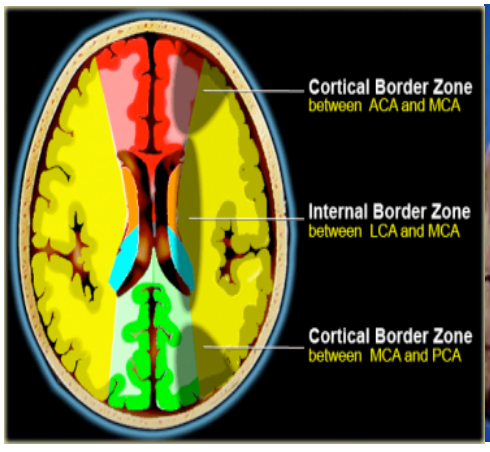
- Wedge-shaped areas of infarction that occur in those regions of the brain and spinal cord that lie at the most distal fields of arterial perfusion

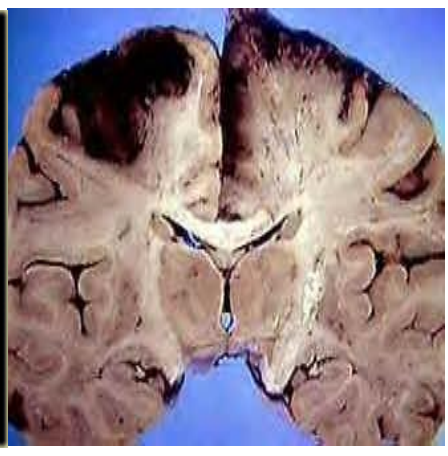
Another definition :an infraction localized to the border zones between the territories of two major arteries in the brain

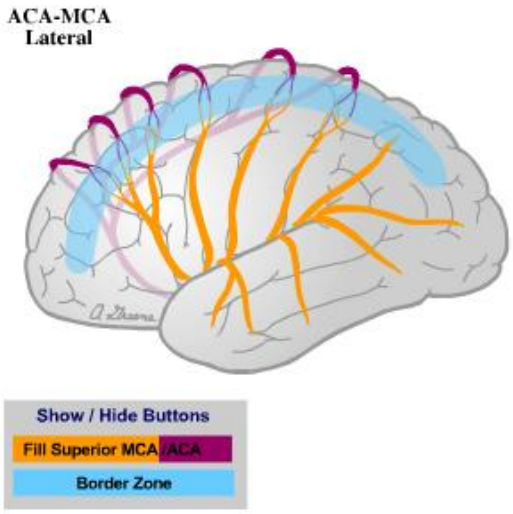
- In the cerebral hemispheres, the border zone between the anterior and the middle cerebral artery distributions is at greatest risk

- Damage to this region produces a band of necrosis over the cerebral convexity a few centimeters lateral to the interhemispheric fissure (between the two hemispheres)

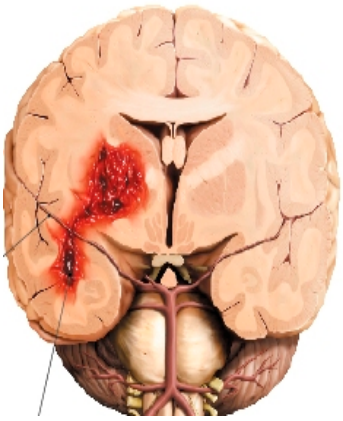
- Border zone infarcts are usually seen after hypotensive episodes.







Intracerebral hemorrhage:



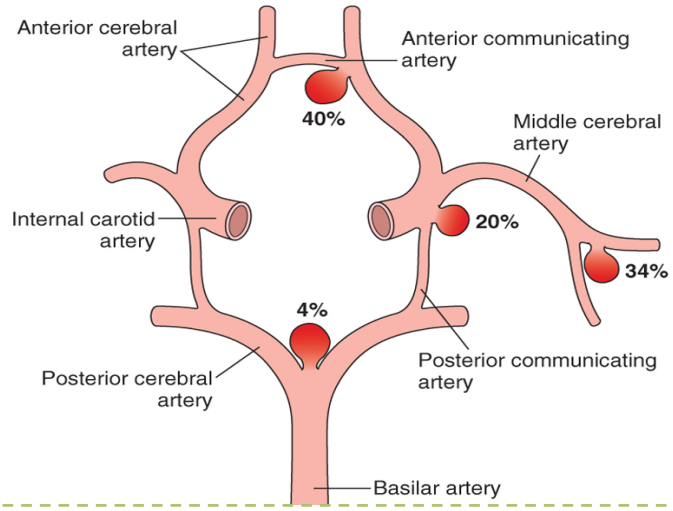
Hemorrhages within the brain(intracerebral)can occur secondary to:

- Hypertension
- Other forms of vascular wall injury (e.g. vasculitis like poly arthritis nodosa, aneyrsms, and aneurysms like berry (saccular) aneurysms)
- Arteriovenous malformation (abnormal connection between veins and arteries, abnormally rapid rate of blood flow frequently cause blood pressure inside the vessels)

Patients with aneurysms sometimes hear murmurs in their ears. Especially in young females , if the patient had a murmur and a headache also the aneurysm may be ruptured.

- An intraparenchymal tumor (if there is a tumor it may bleed for example, the glioblastoma , Where the vessels that undergo endothelial cell proliferation become weak may rupture and cause hemorrhage).

Hemorrhages associated with the dura (in either subdural or epidural spaces) make up a pattern associated with trauma (discussed in another lecture)

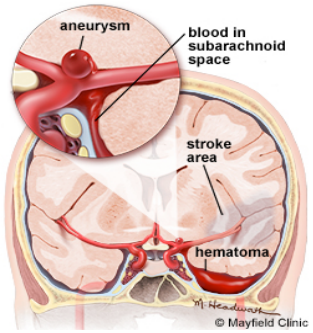


The rupture occur when an increase in blood pressure happens such as while exercising

Illustration showing common sites of berry (saccular) aneurysms. Note that about 90% of saccular aneurysms occur in the anterior circulation near major arterial branch points.

Most frequent side of this aneurysm-saccular- (40%) is between the anterior communicating and the anterior cerebral artery. And the least frequent is at the junction of the posterior cerebral arteries.

Subarachnoid Hemorrhage:



Causes of subarachnoid hemorrhage:

- Rupture of a saccular (berry) aneurysm (The most frequent cause significant) the patient is usually of young age and complains of a headache.
- vascular malformation
- trauma (in which case it is usually associated with other signs of the injury)
- rupture of an intracerebral hemorrhage into the ventricular system
- hematologic disturbances
- tumors

Berry Aneurysm happens in circle of Wiliis

- Rupture can occur at any time, but in about one-third of cases it is associated with acute increases in intracranial pressure, such as withstraining at stool or sexual orgasm
- Blood under arterial pressure is forced into the subarachnoid space, and individuals are stricken with sudden, excruciating headache (classically described as "the worst headache I've ever had") and rapidly lose consciousness
- Between 25% and 50% of individuals die with the first rupture, although those who survive typically improve and recover consciousness in minutes
- Recurring bleeding is common in survivors; itis currently not possible to predict which individuals will have recurrences of bleeding
- The prognosis worsens with each episode of Bleeding
- About 90% of saccular aneurysms occur in the anterior circulation near major arterial branch points
- mmultiple aneurysms exist in 20% to 30% of cases. Although they are 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, such that aneurysmsgreater than 10 mm have a roughly 50% risk of bleeding per year
- In the early period after a subarachnoid hemorrhage, there is a risk of additional ischemic injury from vasospasm involving other vessels (As the blood is lost other blood vessels constrict in order to prevent blood loss and that could cause ischemia in their regions)
- In the healing phase of subarachnoid hemorrhage, meningeal fibrosis and scarring occur, sometimes leading to obstruction of CSF flow as well ainterruption

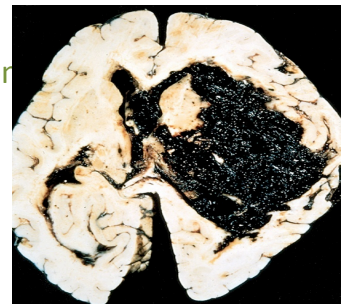
In general, hemorrhage is due to weakness of the vessel wall or due to aneurysm

of the normalpathways of CSF resorption complication diseases, like hydrocephalus and adhesions causing obstruction of the CSF pathway.

Hypertensive Cerebrovascular Disease:

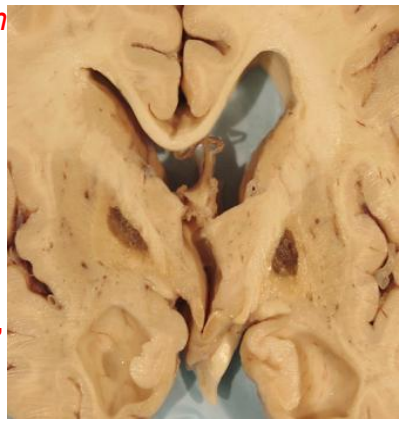
The most important effects of hypertension on the brain include:

- Massive hypertensive intracerebral hemorrhage (discussed earlier, most important)
- Lacunar (small spaces) infarcts .
- Slit hemorrhages (elongated opeing)
- Hypertensive encephalopathy (all the diseases from hypertension)



The latter three happen because of hyalinization of arteries and cause abr function of blood vessels

- Hypertension affects the deep penetrating arteries and arterioles that supply the basal ganglia and hemispheric white matter and the brain stem especially the pons.
- Hypertension causes several changes, including hyaline arteriolar sclerosis in arterioles weaker than are normal vessels and are more vulnerable to rupture
- In some instances, chronic hypertension is associated with the development of minute aneurysms in vessels that are less than 300 μm in diameter Charcot-Bouchard microaneurysms *(microaneurysms in th caused by hypertention).These aneurysms can easily rupture*



Examples on the hypertensive cerebrovascular diseases:

Lacunar infarcts:

- small cavitary infarcts

- most commonly in deep gray matter (basal ganglia and thalamus), internal capsule, deep white matter, and pons

- consist of cavities of tissue loss with scattered lipid-laden macrophages and surrounding gliosis

- depending on their location in the CNS, lacunes can either be clinically silent or cause significant neurologic impairment (two types : asymptomatic , symptomatic)

Slit hemorrhage:

- rupture of the small-caliber penetrating vessels and the development of small hemorrhages

• in time, these hemorrhages resorb, leaving behind a slit like cavity surrounded by brownish discoloration

Petechiae are Minute (1- to 2mm) Hemorrhages that are the smallest kind seen on skin and mucus Membranes

Fibrinoid necrosis is a special form of necrosis usually seen in immune reactions involving blood vessels (fibrin-like)

Acute hypertensive encephalopathy:

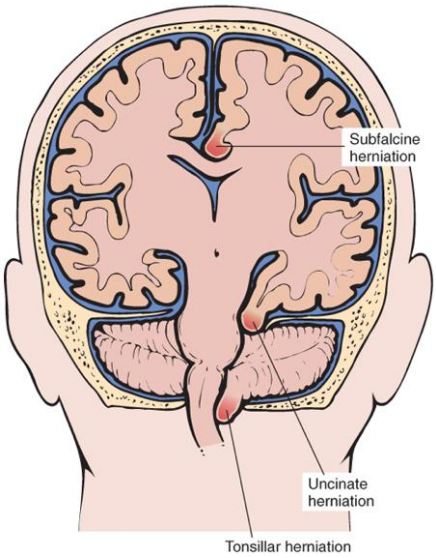
A clinicopathologic syndrome:

• Diffuse cerebral dysfunction, including headaches, confusion, vomiting, and convulsions, sometimes leading to coma

• Does not usually remit spontaneously

• May be associated with an edematous brain, with or without transtentorial or tonsillar herniation

This condition may cause sever pressure on certain parts by bones like the occulomotor nerve and the base of the brain. When the brain stem is pushed at the foramen magnum, this causes intense pressure on it where it can lead to damage to the respiratory and cardiac centers in the brain stem and then cardiorespiratory arrest and death.



Vasculitis:

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

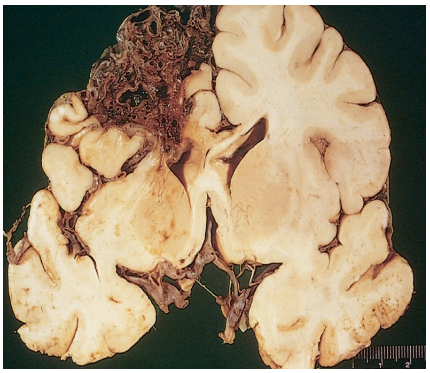
(such as toxoplasmosis, aspergillosis, and CMV encephalitis)

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



It is most dangerous and most important of the four types of vessel malformation that can occur in the vessels of the brain. It is twice common in males than in females. They are present clinically.

So what can cause or contribute to a stroke?

- Hypertension
- Athersclerosis
- Thrombophilia, e.g. Sickle cell anemia
- Embolic diseases
- Systemic hypoperfusion/ Global hypoxia, e.g. shock
- Vascular malformations
- Vasculitis

Amyloid deposition in the vessels greatly increases risk of rupture.
It can be seen when the tissue is stained with Congo Red .

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

Homework :

What are the risk factors of stroke?
Have been explained .

Define: Transient ischemic attack
**transient episode of neurologic dysfunction caused by* ischemia.
**Is when blood flow to a part of the*
brain stops for a brief period of time.

Questions:

The area which is less susceptible to focal ischemia is :
- a- Thalamus
- b- Basal ganglia
- c- Cerebral cortex
- d- Deep white matter

Which cell is present first in ischemia :
- a- Neutrophil
- b- Red neuron
- c- Macrophage
- d- Fibroblast

A young patient comes to the ER complaining of an extreme headache, mentioning that he has lost consciousness sometimes. He was diagnosed with subarachnoid hemorrhage. What is the most common cause:
- a- Arteriovenous malformation
- b- Tumor
- c- Hematologic disturbances
- d- Ruptured berry aneurysm

Small cavitary infarcts in the brain of a hypertensive patient are described as: a- Slits
- b- Lacunar infarcts
- c- Hypertensive encephalopathy
- e-liquefactive necrosis

A male with circulatory problems developed lacunar infarcts near the basal ganglia, what is the most likely cause of these infarcts?

a- hypertension
b- hypotension
c- trauma

A 35 year old male on anti coagulants travelled to Jeddah with friends and left his medication, later on, he developed weakness in his right arm and loss of vision. what is most likely cause for his symptoms?

a- Embolic stroke
b- Transient ischemic attack

leading cause to stroke?

a- atherosclerosis
b- arteriovanous malformation
c- hypertension
d- vasculitis

We used some of last year's team work , thanks for them