Vascular Diseases of the central Nervous System:

I. They are a major cause of death in the developed world and are the most prevalent cause of neurologic morbidity caused by pathologic processes involving the blood vessels.

II. The three main pathogenic mechanisms are: Thrombotic occlusion of vessels, Embolic occlusion of vessels, Vascular rupture.

III. The brain is a highly oxygen-dependent tissue that requires a continual supply of glucose and oxygen from the blood.

IV. Although it constitutes no more than 2% of body weight, the brain receives 15% of the resting cardiac output and is responsible for 20% of total body oxygen consumption.

V. cerebral blood flow normally remains stable over a wide range of blood pressure and intracranial pressure because of autoregulation of vascular resistance.

- According to pathophysiology and pathologic anatomy, cerebrovascular diseases are divided into two main processes:

A. Hypoxia, ischemia and infarction

B. Hemorrhage: accompanies rupture of vessels and leads to direct tissue damage as well as secondary ischemic injury.

- Stroke is the clinical designation applied to all of these conditions when symptoms begin acutely.
- If the brain hypo perfusion is sever it will result in ischemic brain death.

A. Hypoxia, ischemia, infarction:

➢ Hypoxia

The brain may be deprived of oxygen by two general mechanisms:

• Functional hypoxia, caused by a low partial pressure of oxygen (e.g., high altitude), impaired oxygen-carrying capacity (e.g., severe anemia, carbon monoxide poisoning), or toxins that interfere with oxygen use (e.g., cyanide poisoning).

هون السبب مش انه صار دمار للاوعيه الدمويه او اي اشي داخل الدماغ الدم الواصل الدماغ تمام لكن مافيه الكميه المناسبه لحاجة الدماغ من الاوكسجين

• Ischemia, either transient or permanent, due to tissue hypo perfusion, which can be caused by hypotension, vascular obstruction, or both هون صاراي اشي قلل الدم الواصل للدماغ

In terms to clinical presentation they vary from being acute like stroke or sever like brain death:

- The acute results :

▶ The most sensitive neurons to transient global ischemia are; مهمات ركزت عليهم

i. The pyramidal cells of the hippocampus (especially) CA1 neurons.

ii. Cerebellar purkinji cells.

iii. Pyramidal neurons in the cerebral cortex produces a pattern called pseudolaminar Necrosis.

	Stroke	Transient ischemic attack(TIA)	Global cerebral ischemia.
Generally اشياء حكتهم هي عن كل وحده	Acute in onset , sudden ,irreversible cerebral damage	Accumulative disorder ,no irreversible cerebral damage , emboli	No irreversible cerebral damage
Cause	Ischemia or hemorrhage	small emboli from the carotids or vertebrobasilar circulation	Widespread ischemic-hypoxic injury can occur in the setting of severe systemic hypotension, usually when systolic pressures fall below 50 mm Hg, as in cardiac arrest and shock.
Effected brain portion	Abrupt onset of focal or global neurological Symptoms.	Variable	Globally affecting the brain
Duration of signs and symptoms	The symptoms must continue for more than 24 hours	The neurologic symptoms resolve within 24 hours	The clinical outcome varies with the severity and duration of the insult
The result	There should be permanent damage to the brain	No irreversible tissue damage	When the insult is mild, there may be only a transient post ischemic confessional state, with eventual complete recovery.

- Brain death

- Other patients meet the clinical criteria for "brain death," including:

1. Evidence of diffuse cortical injury.(isoelectric, or "flat," electroencephalogram (EEG)2. And brain stem damage, including absent reflexes and respiratory drive.

On morphological appearance

- In the setting of global ischemia, the brain is swollen, with wide gyri and narrowed sulci.
- The cut surface shows poor demarcation between gray matter and white matter.

On histological appearance:

The histopathologic changes that accompany irreversible ischemic injury (infarction) are grouped into three categories	**Early changes**	**Subacute changes**	**Repair**
Time duration	occurring 12 to 24 hours after the insult	occurring at 24 hours to 2 weeks	seen after 2 weeks
Cellular event تابع للearly الخلايا الي رح تنصاب كمانastrocytes and oligodendroglia **After this, the reaction to tissue damage begins with infiltration of neutrophils**	microvacuolation, followed by cytoplasmic eosinophilia, and later nuclear pyknosis and karyorrhexis which is called acute neuronal cell change (red neurons)	necrosis of tissue, influx of macrophages, vascular proliferation, and reactive gliosis	removal of necrotic tissue and gliosis

➢Infarctions

	Border zone ("watershed") infarcts	Focal Cerebral Ischemia	Embolic infarctions	Thrombotic occlusions
Site of occurrence	occur in regions of the brain and spinal cord that lie at the most distal portions of cerebral hemispheres, the border zone between the anterior and the middle cerebral artery distributions is at greatest risk. Damage to this region produces a wedge-shaped band of necrosis over the cerebral convexity a few centimeters lateral to the interhemispheric fissure.rterial territories	The circle of Willis or cortical-leptomeningeal anastomoses can limit damage in some regions there is little if any collateral blood flow to structures such as the thalamus, basal ganglia, and deep white matter, are the once mostly affected which are supplied by deep penetrating vessels	Emboli tend to lodge where vessels branch or in areas of stenosis, usually caused by atherosclerosis	carotid bifurcation, the origin of the middle cerebral artery, and either end of the basilar artery

Cause	after hypotensive episodes	Cerebral arterial occlusion leads first to focal ischemia and then to infarction in the distribution of the compromised vessel The size, location, and shape of the infarct and the extent of tissue damage that results may be modified by collateral blood flow.	Cardiac mural thrombi are a frequent source of emboli; myocardial dysfunction, valvular disease, and atrial fibrillation are important predisposing factors. Thromboemboli also arise in arteries, most often from atheromatous plaques in the carotid arteries or aortic arch. Deep leg veins and fat emboli, usually following bone trauma.	Thrombotic occlusions causing small infarcts of only a few millimeters in diameter, so-called "lacunar infarcts," occur when small penetrating arteries occlude due to chronic damage, usually from long-standing hypertension

Infarcts can be divided into two broad groups all of which are caused by thrombotic occlusions:

	Nonhemorrhagic infarcts	Hemorrhagic infarcts
cause	result from acute vascular occlusions and may evolve into	There is reperfusion of ischemic tissue, either through collaterals or after dissolution of emboli
Morphological	✓ During the first 6 hours, the tissue is unchanged in appearance, but by 48 hours, the tissue becomes pale, soft, and swollen. ✓ From days 2 to 10, the injured brain turns gelatinous and friable, and the boundary between normal and abnormal tissue becomes more distinct as edema resolves in the adjacent viable tissue. ✓ From day 10 to week 3, the tissue liquefies, eventually leaving a fluid-filled cavity, which gradually expands as dead tissue is resorbed	Usually manifest as multiple, sometimes confluent, petechial hemorrhages. The microscopic picture and evolution of hemorrhagic infarction parallel those of ischemic infarction, with the addition of blood extravasation and resorption. In individuals with coagulopathies, hemorrhagic infarcts may be associated with extensive intracerebral hematomas.

Microscopically	The tissue reaction follows a characteristic sequence. After the first 12 hours, ischemic neuronal change (red neurons)) and cytotoxic and vasogenic edema appear. Endothelial and glial cells, mainly astrocytes, swell, and myelinated fibers begin to disintegrate.	During the first several days neutrophils infiltrate the area of injury, but these are replaced over the next 2-3 weeks by macrophages. Macrophages containing myelin or red blood cell breakdown products 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 cytoplasmic extensions.
		After several months, the striking astrocytic nuclear and cytoplasmic enlargement regresses. 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

B. Hemorrhage:

	Intracranial Hemorrhage	Cerebral Amyloid AngiopathyCAA	Subarachnoid Hemorrhage	Saccular Aneurysms	Brain Aneurysms
cause	Rupture of a small intraparenchymal vessel. Hypertension is the leading underlying cause, and brain hemorrhage accounts for roughly 15% of deaths among individuals with chronic hypertension	same amyloidogenic peptides as those found in Alzheimer disease deposit in the walls of medium- and small-caliber meningeal and cortical vessels.	rupture of a saccular(berry) aneurysm. vascular malformation, trauma, rupture of an intracerebral hemorrhage into the ventricular system, coagulopathies, and tumors.	In about one-third of cases, rupture of a saccular aneurysm occurs at the time of an acute increase in intracranial pressure. The aneurysms are not present at birth but develop over time because of underlying defects in the vessel media.	Other types of aneurysms include: 1. atherosclerotic aneurysm , mostly of the basilar artery 2. Mycotic aneurysms 3. Traumatic aneurysms 4. Dissecting aneurysm

Most affected site	basal ganglia, thalamus, pons, and cerebellum	the lobes of the cerebral cortex (lobar hemorrhages). CAA also results in small (<1 mm) cortical hemorrhages (microhemorrhages)	About 90% of saccular aneurysms occur in the anterior circulation near major arterial branch points ,multiple aneurysms exist in 20% to 30% of cases.		
Pathogeneses	Spontaneous (nontraumatic) intraparenchymal hemorrhages	Amyloid deposition weakens vessel walls and increases the risk for hemorrhages, which differ in distribution from those associated with hypertension.	In about one-third of cases, rupture of a saccular aneurysm occurs at the time of an acute increase in intracranial pressure. Blood under arterial pressure is forced into the subarachnoid space		
clinically	Clinically devastating when it affects large portions of the brain or extends into the ventricular system; alternatively, it can affect small regions	The amyloid confers a rigid, pipe-like appearance and stains with Congo red.	the patient is stricken with sudden, excruciating headache (known as a thunderclap headache, often		

	and be clinically silent.		described as “the worst headache I’ve ever had”) مهمه ركزت عليها and rapidly loses consciousness. Between 25% and 50% of affected individuals die from the first bleed, and recurrent bleeds are common in survivors.		

Hypertensive cerebrovascular diseases:

Hypertension causes hyaline arteriolar sclerosis of the deep penetrating arteries and arterioles that supply the basal ganglia, the hemispheric white matter, and the brain stem.
Affected arteriolar walls are weakened and are more vulnerable to rupture.
In some instances, minute aneurysms (Charcot-Bouchard microaneurysms) form in vessels less than 300 µm in diameter.
Effect of hypertension on the brain (other than Massive hypertensive intraparenchymal hemorrhage) include:
1. Lacunar infarcts

2. Slit hemorrhages

3. Acute hypertensive encephalopathy

	Lacunes or lacunar infarcts(Small cavity infarcts)	Slit hemorrhages	Hypertensive encephalopathy
Size and most affected areas	just a few millimeters in size, that are found most commonly in the deep gray matter (basal ganglia and thalamus), the internal capsule, the deep white matter, and the pons	development of small hemorrhages	
Cause and pathogeneses	They are caused by occlusion of a single penetrating branch of a large cerebral artery.	Hypertension can lead to rupture of the small caliber blood vessels and lead to development of small hemorrhages. With time these hemorrhages resorb leaving behind a slit-like spaces called slit hemorrhages.	arising in the setting of malignant hypertension. - Most often is associated with sudden sustained rises in diastolic blood pressure to greater than 130 mm Hg and characterized: A. By increased intracranial pressure due to loss of autoregulation and

			forceful over distention of blood vessels, leading to fluid extravasation (hydrostatic edema). B. Global cerebral dysfunction, manifesting as headaches, confusion, vomiting, convulsions, and sometimes coma. - Rapid therapeutic intervention to reduce the intracranial pressure is essential, because this syndrome does not remit spontaneously.

MICROSCOPICAL AND MACROSCOPICAL FEATURES

- Postmorteum examination shows edematous brain with or without trantentorial or tonsillar Herniations.

- Microscopic examination shows Fibrinoid necrosis and thrombosis of arterioles and capillaries ASSCOITAED with microinfarcts and microhemorrhages

Inflammatory processes that involve blood vessels:

A. Infectious vasculitis is common in the setting of immunosuppression and in opportunistic infection such as aspergillosis and CMV encephalitis.

B. Primary angiitis of the CNS:

- Is an inflammatory disorder that involves multiple small to medium-sized parenchymal and subarachnoid vessels.

- Characterized by chronic inflammation, multinucleated giant cells and destruction of the vessel wall.

C. Granulomas if present it called granulomatous angiitis of the central nervous system.

- Affected individuals may present with diffuse encephalopathy or multifocal clinical picture often with cognitive dysfunction.

- Patients improve with steroids or immunosuppressive therapy