CEREBROVASCULAR DISEASES

They are brain disorders caused by pathologic processes involving blood vessels.

three main pathogenic mechanisms are: (1) thrombotic occlusion, (2) embolic occlusion, and (3) vascular rupture.

Thrombosis and embolism have similar consequences for the brain: loss of oxygen and metabolic substrates, resulting in infarction or ischemic injury of regions supplied by the affected vessel.

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

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)

• **Ischemia:** either transient or permanent, due to tissue hypoperfusion, which can be caused by hypotension, vascular obstruction, or both.

Global Cerebral Ischemia

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.

The clinical outcome varies with the 1- severity and 2- duration of the insult.

Neurons are more susceptible to hypoxic injury than are glial cells, and the most susceptible neurons are the pyramidal cells of the hippocampus and Purkinje cells of the cerebellum.

In severe global cerebral ischemia, widespread neuronal death occurs, patients who survive often remain severely impaired neurologically.

MORPHOLOGY

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

Histopathologicaly: the changes that accompany infarction are grouped into three categories.

- **Early changes**: occurring 12 to 24 hours after the insult, include acute neuronal cell change (red neurons) Similar changes occur somewhat later in astrocytes and oligodendroglia. After this, the reaction to tissue damage begins with infiltration of neutrophils.

- **Subacute changes**, occurring at 24 hours to 2 weeks, include necrosis of tissue, influx of macrophages, vascular proliferation, and reactive gliosis.
- **Repair,** seen after 2 weeks, is characterized by removal of necrotic tissue and gliosis.

Border zone ("watershed") infarcts occur in regions of the brain and spinal cord that lie at the most distal portions of arterial territories. They are usually seen after hypotensive episodes. 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 wedge-shaped band of necrosis over the cerebral convexity a few centimeters lateral to the interhemispheric fissure.

Focal Cerebral Ischemia

Cerebral arterial occlusion leads first to focal ischemia and then to infarction in the distribution of the compromised vessel.

Collateral blood flow (e.g. circle of Willis) may modified: The size, location, and shape of the infarct and the extent of tissue damage that results. By contrast, there is little if any collateral blood flow to structures such as the thalamus, basal ganglia, and deep white matter, which are supplied by deep penetrating vessels.

Embolic infarctions are more common than thrombosis. 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.

The territory of the middle cerebral artery, is most frequently affected by embolic infarction. Emboli tend to lodge where vessels branch or in areas of stenosis, usually caused by atherosclerosis.

Thrombotic occlusions causing cerebral infarctions usually are superimposed on atherosclerotic plaques; common sites are the carotid bifurcation, the origin of the middle cerebral artery, and end of the basilar artery and may accompanied by distal embolization.

Lacunar infarcts: Thrombotic occlusions of small penetrating arteries due to chronic damage, (hypertension) causing small infarcts of only a few millimeters in diameter.

Classification of infarction: Infarcts can be divided into two broad groups:

1- ***Nonhemorrhagic infarcts*** result from acute vascular occlusions and may evolve into hemorrhagic infarcts when there is reperfusion of ischemic tissue, either through collaterals or after dissolution of emboli.

MORPHOLOGY

The macroscopic appearance of a nonhemorrhagic infarct evolves over time.

1- first 6 hours no tissue changed.

2- By 48 hours, the tissue becomes pale, soft, and swollen.

3- From days 2 -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.

4- day 10 - week 3, the tissue liquefies leaving a fluid-filled cavity.

Microscopically: the tissue reaction follows a characteristic sequence.

- Ischemic neuronal change (red neurons) and edema.
- Endothelial and glial cells swell, and myelinated fibers begin to disintegrate.
- Neutrophils infiltrate the area of injury, to be 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.

***2-Hemorrhagic infarcts*:** usually manifest as multiple, petechial hemorrhages. The microscopic picture and evolution of hemorrhagic infarction parallel those of ischemic infarction, with the addition of blood extravasation and resorption.

Intracranial Hemorrhage: Hemorrhages within the brain are caused by:

1) Hypertension and other diseases leading to vascular wall injury,

2) Structural lesions such as arteriovenous and cavernous malformations.

3) Tumors.

Subarachnoid hemorrhages most commonly are the result of ruptured aneurysms but also occur with other vascular malformations.

Subdural or epidural hemorrhages usually are associated with trauma.

Primary Brain Parenchymal Hemorrhage

Spontaneous (nontraumatic) intraparenchymal hemorrhages are most common in mid to late adult life. Most are due to the 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. Intracerebral hemorrhage can be clinically devastating when it

affects large portions of the brain or extends into the ventricular system; alternatively, it can affect small regions and be clinically silent.
Hypertensive intraparenchymal hemorrhages typically occur in the basal ganglia, thalamus, pons, and cerebellum. If the individual survives the acute event, gradual resolution of the hematoma ensues, sometimes with considerable clinical improvement.

MORPHOLOGY
In acute intracerebral hemorrhage, the extravasated blood compresses the adjacent parenchyma. With time, hemorrhages are converted to a cavity with a brown, discolored rim.
Microscopic examination, early lesions consist of clotted blood surrounded by edematous brain tissue containing neurons and glia displaying morphologic changes typical of anoxic injury.
Eventually the edema resolves, pigment- and lipid-laden macrophages appear, and proliferation of reactive astrocytes becomes visible at the periphery of the lesion.

Subarachnoid Hemorrhage: cause by

1- Rupture of a saccular (berry) aneurysm: it is the most frequent cause of clinically significant nontraumatic subarachnoid hemorrhage.
2- Other types of aneurysm e.g atherosclerotic, Mycotic, Traumatic and dissecting aneurysms.
3- Vascular malformation
4- Trauma,
5- Rupture of an intracerebral hemorrhage into the ventricular system,
6- Coagulopathies,
7- Tumors.

Saccular Aneurysms (berry)
In about one-third of cases, rupture of a saccular aneurysm occurs at the time of an acute increase in intracranial pressure, such as occurs with straining at stool or sexual orgasm. Blood under arterial pressure is forced into the subarachnoid space, and the patient is stricken with sudden, excruciating headache (known as a thunderclap headache) and rapidly loses consciousness. Between 25% and 50% of affected individuals die from the first bleed, and recurrent bleeds are common in survivors. About 90% of saccular aneurysms occur in the anterior circulation near major arterial branch points; multiple aneurysms exist in 20% to 30% of cases.

The aneurysms are not present at birth but develop over time because of underlying genetic defects in the vessel media.
There is an increased risk for aneurysms in patients with autosomal dominant polycystic kidney disease and genetic disorders of extracellular matrix proteins (e.g., Ehler-Danlos syndrome). The probability of rupture increasing with size. For example, aneurysms larger than 1 cm in diameter have a roughly 50% risk for bleeding per year. Atherosclerotic, mycotic, traumatic, and dissecting aneurysms also occur intracranially. The last three types (like saccular aneurysms) most often are found in the anterior circulation, whereas atherosclerotic aneurysms frequently are fusiform and most commonly involve the basilar artery.

Hypertensive Cerebrovascular Disease

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. The effect of hypertension on cerebral blood vessels are:

- Rupture: The walls of the affected arteriolar are weakened and are more vulnerable to rupture.
- Rupture of the small-caliber penetrating vessels may occur, leading to the development of small hemorrhages. In time, these hemorrhages resorb, leaving behind a slitlike cavity (slit hemorrhage) surrounded by brownish discoloration.
- Minute aneurysms (Charcot-Bouchard microaneurysms) form in vessels less than 300 μm in diameter.
- Lacunes or lacunar infarcts are small cavitary infarcts, 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. They are caused by occlusion of a single penetrating branch of a large cerebral artery. Depending on their location, lacunes can be silent clinically or cause significant neurologic impairment.
- Acute hypertensive encephalopathy most often is associated with sudden sustained increases in diastolic blood pressure to greater than 130 mm Hg. It is characterized by increased intracranial pressure and global cerebral dysfunction, manifesting as headaches, confusion, vomiting, convulsions, and sometimes coma.