PATHOLOGY

SHEET NO. 2

WRITER : Leen M. Hadidi

CORRECTOR : Hadeel Nidal Othman

DOCTOR : Dr. Maha Shomaf

CENTRAL NERVOUS SYSTEM TRAUMA

- Trauma to the brain and spinal cord is a significant cause of death and disability.
- Severity and site of injury affect the outcome. Injury of several cubic centimeters of brain parenchyma may be:
  - clinically silent (if in the frontal lobe).
  - severely disabling (spinal cord).
  -fatal (involving the brain stem).

- A blow to the head may be: penetrating or blunt, open or a closed injury.

- The magnitude and distribution of traumatic brain lesions depend on :
1-the shape of the object causing the trauma
2-the force of impact
3- whether the head is in motion at the time of injury

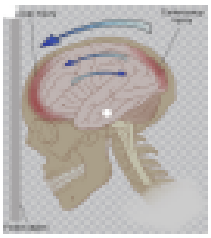
- Severe brain damage can occur in the absence of external signs of head injury.

- Severe lacerations and even skull fractures do not necessarily indicate damage to the underlying brain.

- In addition to skull or spinal fractures, trauma can cause :
  1-parenchymal injury.
  2-vascular injury.
  3-combinations of both.

- Traumatic **Parenchymal Injuries**, Types of brain injury :
  1- contusions.
  2- laceration.
  3- diffuse axonal injury.
  4- concussion.

#contusions[1]**:-** brain injury that occurs from collision of the brain with the skull **>>** at the site of impact (a **coup injury**), **or** on the opposite side (**contrecoup injury**) due to the pressure.



A contusion is caused by rapid tissue displacement, disruption of vascular channels, and subsequent hemorrhage, tissue injury, and edema.

- Since they are the points of impact, crests of gyri are most susceptible.
- The cerebral cortex along the sulci is less vulnerable .

The most common locations where contusions occur correspond to the most frequent sites of direct impact and to regions of the brain that overlie a rough and irregular inner skull surface, such as :

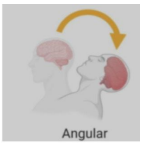
1-the frontal lobes. 2-the orbital gyri. 3-the temporal lobes.

#laceration:- penetration of the brain, either by a projectile such as a bullet or a skull fragment from a fracture.
- Occurs, with tissue tearing, vascular disruption, hemorrhage, and injury along a linear path.

[1] contusions happen when there is impact of an object with the head.

#diffuse axonal injury:-

• Although injury to the surface of the brain is often the most dramatic, widespread injury to axons within the brain can also happen.
• The movement of one region of the brain relative to another is thought to lead to the disruption of axonal integrity and function.
• Angular acceleration alone in the absence of impact may cause axonal injury as well as hemorrhage.



Video for angular acceleration:
https://youtu.be/Z6fImYkBeK0

• Diffuse axonal injury is characterized by the wide but often asymmetric distribution of axonal swellings that appears within hours of the injury and may persist for much longer. •
As many as 50% of patients who develop coma shortly after trauma, even without cerebral contusions, are believed to have white matter damage and diffuse axonal injury.
• Although these changes may be widespread, lesions are most commonly found near the angles of the lateral ventricles and in the brain stem.
Some neurons may be affected more than others depending on the force direction.

#Concussion:- describes reversible altered consciousness from head injury in the absence of contusion.
• The characteristic transient neurologic dysfunction includes :
1-loss of consciousness.
2-temporary respiratory arrest.
3-loss of reflexes.
Although neurologic recovery is complete, amnesia for the event persists. not important *for amnesia:Youtube
The pathogenesis of the sudden disruption of nervous activity is unknown.

- Traumatic **Vascular Injury** :

Vascular injury:- is a frequent component of CNS trauma and results from direct trauma and disruption of the vessel wall, leading to hemorrhage.
(The treatment might prevent the development of permanent damage to the parenchyma).
Depending on which vessels rupture, hemorrhage may occur in any of several compartments:

1- epidural
2- subdural.
3- subarachnoid.
4- intra-parenchymal

Subarachnoid and intraparenchymal hemorrhages most often occur at sites of contusions and lacerations.

Epidural Hematoma

- The dura is normally tightly applied to the inside of the skull fused with the periosteum.
- Vessels that run in the dura most importantly **the middle meningeal artery** are vulnerable to injury particularly with skull fractures.

- In children in whom the skull is deformable, a temporary displacement of the skull bones may tear a vessel in the absence of a skull fracture.
- Once a vessel has been torn, the accumulation of blood under arterial pressure can cause separation of the dura from the inner surface of the skull.
- The expanding hematoma has a smooth inner contour that **compresses the brain surface**.
- Clinically, patients can be lucid for several hours between the moment of trauma and the development of neurologic signs.
- An epidural hematoma may expand rapidly and is a **neurosurgical emergency** requiring prompt drainage>> to release pressure.

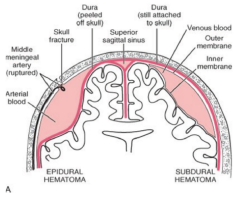
Subdural Hematoma

- The rapid movement of the brain that occurs in trauma can tear **the bridging veins** that extend from the cerebral hemispheres through the subarachnoid and subdural space to empty into dural sinuses.
- These vessels are particularly prone to tearing, and their disruption leads to bleeding into the subdural space.
- **Risk factors**:-

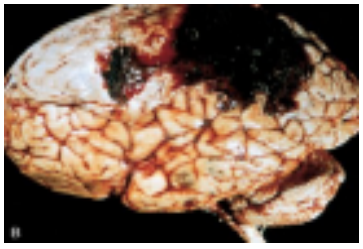
1. **In elderly** patients with **brain atrophy** the bridging veins are stretched out and the brain has additional space for movement, accounting for the higher rate of subdural hematomas in these patients, even after relatively minor head trauma.
2. **Infants** are also susceptible to subdural hematomas because their bridging veins are thin walled. We have a syndrome that can cause subdural hematoma in infants>> shaking baby syndrome.

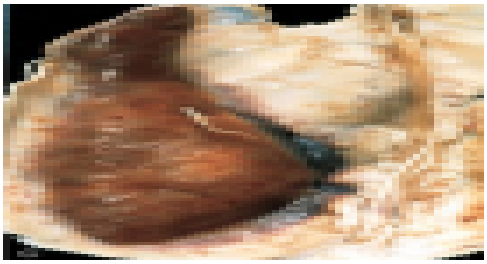
• Subdural hematomas most often become manifest within the first 48 hours after injury.
• They are most common over the **lateral aspects of the cerebral hemispheres**, bilateral in about 10% of cases.

• Neurologic signs are attributable to the pressure exerted on the adjacent brain. • These may be focal, but often the clinical manifestations are nonlocalizing and include headache or confusion.
• In time there may be slowly progressive neurologic deterioration, rarely with acute decompensation.



Gross appearance of epidural hematoma. (B)





Gross appearance of the clot in subdural hematoma. (C)

CEREBROVASCULAR DISEASES

Any abnormality of the brain caused by a pathologic process involving blood vessels.

• The three basic processes are : (1) thrombotic occlusion of vessels.

(2) embolic occlusion of vessels. (3) vascular rupture.
* Thrombosis and embolism cause ischemic injury or infarction of specific regions of the brain, depending on the vessel involved. A similar pattern of injury occurs diffusely when there is complete loss of perfusion (or delivery of oxygen and metabolic substrate).

• The first two share many characteristics, because their effect on the brain is the same >> **loss of oxygen and metabolic substrates resulting in brain infarction**.
• Hemorrhage accompanies rupture of vessels, leading to direct tissue damage as well as **secondary ischemic injury**.
• "**Stroke**" is the clinical designation that applies to **all these conditions**, particularly when symptoms begin acutely. It's a totally clinical term which describes the presence of a vascular problem without defining the exact disease.

Hypoxia, Ischemia, and Infarction

- The brain requires a constant delivery of glucose and oxygen from the blood.
- Although the brain accounts for only 1% to 2% of body weight, it receives **15% of the resting cardiac output** and accounts for **20% of the total body oxygen consumption**.
- Cerebral blood flow remains **constant** over a wide range of blood pressure and intracranial pressure because of autoregulation of vascular resistance. The brain is a highly aerobic tissue, with oxygen being the limiting substance.
- Neurons can't stand the state of hypoxia.

In a chemical reaction, the limiting reagent, or limiting reactant, is the substance that has been completely consumed when the chemical reaction is complete. *google*

The brain may be deprived of oxygen by any of several mechanisms:

1-functional hypoxia in a setting of : a- A low partial pressure of oxygen

b- Impaired oxygen-carrying capacity-anemia-.

c- Inhibition of oxygen use by tissue.

2-**ischemia:** a- Transient. b- Permanent.

Cessation of blood flow can result from:
1- Reduction in perfusion pressure, as in hypotension.
2- Secondary to vascular obstruction.
3- Both .

Global Cerebral Ischemia

• widespread ischemic/hypoxic injury occurs when there is a generalized reduction of cerebral perfusion, usually below systolic pressures of less than 50mmHg, such as in:
1-cardiac arrest. 2-shock. 3-severe hypotension.

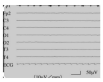
#Clinical manifestation:-
• The clinical outcome varies with the severity of the insult,
a- when mild >> there may be only a transient postischemic confusional state, with eventual **complete recovery**. However, Irreversible damage of CNS tissue does occur in some individuals who suffer mild or transient global ischemic insults.
• **Neurons are much more sensitive to hypoxia than are glial cells.**

• **There is also variability in the susceptibility of different populations of neurons in different regions of the CNS.**

• The most susceptible cells to ischemia of short duration are :
1-pyramidal cells of the Sommer sector (CA1) of the hippocampus.
2-Purkinje cells of the cerebellum.
3-pyramidal neurons in the neocortex.

b- In severe global cerebral ischemia, **widespread neuronal death** irrespective of regional vulnerability occurs.
Individuals who survive in this state often remain severely impaired neurologically and deeply comatose (**persistent vegetative state**).

a test or record of brain activity, flat on EEG indicates an irreversible coma.

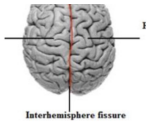


• The clinical criteria for "**brain death**" include:
1-evidence of diffuse cortical injury
(isoelectric, or "flat," electroencephalogram).
2-brain stem damage including absent reflexes and respiratory drive.

• When patients with this pervasive form of injury are maintained on mechanical ventilation, the brain gradually undergoes an **autolytic process**, resulting in the so-called "**respirator brain**."

Border zone ("watershed") infarcts :you can find this term in other organs such as the GI tract. What is watershed area:- https://youtu.be/Ii9ygvAf5a8
• are 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.
*ischemic lesions that occur in characteristic locations at the junction between two main arterial territories.

• 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.
Border zone infarcts are usually seen after hypotensive episodes.



Focal Cerebral Ischemia

• Cerebral arterial occlusion leads to focal ischemia and -if sustained- to infarction of CNS tissue in the distribution of the compromised vessel.
• The size, location, and shape of the infarct and the extent of tissue damage that results are determined by modifying variables, most importantly **the adequacy of collateral flow**. • The major source of collateral flow is the **circle of Willis**.
• Partial collateralization is also provided over the surface of the brain through **cortical leptomeningeal anastomoses**.
• In contrast, there is little if any collateral flow for the deep penetrating vessels supplying structures such as the thalamus, basal ganglia, and deep white matter

Brain infarction

Occlusive vascular disease of severity sufficient to lead to cerebral infarction may be due to : 1-in situ **thrombosis**. 2-**embolization** from a distant source. *Overall, embolic infarcts are more common*
thrombus start at rough surfaces so the inner lining of the circulation very important

• predisposing factors :
1-Cardiac mural thrombi are a frequent source
2-myocardial infarct >> because of the relaxation of the heart and the stagnation of the blood. 3-valvular disease
4-atrial fibrillation >>because of the stagnation of the blood.

• Thromboemboli arise in:
1-atheromatous plaques within the carotid arteries.
2-paradoxical emboli particularly in children with cardiac anomalies. *Paradoxical Embolism (PDE) occurs when a thrombus crosses an intracardiac defect into the systemic circulation.
3-emboli associated with cardiac surgery.
4-emboli of other material (tumor, fat, or air).

• Common sites of embolization :
1-The territory of distribution of the middle cerebral artery *the direct extension of the internal carotid artery* is most frequently affected by embolic infarction.
2-Emboli tend to lodge where vessels branch or in areas of preexisting luminal stenosis.

The majority of thrombotic occlusions causing cerebral infarctions are due to atherosclerosis. Atherosclerotic stenosis can develop superimposed thrombosis, accompanied by anterograde extension, fragmentation, and distal embolization.
• the most common sites of primary thrombosis are :
1-the carotid bifurcation.
2-the origin of the middle cerebral artery.
3-at either end of the basilar artery.

• Infarcts can be divided into two broad groups based on their macroscopic and corresponding radiologic appearance :
1-**Non Hemorrhagic infarcts.**
Can be treated with thrombolytic therapies, if identified shortly after presentation. Usually related to ischemia.
2-**Hemorrhagic infarcts.**
Multiple, sometimes confluent, petechial hemorrhages.
The hemorrhage occurs secondary to reperfusion of ischemic tissue, either through collaterals or after dissolution of intravascular occlusions.

Intracranial Hemorrhage

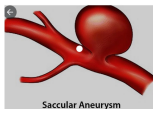
• Hemorrhage within the skull can occur in a variety of locations, and each location is associated with a set of underlying causes.

• Hemorrhages within the brain itself can occur secondary to :
1-hypertension or other forms of vascular wall injury.
2-arteriovenous malformation.
3-cavernous malformation.
4-intraparenchymal tumor.

Subarachnoid hemorrhages are most commonly seen with **aneurysms (berry aneurysm)**but occur also with other vascular malformations.

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

Primary Brain Parenchymal Hemorrhage>> spontaneous (**non traumatic**) intraparenchymal hemorrhages occur most commonly in mid to late adult life, with a peak incidence at about 60 years of age.



- Most are caused by **rupture of a small intraparenchymal vessel>> Hypertension** is the most common underlying cause.
- Brain hemorrhage accounts for roughly 15% of deaths among individuals with chronic hypertension.

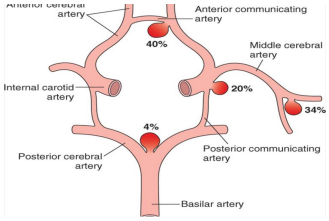
• Hypertensive intraparenchymal hemorrhages typically occur in the :
1-basal ganglia. 2-thalamus. 3-pons. 4-cerebellum .

Clinical manifestations

- The location and size of the bleed will determine the clinical manifestations.
- Intracerebral hemorrhage can be clinically devastating when it affects large portions of the brain and extends into the ventricular system.
- It can affect small regions and be clinically silent.
- Over weeks or months there is a gradual resolution of the hematoma, sometimes with considerable clinical improvement.

Subarachnoid Hemorrhage and Saccular Aneurysms

• Causes :
1-rupture of a saccular (berry) aneurysm. *The most frequent cause of clinically significant subarachnoid hemorrhage*
2- vascular malformation.
3- trauma.
4- rupture of an intracerebral hemorrhage into the ventricular system.
5- hematologic disturbances and tumors.



Clinical manifestations

- Rupture can occur at any time, but in about 1/3 of cases it is associated with acute increases in intracranial pressure (as with straining at stool).
- 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%-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**. *It is currently not possible to predict which individuals will have recurrences of bleeding*

- The prognosis worsens with each episode of bleeding.

- Aneurysms have a roughly 1.3% per year rate of bleeding.
- The probability of rupture increases with the size of the lesion, such that aneurysms greater than 10 mm have a roughly 50% risk of bleeding per year.
- About 90% of saccular aneurysms occur in the anterior circulation near major arterial branch points.
- multiple 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. *it's not congenital*

- **In the early period** after a subarachnoid hemorrhage, there is a risk of additional ischemic injury from vasospasm involving other vessels.
- **In the healing phase** of subarachnoid hemorrhage, meningeal fibrosis and scarring occur, sometimes leading to obstruction of CSF flow as well as interruption of the normal pathways of CSF resorption.

Hypertensive Cerebrovascular Disease

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

1- massive hypertensive intracerebral hemorrhage.
2- lacunar infarcts.
3- slit hemorrhages.
4- hypertensive encephalopathy.

Remember: Hypertension affects the deep penetrating arteries and arterioles that supply the basal ganglia and hemispheric white matter as well as the brain stem.

#Hypertension causes several changes including:
1- hyaline arteriolar sclerosis in arterioles.*Arteriolar walls affected by hyaline change are weaker than are normal vessels and are more vulnerable to rupture.*
2-development of minute aneurysms in vessels that are less than 300 µm in diameter(**Charcot Bouchard microaneurysms**) which can rupture.

Lacunar infarcts Not mentioned by the doctor

- An important clinical and pathologic outcome of arteriolar sclerosis is the development of lacunes or lacunar infarcts.
- These small cavitary infarcts are just a few millimeters wide (<15 mm).
- They are found most commonly in deep gray matter (basal ganglia and thalamus), internal capsule, deep white matter, and pons. -depending on their location in the CNS, lacunae can either be clinically silent or cause significant neurologic impairment-.

Slit hemorrhages Not mentioned by the doctor

- Hypertension also gives rise to rupture of the small-caliber penetrating vessels and the development of small hemorrhages.
- In time, these hemorrhages resorb, leaving behind a slit-like cavity (slit hemorrhage) surrounded by brownish discoloration.

Hypertensive encephalopathy

- Acute hypertensive encephalopathy is a clinicopathologic syndrome **characterized by diffuse cerebral dysfunction** including:
- 1- headaches.
- 2- confusion.
- 3- vomiting.
- 4- convulsions, sometimes leading to coma.
- Rapid therapeutic intervention to reduce the accompanying increased intracranial pressure is required, since the syndrome does not usually remit spontaneously.