# PATHOLOGY

SHEET NO. 1

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بسم الله الرحمن الرحيم

**Basic info** 😬

***Diseases that affect the brain are always serious because the condition may leave a permanent damage of the central nervous system.**

***Central nervous system is composed of two parts:**

**1.central part: a.brain b.spinal cord**

**2.peripheral part: related to the peripheral nerves**

***Diseases that affect each part might be specific or it can be the same process that affect both**

***Functional unit of the CNS is the NEURON ( that doesn't mean it's the only cell there, there are other types of cells that are as important as neurons which have a very vital function supporting the neurons and the normal function of the brain )**

*** Neurons of different types and in different locations have distinct properties including functional roles, distribution of their connections, neurotransmitters used, metabolic. requirements,and levels of electrical activity at a given moment.**

*** Since different regions of the brain participate in different functions, the pattern of clinical signs and symptoms that follow injury depend as much on the region of brain involved as on the pathologic process.**

*** Mature neurons are incapable of cell division and thats why loss of neurons ia a permanent thing ,so destruction of even a small number of neurons essential for a specific function may leave the individual with a neurologic deficit.**

*** In addition to neurons to neurons the CNS contains other cells, such as *astrocytes* and *oligodendrocytes*, which make up the glia.**

# Features of Neuronal Injury.

In response to injury(any stress condition), a number of changes occur in neurons and their processes both axons and dendrites.
*if we examine a brain for a patient within short period of time after death, the changes might not be present. The features and changes start 12 hours after the injury and usually they are obvious and clear after 24 hours.
Within 12 hours of an irreversible hypoxic-ischemic insult, acute neuronal injury becomes evident on routine hematoxylin and eosin (H&E) staining.
Using electron microscopy changes may appear before that but we don't use it.

**The features: [10:00]**

- **1.There is shrinkage of the cell body**

- **2. Pyknosis(clumping of nuclear materiel ,becoming dense in colour, irregular in shape,smaller in size , it can be lost or fragmented) of the nuclei**

- **3. Disappearance of the nucleolus (they are very appearance in normal conditions)**

- **4. Loss of Nissl substance *part of the rough endoplasmic reticulum the site of protein synthesis* with intense eosinophilia of the cytoplasm ("red neurons")**

- **5. The nuclei assumes the angulated shape of the shrunken cell body**

- **6. Injured axons undergo swelling and show disruption of axonal transport**

- **7. The swellings (spheroids) can be recognized on H&E stains and can be highlighted by silver staining or immunohistochemistry.**

- **8. Cell body enlargement and rounding, peripheral displacement of the nucleus, enlargement of the nucleolus, and peripheral dispersion of Nissl substance (central chromatolysis)**

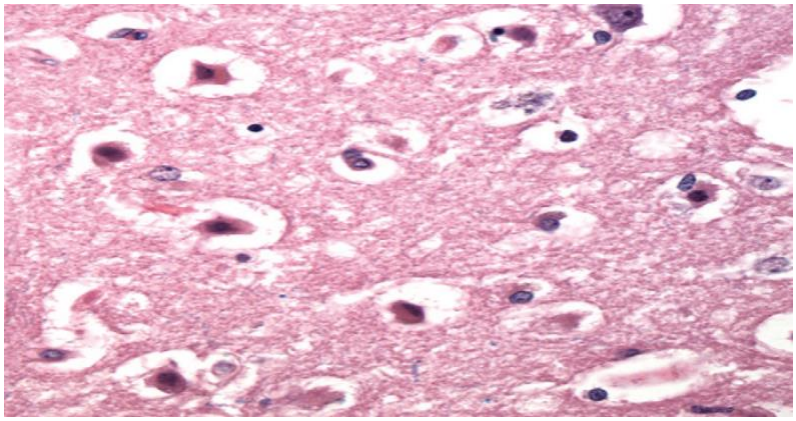
- **9. Acute injuries typically result in breakdown of the blood-brain barrier and variable degrees of cerebral edema. (bbb is very important to keep the normality of the brain )**
  ***Destruction of the bbb is associated with the exposure of the tissue to more substances that may be injurious.**

•**10.Many neurodegenerative diseases are associated with specific intracellular inclusions (e.g., Lewy bodies in Parkinson disease and tangles in Alzheimer disease)**

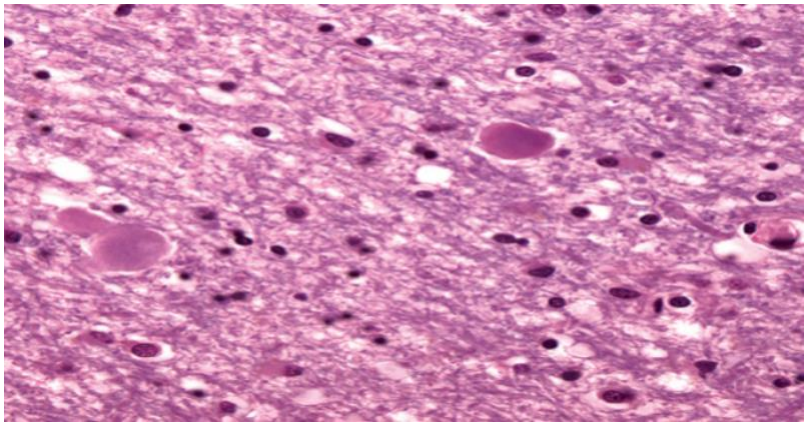
•**11.Pathogenic viruses can also form inclusions in neurons (intranuclear inclusion) like in cytomegalovirus**
•**just as they do in other cells of the body**

•**12. In some neurodegenerative diseases, neuronal processes also become thickened and tortuous (dystrophic neurites)**

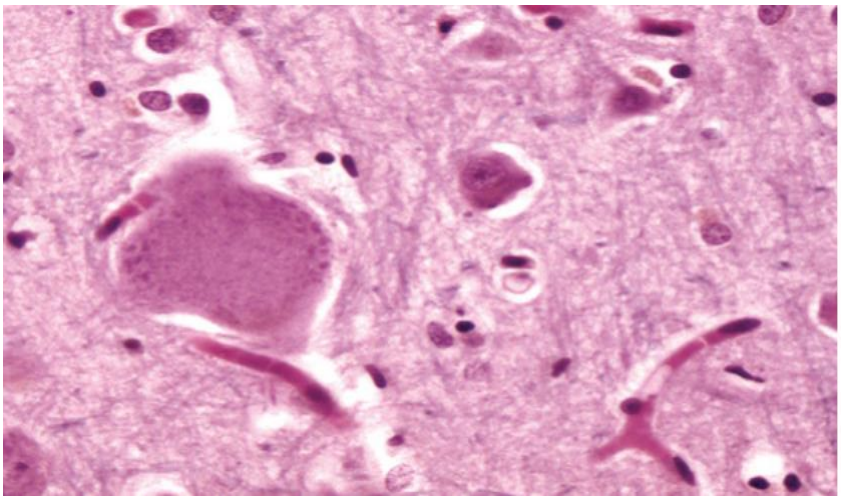
•**13. Neurons also accumulate complex lipids (lipofuscin) in their cytoplasm and lysosomes.(because of the destruction of the cellular membrane) presence of these always indicates a previous exposure to an injurious agent.**



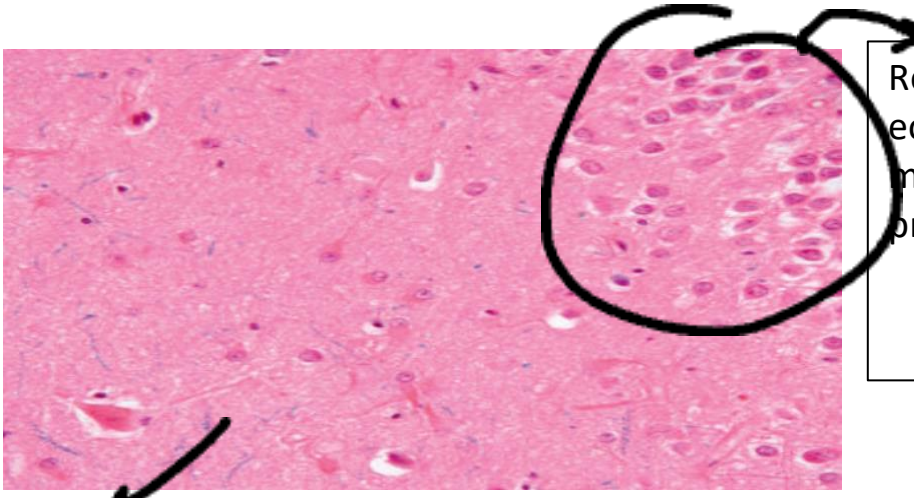
Acute hypoxic-ischemic injury in cerebral cortex, where the individual cell bodies are shrunken, along with the pyknotic nuclei and prominent staining of the cytoplasm by eosin (red neurons)



Axonal spheroids are visible as bulbous swellings at points of disruption or altered axonal transport



Chromatolysis:Swelling of the cell body and peripheral dispersal of the Nissl substance




Reactive astrocytes, with eosinophilic cytoplasm and multiple radiating processes

## Astrocytes in Injury and Repair

Astrocytes are the principal cells responsible for repair and scar formation in the brain, a process termed **gliosis**. (they have an important role to react to the injury because neural cells cannot divide and compensate the loss so the astrocyte come to deal with the process)

In response to injury, astrocytes undergo both **hypertrophy** and **hyperplasia**.

The nucleus enlarges and becomes vesicular, and the nucleolus becomes prominent. The previously scant cytoplasm expands and takes on a bright pink hue, and the cell extends multiple stout, ramifying processes (gemistocytic astrocyte).

***gemisto astrocyte isn't only seen in injured places ,also it can be presented in some tumors like glioblastoma.**

Fibroblasts participate in healing after brain injury to a limited extent except in specific settings (penetrating brain trauma or around abscesses).
In longstanding gliosis, the cytoplasm of reactive astrocytes shrinks
in size and the cellular processes become more tightly interwoven **(fibrillary astrocytes).**
**Rosenthal fibers** are thick, elongated, brightly eosinophilic protein aggregates found in astrocytic processes in chronic gliosis and in some low-grade gliomas
*when we have injury at the brain we need to examine the tissue and be so careful because there's an overlap between the reaction of the cells to the injury and to the tumor. (fibrillary astrocytes and Rosenthal fibers both can be seen in injuries and tumors)

# Changes in Other Cell Types

## 1.Oligodendrocytes

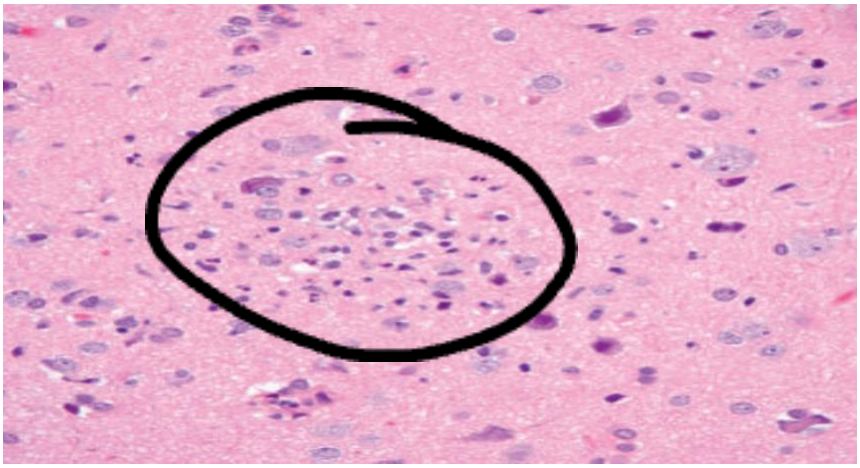
Oligodendrocytes produce myelin
Exhibit a limited spectrum of specific morphologic changes in response to various injuries.
In progressive multifocal leukoencephalopathy, viral inclusions can
be seen in oligodendrocytes, with a smudgy, homogeneous appearing enlarged nuclei.

## 2.Microglial cells

Bone-marrow–derived cells , small in size
Phagocytes of the CNS
When activated by tissue injury, infection, or trauma, they proliferate and become more prominent histologically.
Microglial cells take on the appearance of activated macrophages in areas in the following conditions:

1.Demyelination
2.Organizing infarct (infarct results in cell death or necrosis). [20:00]
3.Hemorrhage
4.In neurosyphilis(an advanced stage of infection) or other infections, they develop elongated nuclei **(rod cells)**

Microglial cells at sites of tissue injury are termed **microglial nodules.**
Similar collections can be found congregating around and phagocytosing injured neurons **(neuronophagia).**



Collection of microglial cells forming
a poorly defined nodule, a common finding in viral infections

## 3.Ependymal cells

line the ventricular system and the central canal of the spinal cord.
Certain pathogens, particularly cytomegalovirus (CMV), can produce extensive ependymal injury and tumors, with typical viral inclusions because they are lining the ventricles so usually the abnormality of these cells is manifested by hydrocephalus.

## 4.Choroid plexus

Is in continuity with the ependyma (which is the lining epithelium), and its specialized epithelial covering is responsible for the secretion of cerebrospinal fluid (CSF).

(22:48)

## EDEMA, HERNIATION, AND HYDROCEPHALUS

The brain and spinal cord exist within the protective and rigid skull and spinal canal, with nerves and blood vessels passing through specific foramina.
The advantage of housing the delicate CNS within such a protective environment is obvious, but this arrangement provides little room for brain parenchymal expansion in disease states.
Disorders that may cause dangerous increases in brain volume within the fixed space of the skull include:

1.Generalized cerebral edema
2.Hydrocephalus
3.Mass lesions such as tumors.

# Cerebral Edema

Cerebral edema is the accumulation of excess fluid within the brain parenchyma.

2 types of edema:

## 1.Vasogenic edema

occurs when the integrity of the normal blood-brain barrier is disrupted, allowing to shift from the vascular compartment into the extracellular spaces of the brain.

- Vasogenic edema can be: (depending in the underlying cause )

1. Localized (e.g., increased vascular permeability due to inflammation or in tumors)
2. Generalized

## 2. Cytotoxic edema

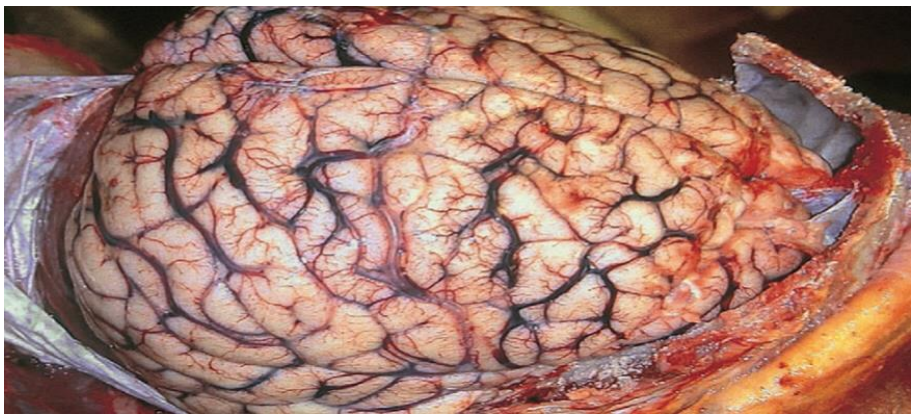
An increase in intracellular fluid secondary to neuronal and glial cell membrane injury as:

1. generalized hypoxic-ischemic
2. exposure to some toxins.

Present of edema within the brain without an obvious underlying cause you should think of cytotoxic edema.

**The edematous brain is softer than normal and often appears to "over fill" the cranial vault.**

**In generalized edema the gyri are flattened, the intervening sulci are narrowed, and the ventricular cavities are compressed**



Cerebral edema

**The surfaces of the gyri are flattened as a result of compression of the expanding brain by the dura mater and inner surface of the skull**

# Hydrocephalus

After being produced by the choroid plexus within the ventricles, CSF circulates through the ventricular system and flows through the foramina of Luschka and Magendie into the subarachnoid space where it is absorbed by arachnoid granulations.
The balance between rates of generation and resorption regulates CSF volume.

**Hydrocephalus: is the accumulation of excessive CSF within the ventricular system.**
It is the consequence of:

1.Impaired flow or resorption
2.Overproduction of CSF, typically seen with tumors of the choroid plexus, only rarely causes hydrocephalus.

3 types of hydrocephalus:

## 1. Noncommunicating hydrocephalus

**If there is a localized obstacle to CSF flow within the ventricular system, then a portion of the ventricles enlarges while the remainder does not.**
**Most commonly is caused by masses (like tumers) obstructing the foramen of Monro or compressing the cerebral aqueduct.**

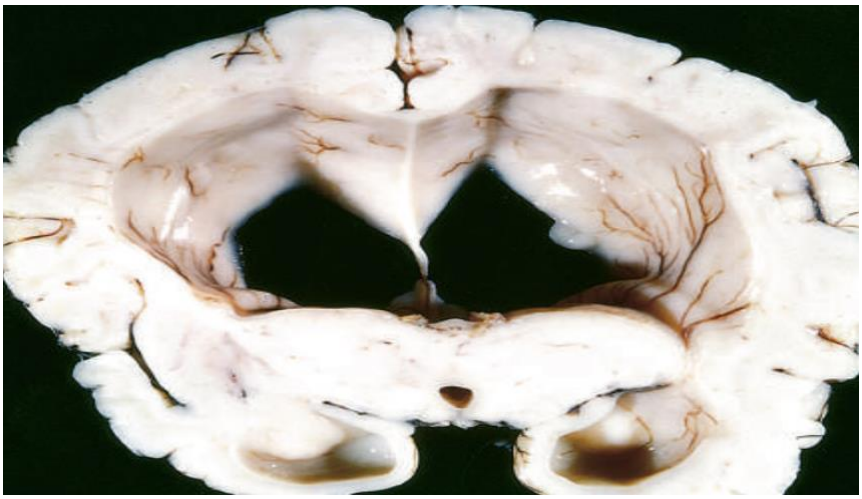
## 2. Communicating hydrocephalus

**The entire ventricular system is enlarged**
**It is usually caused by reduced CSF resorption**

## 3. hydrocephalus ex vacuo

**A compensatory increase in CSF volume following the loss of brain parenchyma as after infarcts or with degenerative diseases.**
**[30:00]**

*If hydrocephalus develops in infancy before closure of the cranial sutures the head enlarges. (in adulthood there is no space to increase in the size the only way is dilation to the ventricles)Once the sutures fuse hydrocephalus causes ventricular expansion and increased intracranial pressure, but with no change in head circumference.



**Hydrocephalus**
**Dilated lateral ventricles seen in a coronal section through the mid-thalamus**

dilatation → pressure → loss of function

## Herniation (displacement part of the brain to another site)

**It occurs when the volume of tissue and fluid inside the skull increases beyond the limit permitted by compression of veins and displacement of CSF resulting in increase in intracranial pressure**
**The cranial vault is subdivided by rigid dural folds (falx and tentorium), and a focal expansion of the brain displaces it in relation to these partitions.**
**If the expansion is sufficiently large, herniation occurs.**
**Herniation often leads to "pinching" and vascular compromise of the compressed tissue, producing infarction, additional swelling, and further herniation.(the herniated part will be swollen because the vessels are compressed so the absorption of fluid is going to be compromised )**

edema → herniation

**3 types of herniation:**

## 1. Subfalcine (cingulate) herniation:

**It occurs when unilateral or asymmetric expansion of a cerebral hemisphere displaces the cingulate gyrus under the edge of falx.(flax is part of the brain membrane)**

**This may be associated with compression of the anterior cerebral artery so any area supplied by the vessel can be affected.**

## 2. Transtentorial (uncinate) herniation

**Occurs when the medial aspect of the lobe is compressed against the free margin of the tentorium.**

**As the temporal lobe is displaced the third cranial nerve is compromised resulting in pupillary dilation and impaired ocular movements on the side of the lesion ("blown pupil") or loss of vision.**

**The posterior cerebral artery may also be compressed resulting in ischemic injury to tissue supplied by that vessel, including the primary visual cortex.**

**If the amount of displaced temporal lobe is large enough the pressure on the midbrain can compress the contralateral cerebral peduncle against the tentorium resulting in hemiparesis ipsilateral to the side of the herniation, so-called false localizing sign.**

**The compression of the peduncle creates a deformation known as : Kernohan's notch.**

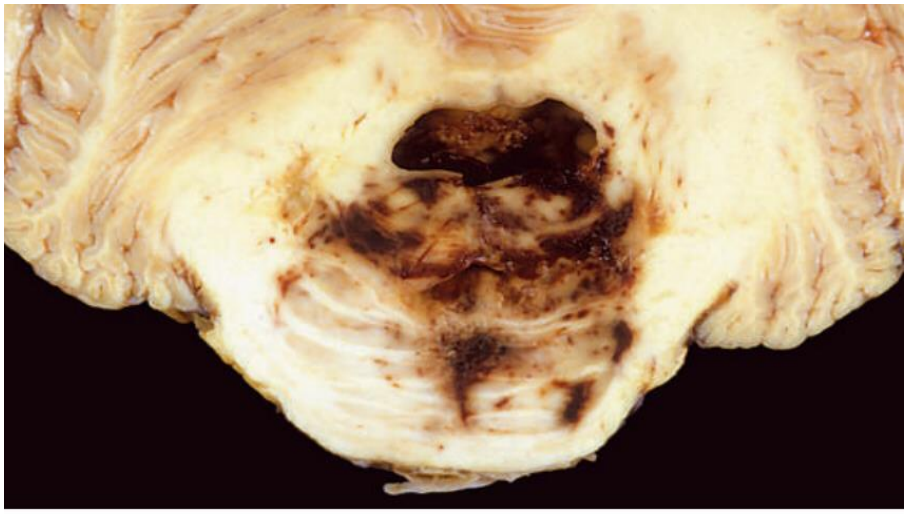
**Progression of transtentorial herniation is often accompanied by linear or flame-shaped hemorrhages in the midbrain and pons, termed *Duret hemorrhages* due to involvement of the small veins that can be torned during the herniation**

**These lesions usually occur in the midline and paramedian regions and are believed to be the result of tearing of penetrating veins and arteries supplying the upper brain stem.**

## 3. Tonsillar herniation (the most serious type)

**It refers to displacement of the cerebellar tonsils through the foramen magnum and it's a narrow foramen that's why if any brain substance restrict in this area, compression will occur**

**This type of herniation is life-threatening, because it causes brain stem compression and compromises vital respiratory and cardiac centers in the medulla.**



**Duret hemorrhage**
**As mass effect displaces the brain downward there is disruption of the vessels that enter the pons along the midline leading to hemorrhage**