PATHOLOGY

LECTURE NO. 1

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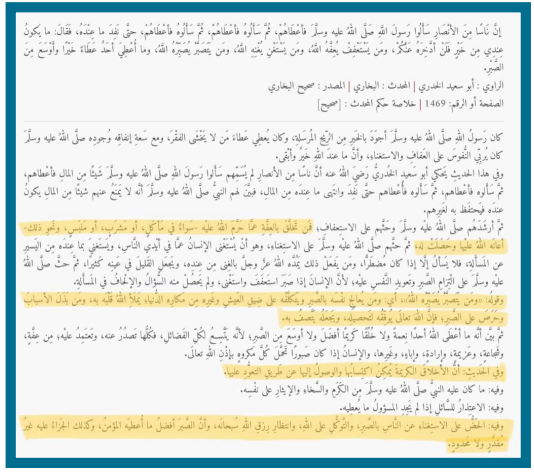

إِنَّ نَاسًا مِنَ الأَنْصَارِ سَأَلُوا رَسُولَ اللَّهِ صَلَّى اللهُ عليه وسلَّمَ فَأَعْطَاهُمْ، ثُمَّ سَأَلُوهُ فَأَعْطَاهُمْ، ثُمَّ سَأَلُوهُ فَأَعْطَاهُمْ، حَتَّى نَفِدَ مَا عِنْدَهُ، فَقَالَ: مَا يَكُونُ عِنْدِي مِنْ خَيْرٍ فَلَنْ أَدَّخِرَهُ عَنْكُمْ، وَمَنْ يَسْتَعْفِفْ يُعِفَّهُ اللَّهُ، وَمَنْ يَسْتَغْنِ يُغْنِهِ اللَّهُ، وَمَنْ يَتَصَبَّرْ يُصَبِّرْهُ اللَّهُ، وَمَا أُعْطِيَ أَحَدٌ عَطَاءً خَيْرًا وَأَوْسَعَ مِنَ الصَّبْرِ.

الراوي : أبو سعيد الخدري | المحدث : البخاري | المصدر : صحيح البخاري

الصفحة أو الرقم: 1469 | خلاصة حكم المحدث : [صحيح]

كان رَسولُ اللهِ صلَّى اللهُ عليه وسلَّمَ أجودَ بالخيرِ من الريحِ المُرسَلةِ، وكان يُعطِي عَطاءَ مَن لا يَخْشَى الفَقْرَ، ومع سَعةِ إنفاقِه وجودِه صلَّى اللهُ عليه وسلَّمَ كان يُربِّي النُّفوسَ على العَفافِ والاستغناءِ، وأنَّ ما عندَ اللهِ خيرٌ وأبقَى.

وفي هذا الحديثِ يَحكِي أبو سَعيدٍ الخدريُّ رَضِيَ اللهُ عنه أنَّ ناسًا مِن الأنصارِ لَمَّ إسْمَهم سَألُوا رَسولَ اللهِ صلَّى اللهُ عليه وسلَّمَ شيئًا مِن المالِ فأعْطاهم، ثمَّ سَألُوه فأعْطاهم، ثمَّ سَألُوه فأعْطاهم حتَّى نَفِدَ وانتهَى ما عندَه مِن المالِ، فبيَّنَ لهم النبيُّ صلَّى اللهُ عليه وسلَّمَ أنَّه لا يَمنَعُ عنهم شيئًا مِن المالِ يكونُ عندَه فيحتفظُ به لغيرِهم.

ثمَّ أرشَدَهم صلَّى اللهُ عليه وسلَّمَ وحثَّهم على الاستعفافِ، فمَن تَخلَّقَ بالعِفَّةِ عمَّا حرَّمَ اللهُ عليه -سواءٌ في مَأكلٍ، أو مَشرَبٍ، أو مَلبسٍ، ونحوِ ذلك- أعانَه اللهُ عليها وحفِظَه بها، ثمَّ حثَّهم صلَّى اللهُ عليه وسلَّمَ على الاستغناءِ، وهو أنْ يَستَغنِيَ الإنسانُ عمَّا في أيدي النَّاسِ، ويَستَغنِيَ بما عندَه مِن اليَسرِ عن المَسألةِ، فلا يَسألُ إلَّا إذا كان مُضطرًّا، ومَن يفعَلْ ذلك يَمُنُّ اللهُ عزَّ وجلَّ بالغِنى مِن عندِه، ويَجعَلِ القليلَ في عينِه كثيرًا، ثمَّ حثَّ صلَّى اللهُ عليه وسلَّمَ على التزامِ الصَّبرِ وتَعويدِ النَّفسِ عليه، لأنَّ الإنسانَ إذا صَبَرَ استَعفَفَ واستَغنَى، ولم يَحتَجْ منه السُّؤالَ والإلحافَ في المَسألةِ.

وفيه: «ومَن يَتصبَّر يُصبِّره اللهُ»، أي: ومَن يُعالِج نفسَه بالصَّبرِ ويحمِلْها على ضيقِ العيشِ وغيرِه مِن مكارِهِ الدُّنيا، يُعِنْه اللهُ عليه، ومَن يَبذُلِ الأسبابَ ويحرِصْ على الصَّبرِ، فإنَّ اللهَ تعالَى يُوفِّقُه لتحصيلِه، ويَجعَلُه يَكتسِبُ به.

ثمَّ بيَّنَ أنَّه ما أُعطِيَ اللهُ أحدًا نعمةً ولا خَلْقًا كريمًا أفضَلَ ولا أوسَعَ مِن الصَّبرِ، لأنَّه يَتَّسِعُ لكلِّ الفَضائلِ، فكلُّها تَصدُرُ عنه، وتَعتَمِدُ عليه، مِن عِفَّةٍ، وقناعةٍ، وعَزيمةٍ، وإرادةٍ، وإباءٍ، وغيرِها، والإنسانُ إذا كان صَبورًا تَحمَّلَ كلَّ مكروهٍ بإذنِ اللهِ تعالَى.

وفي الحديثِ: أنَّ الأخلاقَ الكريمةَ يُمكِنُ اكتسابُها والوصولُ إليها عن طريقِ التخلُّقِ عليها.

وفيه: ما كان عليه النبيُّ صلَّى اللهُ عليه وسلَّمَ مِن الكرَمِ والسَّخاءِ والإيثارِ على نفسِه.

وفيه: الاعتذارُ للسائلِ إذا لم يَجِدِ المسؤولُ ما يعطِيه.

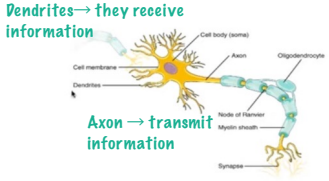
وفيه: الحثُّ على الاستغناءِ عن النَّاسِ بالصَّبرِ، والتَّوكُّلِ على اللهِ، وانتظارِ رِزقِ اللهِ سُبحانه، وأنَّ الصَّبرَ أفضلُ ما أُعطِيَه المؤمنُ، وكذلك الجزاءُ عليه غيرُ مقدَّرٍ ولا محدودٍ.

CNS

Lecture 1

بسم الله الرحمن المستعان

- **The principal functional unit of the CNS is the *Neuron*.**
- **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.**



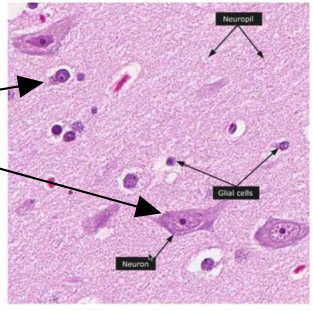
- **Since different regions of the brain participate in different**
- **functions, the pattern of clinical signs and symptoms that follow injury depend as much on the region of brain involved as on the pathologic process**

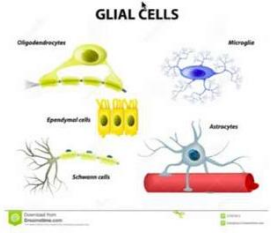
Two types of cells in CNS
1. Parenchymal cell → neuron [functional unit]
2. Supportive cells → glial cells [Oligo dendrocytes, astrocytes , ependymal , microglia]

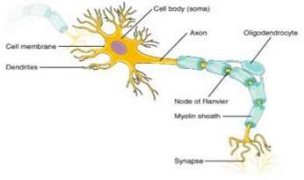
In addition to that → the most important supportive cell in PNS Schwann cells

- **Mature neurons are incapable of cell division 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.**

Small cell → glial cell
Large cell → neuron
No. Of glial cell > no. Of neuron







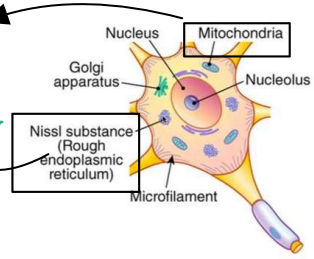
Features of Neuronal Injury.

- In response to injury, a number of changes occur in neurons and their processes both axons and dendrites.
- Within 12 hours of an irreversible hypoxic-ischemic insult, acute neuronal injury becomes evident on routine hematoxylin and eosin (H&E) staining.

In acute injury → that cause death of neuron → the manifestation which we see is red neuron.
Note: acute injury like ischemia or hypoxia , maybe either reversible[swelling of the cell] or irreversible[cell death = red neuron]

- red neuron → response of neurons to irreversible acute damage (we need 12 h to see red neuron after cell damage)
- .if we examine a brain for a patient within short period of time after death, the changes might not be present.

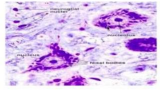
Cell body of neuron have a lots of mitochondria → because it's active cell and need energy , also have lots of rough endoplasmic reticulum [inside RER there are ribosomes which aggregate in cytoplasm and give a violet / bluish color and this aggregation called Nissl substance

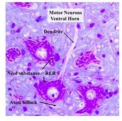


- 1. There is shrinkage of the cell body
- 2. Pyknosis of the nuclei
- 3. Disappearance of the nucleolus
- 4. Loss of Nissl substance with intense eosinophilia of the cytoplasm ("red neurons")
- 5. The nuclei assumes the angulated shape of the shrunken cell body

Hyper chromatic,clumping of nuclear materiel →it can be lost or fragmented

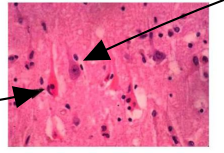
Nissl substance

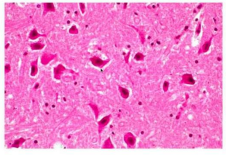




Red neuron :
- Shrinkage
- Hyper chromatic pyknotic nucleus
- Absence of nissl substance

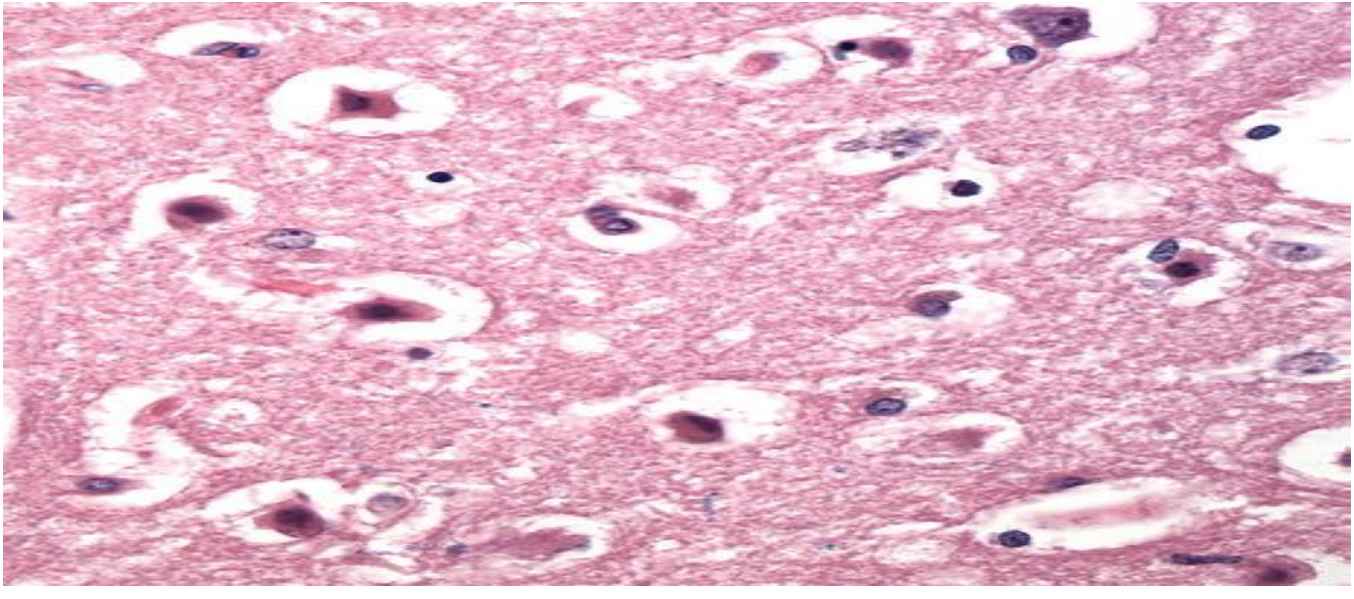
Red neurons





Normal neuron:
- Normal size
- Large nucleus
- Presence of nissl substancel bluish cytoplasm

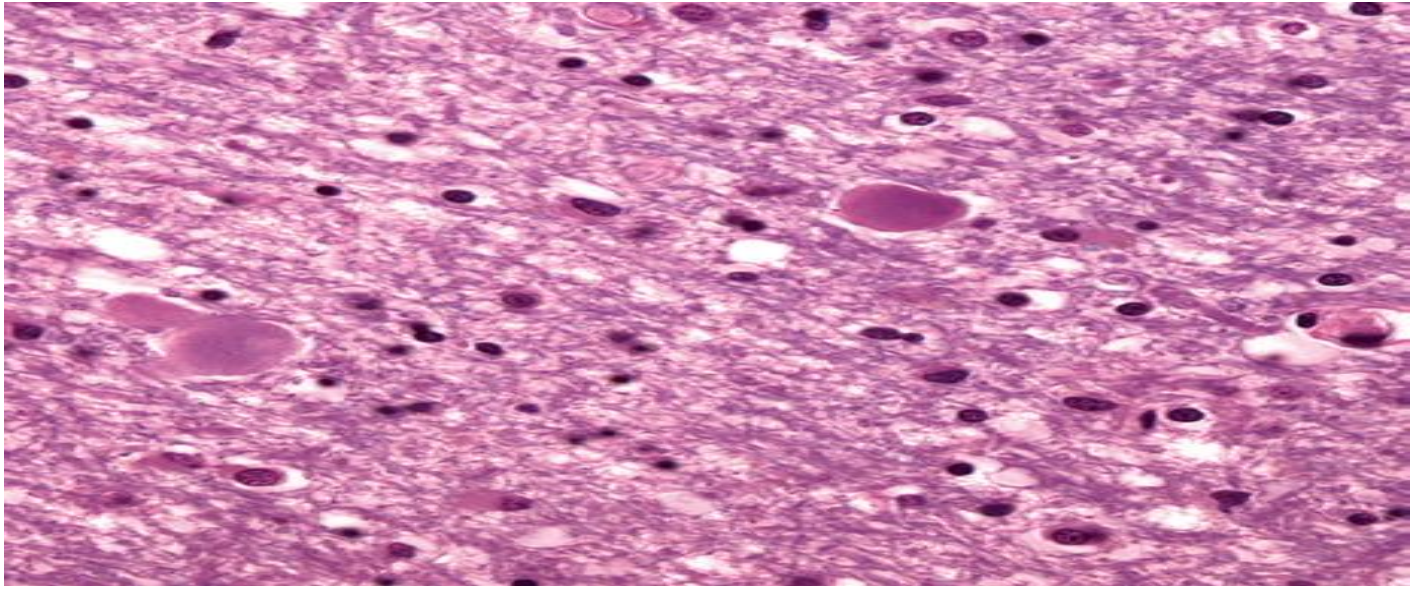
Acute hypoxic-ischemic injury in cerebral cortex, where the individual cell bodies are shrunken, along with the pyknotic nuclei and prominent staining of the cytoplasm by eosin (red neurons)



- 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.

Chronic injury → lead to death of neurons by apoptosis (majority)
Might die by necrosis if there is any infection, inflammation or abscess.
Chronic damage for along time like in alzehaimar disease and neurodegenerative disease → loss of neuron due to apoptosis.

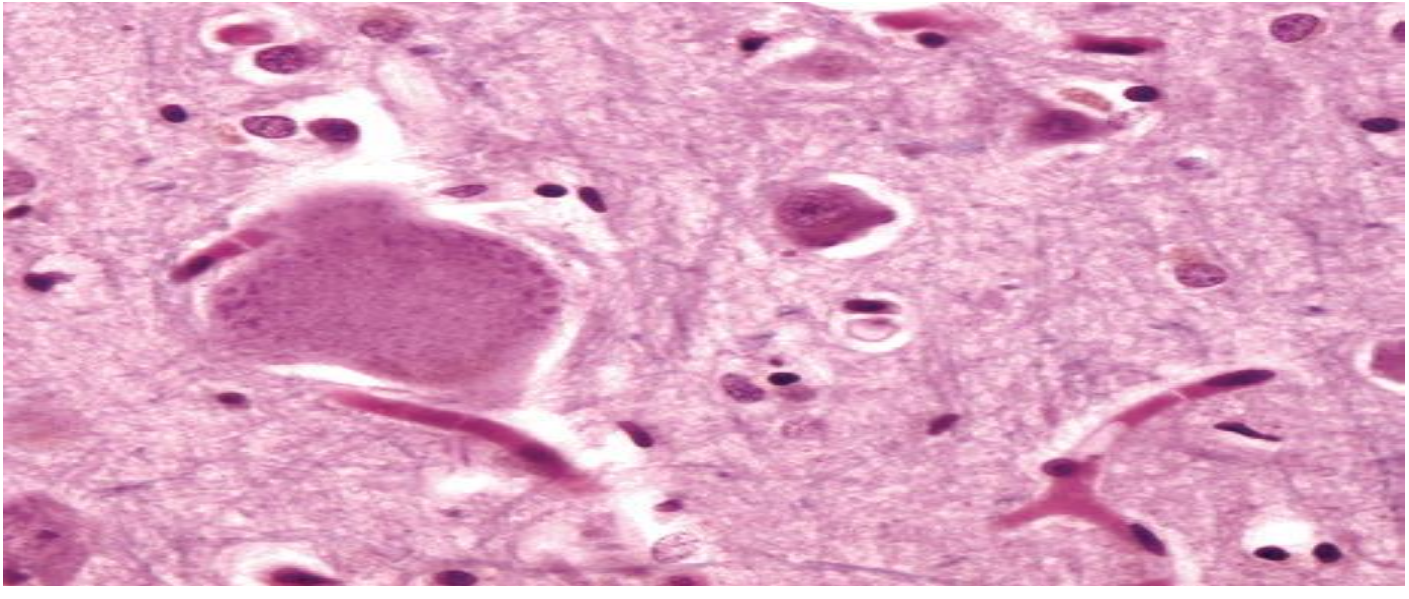
Axonal spheroids are visible as bulbous swellings at points of disruption or altered axonal transport



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

Chromatolysis

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



is very important to keep the normality of the brain

- 9. Acute injuries typically result in breakdown of the blood-brain barrier and variable degrees of cerebral edema
- 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,
- 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)**

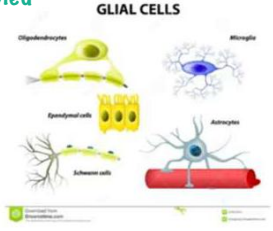
  in their cytoplasm and lysosomes

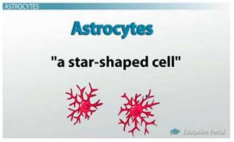
Loss of neuron → permanent lose cause it can't divide and regenerate itself

Glial cells → have ability to enter cell cycle and divide → so, gliosis happened to glial cell

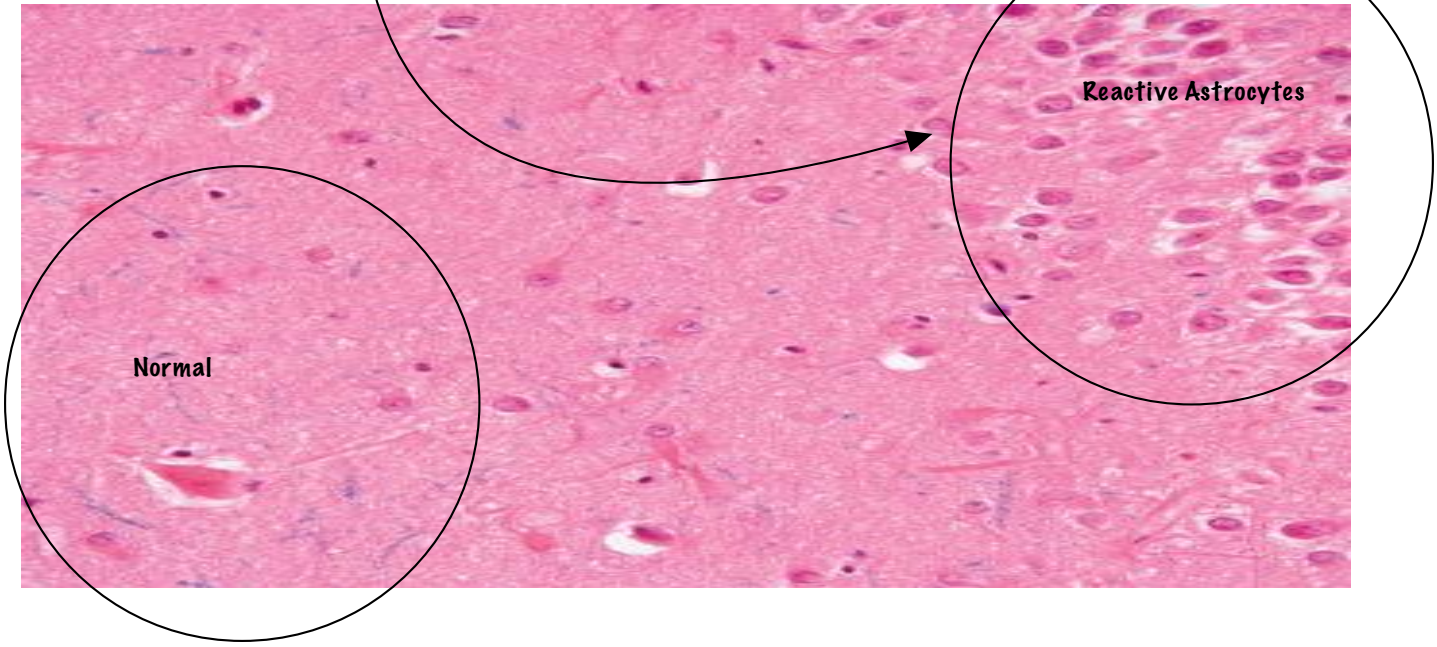
gliosis : not specific reaction to injury lead to increase in glial cell

Glial Cells



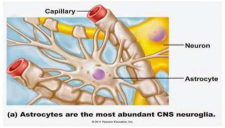


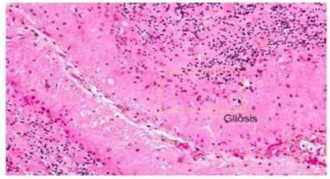
Reactive astrocytes, with eosinophilic cytoplasm and multiple radiating processes



Structural support to neuron , regulate the micro environment to the neuron, decrease the permeability of capillaries (BBB)

Astrocytes in Injury and Repair



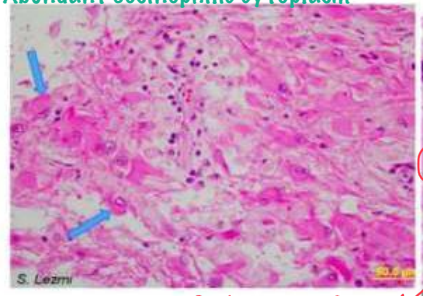


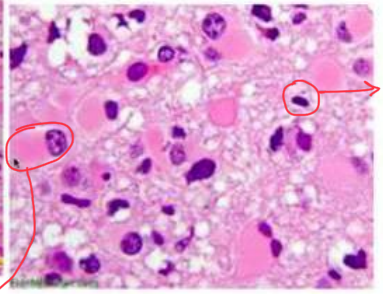
More affected in chronic injury + Most important cell that contribute in Gliosis

- Astrocytes are the principal cells responsible for repair and scar formation in the brain, a process termed **gliosis**. Gliosis: counter part of fibrosis in the rest of the body

Morphologic changes

- In response to injury, astrocytes undergo both hypertrophy and hyperplasia. Mitosis
- The nucleus enlarges and becomes vesicular, and the nucleolus becomes prominent. + Abundant eosinophilic cytoplasm





normal

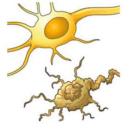
Gemistocyte ← in response to injury

gemisto astrocyte isn't only seen in injured places it can be also be present in some tumors like glioblastoma

- The previously scant cytoplasm expands and takes on a bright pink hue, and the cell extends multiple stout, ramifying processes **(gemistocytic astrocyte).**
- 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)

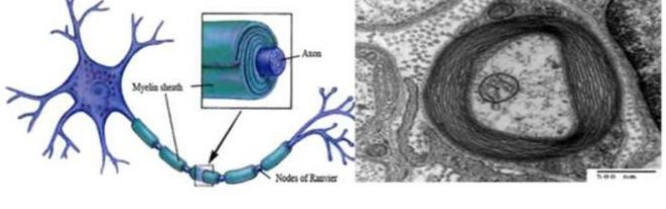
Chronic injury



Changes in Other Cell Types

- **Oligodendrocytes**

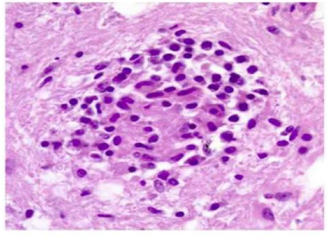
- Oligodendrocytes produce myelin
- Exhibit a limited spectrum of specific morphologic changes in response to various injuries.
- In progressive multifocal leukoencephalopathy, viral inclusions can be seen in oligodendrocytes, with a smudgy, homogeneous appearing enlarged nuclei.



- **Microglial cells**

  Fixed macrophage, originate from monocyte

- Bone-marrow–derived cells
- Phagocytes of the CNS
- When activated by tissue injury, infection, or trauma, they proliferate and become more prominent histologically.

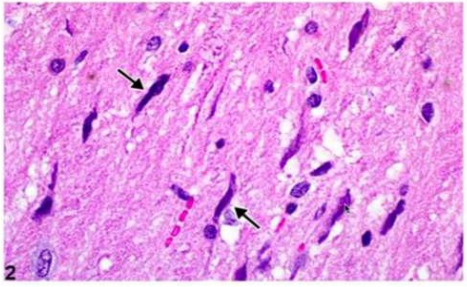


Microglia nodule → collection of macrophages when it's activated and start to phagocyte

Microglial cells take on the appearance of activated macrophages in areas in the following conditions:

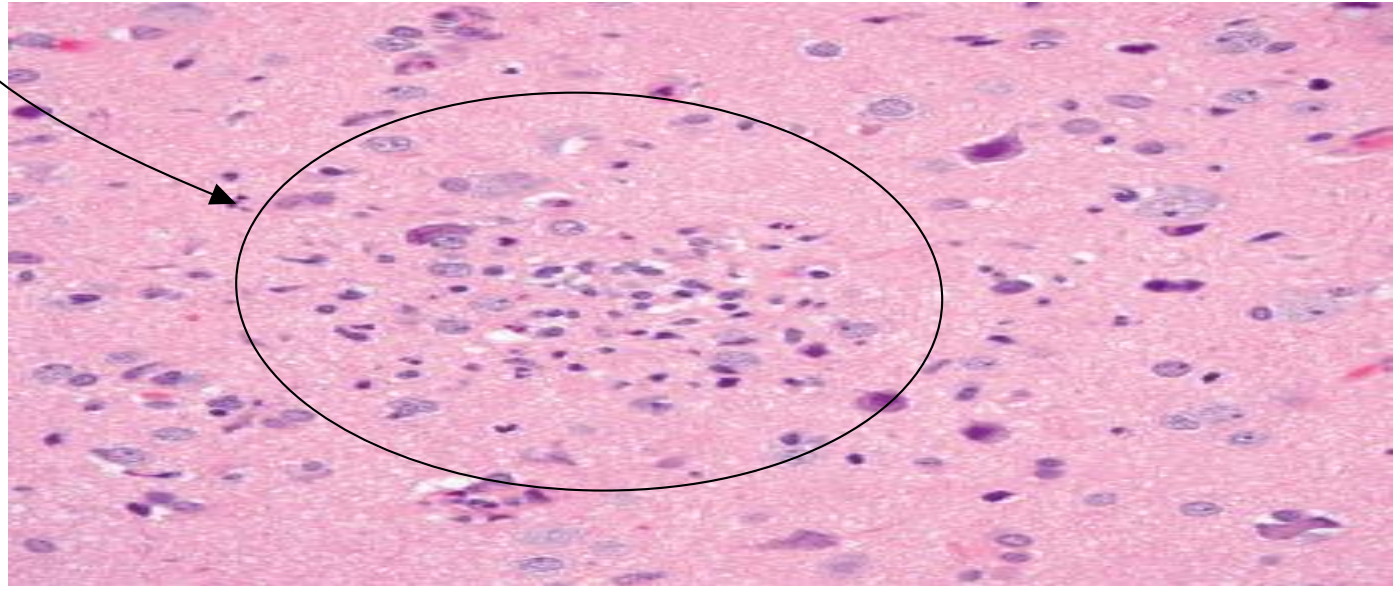
1. Demyelination
2. Organizing infarct
3. Hemorrhage
4. In neurosyphilis or other infections, they develop elongated nuclei **(rod cells)**

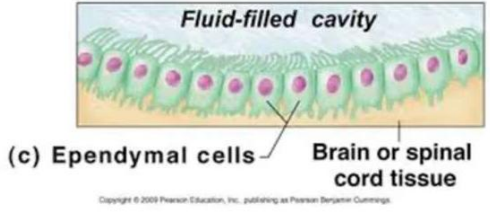
Activated microglial cell called Rod cell → elongated



- 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.





- **Ependymal cells**

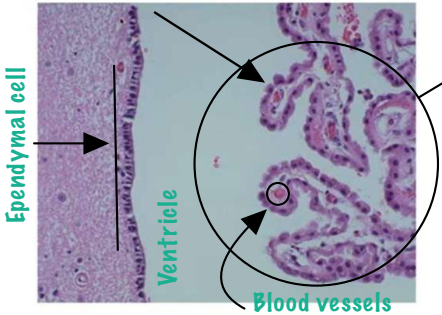
- line the ventricular system and the central canal of the spinal cord.
- Certain pathogens, particularly cytomegalovirus (CMV), can produce extensive ependymal injury, with typical viral inclusions.

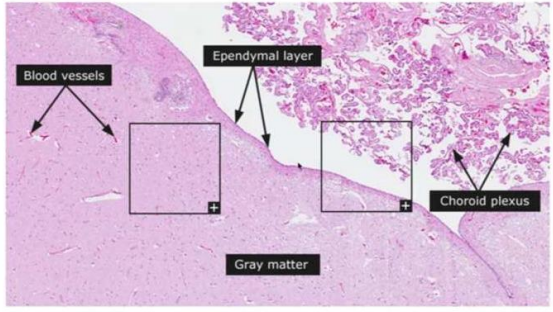
- **Choroid plexus** Extension of Ependymal cells around blood vessels called papillae with vascular course
  * Function of choroid plexus → secrete CSF

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

Choroid plexus

Finger like projection → papillae





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 nis obvious, but this arrangement provides little room for brain parenchymal expansion in disease states.

Skull protects the soft Brain but when volume inside skull increase will lead to increase in intracranial pressure and there is No way to get rid of this increase in volume

Normally → intracranial volume contains volume of CNS 80%, volume of CSF 10% and volume of blood 10%

If there is any lesion (hemorrhage , edema , infection... Etc.→ will be increase the volume which reflected to increase intracranial pressure

- **Disorders that may cause dangerous increases in brain volume within the fixed space of the skull include:**

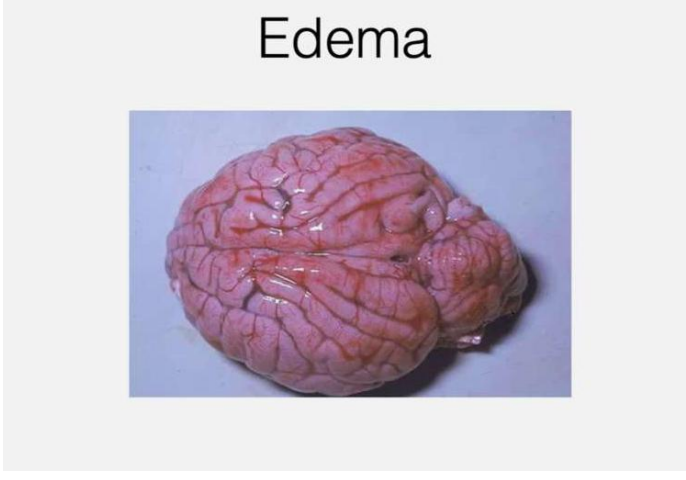
1. **Generalized cerebral edema**
2. **Hydrocephalus** Increase in CSF
3. **Mass lesions such as tumors.**

Cerebral Edema

Increase in weight of the brain , wide gyri and narrow salci

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

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



- There are two types:

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:**

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:

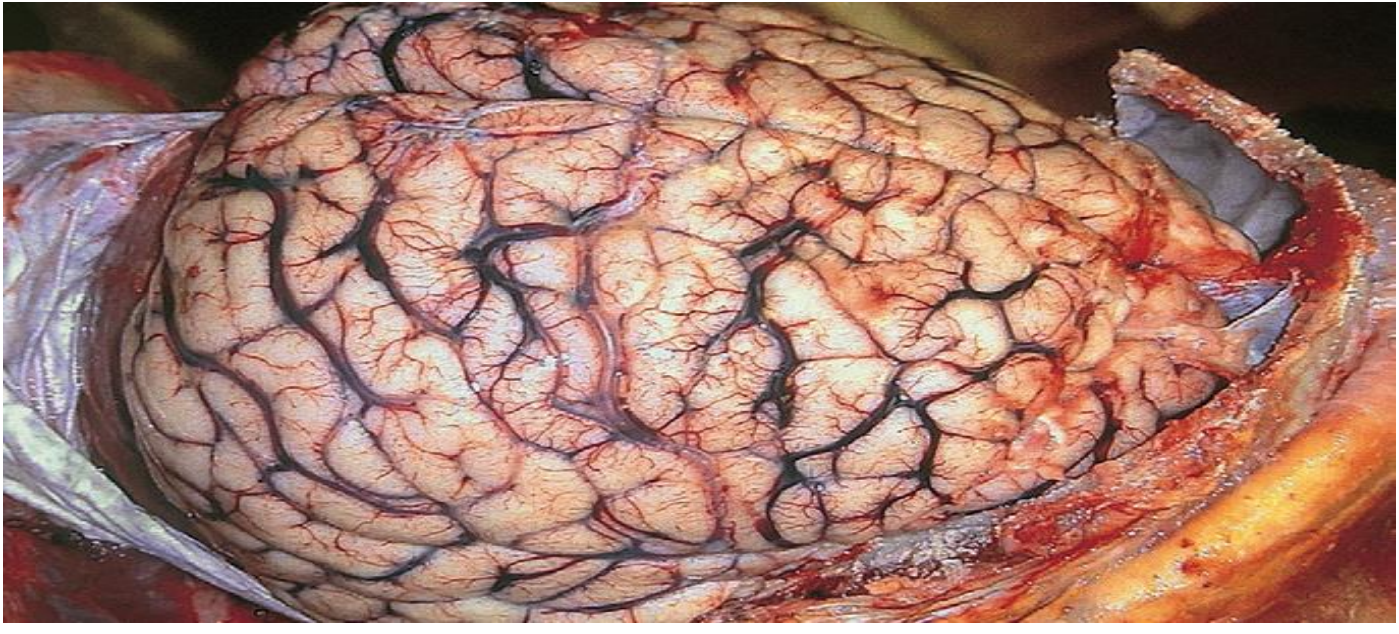
1. generalized hypoxic-ischemic

2. exposure to some toxins.

- **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 (Fig. 22–2).**

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



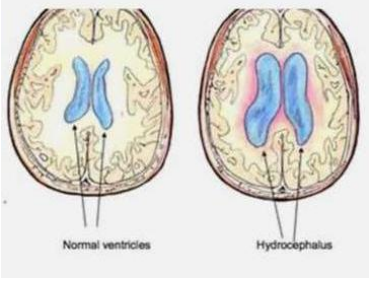
Hydrocephalus

- **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

- **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.**



Types of hydrocephalus

- **1. Noncommunicating hydrocephalus**

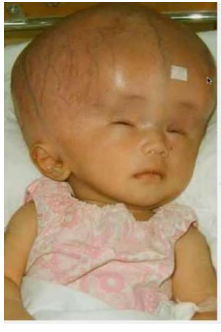
- If there is a localized obstacle to CSF flow within the ventricular system, then a portion of the ventricles enlarges while the remainder does not.

- Most commonly is caused by masses obstructing the foramen of Monro or compressing the cerebral aqueduct

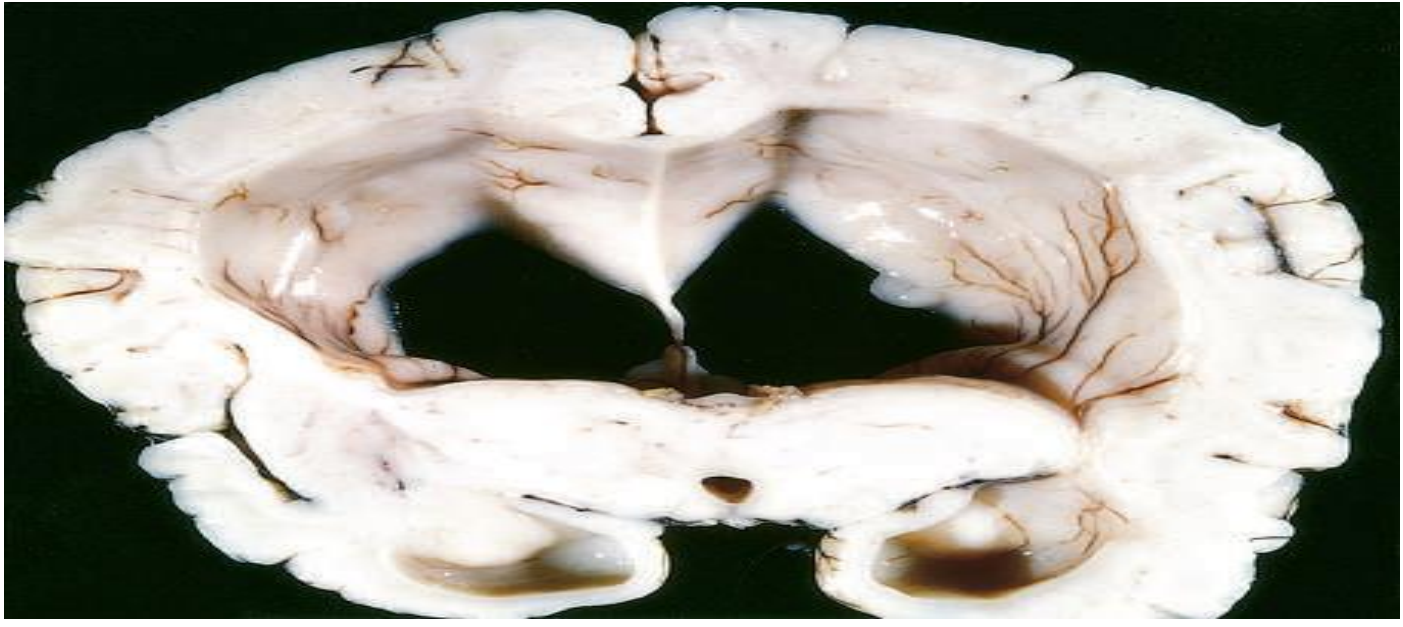
2. Communicating hydrocephalus Generalized

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

- If hydrocephalus develops in infancy before closure of the cranial sutures the head enlarges.
- 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



- **3. hydrocephalus ex vacuo**

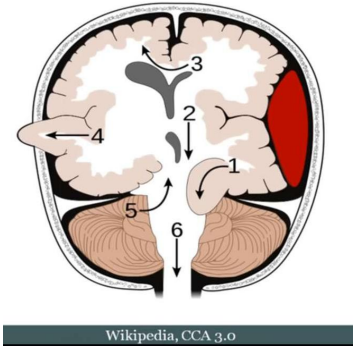
- A compensatory increase in CSF volume following the

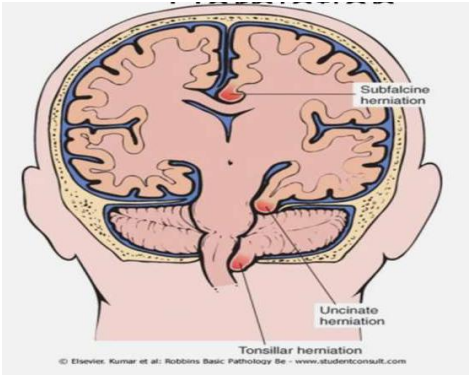
loss of brain parenchyma as after infarcts or with degenerative diseases.

Herniation فتق

the herniated part will be swollen because the vessels are compressed so the absorption of fluid is going to be compromised

- **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**



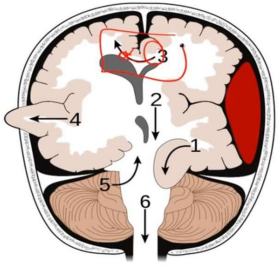


- **The cranial vault is subdivided by rigid dural folds (falx and tentorium), and a focal expansion of the brain displaces it in relation to these partitions.**
- **If the expansion is sufficiently large, herniation occurs.**
- **Herniation often leads to “pinching” and vascular compromise of the compressed tissue, producing infarction, additional swelling, and further herniation.**

There are 3 main 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.**
- **This may be associated with compression of the anterior cerebral artery.**



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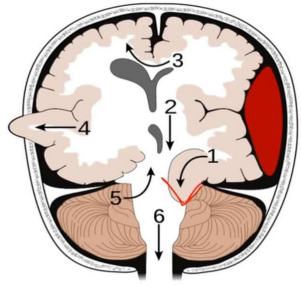

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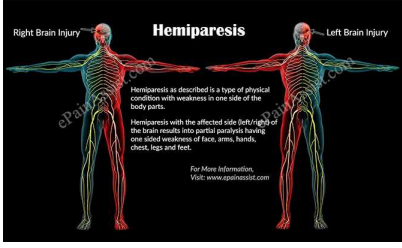
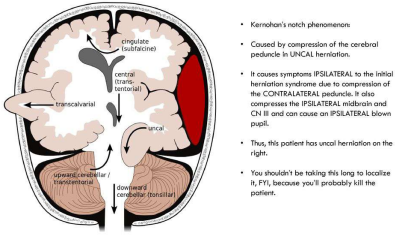
- **2. Transtentorial (uncinate) herniation**

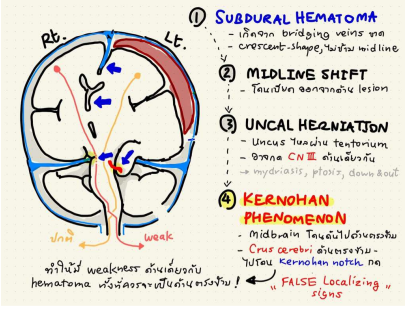
- Occurs when the medial aspect of the lobe is compressed against the free margin of the tentorium.

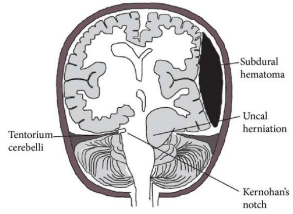
- As the temporal lobe is displaced the third cranial nerve is compromised resulting in pupillary dilation and impaired ocular movements on the side of the lesion (“blown pupil”). or loss of vision.



- **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 a so-called false localizing sign.**



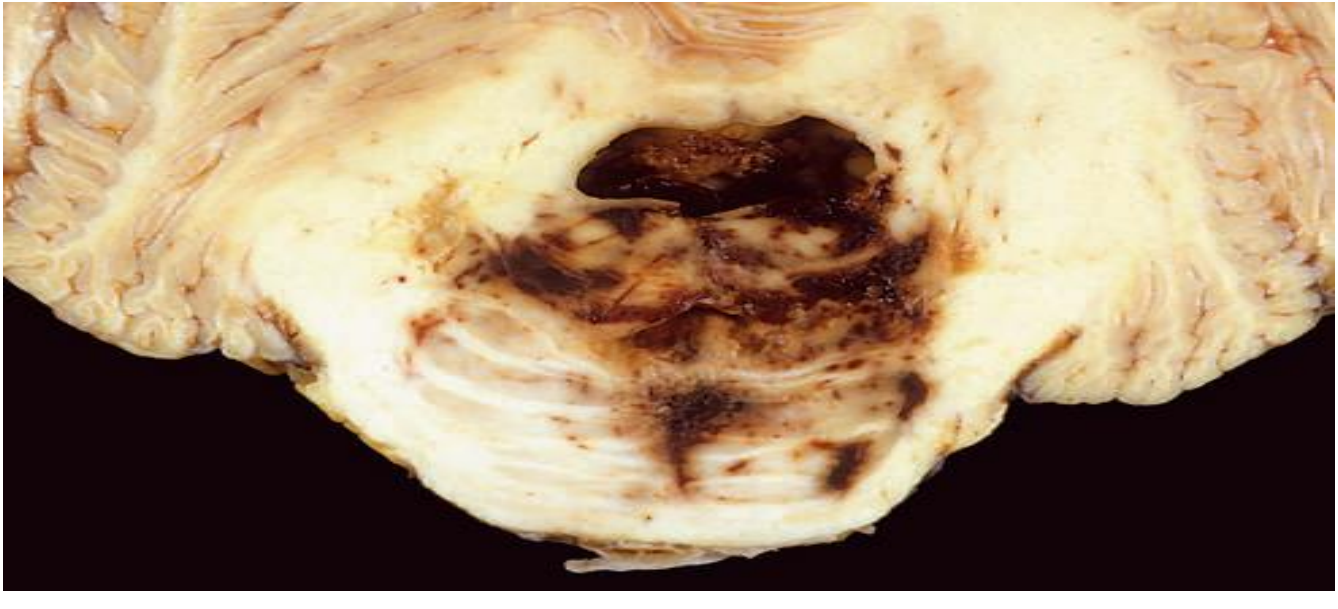




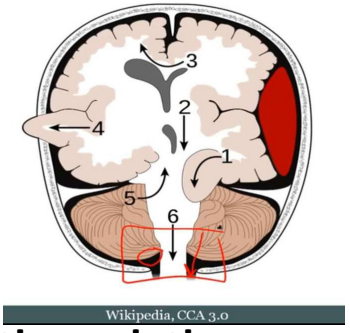
- **The compression of the peduncle creates a deformation known as Kernohan's notch.**
- **Progression of transtentorial herniation is often accompanied by linear or flame-shaped hemorrhages in the midbrain and pons, termed *Duret hemorrhages* (Fig. 22–5).**

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



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**

- It refers to displacement of the cerebellar tonsils through the foramen magnum.

foramen magnum 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.j