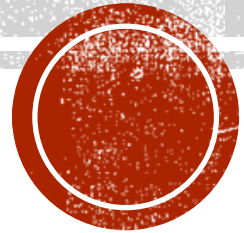
CNS LECTURE 1



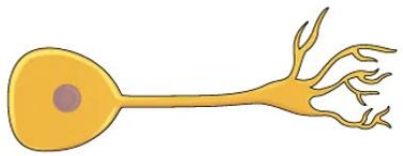
Markers of Neuronal Injury, Edema, Herniation, and Hydrocephalus

Dr. Dua Abuquteish

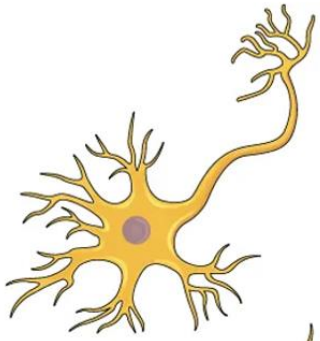
MARKERS OF NEURONAL INJURY

SIGNIFICANT FEATURES IN CNS PATHOLOGY

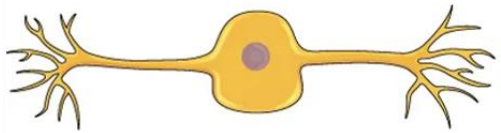
- ✓Extremely susceptible to increased intracranial pressure (I.C.P)
- ✓Highly susceptible to ischemia & hypoxia
- ✓Site of lesion may be more important than its nature
- ✓Selective vulnerability of defined structures to disease processes
- ✓There is no regeneration (**gliosis** not fibrosis)



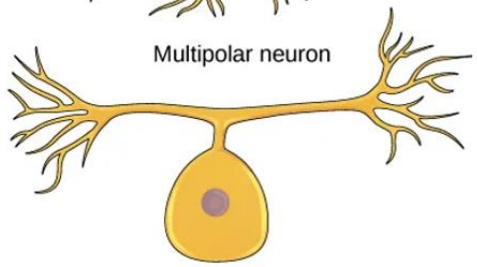
Unipolar neuron



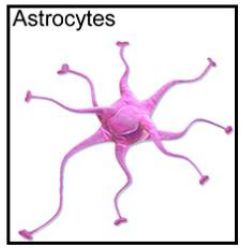
Multipolar neuron

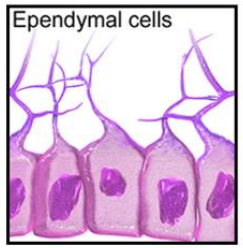


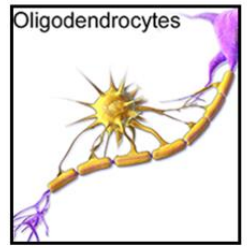
Bipolar neuron

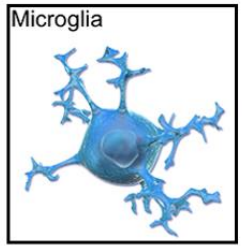


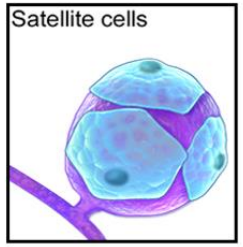
Pseudounipolar neuron

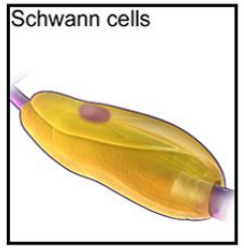












Neurons

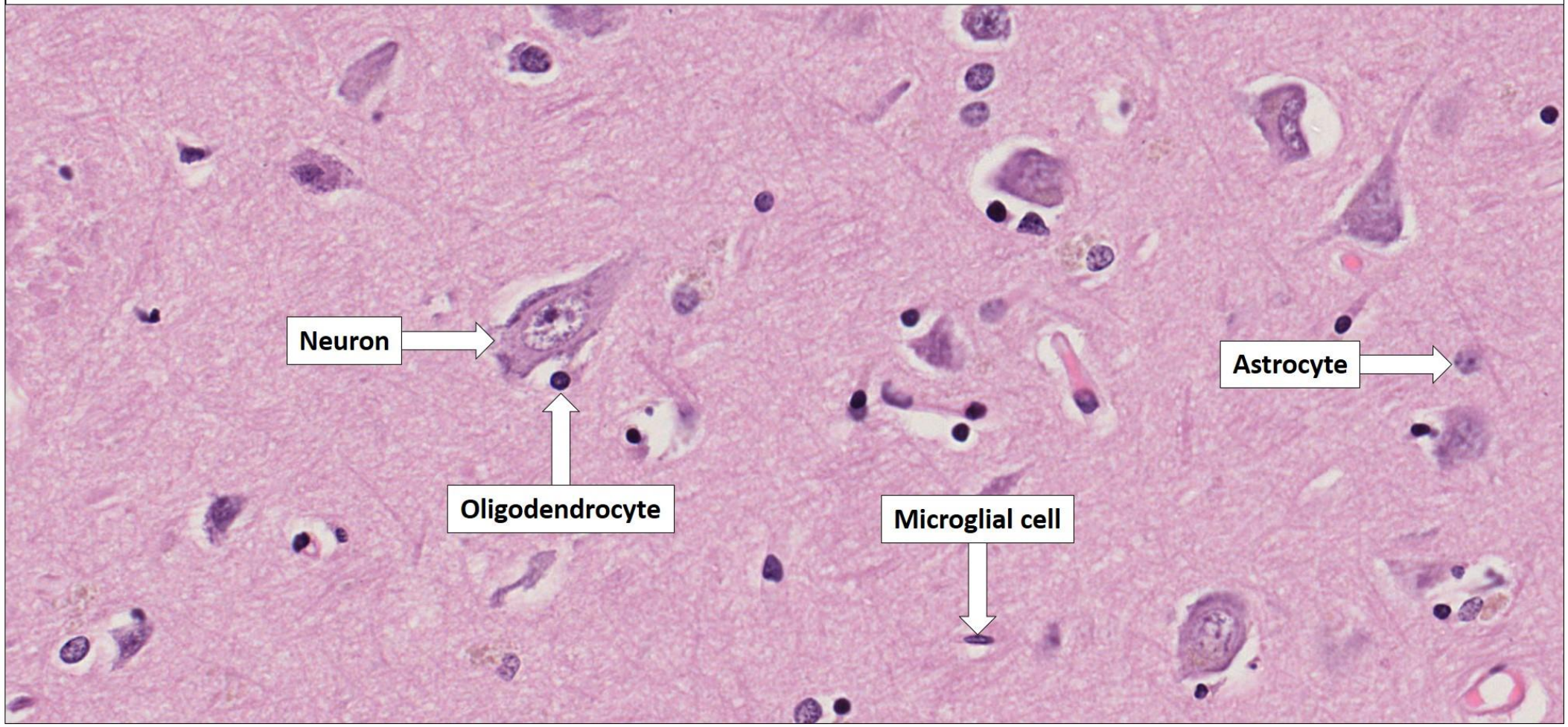
www.majordifferences.com

Glia

neurons are broadly divided into four basic types: unipolar, bipolar, multipolar and pseudounipolar.

Astrocytes, Ependymal cells Oligodendrocytes, Microglia, Satellite cells, Schwann cells

Cerebral cortex (High power):
Neurons typically have large, pale nuclei with prominent nucleoli. The non-neuronal (glial) cells in the grey matter include oligodendrocytes (hyperchromatic, round nuclei and abundant clear-appearing cytoplasm), astrocytes (paler, more elongated nuclei and usually scant cytoplasm), and microglial cells.



CELLS OF CNS

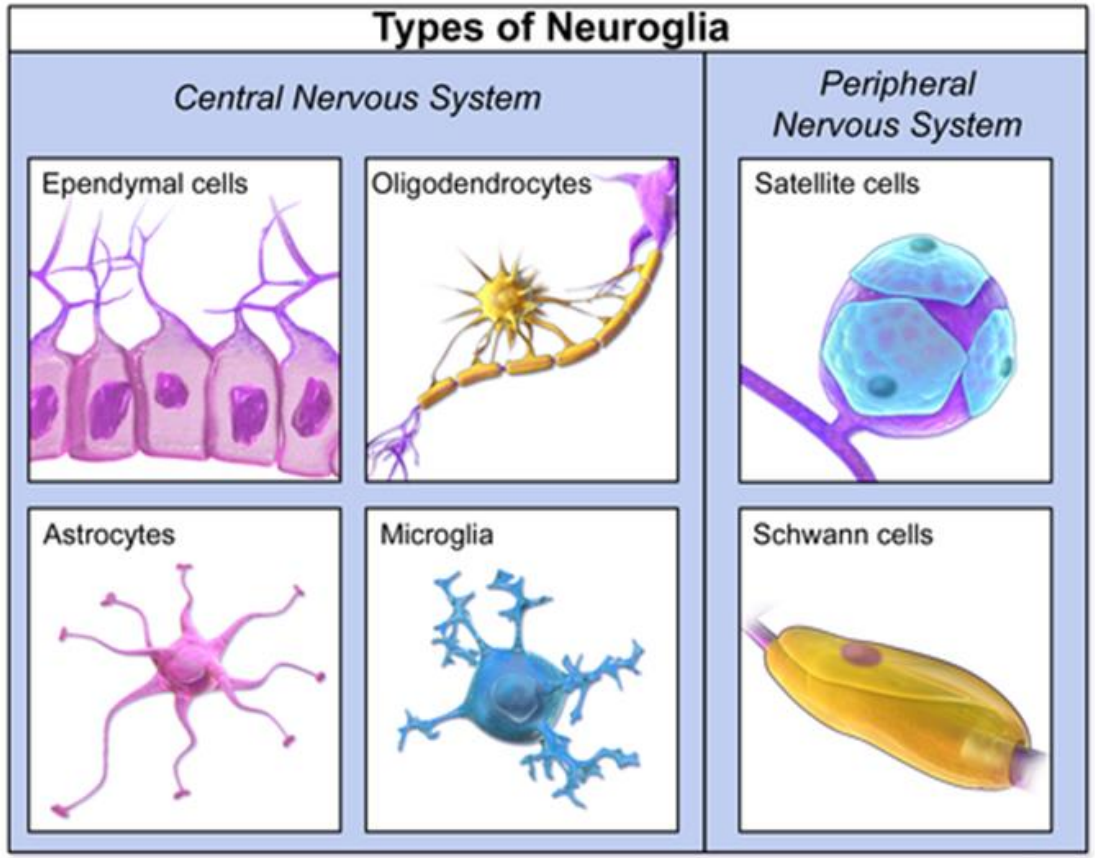
Neurons

Glial cells:

- Astrocyte
- Oligodendrocyte
- Ependymal cells
- Microglia

Meninges :

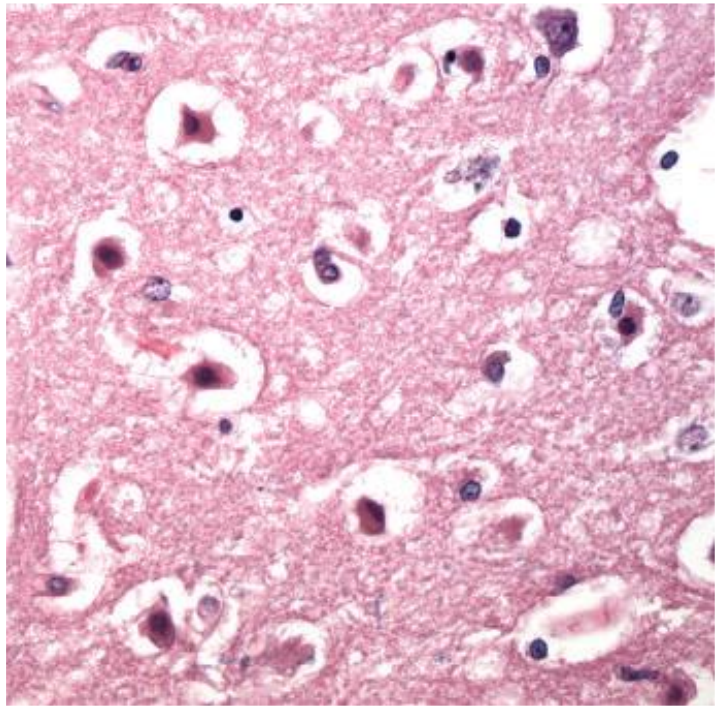
- Meningothelial cells
- Connective tissue & BV



PATTERNS OF NEURONAL INJURY

Acute hypoxic/ischemic injury in cerebral cortex:

Within 12 hours of an irreversible hypoxic/ischemic insult, **acute neuronal injury** becomes evident even on routine H & E staining.



The necrotic neuronal cell bodies & their nuclei are shrunken & pyknotic, loss of Nissl substance, and prominently eosinophilic, so-called ”**red neurons**”

PATTERNS OF NEURONAL INJURY

Axonal reaction:

Axonal injury also leads to cell body enlargement & swelling and dispersion of Nissl substance from the cell center to the periphery **(central chromatolysis**)

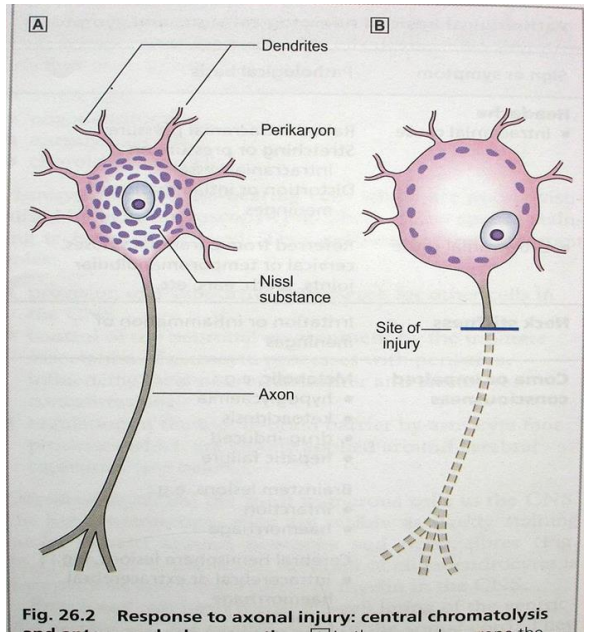
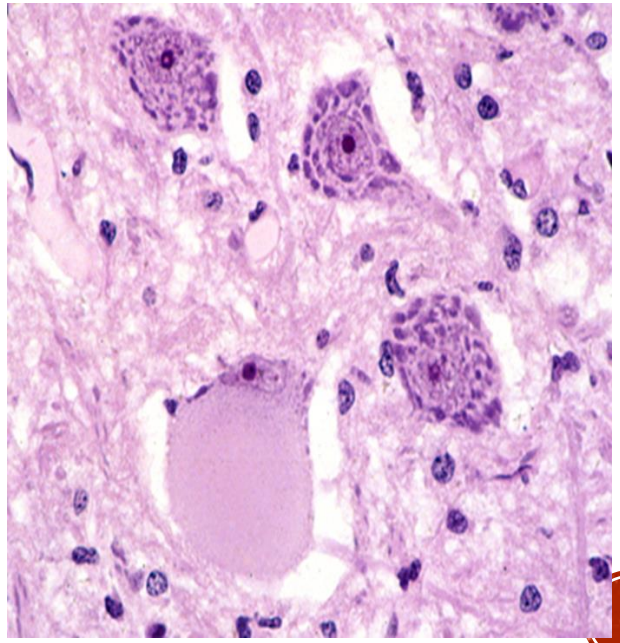


Fig. 26.2 Response to axonal injury: central chromatolysis



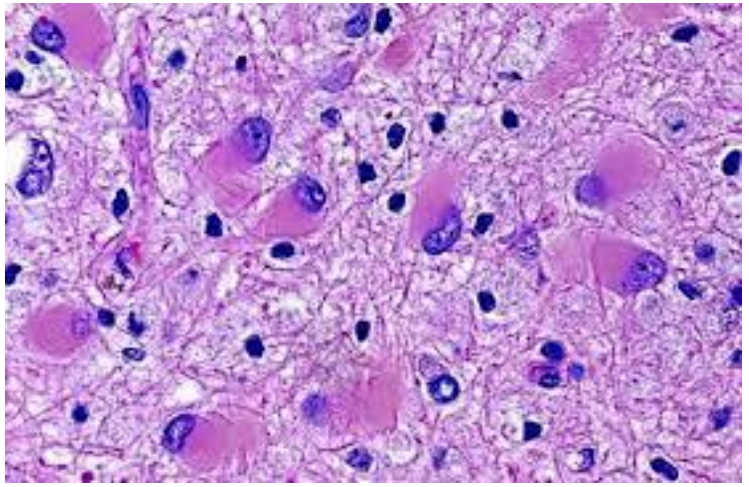
CHRONIC OR SUBACUTE INJURY

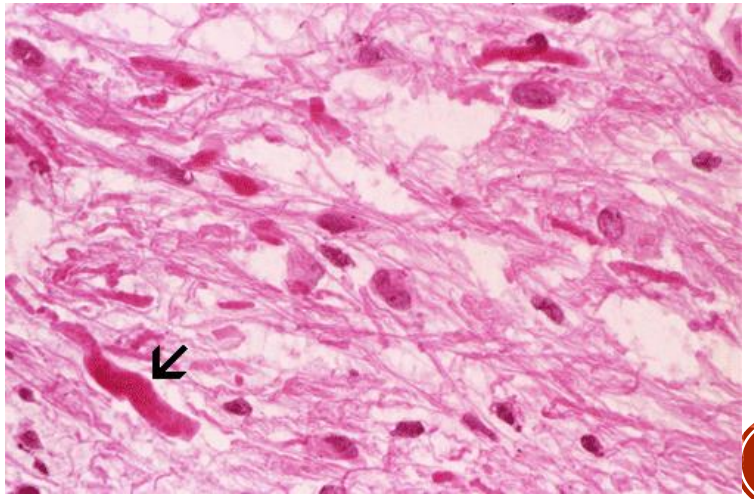
- Degeneration and neuronal loss & replacement by **gliosis** in progressive diseases.

- **Astrocytes** are the principal cells responsible for repair and scar formation in the brain, a process termed gliosis. In response to injury, astrocytes undergo both hypertrophy and hyperplasia.

ASTROCYTE INJURY AND REPAIR

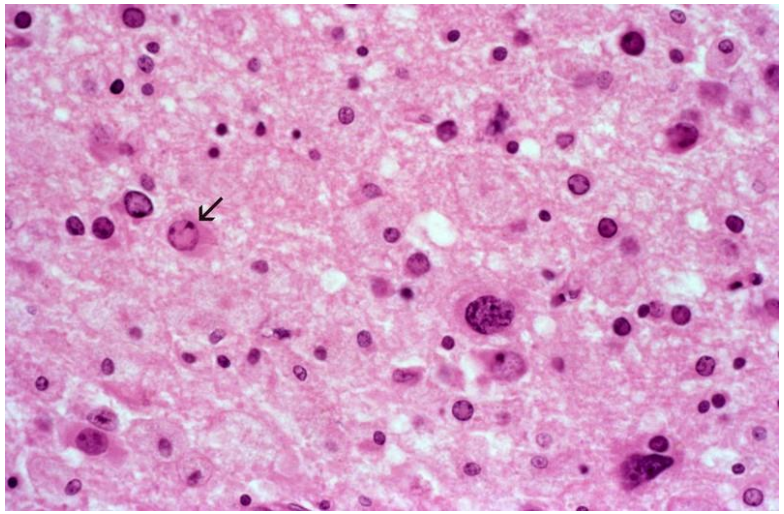
- In response to injury, astrocytes undergoes (**Gliosis**)
- The nucleus enlarges, the nucleolus becomes prominent, and the cytoplasm becomes bright pink hue (gemistocytic astrocyte)
- Unlike elsewhere in the body, fibroblasts participate in healing after brain injury to a limited extent
- Rosenthal fibers are thick, elongated, brightly eosinophilic protein aggregates found in astrocytic processes in chronic gliosis and tumors

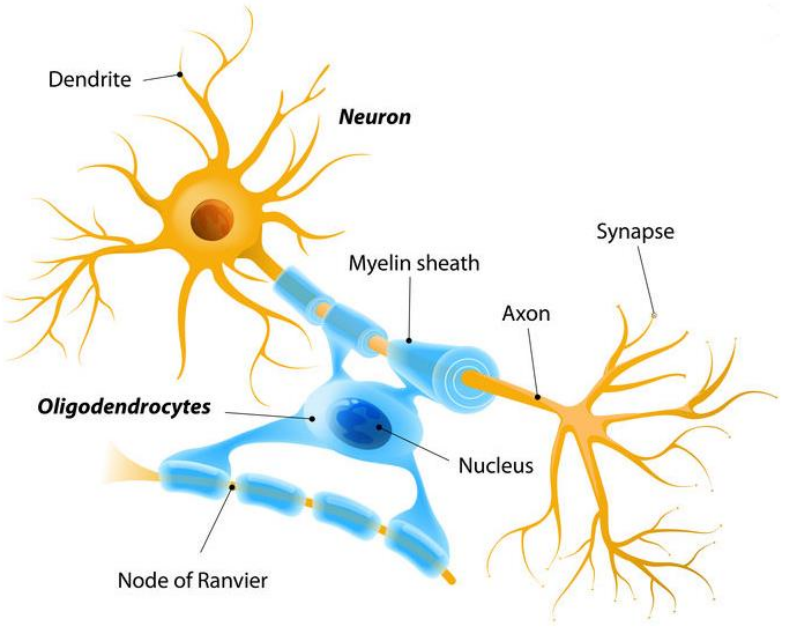




OLIGODENDROCYTES

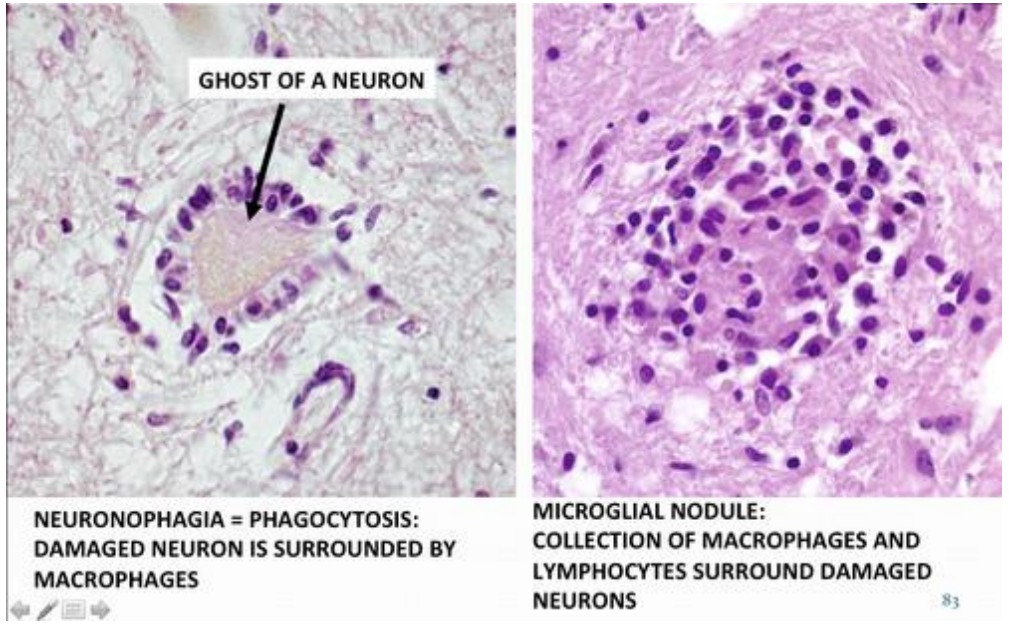
- Produces myelin, exhibit a limited spectrum of changes in response to injuries.
- For example: in progressive multifocal leukoencephalopathy, viral inclusions can be seen in oligodendrocytes.





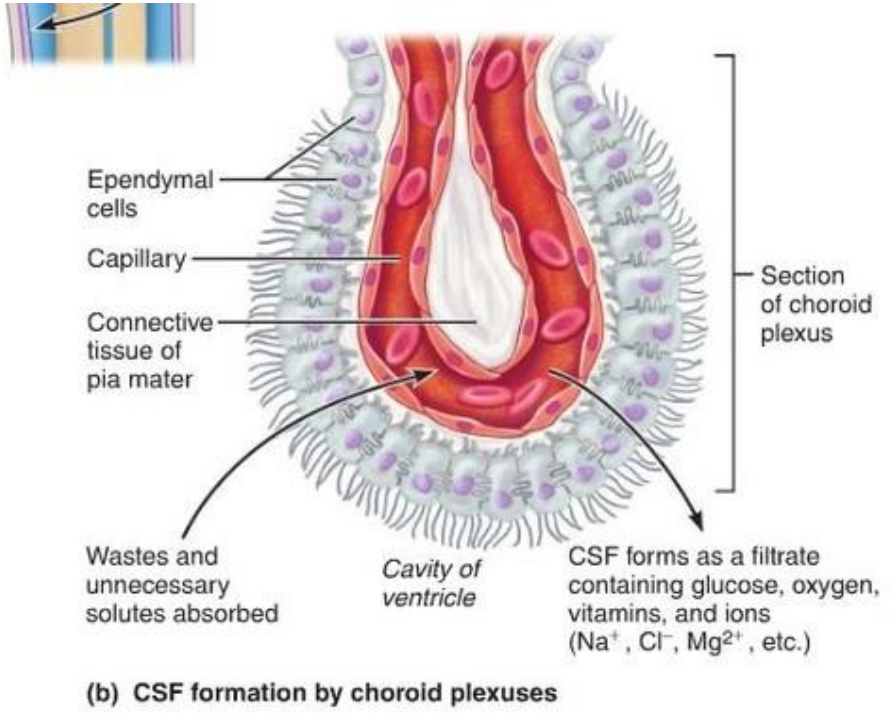
MICROGLIAL CELLS

- **Microglial cells** are long-lived cells that function as the phagocytes of the CNS.
- When activated by tissue injury, infection, or trauma, they proliferate and become more prominent histologically.
- Microglial cells have the appearance of activated macrophages in areas of demyelination, organizing infarct, or hemorrhage
- Aggregates of elongated microglial cells at sites of tissue injury are termed **microglial nodules**
- Collections around and phagocytosing injured neurons **(neuronophagia).**

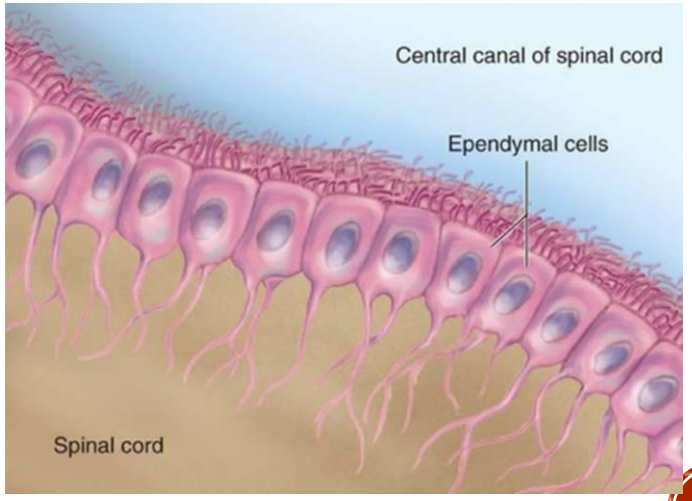


EPENDYMAL CELLS

- Ependymal cells line the ventricular system and the central canal of the spinal cord.
- Certain pathogens, particularly cytomegalovirus (CMV), can produce extensive ependymal injury.
- Choroid plexus is in continuity with the ependyma, and its specialized epithelial covering is responsible for the secretion of cerebrospinal fluid (CSF).



(b) CSF formation by choroid plexuses



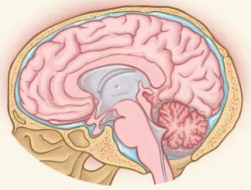
- The brain and spinal cord are encased within the skull and spinal canal, with nerves and blood vessels passing through specific foramina. These rigid structures provide little room for brain expansion in diseases.
- **An increase in the volume of the skull contents (Brain, CSF, & blood) → increase in intracranial pressure (ICP)**
- Increased ICP compromises the blood supply to the brain, resulting in decreased brain perfusion and serious/fatal consequences.

Causes of increase ICP:

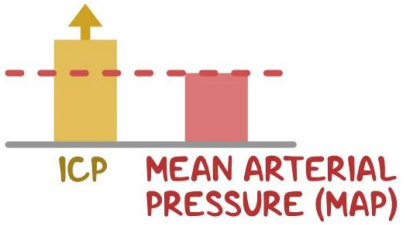
- ❑ Generalized cerebral edema
- ❑ Hydrocephalus
- ❑ Hemorrhages
- ❑ Ischemia
- ❑ Masses (tumors)

↑ INTRACRANIAL PRESSURE (ICP)

⚠ MEDICAL EMERGENCY ⚠



CAN RESULT from:
HEAD INJURY, BLEEDING in BRAIN, TUMORS, INFECTIONS, EXTRA FLUID in BRAIN, STROKE

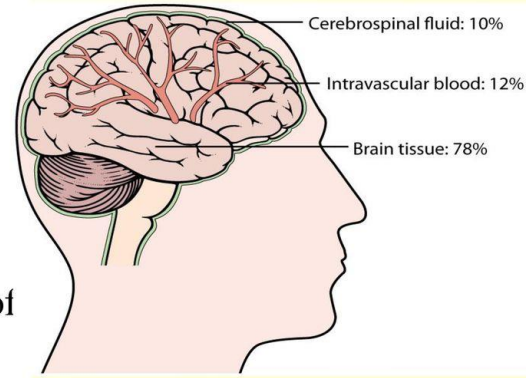


WHEN ICP > MAP, BRAIN CAN NO LONGER RECEIVE ENOUGH O_2

↳ SYMPATHETIC NERVOUS SYSTEM ACTIVATES

↳ THEN PARASYMPATHETIC NERVOUS SYSTEM ACTIVATES

- **ICP is usually measured in the lateral ventricles, with a normal pressure of 0 to 15 mm Hg.**
- brain tissue (1400 g)
- Blood 75 mL
- CSF 75 mL
- the three components are in a state of equilibrium



Symptoms of ICP

Headache
Nausea and Vomiting
Altered Level of Consciousness
Vision Problems
Papilledema
Seizures
Cushing's Triad (a late sign)

CEREBRAL EDEMA

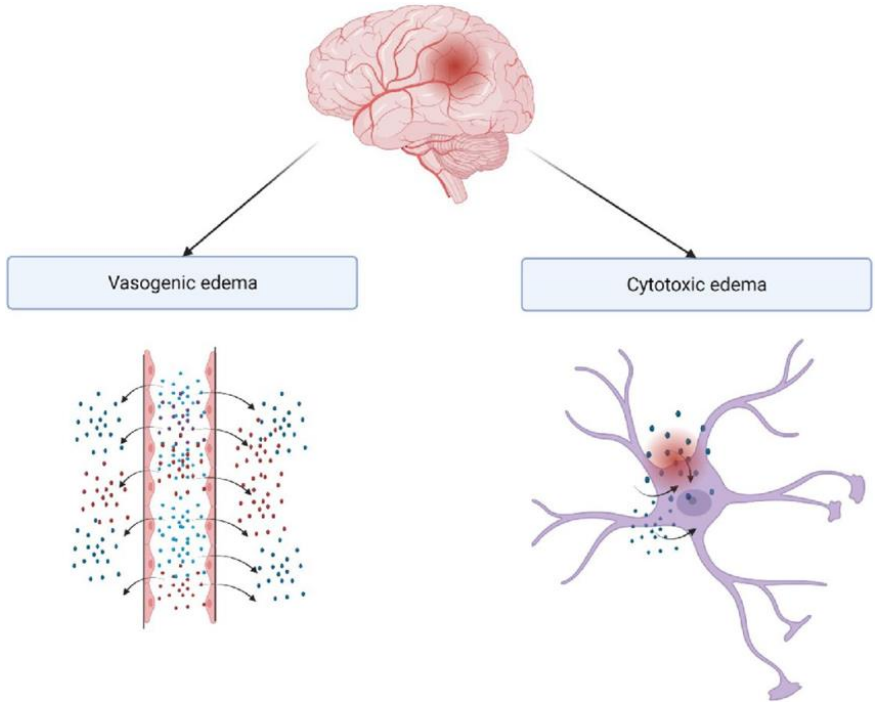
CEREBRAL EDEMA

- Cerebral edema is the accumulation of **excess fluid within the brain parenchyma**
- Cerebral edema commonly present with neurological symptoms, and if severe it can cause ICP, herniation, and death

Two types

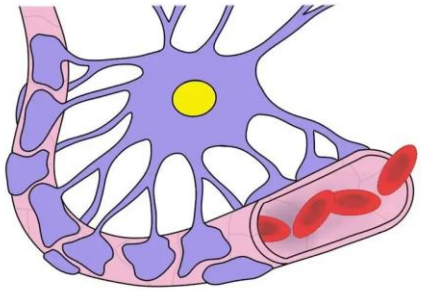
Vasogenic edema

Cytotoxic edema



CEREBRAL EDEMA

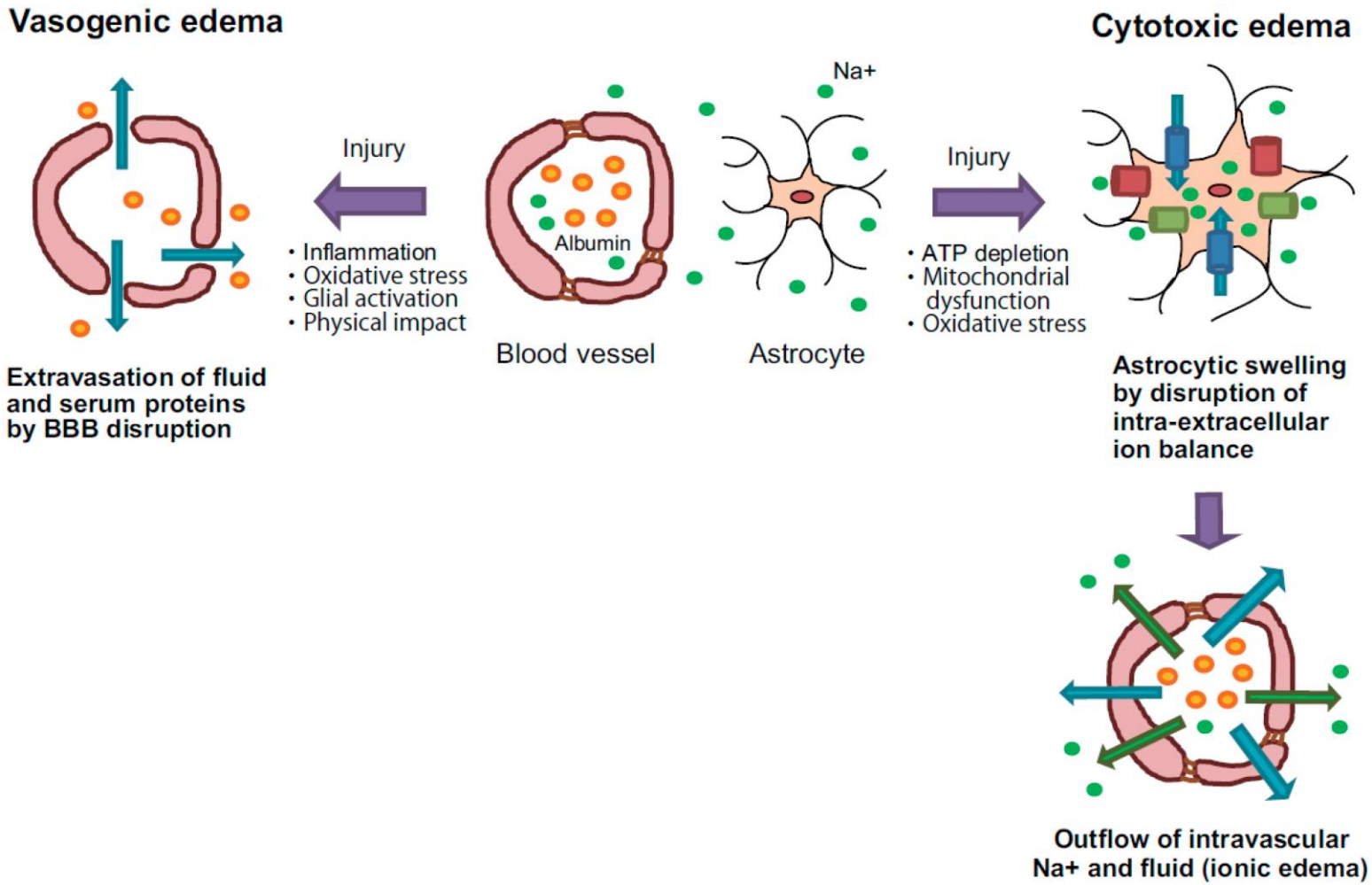
- ***Vasogenic edema*** occurs when the integrity of the normal blood-brain barrier is disrupted, allowing fluid to shift from the vascular compartment into the extracellular spaces of the brain.
- Vasogenic edema can be localized (e.g., inflammation or in tumors) or generalized.



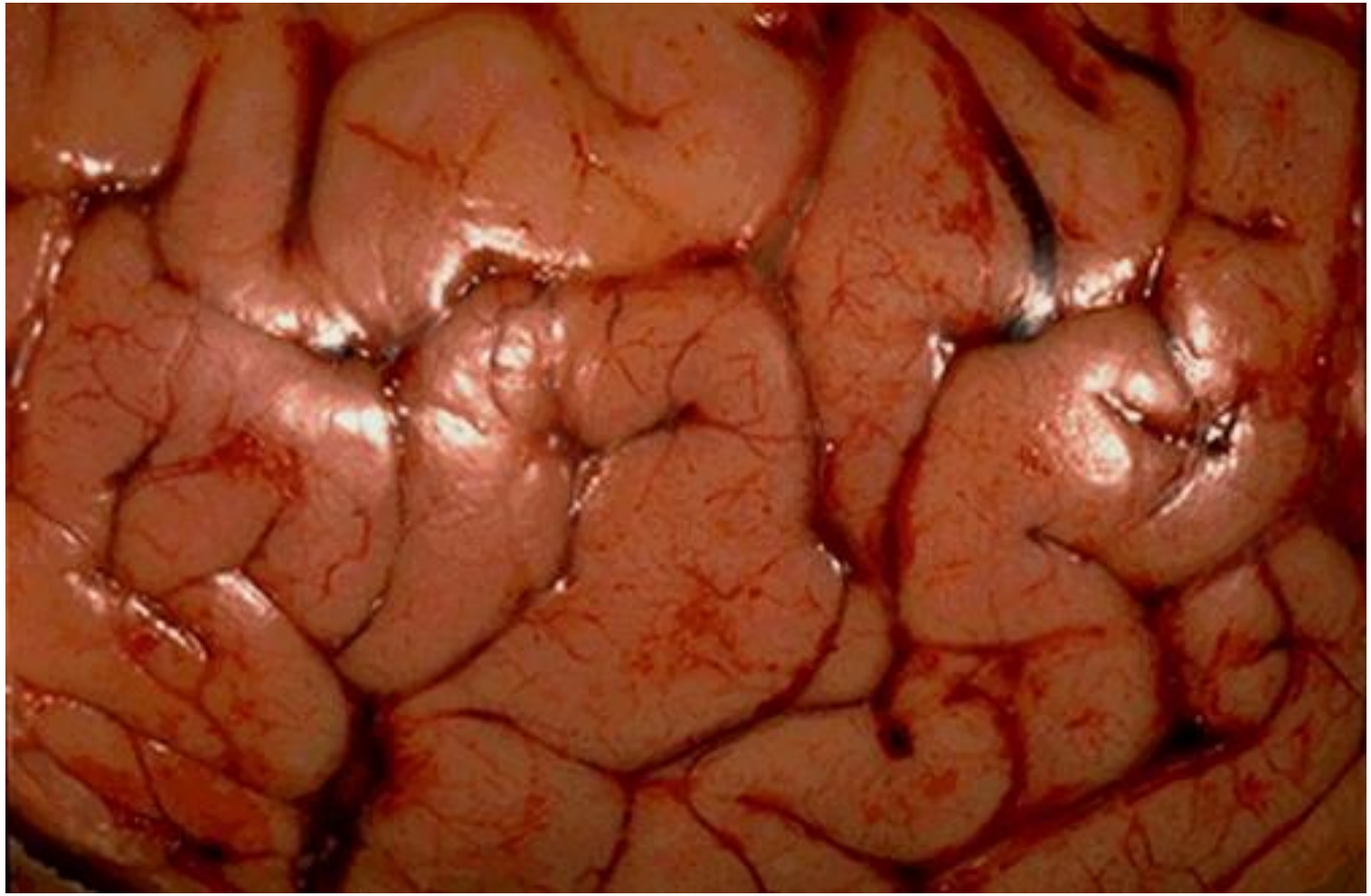
BBB (Blood Brain Barrier)

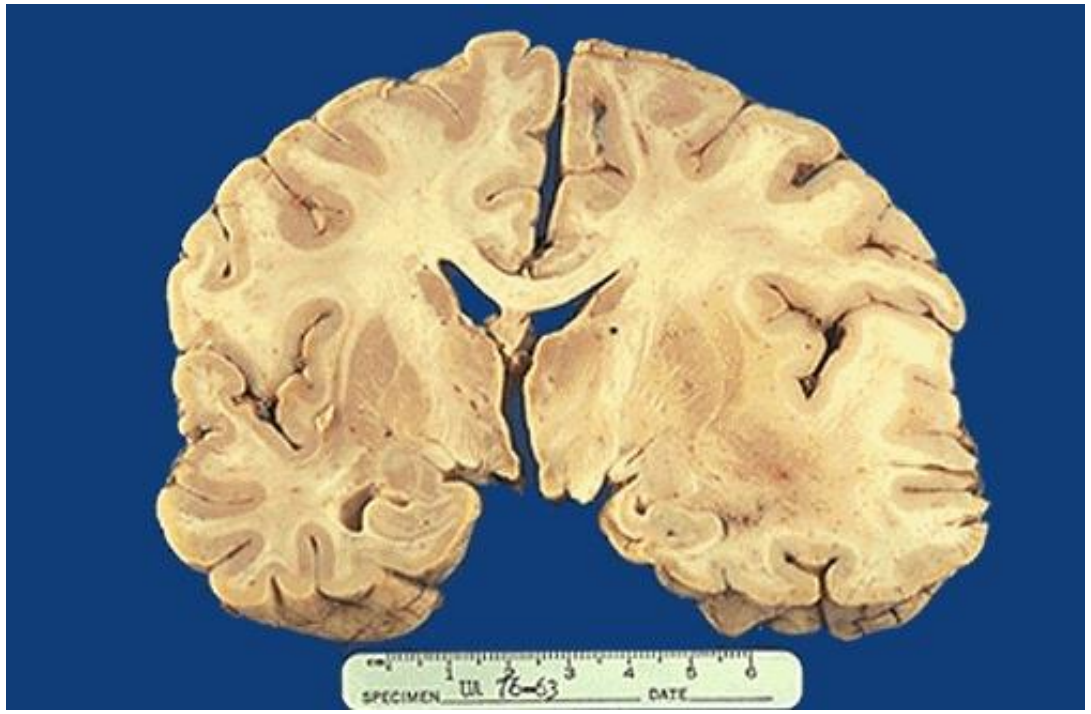
- ***Cytotoxic edema*** is an increase in intracellular fluid secondary to neuronal and glial cell injury, as might follow generalized hypoxic or ischemic insult or exposure to toxins.

CEREBRAL EDEMA

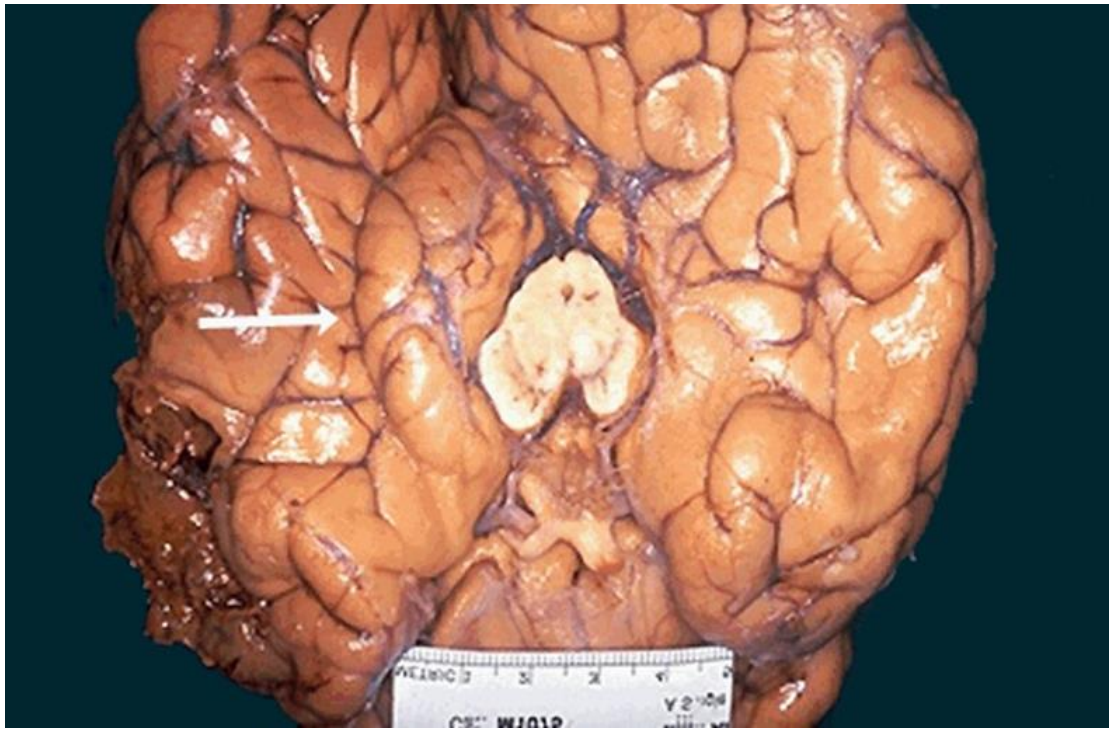


The surface of the brain with cerebral edema demonstrates widened gyri with a flattened surface. the sulci are narrowed.





There is cerebral edema seen at the right which obscures the structures. There is a shift of the midline to the left. Multiple small metastases were the cause for the edema in this case



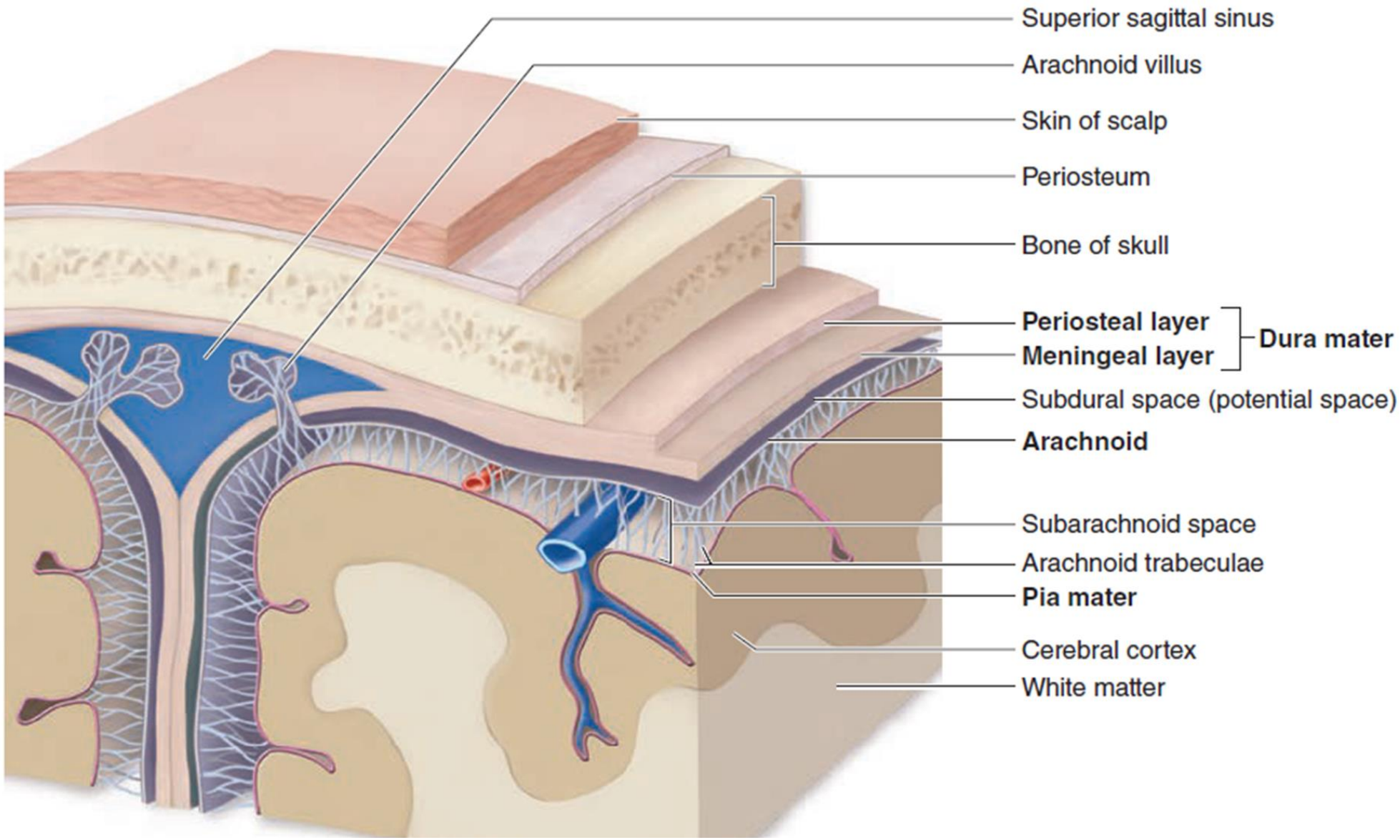
Acute brain swelling is serious. Swelling of the left cerebral hemisphere has produced a shift with herniation of the uncus of the hippocampus through the tentorium, leading to the groove seen at the white arrowhead.

HYDROCEPHALUS

- Choroid plexus produces CSF within the ventricles
- CSF then 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 (arachnoid villi).
- The balance between rates of CSF generation and resorption regulates CSF volume.
- **Hydrocephalus is an increase in the volume of the CSF within the ventricular system.**

Causes:

- Impaired flow or resorption of CSF
- Overproduction of CSF (e.g. some tumors of choroid plexus)


Superior sagittal sinus
Arachnoid villus
Skin of scalp
Periosteum
Bone of skull
Periosteal layer
Meningeal layer
Dura mater
Subdural space (potential space)
Arachnoid
Subarachnoid space
Arachnoid trabeculae
Pia mater
Cerebral cortex
White matter

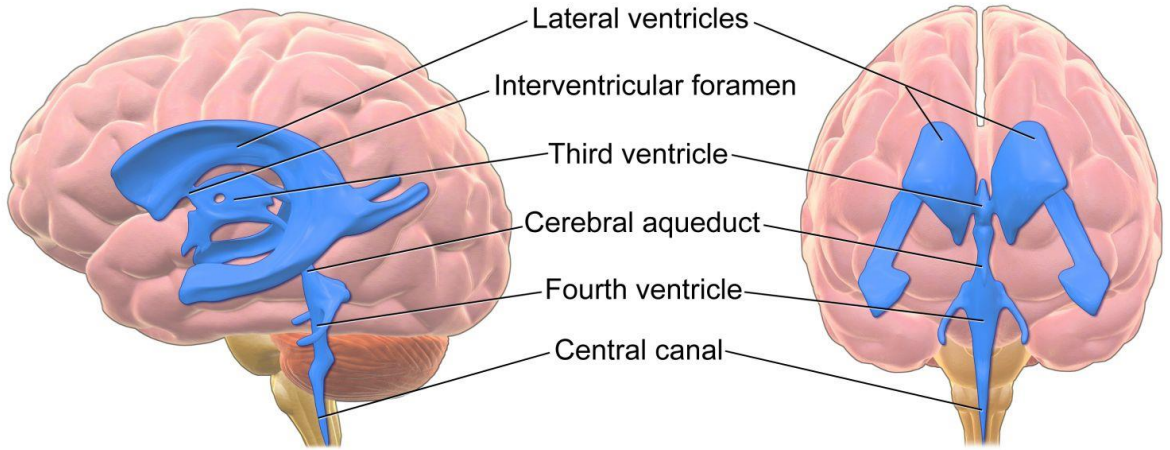
Cerebrospinal Fluid Pathway

Lateral ventricles → Foramen of Monro

Third ventricle → Cerebral aqueduct (of Sylvius)

Fourth ventricle → Foramen of Luschka and Magendie

Subarachnoid space → Arachnoid villi and then to venous drainage system of brain



(lateral view) *(anterior view)*

HYDROCEPHALUS -TYPES

- **Non-communicating hydrocephalus:** there is obstruction to CSF flow within the ventricular system, then a portion of the ventricles enlarges while the remainder does not.

- **Communicating hydrocephalus:** it is usually caused by reduced CSF resorption, and the entire ventricular system is enlarged

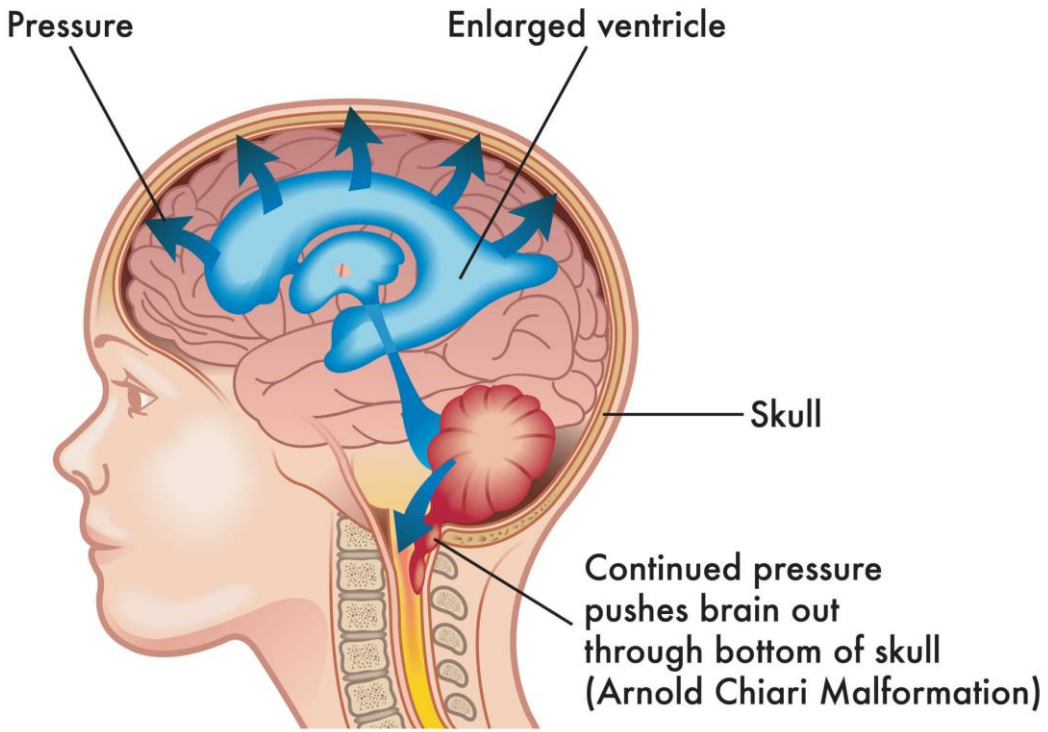
- **Hydrocephalus ex vacuo:** a compensatory increase in CSF volume may occur secondary to a loss of brain volume (e.g., infarction, neurodegenerative disease). In such settings, the hydrocephalus is of no clinical significance.

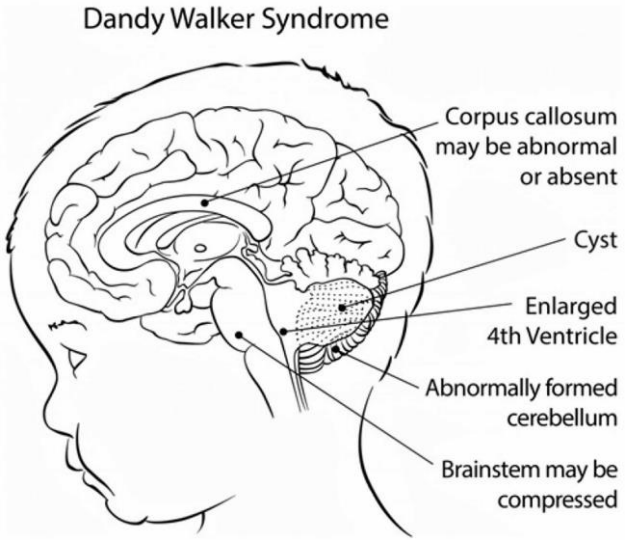
NON-COMMUNICATING HYDROCEPHALUS

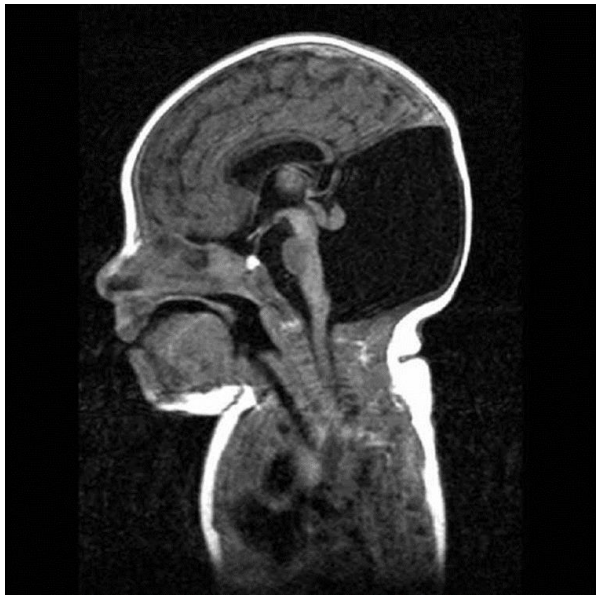
- **Foramen of Monro obstruction:** dilation of one or both lateral ventricles.
- **The aqueduct of Sylvius** obstruction (e.g., atresia, hemorrhage, or tumor) and lead to dilation of both lateral ventricles, as well as the third ventricle.
- **Fourth ventricle obstruction** leads to dilatation of the aqueduct, as well as the lateral and third ventricles (e.g., Chiari malformation).
- **The foramina of Luschka** and **foramen of Magendie** may be obstructed due to congenital malformation (e.g., Dandy-Walker malformation).

Congenital failure of cerebellar vermis to develop so that 4th ventricle is massively dialated and cerebellum is absent; often accompanied by hydrocephalous

Chiari malformation

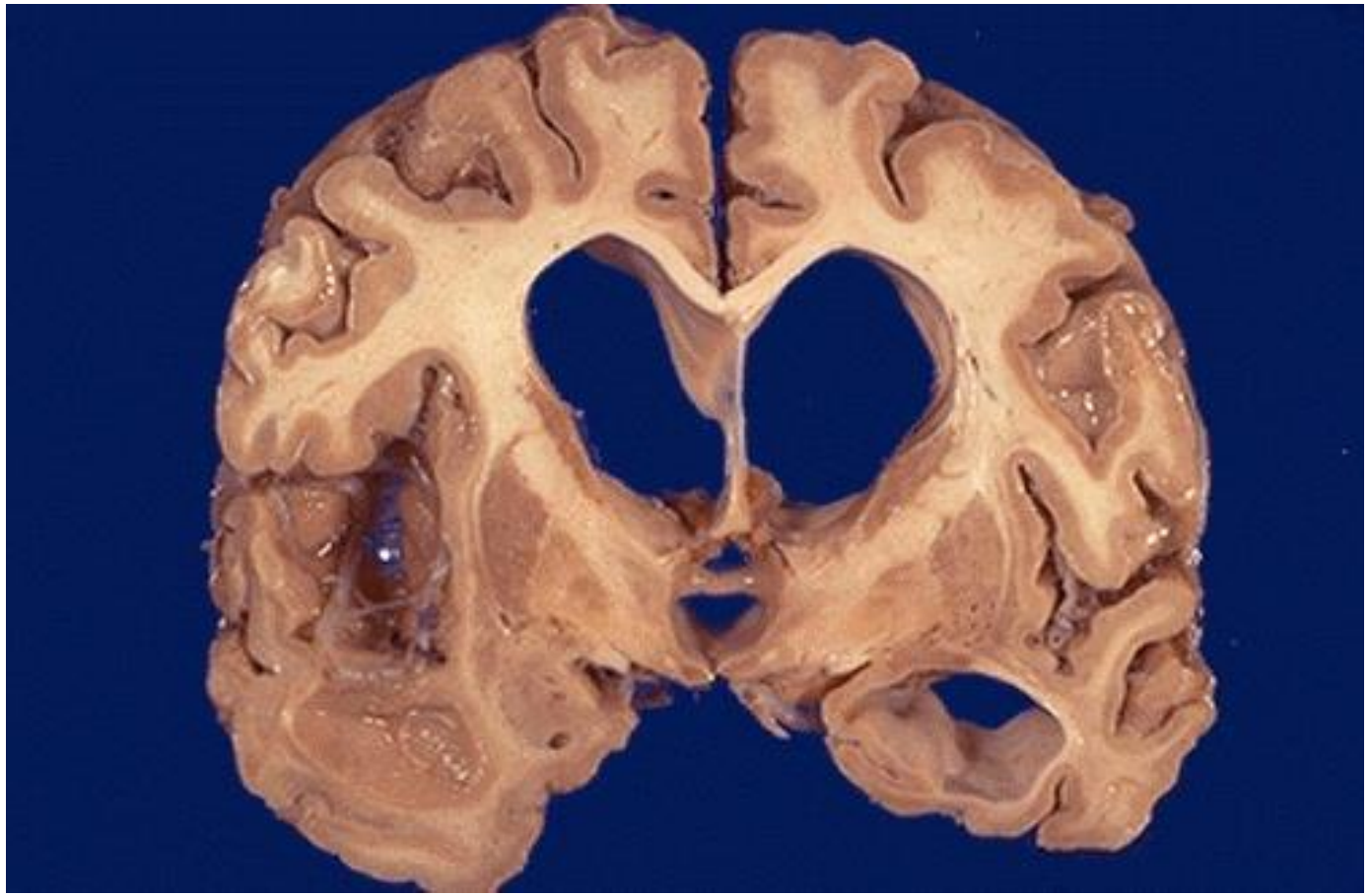




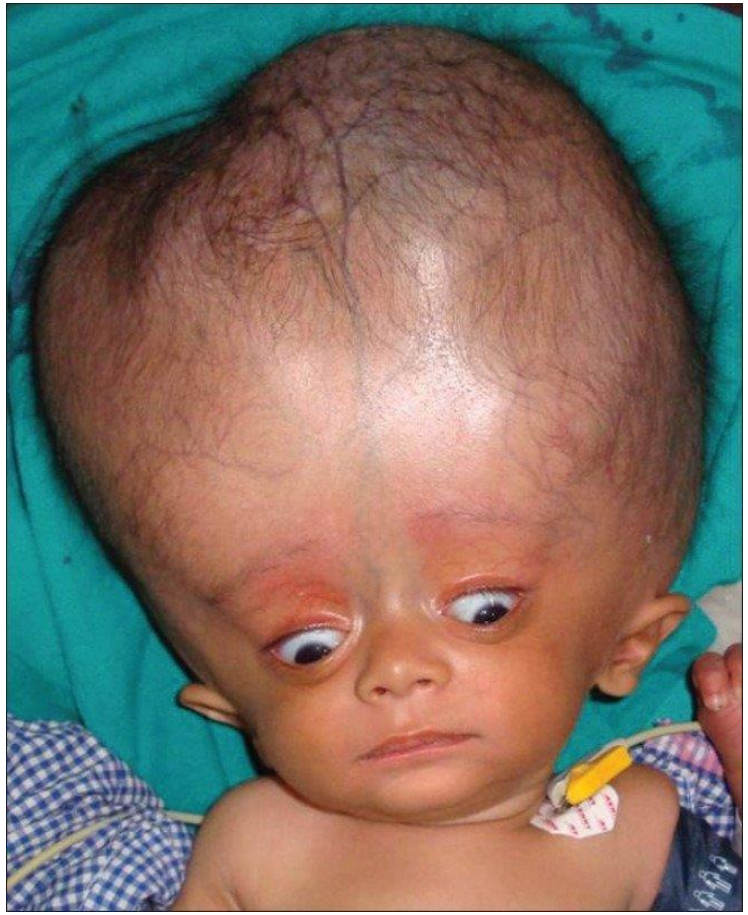


Note the marked dilation of the cerebral ventricles in hydrocephalus.

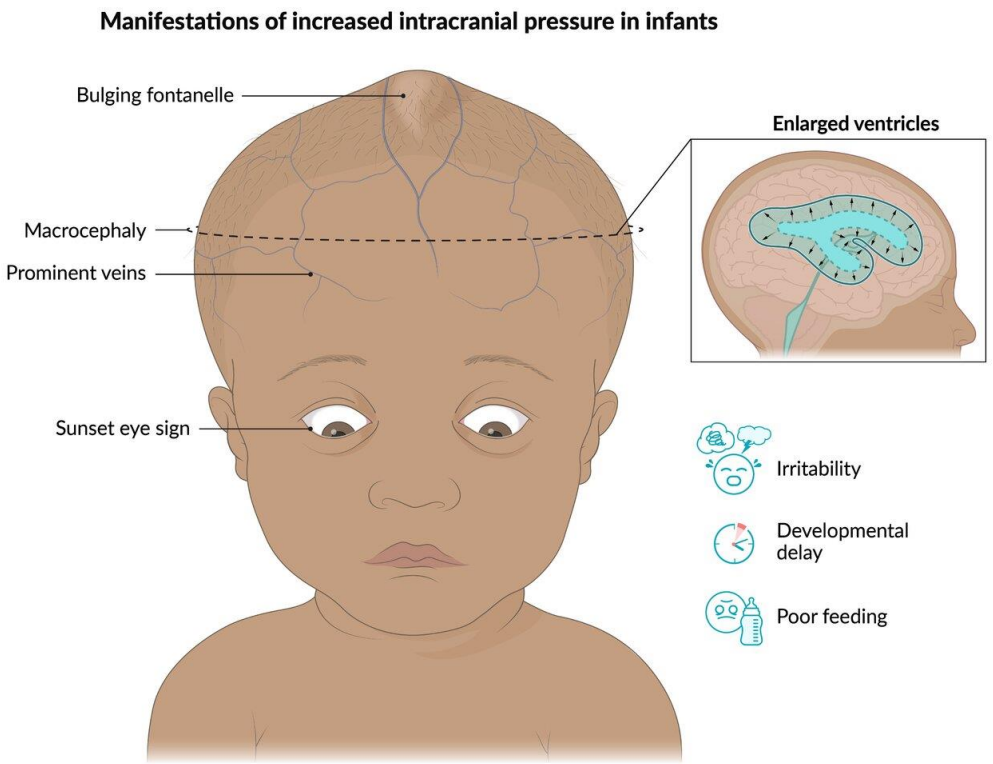
Hydrocephalus can be due to lack of absorption of CSF or due to an obstruction to flow of CSF



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



Symptoms of hydrocephalus in babies and adults



Urinary incontinence (“wet”), gait instability (“wobbly”), and cognitive changes (“wacky”).

Overview of hydrocephalus

	Pathophysiology	Clinical features	Diagnosis

Communicating hydrocephalus	• ↑ CSF production
	• ↓ CSF absorption
		• Typical findings of raised ICP
		  ◦ Headache, nausea, and vomiting
		  ◦ Papilledema
		  ◦ Abducens nerve palsy
		  ◦ Abnormal gait
		  ◦ Impaired consciousness
		  ◦ Cushing triad (irregular breathing, widening pulse pressure, bradycardia)
			• Ultrasonography (children ≤ 18 months of age)
			• MRI or CT (older children and adults)

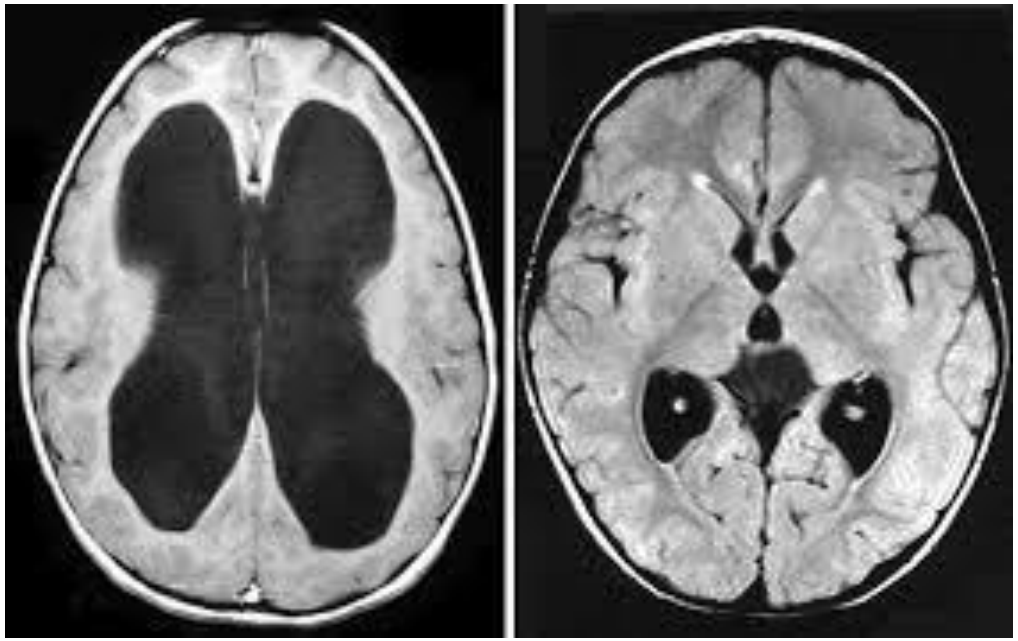
Noncommunicating hydrocephalus	• **Obstructed passage of CSF** from the ventricles to the subarachnoidal space		

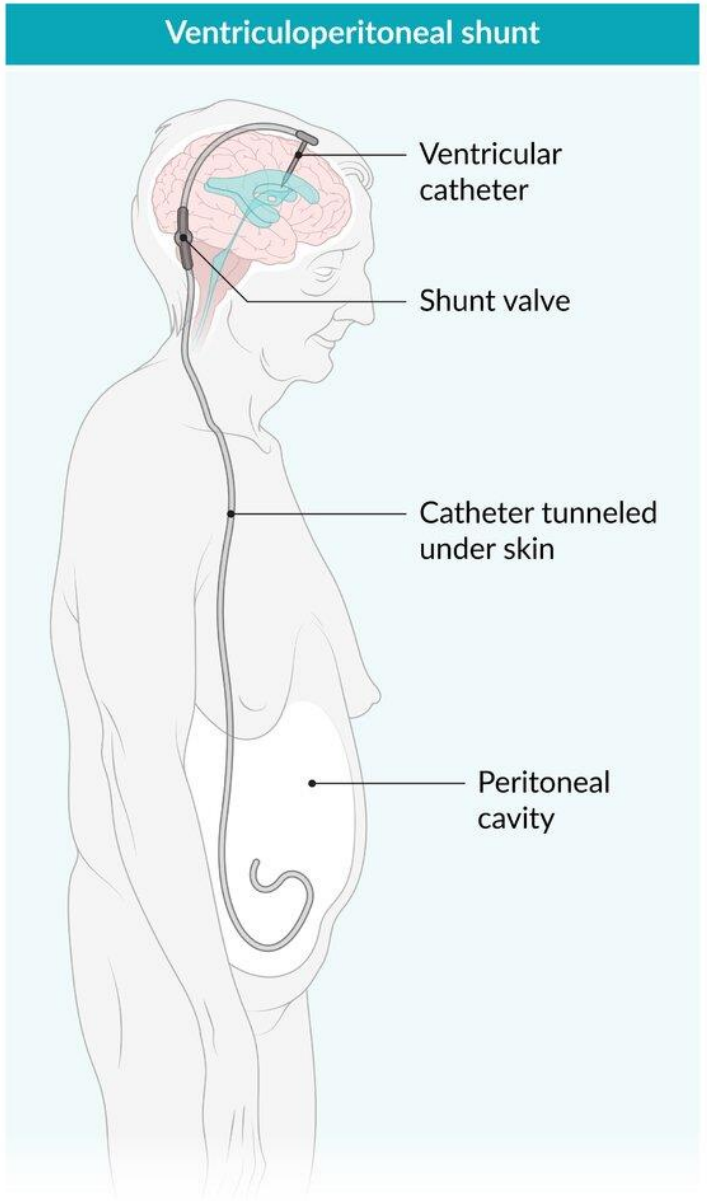
Normal pressure hydrocephalus (NPH)	• **↓ CSF absorption**	• **Classic triad**
		  ◦ **Wet**: urinary incontinence
		  ◦ **Wacky**: dementia
		  ◦ **Wobbly**: frequent falls, broad-based gait with short, shuffling steps (gait apraxia)
			• MRI (initial test)
			• CSF tap test

Hydrocephalus ex vacuo	• Loss of brain tissue	• Symptoms of the underlying condition (e.g., Alzheimer disease, Pick disease)	• Cortical atrophy may be prominent on imaging.

Diagnosis and treatment

CT and MRI scans



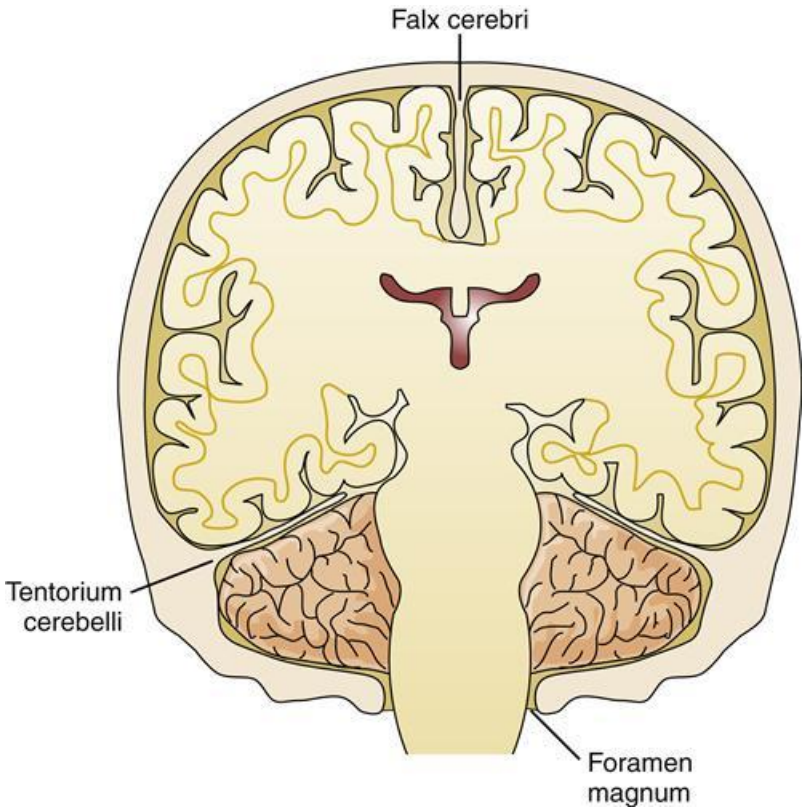


HERNIATION

- Herniation is the displacement of brain tissue from one compartment to another in response to increased ICP

- The intra-cranial compartment is divided by rigid dural folds (falx and tentorium).

- If the pressure is sufficiently high, portions of the brain are displaced across these rigid structures. This herniation often leads to compromise of the blood supply to compressed tissue, producing infarction, swelling, and further herniation.



THERE ARE THREE MAIN TYPES OF HERNIATION

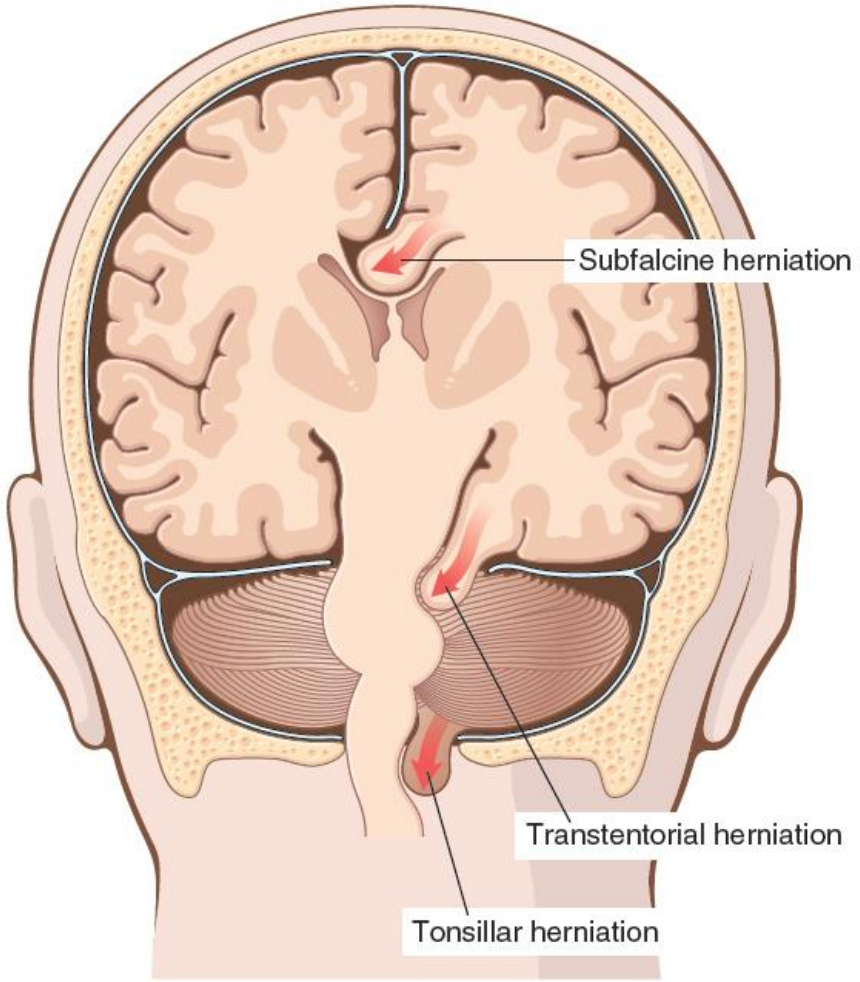
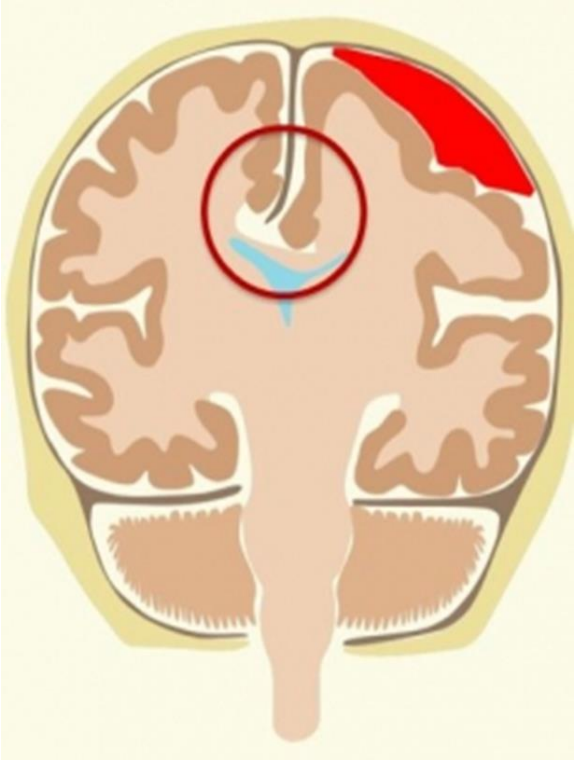


Fig. 23.4 Herniation syndromes. Displacement of brain parenchyma across fixed barriers can be subfalcine, transtentorial, or tonsillar (into the foramen magnum).

1. SUBFALCINE (CINGULATE) HERNIATION

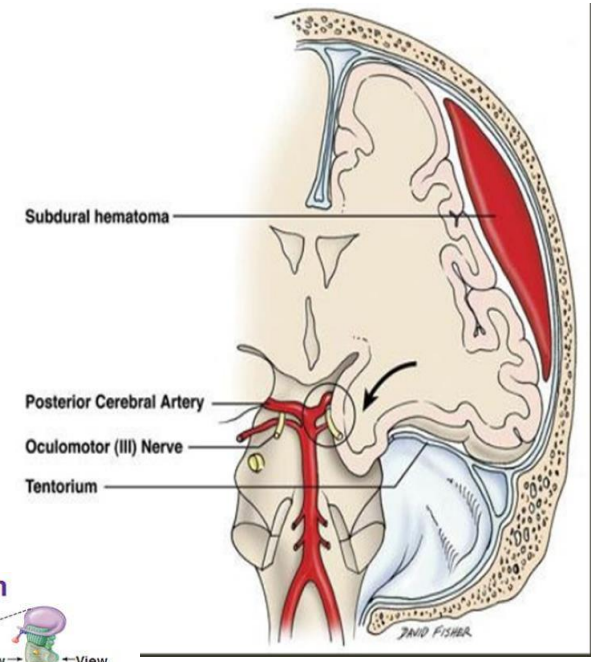
- Herniation of Cingulate gyrus under falx cerebri into the subfalcine space

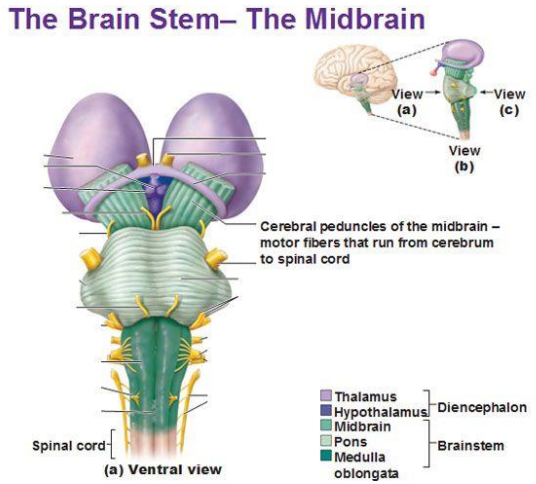
- Compression of branches of Anterior Cerebral Artery causes cerebral infarction



2- *TRANSTENTORIAL (UNCINATE) HERNIATION*

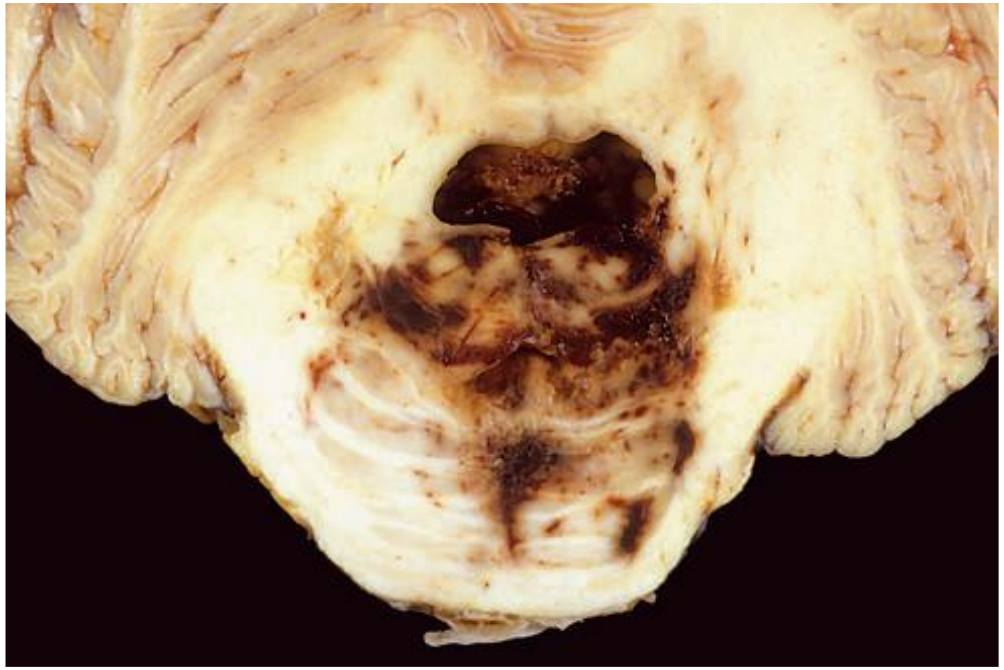
- Herniation of medial temporal lobe through tentorium.
- 3rd Cranial Nerve compression lead to ipsilateral dilated pupil & impaired eye movement
- Pressure on Posterior Carotid Artery lead to Occipital infarction, including visual cortex
- With further displacement of the temporal lobe, pressure on the midbrain may compress the contralateral cerebral peduncle against the tentorium, resulting in hemiparesis ipsilateral to the side of the herniation.





2- TRANSTENTORIAL (UNCINATE) HERNIATION

- Progression of transtentorial herniation is often accompanied by linear or flame-shaped hemorrhages in the midbrain and pons, termed **Duret hemorrhages**

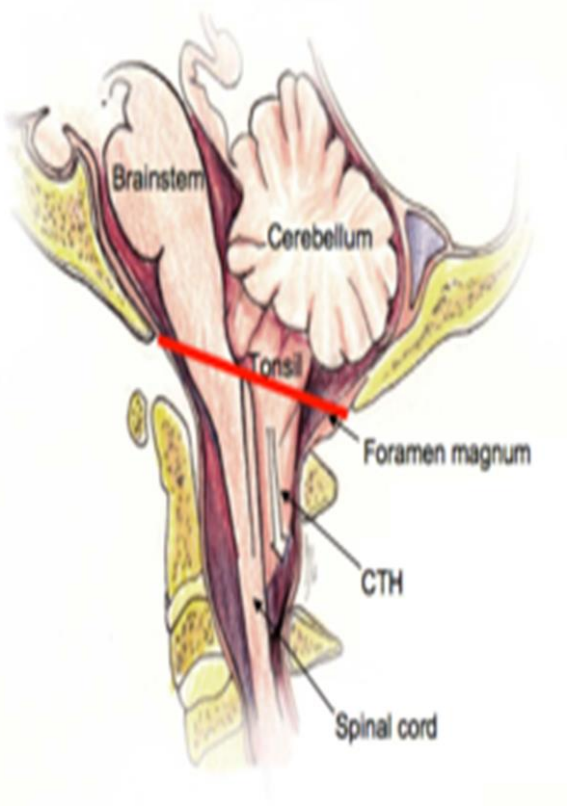


Duret hemorrhage. As mass effect displaces the brain downward, there is disruption of the vessels that enter the pons along the midline, leading to hemorrhage.

3- *TONSILLAR HERNIATION*

- *Tonsillar herniation* refers to displacement of the cerebellar tonsils through the foramen magnum.

- This type of herniation causes brain stem compression and compromises vital respiratory and cardiac centers in the medulla, and is often fatal.



DEVELOPMENTAL ANOMALIES

Neural tube defects :

- **Anencephaly:** absence of skull and brain

- There is no cure or standard treatment for anencephaly and the prognosis for patients is death.
- Most anencephalic fetuses do not survive birth, accounting for 55% of non-aborted cases. Infants that are not stillborn will usually die within a few hours or days after birth

DEVELOPMENTAL ANOMALIES

Neural tube defects :

- **Spina bifida :**

- Failure of posterior vertebral arch to close
- Spina bifida occulta (asymptomatic)
- Spina bifida - cystic protrusion of underlying tissue :

  1.Meningocele - meninges protrude
  2.Meningomyelocele - meninges and spinal cord protrude