



# Pathology

## CNS Revision

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## Pathology

# CNS Congenital Anomalies & Hydrocephalus

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Neural tube defects

Forebrain malformations

## Congenital Malformations

Posterior fossa malformations

Spinal cord malformations

Hydrocephalus

# Congenital Malformations of the CNS

## \* Causes:

- Unknown,
- Genetic factors,
- Environmental factors: Teratogens (e.g. chemicals, infectious agents)
- Maternal conditions: e.g. Folic acid deficiency early in pregnancy, alcoholism.

## \* Classification:

- Neural tube defects
- Forebrain malformations
- Posterior fossa malformations
- Spinal cord malformations

# Neural tube defects

Failure of a part of the neural tube to close  
→ malformations involving neural tissue, meninges, and overlying bone or soft tissues.

- Maternal serum level of alpha-fetoprotein (MSAFP) is used to screen neural tube defects (elevated).

## Classification:

- Spinal neural tube defects
  - Spina bifida occulta
  - Meningocele
  - Myelomeningocele
- Cranial neural tube defects
  - Anencephaly
  - Encephalocele

# Neural tube defects

## A. Spinal neural tube defects

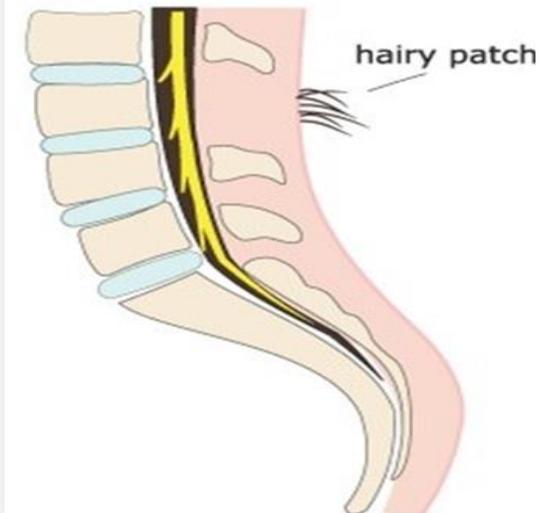
Site: lumbo-sacral region (mostly S1 to S2).

**Spina bifida occulta:** (least severe type)

- A bone gap of the vertebral spine.
- Other layers are normal.
- No opening on the back.
- Associated with moles, angioma, lipoma, and a hair patch over the affected area.
- Clinically: Very few cases have symptoms as: back pain, scoliosis, leg weakness and bowel or bladder dysfunction.

Spina bifida occulta

(opened posterior vertebral body)



# Neural tube defects

## Meningocele:

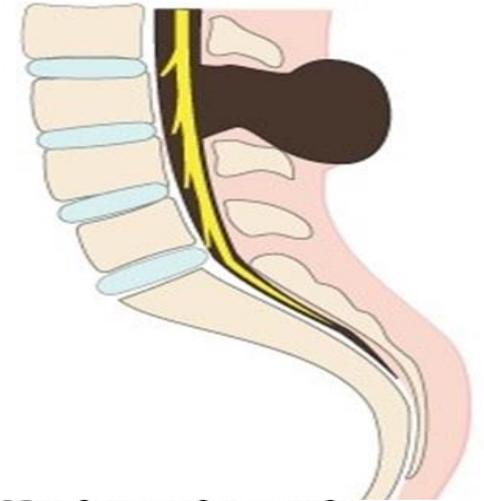
- The meninges are protruded through the bone opening forming a CSF-filled sac.
- The rarest type of spinal defects.

## Myelomeningocele: (most severe type)

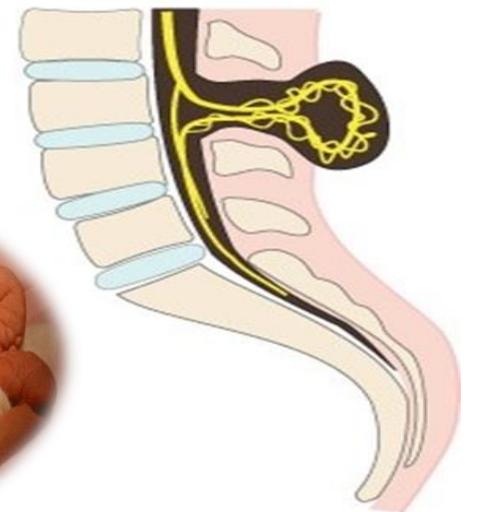
- Protrusion of a segment of spinal cord and nerves within a meningeal sac through the back, leads to:
  - Bowel and bladder dysfunction, or total paralysis of the lower limbs.
  - Risk of infections.



**Meningocele**  
(protrusion of the meninges)



**Myelomeningocele**  
(protrusion and opened spinal cord)



# Neural tube defects

## B. Cranial neural tube defects

### Encephalocele:

Cranial defect with a sac-like protrusion of malformed brain tissue and membranes. It most often occurs in the occipital region.



### Anencephaly:

Absence of most of the brain and calvarium. Incompatible with postnatal life.



# Forebrain malformations

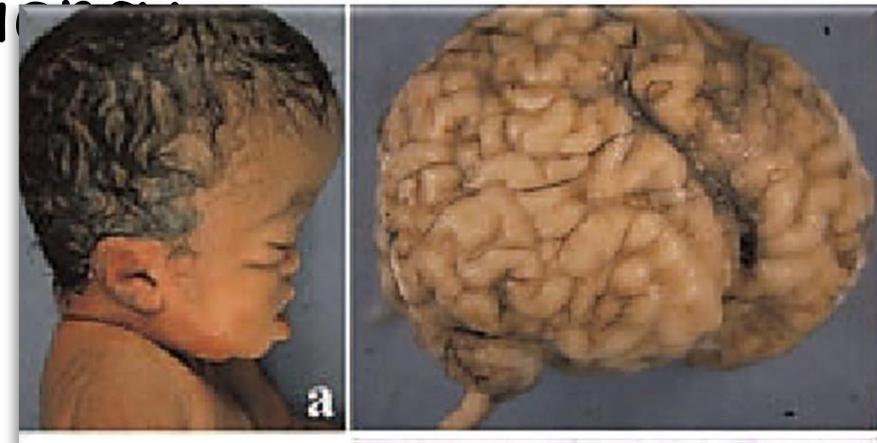
## Microencephaly: (more common)

Small brain volume, with a small head circumference. Caused by:

- Chromosomal abnormalities,
- Fetal alcohol syndrome
- Intrauterine human immunodeficiency virus 1 (HIV-1) infection.

## Megalencephaly:

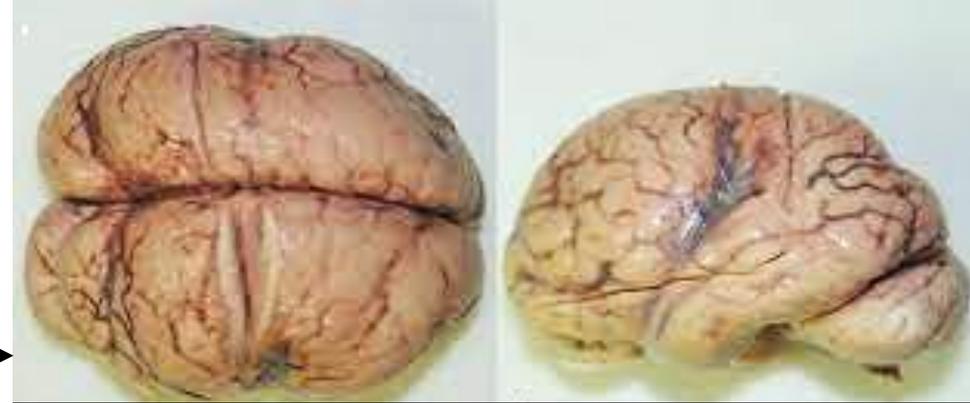
Large brain volume (less common).



# Forebrain malformations

## Lissencephaly:

- Reduction in the number of gyri, or
- no gyral pattern (agyria).

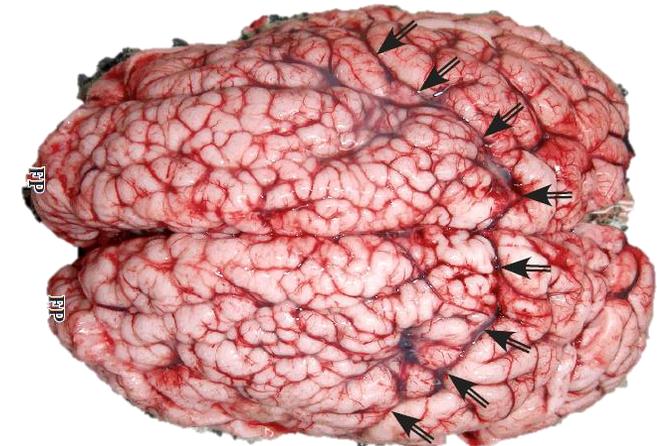
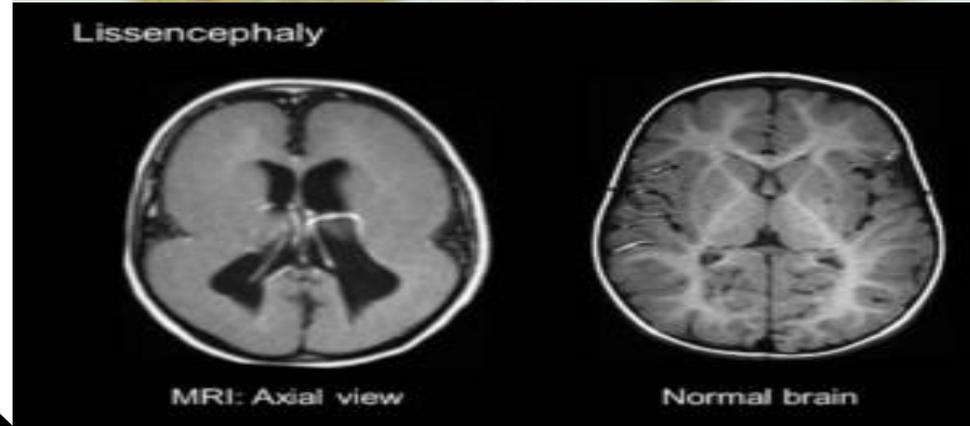


## Polymicrogyria:

Increased number of abnormal gyri with altered cortical structure.

## Neuronal heterotopia:

- A collection of neurons in inappropriate locations
- (defect in migration) → epilepsy.



# Posterior fossa malformations

## 1. Chiari malformations:

### Type I:

- Low-lying cerebellar tonsils into the vertebral canal → **medullary compression**.
- Associated with **syringomyelia**.

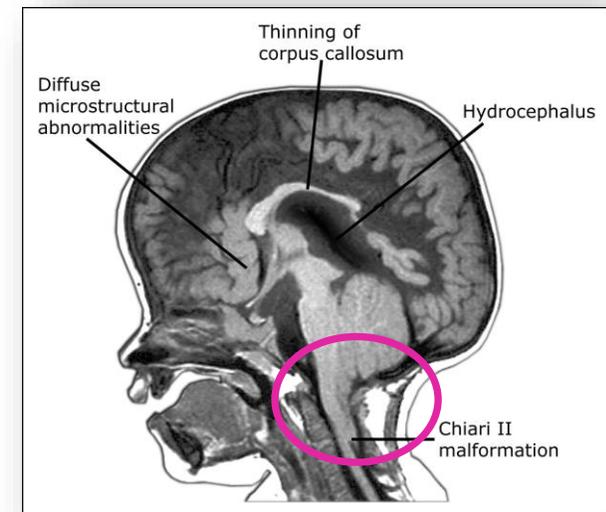
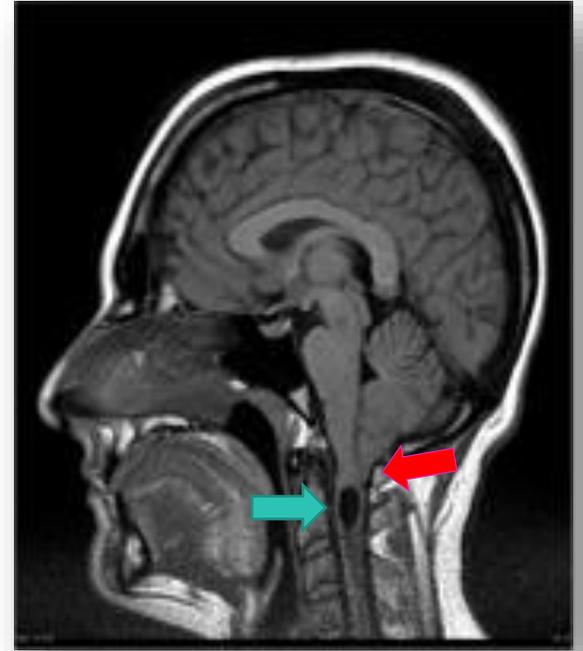
### Type II:

- Extension of cerebellar vermis through the foramen magnum → **hydrocephalus**.
- Associated with **myelomeningocele**.

## 2. Dandy-Walker malformation:

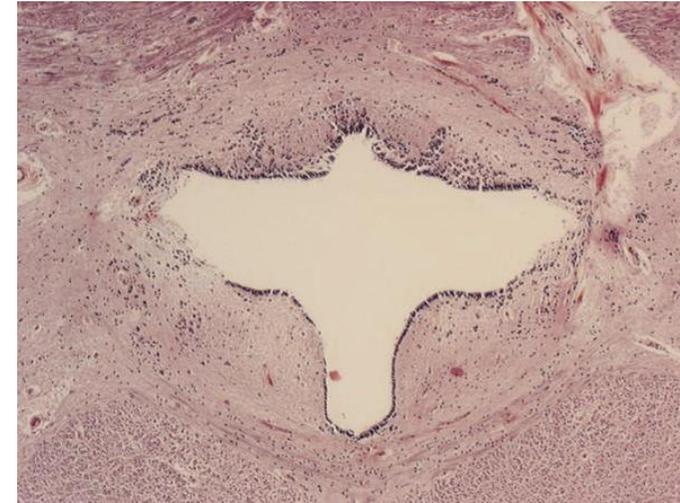
Enlarged posterior fossa, absent cerebellar vermis with a large midline cyst

## 3. Aqueductal stenosis → hydrocephalus.



# Spinal cord malformations

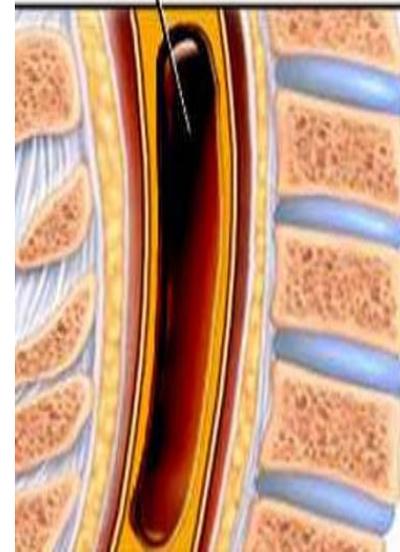
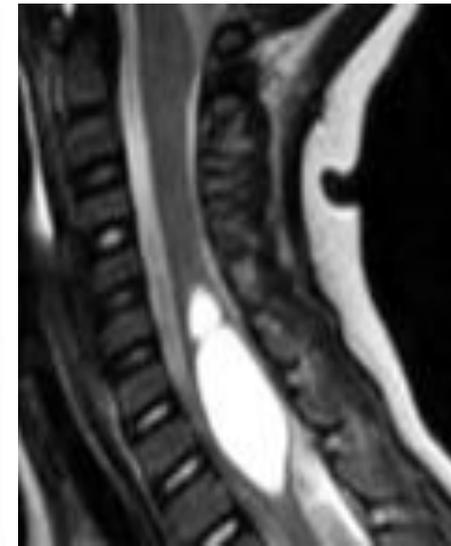
1. **Hydromyelia:** Expansion of the central canal of the cord. →



2. **Syringomyelia (syrinx):** A central fluid-filled cleft-like cavity in the cord → loss of pain and temperature sensation in the upper extremities.

## Syringomyelia

Fluid-filled cyst (syrinx)



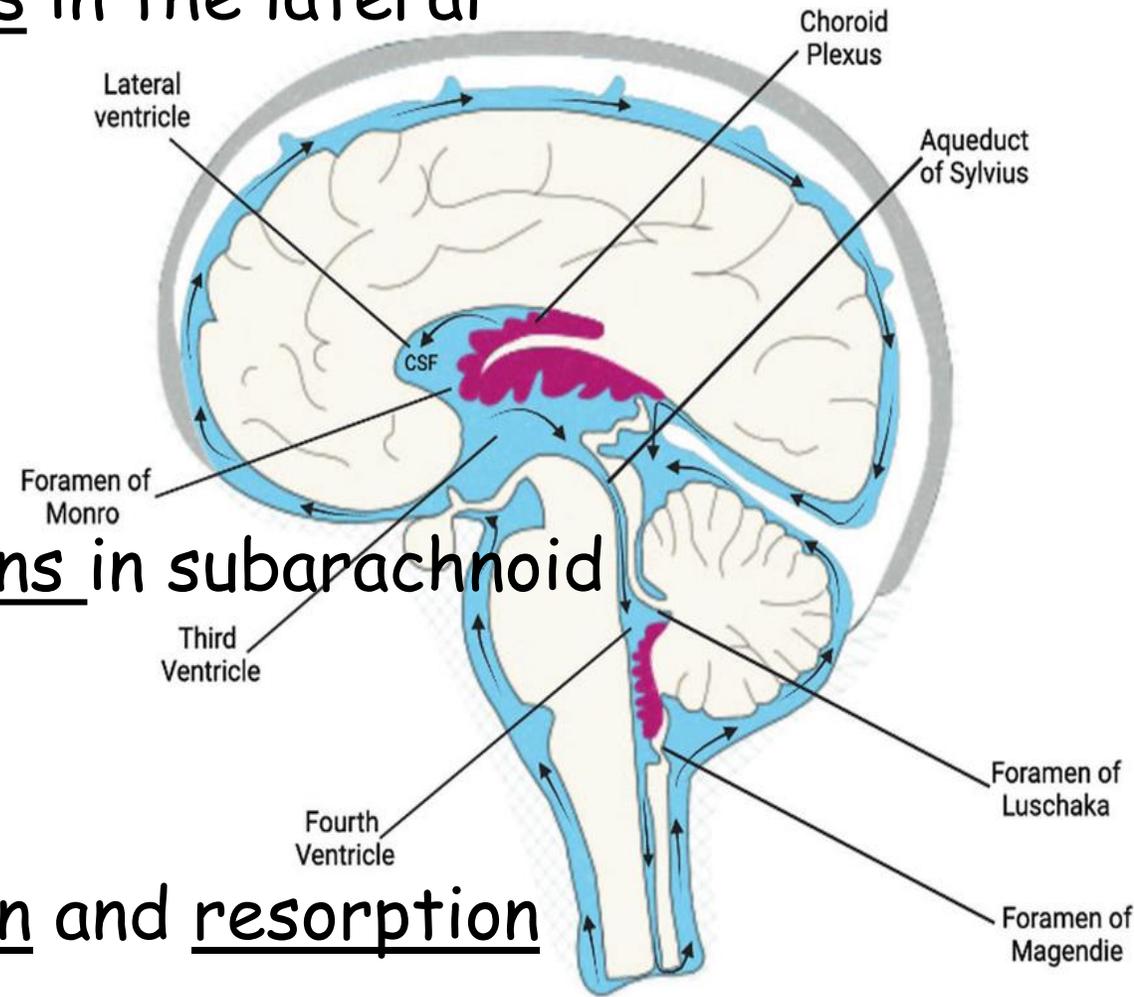
## Now....Answer this

Which of the following characterizes Arnold-Chiari malformation type II?

- A. Low-laying cerebellar tonsils into the vertebral canal.
- B. A central fluid filled cavity in the spinal canal.
- C. Enlarged posterior fossa with large midline cyst.
- D. Extension of cerebellar vermis into the foramen magnum.
- E. Sac-like protrusion of malformed brain tissue and membranes via defect.

# CSF Circulation

1. CSF is produced by choroid plexus in the lateral ventricles →
  2. 3<sup>rd</sup> ventricle →
  3. Aqueduct of Sylvius →
  4. 4<sup>th</sup> ventricle →
  5. Foramina of Magendie →
  6. Resorbed by arachnoid granulations in subarachnoid space →
  7. The dural venous sinuses →
  8. Blood stream.
- The balance between CSF production and resorption regulates its volume.



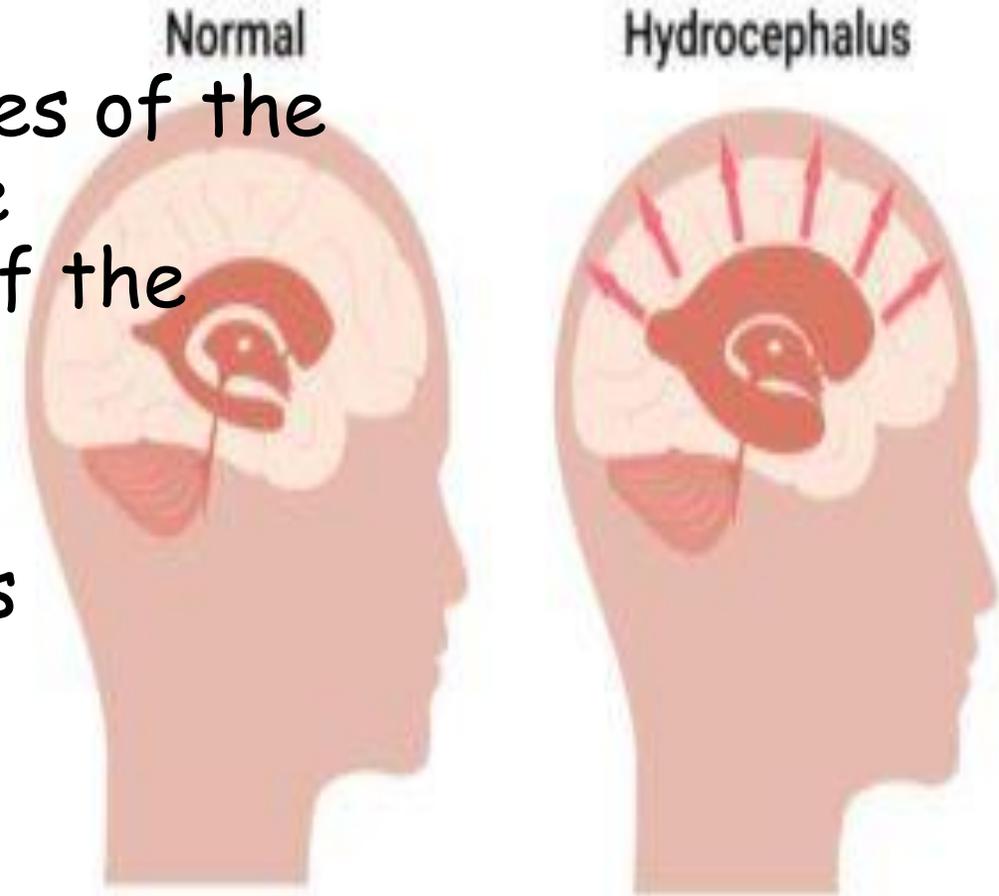
# Hydrocephalus

## Definition:

Abnormal dilatation of the ventricles of the brain due to increased C.S.F volume associated with pressure atrophy of the brain tissue.

## Pathogenesis, causes: 3 mechanisms

1. Increased CSF production
2. Decreased CSF resorption
3. CSF flow obstruction



# Hydrocephalus

## 1. Increased CSF production

- Choroid plexus neoplasms (papilloma, carcinoma)
- Choroiditis.

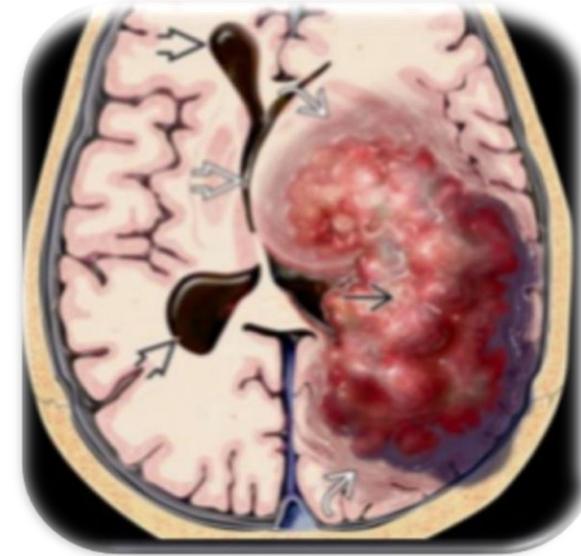
## 2. Decreased CSF resorption

### • Congenital:

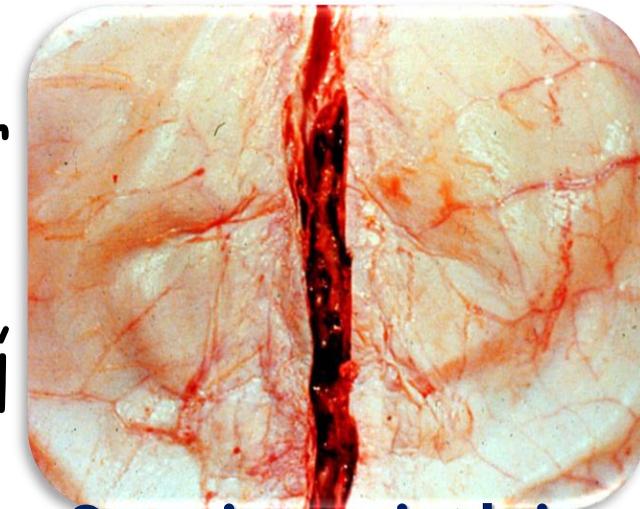
Agensis, aplasia or hypoplasia of arachnoid granulations.

### • Acquired:

- Fibrosis of arachnoid granulations (after meningitis or subarachnoid hemorrhage).
- Space occupying lesions (abscess, hematoma, tumor → compress the brain against the skull compromising the arachnoid granulations).
- Superior sagittal sinus thrombosis.



Choroid plexus carcinoma



Superior sagittal sinus thrombosis

# Hydrocephalus

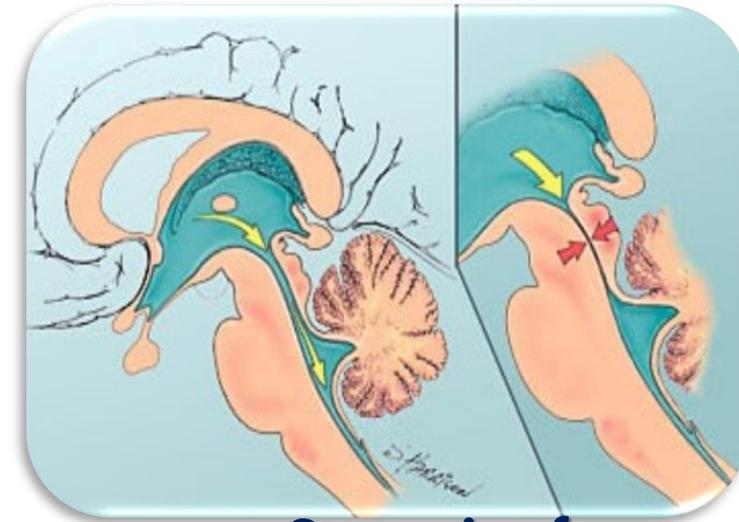
## 3. CSF flow obstruction

### Congenital:

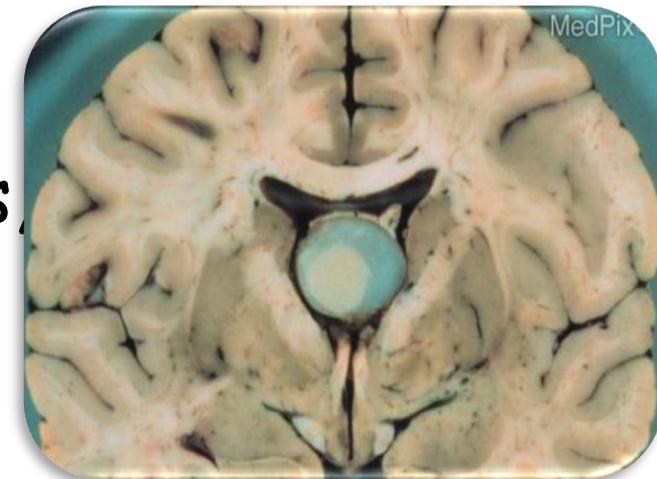
- Stenosis of aqueduct of Sylvius.
- Obstruction or stenosis of foramina of Luschka and Magendie.
- Chiari type II malformation.

### Acquired:

- 3rd ventricle cyst or glioma.
- Adhesions of 4th ventricle foramina (post-meningitis, post-subarachnoid hemorrhage).
- Adhesions of arachnoid space (post-meningitis, post-subarachnoid hemorrhage).
- Space occupying lesions (abscess, hematoma or tumor compress the brain to the skull compromising the subarachnoid space).



**Stenosis of aqueduct of Sylvius**

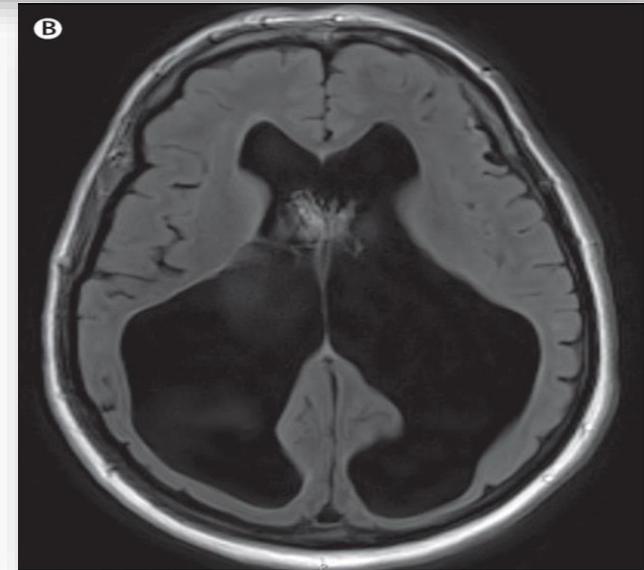
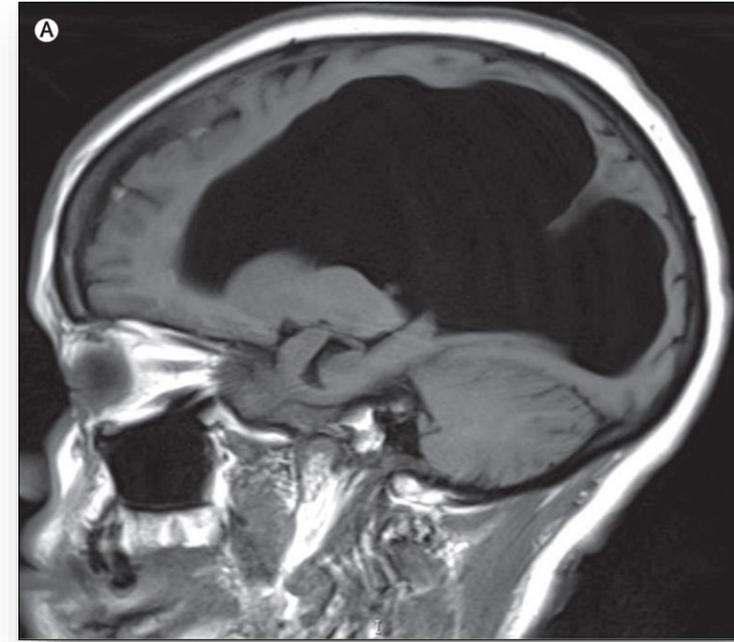


**Third ventricle cyst**

# Hydrocephalus

## Types of hydrocephalus:

- **Communicating:** The ventricles communicate with the subarachnoid space (mainly increased production).
- **Non-communicating:** The ventricles are not communicating with the subarachnoid space (mainly obstruction to CSF flow).
- **Compensatory hydrocephalus:** increased amount of CSF to compensate loss of brain tissue (atrophy, infarcts, surgery).



# Hydrocephalus

## Pathological effects of hydrocephalus:

- Permanent dilation of the ventricular systems proximal to the site of obstruction.
- Raised ventricular C.S.F pressure.
- Pressure atrophy of brain tissue.
- Skull changes:

In children:

-Enlarged Skull.

-Separated Sutures

-Thin Bones

-Mental deficiency.

In adults:

- Head does not enlarge (sutures and fontanelles are closed)
- Skull bone show varying degrees of convolutional markings.



## Now....Answer this

A 3-month-old female infant was presented to the pediatrician by abnormally increased head circumference, thin skull bones, wide fontanelles and separate skull sutures. Neurologic examination revealed affected neurologic status. What is the most-likely cause for this condition?

- a. Choroid plexus carcinoma
- b. Atrophic loss of brain tissue
- c. Superior sagittal sinus thrombosis
- d. Narrowing (stenosis) of aqueduct of Sylvius
- e. Post-inflammatory fibrosis of arachnoid granulations



## Pathology

# CNS Infections

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# Agenda

CNS Infection

Bacterial

Viral

Prion disease

# CNS Infections

## Routes of Infection:

1. Hematogenous: most common; by arterial circulation, or retrograde venous spread from veins of the face.
2. Direct implantation: traumatic, iatrogenic (e.g. lumbar puncture) or with congenital malformations (e.g. meningomyelocele).
3. Local spread: from adjacent structures, such as: air sinuses, teeth, skull, or vertebrae.
4. Nerve spread: Viruses transported along the peripheral nerves as in rabies and herpes zoster viruses.

# CNS Infections

## Classification:

- **Bacterial:**
  - Acute suppurative (bacterial or pyogenic) meningitis
  - Focal suppurative infections: Brain abscess, Extradural Abscess, Subdural empyema.
  - Chronic bacterial meningoenkephalitis: (TB, Syphilis).
- **Viral:**
  - Viral (aseptic) meningitis.
  - Viral encephalitis and meningoenkephalitis: Herpes Simplex Virus Type 1 and 2, Varicella-Zoster Virus, Cytomegalovirus (CMV), JC polyomavirus and Human Immunodeficiency Virus (HIV).
  - Brainstem and Spinal cord infection: Rabies and Polio Viruses.
- **Parasitic:** Toxoplasmosis, Cysticercosis, Malaria, Amoebiasis.
- **Fungal:** Candida, Aspergillus, Mucor-mycosis, ...
- **Prion Diseases.**

# Acute Pyogenic Meningitis

Acute suppurative inflammation of leptomeninges involving the subarachnoid space.

## Organisms:

- In neonates: *Escherichia coli* and group B streptococci.
- Young children: *Haemophilus influenzae*.
- In adolescents and young adults: *Neisseria meningitidis*.
- In older adults, *Streptococcus pneumoniae* and *Listeria monocytogenes*.

## Routes of infection:

- Blood born
- Direct spread
- Penetrating wounds

# Acute Pyogenic Meningitis

## Clinical features:

- Signs of systemic infection (e.g. fever)
- Signs of meningeal irritation (headache, irritability, neck stiffness, confusion)

## CSF changes (lumbar puncture):

- Turbid,
- Increased pressure,
- Increased protein,
- Low glucose,
- Excess neutrophils,
- Bacteria detected in smear or by culture.

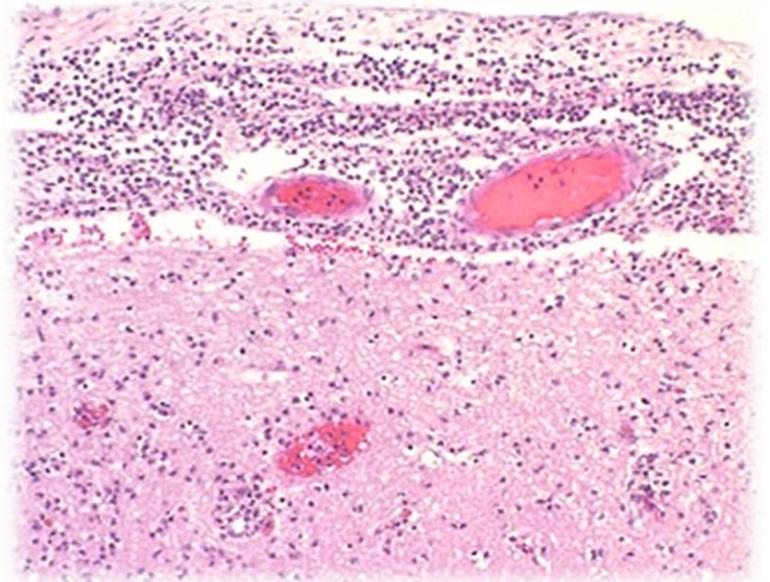
# Acute Pyogenic Meningitis

## Gross:

- 1-The leptomeninges:
  - Hyperaemic ( dilated leptomeningeal vessels), thick opaque, tense
  - The subarachnoid space is filled with yellow pus more apparent at the base of the brain
- 2-The brain: is edematous
- 3-The ventricles: are moderately dilated, contain turbid CSF

## Microscopic:

- Neutrophils and pus cells fill the subarachnoid space and the leptomeninges.
- Edema around the congested blood vessels.
- Brain underneath show oedema and cellular degeneration.



# Acute Pyogenic Meningitis

## Complications:

\*Spread of infection:

- Meningo- encephalitis and small brain infarcts.
- Subdural abscess and sinus thrombophlebitis.
- Meningococcal septicemia may occur when big number of meningococci reach the blood. This can cause bilateral suprarenal hemorrhage and acute suprarenal failure (water- house Friedrichsen syndrome).

\*Nerve paresis especially 3,4,6. caused by Pressure of the exudates and late Fibrous adhesions

\*Hydrocephalus (Increased intracrainal pressure), caused by Pressure of the exudates and late Fibrous adhesions

# Brain Abscess

## Causes:

Pyogenic bacteria, (strept. and staph.)

## Routes of infection:

- External from opened injury, mastoiditis or otitis media, frontal sinusitis.
- Blood spread from suppuration or septic emboli.

## Acute abscess:

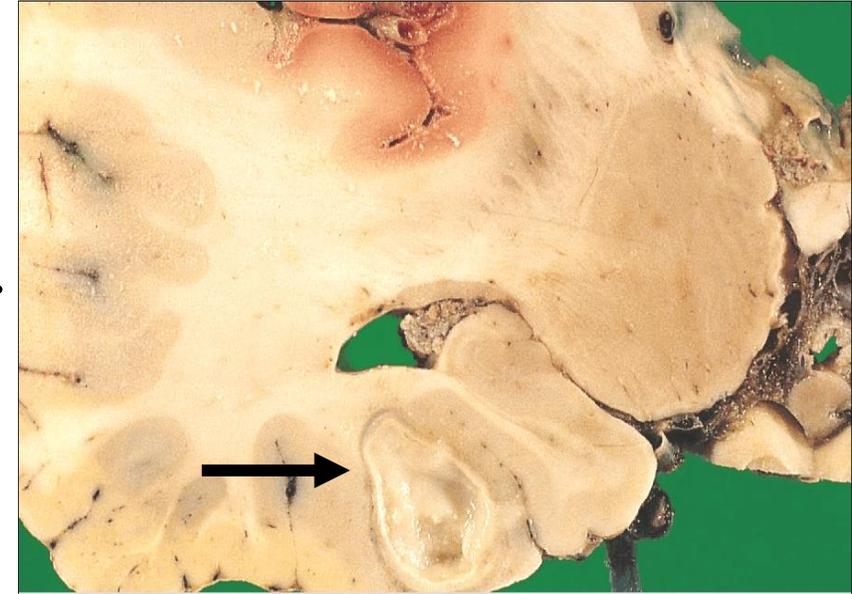
- Cavity filled with pus, surrounded by area of congestion and has irregular shreddy lining.

## Chronic abscess:

- Develops after 3-6 weeks.
- Has fibrous wall of fibroglia and the lining is smooth.

## Complications:

- Direct spread produces suppurative encephalitis, subdural abscess, sinus thrombophlebitis and extradural abscess.
- Rupture into ventricular system (ventriculitis) or subarachnoid space producing meningitis.



# Acute Viral (Aseptic) Meningitis

Acute inflammation of leptomeninges in absence of bacteria by culture.

## Cause:

- Most commonly **enteroviruses** (polio-, echo-, coxackie-).

## C/P:

- Signs of meningeal irritation, fever, and alterations of consciousness of relatively acute onset.

## CSF changes:

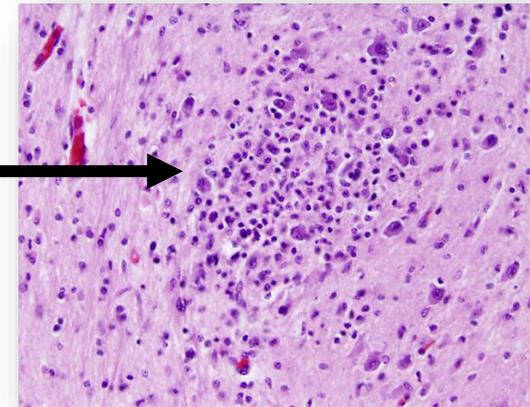
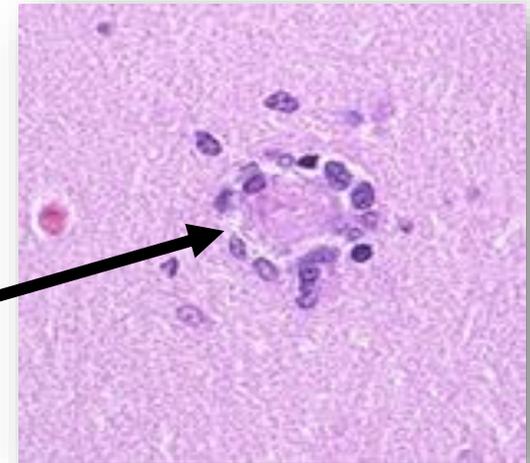
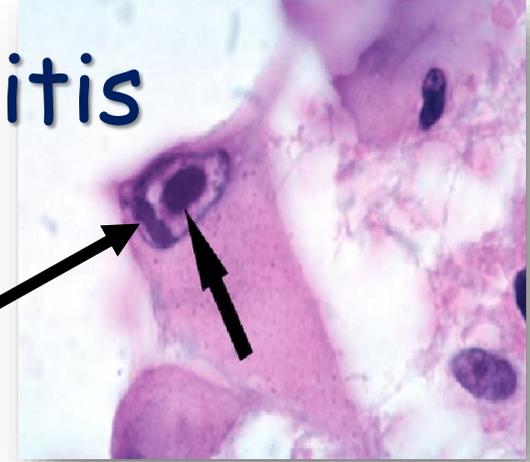
- Lymphocytosis,
- Mild to moderate increase in protein,
- Normal glucose.

**Fate:** Usually self-limited.

# Viral Encephalitis / Meningoencephalitis

## General Features:

- generalized viraemia which in a proportion of cases is followed by localization in the C.N.S
- virus multiply within the nerve cells:
  - Nissel degeneration
  - inclusion bodies (virus particles)
- Nerve cell necrosis, which are removed by microglia (neuronophagia).
- hyperemia and mononuclear cell inflammatory response with collection of macrophage (Microglial nodules).
- Healing occur by glial scar (gliosis).



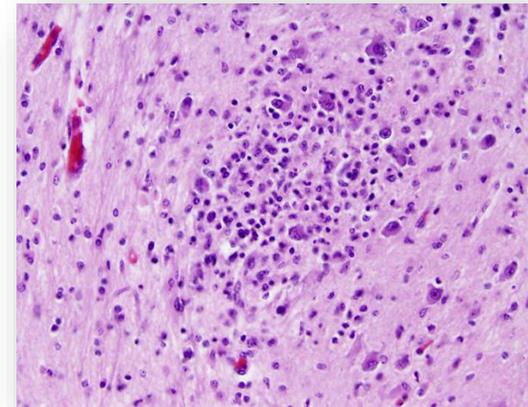
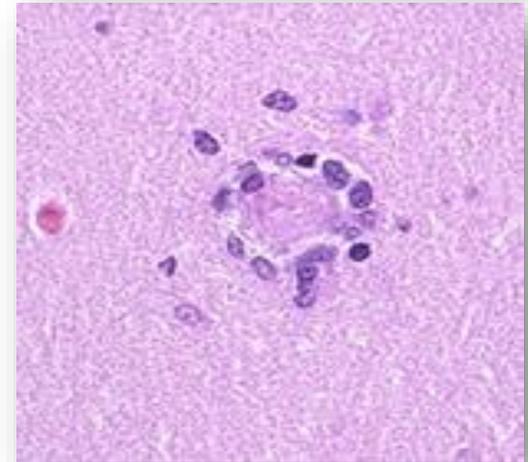
# Viral Encephalitis / Meningoencephalitis

## 1. Herpes Simplex Virus (HSV):

### Type 1:

- Affects children in the **temporal and inferior frontal lobes**.
- Acute viral infection of sensory nerve ganglia, its nerve and its area of supply (skin or mucous membrane). It produce redness and vesicles which ulcerate without scar
- **Cowdry type A** bodies are intranuclear inclusion bodies.

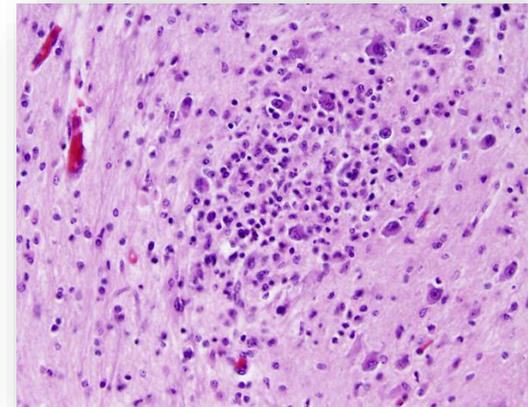
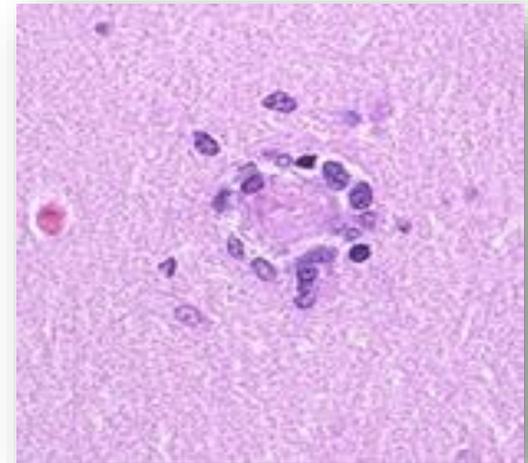
**Type 2:** Affects **immunocompromised** adults and **neonates born by vaginal delivery** of actively infected mother.



# Viral Encephalitis / Meningoencephalitis

## 2. Varicella-Zoster Virus:

- An acute viral infection of adults, immune deficient individuals
- It is due to recurrence of latent varicella (chicken pox) infection
- Common Sites:
  - Posterior root ganglia of lower cervical and upper thoracic and Gasserian ganglia (Fifth nerve)
  - Traverse from the affected ganglia along the sensory nerves to skin
  - In the skin it cause pain, redness and vesicles (shingle) containing serous or hemorrhagic exudate
  - The vesicles occur in the dermatome supplied by the affected sensory neuron.
- The virus may spread to brain causing encephalitis



# Viral Encephalitis / Meningoencephalitis

## 3. Cytomegalovirus (CMV):

Age: Adult infection and intrauterine infection:

Site: Periventricular region.

- Microcephaly & periventricular calcification in newborn.

M/E: Large cells with cytomegalic intranuclear inclusions.

## 4. Human Immunodeficiency Virus (HIV; AIDS):

### Pathological lesions:

1-Acute aseptic meningitis.

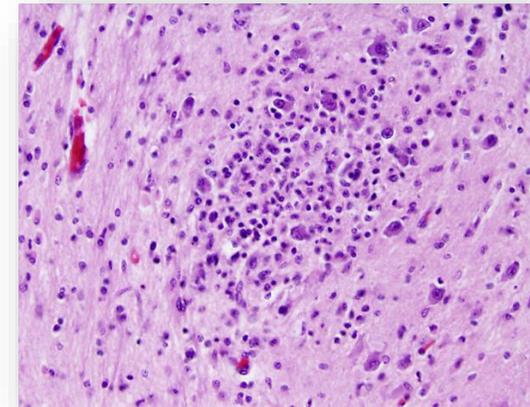
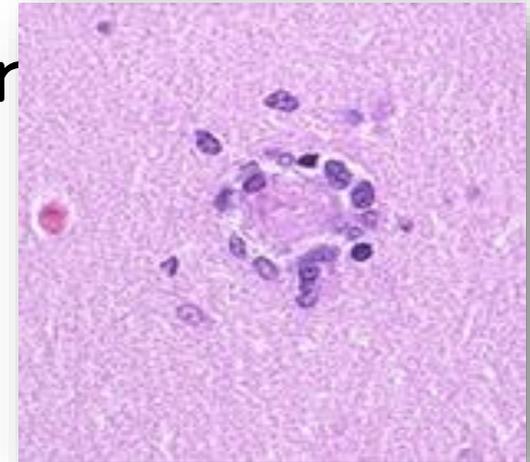
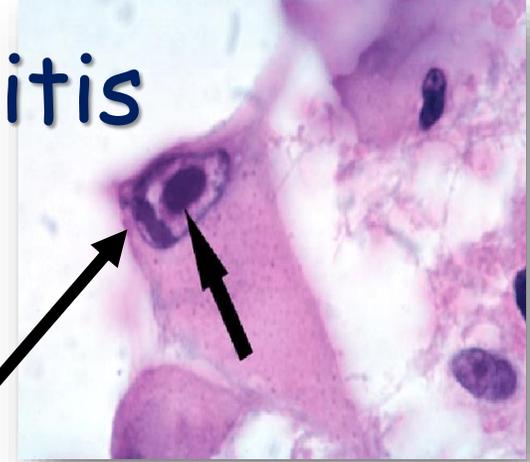
2-Subacute HIV encephalitis.

3-Opportunistic infections (Fungal, parasitic, viral).

4-Leukoencephalopathy (myelinopathy).

5-Tumors as cerebral lymphoma.

-Congenital HIV encephalitis is more severe than the adult and may result in microcephaly.



# Viral Encephalitis / Meningoencephalitis

## 5. Rabies:

**Cause:** Rabies virus

**Method of infection:** Bites of rabid animals, spread along the peripheral nerves to the C.N.S.

**Site of affection:** brain stem, hypothalamus, hippocampus cerebellum and dorsal root ganglia

**N/E:** Swelling and hyperemia of the affected tissue

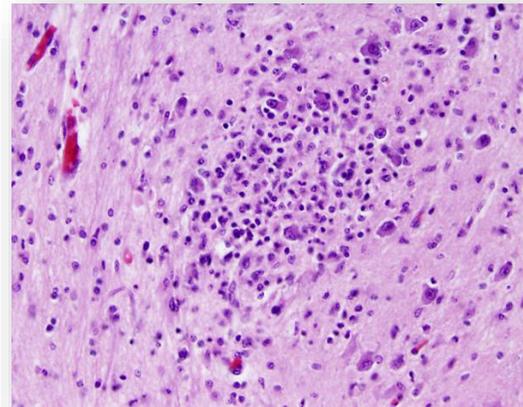
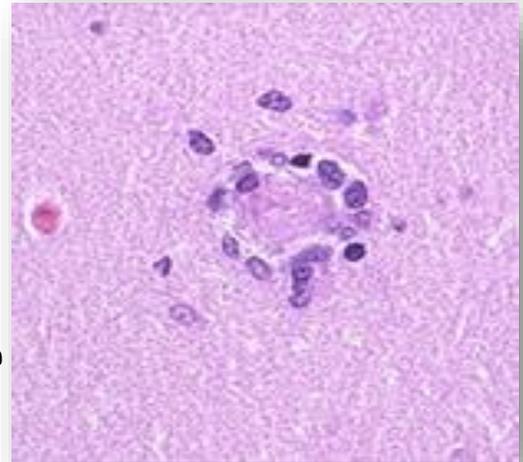
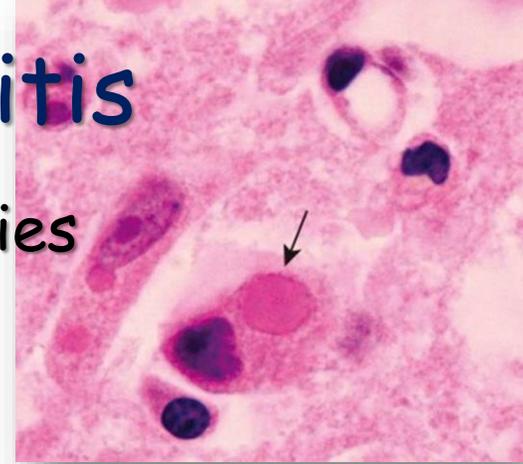
**M/E:-** Diffuse encephalomyelitis of nerve cells.

- Swelling and necrosis, vascular dilation, perivascular infiltration by plasma cells and lymphocytes
- Negri bodies (eosinophilic intracytoplasmic inclusions) are more common in hippocampus and cerebellum

**Clinically:**

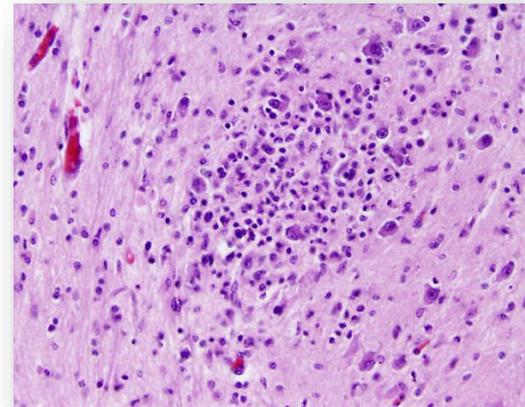
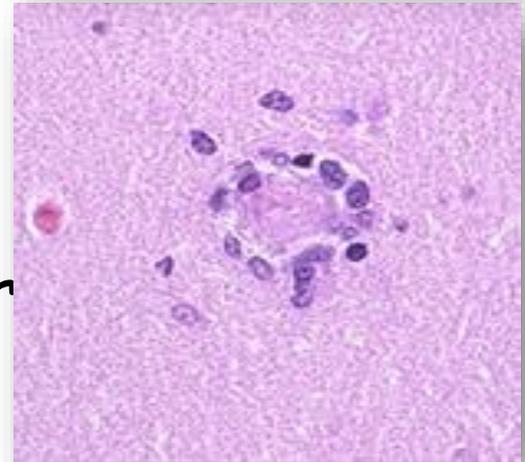
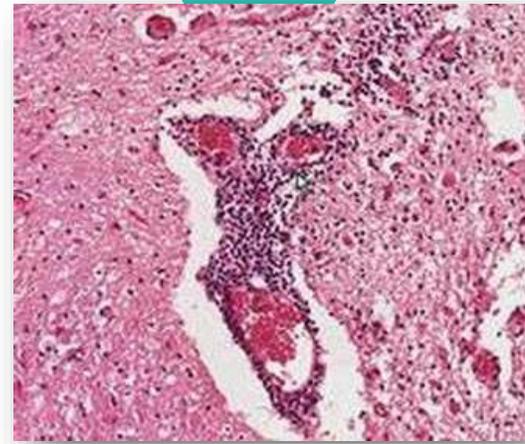
- Hyperexcitability, hydrophobia caused by spasm of Pharynx, usually fatal.

Negri bodies



# Poliomyelitis

- Acute viral infection of the anterior horn cells by Polio virus; an enterovirus transmitted by ingestion
- Incubation periods 1-3 weeks
- Stage of diseases:
  - Intestinal stage 5 days
  - Viraemia stage 5 days
  - Neural stage at which the virus attaches the anterior horn cells of the spinal cord (rarely brain stem)
- N/E: Swelling, hyperemia of the cervical and lumbar anterior horn gray matter.
- M/E: Degeneration and necrosis of anterior horn cells, Perivascular mononuclear inflammatory cells and neuronophagia.



# Poliomyelitis

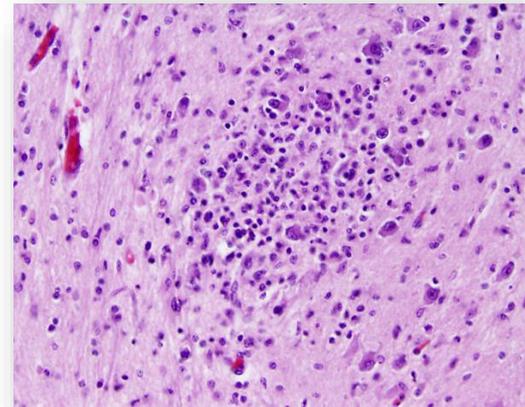
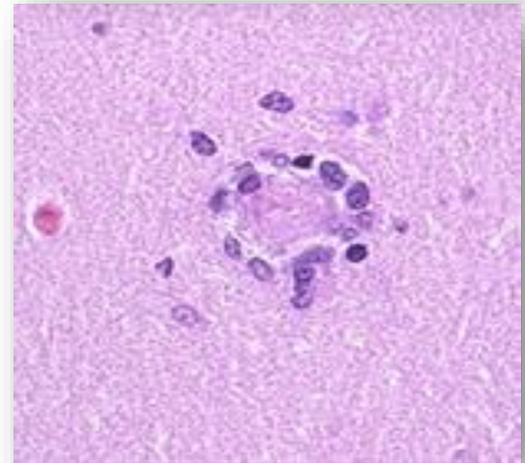
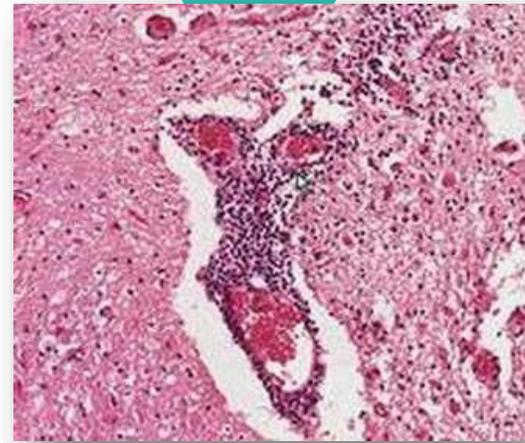
Fate: Healing by gliosis is followed by:

I- Degeneration and thinning of the related peripheral nerves

II- Neuropathic muscular atrophy and replacement by fibrofatty tissue of the related muscles.

C/P:

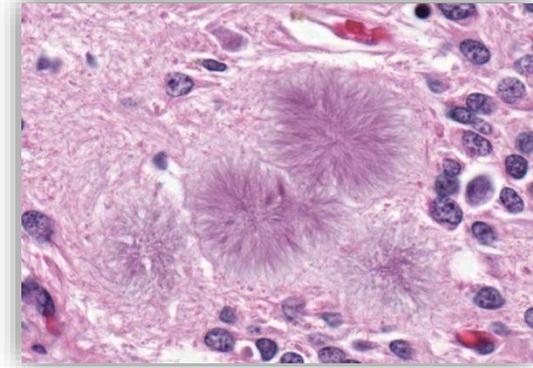
- Permanent flaccid paralysis (about 1% of cases): muscle wasting and hyporeflexia in the corresponding region of the body **mostly lower limbs**.
- Post-polio syndrome: progressive weakness, decrease in muscle mass and pain (affects polio survivors many years after recovery from an initial acute attack of the poliomyelitis virus).



# Prion Disease

Very rare diseases (**forms**: sporadic, familial, iatrogenic, and mad cow disease).

- Infective agent is an abnormal misfolded cellular protein called **prion**.
- It causes fatal and transmissible neurodegenerative diseases in humans and many other animals.
- The primary method of infection is through ingestion (infected meat products) or less commonly inoculation (e.g. medical instrument).



**PrP Misfolded cellular protein**



## Pathology

# Cerebrovascular Diseases

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# Cerebrovascular Diseases

Hypoxia & Ischemia & Infarction

Intracranial Hemorrhage

Hypertensive Diseases

Aneurysms

Vascular malformations

# Cerebrovascular Diseases

Brain disorders involving blood vessels.

## 1. Hypoxia, Ischemia, and Infarction

- A. Global cerebral ischemia
- B. Focal cerebral ischemia & infarction

## 2. Intracranial Hemorrhage

- A. Intra-parenchymal,      B. Subarachnoid,  
C. Subdural,                      D. Extradural

## 3. Hypertensive Cerebrovascular Diseases

## 4. Other Vascular Diseases:

- A. Aneurysms
- B. Vascular malformations
- C. Cerebral amyloid angiopathy
- D. Vasculitis

# Hypoxia, Ischemia, and Infarction

## Global cerebral ischemia:

Widespread ischemic-hypoxic brain injury.

### Cause:

Severe systemic hypotension (systolic pressure below 50 mm Hg) as in cardiac arrest and shock.

**Clinical outcome:** Varies with severity and duration.

- Mild, transient → complete recovery.
- Moderate → damage to vulnerable areas.
- Severe, long-standing → widespread neuronal death.

Neurons are more liable to hypoxic injury than glial cells.

(most susceptible neurons are the pyramidal cells of the hippocampus and neocortex and Purkinje cells of the cerebellum.)

- Patients who survive suffer severe neurologic impairment.

# Hypoxia, Ischemia, and Infarction

## Global cerebral ischemia:

- N/E:**
- Brain swelling, wide gyri & narrow sulci
  - Poor grey /white matter demarcation

## M/E:

### Early changes:

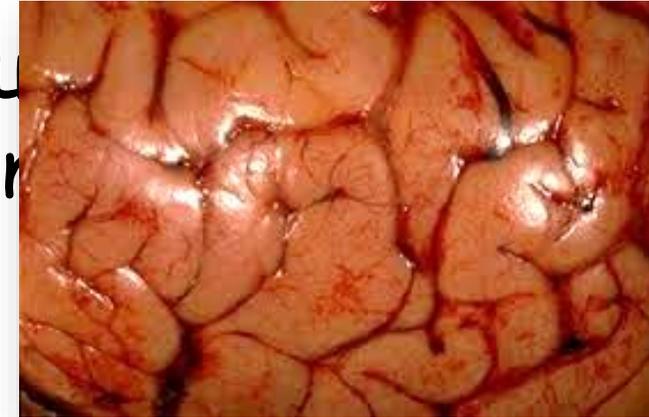
- **Red neurons** (cytoplasmic eosinophilia, nuclear dissolution).
- Similar changes occur in astrocytes and oligodendroglia.

### Subacute changes:

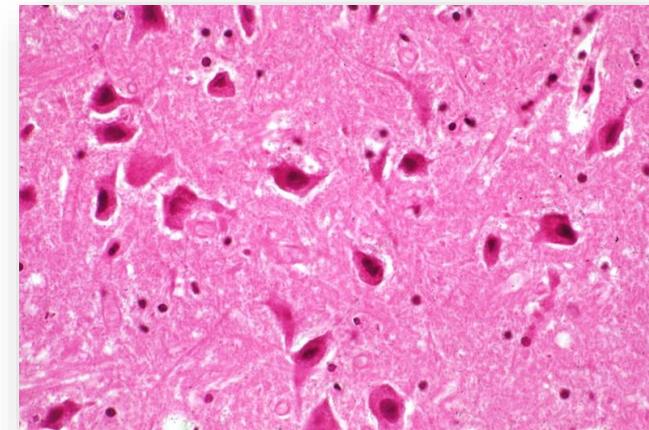
- Necrosis,
- Phagocytic cells remove necrotic tissue.

### Repair:

- Loss of organized CNS structure.
- Gliosis.



Brain swelling



Red neurons

# Hypoxia, Ischemia, and Infarction

## B. Focal Cerebral Ischemia

Leads to infarction (cerebral stroke) in the distribution of the occluded vessel by embolus or thrombus.

\*The presence of collaterals protects against infarction:

- **Thalamus, basal ganglia** and **deep white matter** are more affected due to deficient collaterals.
- **Circle of Willis** and **cortical leptomeningeal surface** are protected by collaterals.

**\*Clinically:** Neurologic deficit according to the area supplied by the affected vessel.

# Hypoxia, Ischemia, and Infarction

## B. Focal Cerebral Ischemia

**Embolic infarcts:** More common.

- Source of emboli:

1. Cardiac mural thrombi.

2. Valvular vegetations.

3. Atheromatous plaques within the carotid arteries or aortic arch.

**Thrombotic infarcts:** Less common.

- Sources of thrombi:

1. Thrombosis on top of atherosclerosis of the origin of the middle cerebral artery, and end of the basilar artery.

2. Thrombi of dural venous sinuses or deep cerebral veins (less common).

# Hypoxia, Ischemia, and Infarction

## B. Focal Cerebral Ischemia

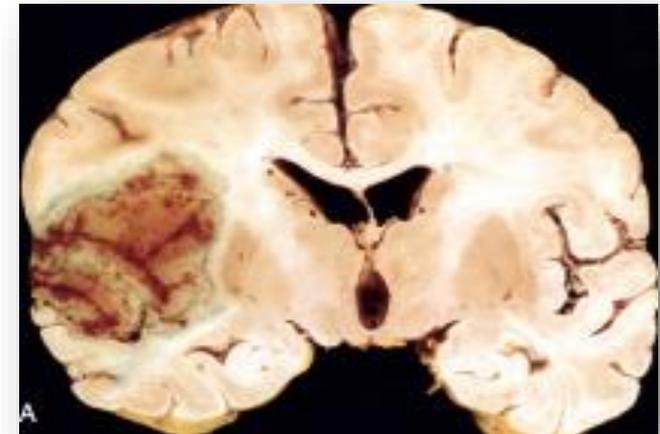
**NE: Types and morphology of infarcts:**

**Non-hemorrhagic Infarct:**

- Early: Pale, opaque.
- Liquefactive necrosis → creamy fluid-filled cavity.
- Healing → destruction of cortex + gliosis.

**Hemorrhagic infarct: Due to:**

- Reperfusion of ischemic tissue  
(collaterals or therapeutic/spontaneous dissolution of emboli).
- Infarcts caused by venous occlusion.



# Hypoxia, Ischemia, and Infarction

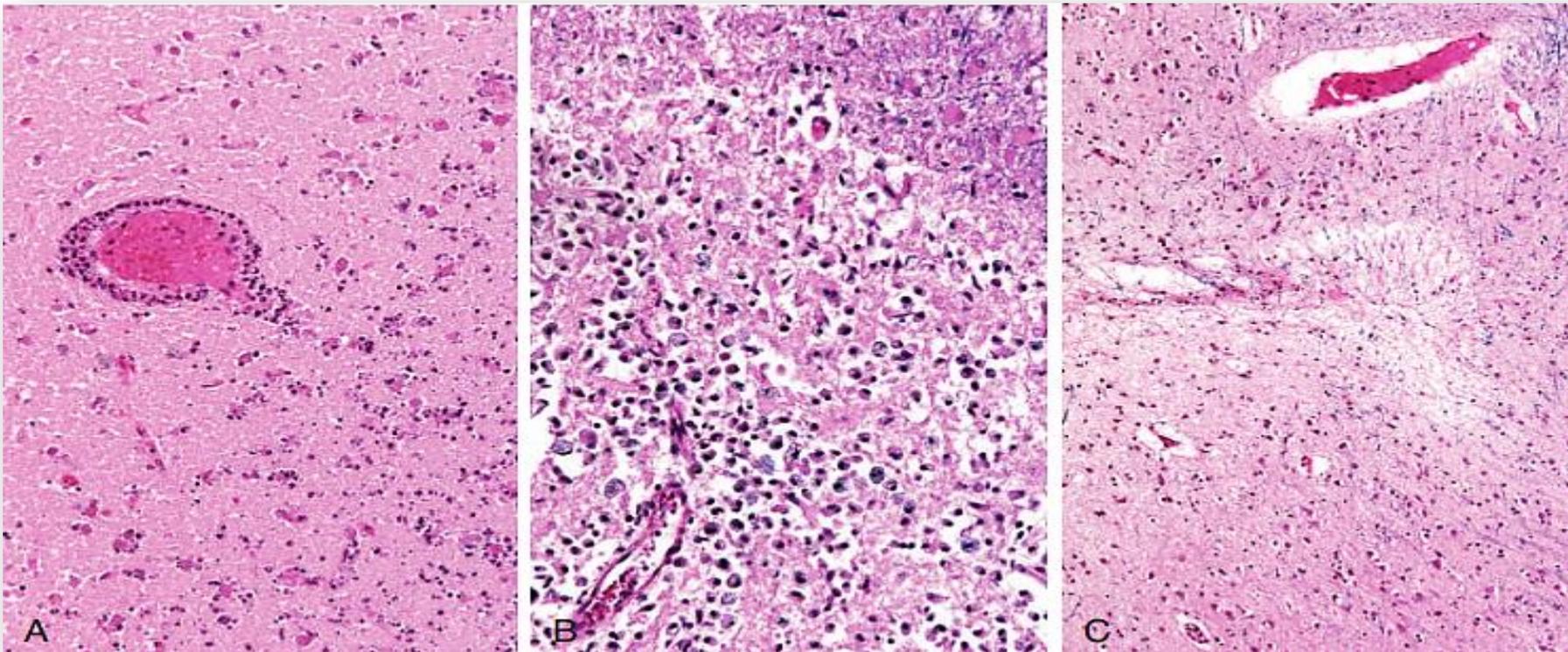
## B. Focal Cerebral Ischemia

**ME:** Cerebral infarction stages:

A. Early infarct (red neurons) with neutrophil infiltration

B. By day 10, influx of phagocytic cells

C. Old infarct with tissue loss and residual gliosis



# Intracranial Hemorrhage

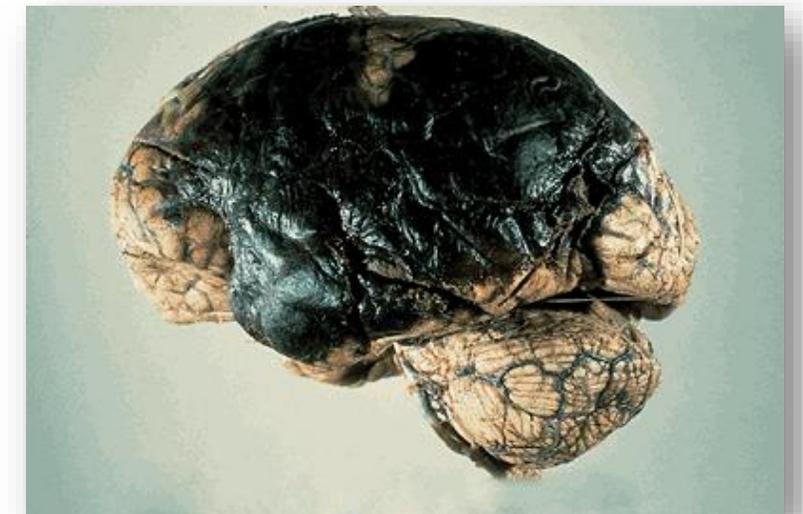
## A. Intra-parenchymal hemorrhage:

- Most common in hypertension.
- Atherosclerosis.
- Tumors.
- Cerebral contusions (trauma).
- Clotting disorders.
- Cerebral amyloid angiopathy.
- Vascular malformations.



## B. Subarachnoid hemorrhage:

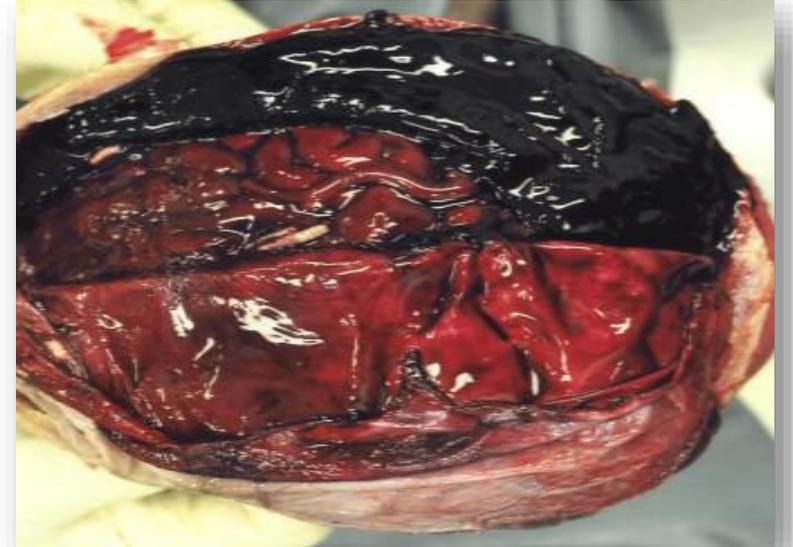
- Ruptured aneurysms
- Vascular malformations
- Brain trauma.



# Intracranial Hemorrhage

## C. Subdural hemorrhage (hematoma):

- Caused by rupture of venous sinuses or bridging subduralcerebral veins.
- Common in: old patients with
- brain atrophy, alcoholics.



## D. Epidural (Extradural) hemorrhage :

- Caused by traumatic skull fracture, especially temporal or parietal bones (tear of middle meningeal artery).
- Expands rapidly (arterial bleeding) with rapid increase of ICP
- It is a neurosurgical emergency (drainage and repair to prevent death).

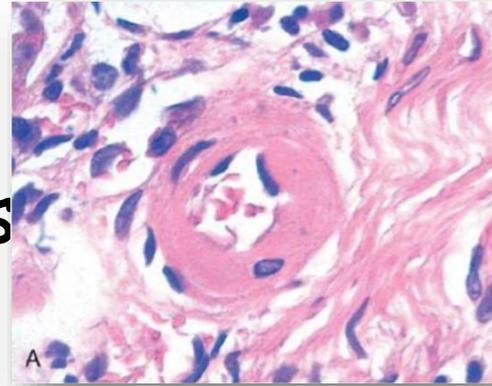


# Hypertensive Cerebrovascular Diseases

**Sites:** Thalamus, basal ganglia, deep white mater, internal capsule and pons.

## **Lesions:**

1. Hyaline arterio-sclerosis of cerebral arterioles
2. Charcot-Bouchard microaneurysms,
3. Lacunar infarcts: few millimeters in size,
4. Slit hemorrhages: Rupture of the small penetrating vessels,
5. Massive intra-parenchymal hemorrhage: arterial
6. Cerebral edema,
7. Acute hypertensive encephalopathy: if diastolic blood pressure exceeds 130 mm Hg. (mostly) → cerebral dysfunction, headaches, confusion, vomiting, convulsions, and sometimes coma.



**Hyaline arteriosclerosis**

# Cerebral Aneurysms

## Types:

1. Congenital berry aneurysms:
2. Microaneurysms of essential hypertension (Charcot-Bouchard).
3. Atheromatous aneurysms.
4. Traumatic aneurysms.
5. Mycotic aneurysms: emboli of bacterial endocarditis.

## Clinical effects:

- Pressure on the surrounding,
- Rupture and subarachnoid or intraparenchymal hemorrhage.
- Thrombosis and calcifications lead to acute ischemia (Infarction) or chronic ischemia ( brain atrophy).

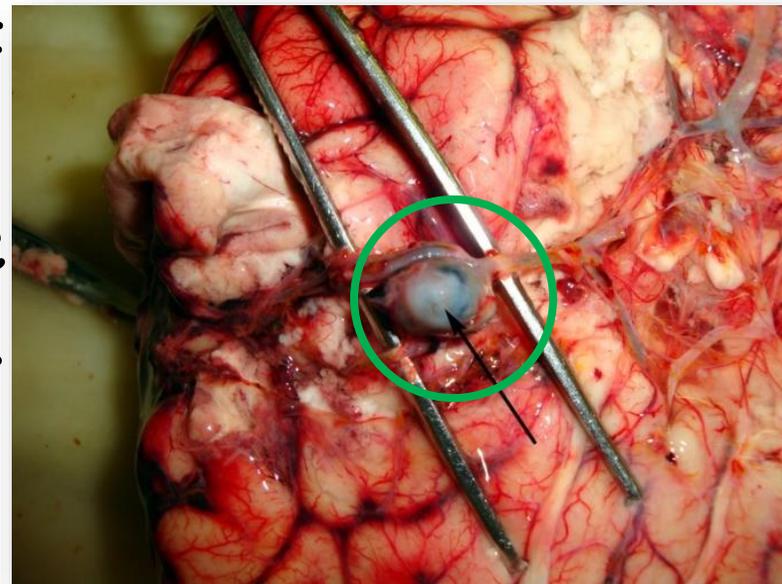
# Cerebral Aneurysms

**Congenital saccular berry aneurysms:**

**Site:** circle of Willis (small, multiple).

**Pathology:** internal elastic lamina & medial weakness at bifurcation of arteries causing saccular aneurysm.

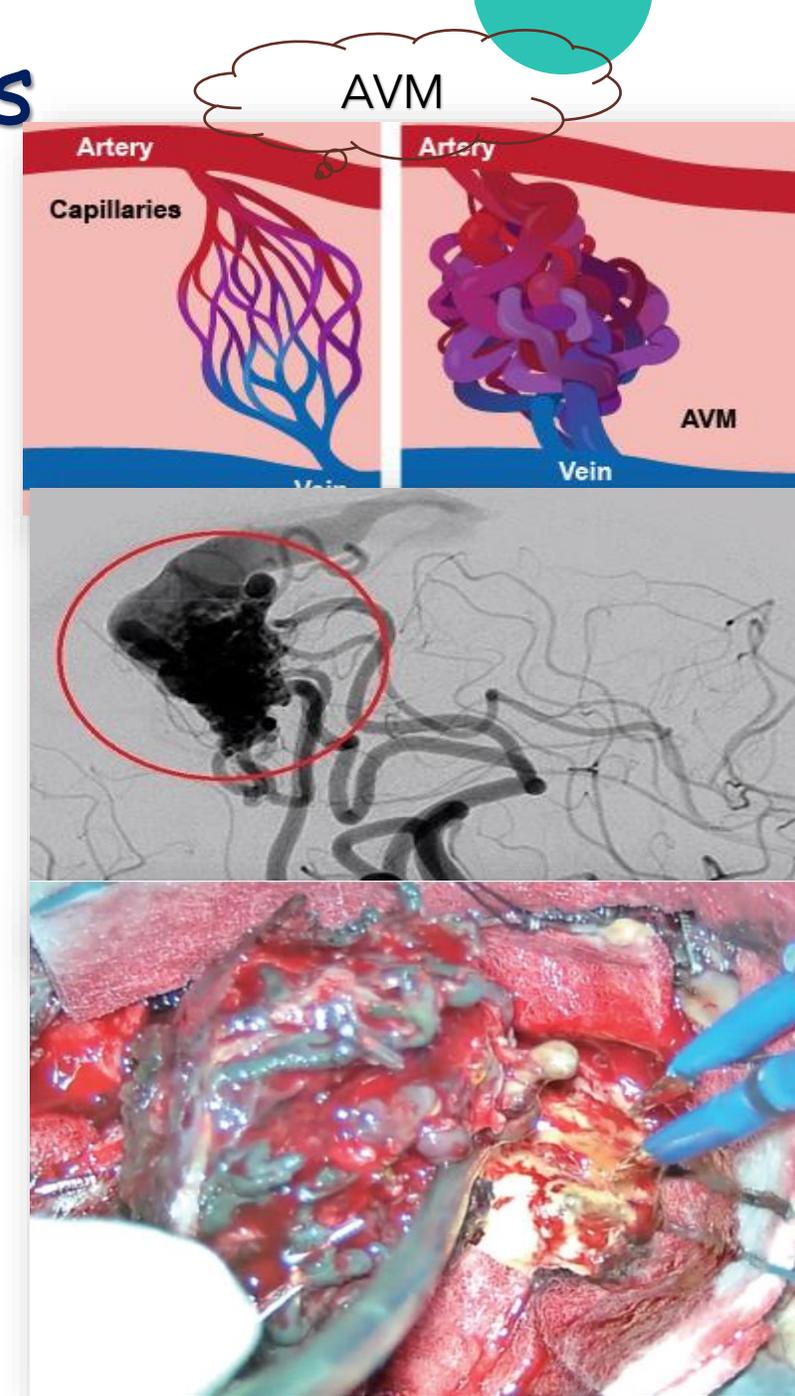
- Most frequent cause of spontaneous subarachnoid hemorrhage (sudden severe headache and loss of consciousness).
- Rupture associates straining (increase intracranial pressure. e.g. constipation, severe cough.....).



# Vascular Malformations

## Variants:

1. Arterio-venous malformations (AVMs)
  2. Cavernous malformations (hemangiomas),
  3. Capillary telangiectasias,
  4. Venous angiomas.
- The most dangerous malformation is **AVM**.
  - Appears as tangled network of worm-like vascular channels.
  - Leads to: mixed intra-parenchymal or subarachnoid hemorrhages





## Pathology

# Tumors of the Nervous System

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# Tumors of Nervous System

Gliomas

- Astrocytoma
- Oligodendroglioma
- Ependymoma

Embryonal tumors

Medulloblastoma

Tumors of Meninges

Meningioma  
Nonmeningothelial

Tumors of peripheral nerves.

Schwannoma  
Neurofibroma

Metastatic tumors.

Hemopoietic tumors.

Plasmacytoma  
Lymphoma

# Classification of Nervous System Tumors

## 1- Gliomas:

- Astrocytoma
- Oligodendroglioma
- Ependymoma

## 2- Embryonal tumors:

- Medulloblastoma.

## 3- Tumors of Meninges:

- Meningioma
- Mesenchymal  
Nonmeningothelial  
tumors

## 4- Tumors of peripheral nerves.

- Schwannoma
- Neurofibroma
- Malignant nerve sheath tm

## 5- Hemopoietic tumors

- Plasmacytoma
- Lymphoma

## 6- Germ cell tumors

## 7- Tumors of seller region

- Pituitary tumors
- Craniopharyngioma

## 8- Choroid plexus tumors:

- Choroid plexus papilloma.
- Choroid plexus carcinoma.

## 9- Pineal body tumors

- Pinealoma
- Pineoblastoma

## 10- Metastatic tumors

# Gliomas

## Astrocytomas

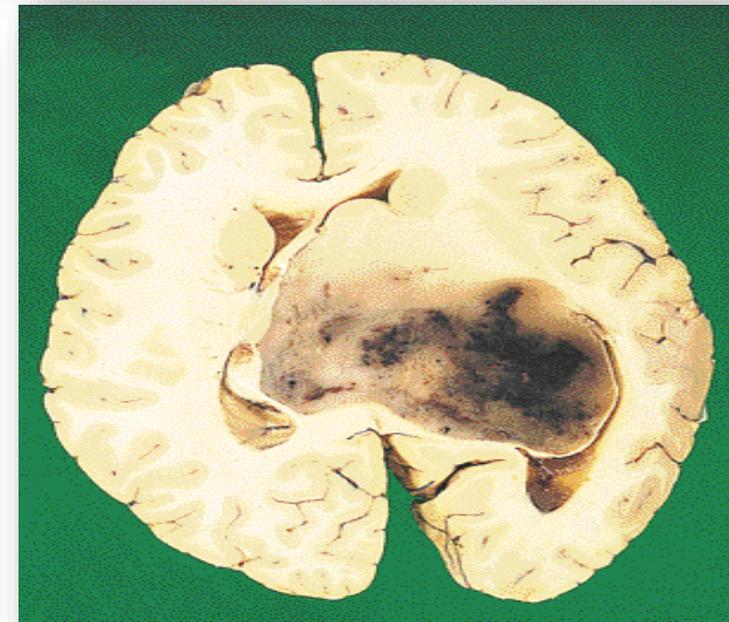
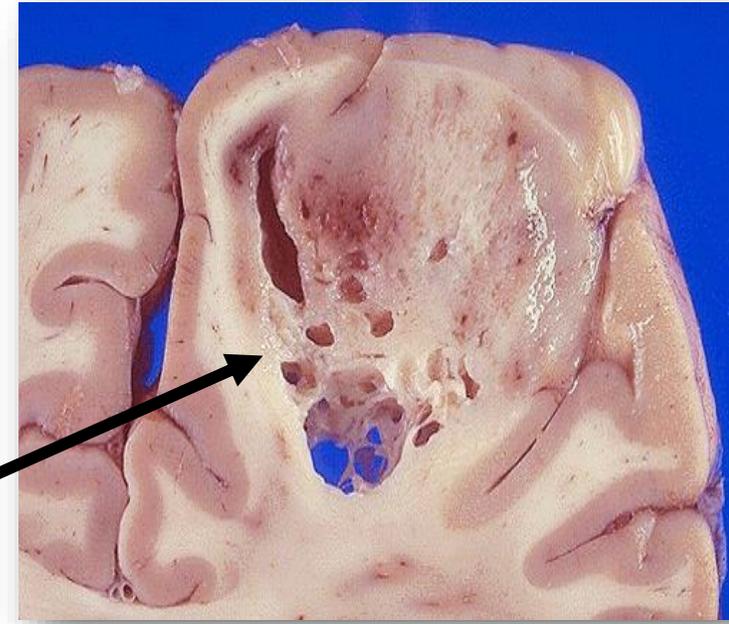
Tumors of astrocytes are the commonest glioma.

### Site:

- Cerebellum of children.
- Cerebrum of adults.

### N/E:

- Soft grey mass with ill-defined outline. The cut surface shows areas of cystic degeneration.
- In high grade forms it shows necrosis and hemorrhages.



# Gliomas

## Astrocytomas

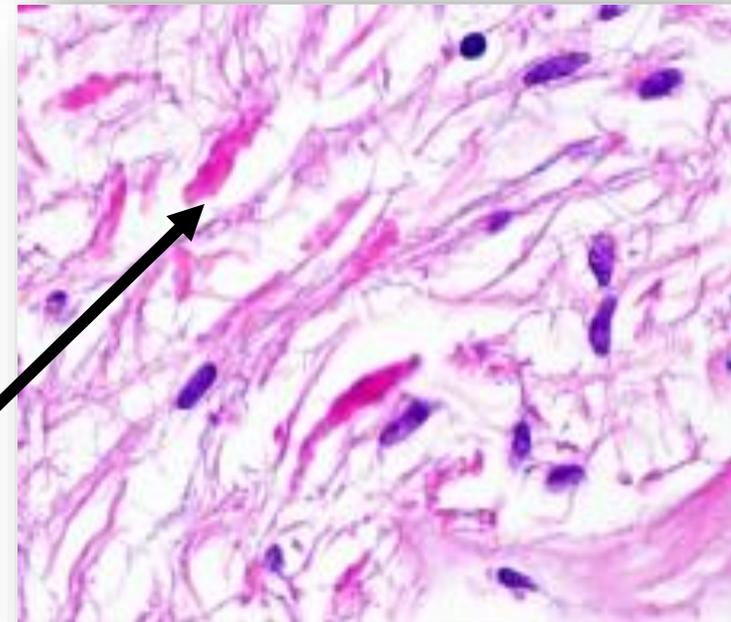
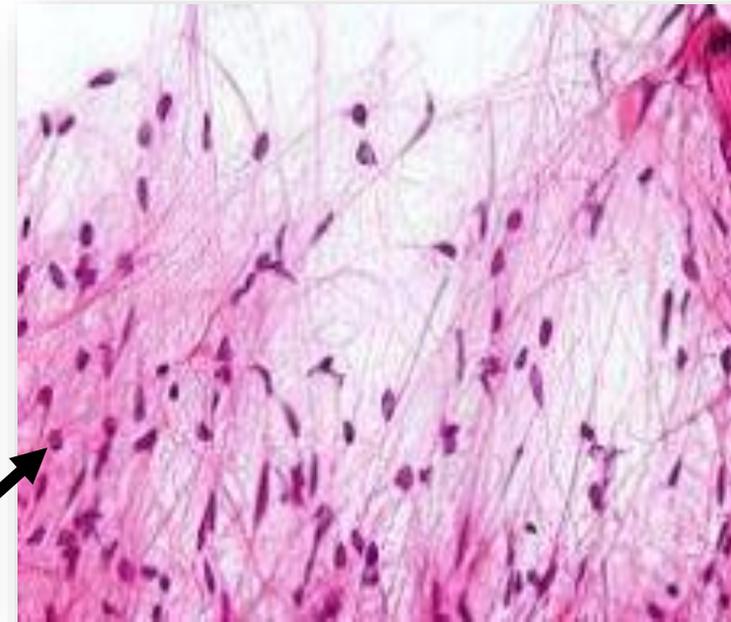
M/E:

- Neoplastic Astrocytes, branched cells with fibrillary background it may be of variable grades of differentiation.

1) Localized astrocytomas:

**Pilocytic astrocytoma ---grade I**

- Mildly cellular, formed of mature astrocytes within excess fibrillary back ground, cells are bipolar with stroma of eosinophilic elongated and coma shaped fibers (Rosenthal fibers).



# Gliomas

## Astrocytomas

### 2) Diffuse astrocytomas:

#### a) Diffuse fibrillary astrocytoma ---grade II:

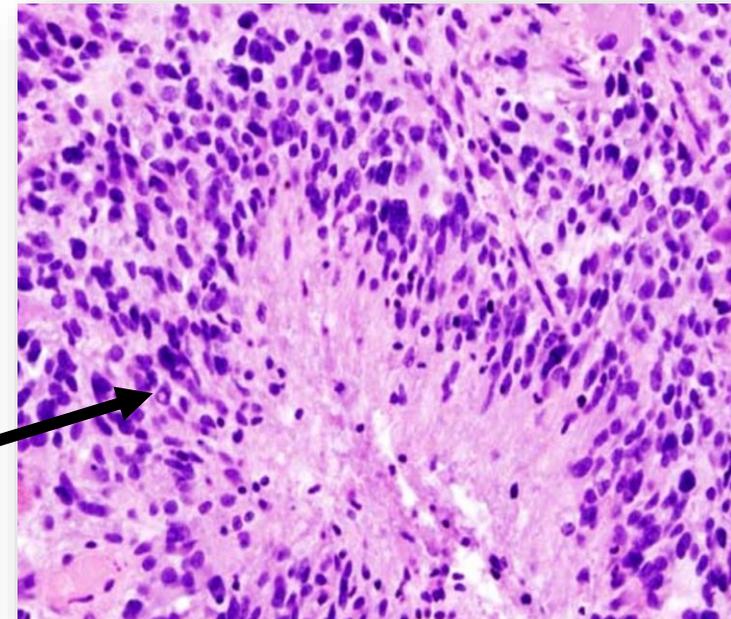
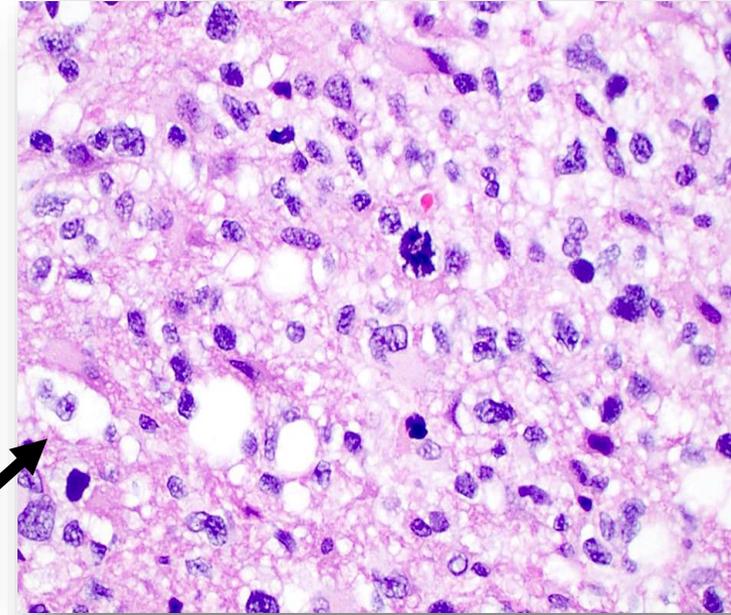
- Hypercellular, formed of pleomorphic astrocytes within excess fibrillary background. A subtype of Grade II diffuse astrocytoma show Large astrocytes with excess eosinophilic cytoplasm and eccentric nuclei ; called gemistocytic astrocytoma.

#### b) Anaplastic astrocytoma---- grade III:

- Formed of pleomorphic less mature astrocytes with excess mitosis without necrosis

#### c) Glioblastoma Multiforme -----grade IV:

- Formed of primitive astrocytes with marked pleomorphism, Giant cells, mitosis, necrosis (palisaded), vascular endothelial proliferation (glomeruloid).



# Gliomas

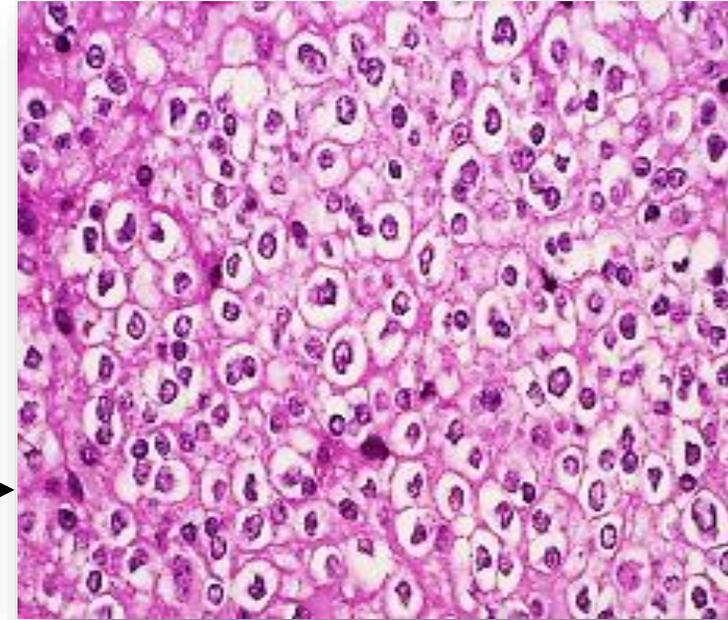
## Oligodendroglioma

From oligodendroglia cells of cerebrum.

Middle age.

**N/E:** pink, Firm with cyst formations and calcification.

**M/E:** Rounded cells, with uniform round nuclei and clear cytoplasm with focal of calcification. →



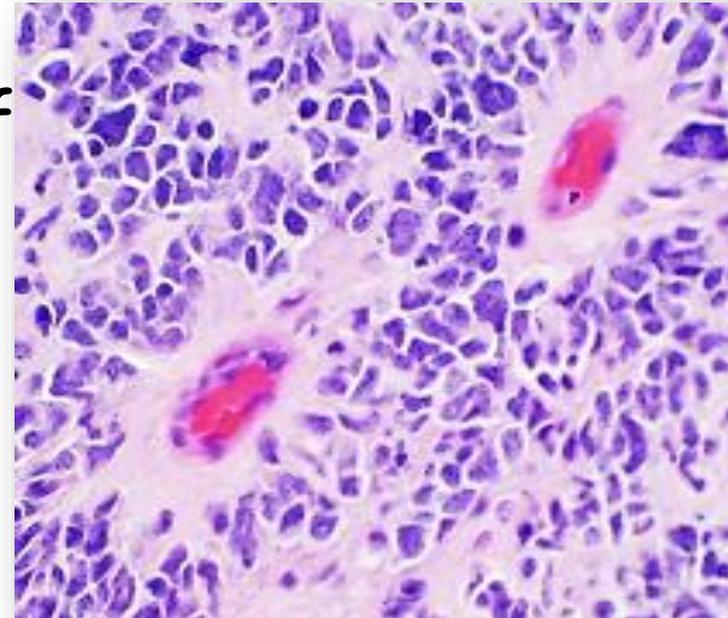
## Ependymoma

From ependymal cells lining the ventricles, commonly the 4th ventricle and Lower part of the spinal cord

Children and young adults.

**N/E:** Fleshy vascular mass with calcification.

**M/E:** Elongated cells arranged perivascular in pseudorosettes. →



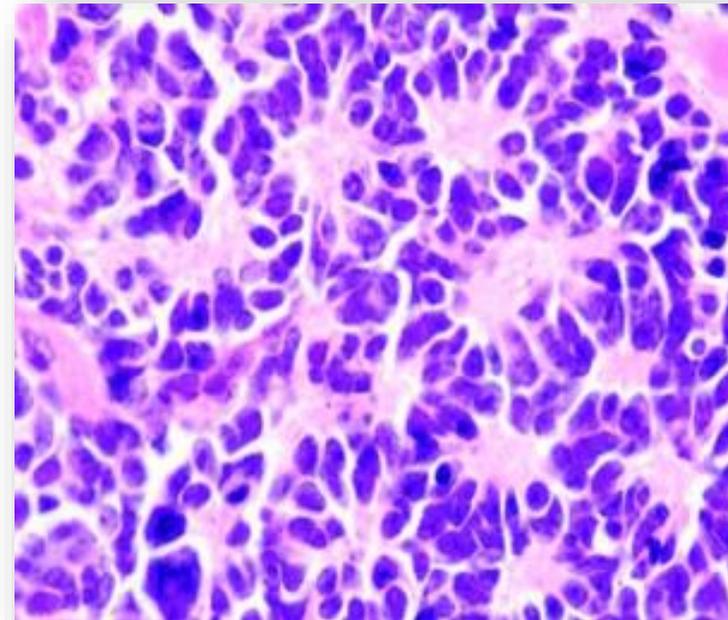
# Embryonal tumors

## Medulloblastoma

- Common childhood brain tumor
- At the roof of 4th ventricle

**N/E:** Fleshy soft grey mass projections in the 4th ventricle may penetrate the brain to reach the subarachnoid space.

**M/E:** Small dark stained cells arranged in rosettes.



# Tumors of Meninges

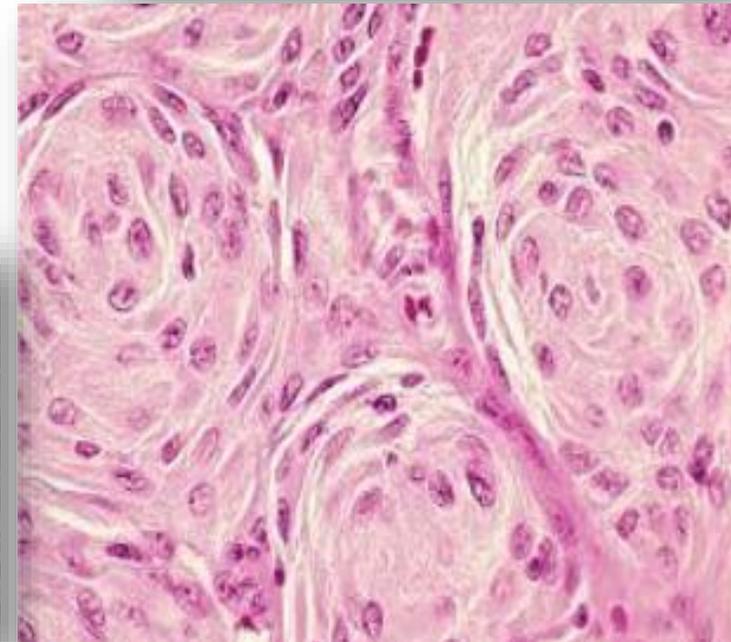
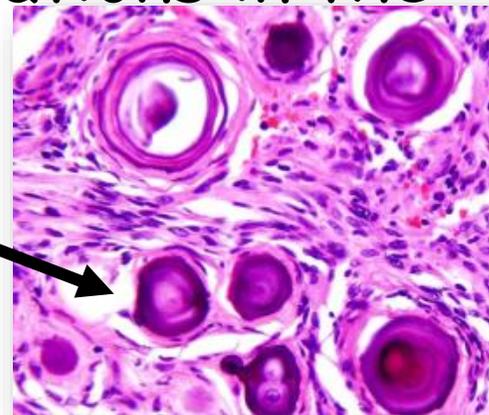
## Meningioma

- In adults common in females.
- Originates from the endothelial cells of the arachnoid villi

**N/E:** Rounded firm capsulated tumor attached externally to the dura and imbedded in the brain tissue internally.- Cut surface: greyish white and often show whorly appearance.

**M/E:** Formed of spindle shaped cells arranged in concentric layers with calcifications in the center (Psammoma bodies).

Meningioma may turn malignant.



# Tumors of peripheral nerves

## Schwannoma

-It is a benign tumor of cranial and spinal nerves, originate from schwann cells which cover the peripheral nerves.

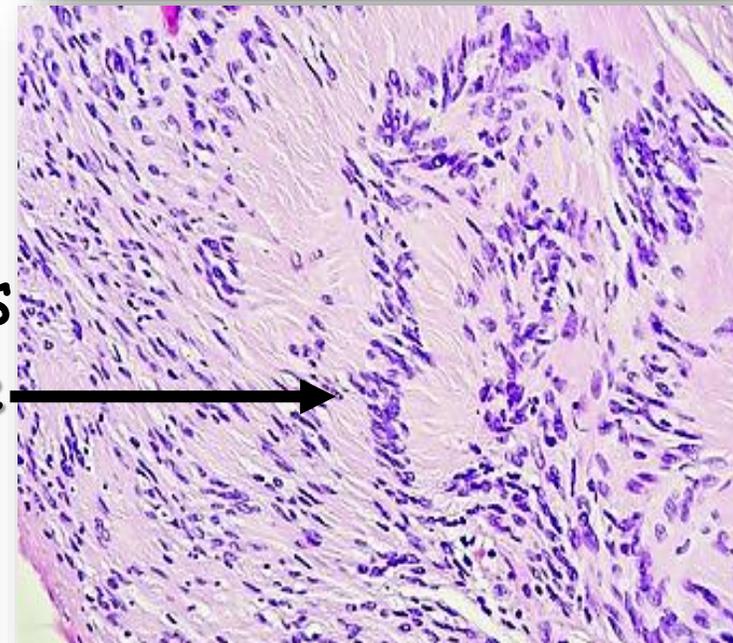
- Age: 50-60 years.

**N/E:** Acoustic neuroma of 8th cranial nerve at the base of the brain (cerebello- pontine angle)

Solitary mass, capsulated, firm round or fusiform with the related nerve at one side

Cut surface is grey white and may show cysts

**M/E:** Spindles shaped cells arranged in bundles with rod- shaped nuclei side by side in palisade manner with reticular and collagen fibers in between.



# Tumors of peripheral nerves

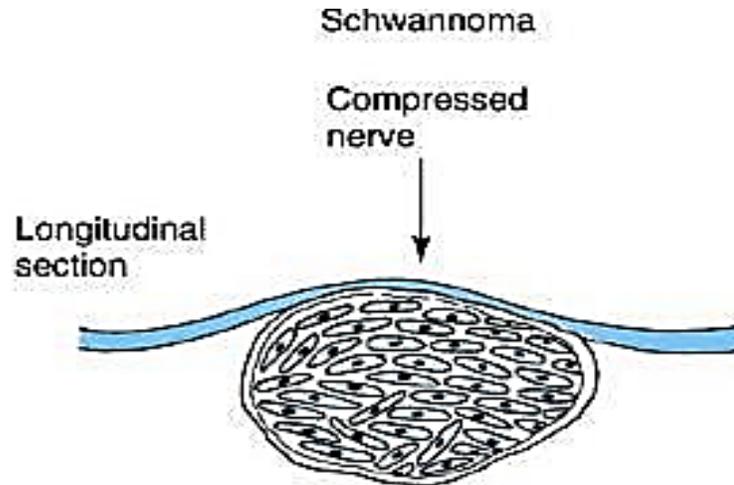
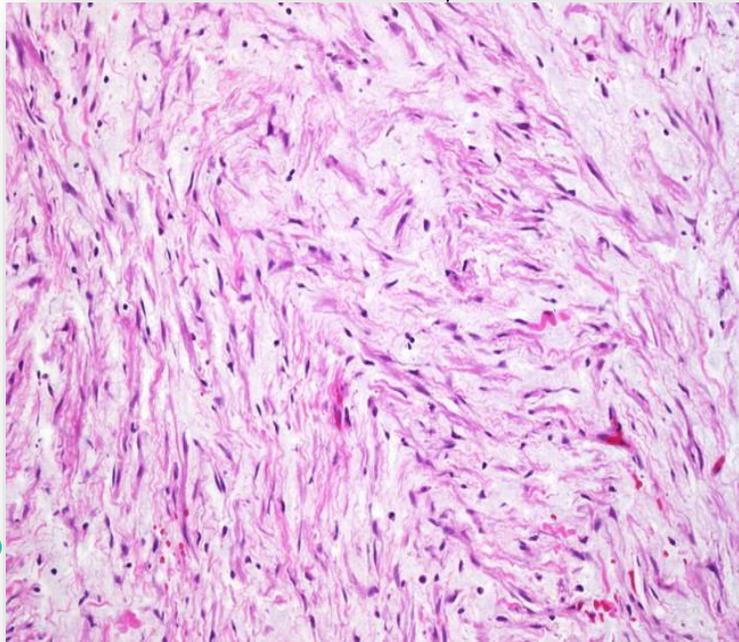
## Neurofibroma

**N/E:** Fusiform mass through which the nerve pass Firm grey unencapsulated.

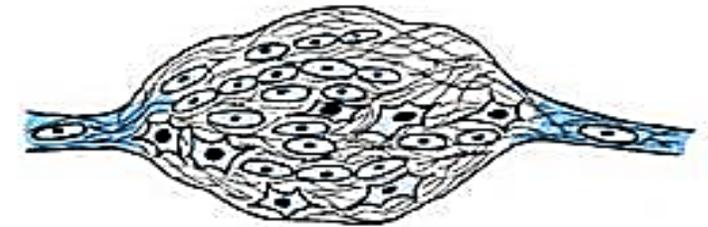
**M/E:** Spindle shaped cells in bundles with fibrous stroma and neurofibres.



Neurofibroma



- Tumor encapsulated
- Separable from nerve of origin
- Composed of Schwann cells



- Tumor not encapsulated—represents expanded nerve
- Composed of mixture of Schwann cells and fibroblasts and contains axons

# Tumors of peripheral nerves

## Neurofibroma

Multiple neurofibromatosis. (Von-Reckling-Hausen disease).

- Hereditary autosomal dominant hamartoma.
- Multiple neurofibromas of cutaneous nerves.
- Cafe au lait skin patches of skin hyperpigmentation.
- Localized or diffuse overgrowth of fibrous tissue of overlying skin (Elephantiasis neuromatosa).

Prognosis:

- Malignant transformation is common than in schwannoma. (10%)



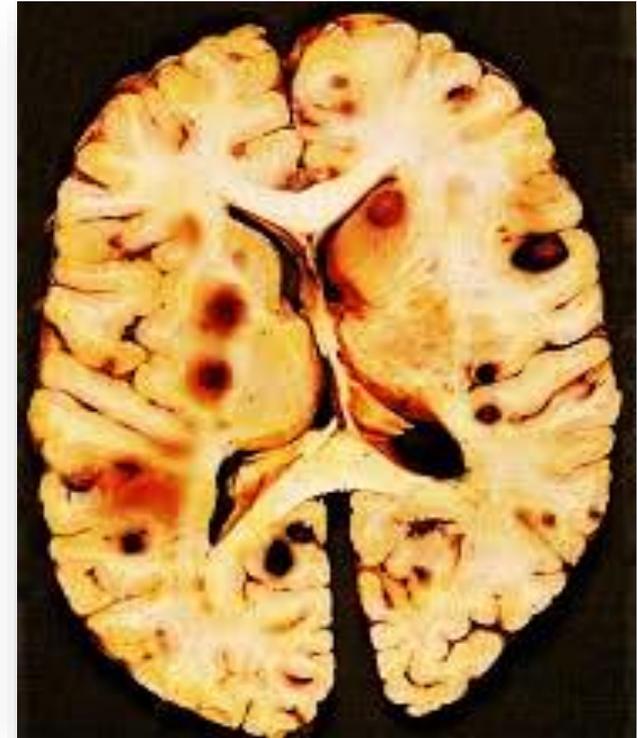
# Metastatic tumors

The most common malignant tumor in the brain representing 30% of brain tumors.

- Majority are carcinomas.
- Occur mostly in older people.
- They reach the C.N.S. through arteries or vertebral system of veins.
- Common sources: carcinomas of lungs, breast and kidney

**N/E:** Multiple nodules of variable size in the cerebrum at junction of grey and white matter surrounded by oedema, show hemorrhage, necrosis and cyst formation

**M/E:** As primary tumor and in relation to blood vessels



# Effect of intracranial tumors

## Local effects:

- Compression and destruction of the affected site lead to neurologic deficit such as hemiplegia.
- Hydrocephalous.
- Increased intracranial tension caused by increased intracranial contents by:
  - Tumor mass
  - Cerebral oedema due to compression of the veins by tumour obstruction of C.S.F. pathway.

## Manifestations:

- Headache with projectile vomiting
- Papilloedma (blurring of vision) oedema of optic disc due to compression of retinal veins.
- Brain herniation.



# Pathology

## Disease of Eye & Ear

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Blepharitis

Conjunctivitis

Keratitis

Eye

Retinoblastoma

Rhabdomyosarcoma

Otitis media

Otitis externa

Otitis interna

Ear

Glomus tumor

Acoustic neuroma

# Diseases of Eye

## Blepharitis

Inflammation of the eye lid.

### Causes:

- Allergies
- Dandruff (seborrheic dermatitis)
- Parasitic as lice or mites in eyelashes
- Meibomian gland dysfunction (MGD)

### Symptoms:

- Redness & swelling
- Itching.
- Pain
- Discharge that forms a crust at the lid margin during night that may prevent eyes from opening in the morning.



# Diseases of Eye

## Blepharitis

### Complications:

#### Stye:

- Acute suppurative inflammation of sebaceous glands or follicles (Boil) of eyelid
- very painful. At the eyelid's edge

#### • Chalazion:

- Granulomatous inflammation of in obstructed meibomian glands.
- Slowly growing lid nodule.
- M/E: Lipogranuloma (empty spaces surrounded by epithelioid with multinucleated giant cells, fibrosis)



# Diseases of Eye

## Conjunctivitis

Inflammation of the conjunctiva.

### Causes:

- Viral infection (Adenovirus, Herpes simplex and herpes zoster)
- Bacterial infection
- Allergic reaction.

### Symptoms:

- Redness
- Itching.
- Gritty feeling
- Discharge that may form a crust
- Lacrimation.
- Sensitivity to light, called photophobia



# Diseases of Eye

## Keratitis

Inflammation of the cornea.

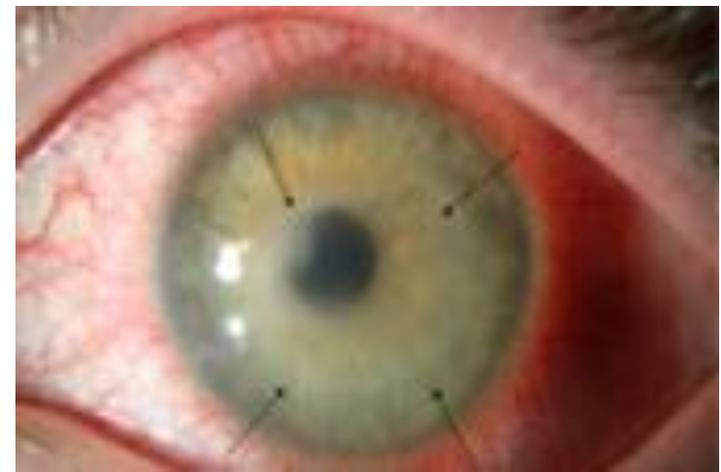
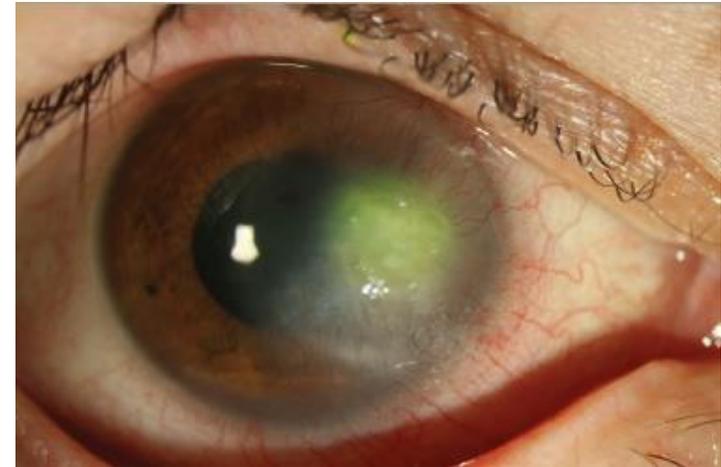
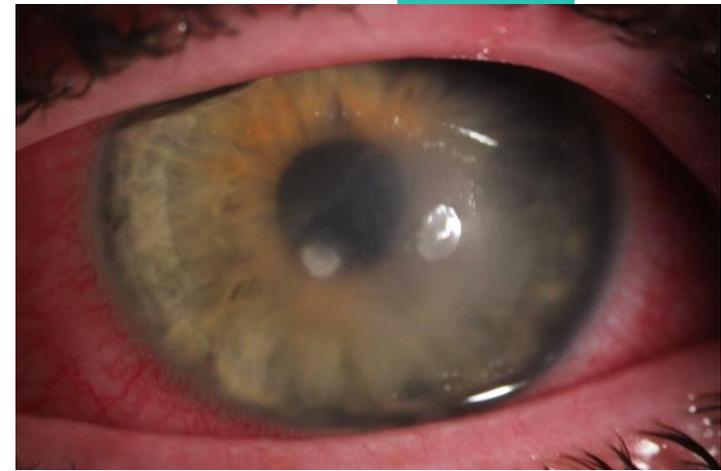
### Causes:

#### Infectious keratitis

- Bacterial
- Viral
- Fungal
- Parasitic (*Acanthamoeba*)

#### Noninfectious keratitis

- Injury
- Eyelid disorders
- Dry eye syndrome
- Exposure to intense ultraviolet (UV) light (photokeratitis)



# Diseases of Eye

## Keratitis

### Bacterial keratitis:

Common in contact lenses wearer from contaminated eye drops or contact lens solution.

### Viral keratitis:

- Herpes simplex virus, Chicken pox virus.

The repeated infections are triggered by stress, an impaired immune system, or exposure to sunlight.

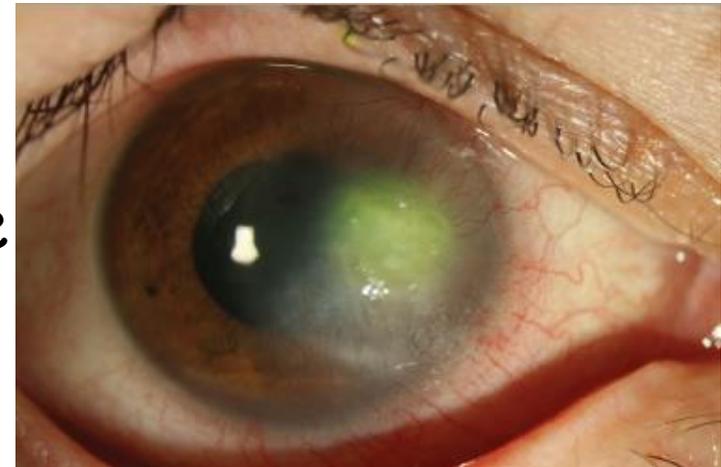
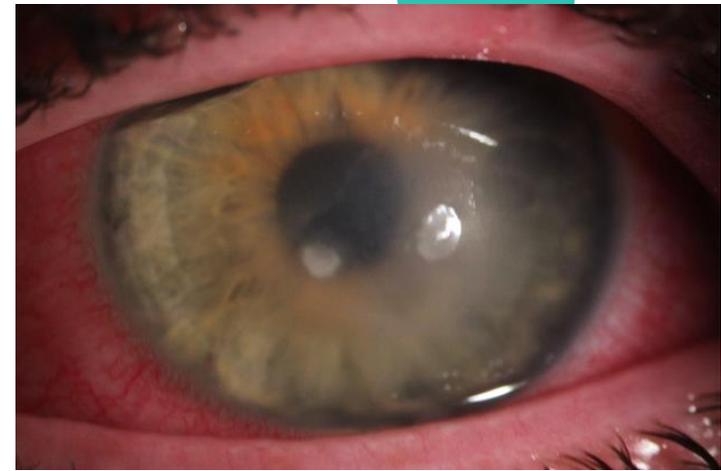
### Parasitic keratitis:

- Acanthamoeba

Poor contact lens hygiene, Exposure to water (like swimming pools) while wearing contact lenses.

### Eyelid disorders:

If the eyelid does not close properly, the cornea can dry out, and keratitis can develop



# Diseases of Eye

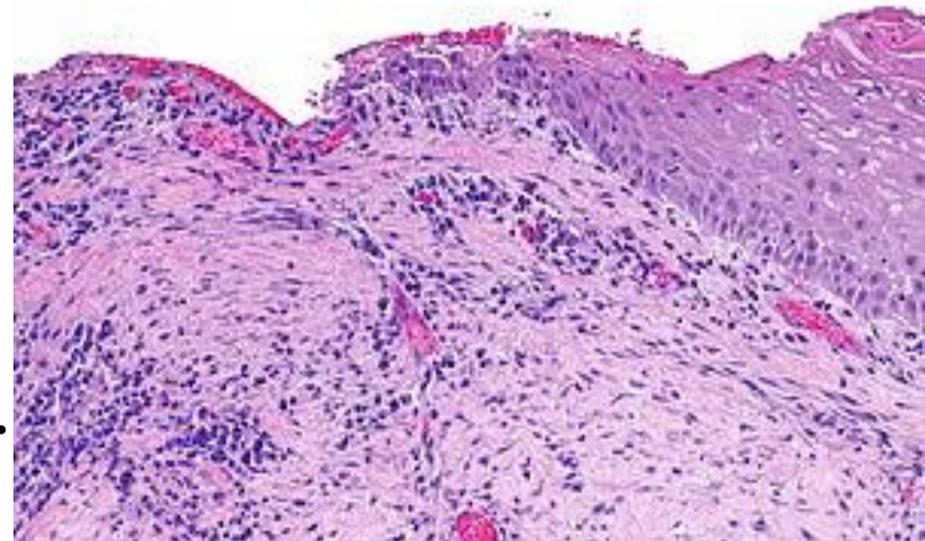
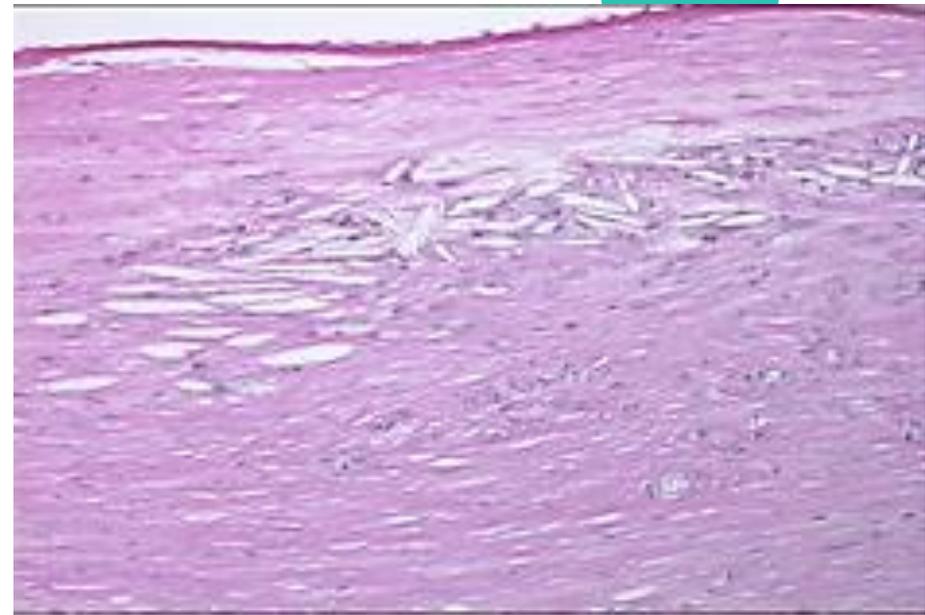
## Keratitis

### Pathologic features:

- Stromal edema. →
- Corneal ulceration may lead to fibrosis with final fibrosis and opacity.
- Rapid neovascularization.
- Stromal mixed inflammatory infiltrates could be focal, or diffuse.

### Clinical features:

- Eye redness.
- Eye pain.
- Excess tears or other discharge.
- Blurred vision due to edema or opacities.
- Photophobia.
- Foreign body sensation



# Eye Tumors

## **Eyelid:**

1. Squamous cell papilloma.
2. Basal cell papilloma.
3. Sebaceous adenoma.
4. Nevi.

## **Conjunctiva & cornea:**

1. Squamous cell papilloma.
2. Nevi

## **Intraocular:**

1. Nevus.

## **Eyelid:**

1. Squamous cell carcinoma.
2. Basal cell carcinoma.
3. Sebaceous adenocarcinoma.
4. Malignant melanoma.

## **Conjunctiva & cornea:**

1. Squamous cell carcinoma.
2. Malignant melanoma.

## **Intraocular:**

1. Melanoma.
2. Lymphoma
3. Retinoblastoma.

## **Intraorbital:**

- lymphoma.  
Rhabdomyosarcoma.

# Eye Tumors

- \* The most common malignant tumor of the eye lid is **Basal cell carcinoma** followed by **Sebaceous adenocarcinoma**.
- \* The most common primary ocular malignancy in the adults is **Uveal Melanoma**.
- \* The most common malignant ocular tumor in Children is **Retinoblastoma**.
- \* The most common malignant orbital tumor in Children is **rhabdomyosarcoma**

# Eye Tumors

## Retinoblastoma

- The most common malignant ocular tumor in children. →
- Present at birth or in early childhood (<4 years old).
- 40% of cases are familial; carrying mutation in Rb1 gene; with tendency of bilateral tumors
- Tumor occurs when both alleles of the retinoblastoma 1 gene (RB1) are inactive

### NE:

- Greyish white mass within the retina with areas of calcification and yellow necrosis.



# Eye Tumors

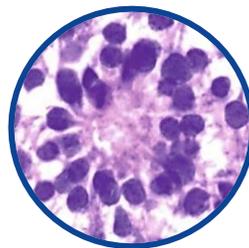
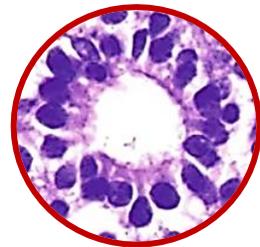
## Retinoblastoma

### M/E:

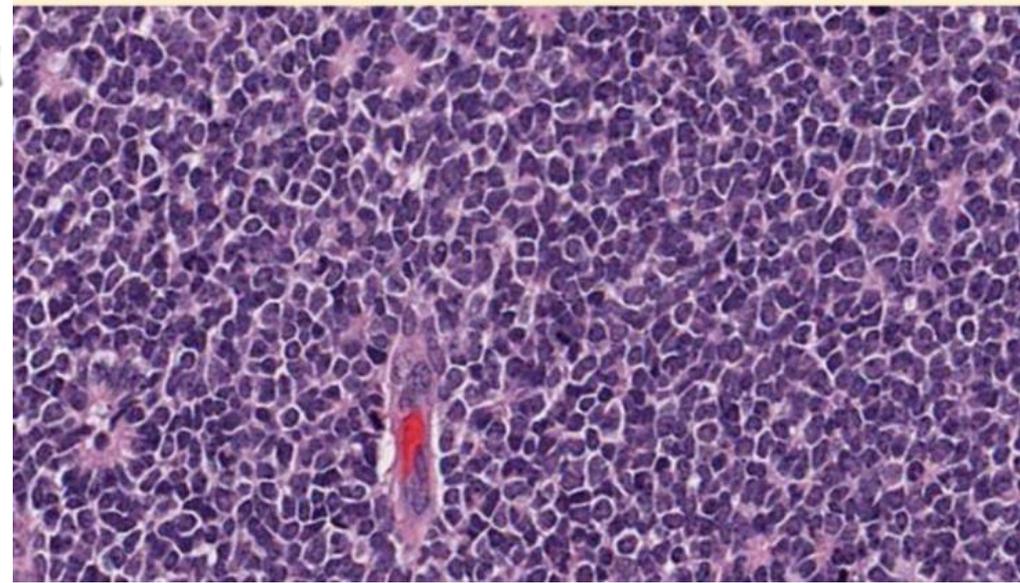
- Embryonal tumor consists of small round blue cells with hyperchromatic nuclei and scant cytoplasm arranged in sheets.

- The tumor cells show characteristic rosettes (tends form photo-receptor elements)

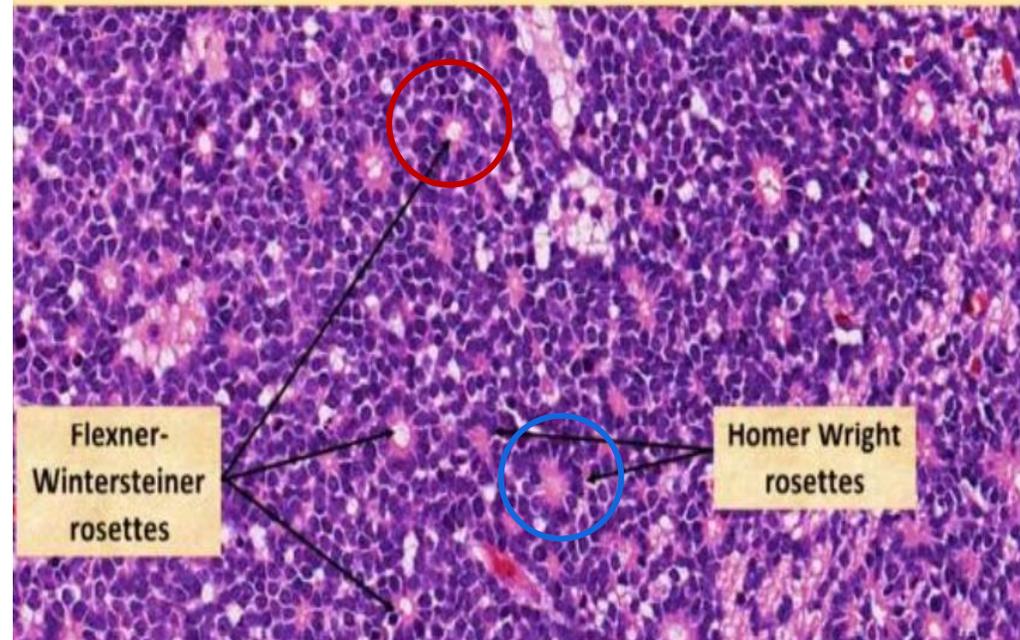
where the tumor cells are arranged around a lumen or around neurofibrillary structure.



High Power: Intensely basophilic nuclei and scanty cytoplasm



ROSETTES



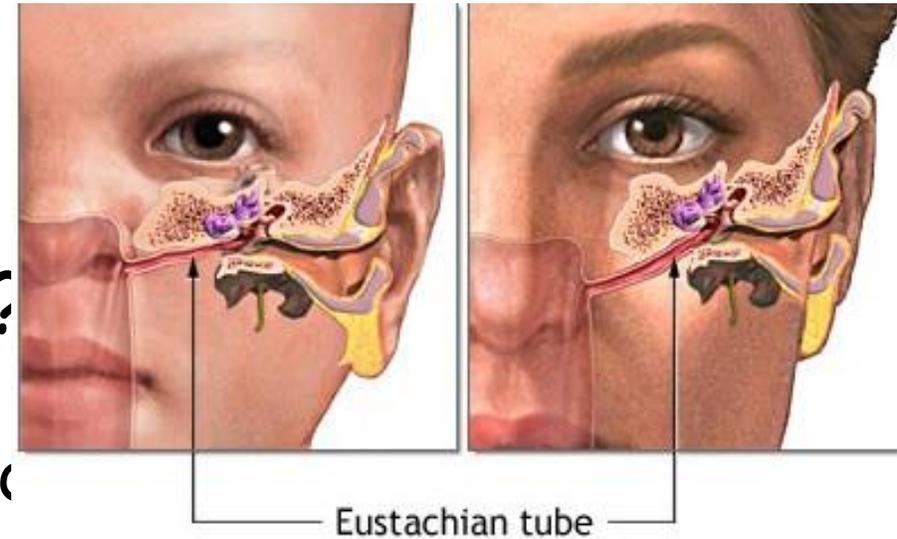
# Diseases of Ear

## Otitis Media

Inflammation of the middle ear.

### Risk factors:

- Children in first 2-4 years of life ???
  - Immune system not fully developed
  - Eustachian tube is easier to get blocked as it is shorter, more horizontal with narrower opening
  - Adenoids show infection or hyperplasia
- Bottle feeding (in supine position)
- Day care (kid-to-kid)
- Craniofacial anomalies as cleft palate
- Ciliary dysfunction as in exposure to cigarette



# Diseases of Ear

## Otitis Media

### Etiology:

\**S. pneumoniae* - 40-45%

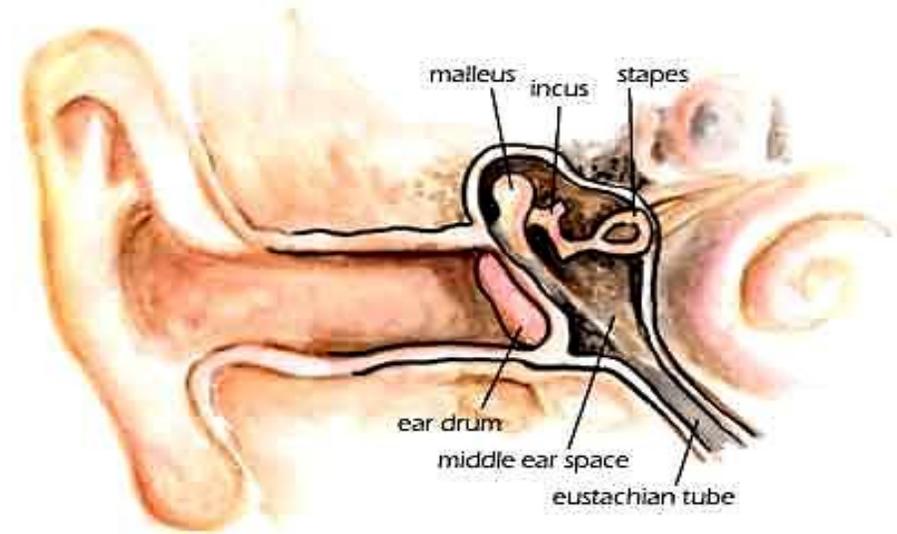
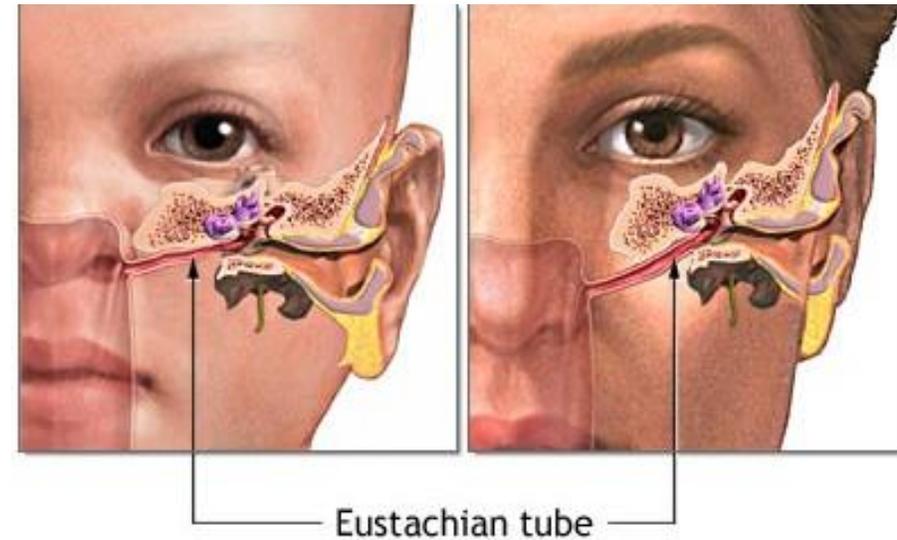
\**H. influenzae* - 30-35%

Others:

*Moraxella catarrhalis*,  
Group A strep, staph,  
Viral

### Routes:

- Via eustachian tube: the most common.
- Via external ear: tympanic membrane perforation.
- Direct spread from mastoiditis.
- Blood-born: very rare.



# Diseases of Ear

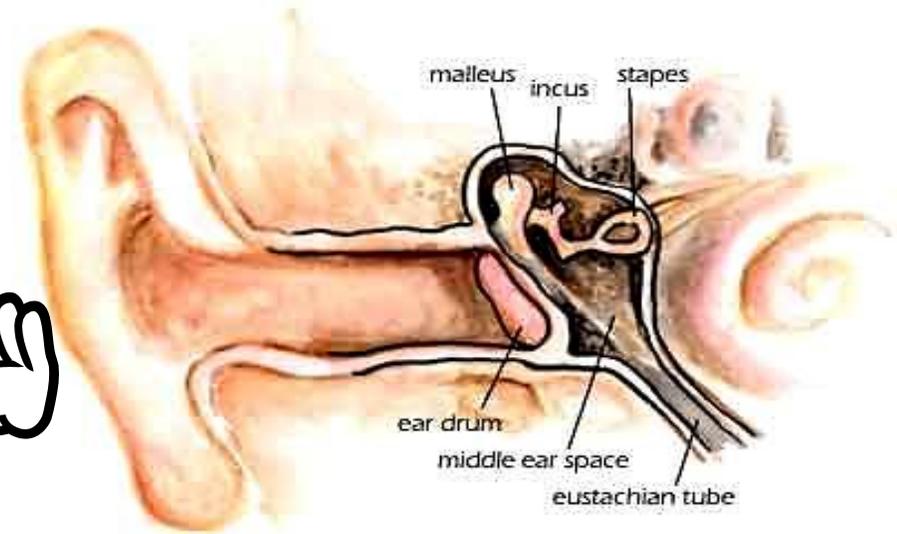
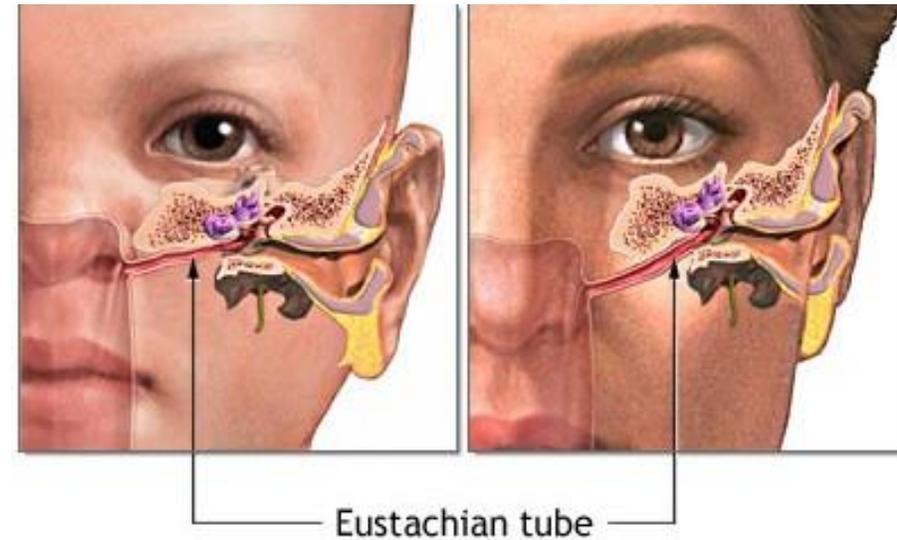
## Otitis Media

### Classification:

- Acute Otitis media:
- Otitis Media with effusion (OME):
- Chronic otitis media:
  - OM lasting 6 weeks or more
  - Chronic suppurative
  - Cholesteatoma

### Complications:

- Hearing loss; conductive, temporary
- Facial nerve Paralysis
- Spread of infection:
  - Labyrinthitis, Mastoiditis
  - Intracranial as meningitis & brain abscess



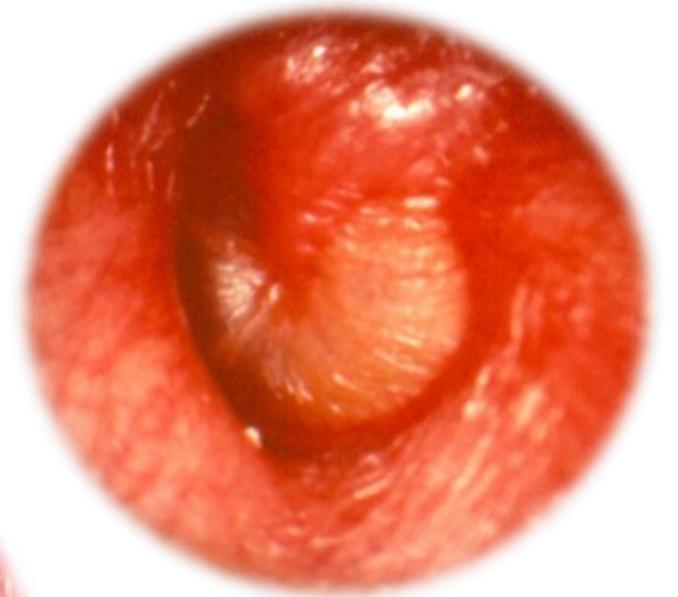
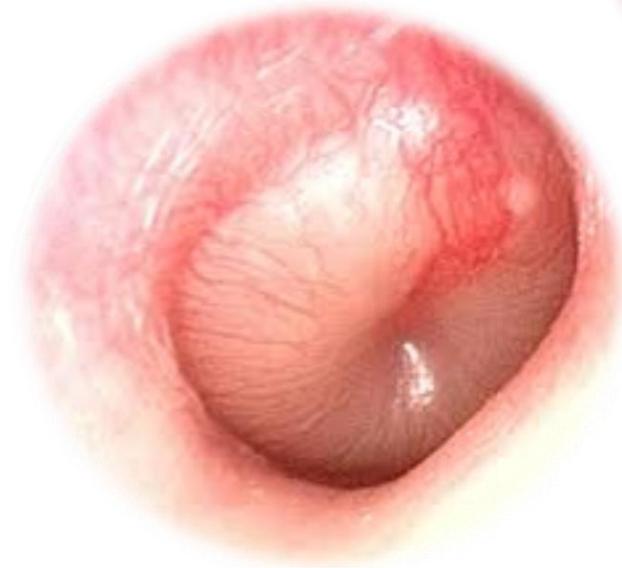
# Diseases of Ear

## Otitis Media

### Acute otitis media:

#### Tympanic membrane:

- Opaque, thick
- Bulging/injected (erythematous)
- Loss of anatomic landmarks
- Reduced mobility
- Purulent effusion



# Diseases of Ear

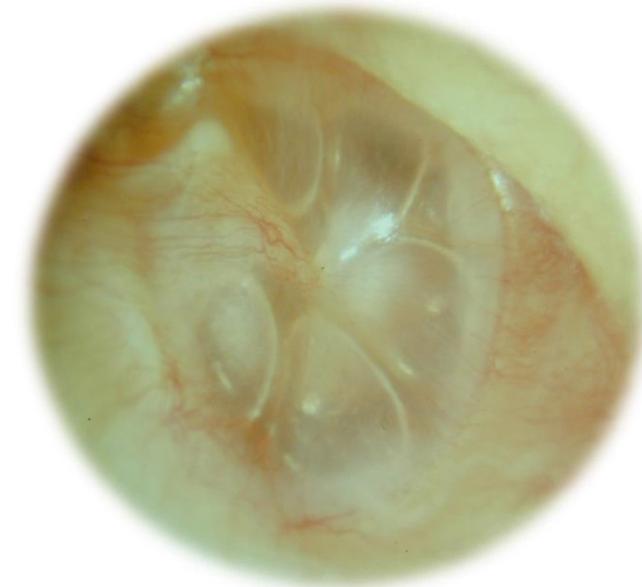
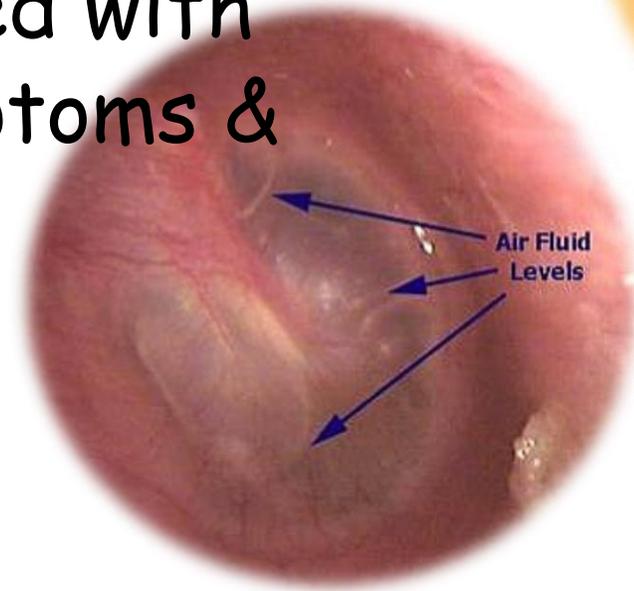
## Otitis Media

### Otitis media with effusion:

Effusion with intact tympanic membrane, **not** associated with acute inflammatory symptoms & signs.

Tympanic membrane:

- Translucent or opaque
- Gray/pink
- Reduced mobility
- Effusion (thick mucoid) +/- air.

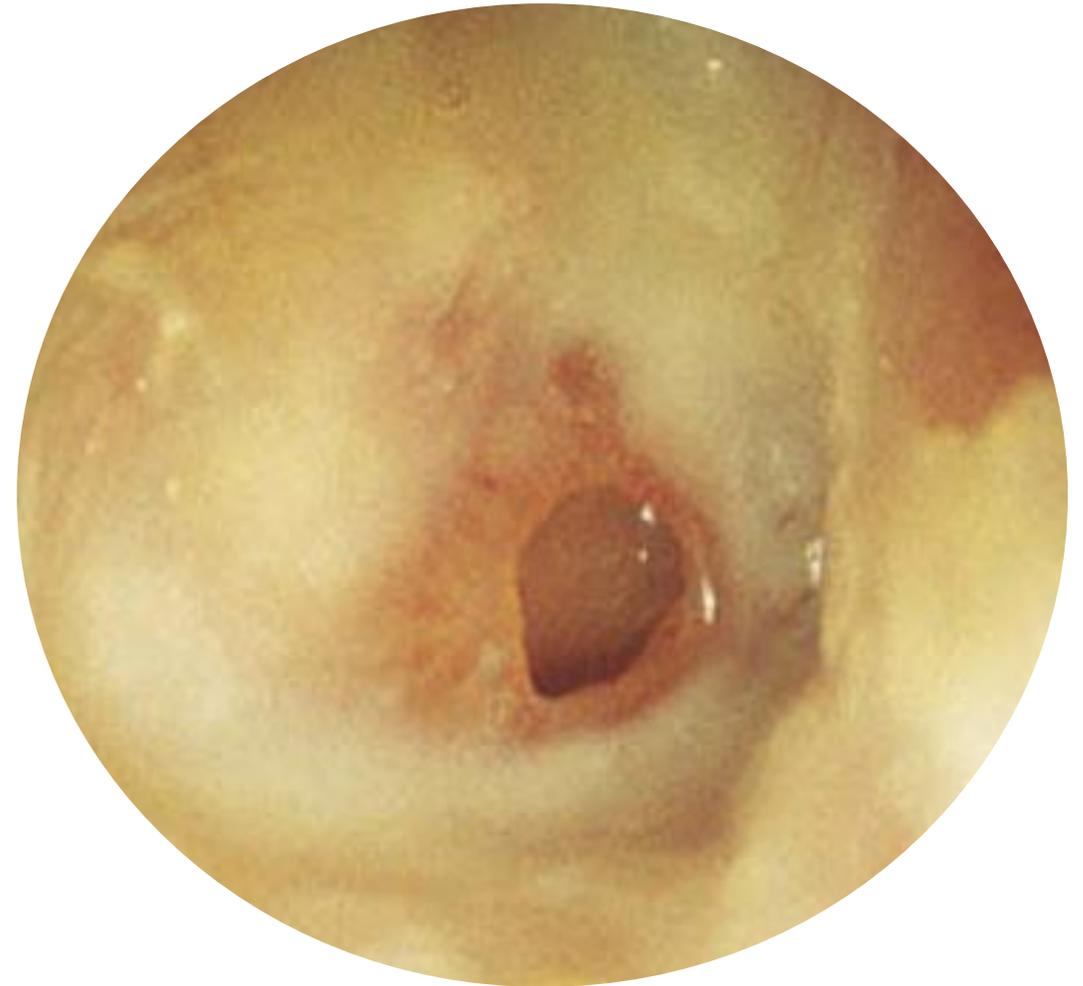


# Diseases of Ear

## Otitis Media

### Chronic suppurative otitis media:

- Chronic tympanic membrane perforation, fibrosis, calcification
- Purulent discharge (mucopurulent otorrhea)
- Conductive hearing loss

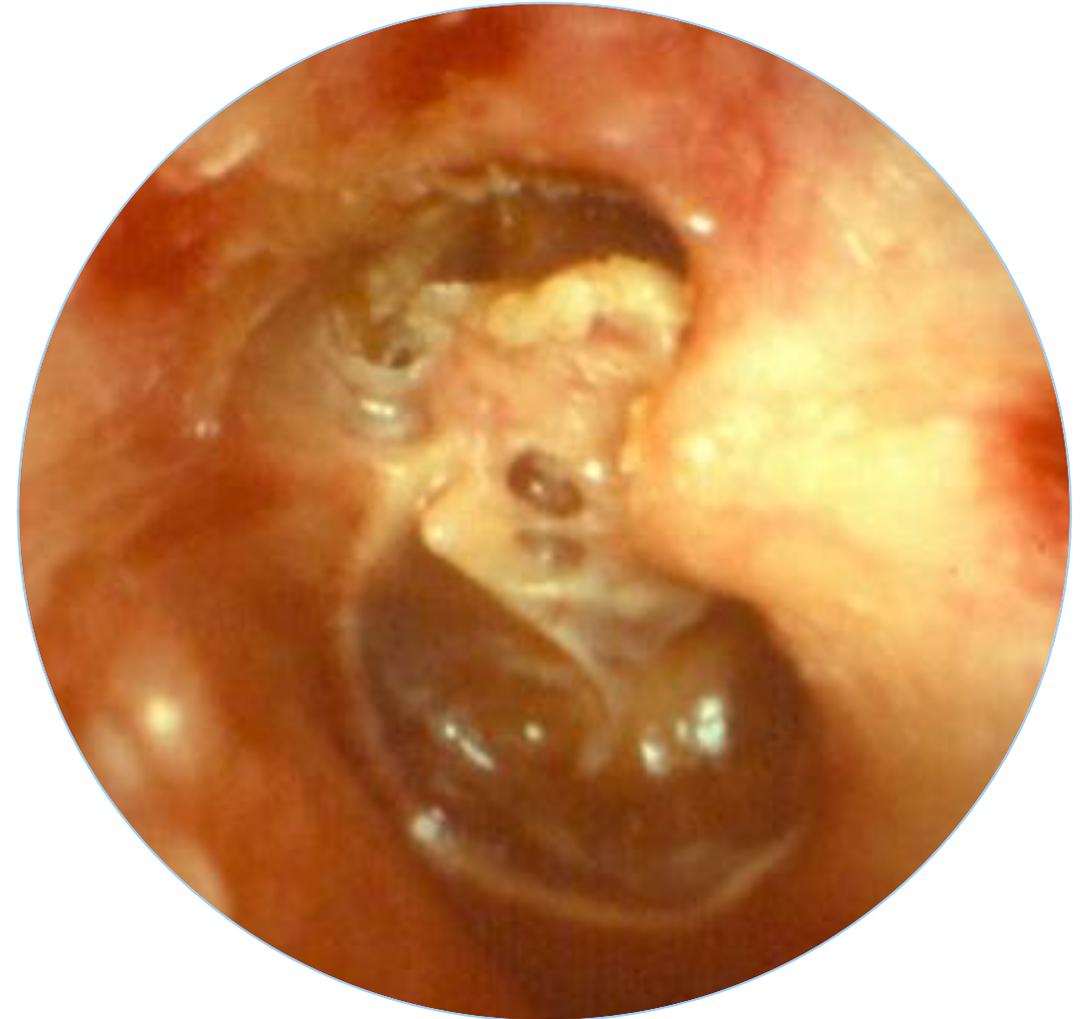


# Diseases of Ear

## Otitis Media

### Chronic otitis media with cholesteatoma:

- Accumulation of squamous epithelium with keratin + cholesterol clefts + large number of histiocytes. in middle ear & mastoid
- Osteolytic (osteoclastic inflammation)
- Often accompanied by chronic otorrhea



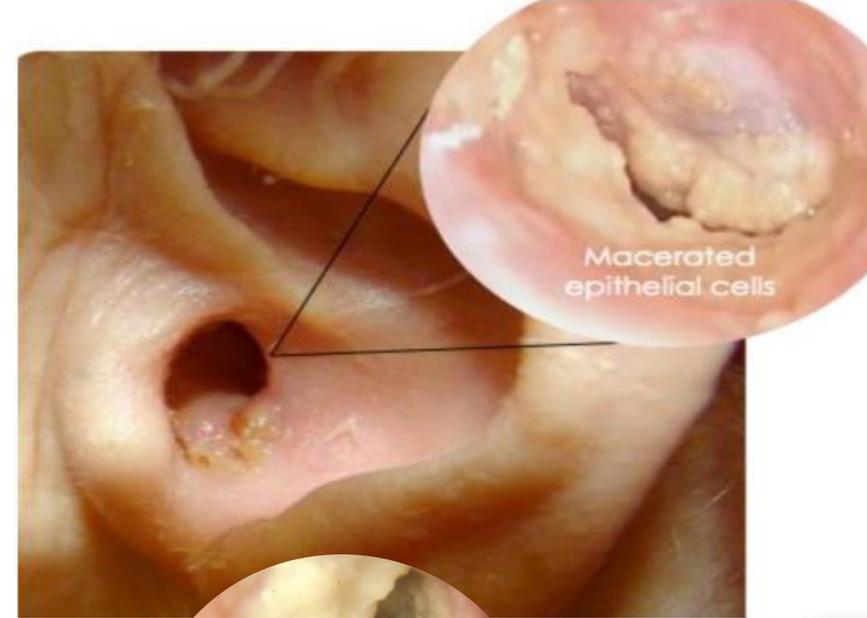
# Diseases of Ear

## Otitis Externa

Infection of the skin and subcutis of the external auditory canal

### Types:

- 1- Acute diffuse otitis externa
- 2- Circumscribed otitis externa.
- 3- Chronic otitis externa.
- 4- Malignant (Necrotizing) otitis externa



## Otitis Interna

- Commonly known as labyrinthitis or vestibular neuritis.
- Caused mainly by viral infection.
- Symptoms include vertigo, dizziness, a ringing sound in your ears

# Ear Tumors

- Tumors of external ear:  
Cerumen-gland tumors
- Tumors of middle ear:  
Jugular paraganglioma  
(glomus tumor).
- Tumors of inner ear:  
Acoustic neuroma.

# Ear Tumors

## Schwannoma

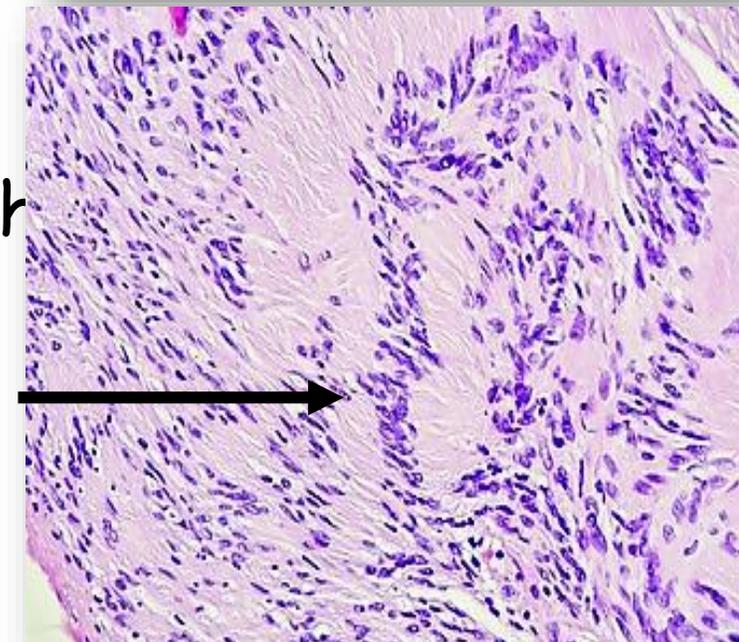
- It is a benign tumor called Acoustic neuroma of 8th cranial nerve
- Age: 50-60 years.

### N/E:

Solitary mass, capsulated, firm round or fusiform with the related nerve at one side  
Cut surface is grey white and may show cysts

### M/E:

Spindles shaped cells arranged in bundles, with rod-shaped nuclei side by side in palisade manner with reticular and collagen fibers in between.



# Ear Tumors

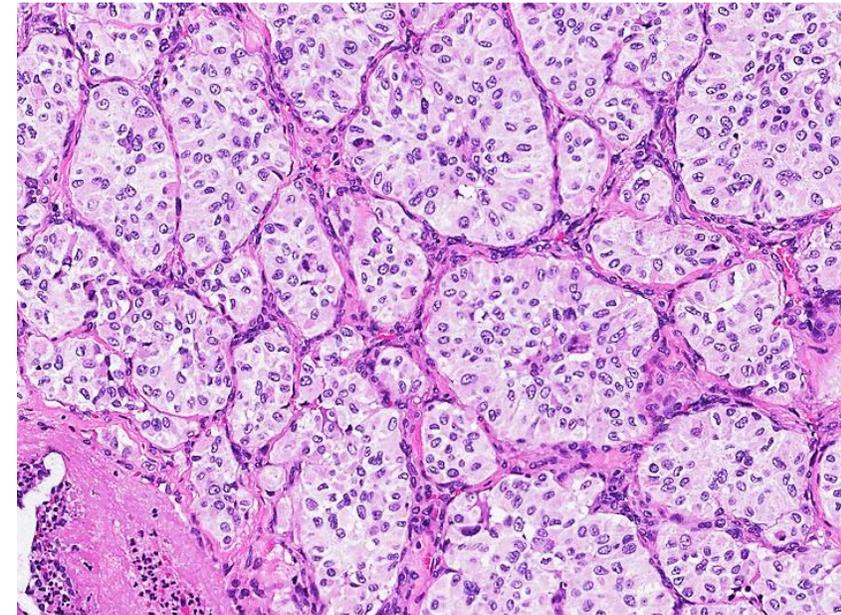
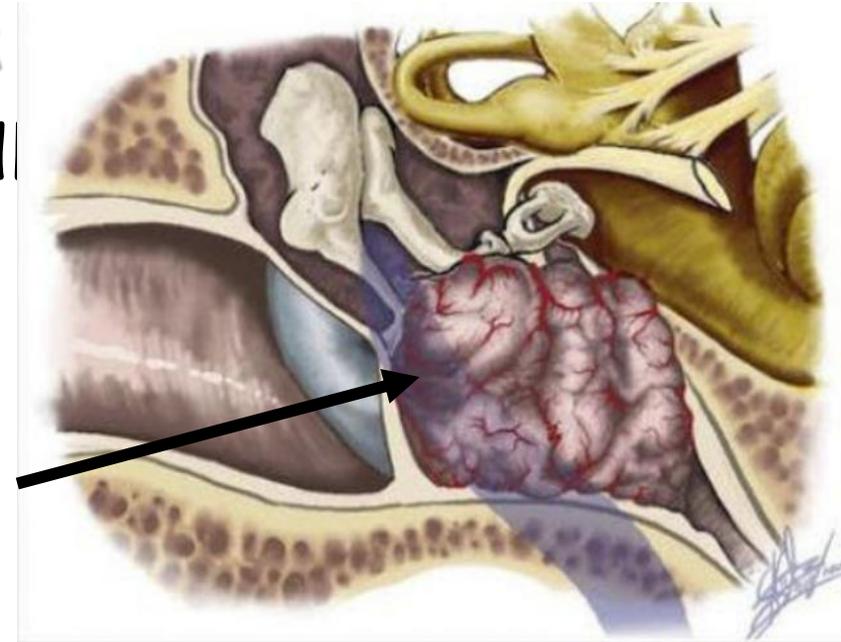
## Jugular para-ganglioma

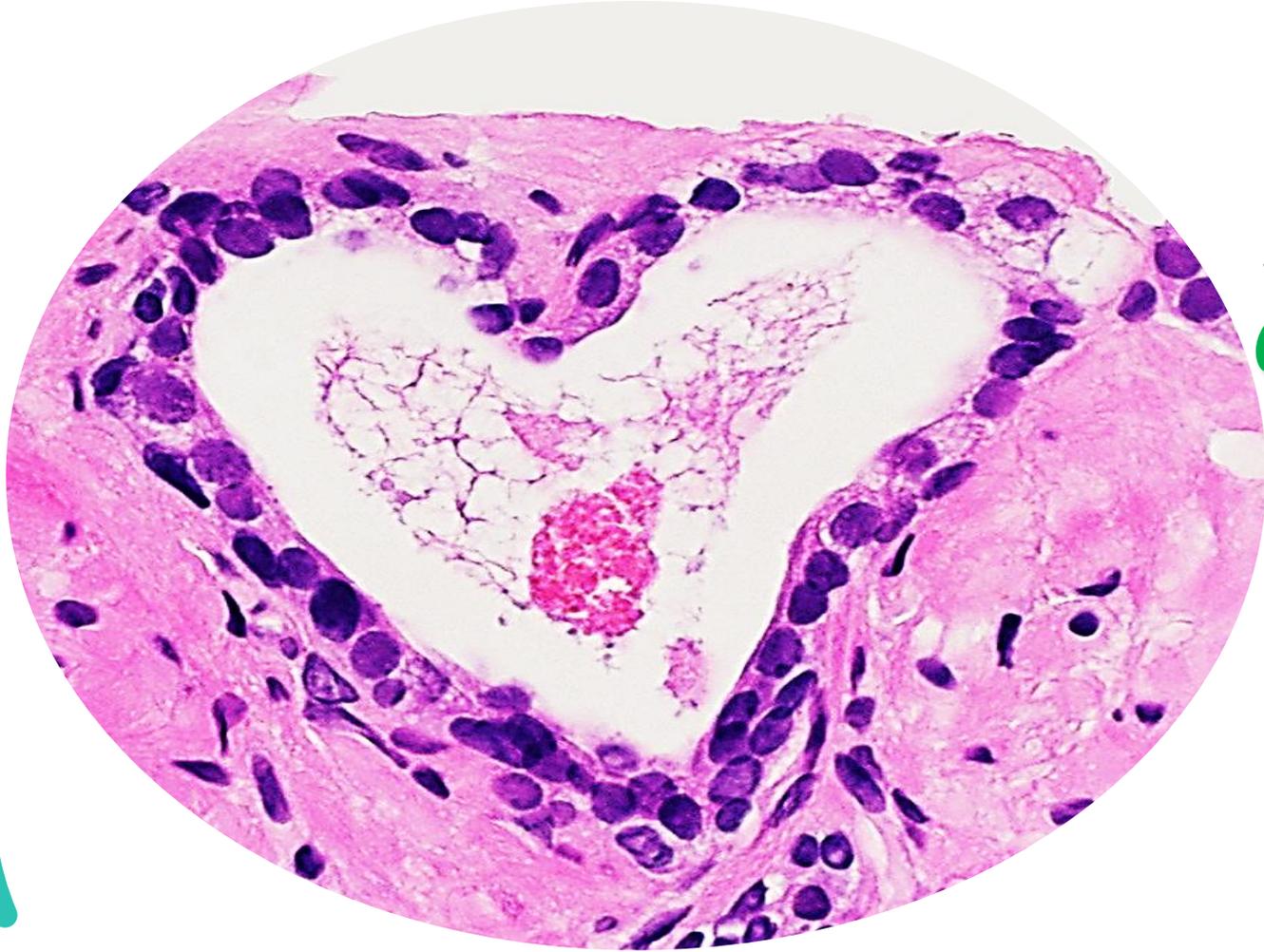
The most common benign tumor of the middle ear. Called *Glomus jugular*- Arise from parasympathetic ganglia.

**M/E:**

Classic organoid/nested pattern called "zellballen"; with fibrovascular stroma separates the nests

1. the central cells are rounded/ovoid chief cells with abundant eosinophilic granular cytoplasm.
2. Spindle cells present at the periphery of nests.





*Thank you*





Discussion & Feedback



# References & recommended readings

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(Robbins Pathology), 2018 ISBN: 978-0-323-35317-5,  
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2. Webpath:

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