

Kuwait University
Faculty of Medicine
DEPARTMENT OF PATHOLOGY
Phase II Curriculum-2011
Central Nervous System Module



CNS tumors and space occupying
lesions (**ID#2396**)

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Weekly Learning Objective(s):

- Describe the origin, localisation and morphological characteristics of primary brain tumours: gliomas, medulloblastomas, meningiomas and Schwannomas. (WLO2429)

Objectives:

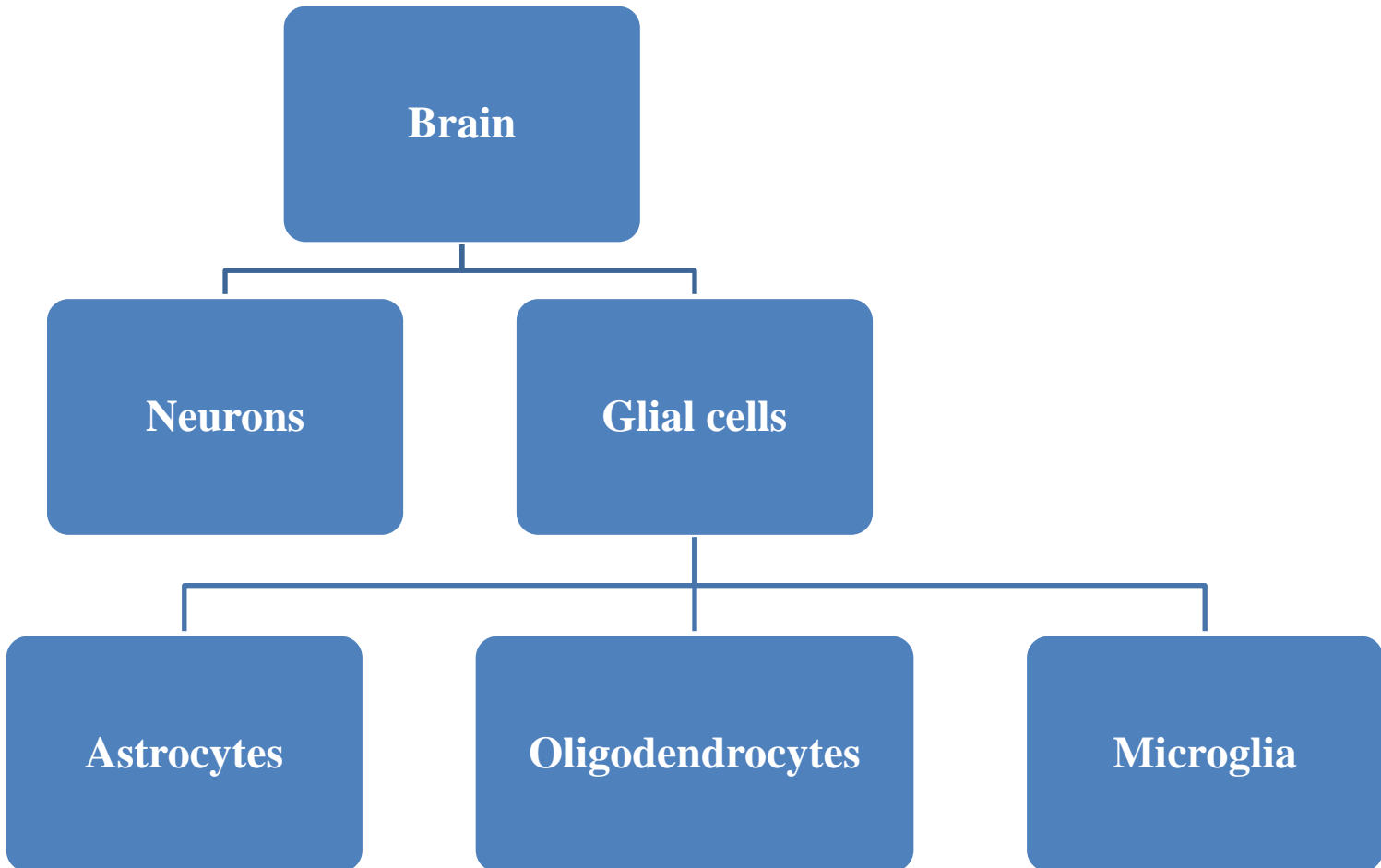
1. Describe the different types of CNS tumours.
2. Describe gross and microscopic features of common CNS tumors.
3. Explain the special aspects of CNS tumours as compared to tumours elsewhere in the body.
4. Explain the differences in the pattern and behaviour of CNS tumours between children and adults.
5. Describe the clinico-pathological features of common CNS tumours.
6. Explain prognostic indicators in CNS tumours.
7. Describe the pathology of other space occupying lesions



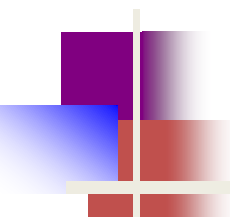
The Brain .. Overview

- Adult brain weighs an average of 1.5 Kg.
- One of the most , if not the most, organ in our bodies
- Hosts about 100 billion neurons and 10x more glial cells organized in distinct and complex functional and anatomical structures.

Cellular components of Brain



Neurons

- 
-
- The main functional and cellular component of the nervous system.
 - They are electrically excitable cells capable of processing and transmitting information signals in the form of action potentials.



Glial Cells

- Supportive role.



Astrocytes

- Functional support: Signal modulation
- Physical support
- Nutritive support



Oligodendrocytes

- Mainly involved in insulation of neurons axons with a lipid-rich membrane called “myelin”.

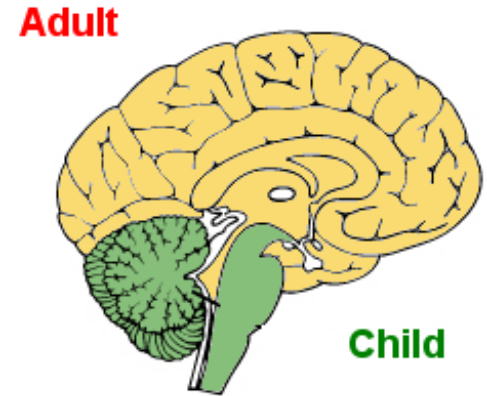


What is a Brain Tumor?

- The World Health Organization (WHO) recognizes 120+ different types of brain tumors
- 3 Basic types:
 - Tumors of the Brain – Gliomas –
 - Tumors to the Brain – Metastases
 - Tumors on the Brain – Meningiomas, Pituitary Tumors, Acoustic Neuromas, etc.

General Considerations

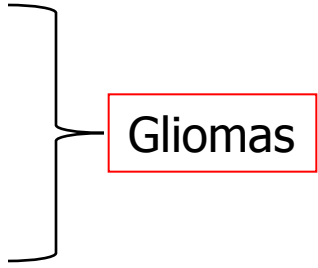
- ❖ **CNS tumors – second commonest tumor in children and sixth in adults.**
- ❖ Peak incidence at 1st and 5th decades
- ❖ Supratentorial tumors in adults
- ❖ **In adults – 70% are supratentorial**
- ❖ Infratentorial tumors in childhood
- ❖ **In children – 70% are sited in the posterior fossa and are intrinsic.**



Classification - CNS tumours

Cell of origin	CNS tumour
■ Glial cells (Astrocyte, Oligodendrocyte, ependyma, Primitive Glial cell-microglia)	Astrocytoma, oligodendroglioma, ependymoma, glioblastoma
■ Primitive Neuroectodermal cells	Medulloblastoma,
■ Arachnoidal cell	Meningioma
■ Nerve sheath cells	Schwannoma, neurofibroma
■ Lymphoreticular cells	Lymphoma

CNS Tumours

- **Intrinsic** of glial origin
 - (all primary in children 65% primary in adults)
 - astrocytomas
 - glioblastoma
 - oligodendroglioma
 - ependymoma
 - choroid plexus papilloma
 - PNET – medulloblastoma
 - Hemangioblastoma
 - Lymphoma
 - **Extrinsic** – meninges, Cranial + spinal nerve roots
 - Metastasis
 - meningioma
 - schwannoma
 - neurofibroma
- 
- Gliomas

Clinicopathological features

Brain tumours may present clinically in two main ways:

- **Local effects**

- Destruction of functional neural tissue → ***neurologic deficit*** → ***sensory or motor or both.***
- Irritates function area → involuntary release of neuronal activity – ***manifest as seizure.***
 - Epilepsy with a temporal lobe tumour
 - paraplegia with a spinal cord tumour

- **Mass effects+ surrounding edema** → raised intracranial pressure → headaches and vomiting

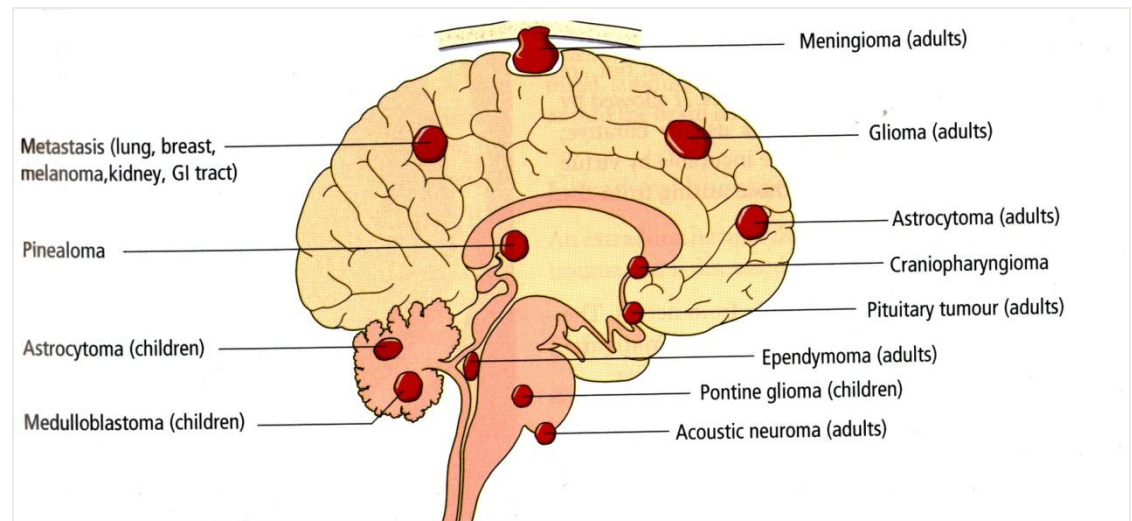
- posterior fossa tumours present with hydrocephalus, particularly in children.

- **Intracranial herniation** is a common mode of death

SPREAD

- Primary CNS neoplasms **virtually never metastasise to other organs.**
- **Infiltration** of adjacent tissues both within the nervous system and its coverings (including the skull) is common, for example in meningioma.
- seeding to remote parts of the nervous system by the **CSF pathway** for example medulloblastomas.

Age of the patient – Location of tumor



•Astrocytic neoplasm

Cerebrum – middle of life + old age

Cerebellum + pons – childhood

Spinal cord – young adults

•Oligodendrogliomas – cerebrum

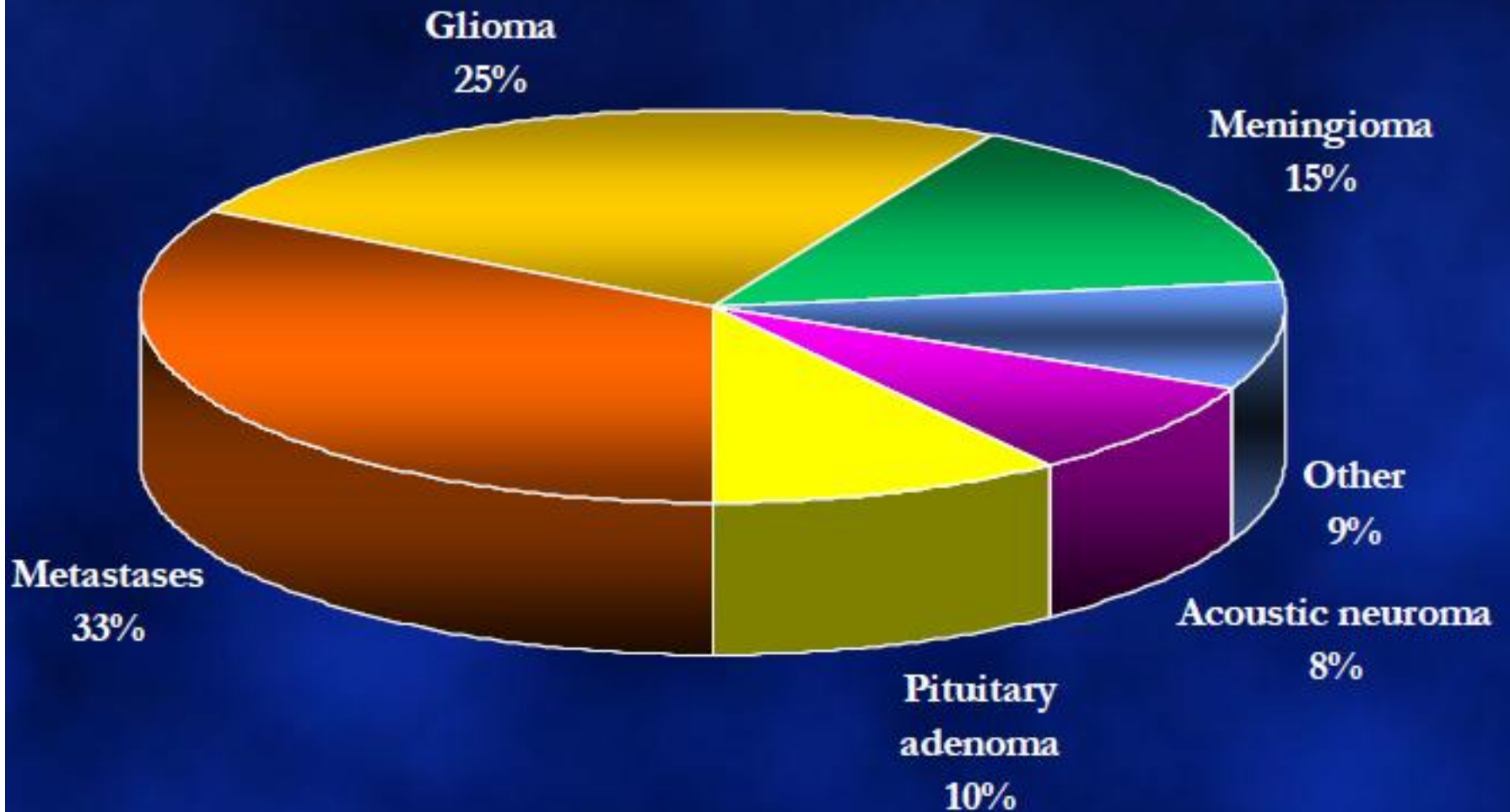
•Ependymoma

- IV ventricle in first three decades

- Spinal cord filum terminale

•Medulloblastoma – Cerebellum - Childhood

Intracranial Neoplasms



Incidence of Intracranial Gliomas (All Ages)

Glioblastomas 55%

Astrocytomas 20%

Ependymomas 5%

Medulloblastomas 5%

Oligodendrogliomas 5%

Choroid plexus lesions, cysts, etc 10%



Incidence of Intracranial Gliomas [children]

- Astrocytomas [50%]
- Medulloblastoma [45%]
- Ependymomas [5%]

Astrocytic neoplasms

Epidemiology

- **60% of brain tumors**
- **7-10 cases/100,000 per year**
- **Grade I astrocytomas (pilocytic) in cerebellum, brainstem, and optic nerves of children**
- **Grade II astrocytomas in the cerebral hemispheres of 20-40 year old individuals**
- **High grade astrocytomas seen in older individuals**

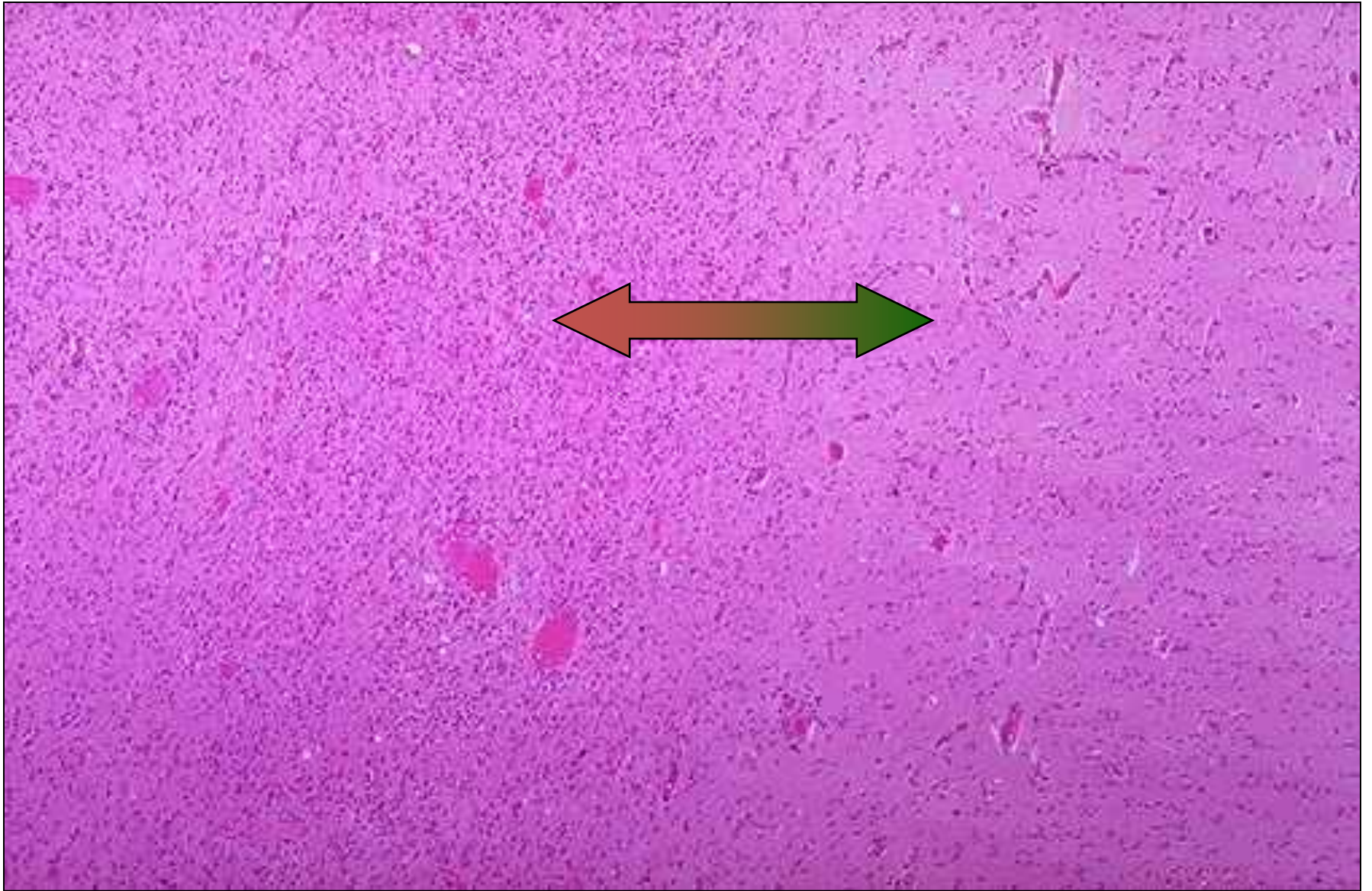
Astrocytoma:

- Headache, seizures & neurological deficits.
- 4 tier grading system.
 - Anaplasia, cellular pleomorphism
 - Mitotic activity,
 - Necrosis &
 - Endothelial proliferation.
- Well differentiated – low grade
- Anaplastic - high grade
- Glioblastoma multiforme.

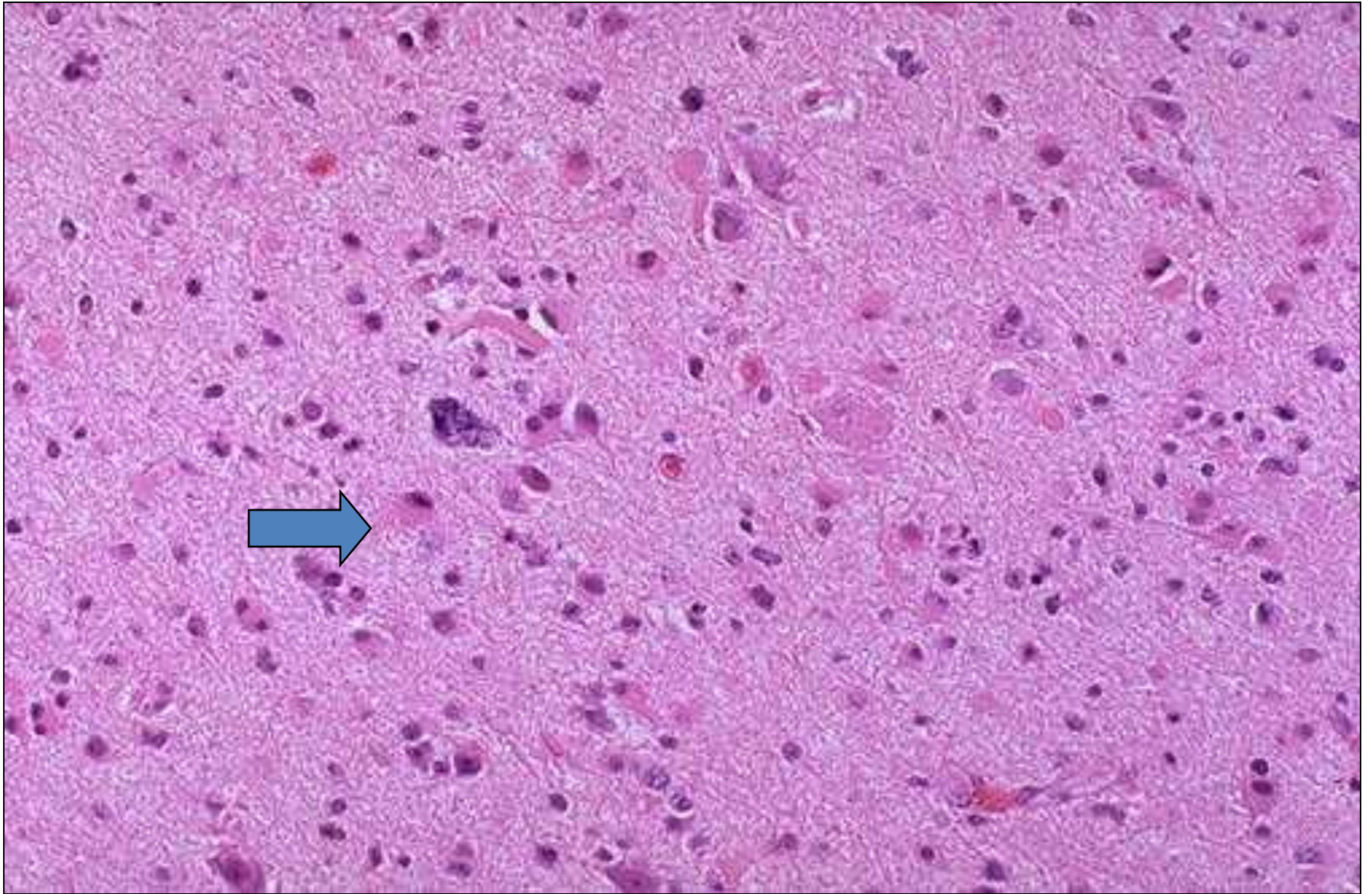
Astrocytoma: microscopic

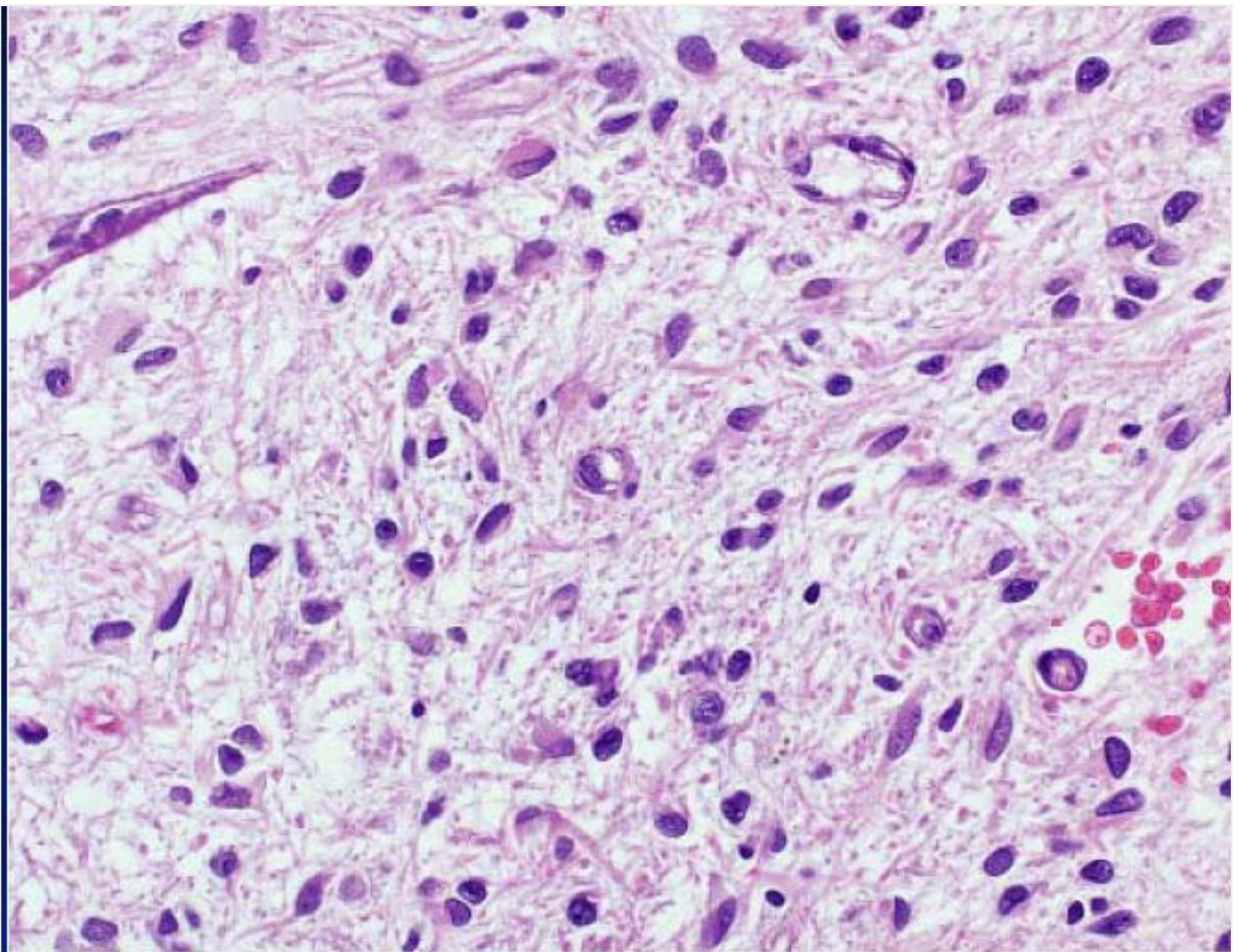
- **Low grade-** hypercellularity, pleomorphism
- **Anaplastic- high grade** – plus will have more mitosis & vascular endothelial proliferation
- **Glioblastoma multiforme-** plus necrosis and pseudopalisades. Grossly variegated appearance (multiforme)

Astrocytoma



Astrocytoma

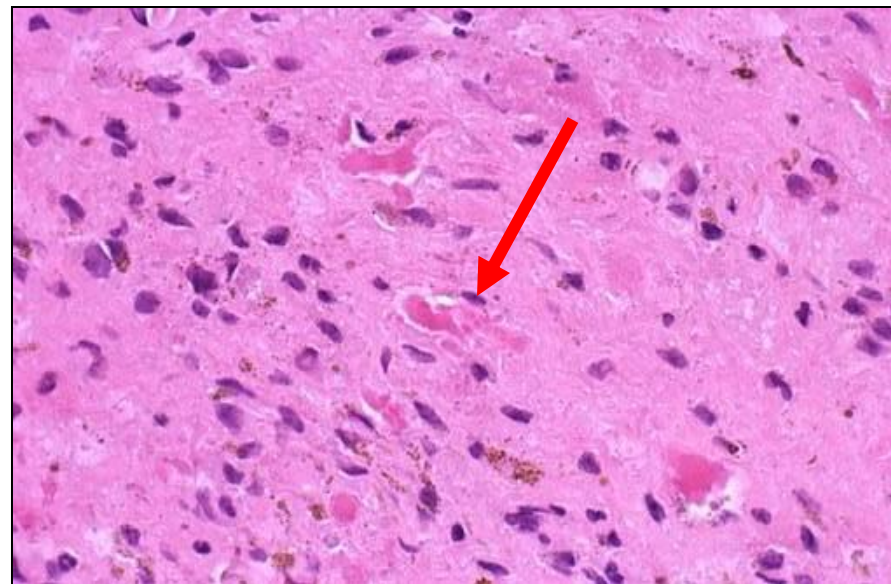
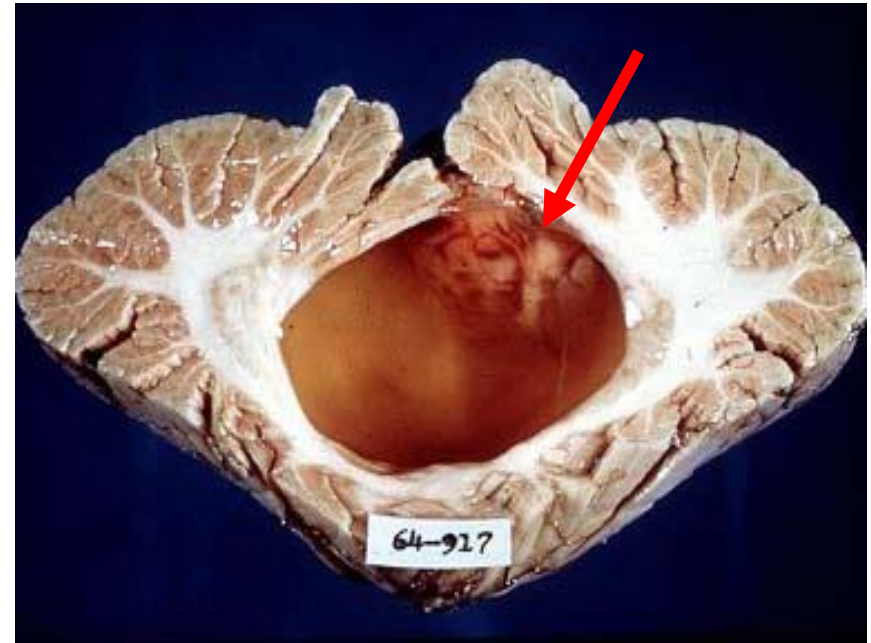


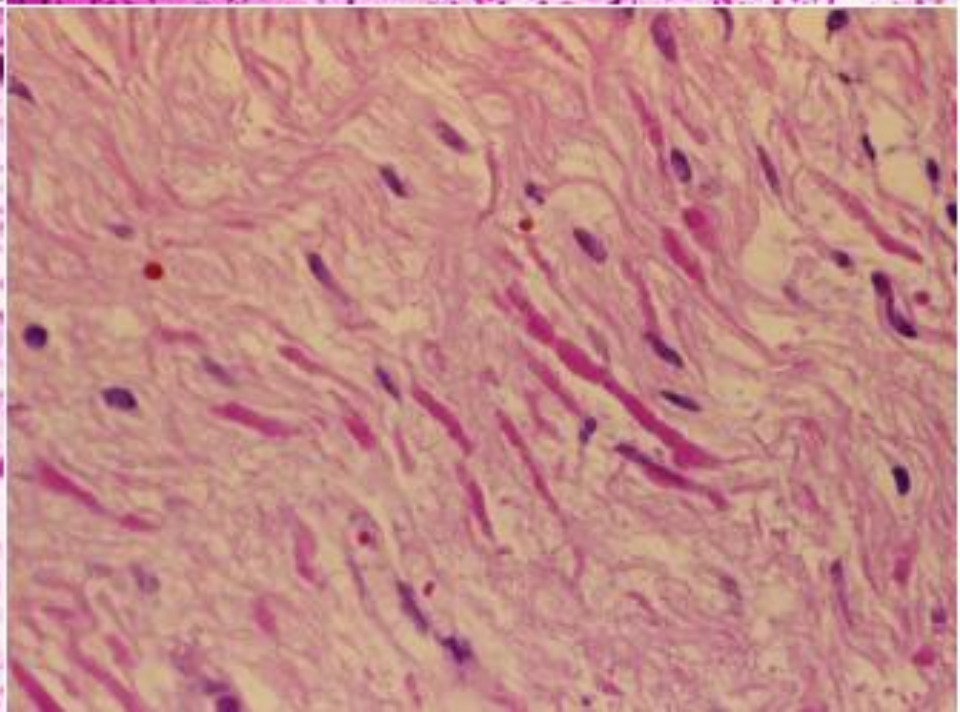
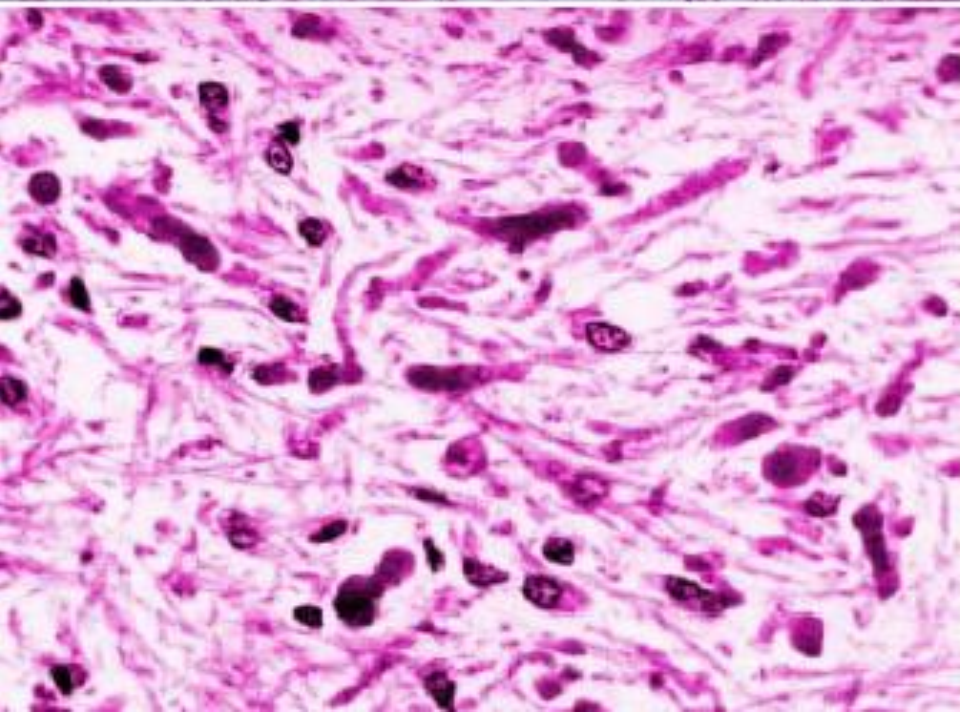
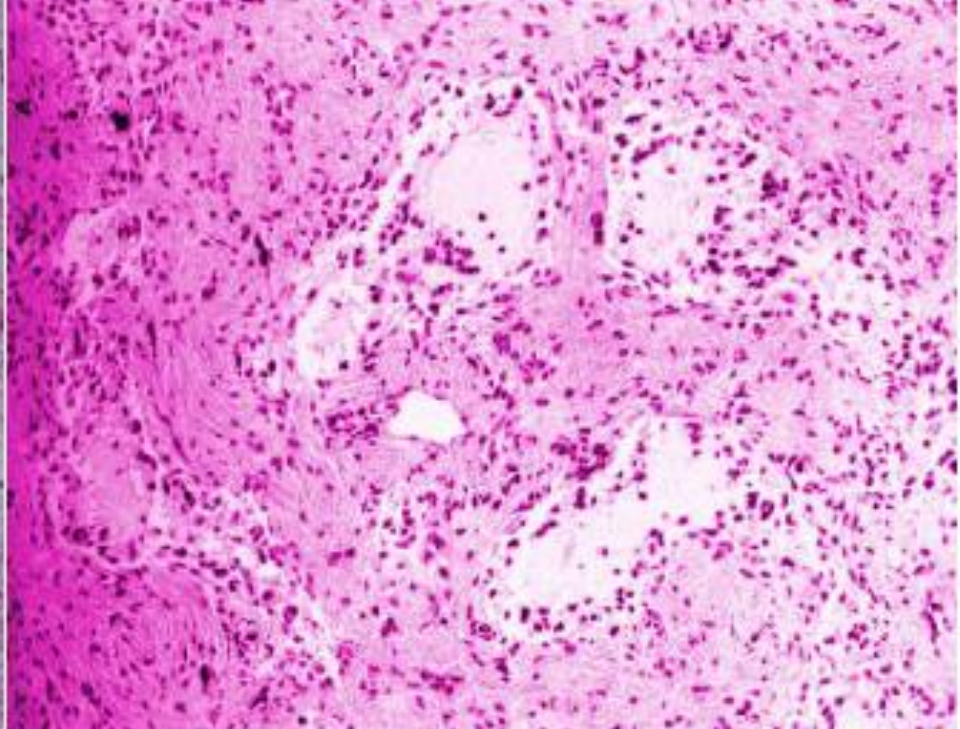
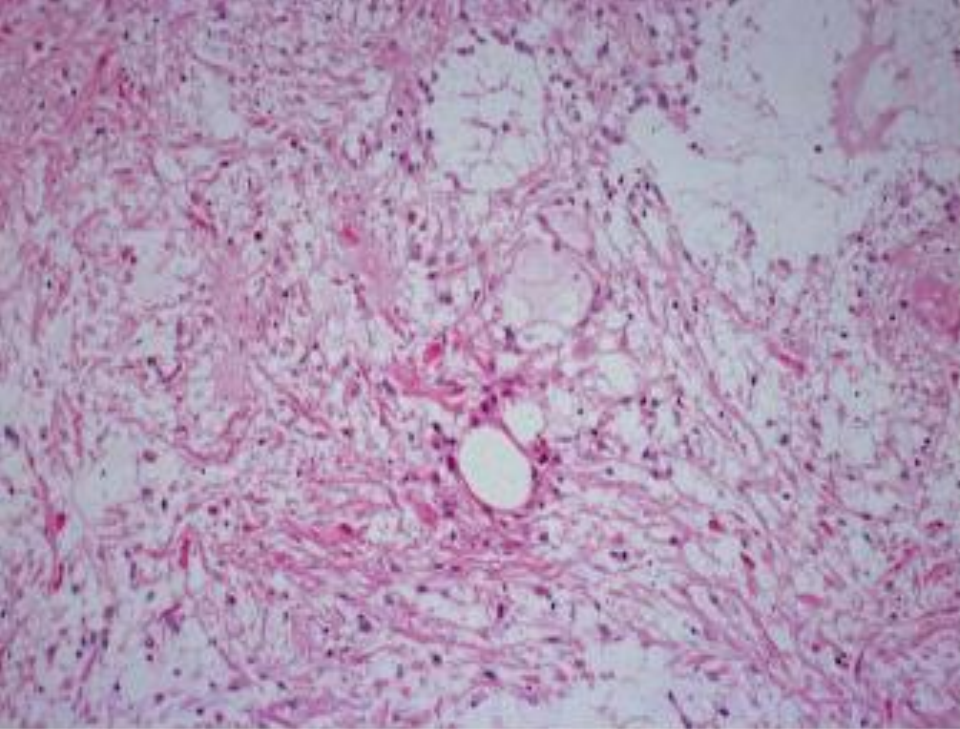




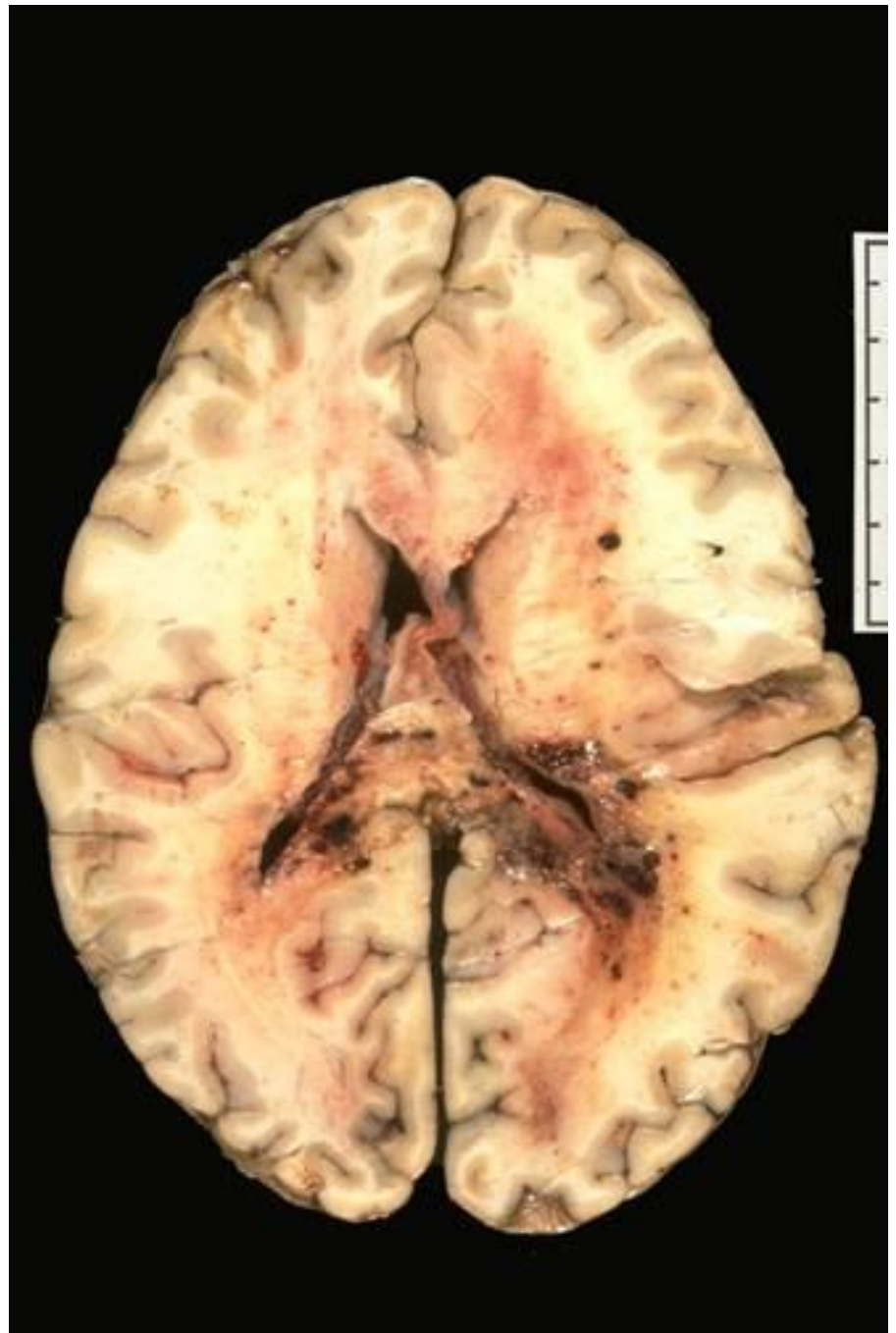
Pilocytic astrocytoma

- Common in childhood
- Most slow growing of the gliomas
- Sites: below the tentorium, posterior fossa-cerebellum, around III V., optic nerve
- Grossly well circumscribed gelatinous mass - cystic with mural nodule
- Microscopic
 - elongated hair-like (pilo) stellate astrocytic cells – loosely knit
 - Rosenthal fibers

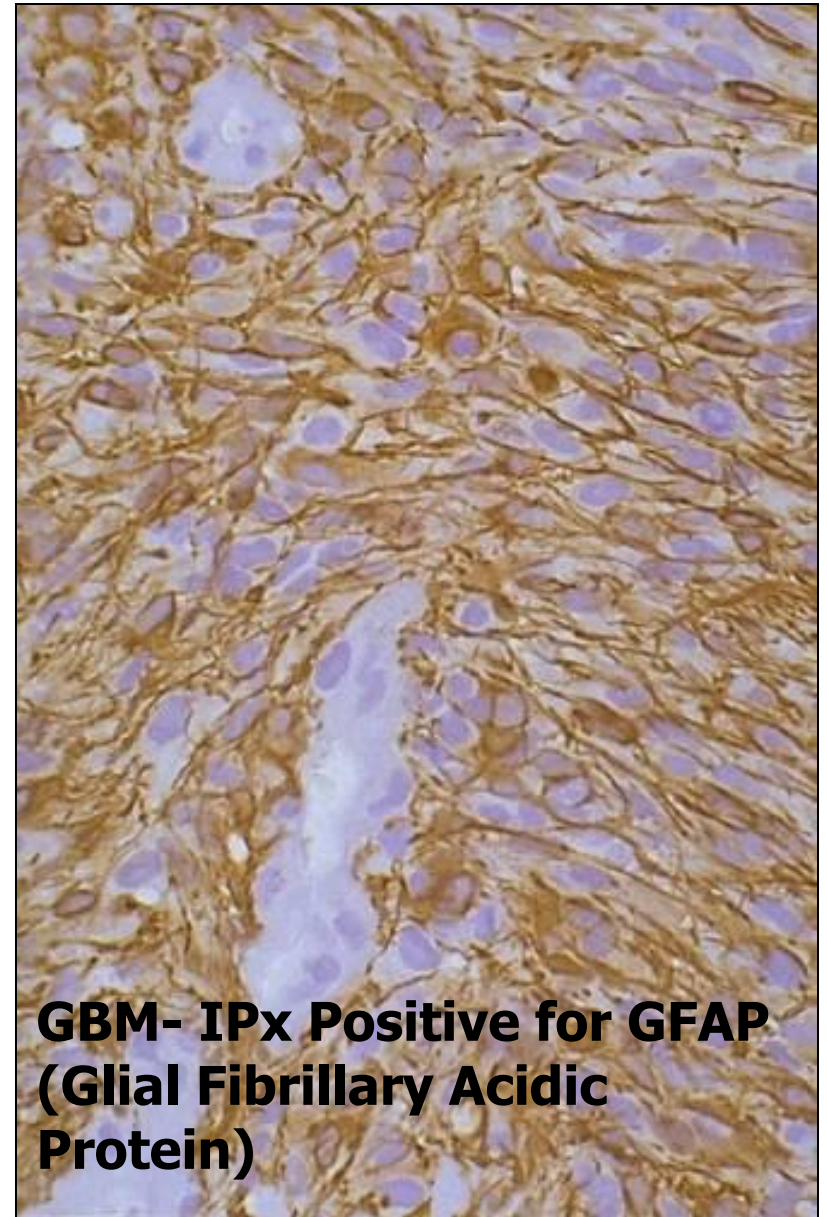
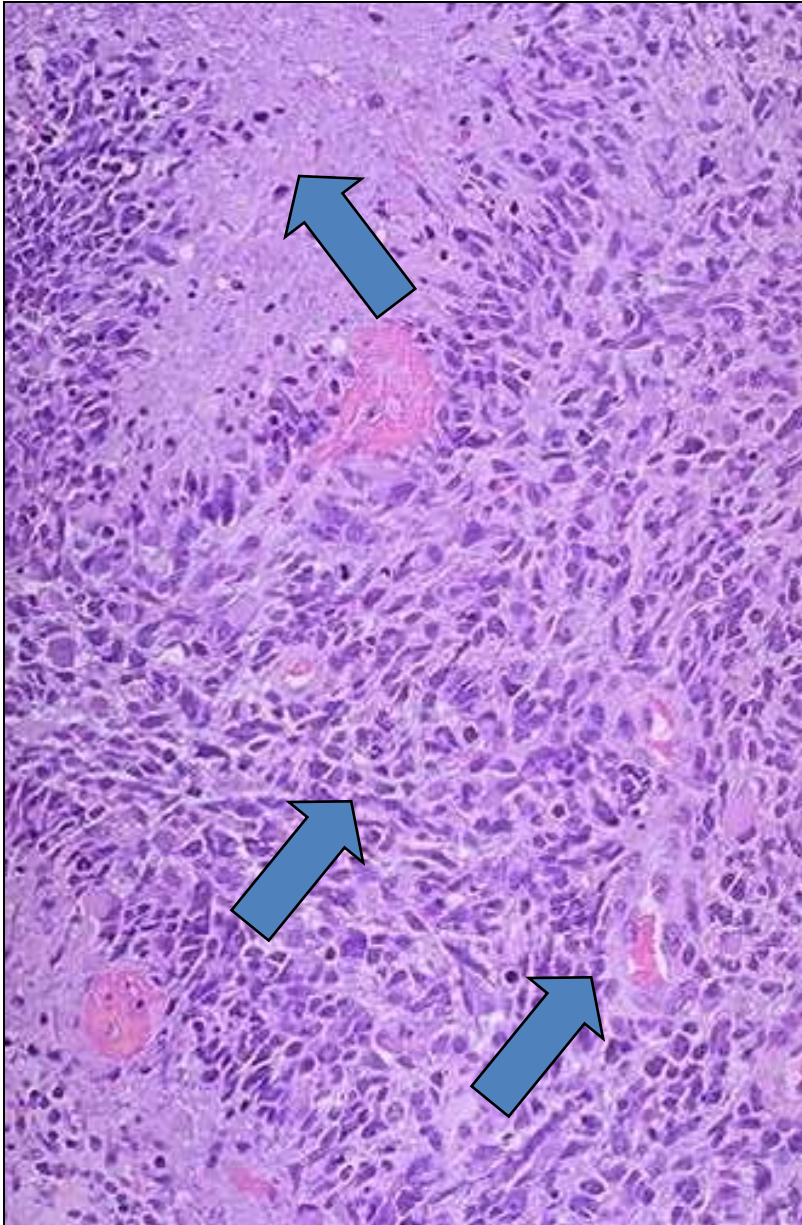




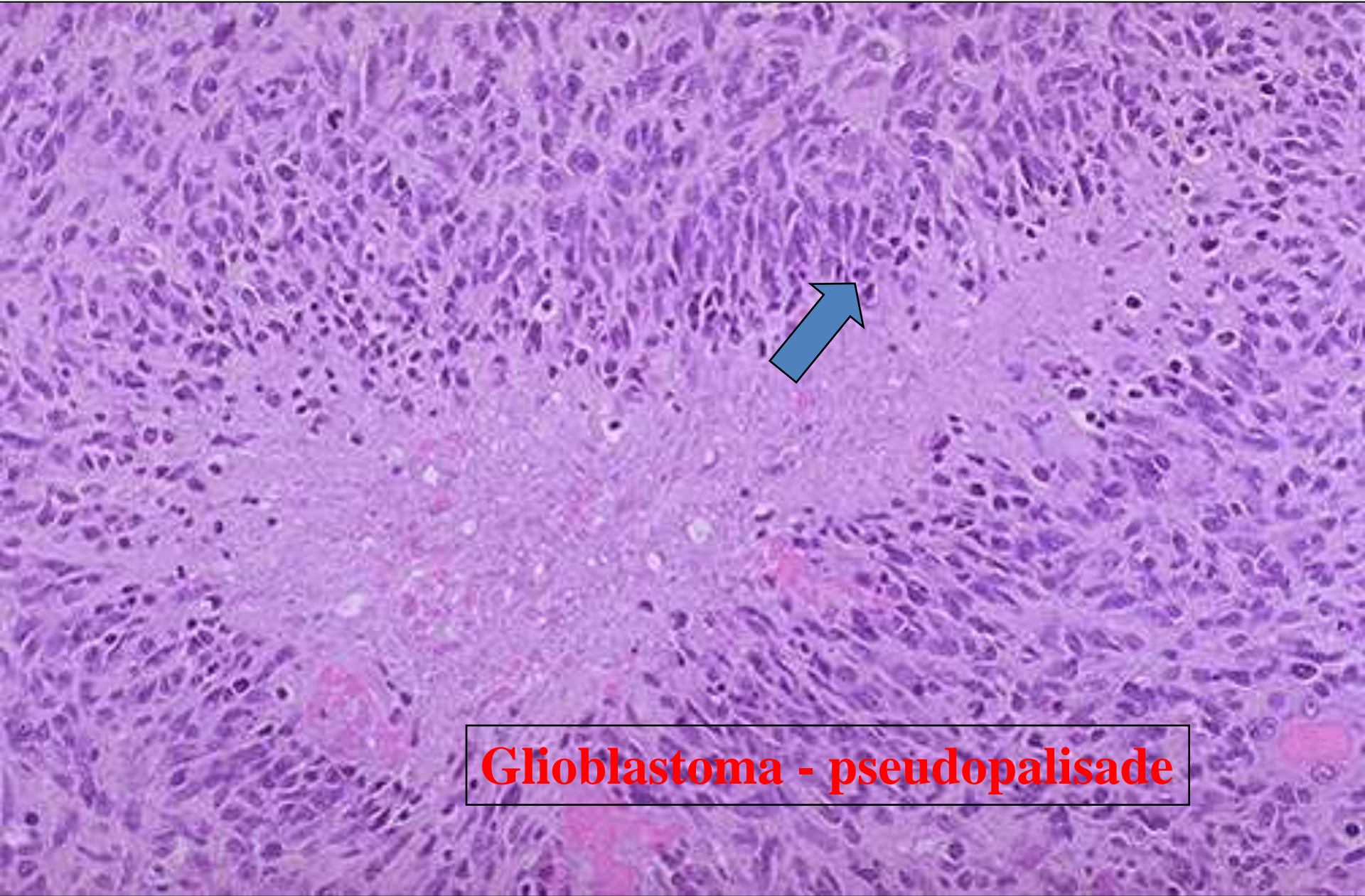
Glioblastoma Multiforme



Glioblastoma Multiforme



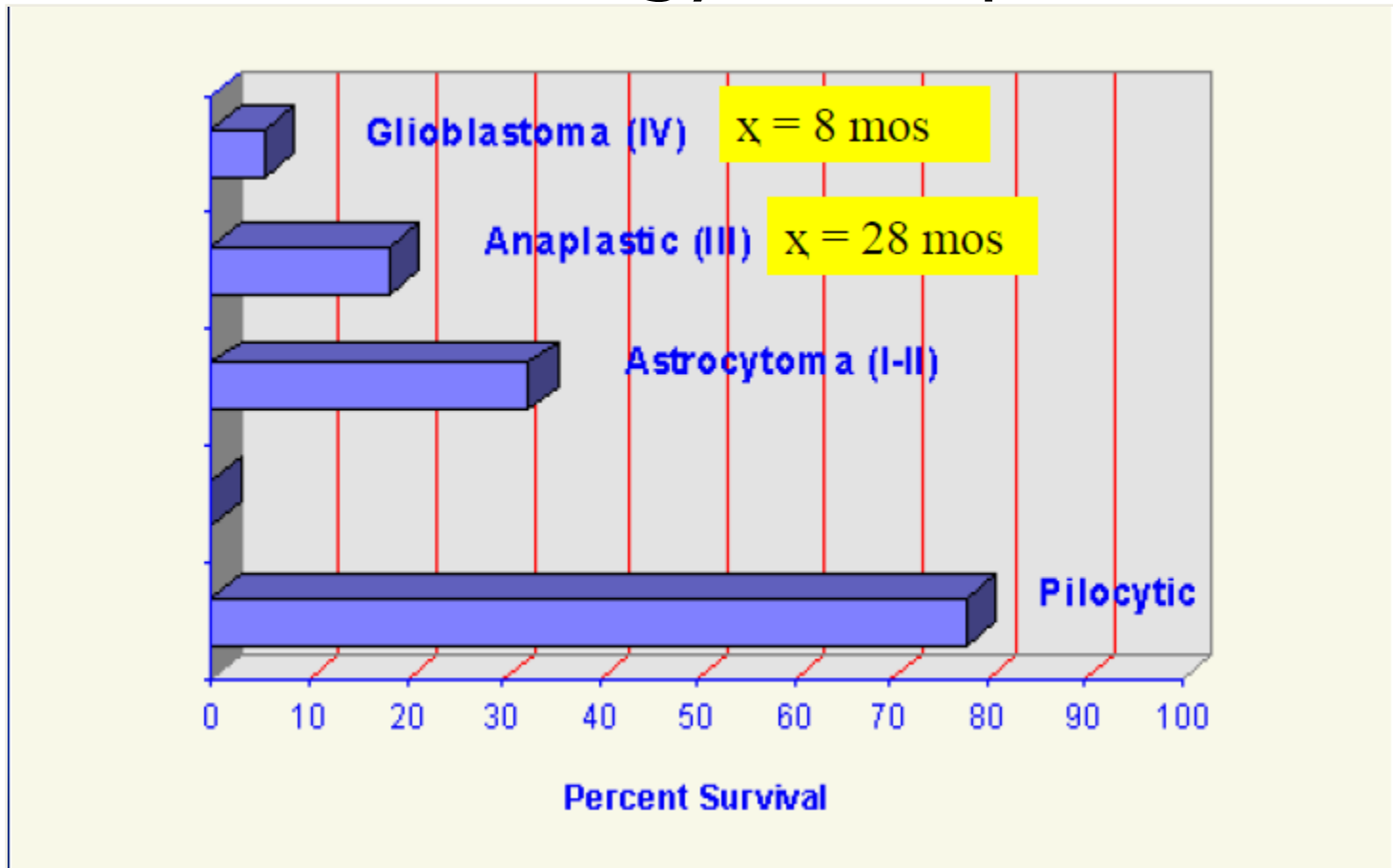
Glioblastoma Multiforme



Glioblastoma - pseudopalisade

Prognosis

- Age of patient
- Size, site and histology of neoplasm



Astrocytomas

Adults:

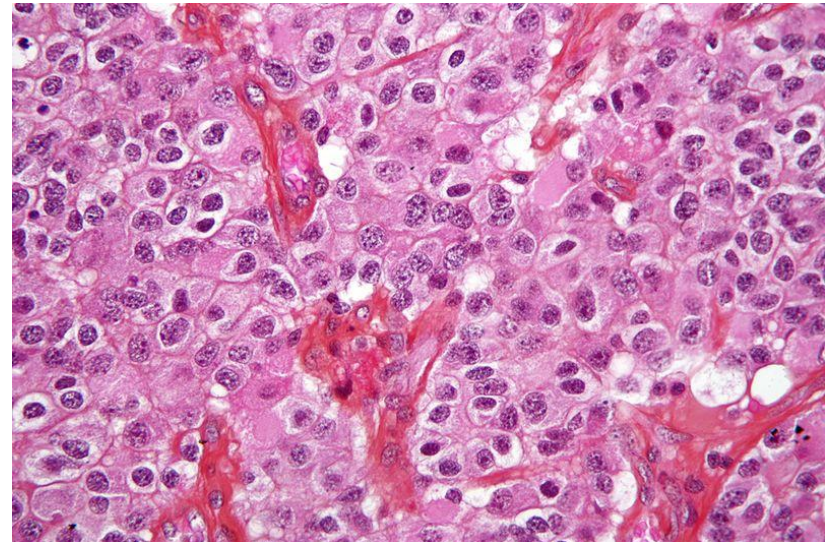
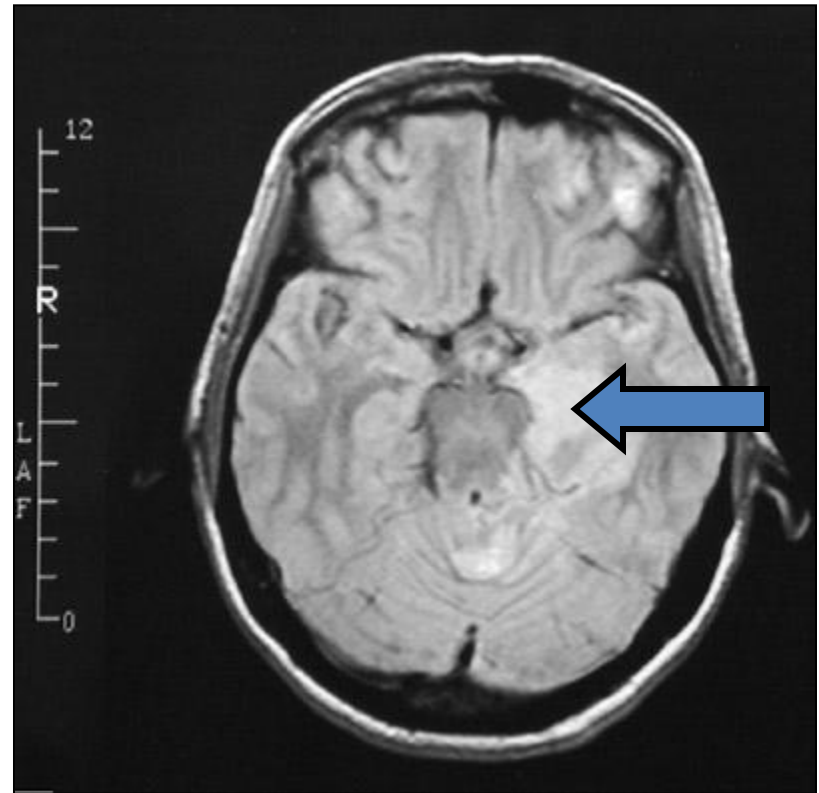
Supratentorial
Solid
Malignant
Fibrillary

Childhood:

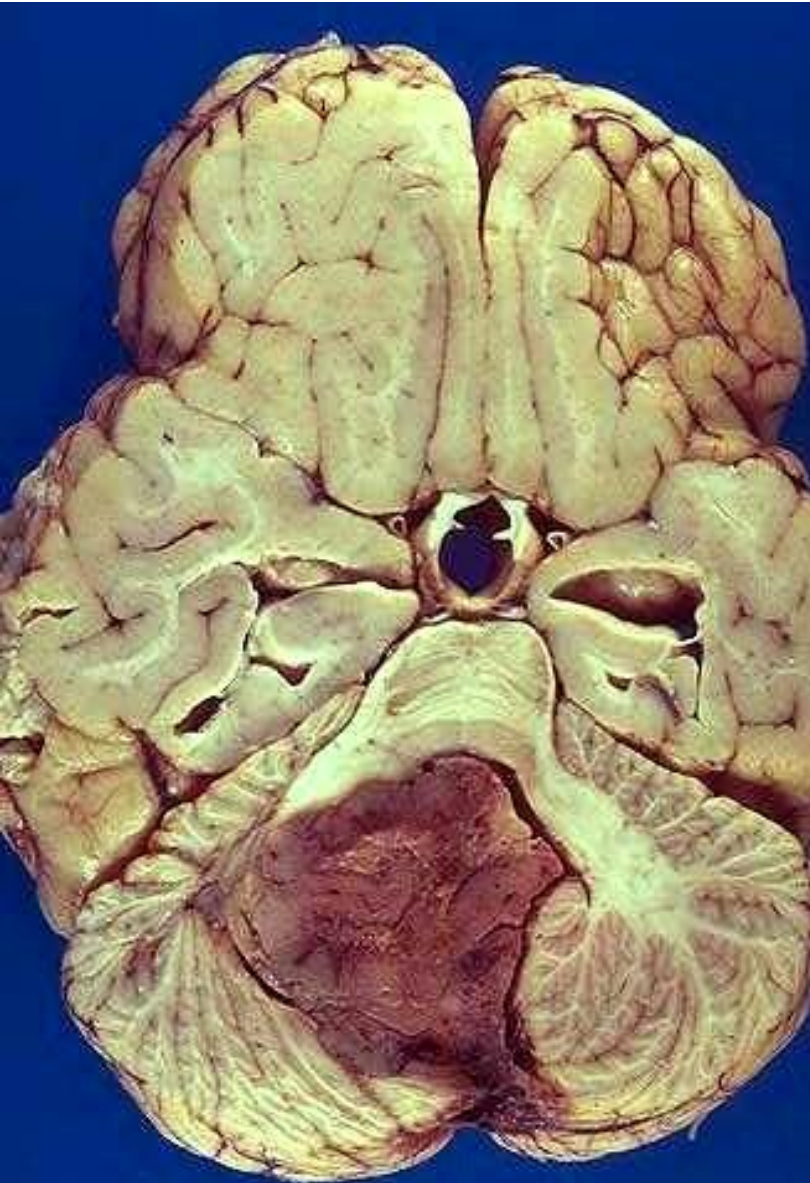
Infratentorial
Cystic
Benign
Pilocytic

Oligodendroglioma

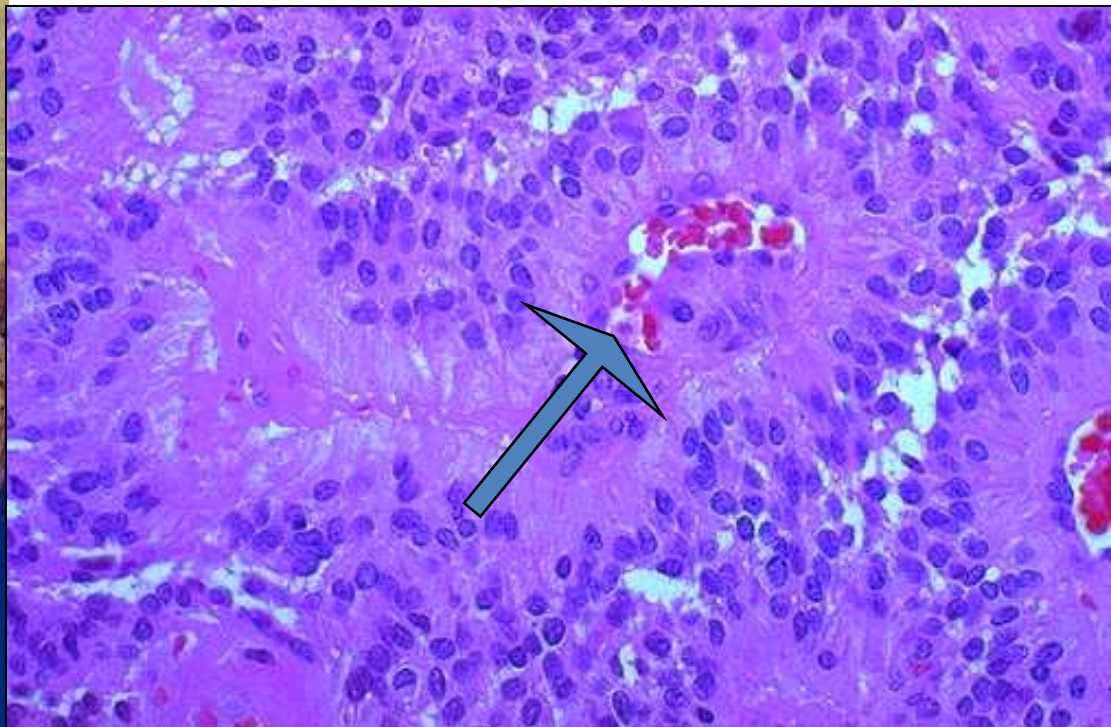
- Cells of origin:
Oligodendrocytes
- Common in cerebral hemispheres
- Calcifications common among all gliomas
- Grades:
Low grade
Anaplastic
- 1P19 +19q LOH
sensitive to therapy



Ependymoma

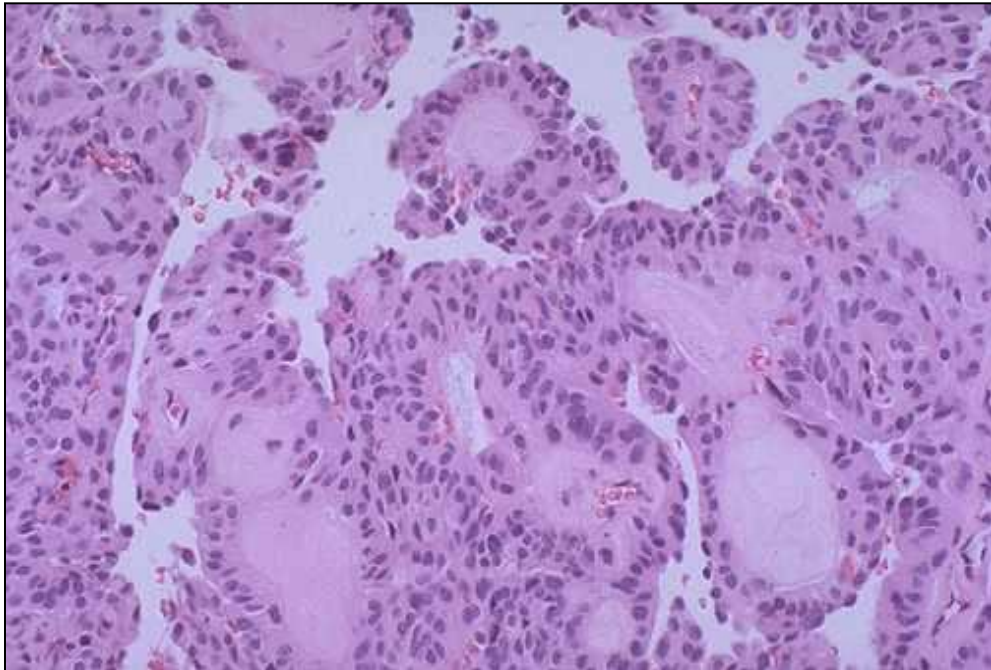


- Arises from the ependymal surface usually in the fourth ventricle and projects into the CSF pathway.
- Tumors are well differentiated
- Invasion of adjacent CNS tissue is uncommon.



Spinal Ependymoma

- A special variant, the myxopapillary ependymoma occurs in the cauda equina region in the adults

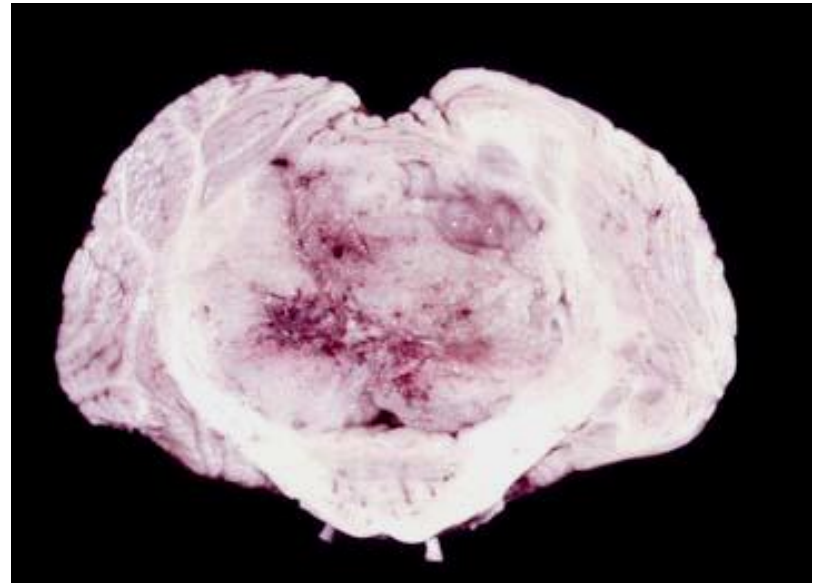


Neuroectodermal Tumors

- Origin from primitive blast cells.
- Rosettes – attempt at nerve formation
 1. Medulloblastoma – Cerebellum c-Myc aggressive phenotype
 2. Retinoblastoma - Retina
 3. Neuroblastoma – Sympathetic nervous system/Adrenal glands/N-Myc amplification aggressive phenotype
 4. Ganglioneuroma - Mediastinum

Medulloblastoma

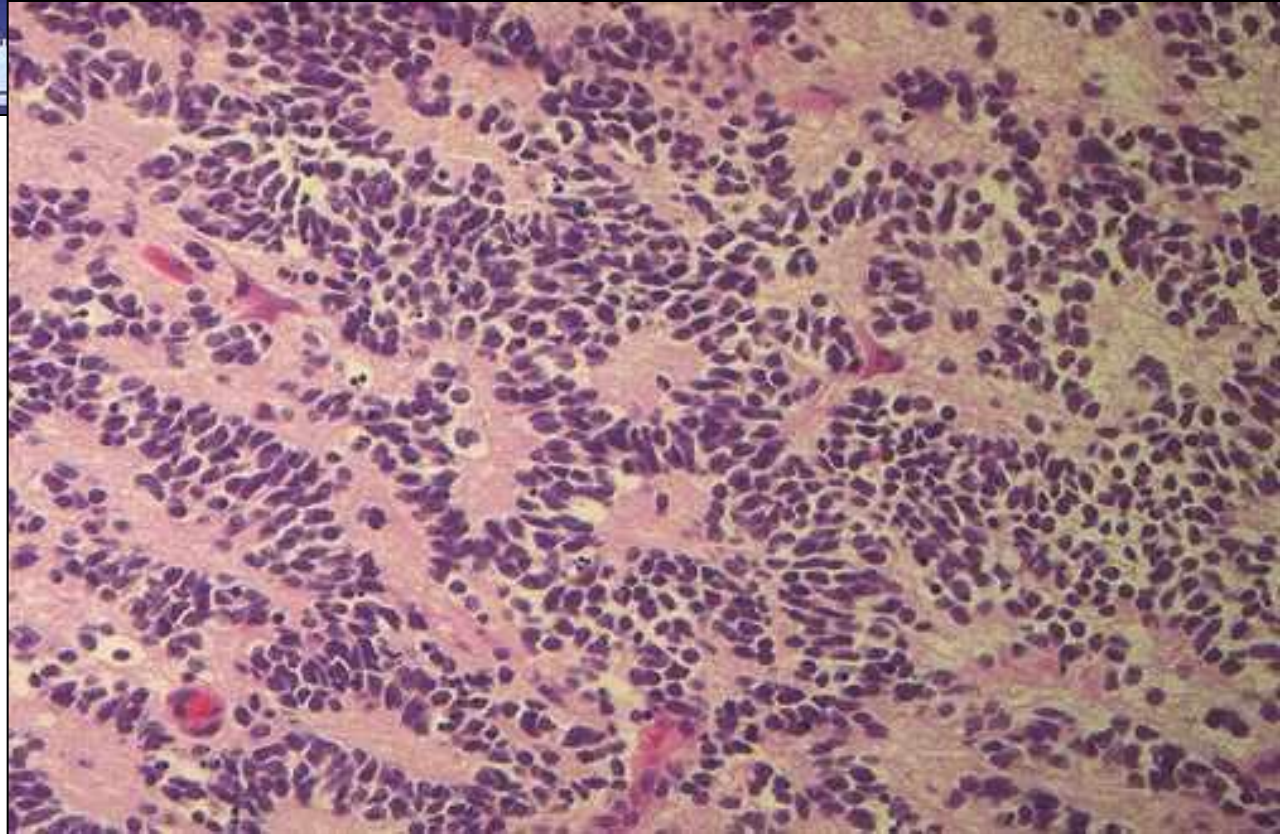
- Origin: primitive neuroectodermal cells
- Age: 1st decade of life. Most common brain tumor at this age.
- Site: vermis of cerebellum
- May cause hydrocephalus
- Meningeal infiltration is frequent and CSF seeding / subarachnoid dissemination is common
- C-Myc amplification aggressive phenotype



Medulloblastoma



cm 1 2 3 4 5
SPECIMEN UA73-240 DATE

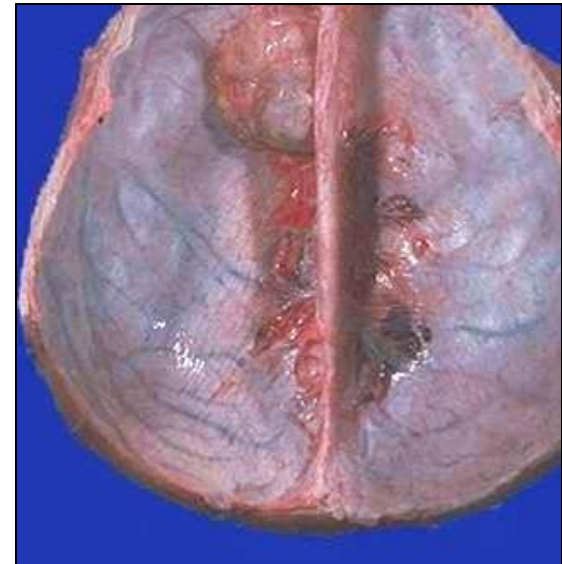
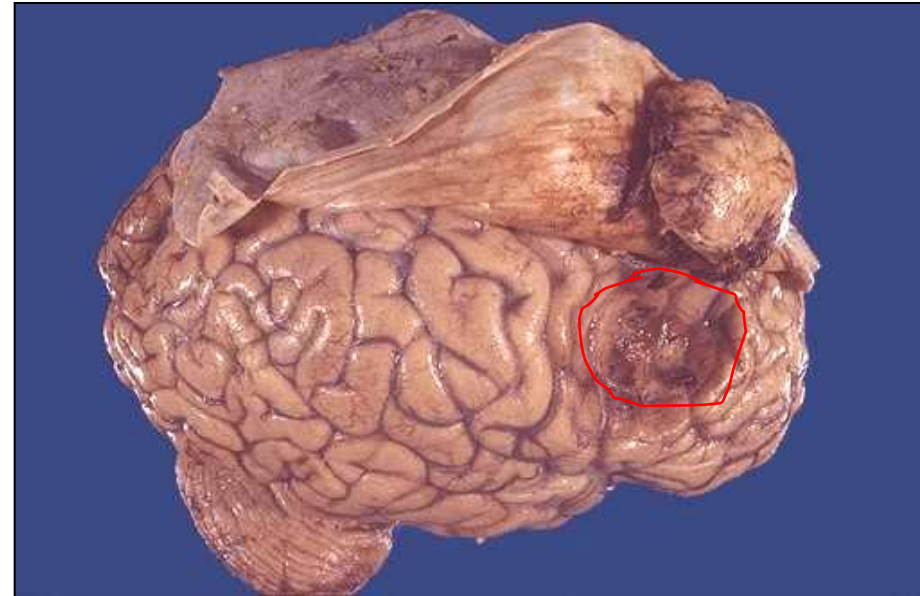


Lymphoma

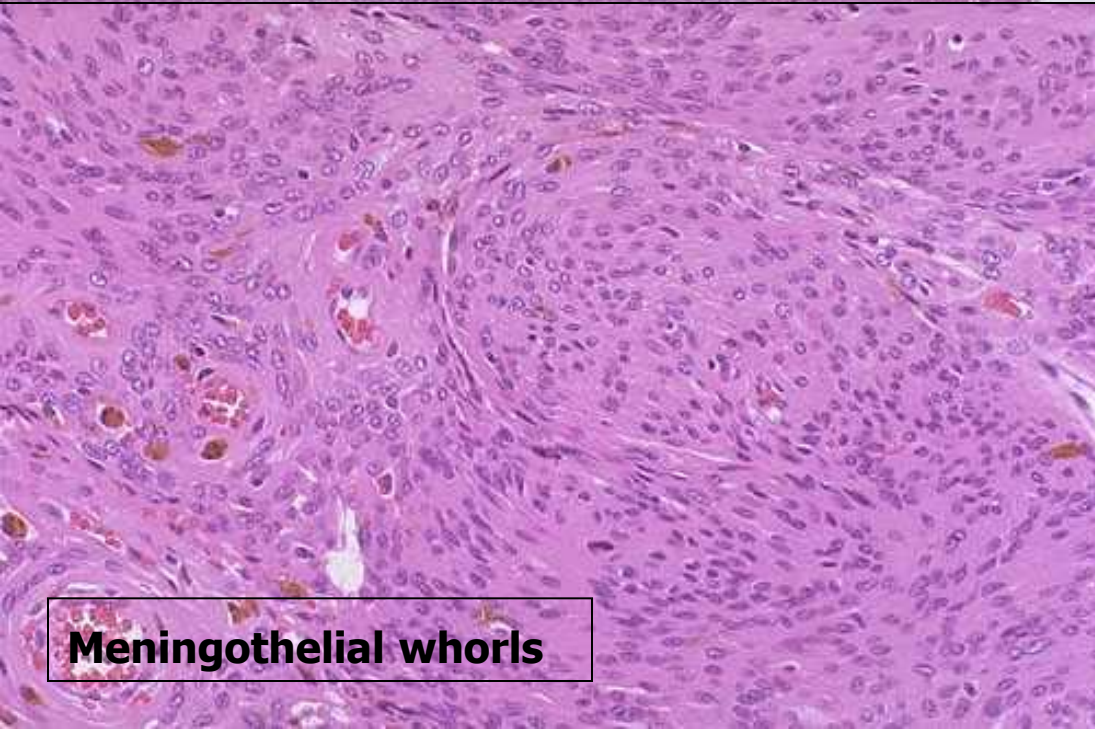
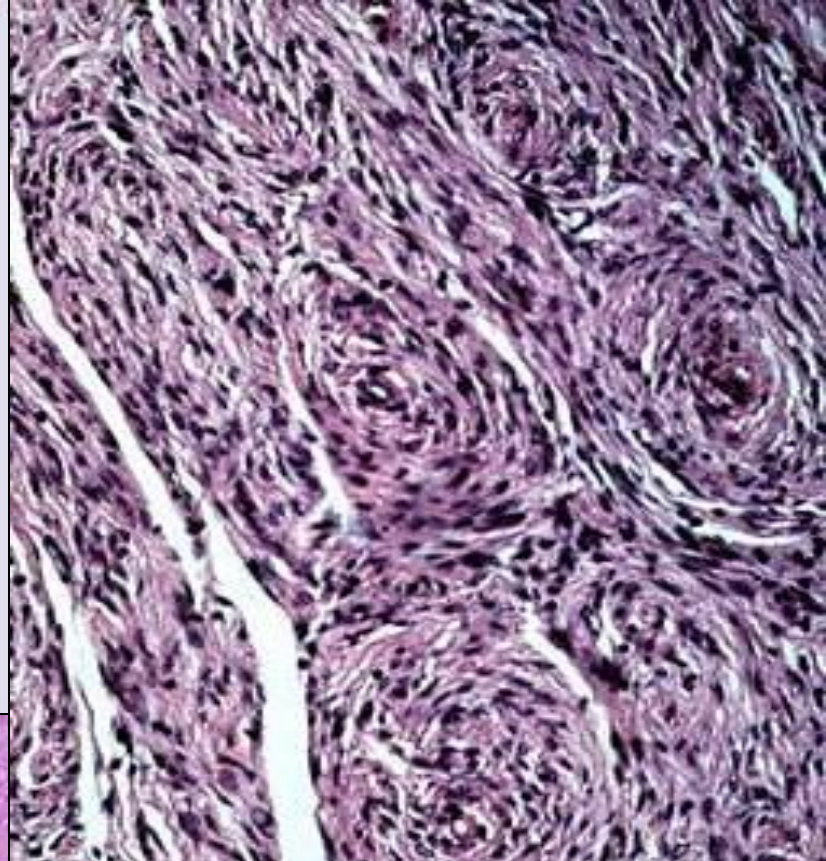
- Rare
- Primary lymphomas have an increased frequency in immunosuppressed individuals and AIDS patients
- EBV implicated in these neoplasms
- Mostly high grade NHL of B-cell type
- Have a poor prognosis

Meningioma:

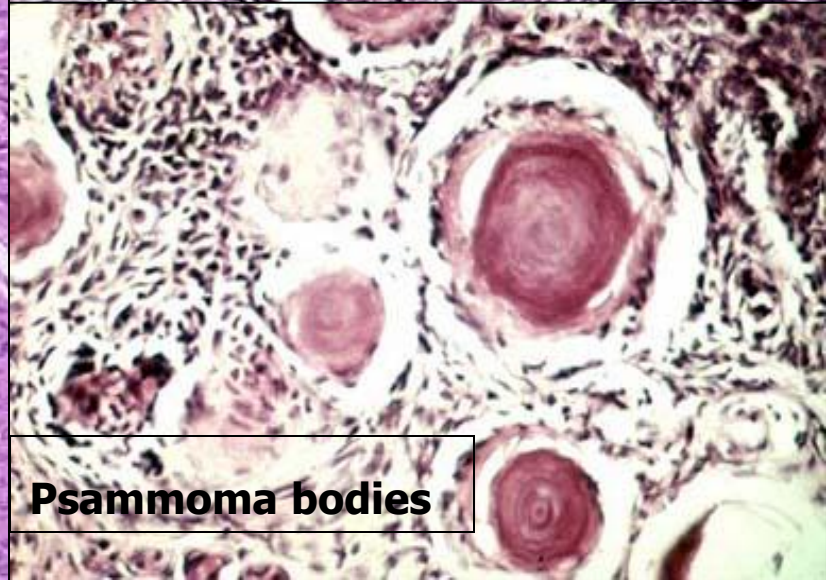
- Arise from meningotheelial cells of arachnoid granulations.
- Adjacent to venous sinuses.
- Common sites – parasagittal region, sphenoidal wing, olfactory groove, foramen magnum
- Nodular, capsulated, slow growing-Benign
- Form whorls of cells
- Psammoma bodies in the center.
- Effect by pressure.
- No infiltration or metastasis (Benign).



Meningioma



Meningothelial whorls



Psammoma bodies

Tumors of Nerve Roots and Peripheral Nerves

1. Schwannoma

8th Cranial nerve (Acoustic sch.)

Spinal roots, posterior

Peripheral nerves

2. Neurofibroma

Spinal Roots, [dorsal nerve roots] rare

Peripheral nerves

3. Malignant variants

Malignant peripheral nerve sheath tumor
(MPNT)

Rare

Nerve Sheath Tumors:

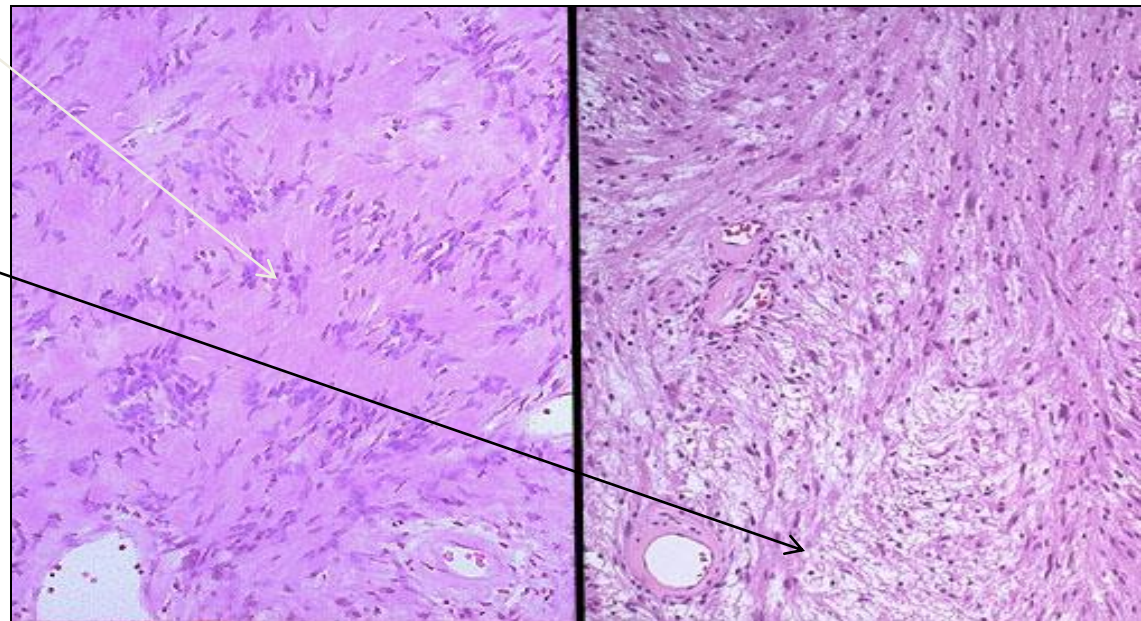
- **Neurofibroma:**
 - Epi & endoneurial fibroblasts.
 - Form whorls of fibroblasts
 - Well differentiated, benign,
 - Two types:
 - **Classic form** - Cutaneous / nerve - Solitary collagen matrix, spindle cells,
 - **Plexiform** - Multiple, infiltrative, myxoid.



Nerve Sheath Tumors:

■ Schwannoma:

- Benign.
- Encapsulated:
- Note the more cellular "Antoni A" pattern on the left with palisading nuclei surrounding pink areas (Verocay bodies).
- On the right is the "Antoni B" pattern with a looser stroma, fewer cells, and myxoid change.





- **Acoustic Schwannoma**
- Vestibular branch of 8th cranial nerve in the region of the cerebello-pontine angle

Neurofibromatosis - Von Recklinghausen

- Dominant inheritance
- Multiple neurofibromas
 - Central - CNS
 - peripheral nerves
- Increased incidence of:
 - meningioma
 - glioma
 - schwannoma - bilateral VIII N.
- Cafe-au-lait (melanosis) in skin
- Elephantiasis: increased connective tissue

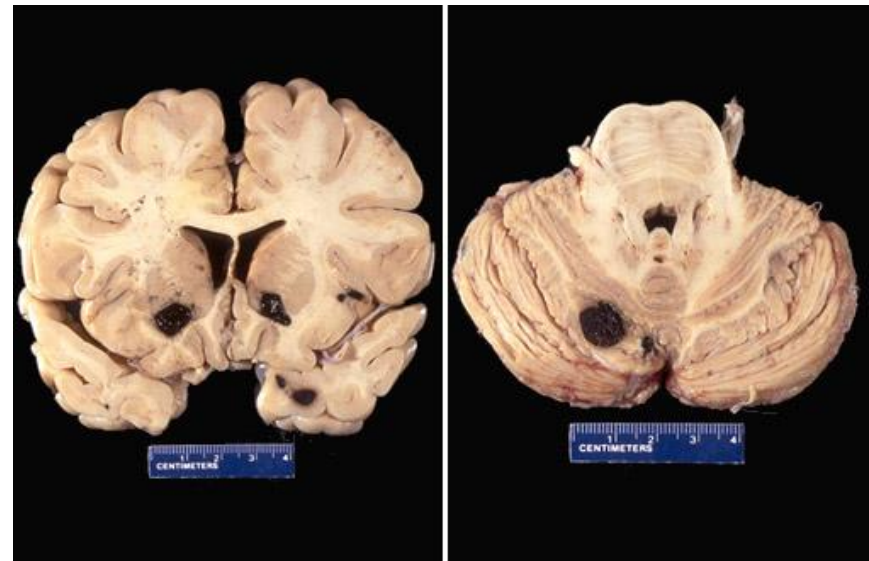
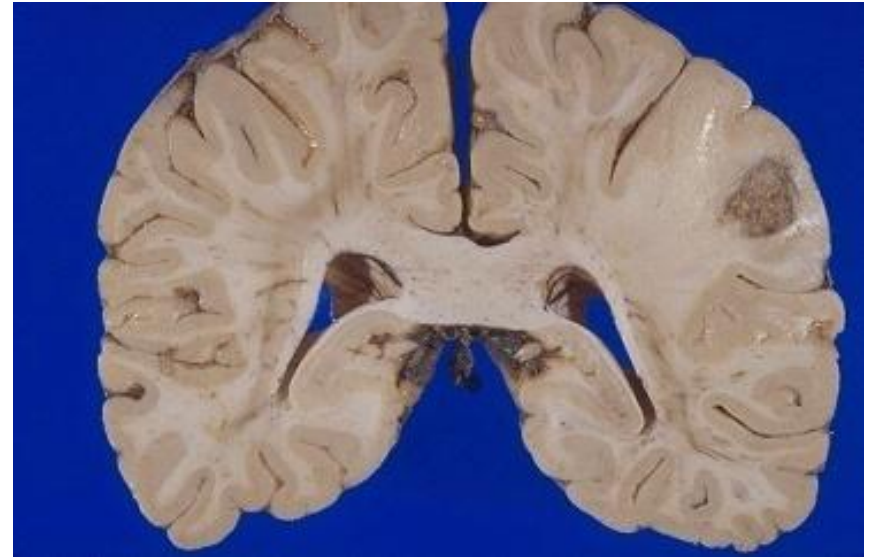


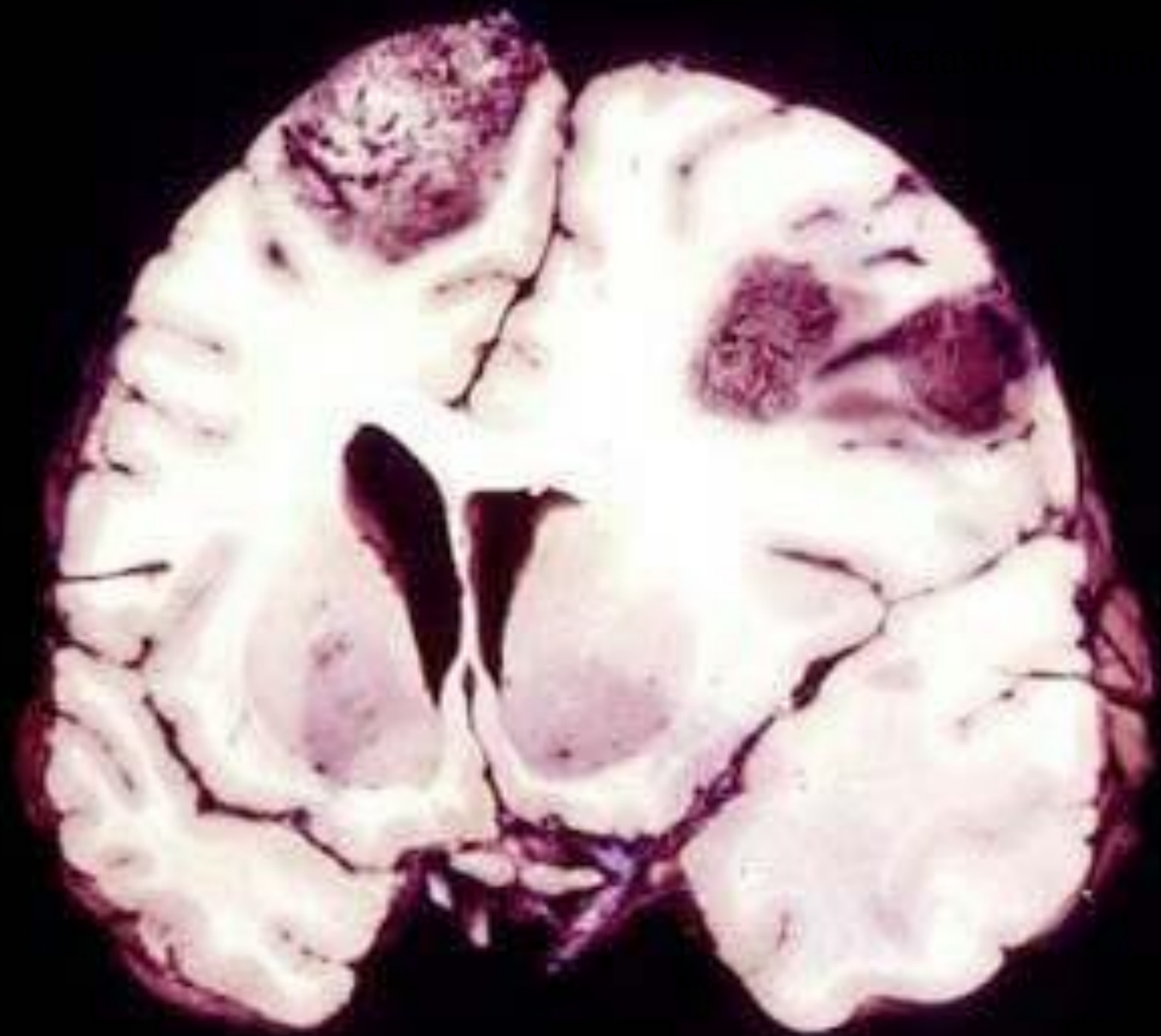
Neurofibromatosis:

- Type I (common):(AD, 17q, 1:3000)
 - Plexiform & solitary neurofibromas
 - Optic nerve gliomas, Lisch nodules, Café au lait spots.
- Type II (rare):(22q, 1:40,000)
 - Bilateral acoustic schwannoma/osis
 - Multiple meningioma/osis, ependymoma of spinal cord

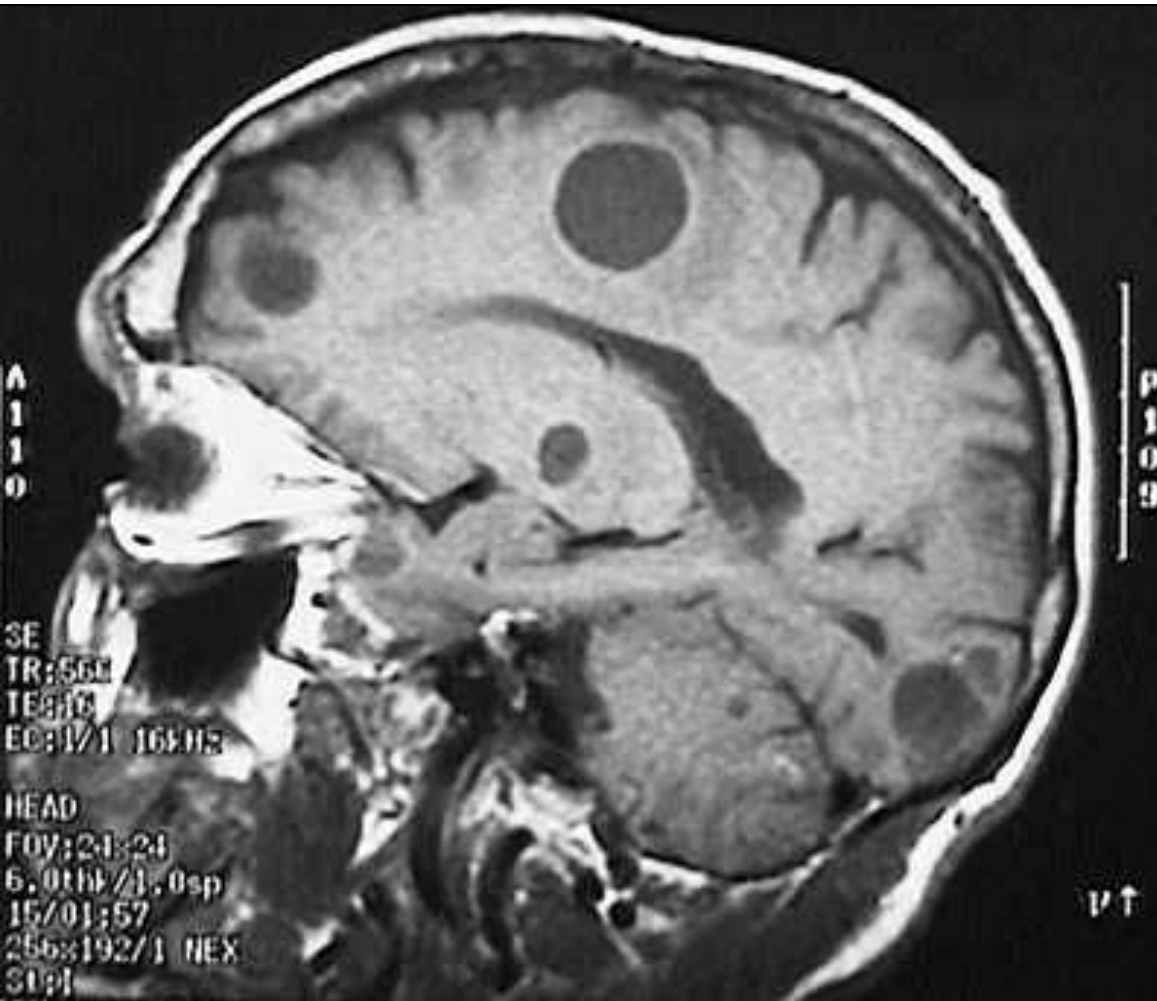
Metastatic Tumours

- Most common brain tumor in adults
- Compression and invasion
- Metastasis
 - hematogenous
 - direct spread
- Most are in cerebrum
- Occurs at boundary of grey and white matter
- Breast, lung, kidney, colon, melanoma
- Discrete, globoid, sharply demarcated tumors. Amenable to surgical resection
- Extradural metastasis presents as paraplegia





Brain Metastasis



Seriousness of Brain injuries and disorders



- Brain **limited** self-renewal capability
- Current mode of therapy is inadequate

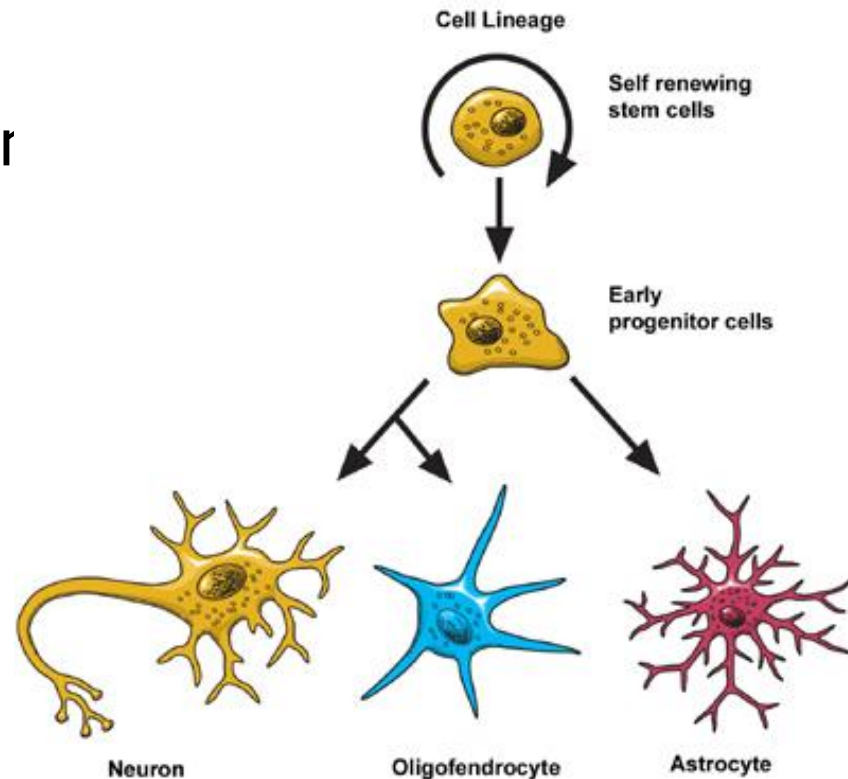


We need a new approach ...

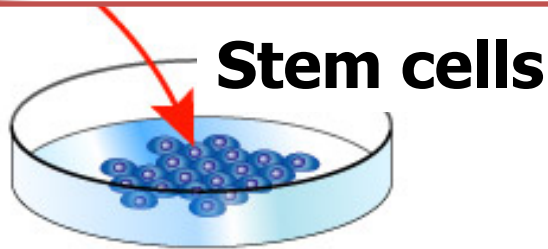
- To compensate the brain for the lost neural tissues.
- But ...organ donation doesn't apply here
...

Stem cell .. The hope

- Unspecialized cells that are capable of :
 - Self-renewal
 - Differentiation



The Strategy



**Neural
differentiation**



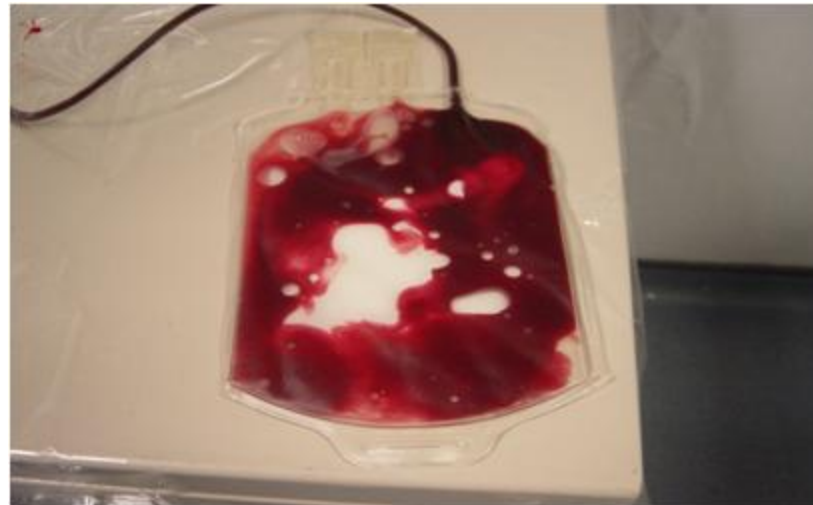
**In
Laboratories**



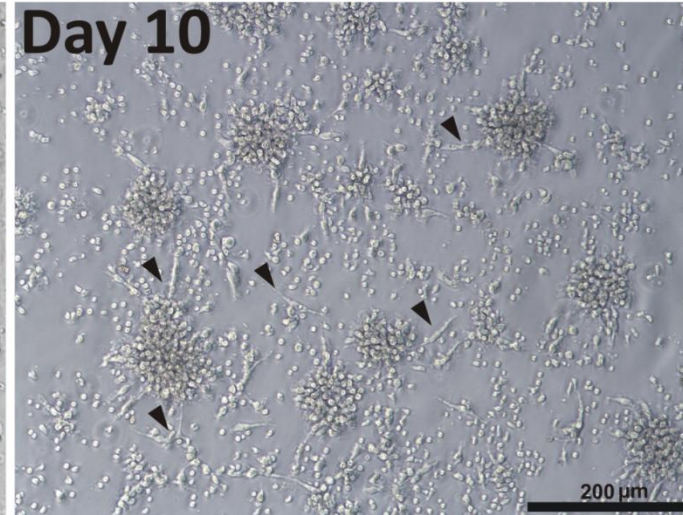
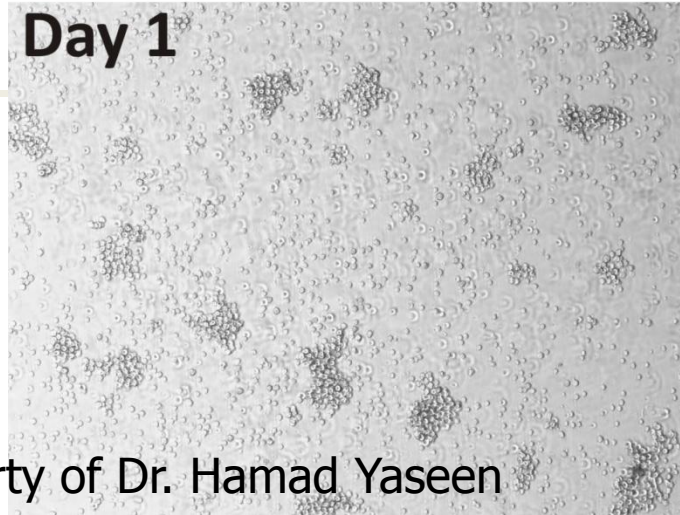
**Transplanting
generated
neural tissue**

In Clinics

An Example .. Umbilical cord blood stem cells



Umbilical cord blood stem cells



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bFGF
EGF

RA
BDNF
EGF

cAMP
NGF
BDNF
EGF

Early neural commitment

Neuronal differentiation

Neuronal maturation

Day 0

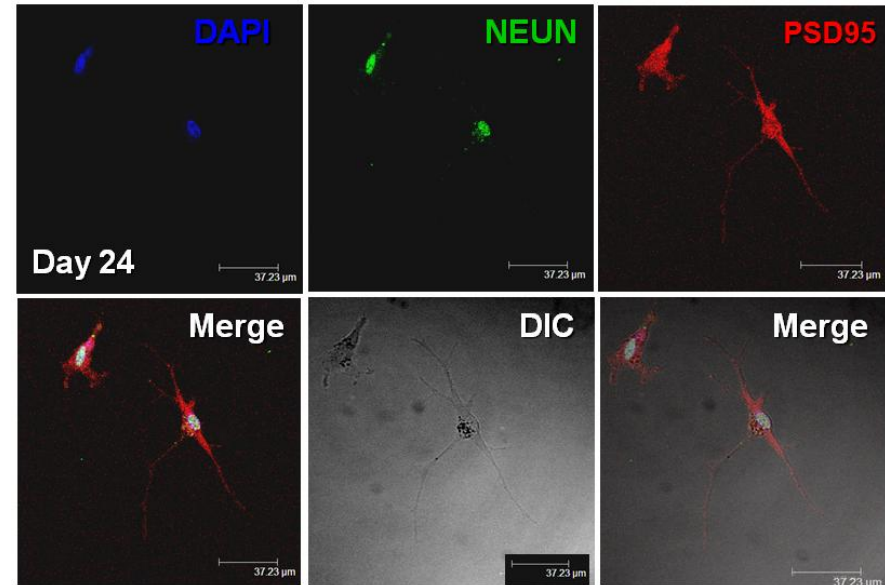
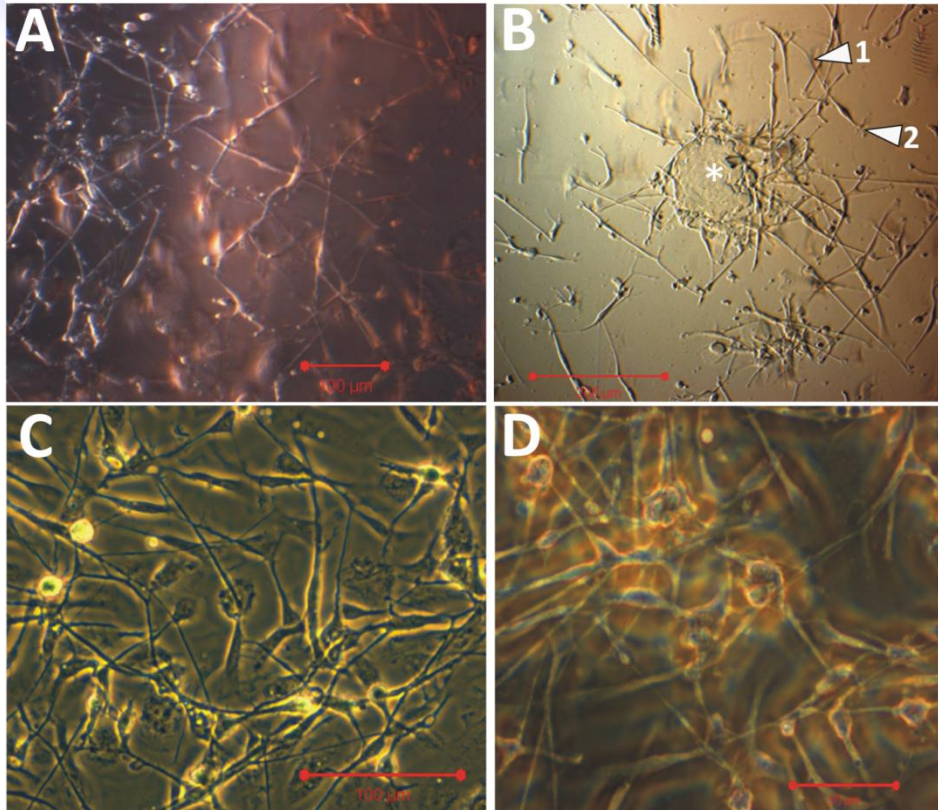
Day 10

Day 17

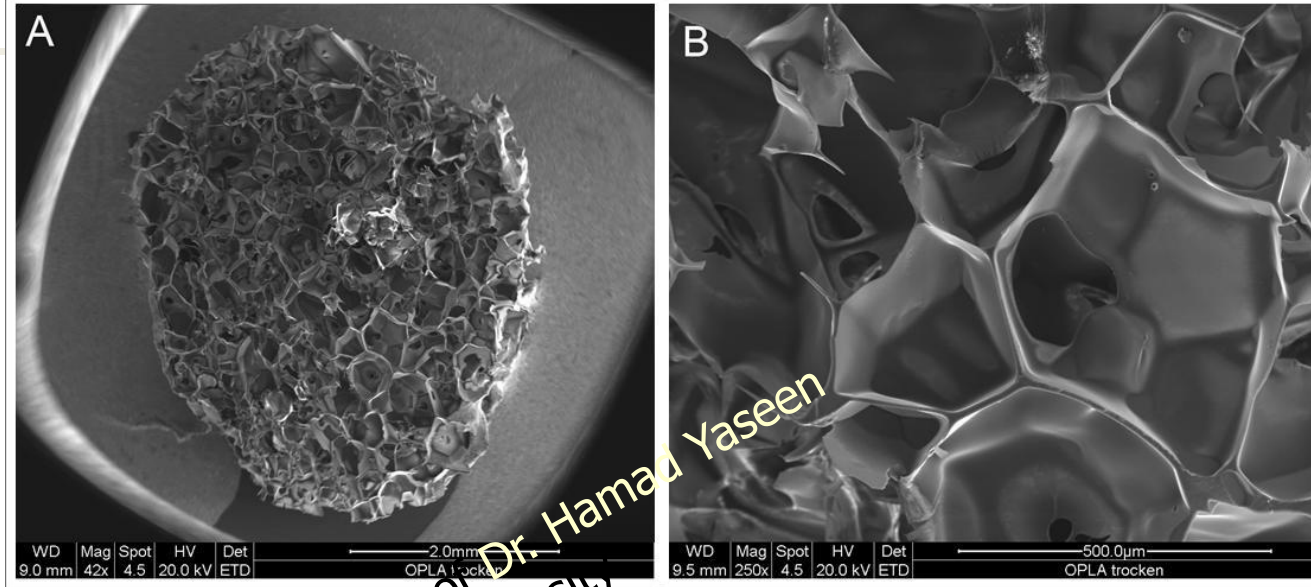
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Neural differentiation

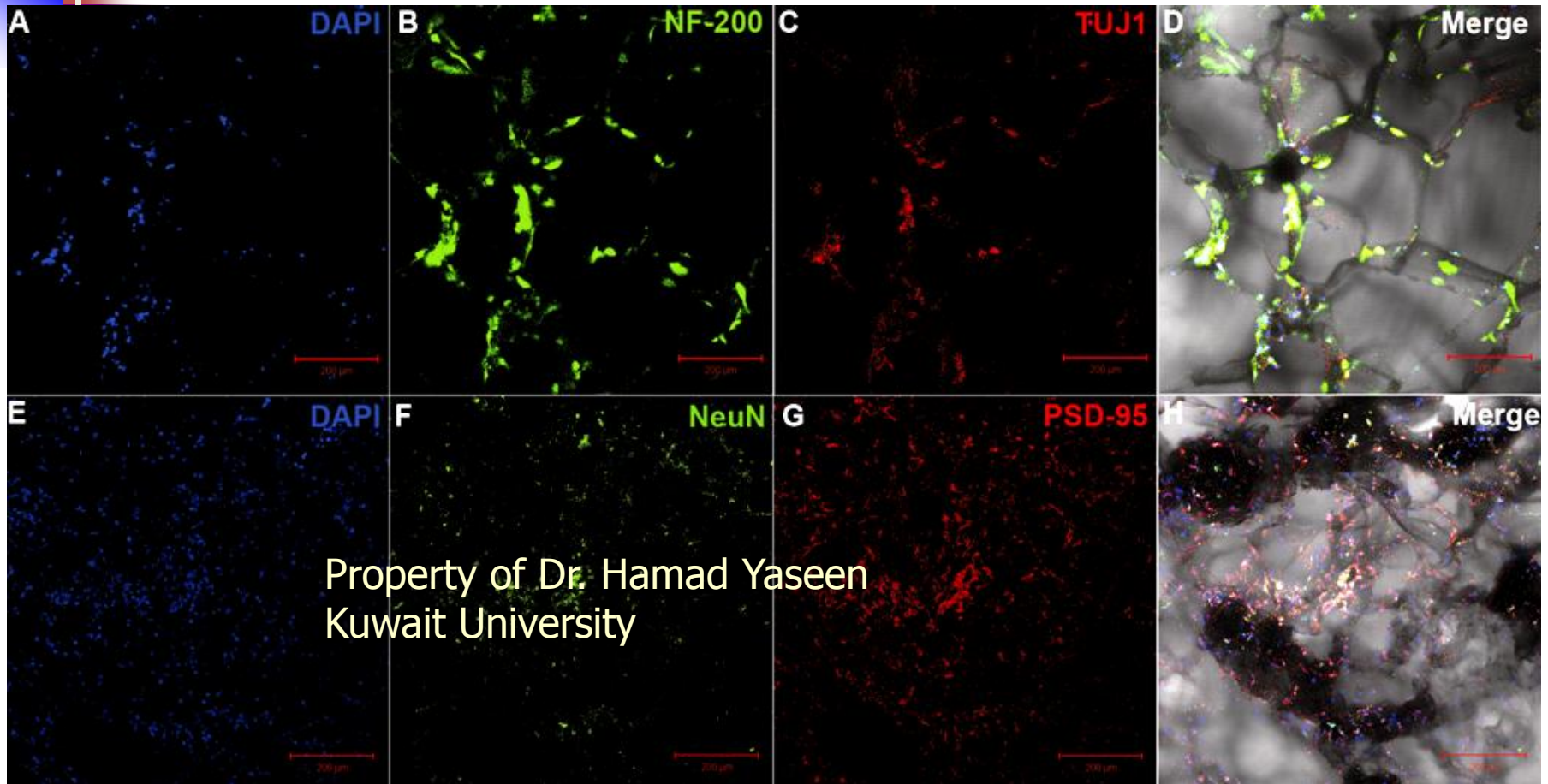
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Generating 3D neural tissues



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Any Questions?
Thank you
