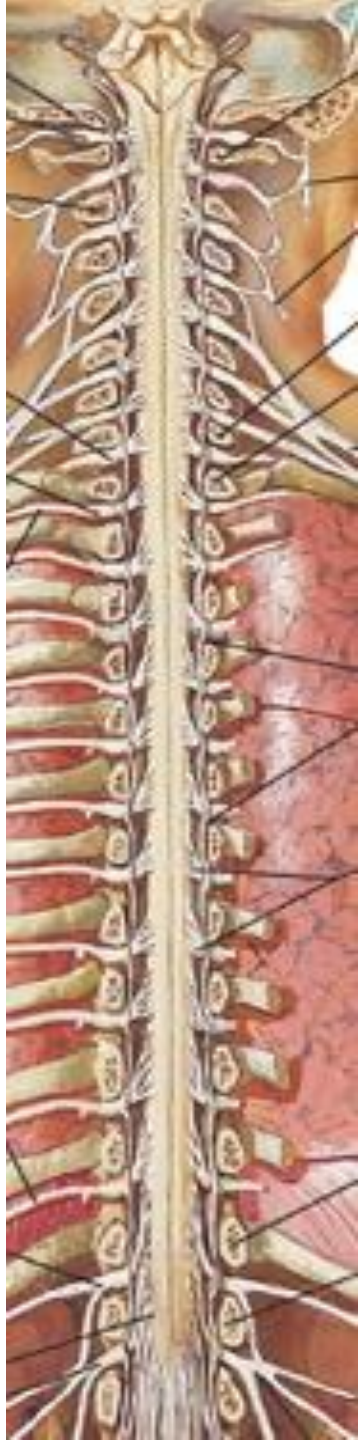
TUMORS

of

CNS



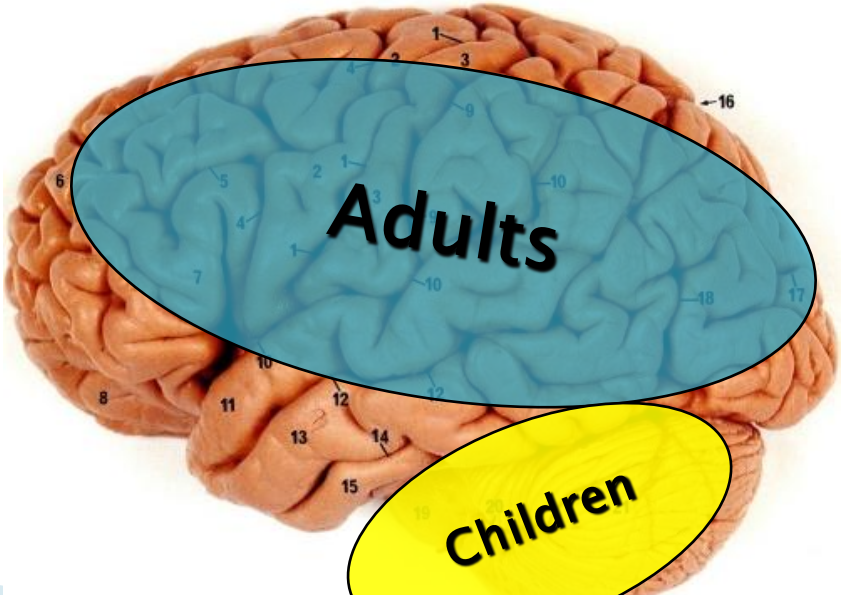
Primary CNS Tumours

- **Age:** Double peak; 1st & 6th decades.
- Tumors in *childhood* differ from those in *adults* both in histologic subtype & location.

Generally:

- The annual incidence of CNS tumors ranges from 10- 17 / 100,000 persons for intracranial tumors and 1 - 2 / 100,000 persons for intraspinal tumors

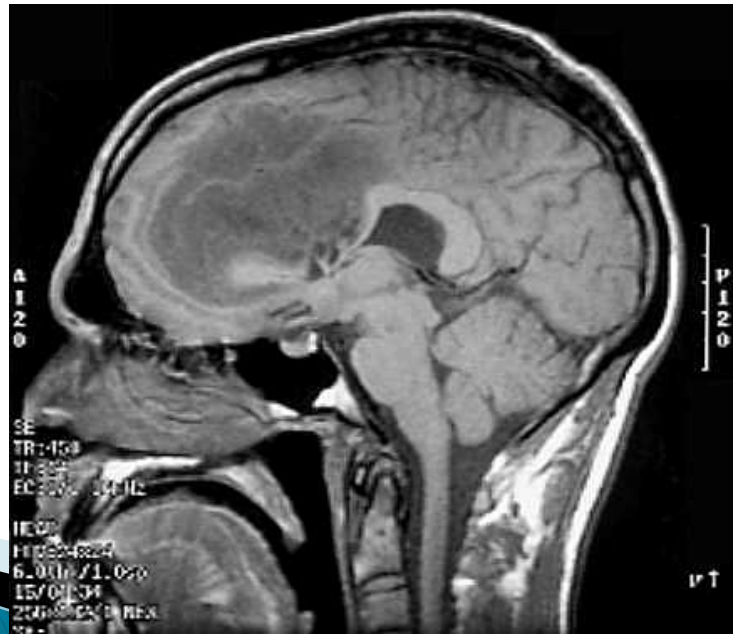
- ½ - ¾ are primary tumors, and the rest are metastatic.
  - *In children:* 20% of all pediatric tumors. 70% are infratentorial and usually primary.
  - *In adults:* 70% are supratentorial (posterior fossa) & are primary OR metastasis.



Characteristic features of brain tumors

- **NO** premalignant or in situ stages.

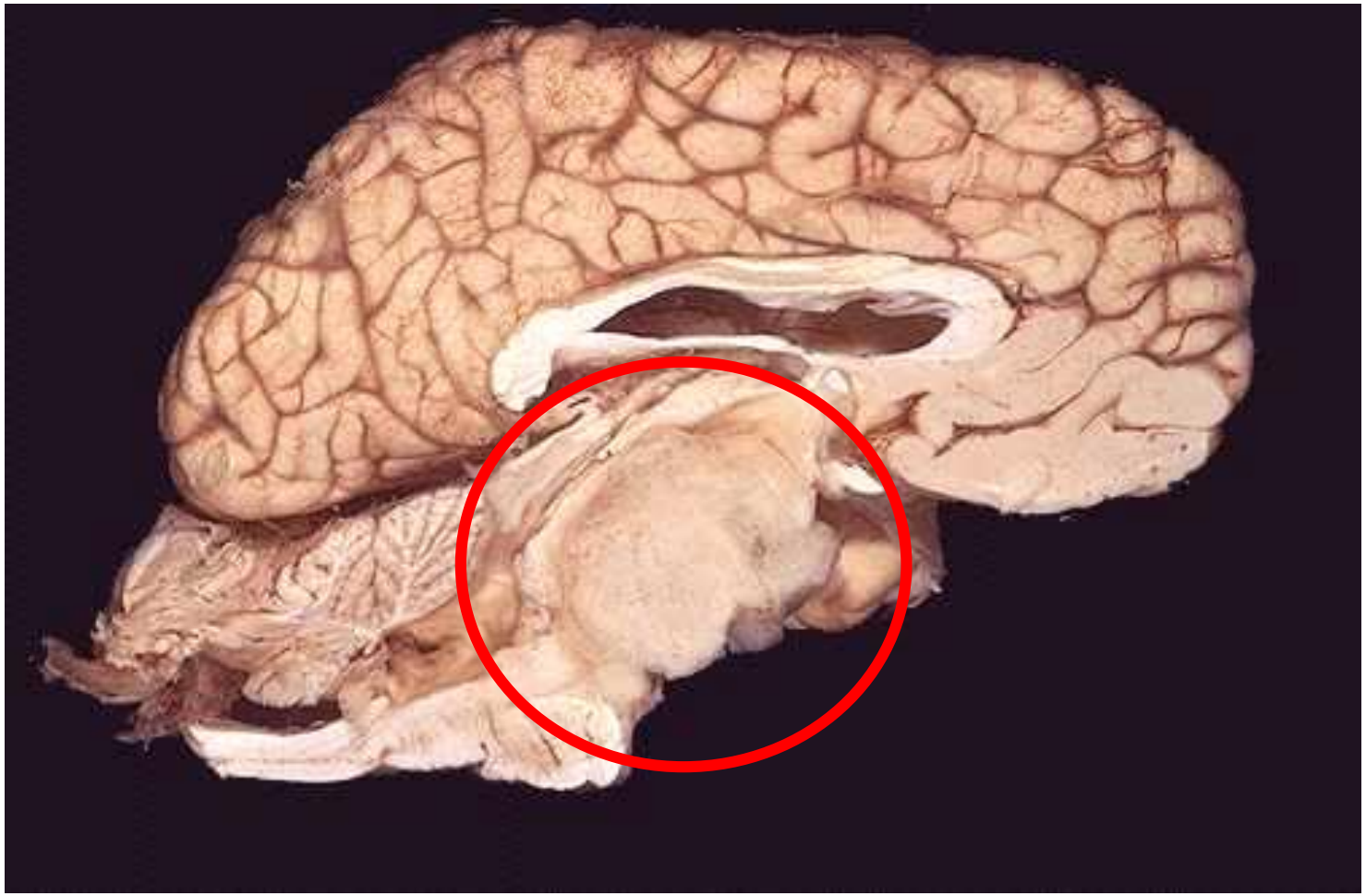
- Large area of **INVASION** (even low-grade tumors) leading to:
  - →Serious clinical deficits*, non-resectability & poor prognosis.



Characteristic features of brain tumors

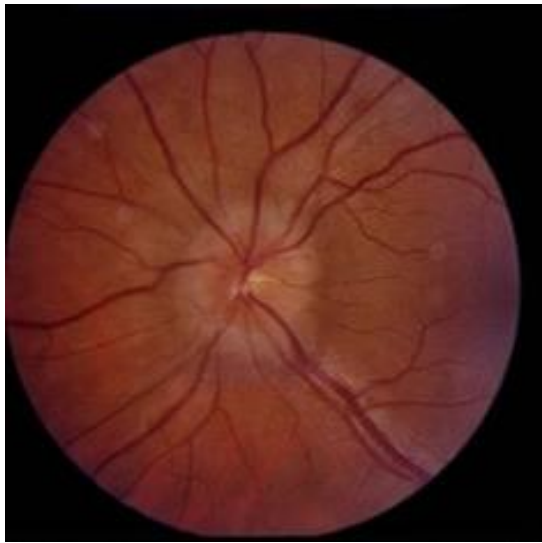
- The ***anatomic site*** of the neoplasm can influence **OUTCOME** regardless the tumor type, due to *local effects* (as benign meningioma*) OR *non-resectability* (as brain stem gliomas).

- **Rarely spread** (metastasized) outside of the CNS (even highly malignant gliomas); BUT, some can spread to other sites through subarachnoid space along the neuroaxis.

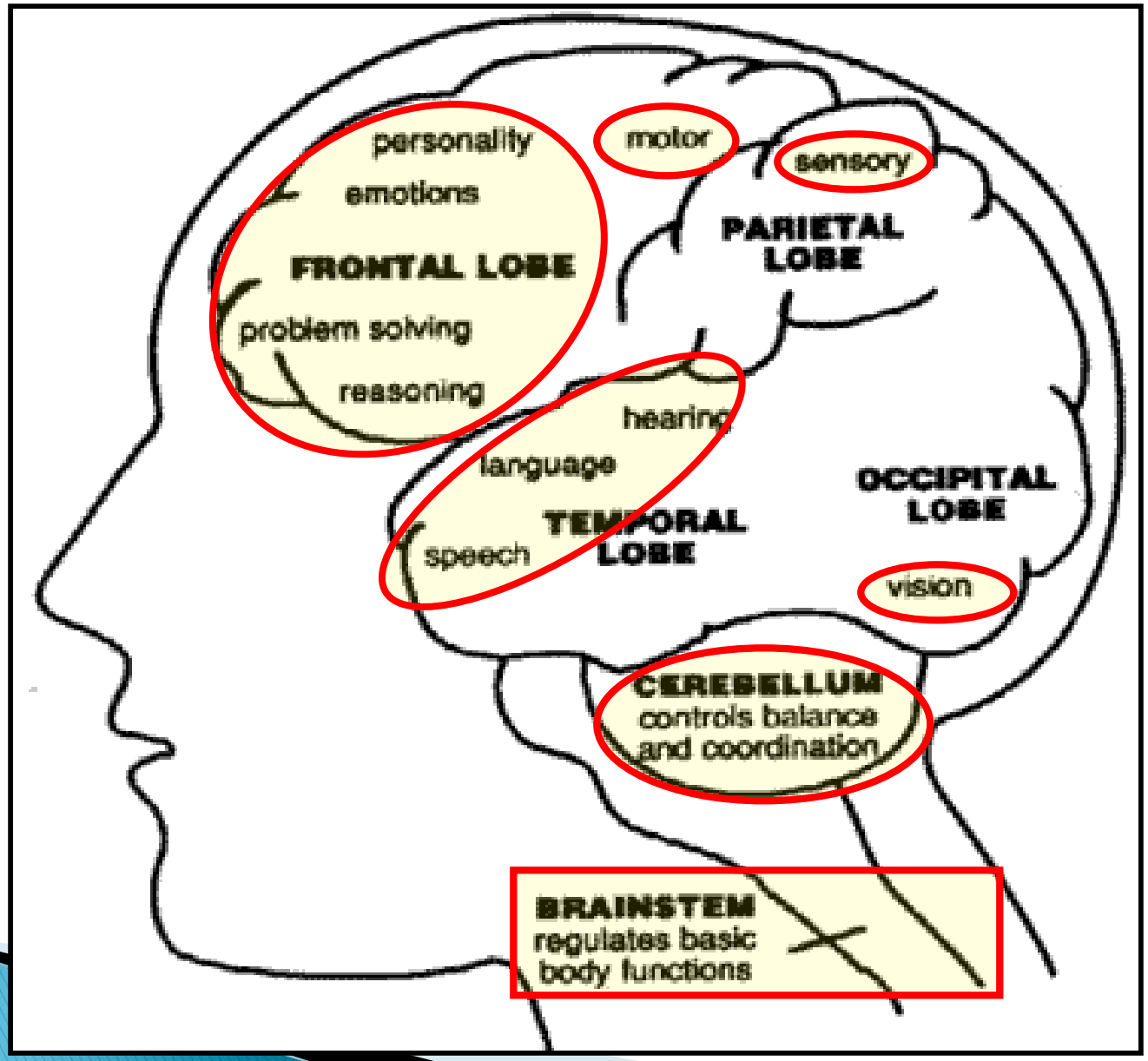


Clinical presentation*

- **Related to:**
  - **Localizing signs:** Nerve & tract deficits, seizures, paralysis … etc.
  - **± ↑ ICP:** Headache (morning), vomiting, slow pulse, papilloedema …



CNS Anatomy – Clinical presentation

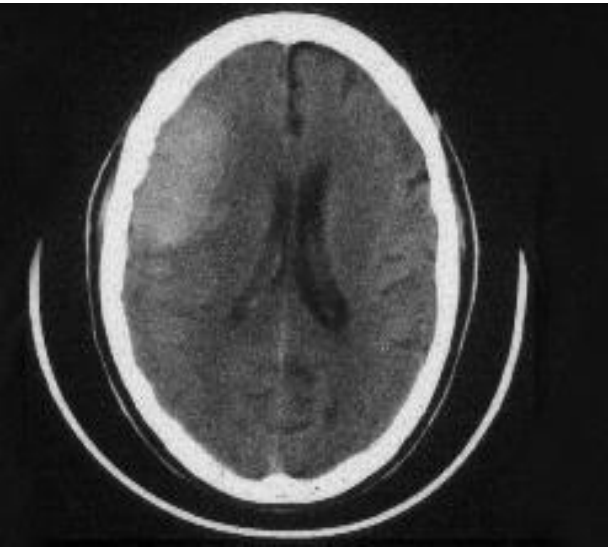


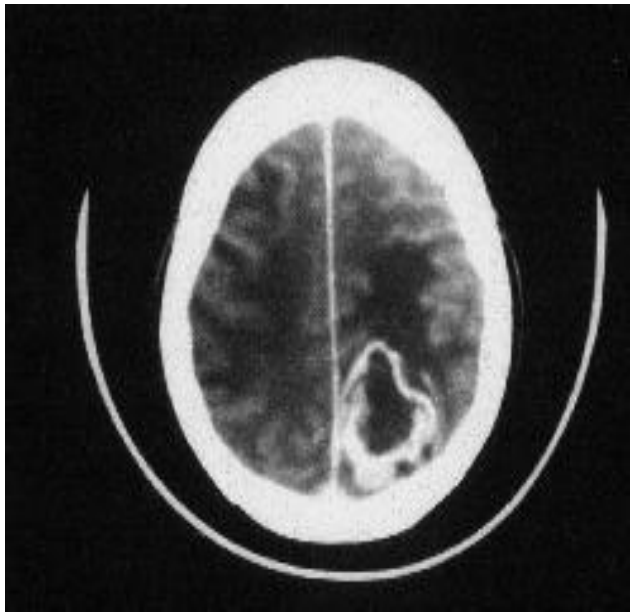
CNS Tumors
Clinical Features–Pathogenesis

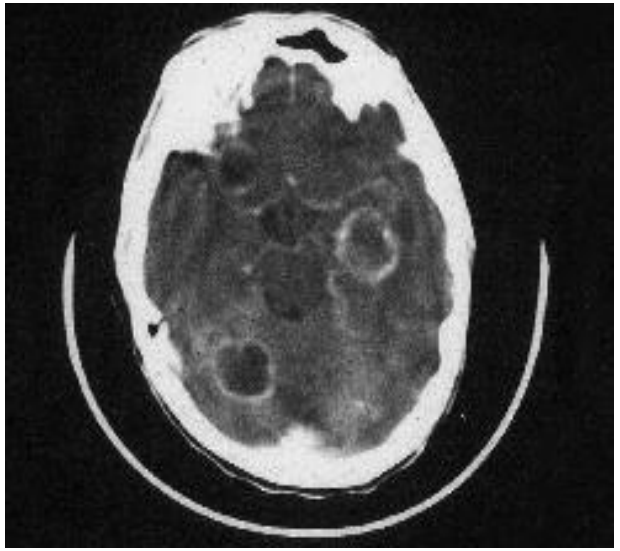
Headaches (morning)	Increased ICP
Papilloedema	Increased ICP
Nausea or vomiting	ICP – Medulla ob.
Bradycardia	ICP – Parasymp.
Seizures (convulsions).	Irritation.
Drowsiness, Obtundation	Brain Stem compress
Personality or memory	Frontal lobe
Changes in speech	Temporal lobe
Limb weakness	Motor area
Balance/Stumbling	Cerebellum
Eye movements or vision	Optic tract, occipital.

Approach

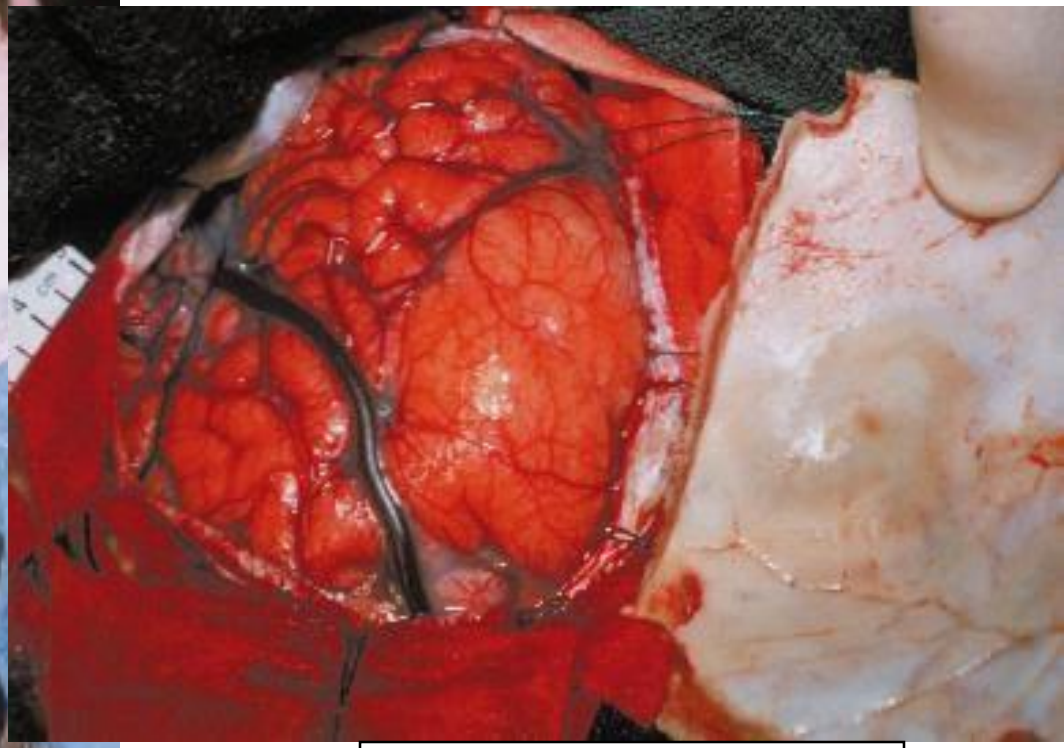
- History
- Physical & **neurologic** Ex
- Lumber puncture (including cytology)
- CT
- MRI
- Brain angiography
- Biopsy







Stereotactic Biopsy



Craniotomy

Primary Tumours - Aetiology

- **Environmental:**
  - *Radiation:* Often 5-25 years after treatment of pituitary adenoma or craniopharyngioma.
    - *Cell phones* ???:* Mobile phones use electromagnetic radiation → Possibly carcinogenic (IARC 2011).
  - *Immunosuppression* (as lymphomas).
  - *Viral & Chemical carcinogens*
- **Genetic:**
  - *Sporadic (as P53, EGFR …).*
  - *Familial (inherited familial tumor syndromes).*

Classification of Tumors :

- **Classified according to:**
  - → Cell of origin & degree of differentiation .

- However, slowly growing entities may undergo **transformation** into more aggressive tumors.

- *WHO grading system* important for treatment and prognosis.

1. Gliomas*:
   i. *Diffuse gliomas (common)*
      a. Astrocytoma (many variants)
      b. Oligodendroglioma
      c. Mixed
   ii. *Solid gliomas (less common)*
      Ependymoma

2. Neuronal Tumors:
   i. Central neurocytoma
   ii. Ganglioglioma
   iii. Dysembryoplastic neuroepithelial tumor

3. Embryonal (Primitive) Neoplasms:
   Medulloblastoma

4. Meningiomas:

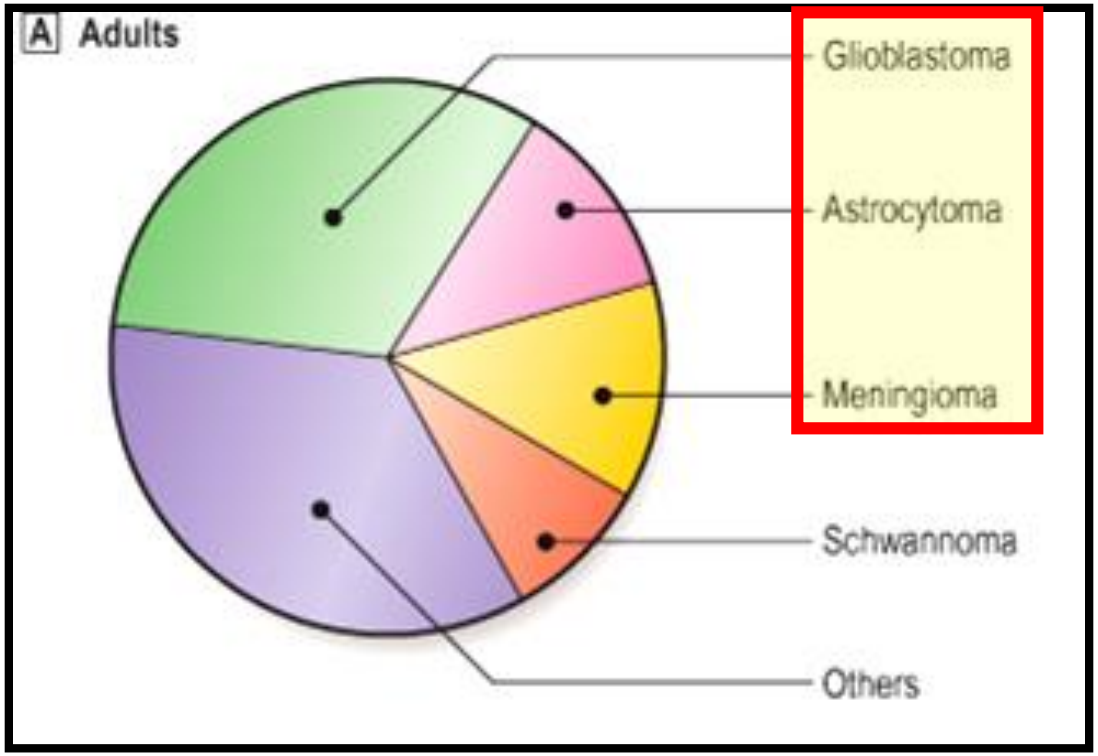
5. Nerve Sheath:
   i. Schwannoma
   ii. Neurofibroma

6. Other Parenchymal Tumors:
   i. Primary CNS Lymphoma
   ii. Germ Cell Tumors

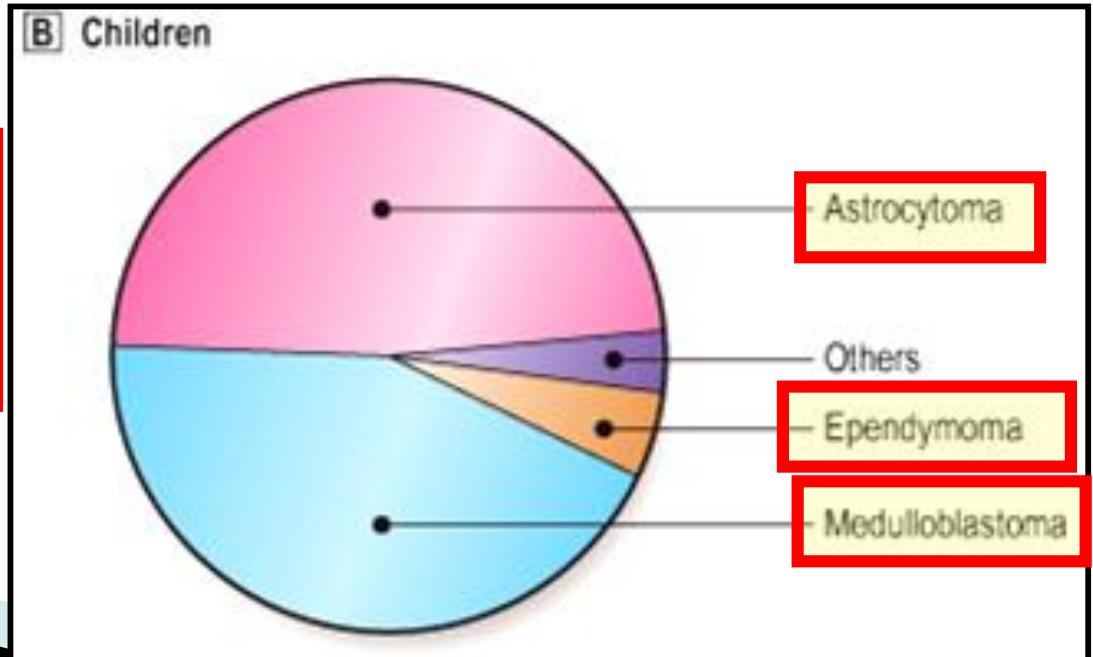
7. Metastatic Tumors.

Commonest tumors in:

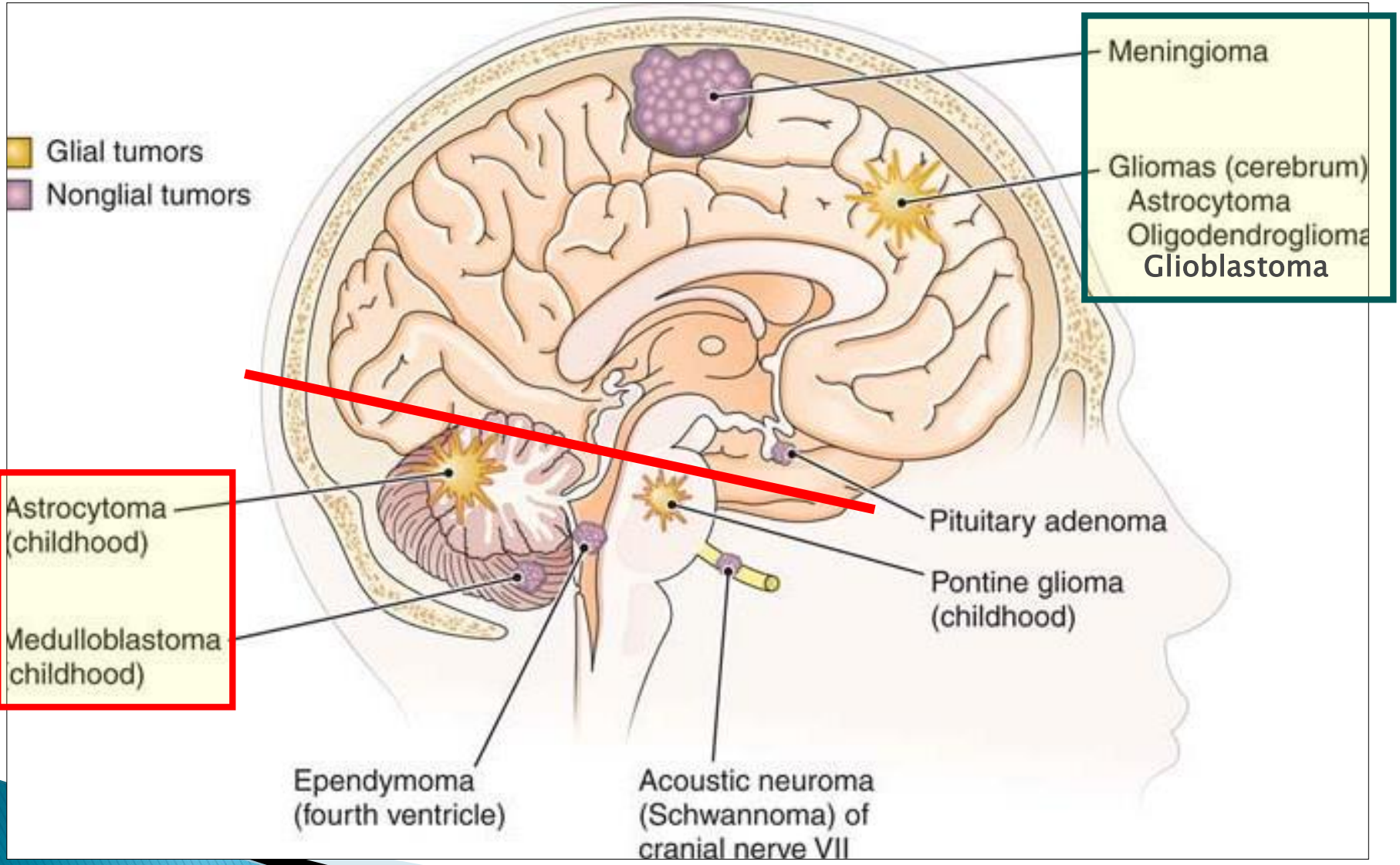
- **Adults:**
  1. Metastasis.
  2. Glioblastoma
  3. Astrocytoma
  4. Meningioma



- **Children:**
  1. Astrocytoma
  2. Medulloblastoma
  3. Ependymoma



CNS Tumors


Glial tumors
Nonglial tumors
Meningioma
Gliomas (cerebrum)
Astrocytoma
Oligodendroglioma
Glioblastoma
Astrocytoma (childhood)
Medulloblastoma (childhood)
Pituitary adenoma
Pontine glioma (childhood)
Ependymoma (fourth ventricle)
Acoustic neuroma (Schwannoma) of cranial nerve VII

Gliomas

1. Astrocytoma

- Commonest glial tumor.
- WHO Grading, depends on:
    1. Nuclear pleomorphism
    2. Mitotic activity
    3. **NECROSIS**
    4. **Vascular proliferation**
- High grade tumors (as Glioblastoma) can arise from *transformation* of low grade gliomas **OR** can occur *de novo.*

Gliomas

1. Astrocytoma

A. Pilocytic astrocytoma:

- Children and young adults.
- Commonly cerebellum (sometimes 3rd ventricle or optic nerve*).
- Relatively benign.

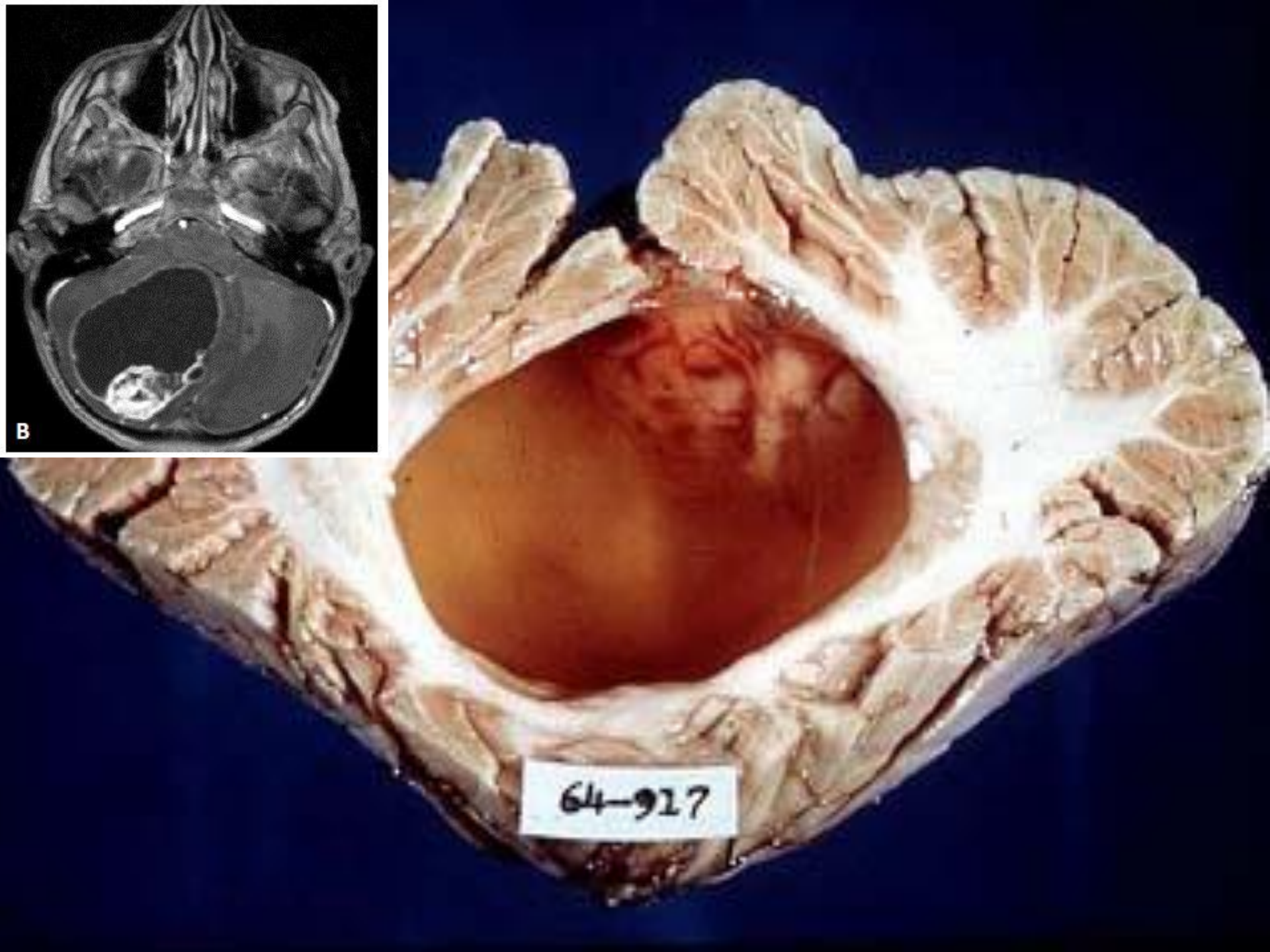
B. Diffuse (Fibrillary) astrocytoma:

- 4th to 6th decade.
- Commonly cerebral hemisphere
- Variable grades:
  - Well differentiated astrocytoma
  - Anaplstic astrocytoma
  - Glioblastoma multiforme

Pilocytic astrocytoma

(WHO grade I)

- **Gross:**
  - Often cystic* (with mural nodule) or well circumscribed solid mass.
- **Microscopic:**
  - Bipolar cells with long, thin "hairlike" processes.
  - Microcysts & Rosenthal fibers & eosinophilic granular bodies are commonly seen.
  - **NO** or rare mitosis & necrosis.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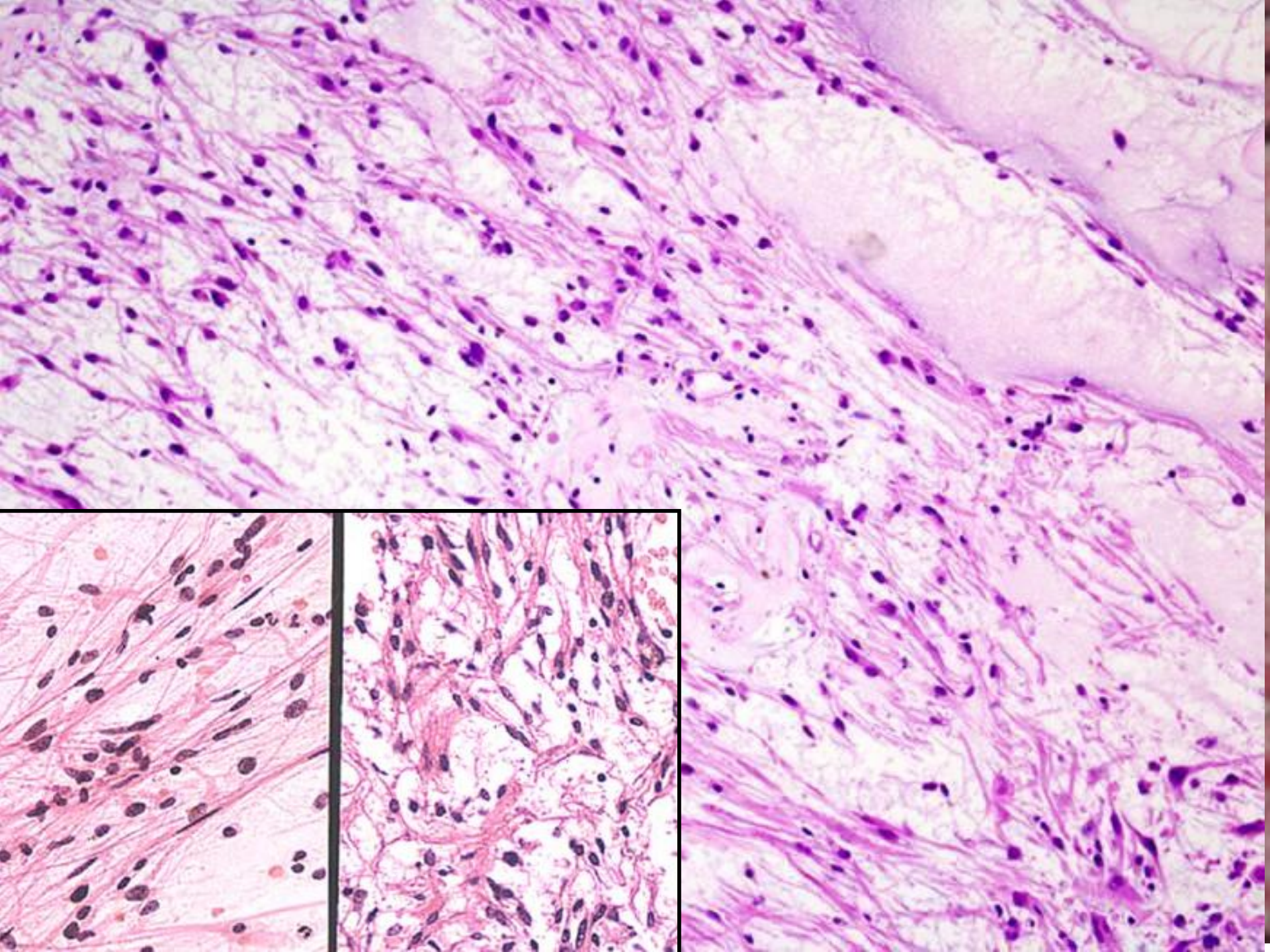
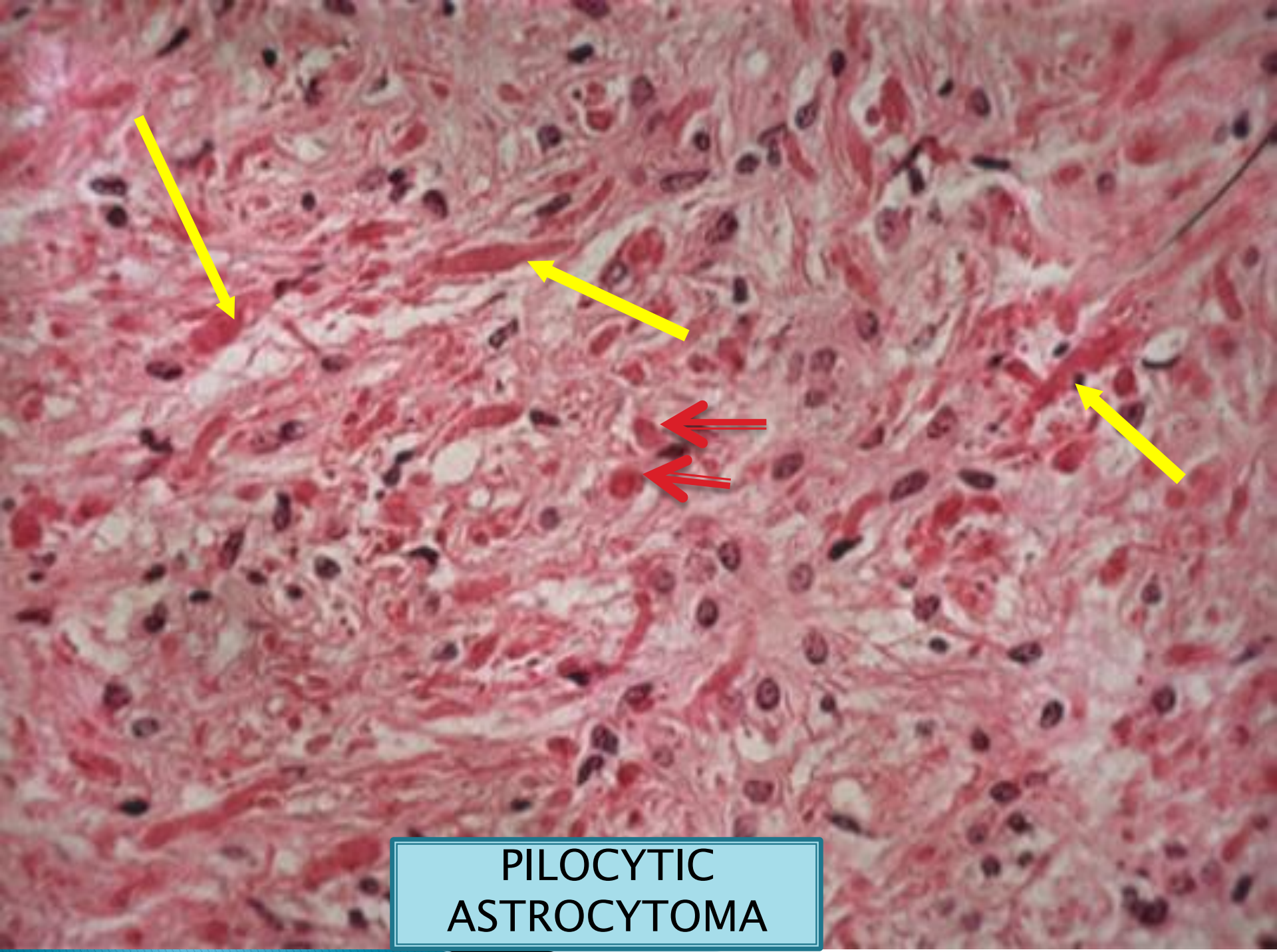
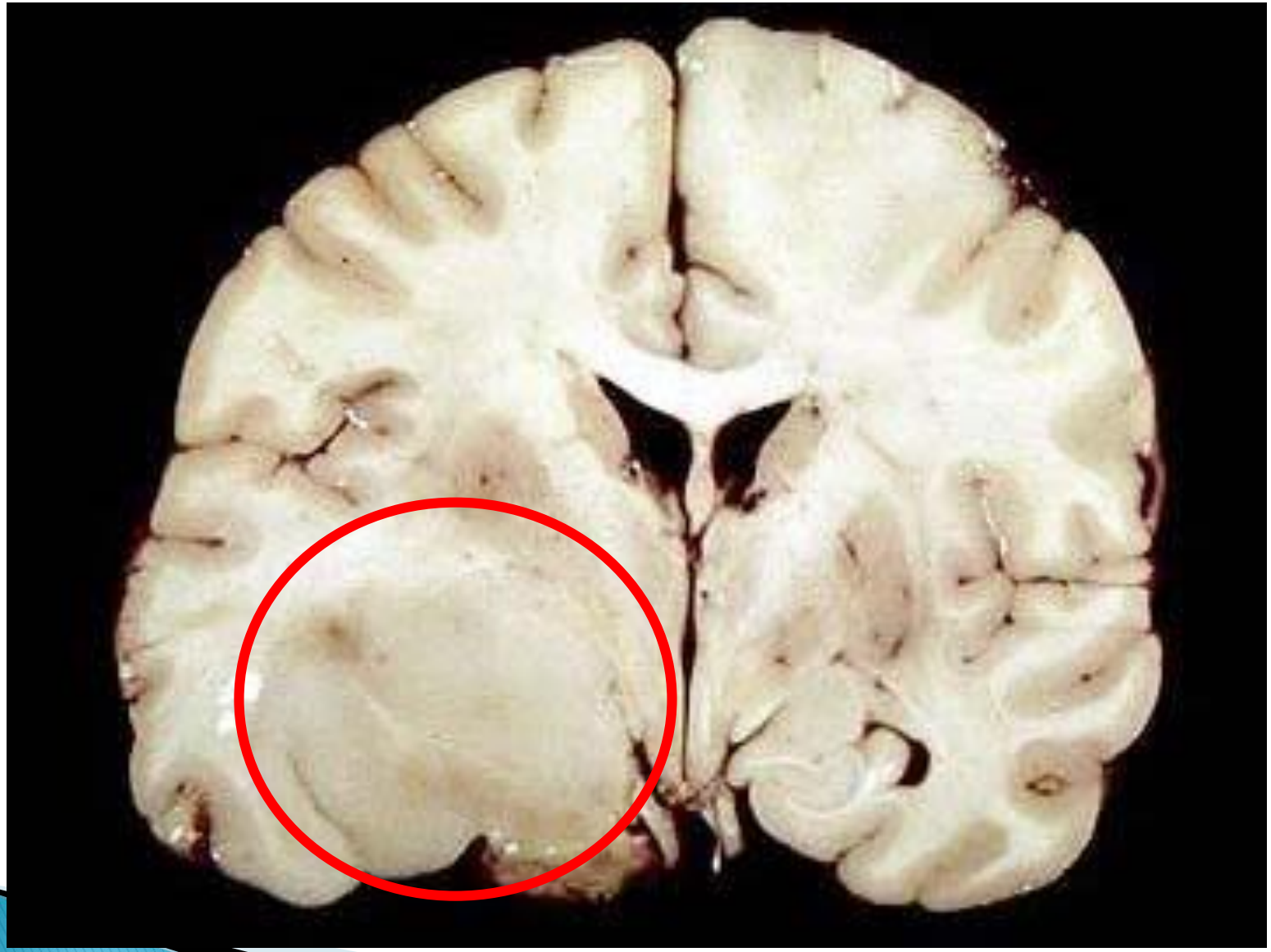
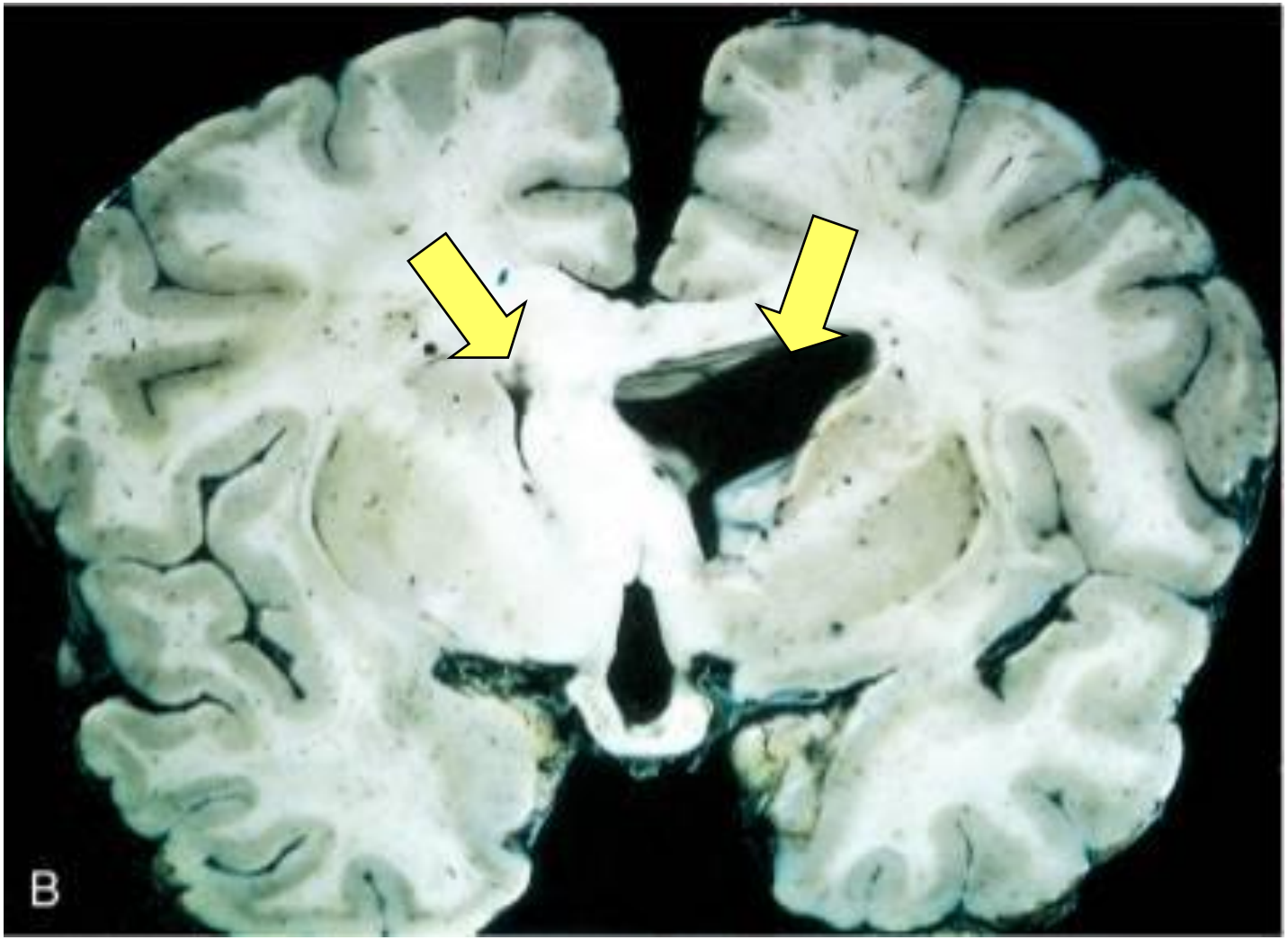



PILOCYTIC
ASTROCYTOMA

Well differentiated astrocytoma
(WHO grade II)

- Static or progress slowly* (mean survival of more than 5 years).
- **Gross:**
  - Poorly defined infiltrative tumor extending beyond the grossly evident margins (no clearly defined margin).
- **Microscopic:**
  - Mild-moderate ↑ cellularity, minimal pleomorphism, & fine fibrillary background.

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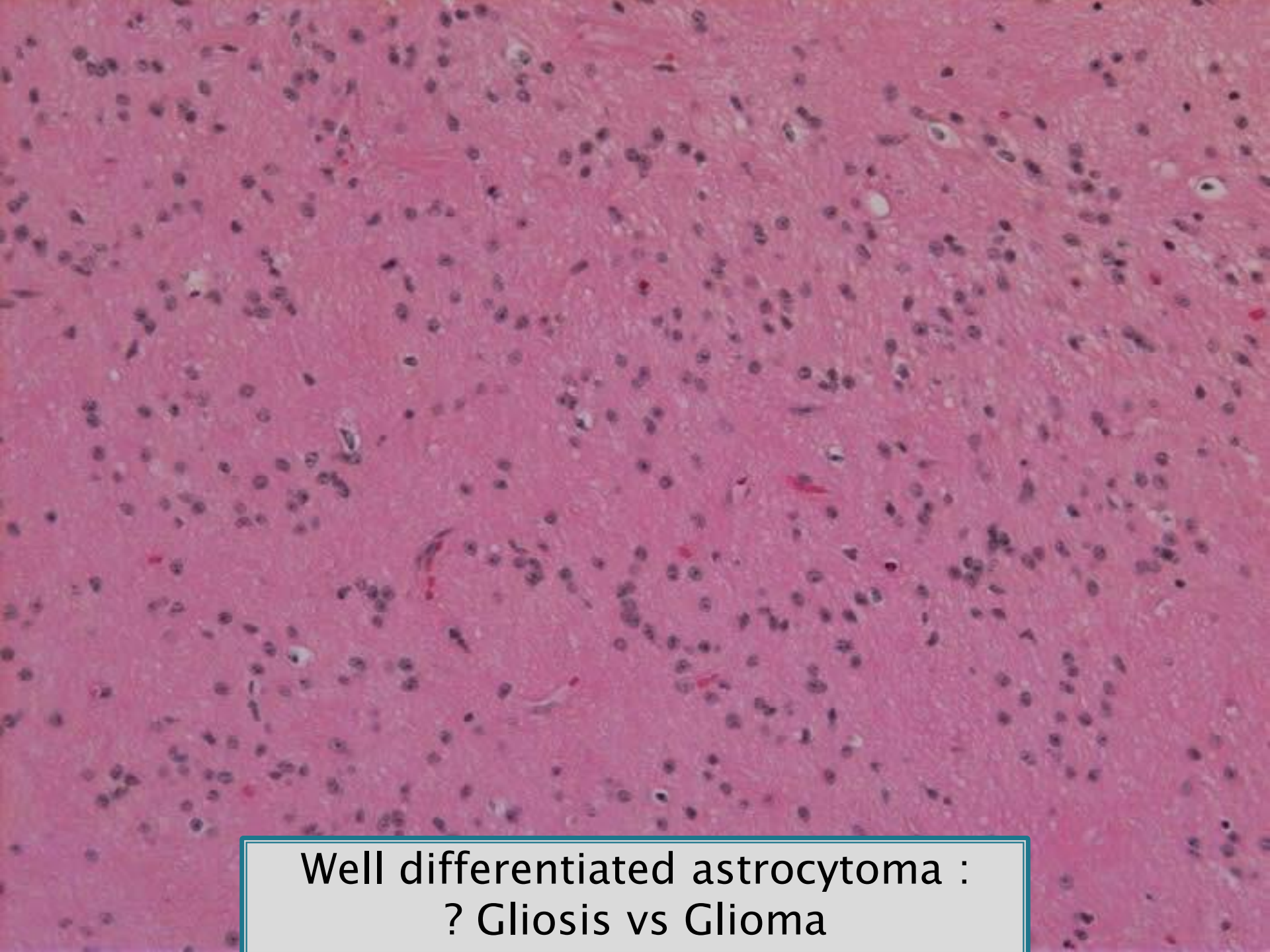
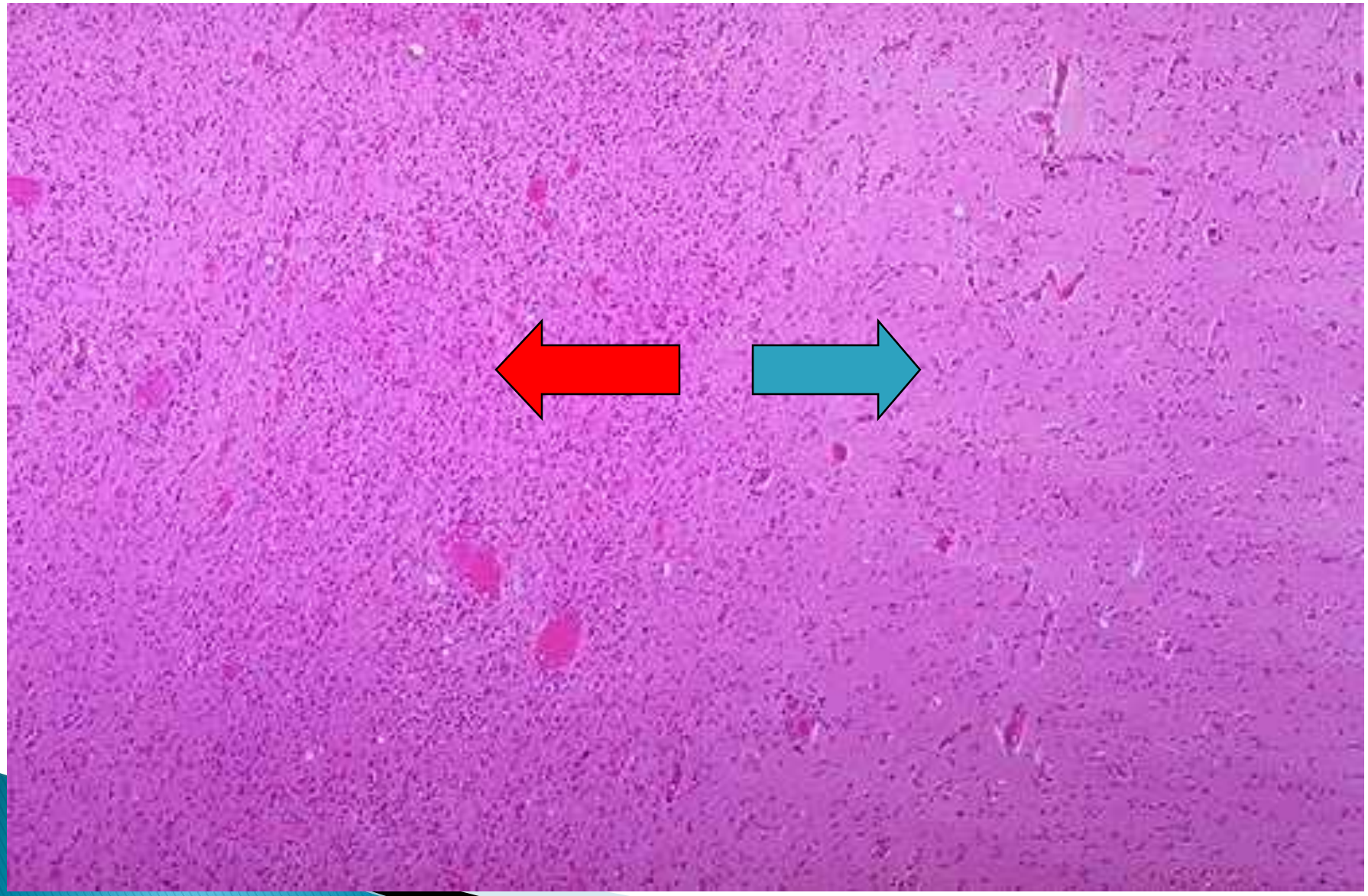


Well differentiated astrocytoma :
? Gliosis vs Glioma

Glioma

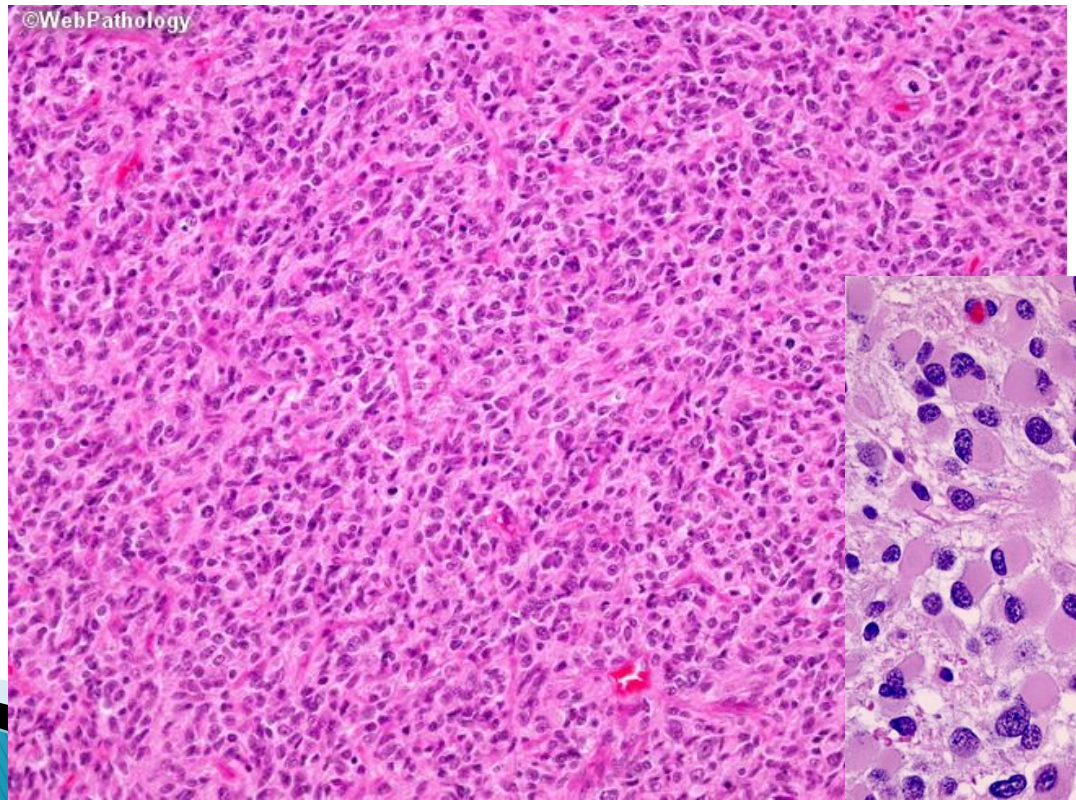
Brain Normal

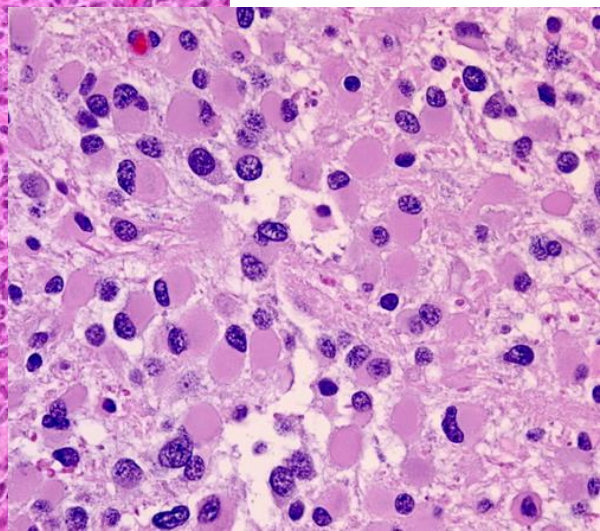


Anaplastic astrocytoma

(WHO grade III)

- **Microscopic:**
  - More cellularity, pleomorphic & **mitosis**.
  - **NO** palisading necrosis or microvascular proliferation





Glioblastoma

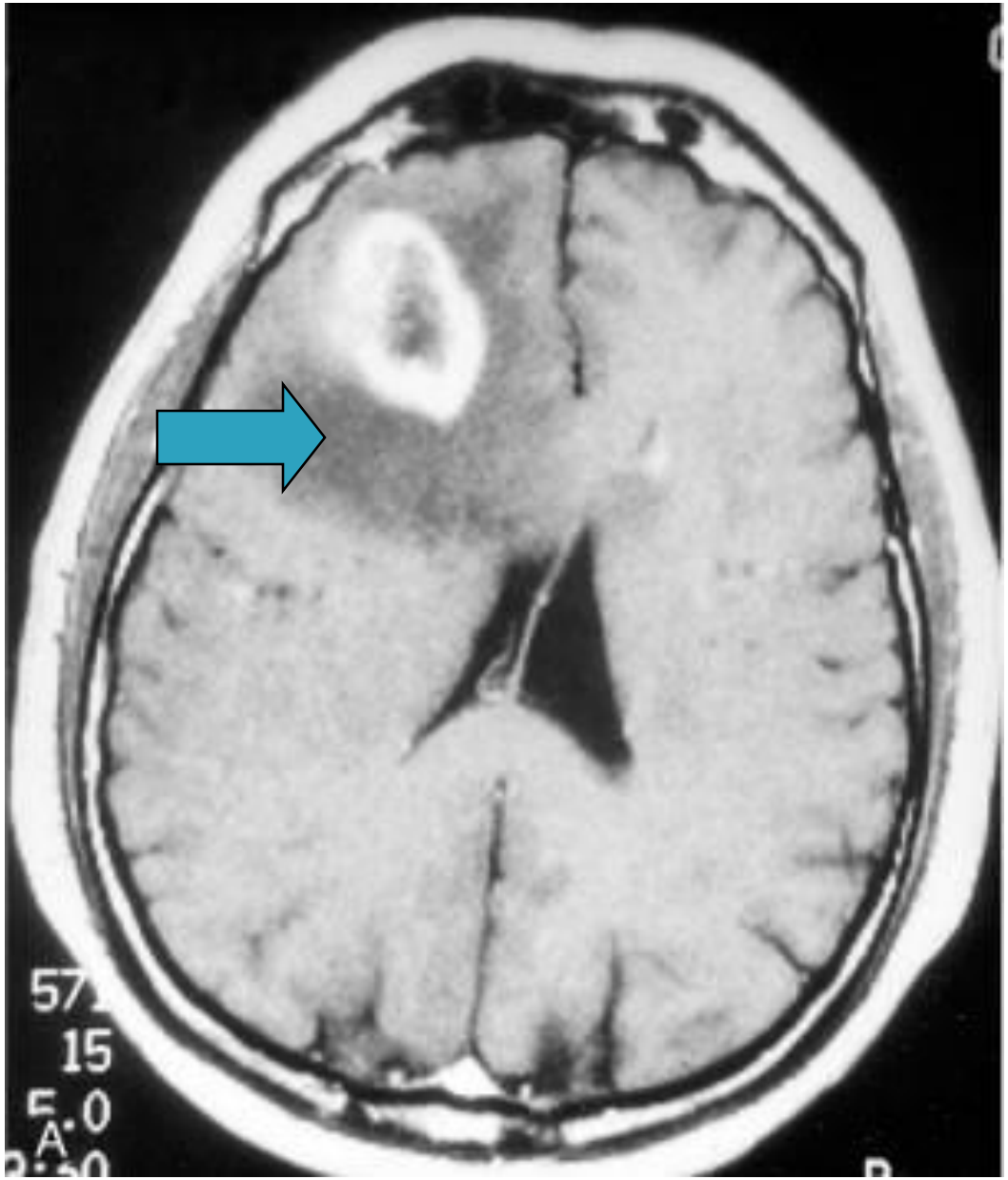
(WHO grade IV)

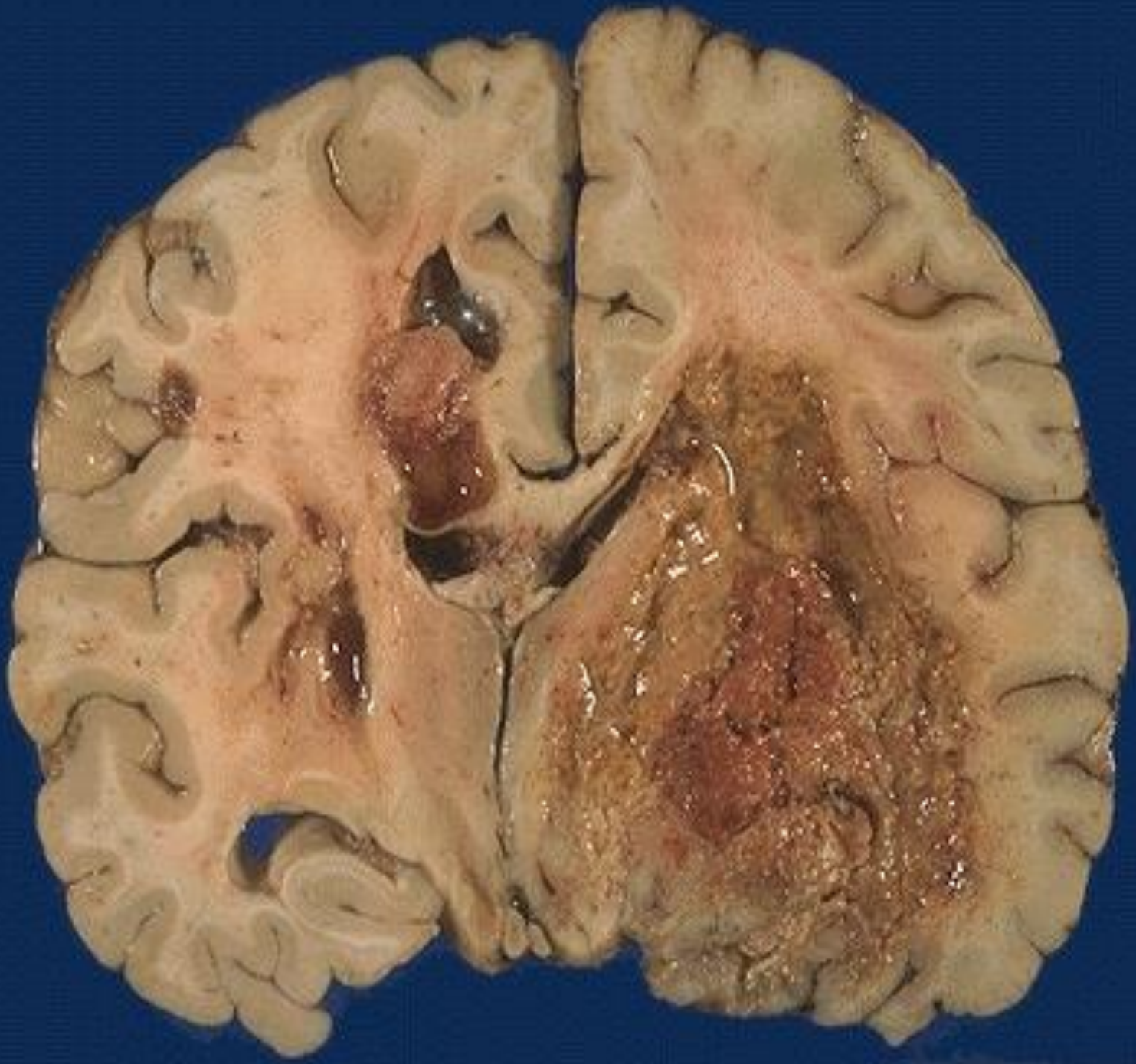
- **CT/MRI:**
  - Supratentorial enhancing tumor with surrounding edema.

- **Microscopic:**
  - Similar to anaplastic astrocytoma with:
    - **Palisading necrosis**
    - **± Microvascular (glumeruloid) proliferation**

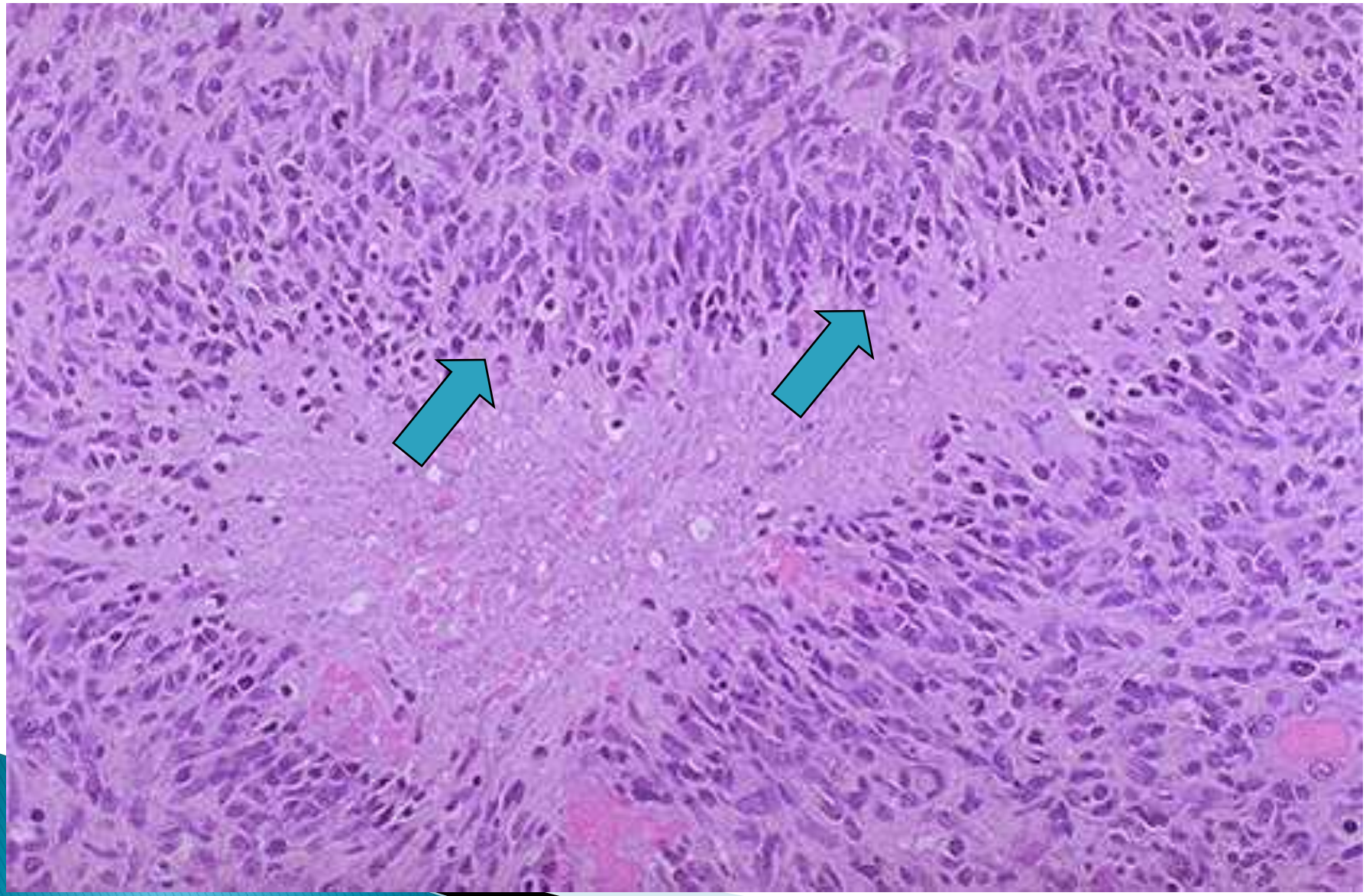
- **Prognosis:**
  - Very poor; with treatment, the median survival is only ***15 months***.
  - De-novo GBM has a **worse** Px than secondary GBM.

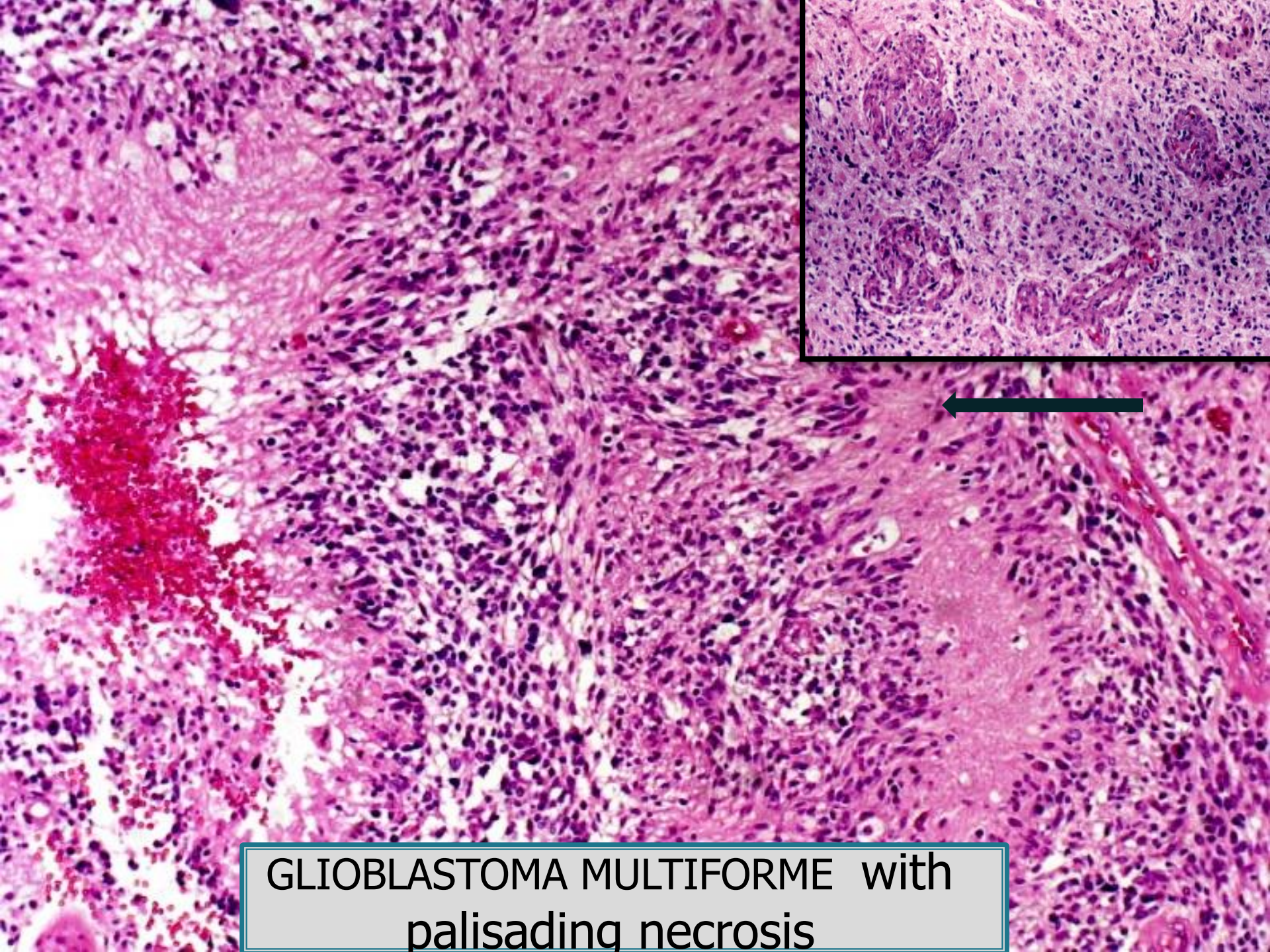
Glioma: Enhancement with peritumoral edema.





GBM





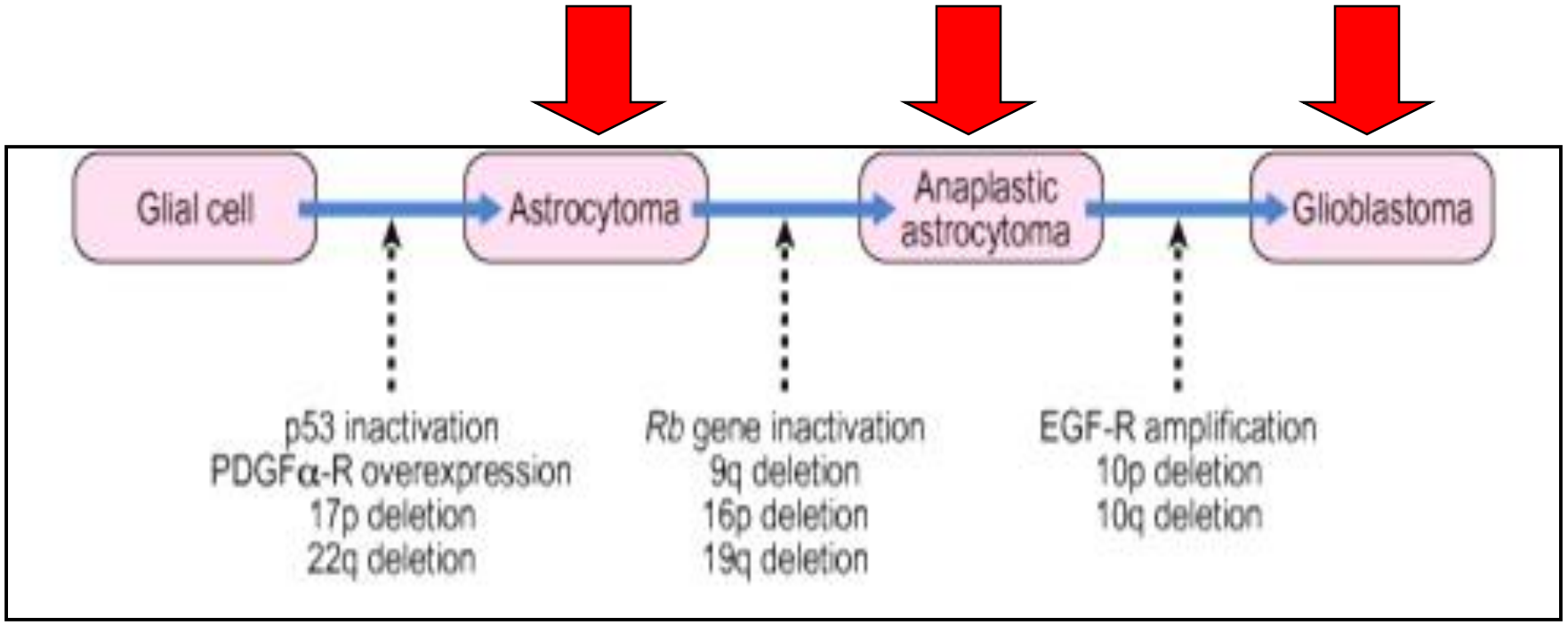
GLIOBLASTOMA MULTIFORME with palisading necrosis

Genetics mutation associated with astrocytomas

- **Pilocytic astrocytoma:**
  - Serine-threonine kinase BRAF
- **Lower grade astrocytoma:**
  - Isocitrate dehydrogenase (**IDH1** and IDH2).
- **GBM:**
  - Inactivation of p53 & Rb (*Secondary* GBM + low grade astro.)
  - Activation of PI3K.
  - Amplification of EGFR (*Primary* GBM).

Genetic abnormalities in Glioma:

Low grade → Anaplastic → GBM



Gliomas

2. Oligodendroglioma:

- More in 4th & 5th decades
- In frontal or temporal lobes→ favors white matter.
- Deletions of chromosomes *1p and 19q* is common → indicates high response to chemo & radiotherapy.
- Better prognosis than that for patients with astrocytomas of similar grade**.

Gliomas

2. Oligodendroglioma:

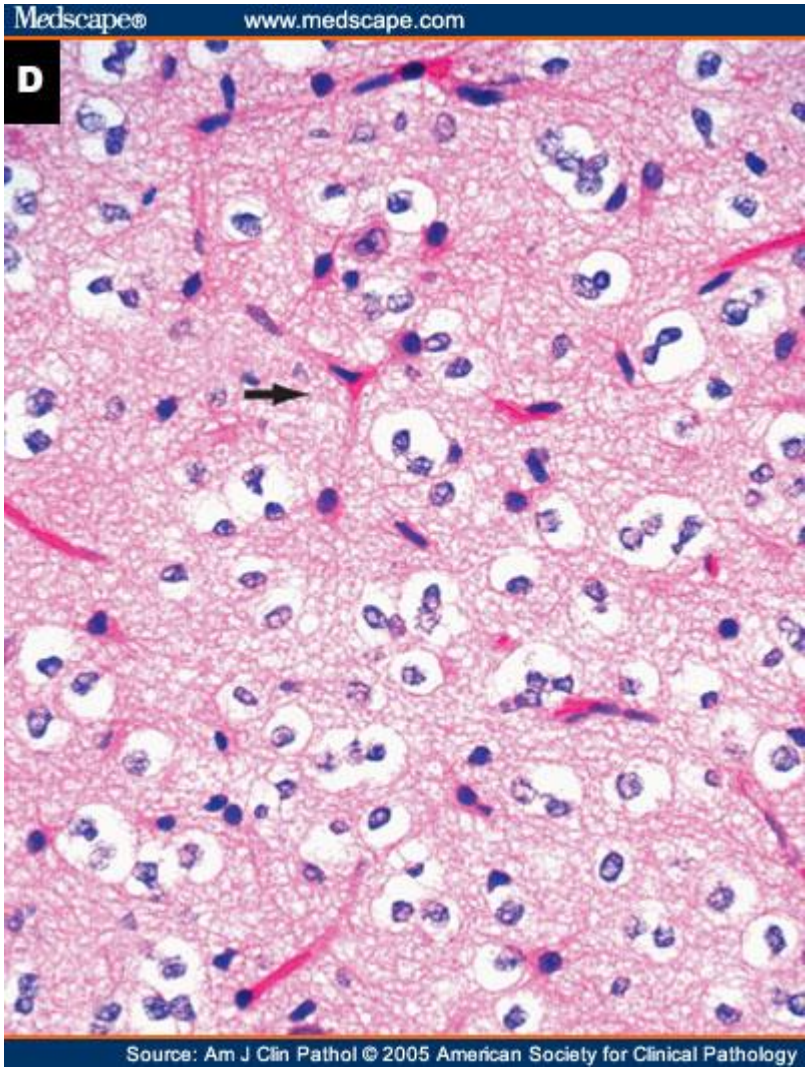
- **Gross:**
  - Mass with cysts, hemorrhage & **calcification**
- **Microscopic & WHO grades:**

A. Typical (Grade II):

- Small uniform cells surrounded by clear cytoplasm (FRIED EGG APPEARANCE).
- Delicate capillaries.
- Calcifications (90%).
- Absent or minimal mitosis.

B. Anaplastic (Grade III):

- More cellularity, pleomorphism & mitosis.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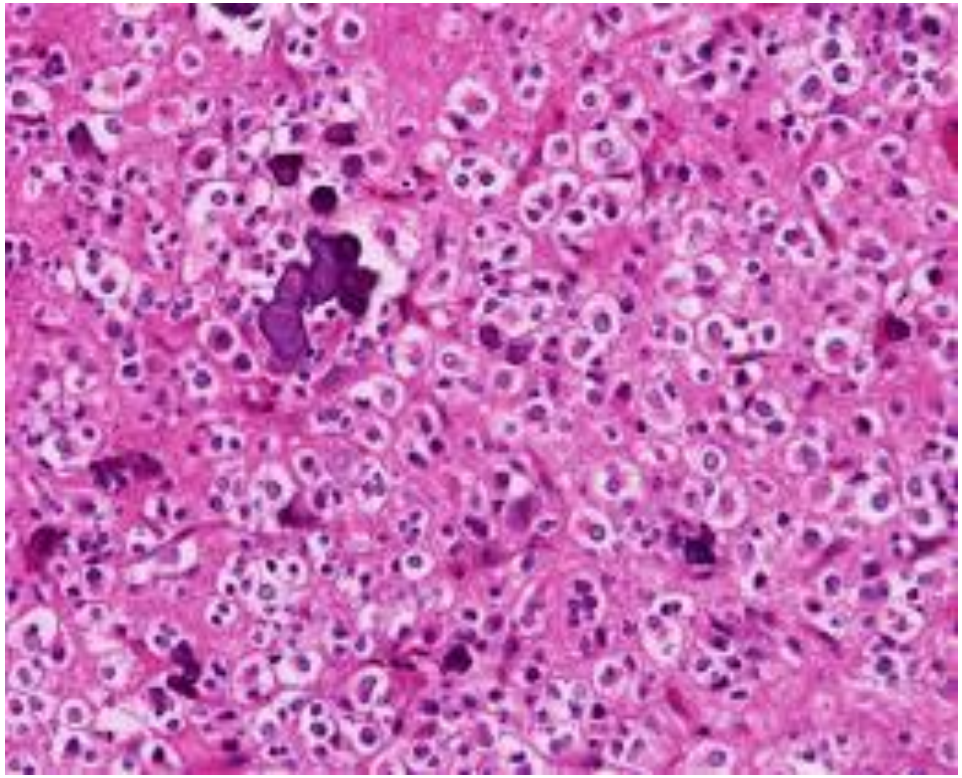


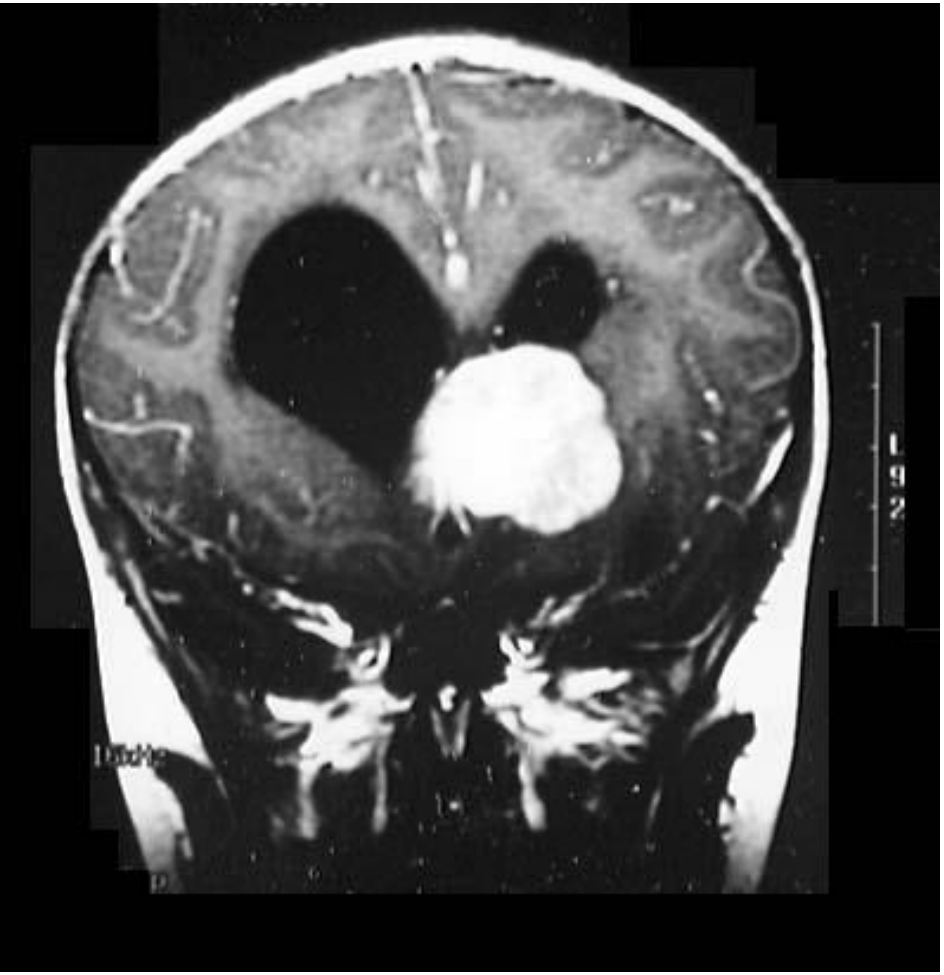
3. Ependymoma

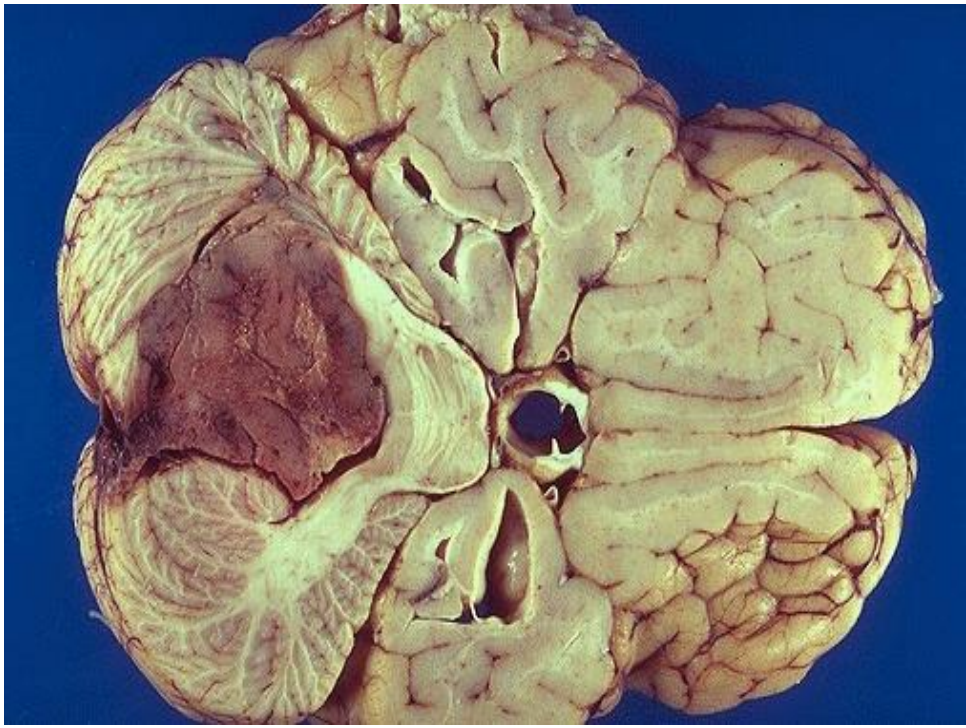
- Arise from ependyma-lined ventricular system*→ Can cause hydrocephalus & metastesize by CSF:
  - <20 yrs → 4th ventricle
  - >20 yrs → Spinal cord***
- **Microscopic & WHO grading:**

A. Typical (Grade II) → Regular cells forming:

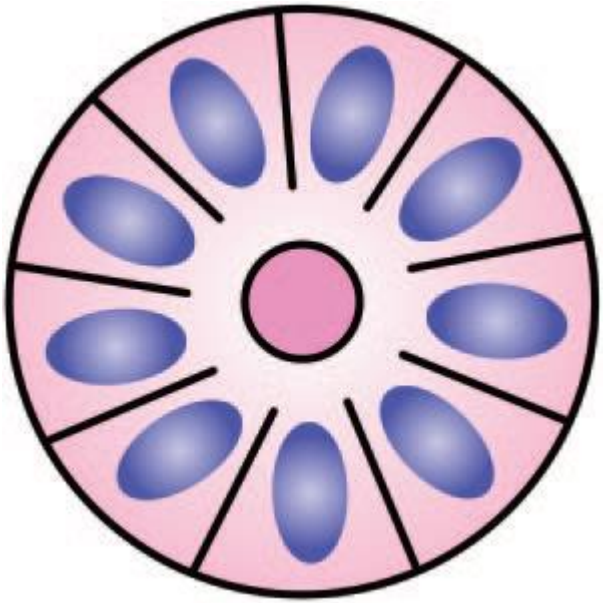
- **Ependymal true rosettes**
- **Perivascular pseudorosettes**

B. Anaplastic (Grade III).

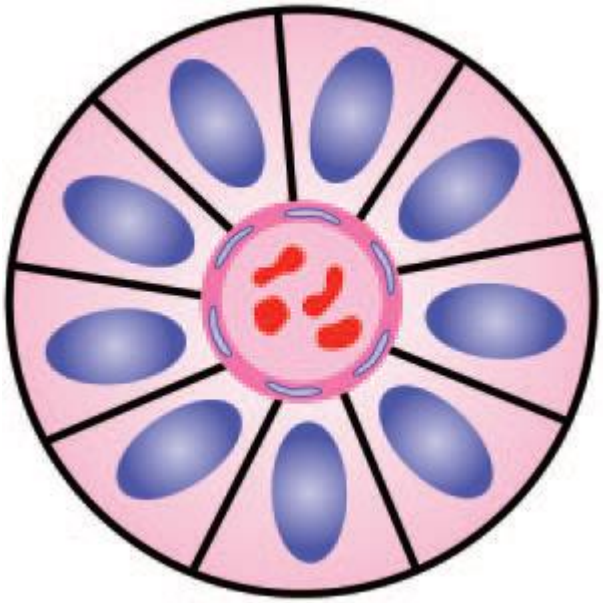


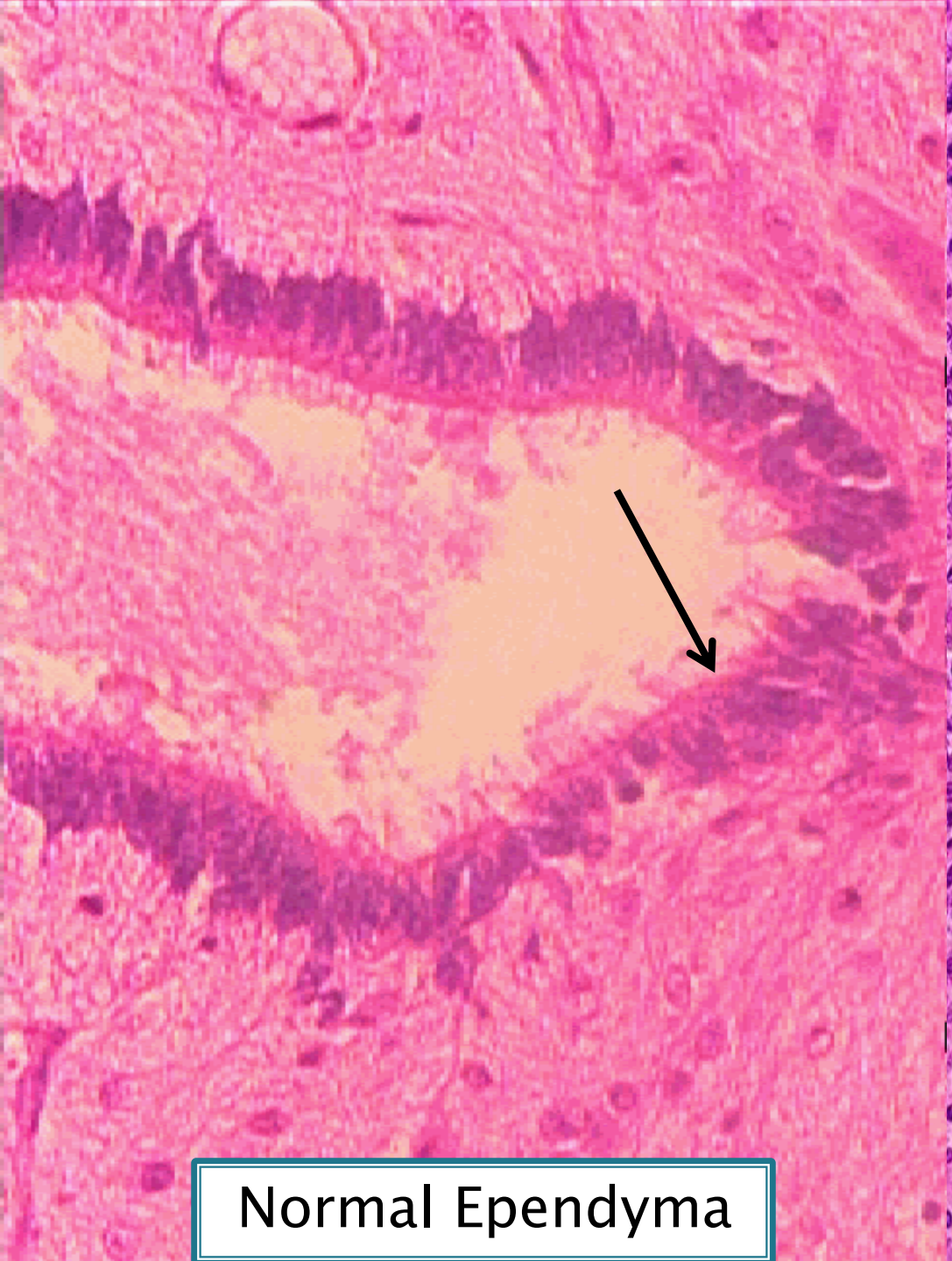


True Rosette

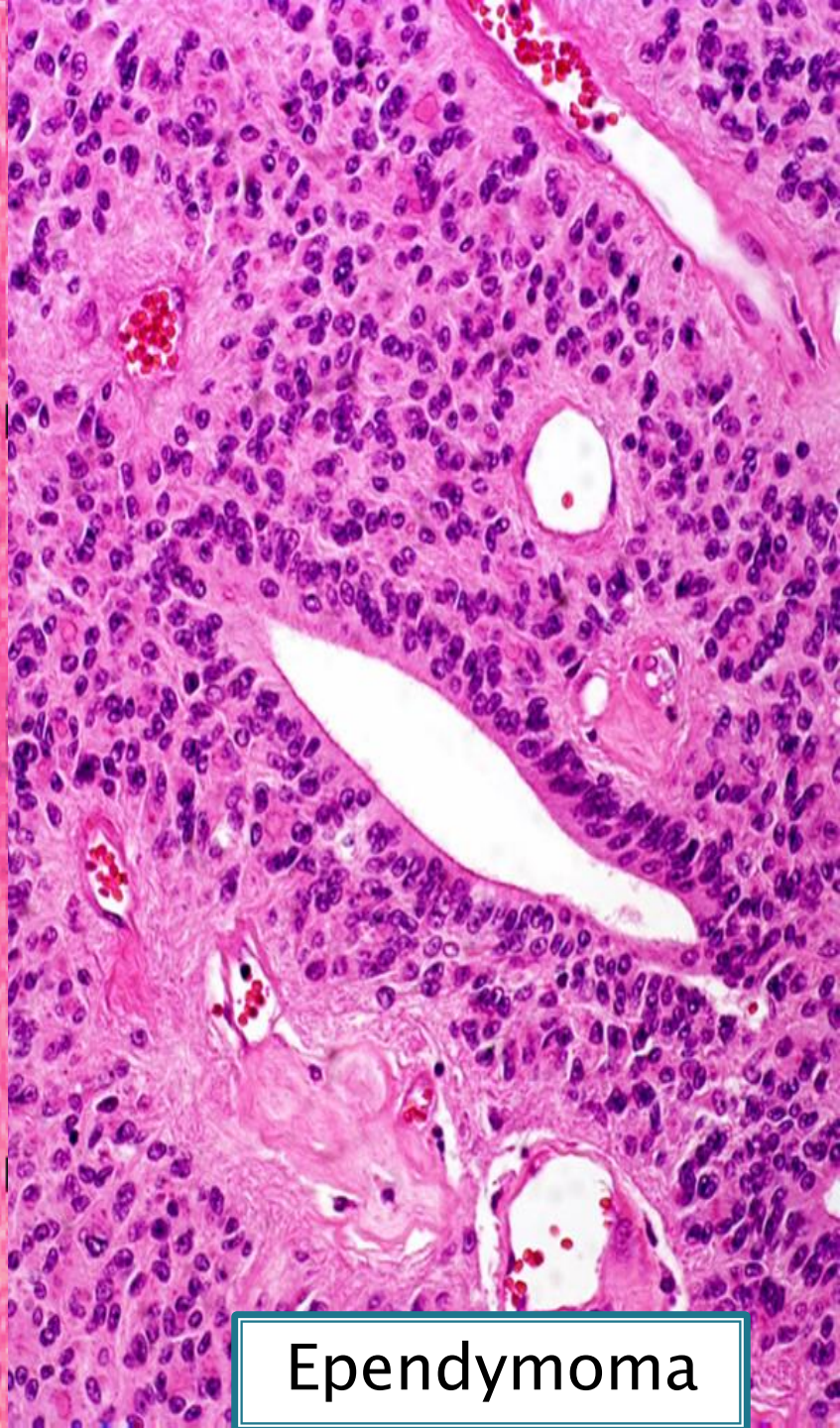


Perivascular Pseudorosette

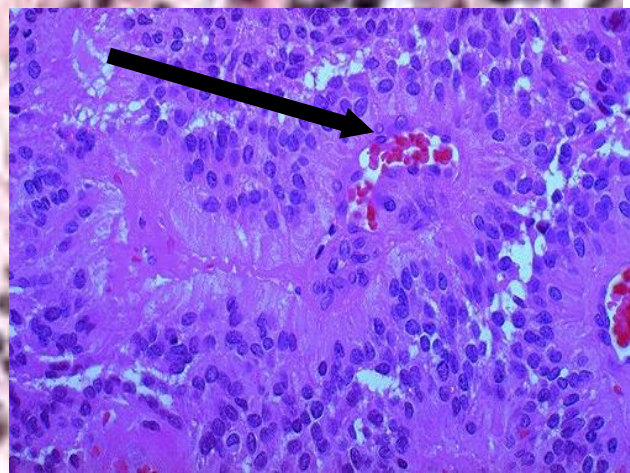




Normal Ependyma



Ependymoma

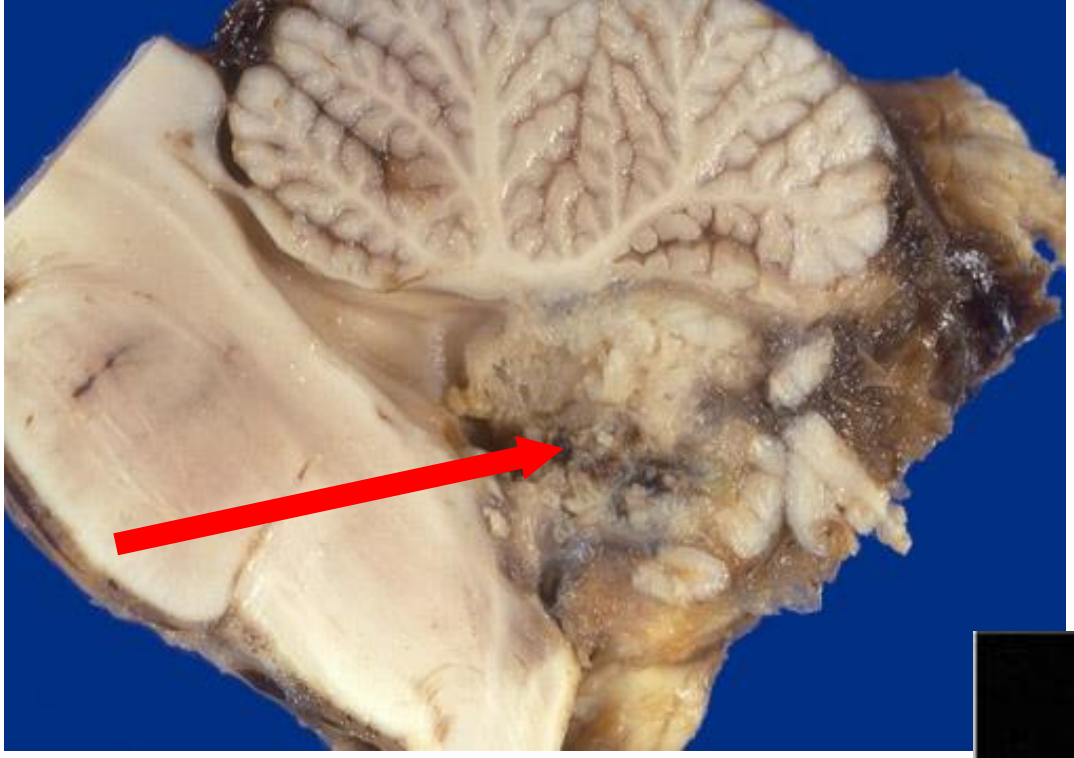


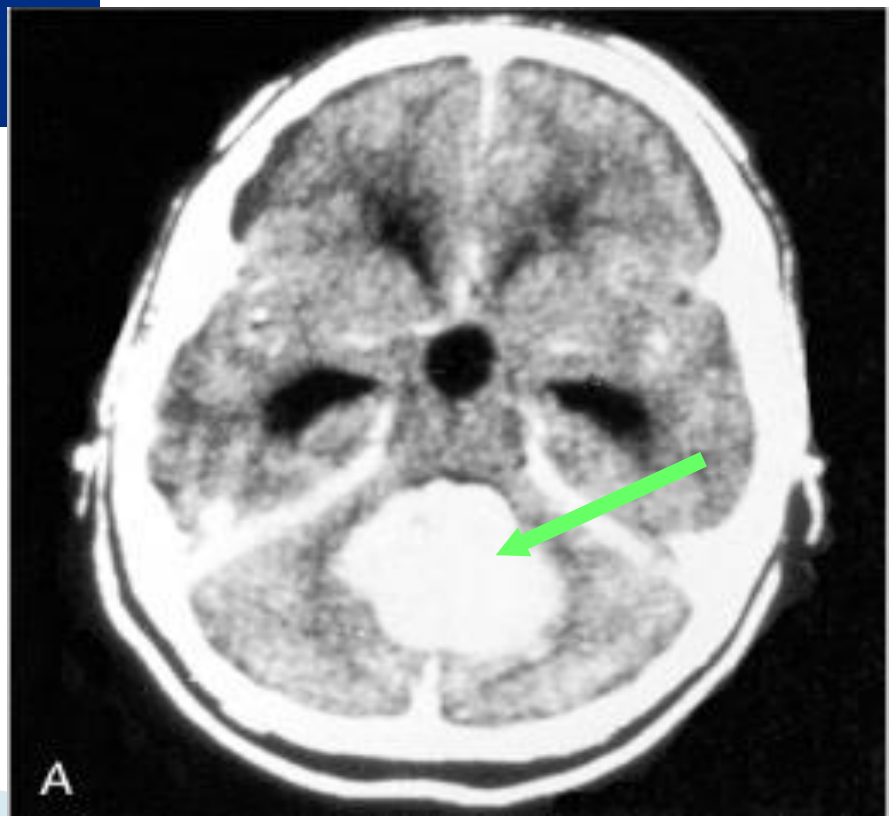
Embryonal (Promitive) Neoplasms

Medulloblastoma

WHO grade VI

- A primitive neuroectodermal tumor (**PNET**) composed of *undifferentiated small blue round cells*.
- **20**% of pediatric brain tumors:
  - Children → Midline cerebellum or roof of 4th ventricle.
  - Young adults → Lateral cerebellum.
- Manifests with hydrocephalus & ↑ICP early.
- Spread through CSF.





Medulloblastoma

➢ Microscopic:

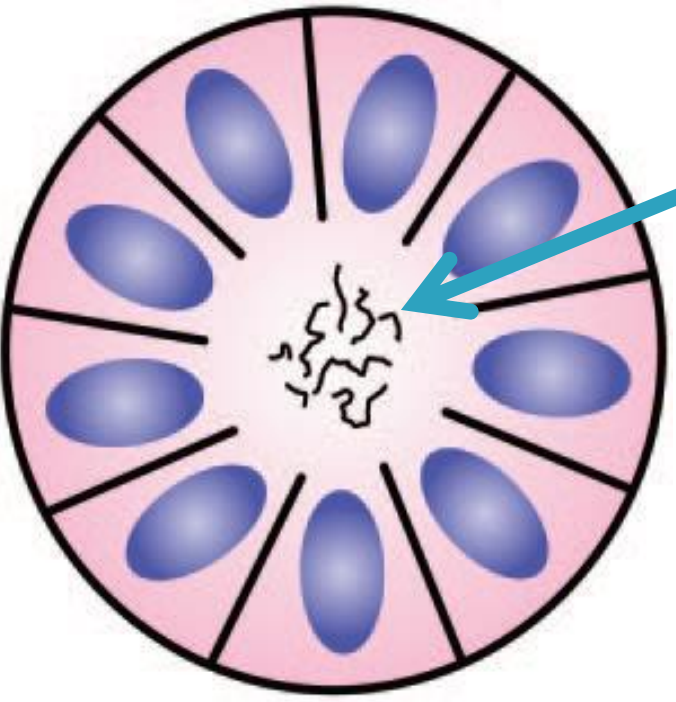
- Cellular tumor composed of small blue round cells with numerous mitoses & ***Homer - Wright Rosettes.***

➢ Genetics:

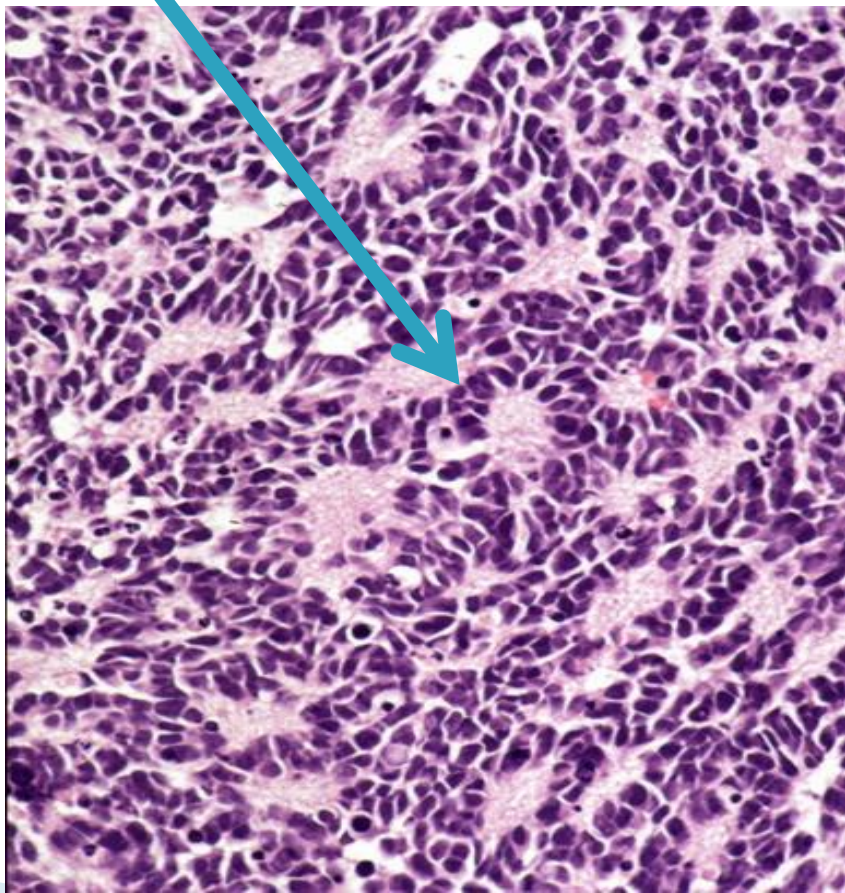
- MYC amplification (bad Px).
- WNT mutation (good Px).
- Sonic hedgehog (?).

➢ Prognosis & treatment:

- Without treatment → very poor.
- With treatment (since it is radiosensitive) → 75% 5-year survival rate (BUT!!!).



Neurofibrillary center



Homer Wright R. in Medulloblastoma

Meningioma

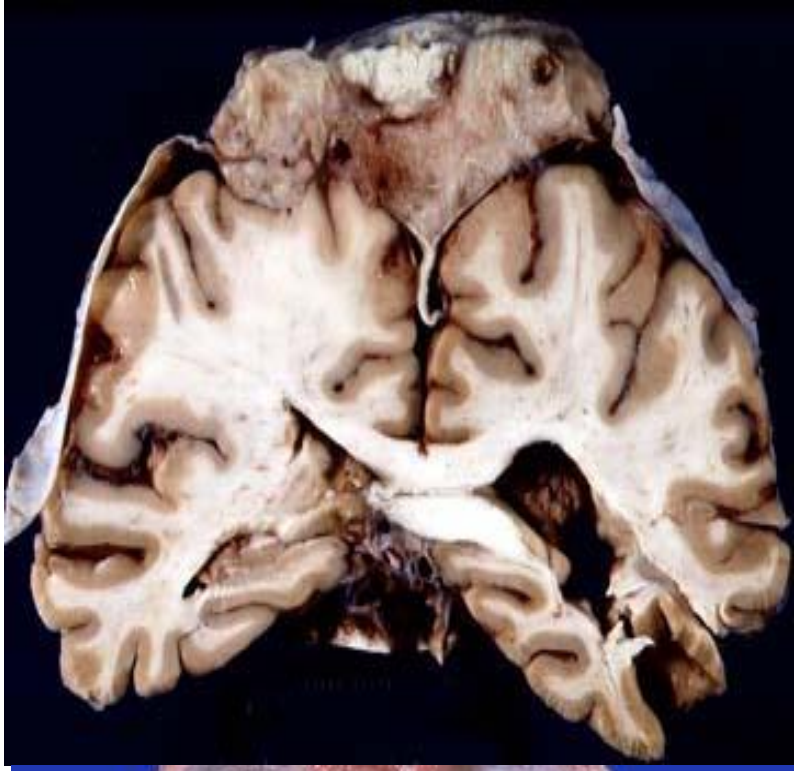
- Arise from arachnoid meningiothelial cell on surface of brain or spinal cord.
- **Sites:** Parasagital (Falx), sphenoid….
- Most in adult females → Tumor cells contain PROGESTERON receptors
- 50% are associated with **NF2** mutation.

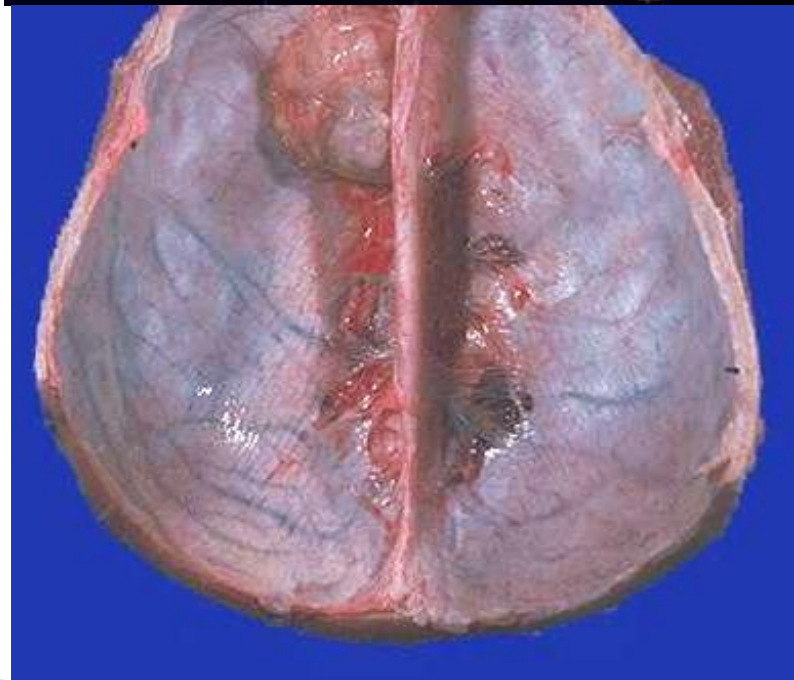
Gross:

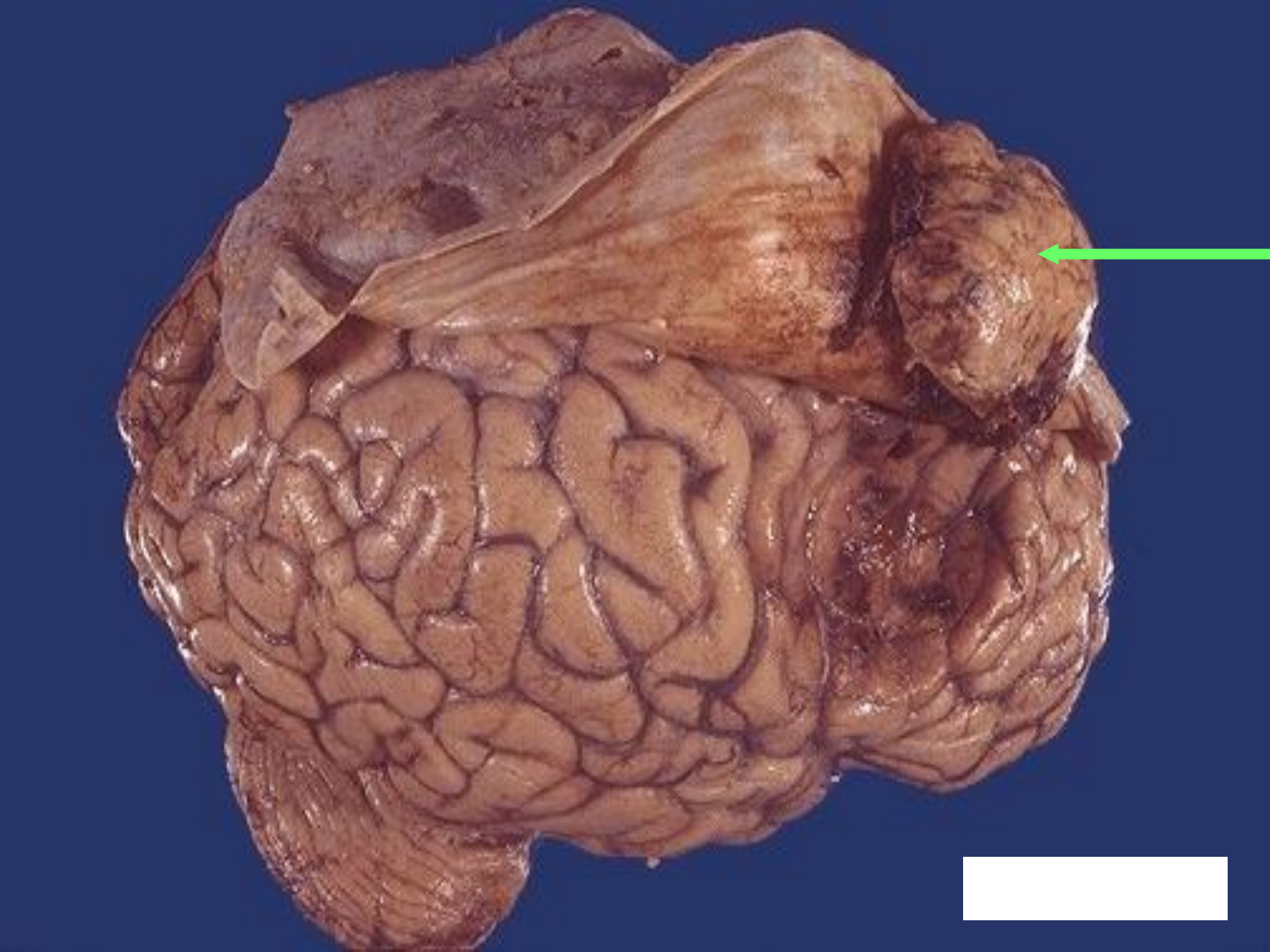
- Well defined solid dural based mass → Compressing brain but *easily* removed.

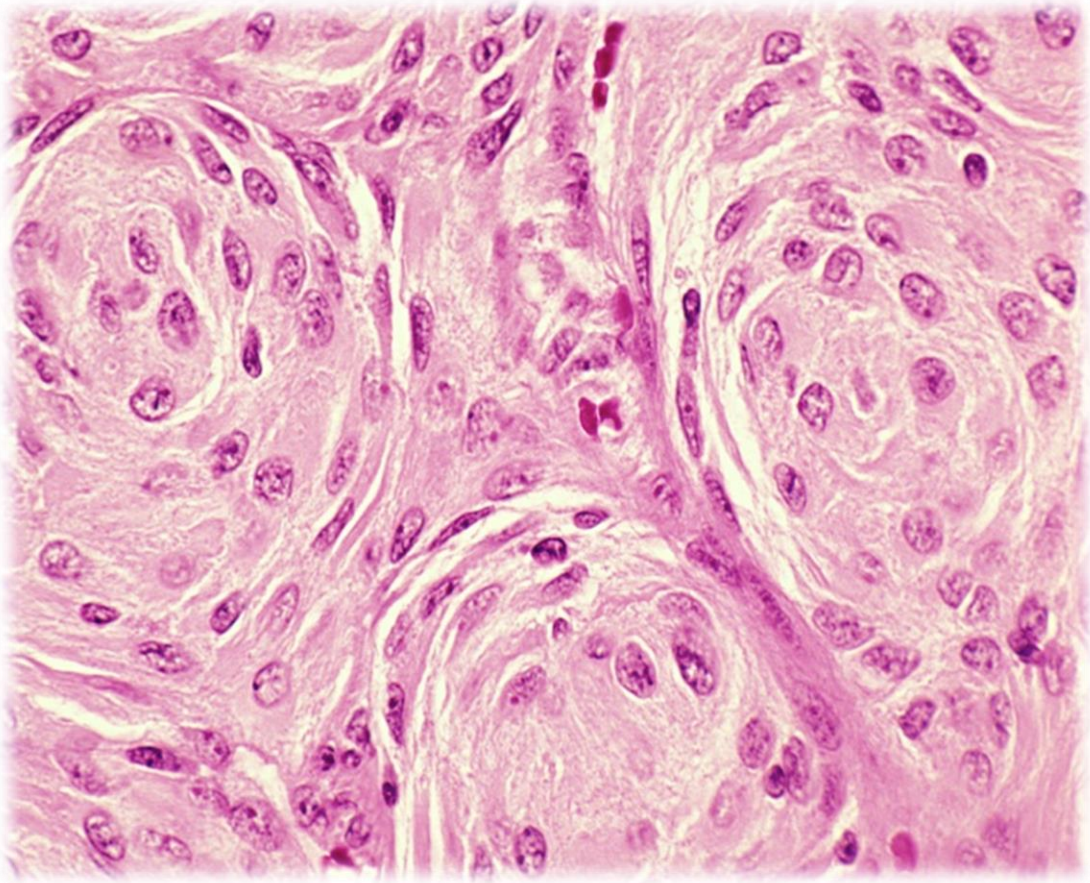
- Can invade the skull & venous sinuses, but this does not affect prognosis

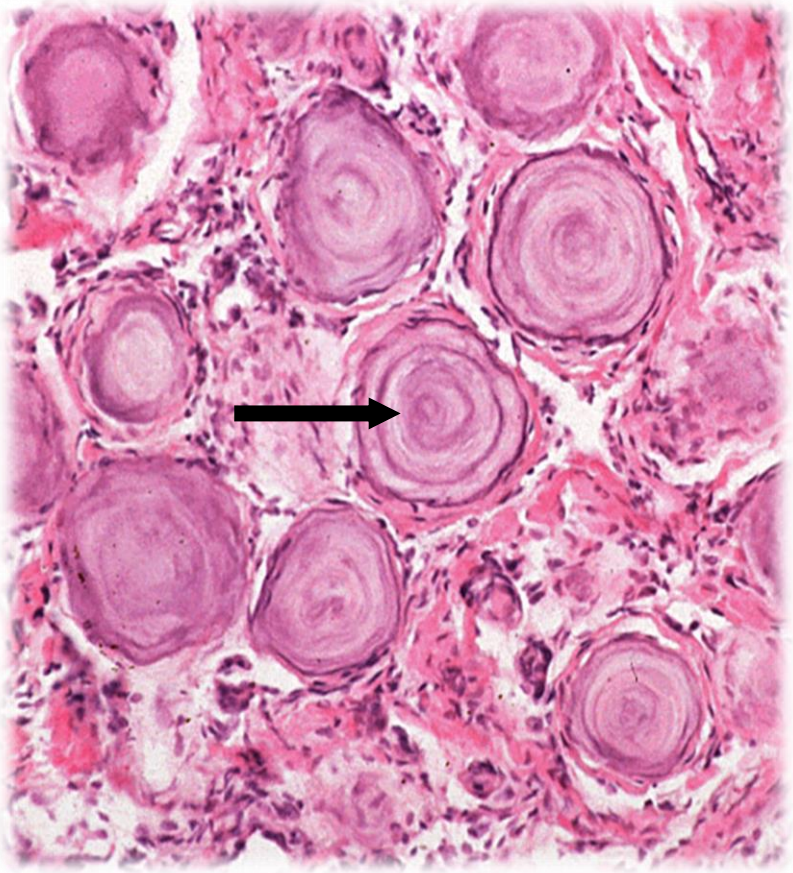
- Can invade the underlying brain → **IMPORTANT** in prognosis







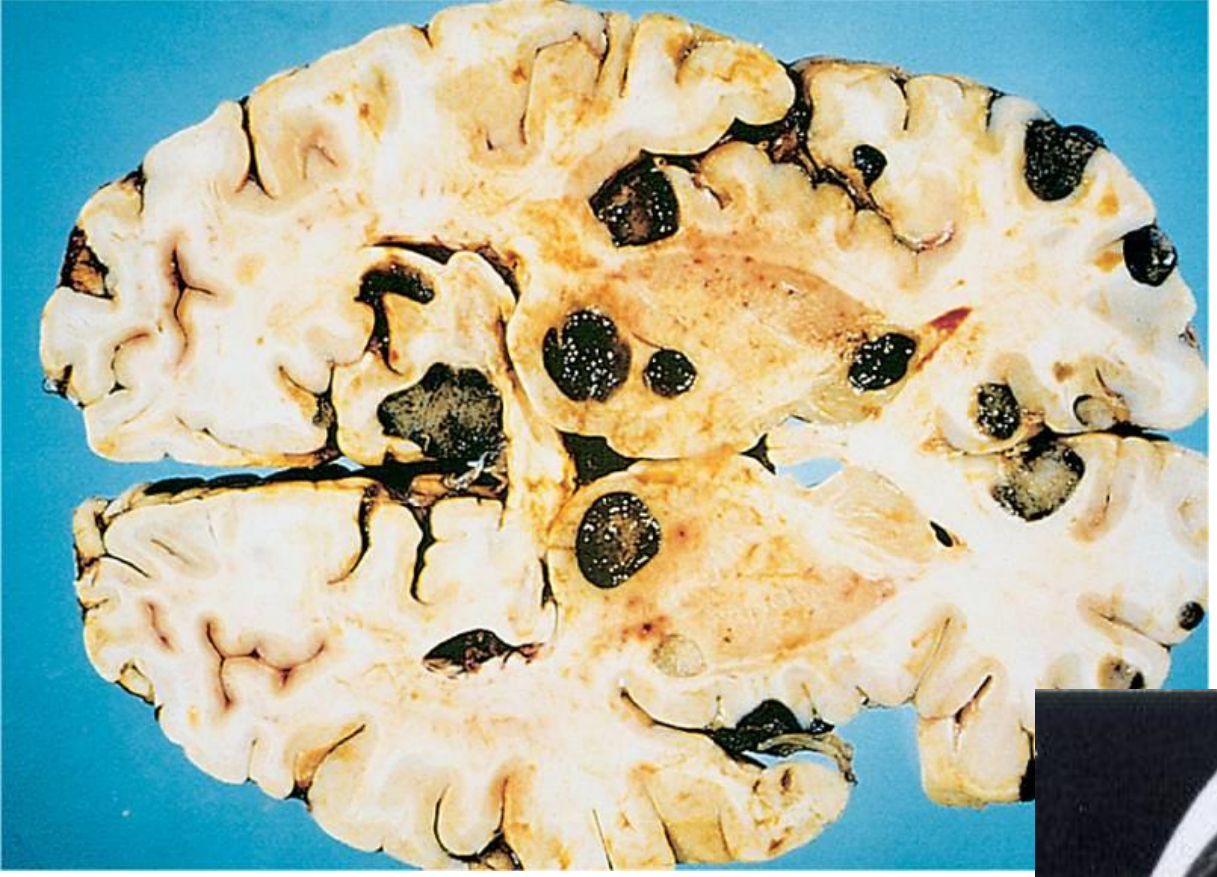


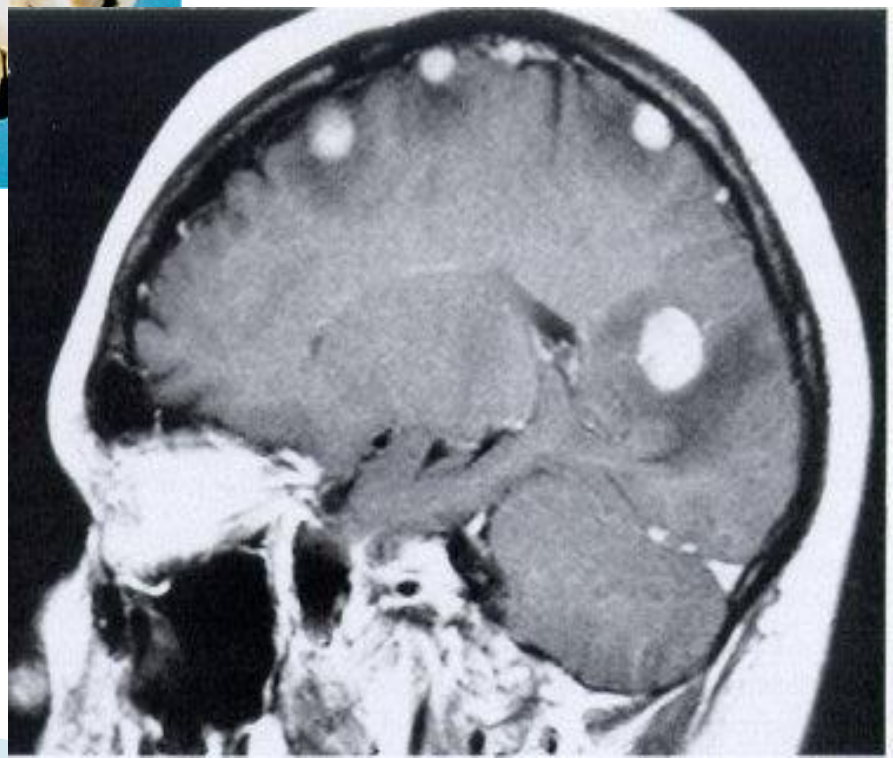


Psammoma bodies are diagnostic of meningiomas in brain tumors

Metastatic CNS tumors

- Majority are **CARCINOMAS** disseminate via blood → forming multiple sharply demarcated masses at Grey-white matter junction OR at border zone between MCA and PCA with marked surrounding edema.

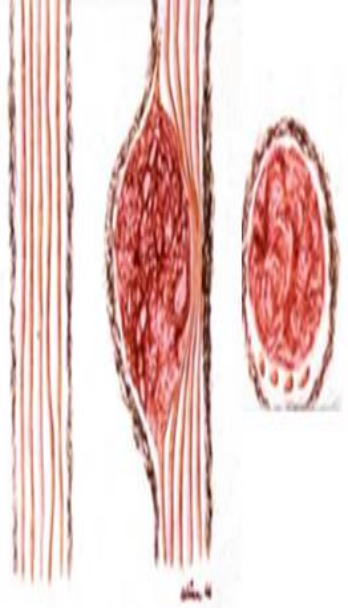




- Origin of solid primary tumors:
  - Lung (most common)
  - Breast
  - Melanoma
  - Kidney
  - Gastrointestinal

- Less common but with special propensity for brain metastasize:
  - Germ cell tumours
  - Thyroid

Spinal Cord tumors :



- Extraspinal: Metastatic, Lymphoma
- Extradural intraspinal : Metastatic, Lymphoma
- Intradural :

  Extramedullary : Schwannoma

  Meningioma

  Intramedullary : Ependymoma

  Astrocytoma

Tumours of Peripheral Nervous System :

- Majority are composed of cells that show evidence of *Schwann cell differentiation.*

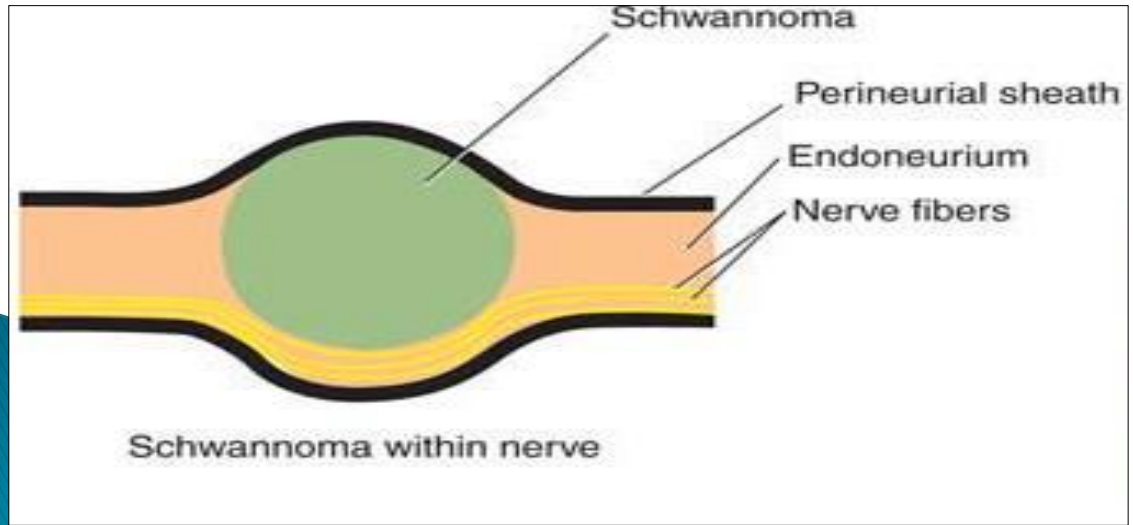
1. Schwannoma.
2. Neurofibroma.
3. Malignant peripheral nerve sheath tumor (MPNST).

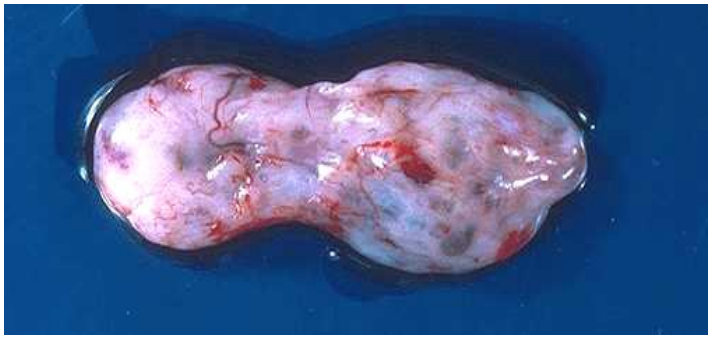
- Although majority arise along the course of a peripheral nerve, few arise close to the brain, mainly schwanoma at cerebellopontine angle.

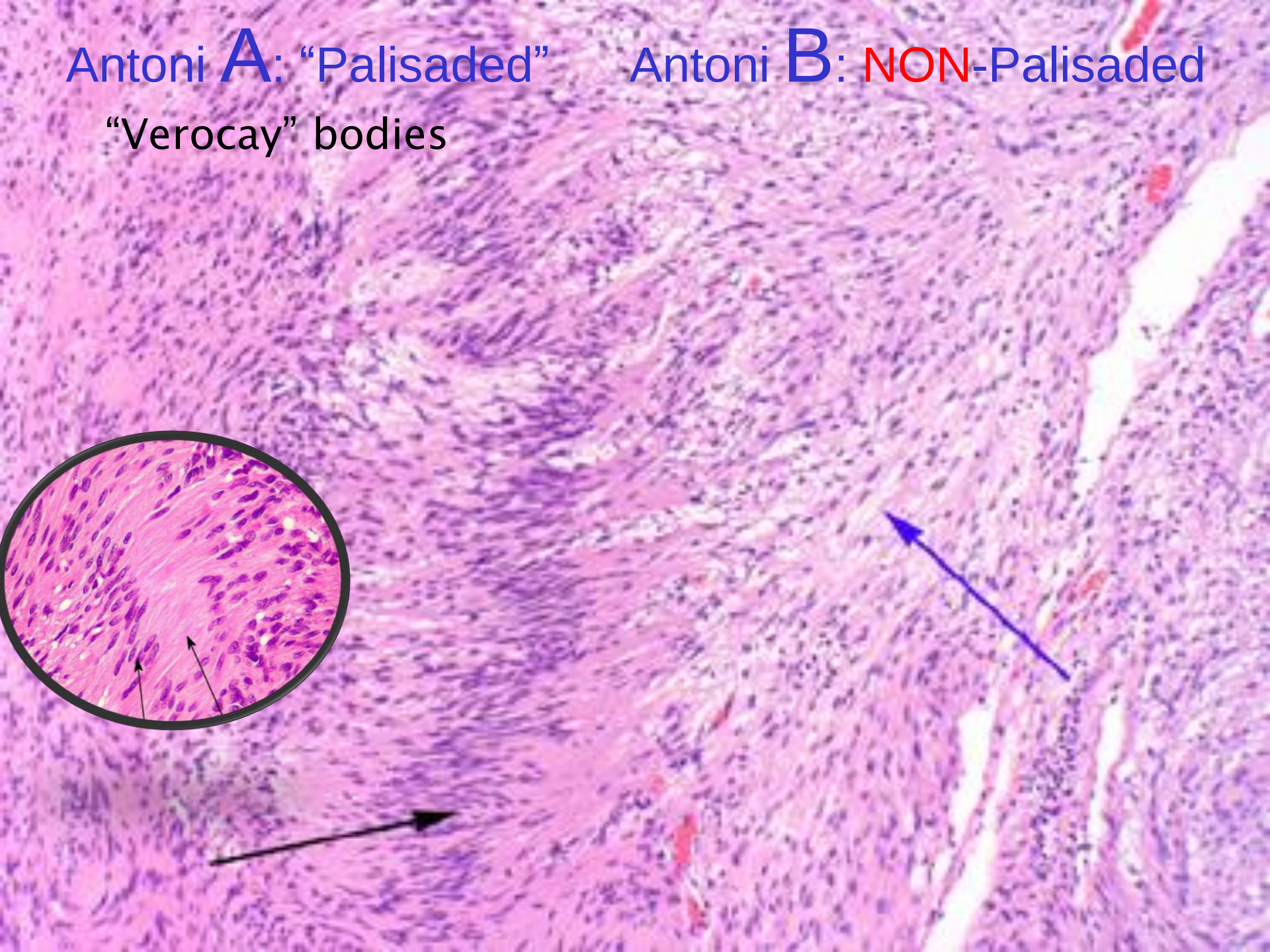
- They are usually solitary , but may be multiple in the Familial Tumor Syndromes (NF).

Schwannoma

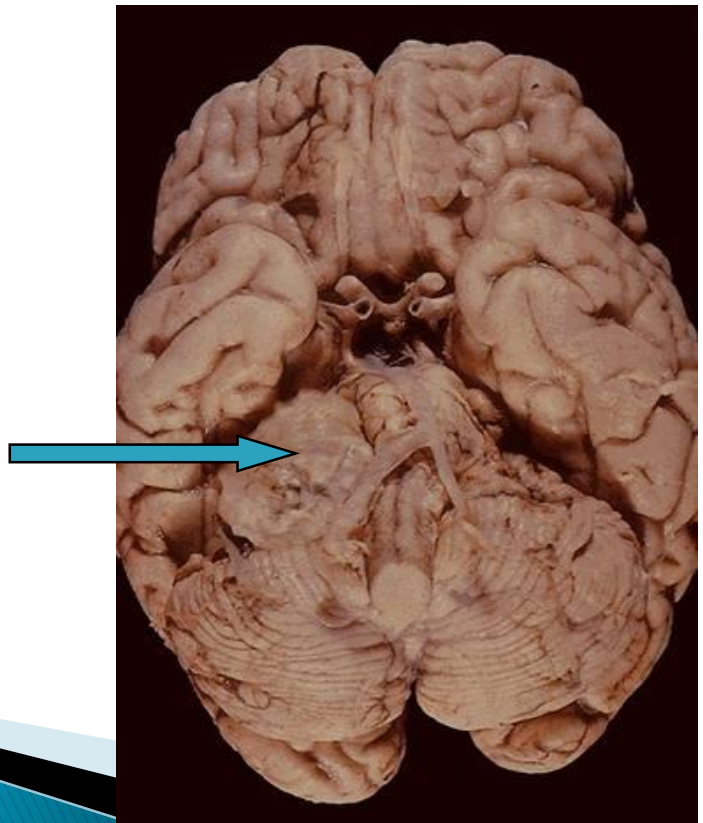
- Benign tumor.
- Can be **sporadic** (ass. with NF2 gene mutation) or **familial** (Neurofibromatosis-2).
- **Gross:**
  - *Encapsulated* masses that abut the associated nerve <u>without</u> invading it.






Antoni A: "Palisaded"
Antoni B: NON-Palisaded
"Verocay" bodies

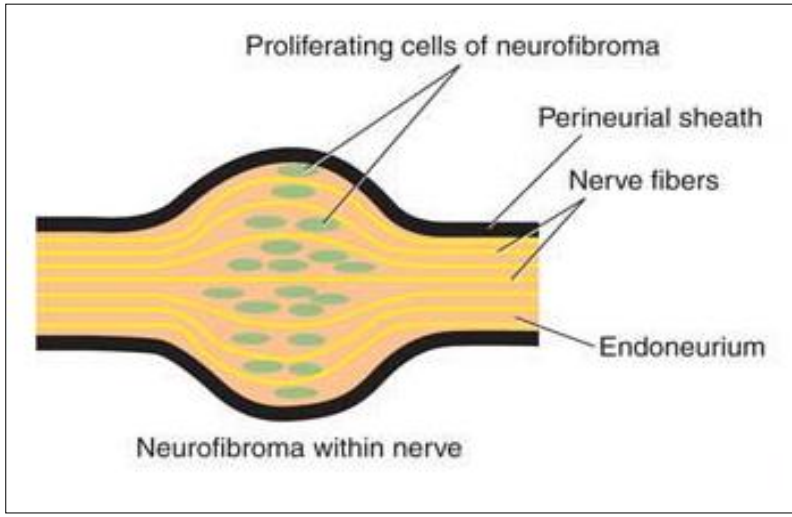
- **Clinical features:**
- Related to nerve compression.
- ***Acoustic neuroma:***
  - Schwannomas occur at the cerebellopontine angle leading to tinnitus & hearing loss.



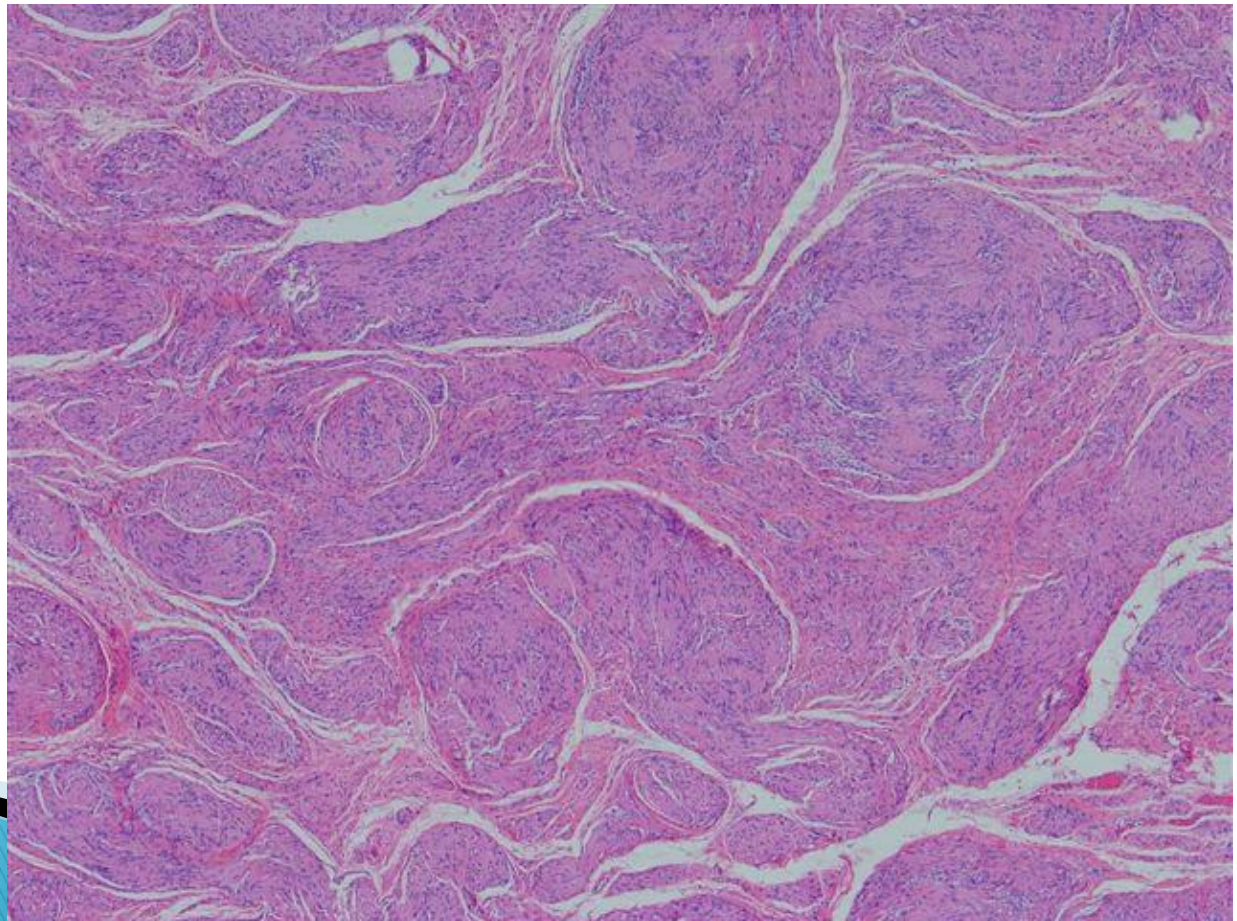
Neurofibroma

- Benign tumor composed of neoplastic Schwann cells admixed with perineurial- like cells, fibroblasts, mast cells …
- Can be **sporadic** (ass. with NF2 gene mutation) or **familial** (Neurofibromatosis-1).

1. Superficial cutaneous neurofibromas.
2. Diffuse neurofibromas
3. **Plexiform neurofibromas:**
   → Has the highest risk to transformed into **MPNST**



- **Clinical features:**
  - Nodulular or diffuse lesion in skin or SC. tissue.
- **Microscopic:**



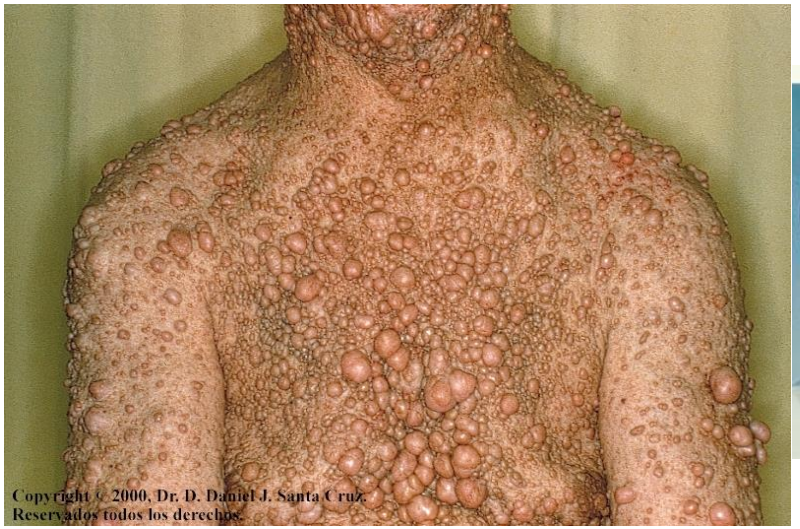
Inherited familial tumor syndromes

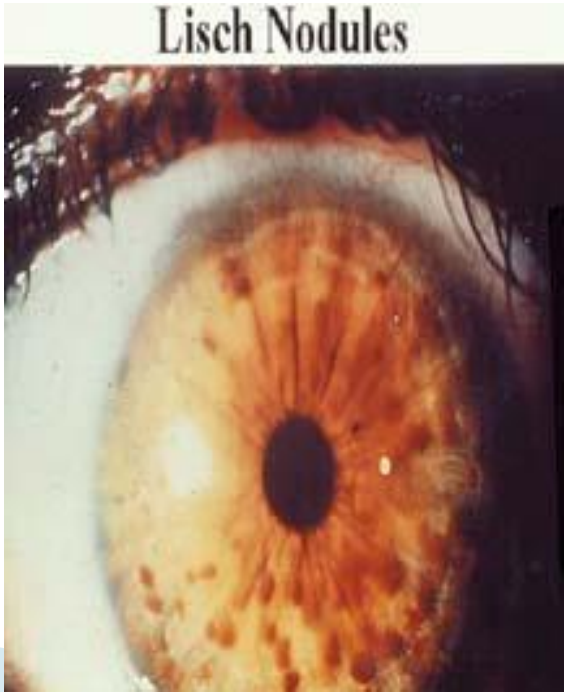
Most are **AD** disorders.

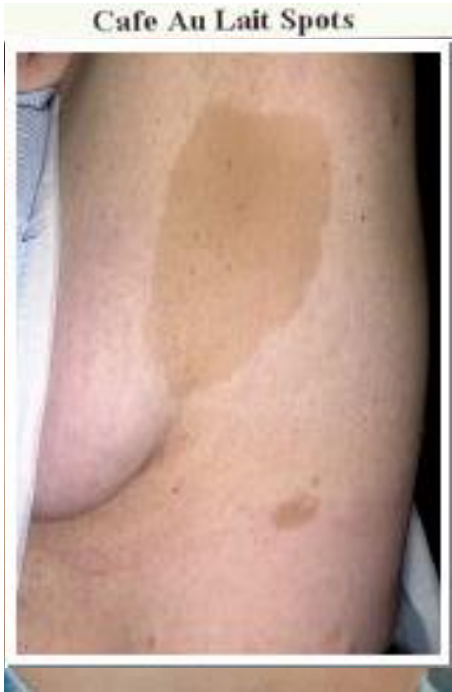
- **Neurofibromatosis Type I & Type II –**
  Variety of CNS & peripheral nerve tumors ± other systemic manifestations
- **Tuberous sclerosis – CNS hamartomas ,astrocytoma, subependymoma (TUBERS), extracerebral lesions including benign skin lesions, renal angiomyolipoma ..etc**
- **Von Hippel-Lindau – hemangioblastoma , renal carcinoma , renal cysts ……. etc**
- **Li-Fraumeni – inherited p53 mutation → glioma, many types of tumors.**

Neurofibromatosis-1

- Neurofibromas± Sarcomatous trans -formation
- Glioma of optic nerve
- Meningioma
- Café-au-lait spots
- Pigmented nodules of iris







Neurofibromatosis-2

- **Bilateral acoustic neuromas.**
- **Multiple meningiomas (more than NF1)& ependymomas.**

Thank you