



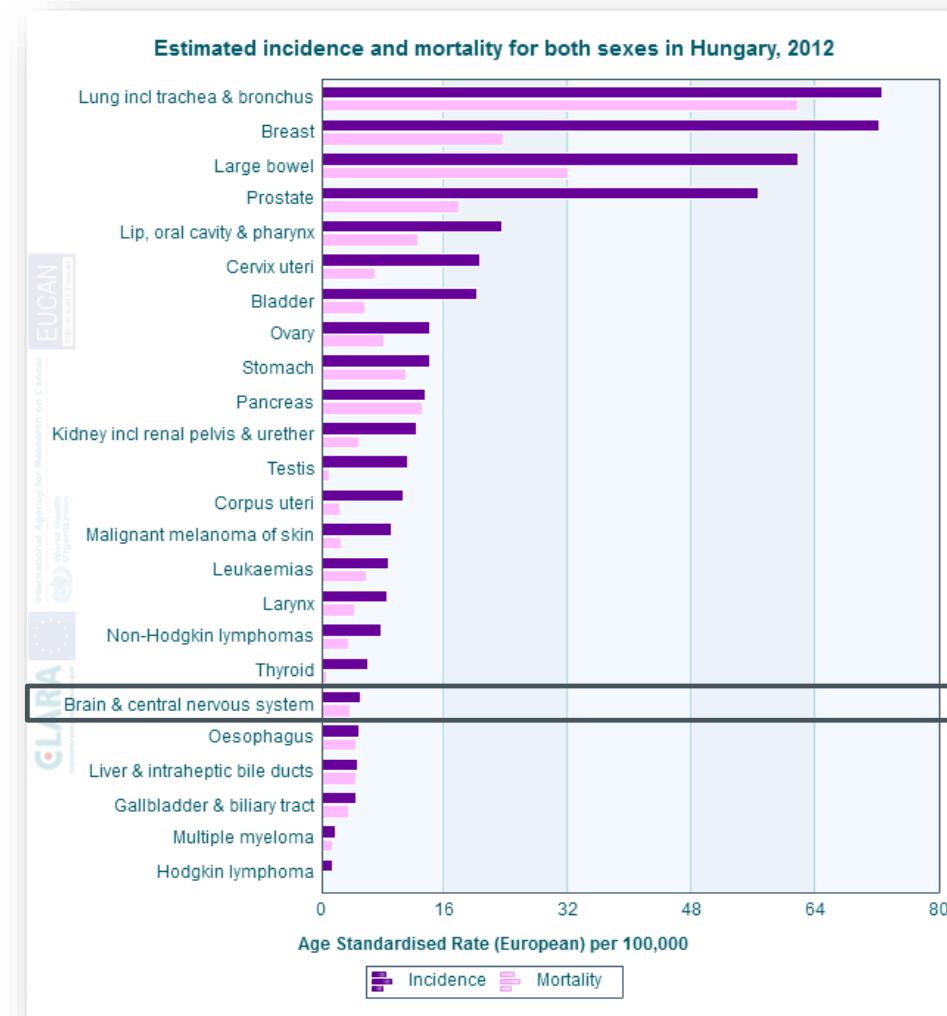
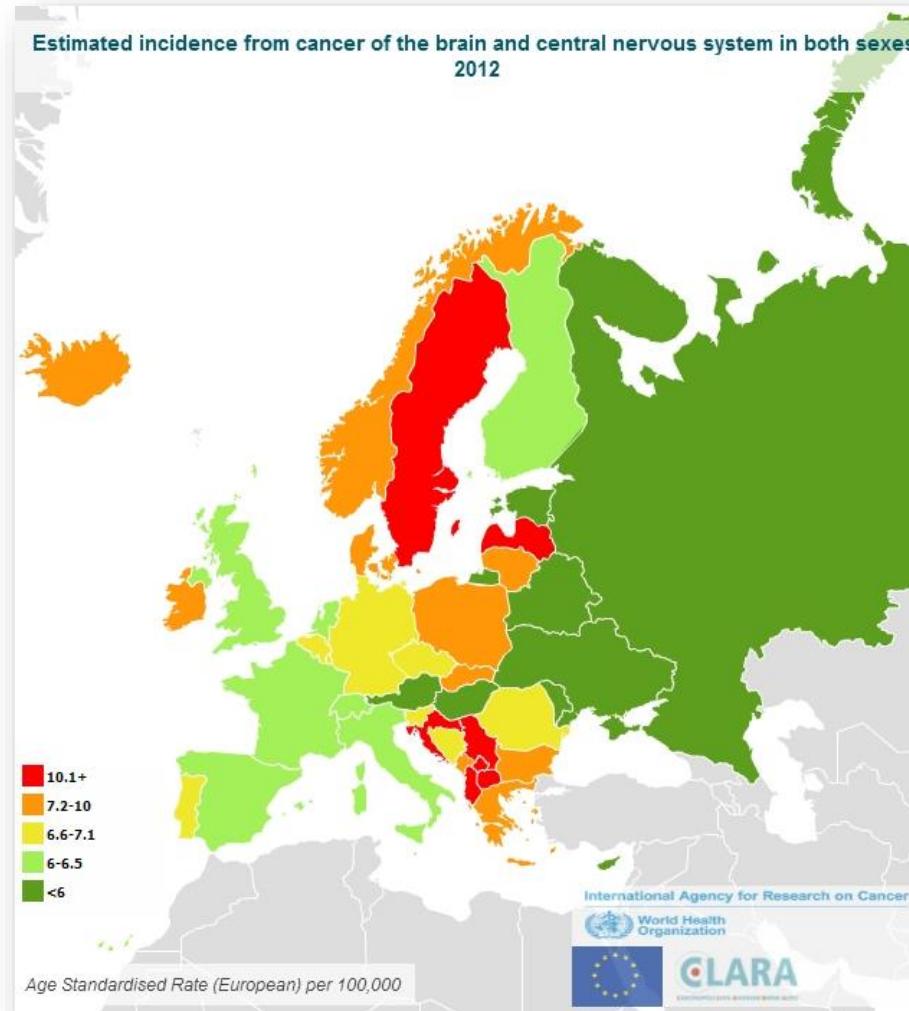
NEUROPATHOLOGY NEOPLASIA

HAJNALKA RAJNAI



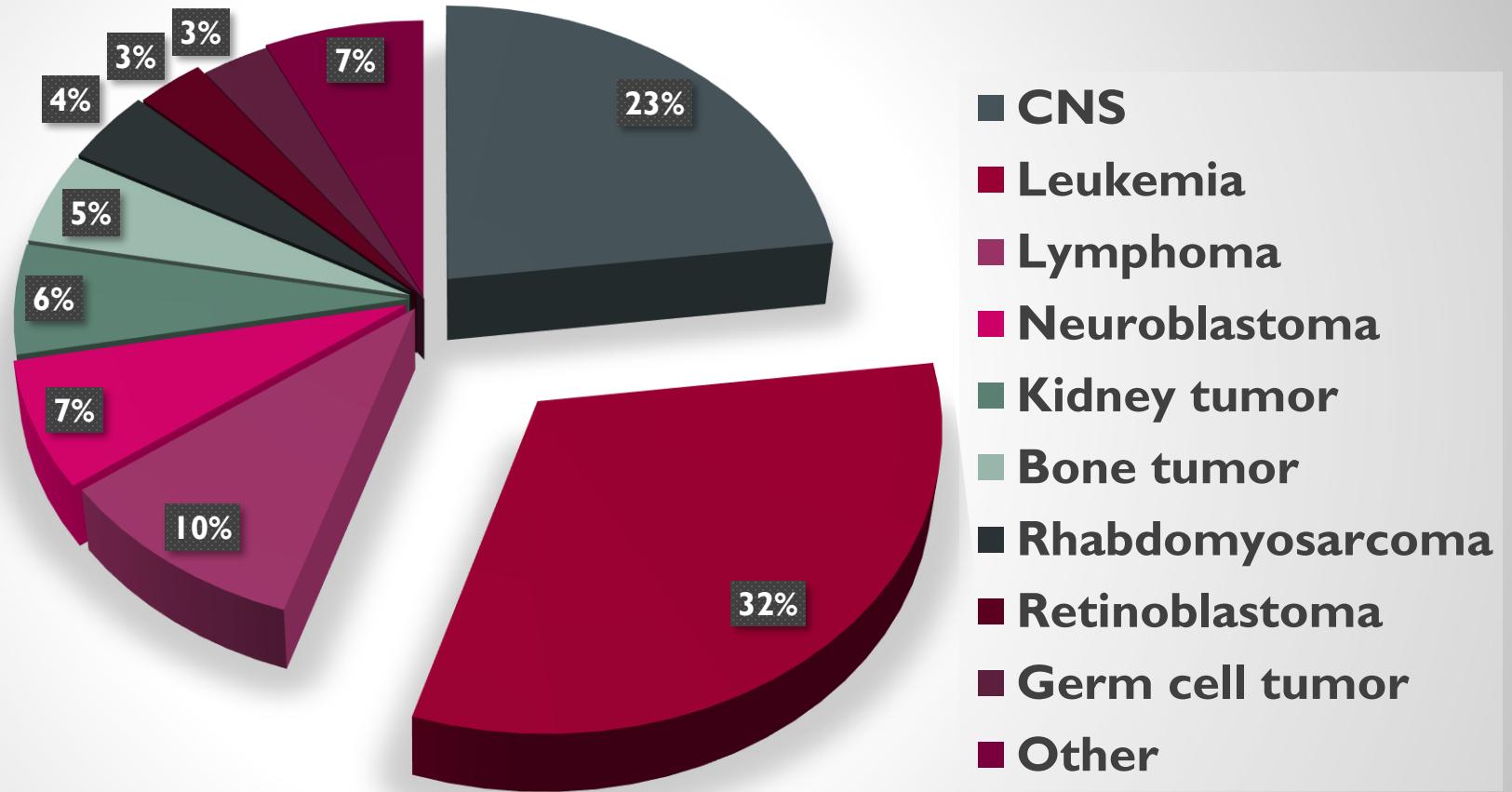


PRIMARY CNS NEOPLASIAS





INCIDANCE OF CHILDHOOD NEOPLASMS





PRIMARY TUMORS OF THE CNS



Gliomák



Neuronal or mixed glioneural tumors



Choroid plexus neoplasms



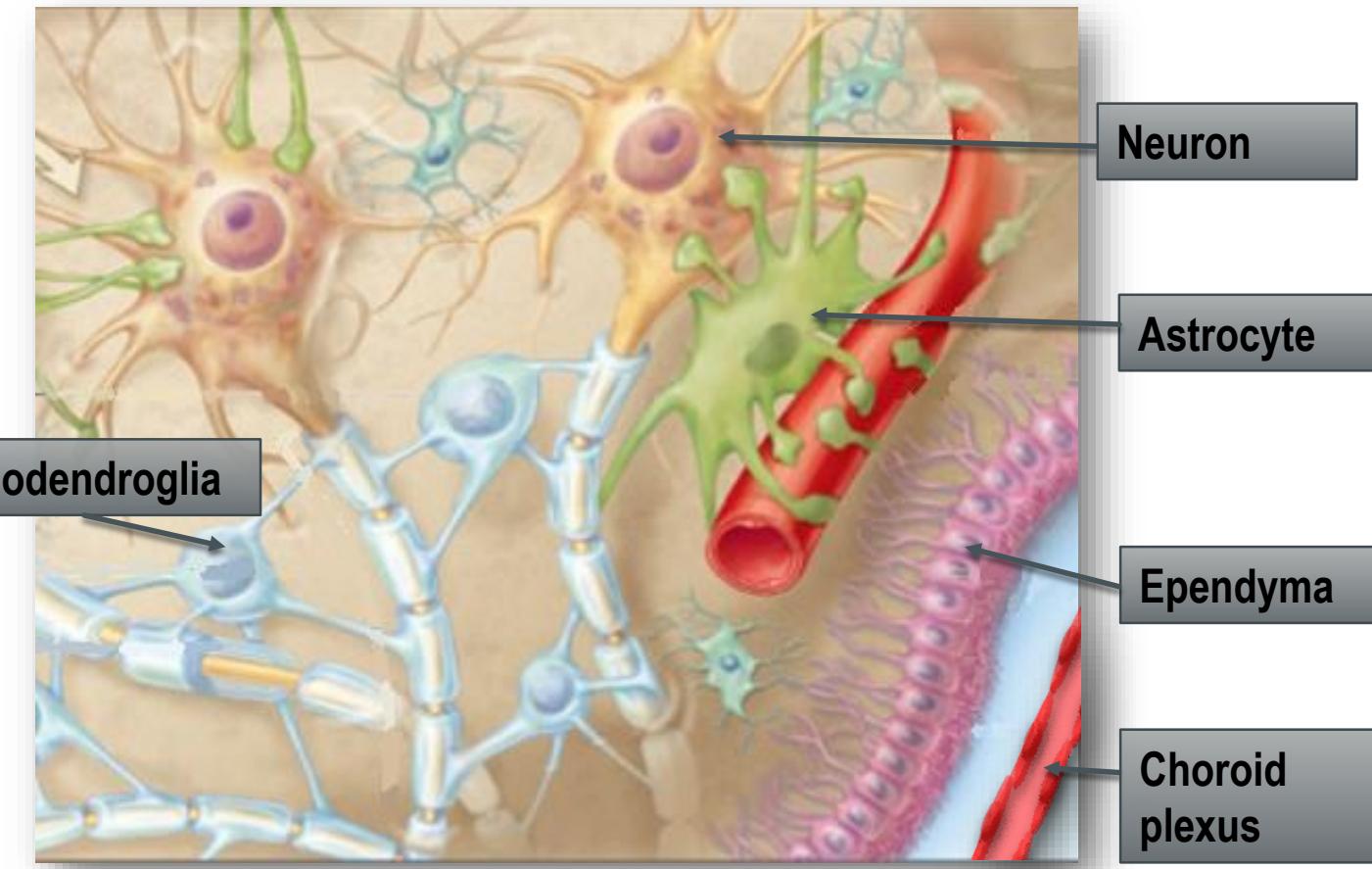
Embryonal tumors



Meningial tumors



- Other parenchymal tumors
- Haematologic malignancies
 - Germ cell tumors





CHARACTERISTICS

- Diagnosis
 - Age
 - Sex
 - Site of neoplasm
 - Family history
- Do not have premalignant or in situ stages
- Rarely spread outside of the CNS

Grade

- Predicting the biological behaviour
- Grade I
 - Low proliferative potential
 - Possibility of curative resection
- Grade II
 - Infiltrative
 - Often recur
 - Progression
- Grade III
 - Histological evidence of malignancy
 - High mitotic activity, atypia
- Grade IV
 - Cytologically malignant
 - Rapid disease evolution



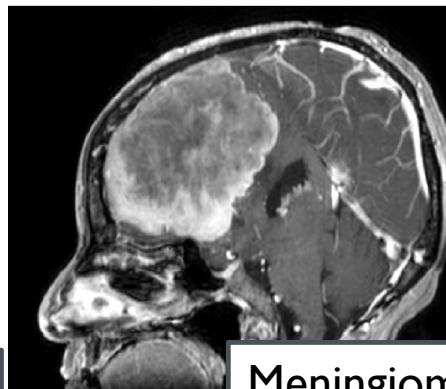
SYMPTOMS

Depends on site of tumor and growth speed

Symptoms of increased ICP

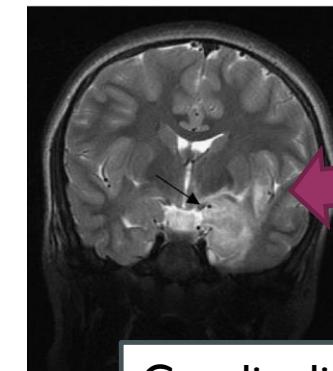


GBM



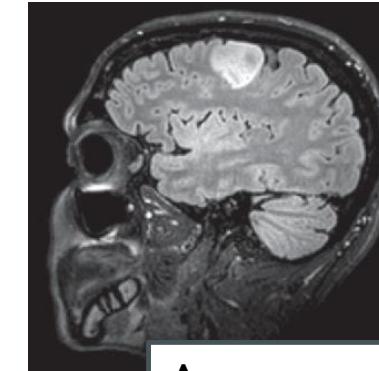
Meningioma

Epilepsy



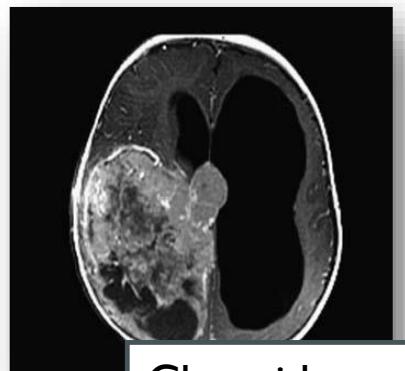
Ganglioglioma

Focal deficits



Astrocytoma

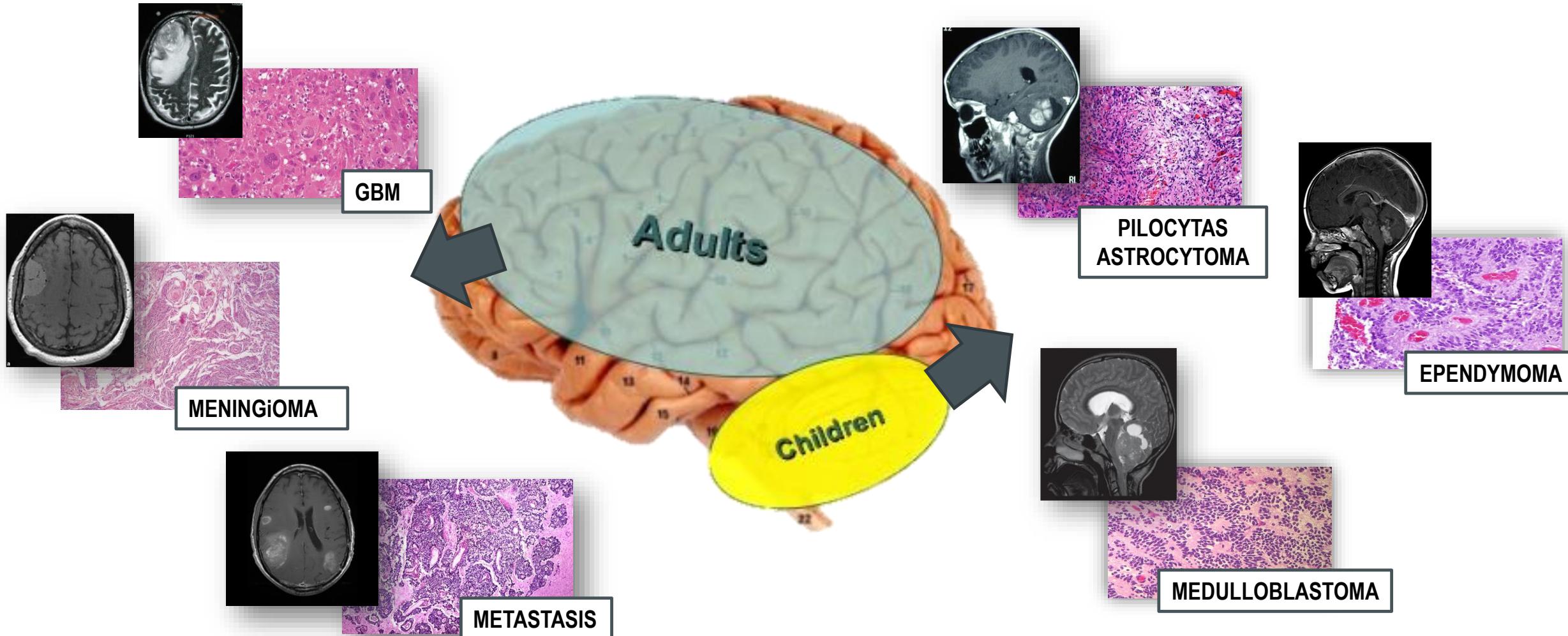
Hydrocephalus



Choroid
Plexus cc



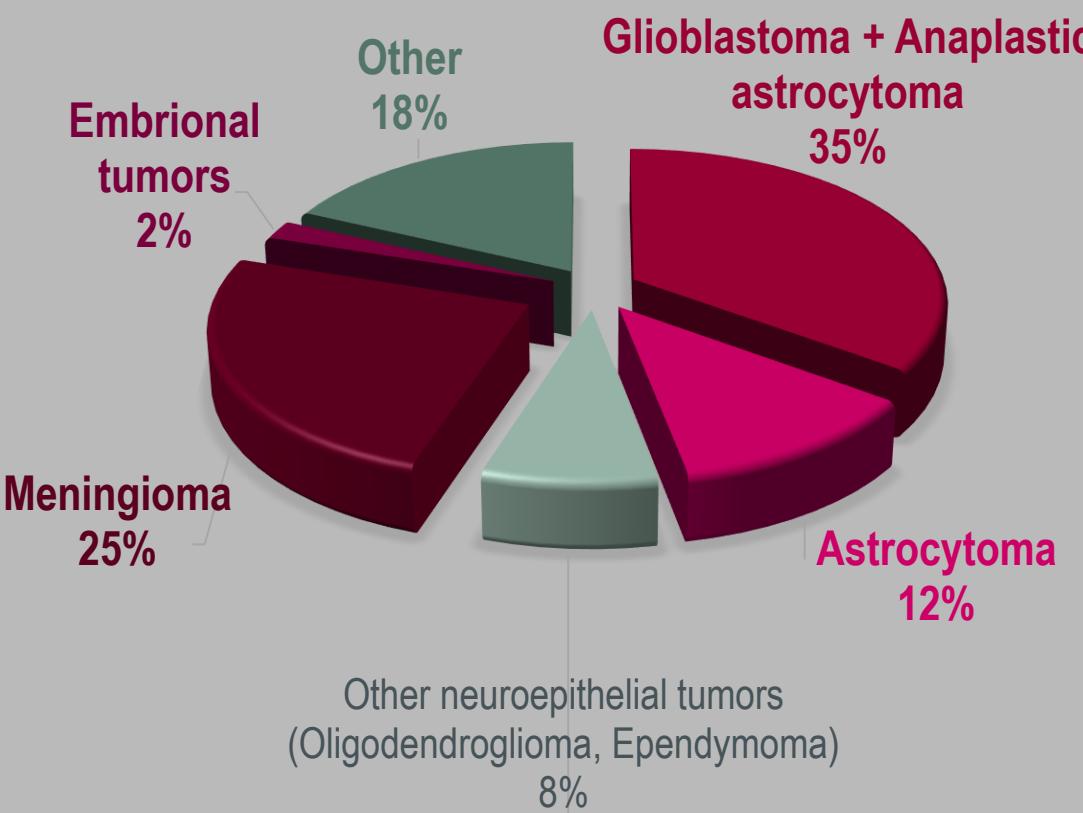
PRIMARY TUMORS OF THE CNS



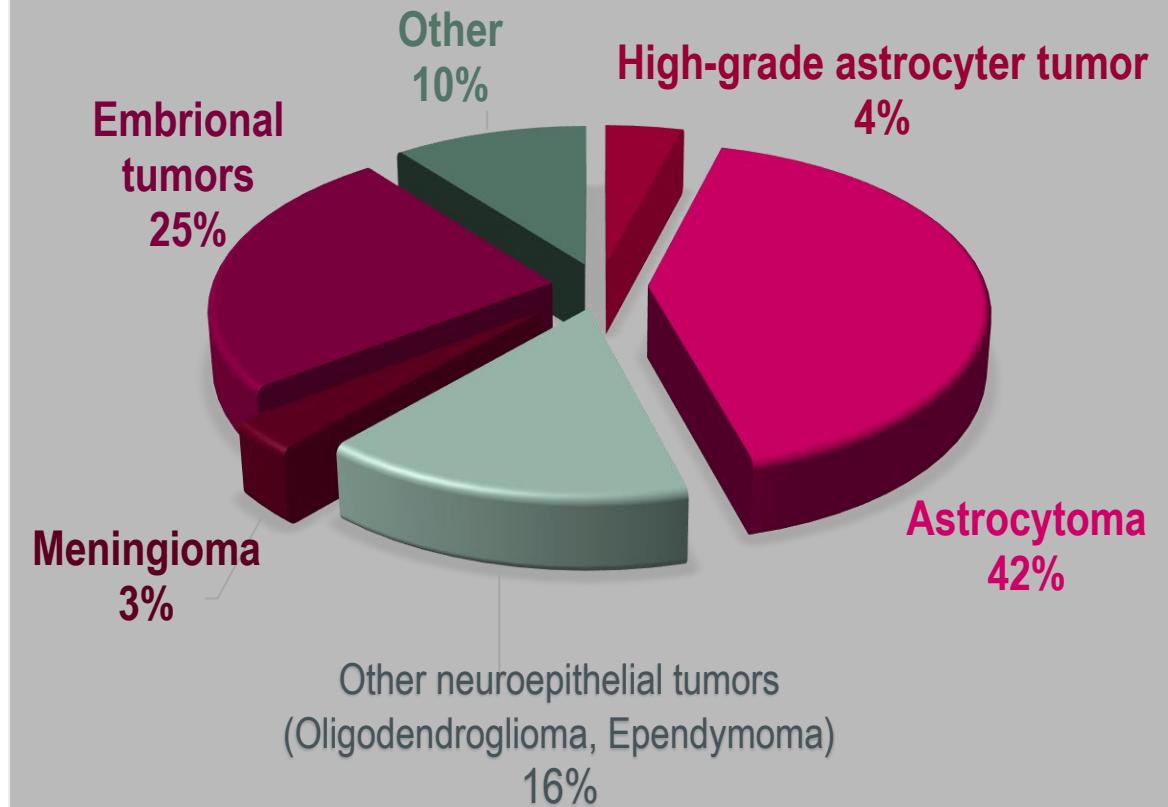


PRIMARY TUMORS OF THE CNS

ADULT CNS TUMORS

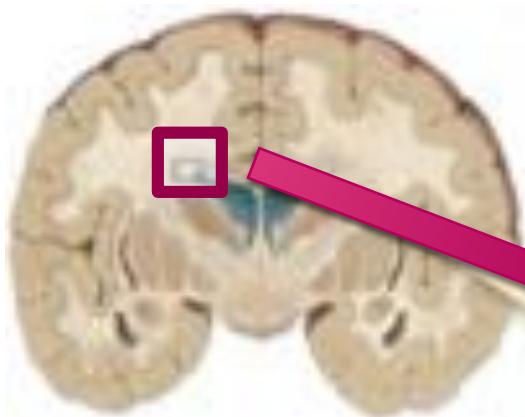


PEDIATRIC CNS TUMORS

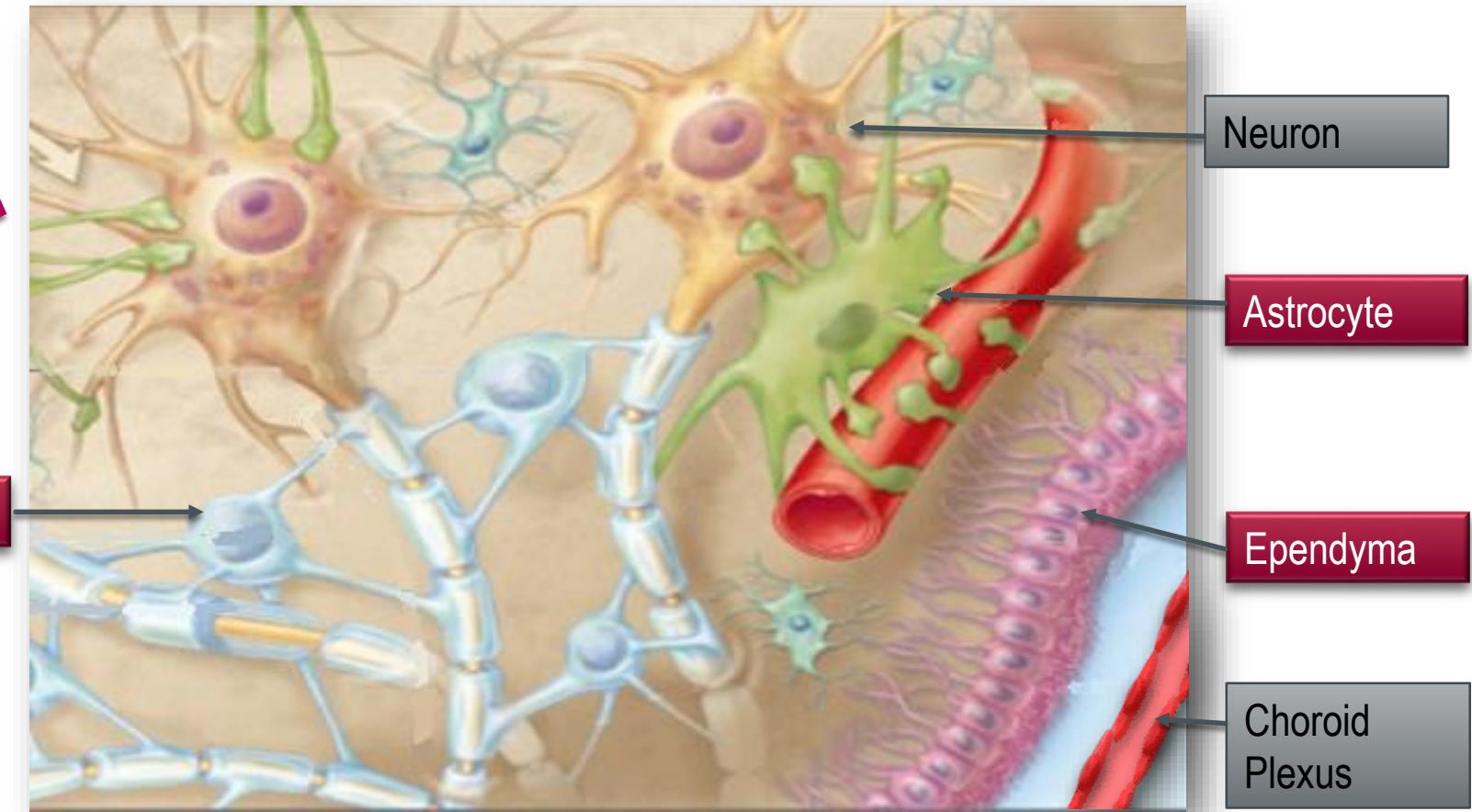




I. GLIOMAS



Oligodendroglia





GRADE I
GRADE II
GRADE III
GRADE IV



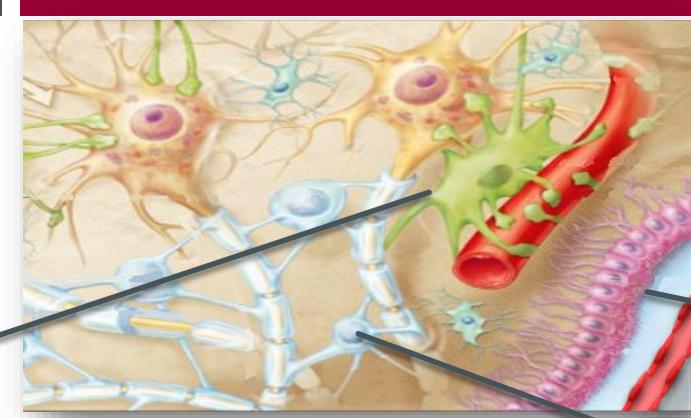
Astrocytomas

Pilocytic astocytoma

Diffuse astocytoma

Anaplastic astocytoma

Glioblastoma

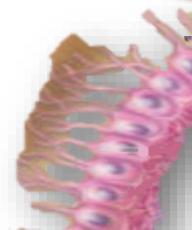


Oligodendrogliomas



Oligodendroglioma

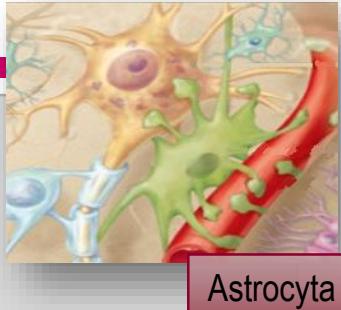
Anaplastic Oligodendroglioma



Ependymomas

Ependymoma

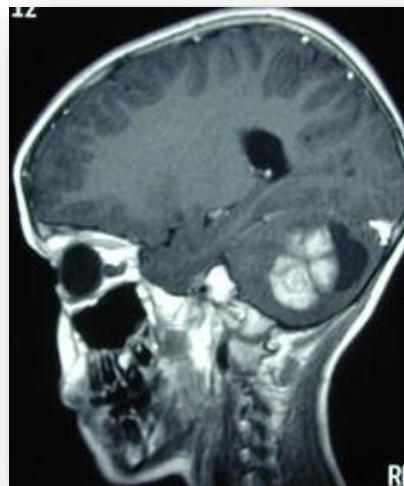
Anaplastic Ependymoma



CNS Tumors with astrocytic differentiation

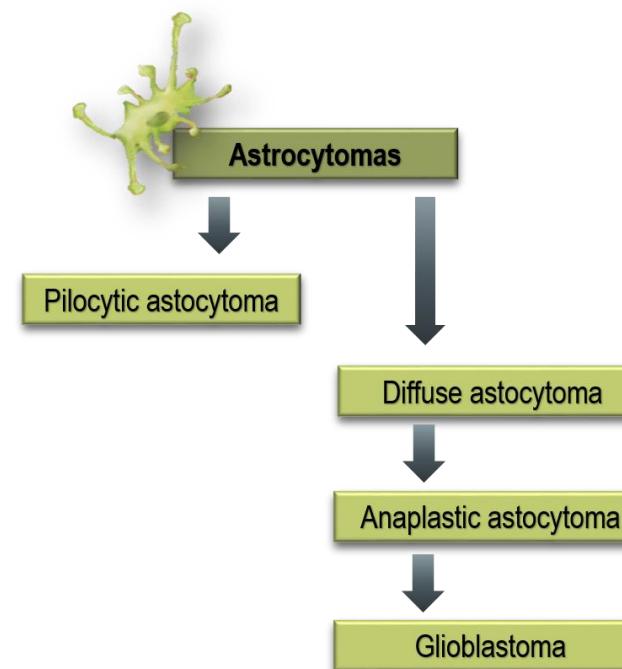
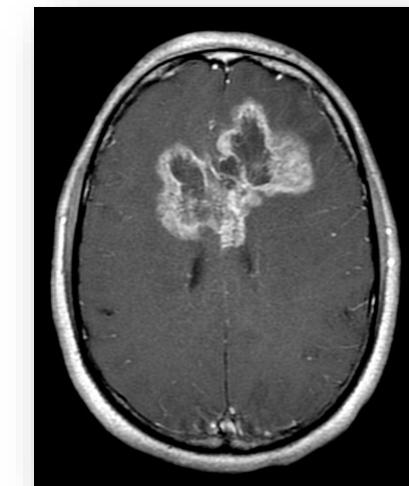
Pilocytic astrocytoma (Grade I)

- Children, young adults
- Localised
- Posterior fossa

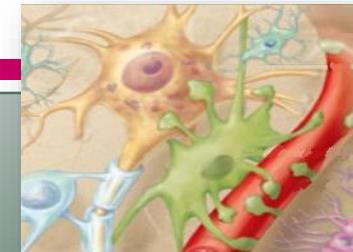


Diffuse astrocytomas (Grade II-IV)

- Middle aged, older patients
- Infiltrating
- Hemispherical

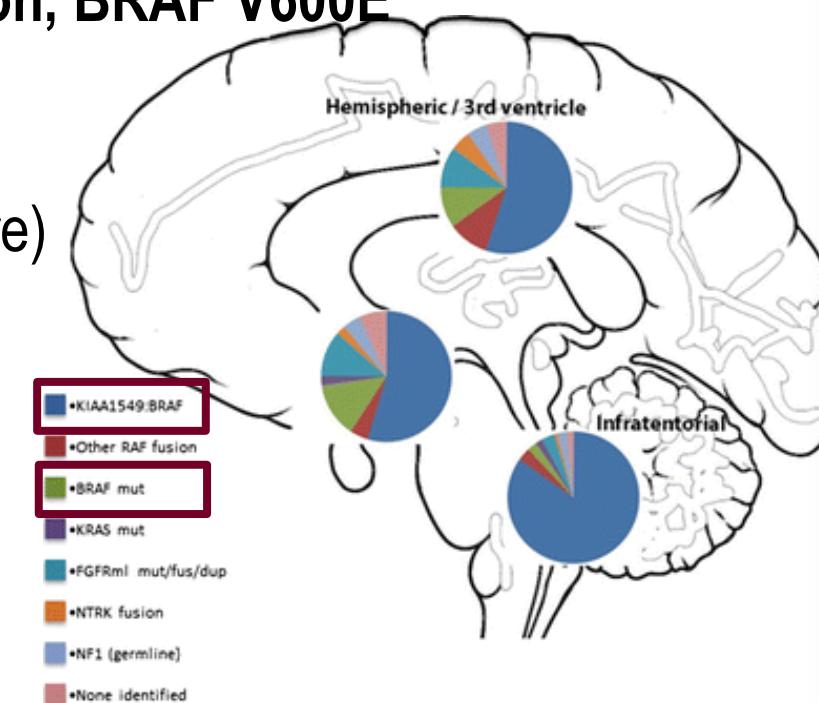
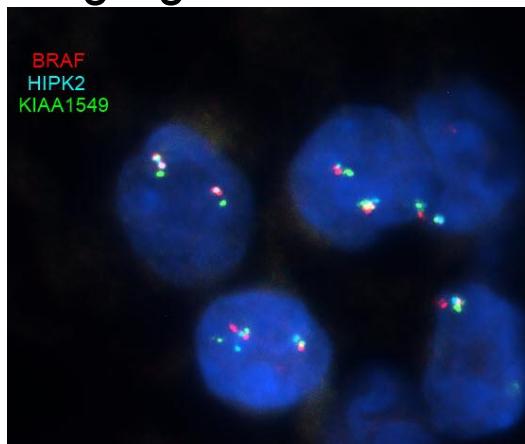


Pilocytic astrocytoma (Grade I)



Astrocyta

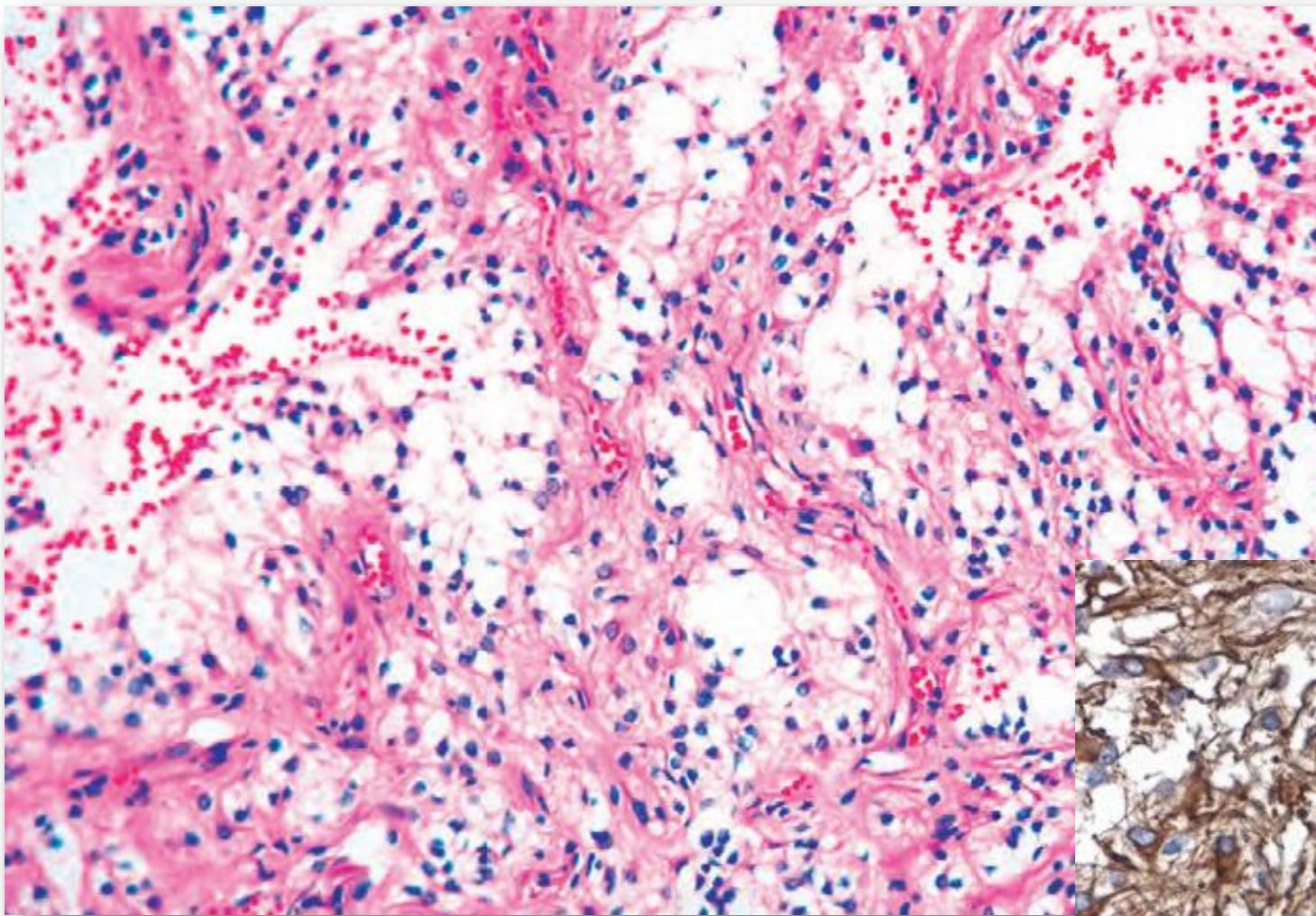
- Children and young adults
- Common(18%) benign CNS tumor in children
- Most commonly infratentorial – Cerebellum
- **BRAF/KIAA1549 translocation, BRAF V600E**
- MAPK pathway mutations
- High-grade transformation (rare)



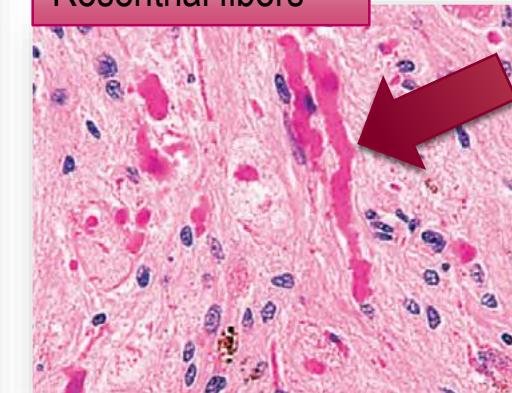
Pilocytic astrocytoma (Grade I)



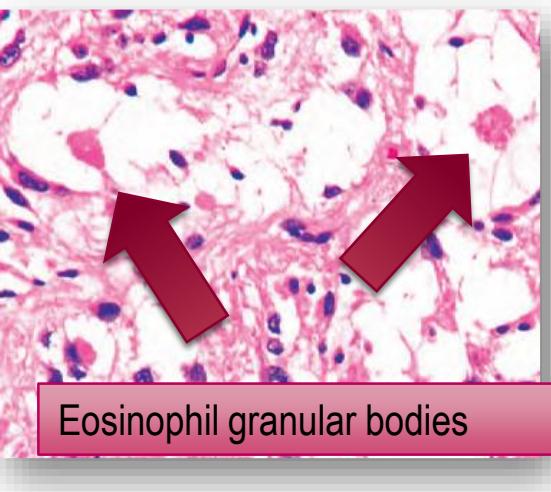
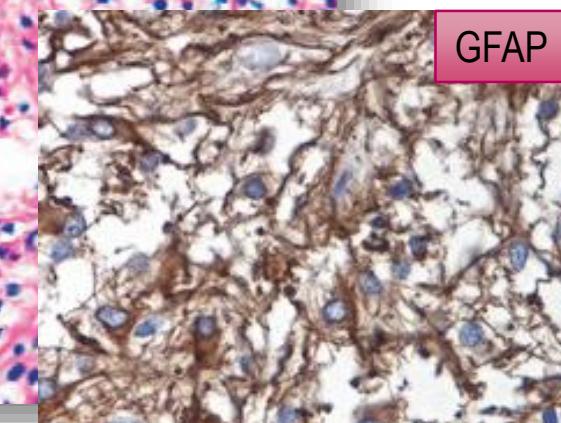
Astrocyte



Rosenthal fibers



GFAP



Eosinophil granular bodies



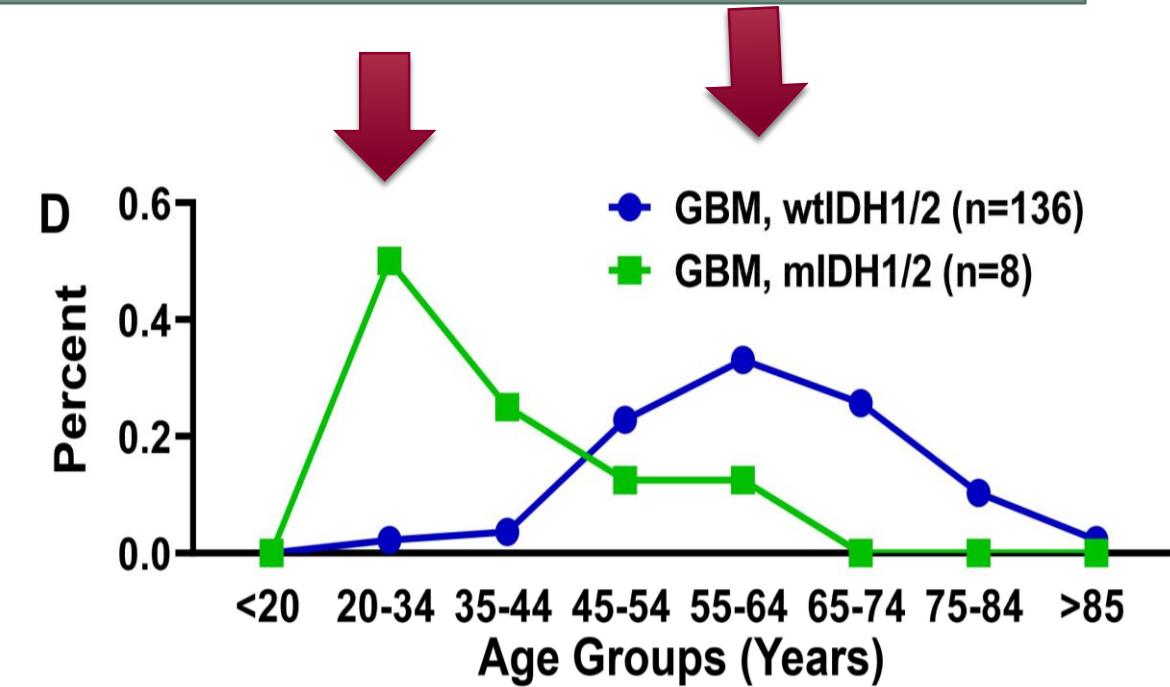
Diffuse gliomas with astrocytic differentiation (Grade II-IV)

- Two age groups
 - 20-35 years
 - Grade II → Grade III → Grade IV
 - IDH gene mutation
 - >60 years
 - Grade IV
- Hemispherical – Focal neurological deficits

Well-differentiated diffuse astrocytoma Grade II

Anaplastic astrocytoma Grade III

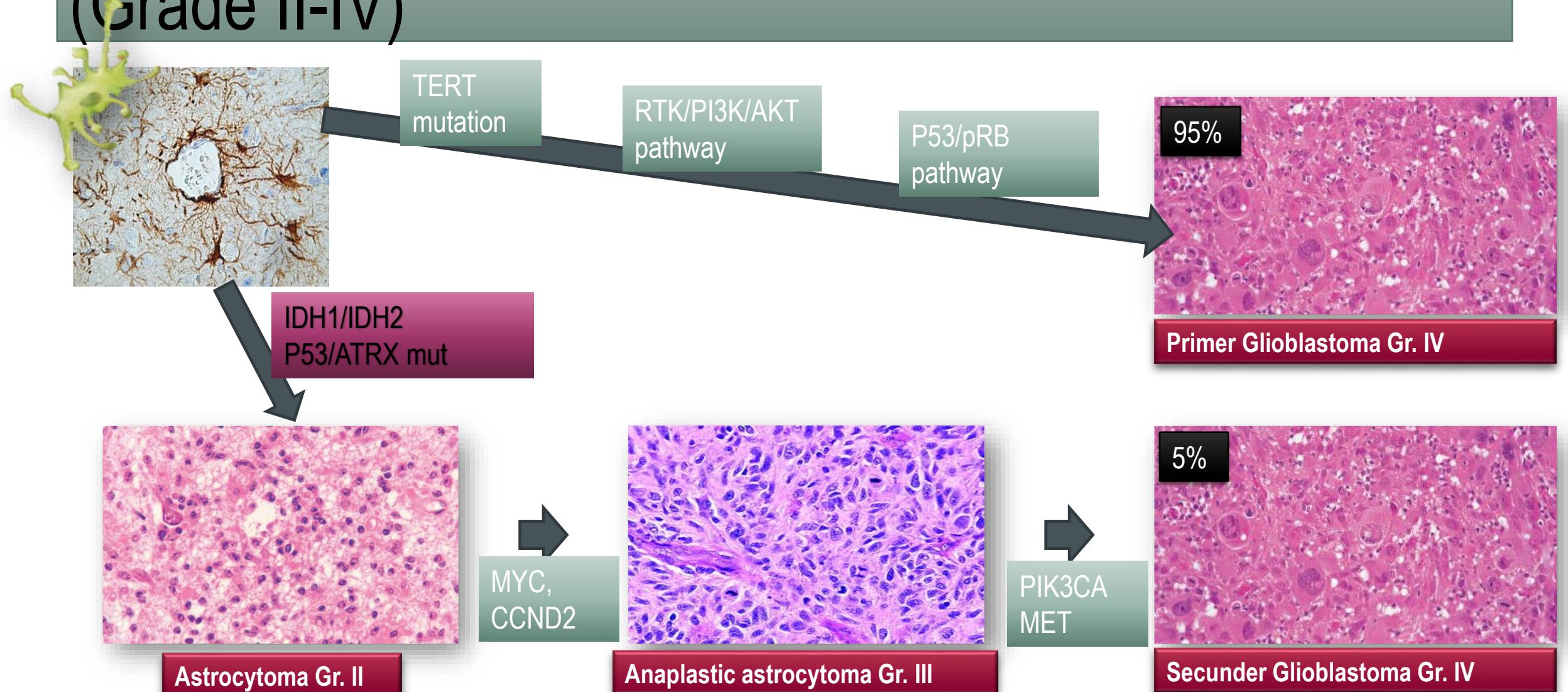
Glioblastoma Grade IV



- Similar prognosis in both age groups
- Survival: 15-20 months

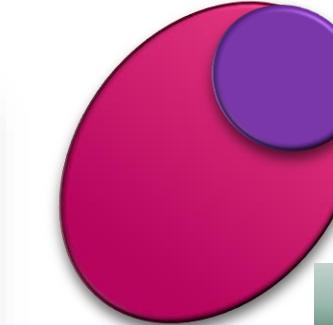
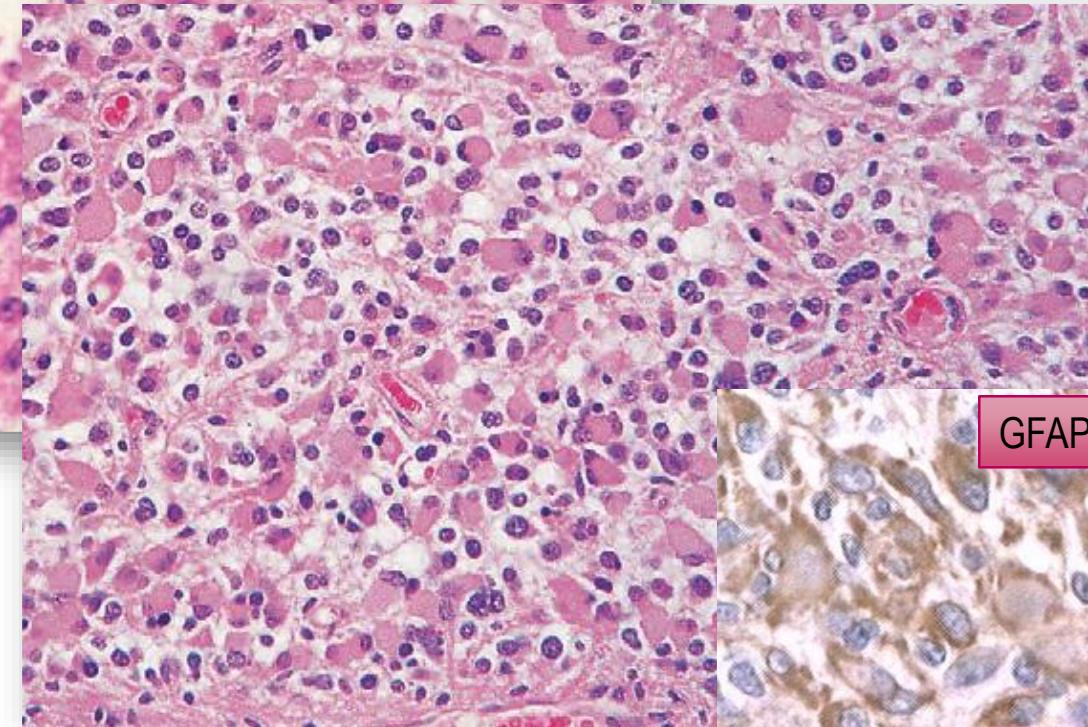
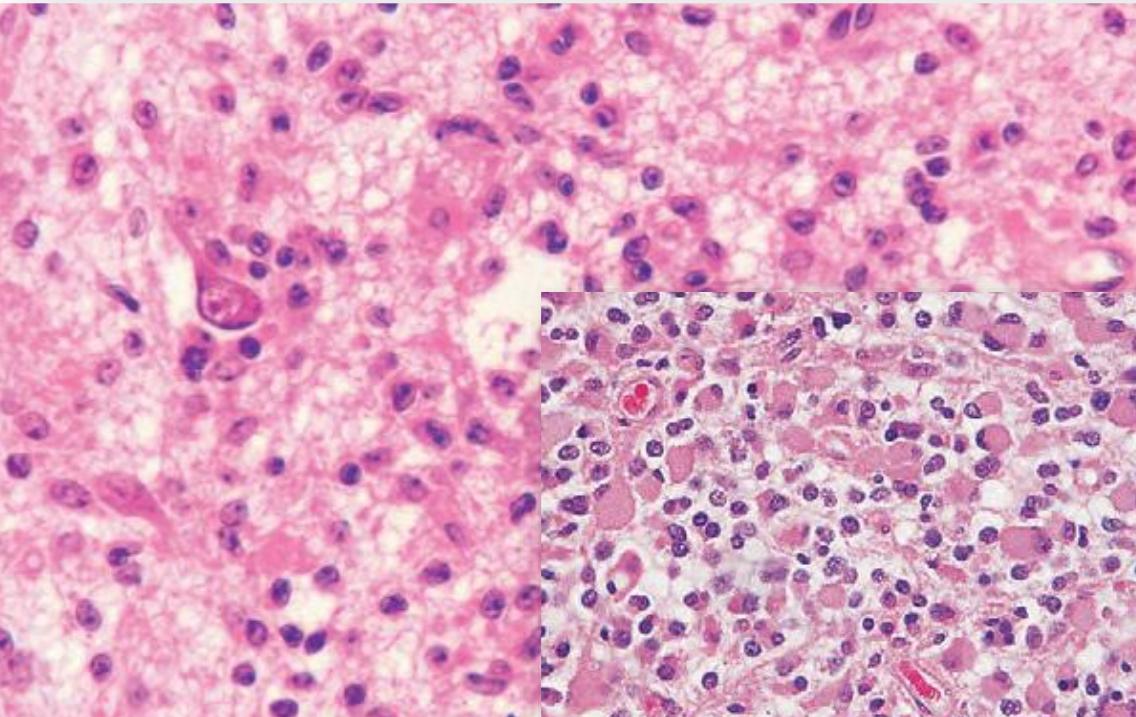


Diffuse gliomas with astrocytic differentiation (Grade II-IV)

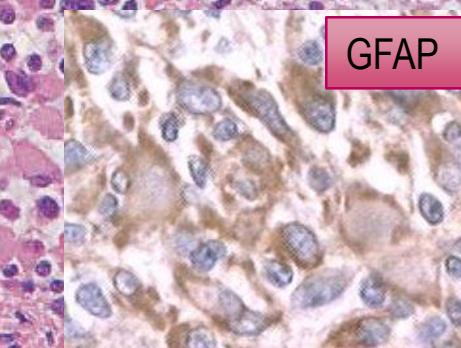


Diffuse astrocytoma Grade II

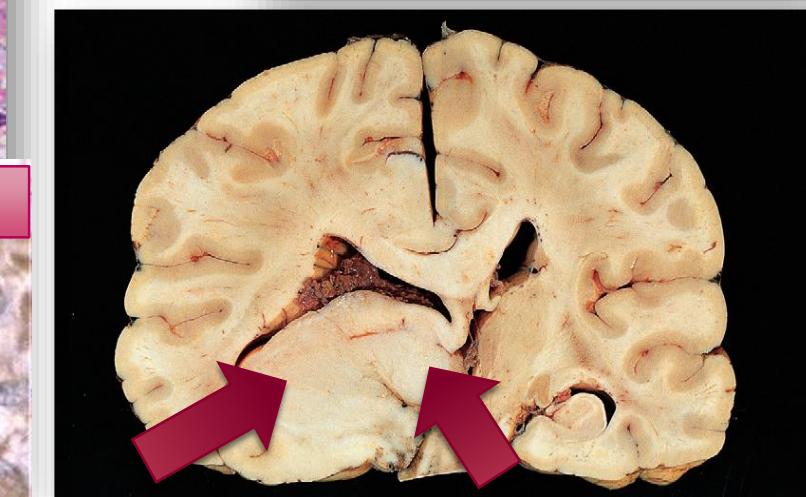
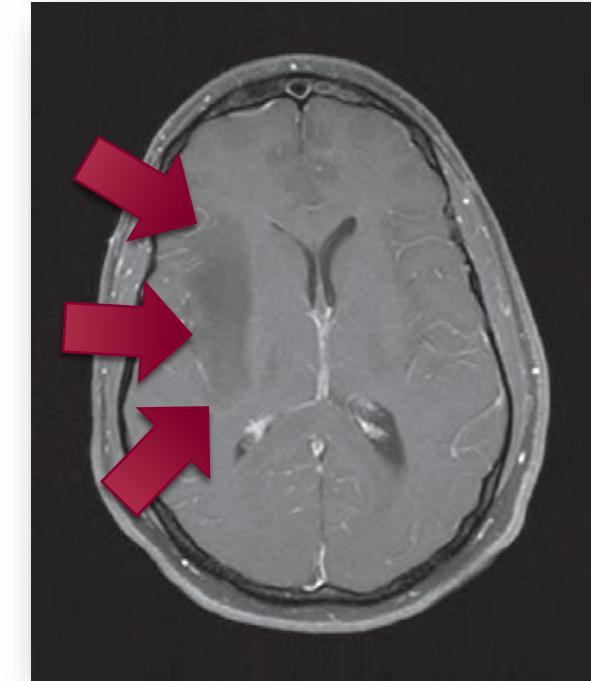
- Atypia+ High cellularity



Gemistocyte

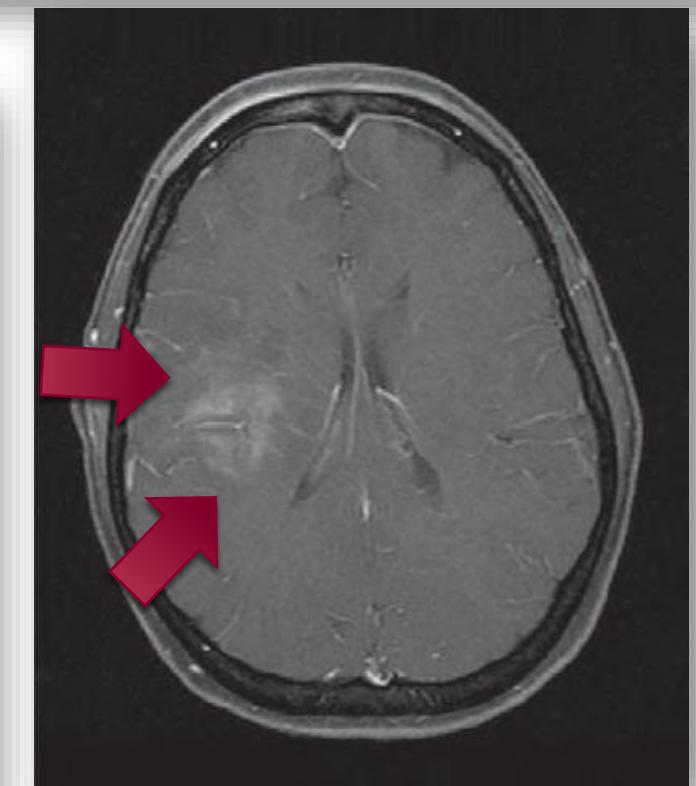
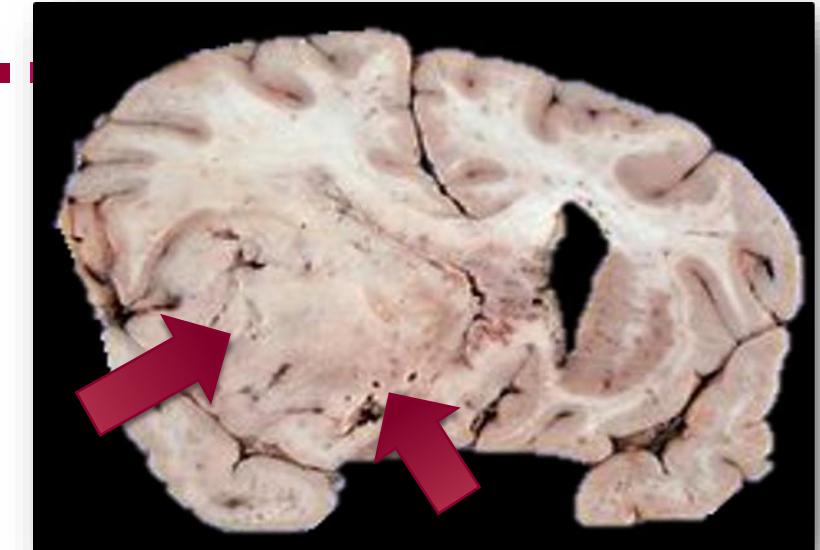
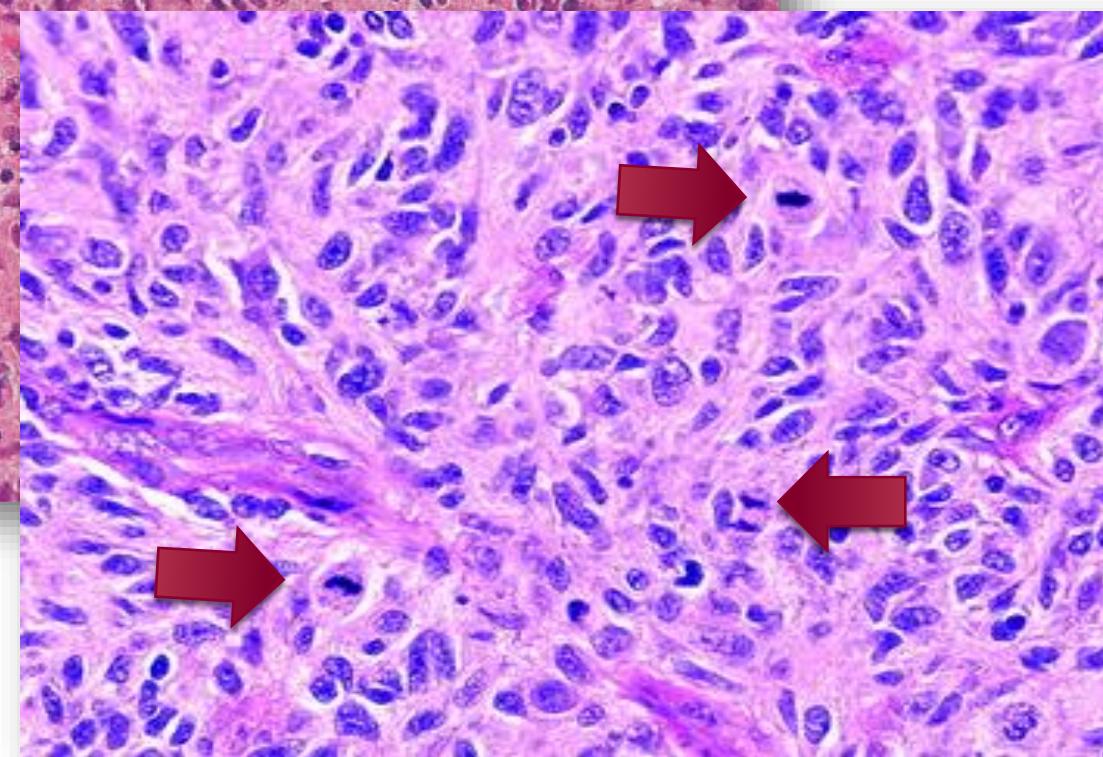
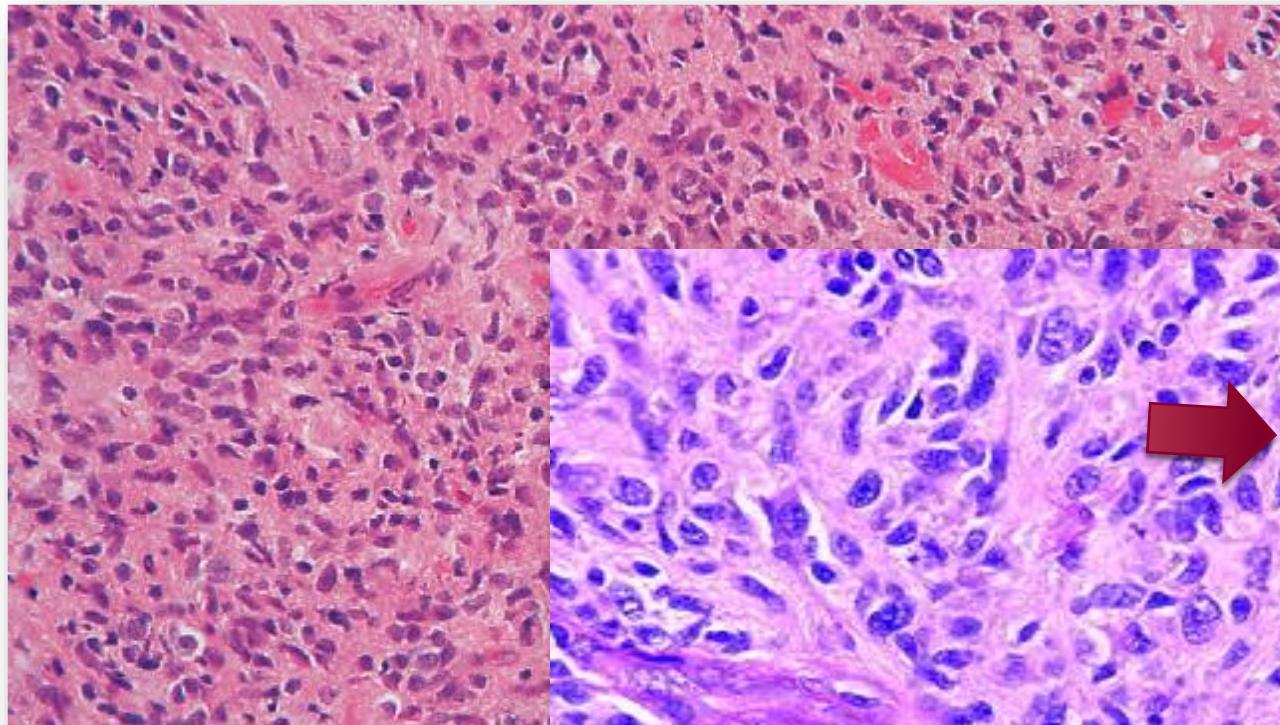


GFAP



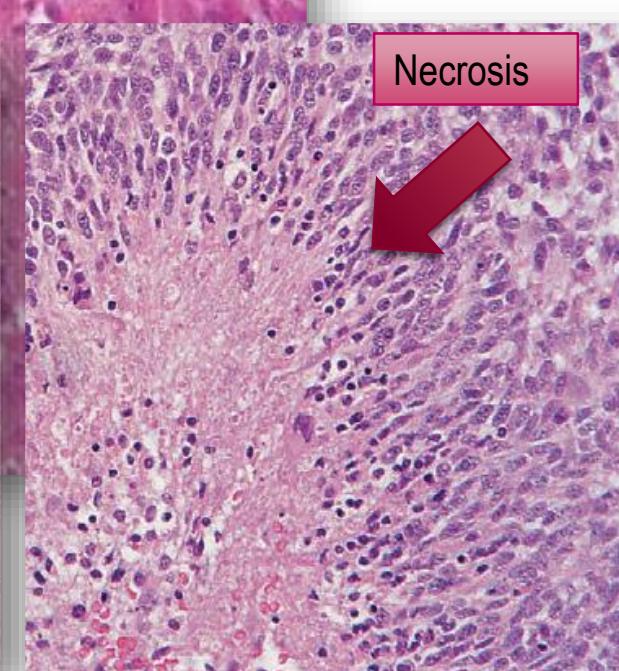
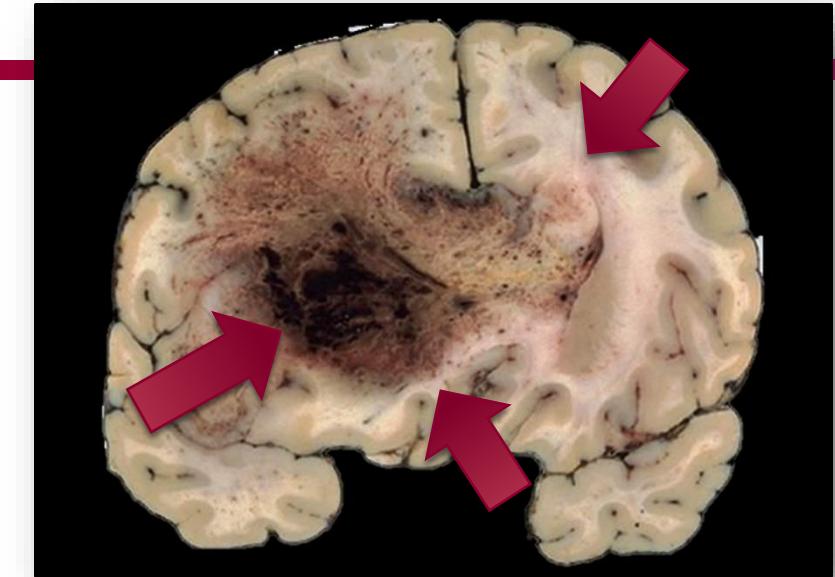
Anaplastic astrocytoma Grade III

- Atypia + High cellularity + High mitotic activity



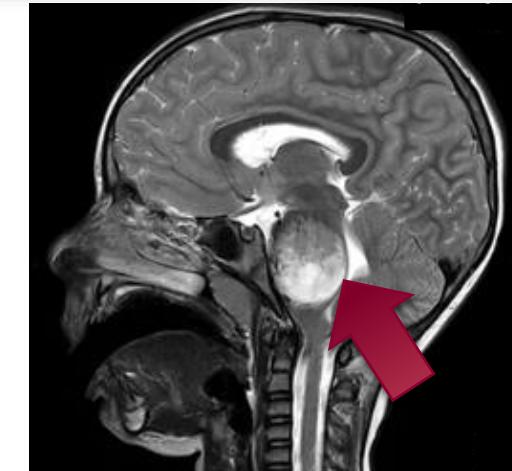
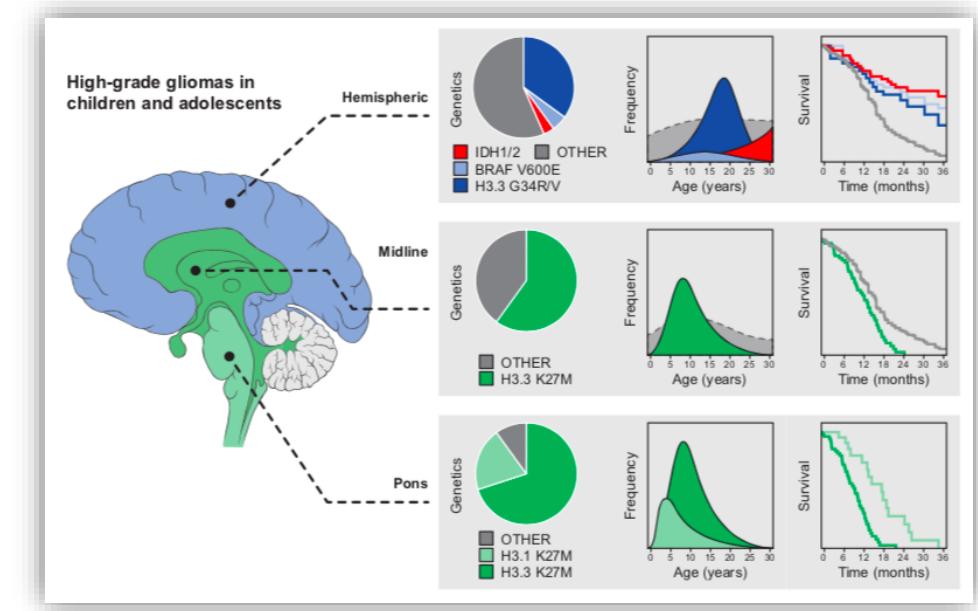
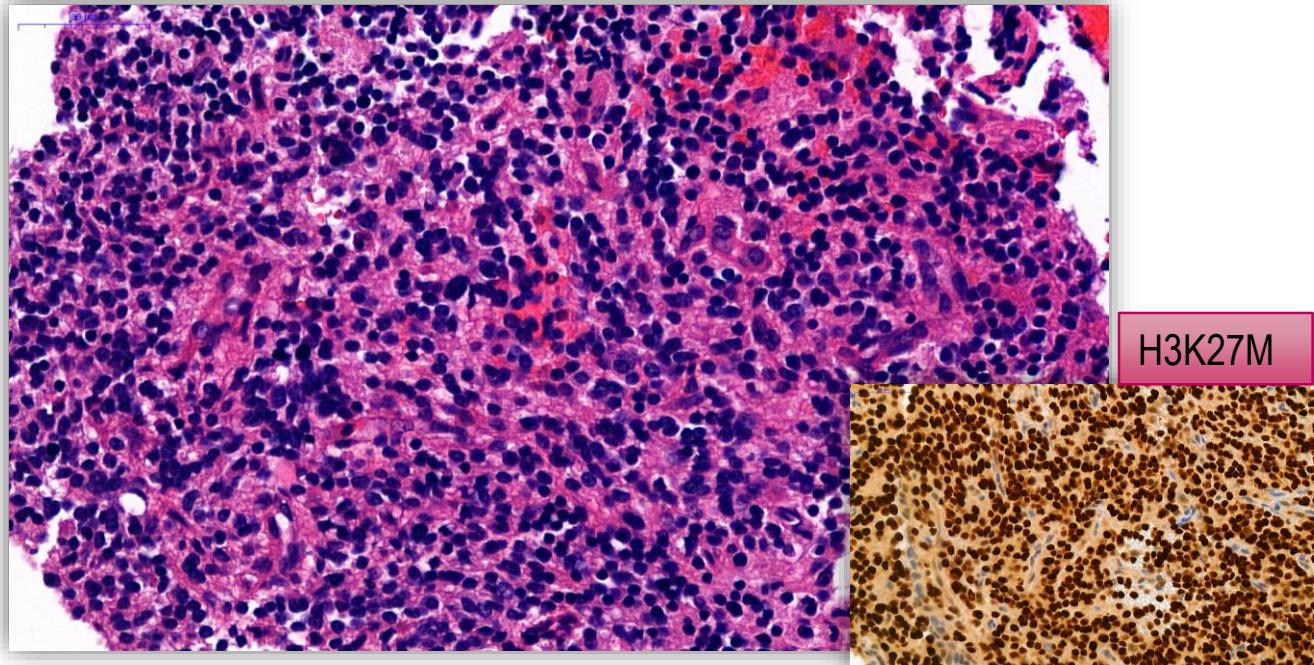
Glioblastoma Grade IV

- Atypia + High cellularity + High mitotic activity + Necrosis/Endothel proliferation



DIFFUSE MIDLINE GLIOMA, H3 K27M MUTANT (GRADE IV)

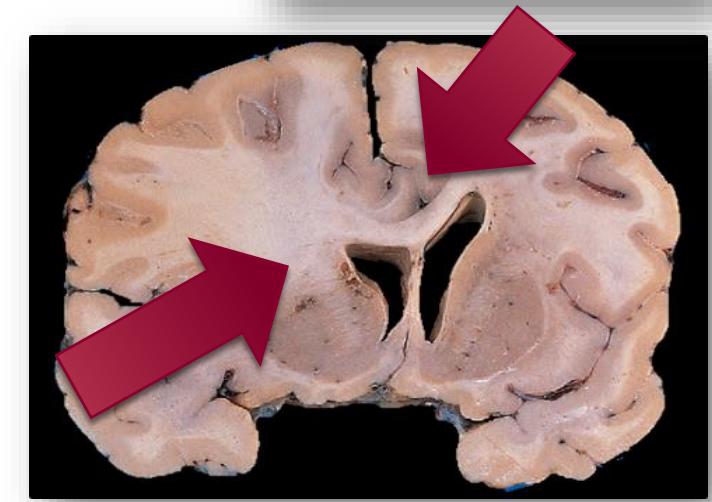
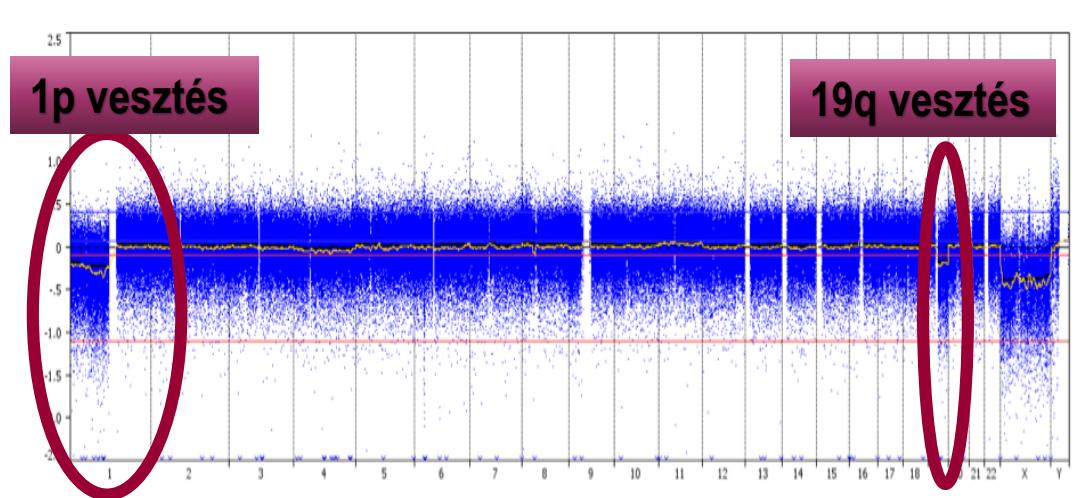
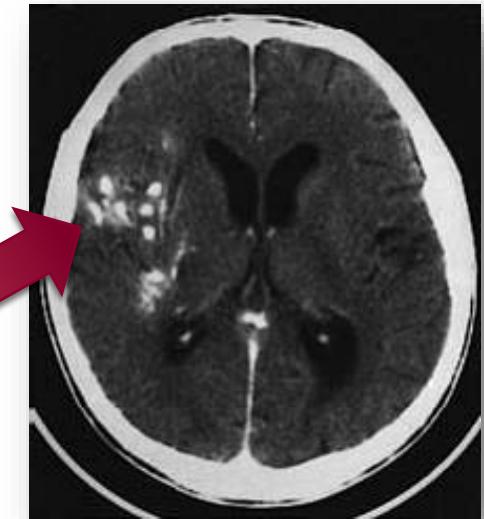
- 5 - 10 years of age, but older age groups
- 10% of all malignant pediatric CNS tumors
- Brainstem, thalamus and spinal cord
- High-grade even if low-grade morphology (~10%)





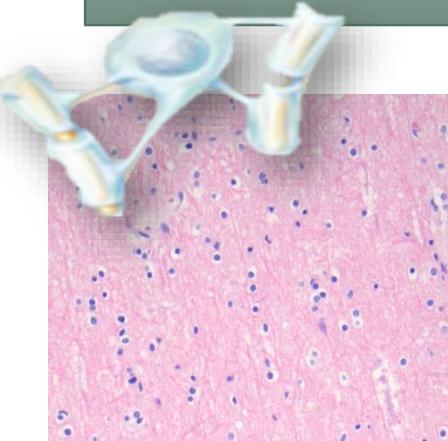
Oligodendroglial tumors(Grade II-III)

- Fourth and fifth decades of life
- Cerebral hemispheres – Seizure, headache
 - Frontal, temporal lobe
- 1p 19q codeletion

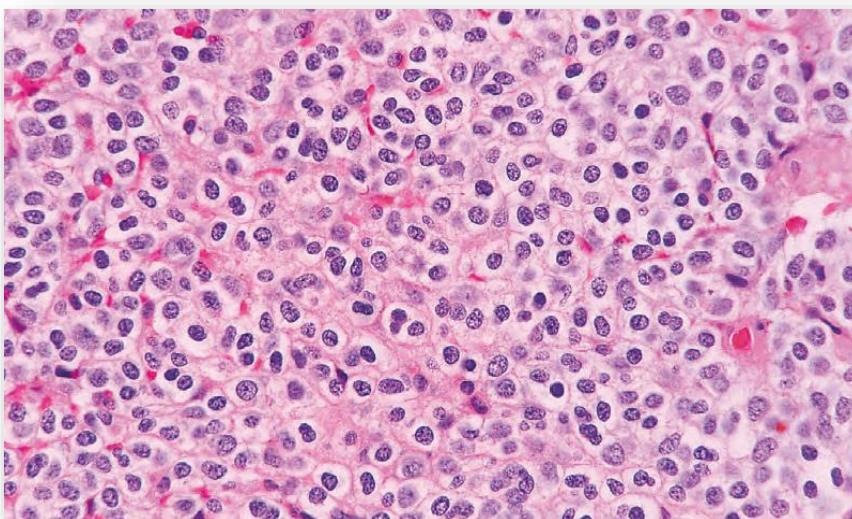




Oligodendroglial tumors(Grade II-III)

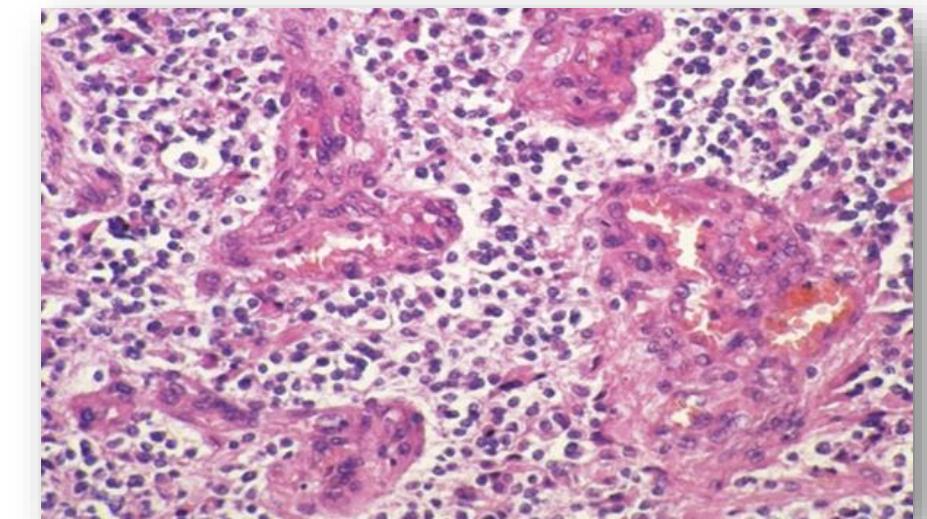


IDH1/IDH2
1p/19q codeletion, TERT,
CIC FUBP1



Oligodendrogloma Gr. II

CDKN2A

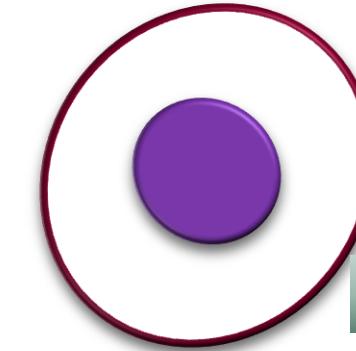
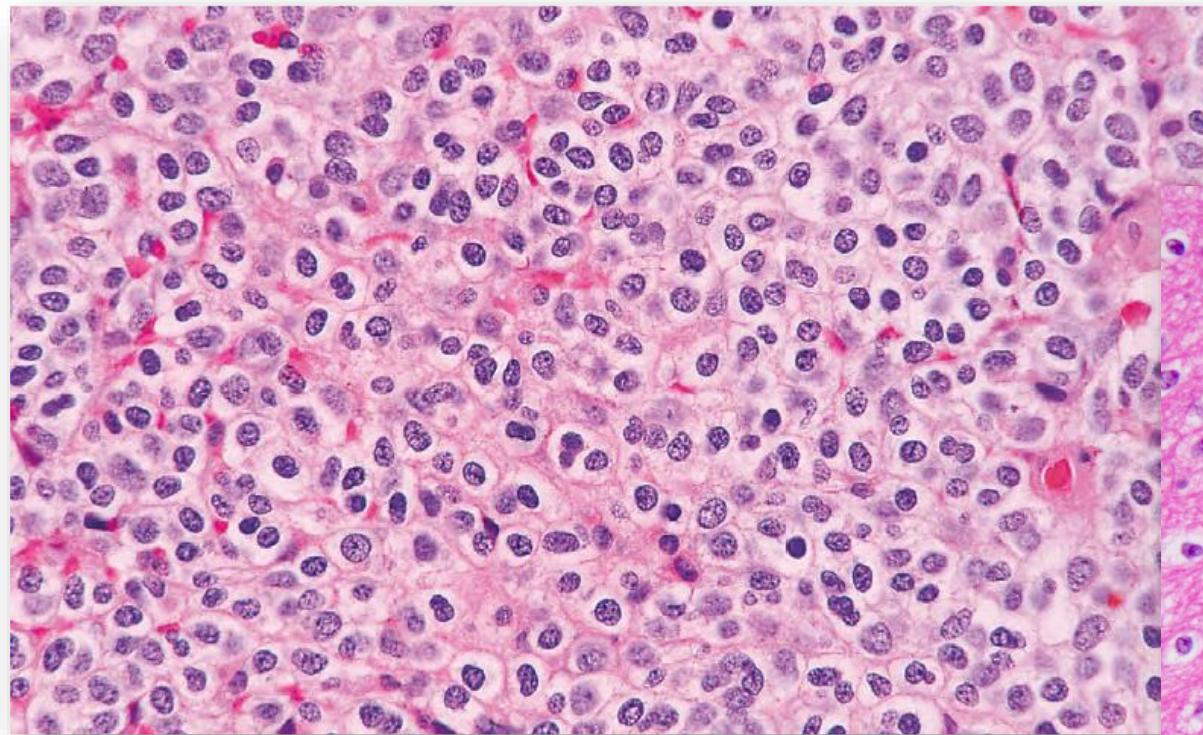


Anaplastic oligodendrogloma Gr. III

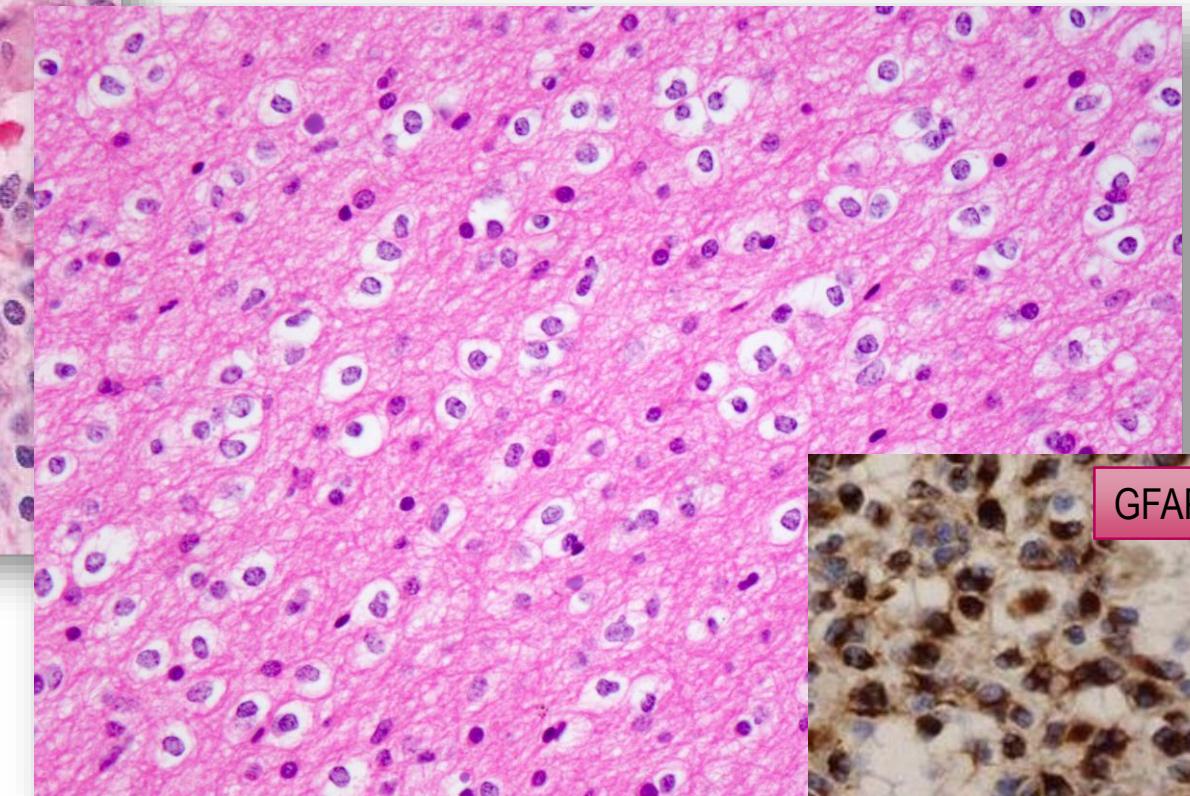


Oligodendroglioma Grade II

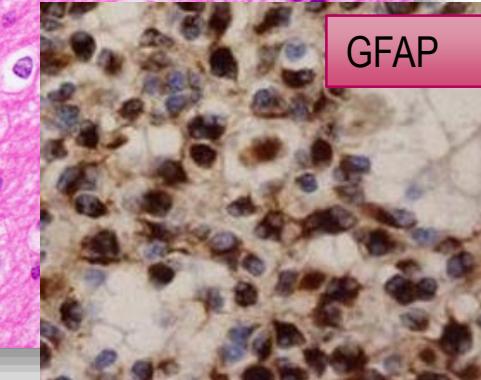
- Atypia+ High cellularity



Fried-egg cells



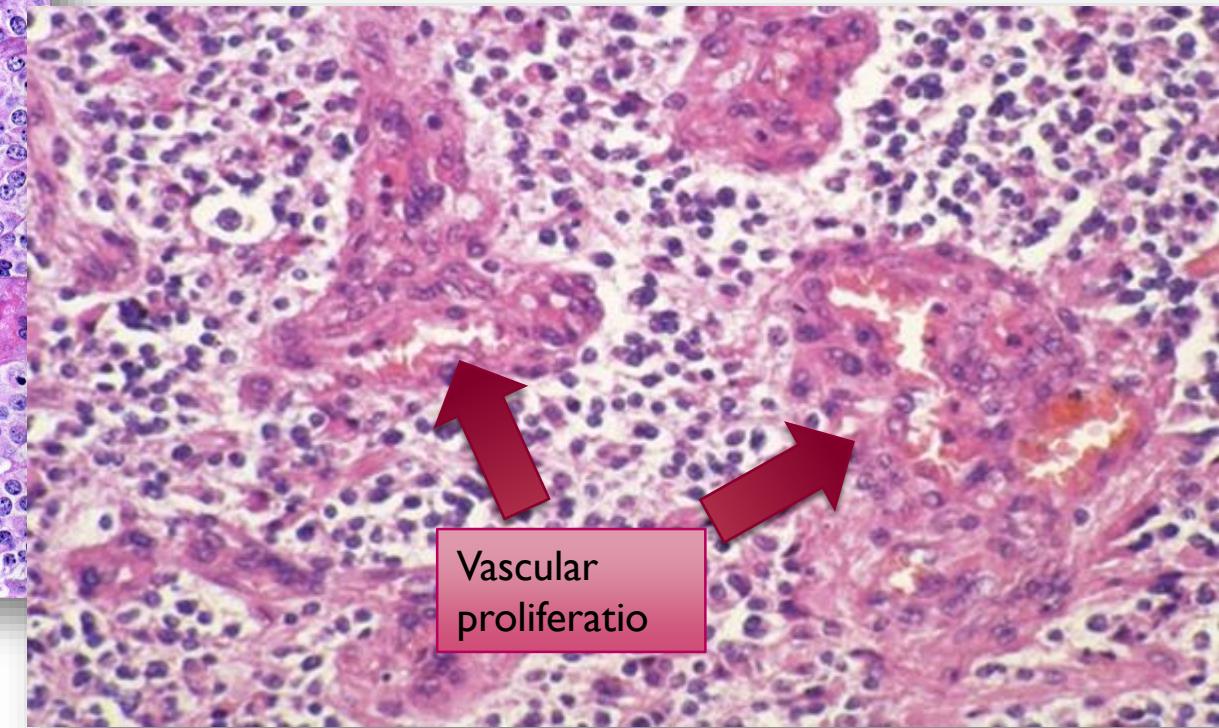
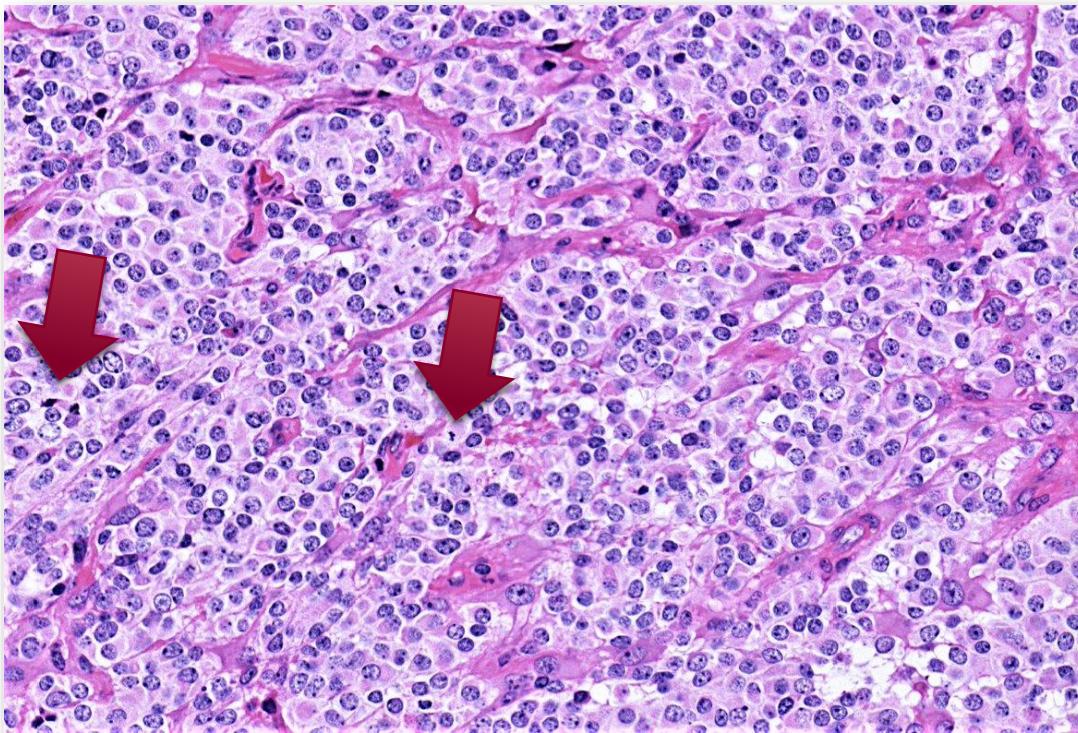
GFAP





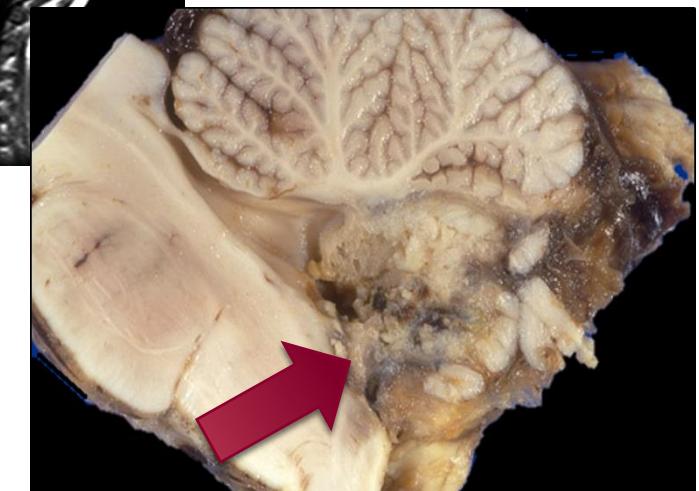
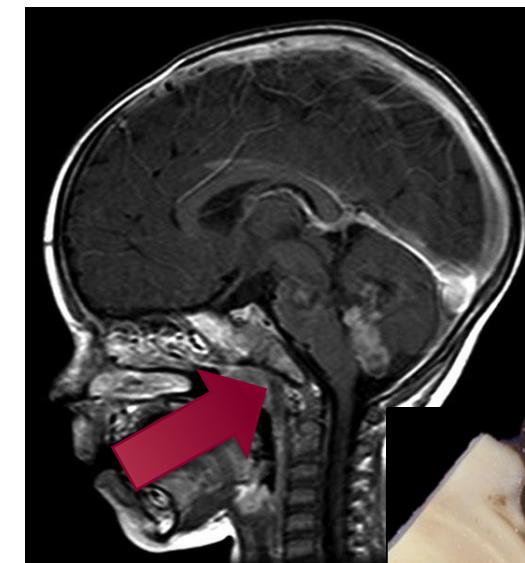
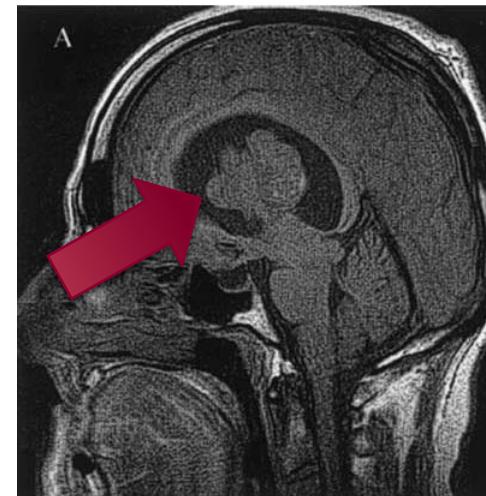
Anaplastic oligodendrogloma Grade III

- Atypia + High cellularity + High mitotic activity + Necrosis/Endothel proliferation

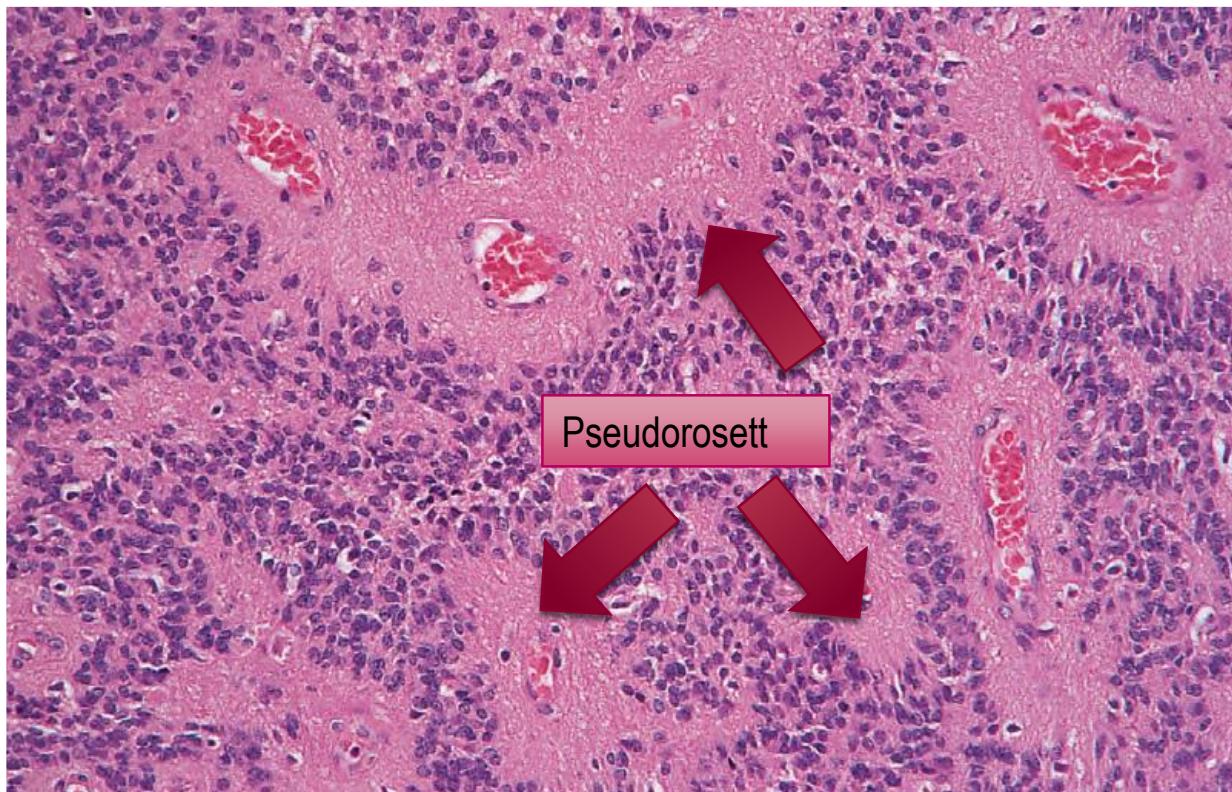


Ependymal tumors

- Supratentorial
 - Lateral ventricles
 - Young adults
- Infratentorial
 - 4th ventricle
 - Childhood
- Spinal ependymoma
 - Canalis centralis
 - 20-40 years of age

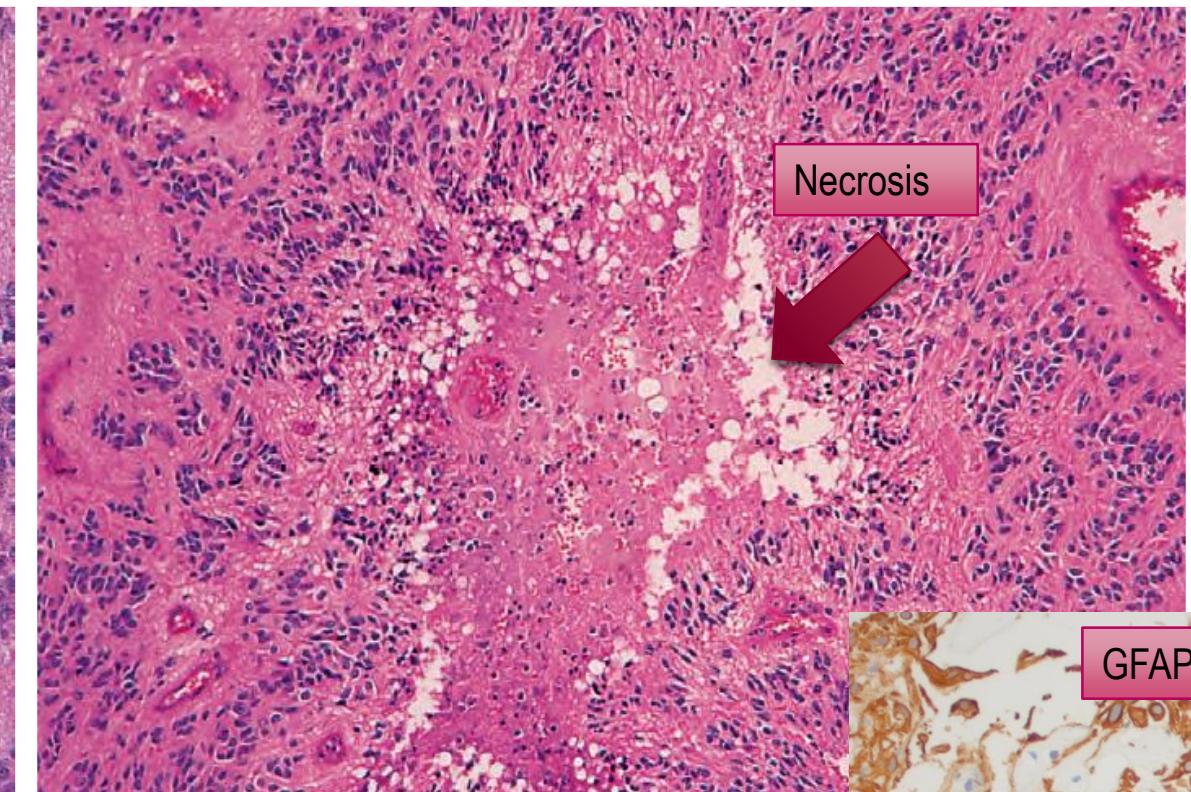


Ependymoma Grade II



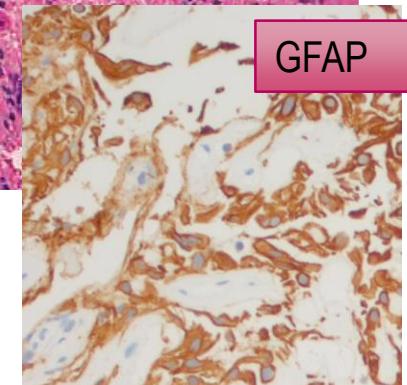
Pseudorosette

Anaplastic ependymoma Grade III

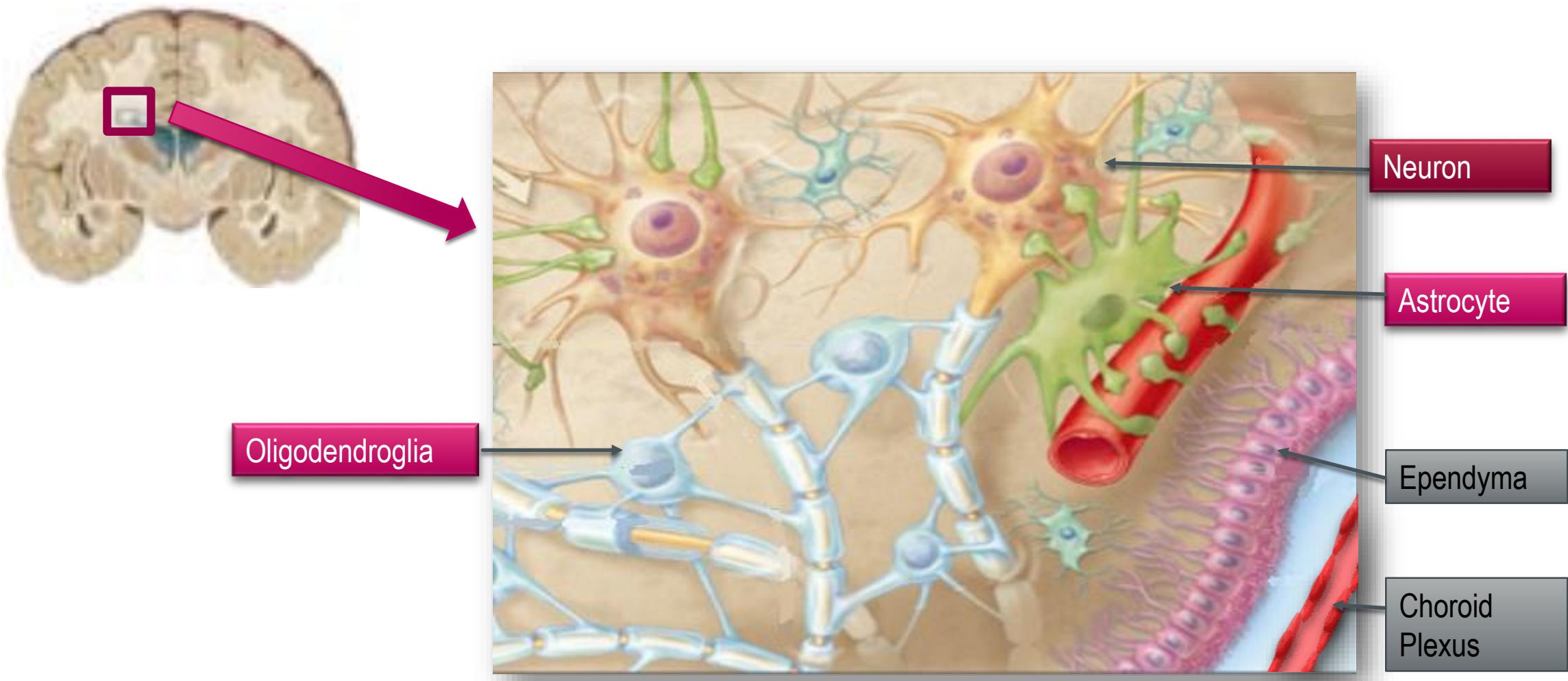


Necrosis

GFAP

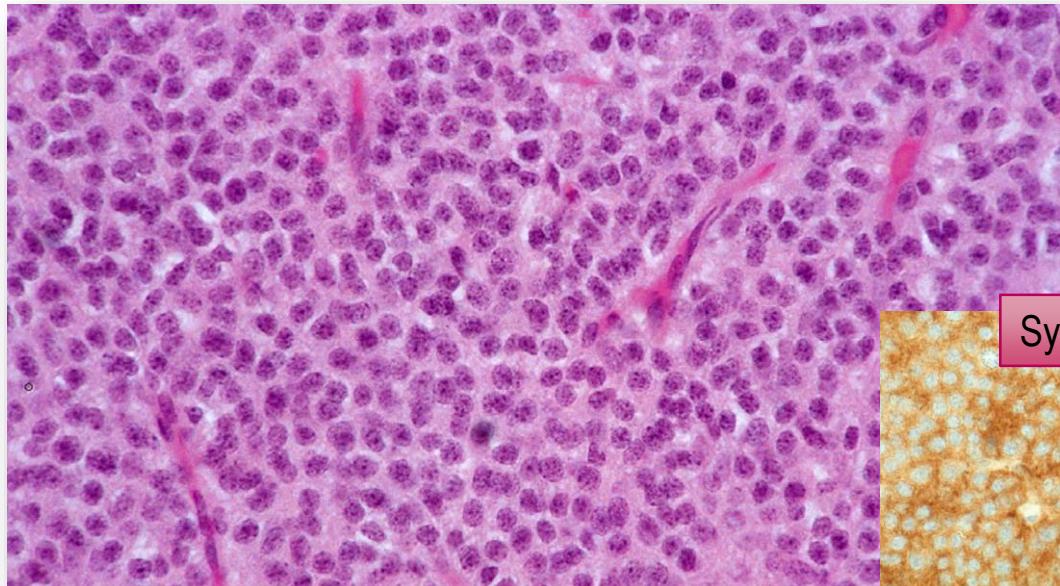


II. NEURONAL/GLIONEURONAL TUMORS

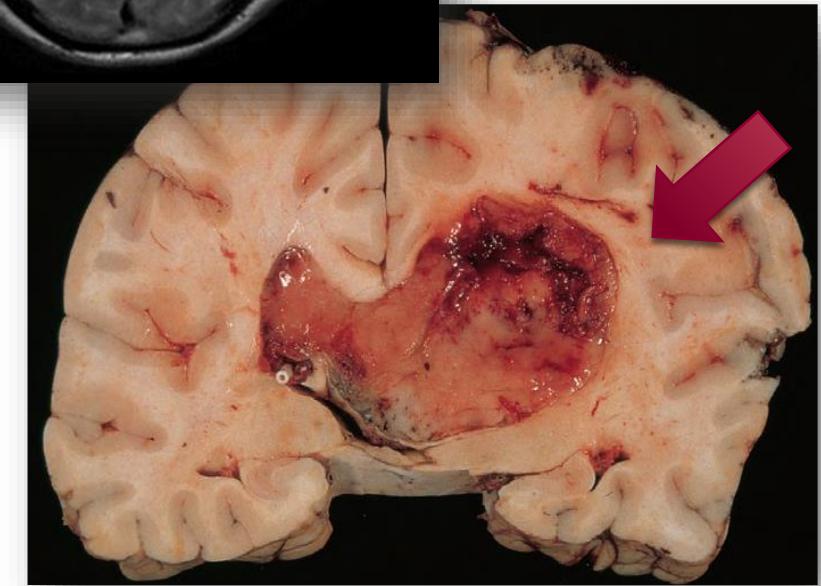
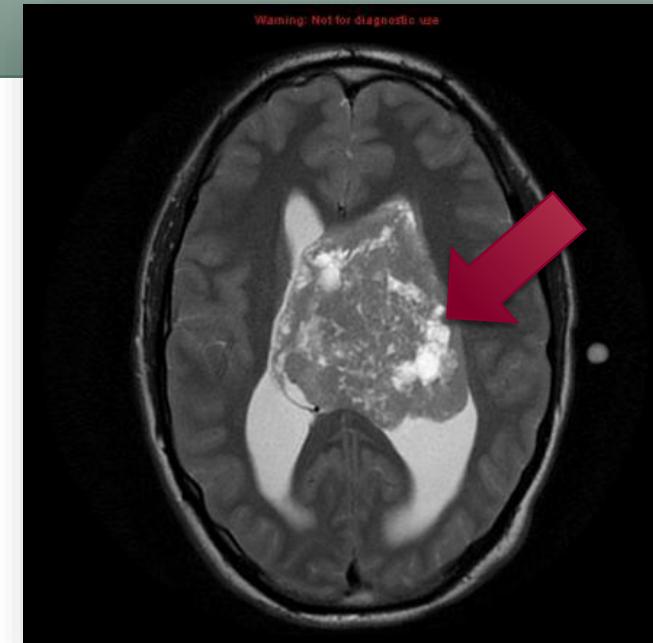


Central neurocytoma Grade II

- Young adults
- Rare tumor
- Location:
 - Lateral or 3rd ventricle
 - Septum pellucidum

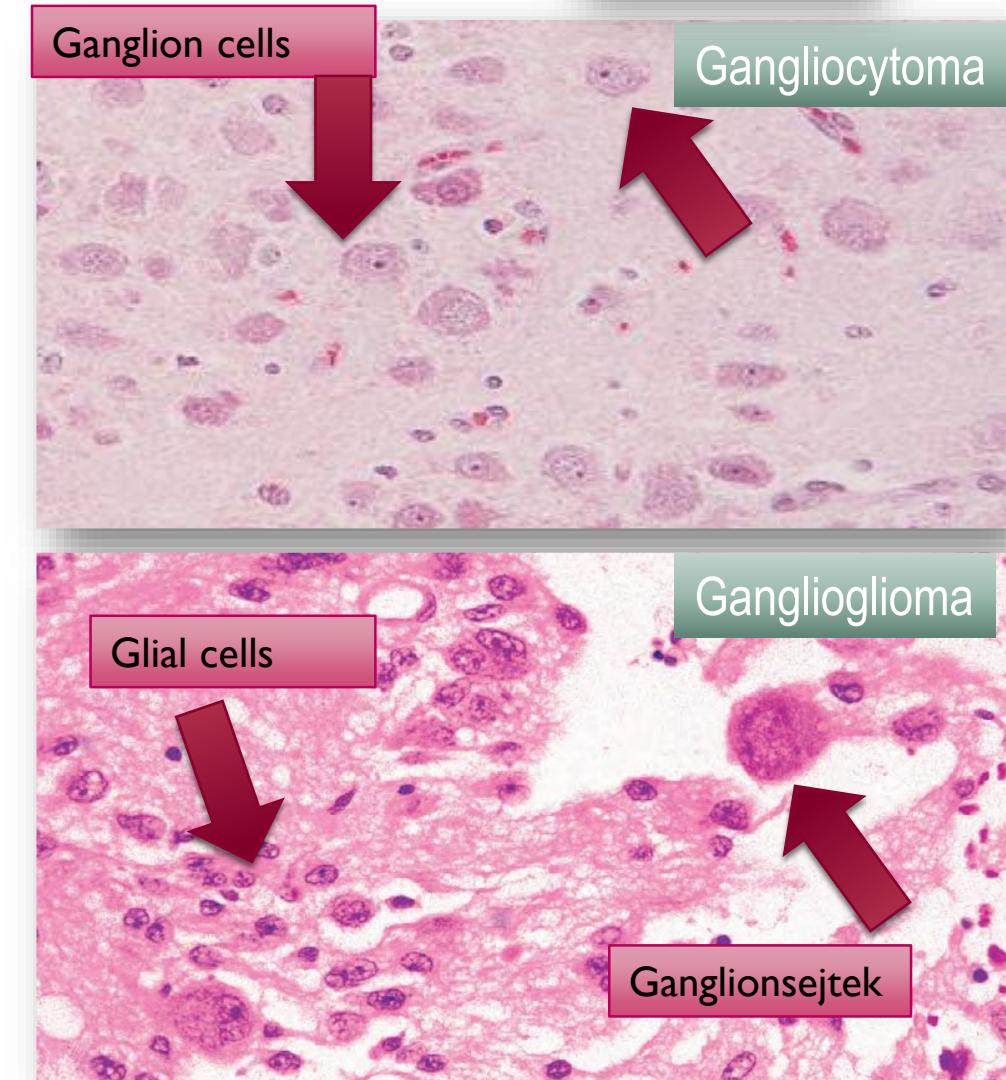
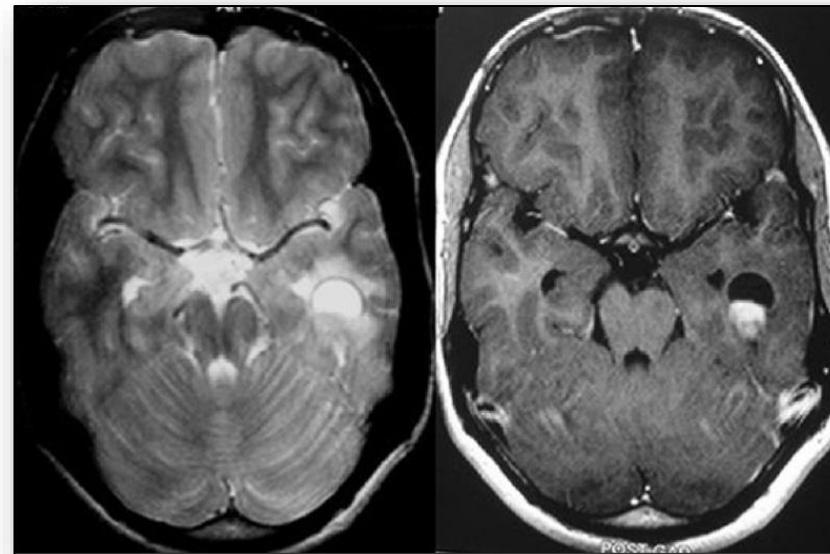


Synaptophysin



Gangliocytoma, ganglioglioma Grade I

- Children, young adults
- Temporal lobe
 - Epilepsy
- **BRAF gene mutation (BRAF V600E v. BRAF/KIAA tr)**
- Mature appearing neurons ± Glial cells
- Glial component – with time anaplastic

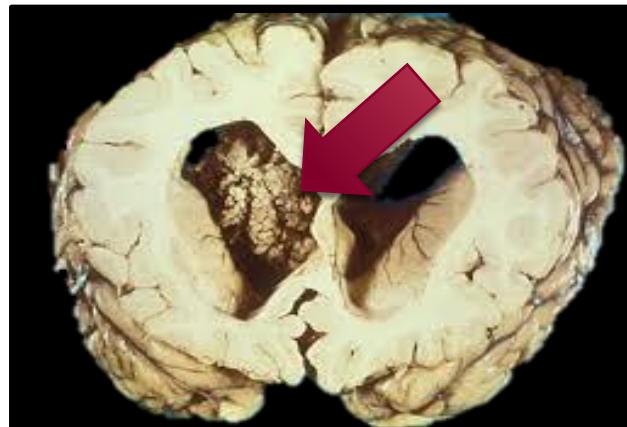
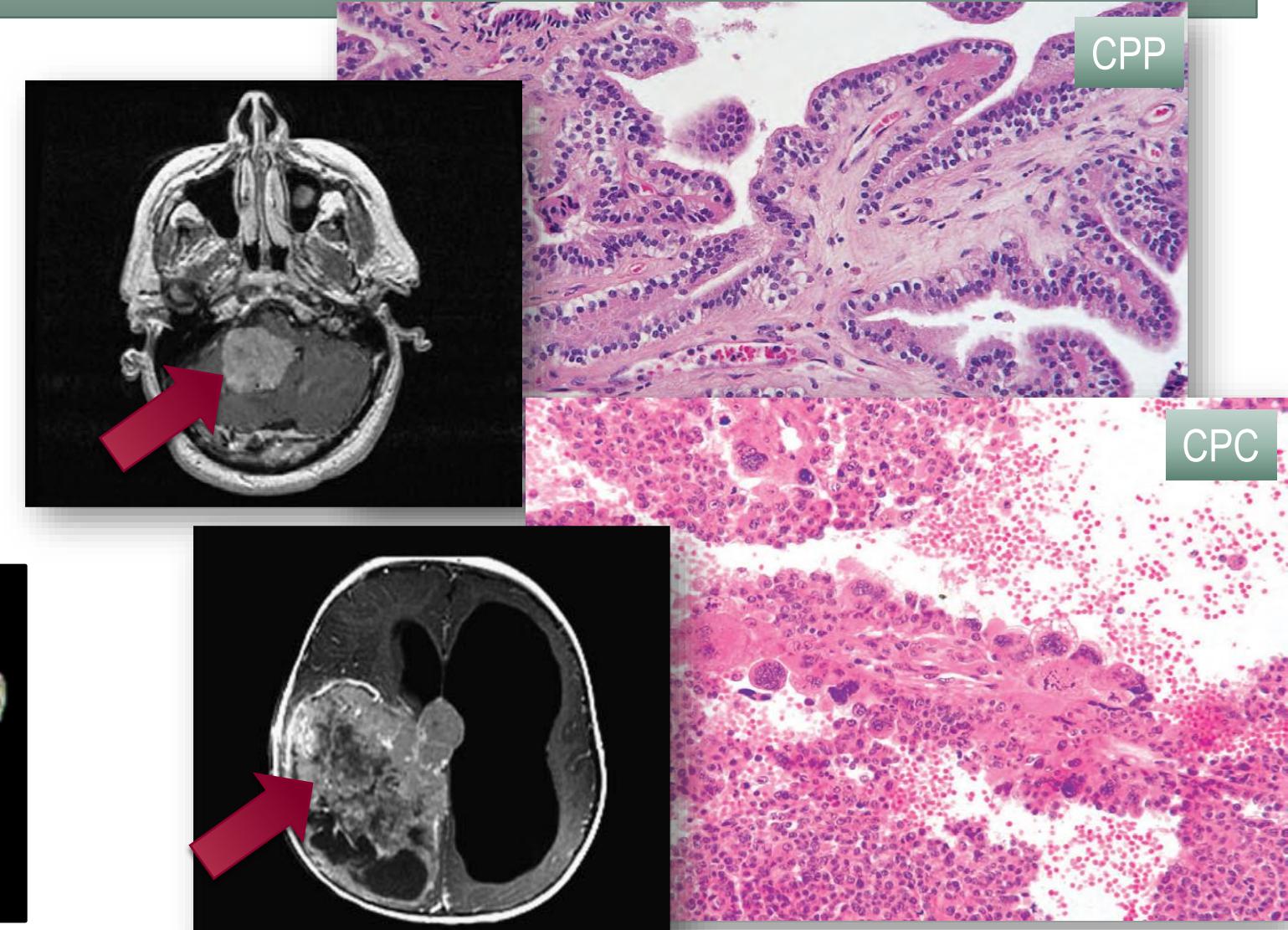


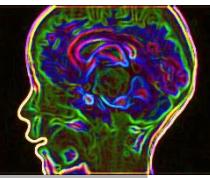
III. CHOROID PLEXUS NEOPLASMS



Choroid plexus papilloma/ Choroid plexus carcinoma

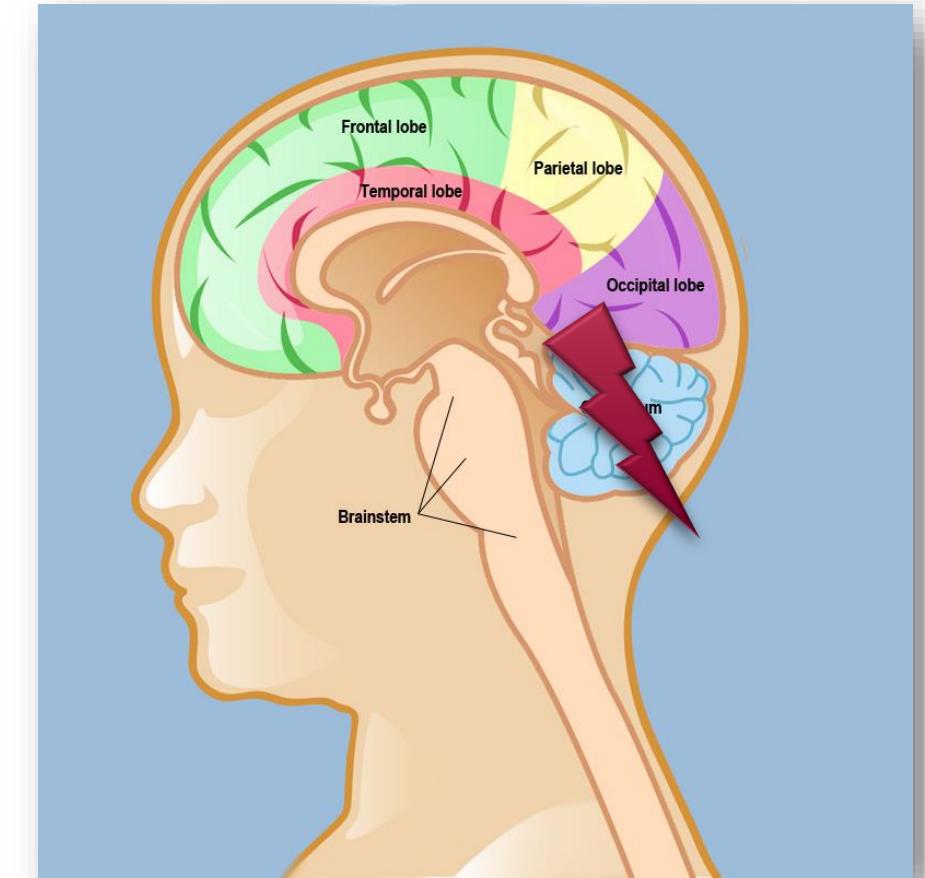
- Children
- Lateral or 4th ventricle
- Papilloma
 - More common
- Carcinoma
 - TP53 mutation
 - Poor prognosis





IV. EMBRIONAL NEUROEPITHELIAL TUMORS

- Predominance in children
- Disseminate through CSF pathways
- Small undifferentiated cells
- High mitotic index, widespread apoptosis
- Potential for divergent neuroepithelial differentiation





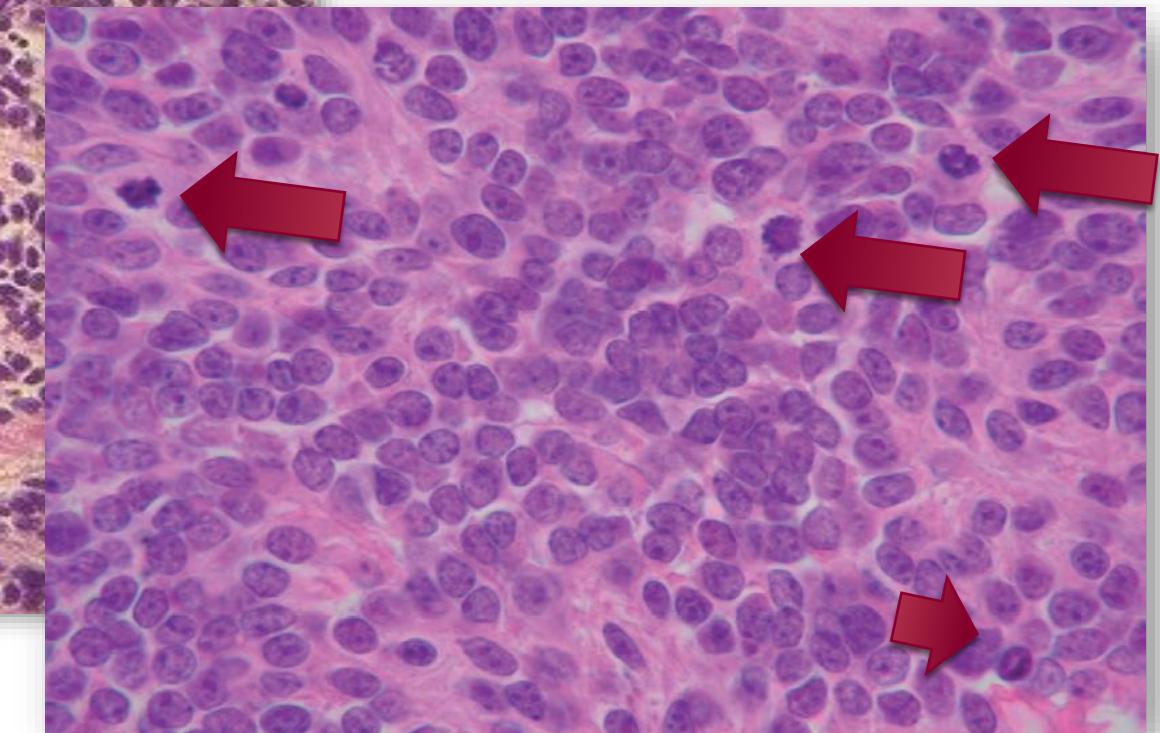
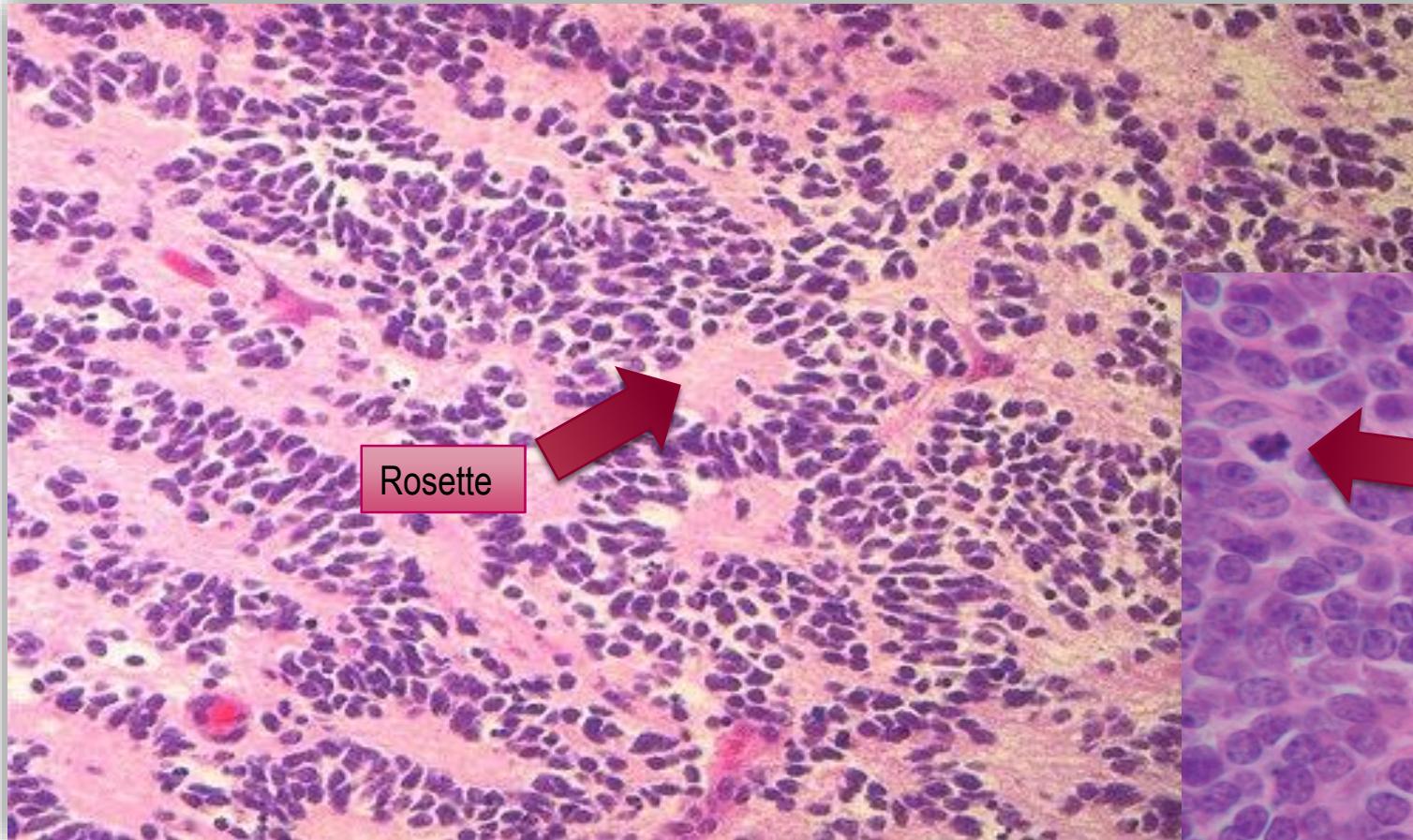
Medulloblastoma Grade IV

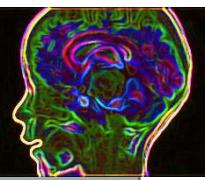
- 20% of pediatric brain tumor
- Infratentorial, 4th ventricle
- Four molecular subgroups :
 - WNT- activated (10%)
 - Sonic hedgehog (SHH)-activated (30%)
 - Group 3 (20%)
 - Group 4 (40%)





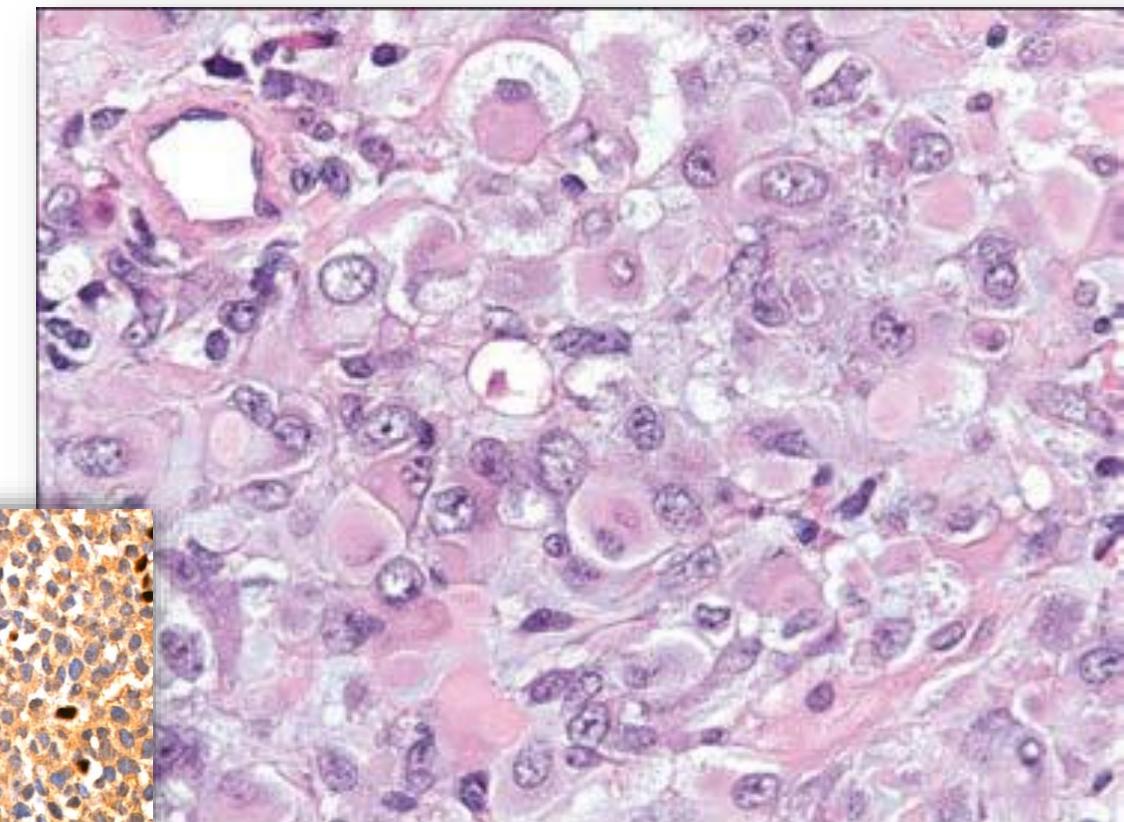
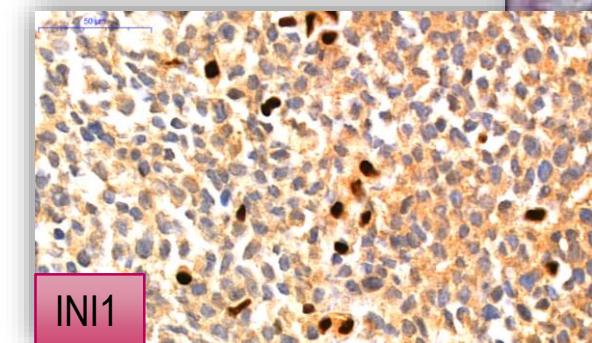
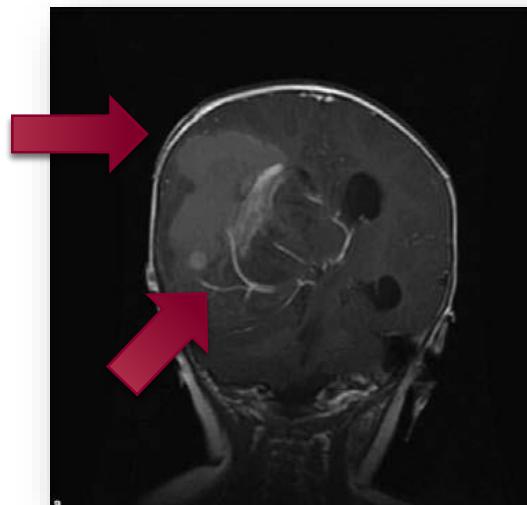
Medulloblastoma Grade IV



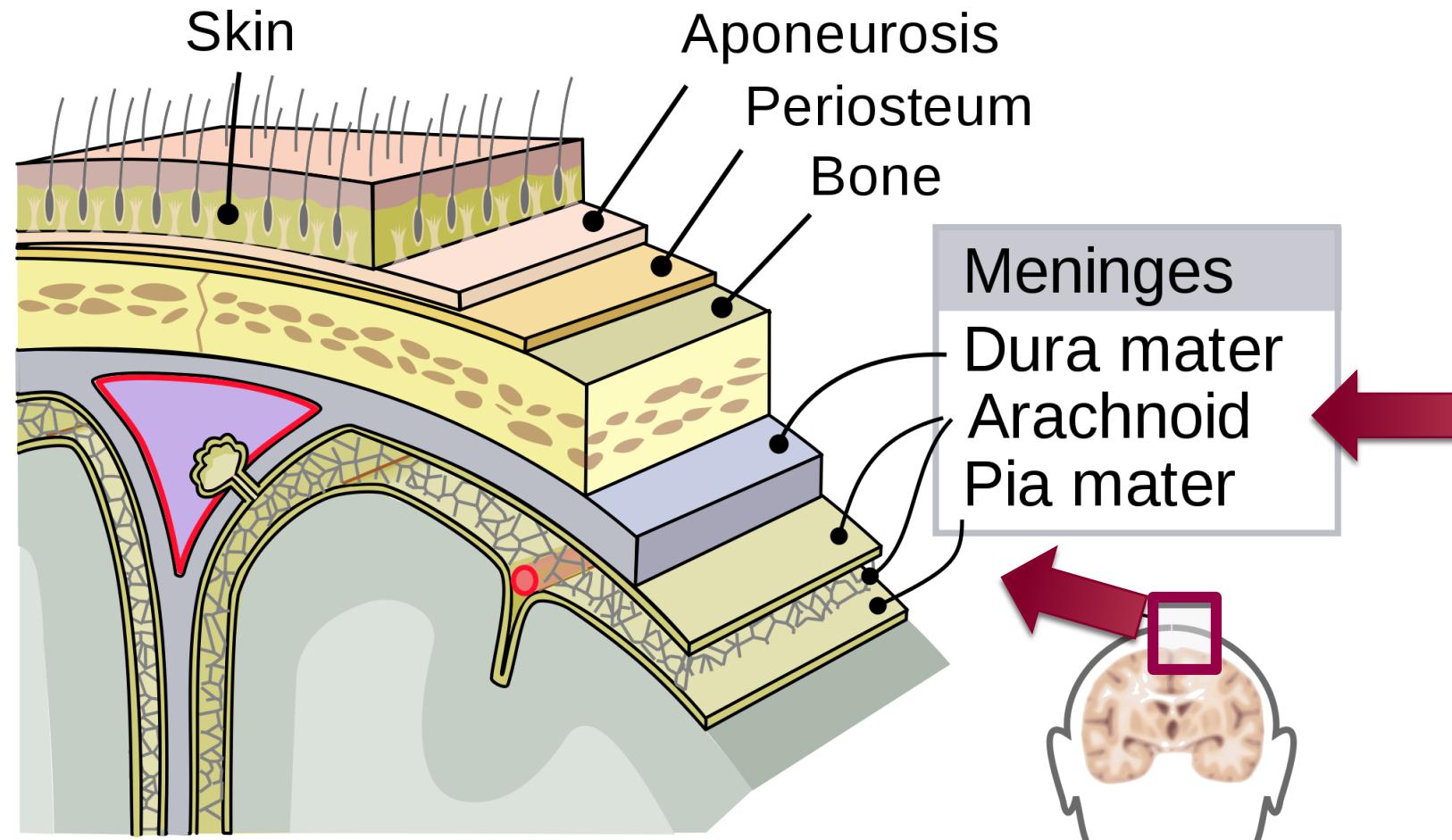


Atypical Teratoid Rhabdoid Tumor (AT/RT) Grade IV

- Most commonly <5, years (most patients <1)
- Very poor prognosis
- 1% Childhood CNS tumors
- 10% Infant CNS tumors
- Supratentorial common, but anywhere
- INI1/SMARCB1 loss

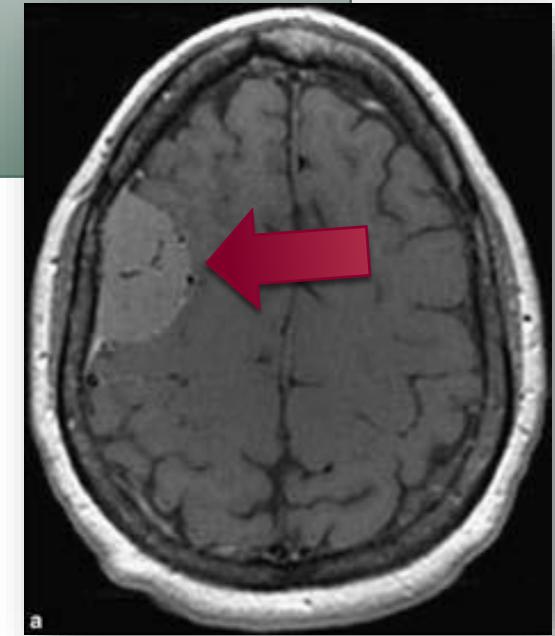
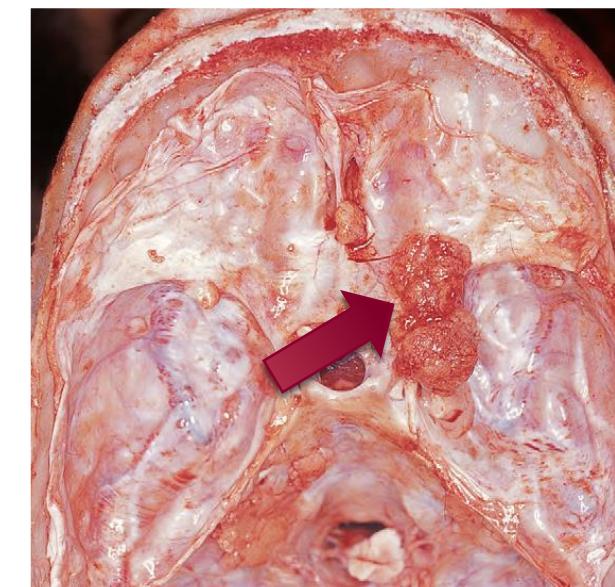


V. MENINGIOMAS

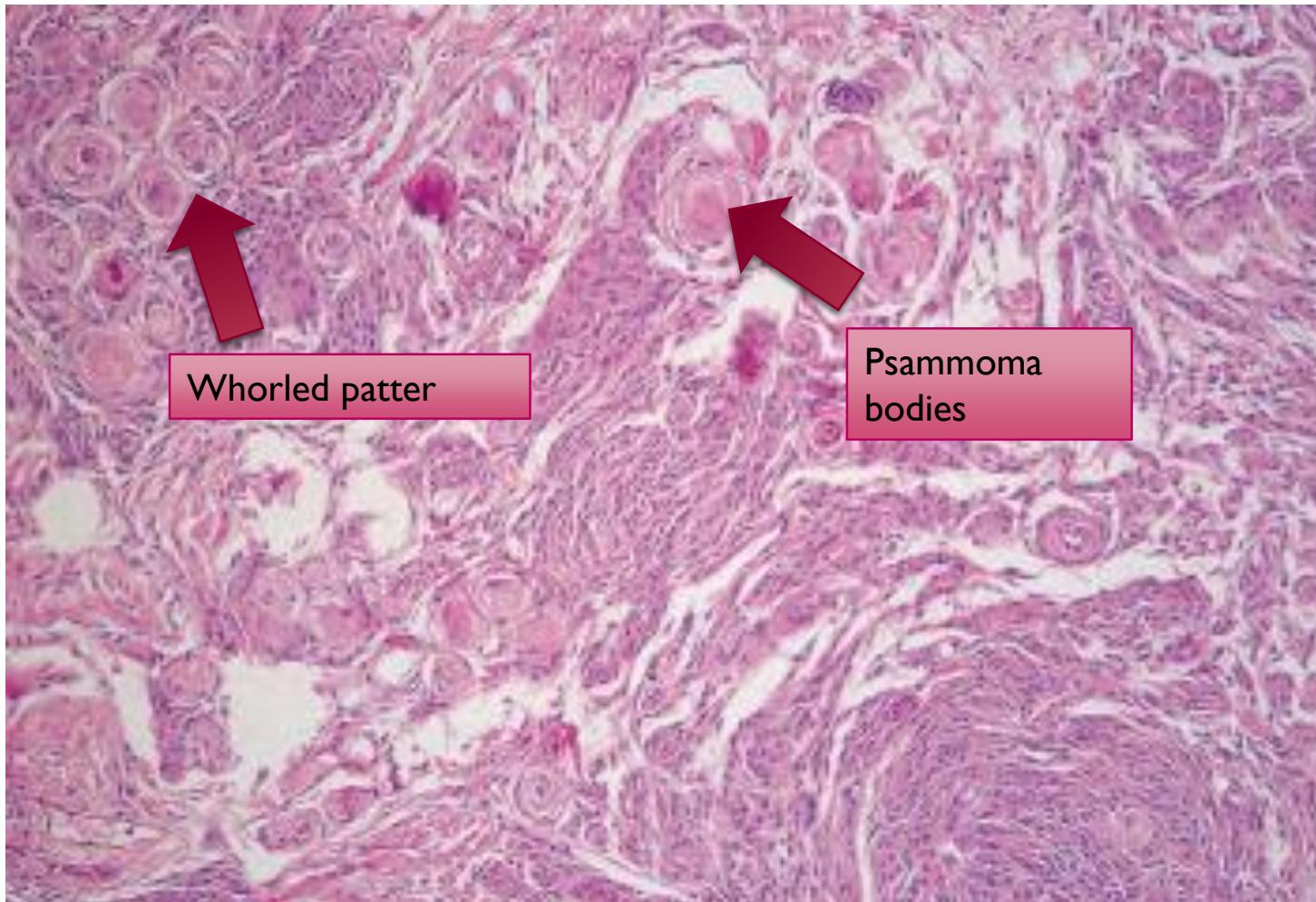


Meningeoma Grade I.

- Incidence increases with age
- Primary CNS tumors ~30% meningioma
- External surfaces or intraventricular (Rare)
- Focal neurological deficits
- Several histological variants



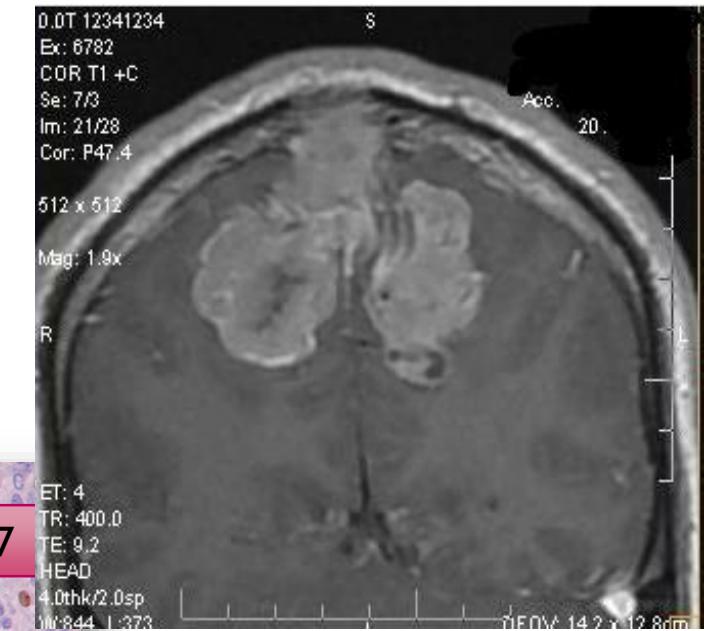
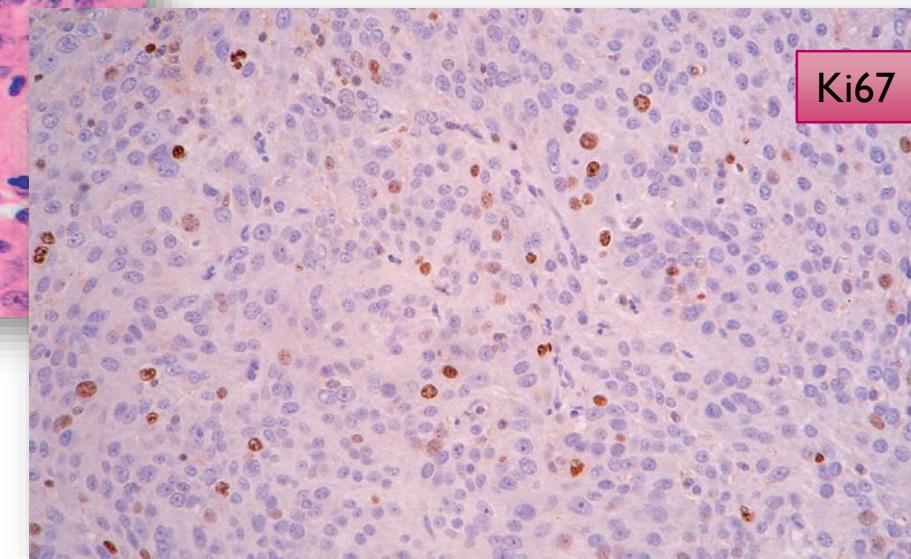
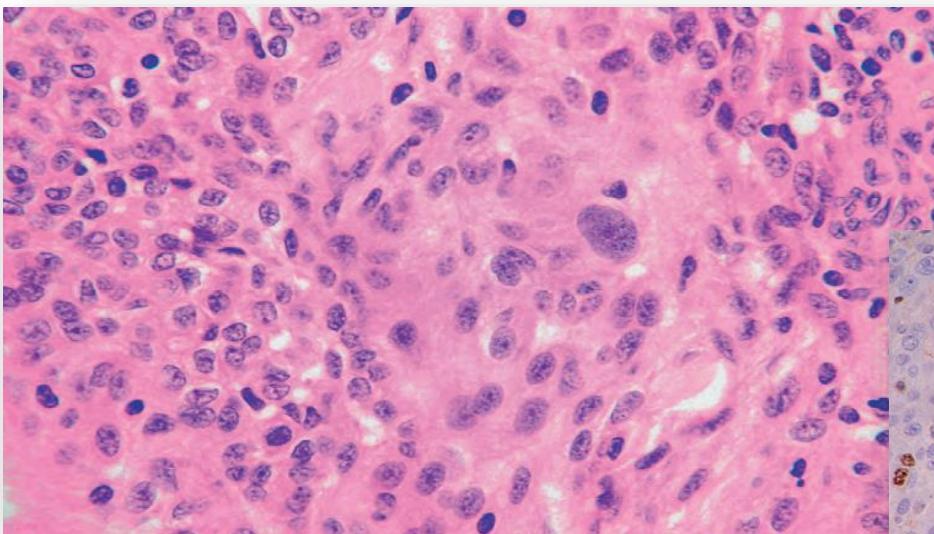
Meningeoma Grade I.



Several histological variants:
Meningothelial
Fibrosus
Transicinal
Psammomatous
Angiomatous
Microcystic
Secretory
Lymphoplasmocyte rich
Metaplastic

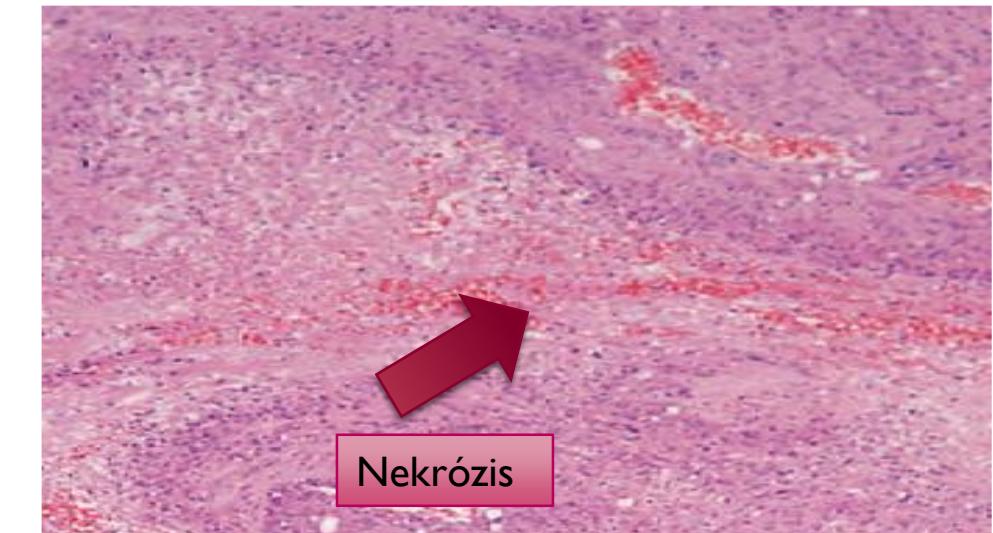
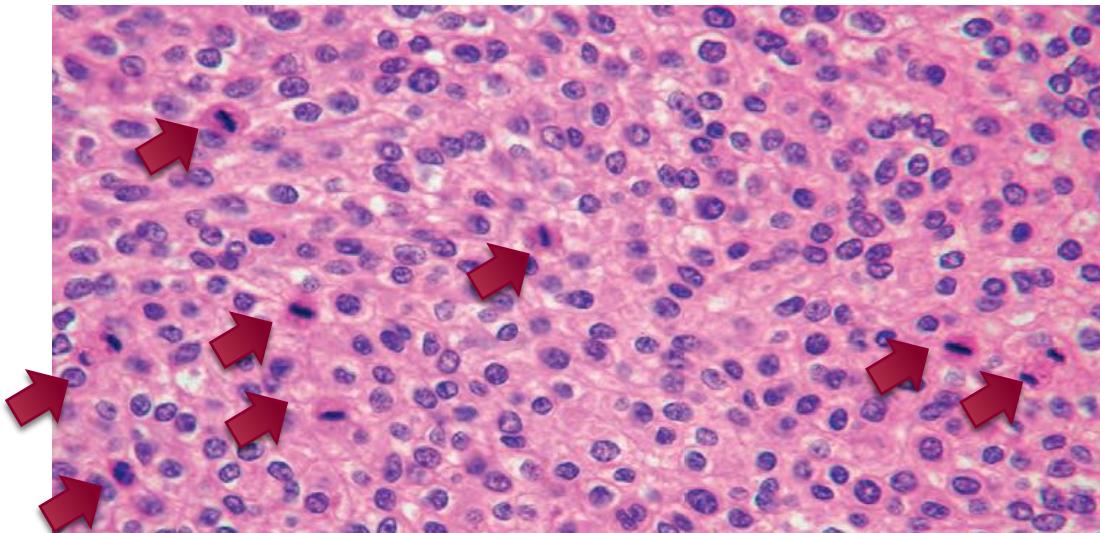
ATYPICAL MENINGEOMA GRADE II.

- Grade II variants: Chordoid, clear cell, atypical
- Clear cell : Childhood lumbal tumor
- Brain invasion – Grade II



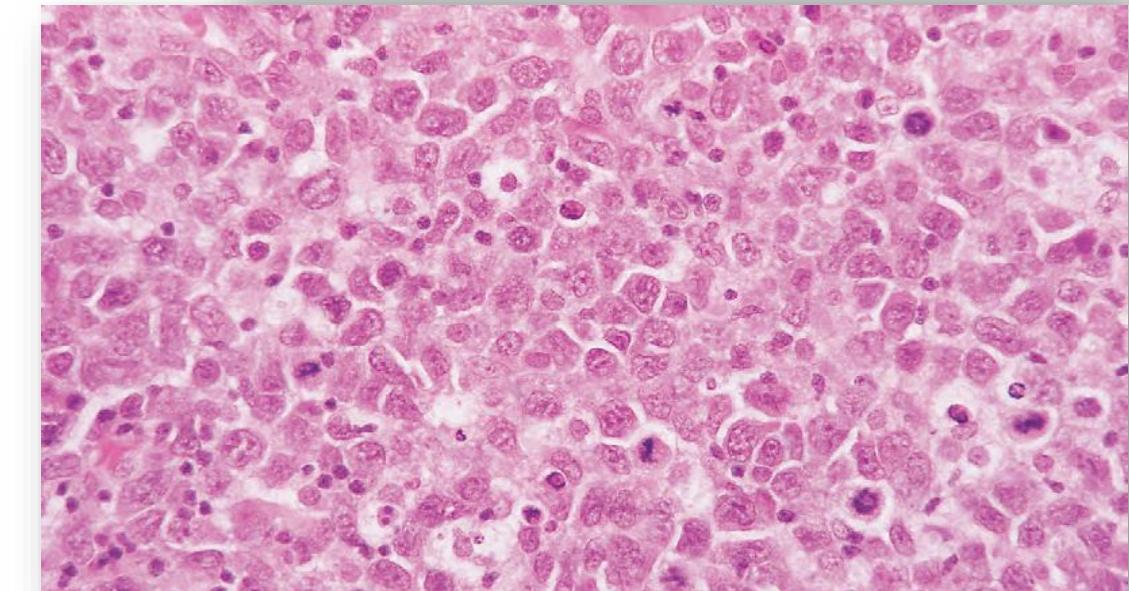
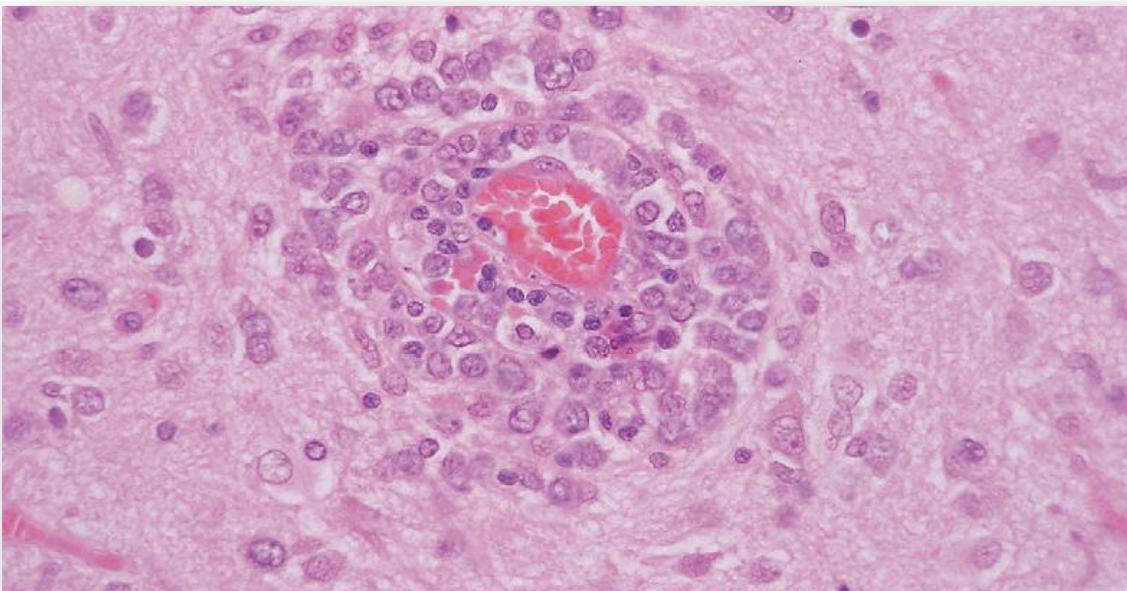
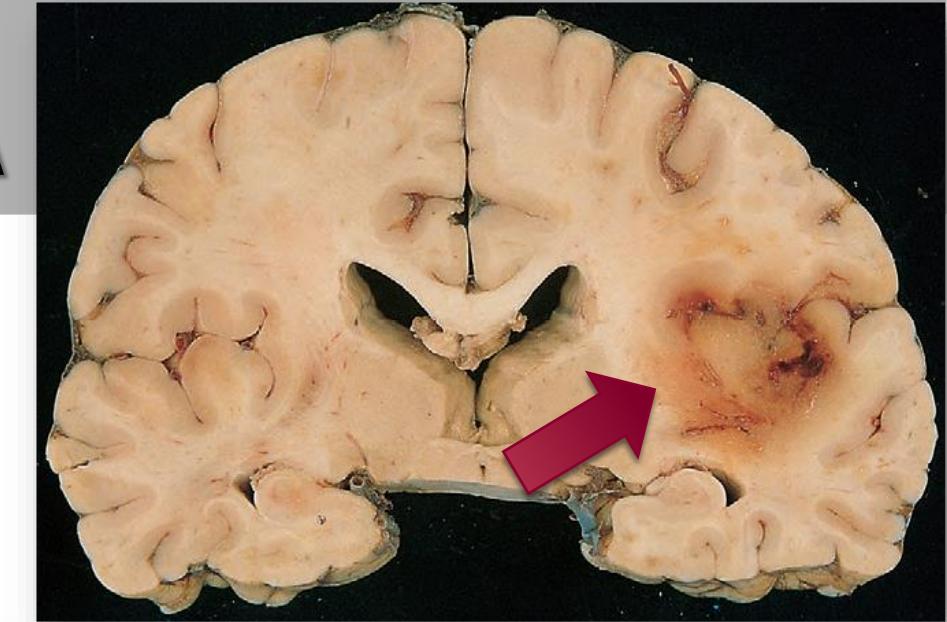
ANAPLASTIC MENINGEOMA GRADE III.

- Grade III variants: Papillary, rhabdoid, anaplastic
- Difficult differential diagnostics



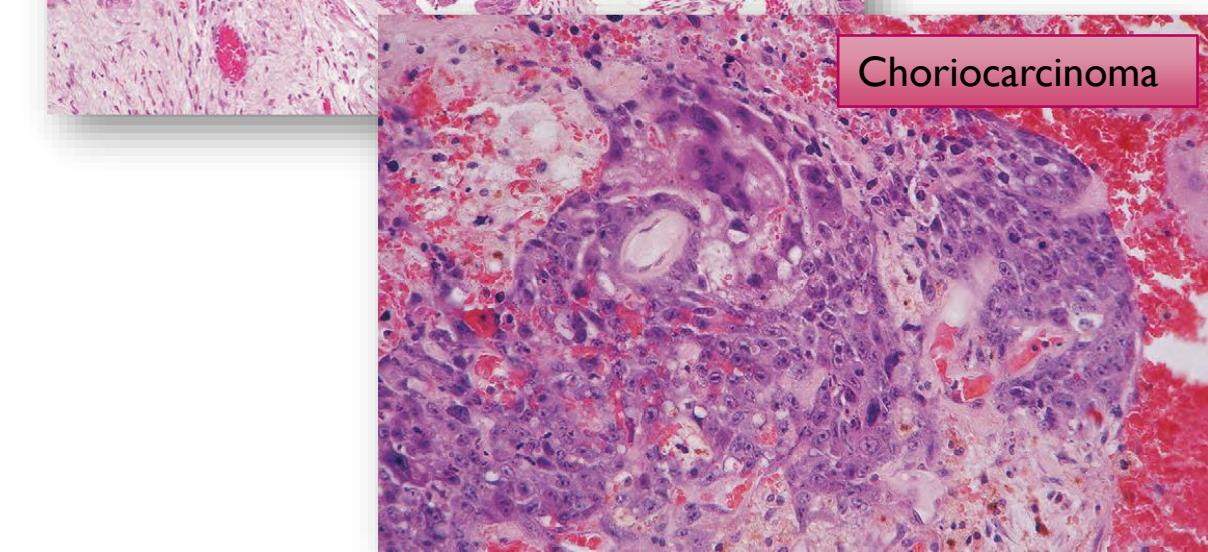
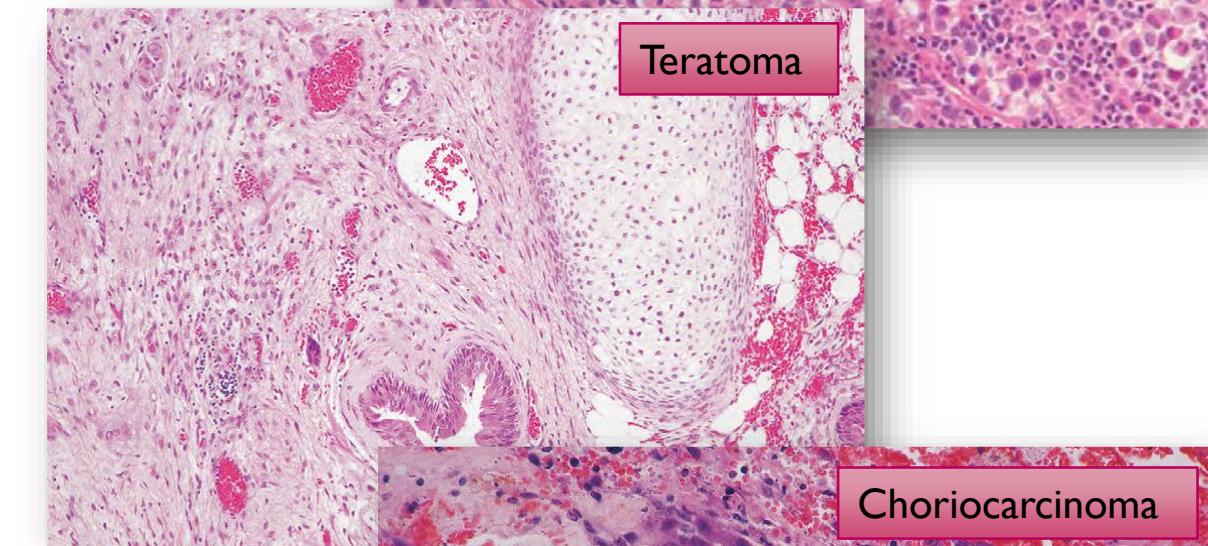
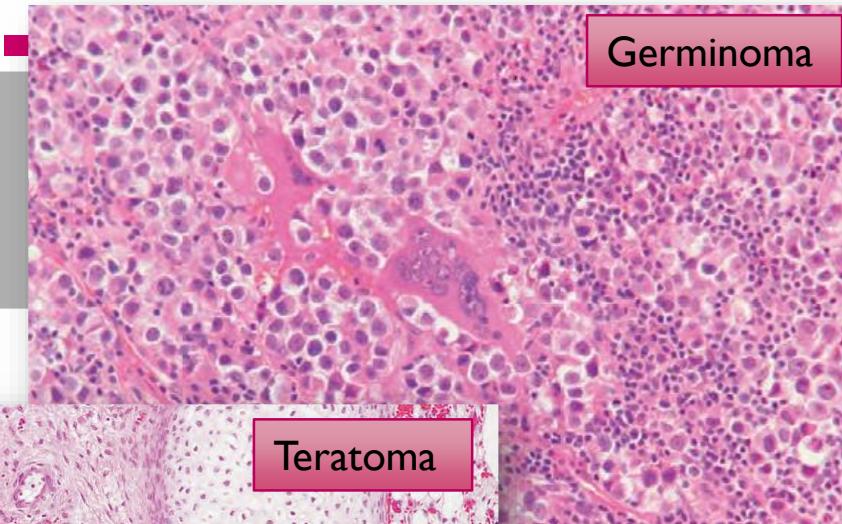
VI. PRIMARY CNS LYMPHOMA

- DLBCL type
- Immunosuppressed patients - EBV+
- But Not only!



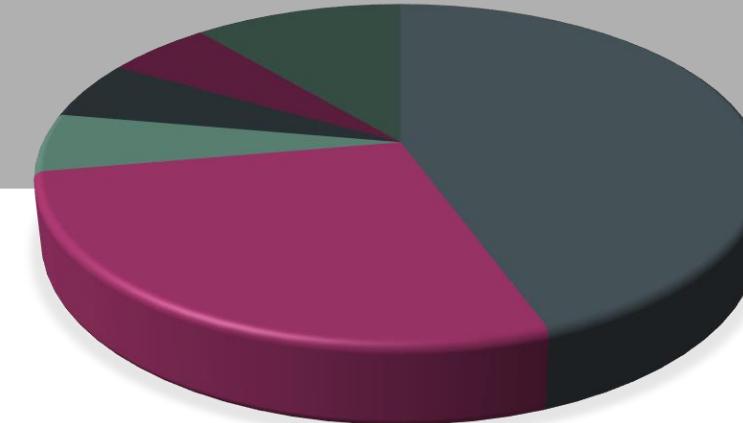
VII. CNS GERM CELL TUMORS

- Germinoma - 50%
 - Teratoma - 20%
 - Mature teratoma
 - Immature teratoma
 - Teratoma with malignant transformation
 - Yolk sac tumor
 - Embryonal carcinoma
 - Choriocarcinoma
 - Mixed tumor - 25%
- } 5%

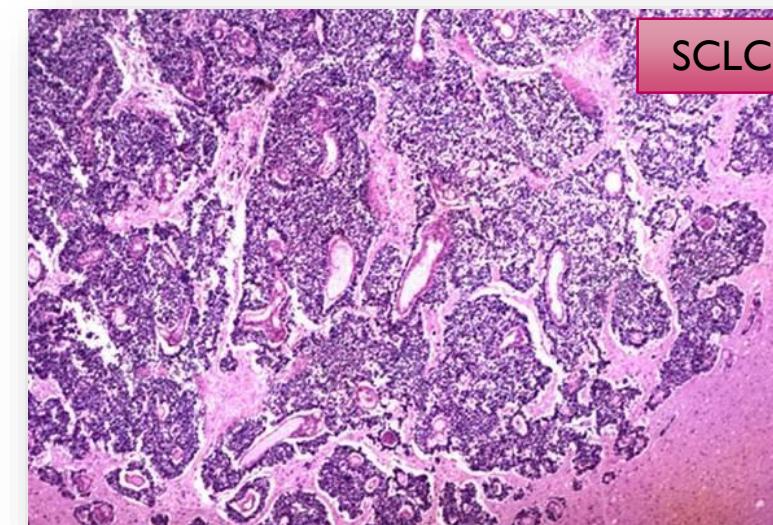
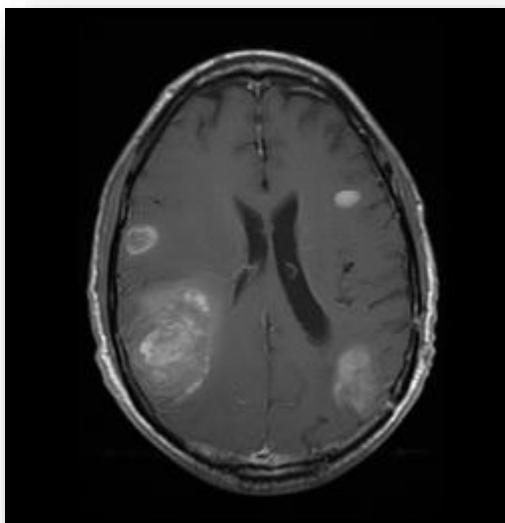


VIII. METASTATIC TUMORS

- 25-50% of all CNS tumors
- Gray-white junction
- Sharply demarcated masses
- Perifocal edema



- Lung tumor
- Breast tumor
- Melanoma
- Gasrointestinal tumor
- Kidney
- Other





NEUROPATHOLOGY INFECTIONS

HAJNALKA RAJNAI



INFECTIOUS AGENTS

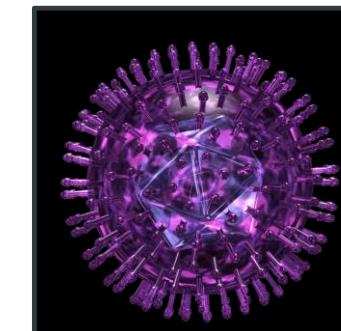
I. Bacterial infection

- Bakterial meningitis
- Brain abcessus
- Tuberculosis
- Neurosyphilis



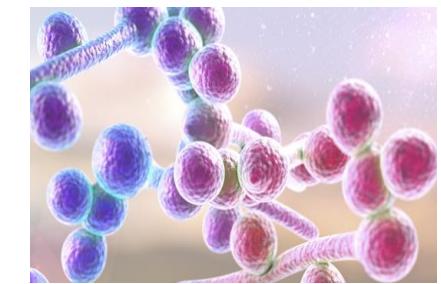
2. Viral infection

- Viral meningitis
- Herpesvirus
- Cytomegalovirus
- Poliovirus
- Rabies
- HIV
- Progressive multifocal leukoencephalopathy



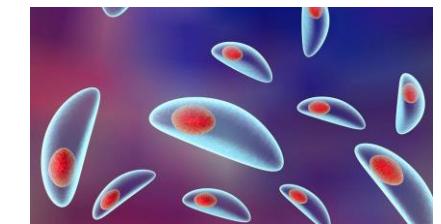
3. Fungal infection

- Candida
- Mucormycosis
- Aspergillus
- Cryptococcus



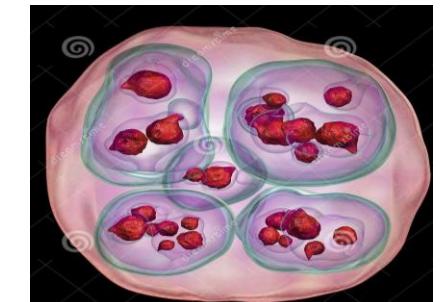
4. Protozoal infection

- Toxoplasma



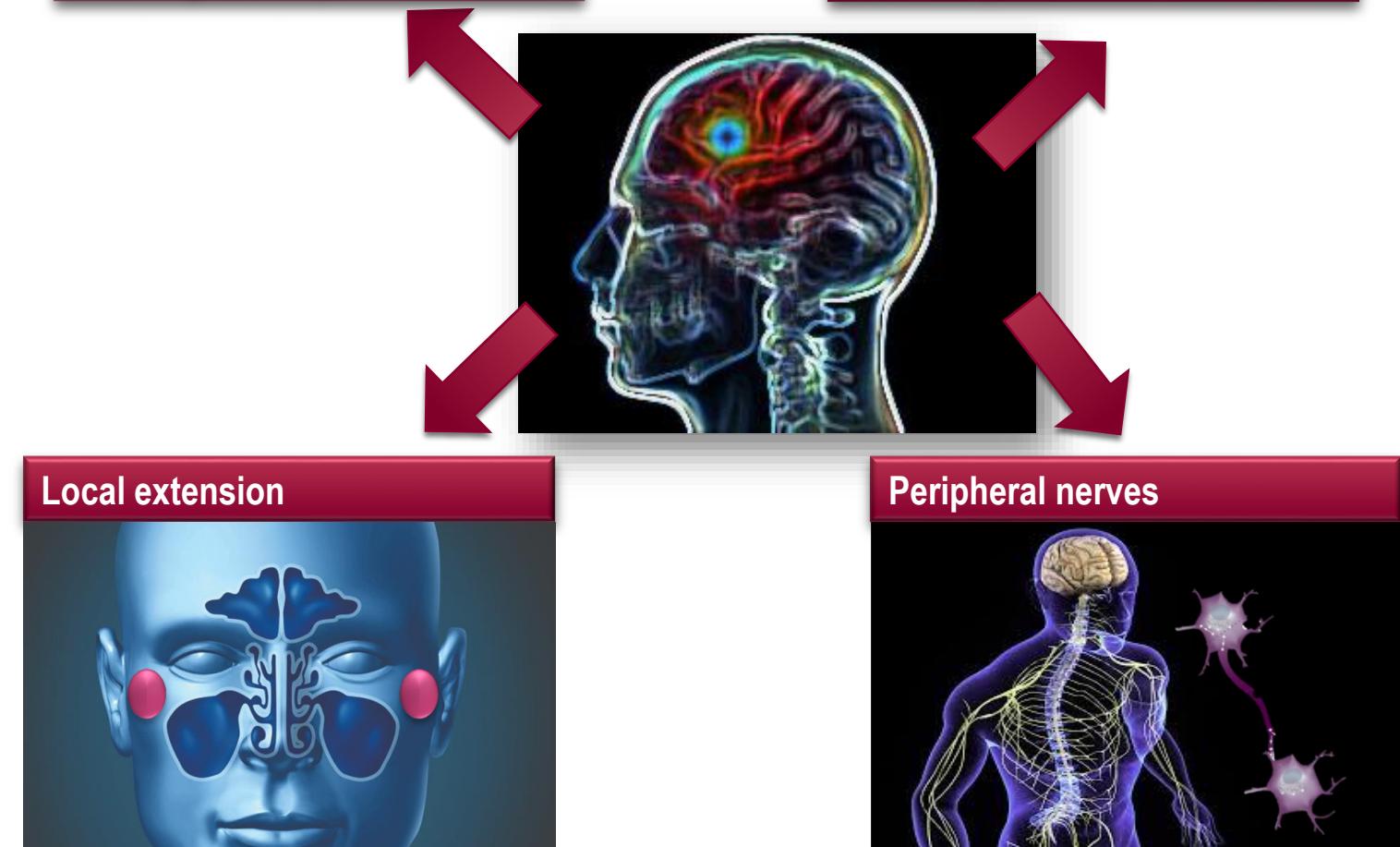
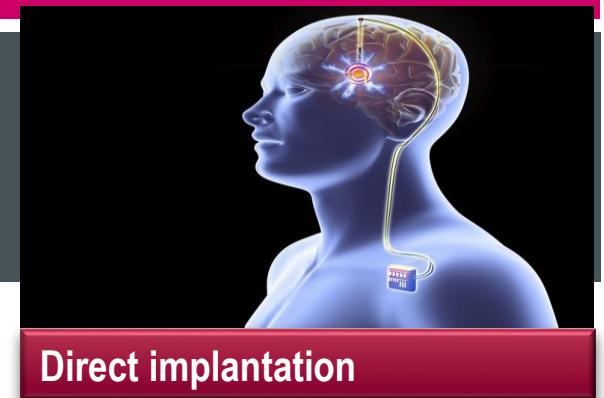
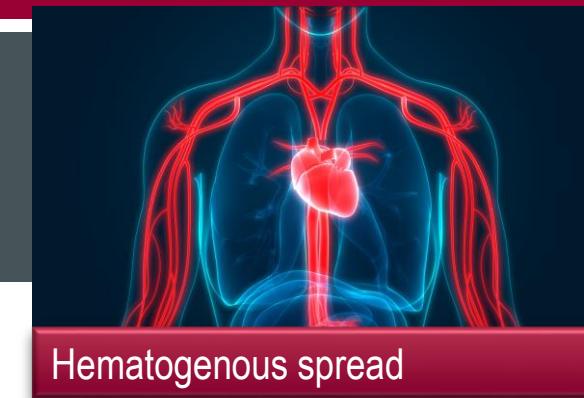
5. Parazite infection

- Cystercosis
- Echinococcus



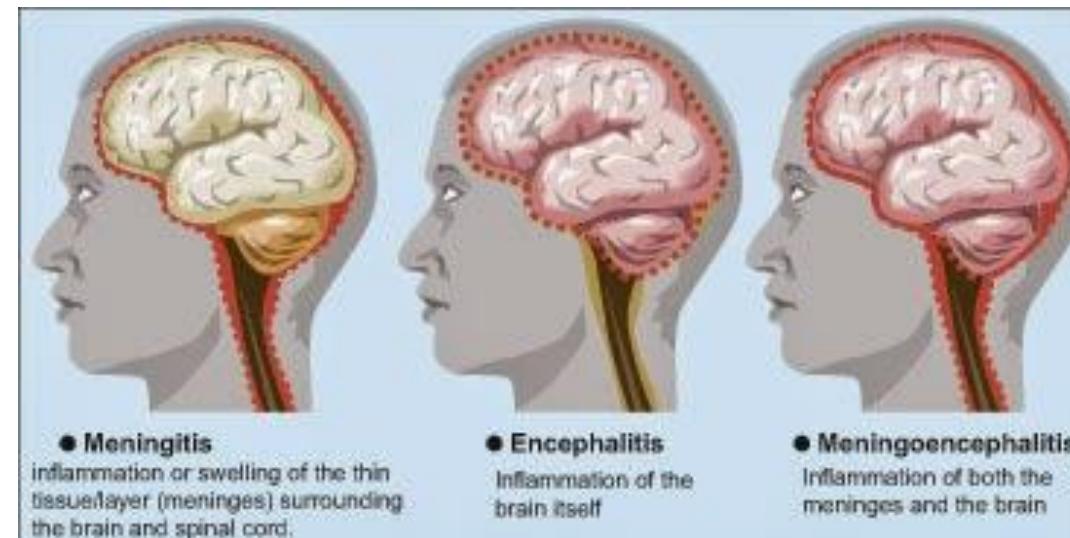
SPREAD

1. Hematogenous spread
2. Direct implantation
 - Trauma, iatrogenic (Epilepsy, surgery)
3. Local extension
 - Sinuses, Otitis media, Congenital malformations
4. Retrograde, peripheral nerves



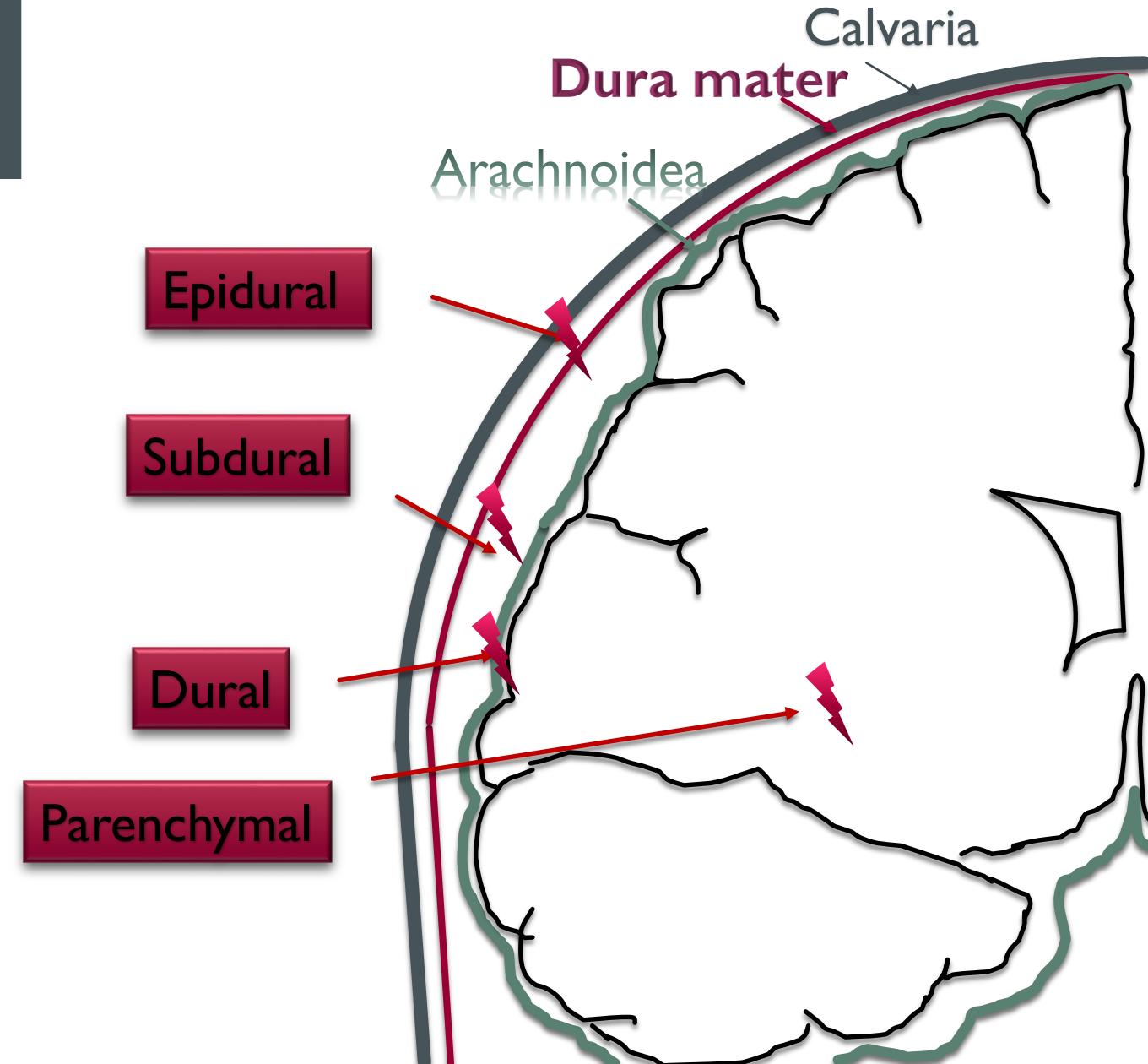
LOCATION

- 1. Parenchyma:** encephalitis , myelitis, encephalomyelitis.
- 2. Meninges:** meningitis, pachymeningitis.
- 3. Parenchyma and Meninges:** meningoencephalitis.



LOCATION

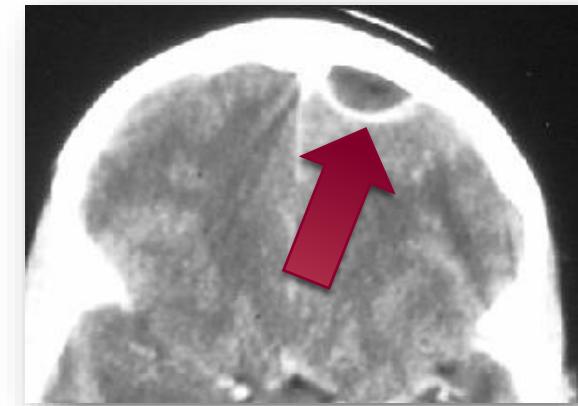
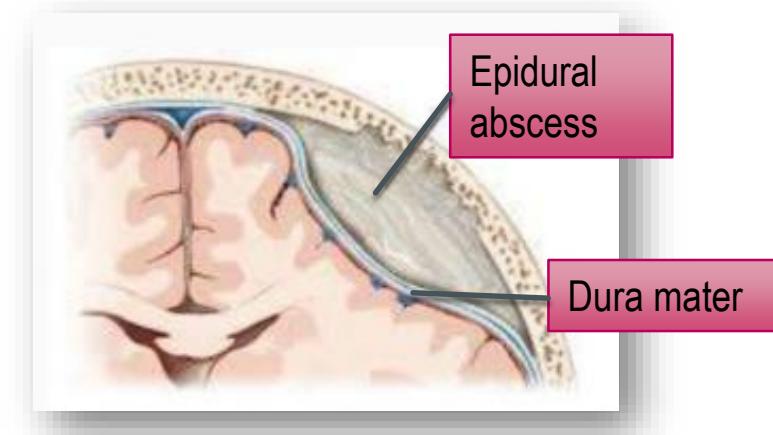
1. Epidural infection
2. Subdural infection
3. Dural infection – meningitis
4. Parenchymal infections –
Encephalitis



EPIDURAL AND SUBDURAL INFECTIONS

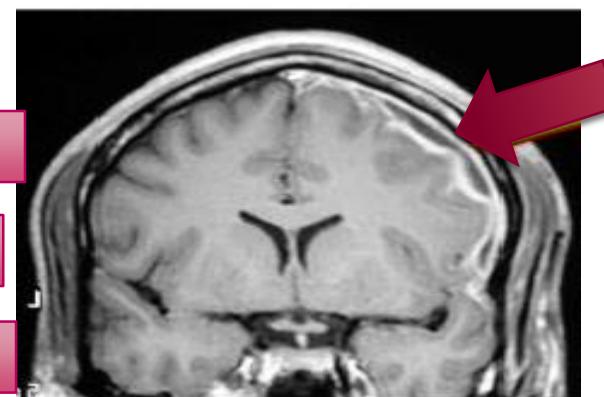
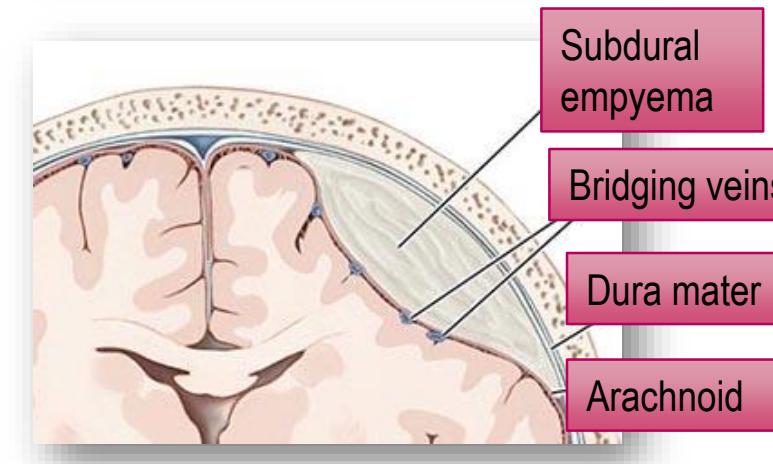
Epidural abscess

- Local spread – sinuitis, osteomyelitis
- Bacterial, fungal
- Spinal - spinal cord compression



Subdural empyema

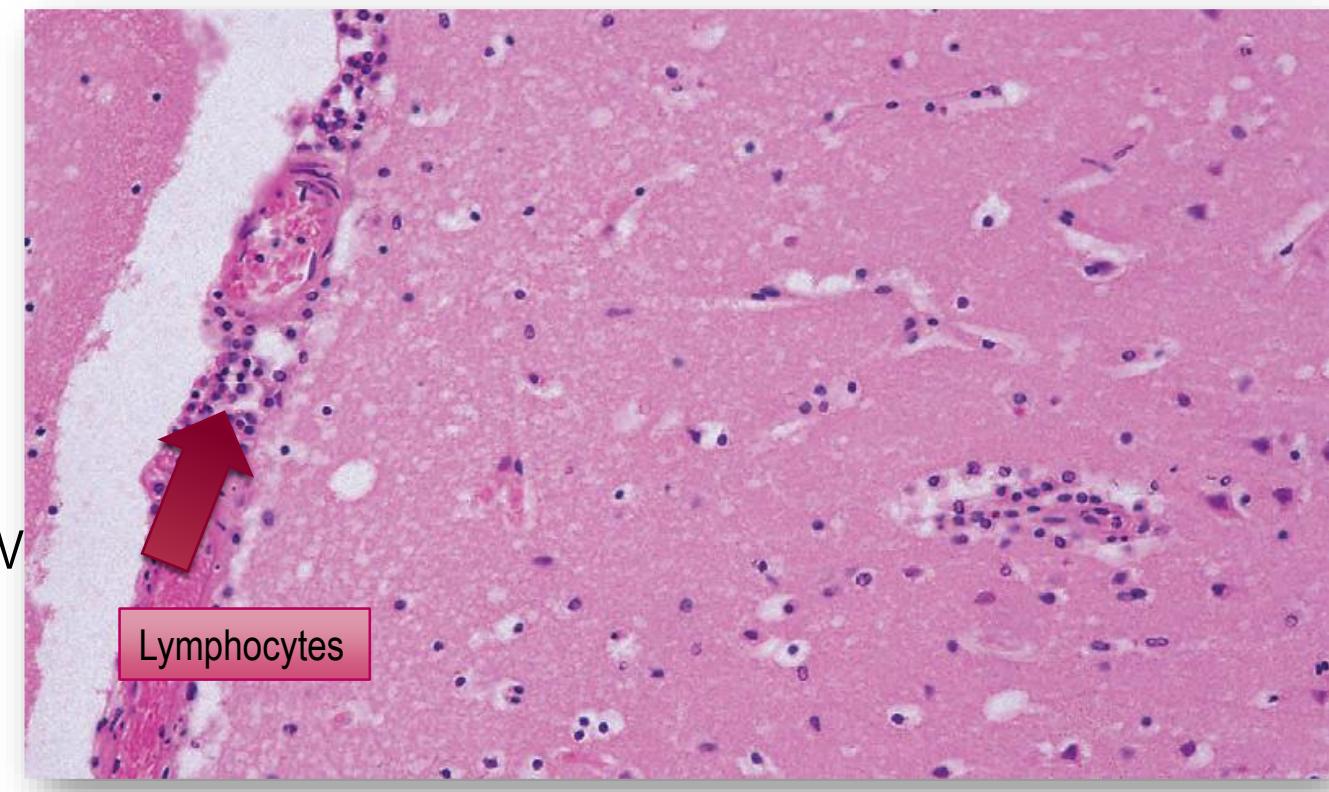
- Local spread – sinus, otitis
- Arachnoid, subarachnoid space is unaffected
- Thrombophlebitis in the bridging veins



MENINGITIS

Aseptic/Viral meningitis

- Mostly associated with encephalitis
- Mild meningeal symptoms
- Viral agents:
 - Echovirus
 - Coxsackie B
 - Coxsackie A
 - Herpes simplex virus (HSV)-2
 - Mumps
 - Human immunodeficiency virus (HIV)
 - Lymphocytic choriomeningitis virus
 - Arbovirus
 - Rubeola
 - Parainfluenza virus
 - Adenovirus



Bacterial meningitis

1. Neonates

- Escherichia coli
- B Streptococcus

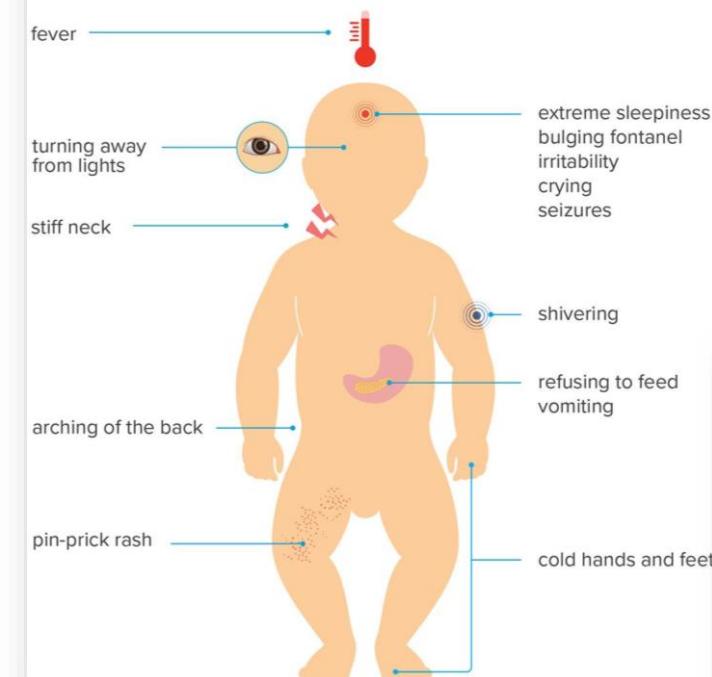
2. Children young, adults

- Neisseria meningitidis
- Streptococcus pneumoniae

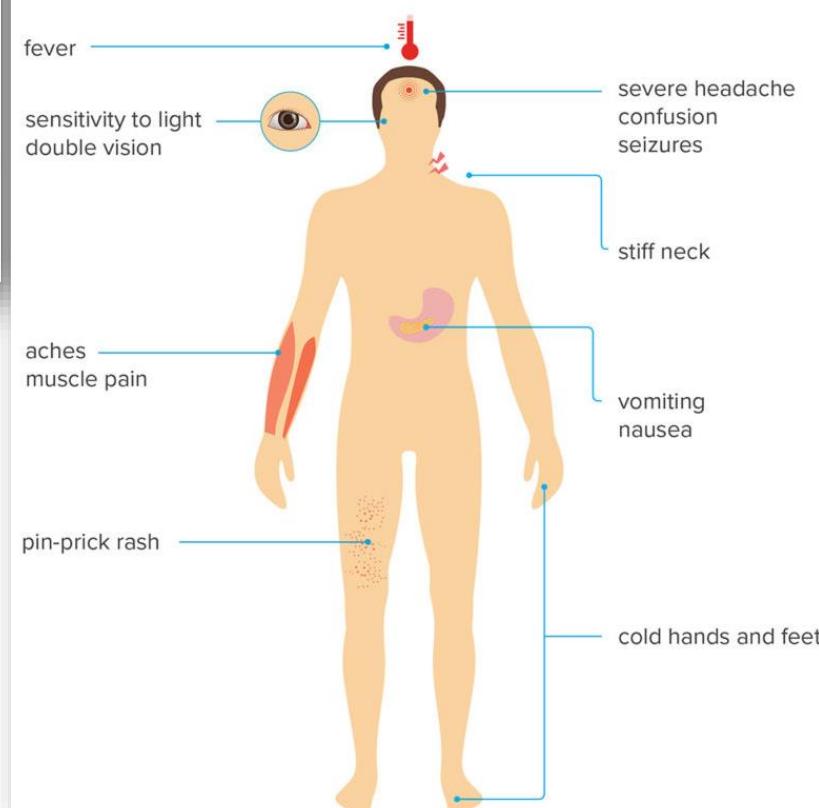
3. Older individuals

- Streptococcus pneumoniae
- Listeria monocytogenes

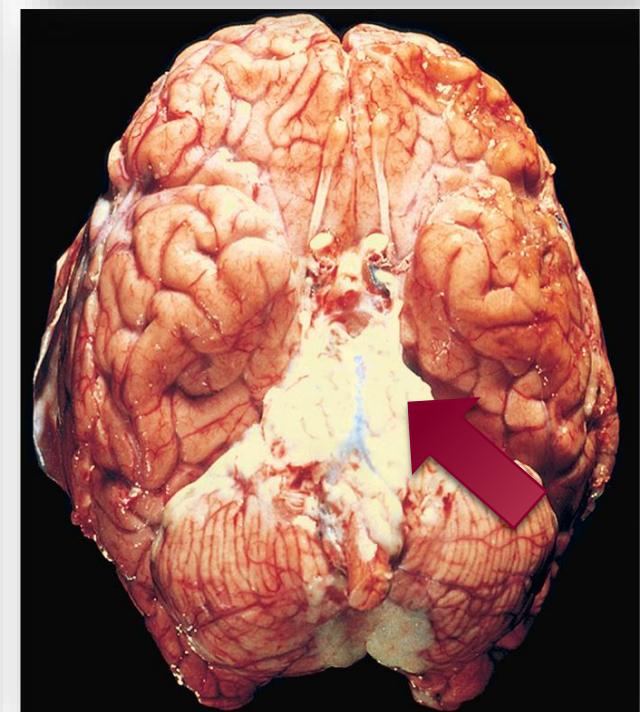
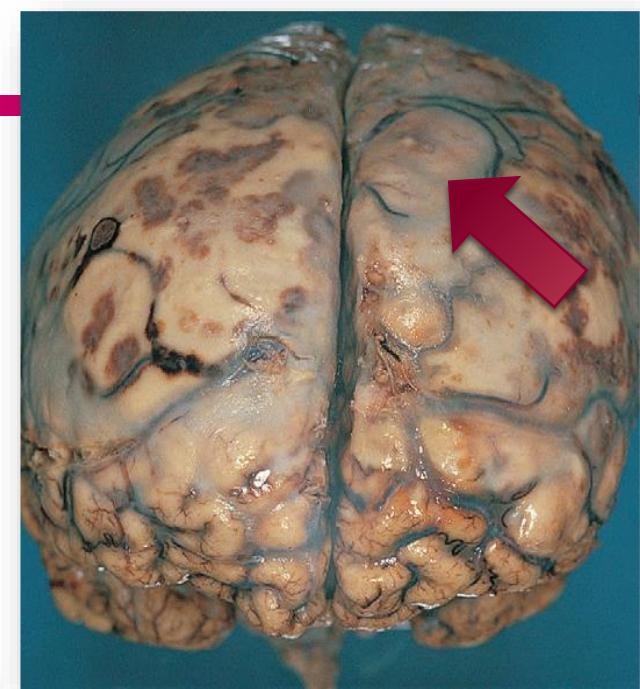
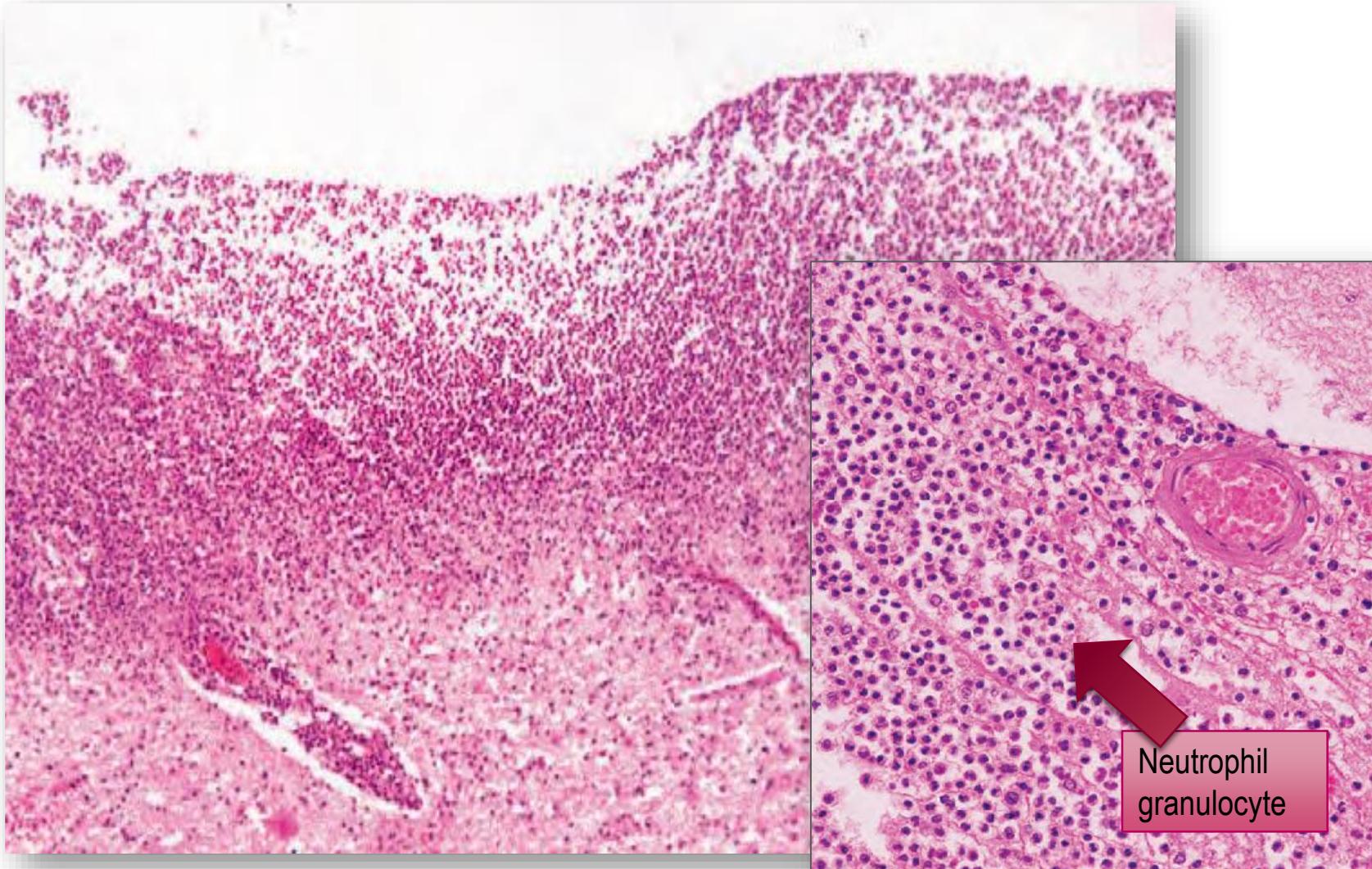
Meningitis in Infants



Meningitis in Adults



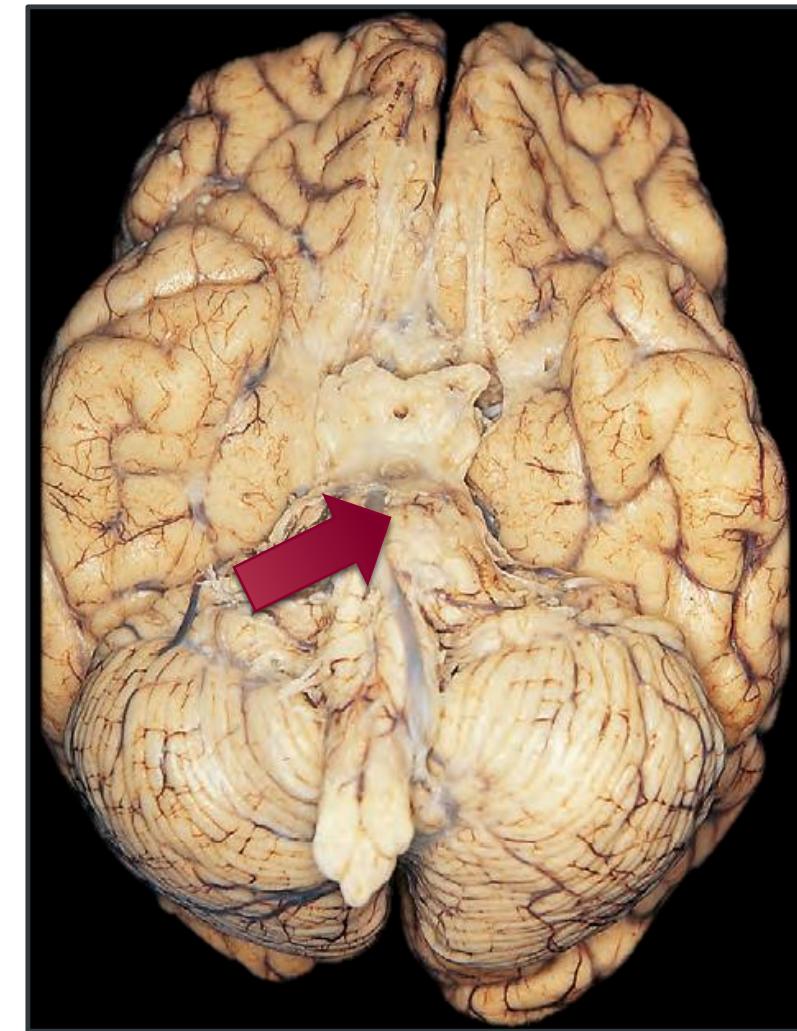
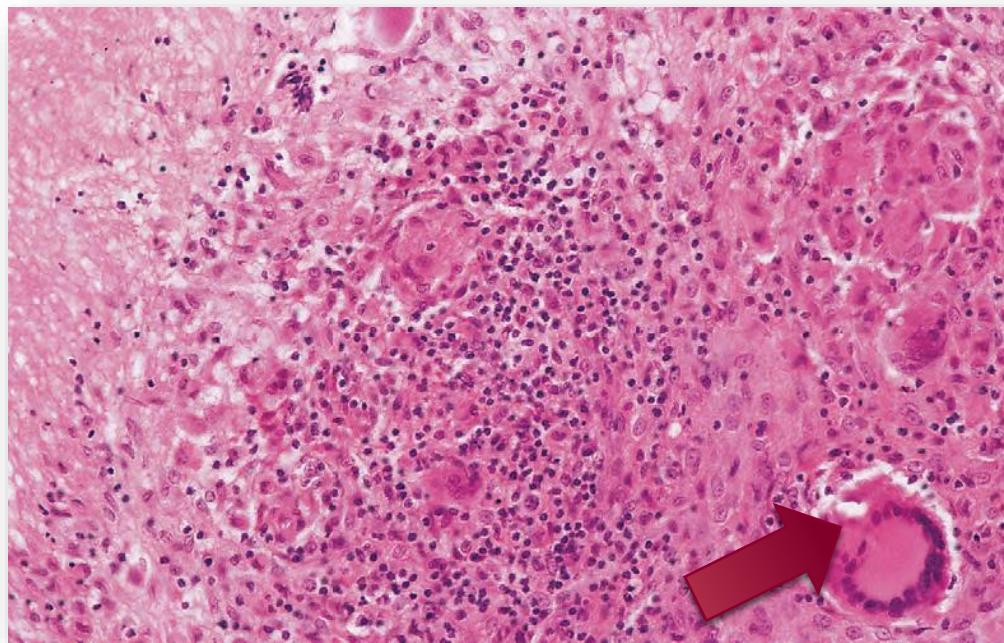
Bakterial meningitis



Chronic meningitis

Mycobacterium tuberculosis

- Meningitis – Fibrinous exudate
- Intraparenchymal mass (tuberculoma)
- Chronic tuberculous infection - arachnoidal fibrosis - hydrocephalus



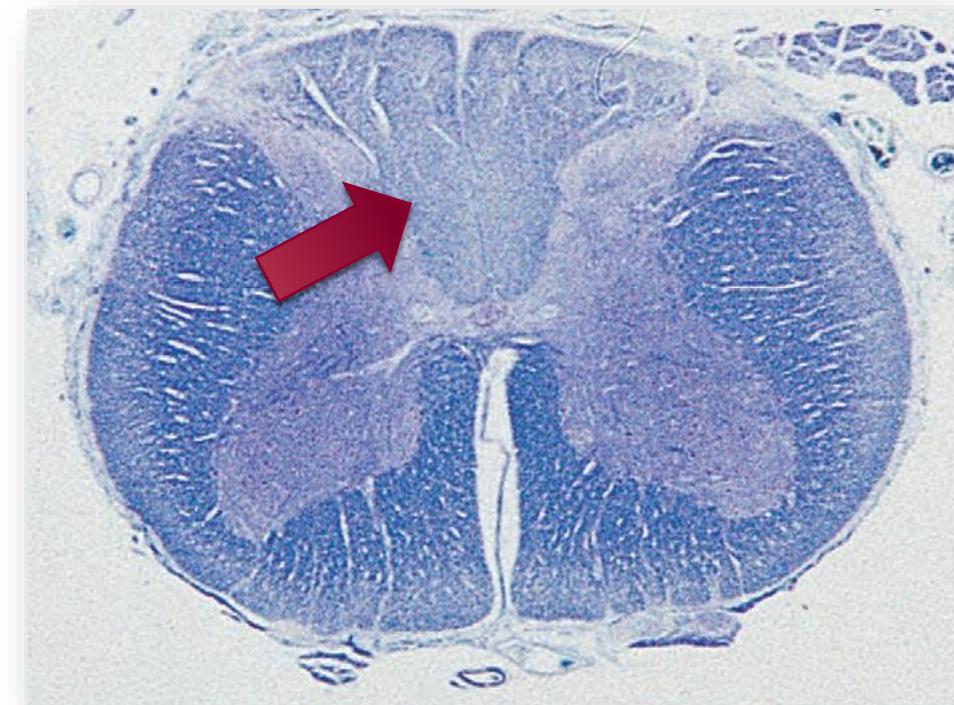
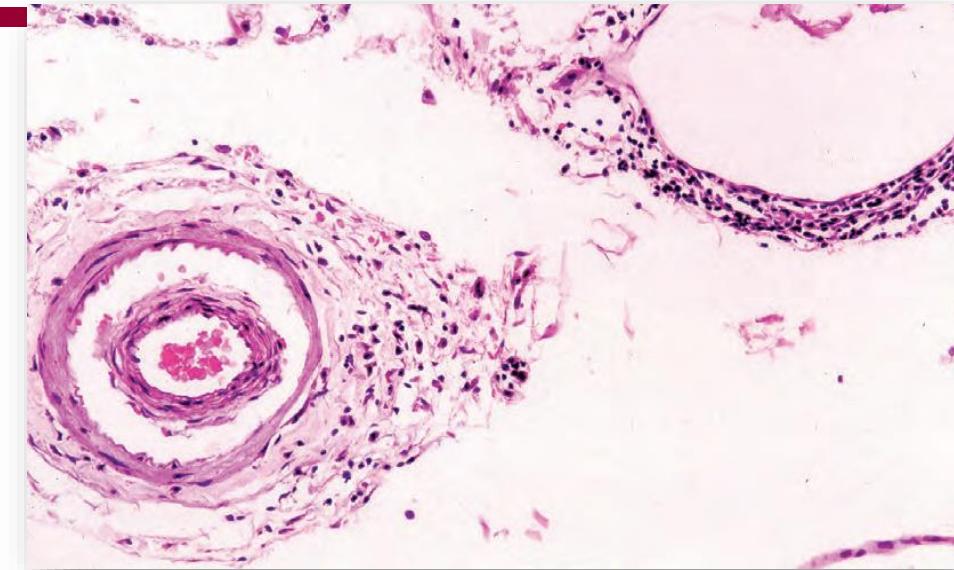
Spirochaetal infections

A. Neurosyphilis (3rd stage) – *Treponema pallidum*

- 10% of persons with untreated infection
- 1. Chronic meningitis/meningovascular neurosyphilis
 - Involves the base of the brain
- 2. Paretic neurosyphilis
 - Neuron loss – loss of mental, physical functions
- 3. Tabes dorsalis
 - Sensory nerves in the dorsal roots
 - Sensory ataxia

B. Neuroborreliosis – *Borrelia burgdorferi*

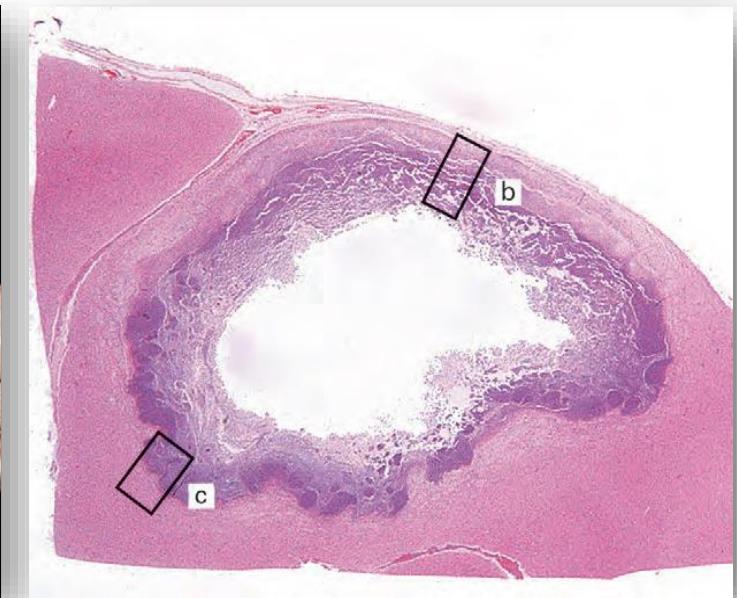
- Aseptic meningitis
- Facial nerve palsies
- Mild encephalopathy
- Polyneuropathies



PARENCHYMAL INFECTIONS

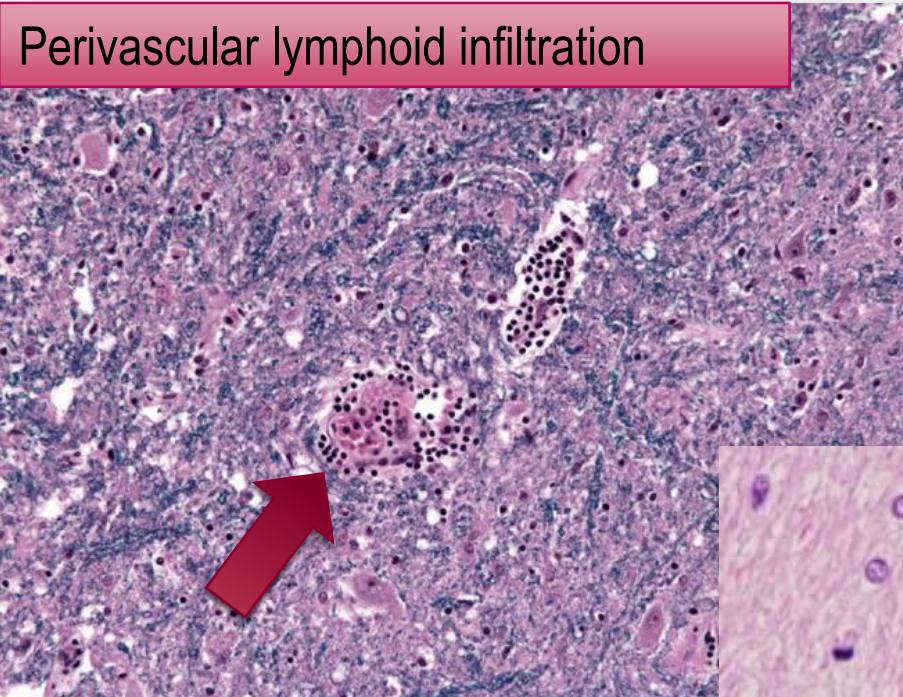
Brain abscesses

- Bacterial infections
- Spread:
 - Direct implantation
 - Local extension
 - Hematogenous spread
- Symptoms - Focal

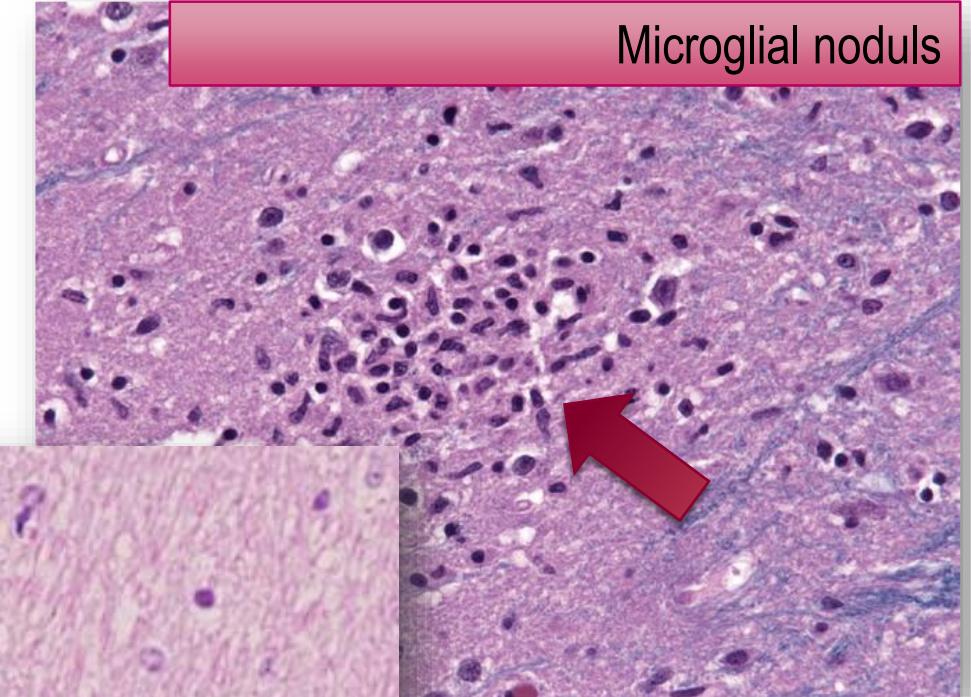


Viral encephalitis

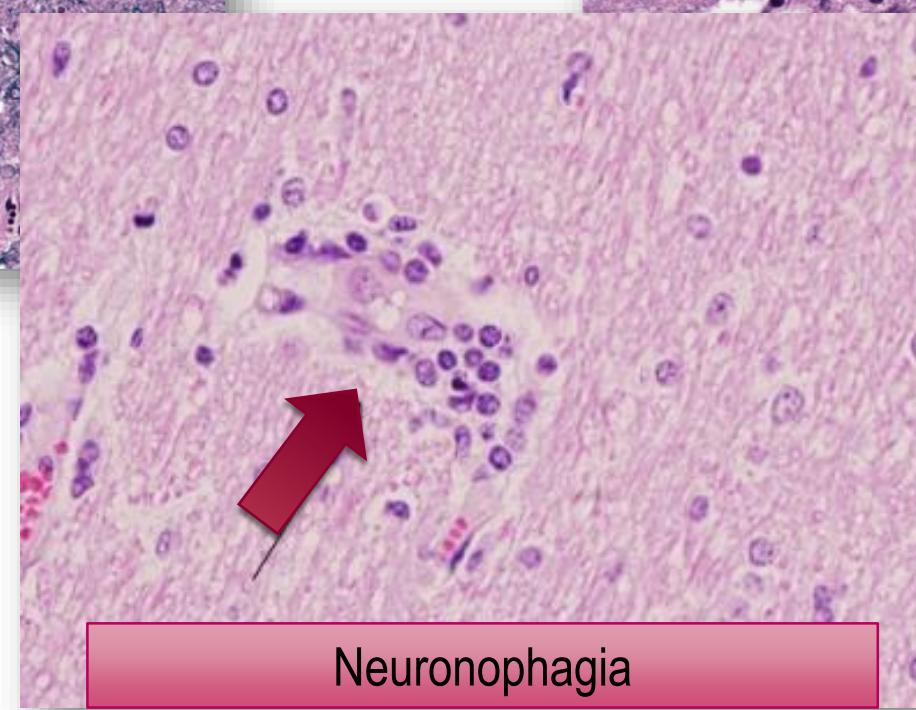
Perivascular lymphoid infiltration



Microglial nodules



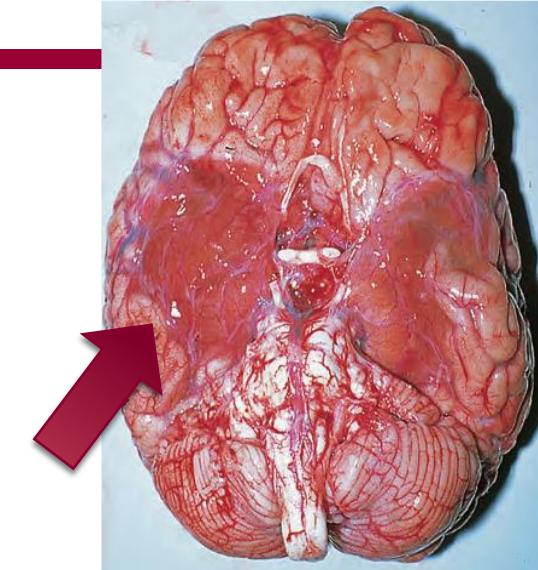
Neuronophagia



Herpes virus

A. Herpes simplex-1

- Children and young adults
- Frontal, temporal lobe involvement
- Necrotizing encephalitis



Necrotizing encephalitis

B. Herpes simplex-2

- Adults
- Viral meningitis
- Primary HSV genital inf - neonates



Cowdry A body

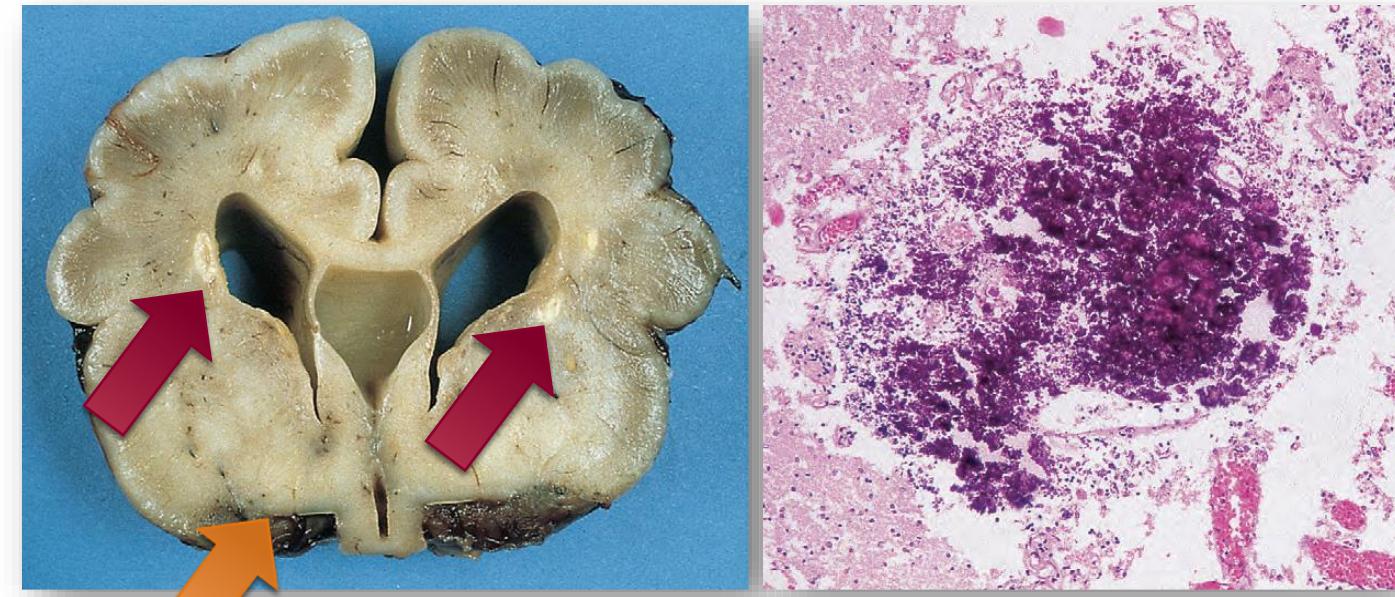
C. Varicella zoster

- Immunosuppressed patients
- HZV encephalitis

Cytomegalovirus

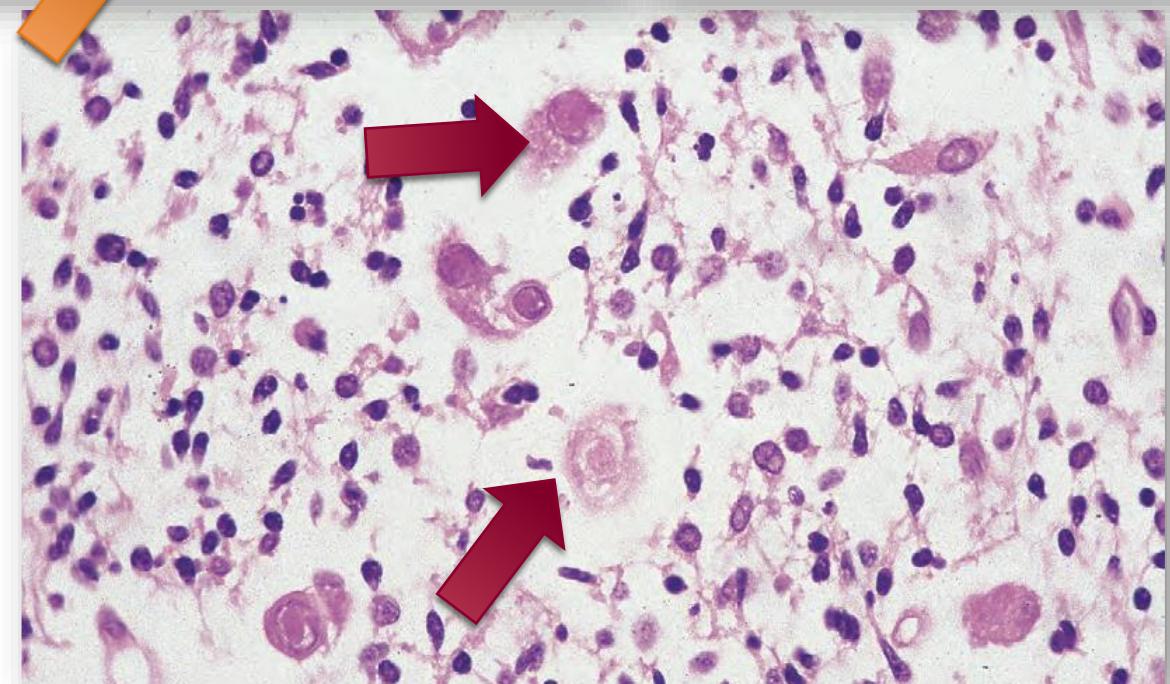
A. Fetal infection

- **TORCH**
- Periventricular necrosis
- Microcephalia
- Periventricular calcification



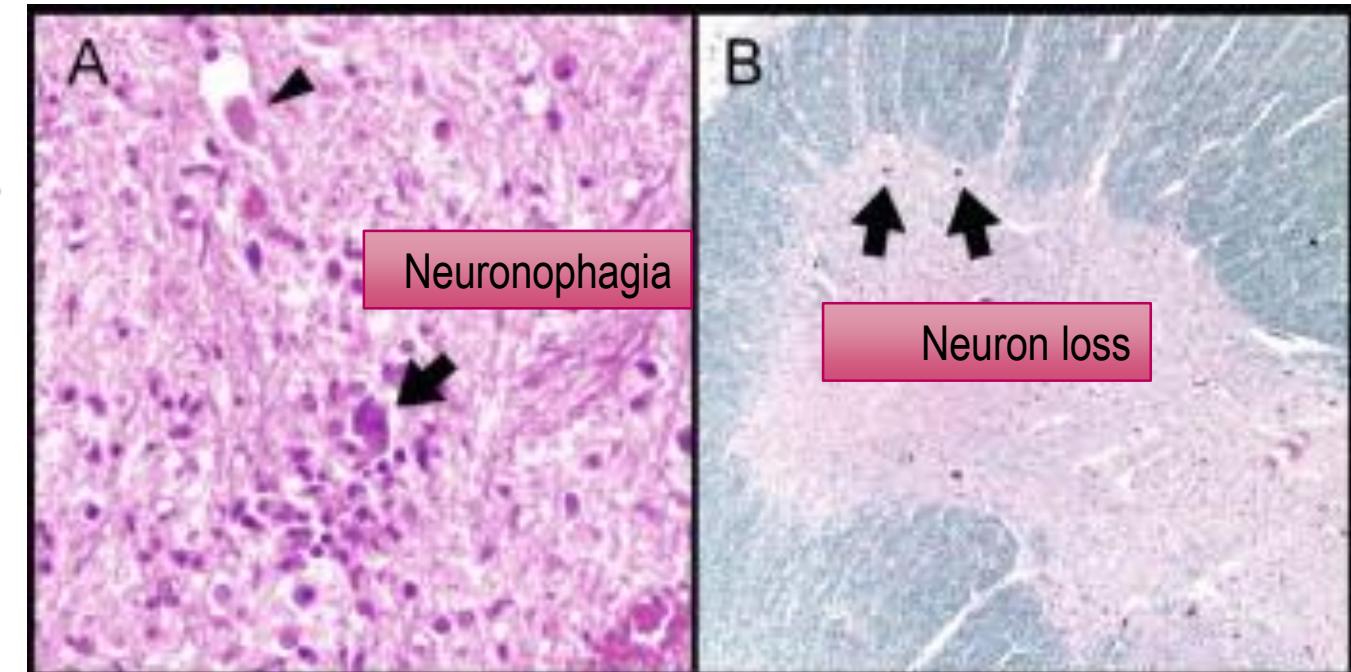
B. Adult infection

- Immunosuppressed patients
- Periventricular
- Subacute encephalitis



Poliovirus

- Gastroenteritis – Secunder CNS spread
 - **Poliomyelitis anterior acuta /Paralytic poliomyelitis**
 - Damages motor neurons in the spinal cord and brain stem
 - Flaccid paralysis with muscle wasting and hyporeflexia
- 25 to 35 years – **Postpolio syndrome**
 - Progressive weakness, pain

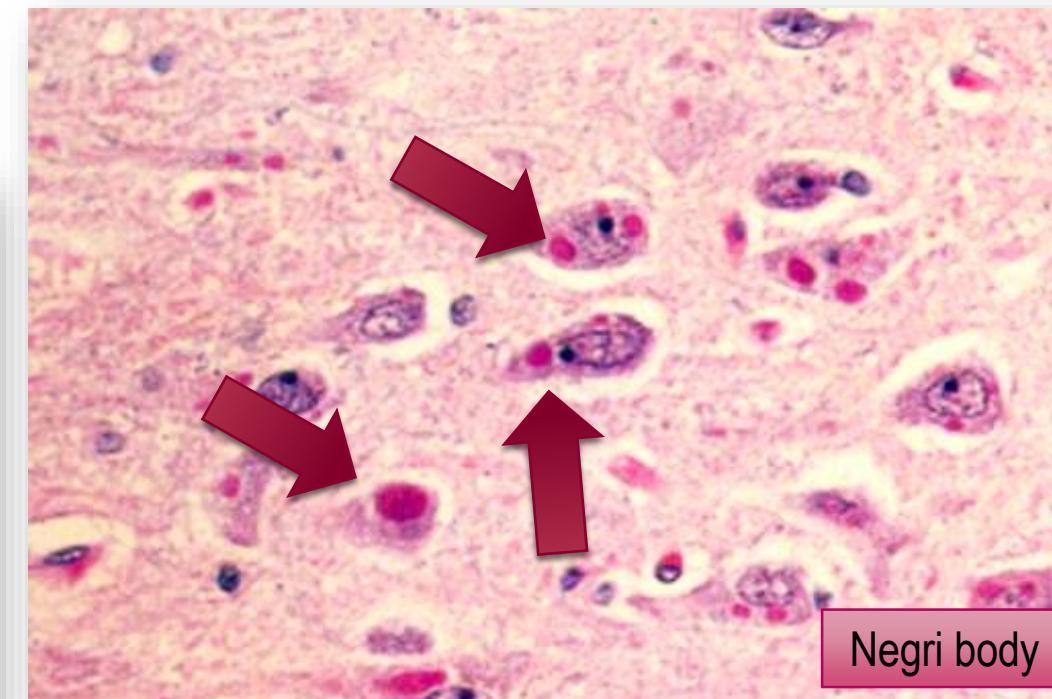
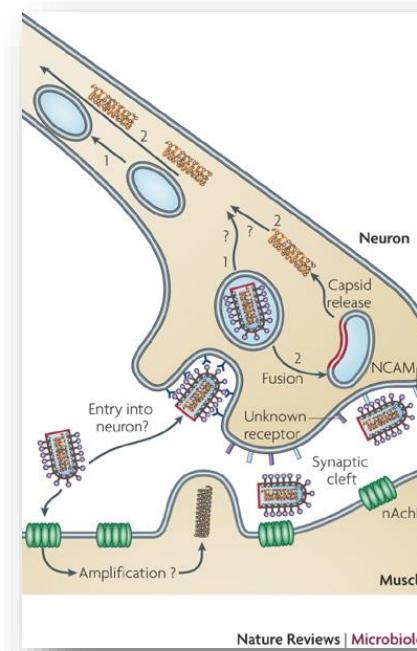


Retrograde trans-synaptic spread

Rabies Virus

Rabies

- Rabid animals, usually by a bite
- Ascending along the peripheral nerves
 - The incubation period depends on the distance between the wound and the brain
- Symptoms:
 - Non specific
 - Signs of CNS excitability
 - Pain, hydrophobia
 - Mania-coma



Human Immunodeficiency virus

A. Asepticus meningitis

- Within 1 to 2 weeks in about 10% of patients

B. HIV Encephalitis (HIVE)

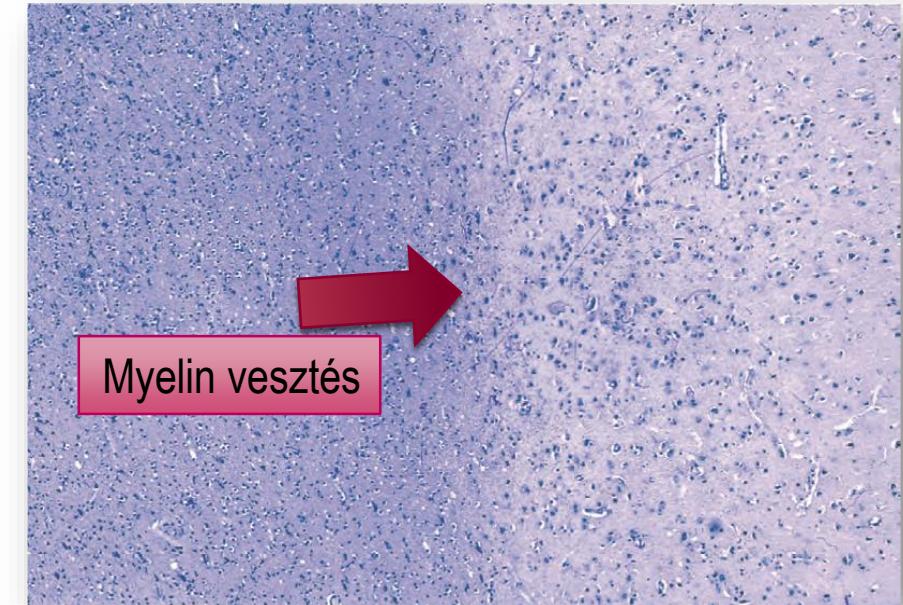
- Perivascular lymphoid infiltration
- Myelin loss in the hemispheres (Leukoencephalopathia)
- Microglial noduls
- Giant cells

C. Opportunistic infections

- Toxoplasma
- Cryptococcal
- Progressive multifocal leukoencephalopathy (PML)
- Cytomegalovirus (CMV)

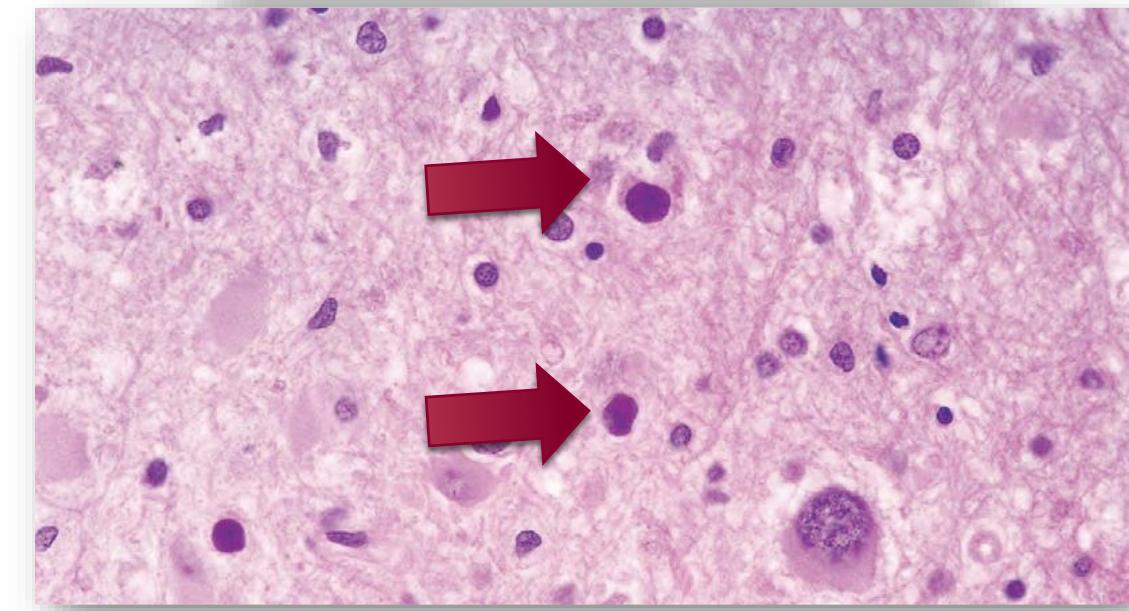
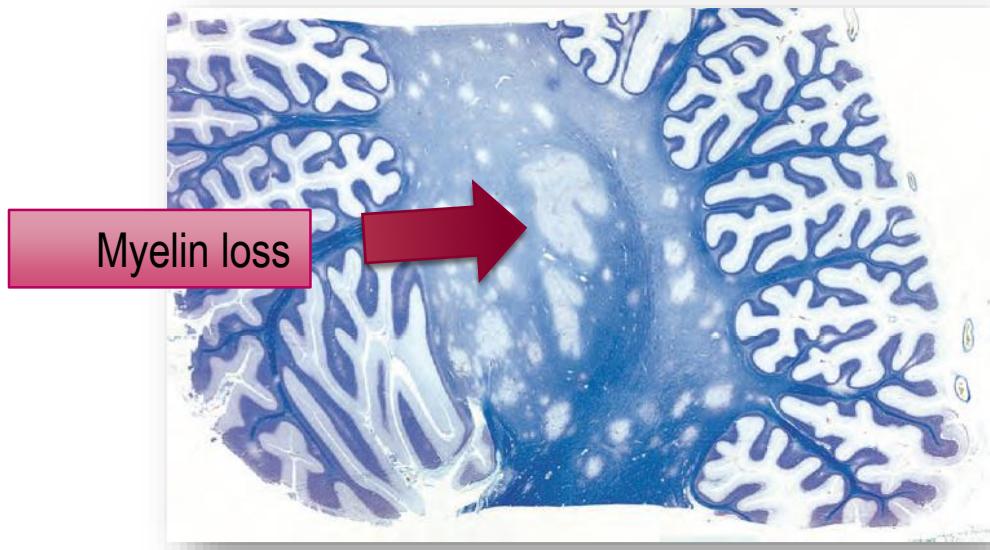
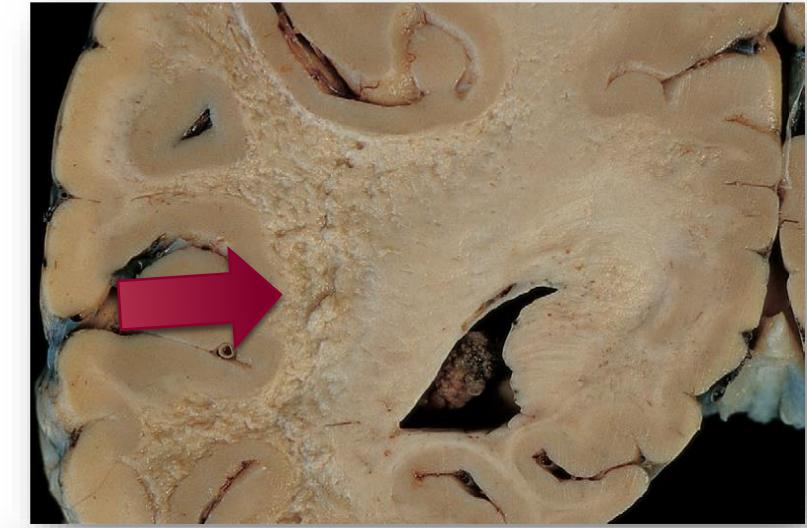
D. Primary CNS lymphoma

- EBV +



JC virus / Progressive multifocal leukoencephalopathy (PML)

- Polyoma virus
- Infects oligodendroglial cells
 - Demyelinisation
 - White matter – Hemispheres, Cerebellum
- Progressive neurologic symptoms



Fungal infections

A. *Candida Albicans*

- Multiplex microabscesses

B. *Mucormycosis*

- Nasal cavity, sinus infection
- Direct extension, Vascular invasion

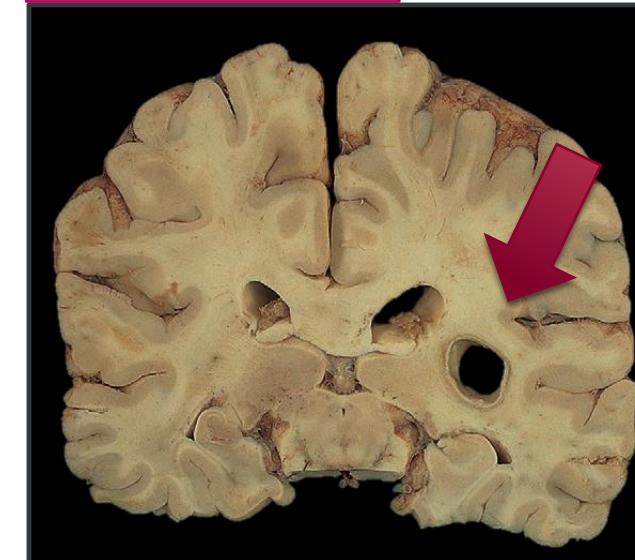
C. *Aspergillus fumigatus*

- Hemorrhagic infarctions
- Vascular invasion

D. *Cryptococcus neoformans*

- Meningitis, Meningoencephalitis
- Fulminant

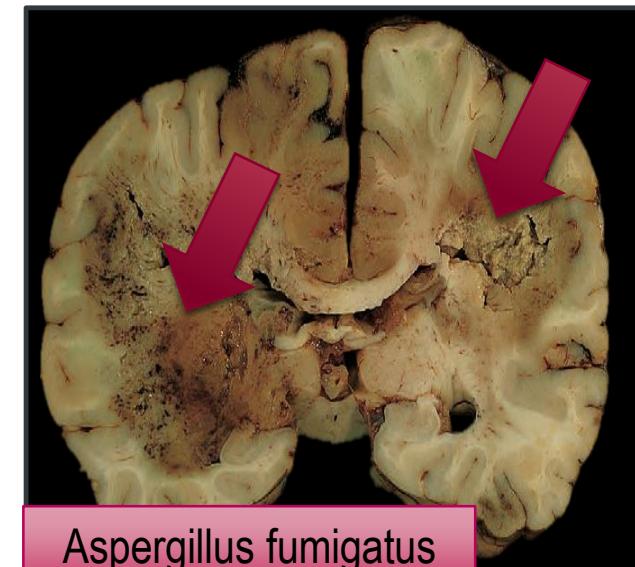
Candida albicans



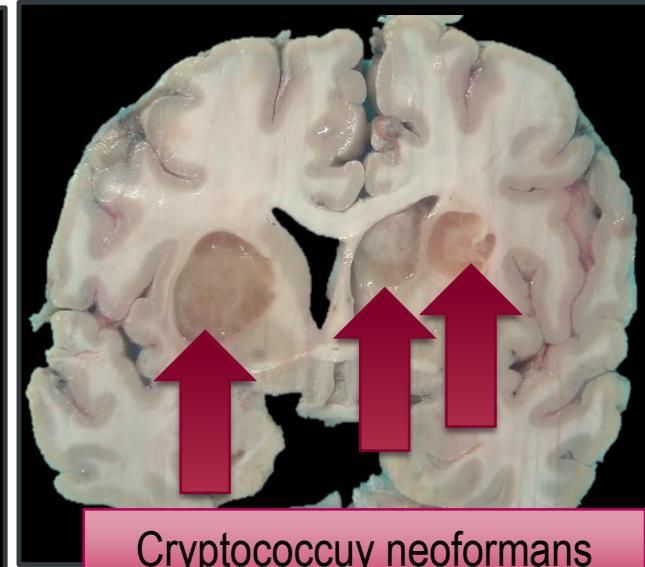
Mucormycosis

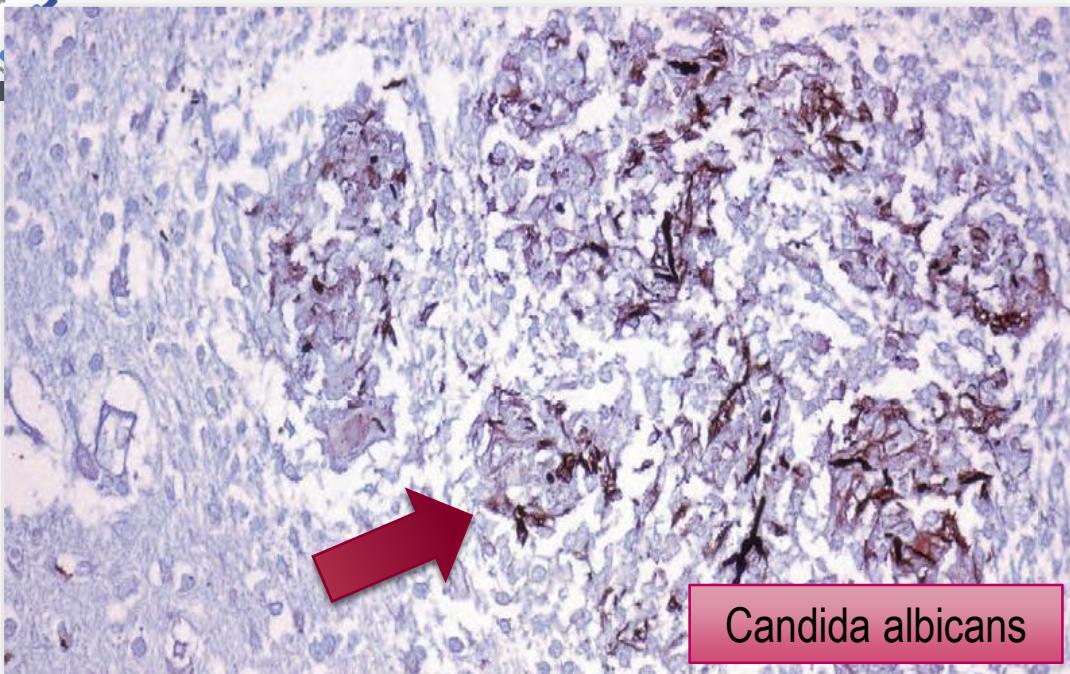


Aspergillus fumigatus

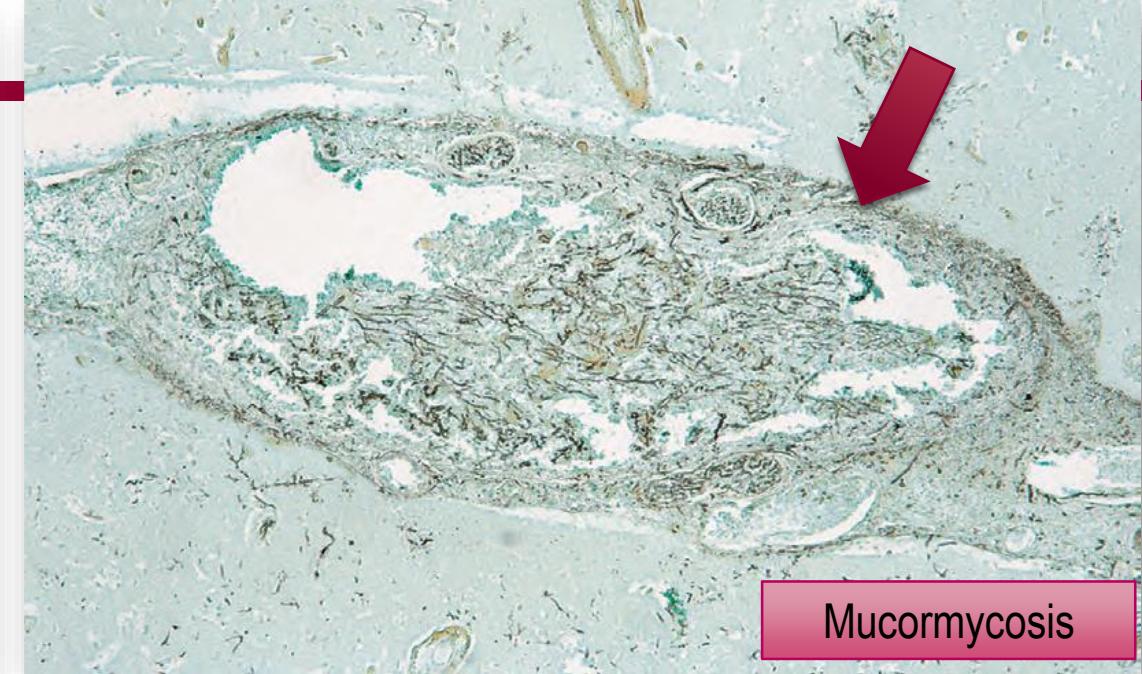


Cryptococcuy neoformans

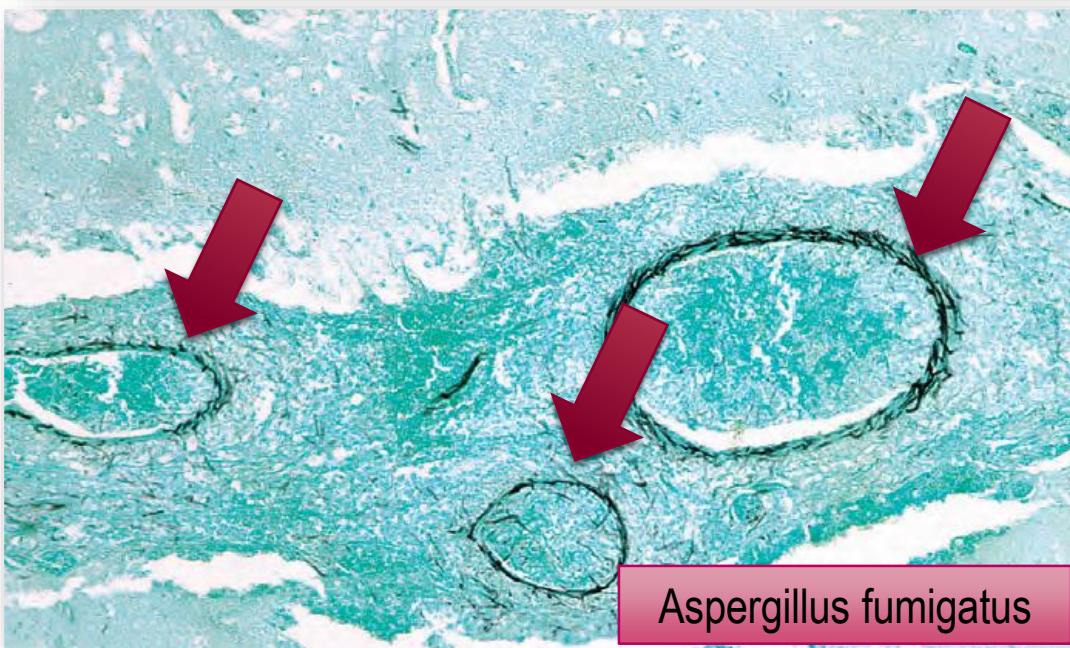




Candida albicans



Mucormycosis



Aspergillus fumigatus



Cryptococcus neoformans

Protozoal infections - Toxoplasmosis

Toxoplasma gondii

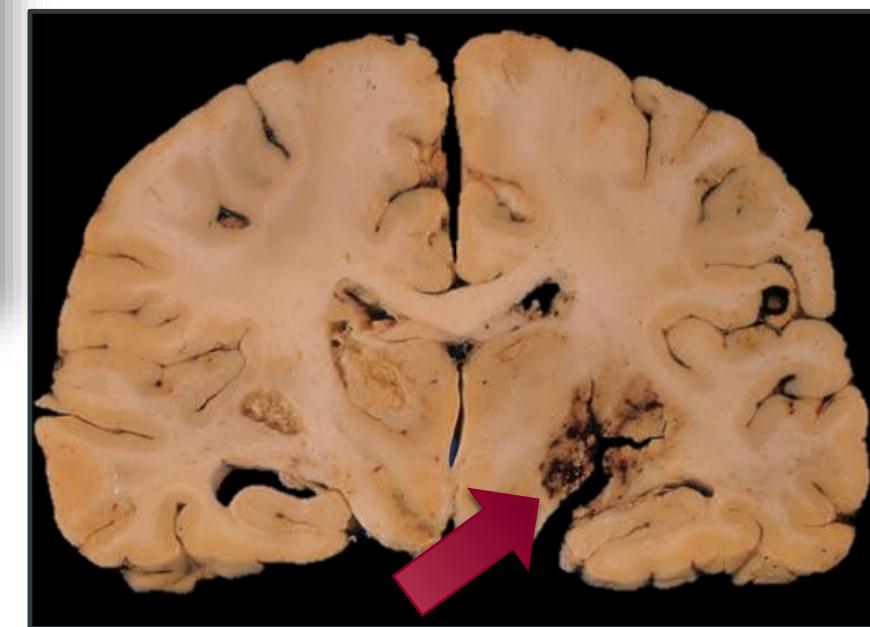
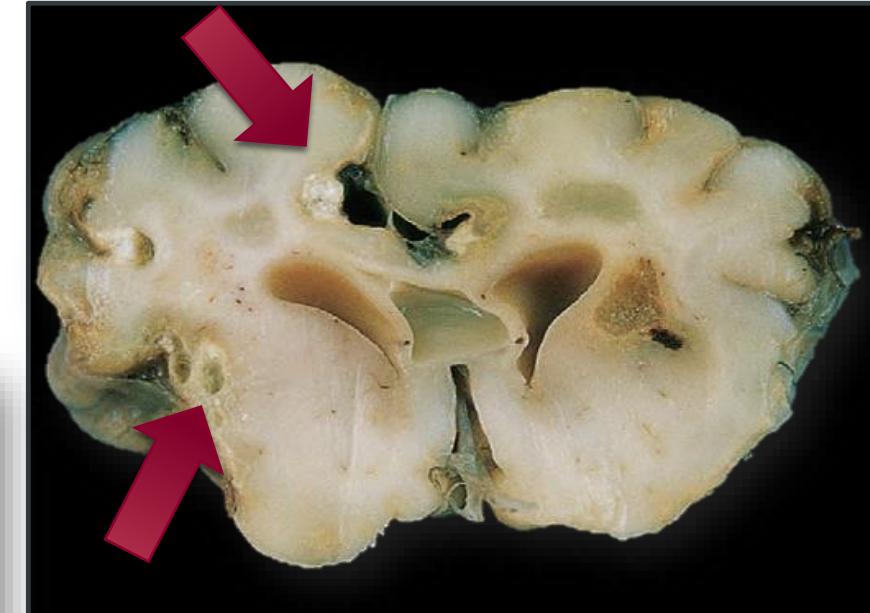
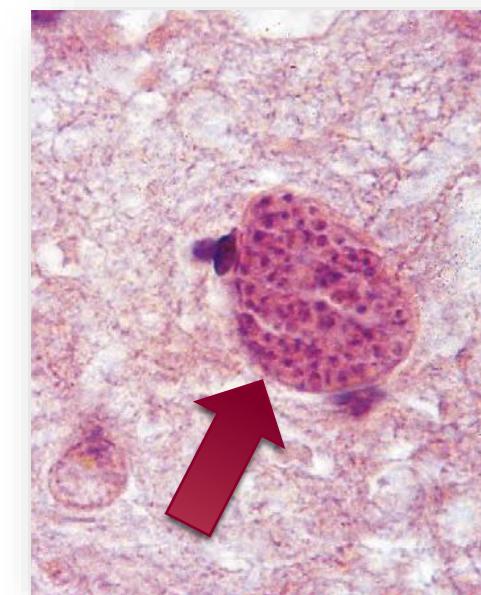
- Humans intermedier hosts
- Definitive host - Cat

A. Fetal infection

- TORCH
- Chorioretinitis
- Hydrocephalus
- Intracranial calcification

B. Adult infection

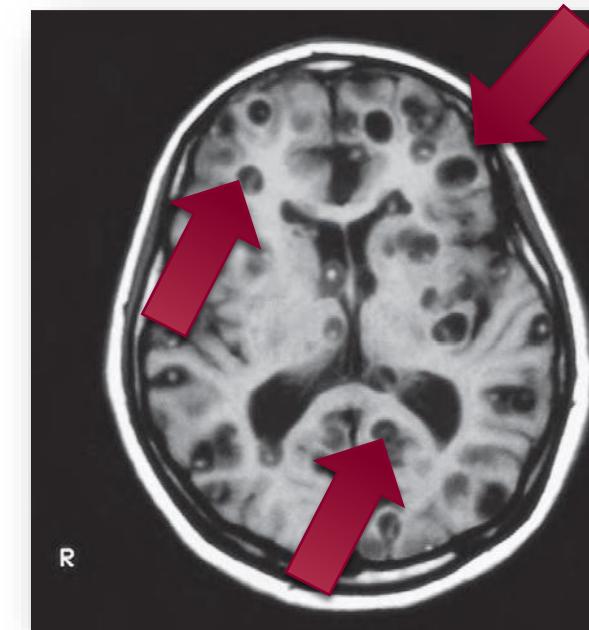
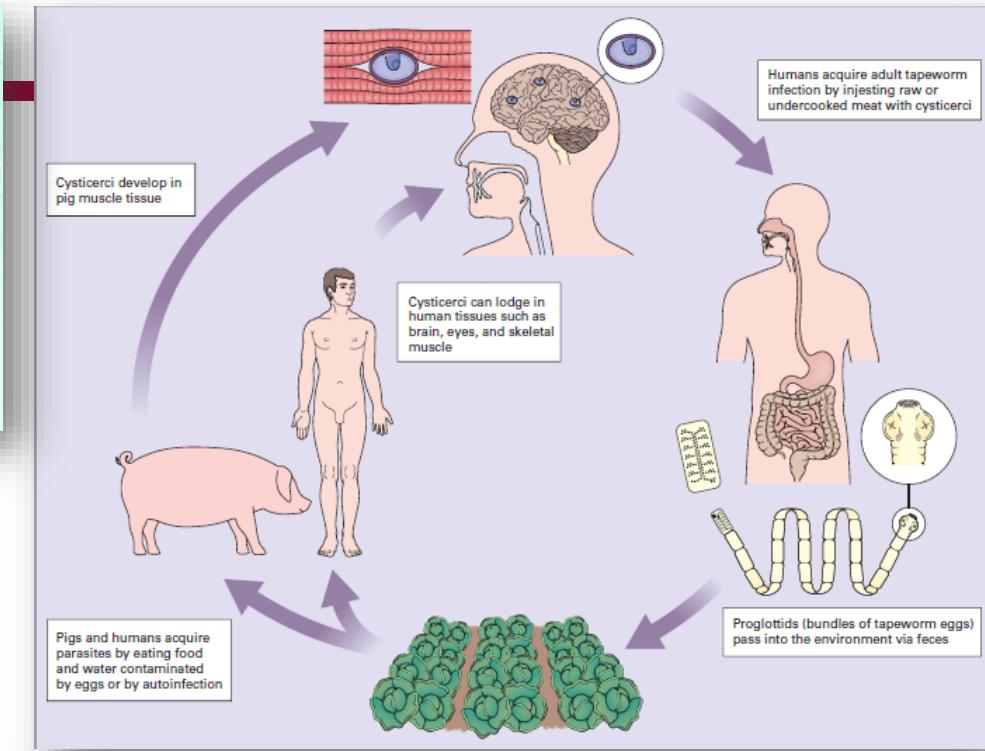
- Immunosuppressed adults
- Subacute symptoms
- Evolving in 1 or 2 week period
- Focal-diffuse



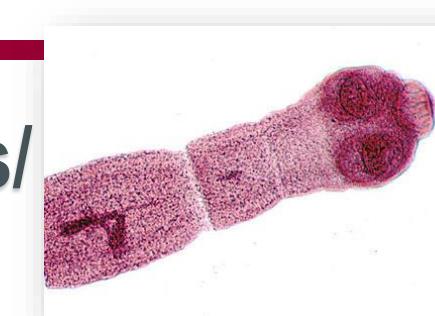
Parasitic Infections

Tenia solium - Cysticercosis

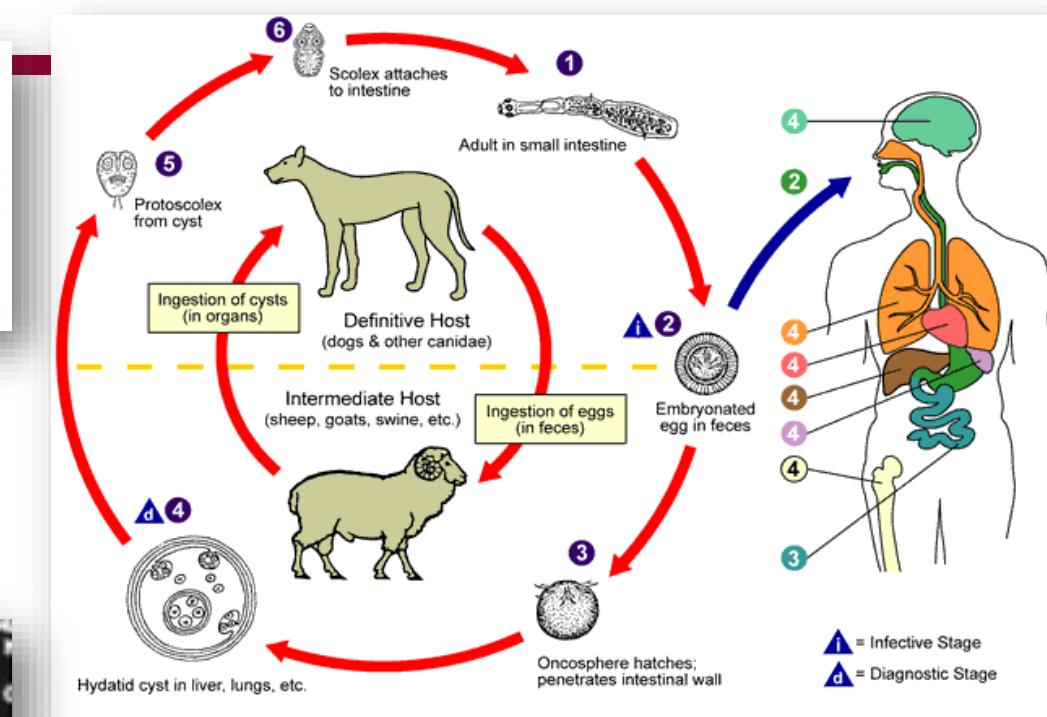
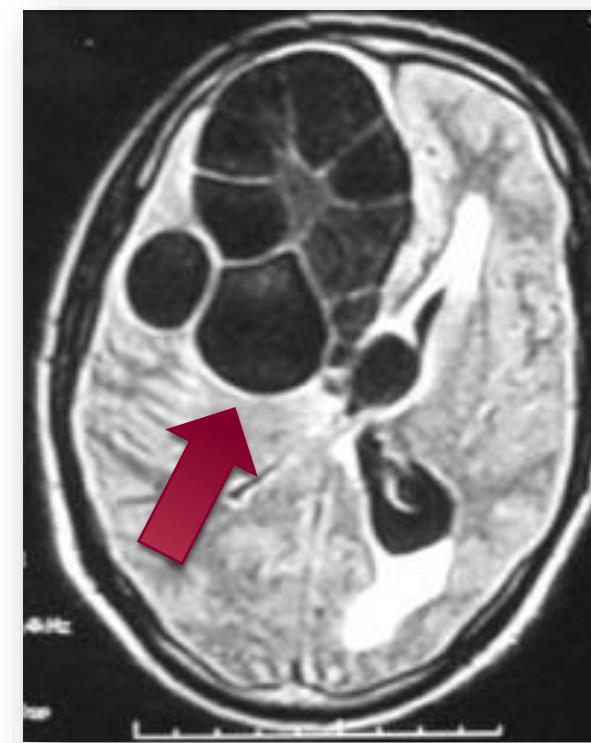
- End-stage infection
 - Larval organisms leave the lumen of the gastrointestinal tract
 - Encyst – Brain – subarachnoid space
- Symptoms
 - Focal symptoms
 - Epilepsy



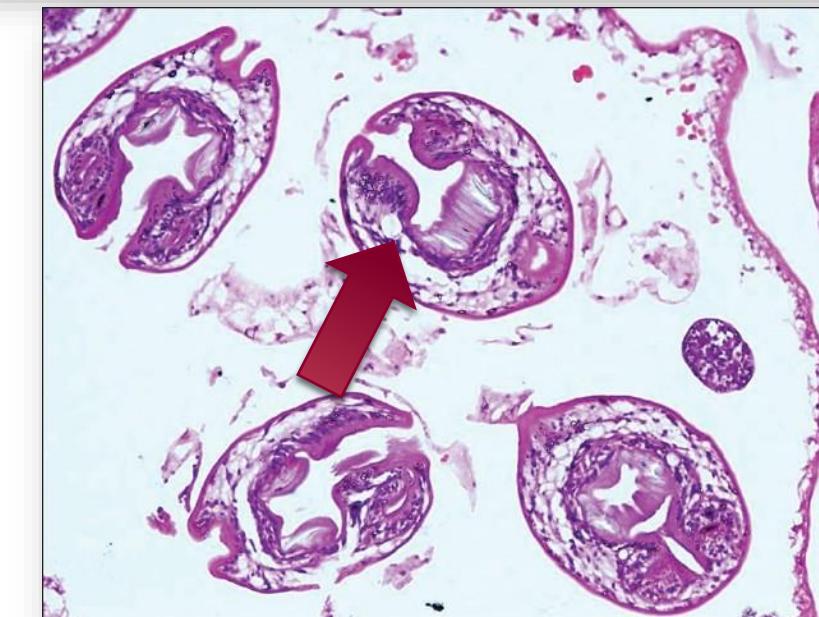
Echinococcus /Hydatidosis/



- Childhood
- Contact with dogs
 - Encysts – Usually liver, lung rarely brain



- Symptoms
 - Focal signs
 - Epilepsy





- Robbins Basic Pathology, 10th Edition
- Neuropathology: A Reference Text of CNS Pathology, 3rd Edition

