

# CNS Tumors

## Pathology

# CNS Tumors

## Incidence

- The annual incidence of tumors of the CNS ranges from:
  - 10 to 17 per 100,000 persons for intracranial tumors
  - 1 to 2 per 100,000 persons for intraspinal tumors
- About half to three-quarters are primary tumors, and the rest are metastatic

# CNS Tumors

## and childhood

- Tumors of the CNS are a large proportion of cancers of childhood, accounting for as many as 20% of all tumors
- CNS tumors in childhood differ from those in adults both in histologic subtype and location
- In childhood, tumors are likely to arise in the posterior fossa, while in adults they are mostly supratentorial

# CNS Tumors

## General characteristics

- The anatomic site of the neoplasm can have lethal consequences irrespective of histological classification (i.e. benign tumors can be fatal in certain locations)
  - *examples on such locations?*
- These tumors do not have detectable premalignant or in situ stages comparable to those of carcinomas
- The pattern of spread of primary CNS neoplasms differs from that of other tumors:
  - rarely metastasize outside the CNS
  - the subarachnoid space does provide a pathway for spread
    - *What are the layers that surround subarachnoid space?*

# CNS Tumors

## General characteristics

- Even low-grade lesions may infiltrate large regions of the brain, leading to serious clinical deficits, nonresectability, and poor prognosis

# CNS Tumors

## General manifestations

- Seizures, headaches, vague symptoms
- Focal neurologic deficits related to the anatomic site of involvement
- Rate of growth may correlate with history

# CNS tumors

## Classification

- May arise from:
  - cells of the coverings (meningiomas)
  - cells intrinsic to the brain (gliomas, neuronal tumors, choroid plexus tumors)
  - other cell populations within the skull (primary CNS lymphoma, germ-cell tumors)
  - they may spread from elsewhere in the body (metastases)

# CNS Tumors

## Gliomas

- *Astrocytomas*
- *Oligodendrogliomas*
- *Ependymomas*



# CNS Tumors

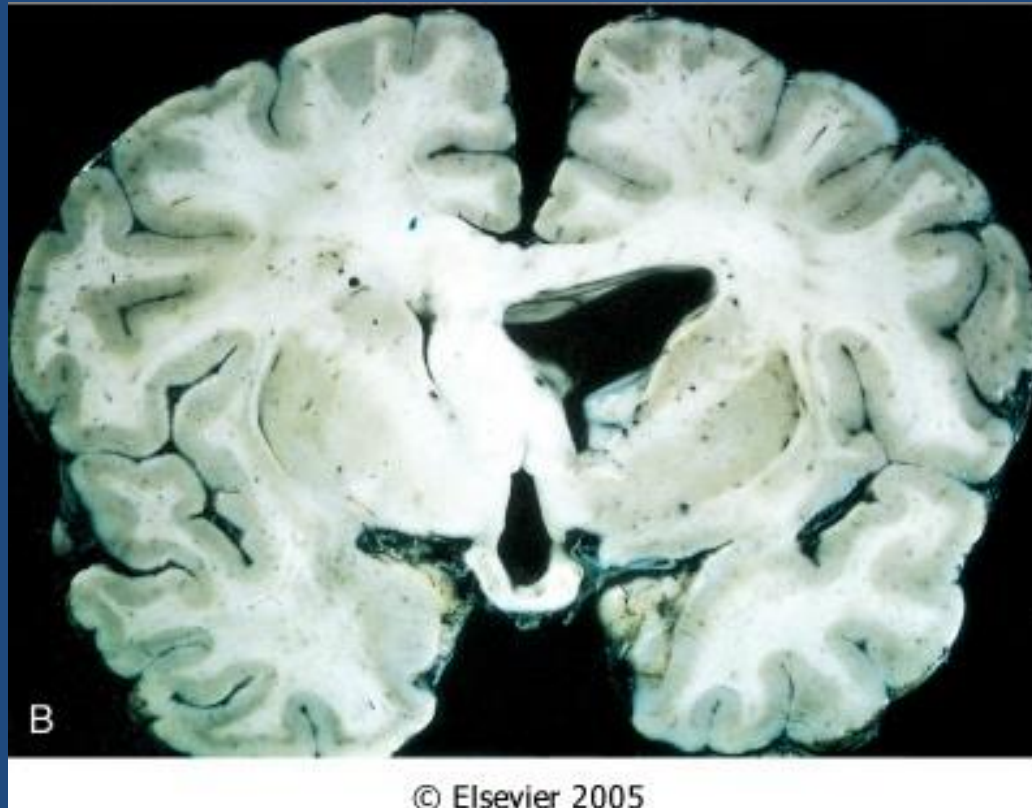
## *Astrocytomas*

- Fibrillary:
  - 4<sup>th</sup> to 6<sup>th</sup> decade
  - Commonly cerebral hemisphere
  - Variable grades:
    - Diffuse astrocytoma (**Grade II**)
    - Anaplastic astrocytoma (**Grade III**)
    - Glioblastoma (**Grade IV**)
- Pilocytic ( **Grade I** )
  - Children and young adults
  - Commonly cerebellum
  - Relatively benign

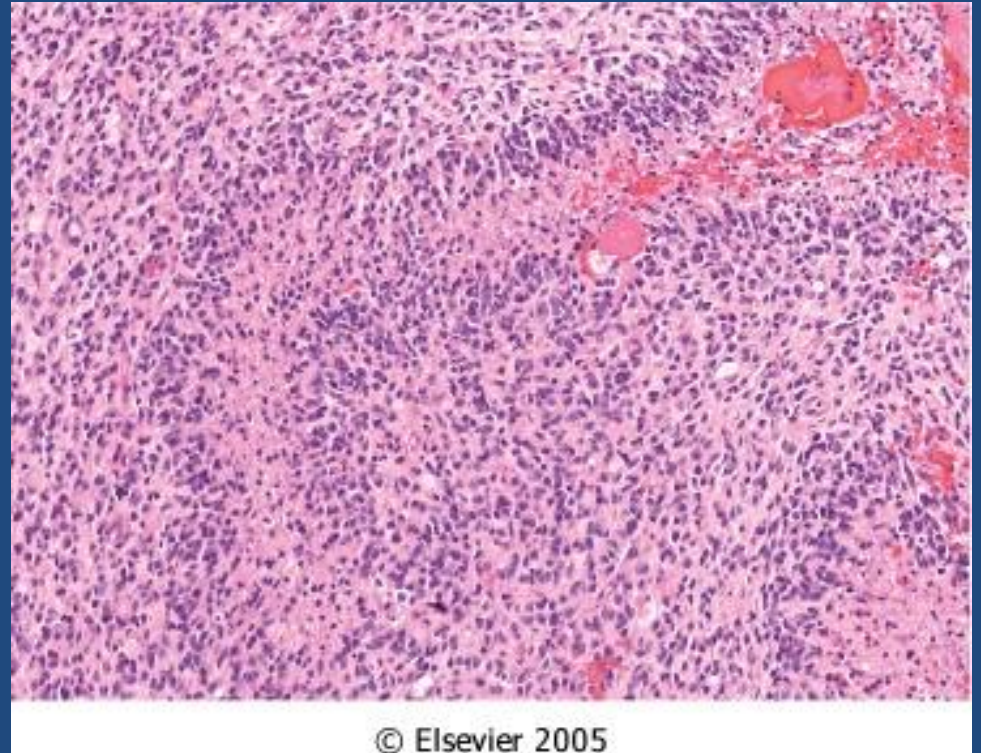
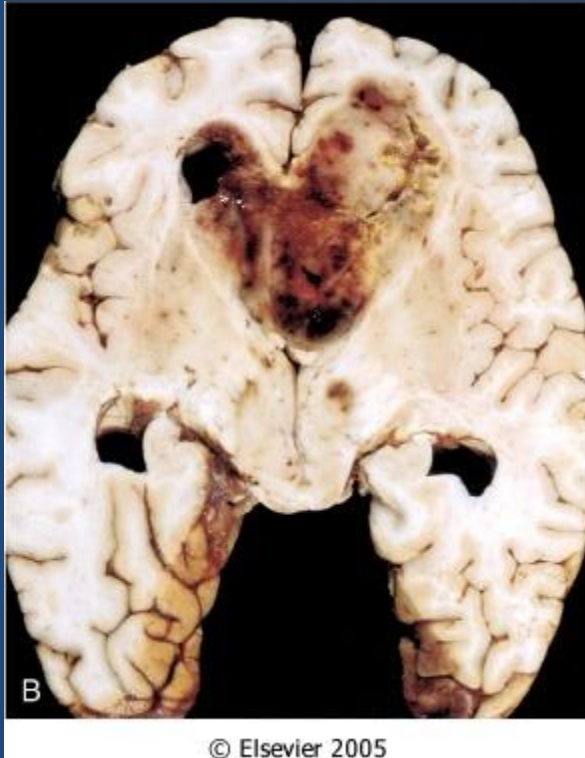
# CNS Tumors

## Fibrillary Astrocytoma

- Well differentiated “diffuse astrocytoma” (WHO grade II) :
  - Static or progress slowly (mean survival of more than 5 years)
  - Moderate cellularity
  - Variable nuclear pleomorphism
- Less differentiated (higher-grade) :
  - Anaplastic astrocytoma (WHO grade III)
    - More cellular
    - Greater nuclear pleomorphism
    - Mitosis
  - Glioblastoma (WHO grade IV) :
    - With treatment, mean survival of 8-10 months
    - All the features of anaplastic astrocytoma, plus:
      - *Necrosis and/or vascular or endothelial cell proliferation*



- Note that diffuse astrocytoma are poorly demarcated



- GBM
  - Pseudopalisading necrosis
  - AND/OR
  - Vascular proliferation

# CNS Tumors

## Astrocytoma

- Mutations that alter the enzymatic activity of two isoforms of the metabolic enzyme isocitrate dehydrogenase (IDH1 and IDH2) are common in lower-grade astrocytomas

# CNS Tumors

## Glioblastoma

- **Secondary** glioblastomas share *p53* mutations that characterized low-grade gliomas
- While **primary** glioblastomas are characterized by amplification of the epidermal growth factor receptor (*EGFR*) gene

# CNS Tumors

## Pilocytic Astrocytoma

- Often cystic, with a mural nodule
- Well circumscribed
- "hairlike"=pilocytic processes that are GFAP positive
- Rosenthal fibers & hyaline granular bodies are often present
- Necrosis and mitoses are typically absent



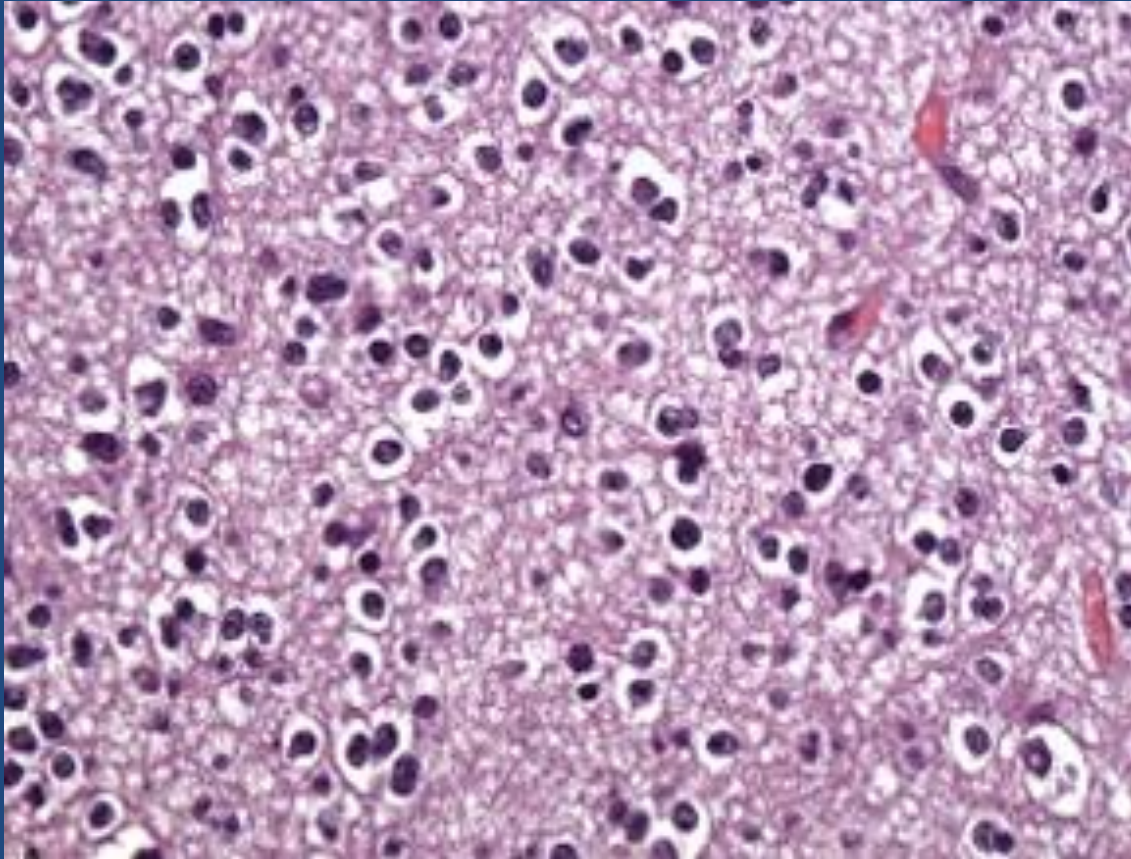




# CNS Tumors

## Oligodendroglioma

- The most common genetic findings are loss of heterozygosity for chromosomes 1p and 19q
- Fourth and fifth decades
- Cerebral hemispheres, with a predilection for white matter
- Better prognosis than do patients with astrocytomas (5 to 10 years with Rx)
- Anaplastic form prognosis is worse



- In oligodendroglioma tumor cells have round nuclei, often with a cytoplasmic halo
- Blood vessels in the background are thin and can form an interlacing pattern

→ *What additional features are needed for anaplastic oligodendroglioma?*



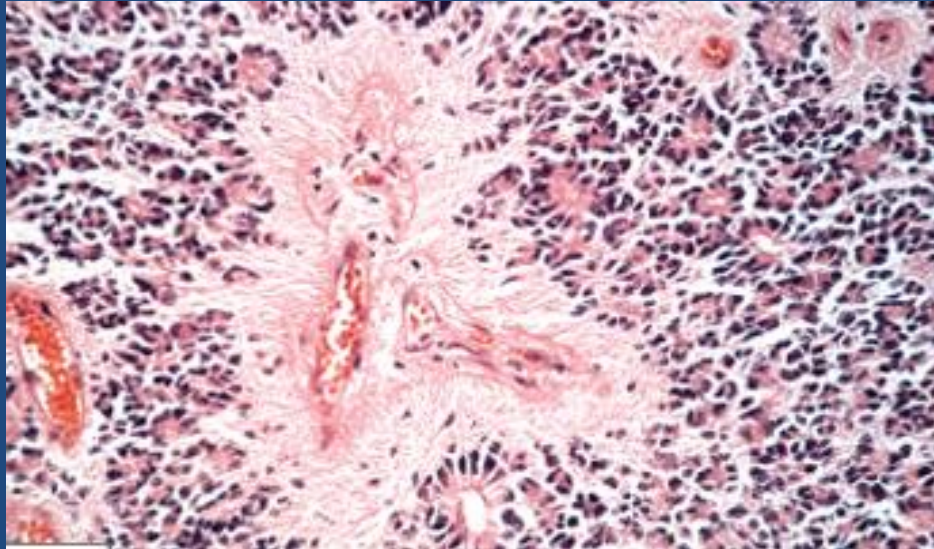
# CNS Tumors

## Ependymoma

- Most often arise next to the ependyma-lined ventricular system, including the central canal of the spinal cord
- Occurs in the first two decades of life, they typically occur near the fourth ventricle
- In adults, the spinal cord is their most common location

# CNS Tumors

## Ependymoma



- Tumor cells may form round or elongated structures (**rosettes**, canals)  
→ *what is a rosette?*
- **perivascular pseudo-rosettes**
- Anaplastic ependymomas show increased cell density, high mitotic rates, necrosis and less evident ependymal differentiation



# CNS Tumors

## Meningioma

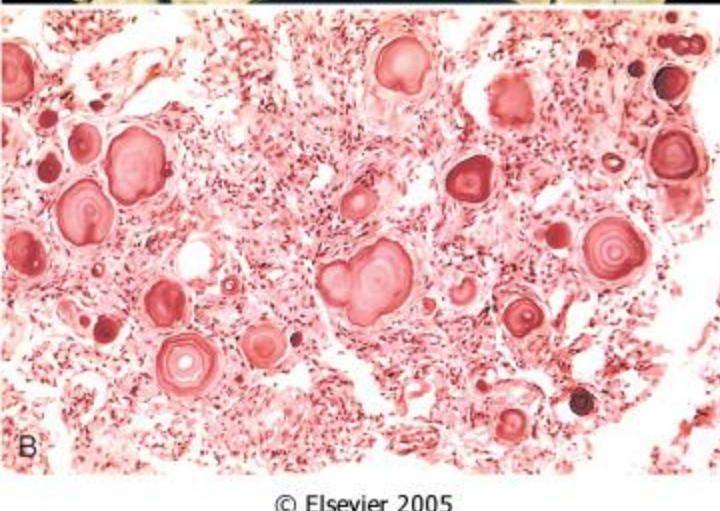
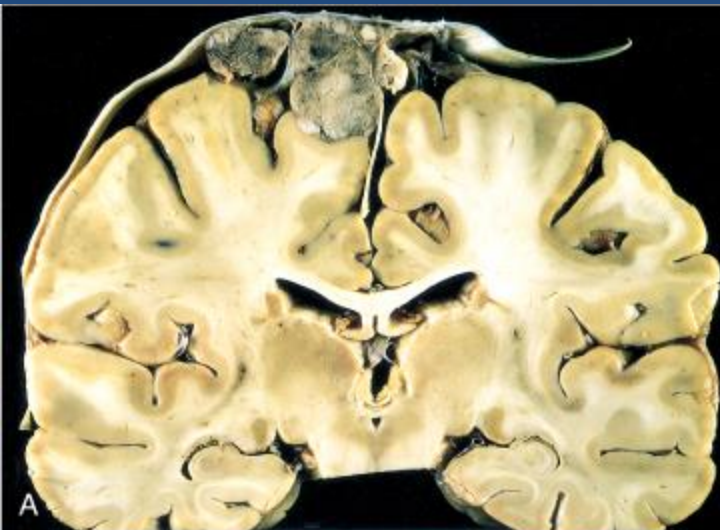
- Predominantly benign tumors of adults
- Origin: meningothelial cell of the arachnoid



# CNS Tumors

## Meningioma

- Well demarcated
- Attached to the dura with compression of underlying brain
- **Whorled** pattern of cell growth and **psammoma** bodies





# CNS Tumors

## Meningioma

- Main subtypes:
  - Syncytial
  - Fibroblastic
  - Transitional
- Also note:
  - Atypical meningiomas
  - Anaplastic (malignant) meningiomas

# CNS Tumors

## Meningioma

- Although most meningiomas are easily separable from underlying brain, some tumors infiltrate the brain.
- The presence of brain invasion is associated with increased risk of recurrence.



# CNS Tumors

## Medulloblastoma

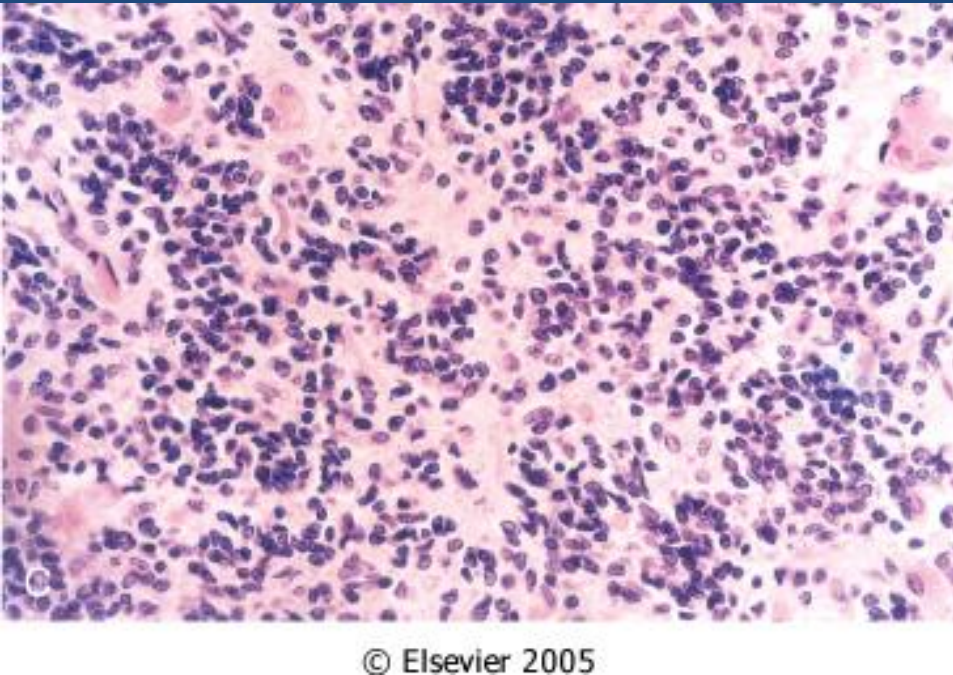
- Children and exclusively in the cerebellum
- Neuronal and glial markers may be expressed, but the tumor is often largely undifferentiated
- The tumor is highly malignant, and the prognosis for untreated patients is dismal; however, it is exquisitely radiosensitive
- With total excision and radiation, the 5-year survival rate may be as high as 75%



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# CNS Tumors

## Medulloblastoma



extremely cellular, with sheets of anaplastic ("small blue") cells  
small, with little cytoplasm and hyperchromatic nuclei; mitoses are abundant.



# Nervous system Tumors

## Schwannoma

- Benign
- In the CNS, they are often encountered within the cranial vault in the cerebellopontine angle, where they are attached to the vestibular branch of the eighth nerve (tinnitus and hearing loss)



# Nervous system Tumors

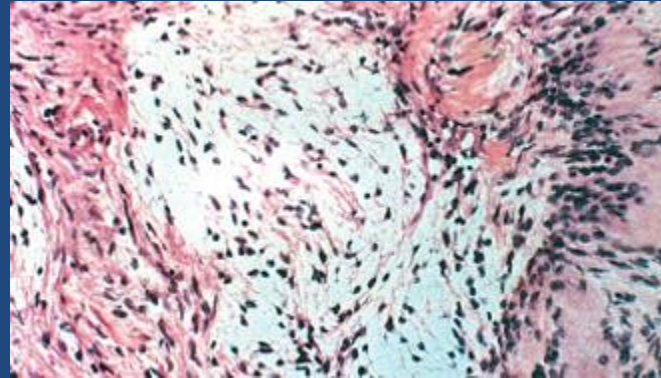
## Schwannoma

- Sporadic schwannomas are associated with mutations in the *NF2* gene
- Bilateral acoustic schwannoma is associated with NF2
- Attached to the nerve but can be separated from it

# Nervous system Tumors

## Schwannoma

- Cellular Antoni A pattern and less cellular Antoni B
- nuclear-free zones of processes that lie between the regions of nuclear palisading are termed Verocay bodies





# Nervous system Tumors

## Neurofibroma

- Examples: (*cutaneous neurofibroma*) or in peripheral nerve (*solitary neurofibroma*)
- These arise sporadically or in association with type 1 neurofibromatosis, rarely malignant
- *plexiform neurofibroma*, mostly arising in individuals with NF1, potential malignancy
- Neurofibromas cannot be separated from nerve trunk (in comparison to schwannoma)



# Nervous system Tumors

## Metastatic tumours

- About half to three-quarters of brain tumors are primary tumors, and the rest are metastatic
- Lung, breast, skin (melanoma), kidney, and gastrointestinal tract are the commonest
- Sharply demarcated masses with edema.





# Homework!

## FAMILIAL TUMOR SYNDROMES

- Describe the inheritance pattern and the main features of:
  - Type 1 Neurofibromatosis
  - Type 2 Neurofibromatosis
- Which one of these two syndromes, has a propensity for the neurofibromas to undergo malignant transformation at a higher rate than that observed for comparable tumors in the general population?

Tip: use the recommended textbook and the internet.

