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 of 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

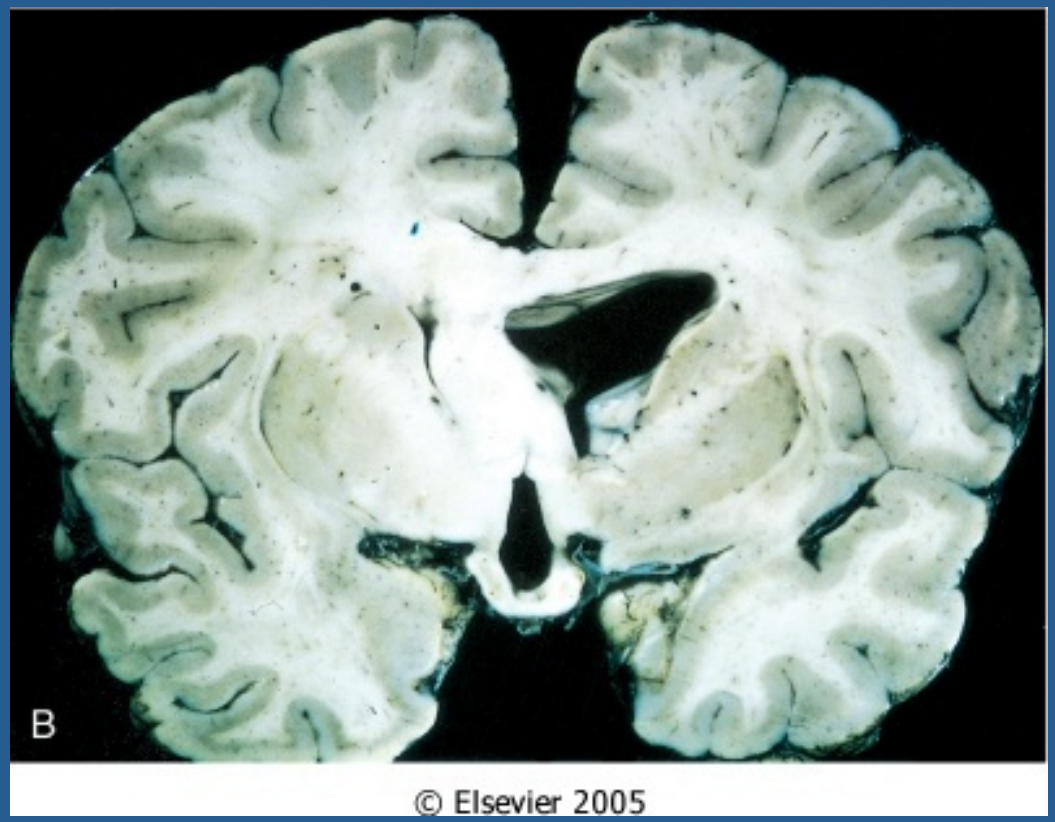
- *Astrocytomas*
- *Oligodendrogliomas*
- *Ependymomas*

CNS Tumors
Astrocytomas

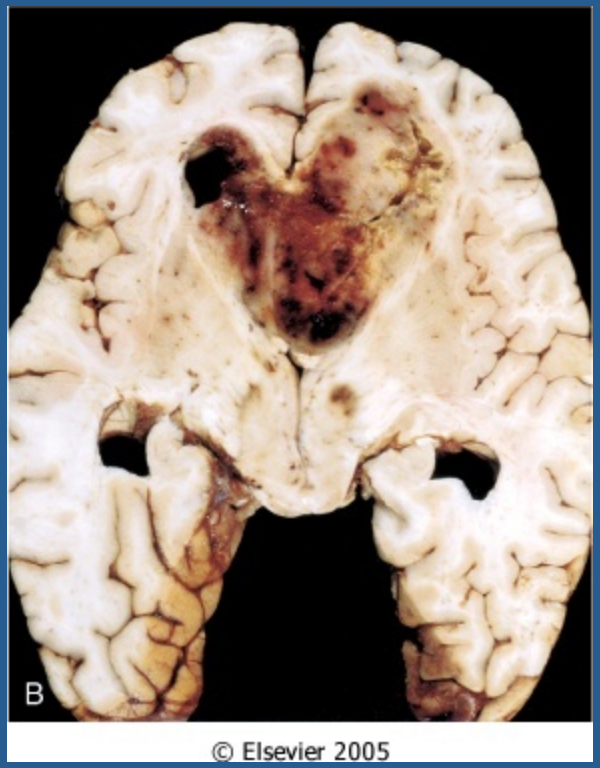
- Fibrillary:
  - 4^{th} to 6^{th} decade
  - Commonly cerebral hemisphere
  - Variable grades:
    - Diffuse astrocytoma **(Grade II)**
    - Anaplastic astrocytoma **(Grade III)**
    - Glioblastoma **(Grade IV)**
- Pilocytic **(Grade I)**
  - Children and young adults
  - Commonly cerebellum
  - Relatively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

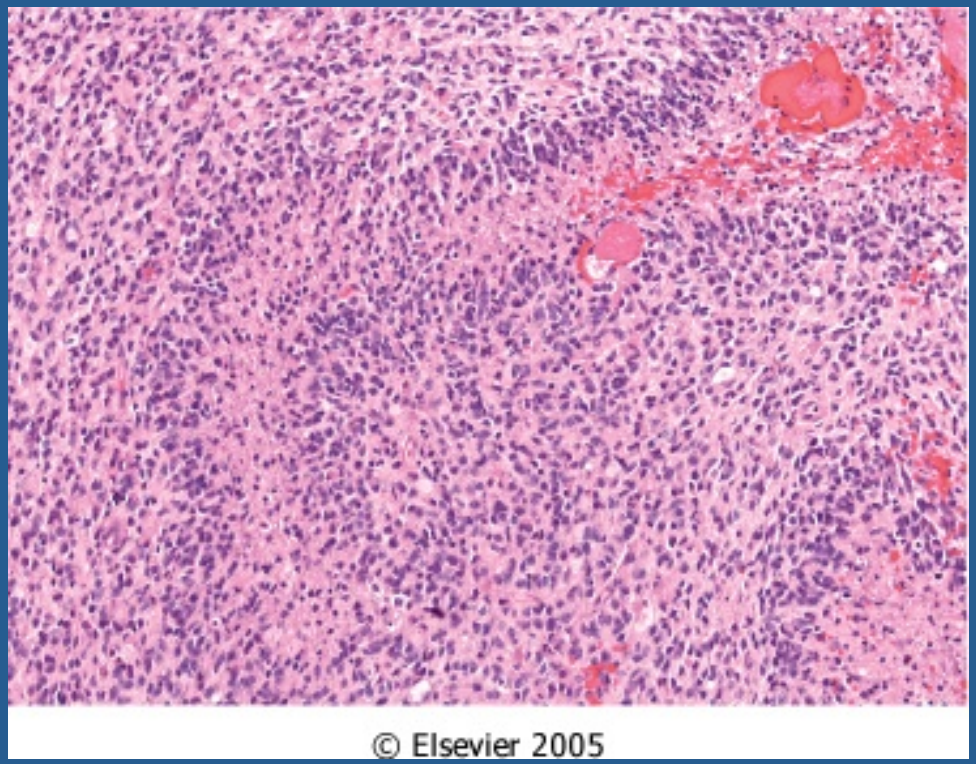
CNS Tumors
Fibrillary Astrocytoma

- 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) :
  - Anaplstic astrocytoma (WHO grade III)
    - More cellular
    - Greater nuclear pelomrophism
    - 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**

    <u>AND/OR</u>
  - **Vascular proliferation**

CNS Tumors
Astrocytoma

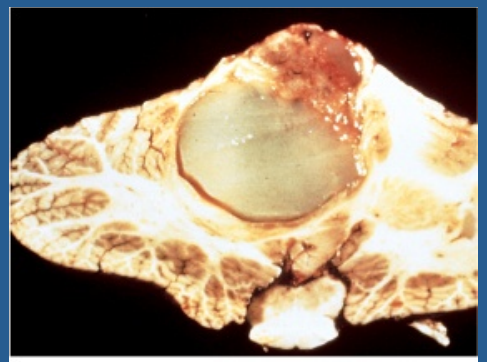
- Mutations that alter the enzymatic activity of two isoforms of the metabolic enzyme isocitrate dehydrogenase (IDH1 and IDH2) are common in lower-grade astrocytomas

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

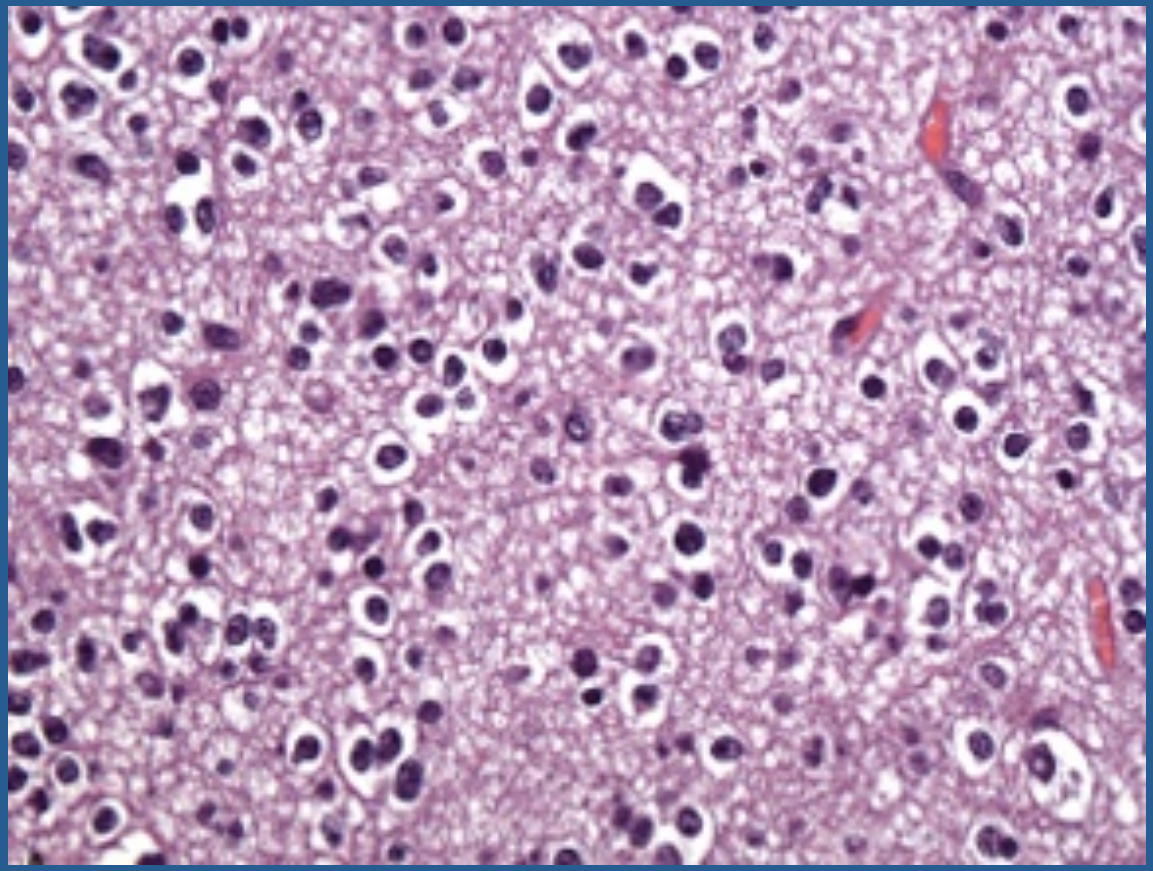
CNS Tumors
Pilocytic Astrocytoma

- 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



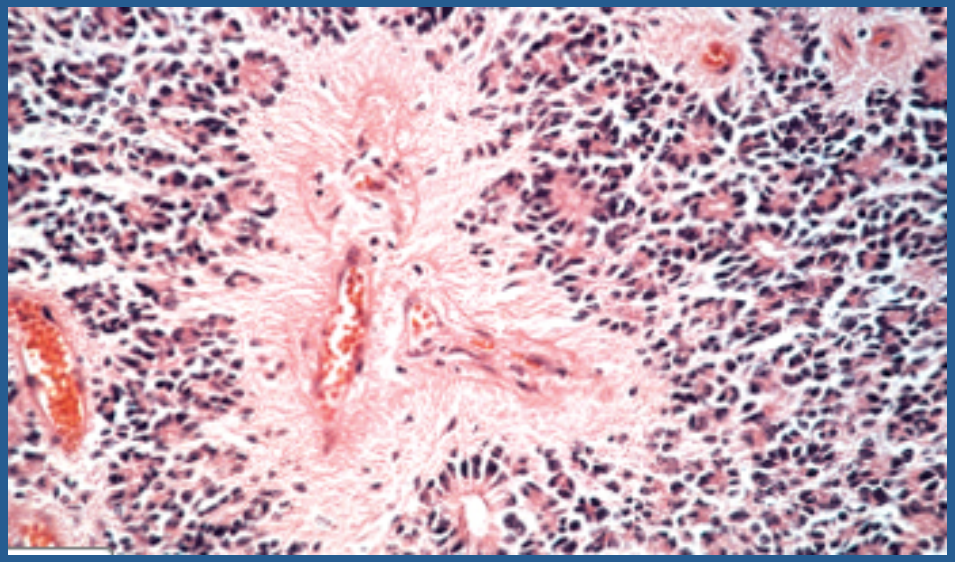
- In oligodendroglioma tumor cells have round nuclei, often with a cytoplasmic halo
- Blood vessels in the background are thin and can form an interlacing pattern

→*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)

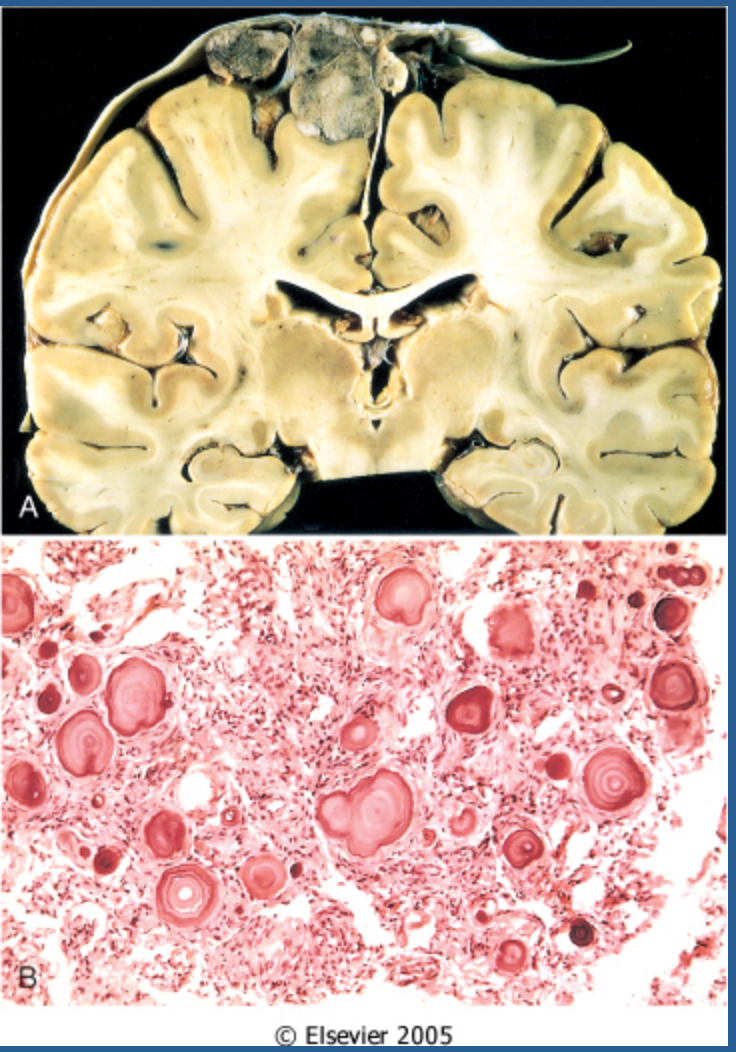
→ *what is a rosette?*

- **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

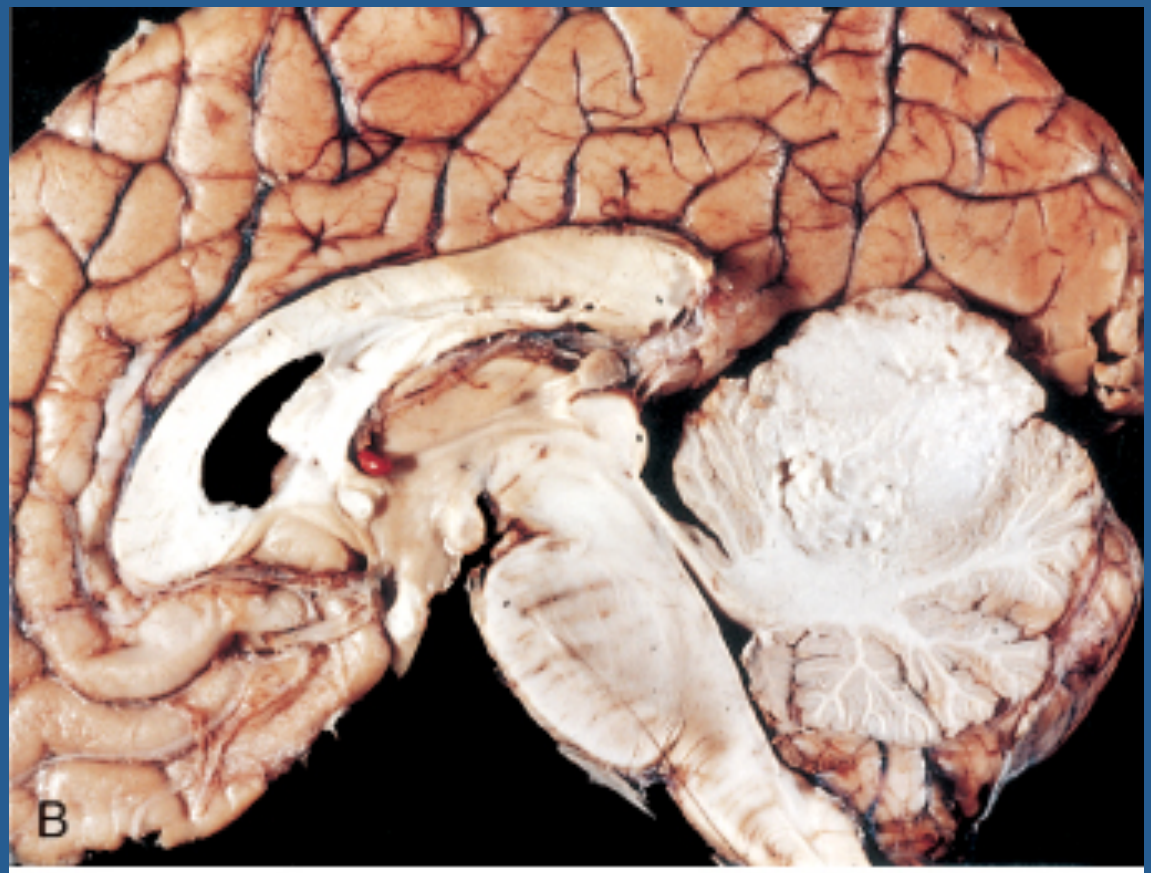
- Main subtypes:
  - Syncytial
  - Fibroblastic
  - Transitional
- Also note:
  - Atypical meningiomas
  - Anaplastic (malignant) meningiomas

CNS Tumors
Meningioma

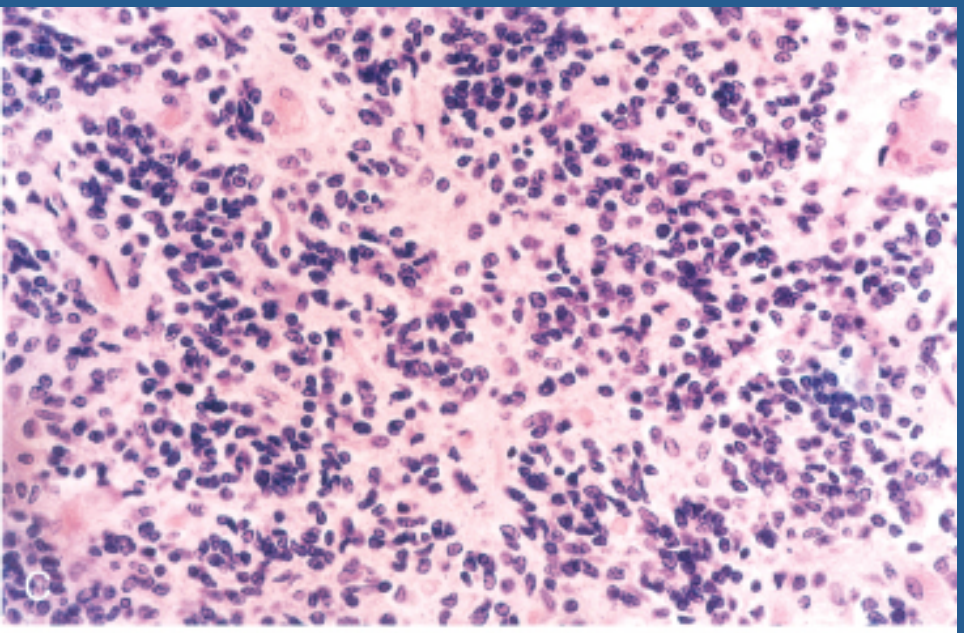
- Although most meningiomas are easily separable from underlying brain, some tumors infiltrate the brain.
- The presence of brain invasion is associated with increased risk of recurrence.

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%



CNS Tumors
Medulloblastoma



extremely cellular, with sheets of anaplastic ("small blue") cells

small, with little cytoplasm and hyperchromatic nuclei; mitoses are abundant.

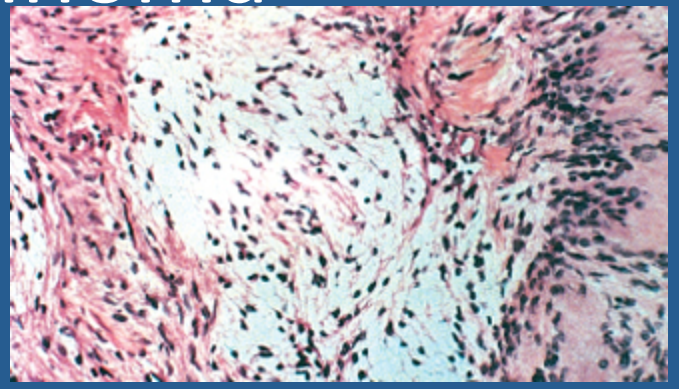
Nervous system Tumors
Schwannoma

- 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



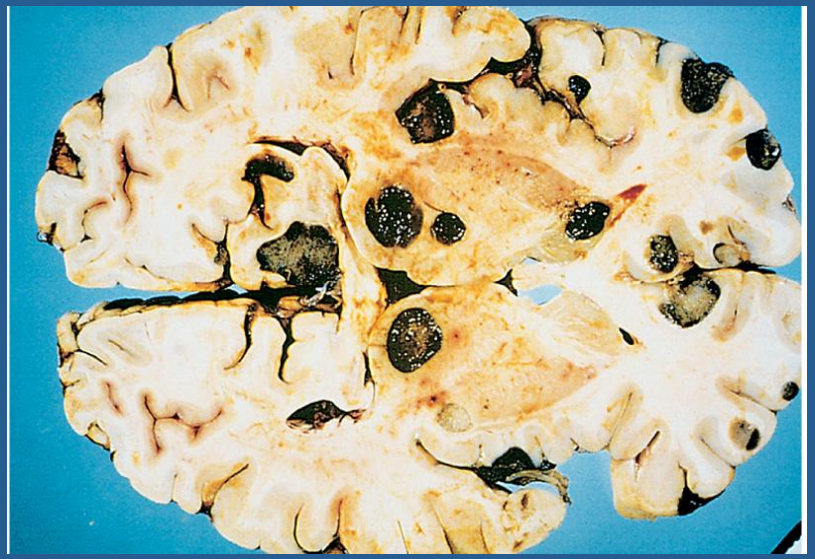
- Cellular Antoni A pattern and less cellular Antoni B
- nuclear-free zones of processes that lie between the regions of nuclear palisading are termed Verocay bodies

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 shcwannoma)

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.