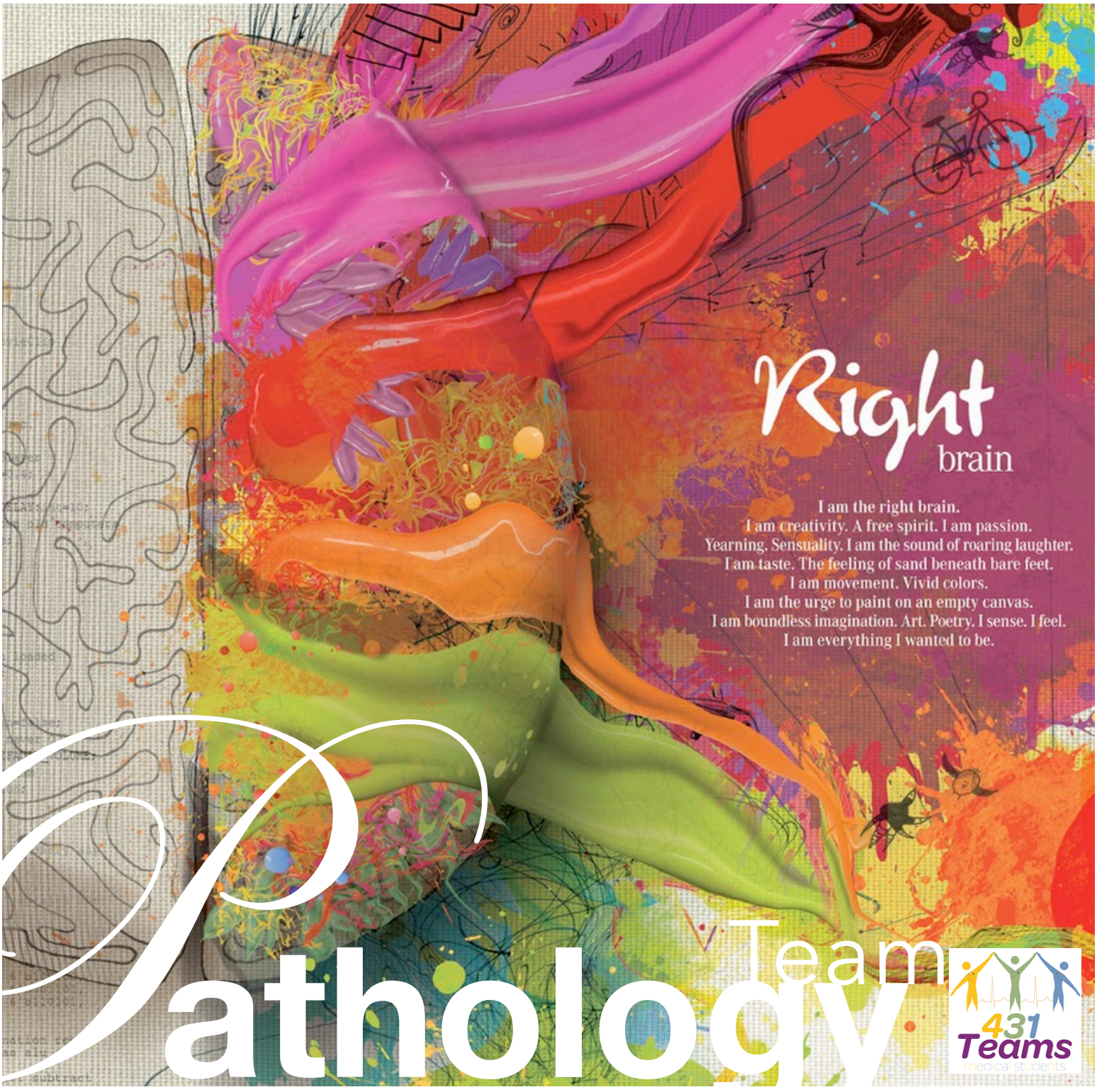

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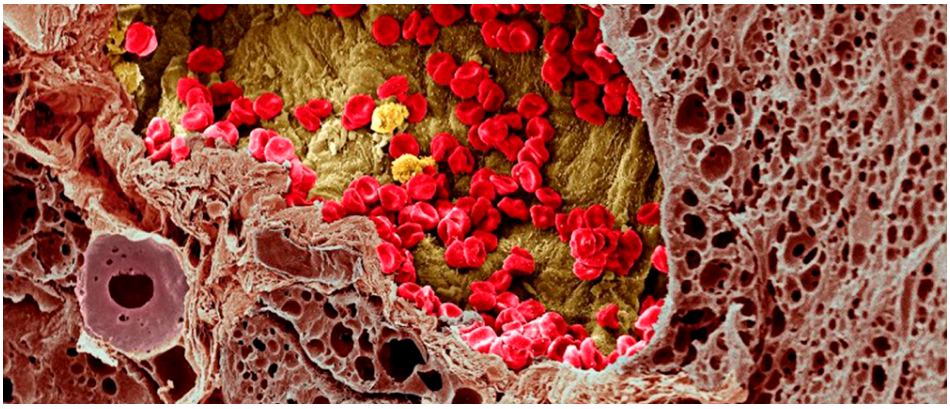
CNS Block

Done by:

Hazim Jokhadar & Sadeem Al dawas

CNS tumors

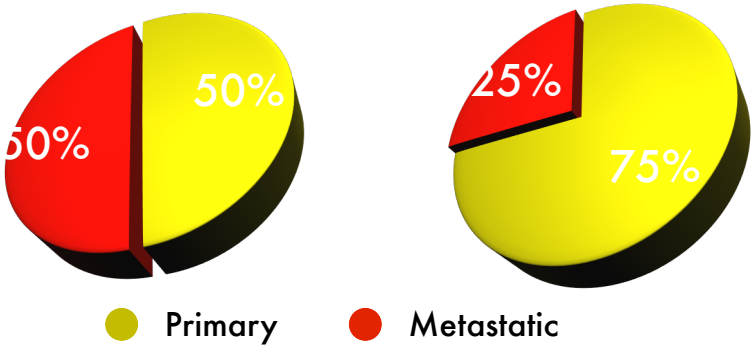


Incidence:

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.

General characteristics

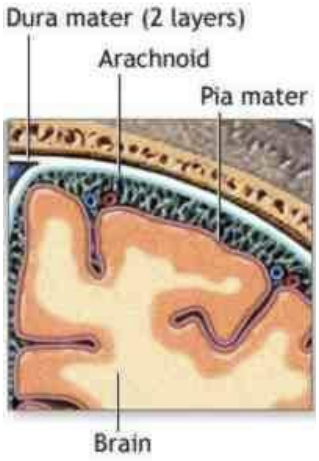
The anatomic site of the neoplasm can have lethal consequences irrespective of histological classification (i.e. benign tumors can be fatal in certain locations)

→ *examples on such locations?* Brain stem

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?*

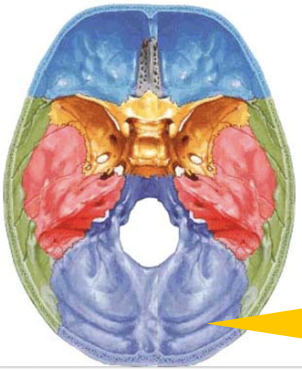


Routes of metastasis:

1- Haematogenous spread.

2- Lymphatic spread.

3- transcoelomic.



Posterior Cranial Fossa

internal surface of the base of skull

the **supratentorial region** of the brain is the area located above the tentorium cerebelli The area of the brain below the tentorium cerebelli is the infratentorial region. The supratentorial region contains the cerebrum, while the infratentorial region contains the cerebellum.

General manifestations

- Seizures, headaches, vague symptoms.
- Focal neurologic deficits related to the anatomic site of involvement.

A focal neurological deficit is a problem with nerve, spinal cord, or brain function. It affects a specific location, such as the left side of the face, right arm, or even a small area such as the tongue.

- Rate of growth may correlate with history.

- Vague symptoms include feeling drowsy, ill, or having a lack of energy or motivation headaches caused by increase of intercrinal pressure.

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).

Gliomas

Astrocytomas

Fibrillary:

- Account for about 80% of adult primary brain tumors.
- Most frequently 4th to 6th decade.
- Commonly found in the cerebral hemisphere.
- Variable grades:

1. Diffuse astrocytoma (Grade II)
2. Anaplstic astrocytoma (Grade III)
3. Glioblastoma (Grade IV)

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) : Anaplstiac astrocytoma (WHO grade III)

- More cellular
- Greater nuclear pelomrophism
- Mitosis

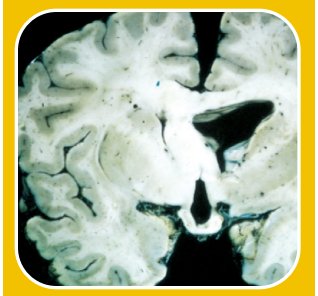
Glioblastoma (WHO grade IV):

- Very poor prognosis, with treatment, mean survival of 8-10 months.
- All the features of anapestic astrocytoma, plus: Necrosis and/or vascular or endothelial cell proliferation.

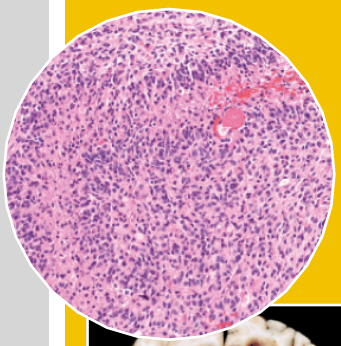
- patient's may present with glioblastoma from the start.
- **secondary** glioblastomas share ***p53*** mutations that characterized low-grade gliomas.
- While **primary** glioblastomas are characterized by amplification of the epidermal growth factor receptor **(*EGFR*)** gene.

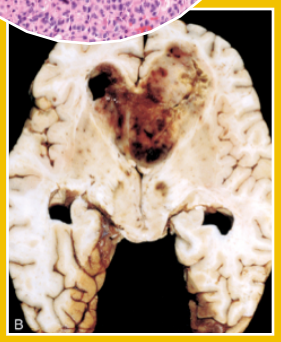
Pilocytic (Grade I):

- Children and young adults.
- Commonly cerebellum.
- Relatively benign.



Note that diffuse astrocytoma are poorly demarcated





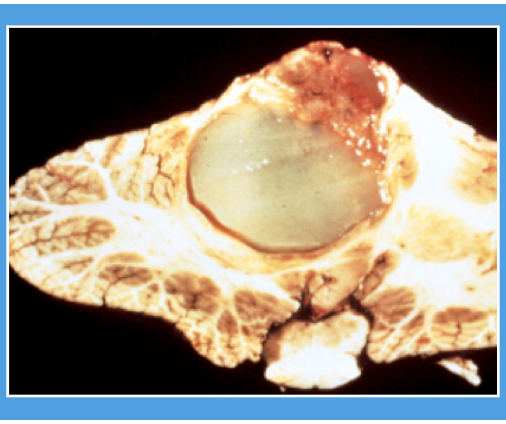
GBM/Glioblastoma Multiforme

Pseudopalisading necrosis AND/OR Vascular proliferation

Glioblastoma = Anaplastic astrocytoma + [Necrosis, Vascular cell proliferation, & pseudo-palisading nuclei]

Pilocytic tumors cont.

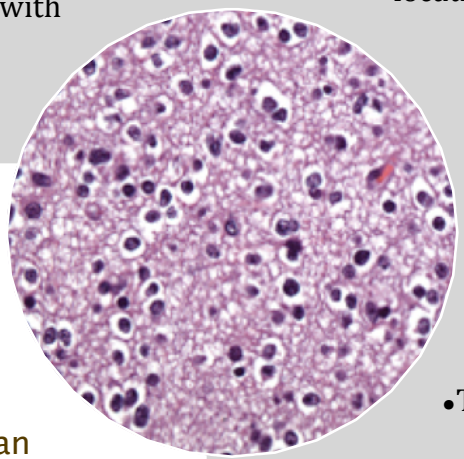
- Often cystic, with a mural nodule.
- **Well circumscribed.**
- "hairlike" = pilocytic processes that are GFAP positive
- Rosenthal fibers & hyaline granular bodies are often present
- Necrosis and mitoses are typically absent



Glial fibrillary acidic protein (GFAP) is a protein that in humans is encoded by the GFAP gene, used to detect glial cells

Oligodendrogliomas

- The most common genetic findings are loss of heterozygosity for **chromosomes 1p and 19q.**
- constitute 5% - 15% of gliomas.
- 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.

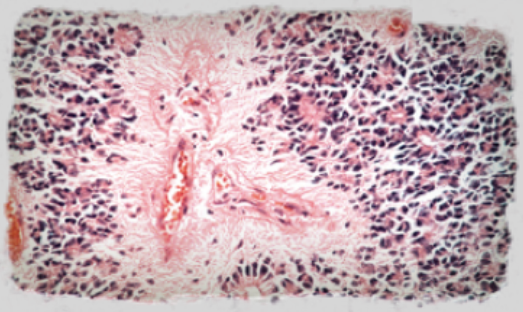
→ *What additional features are needed for anaplastic oligodendroglioma?*

- Increased cell density.
- Nuclear anaplasia.
- Increased mitotic activity.
- Necrosis.

- There is no grade IV in oligodendrocyte.

Ependymomas

- 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.



- Tumor cells may form round or elongated structures (**rosettes,** canals)

→ what is a rosette?

Tumor cells that resemble the embryologic ependymal canal ,with long, delicate Processes extending to the lumen.

A grouping of cells characteristic of neoplasms of neuroblastic or neuroectodermal origin, in which a number of nuclei form a ring from which neurofibrils extend to interlace in the center.

- **More frequently present are perivascular pseudo-rosettes**
- Anaplastic ependymomas show increased cell density, high mitotic rates, necrosis and less evident ependymal differentiation.

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CNS Block

Done by:

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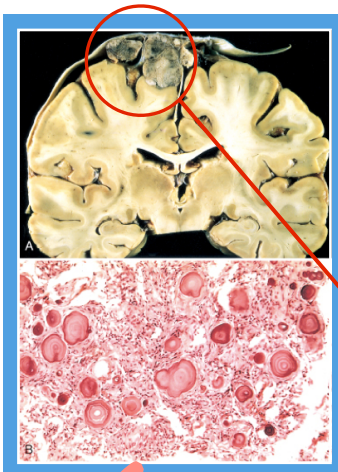


Meningioma

- Predominantly benign tumors of adults.
- Origin: meningothelial cell of the arachnoid.
- Well demarcated.
- Attached to the dura with compression of underlying brain.
- **Whorled** pattern of cell growth and **psammoma** bodies.

ROBBINS

Atypical meningiomas—lesions with a higher rate of recurrence, more aggressive local growth, and a possible need for therapy in addition to surgery—are recognized by several histologic features including a higher mitotic rate.

Anaplastic (malignant) meningiomas are highly aggressive tumors that resemble a high-grade sarcoma, although there is usually some histologic evidence that indicates a meningothelial cell origin.

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.

Meningioma

Histologically Meningioma = Whorled pattern of cells , Psammoma bodies

- Can be in the external surfaces of the brain , as well as within the ventricular system.

Main subtypes:

- Syncytial.
  - Whorled clusters.
- Fibroblastic.
  - Elongated cells with abundant collagen.
- Transitional.
  - Syncytial + fibroblastic features.

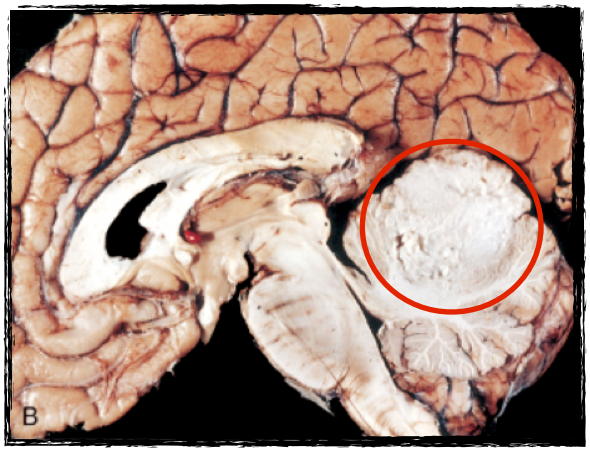
Also note:

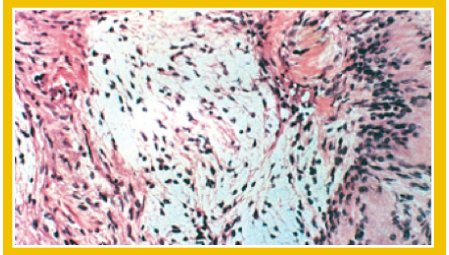
Atypical meningiomas.
Anaplastic (malignant) meningiomas.

- 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.

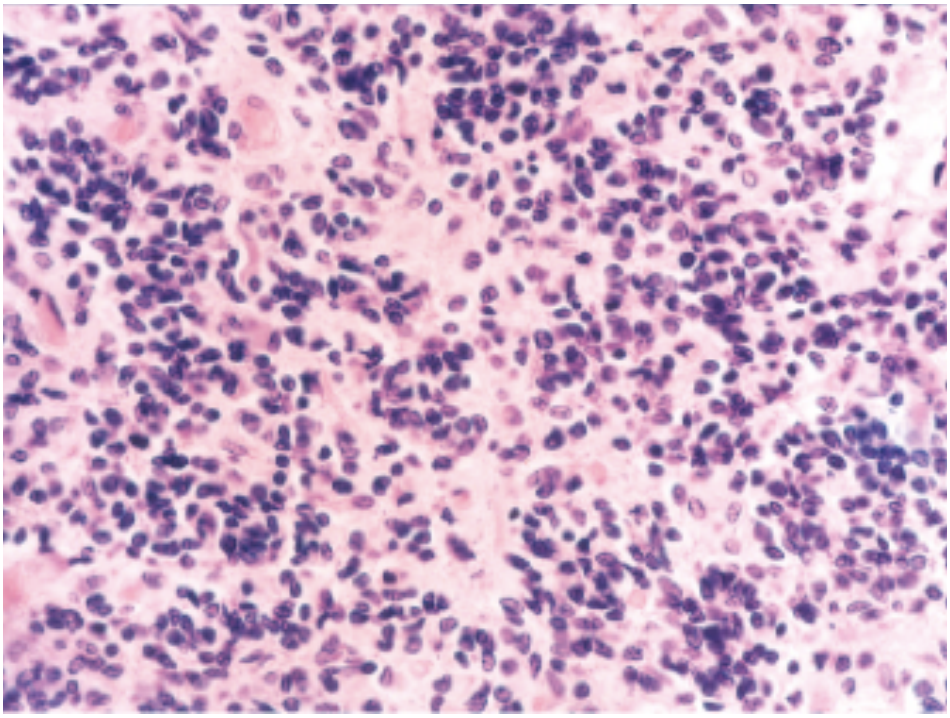
Medulloblastoma

- 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%.





- 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.



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

Metastatic tumors

- 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.

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).
- Sporadic schwannomas are associated with mutations in the *NF2* gene.
- Bilateral acoustic schwannoma is associated with NF_2.
- Attached to the nerve but can be separated from it.

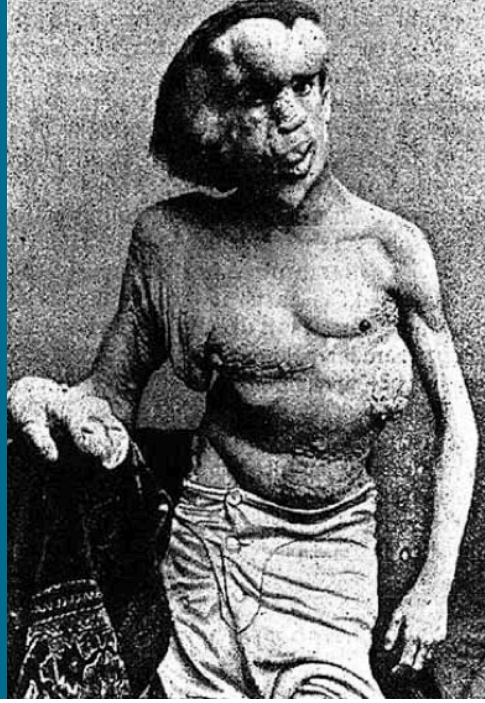
Neurofibroma

- 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).

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?

Type 1 Neurofibromatosis

Answer: ROBBINS, Chapter 23 - the nervous system, pages 900/901

Take home messages:

- Histologic distinction between benign and malignant lesions may be more subtle in comparison to other body systems.

- Even low-grade or benign tumors can have a poor clinical outcome depending on their location.

- The most aggressive and poorly differentiated glial tumor is glioblastoma; it contains anaplastic astrocytes and shows striking vascular abnormalities.

- Metastatic spread of brain tumors to other regions of the body is rare, but the brain is not comparably protected against spread of tumors from elsewhere.