objective

- Understand the infections of the nervous system
- List the most common microorganisms effects the nervous system
- Describe the morphological features of meningitis
- Compare and list the tumors of the Central nervous cyst
- Understand the WHO classification of CNS tumors
- Understand the grading of CNS tumors
- List and describe other parenchymal tumors of the nervous system.

TUMORS

The incidence of CNS tumors is generally low; about 50% to 75% are primary, and the rest are metastatic. In children, they constitute 20% of all tumors with a predilection for the posterior fossa (in adults they are most tumors are supratentorial).

Tumors of the nervous system differ from neoplasms elsewhere in the body

1. *Low-grade lesions may diffusely infiltrate large areas* of the brain, thus associated with poor prognosis.

2. The anatomic site of the tumor can affect the prognosis

a. *it may have lethal consequences* irrespective of the histopathologic type; for example, a benign meningioma, by compressing the medulla, can cause cardiorespiratoryarrest.

a. through influencing the extent of respectability.

3. Even the most highly malignant gliomas rarely metastasize outside the CNS, however, the subarachnoid space does provide a pathway for spread so that seeding along the brain and spinal cord can occur.

GLIOMAS

Gliomas are tumors of the brain parenchyma that histologically resemble different types of glial cells. *The major types of gliomas are astrocytomas, oligodendrogliomas, and ependymomas.*

1. **Astrocytomas:** *the most common of these are fibrillary and pilocytic astrocytomas.*

Fibrillary Astrocytoma account for 80% of adult primary brain tumors. They are most frequent in the ages of 30 to 60 years. Their usual location is the cerebral hemispheres. They show a spectrum of histologic differentiation that correlates well with clinical course and outcome. ***Based on the degree of differentiation, they are classified into three groups:***

a. Astrocytoma (infiltrating astrocytoma) (WHO grade II)
b. Anaplastic astrocytoma (WHO grade III)
c. Glioblastoma multiforme (WHO grade IV)

For well-differentiated astrocytomas, which are slow growing, the mean survival is more than 5 years. Eventually, however, a more rapid growth occurs due to the appearance of anaplastic features. However, many patients present with glioblastoma from the outset. The prognosis of glioblastoma is very poor (mean survival 8 to 10 months despite treatment).

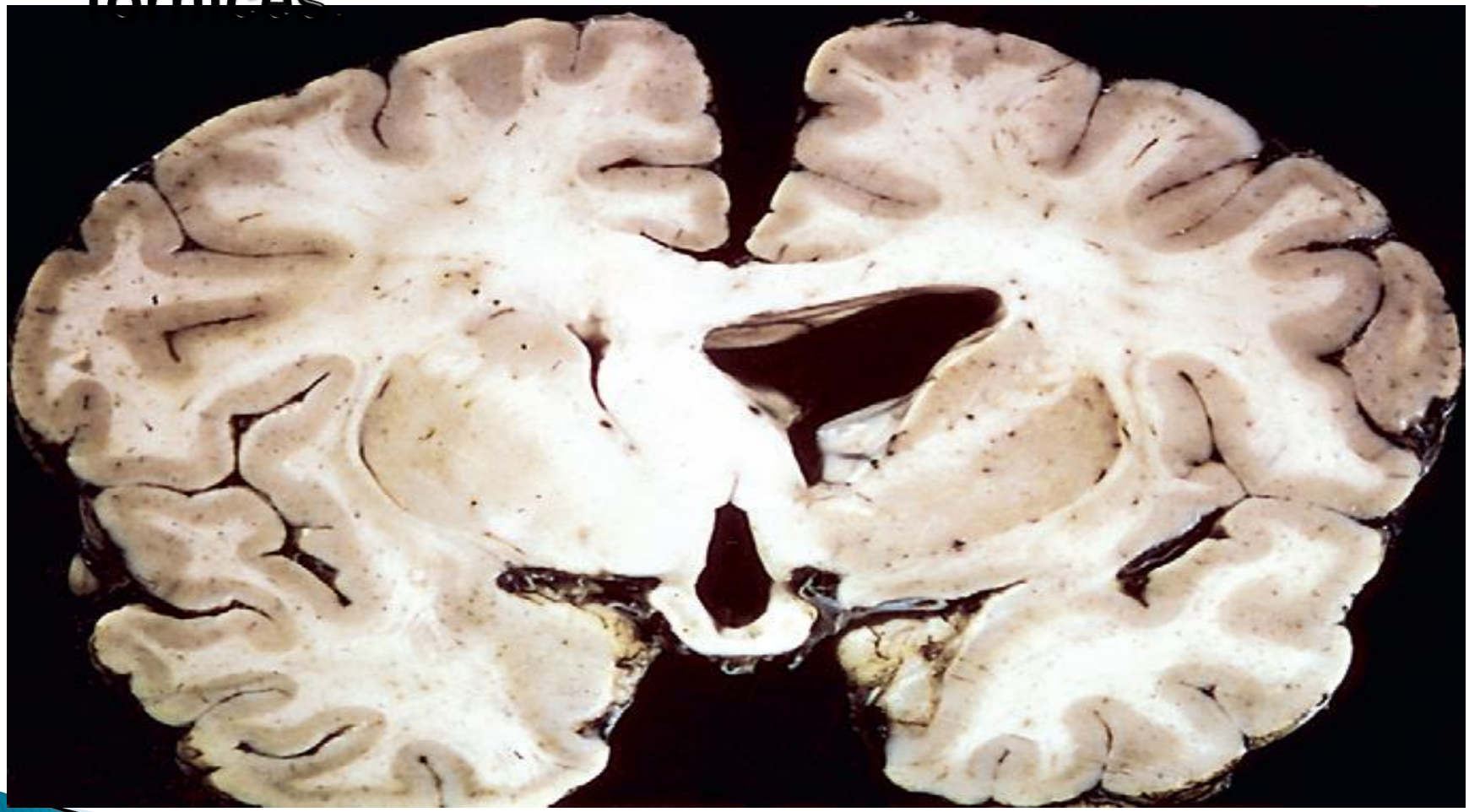
Gross features

- *Low-grade (infiltrating)* astrocytoma is a poorly defined, gray, & infiltrative mass lesion that leads to expansion and distortion of the affected regions of the brain. The cut surface of the tumor is either firm, or soft and gelatinous; cystic degeneration may be seen.
- In glioblastoma, variation in the gross appearance of the tumor from region to region is characteristic. Some areas are firm and white, others are soft and yellow (the result of tissue necrosis), and yet others show regions of cystic degeneration and hemorrhage.

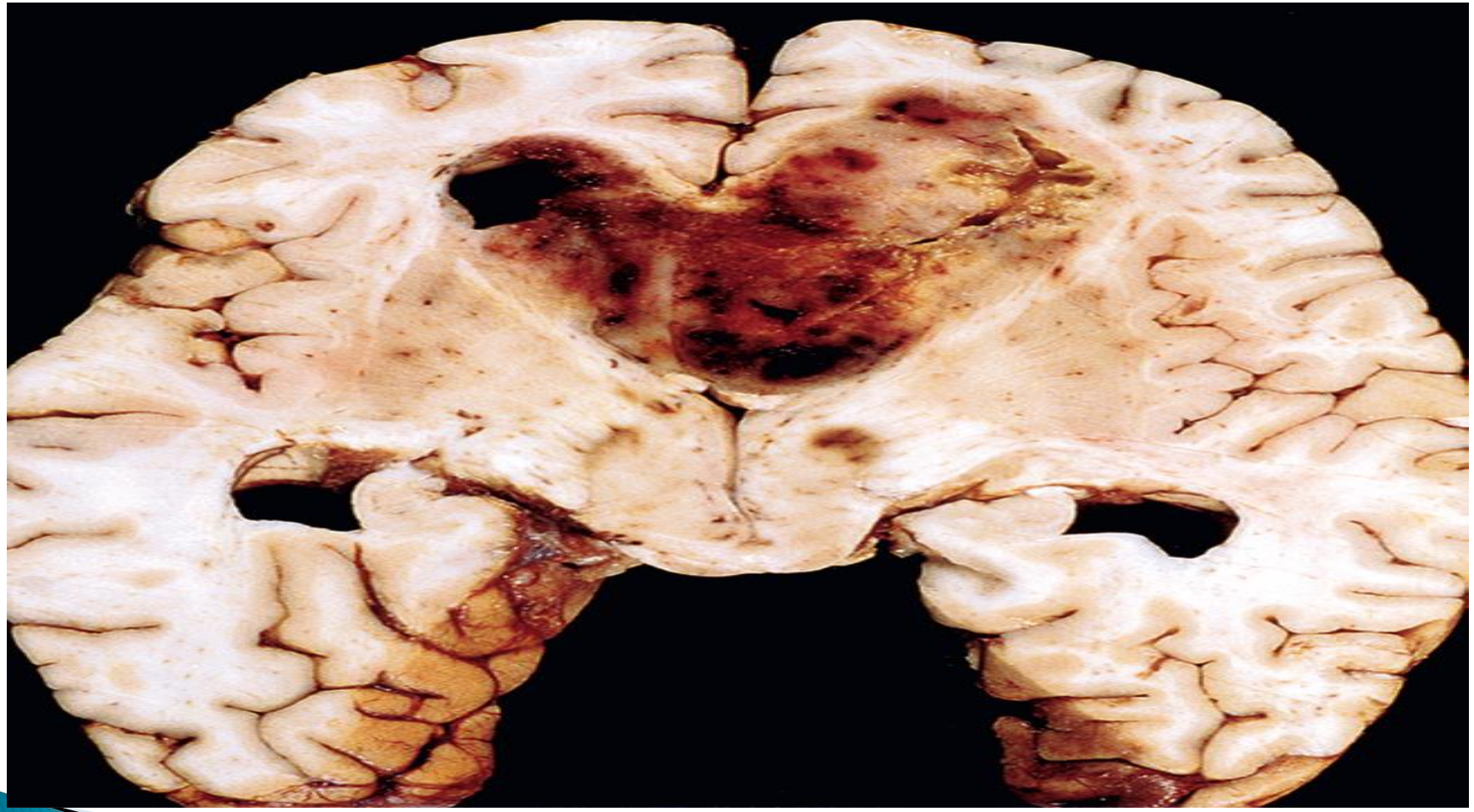
Microscopic features

- Low-grade (infiltrating) **astrocytomas** are characterized by a mild to moderate increase in the number of glial cells, slight nuclear pleomorphism, and an intervening feltwork of fine, GFAP-positive astrocytic cell processes that give the background a fibrillary appearance.

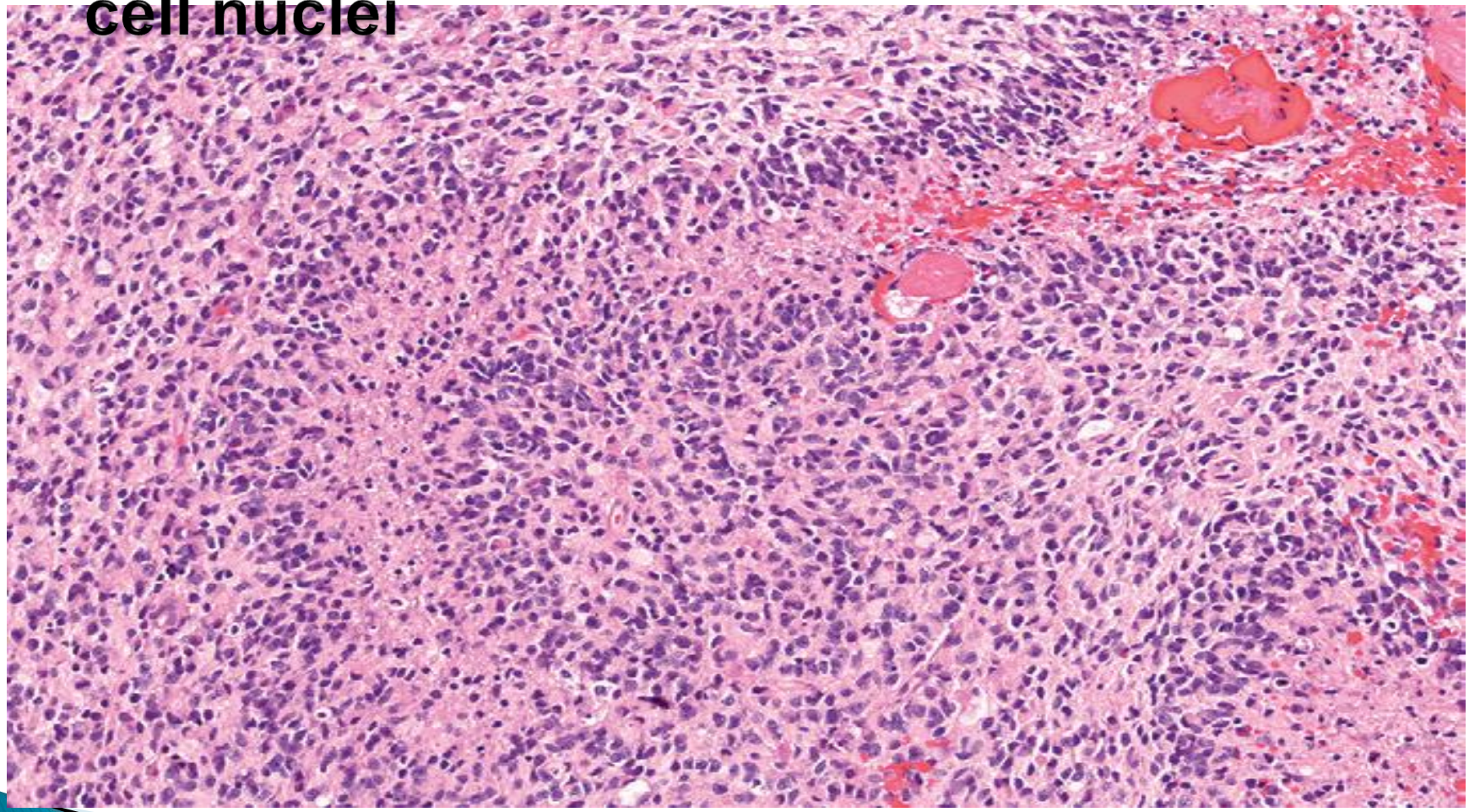
Astrocytomas. A, Low-grade astrocytoma is seen as expanded white matter of the left cerebral hemisphere and thickened corpus callosum and fornices.



B, Glioblastoma appearing as a necrotic, hemorrhagic, infiltrating mass.



C, Glioblastoma is a densely cellular tumor with necrosis and pseudopalisading of tumor cell nuclei



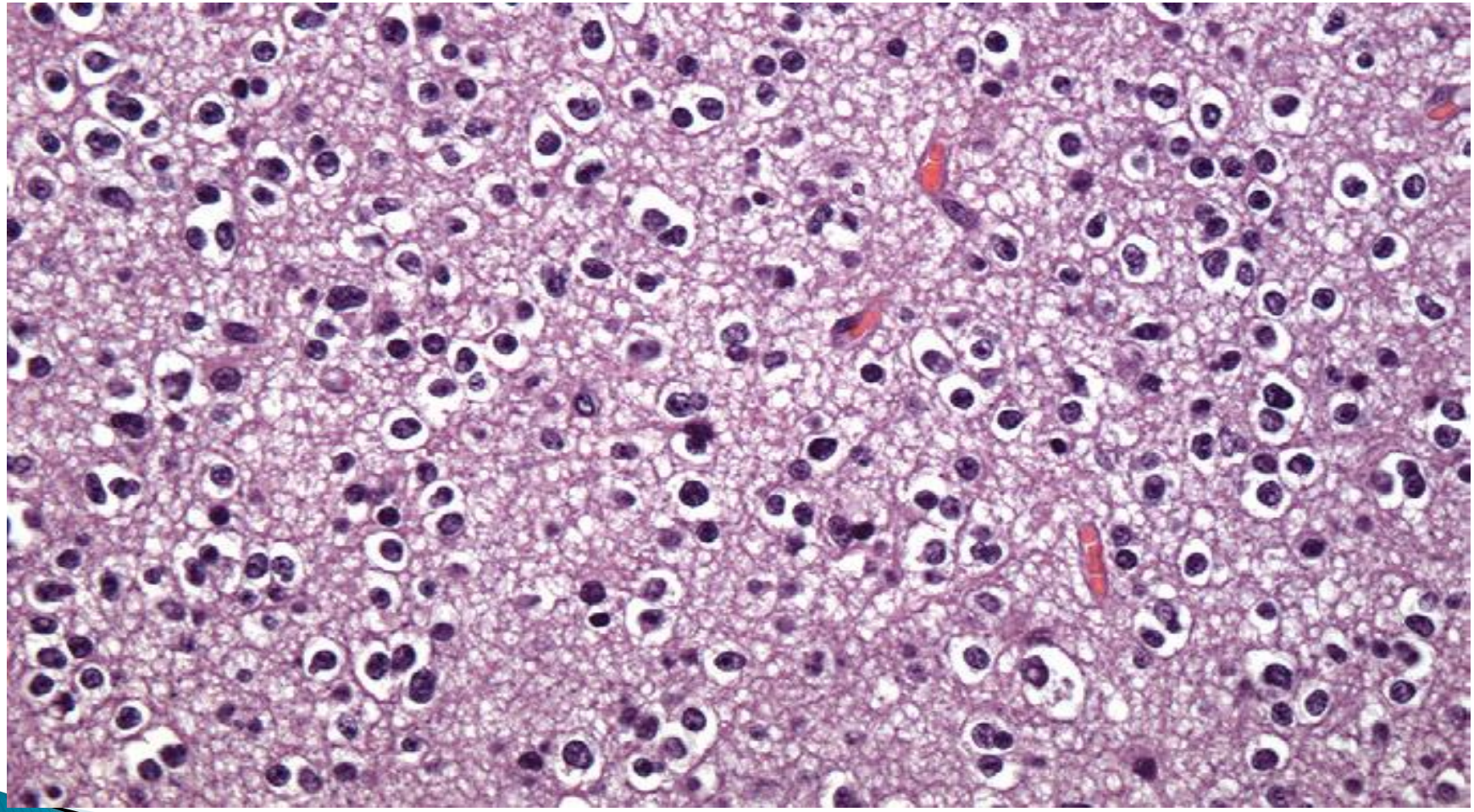
- The tumor cells can be seen infiltrating surrounding normal tissue for some distance from the main lesion.
- ***Anaplastic astrocytomas*** are more densely cellular with greater nuclear pleomorphism; increased mitoses are often observed.
- **Glioblastoma**, have a histologic appearance similar to anaplastic astrocytoma with additional features of *necrosis surrounded by pseudo-palisaded nuclei* &/or prominent *vascular endothelial cell proliferation*.

Pilocytic Astrocytoma (WHO grade I) is a relatively benign tumor, often cystic, that *typically occur in children* and young adults and are *usually located in the cerebellum*. In the cystic variant, there is usually a mural nodule in the wall of the cyst. The tumor is composed of areas with bipolar cells with long, thin "hair-like" processes that are GFAP positive. *Rosenthal fibers,* eosinophilic granular bodies, and microcysts are often present. Necrosis and mitoses are absent. (**Fig. 14-24**)

2.**Oligodendrogliomas** are most common in the 30 to 50 years of age. It is mostly located in the white matter of cerebral hemispheres. The prognosis is generally better than that of astrocytoma.

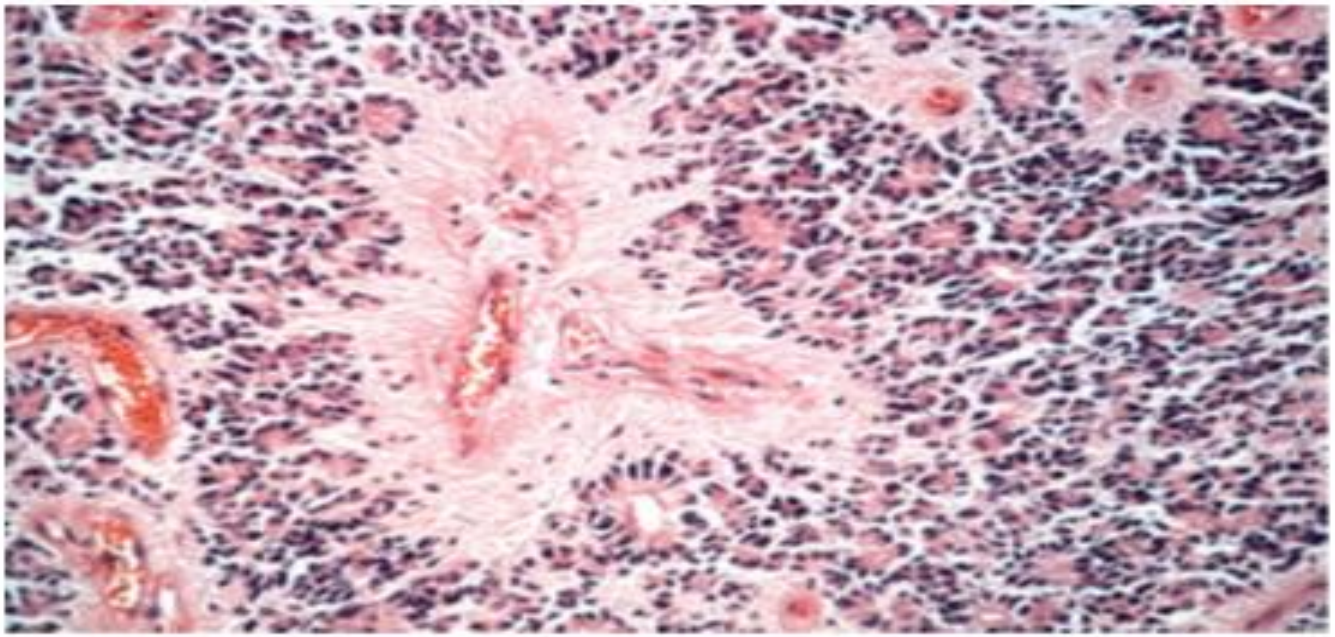
Oligodendrogliomas are infiltrative gelatinous, gray tumors. ***Microscopically,*** the tumor is composed of sheets of *regular cells with spherical vesicular nuclei surrounded by a clear halo of cytoplasm*. It typically contains a *delicate network of anastomosing capillaries (chicken wire– type vasculature)*. Calcifications are frequently present; these range from microscopic foci to massive depositions. The current WHO classification grades oligodendrogliomas into 2 different categories as WHO grade 2 and anaplastic WHO grade 3. Prominent mitotic activity and microvascular/endothelial proliferation are the 2 features that define anaplastic tumors.

A, 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



3. **Ependymoma** most often arises next to the ependyma-lined ventricular system, including the central canal of the spinal cord. In the first two decades of life, they typically occur near the fourth ventricle. In adults, the spinal cord is their most common location. Because ependymomas usually grow within the ventricles, CSF dissemination is a common occurrence. In the fourth ventricle, ependymomas are typically solid or papillary masses projecting from the floor of the ventricle. These tumors are composed of cells with regular, round to oval nuclei. Between the nuclei there is a fibrillary background. *Tumor cells may form round or elongated structures (rosettes)* with long, delicate processes extending into a lumen; more frequently present are *perivascular pseudo-rosettes* in which tumor cells are arranged around vessels with an intervening zone consisting of thin ependymal processes.

Other gliomas.. B, Microscopic appearance of ependymoma.



NEURONAL TUMORS

Central neurocytoma is a low-grade neuronal neoplasm that is typically but not exclusively a periventricular lesion i.e., found within and adjacent to the ventricular system (most commonly the lateral or third ventricles). It is characterized by evenly spaced, round, uniform nuclei and often islands of neuropil.

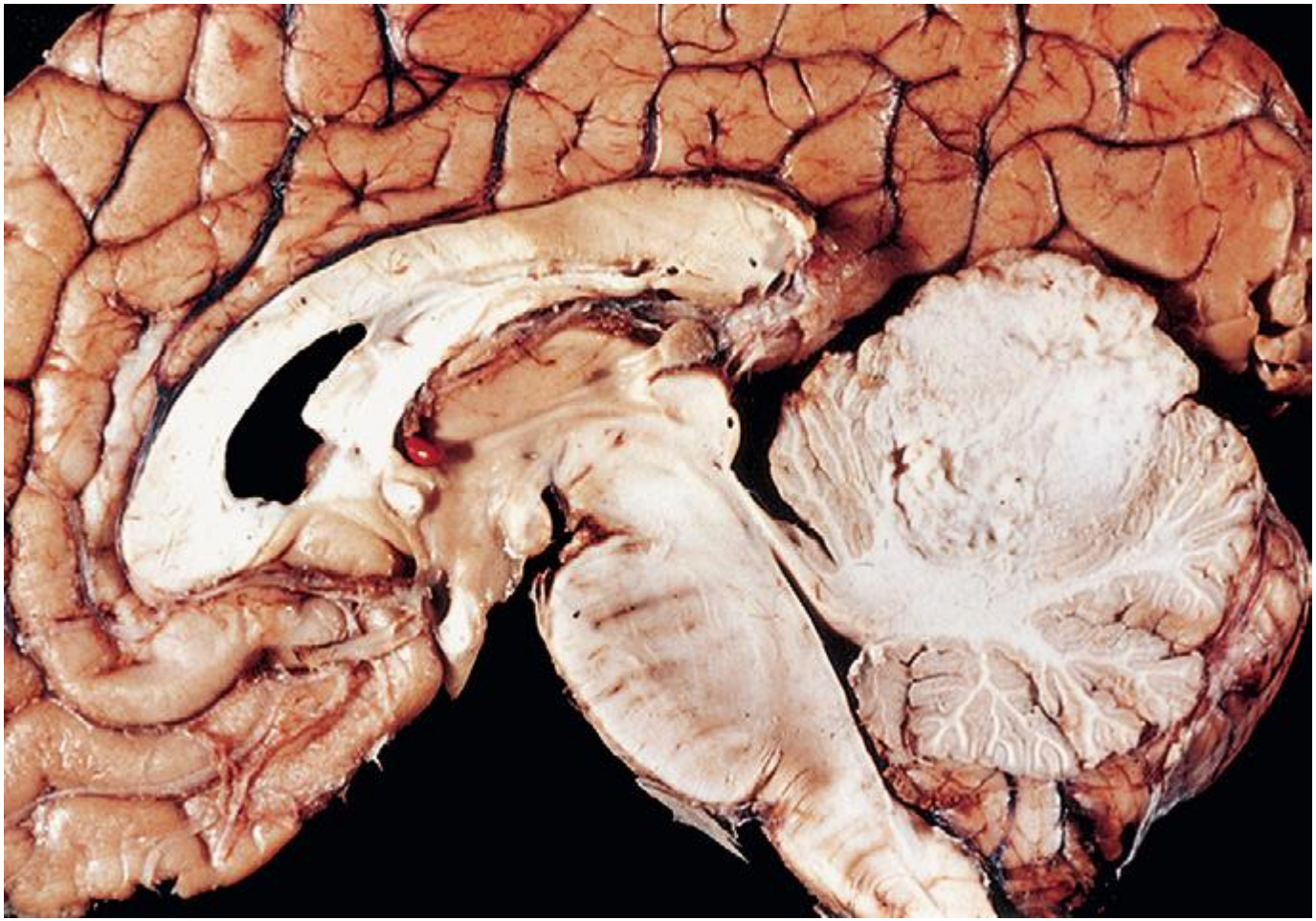
Gangliogliomas are tumors with a mixture of glial elements (looking like a low-grade astrocytoma) and mature-appearing neurons. Most of these tumors are slow growing.

Medulloblastoma *occurs predominantly in children and exclusively in the cerebellum.*

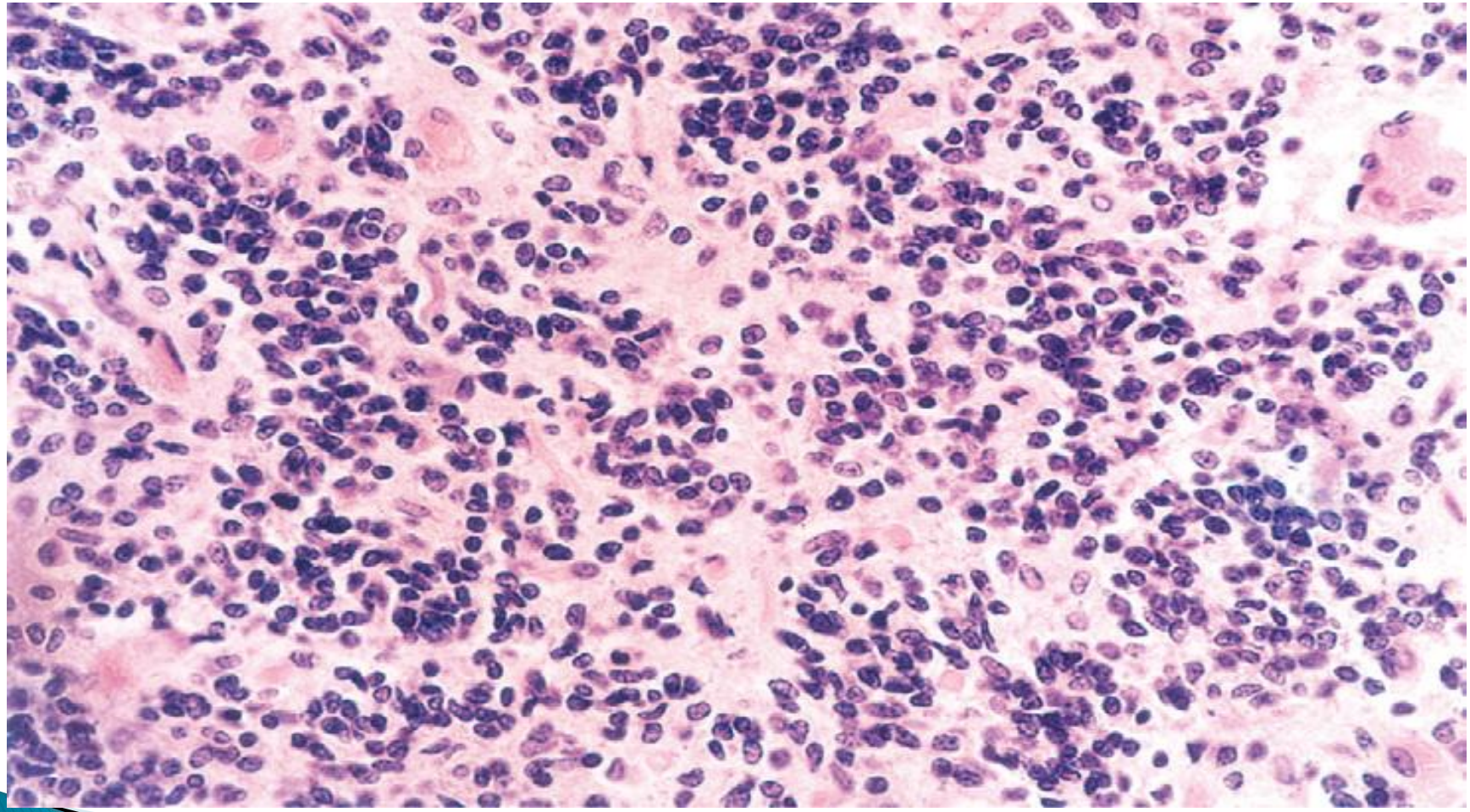
This highly malignant tumor is radiosensitive but without treatment the prognosis is poor.

In children the tumor is located typically in the midline of the cerebellum. It is often well circumscribed, gray, and friable. Medulloblastomas are extremely cellular, with sheets of undifferentiated small cells with little cytoplasm and hyperchromatic nuclei; mitoses are abundant. Some tumors show differentiation along neuronal lines in the form of HomerWright rosettes. The latter consist of tumor cell nuclei disposed in circular fashion about tangled cytoplasmic processes.)

Medulloblastoma. A, Sagittal section of brain showing medulloblastoma with destruction of the superior midline cerebellum



. B, Microscopic
appearance of medulloblastoma.



OTHER PARENCHYMAL TUMORS

Primary Central Nervous System Lymphoma are rare but are the most common CNS neoplasm in immunosuppressed individuals (including transplant recipients and persons with AIDS); under these circumstances the CNS lymphomas are nearly all driven by Epstein-Barr virus. Most of these tumors are diffuse large B-cell lymphomas.

Germ-Cell Tumors occur along the midline, most commonly in the pineal and the suprasellar regions.

They are a tumor of the young, with 90% occurring during the first two decades. Germ-cell tumors in the pineal region show a strong male predominance. The histologic classification of brain germ-cell tumors is similar to that used in the testis, but the CNS equivalent of testicular seminoma is called a germinoma. It should be noted, however, that CNS involvement by a gonadal germ-cell tumor is not uncommon.

MENINGIOMAS

These predominantly benign tumors of adults arise from the meningothelial cell of the arachnoid & are usually attached to the dura. Meningiomas may be found along any of the external surfaces of the brain as well as within the ventricular system, where they arise from the stromal arachnoid cells of the choroid plexus. They cause symptoms through compression of underlying brain. Multiple meningiomas, especially in association with eighth nerve schwannomas or glial tumors, may be a part of neurofibromatosis type 2 (NF2). About half of meningiomas not associated with NF2 still have mutations in the *NF2* gene

Gross features **(Fig. 14-28)**

- They are well-defined dural-based masses that compress underlying brain but
- are easily separated from it.
- On sectioning most meningiomas are grayish-tan and soft. Collagenized
- examples, however, have rubbery texture and whorled or trabeculated cut
- surface.
- Calcification may impart a gritty sensation on cutting.
- Extension into the overlying bone may be present.

Meningioma. A, Parasagittal multilobular meningioma attached to the dura with compression of underlying brain

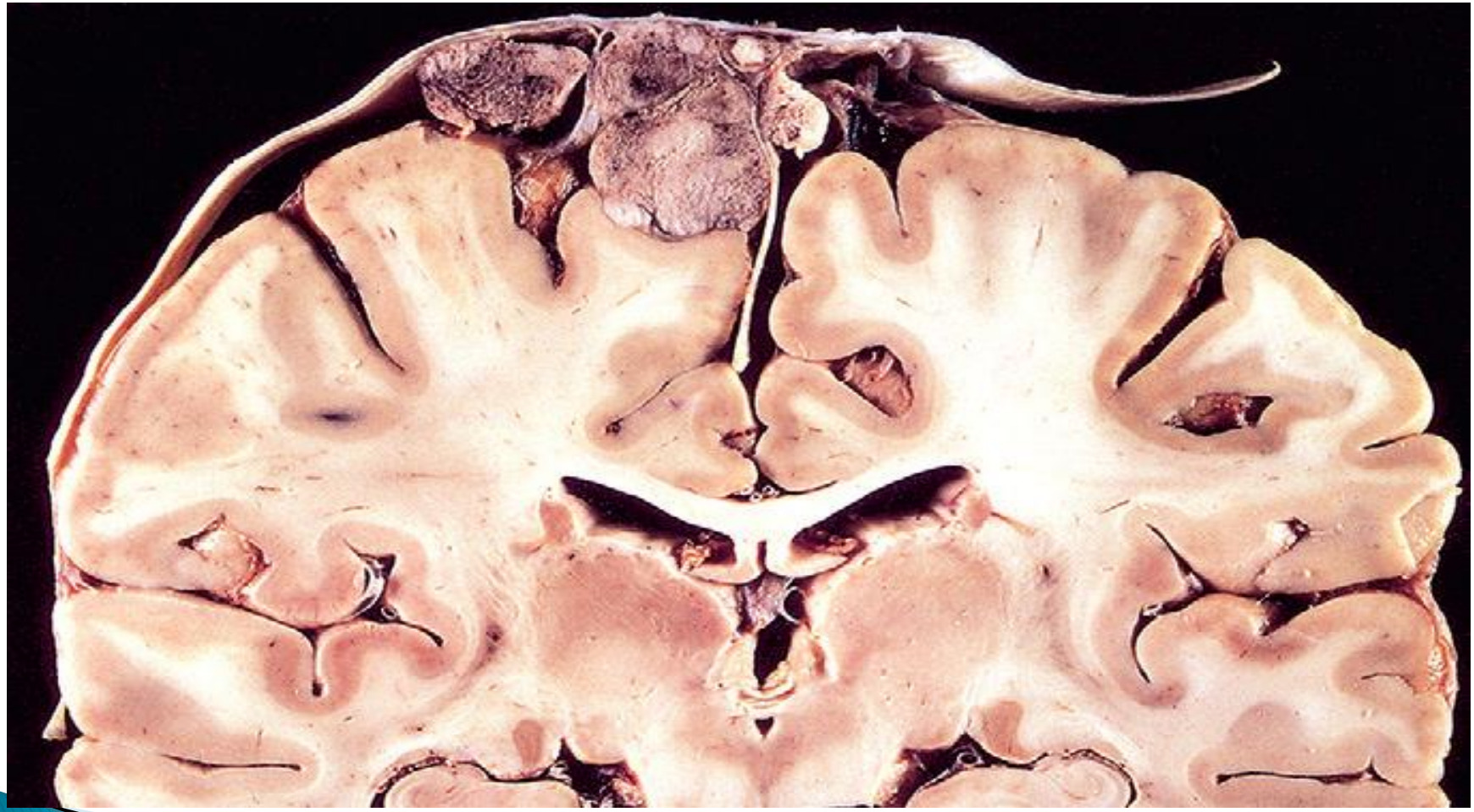
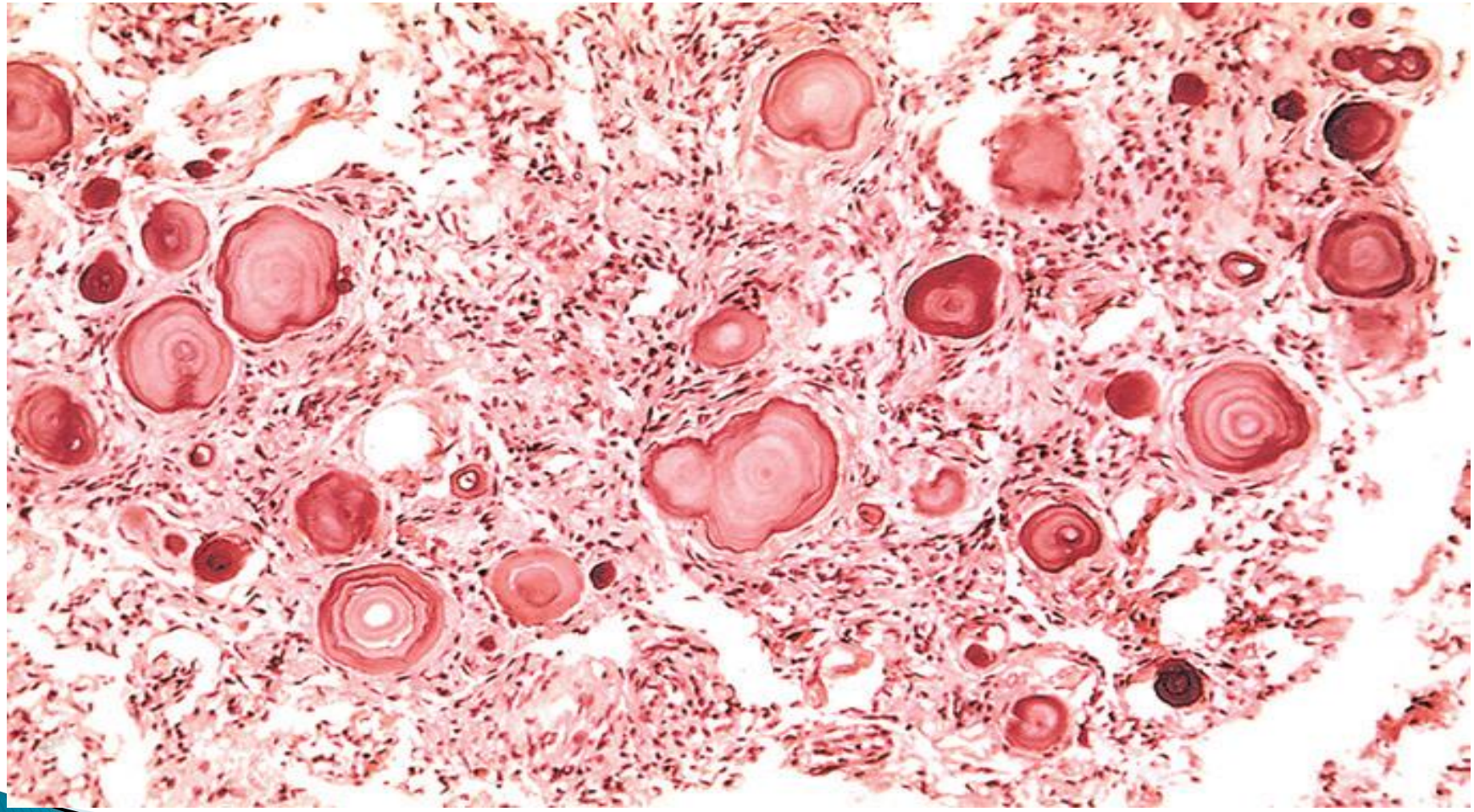


Figure 22–31. B, Meningioma with a whorled pattern of cell growth and psammoma bodies



Microscopic features.

- There are many histologic patterns of meningiomas, including

1. *Syncytial*, showing whorled clusters of tight groups of cells without visible cell membranes

2- Fibroblastic, with elongated cells and abundant collagen deposition between them

3-Transitional, which shares features of the syncytial and fibroblastic types

4- Psammomatous, with numerous psammoma bodies (NB: psammoma bodies may also occur in the above variants but less heavily).

Atypical meningiomas show a higher rate of recurrence, more aggressive local growth. They 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 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

METASTATIC TUMORS

Metastatic lesions, mostly carcinomas, account for 25% to 50% of intracranial tumors. ***The most common primary sites are***

1- lung

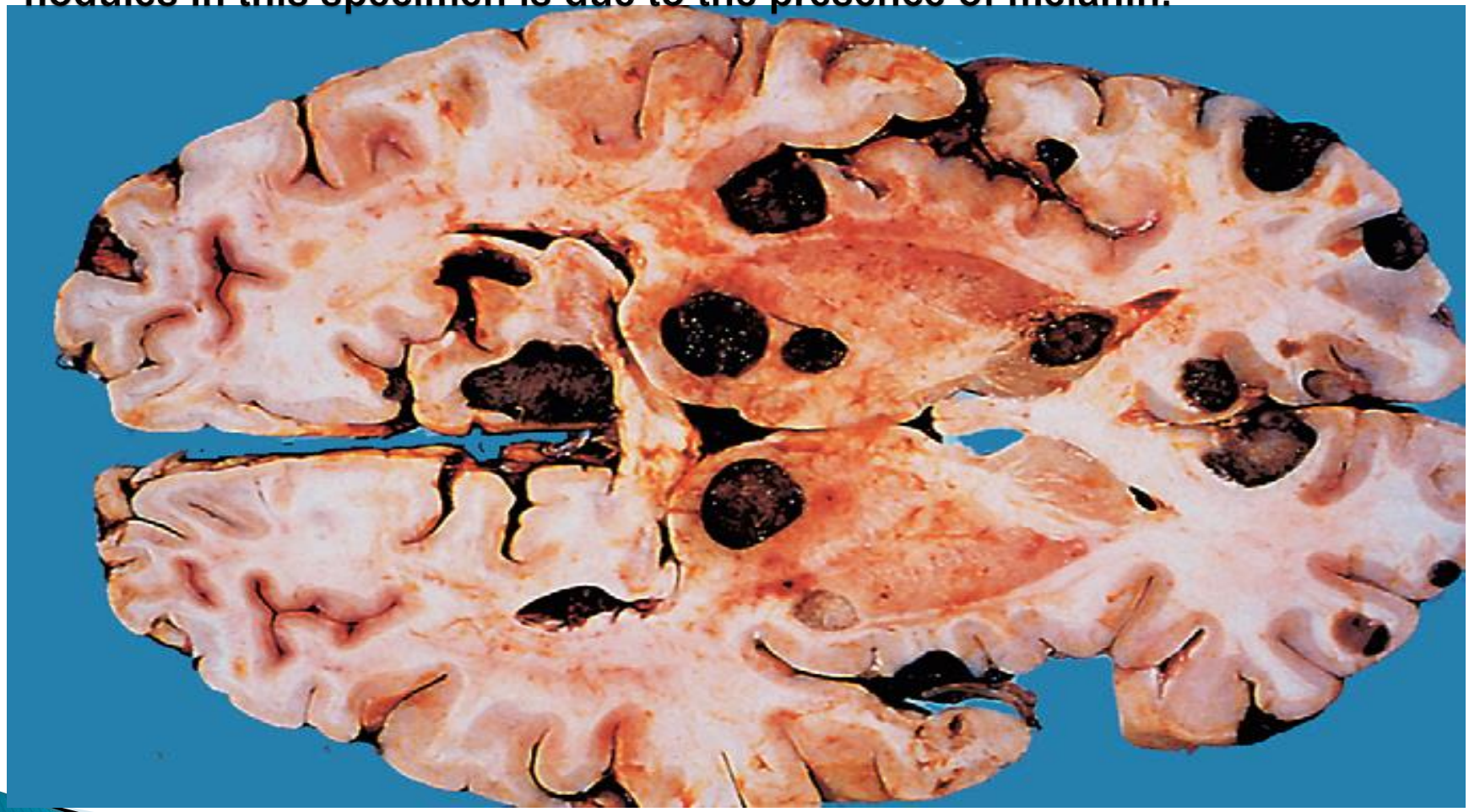
2- breast

3- skin (melanoma)

4- kidney

5-GIT

Figure **Metastatic melanoma. Metastatic lesions are distinguished grossly from most primary central nervous system tumors by their multicentricity**
and well-demarcated margins. The dark color of the tumor nodules in this specimen is due to the presence of melanin.



The meninges are also a frequent site of involvement by metastatic disease. In the brain, metastases form sharply demarcated masses, often at the gray matter-white matter junction, usually surrounded by a zone of edema. The boundary between tumor and brain parenchyma is well defined microscopically as well, with surrounding reactive gliosis.

In addition to the direct and localized effects produced by metastases, *paraneoplastic syndromes* may involve the peripheral and central nervous systems, sometimes even preceding the clinical recognition of the malignant neoplasm. *These syndromes are most commonly associated with small-cell carcinoma of the lung.* There are several manifestations of paraneoplastic syndromes; some characteristic patterns include: *Subacute cerebellar degeneration* resulting in ataxia**,** *Limbic encephalitis* causing a subacute dementia; the pathological changes are centered in the medial temporal lobe, *and* S*ubacute sensory neuropathy* leading to altered pain sensation

DISEASES OF THE PERIPHERAL NERVOUS SYSTEM

Neoplasms of the Peripheral Nervous System

These tumors arise from cells of the peripheral nerve, including Schwann cells, perineurial cells, and fibroblasts. In addition to arising along the peripheral course of nerve, these tumors can arise within the confines of the dura. When they do this, they may cause changes in adjacent brain or spinal cord.

Schwannomas are benign tumors arising from Schwann cells. Symptoms are referable to
local compression of the involved nerve, or to compression of adjacent structures (such as brain stem or spinal cord). They are often encountered in the *cerebellopontine angle*, where they are attached to the vestibular branch of the eighth nerve. These patients often present with tinnitus and hearing loss, and the tumor is often referred to as an ***acoustic neuroma***. Elsewhere within the dura, sensory nerves are preferentially involved, including branches of the trigeminal nerve and dorsal roots. When extradural, schwannomas are most commonly found in association with large nerve trunks. Sporadic schwannomas are associated with mutations in the *NF2* gene on chromosome 22.

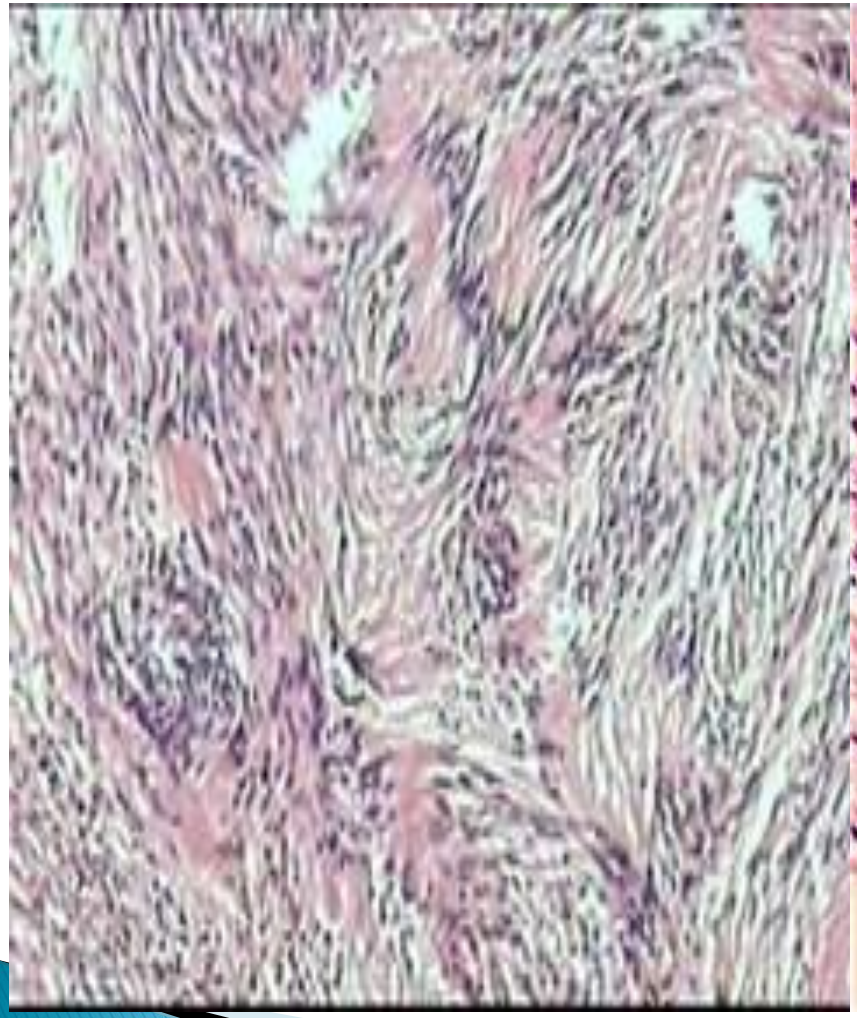
Gross features **(Fig. 14-35)**.

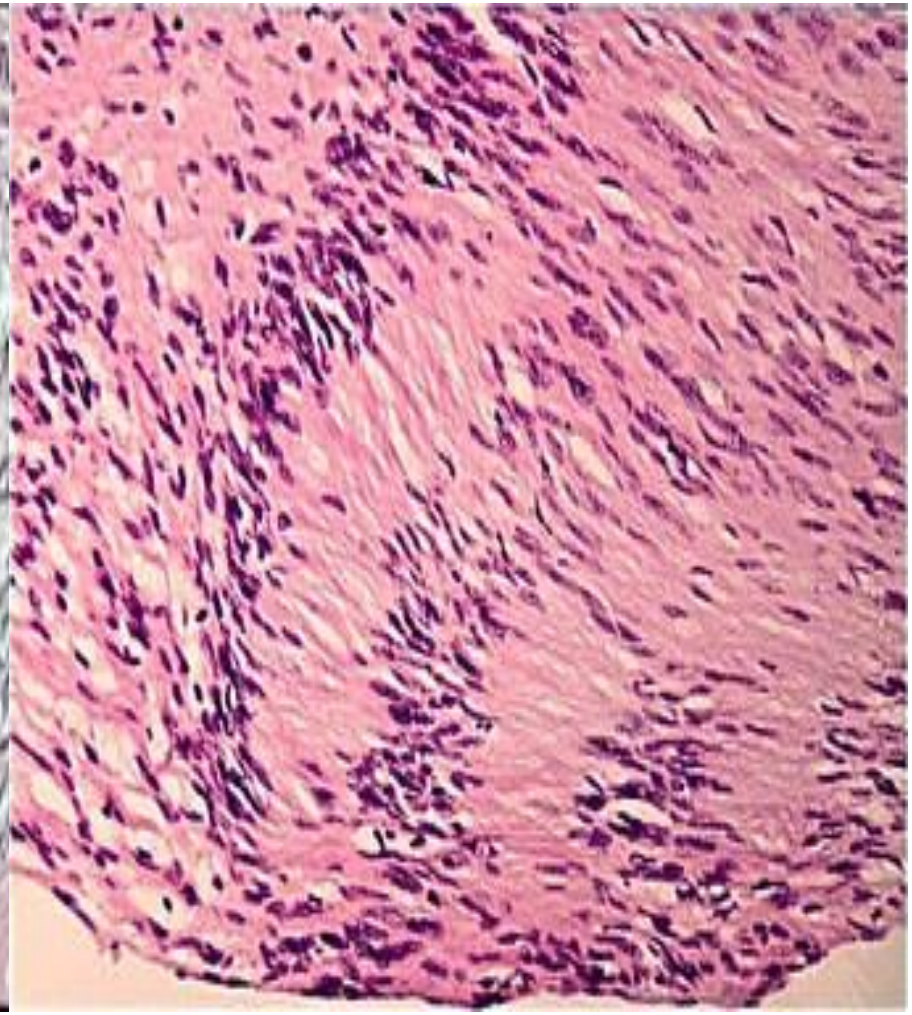
- These tumors are well-circumscribed encapsulated masses that are attached to the nerve.
- They form firm, gray masses sometimes with cystic change.

Microscopically

- There is a mixture of two growth patterns. In the *Antoni A*
- *pattern* of growth, elongated cells are arranged in fascicles
- with their nuclei palisade along "nuclear-free zones" forming
- *Verocay bodies*.
- In the *Antoni B pattern* of growth, the tumor is less densely
- cellular with a loose meshwork of cells along with microcysts

and myxoid changes. In both areas, the cytology of the individual cells is similar, with elongated cell cytoplasm and regular oval nuclei





Neurofibroma

Solitary neurofibromas are mostly cutaneous or involving a peripheral nerve. These arise sporadically or in association with type 1 neurofibromatosis (NF1). The skin lesions are evident as nodules, sometimes with overlying hyperpigmentation; they may grow to be large and become pedunculated. The risk of malignant transformation from these tumors is extremely small, and cosmetic concerns are their major morbidity. The second type is the ***plexiform neurofibroma,*** *mostly arising in individuals with NF1. In the latter situation it is not only difficult to surgically remove these plexiform tumors when they involve major nerve trunks but also their potential for malignant transformation.*

Malignant Peripheral Nerve Sheath Tumors (MPNST) *are highly malignant sarcomas that are locally invasive, frequently leading to multiple recurrences and eventual metastatic spread. Despite their name, these tumors do not arise from malignant transformation of schwannomas. Instead, they arise de novo or from transformation of a plexiform neurofibroma. These tumors can also occur after radiation therapy.*

FAMILIAL TUMOR SYNDROMES *are inherited diseases characterized by the development of hamartomas and neoplasms throughout the body with particular involvement of the nervous system. Most of these syndromes are linked to loss of tumor suppressor genes. The following are autosomal dominant disorders.*

Type 1 Neurofibromatosis (NF1) *is characterized by neurofibromas (plexiform and solitary), gliomas of the optic nerve, and cutaneous hyperpigmented macules (café au lait spots). Individuals with NF1 have a propensity for the neurofibromas to undergo malignant transformation. This is especially true for plexiform neurofibromas.*

Type 2 Neurofibromatosis (NF2) *is characterized by the development of a range of tumors, most commonly bilateral vestibular (acoustic) schwannomas and multiple meningiomas. Ependymomas of the spinal cord also occur.*

Tuberous Sclerosis *is another autosomal dominant syndrome characterized by the development of hamartomas and benign neoplasms involving the brain and other tissues. Seizures, which can be difficult to control with antiepileptic drugs, are associated with the cortical lesion. Extracerebral lesions include renal angiomyolipomas, retinal glial hamartomas, and pulmonary lesions and cardiac rhabdomyomas.*

von Hippel-Lindau Disease *is characterized by the develop hemangioblastomas mostly within the cerebellar hemispheres, and retina. Patients may also have cysts involving the pancreas, liver, and kidneys and have a high propensity to develop renal cell carcinoma of the kidney.*