Mesenchymal tumors, neuroectodermal tumors, pigmented skin lesions

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Should you decide to remember just two slides…basics from the terminology of “cancers“

- **Epithelial** tumors:
- Benign: adenoma (glandular epi), papiloma (surface epi (incl. urothel!))
- Malignant: carcinoma (adenocarcinoma, papilocarcinoma…exc. squamous cell ca, basal cell ca). Carcinoma *in situ*: malignant cells did not perforate basal membrane of the particular epithelium (usually “B9“, exc. urothelial ca in situ)

- **Mesenchymal** tumors:
- Benign: tissue + oma (lipoma, fibroma, myoma, hemangioma, chondromaosteoma…)
- Malignant: tissue + sarcoma (liposarcoma, fibrosarcoma…)
- No “sarcoma in situ“.
- (Exc. Lymphoma, melanoma... Also no “sarcoma in situ“.)

Mesenchymal tumors

- Mesenchymal tumors ("soft tissue tumors") are neoplasms that arise in mesodermal tissues of the body, including skeletal muscle, fat, fibrous tissue, blood vessels and lymphatics
- Malignant are rare, accounting for less than 1% of all malignancies
- Benign are 100 times more common than malignant ones

Mesenchymal tumors

Arise from multipotential mesenchymal stem cells that reside in soft tissues and are classified according to the phenotype they exhibit.

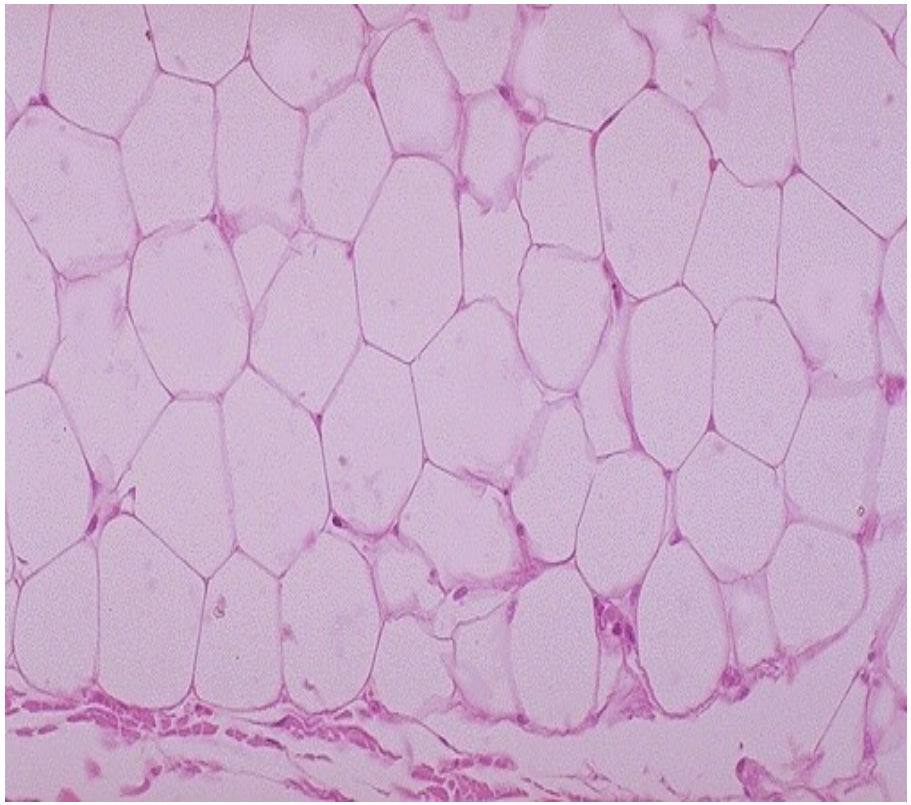
Lipomatous tumors

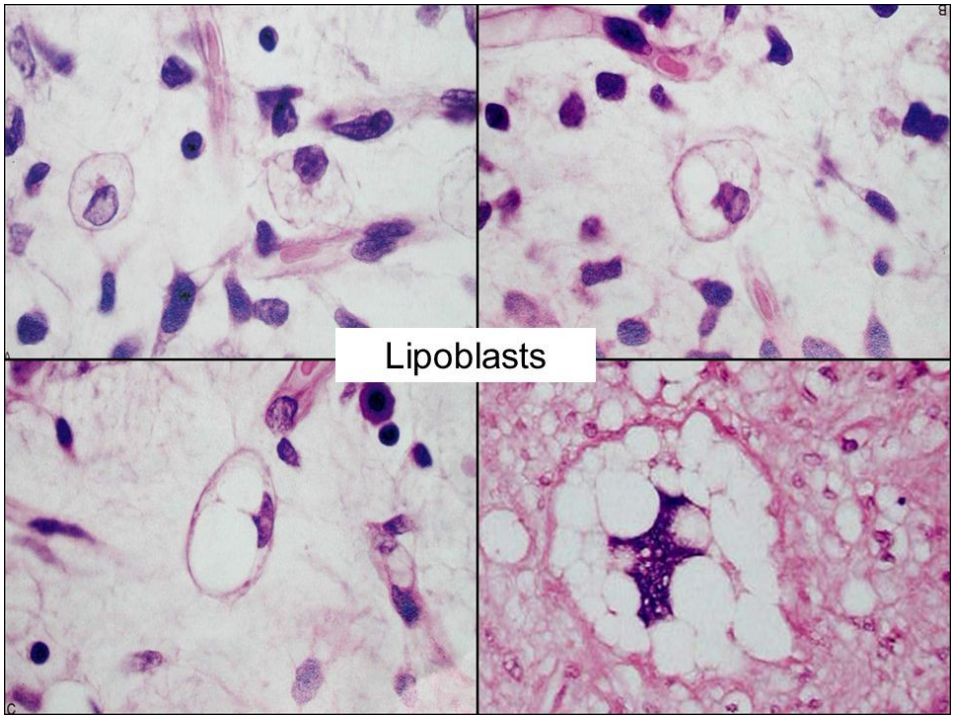
- Lipoma
  - Most common soft tissue tumor
  - Composed of well-differentiated adipocytes
  - Can originate at any site in the body that contains adipose tissue
  - Lipomas are seen mainly in adults
- Liposarcoma
  - Second most common sarcoma in adults
  - 20% of all malignant soft tissue tumors
  - After age 50 years and is most common in the deep thigh and retroperitoneum
  - Tend to grow slowly but may become extremely large

Lipomatous tumors

- Lipoma
  - Encapsulated, soft, yellow lesions that vary in size and may become very large
  - Deeper tumors are often poorly circumscribed
  - Histologically indistinguishable from normal adipose tissue
- Liposarcoma
  - Typically measure 5 to 10 cm in diameter
  - Gross appearances vary depending on the proportions of adipose, mucinous and fibrous tissue
  - **Lipoblast** - a malignant-appearing cell with univacuolated or multivacuolated cytoplasmic fat vesicles indenting the nucleus, that essentially defines a tumor as a liposarcoma

Lipomatous tumors





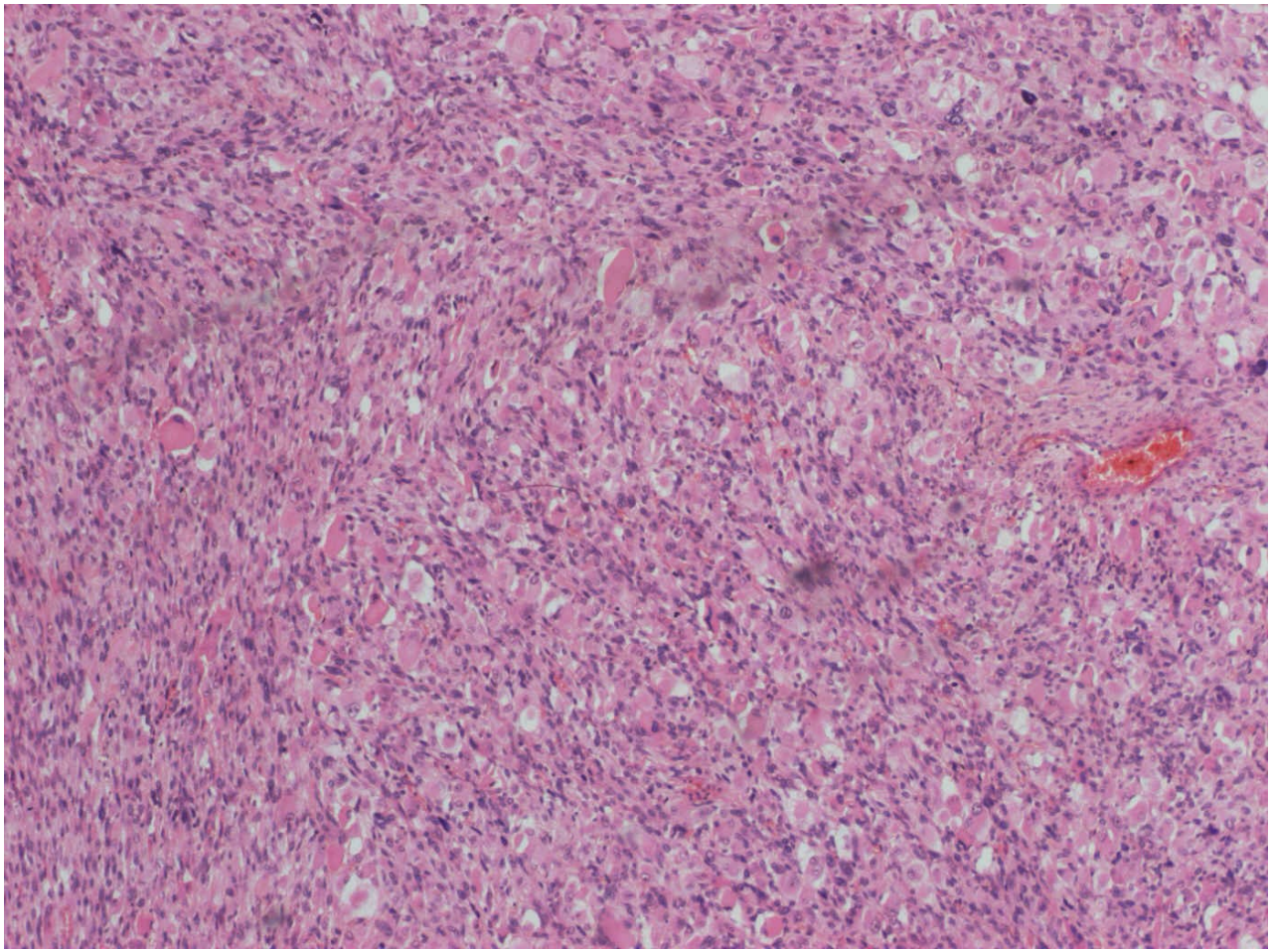
Skeletal muscle tumors

- Rhabdomyoma
  - Extremely rare, usually in heart (+ myxoma – USMLE!)
- Rhabdomyosarcoma
  - Malignant tumor that displays features of striated muscle differentiation
  - Most frequent soft tissue sarcoma of children and young adults, uncommon in adults

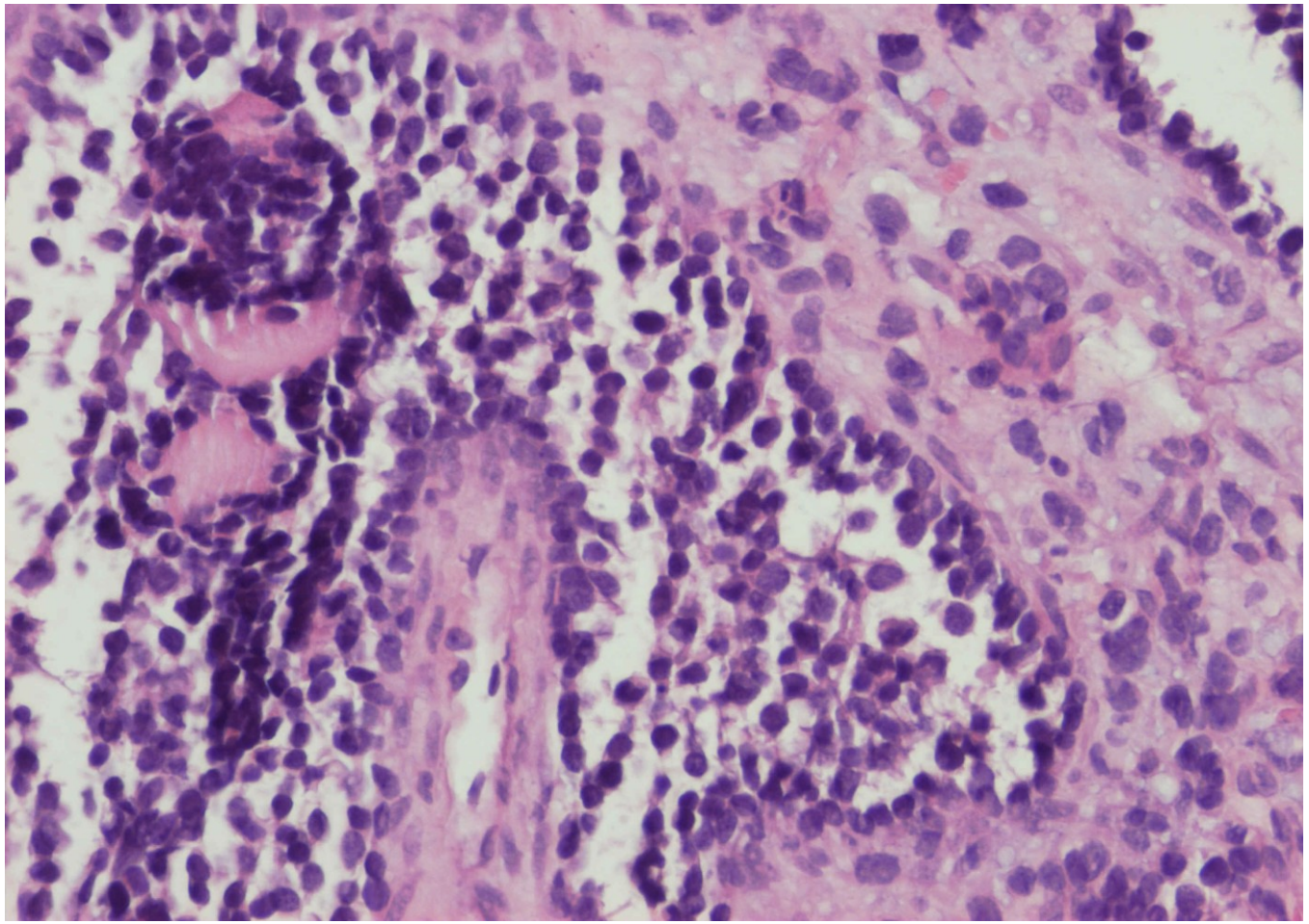
Skeletal muscle tumors

- Rhabdomyoma
- Rhabdomyosarcoma
  - Most of these tumors probably derive from primitive mesenchyme that has retained the capacity for skeletal muscle differentiation
  - 4 subtypes: embryonal, botryoid (sarcoma botryoides, urinary bladder, genitalia) alveolar, pleomorphic)

Skeletal muscle tumors



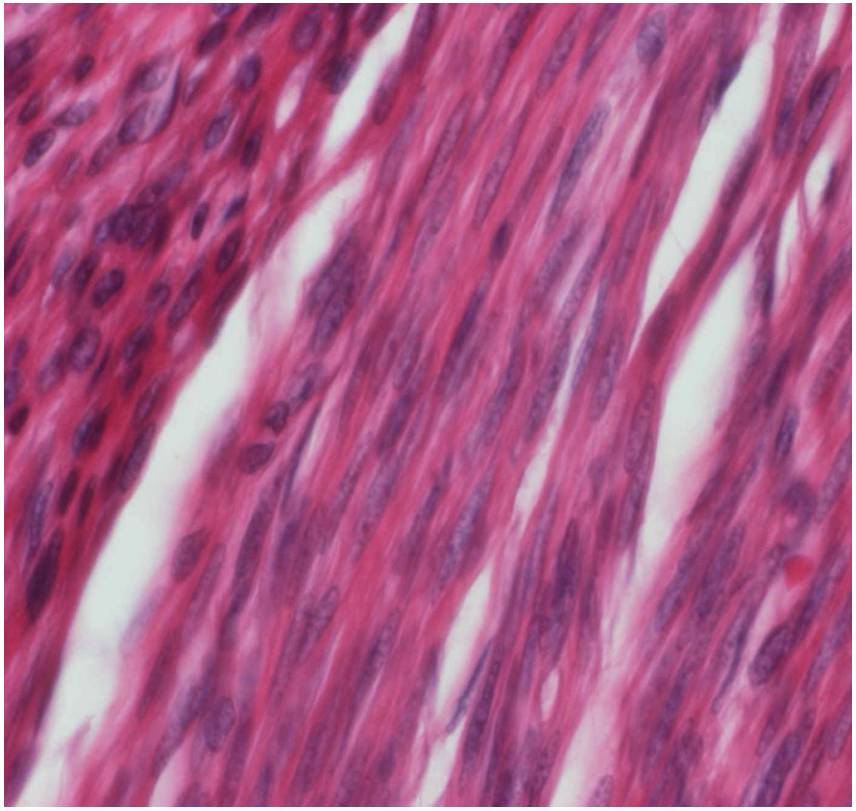
Skeletal muscle tumors

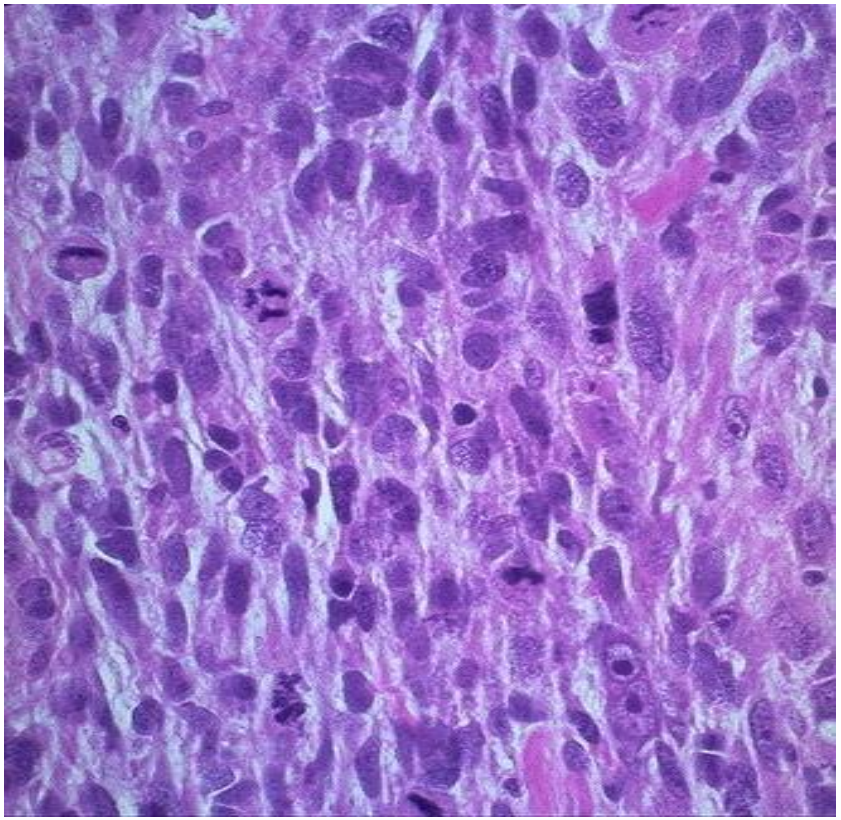


Smooth muscle tumors

- Leiomyoma
  - Usually arises in subcutaneous tissues, or from blood vessel walls in deep somatic tissues, or in myometrium
  - Painful lesions that appear as firm, gray-white, well-circumscribed nodules
  - Microscopically composed of perpendicular fascicles of relatively uniform spindled cells with cigar-shaped nuclei and very low mitotic activity
- Leiomyosarcoma
  - Uncommon tumor of adults that typically arises from the wall of blood vessels in the soft tissue of the extremities or in retroperitoneum or in myometrium
  - Differentiated from leiomyoma mainly by necroses and high mitotic activity
  - Most leiomyosarcomas eventually metastasize, although dissemination may occur as late as 15 or more years after resection of the primary tumor

Smooth muscle tumors

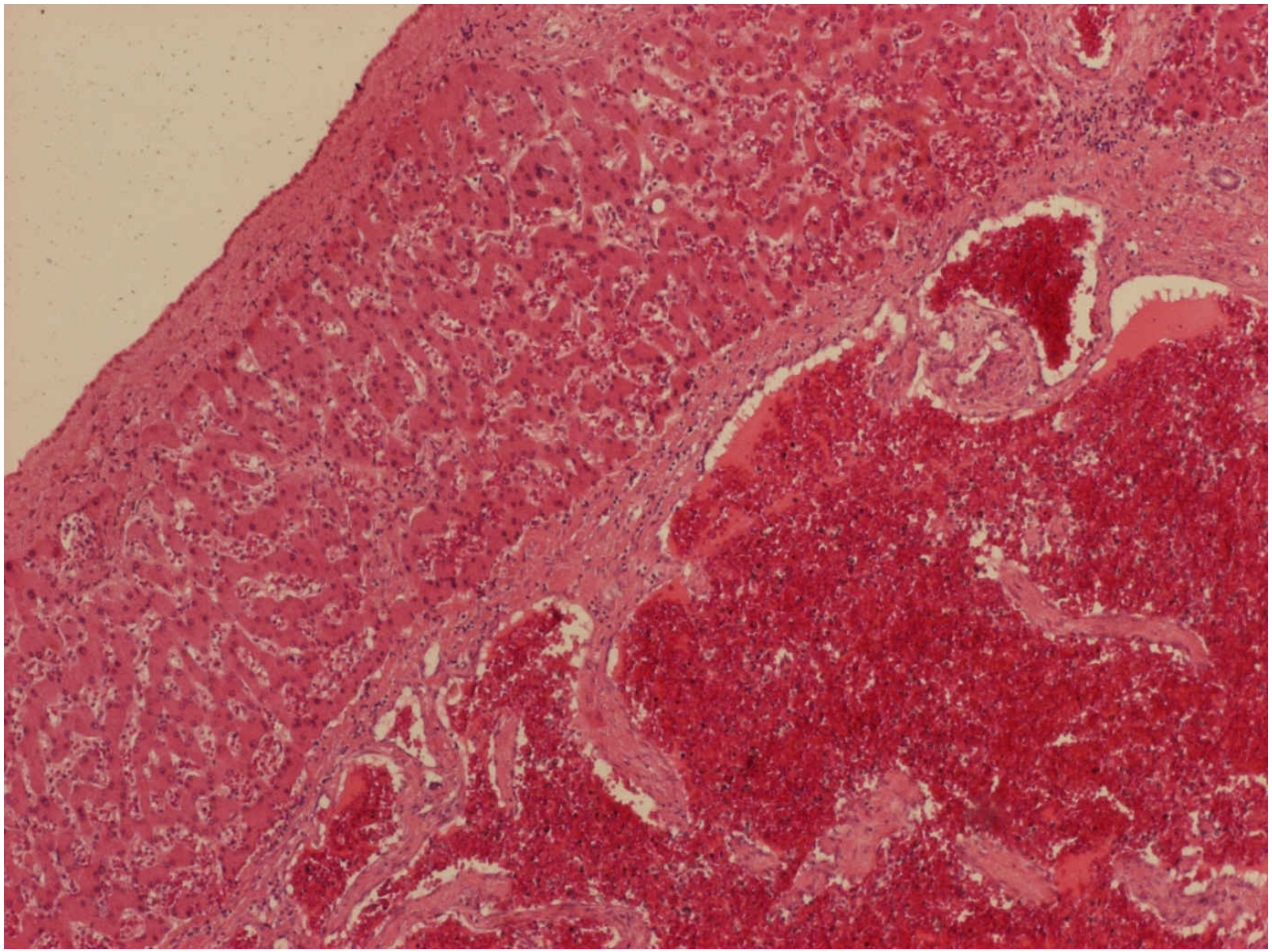




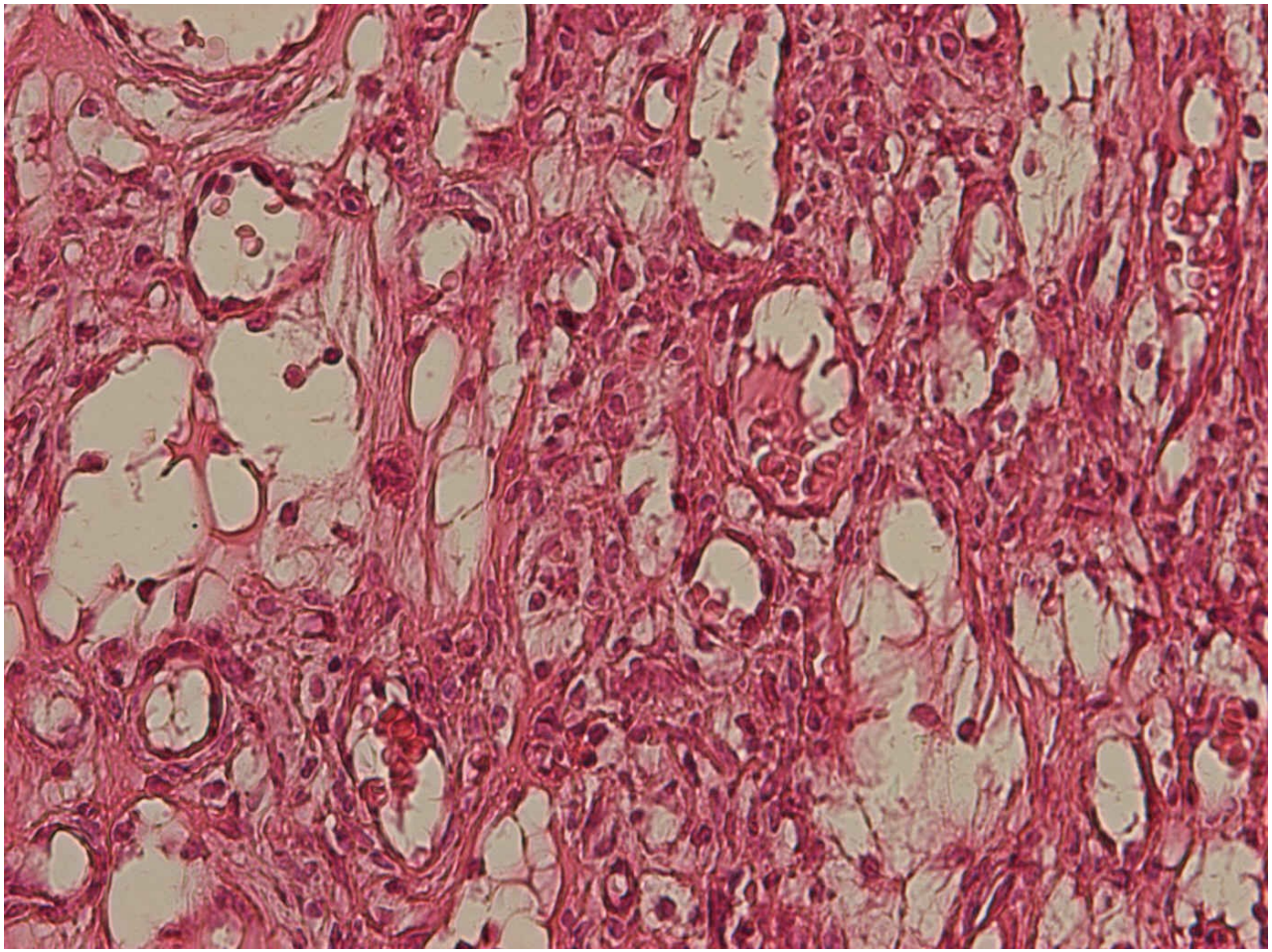
Blood vessels tumors

- Hemangioma
  - Usually occur in the skin but may also be found in internal organs
  - Capillary hemangioma
    - Composed of vascular channels with the size and structure of normal capillaries, var. pyogenic granuloma
  - Arteriovenous hemangioma
    - Composed of arteries and veins, in skin and meninges, can lead to Kasabach Meritt sy
  - Cavernous hemangioma
    - Made of large vascular channels, the liver
- Hemangiosarcoma
  - Rare, occur in either sex and at any age
  - The most common locations are skin, soft tissue, breast, bone, liver and spleen
  - Display varying degrees of differentiation, ranging from those composed mainly of distinct vascular elements to undifferentiated tumors with few recognizable blood channels
  - Kaposi sarcoma (AIDS, HHSV 8)

Blood vessel tumors



Blood vessel tumors

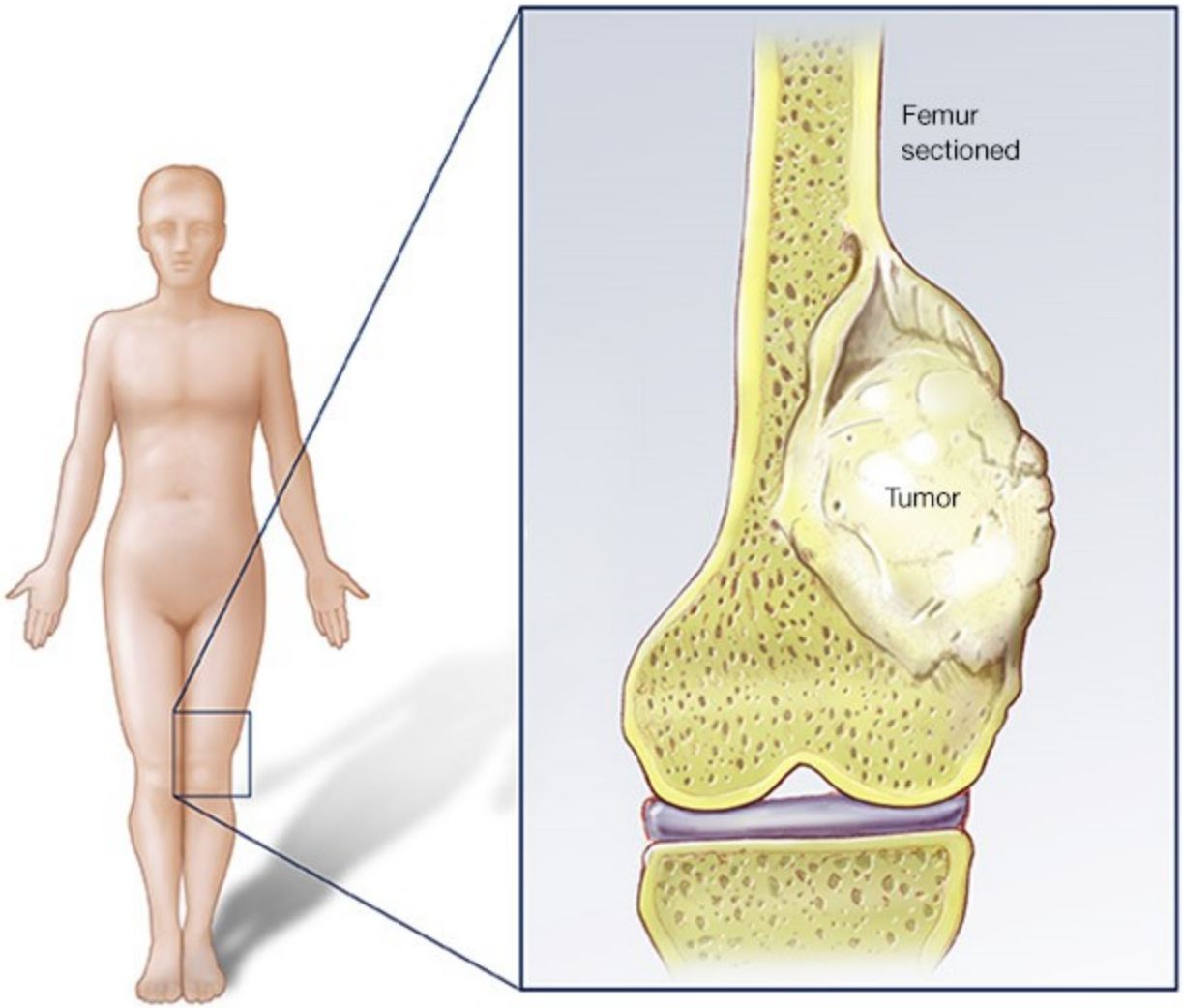


Lymphatic vessels tumors

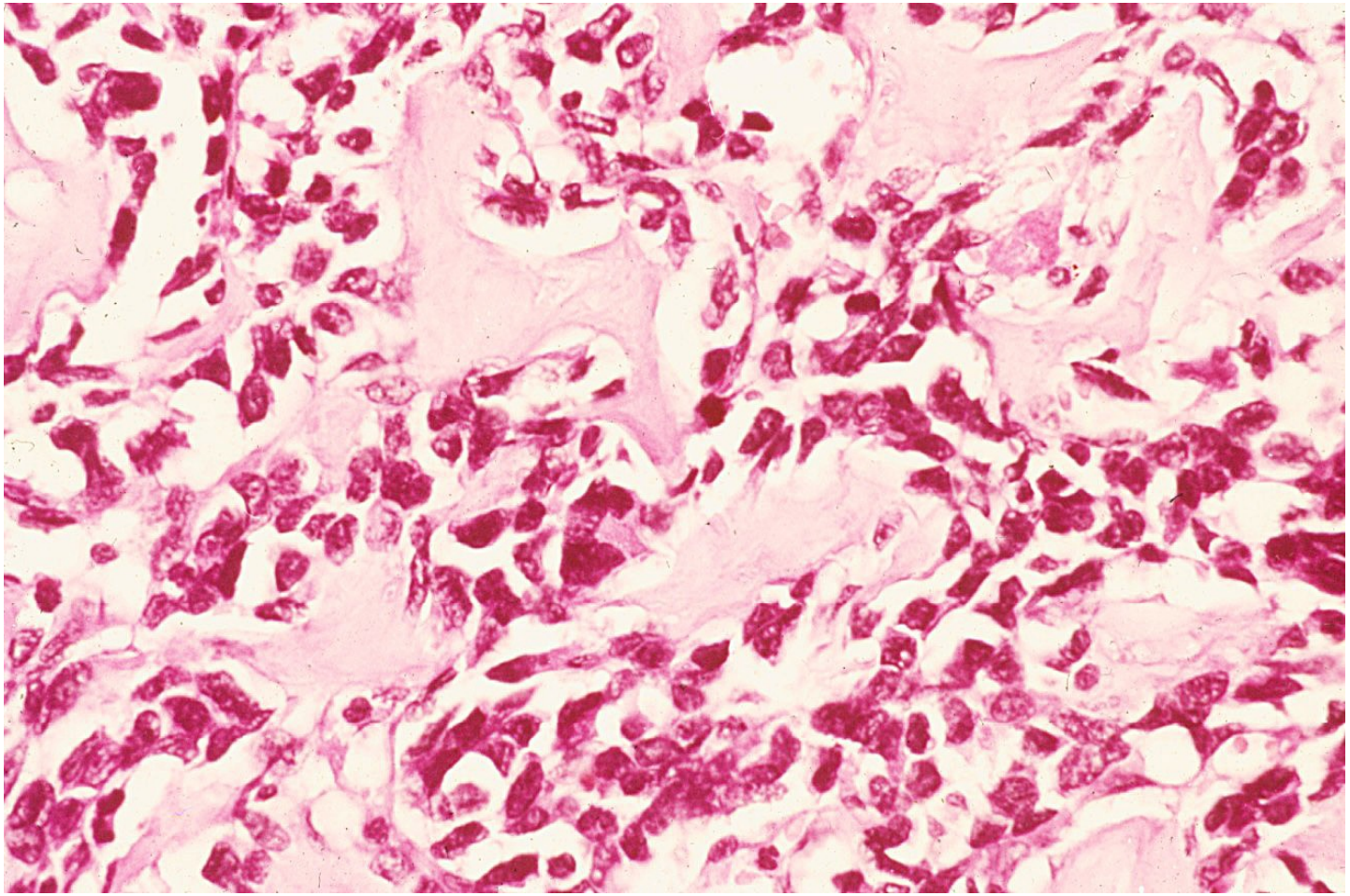
- Lymphangioma
- Capillary, cavernous
- Lymphangiosarcoma

Bone tumors

- Osteoma
  - Benign, slow-growing tumor composed of cortical-type dense bone
  - Multiple osteomas are associated with colonic familial adenomatous polyposis in Gardner syndrome
- Osteoid osteoma
  - Composed of osseous tissue (the nidus) surrounded by a halo of reactive bone formation
  - Very painful
- Osteoblastoma
  - Histologically similar to osteoid osteoma, but larger and not painful
- Osteosarcoma
  - Most common primary malignant bone tumor
  - Represents one fifth of all bone cancers and is most frequent in adolescents between 10 and 20 years old, affecting boys more often than girls (2:1)
  - Highly malignant
  - Often arise near the knee, in the lower femur or upper tibia/fibula
  - 75% arise adjacent to the knee or shoulder
  - Osteoplastic, chondroplastic, fibroplastic variant
  - Codman triangle



Bone tumors

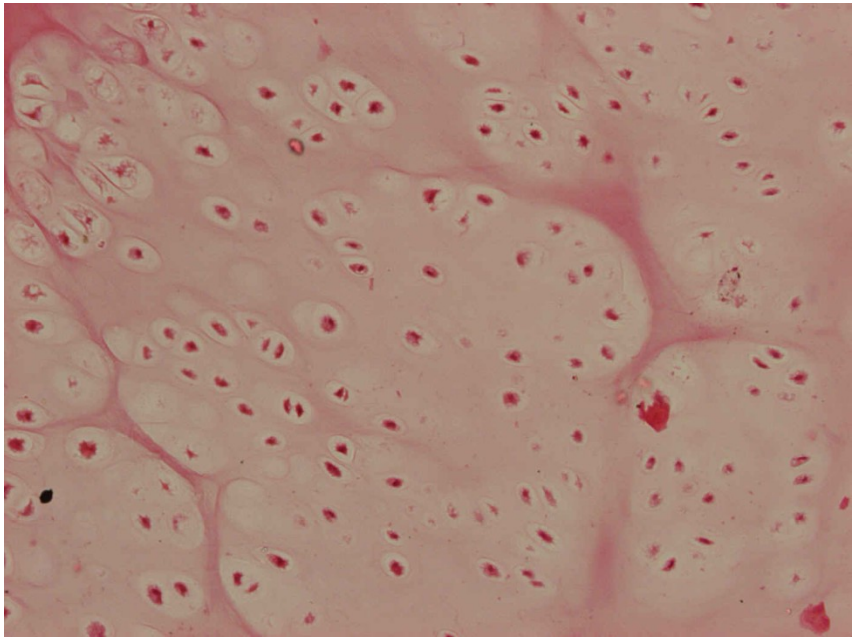


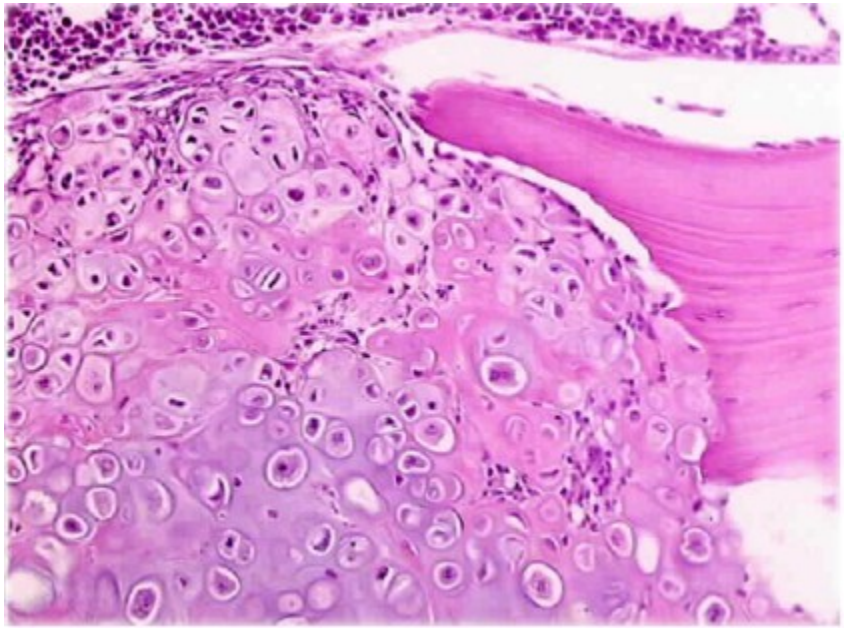
Tumors of cartilage

- Chondroma
  - Most solitary chondromas occur in the metacarpals and phalanges of the hands, the remainder being in almost any other tubular bone
  - On gross examination, solitary chondromas have the semitranslucent appearance of hyaline cartilage, often with a few calcified areas
- Chondroblastoma
  - Uncommon, chondrogenic tumor with predilection for the proximal femur, tibia and humerus, mostly in young (5-25 yrs)

- Chondrosarcoma
  - Malignant tumor of cartilage that arises from a preexisting cartilage rest or chondroma
  - Chondrosarcoma is the second most common primary malignant bone tumor and is more common in men than in women (2:1)
  - Central chondrosarcoma, peripheral chondrosarcoma, juxtacortical chondrosarcoma
  - Older patients than osteosarcoma, hip joint

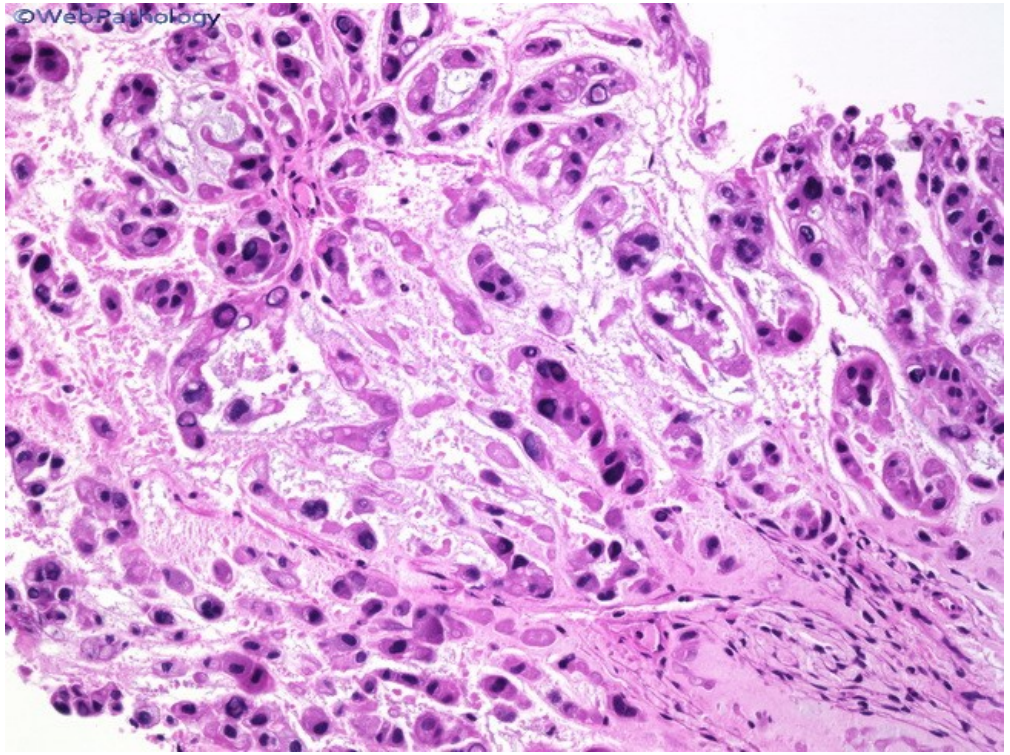
Tumors of cartilage





Chordoma

- NOT chondroma – malignant tumor from the rest of notochord – localised in base of skull, sacral area.



Neuroectodermal tumors

- Tumors of central nervous system (CNS)
- Tumors of peripheral nervous system (PNS)
- Pigmented skin lesions

Tumors of CNS

- Primary CNS cancers account for about 1.5% of all primary malignant tumors
- Metastatic tumors to the CNS are far more common than primary tumors and are a major problem in clinical management
- The broad spectrum of cellular constituents of the CNS (all of the diverse cell types in the CNS) is mirrored by the wide range of tumor types that arise within the brain, spinal cord and their overlying meninges (over 130 different types of CNS neoplasms are recognized and formally codified by the WHO)

Tumors of CNS

- Most brain tumors arise in adults, but some are more common in childhood (the most prominent being medulloblastoma, pilocytic astrocytoma and diffuse pontine astrocytoma)
- In adults, the most common types are meningiomas and gliomas

Tumors of CNS

TUMOURS OF NEUROEPITHELIAL TISSUE

Astrocytic tumours	
Pilocytic astrocytoma	9421/1[1]
Pilomyxoid astrocytoma	*9425/3**
Subependymal giant cell astrocytoma	9384/1
Pleomorphic xanthoastrocytoma	9424/3
Diffuse astrocytoma	9400/3
Fibrillary astrocytoma	9420/3
Gemistocytic astrocytoma	9411/3
Protoplasmic astrocytoma	9410/3
Anaplastic astrocytoma	9401/3
Glioblastoma	9440/3
Giant cell glioblastoma	9441/3
Gliosarcoma	9442/3
Gliomatosis cerebri	9381/3
Oligodendroglial tumours	
Oligodendroglioma	9450/3
Anaplastic oligodendroglioma	9451/3
Oligoastrocytic tumours	
Oligoastrocytoma	9382/3
Anaplastic oligoastrocytoma	9382/3
Ependymal tumours	
Subependymoma	9383/1
Myxopapillary ependymoma	9394/1
Ependymoma	9391/3
Cellular	9391/3
Papillary	9393/3
Clear cell	9391/3
Tanycytic	9391/3
Anaplastic ependymoma	9392/3
Choroid plexus tumours	
Choroid plexus papilloma	9390/0
Atypical choroid plexus papilloma	*9390/1**
Choroid plexus carcinoma	9390/3
Other neuroepithelial tumours	
Astroblastoma	9430/3
Chordoid glioma of the third ventricle	9444/1
Angiocentric glioma	*9431/1**

[1] Morphology code of the International Classification of Diseases for Oncology (ICD-O) (614A) and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /3 for malignant tumours and /1 for borderline or uncertain behaviour.

* The italicised numbers are provisional codes proposed for the 4th edition of ICD-O. While they are expected to be incorporated into the next ICD-O edition, they currently remain subject to change.

Neuronal and mixed neuronal-glial tumours	
Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)	9493/0
Desmoplastic infantile astrocytoma/ ganglioglioma	9412/1
Dysembryoplastic neuroepithelial tumour	9413/0
Gangliocytoma	9492/0
Ganglioglioma	9505/1
Anaplastic ganglioglioma	9505/3
Central neurocytoma	9506/1
Extraventricular neurocytoma	*9506/1**
Cerebellar liponeurocytoma	*9506/1**
Papillary glioneuronal tumour	*9509/1**
Rosette-forming glioneuronal tumour of the fourth ventricle	*9509/1**
Paraganglioma	8680/1
Tumours of the pineal region	
Pineocytoma	9361/1
Pineal parenchymal tumour of intermediate differentiation	9362/3
Pineoblastoma	9362/3
Papillary tumour of the pineal region	*9395/3**
Embryonal tumours	
Medulloblastoma	9470/3
Desmoplastic/nodular medulloblastoma	9471/3
Medulloblastoma with extensive nodularity	*9471/3**
Anaplastic medulloblastoma	*9474/3**
Large cell medulloblastoma	9474/3
CNS primitive neuroectodermal tumour	9473/3
CNS Neuroblastoma	9500/3
CNS Ganglioneuroblastoma	9490/3
Medulloepithelioma	9501/3
Ependymoblastoma	9392/3
Atypical teratoid / rhabdoid tumour	9508/3

TUMOURS OF CRANIAL AND PARASPINAL NERVES

Schwannoma (neurilemoma, neurinoma)	9560/0
Cellular	9560/0
Plexiform	9560/0
Melanotic	9560/0
Neurofibroma	9540/0
Plexiform	9550/0
Perineurioma	
Perineurioma, NOS	9571/0
Malignant perineurioma	9571/3
Malignant peripheral nerve sheath tumour (MPNST)	
Epithelioid MPNST	9540/3
MPNST with mesenchymal differentiation	9540/3
Melanotic MPNST	9540/3
MPNST with glandular differentiation	9540/3

TUMOURS OF THE MENINGES

Tumours of meningothelial cells	
Meningioma	9530/0
Meningothelial	9531/0
Fibrous (fibroblastic)	9532/0
Transitional (mixed)	9537/0
Psammomatous	9533/0
Angiomatous	9534/0
Microcystic	9530/0
Secretory	9530/0
Lymphoplasmacyte-rich	9530/0
Metaplastic	9530/0
Chordoid	9538/1
Clear cell	9538/1
Atypical	9539/1
Papillary	9538/3
Rhabdoid	9538/3
Anaplastic (malignant)	9530/3
Mesenchymal tumours	
Lipoma	8850/0
Angiolipoma	8861/0
Hibernoma	8880/0
Liposarcoma	8850/3
Solitary fibrous tumour	8815/0
Fibrosarcoma	8810/3
Malignant fibrous histiocytoma	8830/3
Leiomyoma	8890/0
Leiomyosarcoma	8890/3
Rhabdomyoma	8900/0
Rhabdomyosarcoma	8900/3
Chondroma	9220/0
Chondrosarcoma	9220/3
Osteoma	9180/0
Osteosarcoma	9180/3
Osteochondroma	9210/0
Haemangioma	9120/0
Epithelioid haemangioendothelioma	9133/1
Haemangiopericytoma	9150/1
Anaplastic haemangiopericytoma	9150/3
Angiosarcoma	9120/3
Kaposi sarcoma	9140/3
Ewing sarcoma - PNET	9364/3
Primary melanocytic lesions	
Diffuse melanocytosis	8728/0
Melanocytoma	8728/1
Malignant melanoma	8720/3
Meningeal melanomatosis	8728/3
Other neoplasms related to the meninges	
Haemangioblastoma	9161/1

LYMPHOMAS AND HAEMATOPOIETIC NEOPLASMS

Malignant lymphomas	9590/3
Plasmacytoma	9731/3
Granulocytic sarcoma	9930/3

GERM CELL TUMOURS

Germinoma	9064/3
Embryonal carcinoma	9070/3
Yolk sac tumour	9071/3
Choriocarcinoma	9100/3
Teratoma	9080/1
Mature	9080/0
Immature	9080/3
Teratoma with malignant transformation	9084/3
Mixed germ cell tumour	9085/3

TUMOURS OF THE SELLAR REGION

Craniopharyngioma	9350/1
Adamantinomatous	9351/1
Papillary	9352/1
Granular cell tumour	9582/0
Pituicytoma	*9432/1**
Spindle cell oncocytoma of the adenohypophysis	*8291/0**

METASTATIC TUMOURS

Tumors of CNS

- Diagnosis
  - Generating a preoperative differential diagnosis of the most likely possibilities based on the patient's clinical information (gender, age, anatomic location)
  - Biopsy or resection of the lesion to obtain a definitive tissue-based diagnosis upon which further clinical management depends
- Clinical signs and symptoms
  - Long history (e.g. several years of poorly controlled seizures, favors more indolent or low-grade disease)
  - Relatively brief history (2-week history of headache, nausea and emesis and localizing signs) favors a higher grade and more aggressively expanding lesion

Tumors of CNS

- Grading
  - Tumor grades according to WHO criteria range from I through IV (I being the lowest grade and IV being the most malignant)
  - Subjective and ill-defined term “benign” should be used with extreme caution, if at all (even WHO grade I tumors can result in a clinical course that entails considerable morbidity and even mortality - anatomic location, growth pattern etc.)

Tumors of CNS

- Meningiomas
- Diffuse astrocytic and oligodendroglial tumors (astrocytomas, oligodendrogliomas)
- Other astrocytic tumors (pilocytic astrocytomas)
- Ependymal tumors
- Embryonal tumors

Meningioma

- Meningiomas are derived from arachnoid (meningothelial) cells that form the outer boundary of the subarachnoid space
- These tumors can arise at any CNS site where arachnoid cells are present

Meningioma

- Meningiomas typically arise in one of three settings:
  - Sporadic – most common
  - Iatrogenic—usually associated with prior cranial irradiation
  - Associated with tumor predisposition syndrome—most commonly neurofibromatosis type 2 (NF2)

Meningioma

- Grade I – „benign“
  - Meningothelial, fibrous, transitional, psammomatous, angiomatous, microcystic, secretory, lymphoplasmacyte rich, metaplastic
- Grade II – atypical
  - Chordoid, clear cell
- Grade III – malignant (anaplastic)
  - Rhabdoid, papillary

Meningioma

- The indolent growth of most meningiomas enables these tumors to enlarge very slowly for years before becoming symptomatic, during which time they displace the brain but do not infiltrate it
- Patients frequently have seizures (particularly with tumors at parasagittal sites over the convexity of the hemispheres) and/or „site-specific signs“ (e.g. tumors of the olfactory groove produce anosmia)

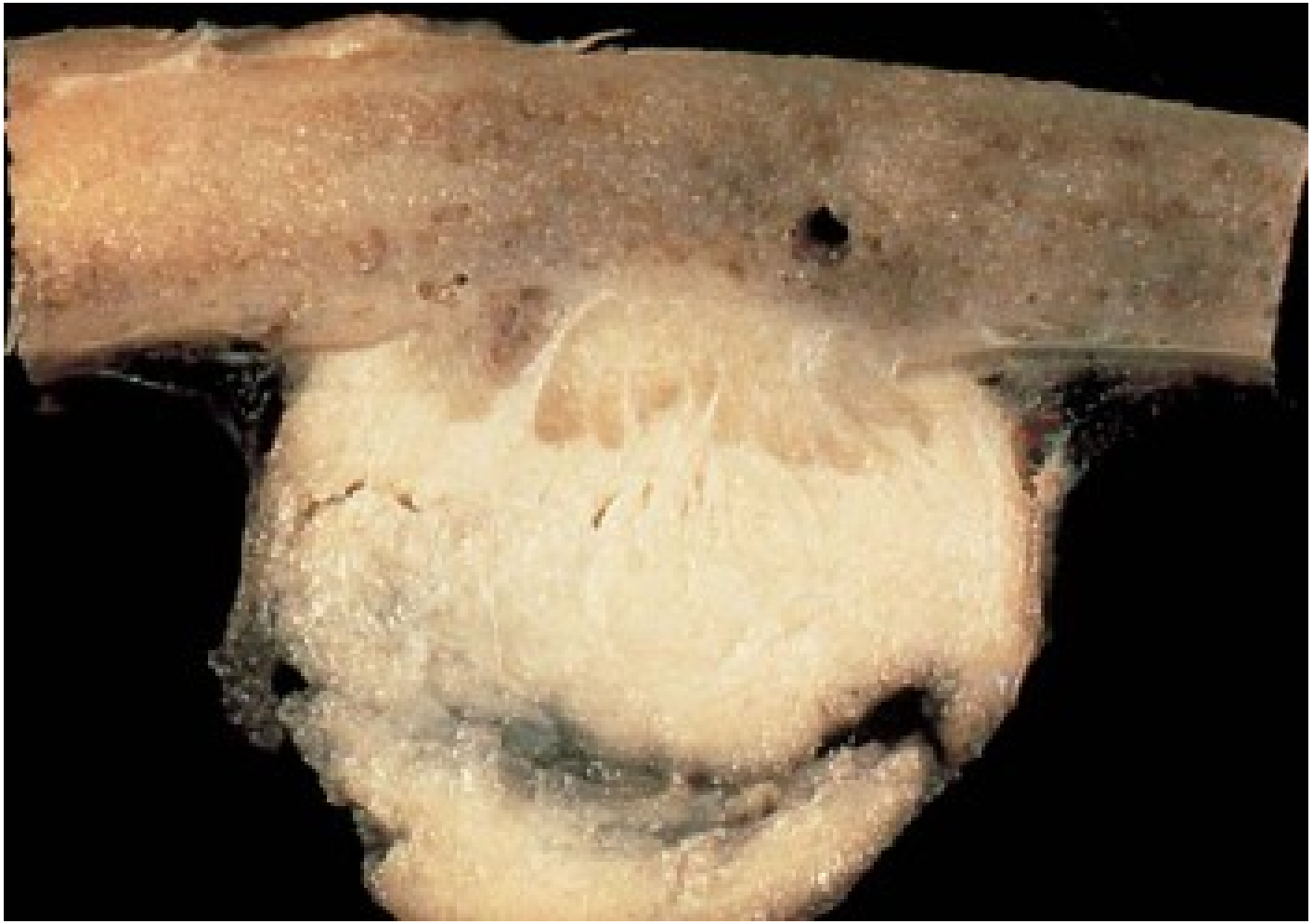
Meningioma

- Invasion of cranial bone is relatively common (even in grade I meningiomas) and growth through the calvarium may create a tumor mass beneath the scalp
- In contrast, invasion of the underlying brain by meningiomas is rare, and such aggressive behavior warrants upgrading to WHO grade II (atypical)

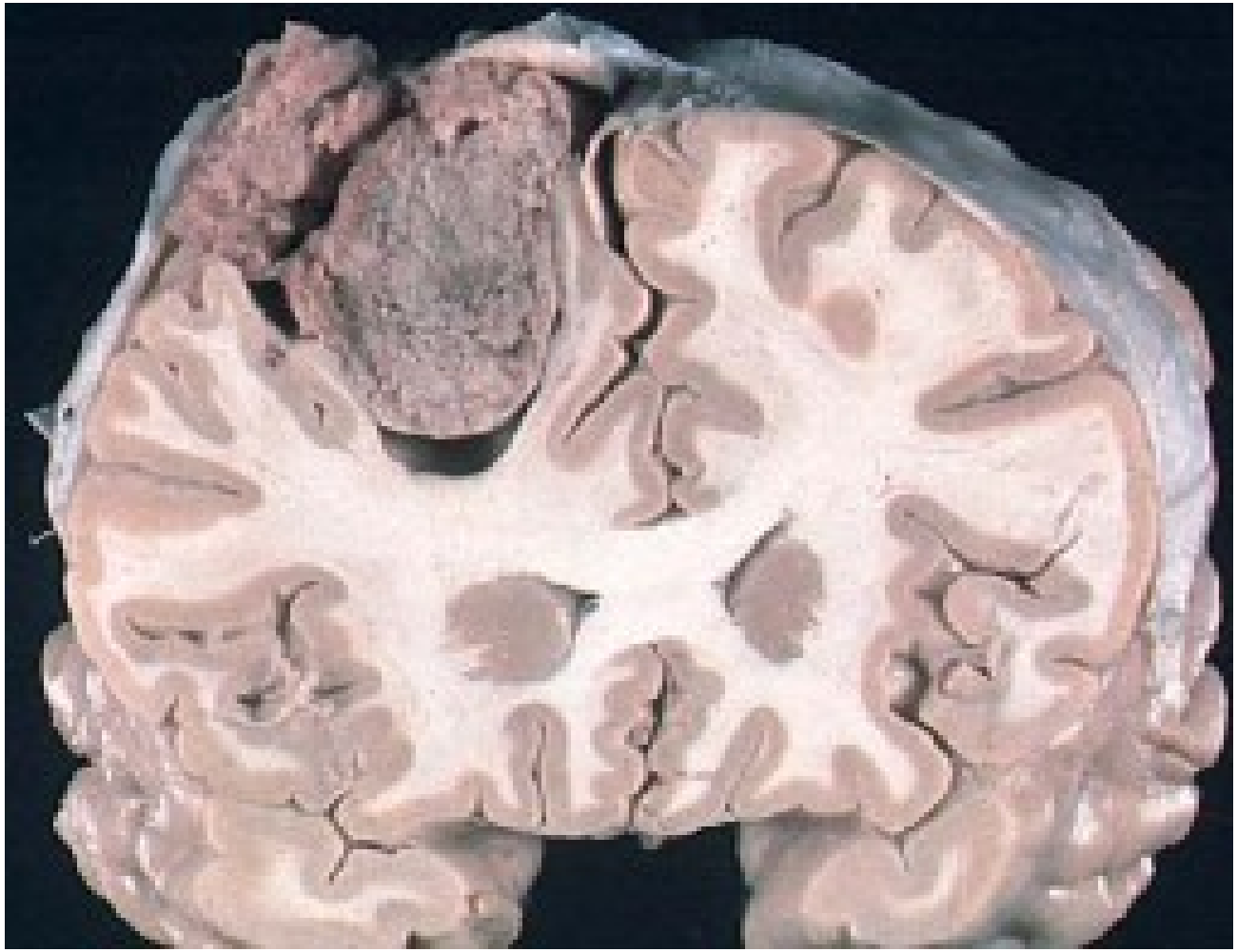
Meningioma

- Usually well-circumscribed dura-based masses of variable size that compress, but do not invade, underlying brain
- Cut surface is fleshy and tan
- Classic histologic hallmark of meningiomas is a whorled pattern, often in association with psammoma bodies (laminated, spherical calcospherites)

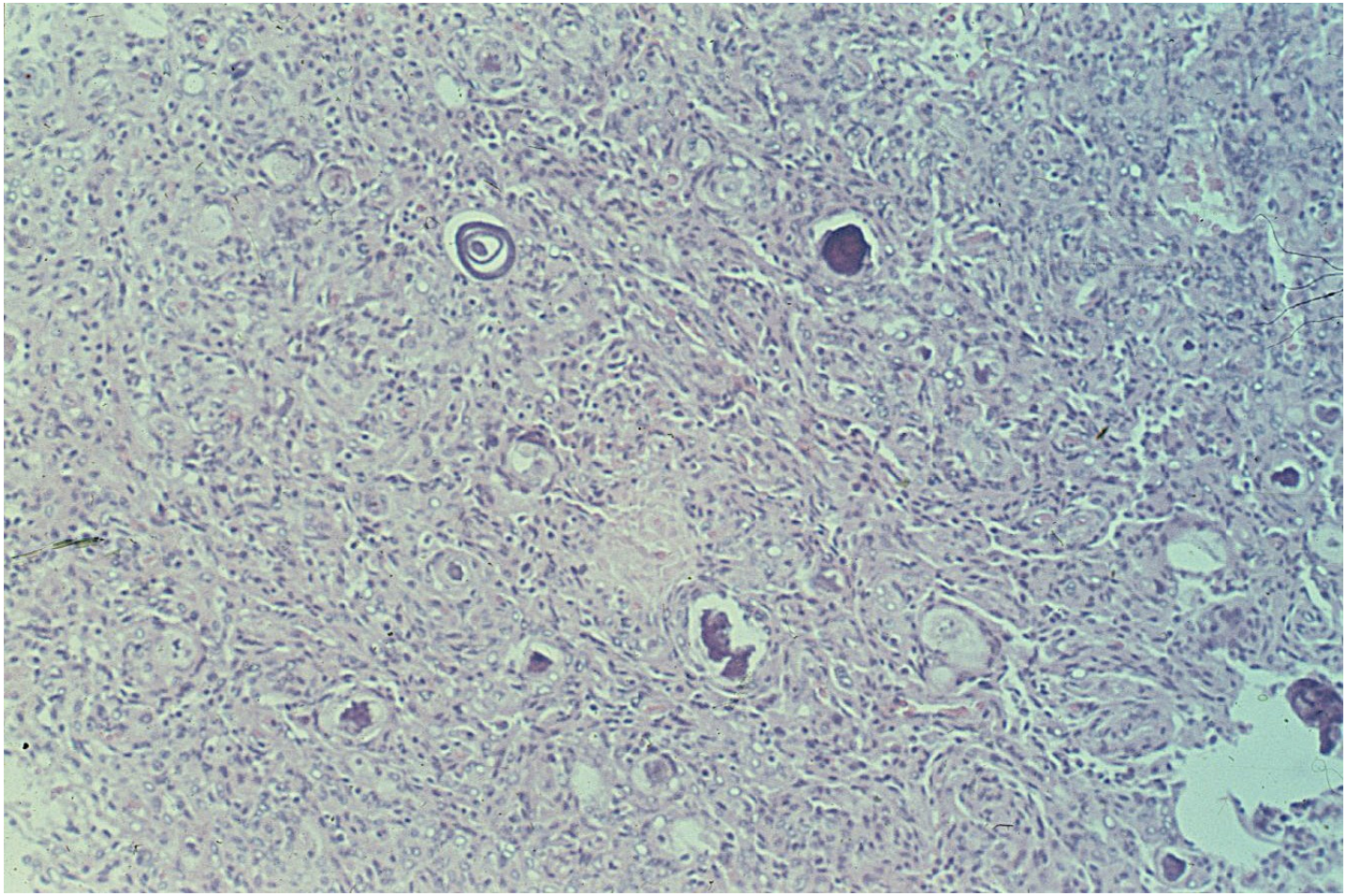
Meningioma



Meningioma



Meningioma



Astrocytic tumors

- Tumors of astrocytic derivation (astrocytomas) are the most common primary brain tumors
  - Diffuse astrocytoma (grade II)
  - Anaplastic astrocytoma (grade III)
  - Glioblastoma (grade IV)
  - Pilocytic astrocytoma (grade I)

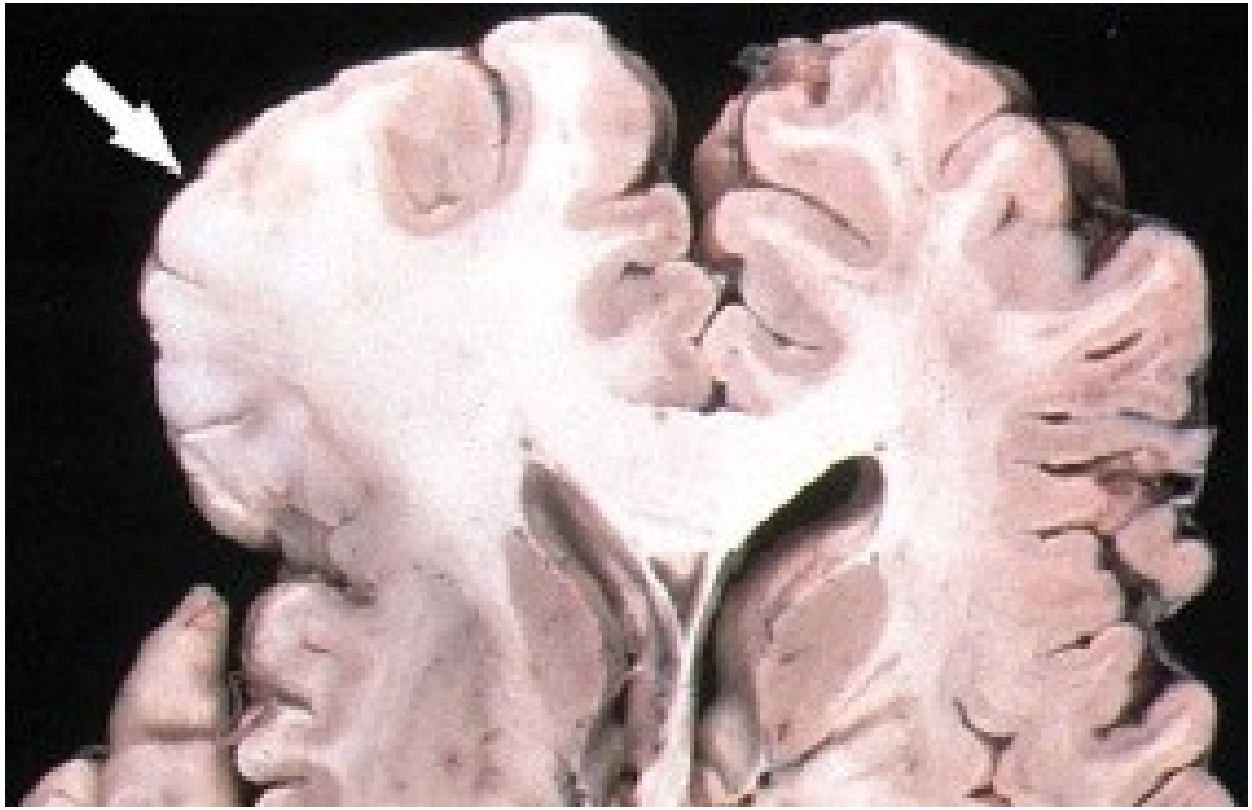
Diffuse astrocytoma

- WHO - …“typically affects young adults and is characterized by a high degree of cellular differentiation and slow growth; the tumour occurs throughout the CNS but is preferentially located supratentorially and has an intrinsic tendency for malignant progression to anaplastic astrocytoma and, ultimately, glioblastoma“...

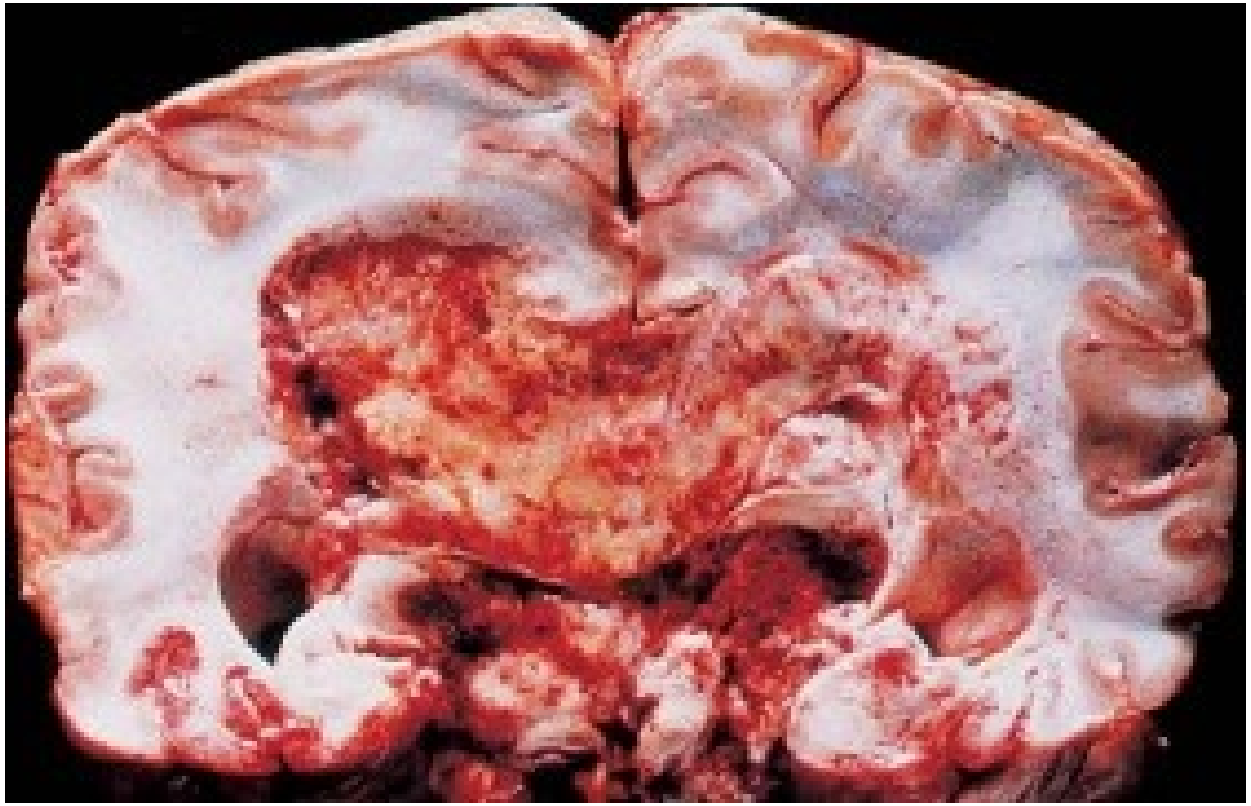
Diffuse astrocytomas

- Ability of individual tumor cells to infiltrate widely through brain and spinal cord parenchyma
- This property reaches its extreme in “gliomatosis cerebri“ (WHO grade III), in which infiltrating glioma cells involve at least three cerebral lobes (and often more) with infiltration into both hemispheres, the brainstem, the cerebellum and even the spinal cord

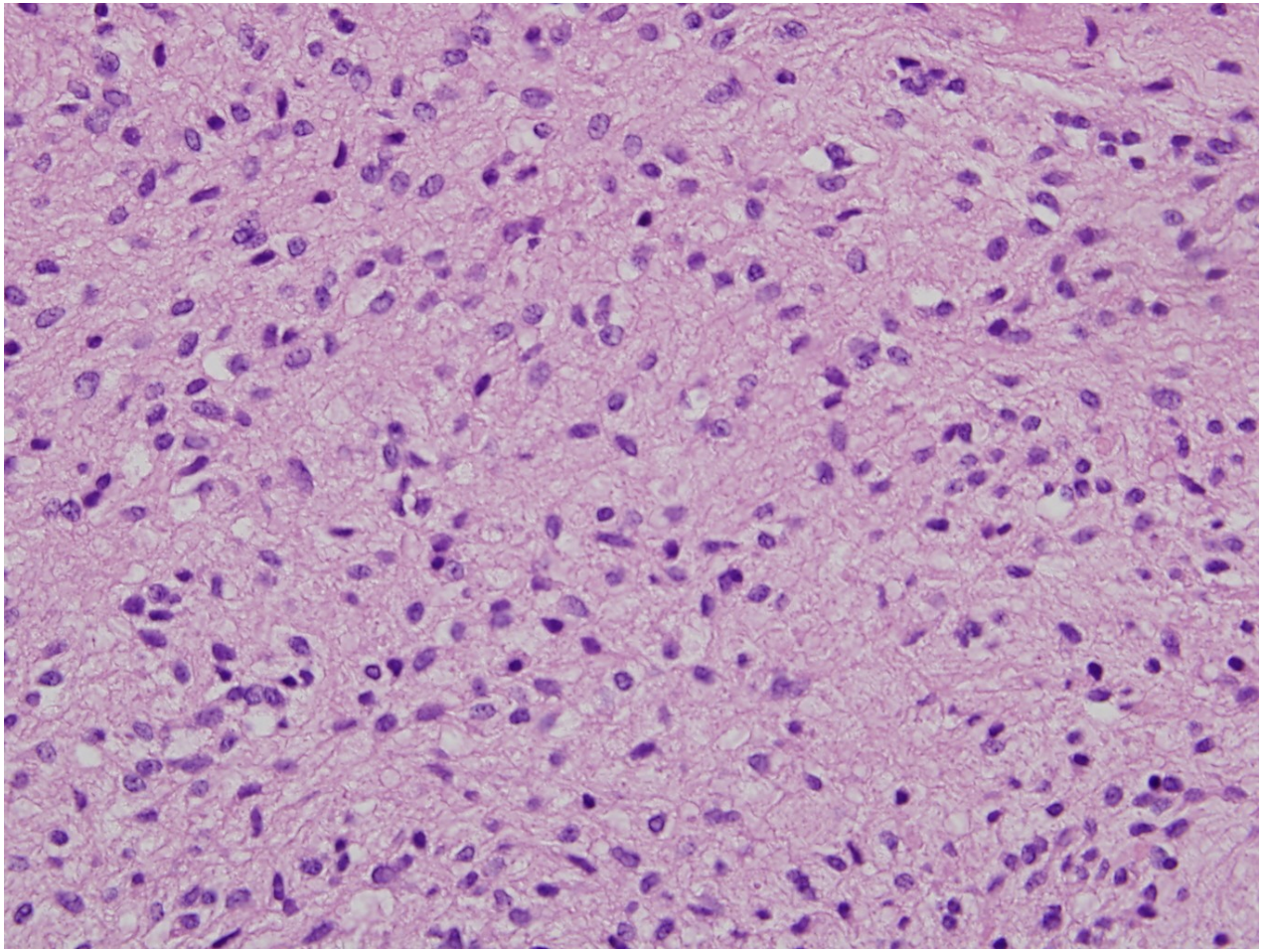
Diffuse astrocytoma



Diffuse astrocytoma



Diffuse astrocytoma



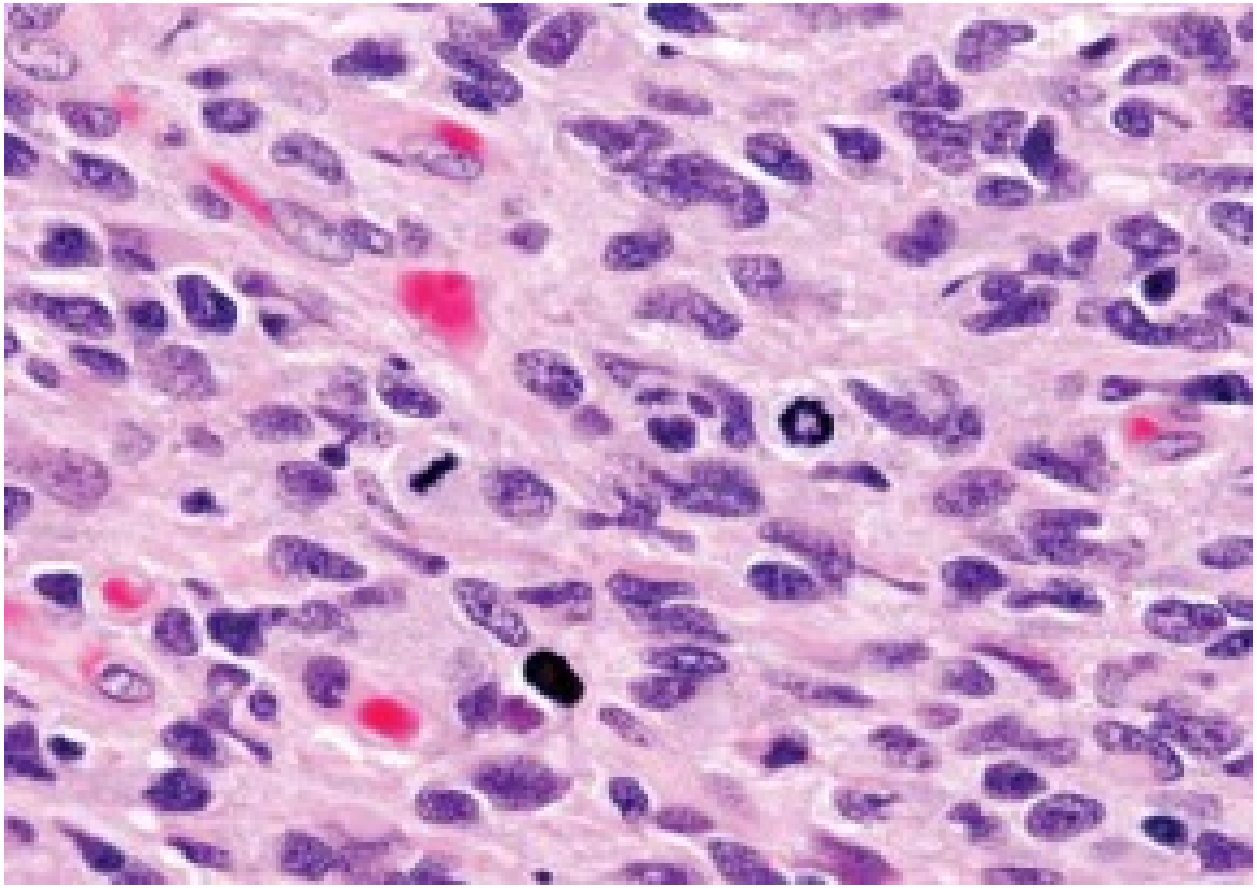
Diffuse astrocytoma

- The mean survival time after surgical intervention is in the range of 6-8 years, with marked individual variation
- Young age at diagnosis has been consistently predictive of a more favourable clinical course, while large tumour size appears to be a negative predictor

Anaplastic astrocytoma

- WHO - …“a diffusely infiltrating malignant astrocytoma that primarily affects adults, is preferentially located in the cerebral hemispheres, and is histologically characterized by nuclear atypia, increased cellularity and significant proliferative activity. The tumour may arise from diffuse astrocytoma WHO grade II or de novo, i.e. without evidence of a less malignant precursor lesion, and has an inherent tendency to undergo progression to glioblastoma“…

Anaplastic astrocytoma



Glioblastoma

- WHO - …“the most frequent primary brain tumor and the most malignant neoplasm with predominant astrocytic differentiation; histopathological features include nuclear atypia, cellular pleomorphism, mitotic activity, vascular thrombosis, microvascular proliferation and necrosis. It typically affects adults and is preferentially located in the cerebral hemispheres. Most glioblastomas manifest rapidly de novo, without recognizable precursor lesions (primary glioblastoma). Secondary glioblastomas develop slowly from diffuse astrocytoma WHO grade II or anaplastic astrocytoma (WHO grade III). Due to their invasive nature, glioblastomas cannot be completely resected, and despite progress in radio/chemotherapy, less than half of patients survive more than a year, with older age as the most significant adverse prognostic factor“…

Glioblastoma

- The vast majority of glioblastomas are sporadic, but a minority arise in the setting of a genetic tumor predisposition syndrome – neurofibromatosis type 1 and Turcot type 1 syndrome (mismatch repair [MMR]/hereditary nonpolyposis colon cancer [HNPCC]–associated Turcot)

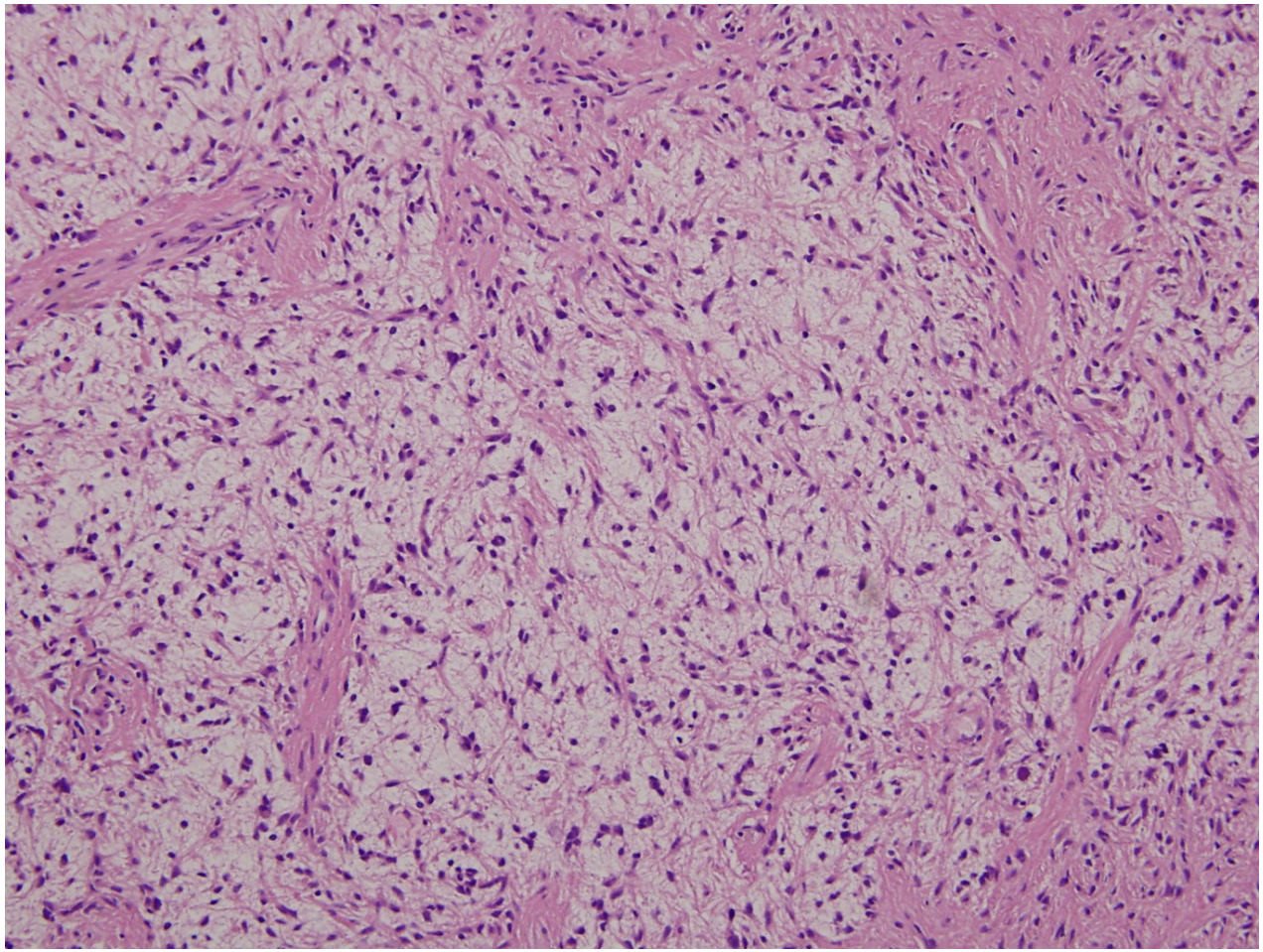
Pilocytic astrocytoma

- In contrast to diffuse astrocytomas, pilocytic astrocytomas do not infiltrate brain or spinal cord parenchyma diffusely and are not prone to undergo anaplastic progression to higher-grade tumors
- Common anatomic locations include the cerebellum, brainstem, optic nerves and third ventricular region

Pilocytic astrocytoma

- WHO - …“a relatively circumscribed, slowly growing, often cystic astrocytoma occurring in children and young adults, histologically characterized by a biphasic pattern with varying proportions of compacted bipolar cells associated with Rosenthal fibers and loose-textured multipolar cells associated with microcysts and eosinophilic granular bodies/hyaline droplets“...

Pilocytic astrocytoma



Oligodendroglial tumors

- Oligodendroglioma (grade II)
- Anaplastic oligodendrolioma (grade III)

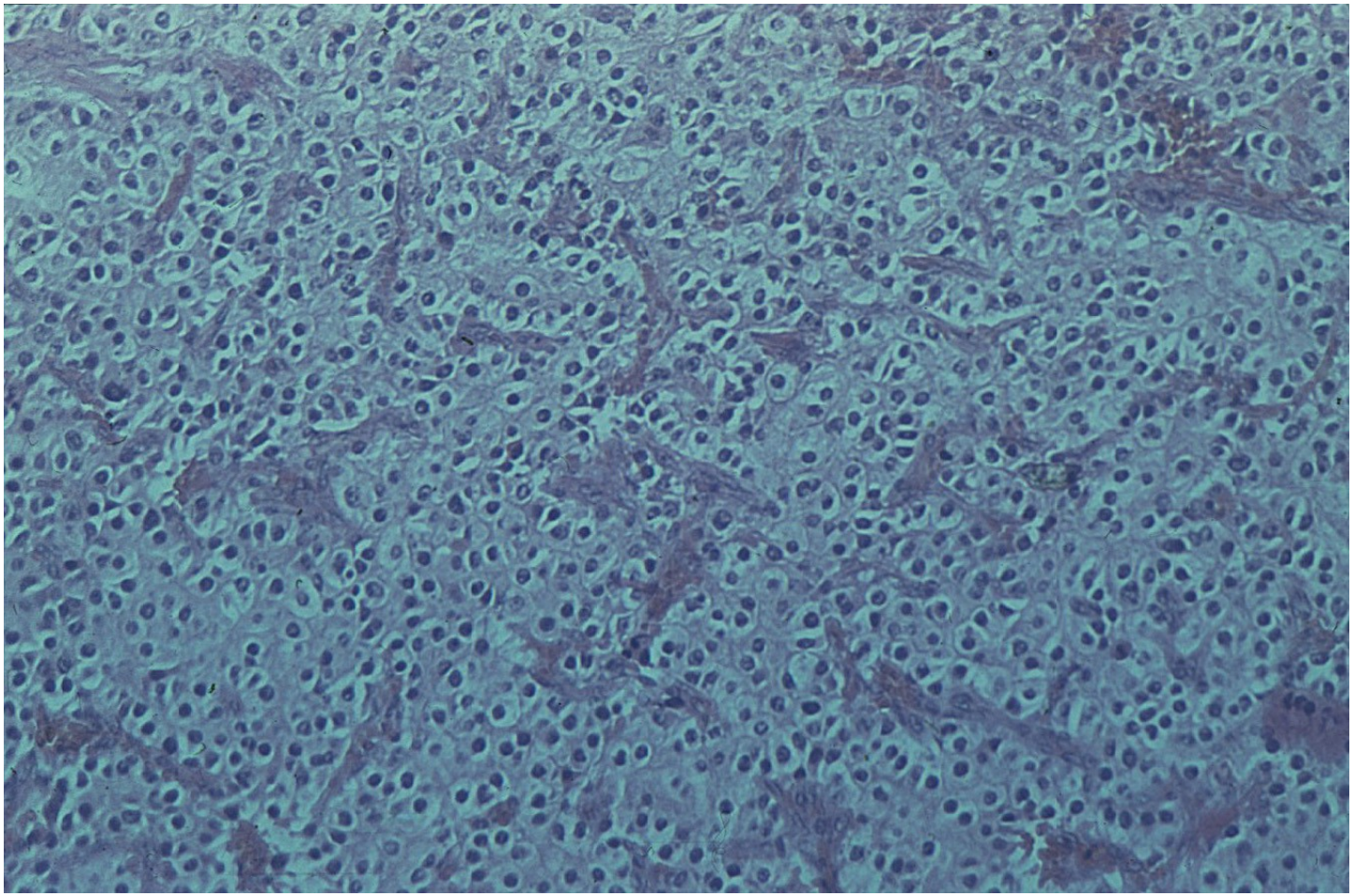
Oligodendroglioma

- WHO - …“a diffusely infiltrating, well-differentiated glioma of adults, typically located in the cerebral hemispheres, composed of neoplastic cells morphologically resembling oligodendroglia and harbouring deletions of chromosomal arms 1p and 19q“…

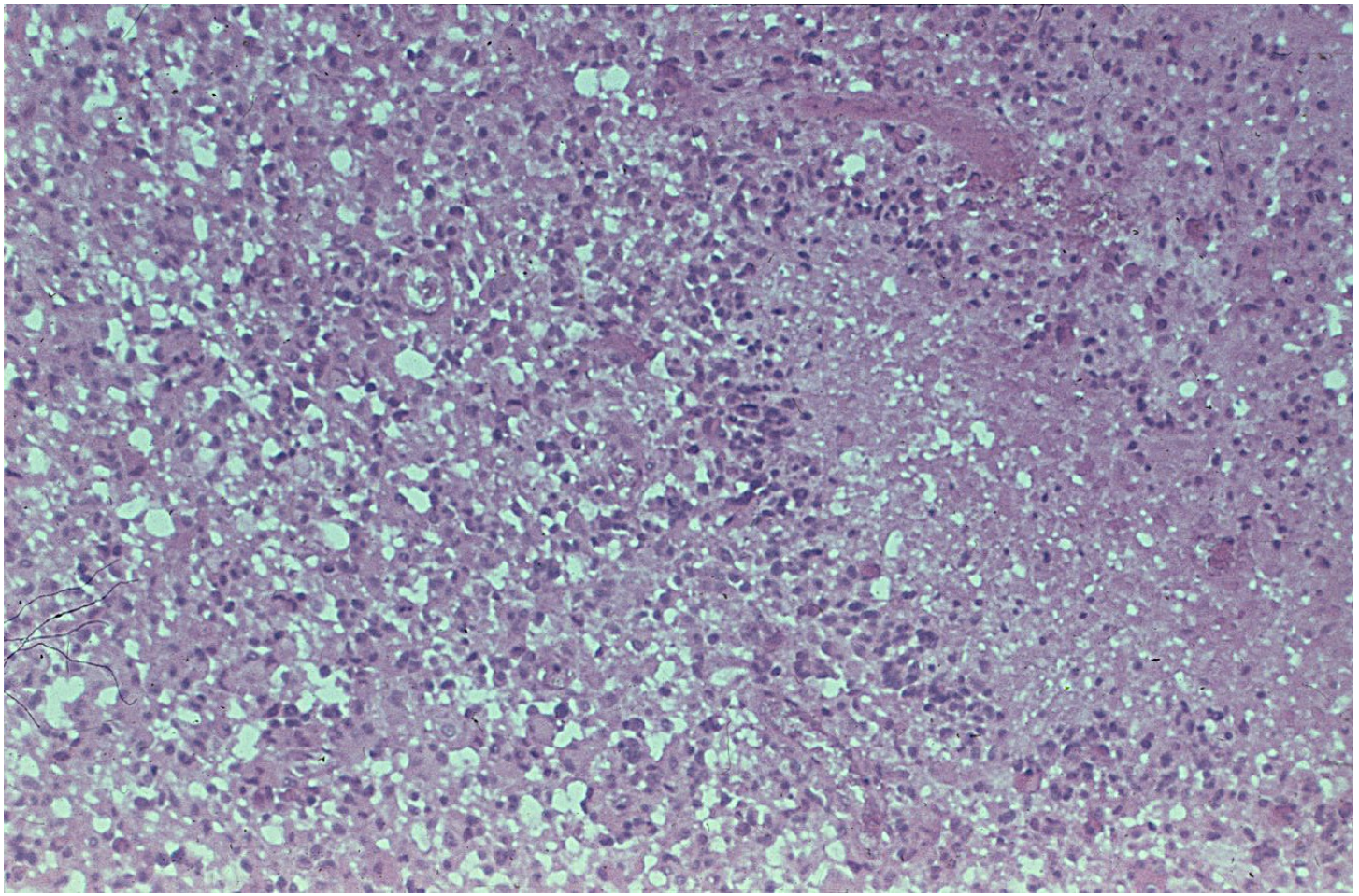
Oligodendroglioma

- Like diffuse astrocytomas, oligodendrogliomas are highly infiltrative tumors. However, their response to treatment and attendant overall survival are much more favorable than for diffuse astrocytomas of comparable grade
- Majority of oligodendrogliomas arise in adults in the fourth and fifth decades, largely in the white matter of cerebral hemispheres

Oligodendroglioma



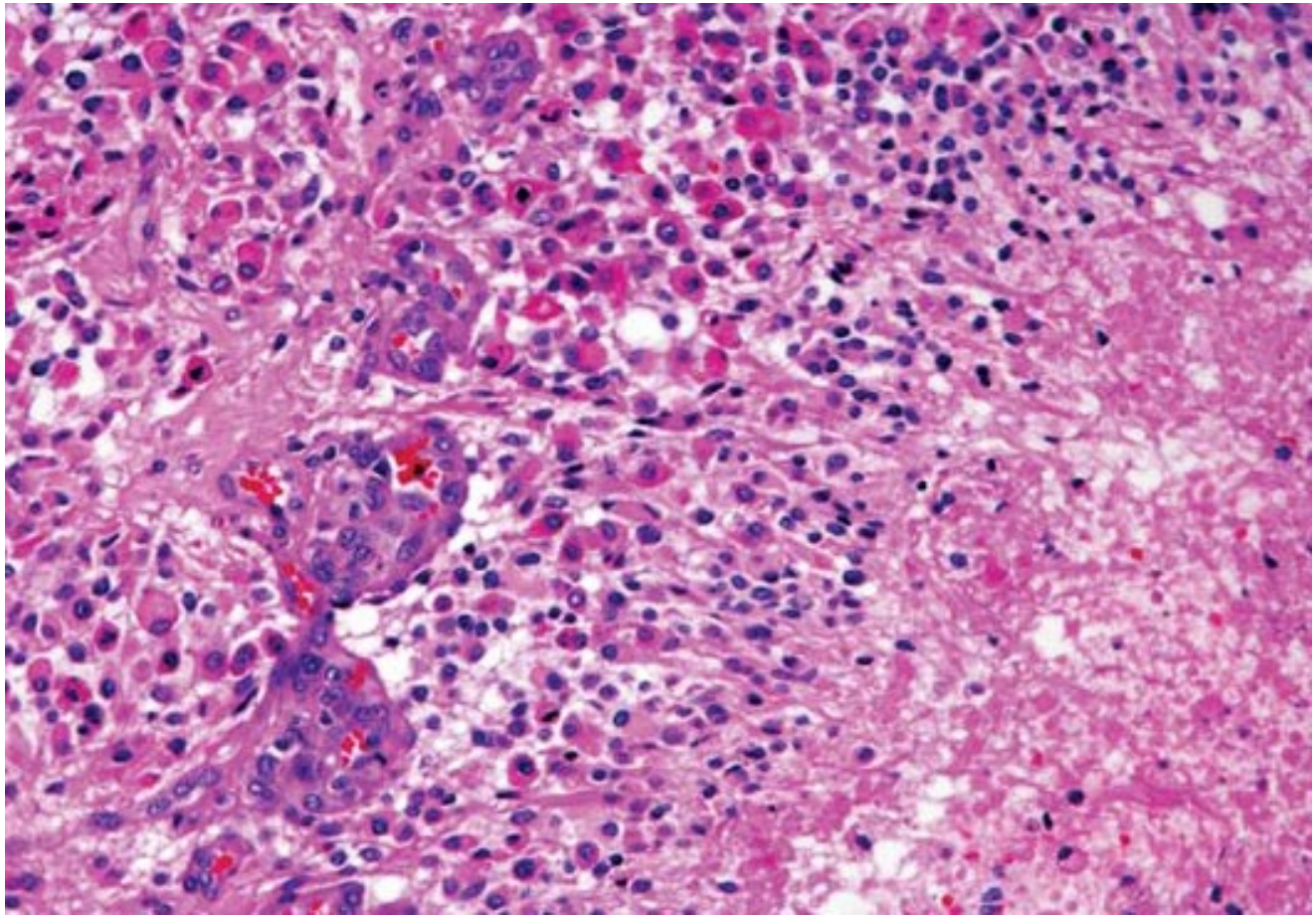
Glioblastoma



Anaplastic oligodendroglioma

- WHO - …“an oligodendroglioma with focal or diffuse histological features of malignancy and a less favourable prognosis“…

Anaplastic oligodendroglioma



Ependymal tumors

- Ependymoma (grade II)
- Anaplastic ependymoma (grade III)

WHO revision 2016 for tumors of astrocytic and oligodendroglial lineage

- Concept of "**integrated diagnosis**"
- Evaluation of **IDH** (isocitrate dehydrogenase) 1,2 expression (both in astrocytomas and in oligodendrogliomas)
- **ATRX** (ataxia telangiectasia retardation X-linked) i astrocytomas
- **Co-deletion 1p19q** in oligodendrogliomas

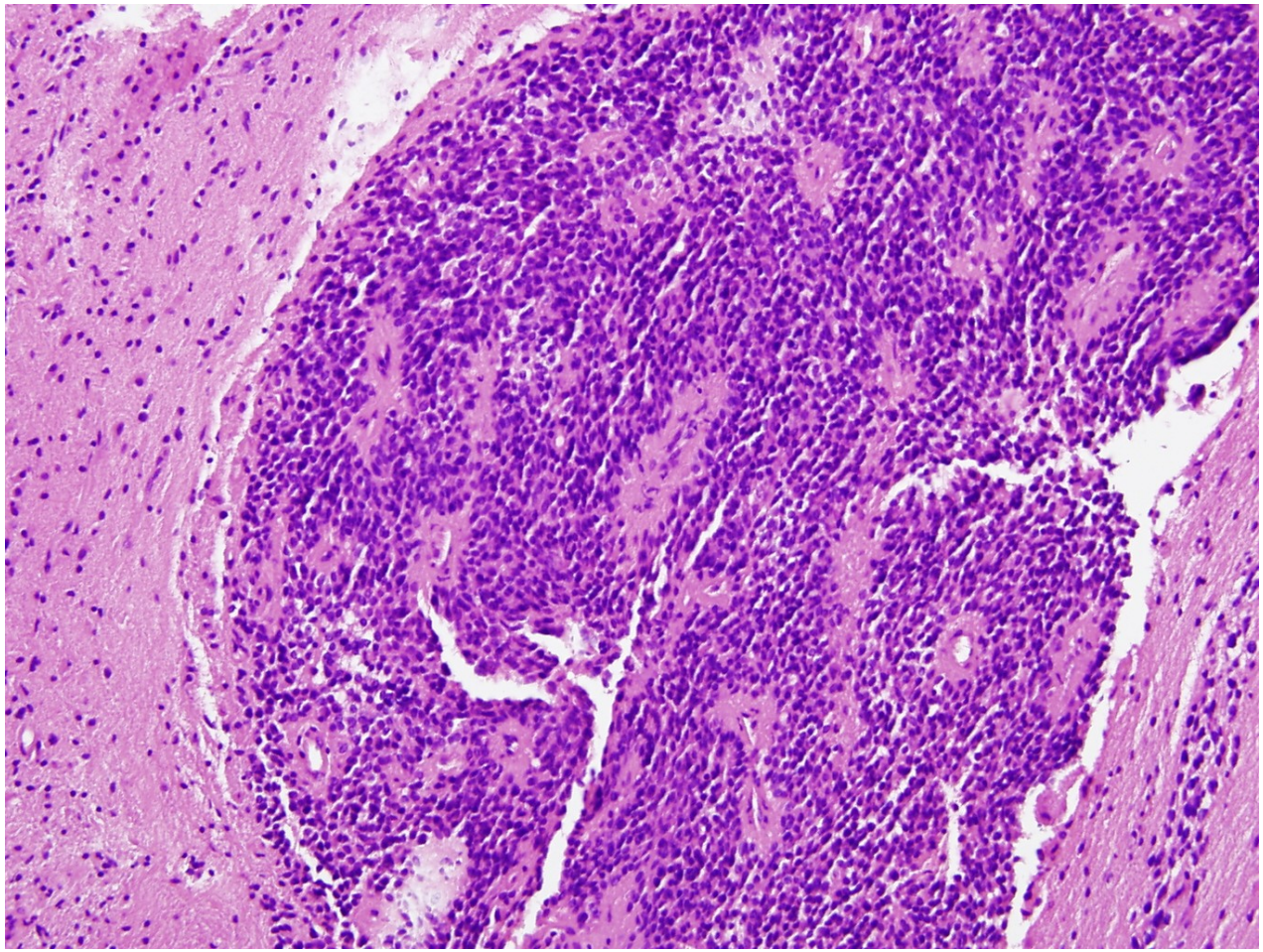
Ependymoma

- WHO - …“a generally slowly growing tumor of children and young adults, originating from the wall of the ventricles or from the spinal canal and composed of neoplastic ependymal cells“…

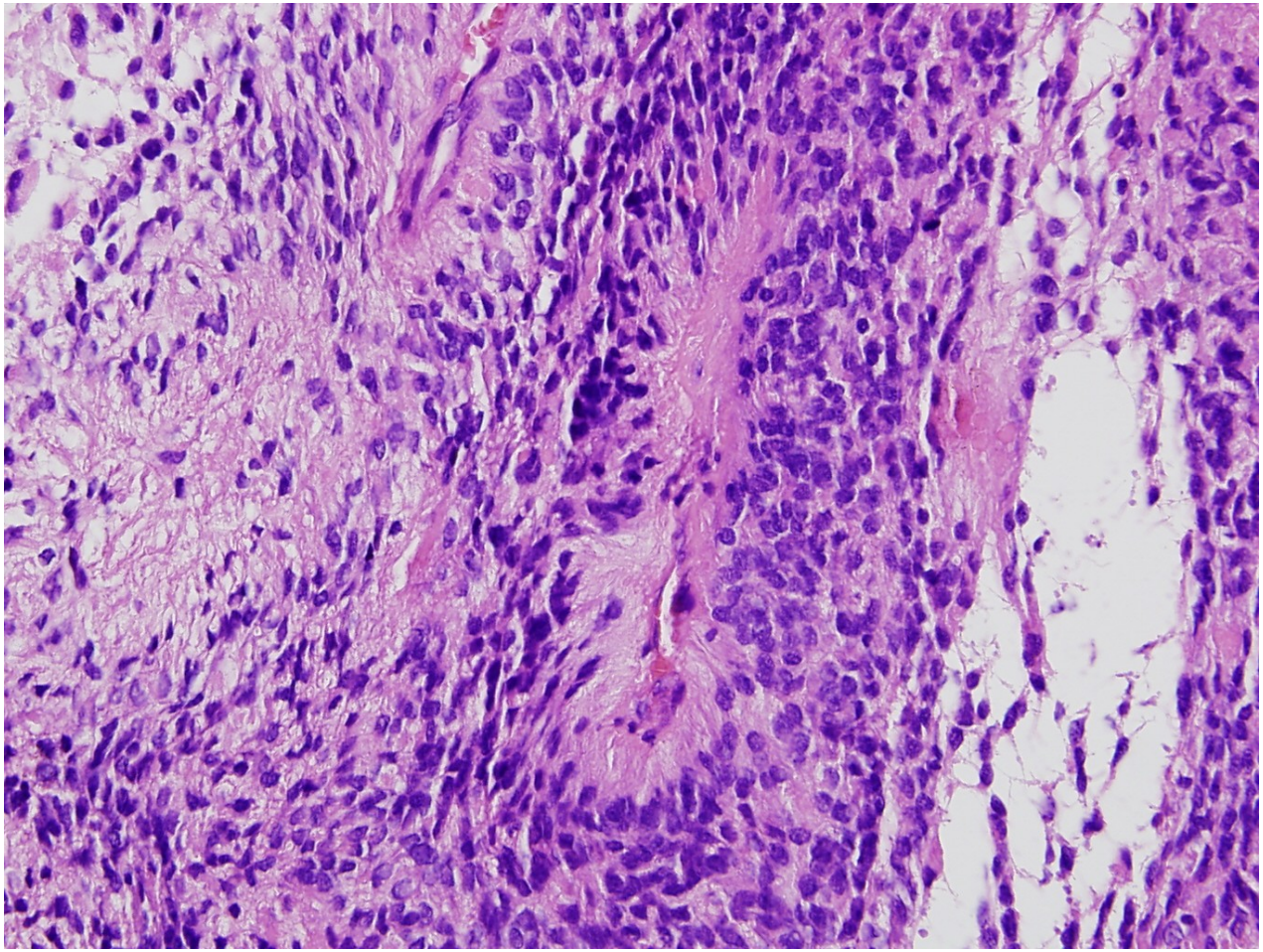
Ependymoma

- Ependymomas grow as relatively circumscribed masses, and so are amenable to surgical resection
- Their primary histologic hallmark is the perivascular pseudorosette, a perivascular cuff of radiating tumor cell cytoplasmic processes

Ependymoma



Ependymoma



Anaplastic ependymoma

- WHO - …“a malignant glioma of ependymal differentiation with accelerated growth and unfavourable clinical outcome, particularly in children; histologically characterized by high mitotic activity, often accompanied by microvascular proliferation and pseudopalisading necrosis“…

Embryonal tumors: medulloblastoma

- WHO - …“a malignant, invasive embryonal tumour of the cerebellum with preferential manifestation in children, predominantly neuronal differentiation, and an inherent tendency to metastasize via CSF pathways“…

  “drop metastases“
- Grade IV

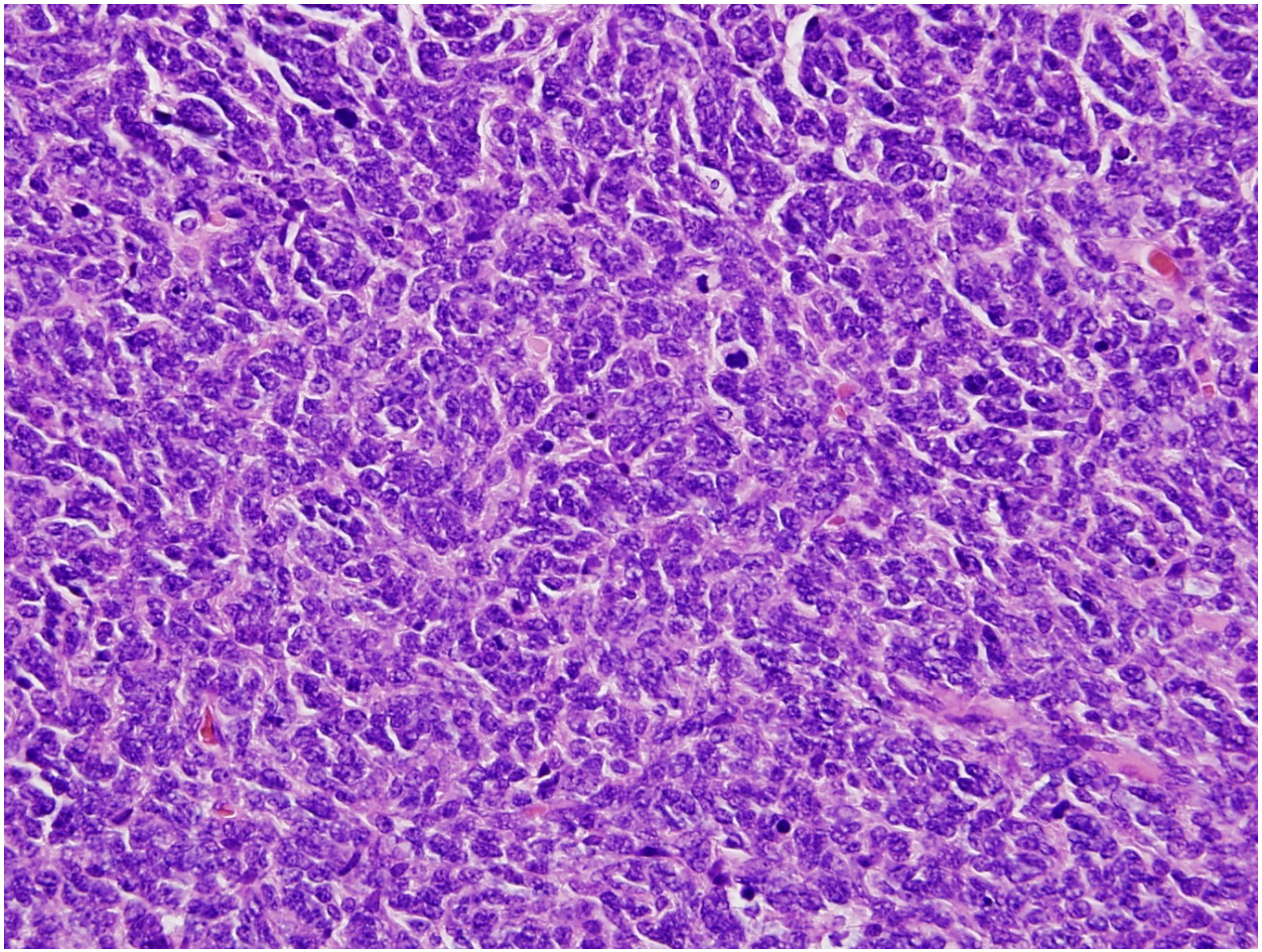
Medulloblastoma

- Peak incidence is at 7 years, but it can also affect adults in the 20- to 45-year old age group
- Childhood medulloblastomas commonly arise in the midline vermis, often expanding to fill the fourth ventricle
- Adult tumors prefer the cerebellar hemispheres

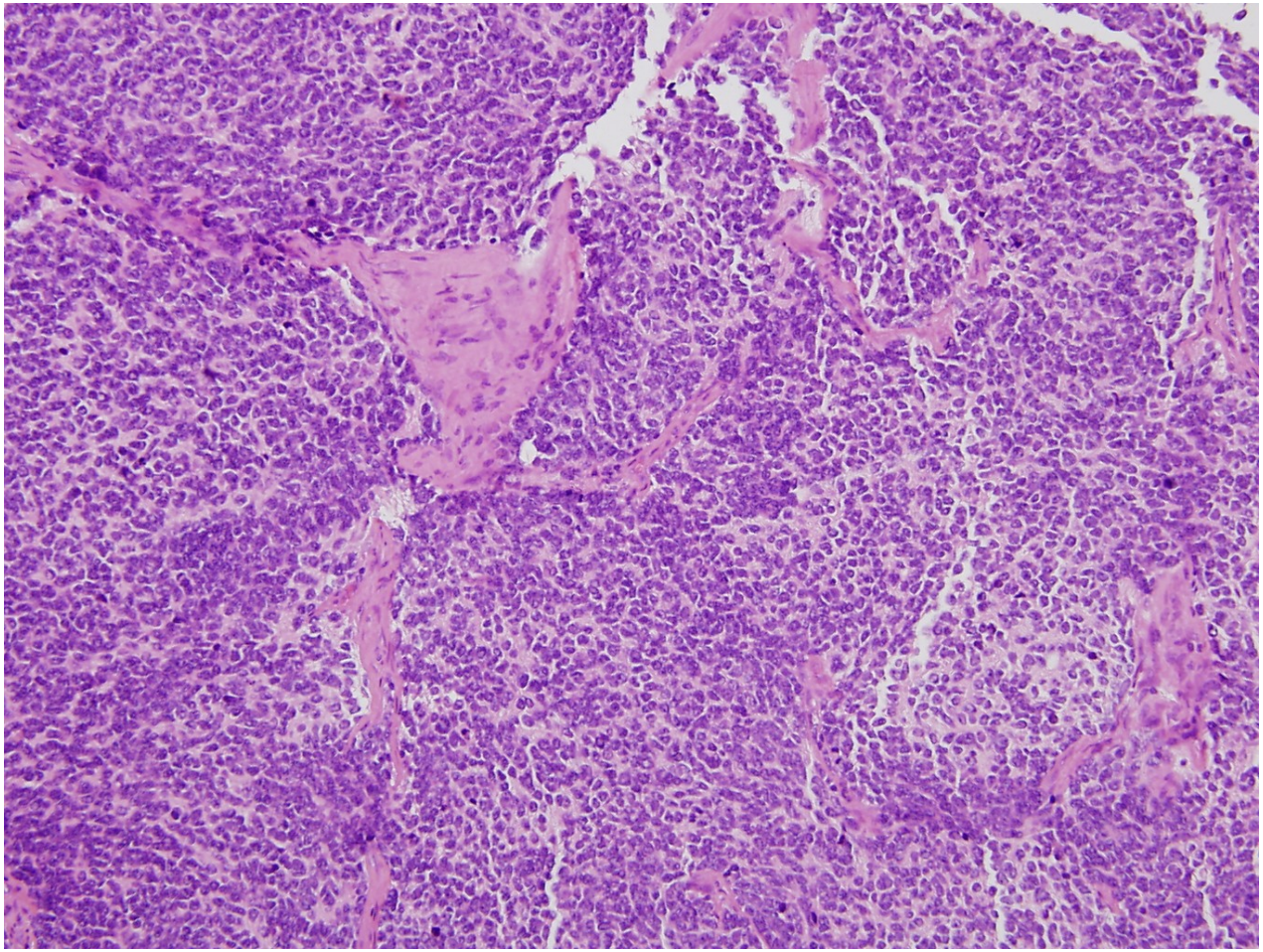
Medulloblastoma

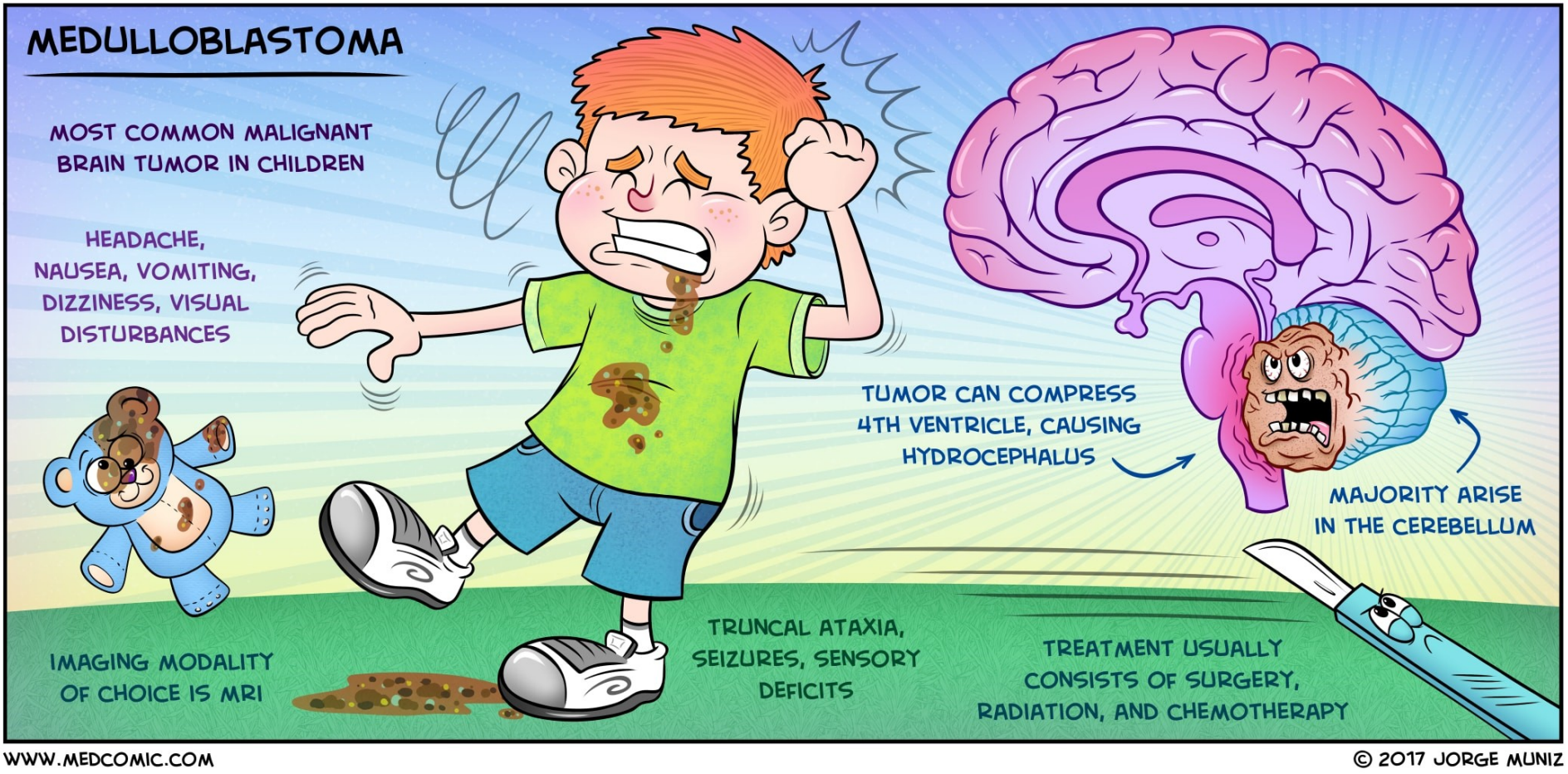
- About one third of patients have leptomeningeal spread at the time of presentation, which is a negative prognostic factor: “drop metastasis“
- Medulloblastoma is thought to arise from stem cells of the fetal external granular layer and/or the periventricular germinal matrix

Medulloblastoma



Medulloblastoma





- Other than medulloblastoma, which tu is the most likely to be in posterior fossa in a kid?
- Is medulloblastoma and neuroblastoma the same tumor?
- Which “blastomas“ are benign?

Tumors of PNS

- Primary PNS tumors are of neuronal or nerve sheath origin
- The most common nerve sheath tumors are schwannoma and neurofibroma
- Neuronal tumors usually arise from the adrenal medulla or sympathetic ganglia (neuroblastoma and ganglioneuroma)

Schwannoma

- Schwannomas are benign, slowly growing, typically encapsulated neoplasms of Schwann cells that originate in cranial nerves, spinal roots or peripheral nerves
- These tumors usually are seen in adults and only very rarely undergo malignant transformation

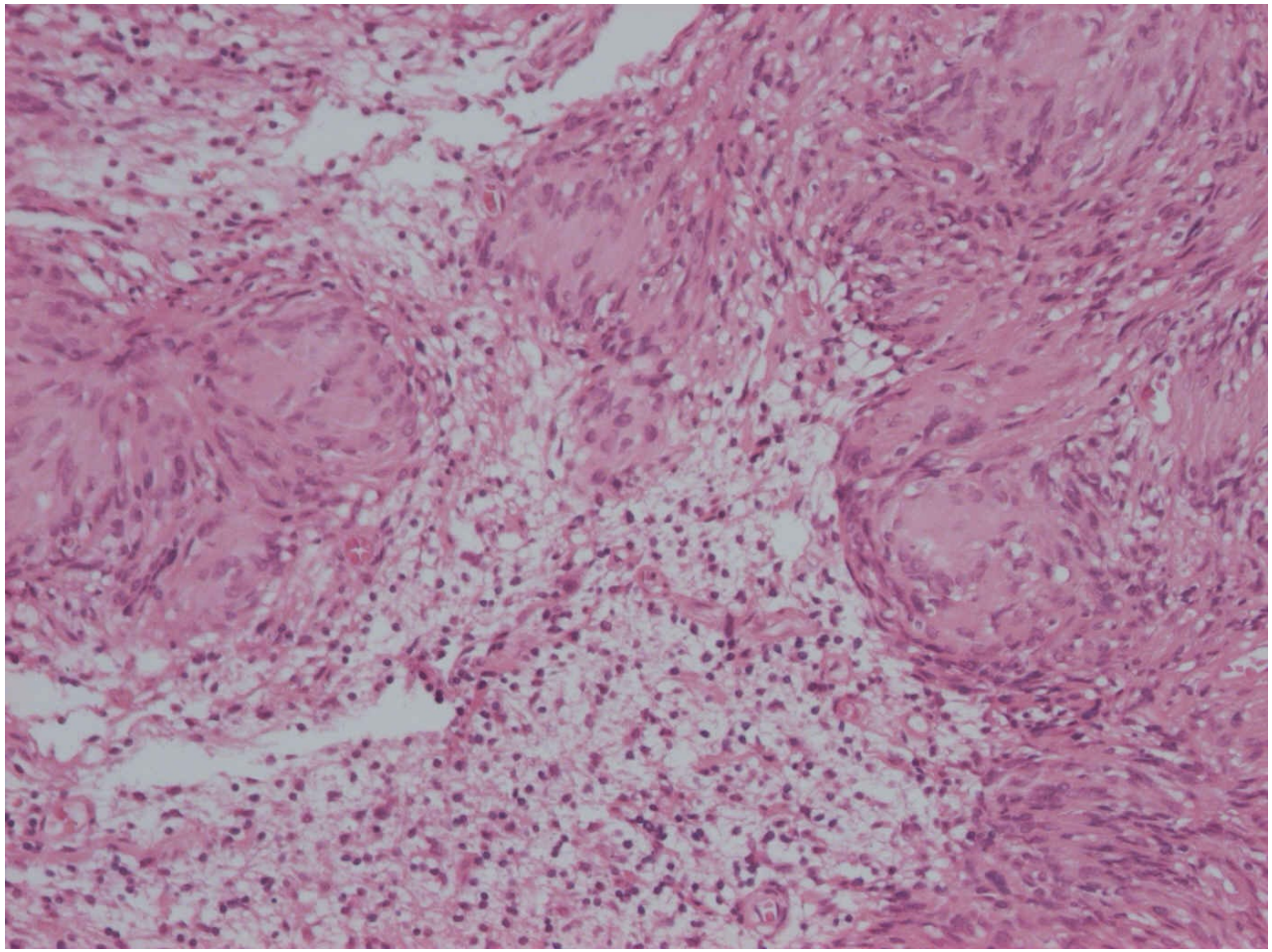
Schwannoma

- Vestibular (acoustic) schwannoma
  - Intracranial schwannomas account for 8% of all primary intracranial tumors
  - Most arise from the vestibular branch of the eighth cranial nerve within the internal auditory canal
  - Most vestibular schwannomas are unilateral and are not associated with NF
  - Bilateral vestibular schwannomas are a defining feature of NF2
- Spinal and peripheral schwannoma
  - Spinal schwannomas are intradural, extramedullary tumors that arise most often from the dorsal (sensory) spinal roots
  - More peripherally located schwannomas usually arise on nerves of the head, neck and extremities

Schwannoma

- The proliferating Schwann cells form two distinctive histologic patterns
  - Antoni A pattern – interwoven fascicles of spindle cells with elongated nuclei, eosinophilic cytoplasm and indistinct cytoplasmic borders. Nuclei may palisade in areas to form structures known as **Verocay bodies**
  - Antoni B pattern – spindle or oval cells with indistinct cytoplasm in a loose, vacuolated background

Schwannoma



Neurofibroma

- Neurofibromas are benign, slowly growing tumors of peripheral nerve, composed of Schwann cells, perineurial-like cells and fibroblasts
- Schwann cells are the neoplastic cells in neurofibromas
- Can be associated with NF1 and have a potential for sarcomatous degeneration to malignant peripheral nerve sheath tumor

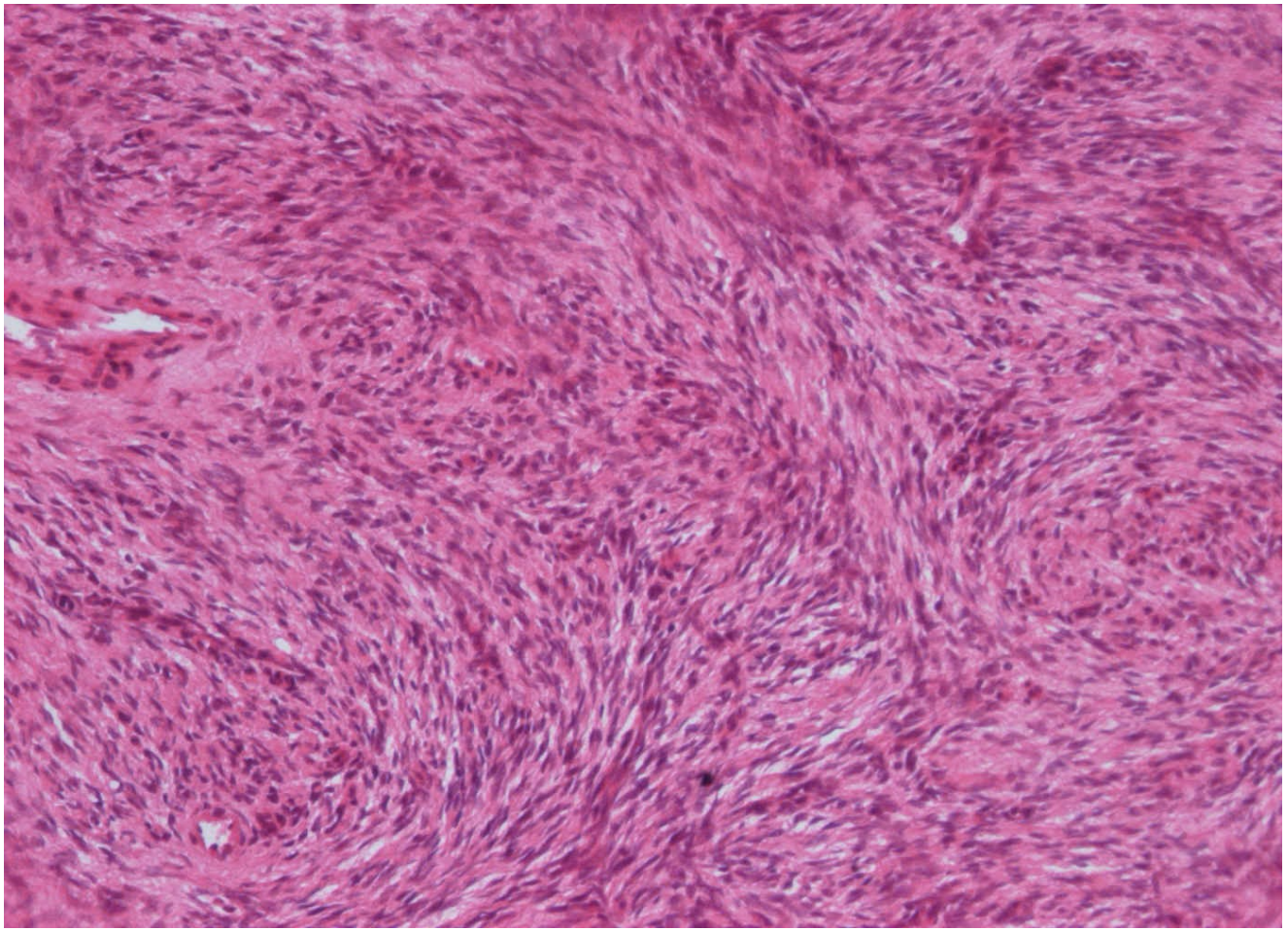
Neurofibroma

- Neurofibromas may be solitary or multiple and may arise on any nerve
- They occur in both children and adults
- Most commonly, they involve skin, subcutis, major nerve plexuses, large deep nerve trunks, retroperitoneum and gastrointestinal tract

Neurofibroma

- Most solitary cutaneous neurofibromas occur outside the context of NF1 and do not have the potential for sarcomatous transformation
- The presence of multiple neurofibromas or one large plexiform neurofibroma is strongly suggestive of NF1 and should prompt a careful search for other stigmata of the disease

Neurofibroma



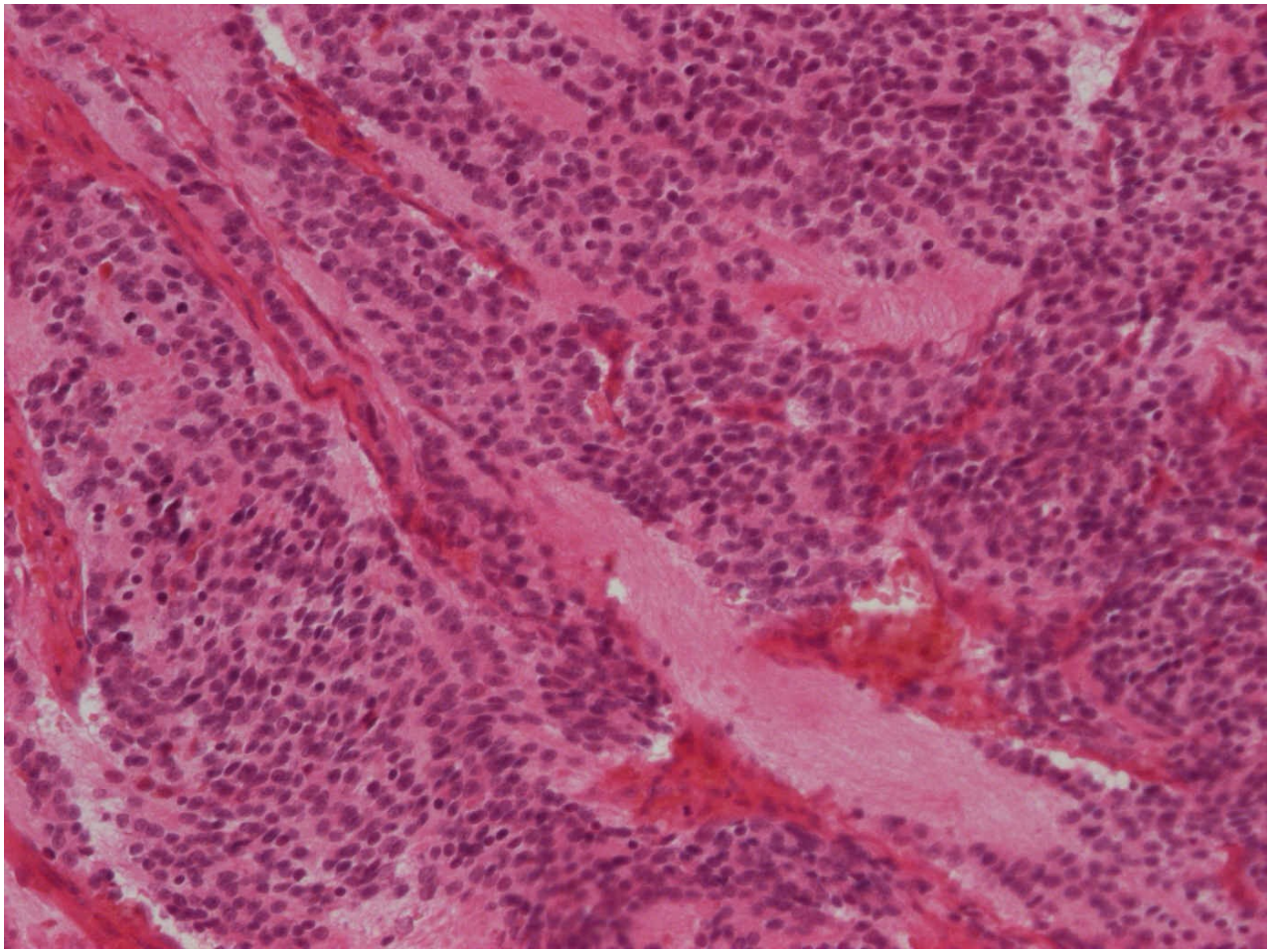
Neuroblastoma (not medulloblastoma!)

- Embryonal malignancy of neural crest origin composed of neoplastic neuroblasts
- Neuroblasts arise from primitive sympathogonia and are intermediates in the development of sympathetic ganglion neurons
- Neuroblastomas are the most common solid extracranial neoplasms of childhood, accounting for up to 10% of all childhood cancers and 15% of cancer deaths in children
- Overall incidence is 1 in 7000, the peak incidence is in the first 3 years

Neuroblastoma

- One third of tumors are in the adrenal, another third elsewhere in the abdomen and 20% in the posterior mediastinum
- Neuroblastomas readily infiltrate surrounding structures and metastasize to regional lymph nodes, liver, lungs, bones and other sites
- Localized neuroblastomas are treated by surgery alone, disseminated tumors require chemotherapy and sometimes irradiation

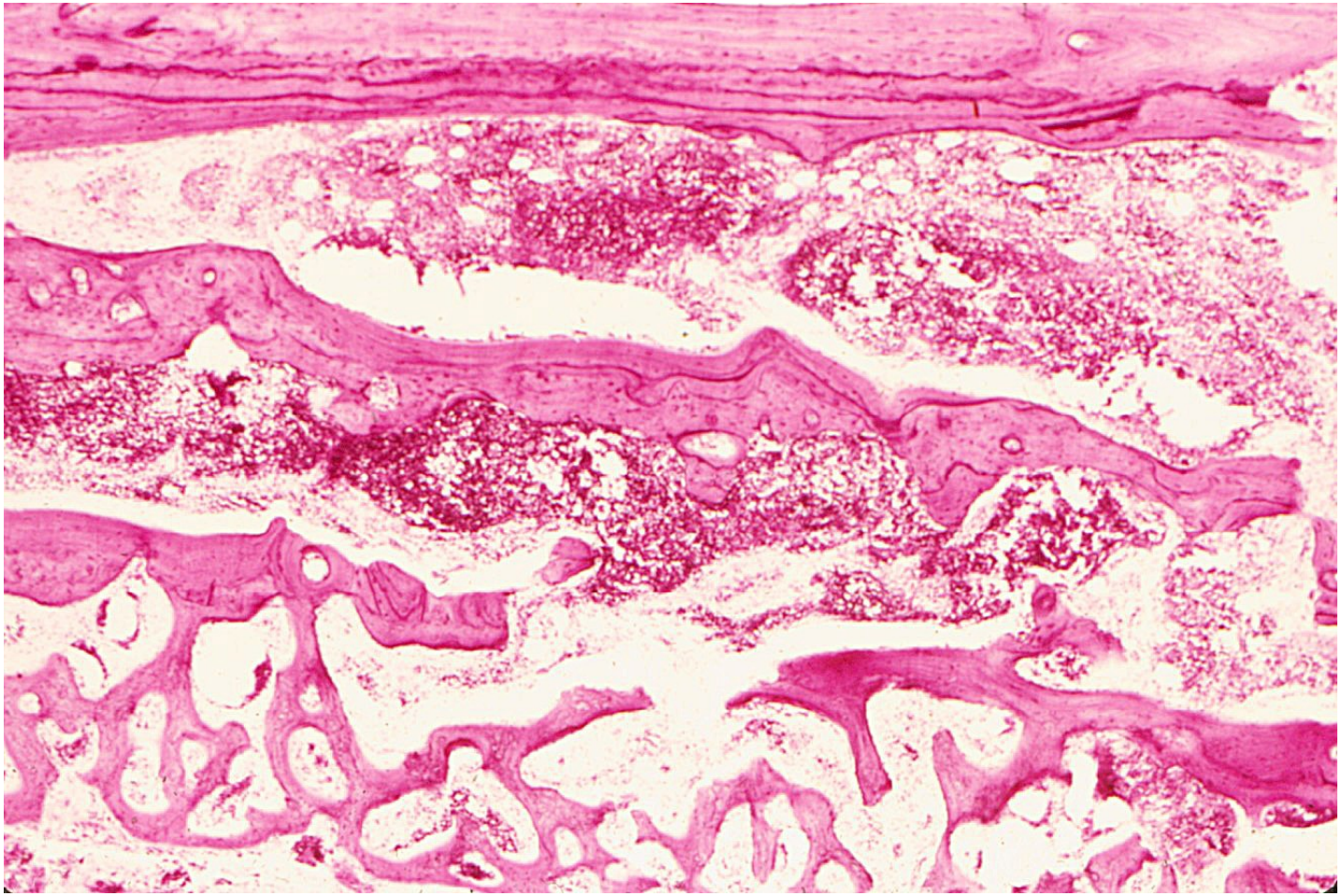
Neuroblastoma



Ewing sarcoma

- Primitive neuroectodermal tumor in childhood
- Uncommon malignant bone tumor composed of small, uniform, round cells
- Represents only 5% of all bone tumors and is found in children and adolescents, with two thirds of cases occurring in patients younger than 20 years
- Primarily a tumor of the long bones (humerus, tibia and femur)
- Prognosis used to be dismal, but with current use of chemotherapy plus radiation and/or surgery, 5-year disease-free survival is between 60% and 75%

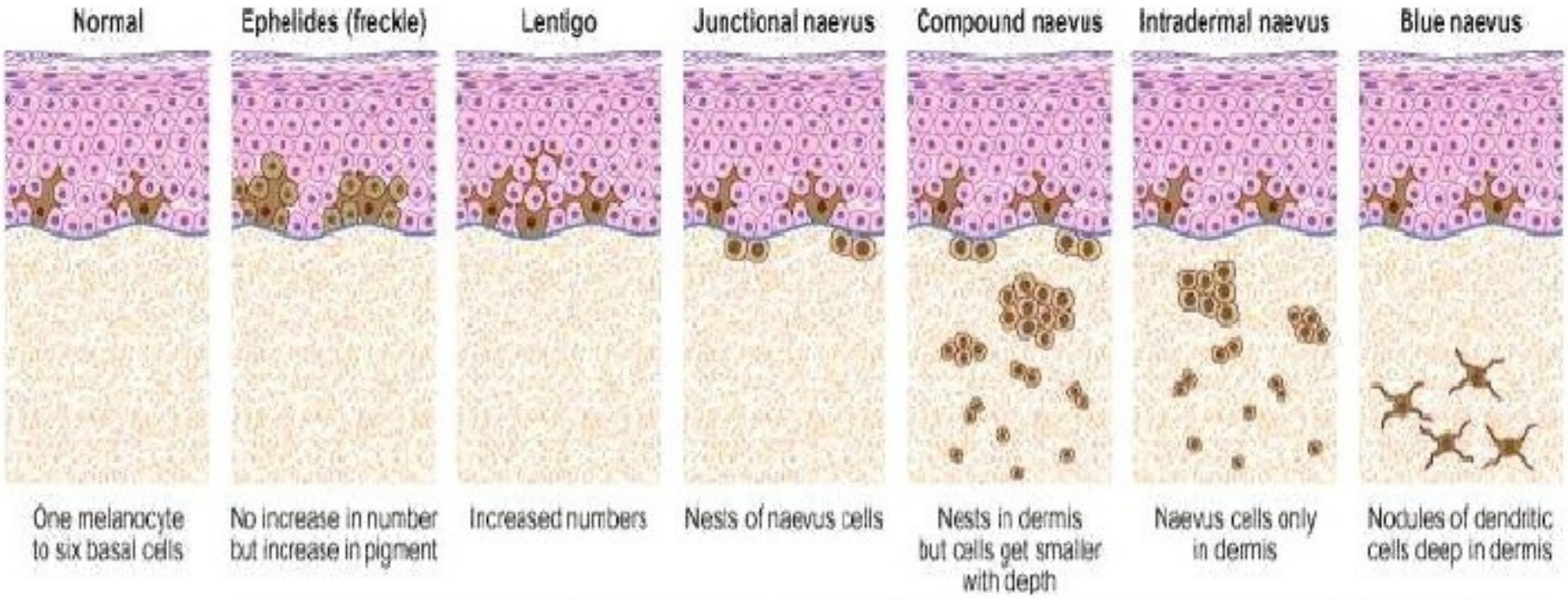
Ewing sarcoma

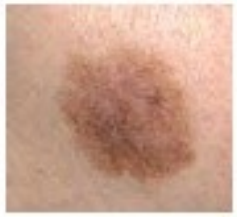


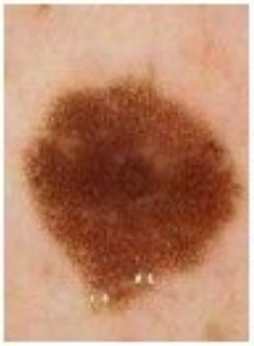
Pigmented skin lesions

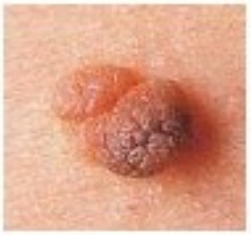
- Ephelides (freckles)
- Lentigo simplex
- Acquired melanocytic nevus (mole)
- Dysplastic nevus
- (Malignant) melanoma

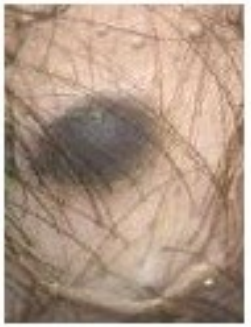
Nevi types & Pathology:











Acquired melanocytic nevus

- Localized benign neoplastic proliferations of melanocytes within the epidermis and/or dermis
- Most people, regardless of skin color, develop 10 to 50 nevi on their skin
- Except for occasional cosmetic significance, nevi are important mainly in relation to melanoma, as markers of individuals at increased risk of developing melanoma and as potential precursors of melanoma

Acquired melanocytic nevus

- A majority of nevi have recently been found to have an activating mutation of the gene encoding the oncogene *BRAF,* which can lead to growth stimulation through the mitogen-activated protein kinase (MAPK) pathway
- After an initial period of growth, nevi are stable lesions that may regress

Acquired melanocytic nevus

Junctional nevus

- melanocytes form nests at the tips of epidermal rete ridges. They tend to lose their dendritic morphology and retain pigment in their cytoplasm

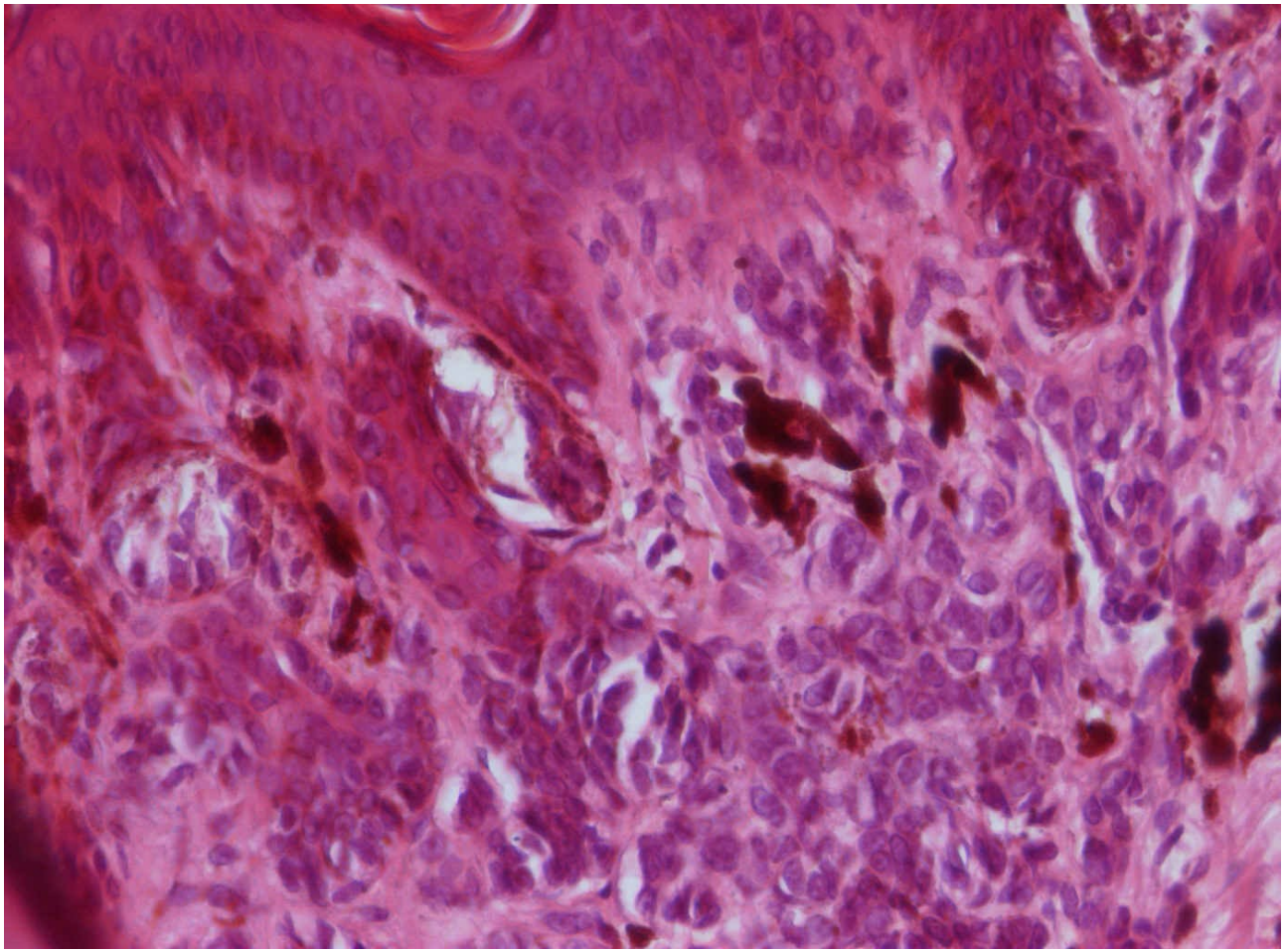
Compound nevus

- nests of melanocytes are seen in the epidermis and some of the cells have migrated into the dermis

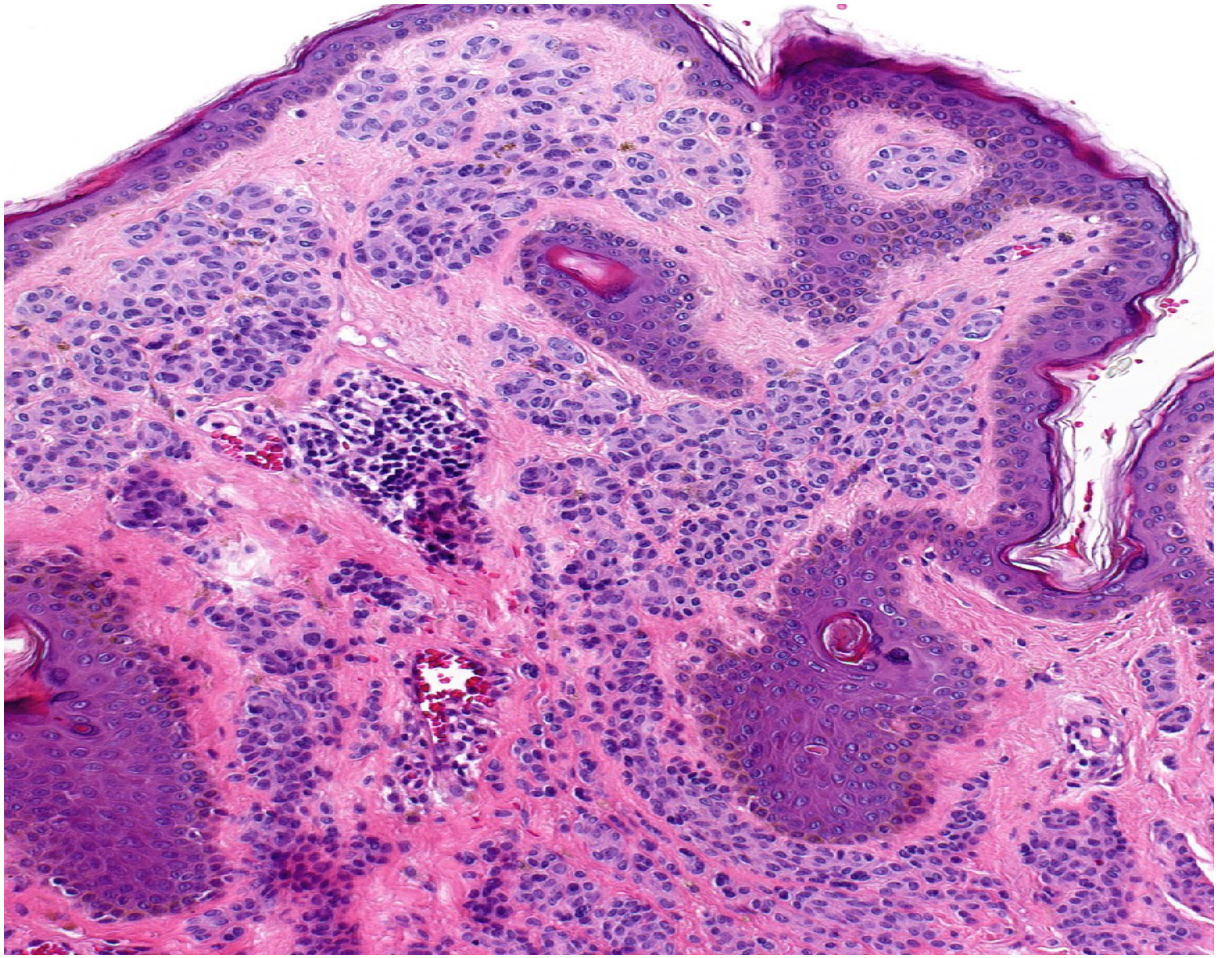
Dermal nevus

- intraepidermal melanocytic growth has ceased and melanocytes are present only in the dermis

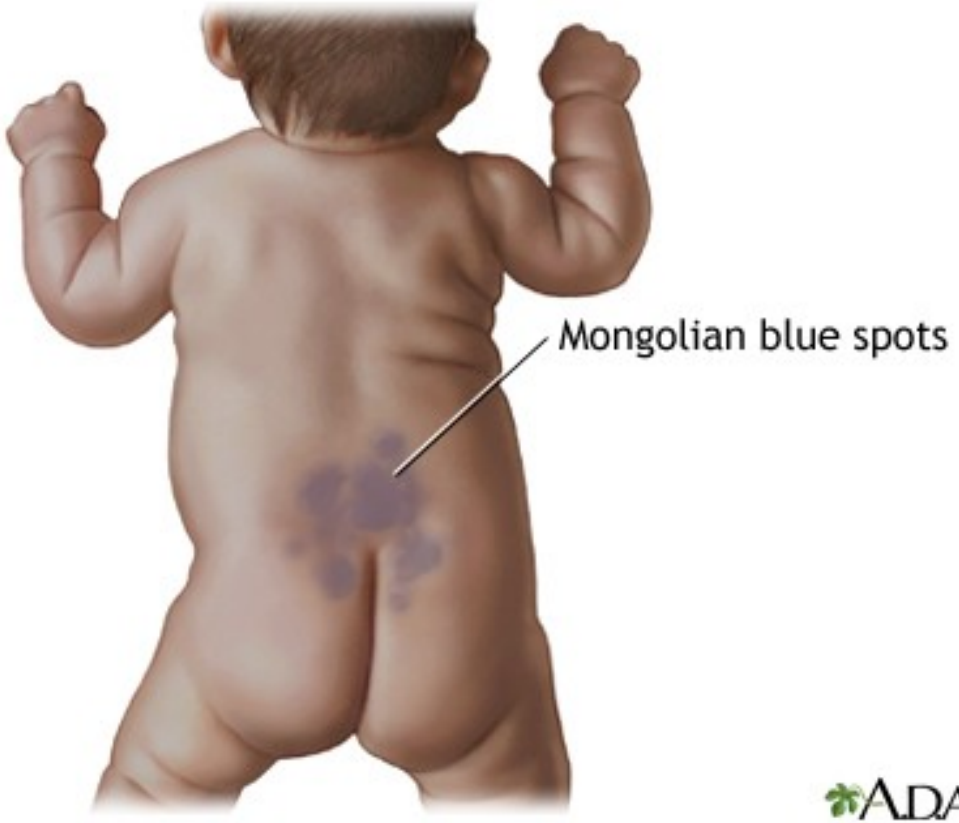
Compound melanocytic nevus



Intradermal melanocytic nevus



Blue nevus

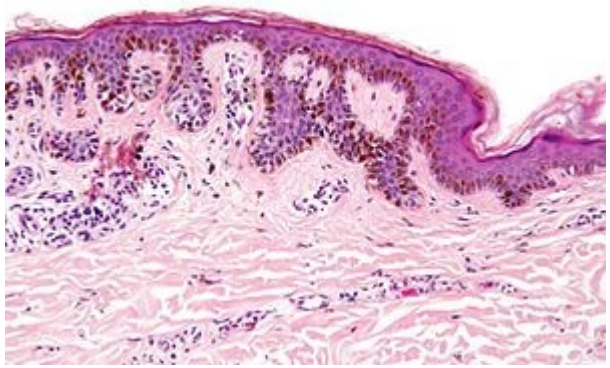


Dysplastic nevus

- Some common acquired nevi do not follow the differentiation described above, and are termed “dysplastic nevi”
- These nevi may show foci of aberrant melanocytic growth and become larger and somewhat irregular peripherally
- Patients with dysplastic nevi are at increased risk of developing melanoma

Dysplastic nevus

- Combination of architectural disorder and cytologic atypia constitutes a dysplastic nevus



Melanoma

- Malignant neoplasm of melanocytes
- The term "melanoma" in current practice is synonymous with previous "malignant melanoma"
- Although not one of the most common cancers overall, it is one of leading causes of cancer mortality in young adults

Malignant melanoma

- Melanomas may evolve through two major stages of progression

  Radial growth phase - the lesion spreads along the radii of an imperfect circle in the skin but remains superficial

  Vertical growth phase - focal area in which the lesion expands in a more or less spherical manner to form a tumor mass, with increasing thickness

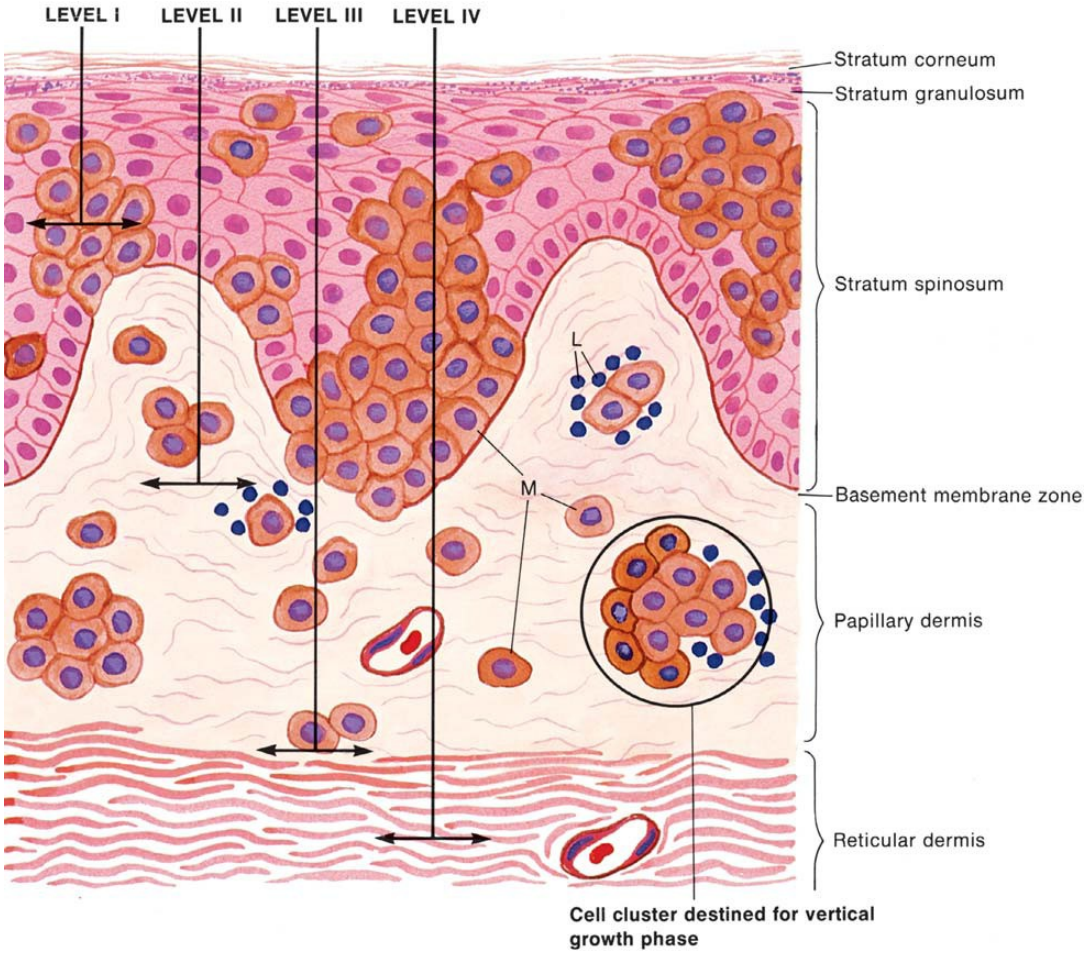
Malignant melanoma

- **Superficial spreading melanoma** (primarily radial growth)
- **Nodular melanoma** (primarily vertical growth)
- **Lentigo maligna melanoma** (melanoma in situ on sun damaged skin)
- **Acral lentiginous melanoma** (most common melanoma in dark skinned people)

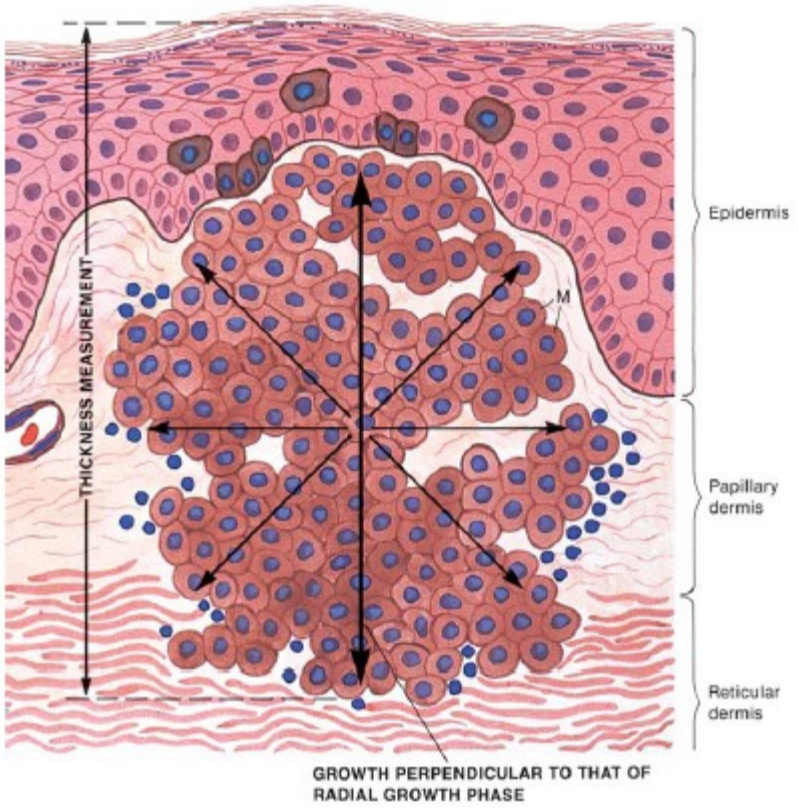
(Malignant) melanoma

- **Melanoma staging**
  - **Clark** level (anatomic)
  - **Breslow** thickness (mm)

Malignant melanoma



Malignant melanoma



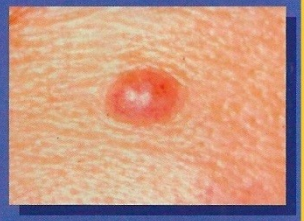
BENIGN

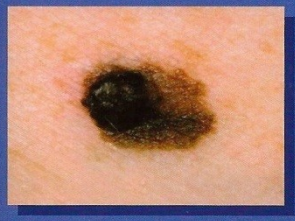
MALIGNANT

ASYMMETRY

This benign mole is not asymmetrical. If you draw a line through the middle, the two sides will match, meaning it is **symmetrical.**

A



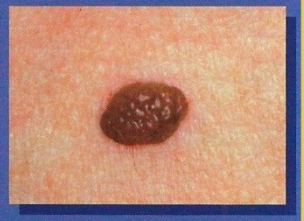


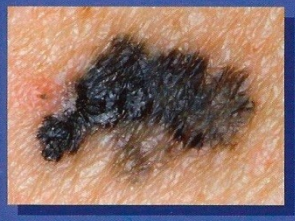
If you draw a line through this mole, the two halves will not match, meaning it is **asymmetrical,** a warning sign for melanoma.

BORDER

A benign mole has **smooth,** even **borders,** unlike the one on the opposite page.

B



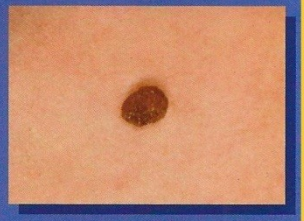


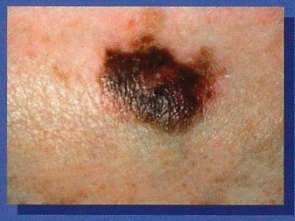
The **borders** of an early melanoma tend to be uneven. The edges may be scalloped or notched.

COLOR

Most benign moles are all **one color**—often a single shade of brown.

C



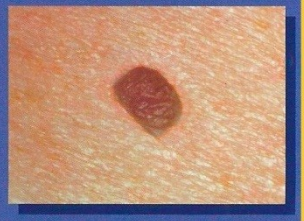


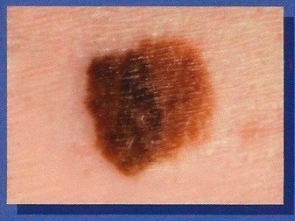
Having a variety of **colors** is another warning signal. A number of different shades of brown, tan or black could appear. A melanoma may also become red, white or blue.

DIAMETER

Benign moles usually have a **smaller diameter** than malignant ones.

D



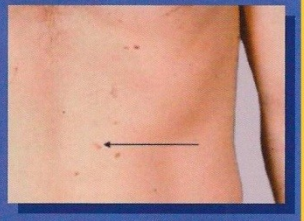


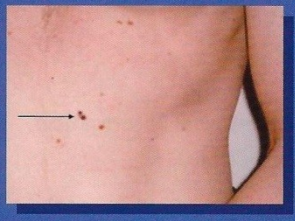
Melanomas usually are **larger in diameter** than the size of the eraser on your pencil (¼ inch or 6mm), but they may sometimes be smaller when first detected.

EVOLVING

Common, benign moles look the **same** over time. Be on the alert when a mole starts to **evolve** or change in any way.

E

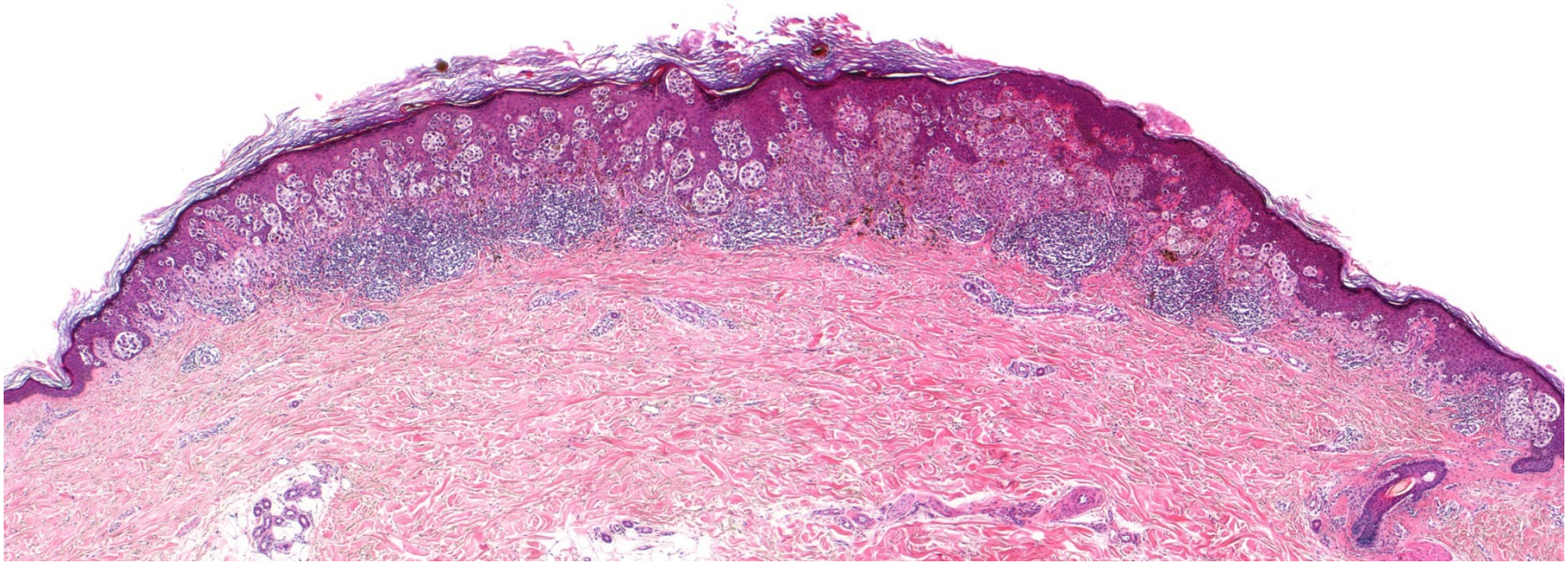




When a mole is **evolving,** see a doctor. Any change—in size, shape, color, elevation, or another trait, or any new symptom such as bleeding, itching or crusting—points to danger.

Source: www.SkinCancer.org

Malignant melanoma



Malignant melanoma