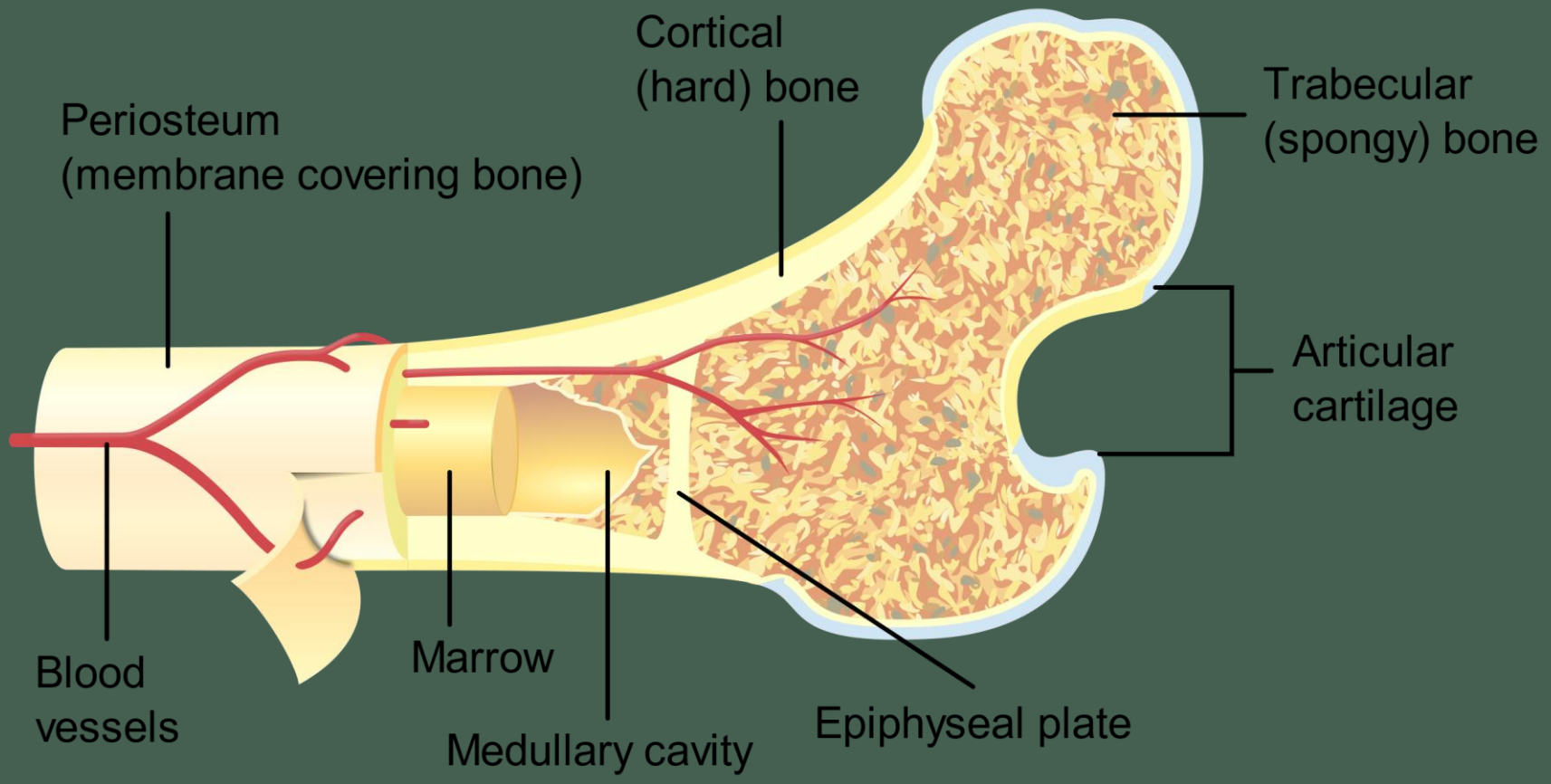
BONE, JOINTS and SKELETAL MUSCLE DISORDERS



BONE PATHOLOGY

BONE TUMORS

Primary bone tumors :

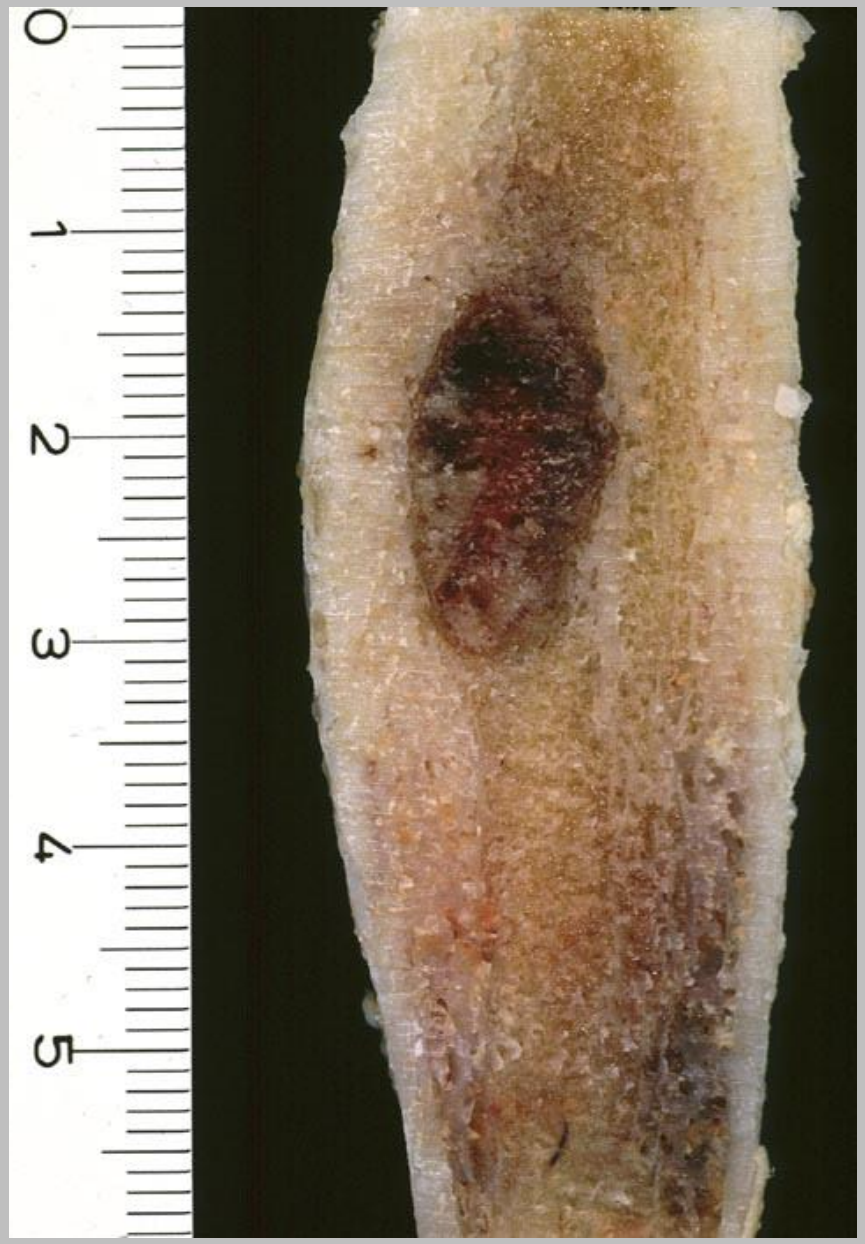
- bone-forming : osteoma, osteoblastoma, osteosarcoma
- cartilage-forming : chondroma, chondroblastoma, chondrosarcoma
- fibrous and fibro-osseous : non-ossifying fibroma, fibrosarcoma
- without normal tissue counterparts : giant cell tumor, Ewing's sarcoma

Metastatic bone tumors :

- most common form of skeletal malignancy
- 75% originate from cancers of breast, prostate, kidney and lung

Osteoma

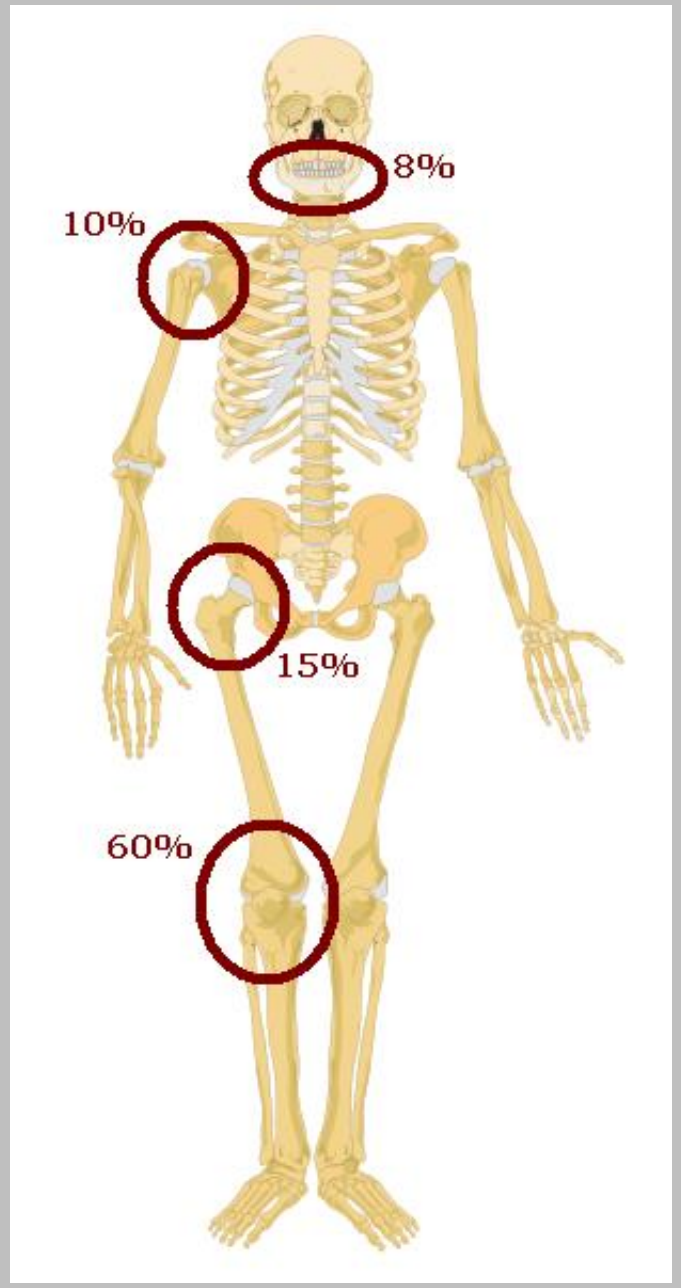
- slow-growing, usually solitary
- arising on or inside the skull and facial bones
- *gross examination* :
  - bosselated, sessile, round/oval
- *microscopy :*
  - woven and lamellar bone deposited in a cortical pattern
  - with Haversian-like systems



https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=004033

Osteosarcoma

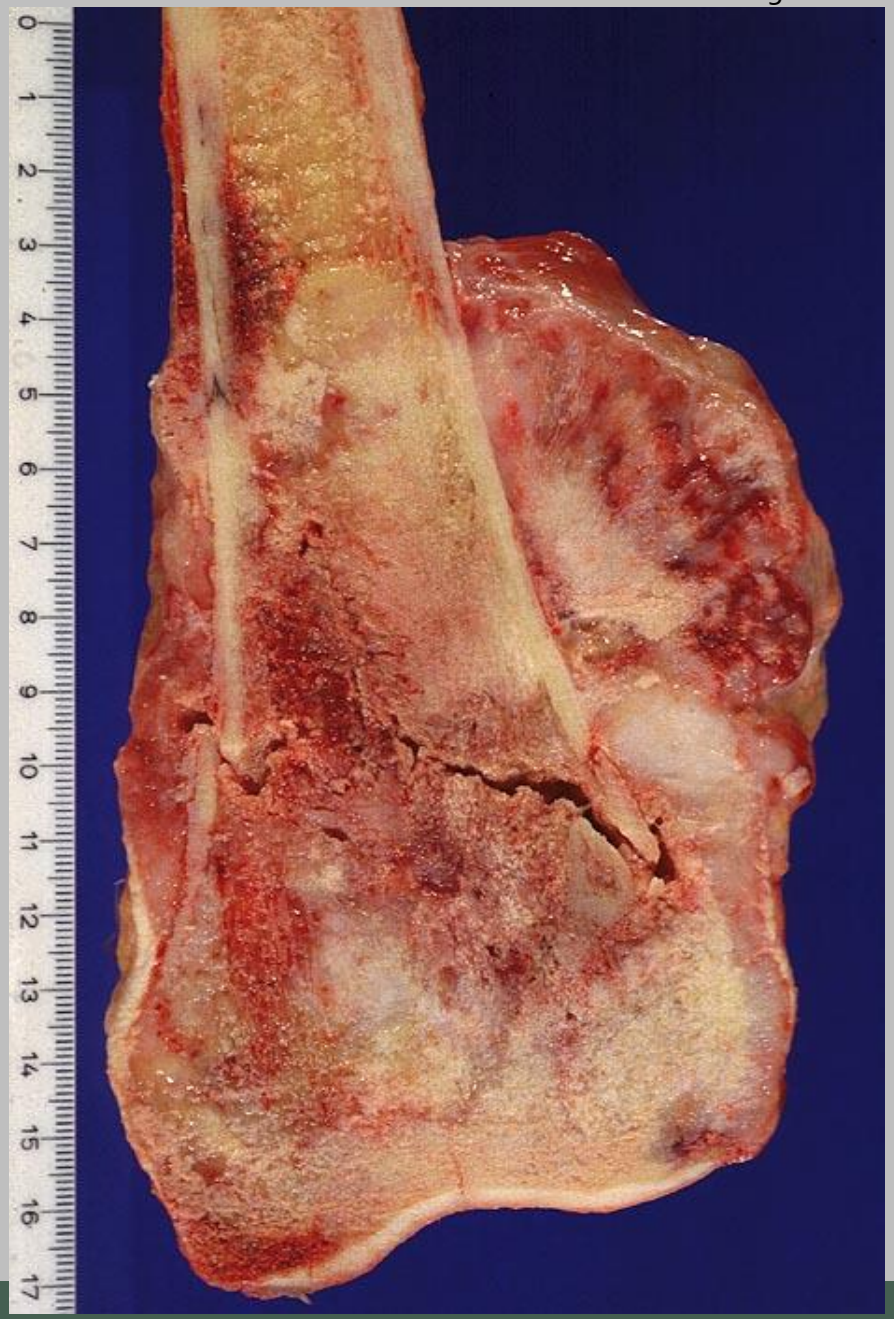
- malignant mesenchymal tumor
- most common primary malignant bone tumor
- frequent in adolescents
- often arise adjacent to :
  - *the knee* (lower femur, upper tibia or fibula
  - *the shoulder* (proximal humerus)
- hematogenous spread to the *lungs*
- long-term survival rate : 60%



Osteosarcoma

Grossly :

- bulky tumors
- hemorrhagic, cystic, soft and bony hard areas
    - destroy the overlying cortex
    - spread into the marrow cavity
    - elevating or perforating the periosteum



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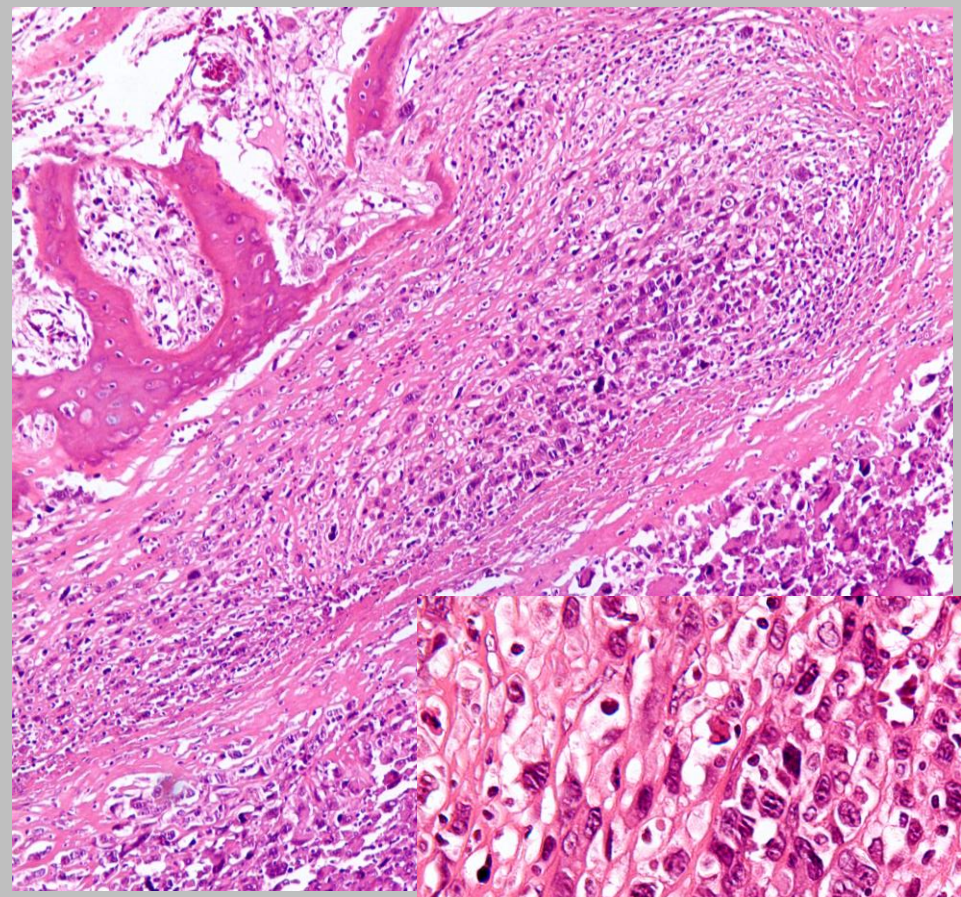
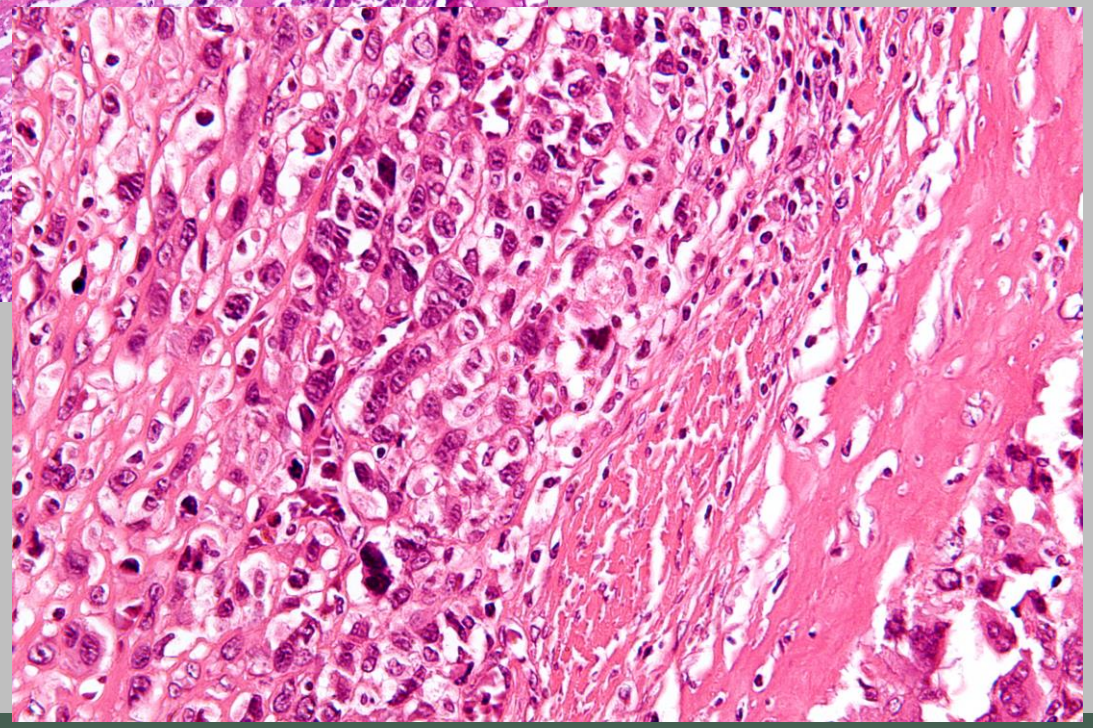
Osteosarcoma

Histologically :

- malignant osteoblasts
  - with varying size and shape
  - having a large, hyperchromatic nuclei
  - with atypical mitoses
- common giant cells
- woven bone, with a coarse, lace-like architecture / broad sheets



High-grade osteosarcoma

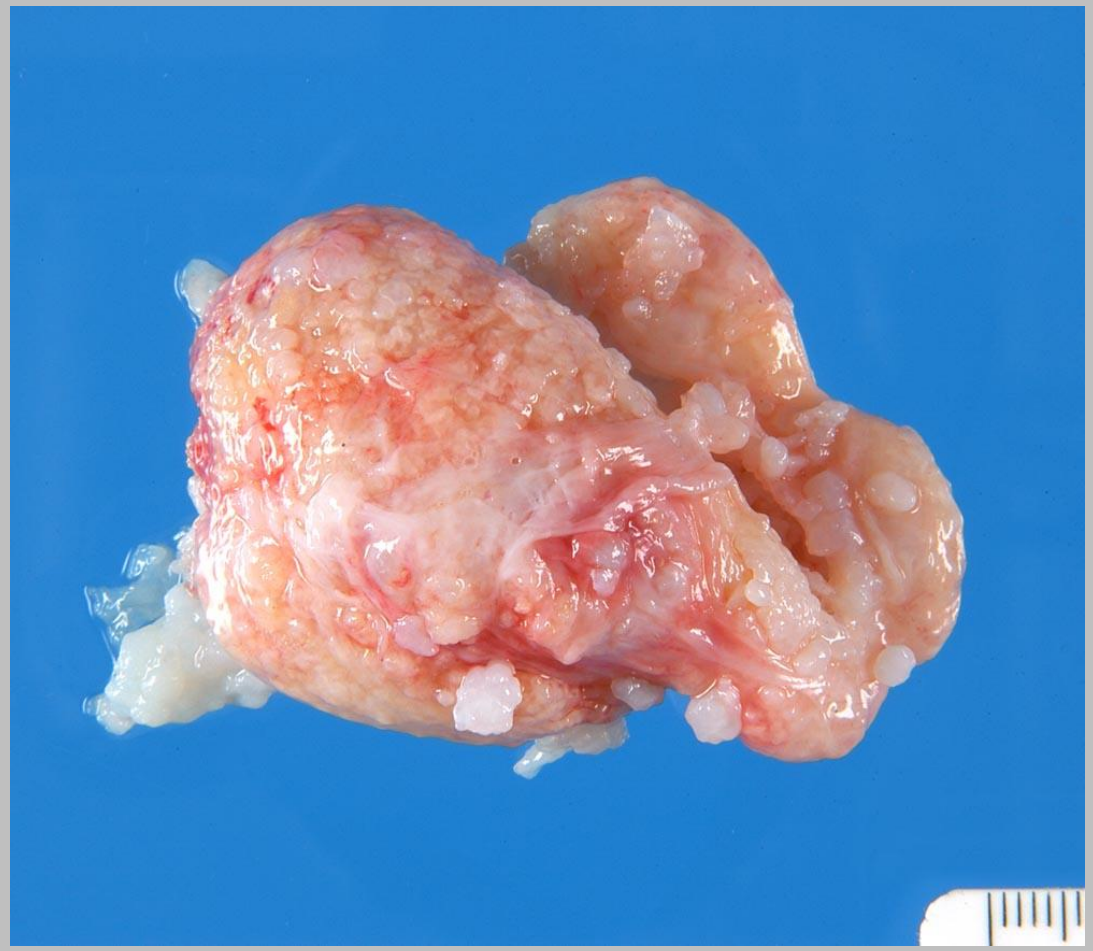


Chondroma

- benign tumors of hyaline cartilage
- usually solitary
- located in the metaphyseal region of tubular bones (hand and feet)
- types :
  - enchondromas (arising within the medullary cavity)
  - subperiosteal or juxtacortical chondromas (arising on the bone surface)

Gross :

- gray-blue, translucent
- *nodular* configuration
- smaller than 3 cm



Synovial chondromatosis

Chondroma

Microscopically :

- circumscribed nodules / lobules well differentiated cartilaginous tissue
- in between lobules, fibro-vascular septa
- the chondrocytes in small lacunae are irregular as number (3 – 6 cells) not only as pairs

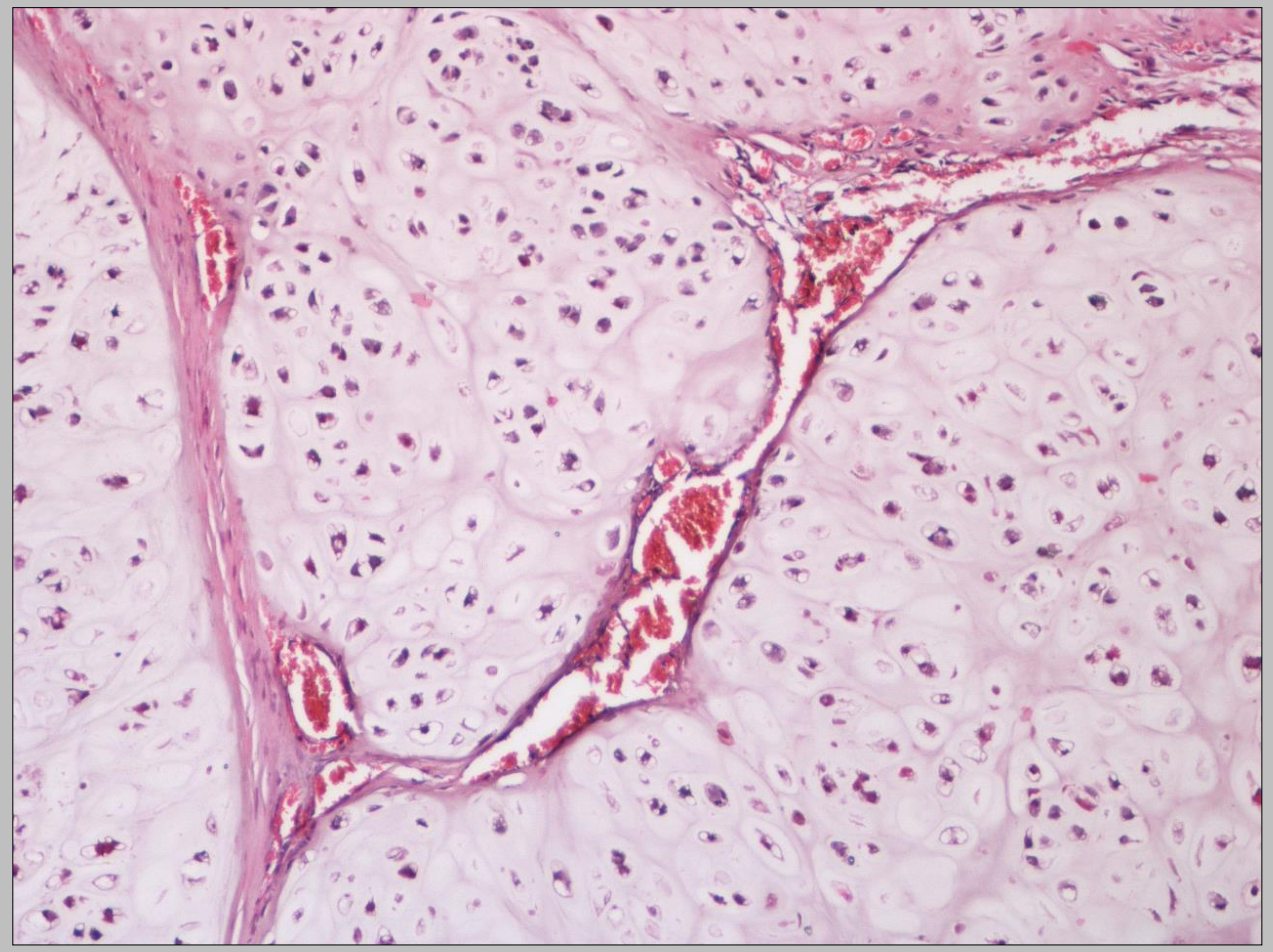


Image from UMF "Victor Babes" Timisoara Morphopathology's archive

Chondrosarcoma

- malignant tumor, originating from cartilage cells
- produces *neoplastic cartilage*
- arises in the central portions of the skeleton

Macroscopically :

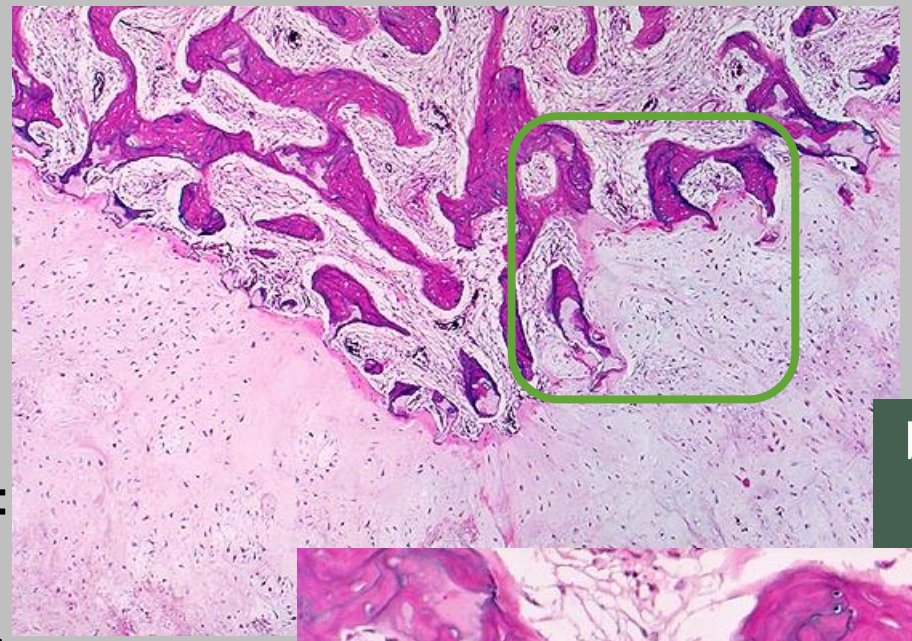
- nodules of gray-white, translucent, glistening tissue
- spotty calcifications
- areas of *necrosis*, *cystic change*, *hemorrhage*

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=009226

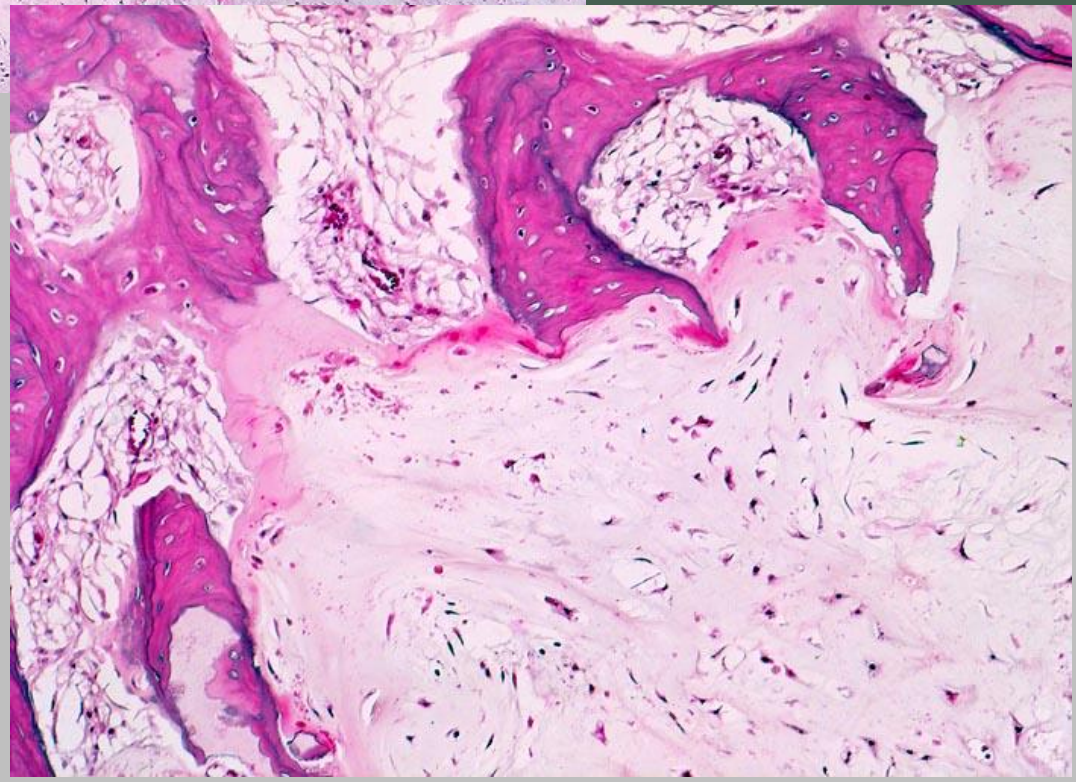
Chondrosarcoma

Microscopically :

- malignant cartilage cells in various stages of maturity
- varying degree of cellularity and atypia:
  - *low-grade:* mild hypercellularity, sparse binucleate cells, few mitoses
  - *high-grade:* marked hypercellularity, extreme pleomorphism, bizarre cells, high mitotic activity



bone destruction at the invasion front



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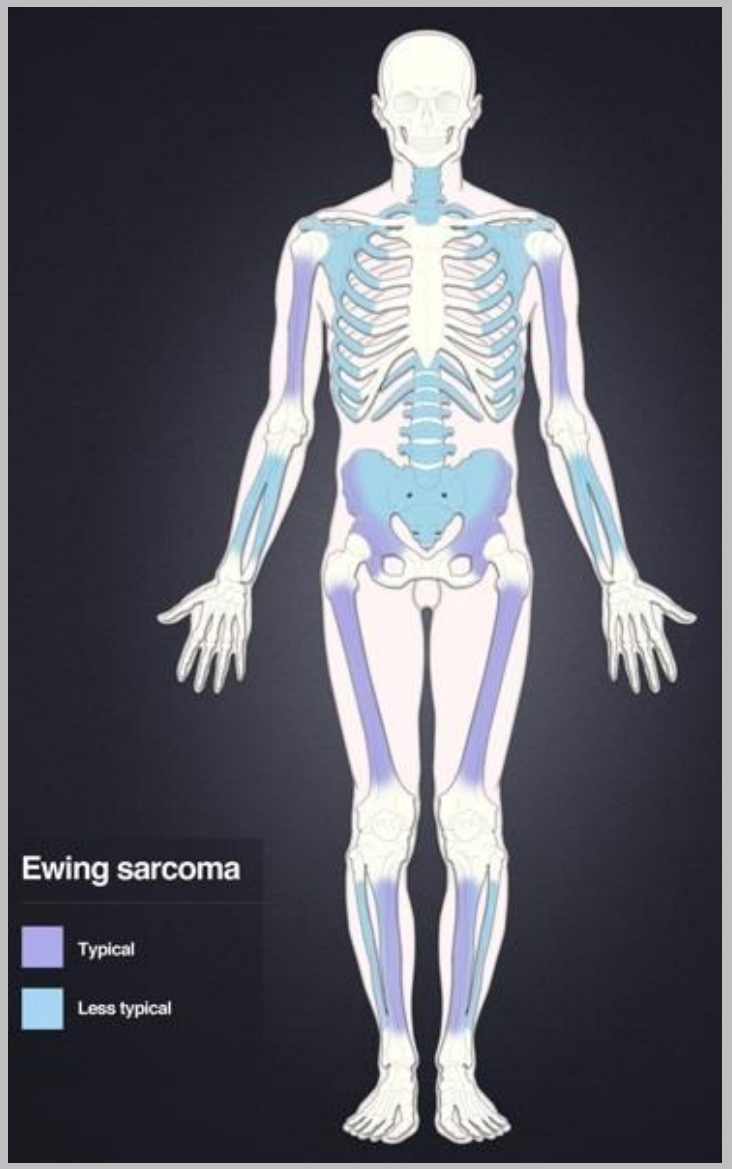
Ewing's sarcoma

- primary malignant small, round cell tumor of the bone
- the 2nd most common bone sarcoma in children
- arises in :
    - the diaphysis of long bones (especially femoral)
    - flat bones of the pelvis



Ewing's sarcoma

Gross :

- arises in the medullar cavity, invading the cortex and the periosteum
- White, fleshy, ill defined tumor with extensive involvement of medulla and cortex with periosteal elevation
- Specimens are usually excised after therapy, and show fibrosis, hemorrhage and necrosis
- soft tissue mass, white-tan

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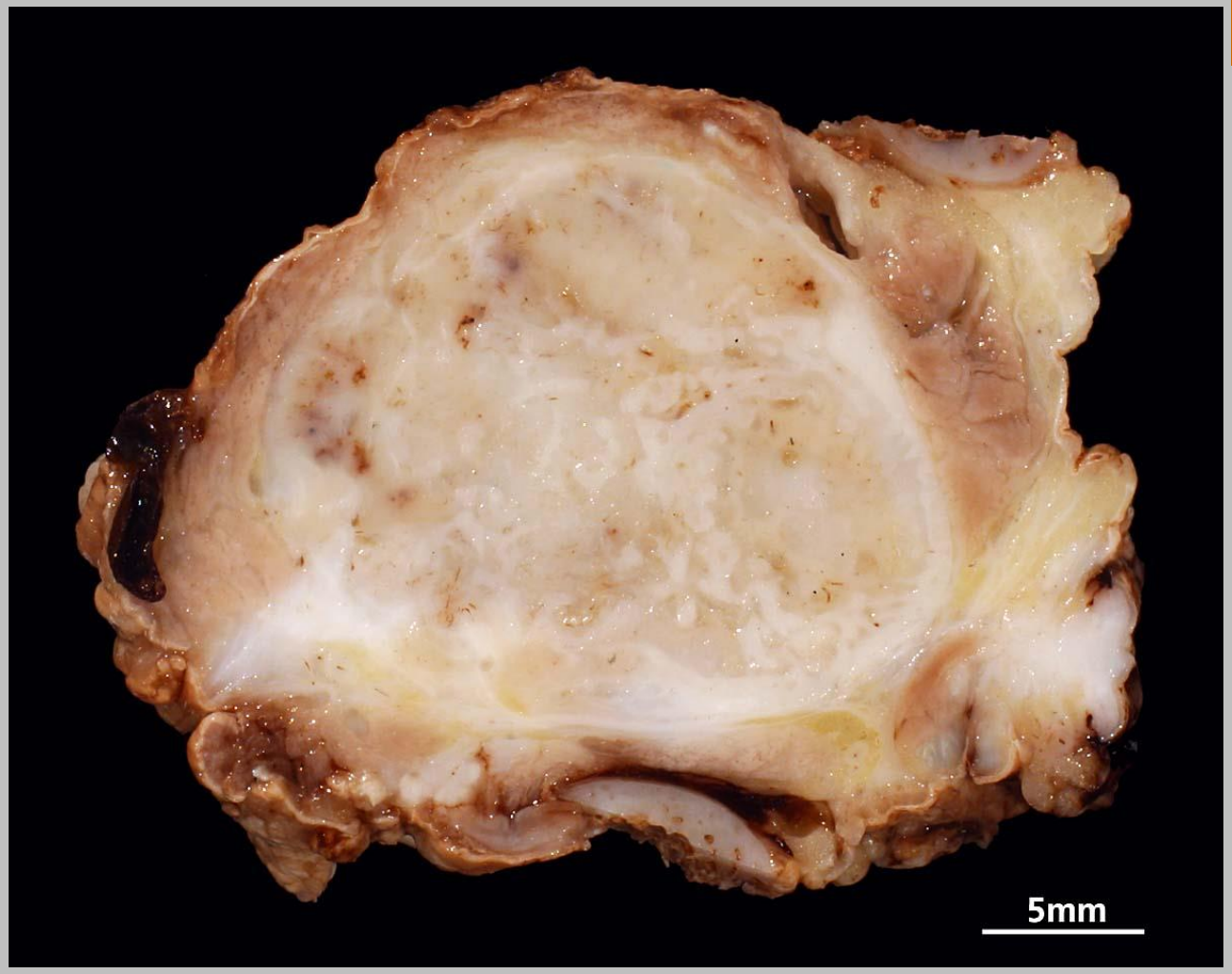
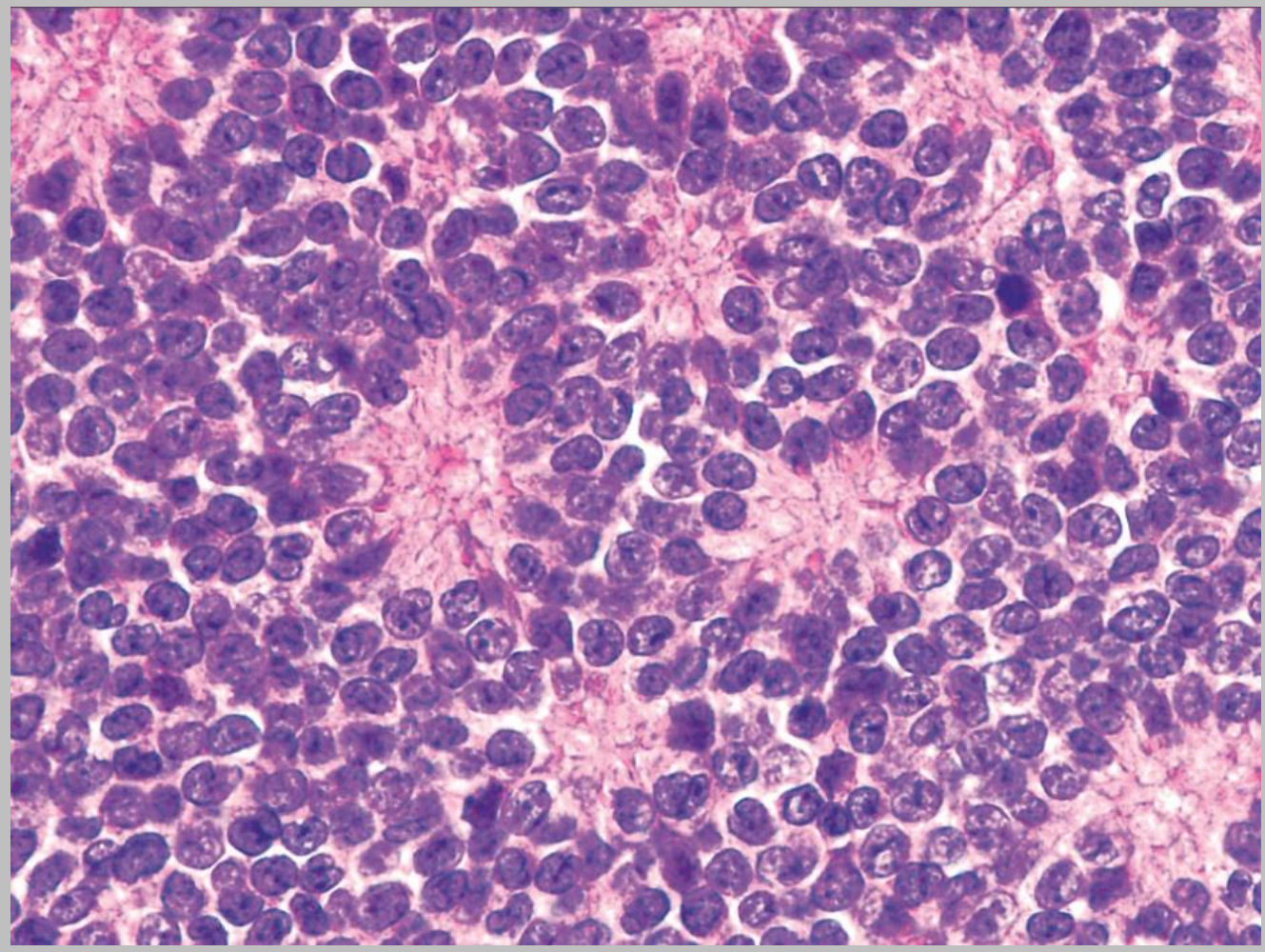
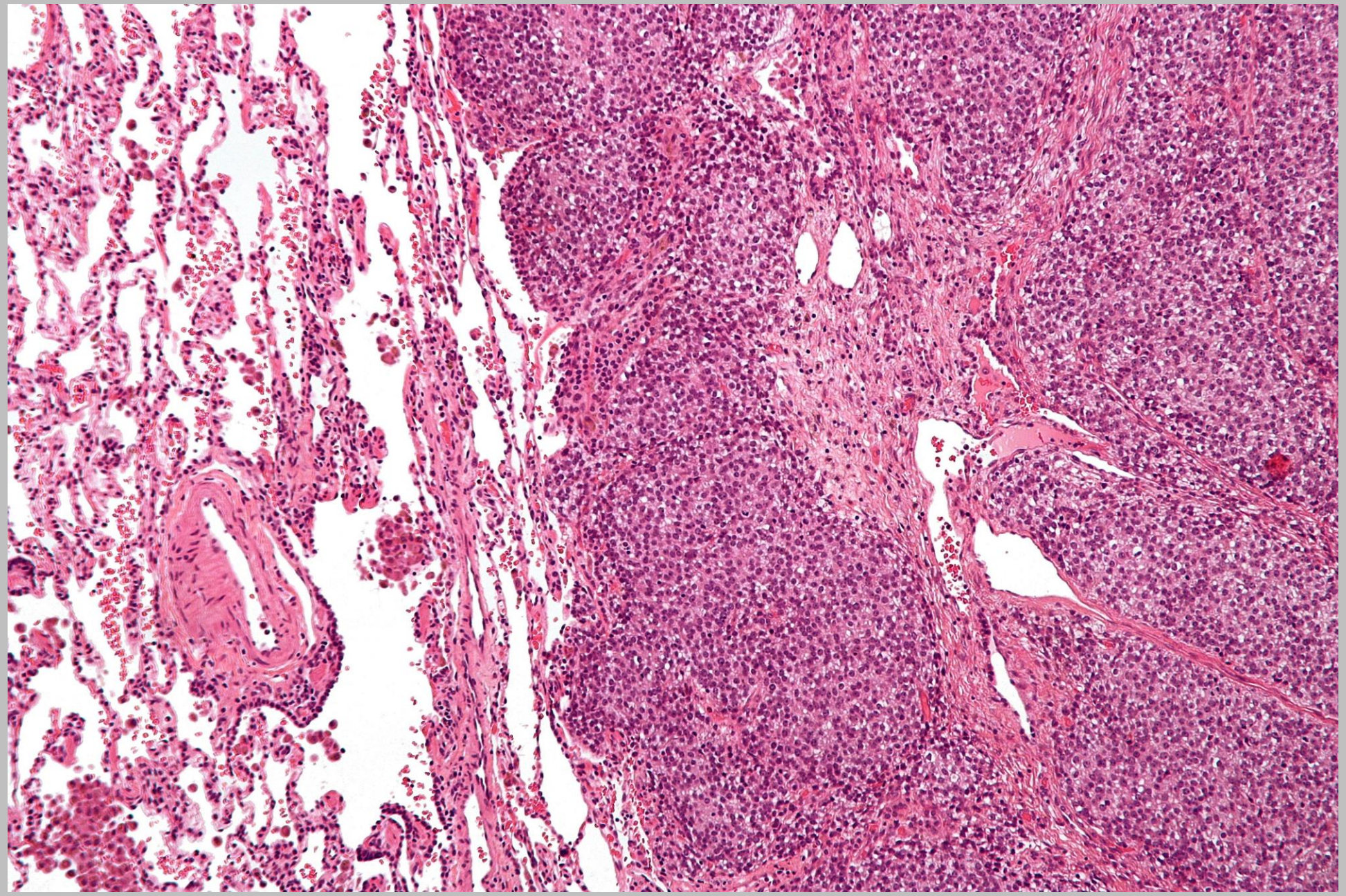


Microscopically :

- sheets of uniform, small, round cells, variably arrayed in rosettes, with neurofibrillary cores (Homer Wright) or central lumens (Flexner-Wintersteiner)
    - slightly larger than lymphocytes
    - scant cytoplasm, may appear clear because of glycogen content
    - with few mitotic figures
- little stroma; fibrous septa



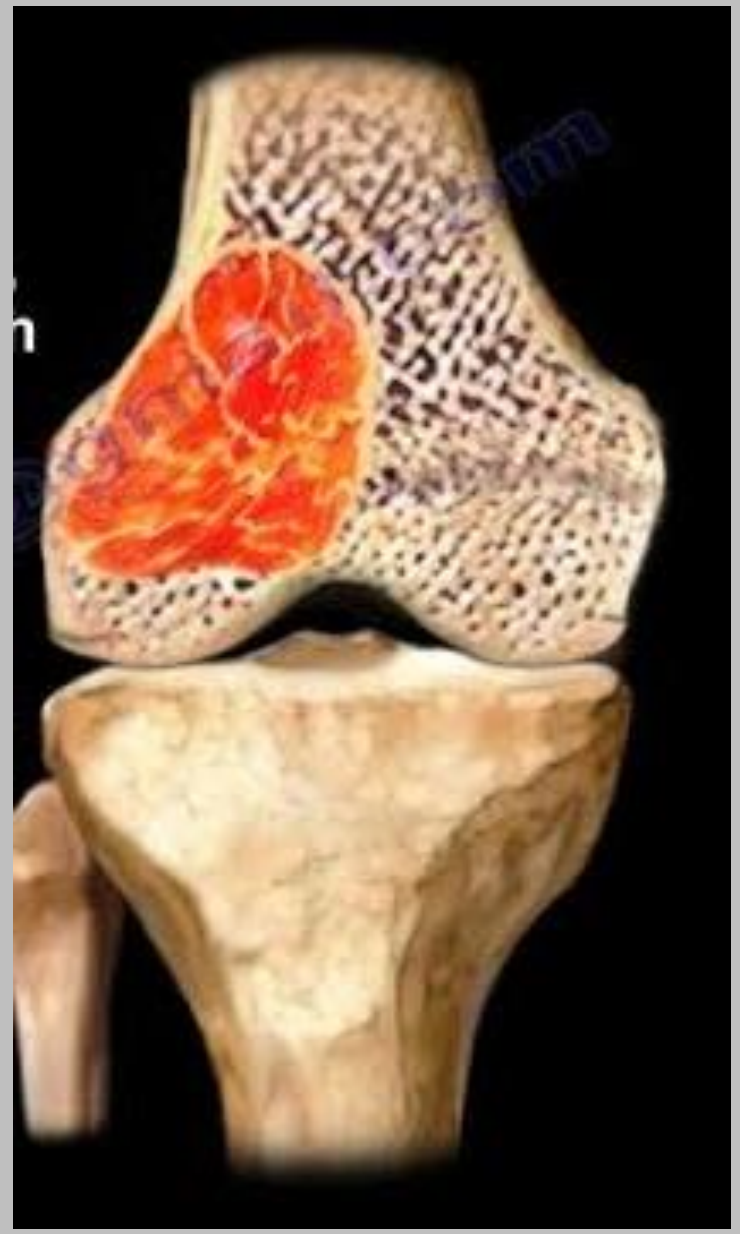
https://pathologyoutlines.com/wick/ewing%20sarcoma%20micro0003.jpg



Lung metastasis of Ewing's sarcoma

Giant cell tumor

- characterized by the presence of multinucleated, osteoclast-type giant cells
- locally aggressive
- *potentially malignant (*pulmonary metastasis in ~2% of cases)
- mostly arising around the knee
- in adults originate at the junction of the metaphysis and the epiphysis of a long bone
- in adolescents they are confined proximally by the growth plate and are limited to metaphysis



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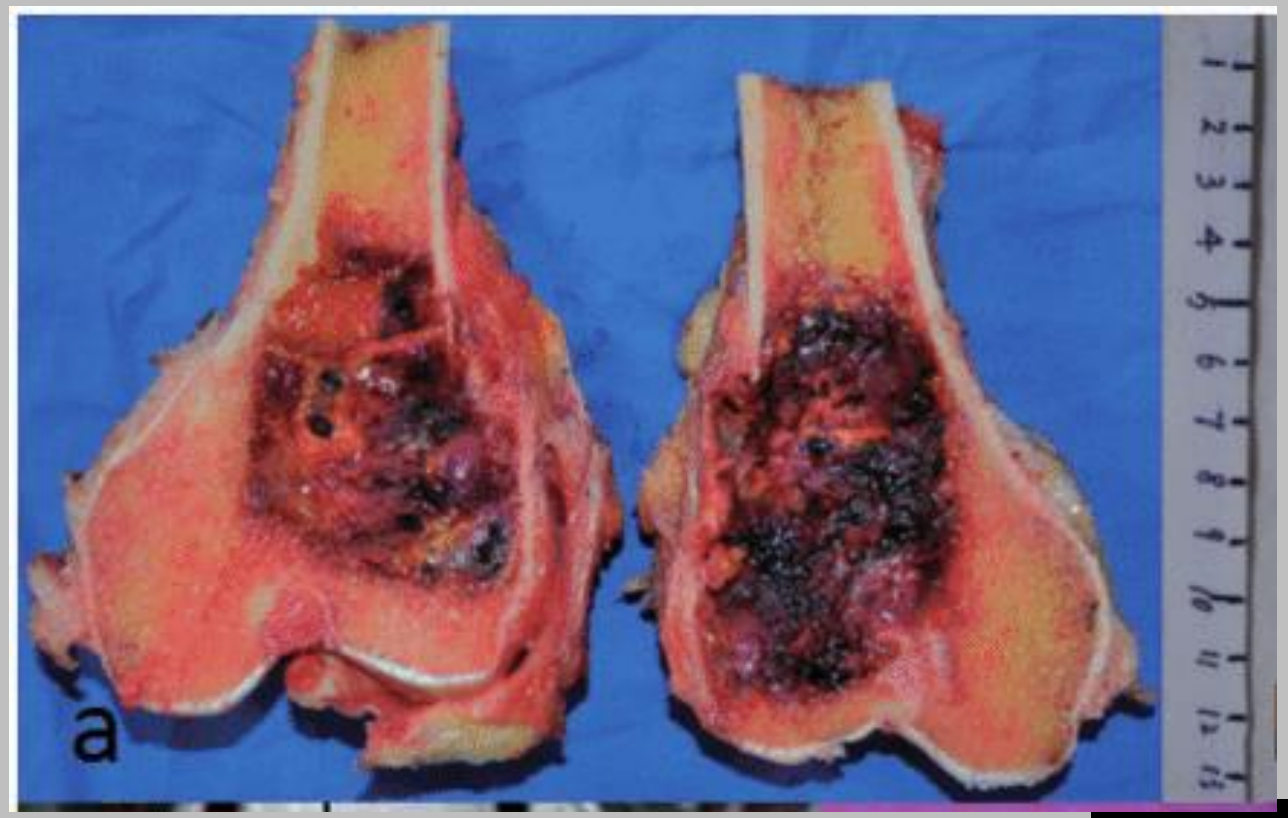
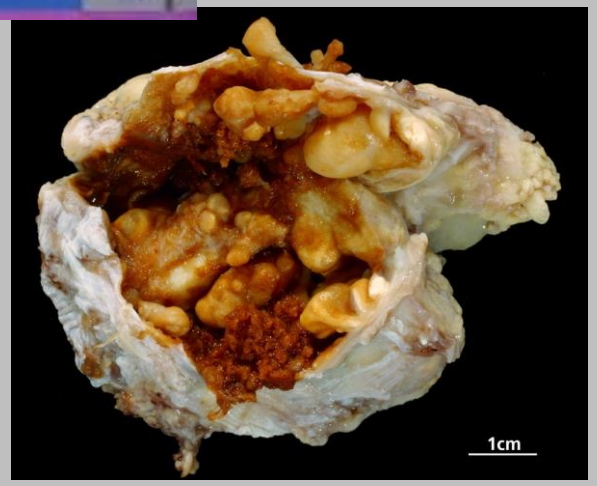


https://www.researchgate.net/publication/319652689/figure/fig3/

Giant cell tumor

Gross :

- large, clearly circumscribed
- soft, without bone or calcification
- light brown with hemorrhage areas



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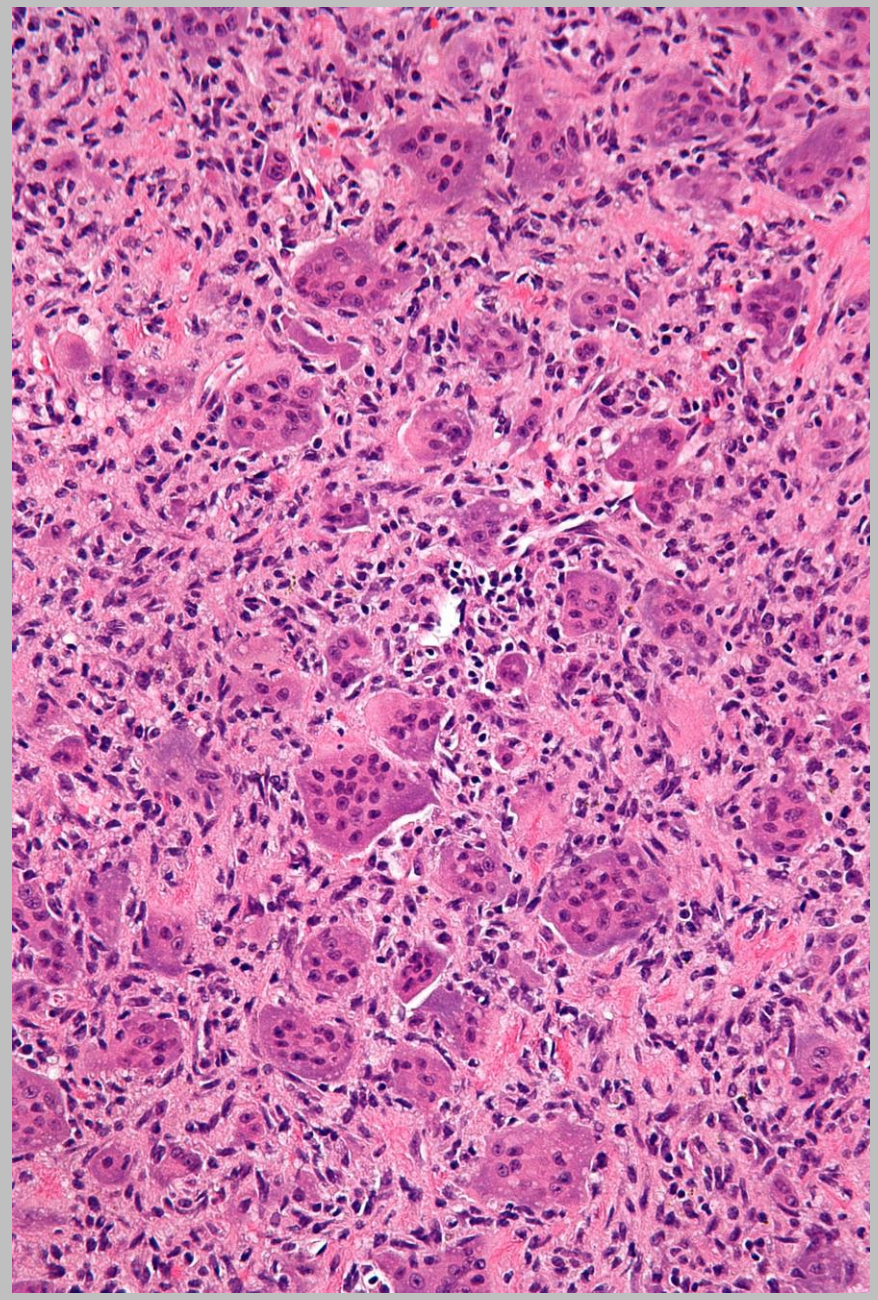
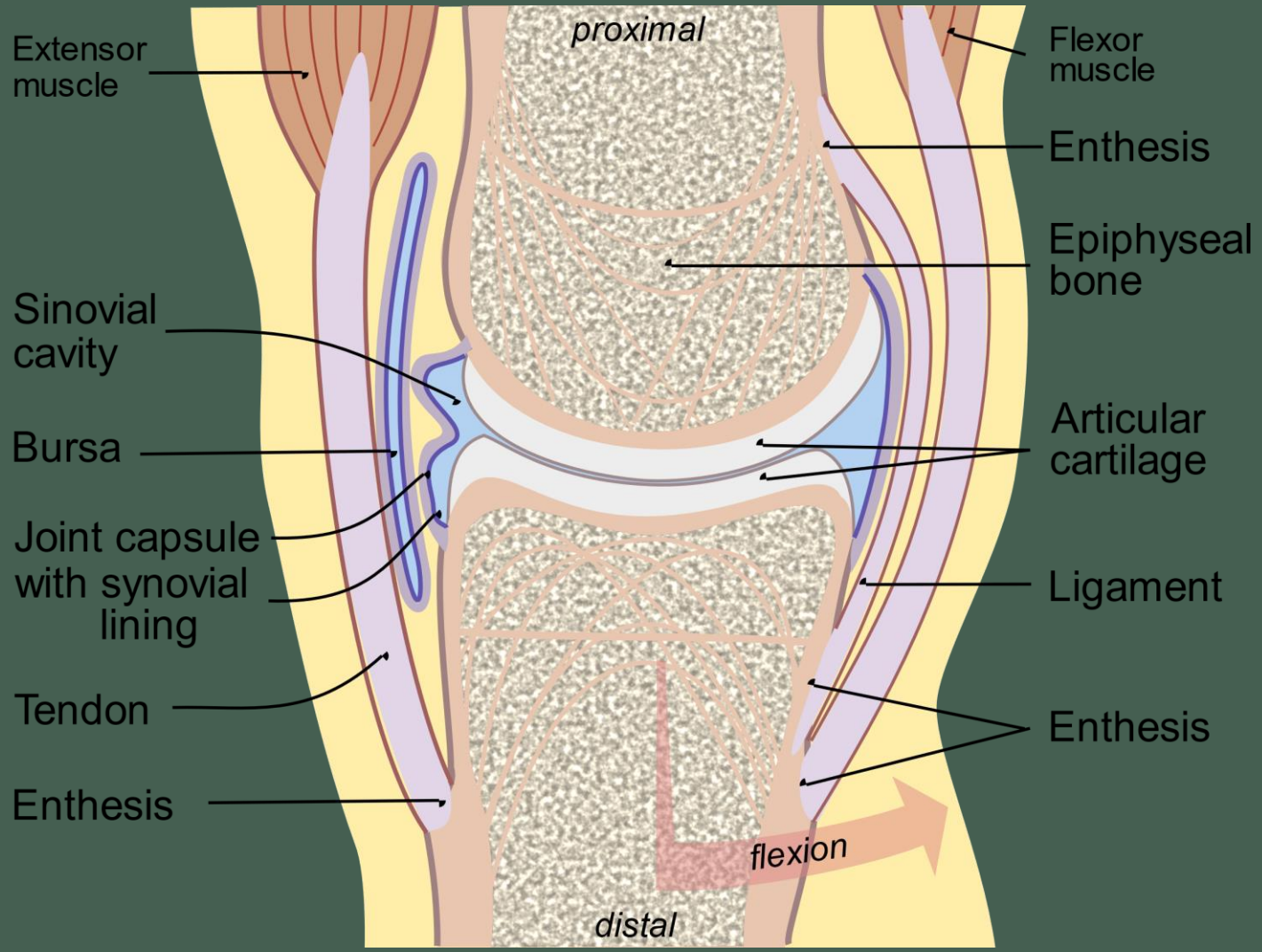
Giant cell tumor

Microscopically :

- two types of cells :
  - mononuclear cells (*the proliferating component*)
    - oval, uniform
    - large nuclei
    - scanty cytoplasm, indistinct cell membranes
    - easily identified mitoses
  - osteoclast-like giant cells
- richly vascularized stroma
    - hemorrhage areas, hemosiderin deposits





JOINTS PATHOLOGY

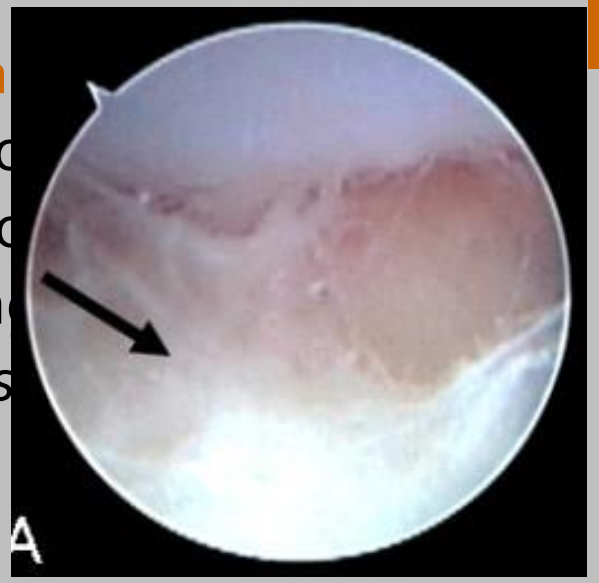
ARTHRITIS

Infectious arthritis

- produced by
  - direct inoculation
  - contiguous spread from a soft tissue abscess
  - hematogenous dissemination in bacteremia
- most common organisms :
  - gonococcus
  - Staphylococcus
  - H. Influenzae
  - Mycobacterium tuberculosis
  - …

Acute suppurative a

- *sudden* develo
  and swollen jo
- restricted ran
- healing with s
  deformities



Tuberculous arthritis

- confluent *tuberculous granulomas with caseous necrosis*
- usually affecting the weight-bearing joint
- insidious onset, gradual progressive pain
- affected synovium may grow as a pannus with bone erosion

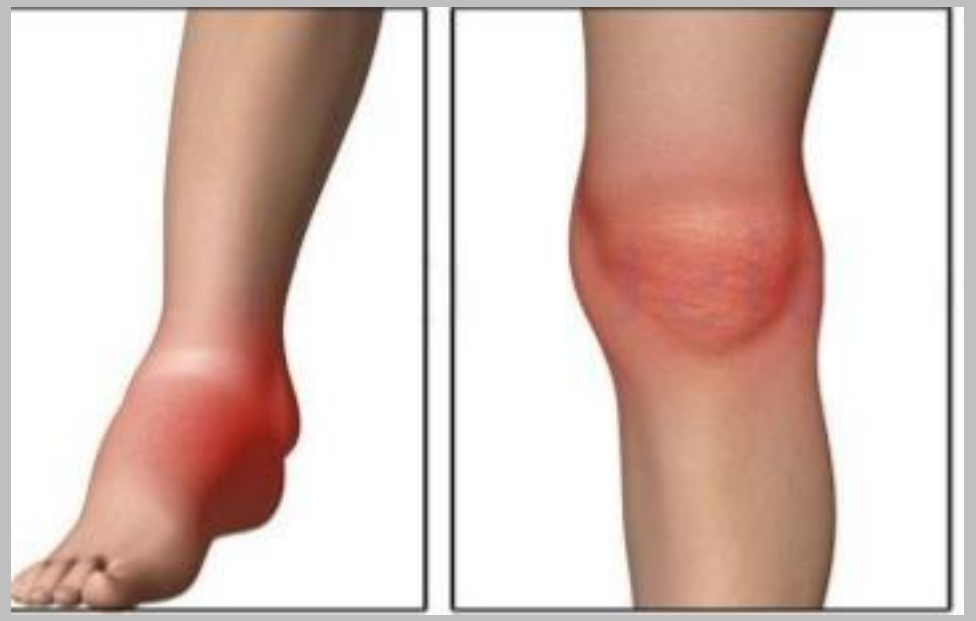
https://upload.wikimedia.org/wikipedia/commons/2/28/SepticArth2011_%28cropped%29.jpg

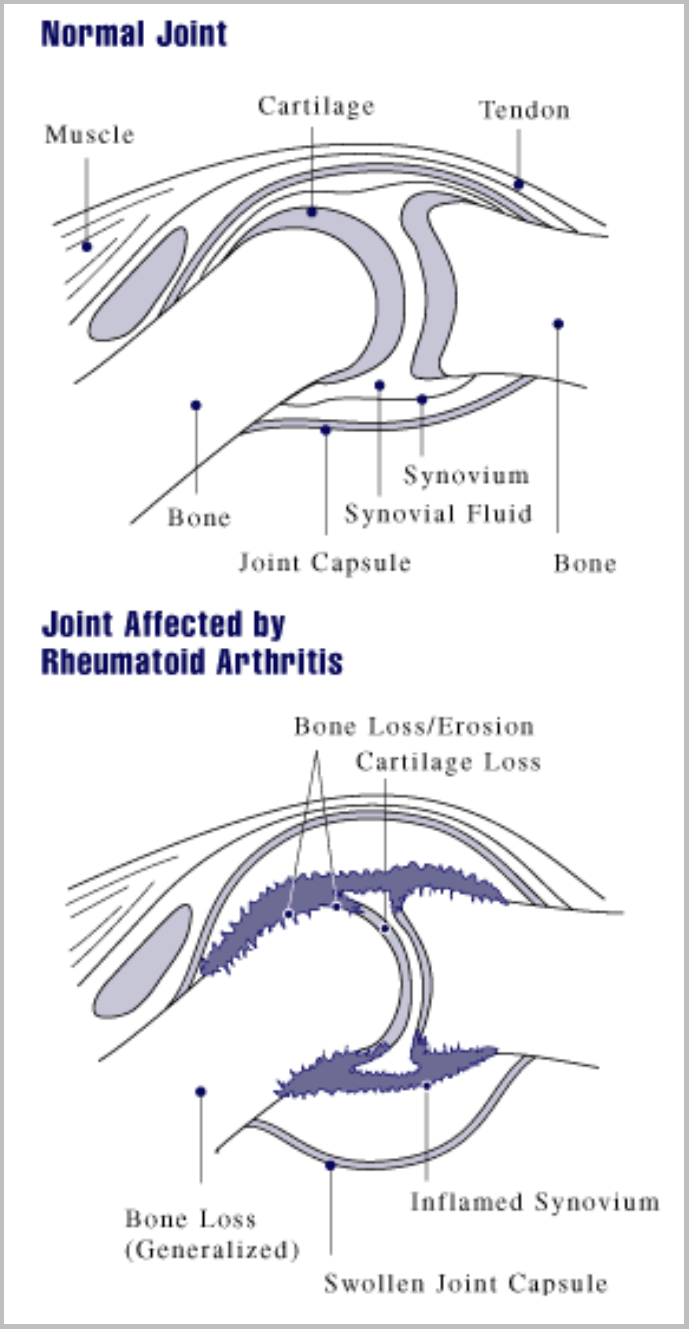
Rheumatic arthritis

- appears in the context of rheumatic fever
    - following a pharyngeal infection with group A beta-hemolytic streptococcus
    - result of an immune response (cross-reaction)
- clinical course : *remission and exacerbation periods*
- usually migratory
- affecting large joints
- resolves without sequelae

The affected joint is painful and swollen. Synovium shows hyperemia, edema and slight leukocyte infiltrate. The synovial fluid is turbid, with more inflammatory cells than normal.

https://image.slidesharecdn.com/acuterheumaticfever-170429014244/95/acute-rheumatic-fever-15-638.jpg?cb=1493430181

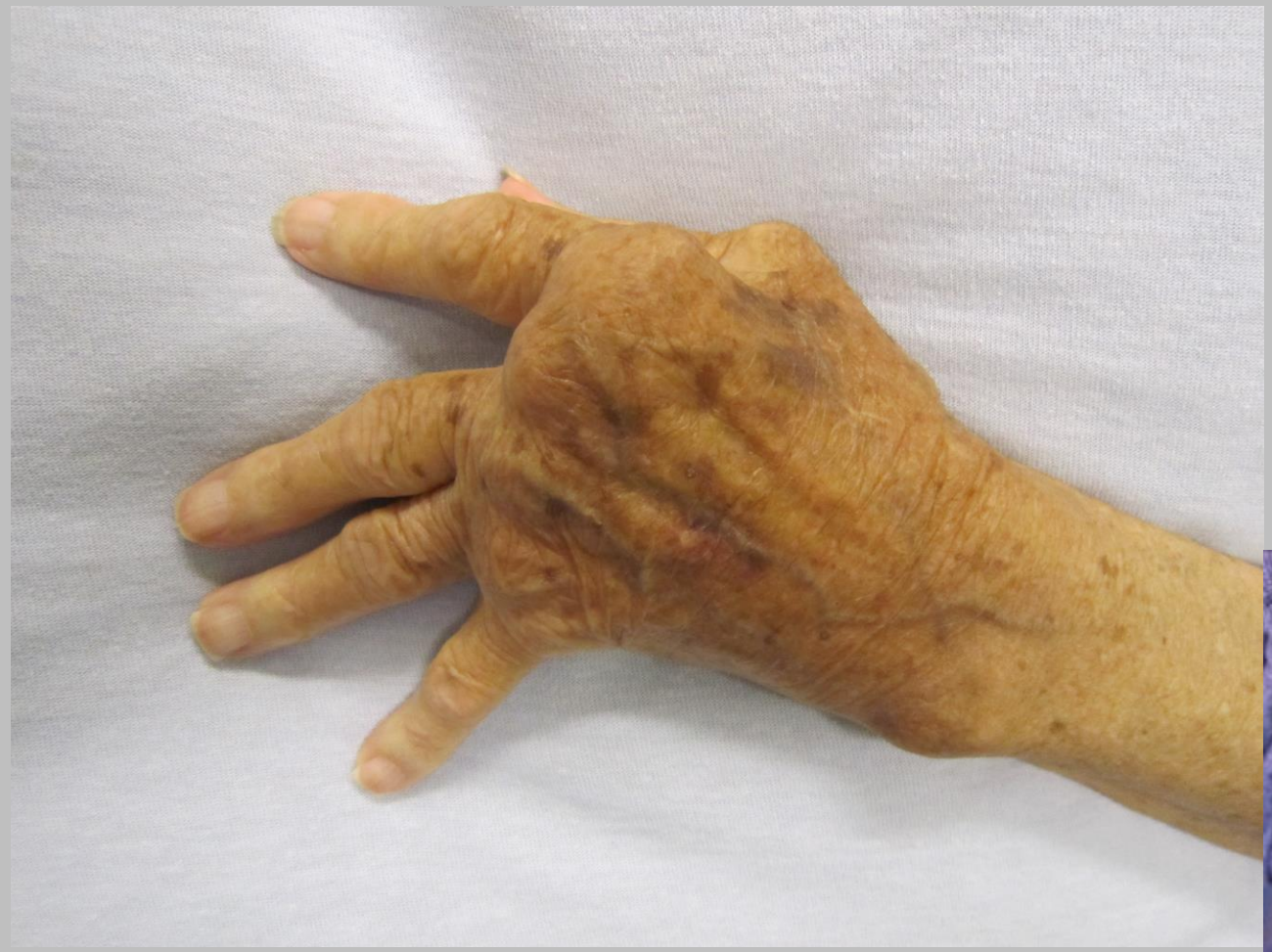




Rheumatoid arthritis

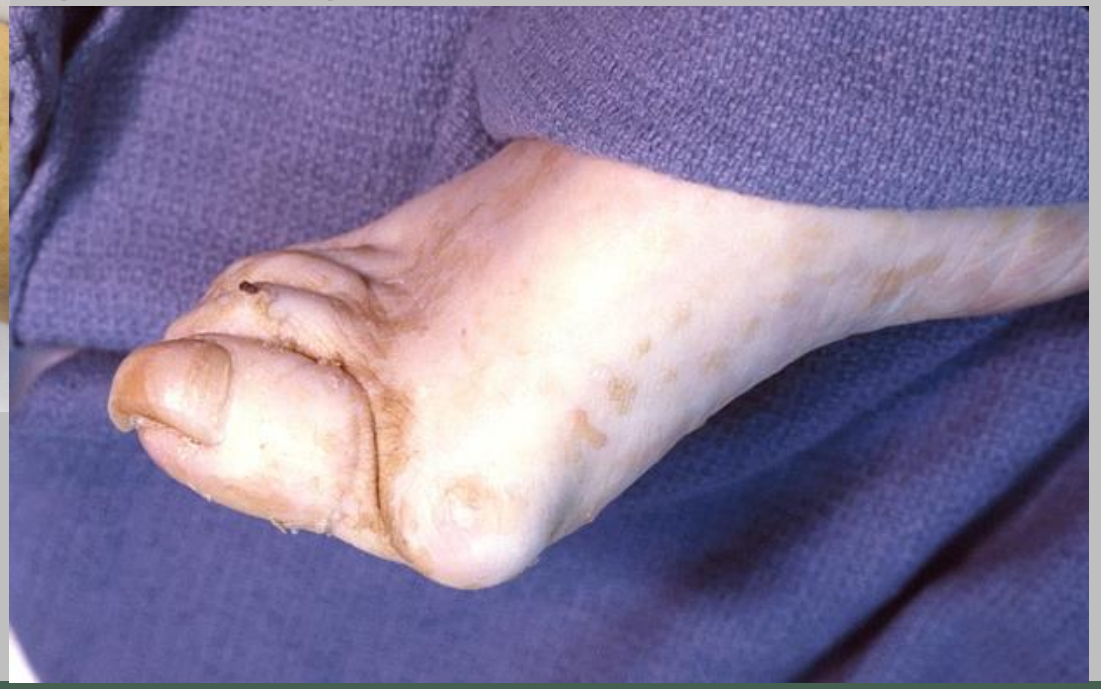
- chronic systemic inflammatory disease
- unknown pathogenesis
- principally attacks diarthrodial joints
- producing a nonsuppurative proliferative synovitis
- clinical course : *remissions, exacerbations*
- clinical manifestations ranging from mild signs to destructive and mutilating disease

Rheumatoid arthritis



By James Heilman, MD - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=11110471

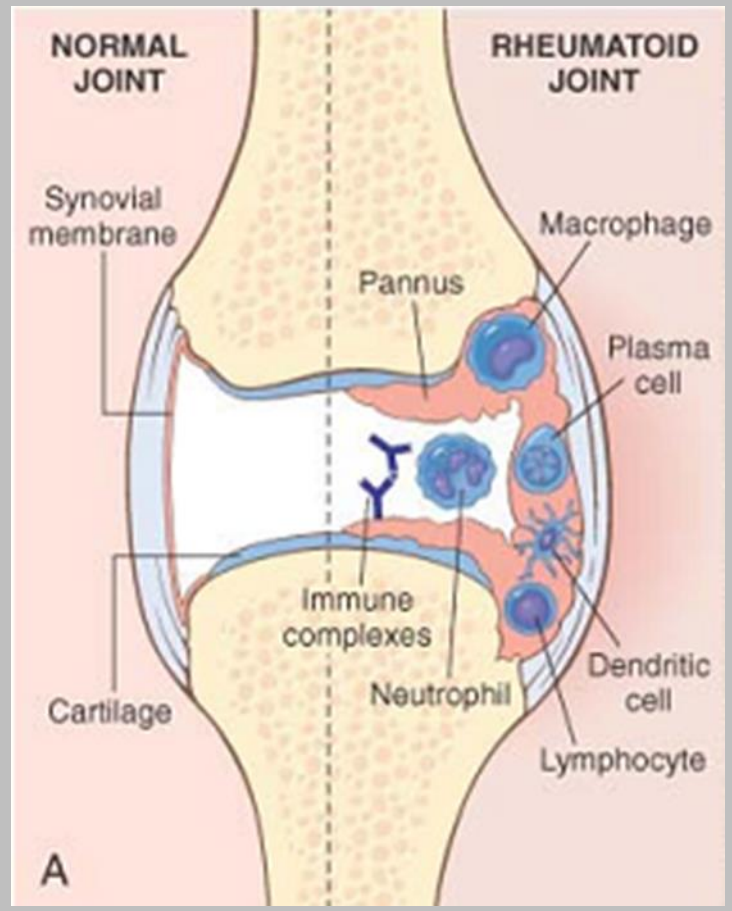
The proximal interphalangeal and metacarpophalangeal joints, elbows, knees, ankles and spine are commonly affected; usually, the joints of extremities are afflicted simultaneously and in a symmetric pattern.

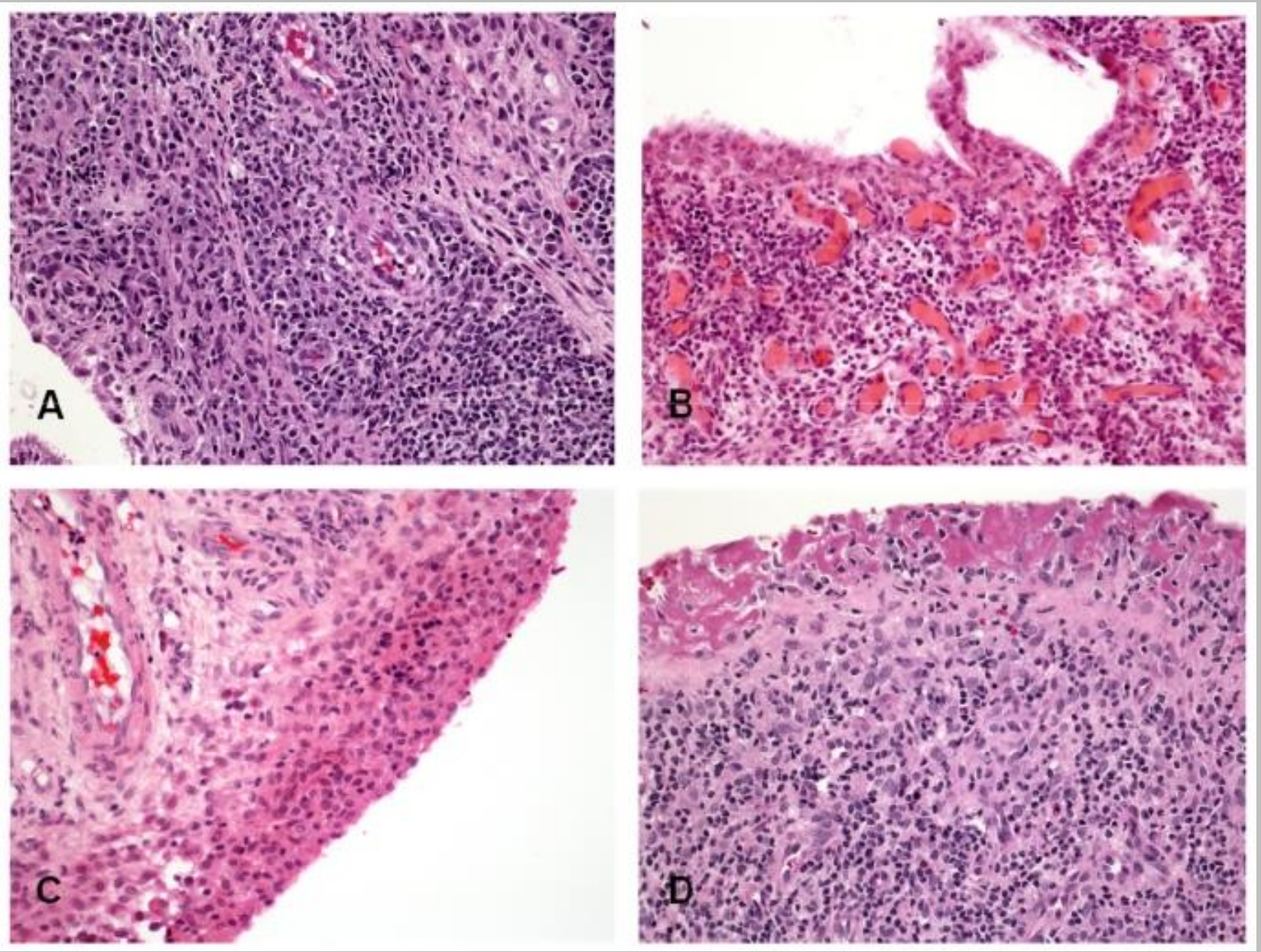


https://peir.path.uab.edu/library/picture.php?/11180/category/77

Rheumatoid arthritis

- synovium :
  - edematous, thickened, hyperplastic
  - covered by *bulbous fronds*
  - eventually, creeps over the articular surface => *pannus*
- stroma :
  - infiltrated by inflammatory cells (chronic-type)
- vascularity :
  - increased, with hemosiderin deposits
- joint space :
  - aggregates of organizing fibrin – *"rice bodies"*
- cartilage :
  - may be destroyed
  - *ankylosis* may ensue





Histopathology of RA synovitis:

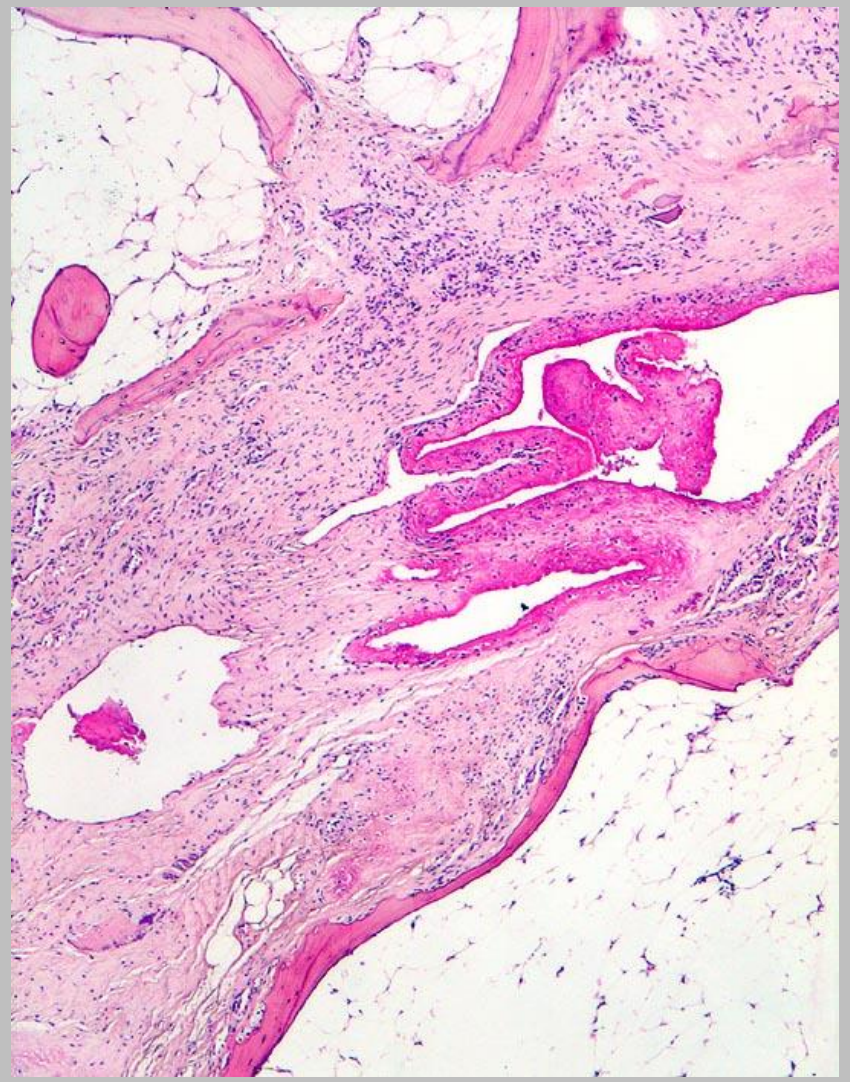
(A) Lymphoid aggregate;
(B) Diffuse lymphocytes infiltrate;
(C) Hyperplasia of the lining layer
(D) Fibrin cap replacing a denuded lining layer.

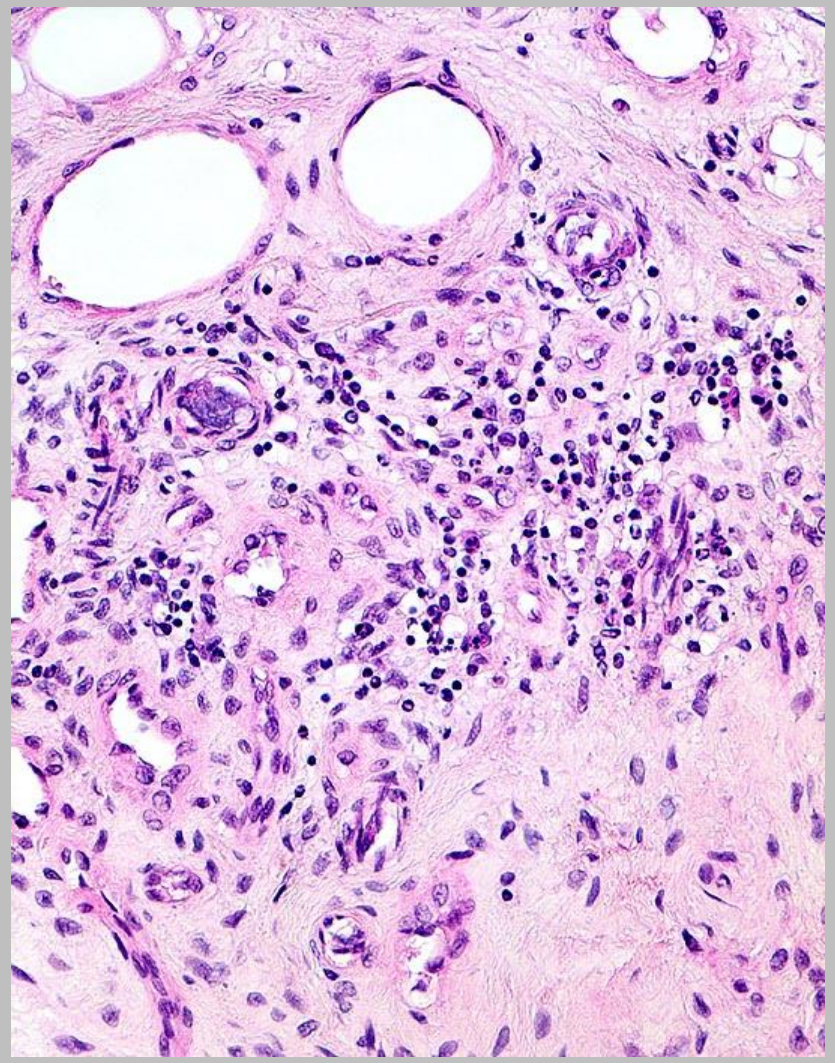
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3263474/bin/TORJ-5-107_F2.jpg

The joint space is filled with Pannus connective tissue (pannus) & fibrin.

Rheumatoid arthritis

Pannus with fibroblasts, capillaries and scattered inflammatory infiltrate.





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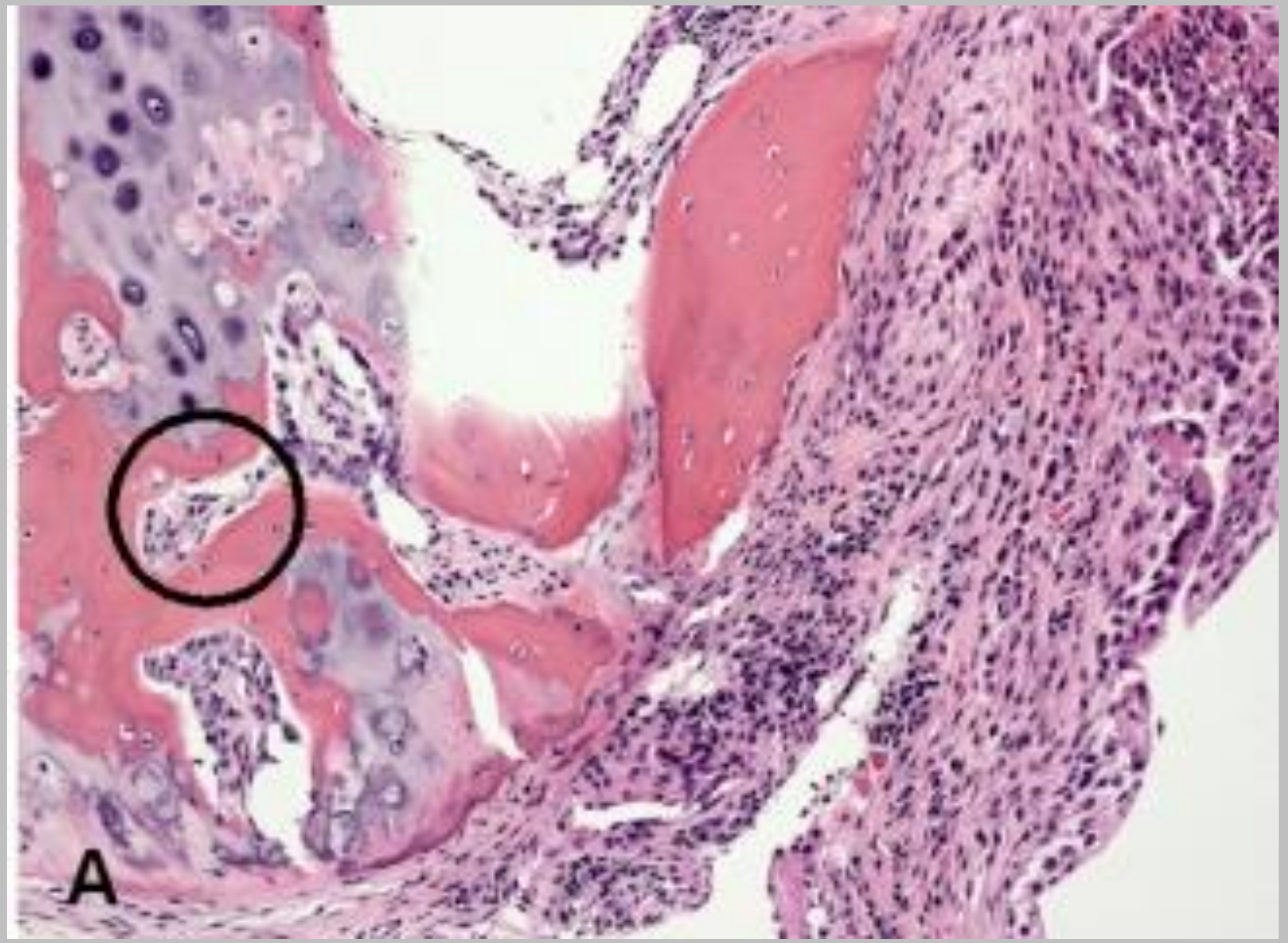
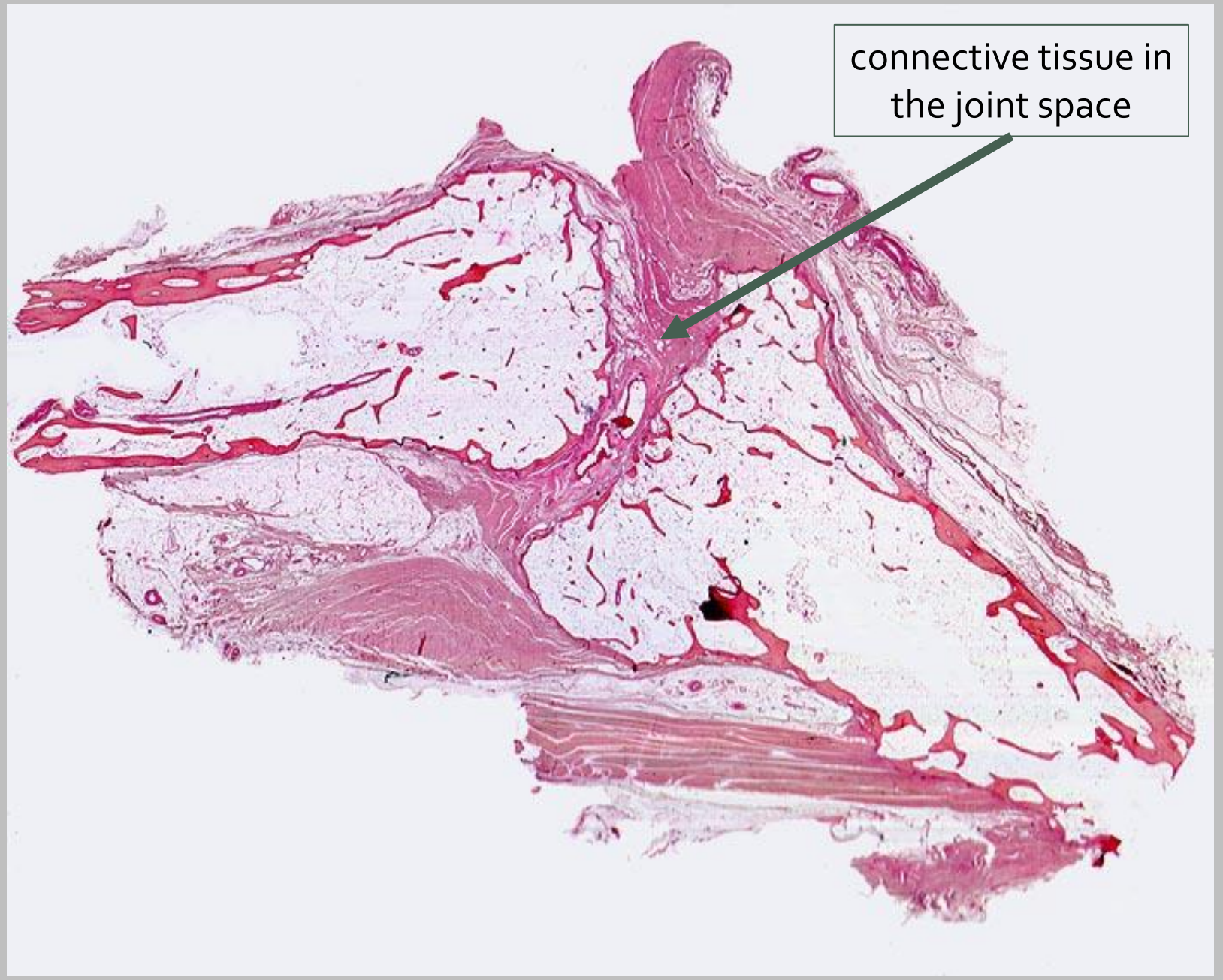


Interface between pannus tissue and bone in a patient with RA. (A) the synovial lesion is invading the adjacent bone.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3263474/bin/TORJ-5-107_F3.jpg



In time, after the cartilage has been destroyed, the fibrocellular pannus bridges the apposing bones forming a fibrous ankylosis that eventually ossifies.

Ankylosis – finger joint

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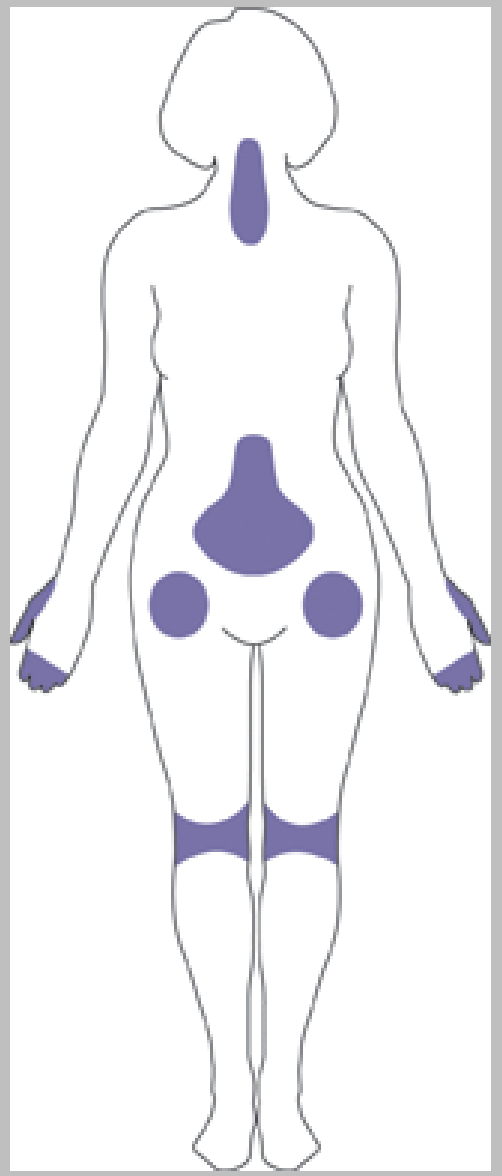


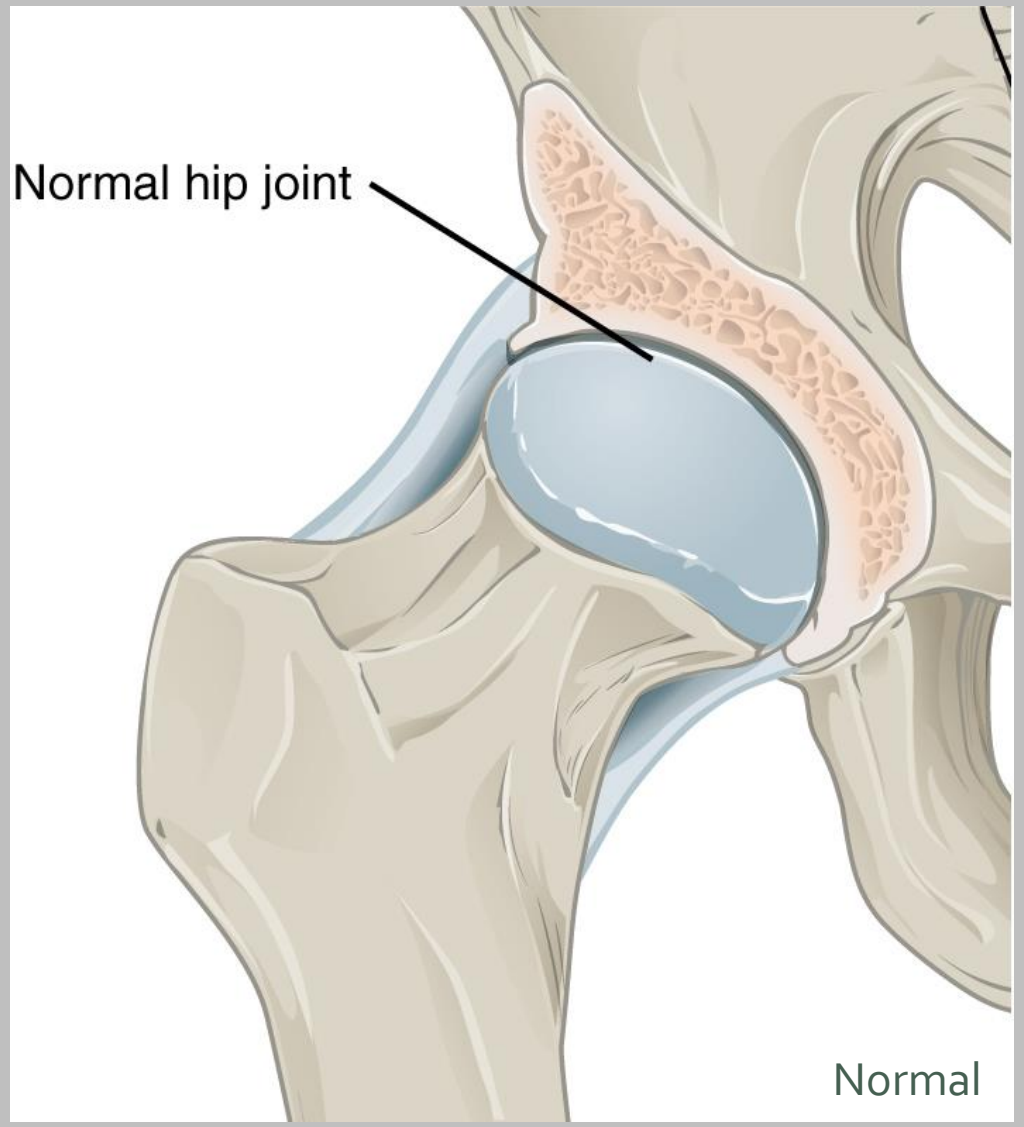
Osteoarthritis

- degenerative joint disease
- progressive erosion of articular cartilage
- appears as an aging phenomenon
- has no apparent initiating cause

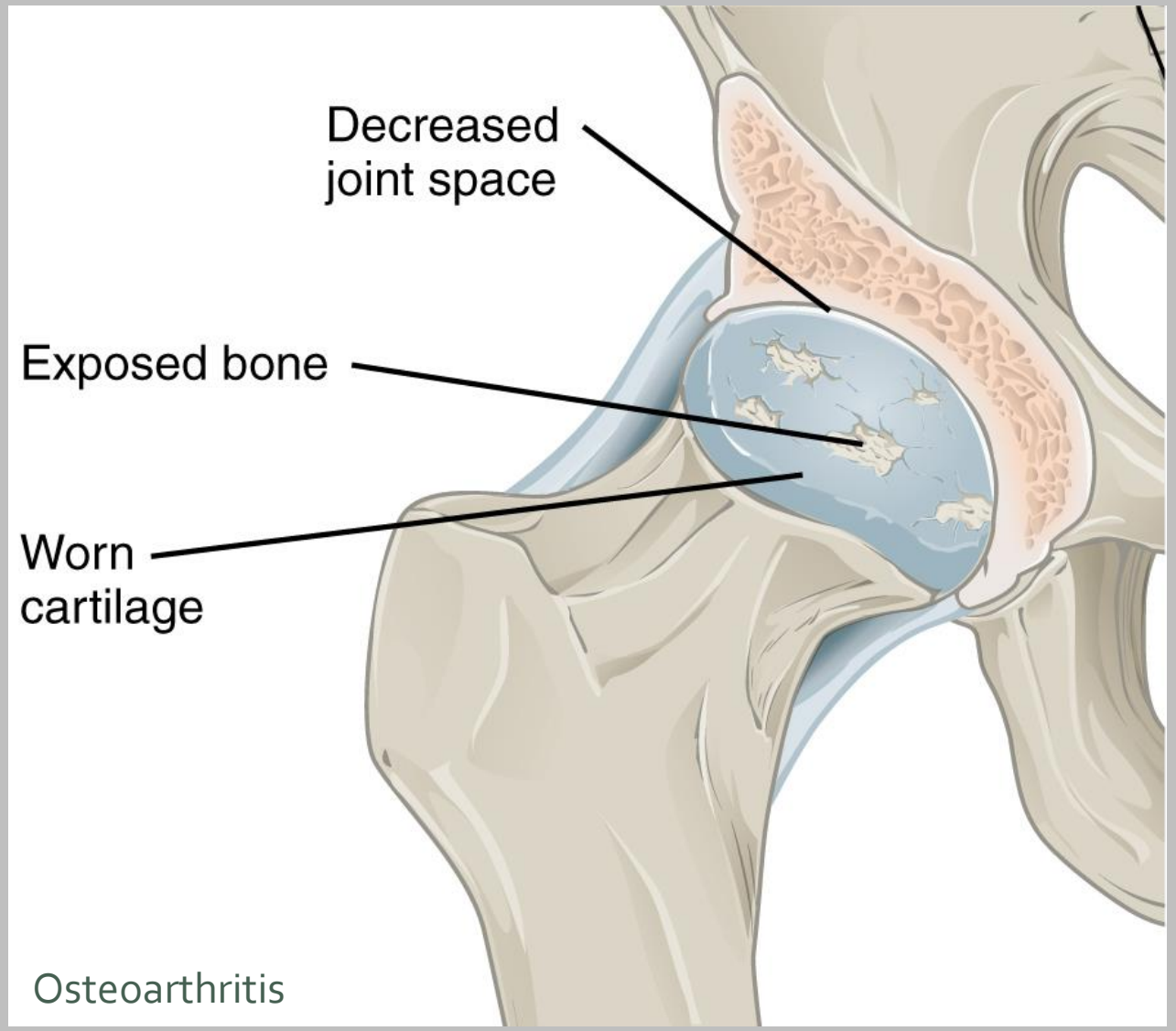
Characteristic symptoms of osteoarthritis:

- ❑ deep, achy pain that worsens in time,
- ❑ morning stiffness, crepitus and limitation of range of movement.

Impingement on spinal foramina by osteophytes results in cervical and lumbar nerve root compression with radicular pain, muscle spasms, muscle atrophy and neurologic deficits



Normal



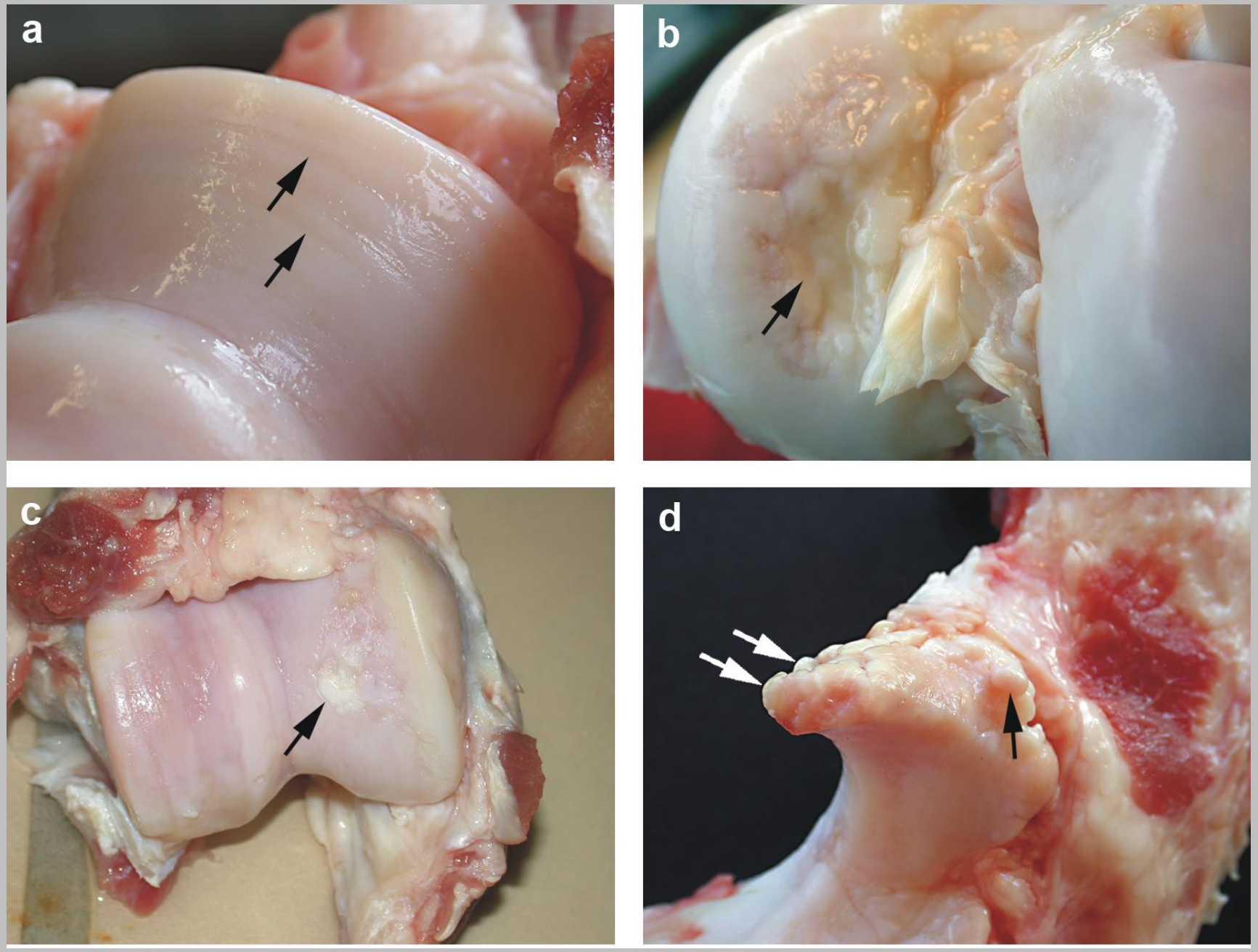
Osteoarthritis

Osteoarthritis

- early stages :
  - granular articular surface
  - softer than normal

- later stages :
  - full-thickness portion of the cartilage: sloughed
  - the exposed subchondral bone plate becomes the new articular surface, that eventually has the appearance of polished ivory (eburnated bone)

- small fractures are common, dislodging pieces of cartilage and bone, that tumble into the joint – "joint mice"
- the fracture gaps allow synovial fluid to enter into the subchondral regions forming fibrous walled cysts
- synovium is congested and fibrotic
- osteophytes (mushroom-shaped) develop at the articular surface margins

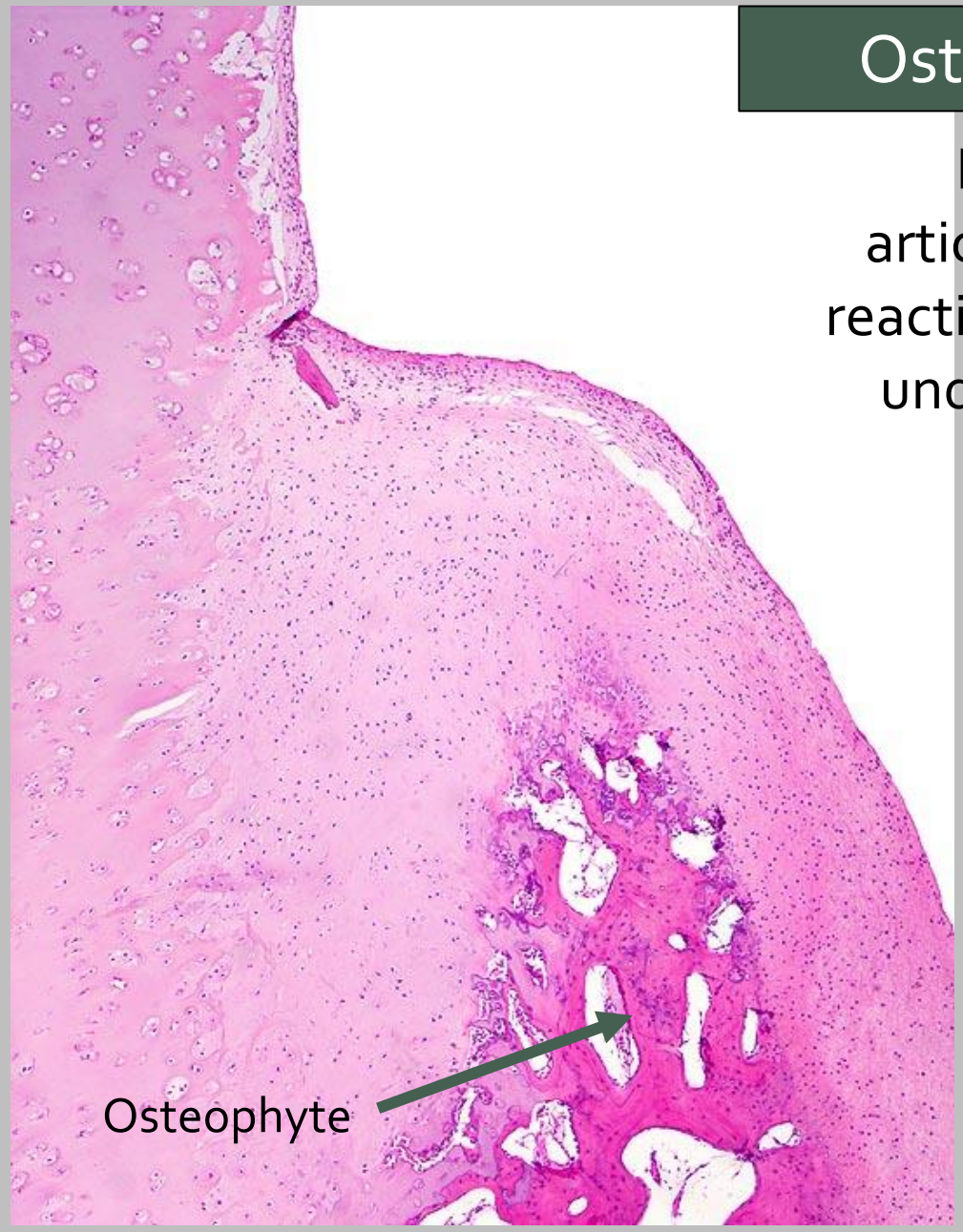


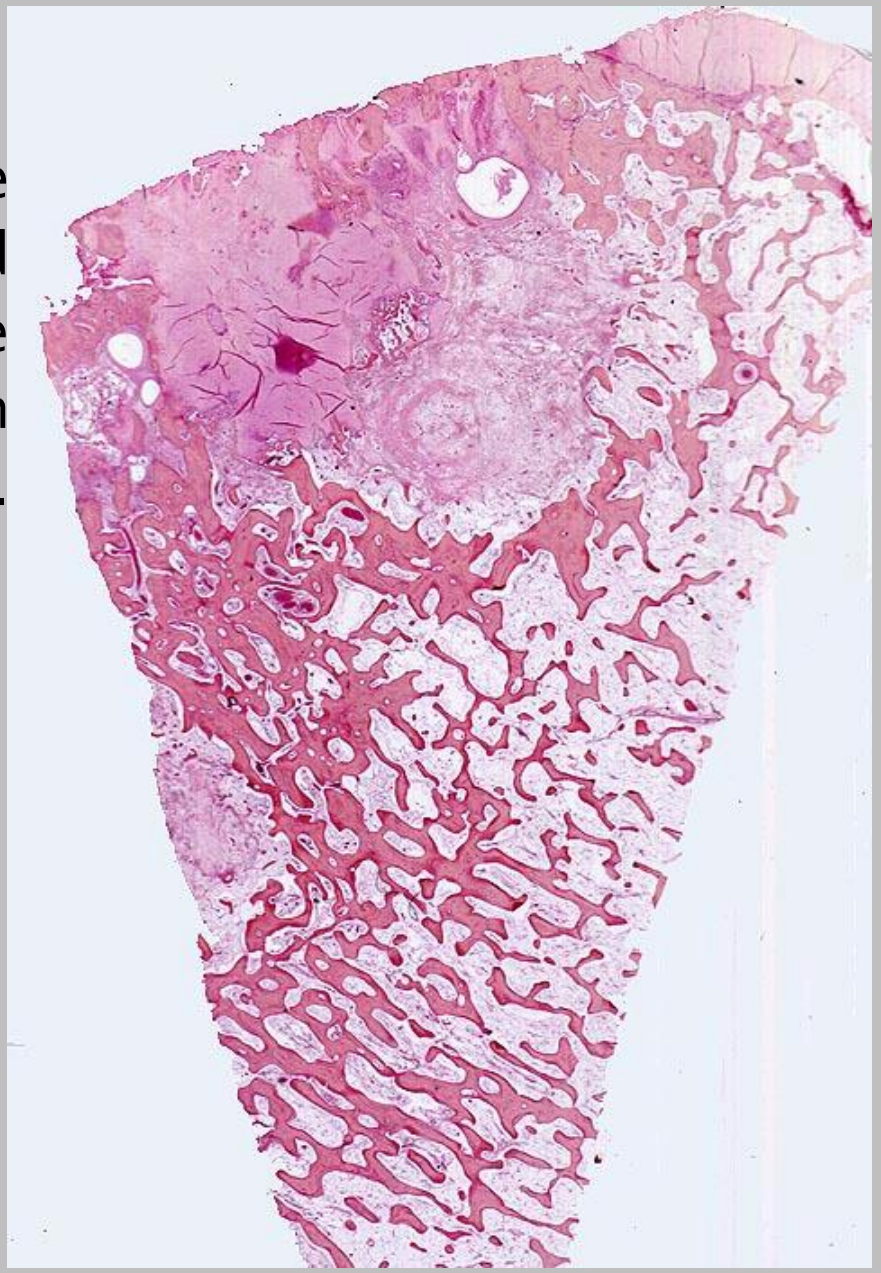
Osteoarthritis

a. cartilage erosion
b. cartilage ulceration
c. cartilage repair
d. marginal osteophytes

Osteoarthritis

Destruction of the articular cartilage and reactive sclerosis of the underlying bone with focal necroses.





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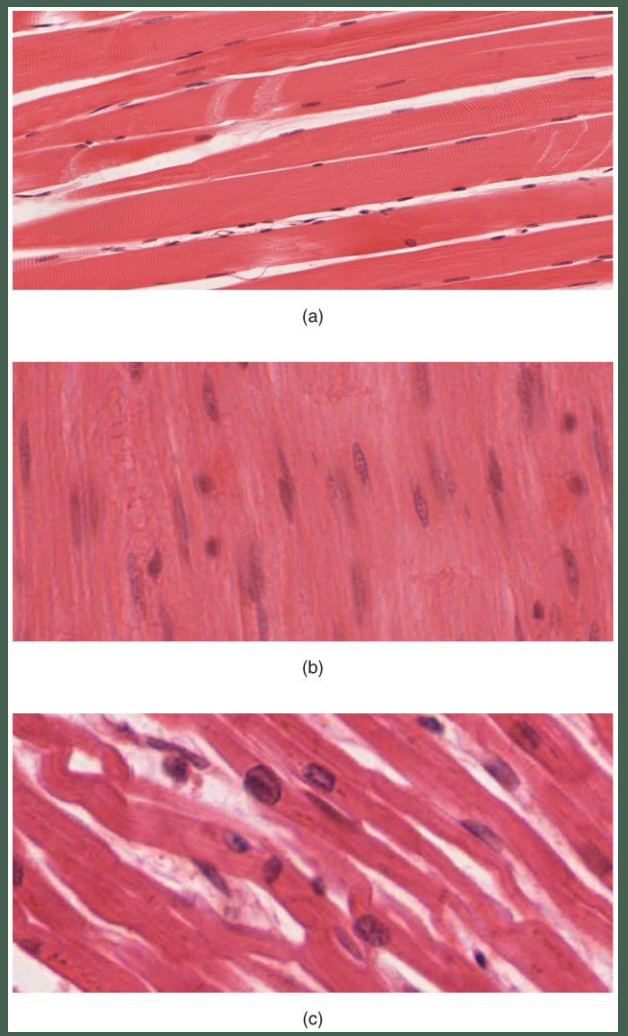


SKELETAL MUSCLE DISORDERS

MUSCULAR DYSTROPHIES

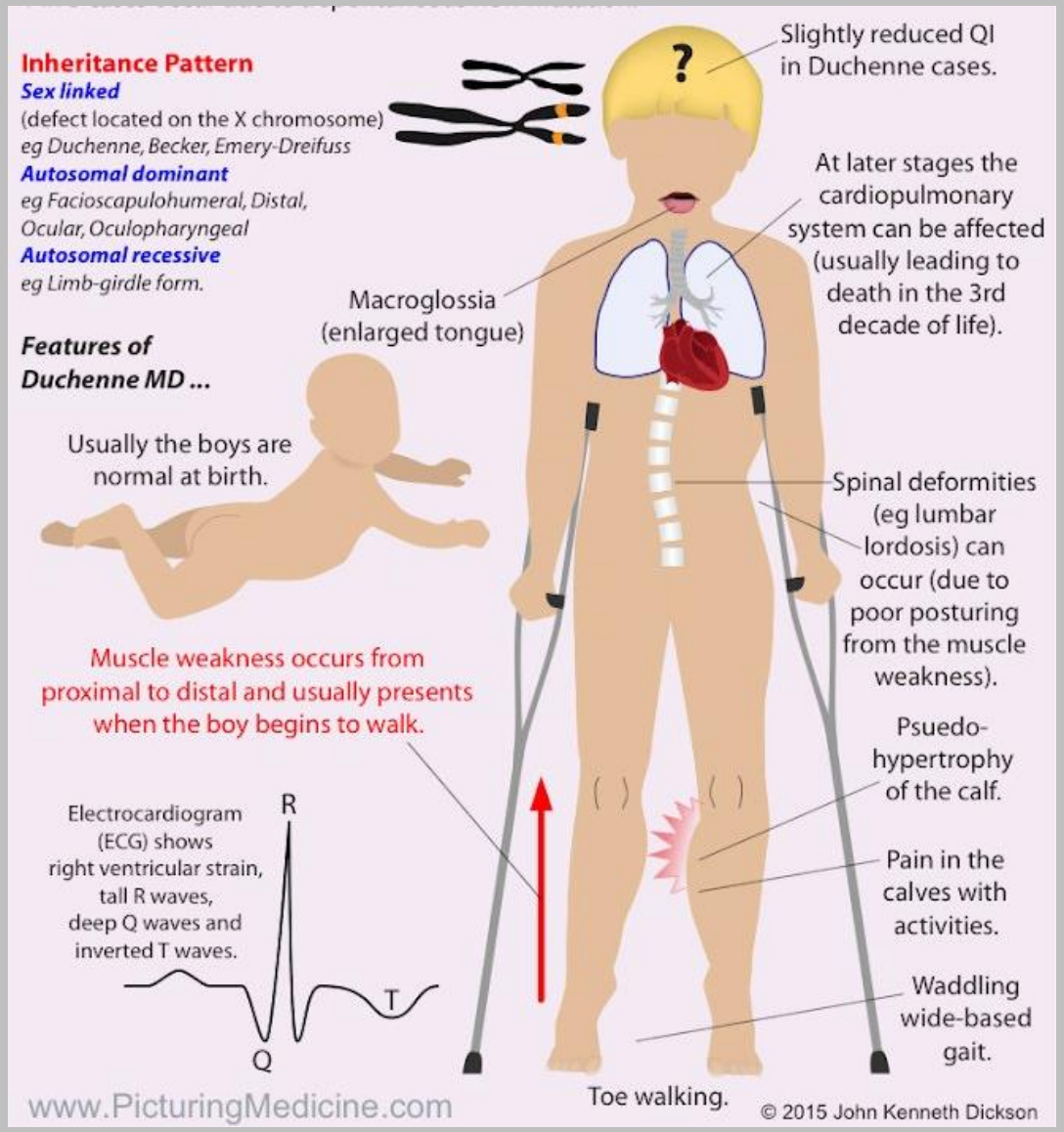
- inherited disorders, characterized clinically by progressive weakness of the voluntary muscles because of primary muscular degeneration

- **Duchenne muscular dystrophy** (X-linked inherited condition: deletion of a gene on the short arm of the X chromosome encoding a protein termed dystrophin, which preserve the integrity of the myocyte membrane during the shape changes associated with contraction**): children, male gender**

- **Myotonic dystrophy** (an autosomal dominant trait): **adults**

Duchenne muscular dystrophy

- *progressive noninflammatory myopathy*
- X-linked inherited condition
- patients become wheelchair-bound by the age of 10, bedridden by 15
- common cause of death : arrhythmia owing to myocardial involvement
- manifests by :
    - muscular atrophy of the muscles
    - replacement by fibrofatty tissue – "pseudohypertrophy"



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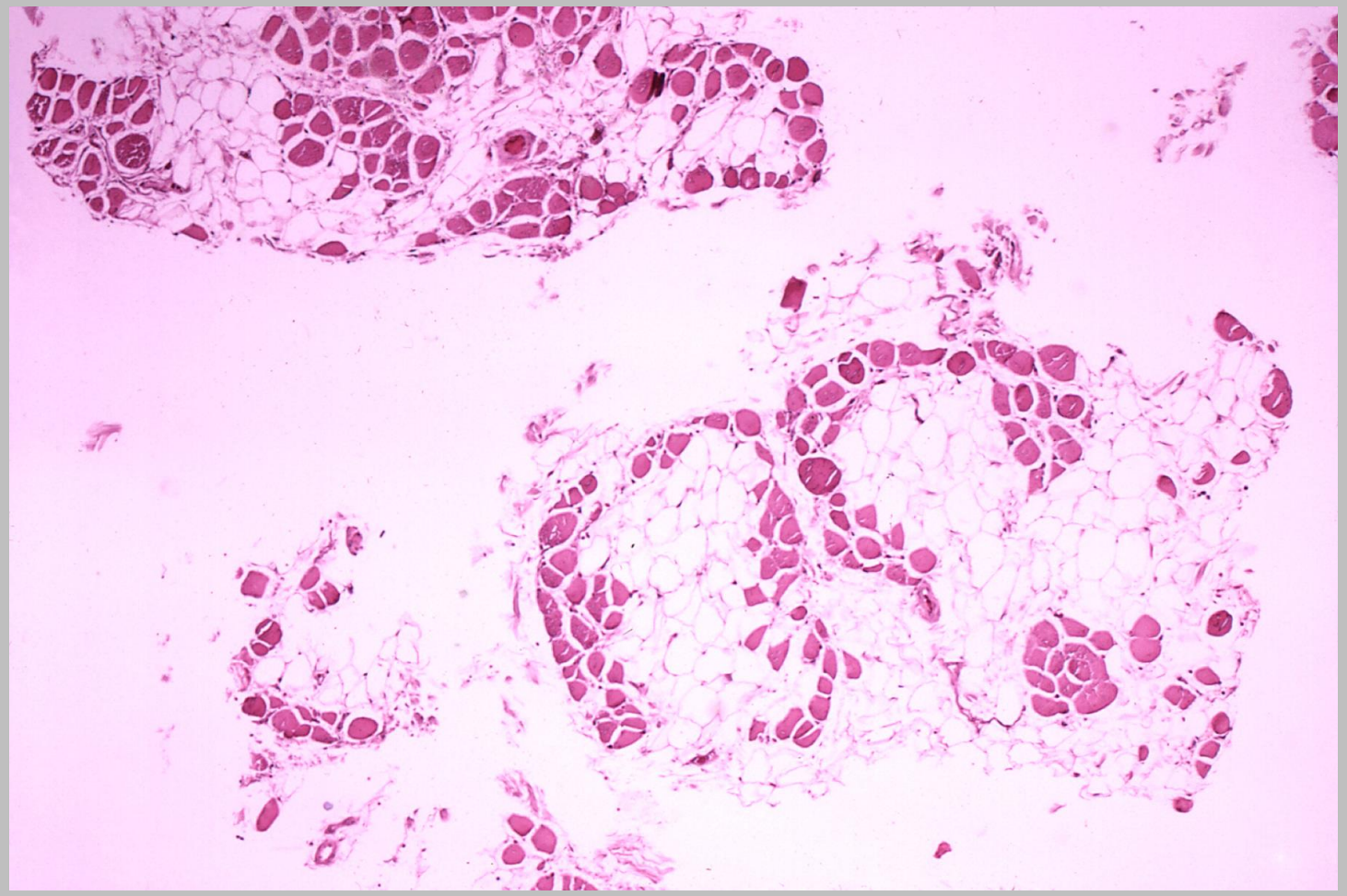

Duchenne muscular dystrophy – gastrocnemius muscle: fibrofatty tissue replacement "pseudohypertrophy"

By Dr. Edwin P. Ewing, Jr. - This media comes from the Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #70. Public Domain, https://commons.wikimedia.org/w/index.php?curid=1049370

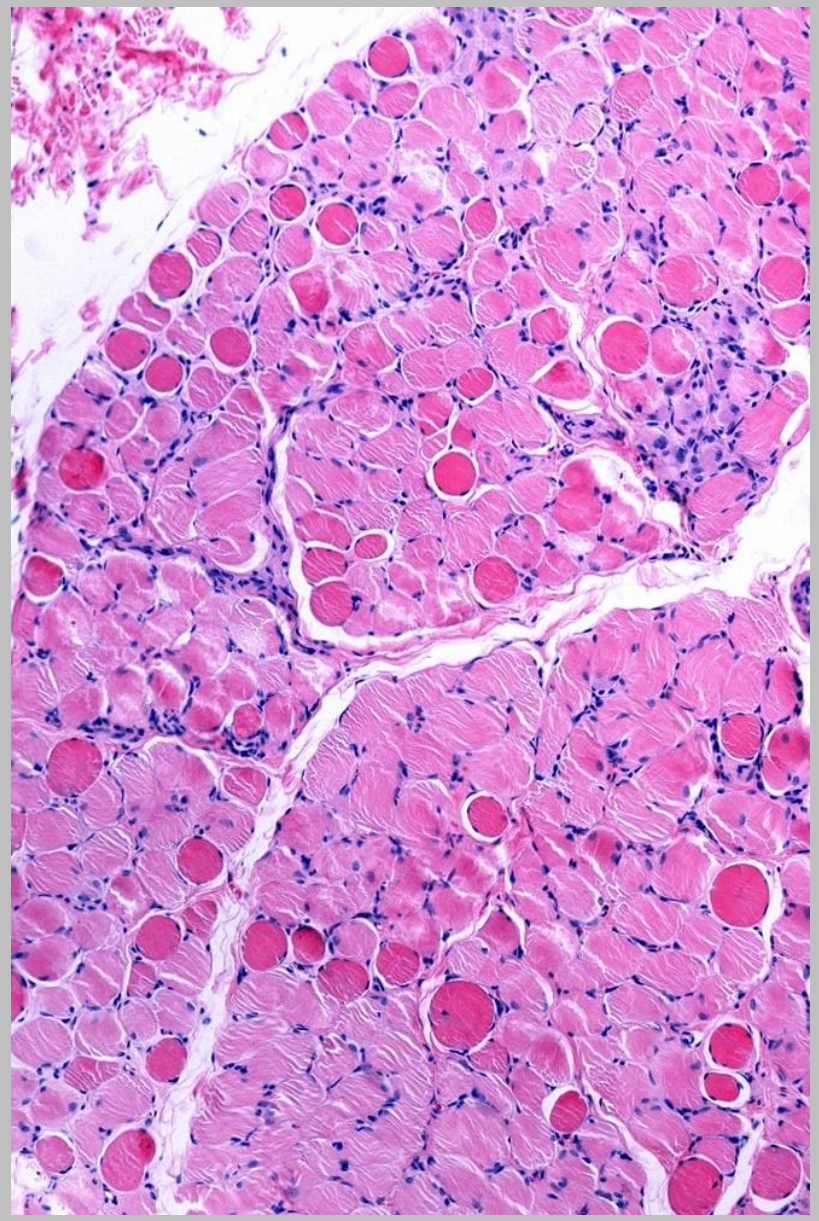

Image Credits: Jose Luis Calvo / Shutterstock.com

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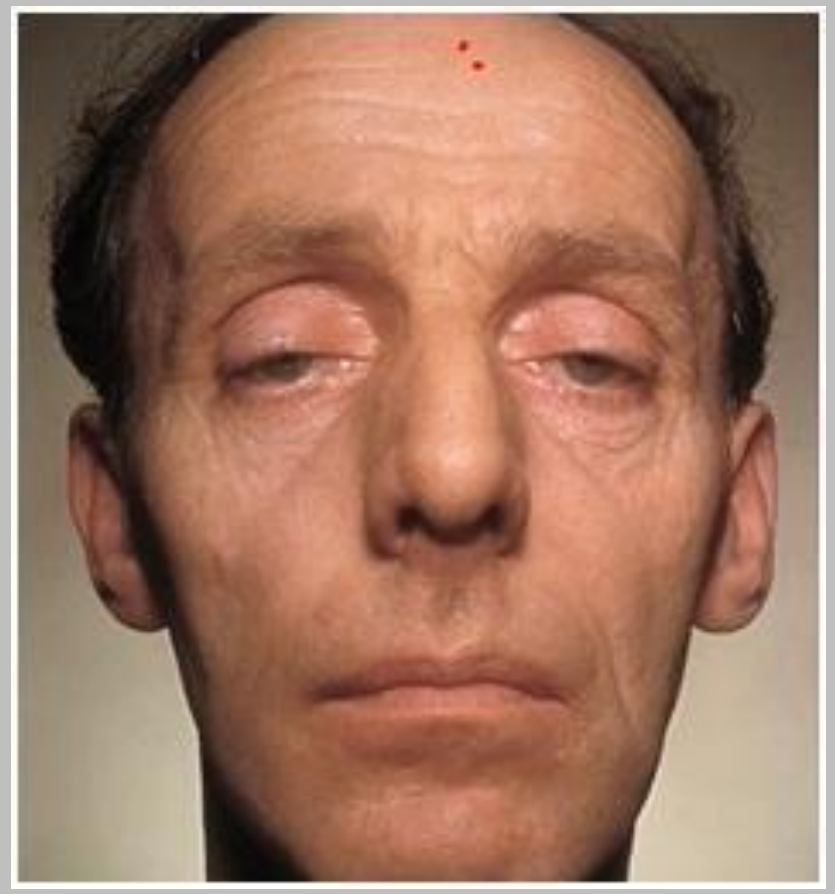

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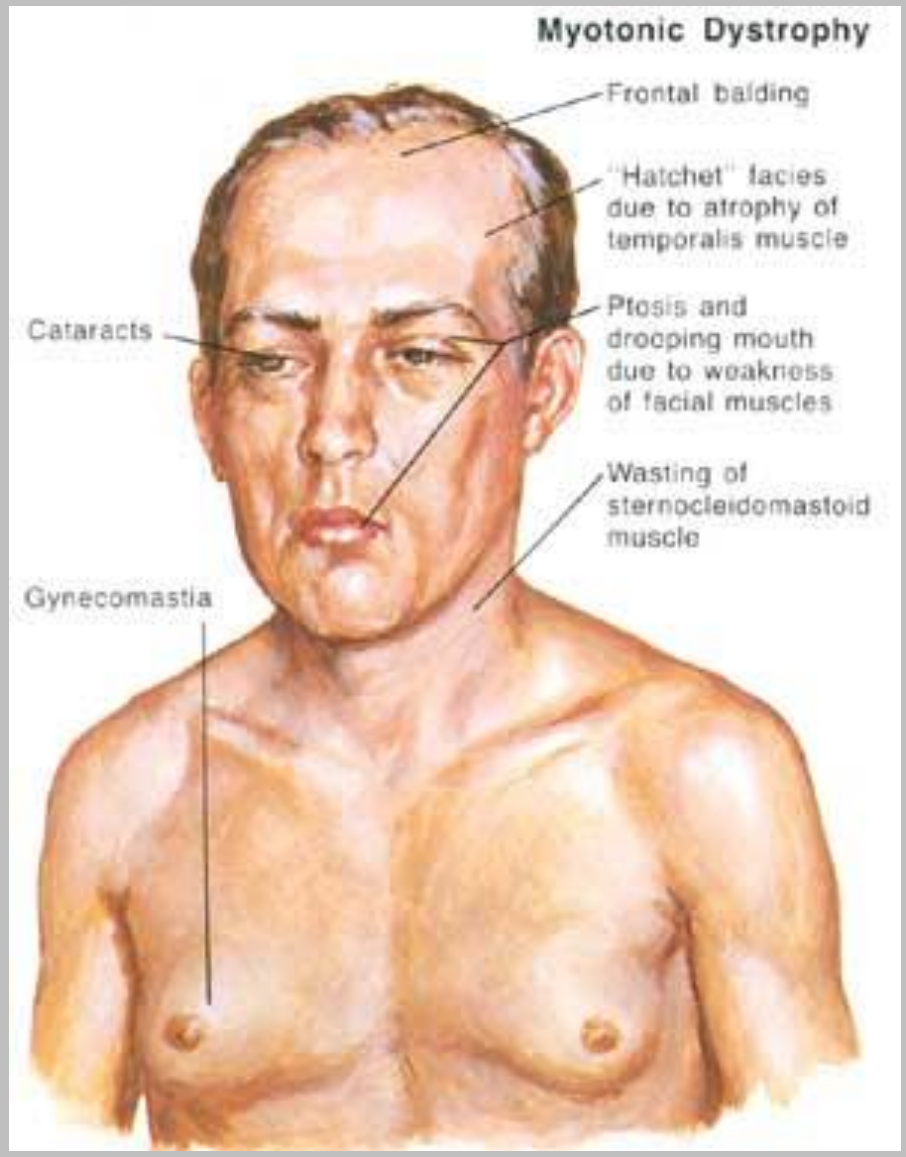
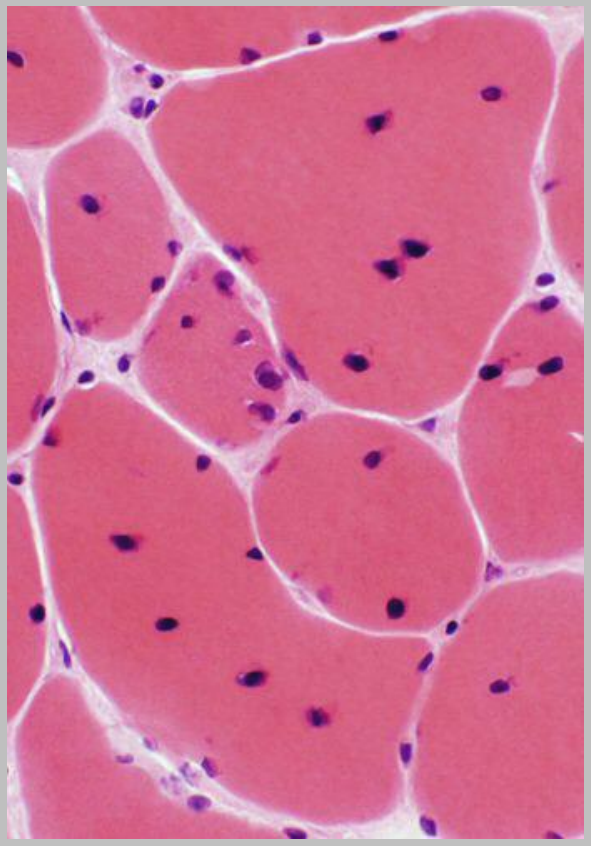


Myopathic changes: Numerous internal nuclei; fiber size variation (HE stain).



INFLAMMATORY MYOPATHIES

Variants :

- **non-infectious muscle disease**

- **infectious myositis**

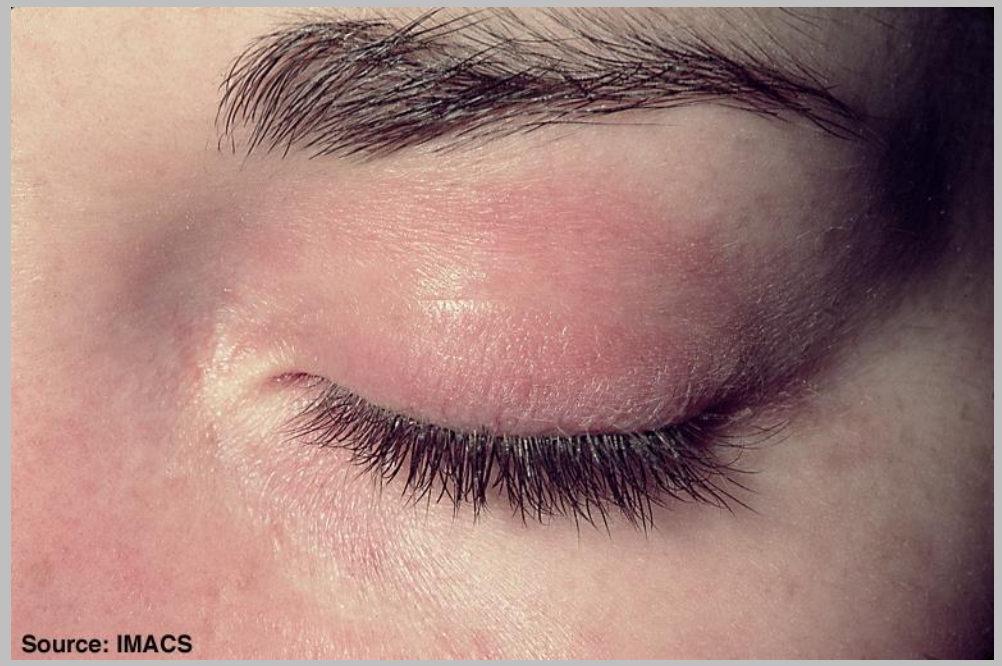
- **inflammatory processes associated with diffuse systemic inflammatory disease** muscle is secondarily affected, in:
  - scleroderma – inflammatory myositis indistinguishable from polymyositis
  - rheumatoid arthritis – muscles adjacent to affected joints

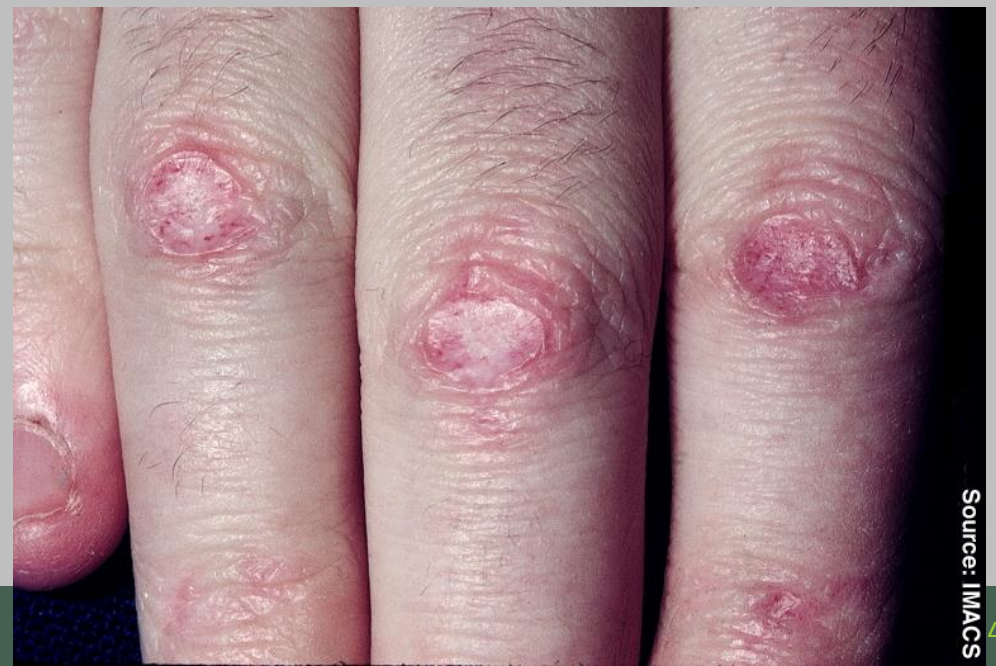
Non-infectious inflammatory myopathies

- autoimmune origin, suggested by :
    - the association with other autoimmune diseases
    - they seem to follow viral infections
    - the detection of autoantibodies
    - evidence of muscle cell injury mediated by cytotoxic T-cells
- three distinct disorders:
    - dermatomyositis
    - polymyositis
    - inclusion-body myositis
- morphological aspects: *presence of inflammatory cells, necrosis and phagocytosis of muscle fibers, mixture of regenerating and atrophic fibers, fibrosis*

Dermatomyositis involves:

- skin :
  - distinct skin rash (heliotrope discoloration)
  - scaling erythematous eruption (knuckles, elbows, knees)
- muscles :
  - slow of muscle contraction
  - layers of atrophic muscle
  - inflammatory infiltrates especially around small blood vessels and *perimysium*





By Elizabeth M. Dugan, Adam M. Huber, Frederick W. Miller, Lisa G. Rider - http://dermatology.cdlib.org/1502/reviews/photoessay/16.jpg, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=9749952

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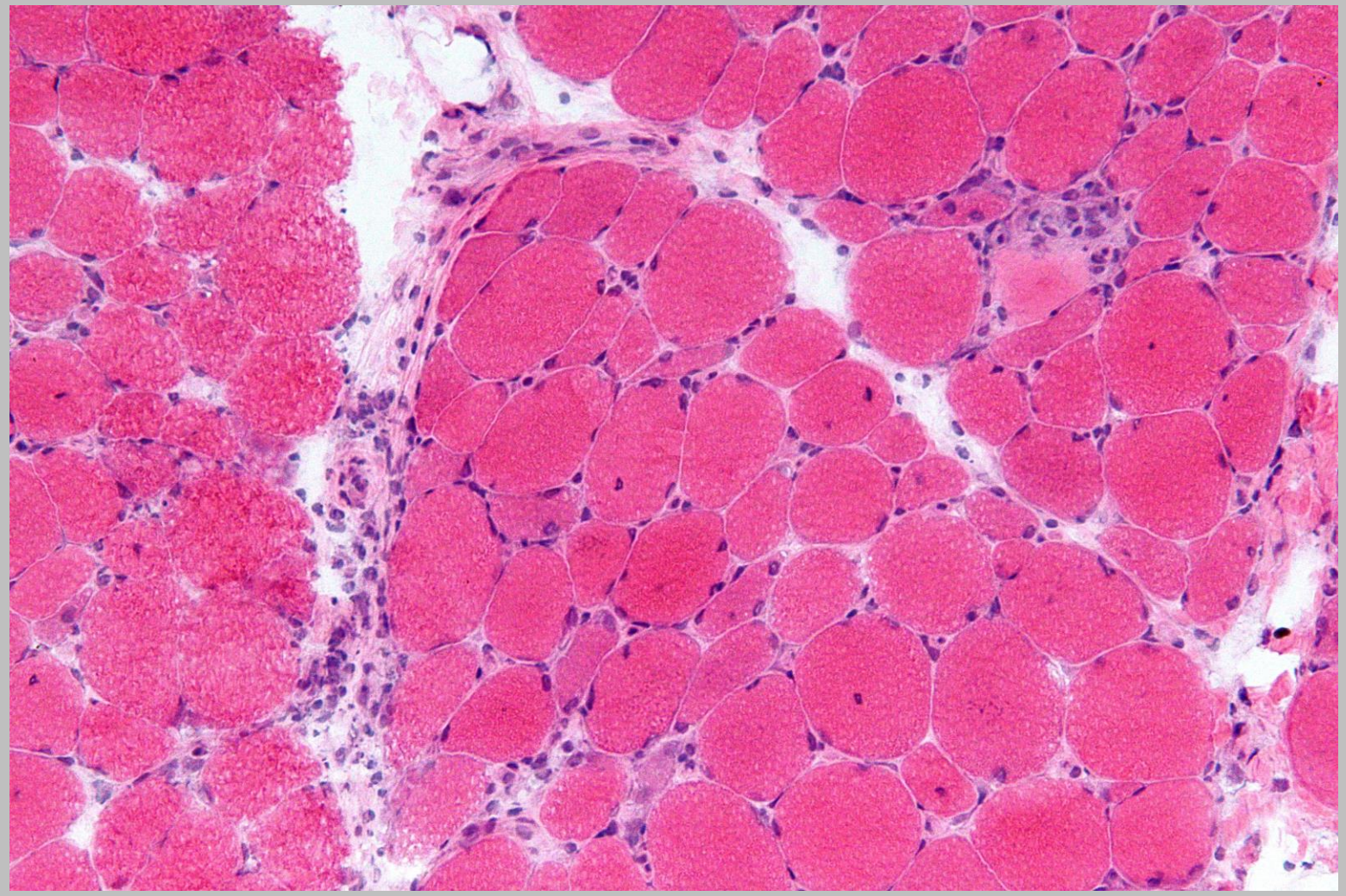
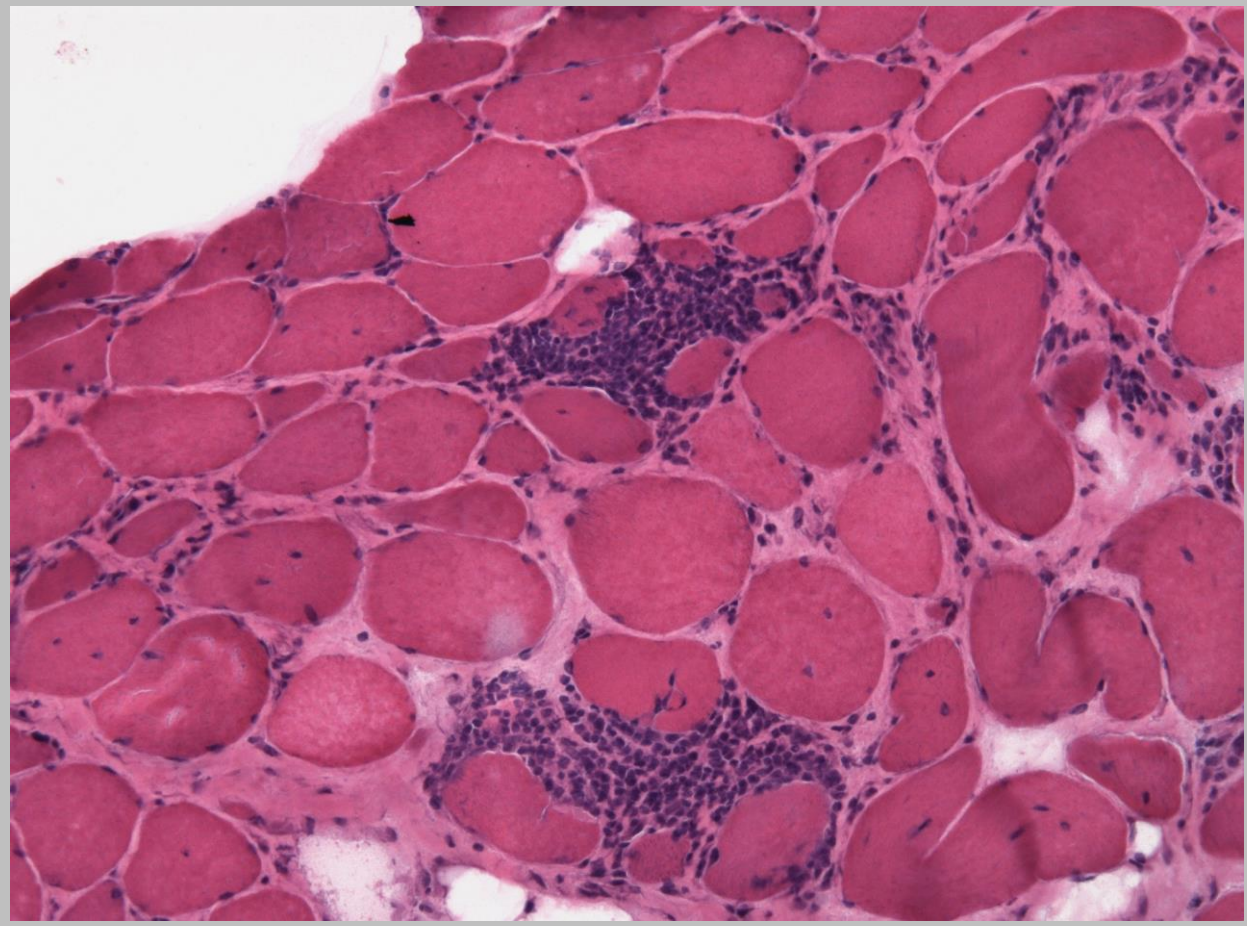


Dermatomyositis

The inflammatory infiltrate in the perimysial connective tissue. Characteristic, a few layers of atrophic fibers are present at the periphery of fascicles. In addition, a dramatic reduction in the intramuscular capillaries can be observed.

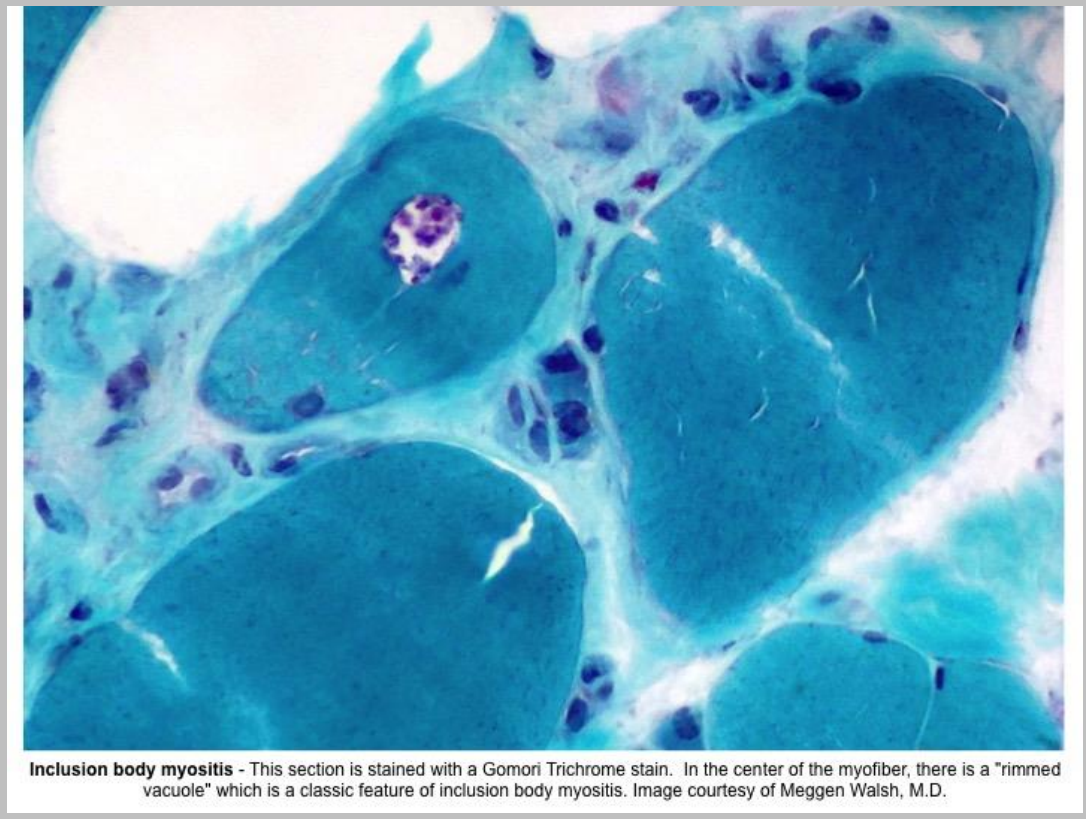
Polymyositis

- similar pattern of muscle involvement as dermatomyositis
  - inflammatory cells present in the *endomysium*
  - necrotic and regenerating fibers are present
  - no vascular injury
- without cutaneous involvement



Inclusion-body myositis

- pattern of inflammatory cell infiltrate – similar with polymyositis
- begins with the involvement of distal muscles
- muscle weakness may be asymmetric
- diagnostic : rimmed vacuoles in myocytes
    - *seen only in frozen sections!!!*



Inclusion body myositis - This section is stained with a Gomori Trichrome stain. In the center of the myofiber, there is a "rimmed vacuole" which is a classic feature of inclusion body myositis. Image courtesy of Meggen Walsh, M.D.

courtesy of AFIP and PathologyOutlines.com
http://www.pathologyoutlines.com/imgau/gomori1.jpg

Infectious myositis

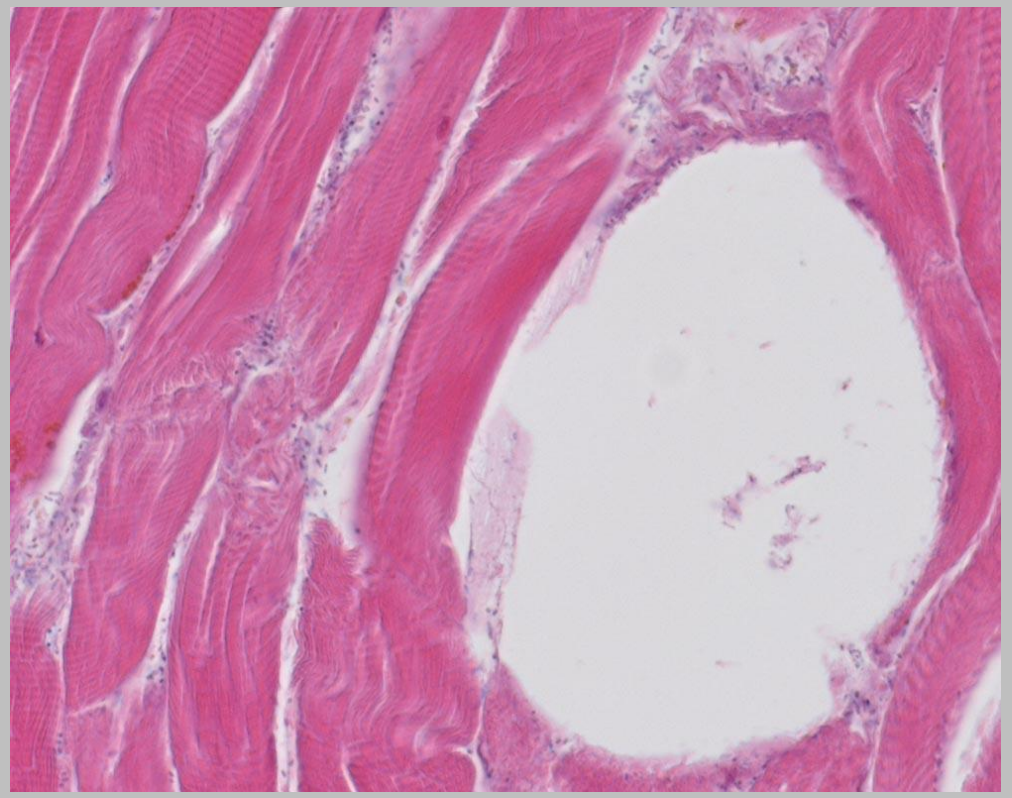
- any pyogenic infection of the soft tissue may produce acute suppurative inflammation

Regarding clostridial infections :

- swollen region, marked edema
- inflamed muscle, soft, blue-black, friable and semi-solid

} gangrene tissue

- microscopically :
  - *severe myonecrosis*
  - *extensive hemolysis*
  - *marked vascular injury, with thrombosis*



Clostridial gangrene – necrotic muscle with gas bubble

CENTRAL NERVOUS SYSTEM TUMORS

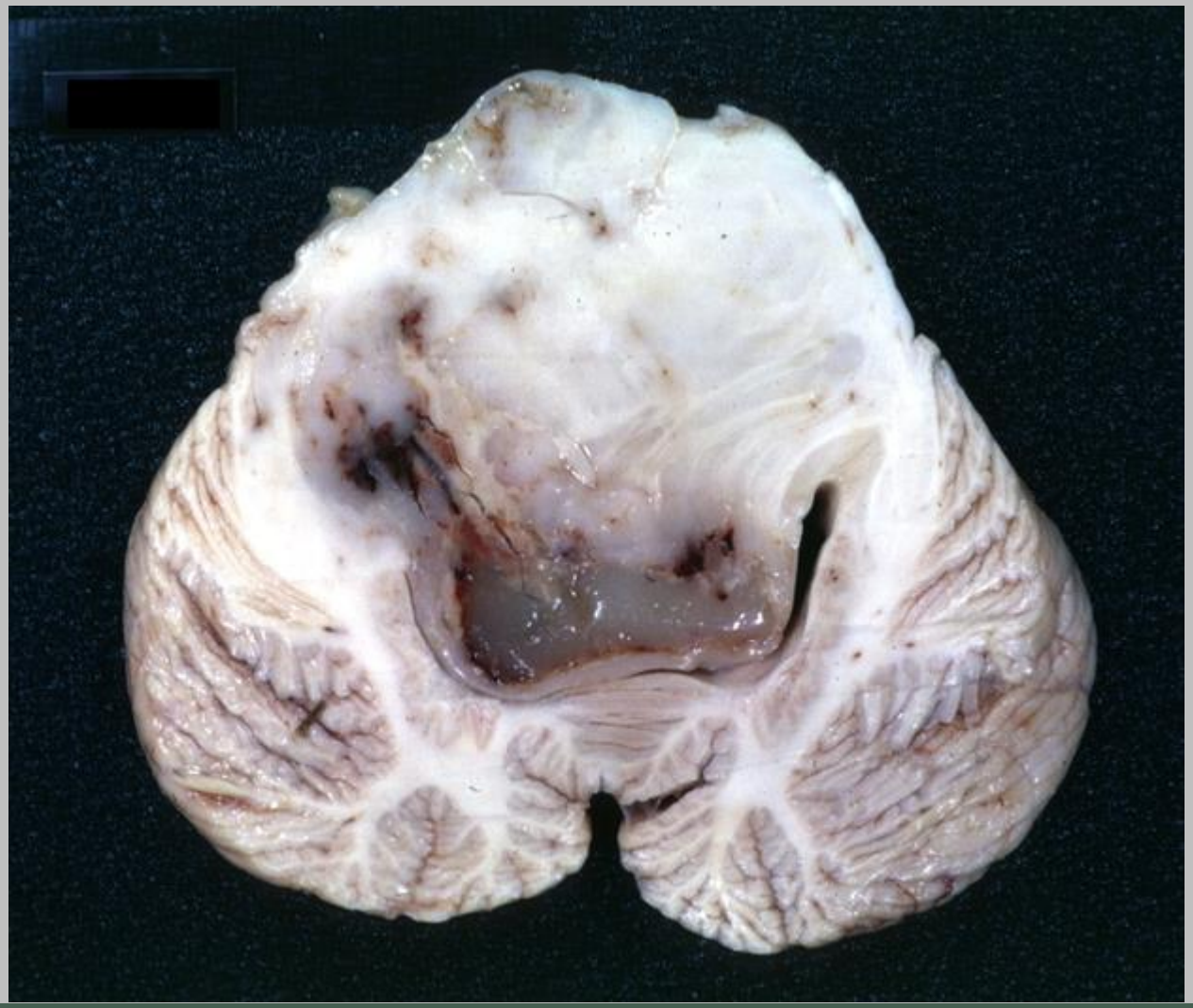
Primary CNS tumors constitute 2% of all "aggressive" neoplasms of the adults (metastatic tumors in brain and spinal cord are more common), and 20% of all cancers of childhood (being second only to leukemia as the most common childhood malignancy and are the most common pediatric solid tumors).

Characteristics that set them apart from neoplastic processes elsewhere in the body:

- ❑ the distinction between benign and malignant tumors is less evident than in other sites: some tumors with the histologic features of a benign neoplasm may infiltrate entire regions of the brain, leading to clinically malignant behavior;
- ❑ conversely, grossly (imagistic + intra-operative) well define-tumors, which apparently could be excised completely, bear the highest malignancy grade (and poor prognosis);
- ❑ in the brain, the surgical procedures are restricted by functional considerations, and some benign lesions may have lethal consequences because of their location.

Astrocytoma is a glioma composed of astrocytes

- develops in the cerebral hemispheres, midbrain, pons, cerebellum and in the spinal cord, predominantly in the thoracic and cervical segments;
- poorly defined, gray-white and infiltrates the brain / spinal cord with an indistinct margin



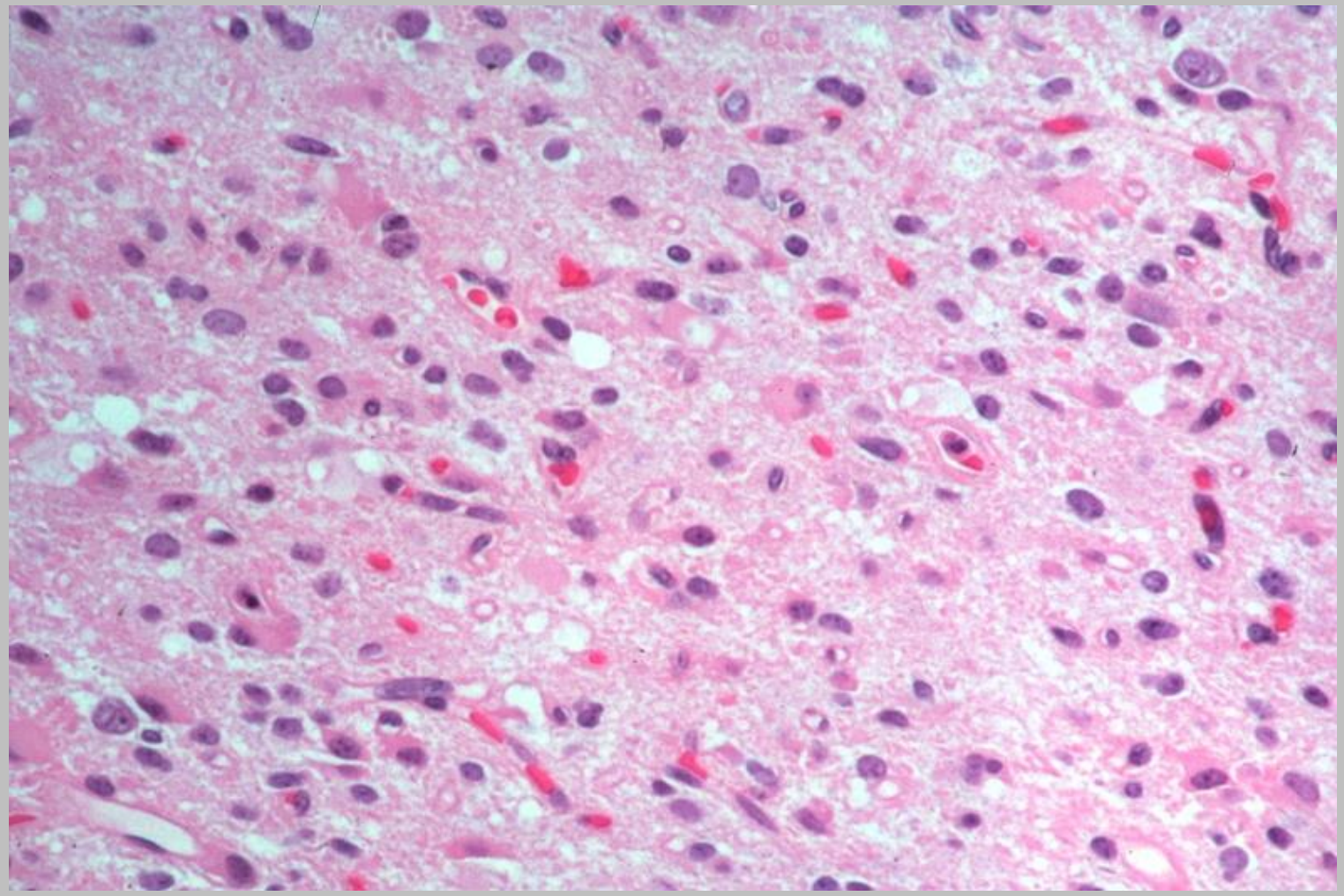
Glioma: Gross fixed tissue horizontal section brain stem and cerebellum with obvious gelatinous appearing neoplasm a pontine glioma

https://peir.path.uab.edu/library/picture.php?/4774/category/81

Astrocytoma

Microscopy:

- denser (compare with normal) cellularity;
- pleomorphic nuclei are dispersed randomly;
- matrix of slender glial cytoplasmatic processes, providing a distinct "fibrillary" appearance;
- microcystic degenerations
- diffuse border / indistinct margin with adjacent non-neoplastic parenchyma



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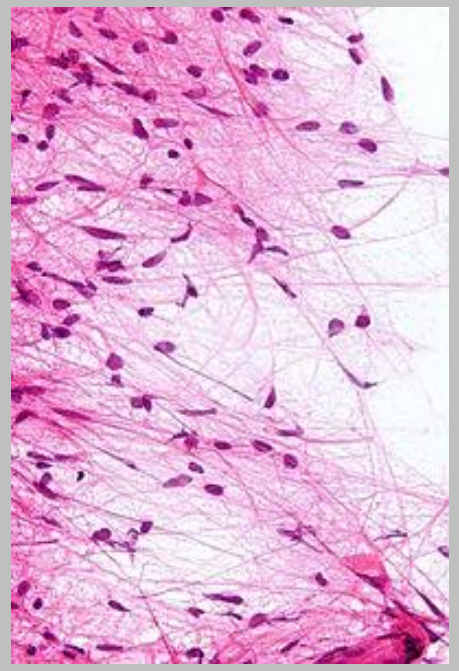
Morphologic variations of astrocytoma:

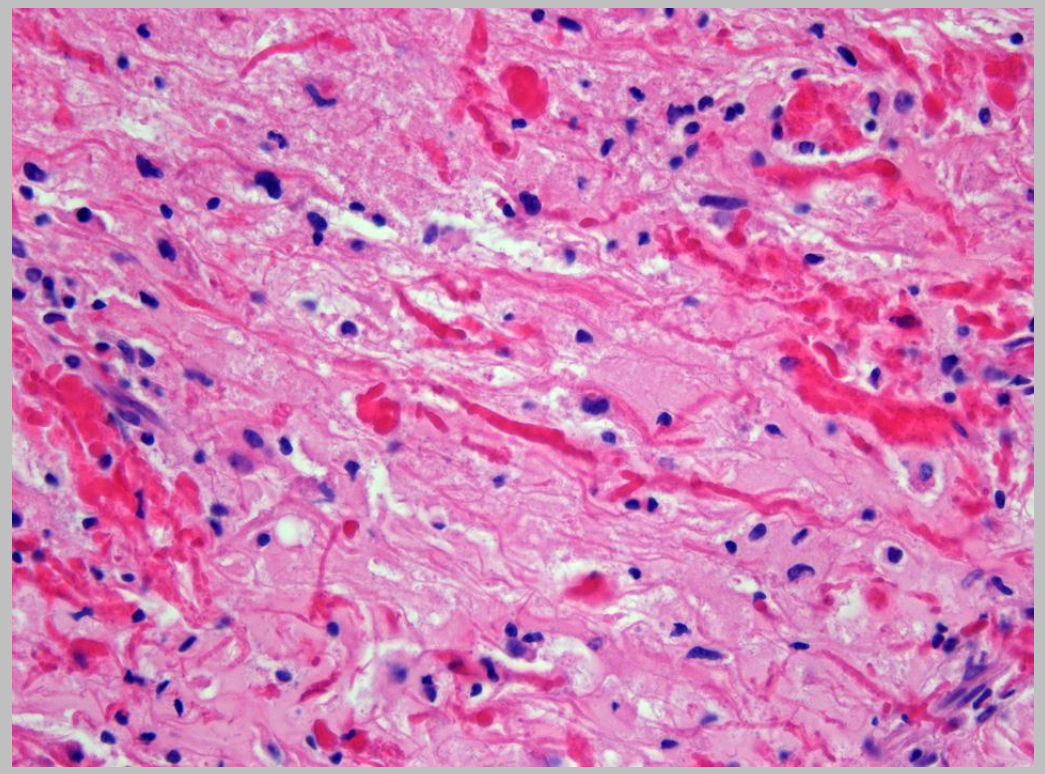
- **Fibrillary astrocytoma** – has intermediately dense glial processes;
- **Gemistocytic astrocytoma** – the tumor cells have abundant, eosinophilic cytoplasm;
- **Pilocytic astrocytoma** – it typically occurs in children and is often cystic; microscopically, the tumor is composed of bipolar cells with long, thin "hair-like" processes and contains Rosenthal fibers and microcysts;
- **Anaplastic astrocytoma** is a less differentiated tumor which is distinguished from the other astrocytomas by greater cellularity, cellular pleomorphism and anaplasia.
- **Glioblastoma multiforme** is the extreme expression of anaplasia among the glial neoplasms

https://upload.wikimedia.org/wikipedia/commons/thumb/b/b1/Pilocytic_astrocytoma_-_smear_-_very_high_mag.jpg/450px-Pilocytic_astrocytoma_-_smear_-_very_high_mag.jpg



Pilocytic astrocytoma, showing characteristic bipolar cells with long pilocytic (hair-like) processes. Smear preparation. H&E stain

https://upload.wikimedia.org/wikipedia/commons/9/94/Rosenthal_HE_40x.jpg



Pilocytic astrocytoma: Rosenthal-fibres, elongated eosinophilic structures , background of thin "hair-like" processes.

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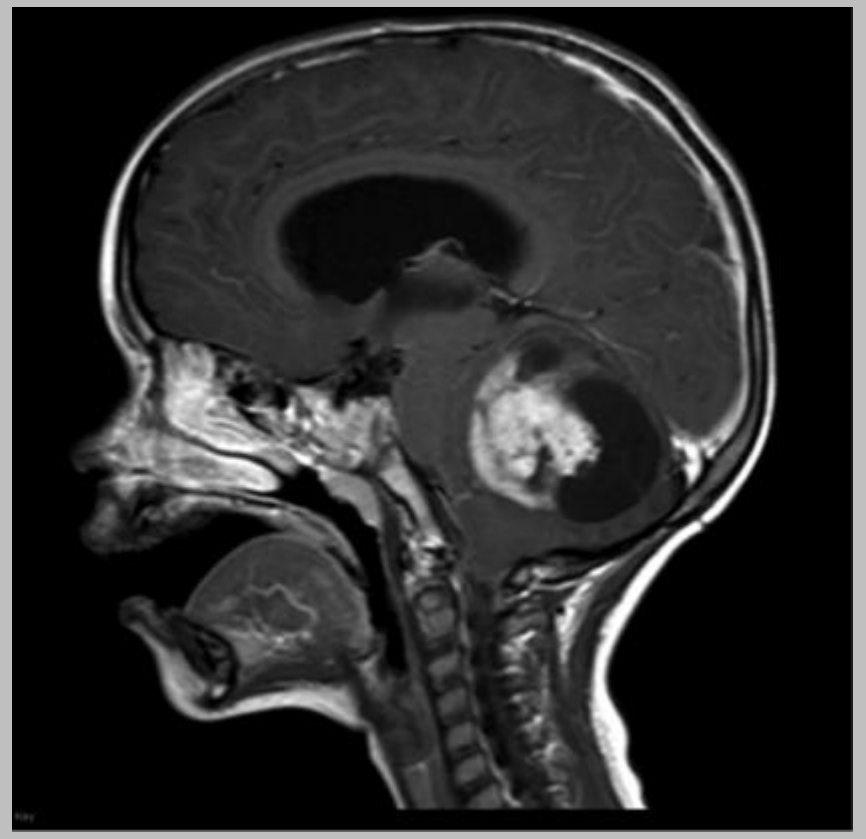


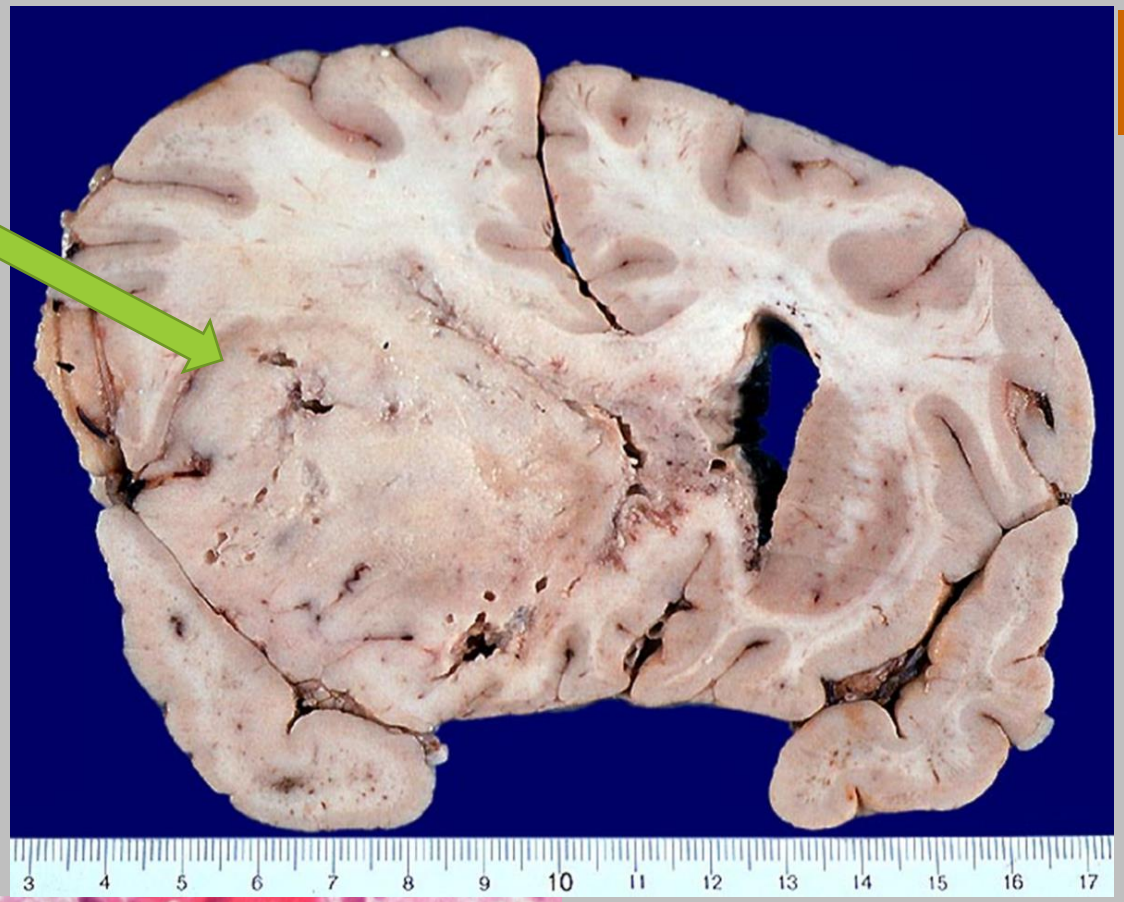
There is a large cystic mass with a brightly enhancing mural nodule in the cerebellum.

http://images.radiopaedia.org/images/25692/371b55cc14912ob9cc64dd4f6febff.jpg

Anaplastic astrocytoma:

gross: left F-T mass with obliteration of left lateral ventricle (anterior horn)

μ: much denser cellularity, greater cellular pleomorphism sometimes with conspicuous plump eosinophilic cells (gemistocytes), diffusely infiltrative margin.



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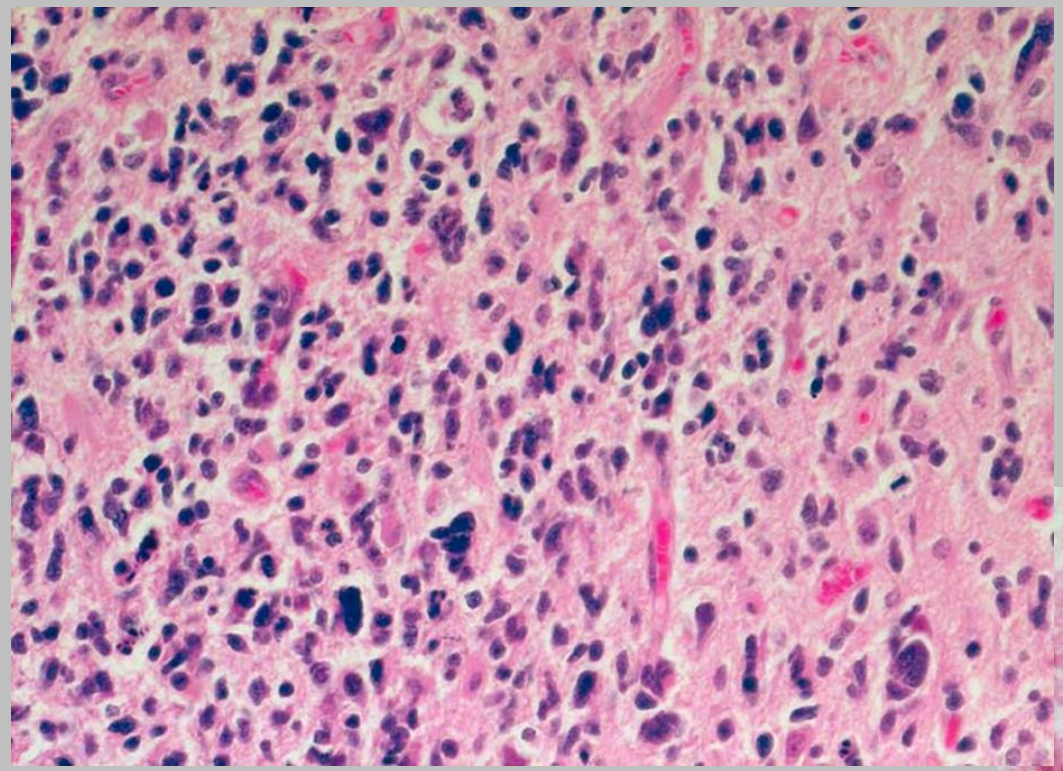

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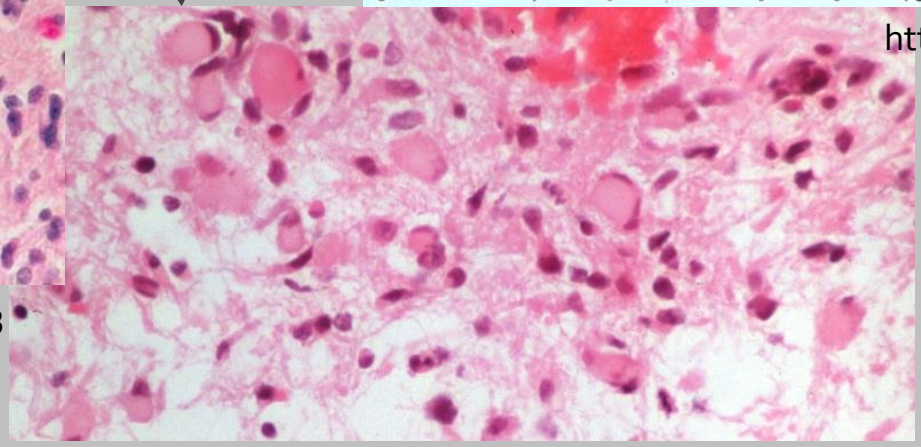

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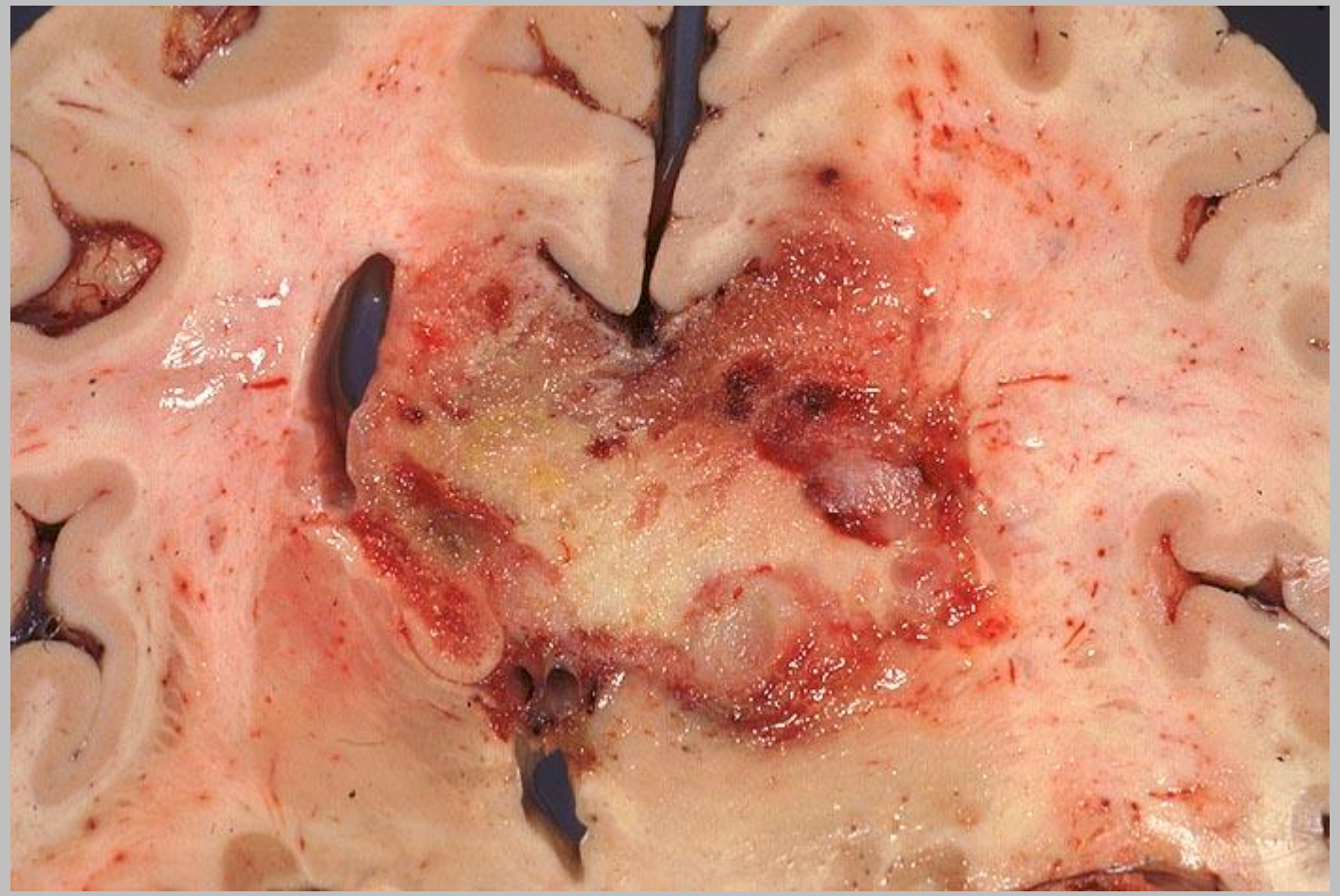

Glioblastoma = the extreme expression of aggressiveness among the glial neoplasms:

- typically infiltrates extensively, frequently crossing the *corpus callosum* and producing a bilateral lesion likened to a butterfly in its gross configuration;
- is a mixture of firm, white areas and softer, yellow foci of necrosis and remote hemorrhage (darker red to brown), as well as cystic change and red areas of recent hemorrhage; it is this appearance that gives its appellation: "multiforme".

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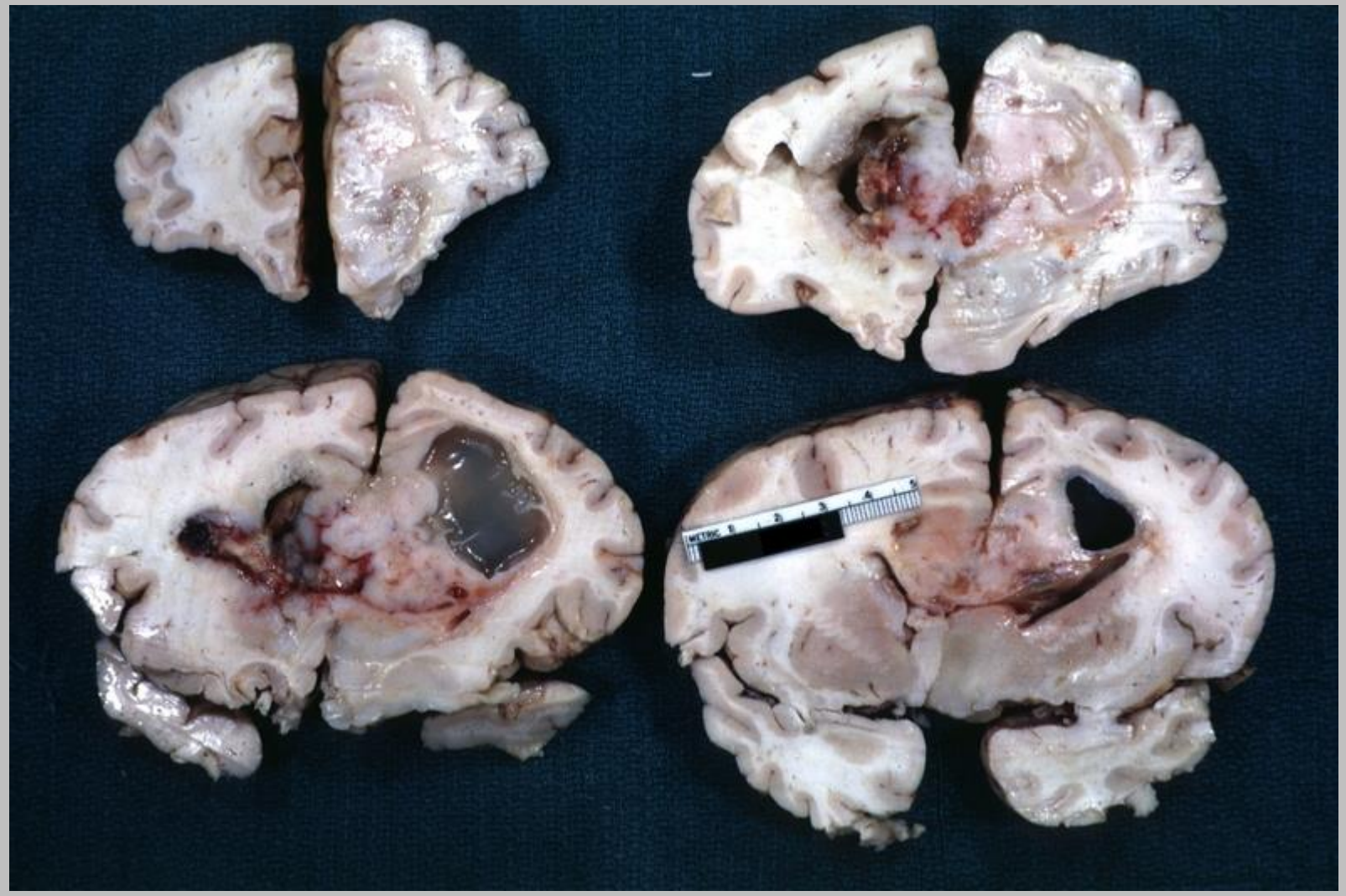

Glioblastoma Multiforme

Gross fixed tissue, coronal successive sections of cerebral hemispheres: large and typical GBM ("butterfly" lesion) that has extended down involving the brainstem.

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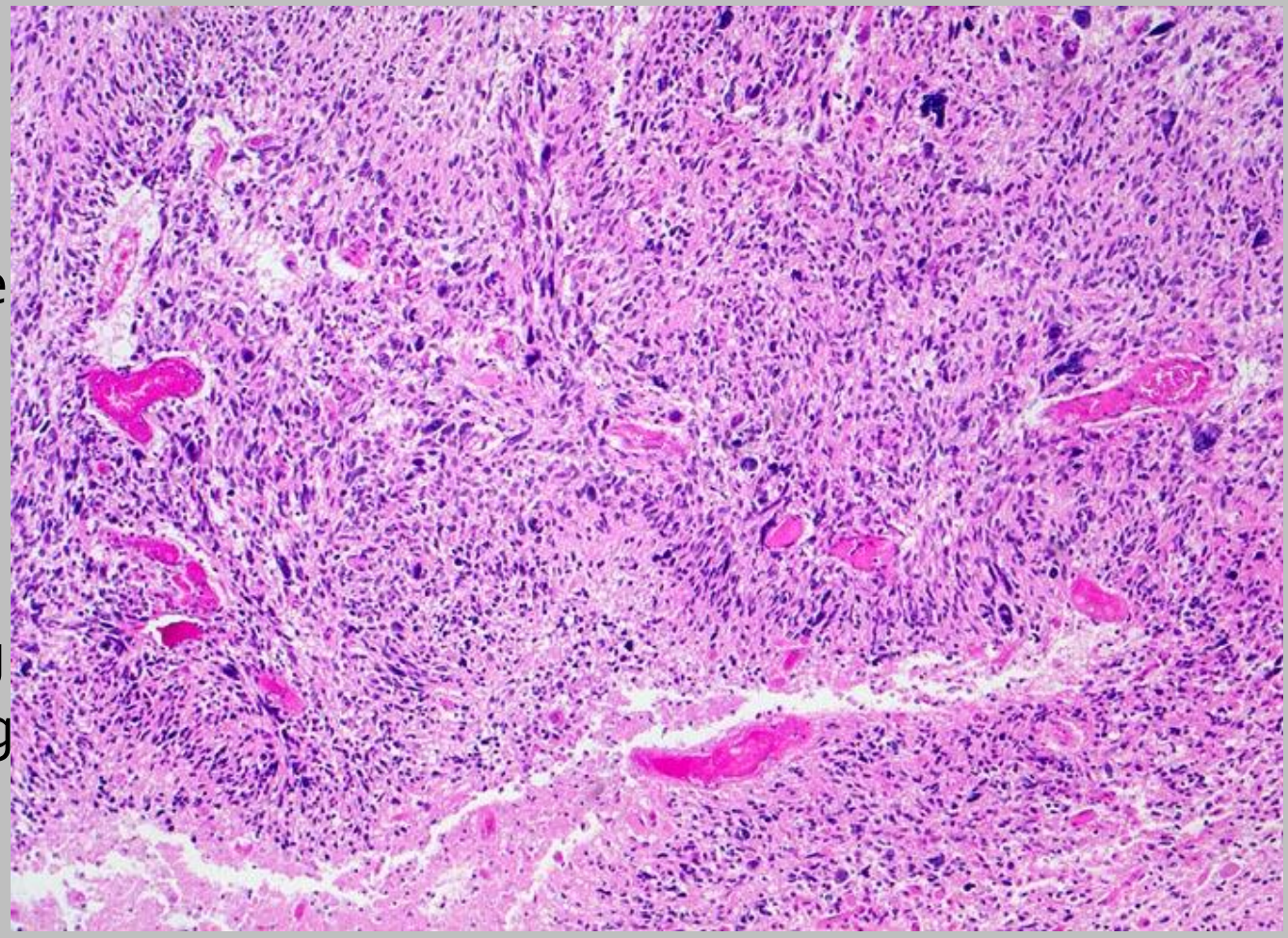
The **cardinal histopathological features** of glioblastoma multiforme (GBM) are:

1. marked cellularity, with variable degrees of cellular pleomorphism and multinucleated cells, frequent mitoses = the extreme expression of anaplasia among the glial neoplasms;
2. serpentine areas of tumor necrosis which occurs in areas of hipercellularity with highly anaplastic tumor cells crowded along the edges of the necrotic regions, producing so-called palisading;
3. endothelial cell proliferation, which creates clusters of small vessels, referred to as "glomeruloid" formations.



Glioblastoma multiforme (GBM): Highly cellular tumor with band-like / serpiginous necrosis.

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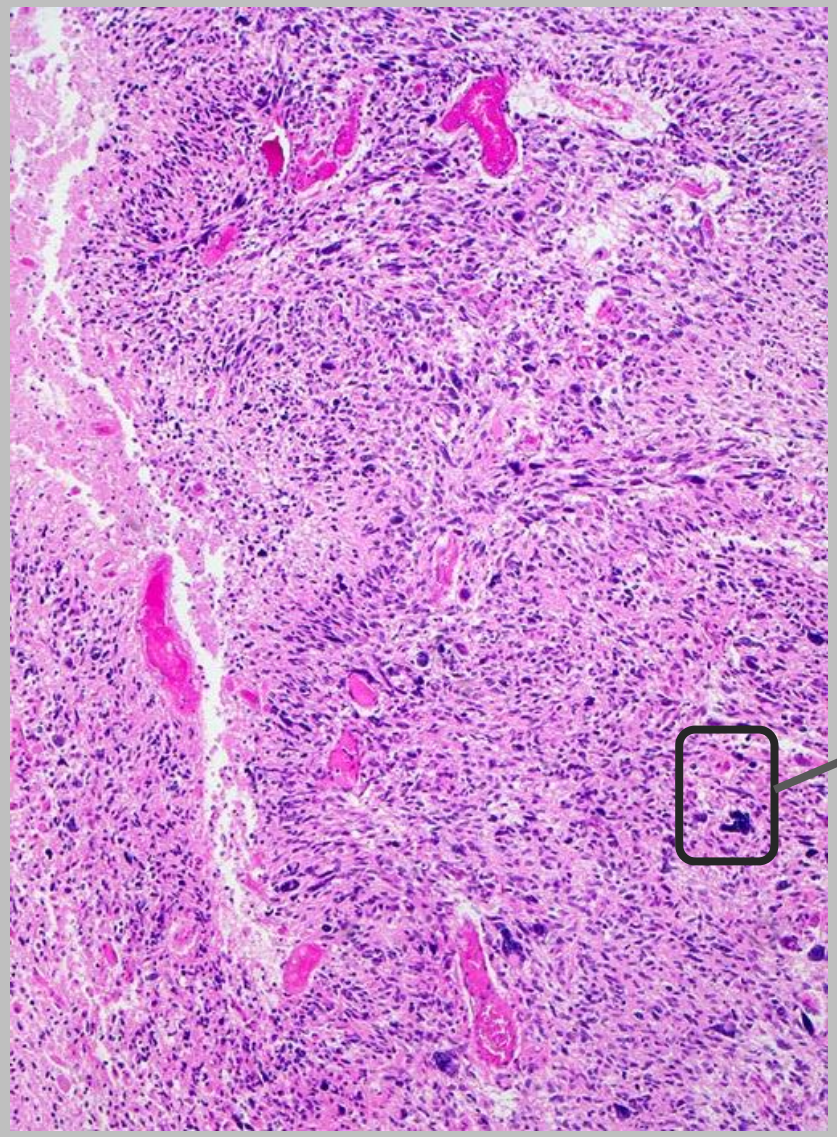

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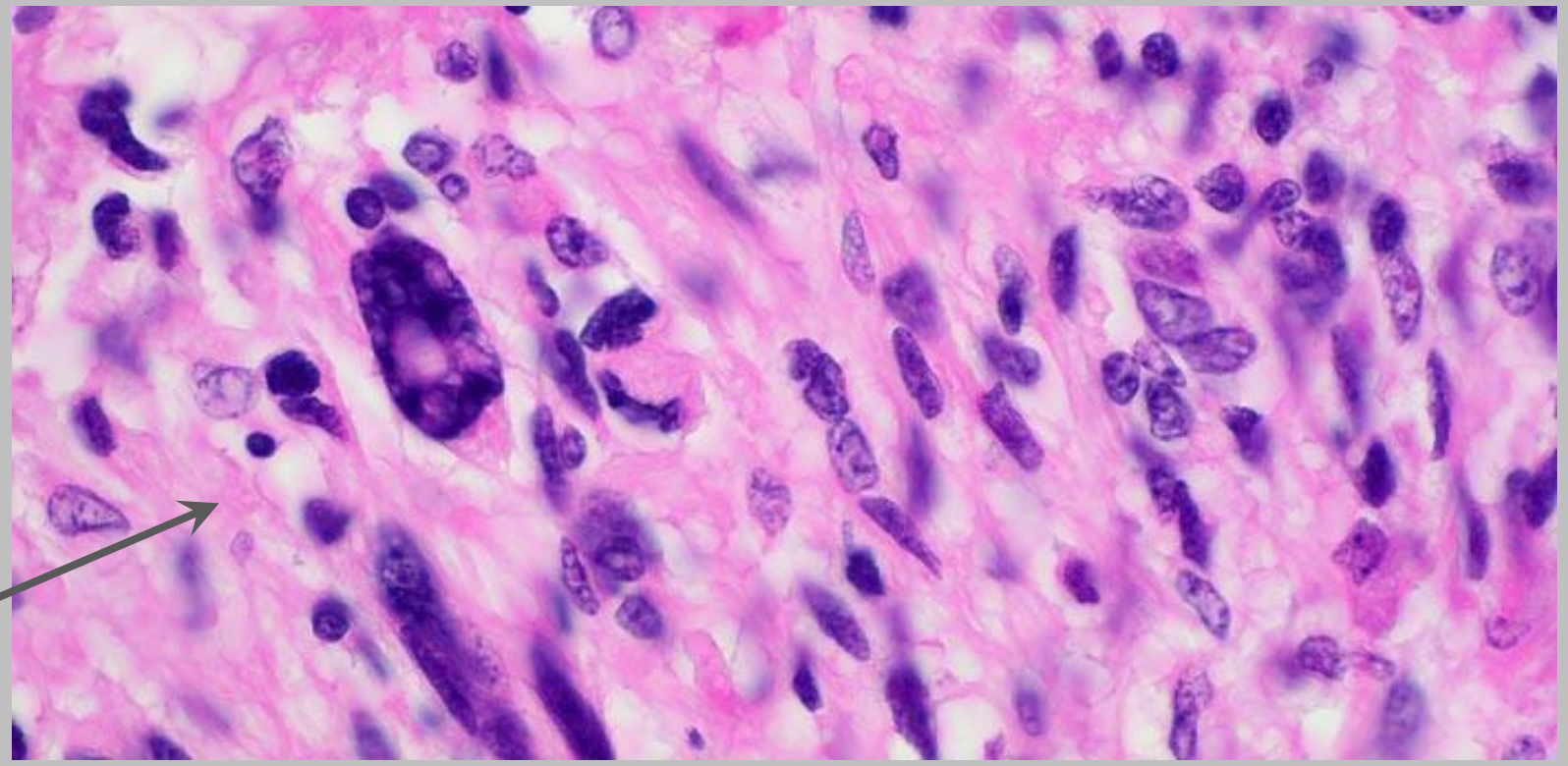

1. **marked cellularity**, with obvious **cellular pleomorphism** and multinucleated cells, even bizzarre cells

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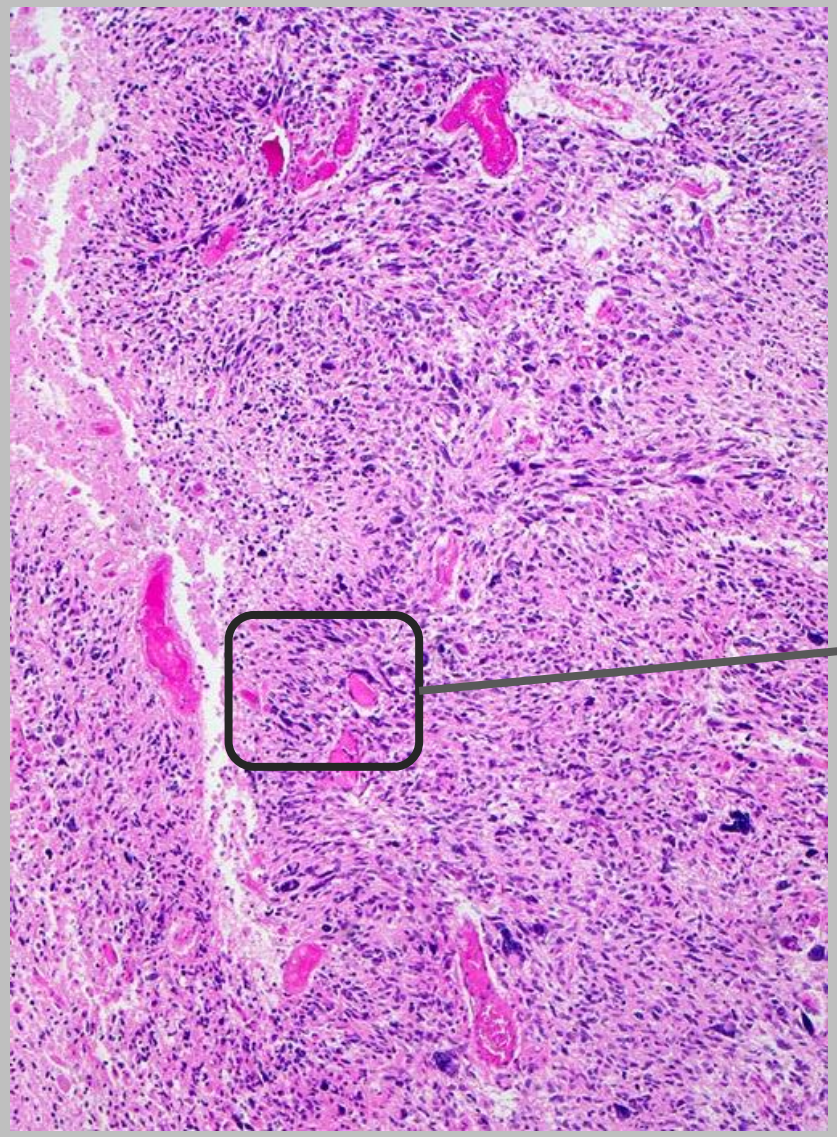

Glioblastoma multiforme (GBM): Highly cellular tumor with band-like / serpiginous necrosis.

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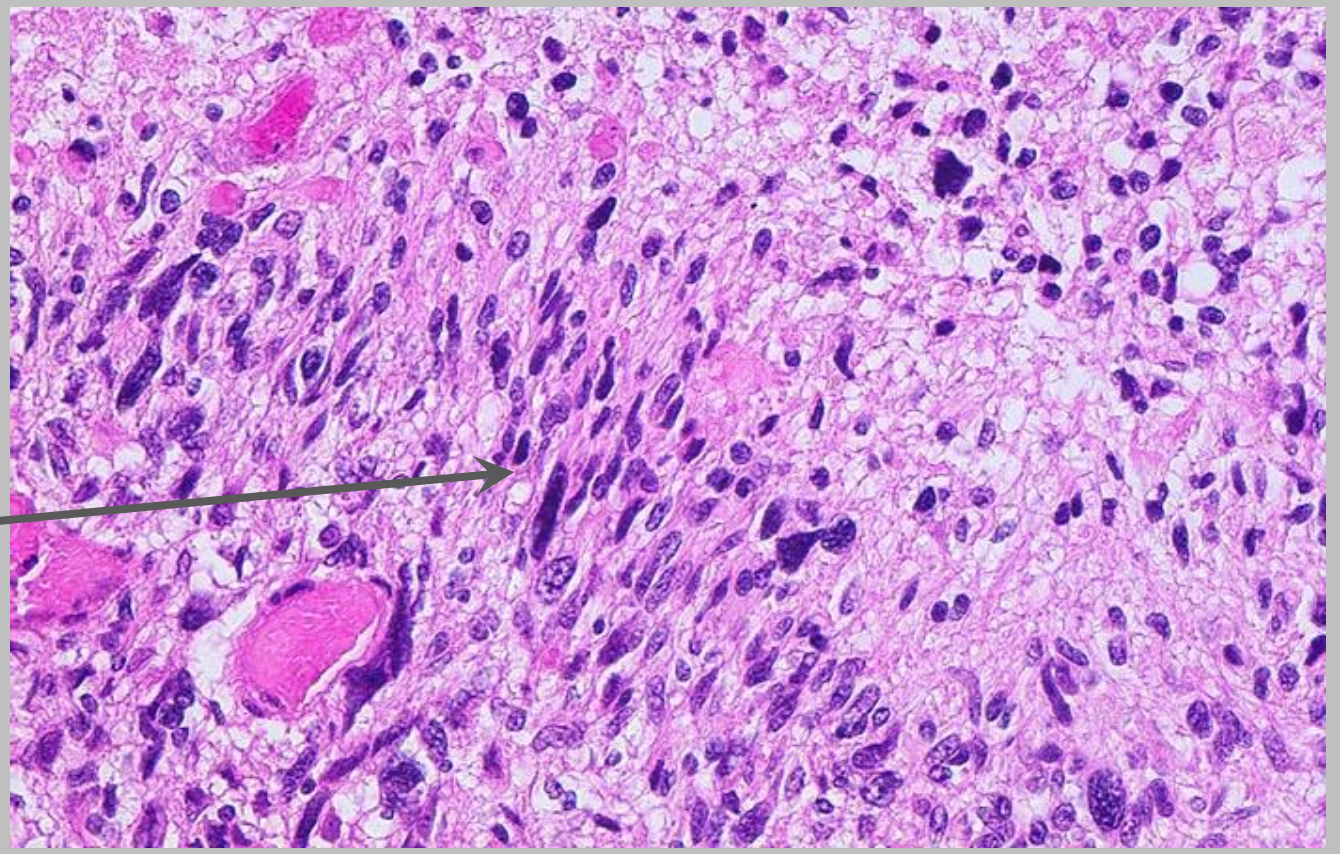

2. Palisading of crowded tumor cells adjacent to tumor necrosis, producing so-called serpiginous or **"pseudopalisading necrosis"**

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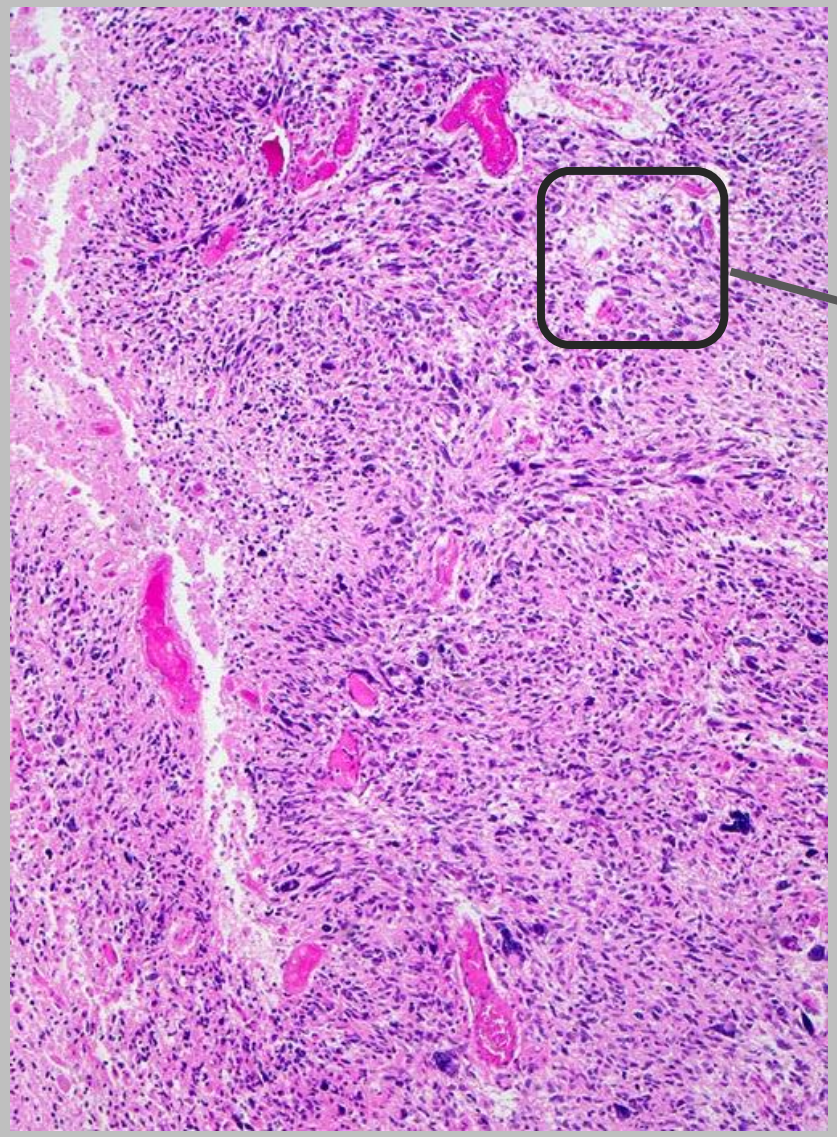

Glioblastoma multiforme (GBM): Highly cellular tumor with band-like / serpiginous necrosis.

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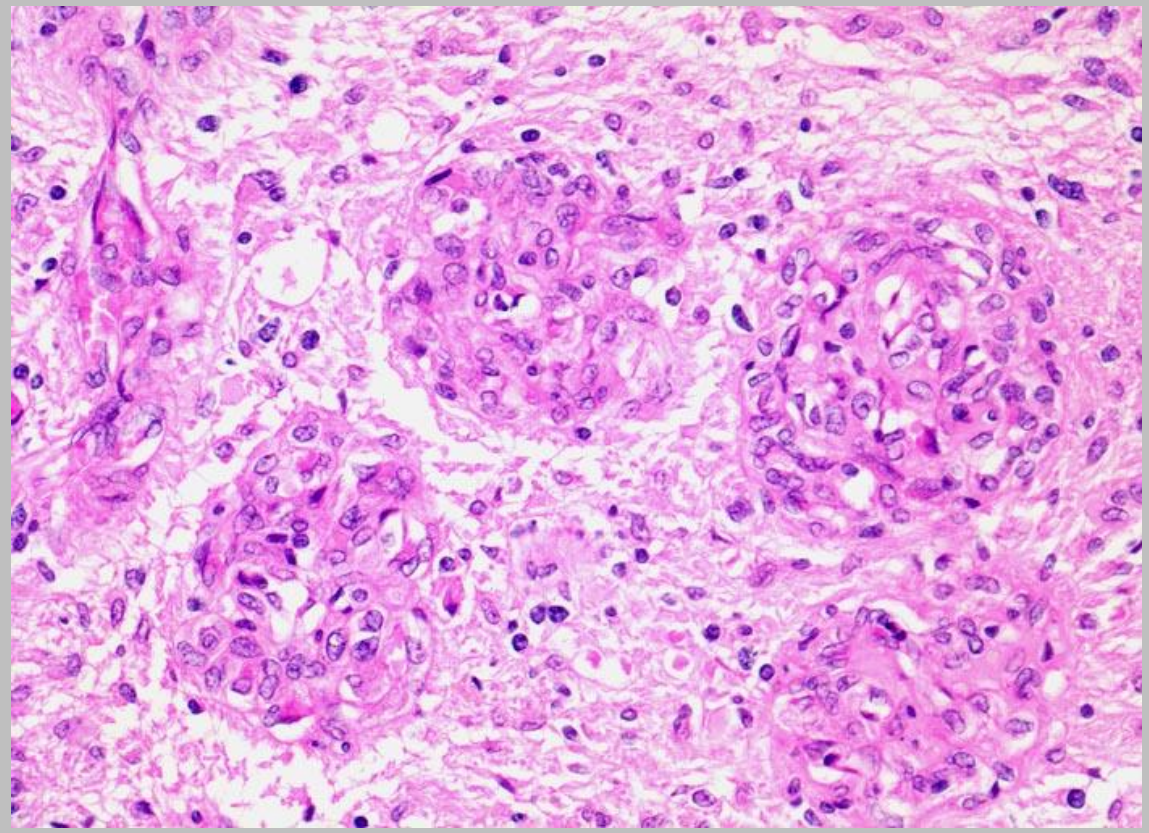

3. endothelial cell proliferation, which creates clusters of small vessels looking like kidney's glomerular / capillaries tufts, referred to as **"glomeruloid" vessels** (formations).

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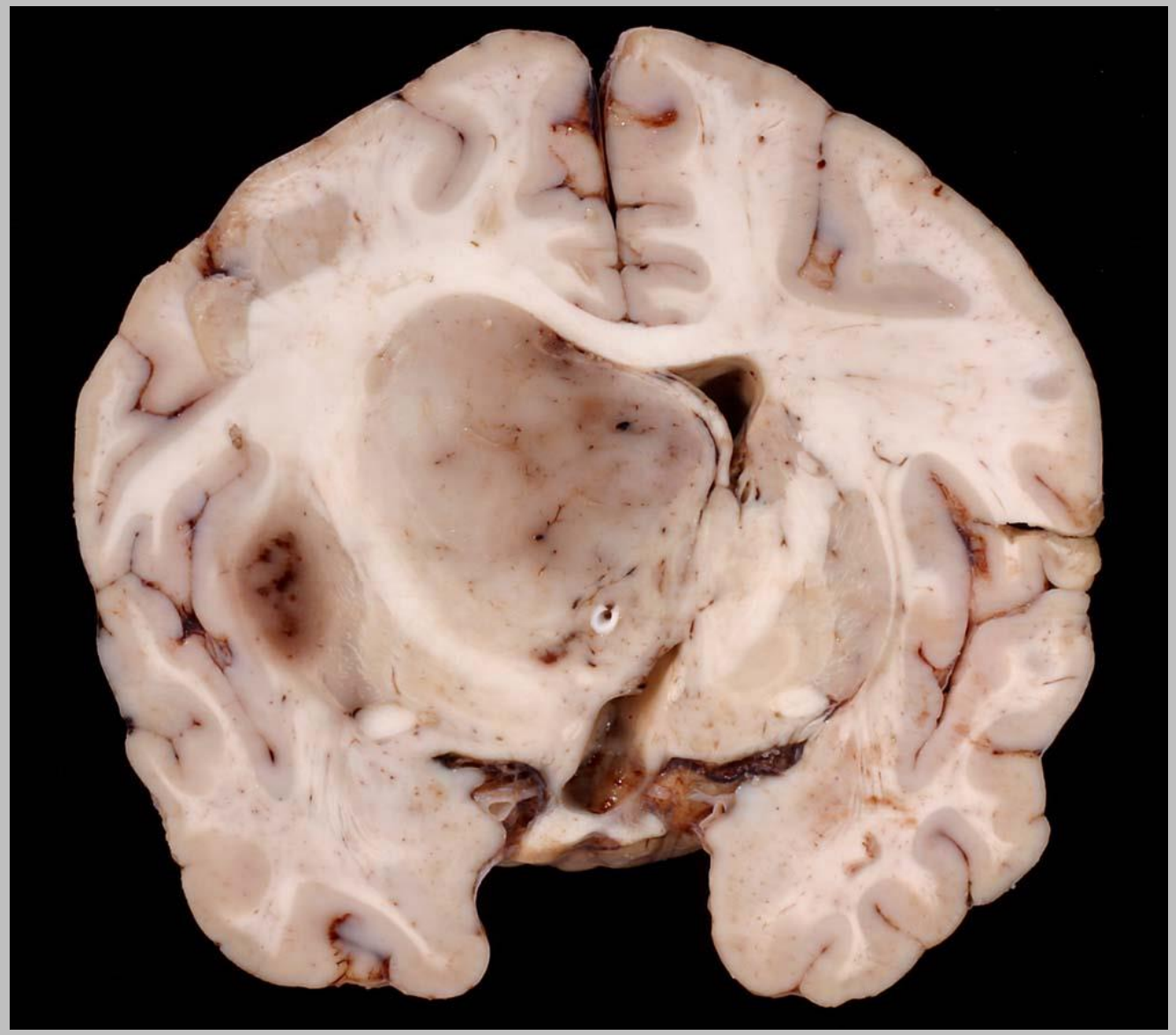
Oligodendroglioma is a glioma composed of oligodendrocytes:

- arises in the white matter, predominantly in the cerebral hemispheres;
- grossly well-circumscribed, gelatinous, gray masses, often with cysts, focal hemorrhage, and calcification.



Oligodendroglioma: grey tumor compressing the left lateral ventricle.

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Oligodendroglioma

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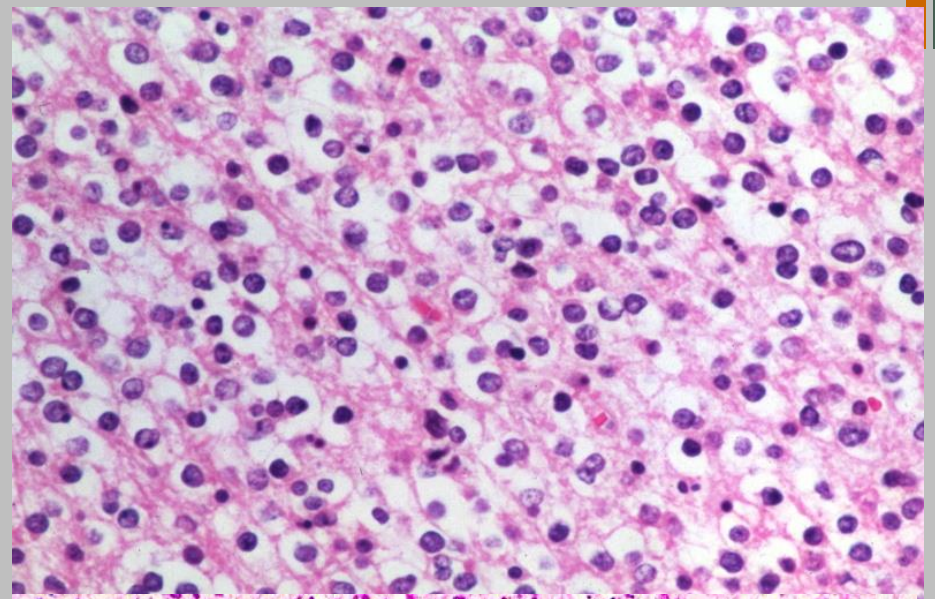

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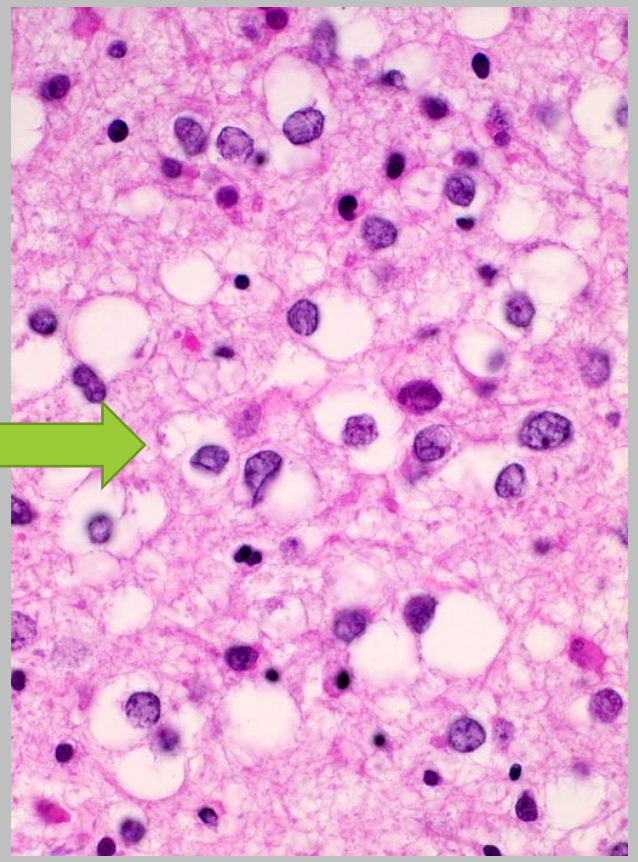
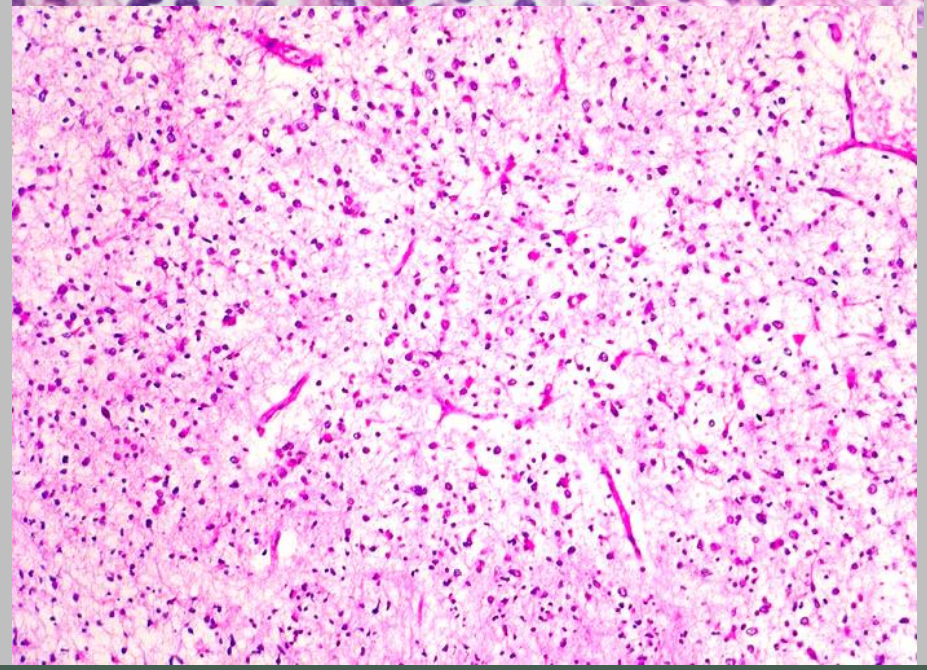
Microscopy:

- sheets of regular cells with spherical nuclei containing finely granular chromatin (similar to normal oligodendrocytes);
- the nuclei are surrounded by a clear halo of cytoplasm, "fried eggs" appearance;
- typically, the tumor contains a delicate network of anastomosing capillaries;
- calcification, present in most cases (90%), ranges from microscopic foci to massive deposition
- diffuse border / indistinct margin with adjacent non-neoplastic parenchyma





ODG: network of branching capillary branching capillaries

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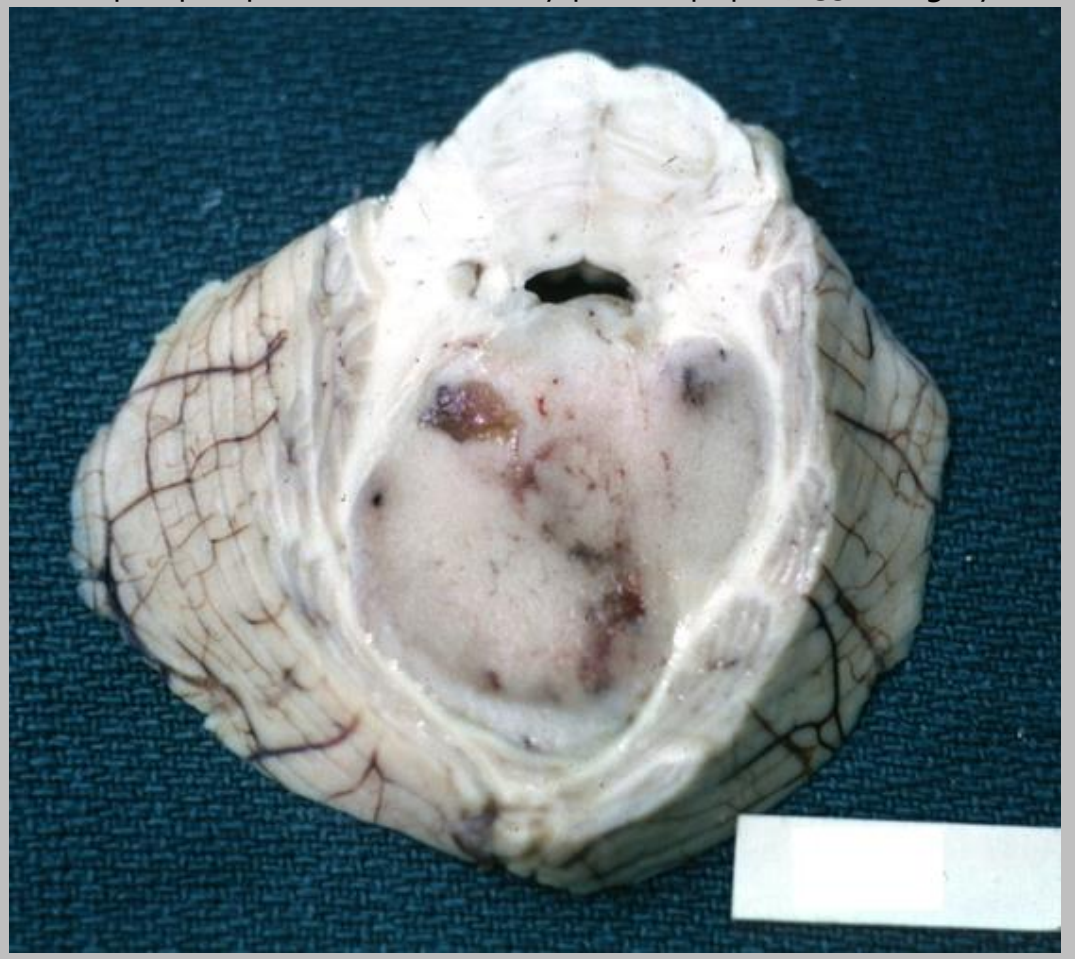
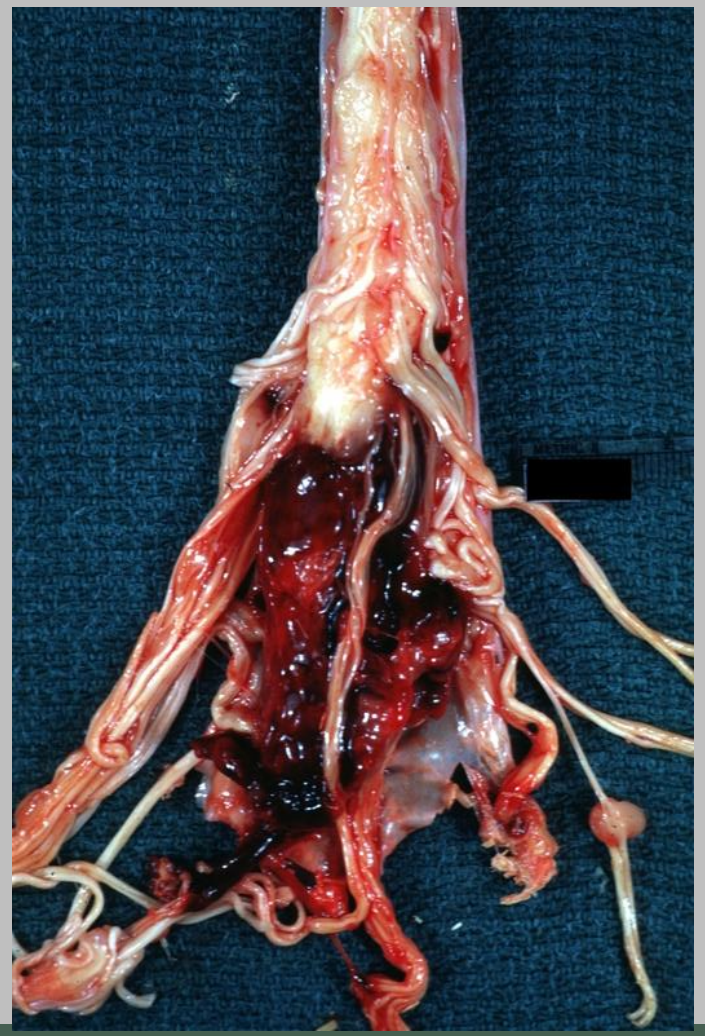
https://peir.path.uab.edu/library/picture.php?/4835/category/81

Ependymoma is a glioma composed of ependymal cells:

- arises next to the ependymal-lined ventricular system, mostly near the fourth ventricle (extending from its floor) or in the spinal cord.



Ependymoma: Gross fixed tissue horizontal section pons and cerebellum obvious neoplasm in the fourth ventricle



Spinal cord and *filum terminale* with an obvious tumor mass, clotted hemorrhage and a mucoid material (probably a myxo-papillary variant of ependymoma).

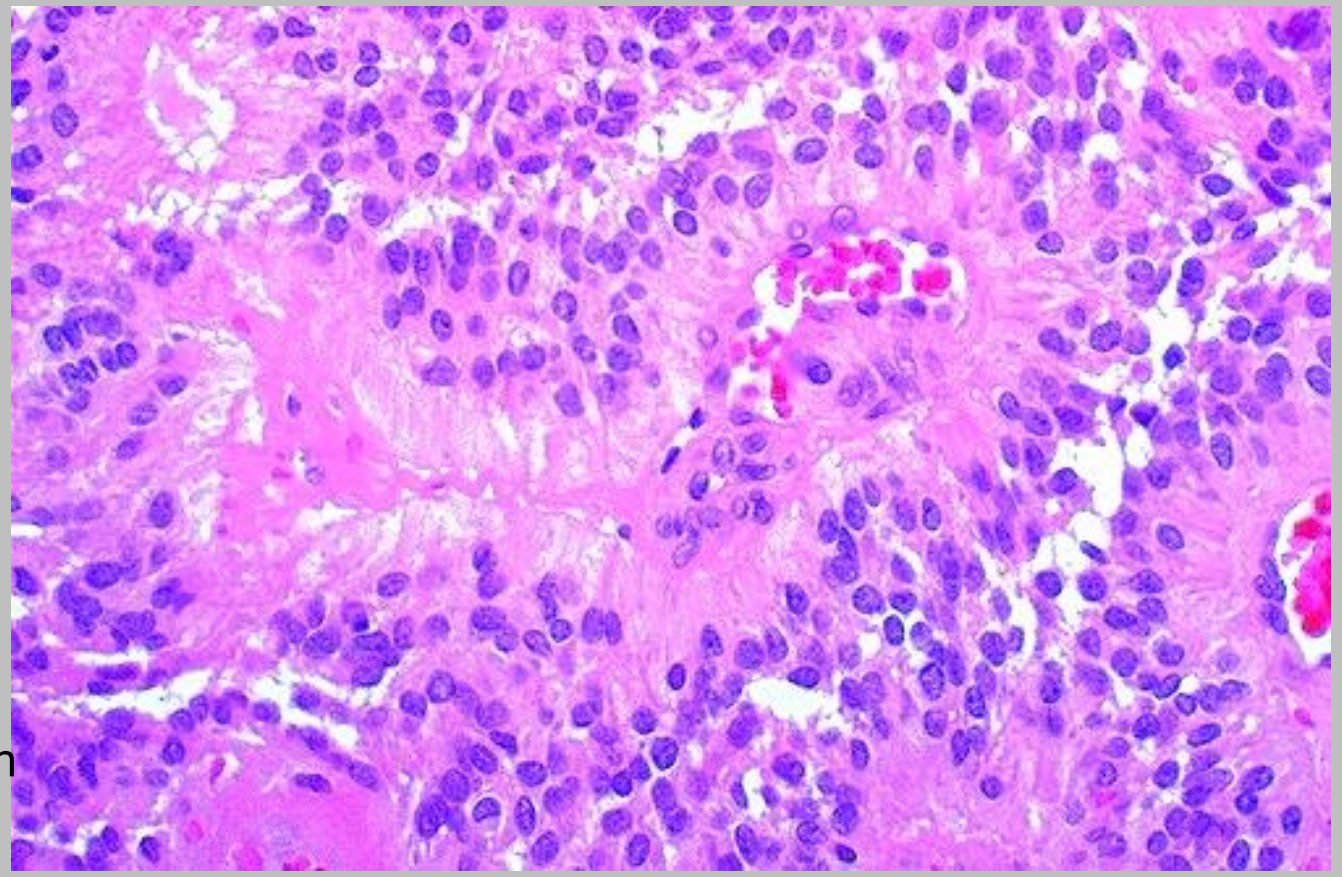
https://peir.path.uab.edu/library/picture.php?/4602/category/81

Ependymoma

https://webpath.med.utah.edu/CNSHTML/CNS122.html

Microscopy:

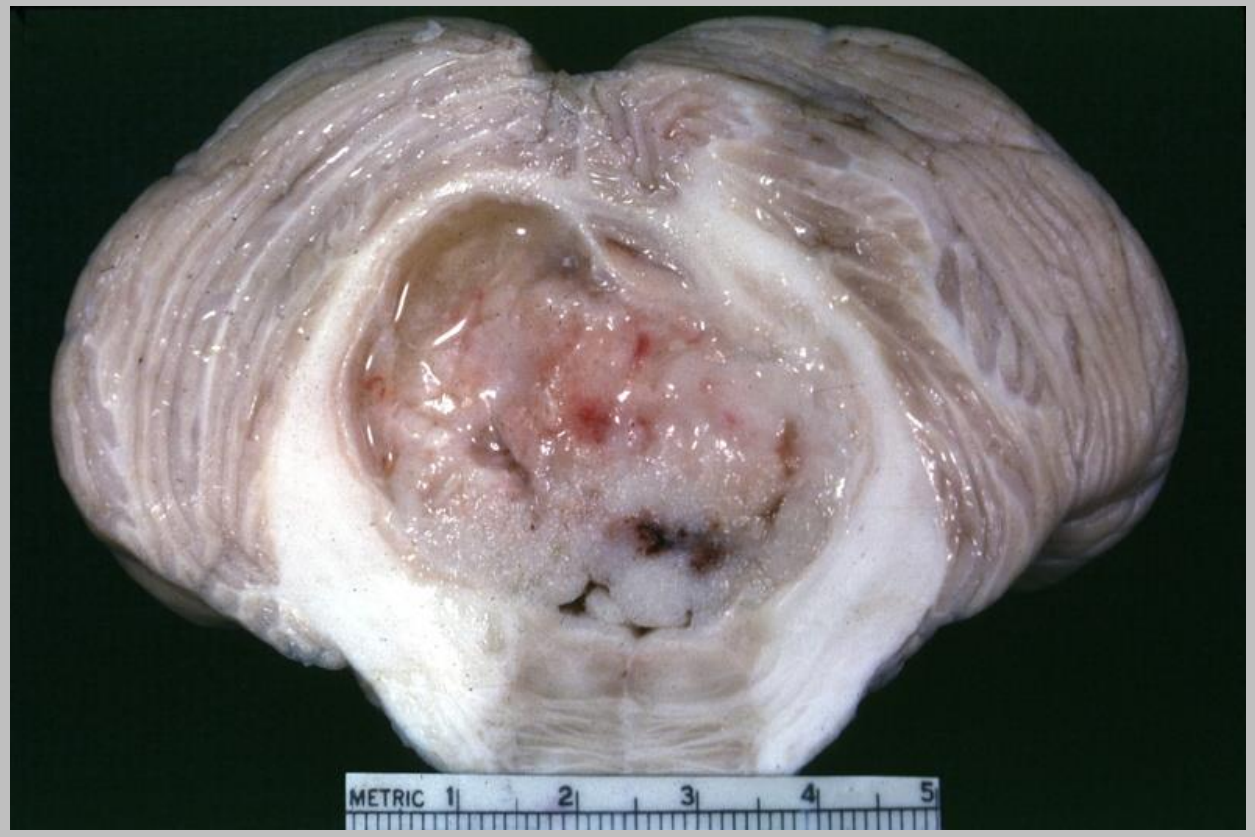
- cells with regular, round to oval nuclei with abundant granular chromatin, disposed in a fine fibrillary background that may be very dense;
- tumor cells may form gland-like structures that resemble the embryologic ependymal canal with long, delicate processes extending into a lumen, forming **ependymal (true) rosettes**; *infrequent finding!!*
- tumor cells are arranged around vessels with an intervening zone (free of nuclei) consisting of thin ependymal processes directed toward the vessel wall - **perivascular rosettes** / pseudorosettes; *common finding!!*
- better demarcated from adjacent non-neoplastic brain than astrocytomas.

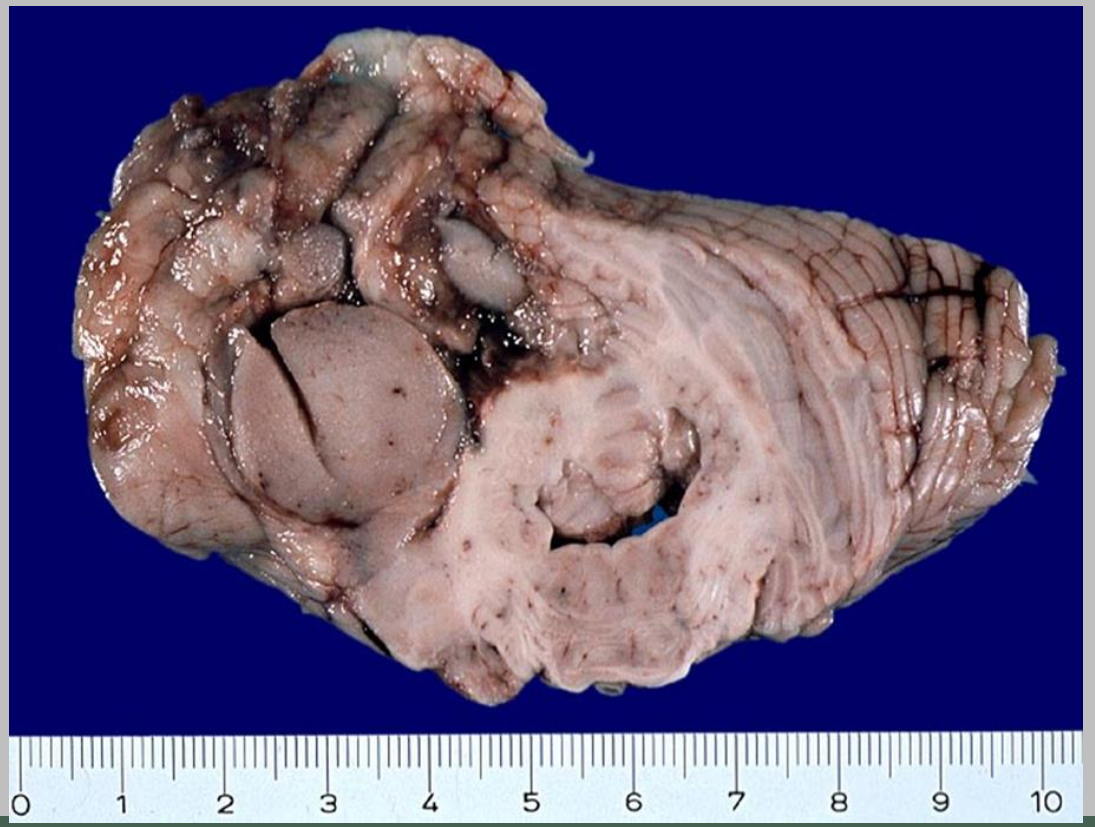


Ependymoma: rosettes (most of them perivascular & single one ependymal? – upper left corner).

***Medulloblastoma* is composed of primitive, undifferentiated cells**:

- predominantly in children (the peak incidence – 7 y-o) and exclusively in the cerebellum;
- the midline of the cerebellum (vermis) – childhood; lateral location (cerebellar hemisphere) more often in adults;
- well circumscribed, gray, and friable and may be seen extending to the surface of the cerebellar folia and involving the leptomeninges.





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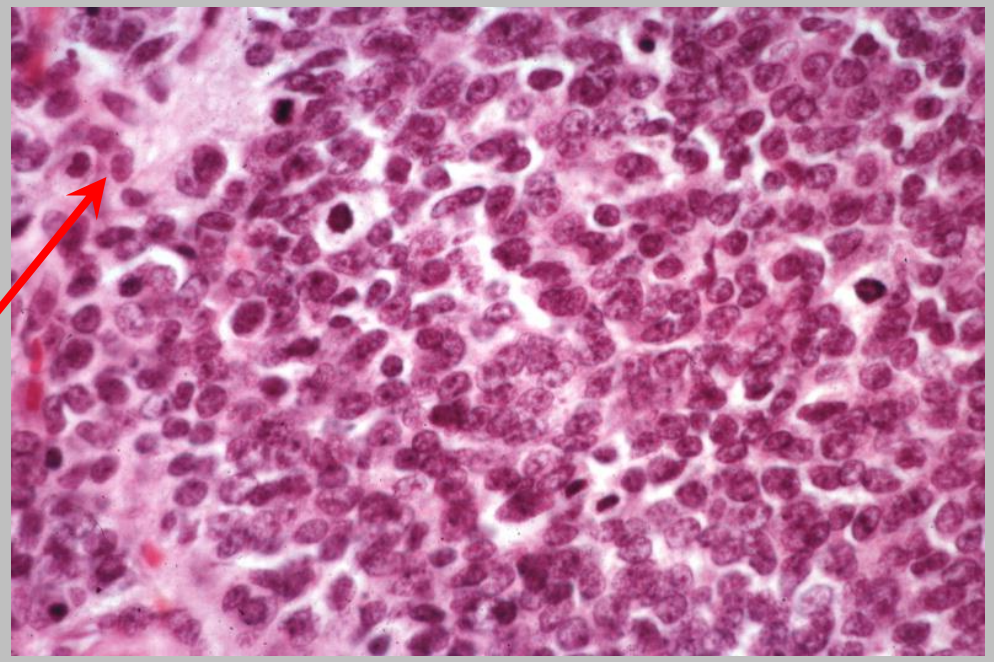
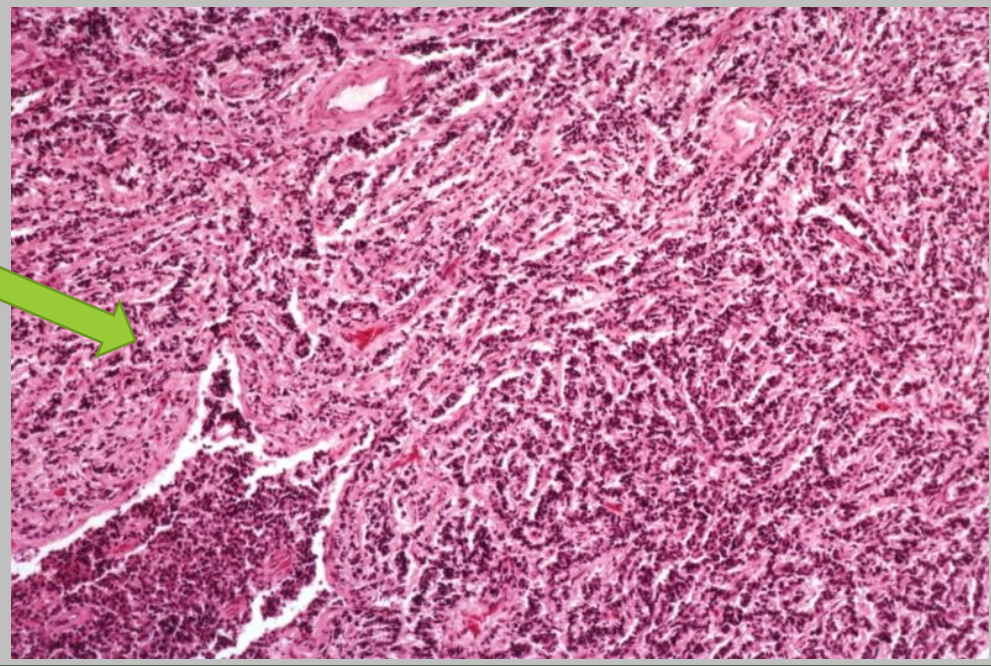
Medulloblastoma

https://peir.path.uab.edu/library/picture.php?/5325/category/82



Microscopy:

- extremely cellular, referred to as a **"blue cells tumor"**;
- nuclei are hyperchromatic, often rounded or elongated, arranged sometimes around a fibrillar core, forming the Homer-Wright **neuroblastic rosettes**
- mitoses are abundant and markers of cellular proliferation are detected in a high percentage in the cells;
- the cells have little cytoplasm and are often devoid of specific features of differentiation ("primitive cells");
- at the edges of the main tumor mass, medulloblastoma cells have a propensity to form linear chains of cells extending through the neuropil to penetrate the pia, and seed into the subarachnoid space: dissemination through the cerebrospinal fluid (CSF), presenting as nodular masses through the neuraxis: a common complication.



https://peir.path.uab.edu/library/picture.php?/5326/category/82

Meningioma arises from the meningothelial cells of the arachnoid:

- are predominantly benign tumors of adults;
- common sites include the parasagittal aspect of the convexity, dura over the lateral convexity, the wing of the sphenoid, olfactory groove, the *sella turcica* or along the spinal cord;
- most appear as solitary, well-circumscribed, masses of variable sizes with a **dural base** that compress underlying brain, but are easily separated from it;
- the mass is usually encapsulated with thin, fibrous tissue and may have a bosselated or polypoid appearance;
- firm, may have a finely gritty consistency, reflecting few calcifications, or they may be extremely calcified with psammoma bodies or even contain metaplastic bone.

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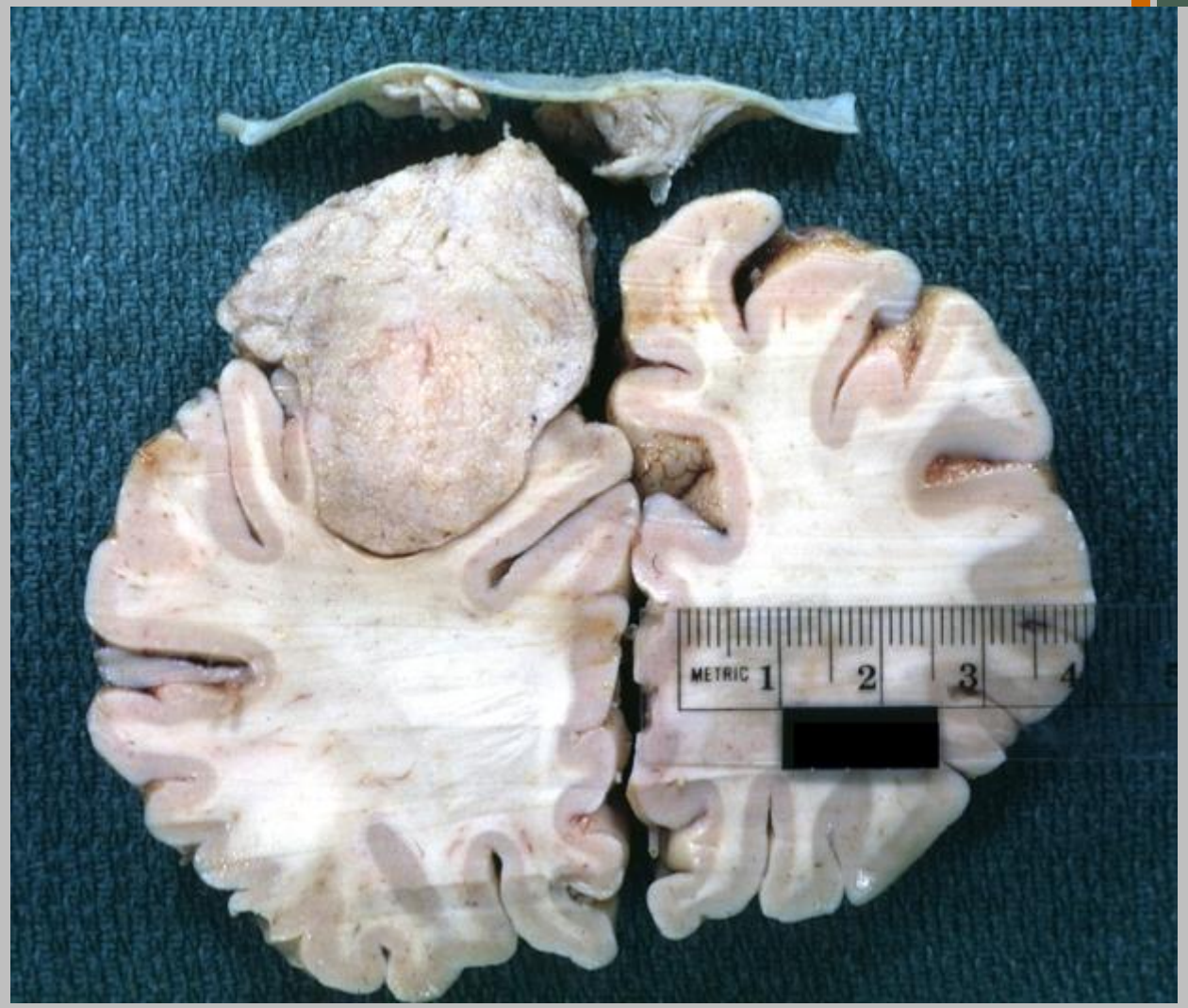

Meningioma: typical meningioma in frontal lobe area, parasagital from convexity *(falx cerebri)*.

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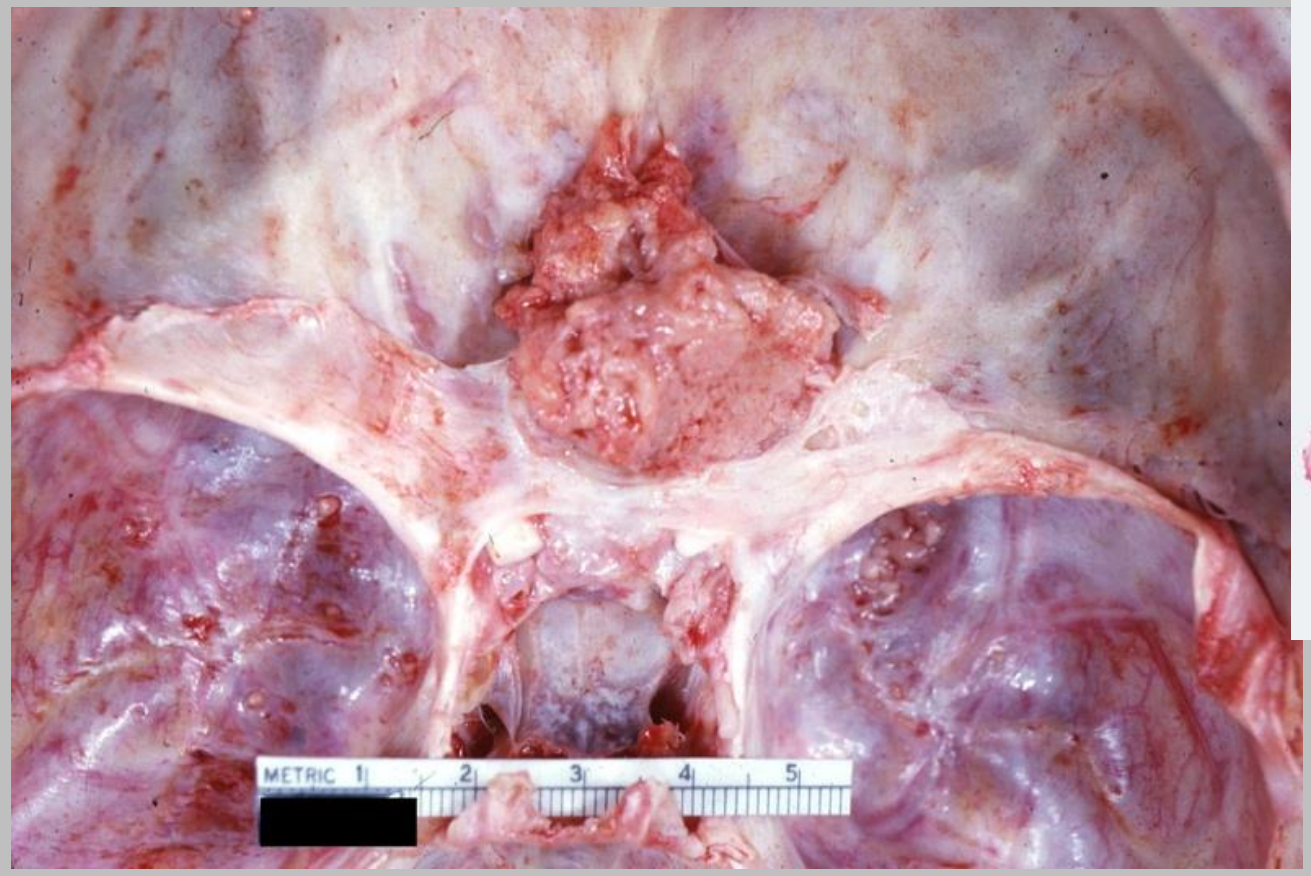
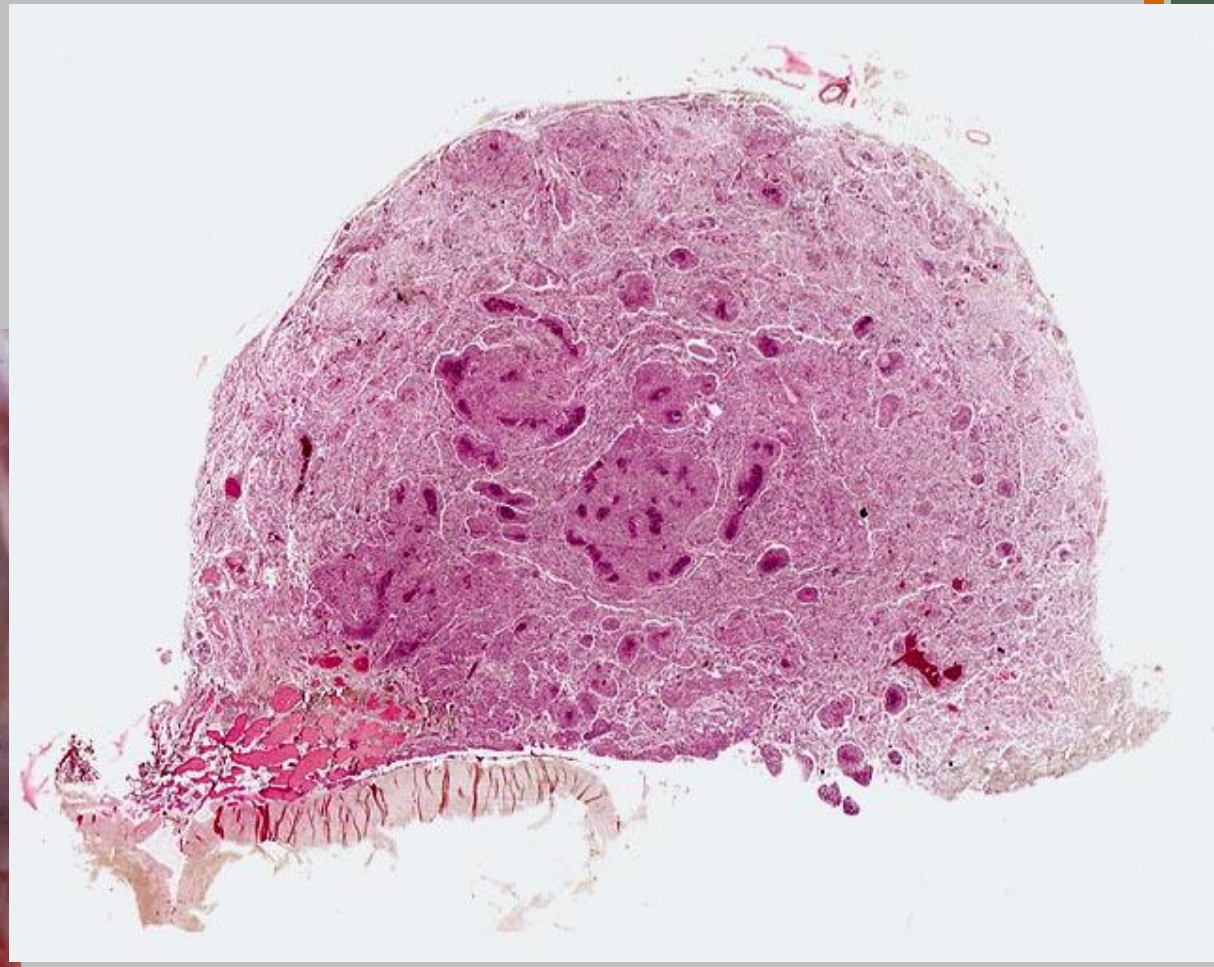
Meningioma of the base of skull with large frontal lesion





Meningioma (whole mount cross section through the base): a well-circumscribed, mass with a *dural insertion* and multiple tiny to large foci of calcification / metaplastic bone throughout the lesion.

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Meningioma

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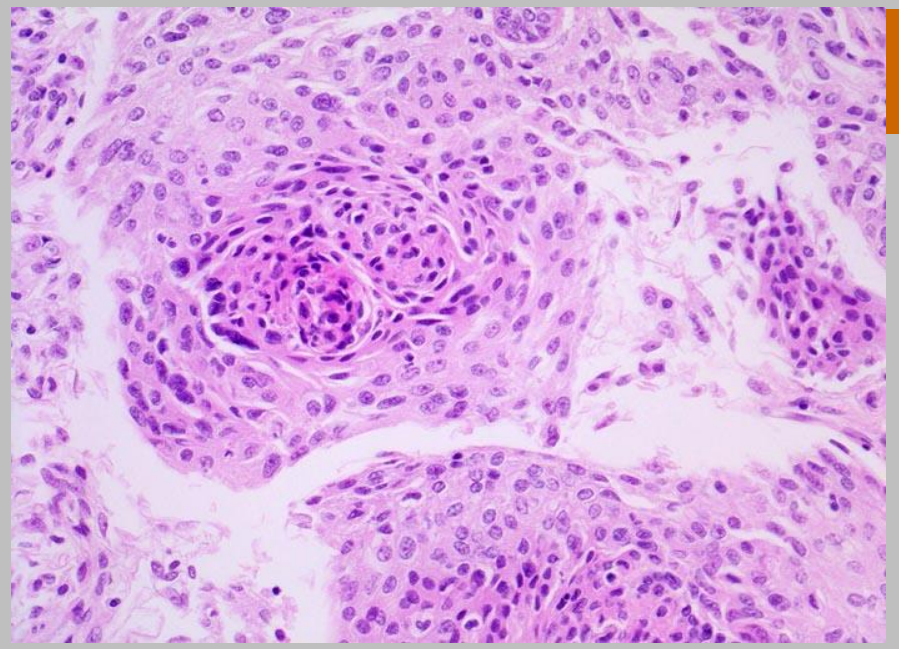


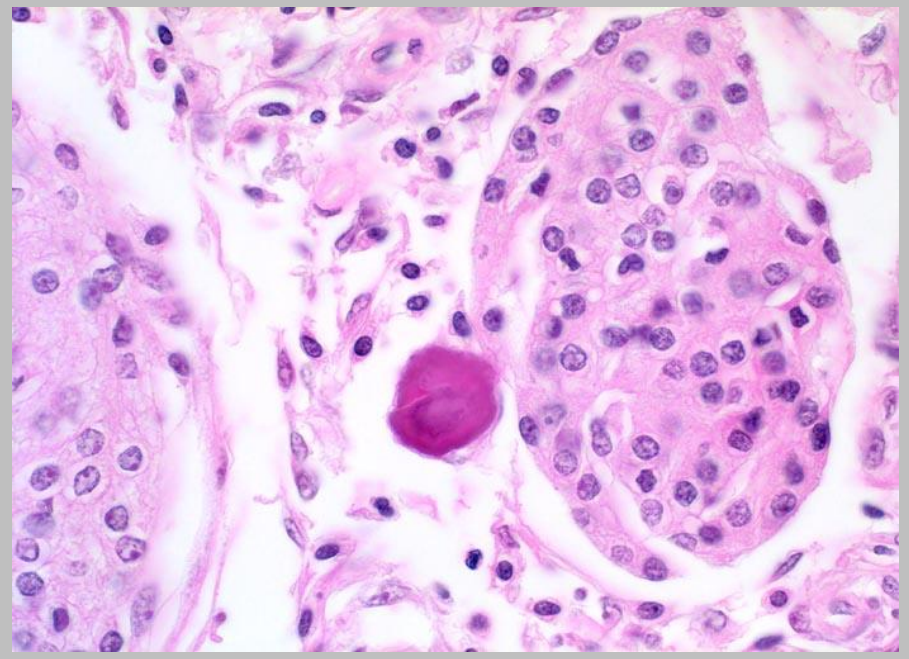
Microscopy:

Typical meningioma - several histologic patterns, more common:

- syncytial / endotheliomatous pattern: lobules and whorled clusters of cells which sit in tight groups, without visible cell membranes:;
- fibroblastic pattern: elongated cells and abundant collagen deposition between them;
- the nuclei are with open chromatin, no visible nucleoli, sometimes, eosinophilic cytoplasm pseudoinclusion
- psammoma bodies in variable number;

Atypical and anaplastic / malignant meningiomas: are unusual tumors and present some particular features:

- single cell infiltration of underlying brain,
- abundant mitoses and
- loss of meningothelial microscopic features (pattern of growing and cyto-nuclear details).



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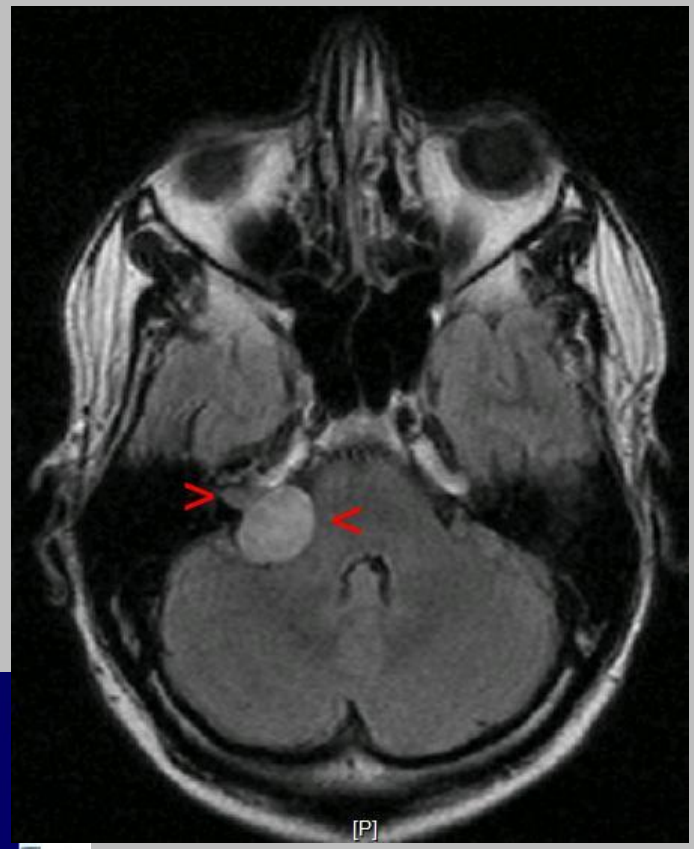
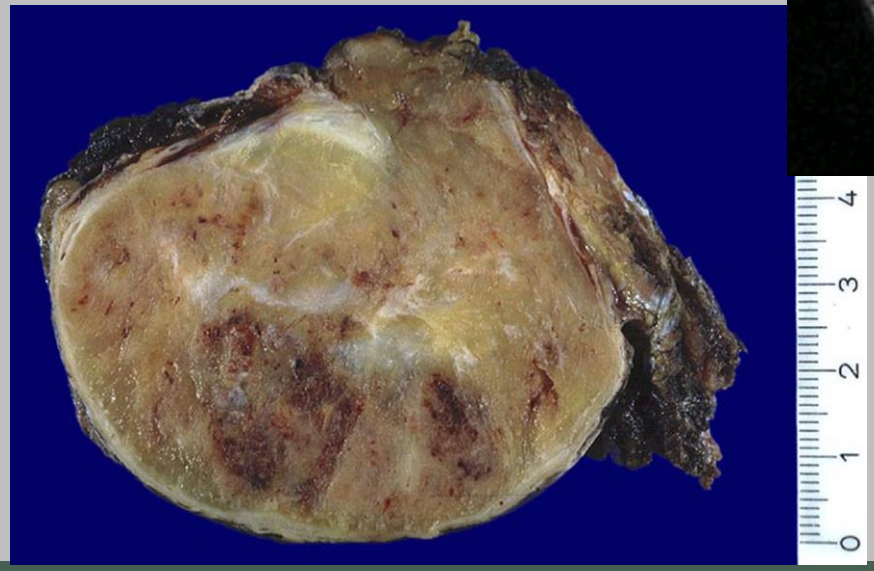
Schwannoma / neurilemmoma / neurinoma arises from Schwann cells:

- within the neurocranium, the most common location is the cerebellopontine angle, attached to the vestibular branch of the eight nerve *(acoustic neurinoma)*;
- *spinal neurinomas* account for 1/3 of all spinal cord tumors; 80% of these tumors arise from intradural nerve roots, especially the dorsal roots;
- well - circumscribed, encapsulated masses that are attached to the nerve but can be separated from it;
- tumors are firm, gray masses but may also have areas of ancient hemorrhages and / or cystic change.

https://upload.wikimedia.org/wikipedia/commons/4/4e/Akustikusneurinom_Mrt.jpg





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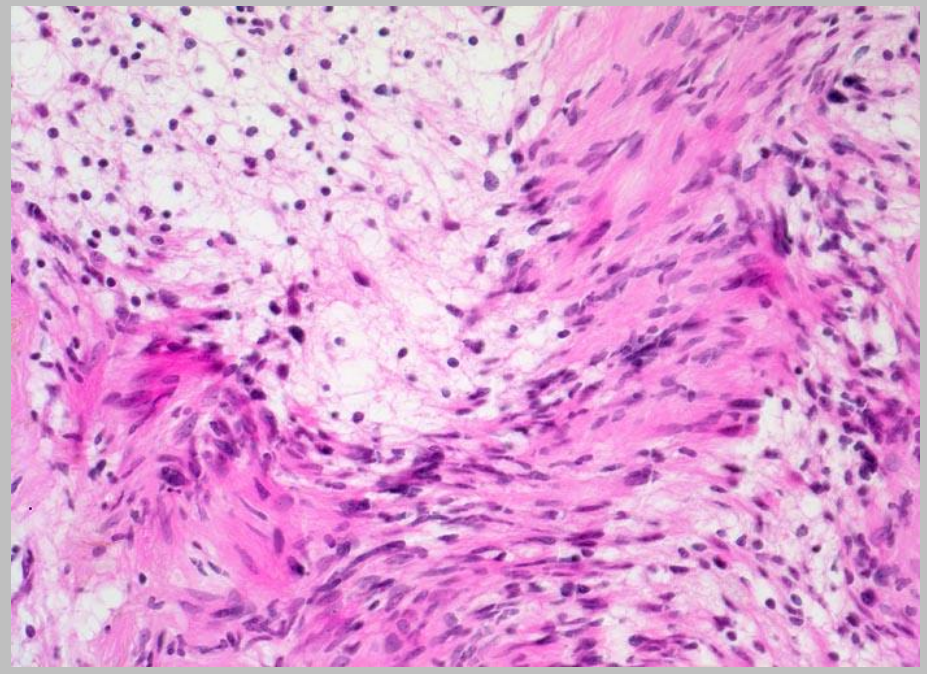
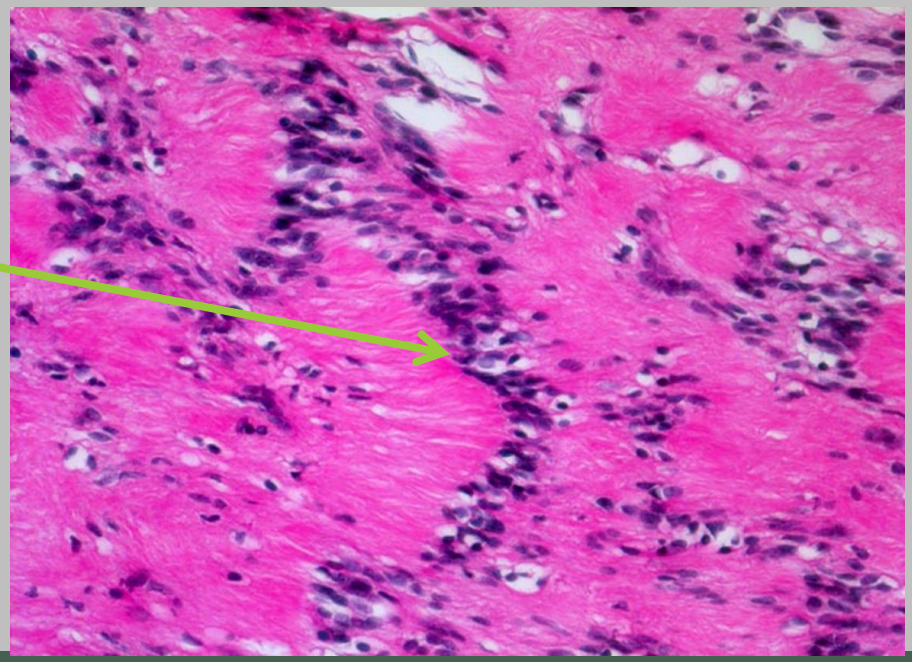


CNS schwannoma

Microscopy:

a mixture of two growth patterns: Antoni A and B**:**

- **Antoni A**: elongated cells with cytoplasmic processes arranged in fascicles presenting moderate to high cellularity with little stroma matrix;
  - the "nuclei-free zones" of processes that lie between the regions of nuclear palisading are termed **Verocay bodies**
- **Antoni B**: a loose network of cells similar to those seen in Antoni A areas, along with microcysts and myxoid change of the ground substance;
- degenerative changes may be found in ancient schwannomas, without prognostic significance.



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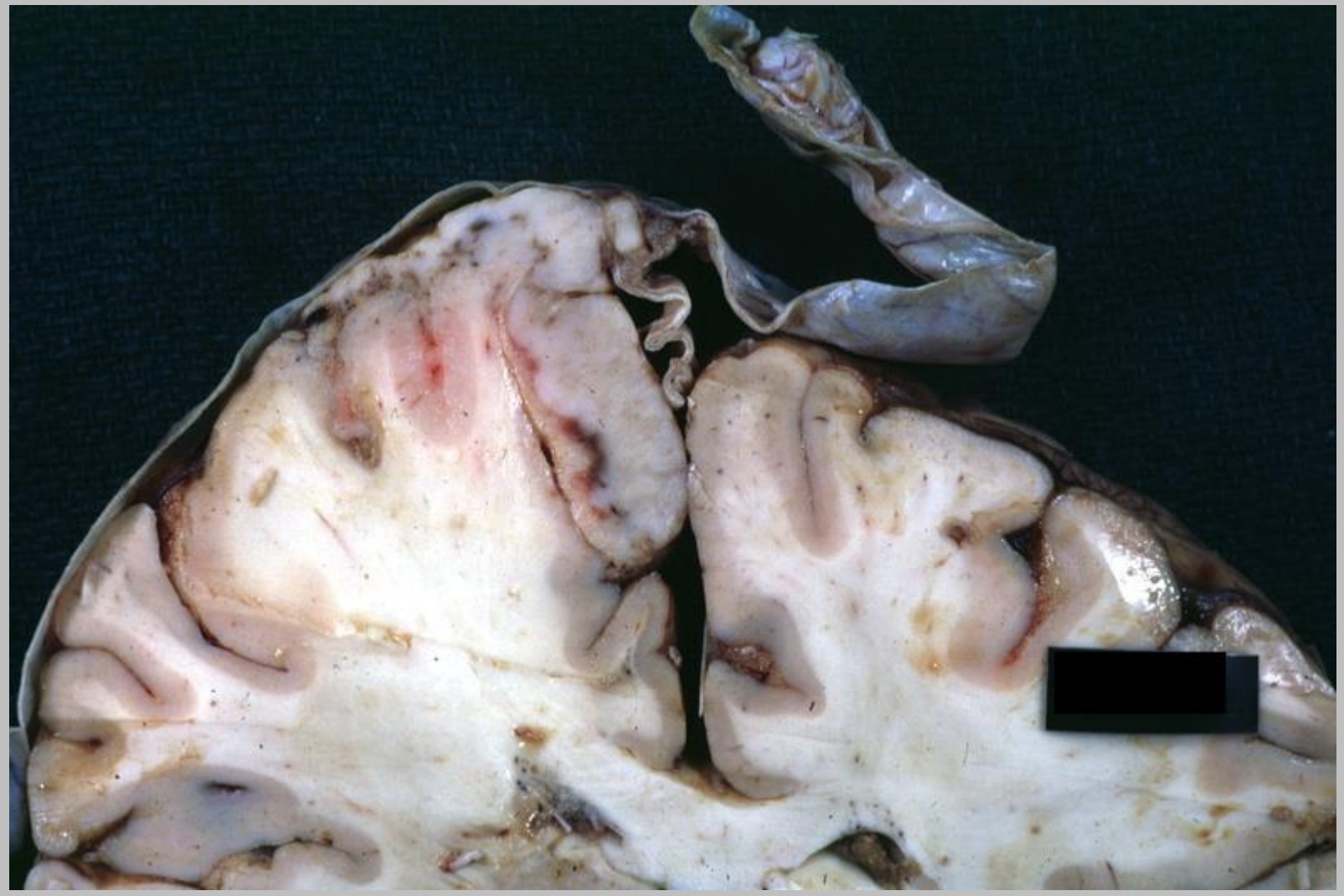
METASTATIC TUMORS far surpass primary CNS tumors in numbers, and malignancies metastatic to the CNS rise major clinical problems.

- Autopsy series show that up to 25% of patients with systemic / disseminated cancers have *CNS metastases*.
- The most common site for brain metastasis is at the *gray–white junction of the cerebral cortex*, but any CNS region may be affected, including the choroid plexus, pineal gland and pituitary gland.
- The most common primary tumors to involve the CNS are *lung* (most frequent for both men and women), *breast*, *melanoma*, kidney and gastrointestinal tract.

Brain metastatic carcinoma: gross illustration of infiltrating neoplasm into the gyrus adjacent to superior sagittal sinus.



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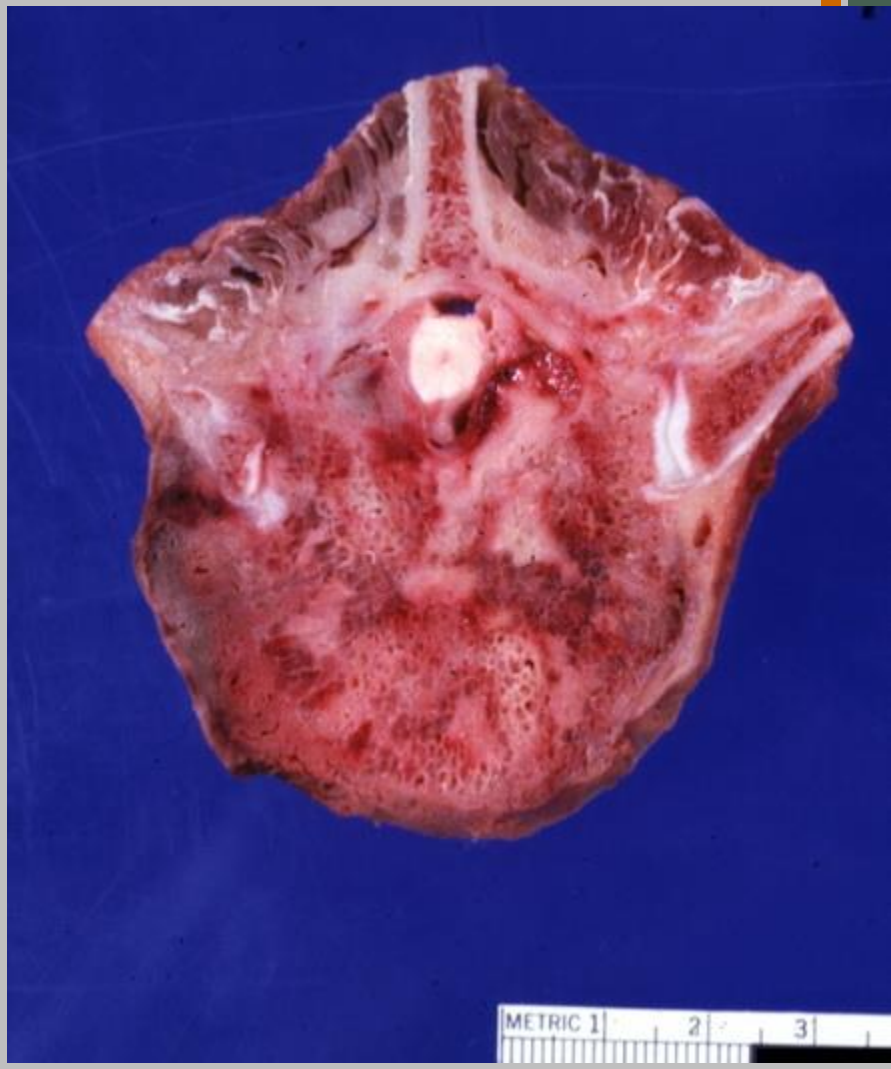

Spinal cord compression due to metastatic carcinoma, gross

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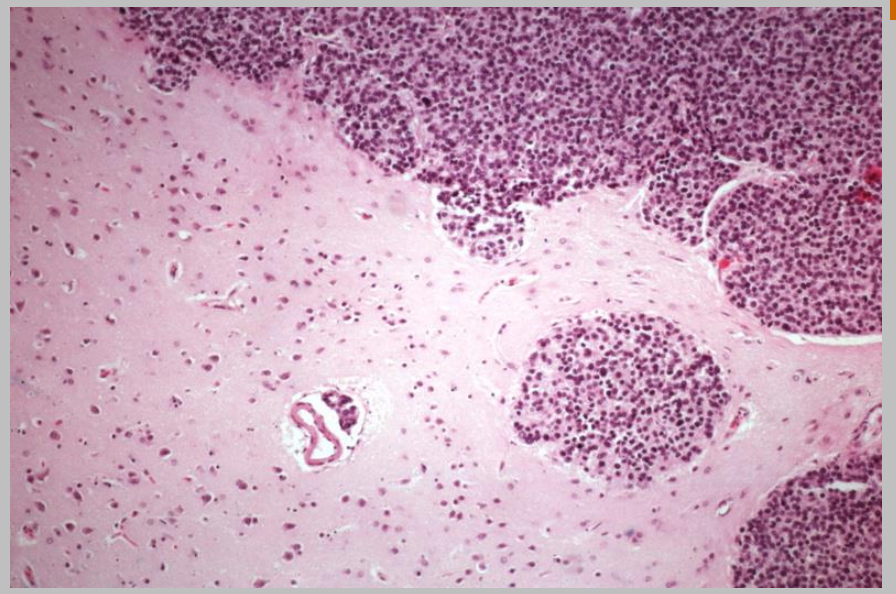
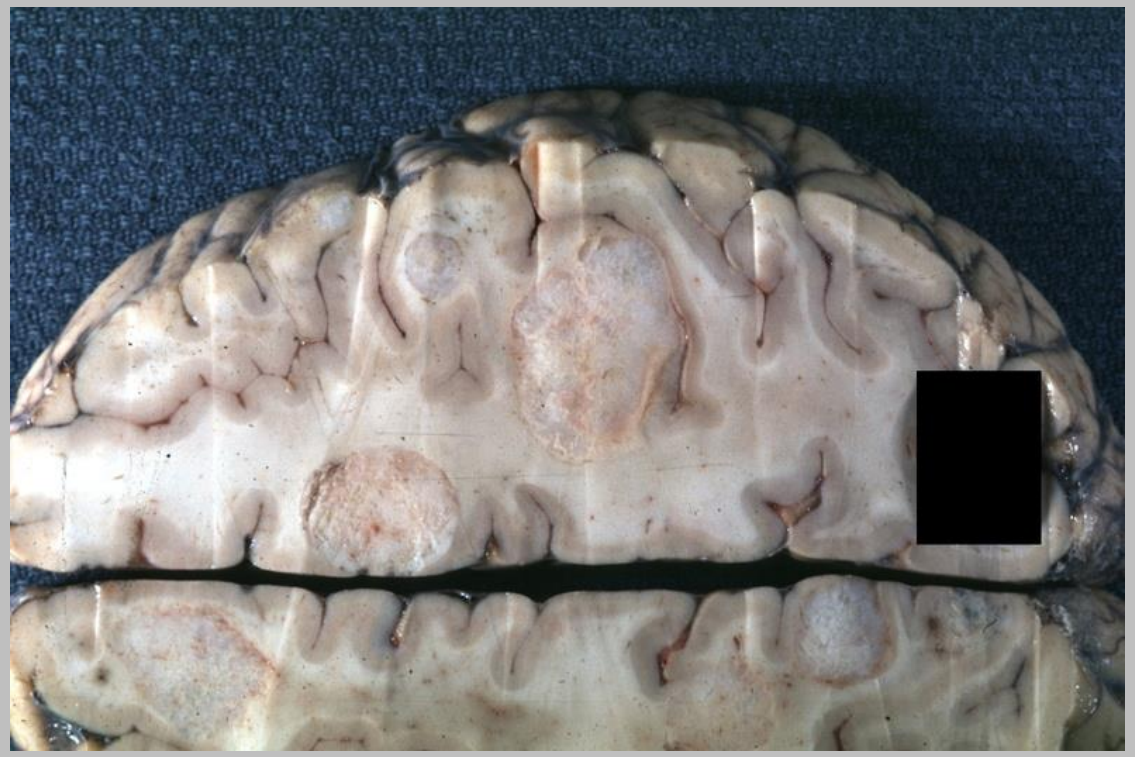
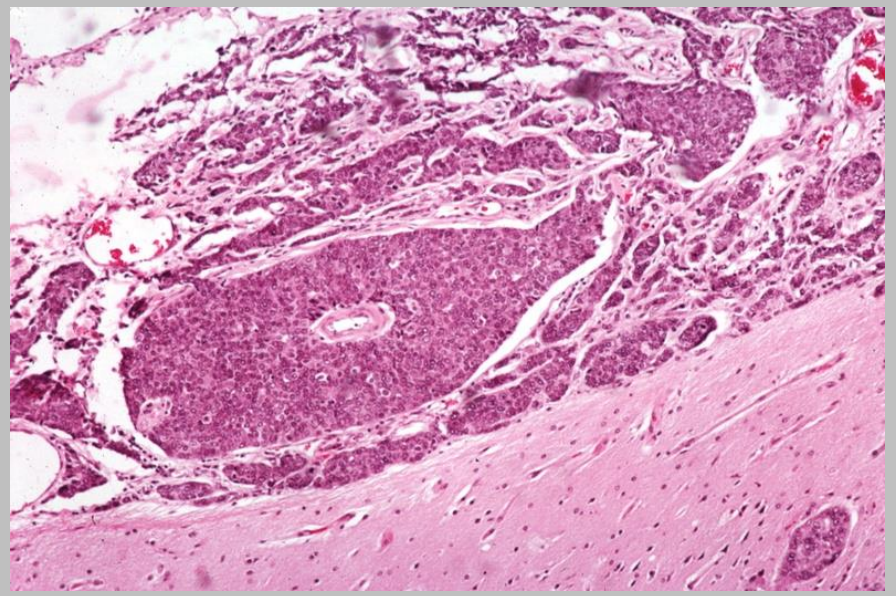
Metastatic CNS carcinoma: small cell carcinoma (lung?)



Brain metastatic carcinoma: multiple metastatic lesions in cerebrum, gross



Metastatic CNS carcinoma: extensive tumor invasion by perivascular Virchow-Robin spaces (breast?)



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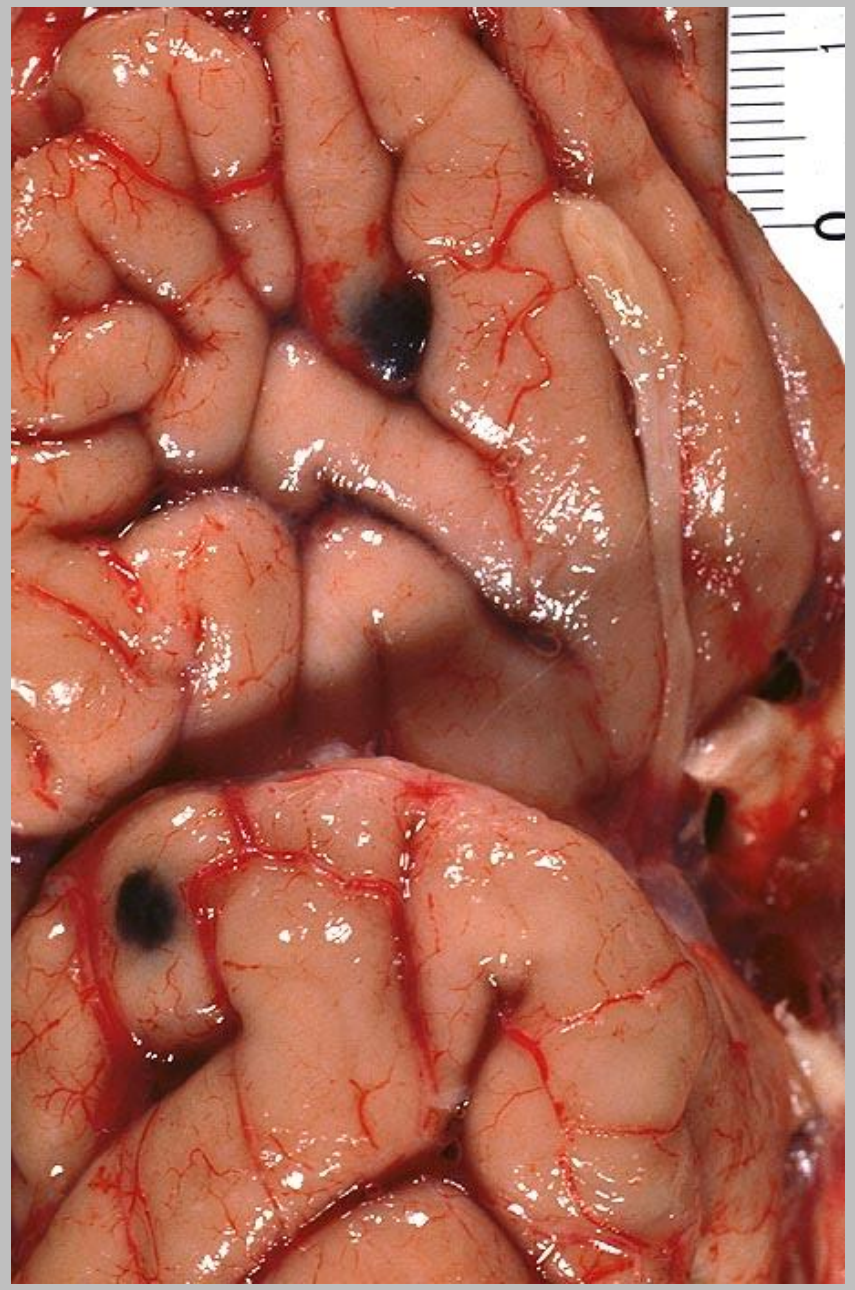

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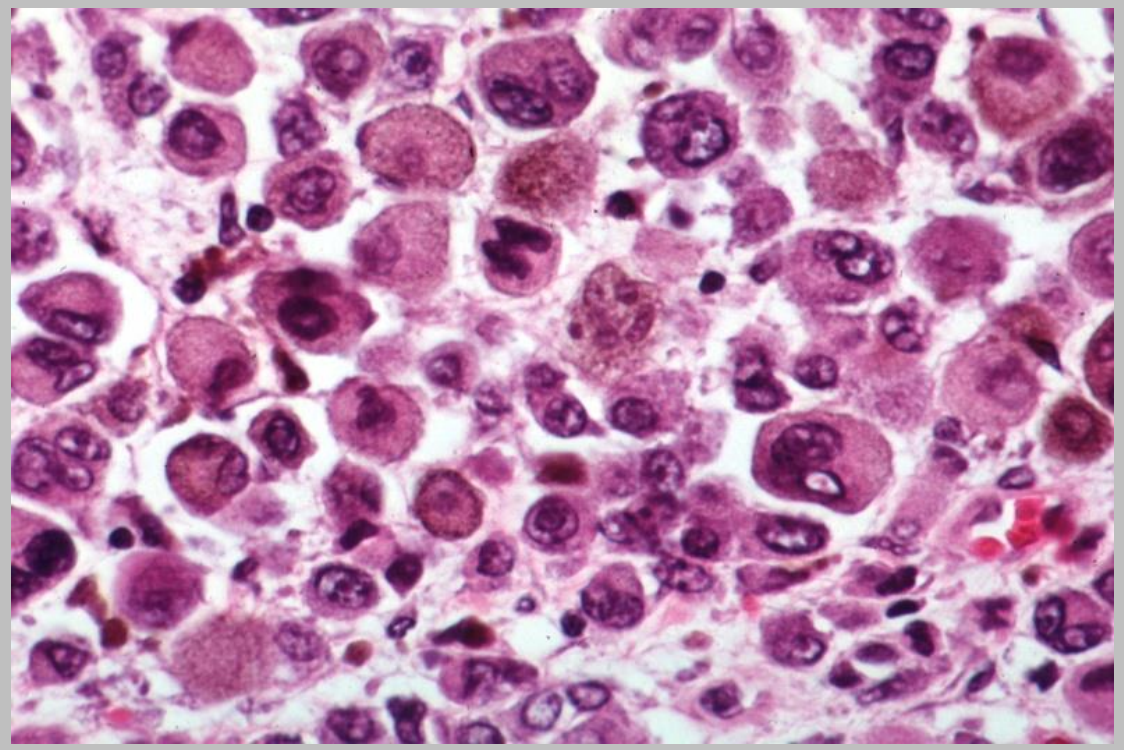

Malignant melanoma: brain metastases.

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