TUMORS OF MESENCHYMAL ORIGIN

LECTURE 12

How do we call them?

- **Remember that cancer (*carcinoma*) is always a malignant tumor derived from the epithelium !!!**
- **Malignant tumors deriving from soft tissues are *sarcoma (pl. –s)***

How do we make the name?

eg. Lipoma	Liposarcoma
Leiomyoma	Leiomyosarcoma
Rhabdomyoma	Rhabdomyosarcoma
Osteoma	Osteosarcoma
Chondroma	Chondrosarcoma

Classification

- Locally malignant tumors
- Malignant tumors
- Benign tumors
- Tumor-like lesions (conditions)

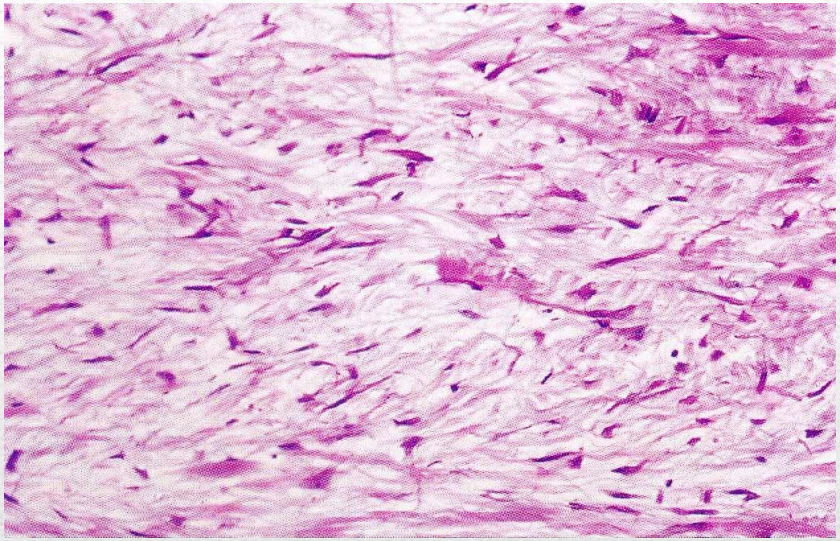
TUMORS OF THE FIBROUS CONNECTIVE TISSUE

THERE IS A VERY LARGE NUMBER OF HYPERPLASTIC LESIONS CLASSIFIED AS TUMORS, SOMETIMES THEIR NATURE IS UNCLEAR, THEY ARE CLASSIFIED AS FIBROMATOSIS AND TUMOR-LIKE HYPERPLASIA

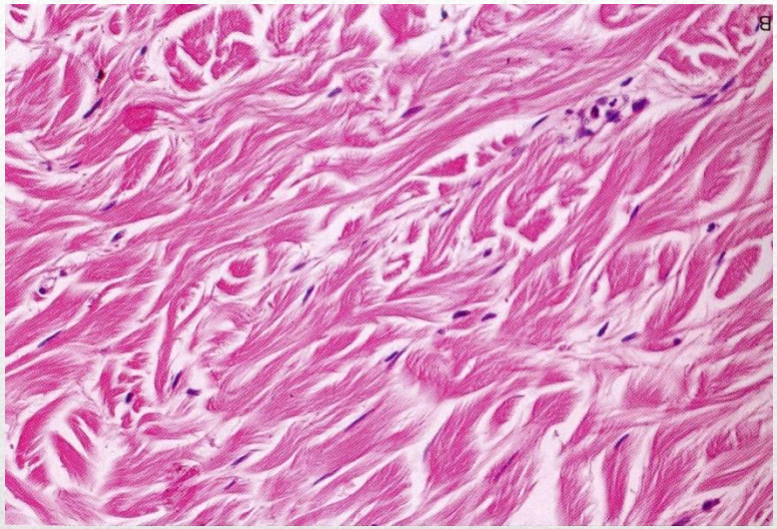
INCLUDED ARE ALSO: BENIGN HYPERPLASIA, TUMORS WITH LIMITED MALIGNANCY AND DEFINED MALIGNANT TUMORS

IT SHOULD KEPT IN MIND THAT HYPERPLASIA OF FIBROUS CONNECTIVE TISSUE IS AN INTEGRAL PART OF OTHER LESIONS, LIKE E.G. FIBROADENOMA, CHONDROFIBROMA ETC.

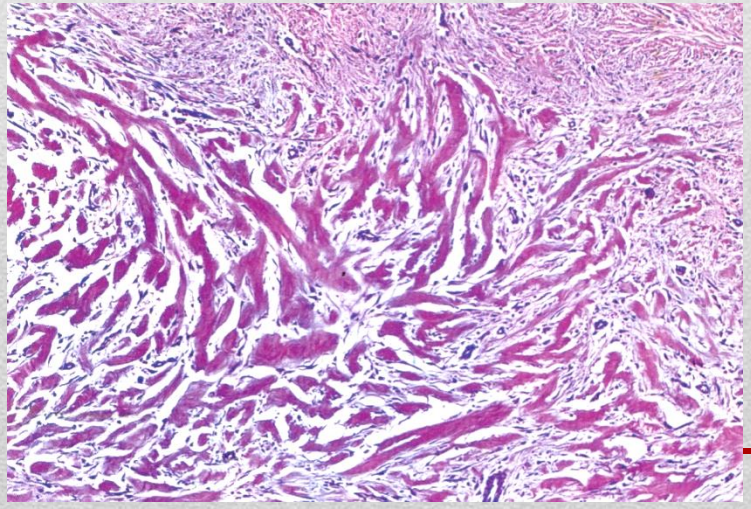
TUMORS OF FIBROUS CONNECTIVE TISSUE (BENIGN) – FIBROBLASTIC/MYOFIBROBLASTIC/FIBROHISTIOCYTIC



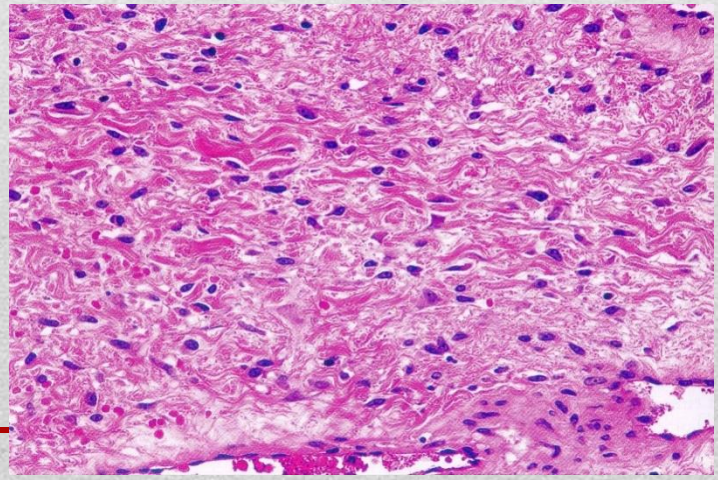
FIBROMA MOLE



FIBROMA DURUM

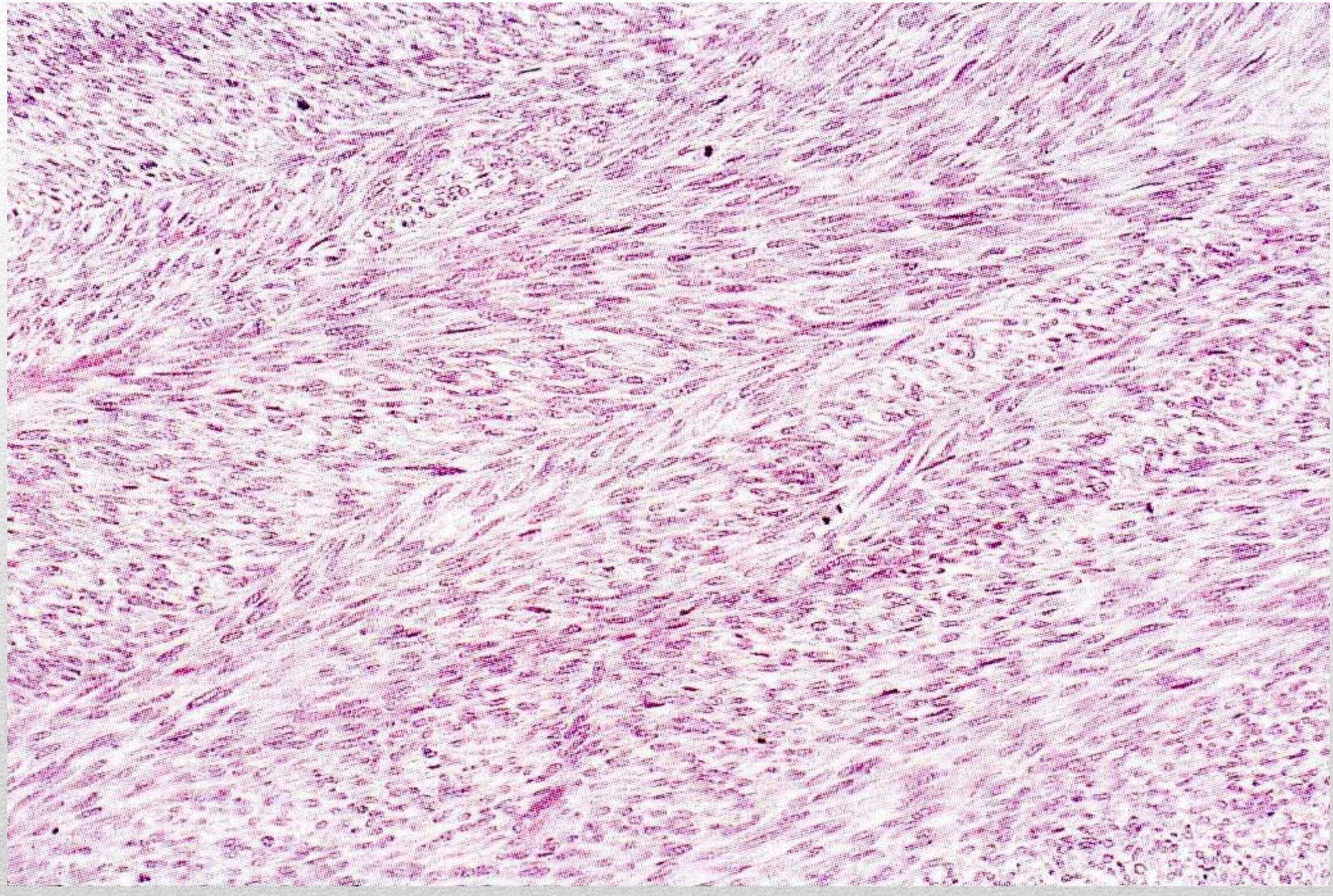


KELOID



FIBROMA IUVENILE - ANGIOFIBROMA

TUMORS OF FIBROUS CONNECTIVE TISSUE (MALIGNANT)



FIBROSARCOMA

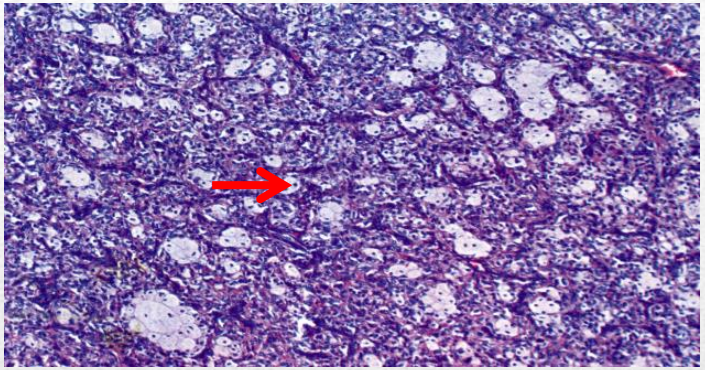
TUMORS OF FIBROUS CONNECTIVE TISSUE

- ***Clinically: LESION OCCURS MOST COMMONLY IN THE SKIN*** **(CAN ALSO OCCUR IN DEEPER TISSUES) – RELAPSES AFTER INCOMPLETE REMOVAL**
- ***Morphologically: TUMOR BUILT OF ONE OR MANY NUCLEATED FOAMY CELLS AND FIBROBLASTS*** **(STORIFORM PATTERN)**
- ***Options:***

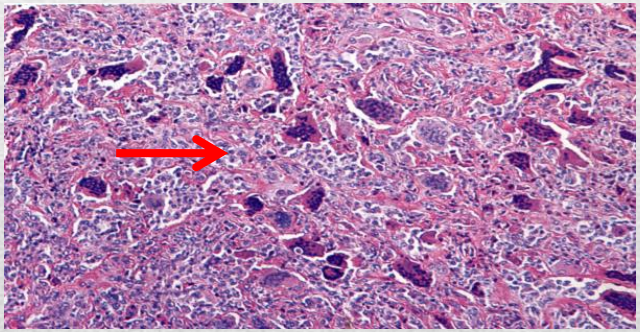
1) **FIBROUS XANTHOMA: BUILT OF NUMEROUS FOAMY CELLS**
2) **GIANT CELL TUMOR: CONTAINS NUMEROUS MULTINUCLEATED GIANT CELLS; IN HANDS, FINGERS (TENDON AREA)**
3) **DERMATOFIBROMA: FIBROUS TUMOR WITH NUMEROUS VESSELS**: ***hemangioma sclerosans***

TUMORS OF FIBROUS CONNECTIVE TISSUE

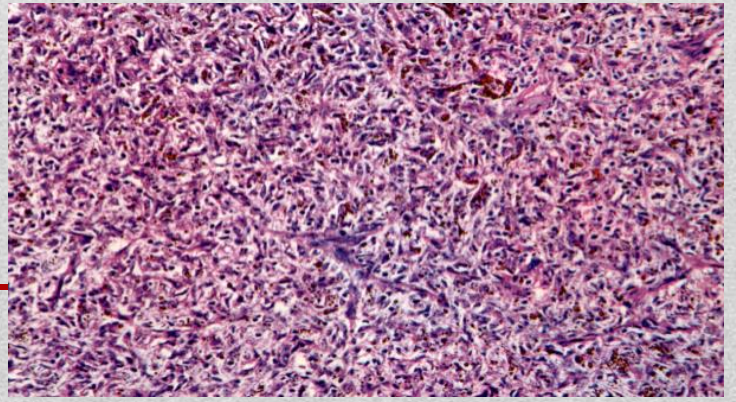
- Fibroxanthoma



- Giant-cell tumor



- Dermatofibroma



TUMORS OF FIBROUS CONNECTIVE TISSUE WITH LOW MALIGNANT POTENTIAL

•THIS IS A GROUP OF NON-CYSTIC LESIONS WITH EXPANSIVE GROWTH

•TENDENCY TO LOCAL RELAPSE IS HIGH

•DO NOT METASTASIZE

•CAN LEAD TO DEATH WHEN IN ORGANS LIKE LUNGS, BRAIN ETC

- **SPECIAL FORMS:**

1) ***CONTRACTURA DUPUYTREN (fibromatosis palmaris)***
2) ***MORBUS PEYRONIE (fibromatosis dolorosa penis)***
3) ***DESMOID:*** **OCCURS ON THE ABDOMEN, IN YOUNG WOMEN AFTER PREGNANCY, CELLS MAY EXPRESS ESTROGENE RECEPTORS**

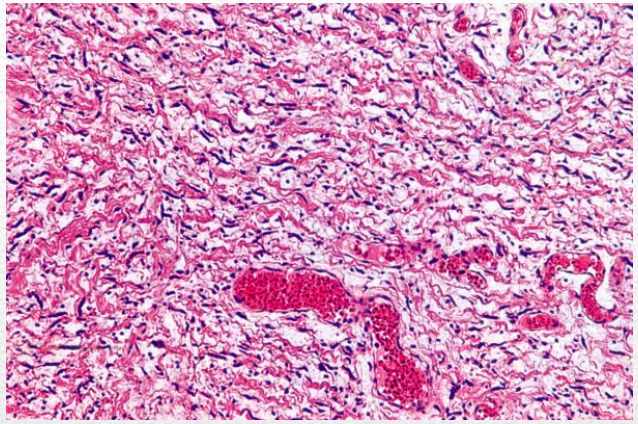
TUMORS OF SCHWANN'S SHEATH

- ***Clinically: MOST COMMONLY OCCURING IN SUBCUTANEOUS TISSUE, RARE IN DEEPER PARTS (CAN BE PEDUNCULATED)***
- ***Options:***

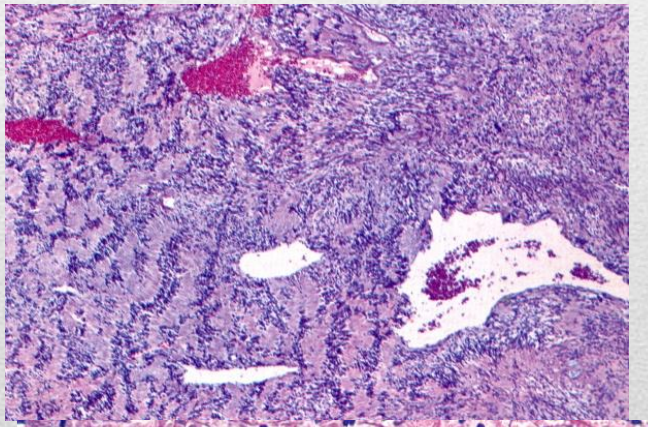
1) **NEUROFIBROMA: most commonly very slightly limited (infiltrations !), built of delicate spindle cells**
2) **NEURILEMMOMA (SCHWANNOMA): sometimes sacculated**
3) **NEUROFIBROMATOSIS RECKLINGHAUSEN: MULTIPLE NEUROFIBROMA in different localizations with discoloration of the skin to *coffee with milk* color*(cafe au lait).* Autosomally dominant inheritance.**
4) **ABRIKOSOW (GRANULAR CELL) TUMOR: occurs in the skin and in the tongue, larynx; causes secondary changes in epidermis and mucosa, nonsacculated, infiltrating**

TUMORS OF SCHWANN'S SHEATH

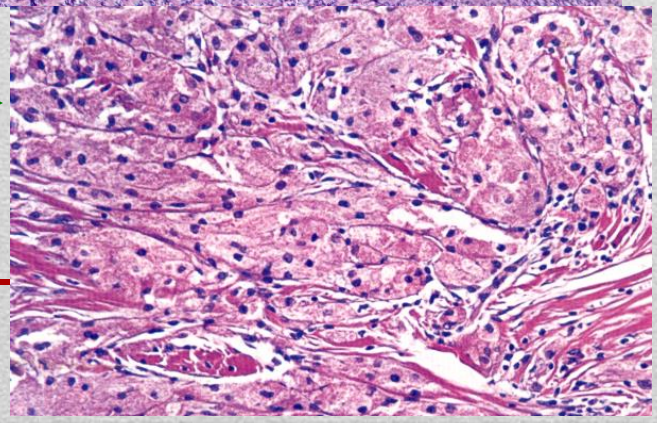
- Neurofibroma



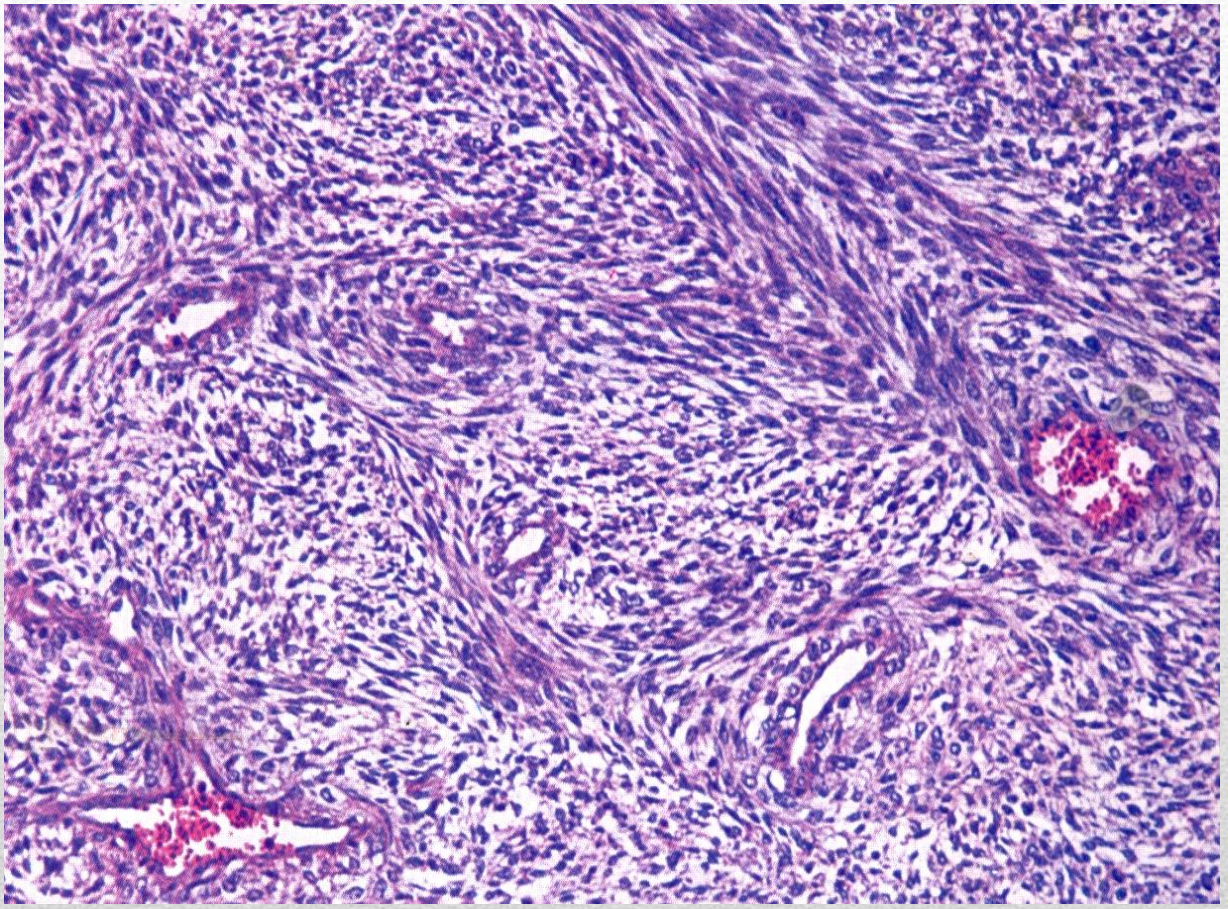
- Neurilemmoma



- Granular cell tumor (tumor Abrikosow))



TUMORS OF SCHWANN'S SHEATH



NEUROFIBROSARCOMA

TUMORS OF ADIPOSE TISSUE

- ***Clinically:*** **MOST COMMONLY OCCURING AS SACCULATED, MACRO- AND MICROSCOPICALLY RESEMBLING FAT TISSUE. MOST COMMONLY ON LIMBS AND BACK. DIFFERENT SIZES**

- ***Malignant Transformation:*** **NEVER OBSERVED IN CASE OF LIPOMA**

- ***Options:***

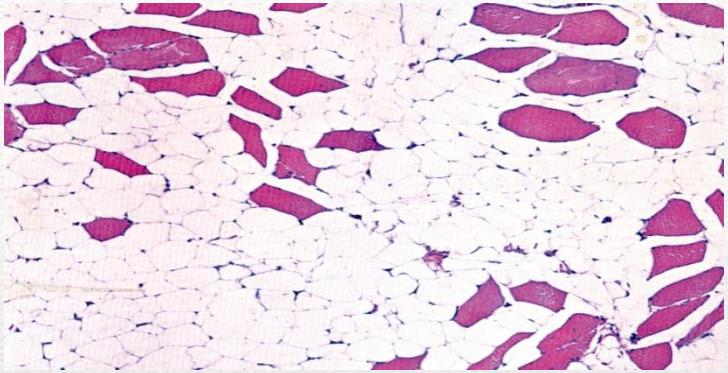
1) <u>LIPOBLASTOMA:</u> RARE, LOBULAR, SACCULATED TUMOR OCCURING MOST COMMONLY IN CHILDREN, BENIGN, SPORADIC RELAPSES

2)<u>HIBERNOMA:</u> RARE, ON NECK AND BETWEEN SCAPULAS FROM BROWN FAT <u>(BEAR FAT</u>), IN CHILDREN AND ADULTS

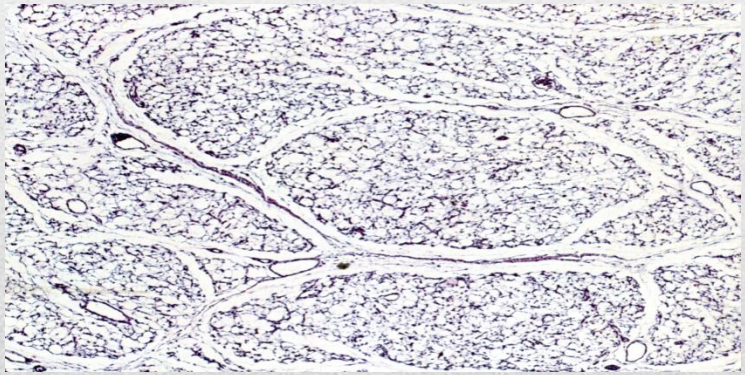
BEAR FAT

BENIGN TUMORS OF ADIPOSE TISSUE

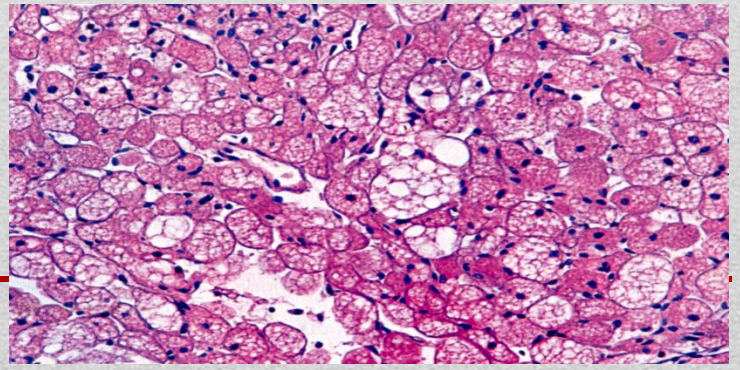
- ***Lipoma***



- ***Lipoblastoma***



- ***Hibernoma***



MALIGNANT TUMORS OF ADIPOSE TISSUE

LIPOSARCOMA: MOST COMMON MALIGNANT TUMOR OF SOFT TISSUES; IN ADULTS, EXTREMELY RARE IN CHILDREN.

MOST COMMONLY GROWS IN RETROPERITONEAL SPACE.

4 Histopathological forms:

liposarcoma lipoma-like, liposarcoma myxomatodes, liposarcoma globocellulare i liposarcoma pleomorphicum.

EACH OF ABOVE HAS A DIFFERENT PROGNOSIS AND CLINICAL COURSE

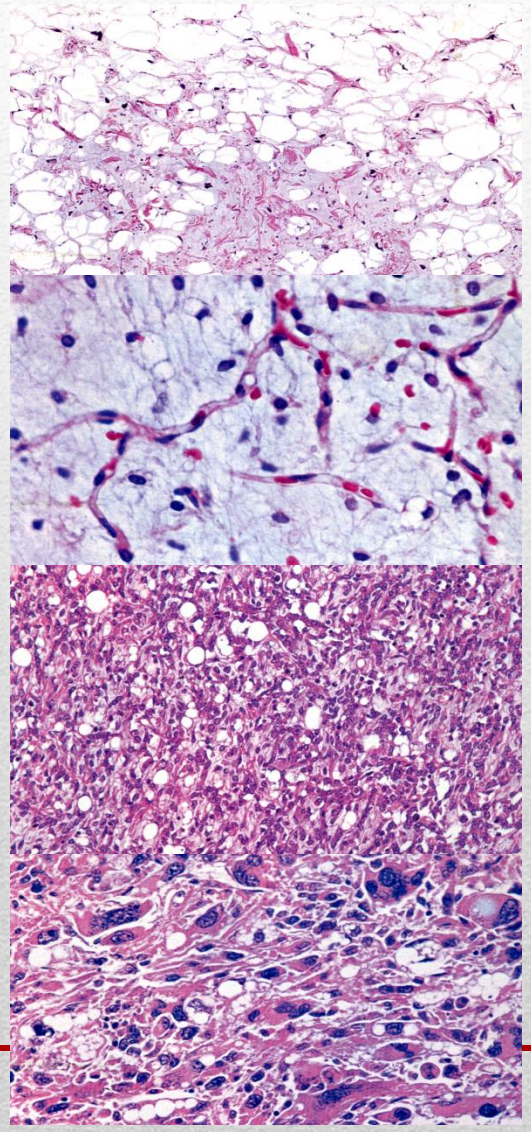
MALIGNANT TUMORS OF ADIPOSE TISSUE

1) Liposarcoma (lipoma like)

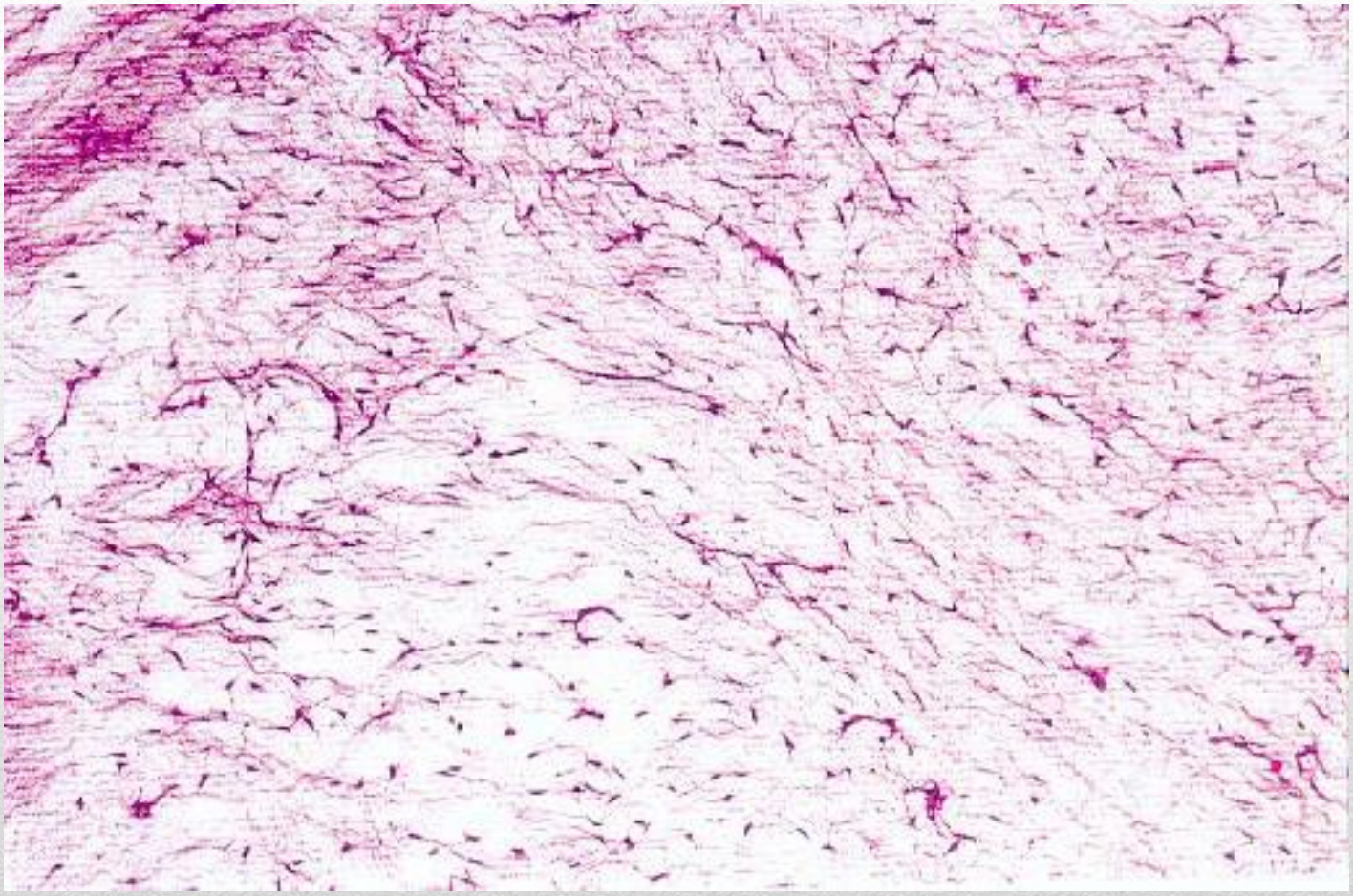
2) Myxoid Liposarcoma

3) Globocellular Liposarcoma

4) Pleomorphic Liposarcoma



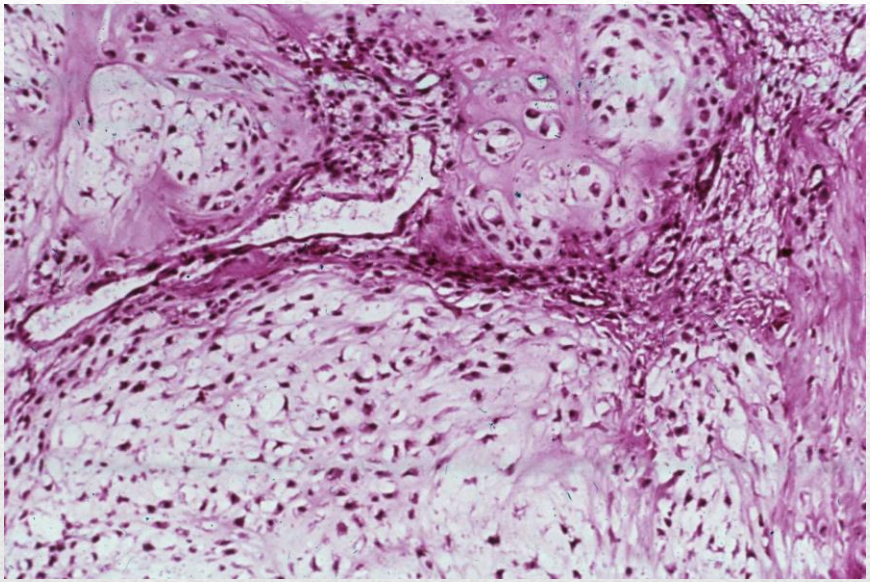
TUMORS OF MYXOMATOUS TISSUE



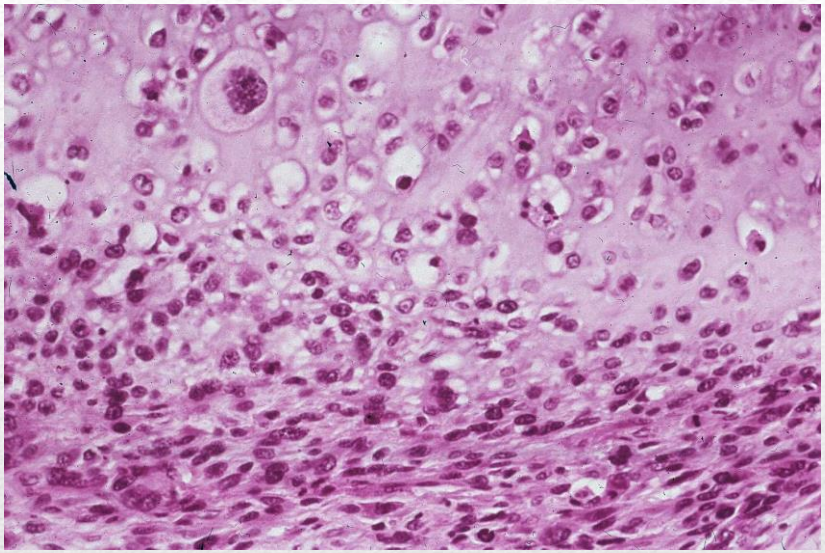
MYXOMA

RARELY SEEN TUMORS (E.G. IN HEART). MOST COMMONLY THE MUCOUS COMPONENT IS SEEN AS A PART OF OTHER MESENCHYMAL TUMORS (FIBROMYXOMA, CHONDROMYXOMA); TENDENCY TO RELAPSE

TUMORS OF CARTILAGINOUS TISSUE



Chondroma



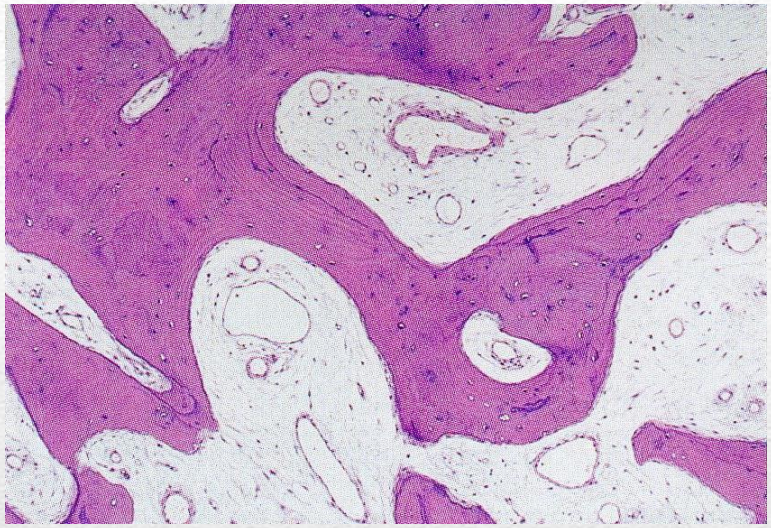
Chondrosarcoma

Generally:

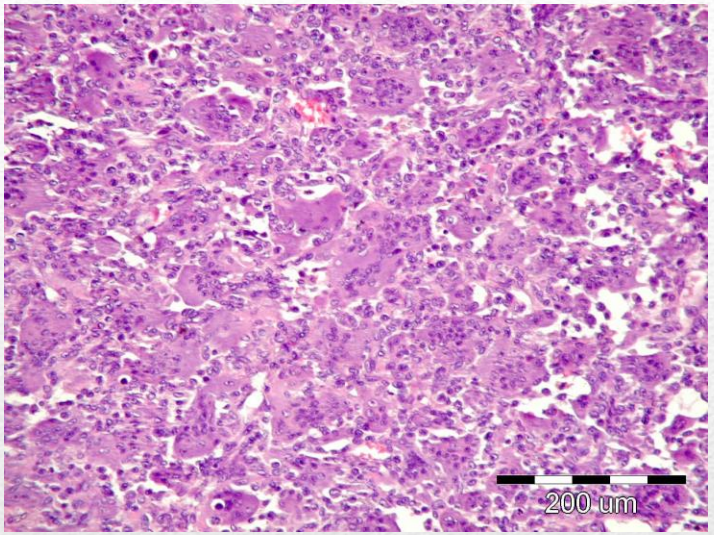
A GROUP OF TUMORS OF DIFFERENT DEGREE OF DIFFERENTIATION MAINLY IN HYALINE CARTILAGE;
BENIGN TUMORS WITH INDISTINCT BORDER FROM BONE.
MALIGNANT FORMS REVEAL SIGNIFICANT INFILTRATING GROWTH.
NUMEROUS CHONDROMA IN OLLIERS SYNDROME

MIXED PROLIFERATIONS, BONE-CARTILAGE (OSTEOCHONDROMA) ARE KNOWN AS EXOSTOSES

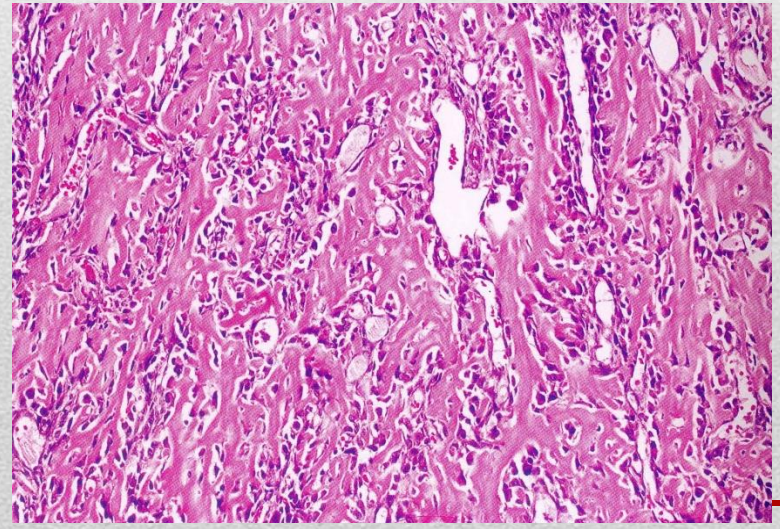
TUMORS OF BONES



OSTEOMA



GIANT-CELL TUMOR - OSTEOCLASTOMA



OSTEOSARCOMA

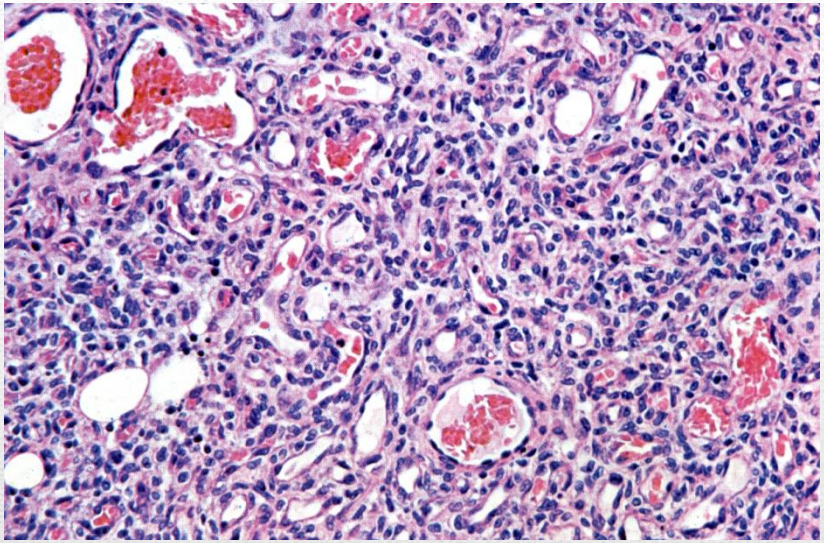
A group of tumors deriving from two groups of cells: osteoblasts and osteoclasts. Many types of growth, in different age groups,commonly located in the metaphyseal parts of long bones

VASCULAR TUMORS

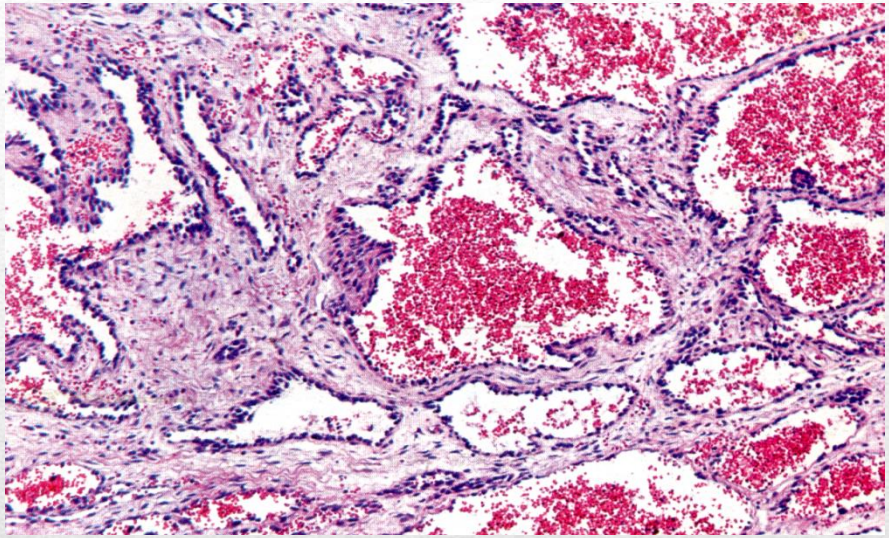
DERIVED FROM BLOOD VESSELS AS WELL AS LYMPHATIC VESSELS

- ***Generally:*** ARE MADE OF NEW VESSELS, COMMON IN CHILDREN, BLUE OR RED IN COLOR; OFTEN SELF-REGRESSIVE
- ***Morphologically:*** there are two basic types, ***capillary hemangioma and cavernous hemangioma***
- Bleeding can sometimes be a serious clinical problem; rapid growth to large sizes angiomas in newborns *(haemangioblastoma)* can be the reason for thrombocytopenia *(Kasabach-Merrit syndrome)*

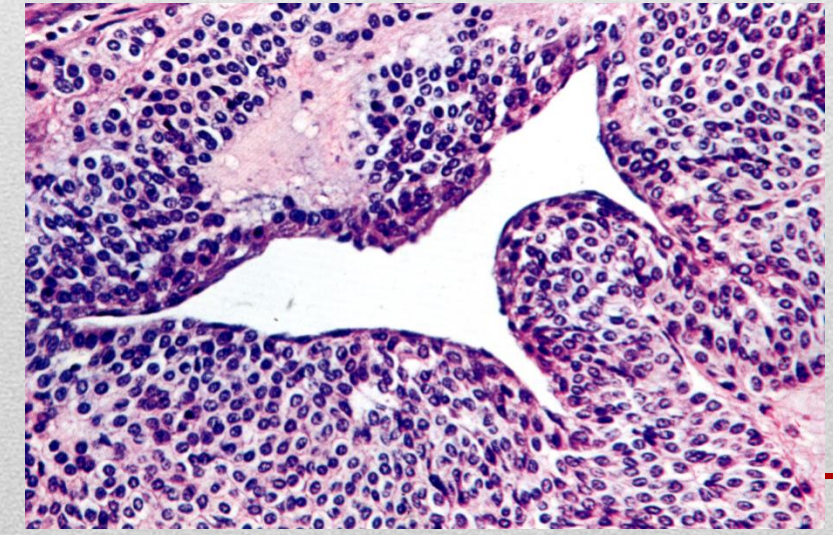
VASCULAR TUMORS



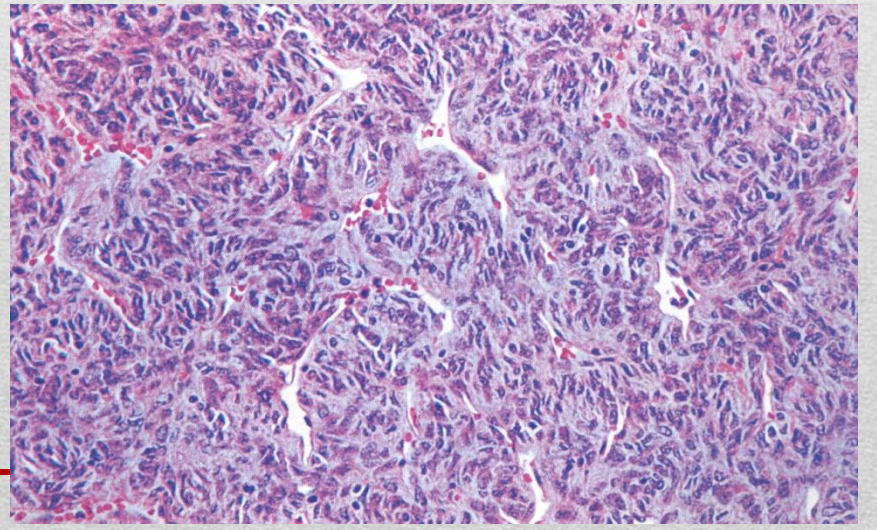
CAPILLARY HEMANGIOMA



CAVERNOUS HEMANGIOMA

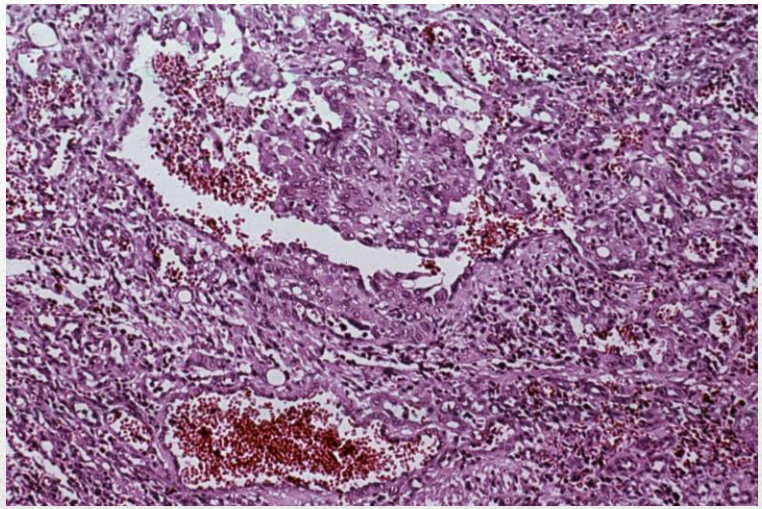


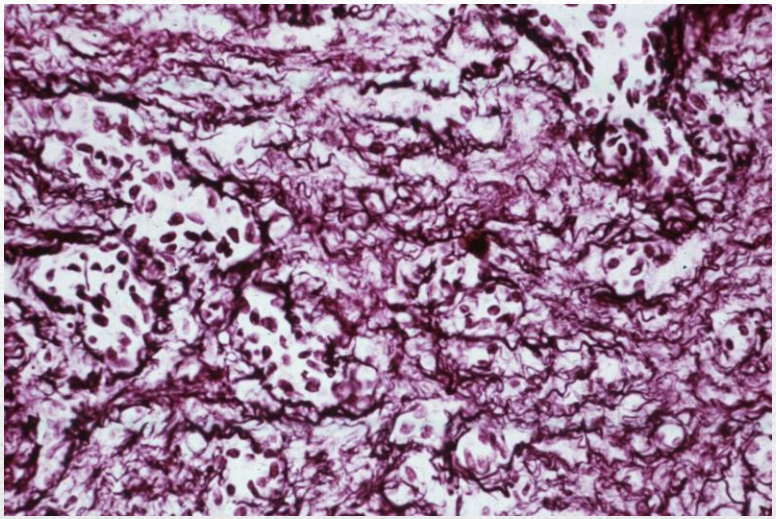
GLOMANGIOMA



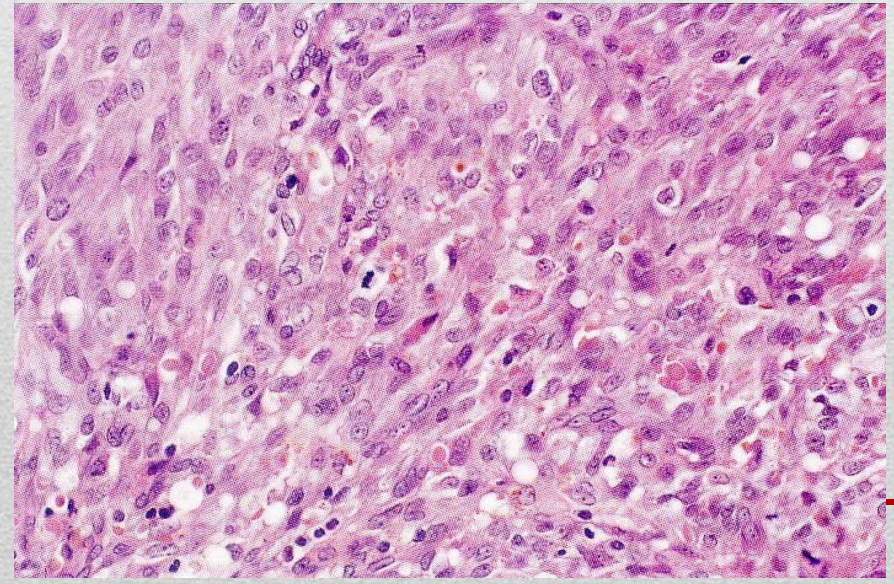
HEMANGIOPERICYTOMA

VASCULAR TUMORS





HEMANGIOENDOTHELIOMA



ANGIOSARCOMA KAPOSI

TUMORS OF MUSCULAR TISSUE

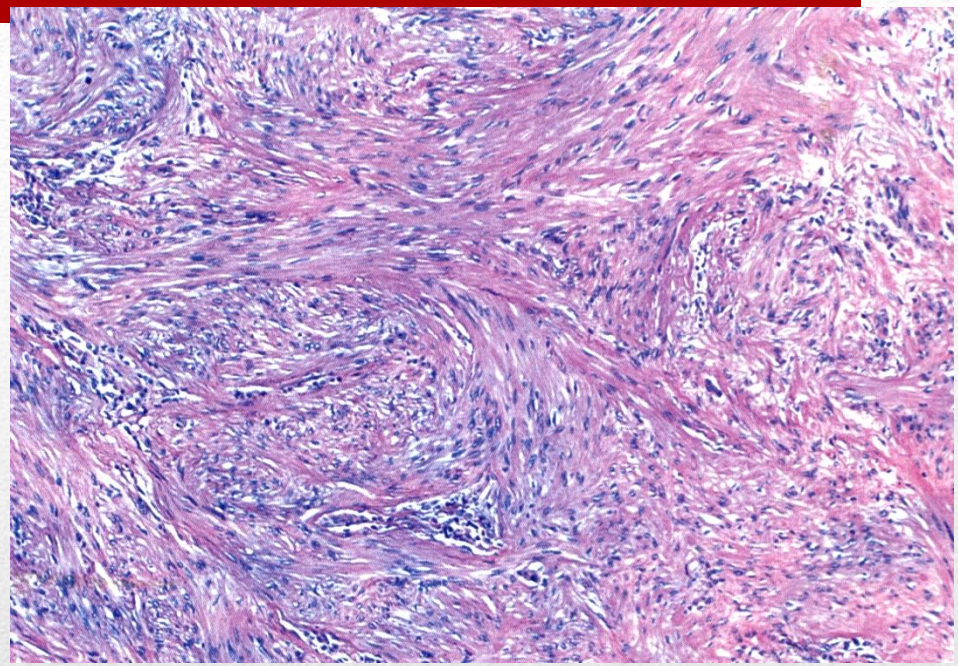
- **LEIOMYOMA: CAN GROW ANYWHERE IN SOFT TISSUES; MOST OFTEN IN UTERUS**

  . encysted (encapsulated) tumor of different sizes built of leiomyoblasts.

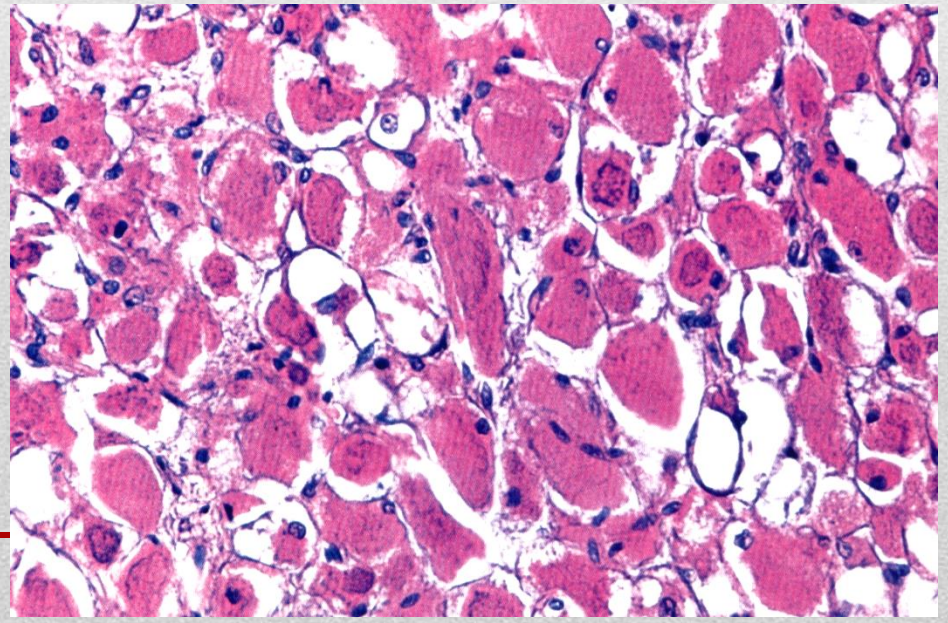
- **Rhabdomyoma*:* occurs in the tongue and vulva, is extremely rare!**

BENIGN TUMORS OF MUSCULAR TISSUE

- **Leiomyoma**



- **Rhabdomyoma**



MALIGNANT TUMORS OF MUSCULAR TISSUE

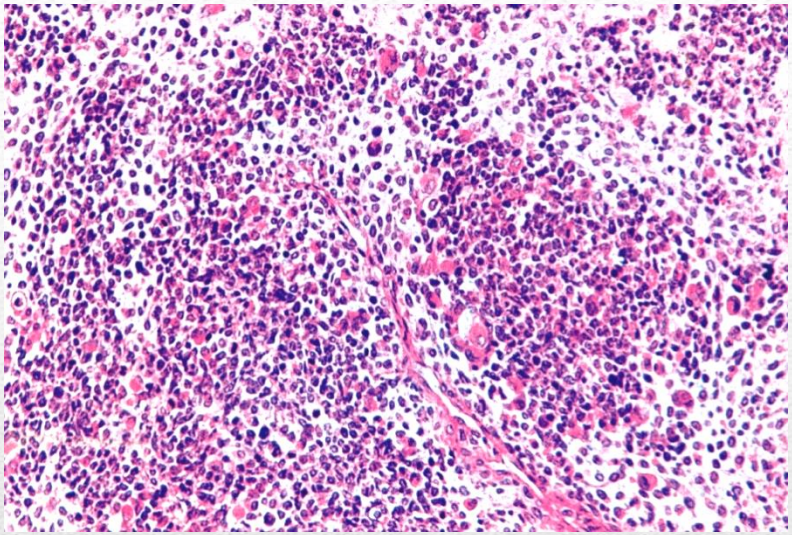
- **RHABDOMYOSARCOMA:** REPRODUCES EMBRYOGENIC MYOGENESIS

1) **EMBRYONAL Rhabdomyosarcoma: TUMOR OF THE CHILDHOOD** before the 6th year of life. Most often located in the facial region (orbit, nasopharynx). Histologically built of small, round cells
2) **BOTRYOID Sarcoma:** a subtype of embryonal occuring in the urogenital area, bile ducts and upper respiratory tract in very young children

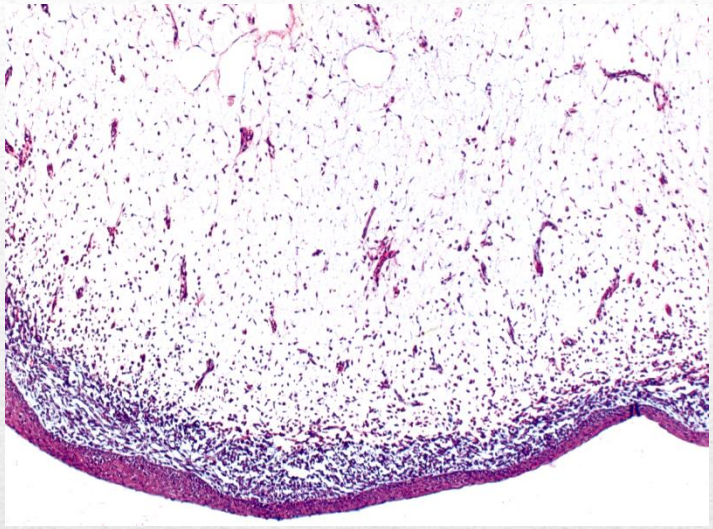
3) ALVEOLAR Rhabdomyosarcoma: reproduces a later stage of myogenesis and also occurs at a later age: between 10 - 25 year of life. Similar locations as the embryonic type and on limbs. Histologically built of small cells like in the embryonic type but there are also larger, more mature myoblasts.

4) **PLEOMORPHIC Rhabdomyosarcoma (ADULT):** it occurs in the 4th to 7th decade of life. 70% of tumors develop deeply in muscles of the thigh.

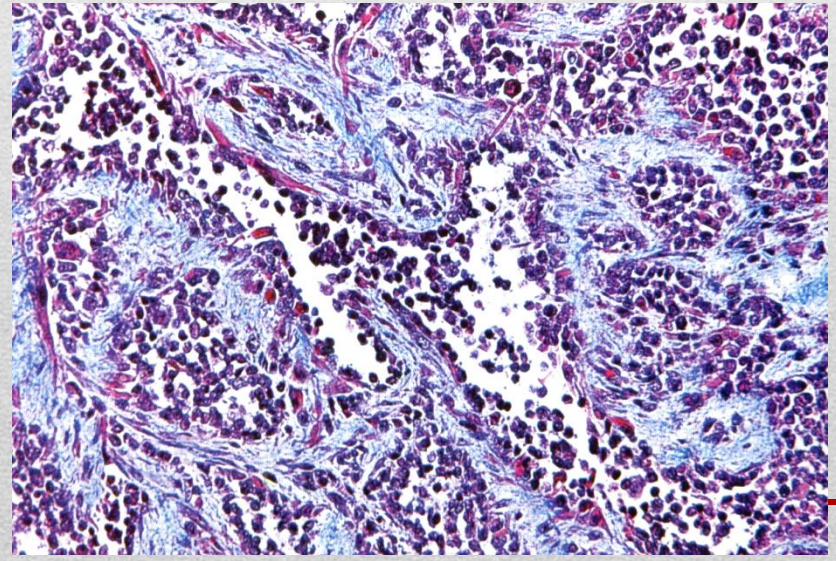
MALIGNANT TUMORS OF MUSCULAR TISSUE



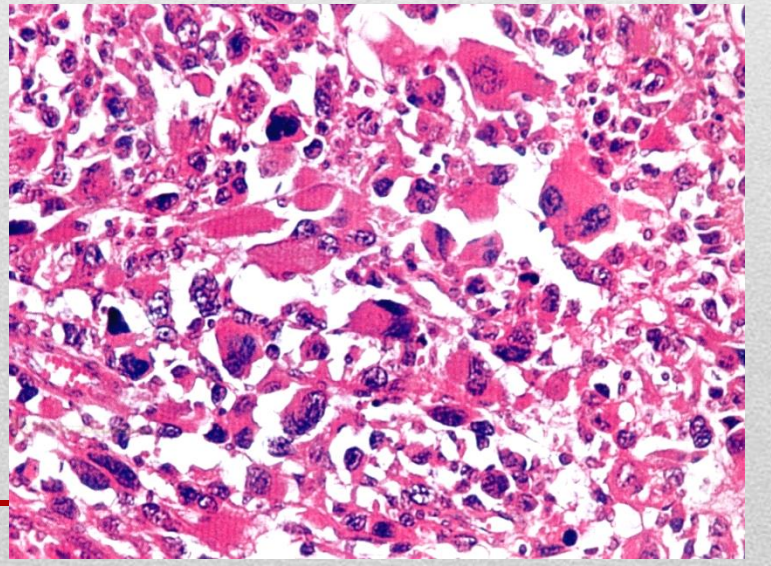
EMBRYONAL RHABDOMYOSARCOMA



BOTRYOID SARCOMA

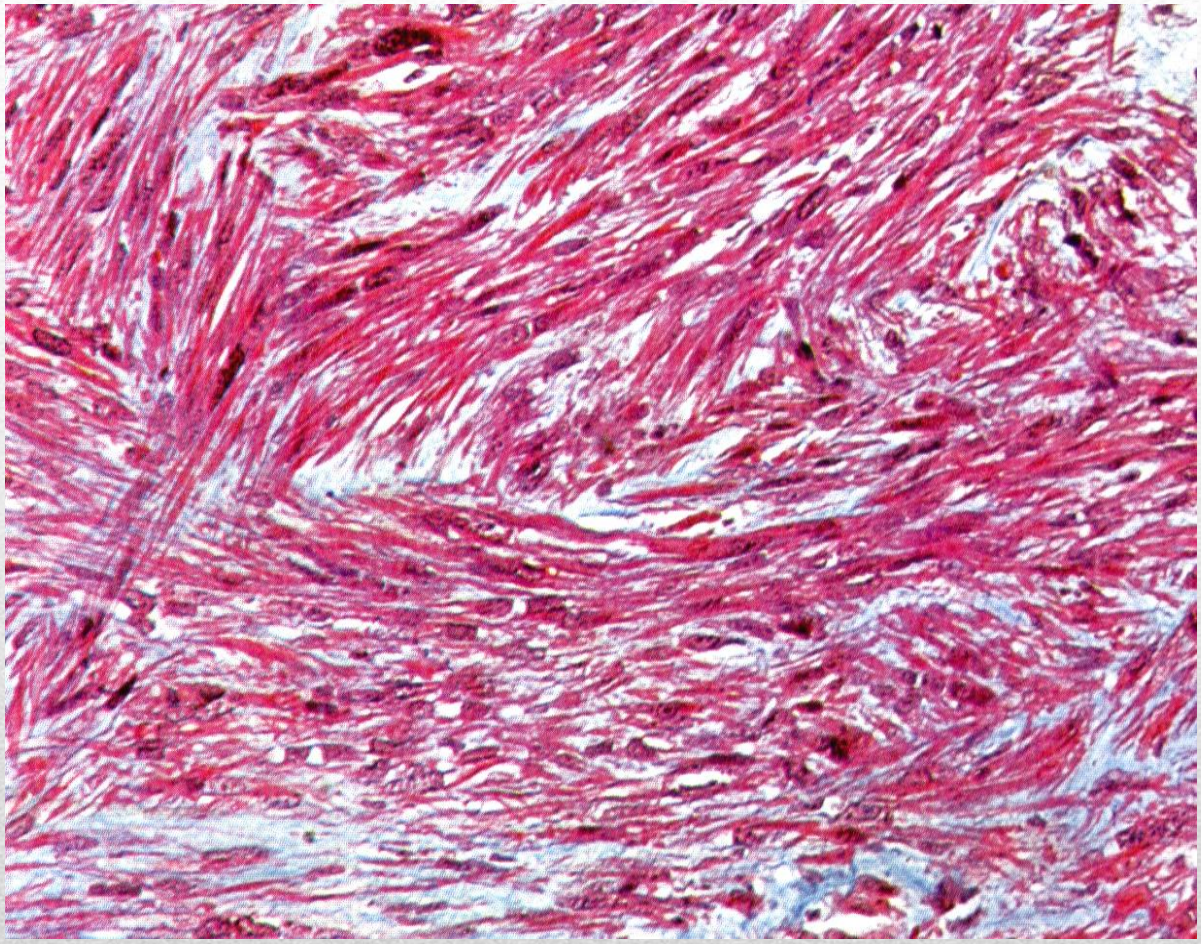


ALVEOLAR RHABDOMYOSARCOMA



PLEOMORPHIC RHABDOMYOSARCOMA

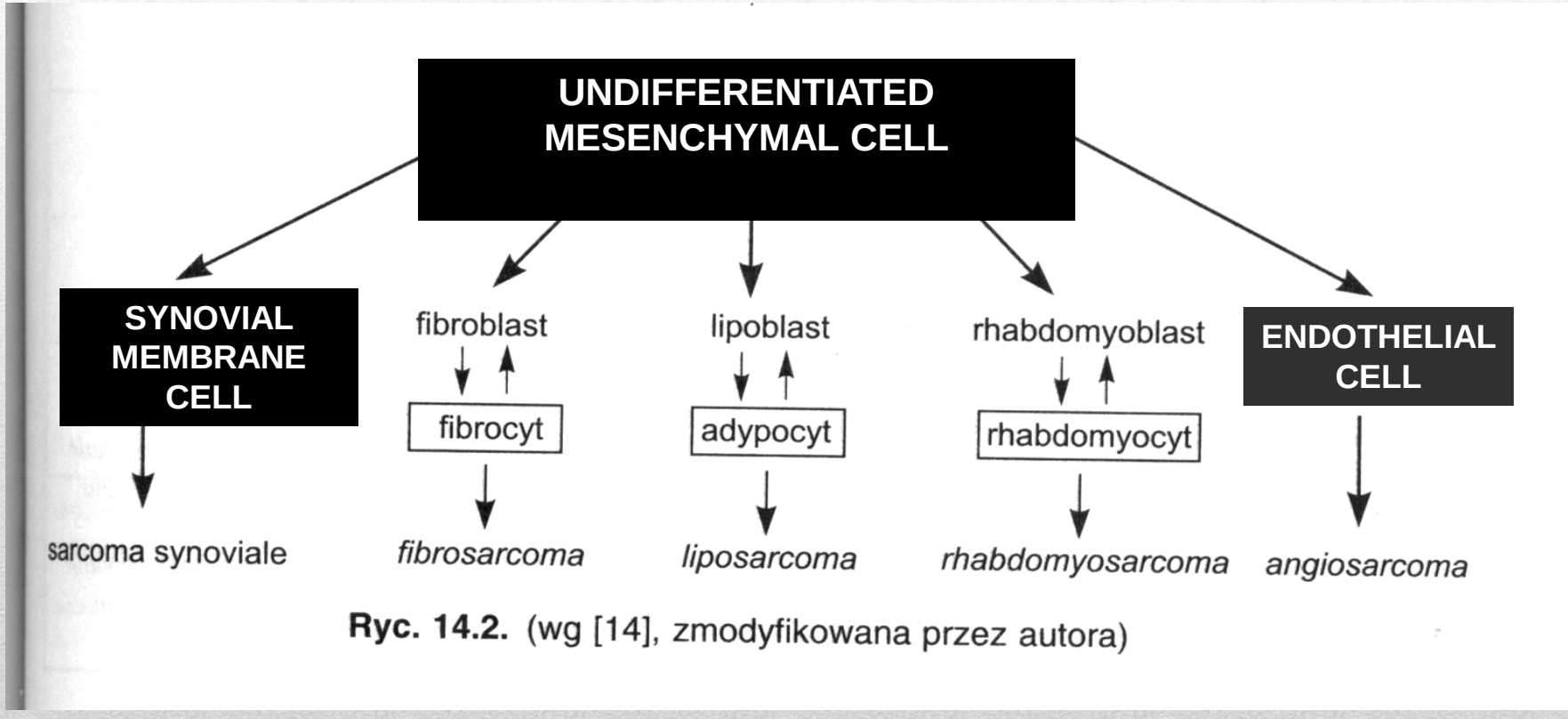
MALIGNANT TUMORS OF MUSCULAR TISSUE



LEIOMYOSARCOMA

MALIGNANT TUMOR OF SMOOTH MUSCLES. RARELY OBSERVED, HIGHLY MALIGNANT; MOST OFTEN SEEN IN THE UTERUS AND ALIMENTARY TRACT

TUMORS OF SOFT TISSUES ARE HETEROLOGOUS IN STRUCTURE AND MAY CONTAIN IMMATURE CELLS; SOME REMAIN VERY PRIMITIVE, SOME CONTAIN MATURE CELLS AND RESEMBLE MATERNAL TISSUE



Ryc. 14.2. (wg [14], zmodyfikowana przez autora)

TUMORS OF SOFT TISSUES

- TUMORS OF SOFT TISSUES CAN BE ENCAPSULATED
- MAY HAVE DISTINCT BORDERS
- THEORETICALLY BENIGN TUMORS ARE ENCAPSULATED WHILE MALIGNANT ARE NOT

THE ENCAPSULATION OR ITS LACK IS NOT A FEATURE WHETHER A TUMOR IS MALIGNANT OR NOT !!!!!!!!!

CLINICAL FEATURES

- Usually arise de novo, not from benign tumors (MPNST may be an exception)
- Do not appear to arise from trauma
- May be caused by radiation therapy (MFH, extraskeletal osteosarcoma), foreign bodies (MFH) or chemical carcinogens (angiosarcoma)
- Recommended to diagnose with FNA, core biopsy or incisional biopsy so appropriate treatment can be determined in advance
- Congenital soft tissue tumors, even with high grade features, rarely have malignant behavior
- Nodal involvement uncommon
- Local recurrences show increased no. of genetic changes

TUMORS OF SOFT TISSUES

Necrosis

NECROSIS AND HEMORRHAGE ARE THE MOST COMMON CHANGES WITHIN MALIGNANT TUMORS

MACROSCOPIC PICTURE

- **MOST SARCOMAS GROW AS SINGLE TUMORS; LOCATED IN DEEPER TISSUES IN CONTRAST TO BENIGN FORMS LOCATED RATHER SUPERFICIALLY; MOST COMMONLY OCCUR IN THE LIMBS AND IN RETROPERITONEAL SPACE**
- **AFTER RESECTION USUALLY REVEAL FLESHY BULGE**

SARCOMA – FLESH-LIKE TUMOR

CRITERIA OF MALIGNANCY

1) **Mitotic activity, including pathological mitosis: localisation of the same type of tumor can influence different criteria of activity, e.g. in leiomyosarcoma in the uterus - should have 10 figures in 10 fields under a large magnification, whereas on the extremities only 1-2 figures.**
2) **Polymorphism of cells**
3) **Necrosis**

These criteria can vary depending on the localization of tumor and histological type.

PROGNOSIS

- **Prognosis depends on the histological type and/or subtype, depth and size of tumor as well as the degree of histological malignancy, G (different systems: NCI-USA, French Federation of Cancer Centers Sarcoma Group)**
- **Mesenchymal tumors metastasize through blood vessels to lungs and liver. Tumors that metastasize mainly through lymphatic vessels are *synovial sarcoma and malignant fibrohistiocytoma*.**

STAGING OF MESENCHYMAL TUMORS

- Significant changes are made in the **8th** edition of the AJCC cancer staging manual for soft tissue sarcomas there is an emphasis on primary anatomic site, due to variability in clinical implications
- This edition divides sarcomas into 4 anatomic sites:
- 1. Extremity and trunk; 2. Retroperitoneum
- 3. Head and neck; 4. Visceral sites
- Staging system applies to soft tissue sarcomas but excludes fibromatosis (desmoid tumor) and Kaposi sarcoma

MOLECULAR/CYTOGENETICS in DIAGNOSTICS

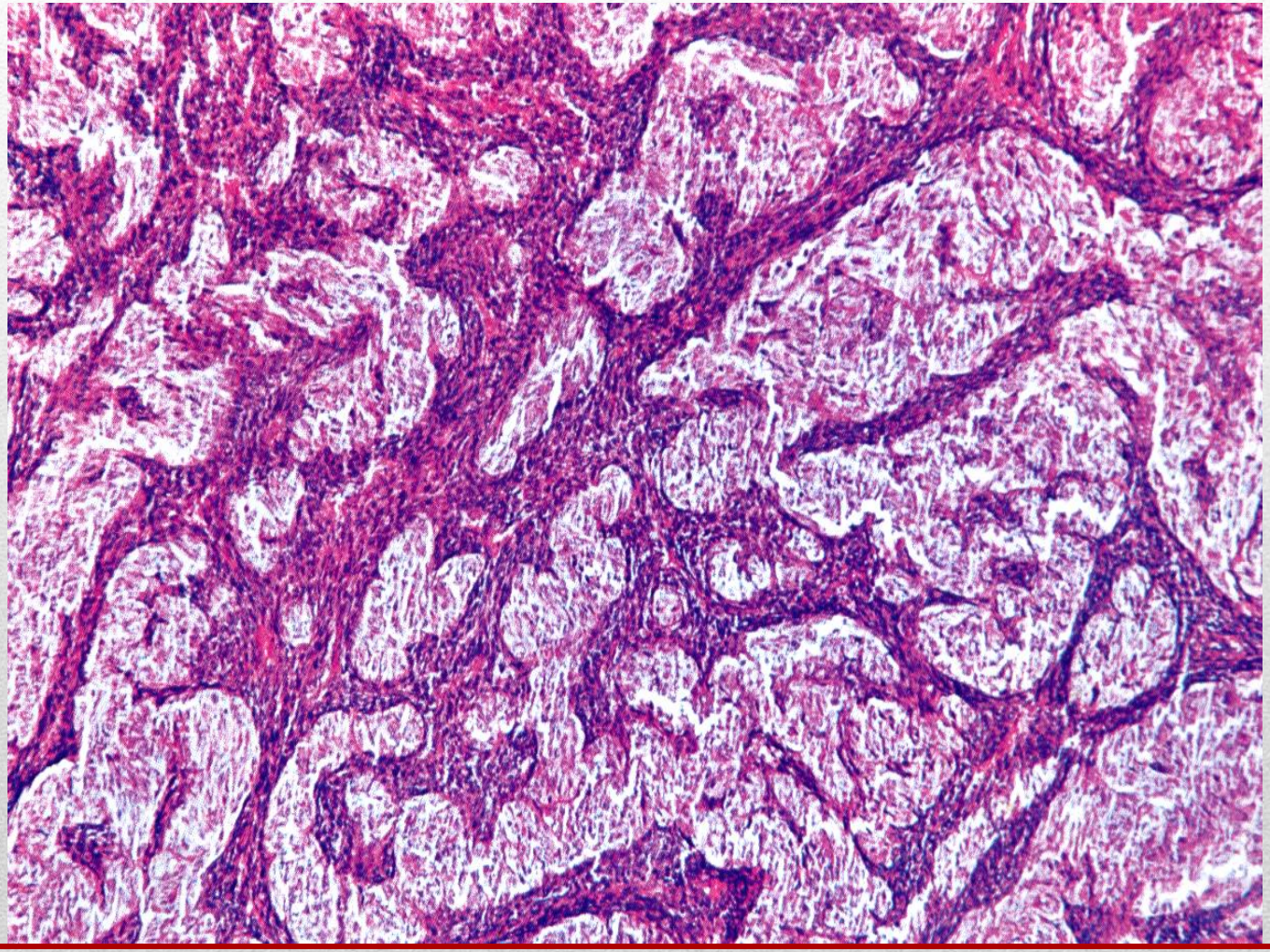
- **RT-PCR or FISH of paraffin-embedded tissue for tumor fusion transcripts is useful, e.g.**
- **1. Rhabdomyosarcoma, alveolar: t(2;13)(q35;q14) - PAX3-FKHR or t(1;13)(p36;q14) - PAX7-FKHR**
- **2. Synovial sarcoma: t(X;18)(p11.23;q11) - SYT-SSX1 or t(X;18)(p11.21;q11) - SYT-SSX2 fusion genes**

SYNOVIAL SARCOMA: DEVELOPS AT EVERY AGE, MOST COMMON BETWEEN 15-35

it develops from synovial epithelial cells. Most commonly occurs on the lower extremities in the knee; can develop anywhere where ligaments are present. Typical histological picture has two patterns: similar to fibrosarcoma and with formations of pseudoglands; single patterns are observed as well; tumor of a long course of many years.

PROGNOSIS IS GENERALLY POOR

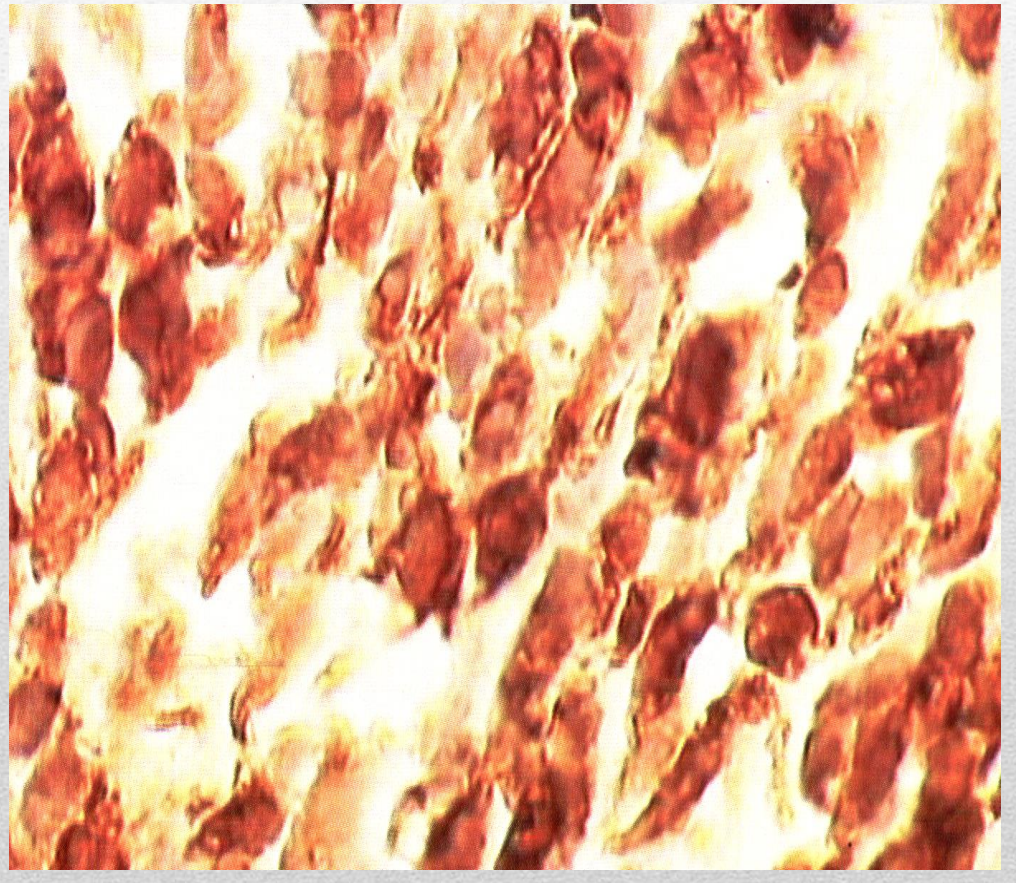
synovial sarcoma



IMMUNOHISTOCHEMICAL DIAGNOSIS - VIMENTIN

VIMENTIN is a filament occuring in the mesenchymal cells

VIMENTIN in rhabdomyosarcoma embryonale cells

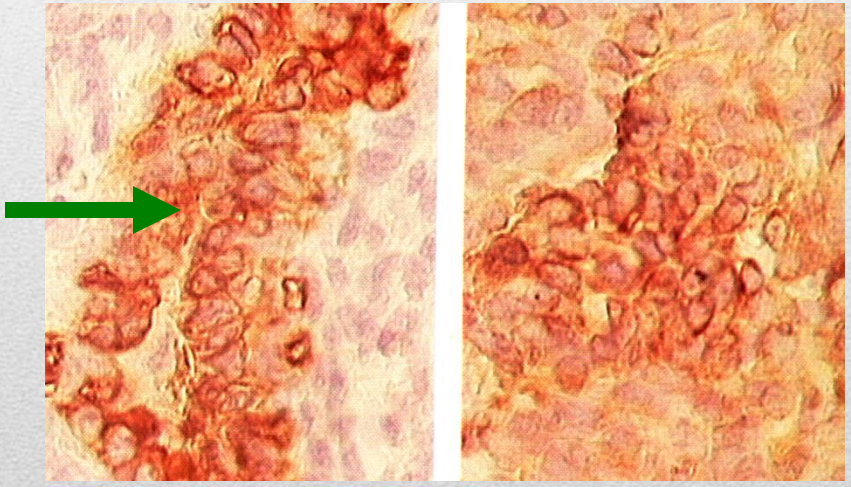


IMMUNOHISTOCHEMICAL DIAGNOSIS

SYNOVIAL SARCOMA

1. Cytokeratin 19 reaction in the gland-like region

2. Vimentin reaction in the spindle-cell region



1. 2.

ARCHITECTURAL PATTERNS

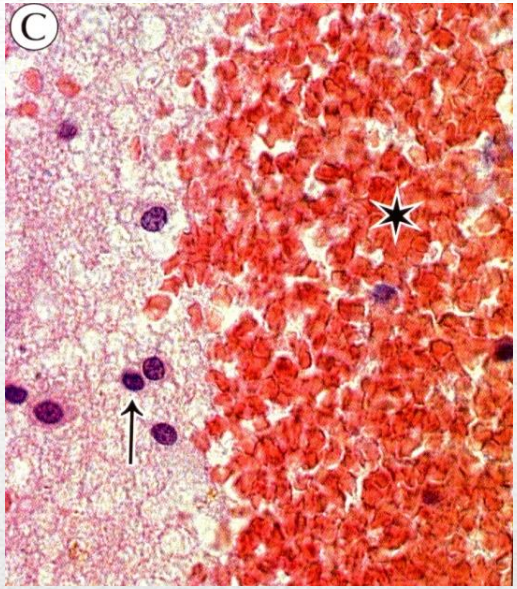
- Alveolar: alveolar rhabdomyosarcoma, alveolar soft parts sarcoma
- Fascicular: fibromatosis, fibrosarcoma, neural tumors (benign or malignant), smooth muscle tumors, synovial sarcoma
- Glandular: adenocarcinoma, biphasic synovial sarcoma, glandular MPNST
- Lobular: clear cell sarcoma, epithelioid sarcoma, extraskeletal myxoid chondrosarcoma
- continued

- Palisading: palisading intranodal myofibroblastoma, Schwann cells (neural tumors), smooth muscle tumors, spindle cell lipoma, synovial sarcoma
- Pericytic vascular: mesenchymal chondrosarcoma, MFH, myopericytoma, solitary fibrous tumor / hemangiopericytoma, synovial sarcoma
- Plexiform: nerve sheath tumors (neurofibroma, schwannoma), plexiform fibrous histiocytoma
- Plexiform vascular: low grade fibromyxoid sarcoma, myxofibrosarcoma, myxoid liposarcoma, nodular fasciitis
- Storiform: dermatofibrosarcoma protuberans (DFSP), fibrohistiocytic tumors, MFH, perineurioma

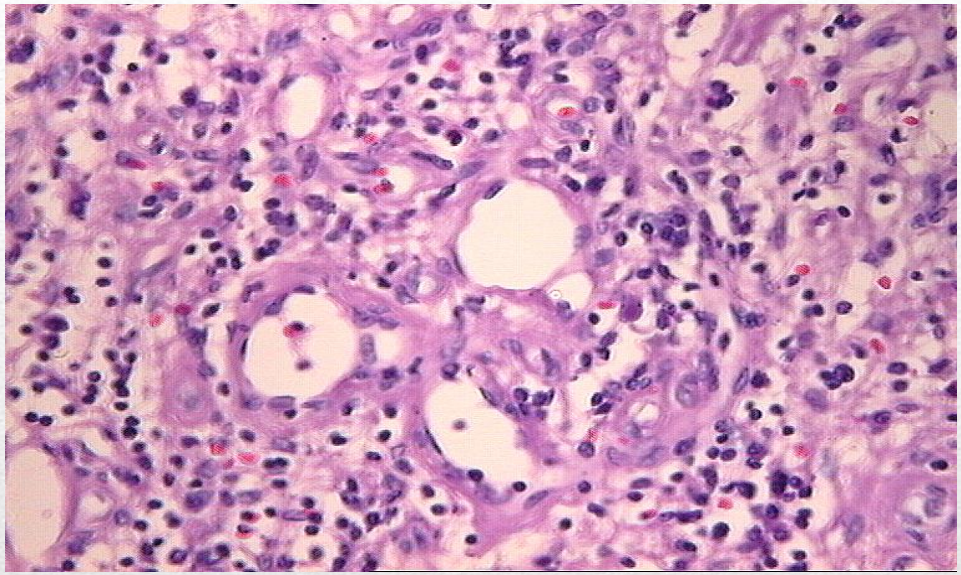
TUMOR-LIKE LESIONS (CONDITIONS) – GENERAL REMARKS

- they are not true tumors but rather a reaction of a tissue to destructive agents – they resemble tumors
- these changes can be of different sizes, routine surgical excision is enough to treat, no relapses
- increased inflammation and hemosiderin deposits are seen in these lesions and around them

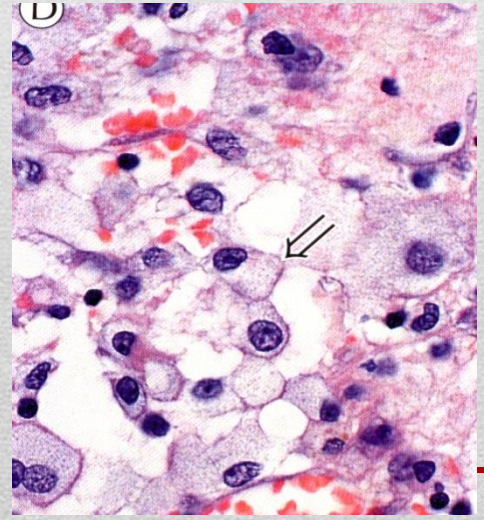
TUMOR-LIKE CONDITIONS



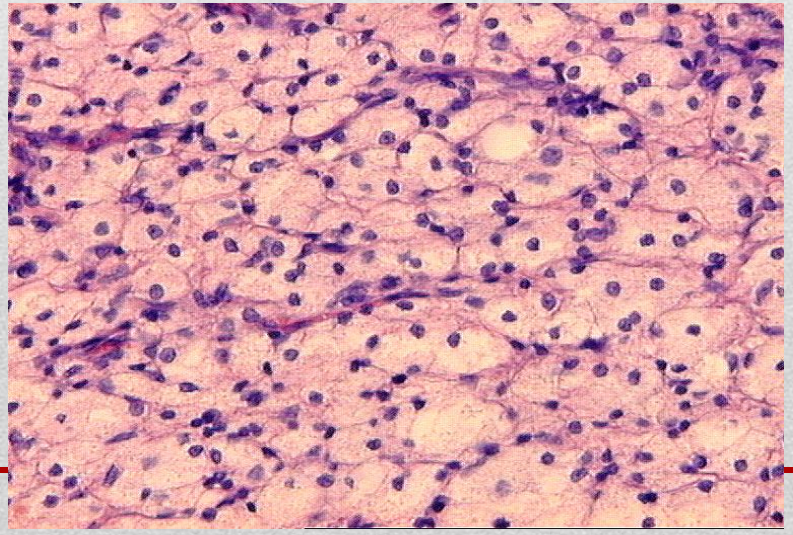
HEMATOMA



PYOGENIC GRANULOMA

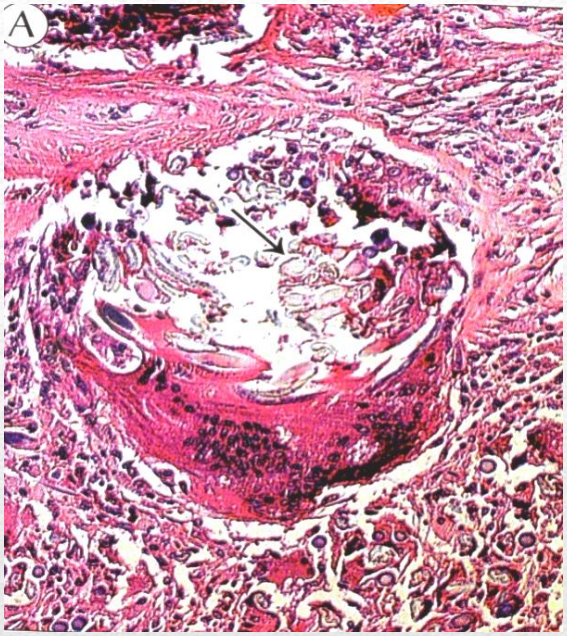


FAT TISSUE NECROSIS

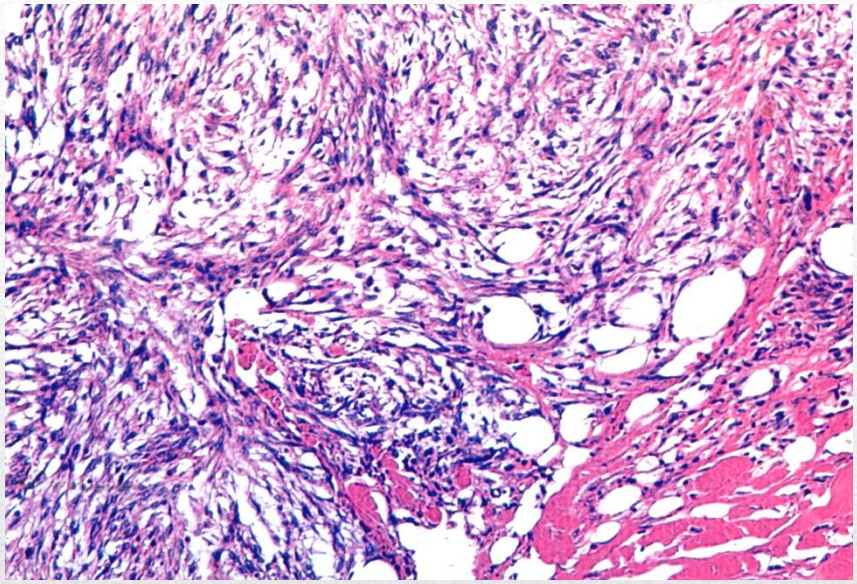


XANTHOGRANULOMA

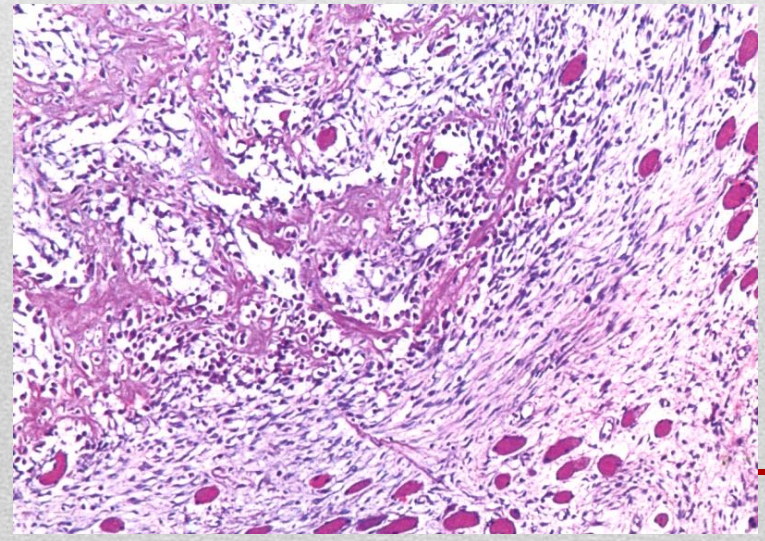
TUMOR-LIKE CONDITIONS



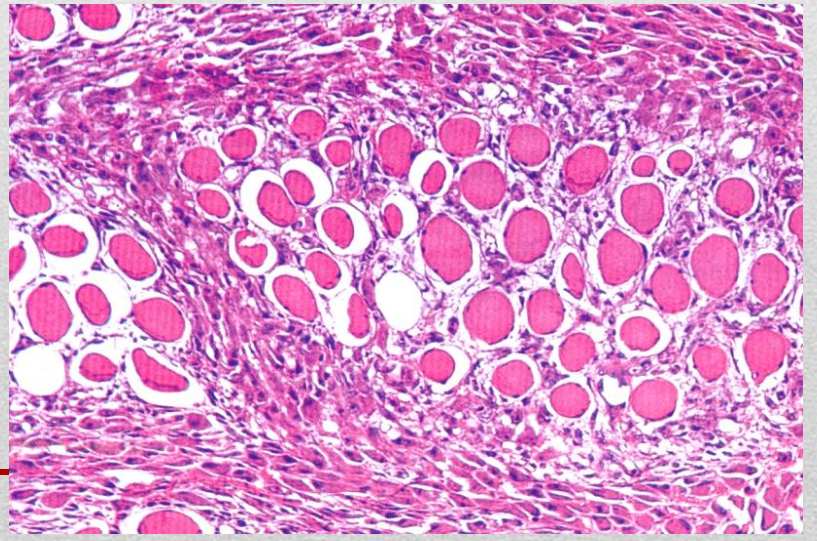
FOREIGN BODY GRANULOMA



NODULAR FASCITIS



MYOSITIS OSSIFICANS



PROLIFERATIVE MYOSITIS

THANK YOU