BONE TUMORS

"Most Commons"

- Most common **PRIMARY** bone tumor = **HEMATOPOIETIC** (40%) *(Multiple Myeloma probably #1)*
- **BENIGN TUMORS MORE COMMON** than Malignant
  - Most common are matrix producing-bone & cartilage; fibrous tumors
- Most common **BENIGN** tumors = **OSTEOCHONDROMA** (**teens & older**) & **Fibrous Cortical Defect**
  - Bone tumors in **CHILDREN & YOUNG ADULTS**, most likely **BENIGN**
- Most common **MALIGNANT** tumor = **OSTEOSARCOMA**, then Chondrosarcoma & Ewings Sarcoma
  - Bone tumors in **ELDERLY**, most likely **MALIGNANT**
- **METASTATIC** tumors are most common **Secondary** bone tumor (from breast, lung, thyroid, kidney, prostate)

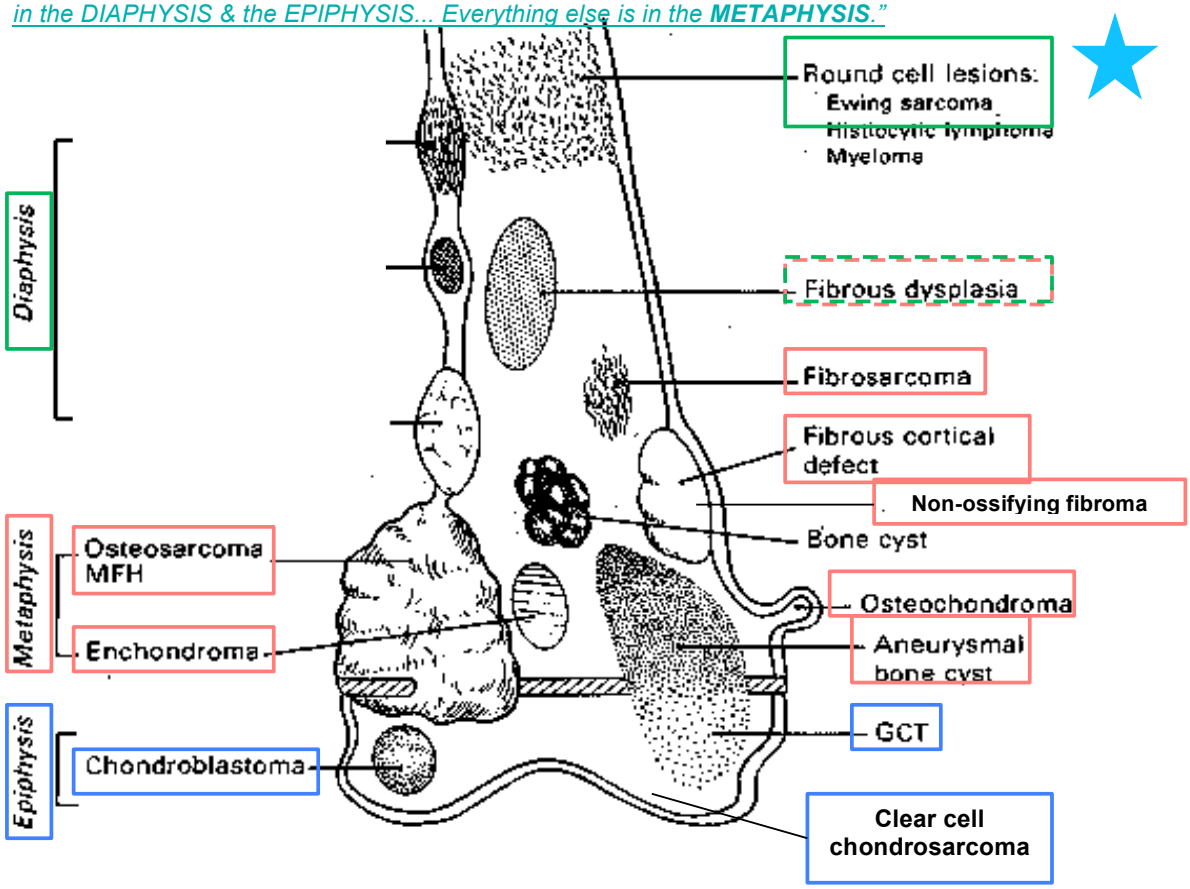
HEREDITARY ASSOCIATIONS

- Li Fraumeni Syndrome (p53 mutation – TSG)
- Hereditary retinoblastoma (Rb mutation – TSG) – **OSTEOSARCOMA**
- ***Be sure to know which are TSG vs. oncogenes. On step, you may get a question that describes a cancer/syndrome you know, but the answer will be "tumor suppressor gene" or "oncogene" rather than p53 or Rb.*
  - *"Patient with an eye tumor & osteosarcoma... What is the most likely gene?* **TSG**!"

OTHER ASSOCIATIONS W/ BONE TUMORS

- Paget Disease
- Metal prosthesis (i.e. artificial hip)
- Chronic osteomyelitis
  - **REMEMBER**: If it is *draining osteomyelitis,* it is associated with **SQUAMOUS CELL CARCINOMA**!
- Bone infarcts
  - **REMEMBER**: *What drug is associated with bone infarcts?* **CORTICOSTEROIDS**
  - *What is disorder is associated with bone infarcts?* **SICKLE CELL DISEASE**

****LOCATIONS –** *"I can't stress enough how important the locations are. Tumors have CLASSIC locations. Learn the ones in the DIAPHYSIS & the EPIPHYSIS... Everything else is in the* ***METAPHYSIS****."*

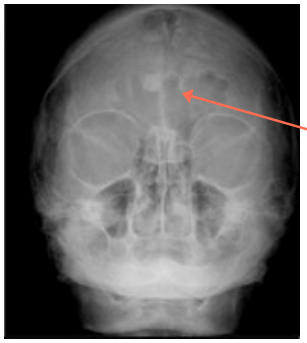


BENIGN BONE TUMORS

- Benign tumors commonly present as **incidental finding** on XR
- May present as pain with slow growing mass OR as **pathologic fracture**

OSTEOMA

- **BENIGN** tumor composed entirely of **BONE**
- Subperiosteal or endosteal **cortex surface**
- Commonly found in **SINUSES, SKULL, & face**
- Typically **incidental finding**, unless obstructing or impinging
  - *It can impinge on brain or obstruct sinus*
- **Gardner Syndrome** – multiple osteomas
  - **Intestinal polyps (FAP)**, epidermal cysts, & fibromatosis
  - *"If this was your pt's XR, next step:* **COLONOSCOPY**!"

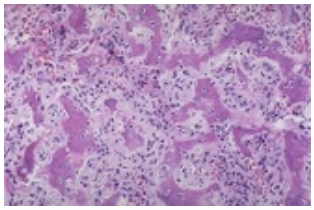


OSTEOMA in Sinus
**This is how it is classically represented*

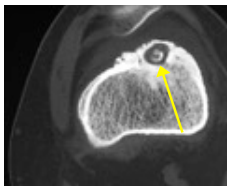
OSTEOID OSTEOMA & OSTEOBLASTOMA

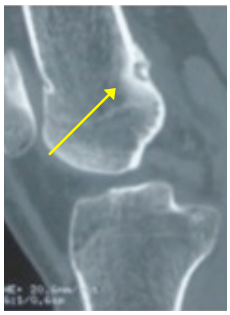
- **BENIGN, BONE-producing tumor**
- Histology is same in both: Osteoblasts on woven bone with loose vascular connective tissue
- **Size is important in dx. Be sure to know the size.*
  - ***Classic question:*** *"Small lesion of the phalanges than it less than 2cm in size. Nidus present. Pain worsens at night, but improves with aspirin."* → **OSTEOID OSTEOMA**

	OSTEOID OSTEOMA	OSTEOBLASTOMA
LOCATION	Metaphysis **Cortex**	Metaphysis **Medulla**
BONES**	Femur/tibia (50%) **Humerus/HANDS/Feet**	**POSTERIOR VERTEBRAE**
SIZE**	**LESS THAN 2 CM**	**MORE THAN 2 CM**
PAIN	Painful; intense at **NIGHT** *Due to PGE_2 produced by osteoblasts*	Dull ache
ASA RELIEF**	Relieved by **ASPIRIN**	NO ASA RELIEF
X-RAY	Central **NIDUS** (lucency) +/- central bone density in **cortex** +/- surrounding bone sclerosis *****DDX****: Osteomyelitis looks similar on XR – FEVER in osteomyelitis is differential*	Radiolucent
TREATMENT	Radioablation	Excision/curettage
HISTOLOGY	*Osteoblasts on woven bone with loose vascular connective tissue*	

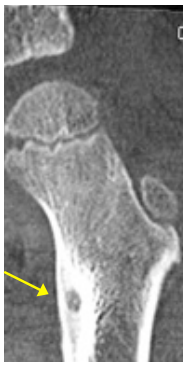


Central Nidus composed of irregular reactive new bone (woven bone)



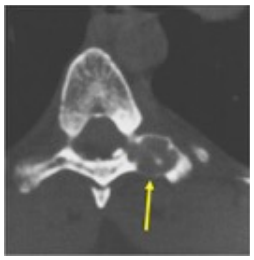


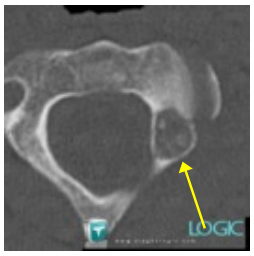
NIDUS in center
-Nidus is a bone-making nodule
-Seen here in **cortex**



Surrounding sclerotic bone very obvious here (dense white)

OSTEOID OSTEOMAS

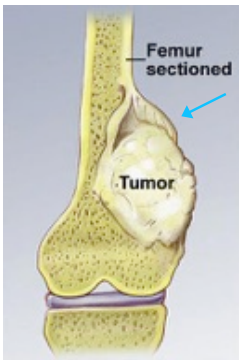


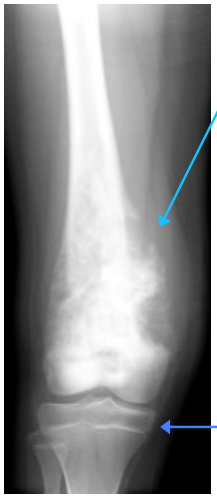


OSTEOBLASTOMAS

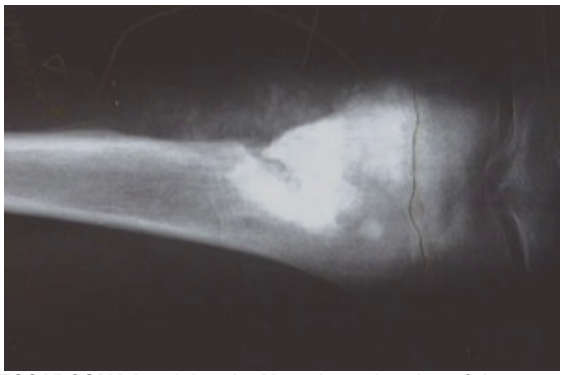
OSTEOSARCOMA

- *By definition, any malignant tumor that **makes osteoid** is considered an osteosarcoma*
- Most Common *Non-Hematopoetic* Malignant PRIMARY bone tumor
- **75% UNDER 20 YEARS OLD** (Classic = **TEENAGER**) → 50% in the **KNEE** – *"proximal tibia, distal femur"*
- In Elderly → Usually secondary to **Paget's Disease**, bone infarction, **prior irradiation**, & in FLAT/LONG BONES
- ***Painful***, enlarging mass
- **"CLASSIC" PRESENTATION OF OSTEOSARCOMA:**
  - **Primary**, solitary, of the long bone (**KNEE**)
  - **METAPHYSIS MEDULLA**
  - Poorly differentiated with boney matrix
- ****X-RAY**: destructive with MIXED lytic + blastic *(destroying bone & making bone)* & ***erodes through cortex***
  - **CODMAN TRIANGLE:** Tumor lifting periosteum
    - ^*The Triangle is NOT specific for osteosarcoma, but it is usually present & a GREAT indicator!*
- Osteosarcoma exhibits **BLOOD-BORNE** metastasis (lungs, bones, brain)
  - 10-20% have lung metastasis at presentation → First-line therapy: ChemoRx
- Long-term survival 60-70%
- Associated with Hereditary Retinoblastoma (RB) & Li-Fraumeni Syndrome (p53)

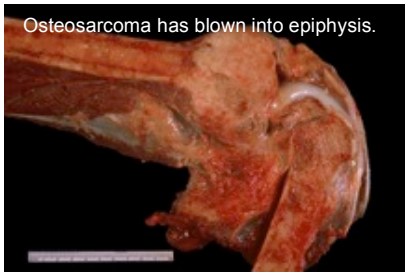


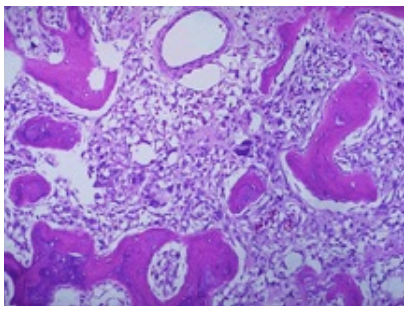


When you look at an X-ray, 1st LOOK FOR A GROWTH PLATE.
If you see a growth plate + Codman Triangle – you should think:
"Classic" Osteosarcoma in a TEENAGER!



OSTEOSARCOMA involving the Metaphyseal region of the upper tibia. The tumor erodes & destroys the bone cortex, extending into soft tissue where irregular tumor bone with calcification is seen. At the L, the periosteum is being lifted up (CODMAN'S TRIANGLE)

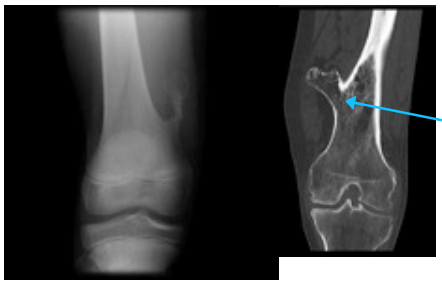


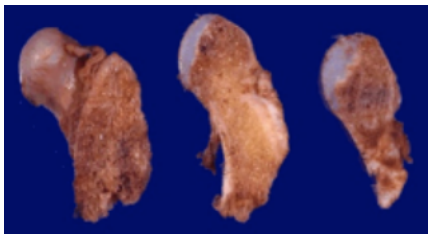


For Step, you should be able to recognize Bone vs. Cartilage on a histological slide, but unlikely you would have to recognize a slide & answer question without proper history in stem.

OSTEOCHONDROMA "Exostosis"

- Most Common **BENIGN** primary bone tumor
- Slow growing mass in the **METAPHYSIS** *near growth plate* of long tubular bones (**KNEE**)
- **XRAY: Mushroom-shaped**, cartilage-capped, **continuity of marrow & cortex** w/ bone, *usually turns away from epiphysis*
- Most common in **TEENS/YOUNG ADULTS** – stops growing with closure of growth plate
- **Multiple Hereditary Exostosis** (AD)
  - Rare risk of **Chondrosarcoma** increased with Hereditary Exostosis
- *Asymptomatic*, until it impinges on nerve or fracture → ***Pain***





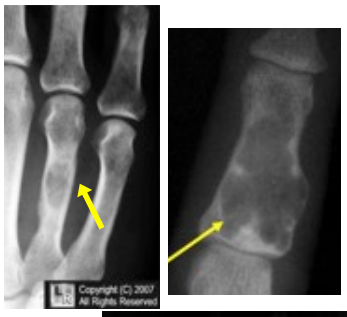
SUBPERIOSTAL CHONDROMA (Juxtacortical Chondroma)

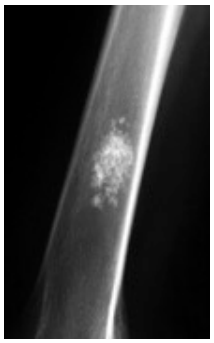
- BENIGN hyaline cartilage tumor found at the surface of bone
- **Age 20-50 "young people"**

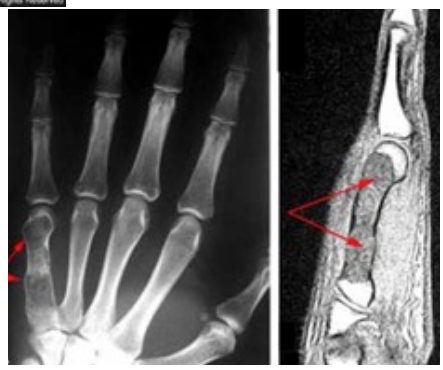
ENCHONDROMA – *"This is an important one to know!"*

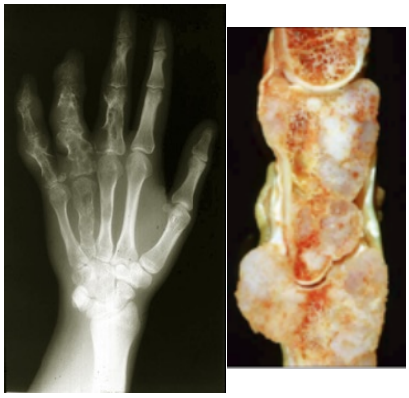
- **BENIGN** hyaline CARTILAGE tumor – ***less than 3cm*** *nodules with peripheral enchondral ossification*
- Enchondroma = "inside the bone"
- Solitary tumor in **METAPHYSIS** (medullary cavity) of tubular bones
- Most Common **INTRAOSSEOUS CARTILAGE** tumor
- Most Common ***(incidental finding)*** bone tumor of the **PHALYNX***
  - *"Most questions on this usually come from the hand."*
- **Age 20-50 y/o – *"young people"***
- Rarely transform to sarcoma. Things to increase risk for **Chondrosarcoma** transformation:
  - **Enchondromatosis (Ollier Disease)**
  - **Maffucci Syndrome**: Enchondromas + hemangiomas
- **X-RAY:** Well-circumscribed lucency w/ a thin rim of dense bone; *if calcified matrix – irregular opacities*

ENCHONDROMA
"You need to be able to recognize this X-ray – Notice the **"SOAP BUBBLE LESIONS"**



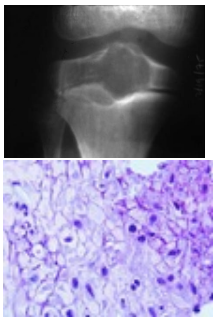






Multiple Enchondromas
Notice the deformity of the bones of his last 3 fingers

CHONDROBLASTOMA

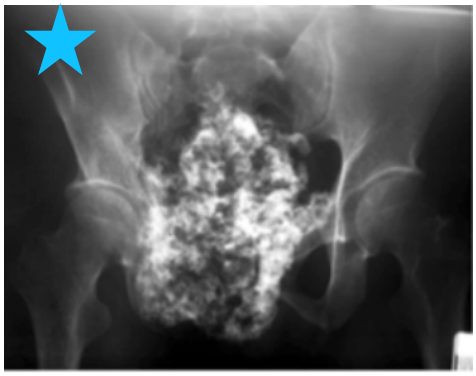


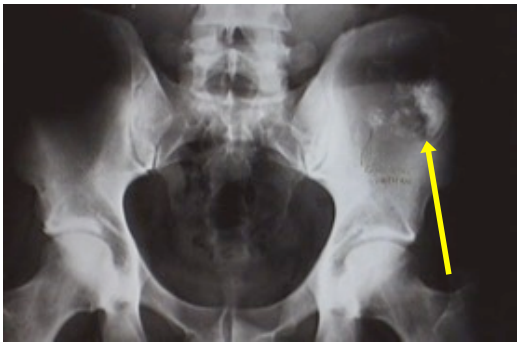
- RARE, BENIGN **CARTILAGE** tumor
- Seen in **Teenagers**
- Most common in **EPIPHYSIS of the KNEE**
- *Painful*
- X**-RAY:** Well-demarcated lucency
- Chondroblasts in hyaline matrix can calcify creating "chicken-wire" pattern

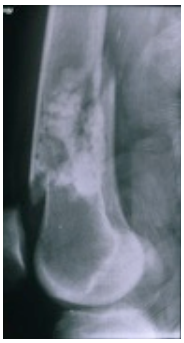
CHONDROSARCOMA

Let's think → Most Common's
TEEN → OSTEOSARCOMA
40 Y/O → CHONDROSARCOMA
PAGET'S DISEASE → OSTEOSARCOMA
IN EPIPHYSIS + TEEN → CHONDROSARCOMA

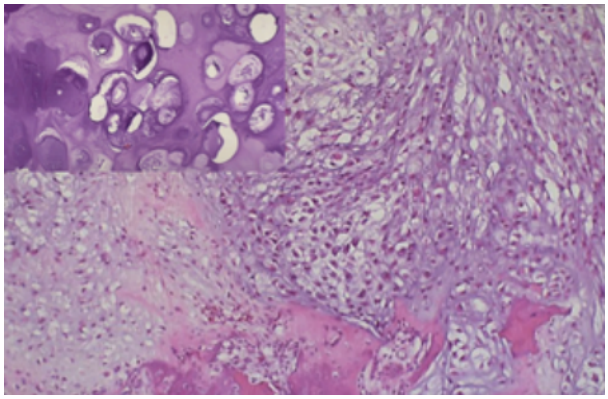
- *Second most common malignant matrix-producing tumor of the bone*
- **MALIGNANT** cartilage* tumor +/- spotty calcifications
- **Most often in patients OVER 40 y/o**
  - BUT... ***Clear Cell Chondrosarcoma = Teens/Young Adults**
    - *Chondrocytes w/ clear cytoplasm*
- Affects **PELVIS**, Shoulder, Ribs
  - Except... **Clear Cell Chondrosarcoma appears in EPIPHYSIS*** of **Long tubular bones** (i.e. limbs)
  - ***If you see a tumor in the EPIPHYSIS in a teenager → Think: Clear Cell Chondrosarcoma!*
  - Remember picture above with LOCATIONS?? Only Giant Cell Tumors (ADULTS), Clear Cell Chondrosarcoma, & Chondroblastomas (RARE) are found in the Epiphysis!
- **15% arise within enchondroma** – *High risk w/ Multiple Enchondromas (Ollier Disease) & Osteochondroma (Multiple Hereditary Exostosis)*
- **X-RAY:** Nodular growth with endosteal scalloping & flocculent densities from calcification – LOOKS LIKE **CLOUD**
- **GROSS EXAM**: grey/white/blue glistening appearance
- **Metastasis** to Lungs & Bone
- *Just be aware that there are Mesenchymal & Dedifferentiated variants of Chondrosarcomas*



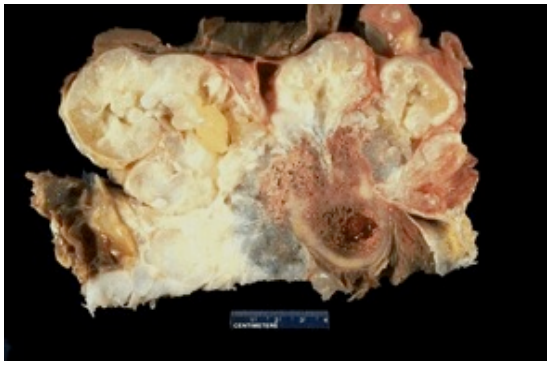




"This is most likely what you're going to see on a test – Something around the pelvis that looks like a **CLOUD!***"*



IT'S CARTILAGE!!



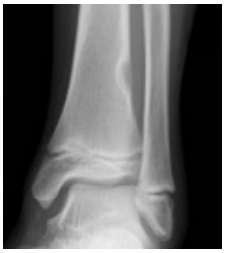
Extensive nodules of white to bluish-white cartilaginous tumor tissue eroding & extending outward from the bone

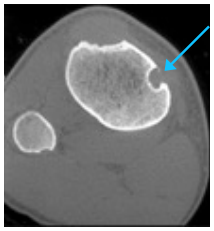
FIBROUS CORTICAL DEFECT & NON-OSSIFYING FIBROMA

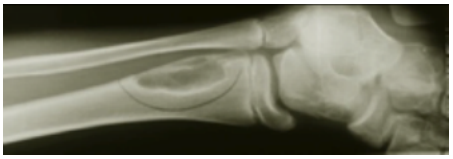
- Grey-yellow-brown tissue composed of **fibroblast & histiocytes** – **NO BONE**
- **X-RAY: LYTIC** lesion in **METAPHYSIS CORTEX** of the **KNEE**

	FIBROUS CORTICAL DEFECT	NON-OSSIFYING FIBROMA
AGE	40% of **Children** *MOST COMMON TUMOR IN **CHILDREN**	**Adolescent**
PRESENTS	**Incidental finding**	Incidental or pathologic fracture
LOCATION	Metaphysis **Cortex** of the **KNEE**	Metaphysis **Cortex** of the **KNEE**
SIZE**	**VERY Small** < 0.5 cm	**VERY Large** up to 6 cm
COURSE	Normally **resolves** into normal bone	**PERSISTS** *Most likely prior fibrous cortical defect*
	Grey-yellow-brown tissue composed of fibroblasts & histiocytes	

"Typical Pictures"



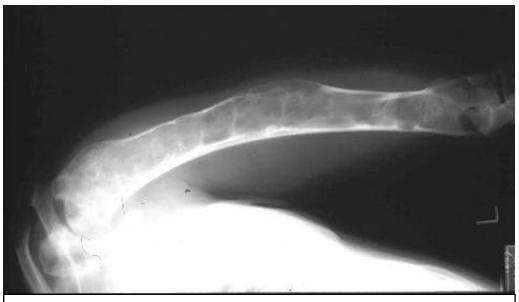




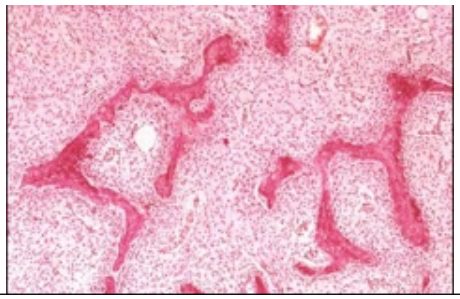
-Skeletally immature
-Large Lesion
-Starts in Cortex

FIBROUS DYSPLASIA

- Occur in **METAPHYSIS** or **DIAPHYSIS**
  - *This is one of only TWO that we have talked about in Diaphysis – Fibrous dysplasia & Ewing Sarcoma*
- **X-RAY**: Ground glass ("**SOAP BUBBLE**" appearance) & well-demarcated intramedullary
- **GROSS EXAM:** tan-white & gritty appearance
- **MICROSCOPY:** "**Classic" Chinese Character** WOVEN bone in fibrous stroma (fibroblasts)
- **MONOSTOTIC Type***most common (70%)
  - Occurs in **TEENS** – *stops w/ growth plate closure*
  - Affects Ribs, Femur, Tibia, Jaws, Calvaria (*skull*), & Humerus – *variety of places*
  - Incidental finding in most cases; can deform the bone
- **POLYOSTOTIC Type**
  - **Mazabruad Syndrome**: Polyostotic Fibrous Dysplasia + soft tissue myxomas
  - ***McCune Albright Syndrome**: Polyostotic Fibrous Dysplasia + café au lait spots + Endocrine dysfunction
    - **ENDOCRINOPATHY**** – *sexual precocity (often), hyperthyroidism, pituitary adenomas with GH, primary adrenal hyperplasia*
      - *8 y/o girl comes in who has started developing breast – DDx: McCune Albright*
      - *Café au lait spots + Bone Lesions = McCune Albright*
    - Hyperactive G-Protein of **GNAS** gene
  - Polyostotic type has increased risk to become malignant



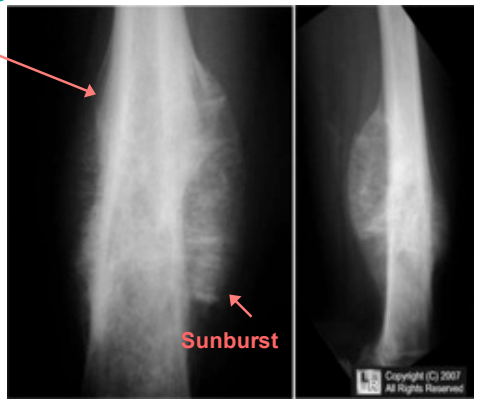
Fibrous dysplasia in Diaphysis going into Metaphysis – Note **"Soap Bubble"** look

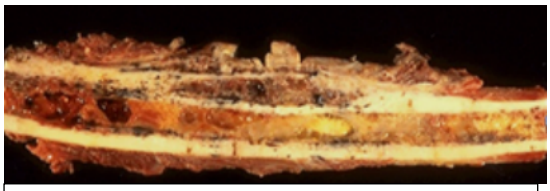


Chinese Characters – *"Classic Picture"*
-No osteoblastic activity

EWING SARCOMA (ES) & PRIMITIVE NEUROECTODERMAL TUMOR (PNET)

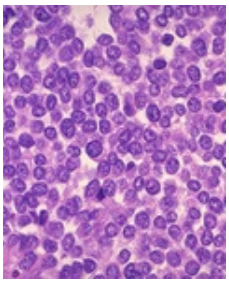
- Translocation: **t(11;22) EWS-FLI1**
- **Under 20 y/o** (80%) – **TEENAGERS**
- **DIAPHYSIS** of long tubular bones (**FEMUR**) & flat bones of **PELVIS**
- ***FEVER***, *anemia*, ***leukocytosis***
  - **This TUMOR has FEVER – Not an infection. Osteomyelitis also has a fever – Due to infection.*
- **X-RAY: LYTIC destruction** with **ONION SKIN** periosteal reaction & **SUNBURST pattern**
  - **Cortical erosion + Soft tissue extension**
- **Small, round (blue) cell** tumor of *bone & soft tissue*, **Glycogen Positive (PAS Stain)**, Homer-Wright Rosettes
- **How to distinguish Osteosarcoma & Ewing Sarcoma on Test**: Osteosarcoma is usually in Metaphysis & Ewing Sarcoma is in DIAPHYSIS



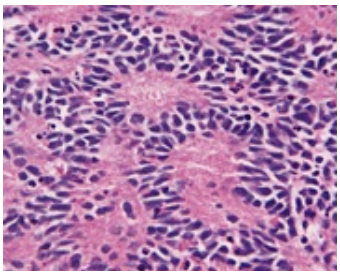


The irregular tan-red-brown tumor mass is breaking through the cortex. More normal fatty marrow is seen at the far right.

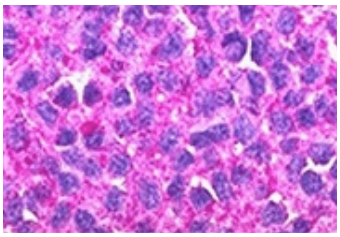
Small Round Blue Cells



ROSETTES

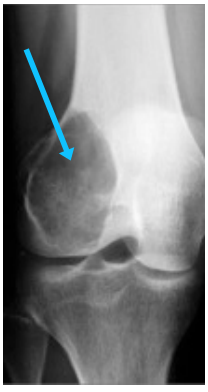


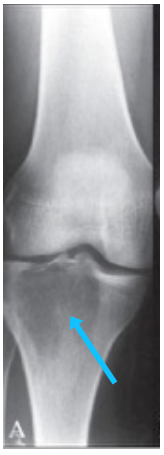
PAS Stain for Glycogen +

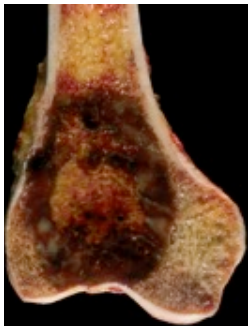


GIANT CELL TUMOR OF BONE

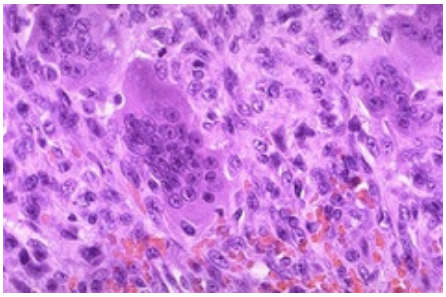
- BENIGN, locally aggressive tumor of **Macrophage/Monocyte** system
  - **Giant cells** (numerous multinucleated cells – 100+ nuclei)
  - Mononuclear cells (oval) express **RANKL** – *RANKL is on Osteoblasts!*
  - Hemorrhage, reactive bone
- Large, cystic red-brown (**hemosiderin**) tumor
- **Adults: EPIPHYSIS**, but may extend *into* ***Metaphysis*** of **KNEES**
- **X-RAY:** LYTIC lesion; may erode cortex into soft tissue w/ thin shell of covering bone
- ***Benign tumor associated with Paget's Disease***





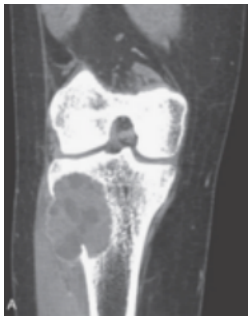


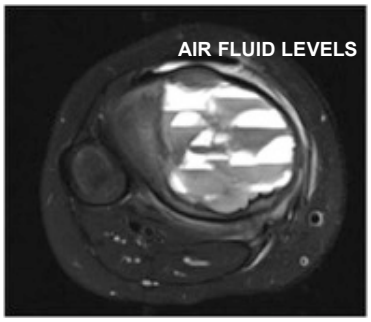
Brown = Hemosiderin

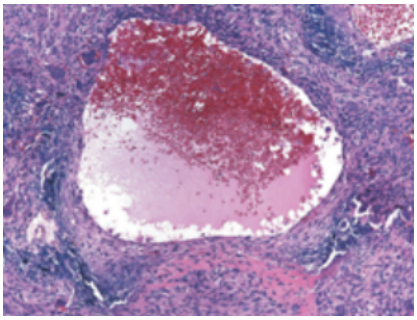


ANEURYSMAL BONE CYST

- Rapidly growing, blood-filled cyst (local)
- **METAPHYSIS** of Long bones & **Vertebrae**
- **Under 20 y/o**
- Most often *pain & swelling*
- **X-RAY**: Eccentric, expansile, well-demarcated – **AIR-FLUID LEVELS!!!!!**
- **HISTOLOGY:** BLOOD-FILLED CYSTS, WOVEN bone w/ **Fibroblasts + Multinucleated Giant Cells** (few)







METASTATIC DISEASE

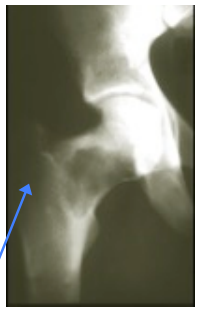
- Most Common form of **Skeletal Malignancy!**
- Pathway of spread: Direct extension, Lymphatic or Hematogenous, Intraspinal seeding (Batson Plexus Veins)

ADULT METASTATIC DISEASE

- 75% are from **PROSTATE** *(usually sclerotic bone response)*, **BREAST**, **KIDNEY**, **LUNG**, **THYROID**
  - *"BLT and a Kosher Pickle" – Breast, Lung, Thyroid, Kidney, Prostate*
- Most often in **AXIAL SKELETON**
- Osteo**blastic** Metastases in Vertebral column + **Male** = Metastatic **PROSTATE** Carcinoma
  - ***Male** comes in with **osteosclerotic bone w/ multiple lesions**:*
    - *If problem is Metabolic – Think: **Paget's Disease***
    - ***If problem is metastasis – Think: Metastatic Prostate!****
- *Female comes in with bone lesion. What should you do with the patient?* **Breast Exam!**

Osteoblastic metastasis from Metastatic Prostate Carcinoma

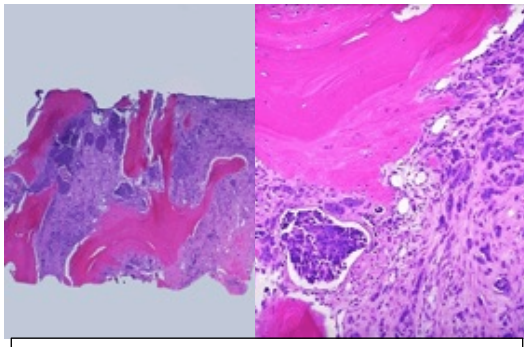
Multiple areas where bone appears to be replaced by yellow-white tissue – Think: METASTATIC TUMOR!



Metastatic Carcinoma, Lytic Lesion

PEDIATRIC METASTATIC DISEASE

- Neuroblastoma
- Wilms Tumor
- Osteosarcoma
- Ewing Sarcoma
- Rhabdomyosarcoma



Bone Metastasis – Ductal Breast Carcinoma

SOFT TISSUE TUMORS

Fatty, Fibrous, Fibrohistiocytic, Skeletal muscle, Smooth muscle, Vascular, Peripheral, Tumors of uncertain histogenesis

SOFT TISSUE TUMORS

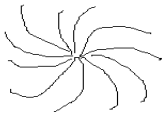
- Usually benign, hematogenous spread to lungs, liver, bone
- Most common in **THIGH**, truck, & retroperitoneum
- Most Common in Children – **Rhabdomyosarcoma**
- Most Common in Young Adults – **Synovial Sarcoma**
- **Bone involved by direct extension or metastasis –** *Touching the bone, but the cortex is not involved*
- Most common cause is UNKNOWN, but associated with radiation, trauma (i.e. mastectomy-angiosarcoma), HHV8: Kaposi's sarcoma, chemical exposure, & thermal burns

GENETIC SYNDROMES

- **Neurofibromastosis Type 1 (Nf1)** – malignant peripheral nerve sheath tumor; *café au lait, lisch nodules*
- **Gardner Syndrome (APC)** – Deep fibromatsosis (desmoid tumors), *multiple osteomas, polyposis*
- **Li-Fraumeni Syndrome (p53)** – soft tissue sarcoma & other malignancies
- **Hereditary Hemorrhagic Telangiectasie (Osler-Weber-Rendu)** – telangiectasias over skin & mucosal surfaces

TUMOR GENETIC CHANGES *These you've got to know! They have become very clinically important.*		
Ewing Sarcoma & Primitive Neuroectodermal Tumor	**t(11;22)**	**EWS-FL1**
Liposarcoma: Myxoid & Round Cell Types	**t(12;16)**	**FAS-DDIT3**
Synovial Sarcoma	**t(X;18)**	**SS18-SSX**
Rhabdomyosarcoma – Alveolar Type	**t(2;13)**	**PAX3-FOX01**
Extraskeletal Myxoid Chondrosarcoma	t(9;22)	CHN-EWS

GENERAL CELL TYPES		
SPINDLE CELL	Rod-shaped, long axis at least 2x short	Fibrous, Schwann cell, Fibrohistiocytic, **Smooth muscle**
SMALL ROUND (BLUE) CELL	Round, little cytoplasm	**Rhabdomyosarcoma PNET/Ewings Sarcoma**
EPITHELIOID (ROUND CELL)	Polyhedral; more cytoplasm	**Epithelioid Sarcoma**
MATRIX PRODUCING	Bone, cartilage	Extra-skeletal Osteosarcooma
BIPHASIC	Spindle + Epithelioid cells	Biphasic **SYNOVIAL SARCOMA**

	GENERAL ARCHITECTURAL PATTERNS	
	**Fascicles of spindle cells**	***Smooth muscle***
	**Short fascicles of spindle cells radiating from center (Storiform, pinwheel-like)**	**Fibrohistiocytic**
	Nuclei in columns (Palisading)	Schwann cell
	**Herringbone** (spindle cell)	**Fibrosarcoma**
	**Biphasic:** Spindle + Epithelioid	**SYNOVIAL SARCOMA**

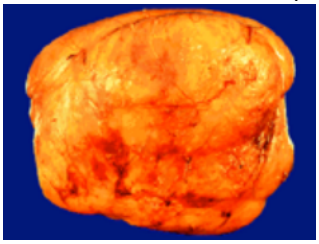
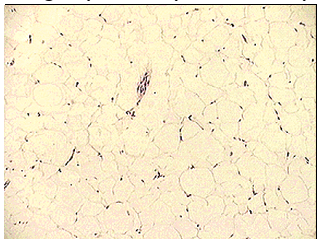
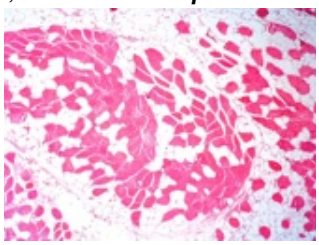
**Architectural patterns brought up in questions – Fascicles=smooth muscle; They'll use terms: "storiform, pinwheel", etc."*

FATTY TUMORS

Lipoma, Liposarcoma: Well-Differentiated, Myxoid/Round Cell, Pleomorphic, Dedifferentiated

LIPOMA

- Most Common **Adult soft tissue tumor**
- ***Benign***, soft, mobile *painless* (except angiolipoma) tumor
- Typically in subcutaneous trunk & proximal extremities
- **GROSS EXAM:** Thinly encapsulated yellow tumor
- **HISTOLOGICAL:** Lobules of mature fat (lots of cleared out spaces) with tiny nuclei
- *There are other variants: fibrolipoma, angiolipoma, spindle cell lipoma,* ***intramusclar lipoma***

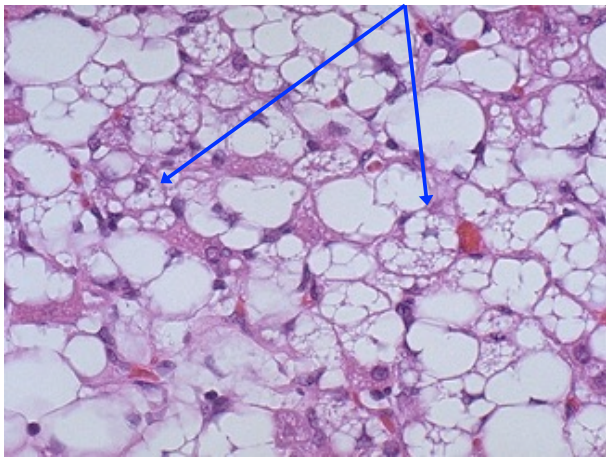
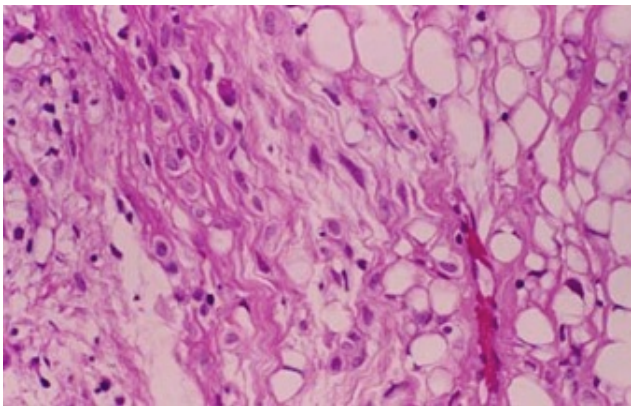
LIPOSARCOMA

- ***Malignant*** tumor of the **Deep Soft Tissues** (**retroperitoneum, proximal extremities**)
- **Mid to late Adulthood (40-60 y/o**)
- **4 Types:** Well-differentiated, Myxoid/Round Cell, Pleomorphic, Dedifferentiated

WELL-DIFFERENTIATED LIPOSARCOMA

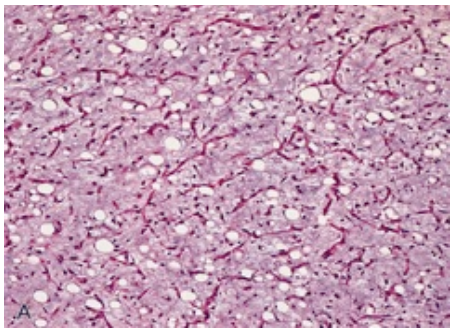
- Most Common type of Liposarcoma
- **MDM2 amplification (inhibits p53) –** *MDM2 used to distinguish lipoma from liposarcoma*
- **GROSS EXAM**: *same as lipoma,* except it is **LARGE** & common in **Retroperitoneum**
  - ***The size is one of the distinguishing features between benign & malignant –*** *Benign tend to be small & malignant tend to be LARGE*
- **HISTOLGY**: *can be very close to benign lipoma*; **Lipoblast** (cytoplasmic vacuoles w/ **scalloped nucleus**) + cytological **atypia in Spindle Cell nuclei** + variation in size of vacuoles *(unusual for lipoma)*
- Tend to be indolent w/ local recurrence – *Locally aggressive, if you excise it & get it all you are usually cured*

Scalloped nuclei

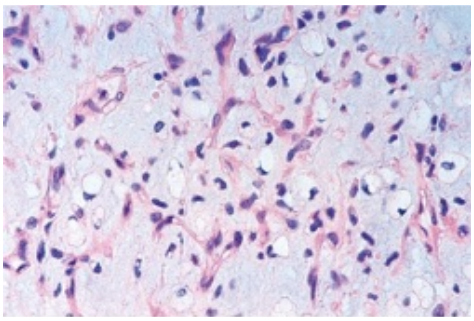



MYXOID/ROUND CELL LIPOSARCOMA

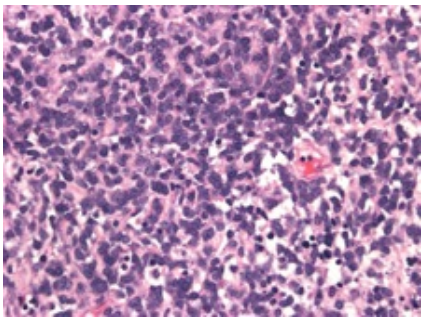
- t(12;16) FUS-DDIT3 fusion protein
- Intramuscular, THIGH
- **Myxoid Liposarcoma** – tends to be **indolent**; watery background; fat + **Chicken Wire Pattern** of vessels; lipoblasts rare
- **Round Cell Liposarcoma** – **aggressive** (progressive – *progressed beyond myxoid changes*); lipoblasts rare



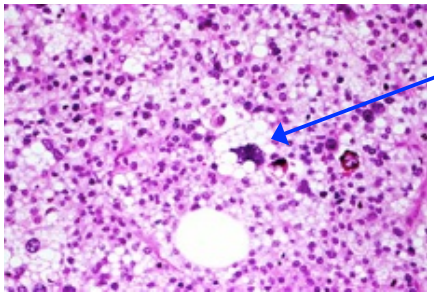
MYXOID LIPOSARCOMA
w/ Chicken Wire Pattern



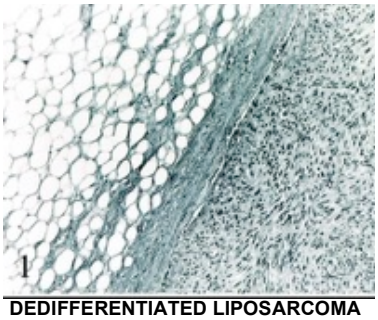
MYXOID LIPOSARCOMA
w/ Lipoblast (Scalloped nuclei)



ROUND CELL LIPOSARCOMA
w/ small, round blue cells



PLEOMORPHIC LIPOSARCOMA w/ Lipoblasts



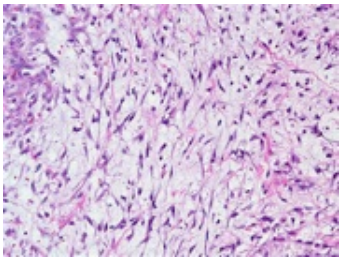
DEDIFFERENTIATED LIPOSARCOMA

FIBROUS (Myofibroblastic) TUMORS/PROLIFERATIONS – Spindle Cells!

Nodular Fasciitis, Myositis Ossificans, Deep Fibromatois (Desmoid), Superficial Fibromatosis, Fibroma, Fibrosarcoma

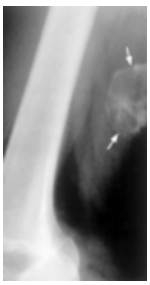
NODULAR FASCIITIS

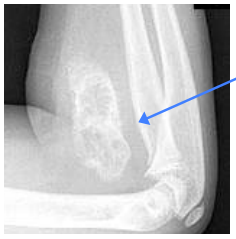
- *Benign reactive proliferation*
- **Most Common** on volvar forearm of Young Adults
- **Solitary, rapidly* growing 2-3 cm** lesion that may be *painful*
- Deep dermis, subcutis, or muscle
- SPINDLE CELL proliferation of myofibroblasts
- Rarely recurs if excised



MYOSITIS (PANNUCULITIS) OSSIFICANS

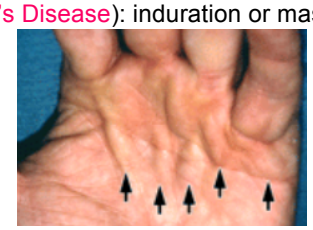
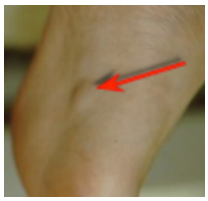
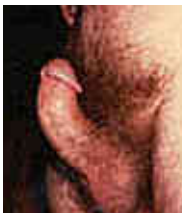
- *Benign reactive proliferation*
- Often in **Athletic adolescents & young adults** w/ ***history of trauma***
- *Looks like Nodular Fasciitis,* but it goes a step further & **MAKES BONE & is larger**
- *Painful*, circumscribed & firm, **3-6 cm**
- Ends as **trabecular bone w/ bone marrow**
- **XRAY**: radiopaque, ossified lesion in soft tissue that does not involve the bone of XR





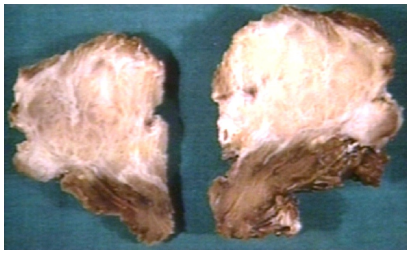
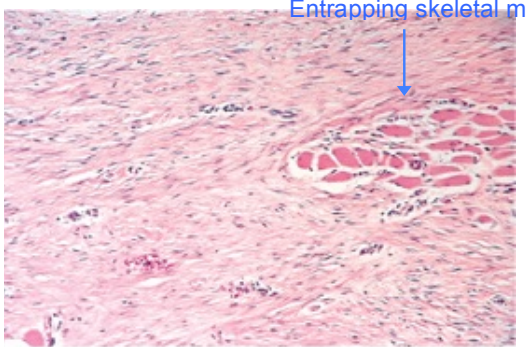
SUPERFICIAL FIBROMATOSIS: Palmar, Plantar, Penile

- Nodular, poorly-defined fascicles of **Fibroblasts** & abundant **Collagen**
- **PALMER** (Dupuytren's Contracture): nodular thickening of palmer fascia; puckers skin & digit (4^{th}/5^{th}) contraction
  - *"You should recognize the way the patient's hand looks – They often cannot open their hand & they will not want to shake your hand... Then you'll notice the nodules."*
- **PLANTAR**: nodular thickening of plantar fascia; usually unilateral, can be painful
- **PENILE** (Peyronie's Disease): induration or mass on dorsolateral penis; causes abnormal curvature of penis, can construct urethra

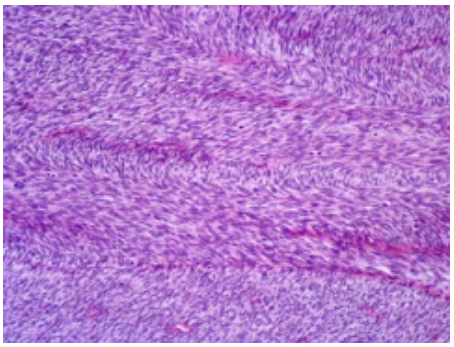
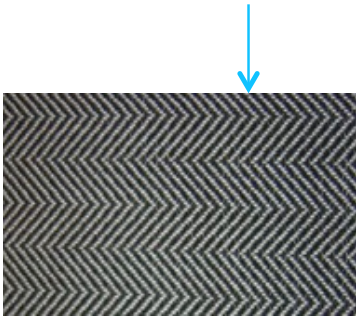
DEEP-SEATED FIBROMATOSIS (Desmoid Tumors)

- Large infiltrative locally aggressive tumors that **do not metastasize**; will recur if not completely excised
- **APC** or **β-catenin** mutations in **Teens-Young Adults (30s)**
- **Large**, **gray-white, poorly-demarcated** on gross exam *(look like scars)*
- **Fibroblasts in fascicles** infiltrate the tissue; **Spindle cells** *(fibrous tissue)*
- **ABDOMINAL** – *anterior abdominal wall*; usually **women during/after pregnancy or C-section**
- **INTRA-ABDOMINAL** – *mesentery & pelvic walls* – **Gardner Syndrome** (FAP)
- **EXTRA-ABDOMINAL** – arms, sometimes breast

FIBROSARCOMA

- RARE, malignant tumor usually found in **Deep Tissue of Extremities**
  - *"It is rare, but I show it because it has a CLASSIC, EASILY TESTABLE picture!"*
- Infiltrative **fish-flesh** with **hemorrhage & necrosis** + **SPINDLE CELLS** w/ areas of **HERRINGBONE PATTERN**
- 50% recur; 25% metastasize!

SKELETAL MUSCLE TUMORS: *MYOD1/Myogenin +, Desmin +*

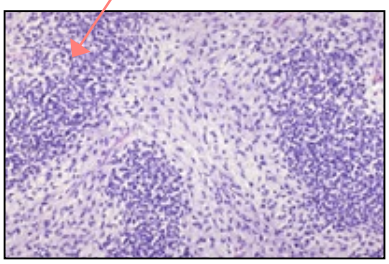
RHABDOMYOSARCOMA

- ***MOST COMMON **Soft Tissue Sarcoma of CHILDHOOD & ADOLESCENCE**; rare after age 20
- **Head/Neck** (Nasal cavity, orbit, middle ear) & **GU tract**
- **Small, round blue cell tumors + Spindle Cells**

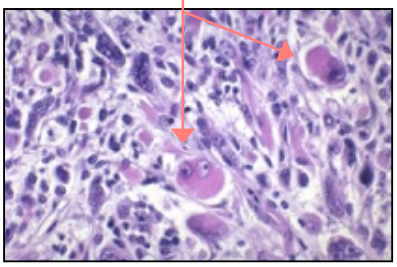
EMBRYONAL RHABDOMYOSARCOMA**

- Majority of Rhabdomyosarcomas (60%) occurring in **Children UNDER 10**
- Soft gray infiltrative mass that **mimics skeletal muscle embryogenesis**
- **SARCOMA BOYRYOIDES** – *Important subtype you need to know!* ***All 3 of these points are VERY TESTABLE!***
  - **Best prognosis** of all embryonal rhabdomyosarcomas
  - **"CLUSTER OF GRAPES"** that produce into lumen of **GU tract (vagina, bladder)**
  - **CAMBIUM LAYER**: Submucosal hypercellular area seen histologically
- **Rhabdomyoblast**: *eccentric eosinophilic cytoplasm*, **Tadpole cells & Strap cells + cross striations**
- **Small, round blue cell tumors + Spindle Cells**
- **EM: Sarcomeres**

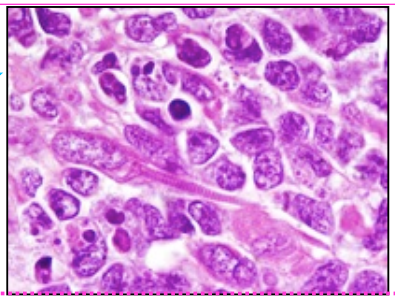
Small, round blue cells



Rhabdomyoblast w/ eosinophilic nuclei

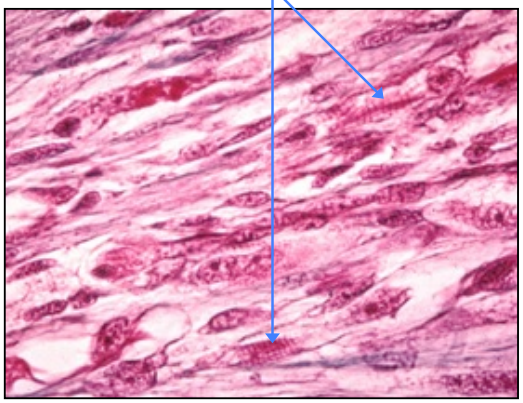


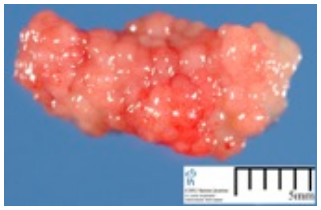
TADPOLE CELL W/ CROSS STRIATIONS



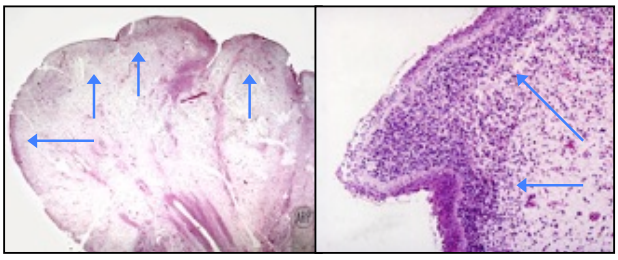
THIS* IS WHAT YOU'RE LOOKING FOR!** *If you see this – It is RHABDOMYOSARCOMA DEFINITELY! You should recognize this picture & this pattern. There is nothing else like it – So it is* ***CLEARLY testable*!!!!*

CROSS STRIATIONS/STRIPES



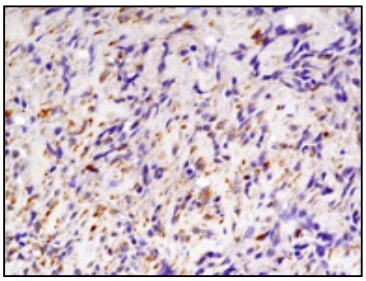


SARCOMA BOTRYOIDES
CLUSTER OF GRAPES
Classic Picture

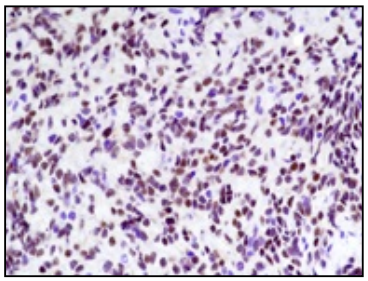


SARCOMA BOTRYOIDES: Cambium Layer

Desmin + Brown Cytoplasm

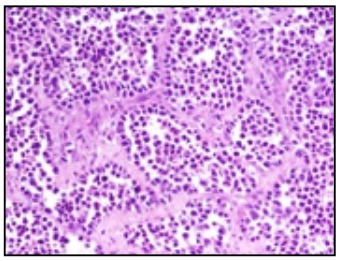


MYOD1 + Brown Nuclei



MYOD1 & Myogenin are SPECIFIC for **SKELETAL MUSCLE ONLY**
+MYOD1 & +myogenin will both stain the nucleus BROWN

Desmin works for **BOTH** Skeletal AND Smooth Muscle!
+Desmin will stain the cystoplasm BROWN

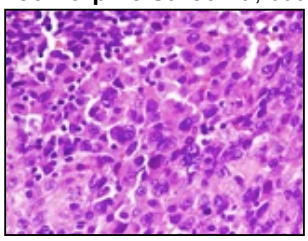


ALVEOLAR RHABDOMYOSARCOMA

- t(2;13) PAX3-FOX01 mutation in a **TEENAGER**
- **POOR PROGNOSIS**
- Deep muscles of extremities (THIGH)
- Fibrous septa divide tumor into ***alveolar-like spaces*** containing discohesive cells, while peripheral cells stick to the wall

PLEOMORPHIC RHABDOMYOSARCOMA

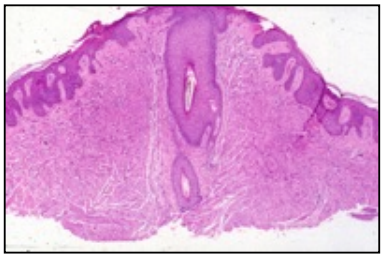
- Rhabdomyosarcoma in Deep Soft Tissue of **ADULTS**
- **POOR PROGNOSIS; *Adults do very poorly with Rhabdomyosarcoma***
- Often **mistaken for Undifferentiated Pleomorphic Sarcoma**, but will have **Desmin +, MyoD1 or Myogenin +**



SMOOTH MUSCLE TUMOR: Spindle Cell, Fascicle; *MYOD1/Myogenin–, Desmin +*

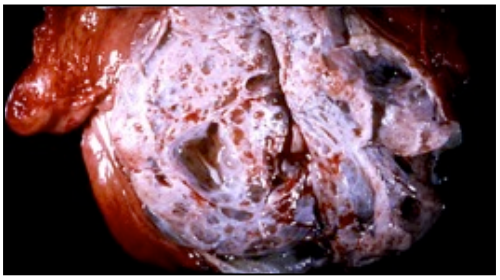
LEIOMYOMA (Fibroids)

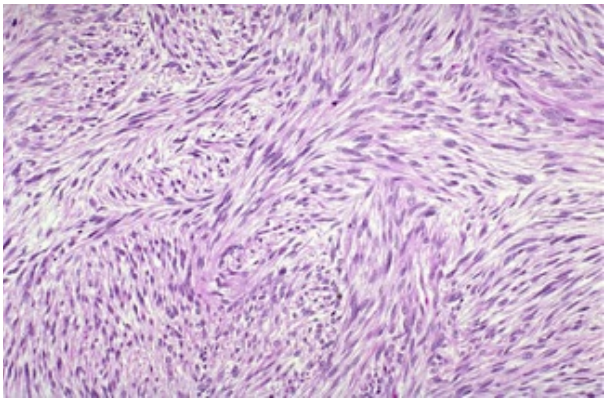
- ***Benign*** smooth muscle tumor;
- MOST COMMON IN THE **UTERUS**
  - **Uterine Leiomyoma** is the most common neoplasm in Women
- Can also occur in **erector pili muscles** (*painful*), nipples, scrotum, labia
- **Fascicles of spindle cells**

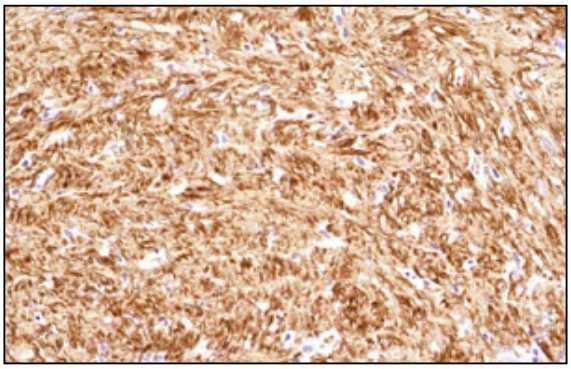


LEIOMYOSARCOMA

- More common in **Females**
- Skin, Deep Extremities, **Retroperitoneum**
- **Large**, heterogenous mass with varying color – *painless & firm*
- **Fascicular Pattern: Eosinophilic spindle cells** – *blunt ended, hyperchromatic nuclei*





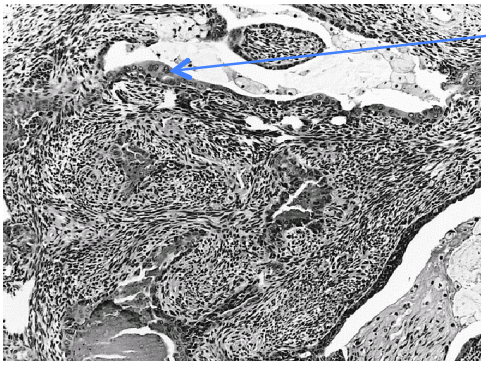


Desmin POSITIVE – Smooth Muscle
+Desmin will stain the cytoplasm BROWN

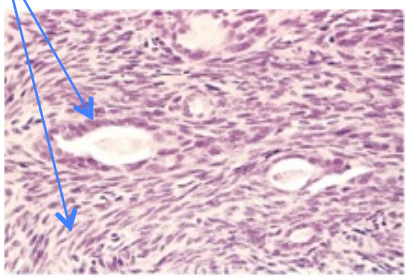
TUMORS OF UNCERTAIN ORIGIN

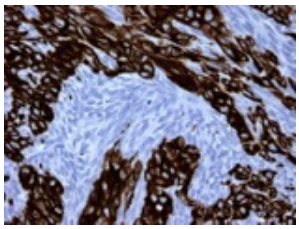
SYNOVIAL SARCOMA*

- **t(X;18) SYT-SSX1** mutation in **Late Adolescent to Young Adult**
- Affects Deep & around Large Joints, especially **KNEE** & **THIGH**
- Often **microcalcifications** on XR
- **BIPHASIC DIFFERENTIATION**** -- *There are other things that show this, but this is the most important!*
  - Epithelial (glands, cords, nests) + Spindle cells in fascicles *"2 populations – This is easy to ask question!"*
- **MONOPHASIC (Spindle Cell) Variant**
  - **Positive** for **Cytokeratins** & **Epithelial Membrane Antigen (EMA)**
    - Epithelial marker + *in epidermis, adenocarcinoma, squamous cell carcinoma, synovial sarcoma*

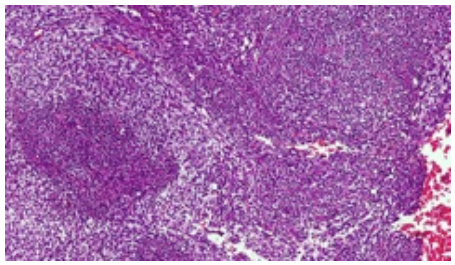


2 cell populations! = DIPHASIC DIFFERENTIATION





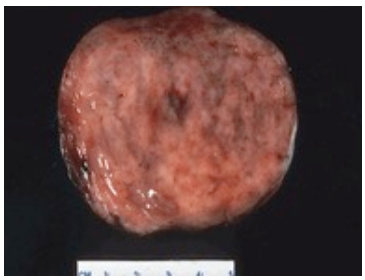
CYTOKERATIN Staining of BIPHASIC SYNOVIAL SARCOMA – Stains epithelioid cells best (brown), spindle are light blue



MONOPHASIC SYNOVIAL SARCOMA
-No epithelial component, SPINDLE CELL only
-MORE COMMON THAN DIPHASIC

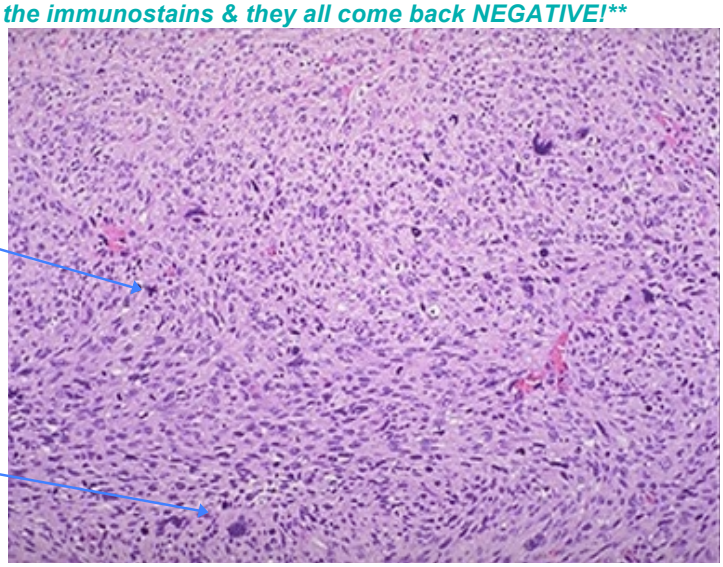
UNDIFFERENTIATED PLEOMORPHIC SARCOMA (Malignant Fibrous Histiocytoma-MFH)

- Group of **aggressive** neoplasms (30-50% metastasis) onset **Mid to Late Adulthood**
- POOR PROGNOSIS – People usually die from this
- **GROSS EXAM:** Large grey, hemorrhagic and/or necrotic
- **HISTOLOGICAL: Spindle cell pleomorphism** & **Storiform Pattern** + mitotic figures & irregular nuclei
- **DIAGNOSIS OF EXCLUSION –** ***You do all the immunostains & they all come back NEGATIVE!****



MITOTIC FIGURE
Looks like an 'X'

HUGE NUCLEUS



OVERVIEW

EPITHELIUM	SKELETAL MUSCLE	SMOOTH MUSCLE	NON-EPITHELIAL
Cytokeratin + EMA +	**MyoD1 +** **Myogenin +** Desmin + Actin +	MyoD1 – Myogenin – Desmin + Actin +	Vimentin +

SPINDLE CELLS	SMALL ROUND BLUE CELLS	BIPHASIC
MYOFIBROBLASTIC Nodular Fasciitis Fibrous Histiocytoma Fibromatosis Myosistis Ossificans Fibrosarcoma **SMOOTH MUSCLE** Leiomyoma Leiomyomosarcoma **UNKNOWN ORIGIN** Monophasic Synovial Sarcoma Undifferentiated Pleomorphic Sarcoma	**SKELETAL MUSCLE** Rhabdomyosarcoma **FAT** Round Cell Liposarcoma **LYMPHOCYTES** Lymphoid Hyperplasia Lymphoma	**UNKNOWN ORIGIN** Synovial Sarcoma

PAINFUL SKIN LESIONS = "Blue ANGEL"
BLUE Rubber Bleb Nevus
Angiolipoma
Neuroma (traumatic)
Glomus tumor
Eccrine spiradenoma
Leiomyoma (cutaneous)