Ewing sarcoma "malignant"	* small blue cell tumor (PNET or primitive neuro ectodermal tumor), "small size tumor cell with large nucleus, little cytoplasm". * second most common sarcoma of bone after osteosarcoma. *** 20>, diaphysis usually between 10 and 20** * translocation is **t(11;22) (q24;q12),**which generates an aberrant transcription factor through fusion of the **EWSR1 gene with the FLI1 gene** * -Trx: neoadjuvant CT followed by surgery; long term survival now reaches 75% * Codman triangle
Giant cell tumor of bone "Benign"	* locally aggressive neoplasm of **adults** العمر مهم **, epiphses** of long bones * **bubble appearance** expanding the cortex of the bone without infiltration to the extracortical space * Histologically: it is sheets wall to wall, multi-nucleated Giant cells or osteoclast like giant cell, so the tumor cell Are the giant cells and the one in between (the single mononuclear cell) *** osteoclast like giant cell: Sometimes they call it osteoclastoma** * rare malignant behavior, cells contain high levels of **RANKL, Trx: curetting or resection**
ANEURYSMAL BONE CYST "Benign"	* characterized by blood – filled cystic spaces and fibrous reaction around it * some argue that (ABC) is not a true neoplasm (probably reactive condition caused by previous trauma or infection) * metaphysis of long bones, Affects adults * -Trx: curetting , resection
Non ossifying fibroma "Benign"	* (a fibroma in the bone), not destroying the surrounding structure, it is not elevating the periosteum, it is well circumscribed * the biopsy looks like benign fibroma (mostly fibroblast some multinucleated giant cell) maybe reactive not a true neoplasm * Other names: fibrous cortical defect (FCD) & metaphyseal fibrous defect (MFD). * Metaphysis in long bone, Histology: bland fibroblastic proliferation, May resolve spontaneously
FIBROUS DYSPLASIA (FD)	*** Not a real tumor; rather a developmental abnormality of bone genesis due to mutations in GNAS1 gene (cAMP mediated osteoblast differentiation)** *** fibrous dysplasia is a group of diseases or syndromes. (forms of FD): 1) Monostotic: affecting one bone, esp: Maxilla and Mandible causing cherubism in children** **2)** Polystotic: multiple bone **3) Mazabraud syndrome: FD (whether it is monostotic or polystotic) + soft tissue myxoma (not a common tumor of soft tissue)** **4) الأهم McCune-Albright syndrome: polystotic FD + café-au-lait skin pigmentation (multiple brownish pigmentation of the skin) + endocrine abnormalities (precocious puberty)** * McCune-Albright syndrome has a **Chinese letters** appearance while in Paget disease the bone appears in a mosaic pattern (pathgnomic)
Ganglion cyst "Benign"	* common condition, a cystic bulge which occurs around the joint and **mainly in the dorsum of the wrist**. Mostly asymptomatic, but sometimes it gets bigger causing pressure on a nerve which is painful, **It is not a true cyst because it does not have a lining.** *** theories about its pathogenesis: 1) Degeneration of joint space leading to pseudocyst formation. (fluid containing bulge) 2) Herniation of synovial membranes** *** Ganglion cyst is probably not a true tumor, it is either herniation or degenerative type of cyst. "**The word ganglion is a misnomer, there is no actual ganglion" ***Treatment: aspiration of tissue (surgical removal). Under the microscope it is a dense fibrovascular connective tissue with myxoid degeneration** **True synovial cyst can occur and is called baker cyst. Baker cyst usually occurs around the knee joint, it presents with large swelling in the posterior aspect of the knee joint (in the popliteal fossa). It is usually a big cyst filled with fluid or a herniation process. Sometimes it causes severe pain, pressure and deep vein thrombosis.**

Tenosynovial giant cell tumor **" Benign"**	*** It is a benign neoplasm of synovium (benign synovial tumor) characterized by a specific translocation: <u>T(1;2)(p13q;37) which affects type IV collagen α-3</u> (signature marker of the genetic abnormality in this tumor)** *** Has two types: 1) Diffuse: more dangerous. called pigmented villonodular synovitis (PVNS) because under the microscope brown pigment is seen which is an evidence of previous bleeding** **And contain brown pigments that are hemosiderin macrophages. Usually affects large joints and most commonly the knee but can affect any joint 2) Localized giant cell tumor of tendon sheath (localized small hands tendons): commonly occurs in the distal aspect of joints of the hand. Sometimes causes pain due to pressure on a nerve. Only treated when symptomatic**
Soft tissue tumors	***** Benign is much more common than malignant * are usually aggressive and metastasize via the **hematogenous pathway into the lungs** * The most common site for sarcomas is in the **extremities, especially the thigh *** Patients with **neurofibromatosis type 1 (NF1) are at higher risk of neurofibrosarcomas**. Patients with **Gardner syndrome, Li-Fraumeni syndrome, OslerWebber-Rendu Syndrome are at higher risk of soft tissue tumors, especially sarcomas** ***** Soft tissue tumors in general **have no precursor** or preneoplastic lesions, unlike dysplasia of the cervix, skin, or colon. Theory is that they arise from **pluripotent mesenchymal stem cell** which acquires somatic mutation producing these tumors * 15-20% of these tumors (especially sarcomas) have a **simple karyotype or a single signature mutation**, 80-85% of sarcomas in general or aggressive malignant soft tissue tumors have a **complex karyotype**, which means there is genomic instability and a lot of mutations. * Diagnosis: grading and staging are important.
Adipose tissue tumors: **1) Lipoma** **"Benign"**	***** MOST COMMON SOFT TISSUE TUMOR. Much more common than liposarcoma * The most common location is subcutaneous tissue. (subcutis) * **Small** and the Pathogenicity is a clone that forms a benign tumor. ***** Gross appearance 1. Well-encapsulated and well circumscribed 2. Soft shiny yellow appearance. ***** Histological appearance: Mature fat cells (adipocytes) ***** Treatment: Excision if they are big, start causing pressure, and their cosmetic appearance is not very good.
2) liposarcoma **"Malignant"**	***** MOST COMMON SARCOMAS IN ADULTS above the age of 50. * The most common location is the Extremities and retroperitoneum * **Larger,** and the Pathogenicity is a clone that forms a malignant tumor * Three types in the histologic appeareance : **1. Well-differentiated**: also called atypical lipomatous tumor. Difficult to diagnose because it looks like lipoma under the microscope. better prognosis. **(MDM2 gene chr 12)** through **FISH analysis 2. Myxoid**: classic, easy to diagnose under the microscope. also good prognosis. t(12,16) **3. Pleomorphic**: the most aggressive type, easy to diagnose, ugly looking. Bad prognosis.
Fibrous tumors: **1) Nodular fasciitis** **"Benign"**	***** Was thought to be a reactive process, recent studies confirm that this process is actually clonal, **t(17;22) producing MYH9-USP6 fusion gene**, Nodular fasciitis maybe **self-limiting** ***** The classic clinical scenario for nodular fasciitis is previous history trauma, and recent rapid increase in the size of the tissue mass * not to Mistakenly diagnose it as malignant, There is a classic appearance of nodular fasciitis under the microscope called **culture-like histology**. It has **spindle cells** which are bland and sometimes have frequent mitosis. Inflammatory cells such as plasma cells, neutrophils, and lymphocytes are sometimes seen as well.

2) Fibromas "Benign"	* very common cutaneous and subcutaneous tumor * usually occurs in the skin and subcutaneous tissue * under the microscope they are planned benign appearing fibroblasts (spindle cells which has fibroblast appearance and immunostim chemical features)
3) Fibrosarcoma "Malignant"	* superficial cutaneous tumors of fibroblasts. * under the microscope they are **cellular, storiform pattern** (The name "storiform" in Latin means (woven), which is a histopathologic sign consists of spindle cells with elongated nuclei radiating from a center point) with increased mitosis.
4) Fibromatoses syndromes: **1- Superficial fibromatoses "Benign"**	* Group of syndromes or diseases in which we will have proliferation of fibroblasts (Tumor-like conditions)- **Fibromatoses syndromes * There are 2 major types: superficial fibromatoses** (which we will explain) and **the deep fibromatoses** (will be explained later) **----------** * occur in cutaneous and subcutaneous area close to the skin, They are **infiltrative lesions** but they are **benign (they do not metastasize) * Hereditary (may run in the family) and Has a negative impact on local function * There are 3 types: 1) Palmar fibromatoses (DUPUYTREN CONTRACTION) occur in the palms of the hands -the palmar fascia in the hand-** (any figure can be involved and they impart the function of the affected finger, difficulty in flexing and extending, and they cause pain**)** **2) Planter fibromatoses: usually occur in the sole of the foot,** they will cause pain, impart on the walking and cause issues when wearing shoes **3) Penile fibromatosis (PEYRONITE DISEASE): occur in the dorsolateral aspect of the penis,** cause painful erection and difficult to treat
2- DEEP FIBROMATOSES (DESMOID TUMOR) "Benign"	* Occur **deep** inside the tissue, invisible usually * Deep infiltrative but bland fibroblastic proliferation; **doesn't metastasize but recur** * **20-30 years, females more common** * Abdominal wall, mesentery and limbs * they have characteristic mutations in **CTNNB1** (responsible for the production of fusion protein **called β-catenin** and when we suspect deep fibromatoses we can utilize this protein because we have special immunohistochemical stain for this protein) or **APC- Adenomatous polyposis coli- genes leading to increased Wnt signaling** * Mostly **are sporadic**; but patients with **Gardner (FAP -familial adenomatous polyposis syndrome) are susceptible** * Difficult to treat * Complete excision is needed to prevent recurrence which is very common, but **complete excision is very difficult** because of the nature of this tumor, the surgeon doesn't know where the tumor start and end. The surgeon takes wide margin -will take 4-5 cm additional safe margins to make sure that he has complete excision * These tumors **(Lethal) kill by local infiltration NOT metastasis**
SKELETAL MUSCLE TUMORS: **1) rhabdomyoma " Benign"**	* Almost all **malignant**; **except rhabdomyoma which is benign**, rare, occurs with **tuberous sclerosis (TSC-Tuberous sclerosis- is a rare multisystem autosomal dominant genetic disease that causes non-cancerous tumor**s to grow in the brain and on other vital organs such as the kidneys, heart, liver, eyes, lungs and skin), **common locations of rhabdomyomas is the tongue and the heart**
2) Rhabdomyosarcoma "Malignant"	* **Rhabdomyosarcoma (RMS) is the malignant** prototype; **most common child sarcoma** * **3 types (embryonal 60%; alveolar 20%; pleomorphic 20%)** * Specific mutations are common * Aggressive tumors; treated by surgery, CT (chemotherapy) +/- RT (radiotherapy) * Rhabdomyosarcomas are **usually large, fleshy and hemorrhagic** tumors * Alveolar type of rhabdomyosarcoma because it looks like the alveoli of the lung * Pleomorphic rhabdomyosarcoma in which the tumor is composed of **small bleu cell tumor**, at electron microscopy you can see the cross striations that will tell us that this is a skeletal muscle malignant tumor

SMOOTH MUSCLE TUMORS: **1) Leiomyoma (LYM) "Benign"**	***** very common; any site but mostly uterus (fibroid leiomyoma of the uterus- ألياف...(patient with one or multiple fibroid complains of menorrhagia and infertility * LYM vary in size and location, well circumscribed**, not infiltrative** * Few can have specific mutations (Fumarate hydratase on chromosome **1q42.3)** • Dx: morphology and histology alone * Histology: **Smooth muscle Cell proliferation, No necrosis, Little mitosis, no hemorrhage**
2) LEIOMYOSARCOMA "Malignant"	***** 10-20% of soft tissue sarcomas * Adults; more in females * Deep soft tissue, extremities and retroperitoneum or from great vessels and uterus (almost 98-99% of smooth muscle tumors of the uterus are leiomyomas, 1-2% are leiomyosarcoma) * Complex genotypes * Hemorrhage, necrosis, increased mitosis (many of them are abnormal) and infiltration of surrounding tissue This is the cervix of the uterus and we can notice the well circumscribe, non-infiltrative, firm white leiomyoma * Trx: depends **on location, size and grade** (high grade sarcomas in thigh or in the uterus are difficult to treat and sometimes we have to add probably additional modalities other than surgery) *** Radiologic**, gross and histologic features of intraabdominal Leiomyosarcoma. Big tumor (10-15) cm with central hemorrhage and necrosis. **Histologically** this tumor is very cellular with clear hemorrhage and necrosis
TUMORS OFUNCERTAIN ORIGIN: **1) Synovial sarcoma "Malignant"**	* Name is misnomer (Although they occur most commonly around joints, however they can occur anywhere) • 10% of all soft tissue sarcomas; **20-40s age** • Deep seated mass of long history, whether it's deep in the joint or deep in the chest or the abdomen • **Translocation T(X;18) (p11;q11) à Makes fusion genes SS18 (signature characteristic) • Histologically: Monophasic (only spindle cells) or biphasic (spindle cells and glands (epithelial cells)** • Trx: aggressive with limb sparing excision + CT to decrease the chance of hematogenous metastasis • 5 years survival 25-65% depending on stage and multi-disciplinary team approach • **Metastasis: lung and lymph nodes** *** Radiologic appearance: Big mass with hemorrhage and heterogenous texture. It's close to the joint but there is no evidence that the origin is from the synovial cells**
2) UNDIFFERENTIATED PLEOMORPHIC SARCOMA (UPS) "Malignant"	***** High grade **mesenchymal sarcomas of pleomorphic** cells that lack cell lineage * Deep soft tissue and extremities * **Old terminology: malignant fibrous histiocytoma (MFH)…**not anymore • **Aneuploid and complex genetic abnormalities** • Large tumors; anaplastic and pleomorphic cells,abnormal mitoses, necrosis * Trx: aggressive with surgery and adjuvant CT +/- RT; poor prognosis *** Histologically: Very ugly bizarre abnormal cells**
3) Uncertainmesenchymal lineage	

EWING SARCOMA	**t(11,22) (q24,q12) transfusion of EWSR1 + FLI1**
FIBROUS DYSPLASIA (FD)	**GNAS1**
TENOSYNOVIAL GIANT CELL TUMOR	**t(1,2) (p13,q37)**
SYNOVIAL SARCOMA	**t(x,18) (p11.2, q11.2) fusion of SS18**
NODULAR FASCIITIS	**t(17,22)**
DEEP FIBROMATOSIS	**Mutation in CTNNB1 or APC genes**
Leiomyoma	**1q42.3**