MSS final

Pathology
Mind maps full material

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Joints overview:

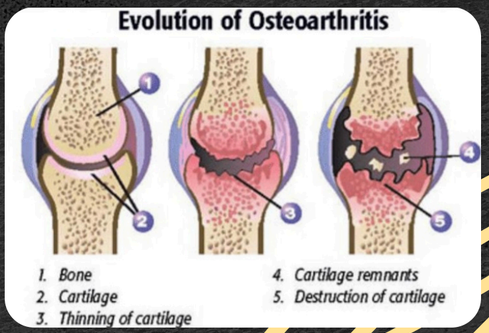
1- Provide motion & stability to our skeleton.

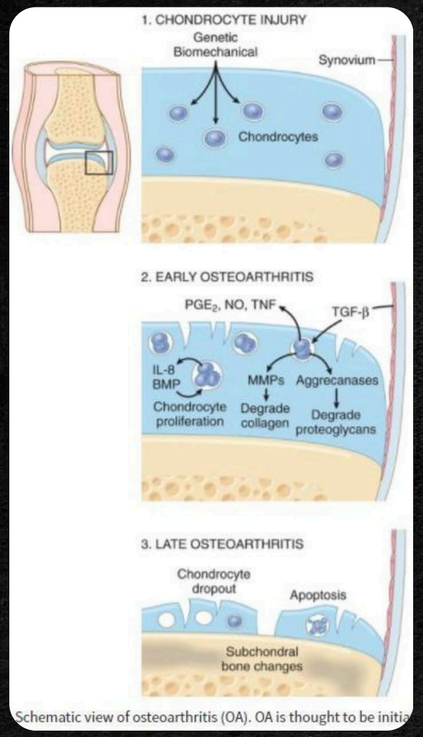
2- divides into:

- **Synovial (cavitated):**
  1- covered by hyaline cartilage(70%water,10% type II collagen),Provide wide motion.
  2- Hyaline cartilage (shockabsorber): no blood supply, no nerves, no lymphatics
  3- very rare to see it tumor mets to cartilage, because it does not have blood supply.
  4- have a synovial membrane: lacks basment membrane.
  - A synoviocytes ------->contains macrophages
  - B synoviocytes ------> which is fibroblast like.
- **Non synovial (solid):**
  1- synarthrosis(ملتصق).
  2- minimal movement, ex: skull.

Joints diseases:

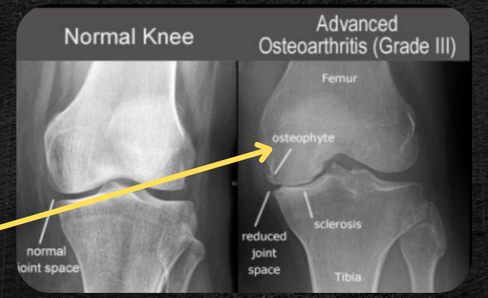
- **OSTEOARTHRITIS (DJD):**
  1- not true – ITIS, degeneration of cartilage.
  2- Insidious, rate of disease increase with age (>50 yr).
  3- Degeneration of cartilage much more repair and proliferation.
  - **Primary(idiopathic):**
    1- caused by aging.
    2- affects few joints.
    3- the most common form of DJD.
  - **Secondary:** Caused by existing diseases.





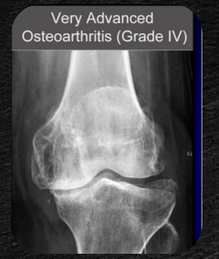
Schematic view of osteoarthritis (OA). OA is thought to be initia

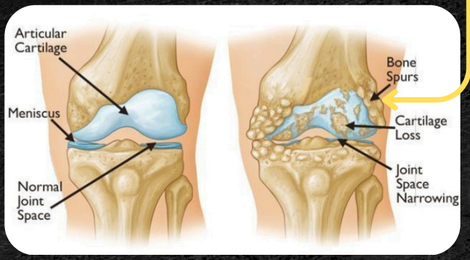
5- severe cases of DJD : 1- eburnation of the bone.
2- cortical sclerosis.
3- penetration to periosteum.
4- cyst formation.
5- osteophytes -------> can cause lock joint.



6- clinical manifestation: 1- Joint pain worsens with use
2- crepitus & range limitation.
3- osteophytes impingement on vertebrae.
4- muscle spasm & atrophy.

7- TX: 1- NSAIDs ------> to decrease inflammation.
2- intra-articular steroids.
3- joint replacement ----------> at severe cases.





Rheumatoid arthritis: 1- Chronic inflammatory autoimmune disease.

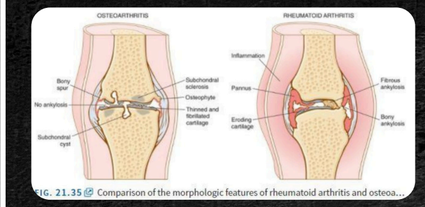
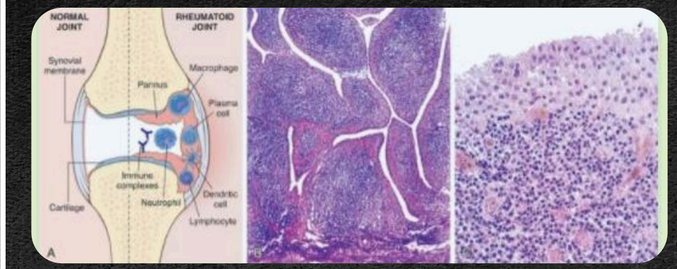


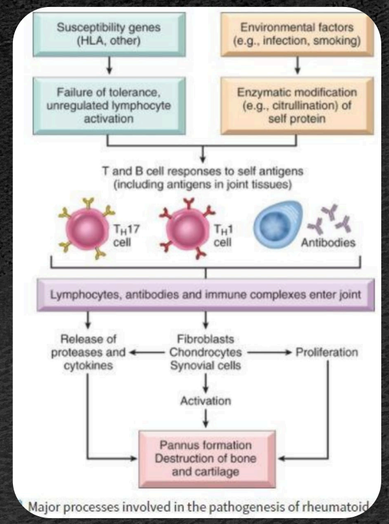
FIG. 21.35 Comparison of the morphologic features of rheumatoid arthritis and osteoa...

2- can cause : 1- nonsuppurative proliferative and inflammatory synovitis.
2- destruction of joints and ankylosis(adhesion of joints).
3- systemic disease, ex : in skin, heart, vessels & lungs.



3- affects females more than males , older more than younger.

4- etiology : caused by : Genetic predisposition + environmental factors.



Major processes involved in the pathogenesis of rheumatoid

5- a- 80% of patients have autoantibodies (IgG & IgM against the Fc portion of their ownIgG [Rheumatoid factor]).
b- 70% of patients have (ACPA).

PATHOGENESIS: 1. IFN-γ (from TH1) → Activates macrophages & synovial cells.

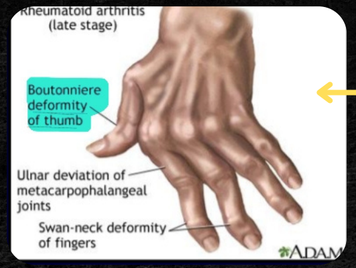
2.IL-17 (from TH17) → Recruits neutrophils & monocytes (early inflammation).

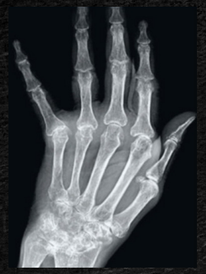
3.RANKL (from T cells) → Stimulates osteoclasts → Bone resorption.

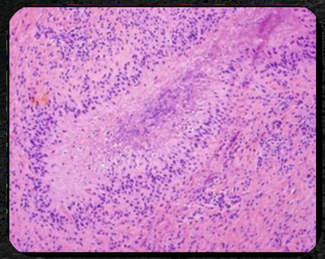
4.TNF (the major player)& IL-1 (from macrophages) → Stimulates resident synoviocytes → Secretion of proteases → Hyaline cartilage destruction.

Remuntled Arthritis clinically: 1- polyarthritis, begins slowly and insidiously.

2- affects symmetrical joints: 1- hands. 2- feet. 3- wrists. 4- ankle. 5- MCP. 6- proximal IPJ.







DX: 1- warm, swollen & painful joints.

2- stiffness of joints when inactive and in the morning.

3- ulnar deviation.

TX: 1- Steroids.

2- MTX(immunosuppressive drug).

3- Anti-TNF.

JUVENILE IDIOPATHIC ARTHRITIS (JIA): 1- Heterogeneous group,arthritis of unknown cause.

2- affect young children <16 years(for at least 6 weeks).

3- Pathogenesis is similar to adult RA, but less severe.

4- characteristics: 1- Oligoarthritis & Systemic disease are more common.

2- Large joints are affected more than small joints.

3-Rheumatoid nodules and Rheum factor are usually absent.

4- usually positive ANA.

Seronegative arthritis (negative ANA) : group of diseases that have similar features: a- Absence of rheumatoid factor.

b- Ligaments pathology rather than synovium.

c- affects sacroiliac joints.

d- Association with HLA-B27 antigen.

e- presence of bony ankylosis (bone fusion).

Ankylosing spondylitis:
1- most common prototype of seronegative arthritis.
2- mainly in adolescent boy, affect axial joints.
3- associated with HLA B27 antigen.

Enteropathic Arthritis: 1- Secondary to bowel infections (salmonella, shigella).
2 positive HLA B27.

Reiter syndrome: 1- can cause arthritis, urethritis/cervicits & conjuctivitis.
2- autoimmune disease initiated by bacterial infection.

Psorotic Arthritis: 1- starts in DIP joints (distal interphalangeal joints).
2- similar to rheumatoid arthritis.

SUPPURATIVE ARTHRITIS: 1- due to Bacterial infection by hematogenous spread.

2-affect: a-< 2 years ------->H. influenza.

b- older children & adults--------> S.aureus.

c- young adults------->Gonococcuss

d- Sickle cell disease------->Salmonella

3-Clinically: 1- sudden acute pain.

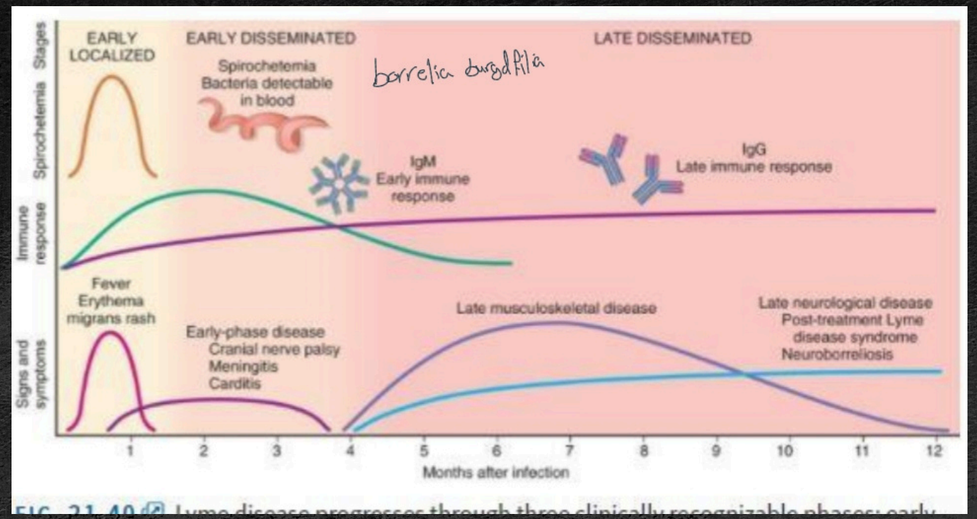
2-swollen and warm joints.

3- affect mainly knee with systemic manifestation (fever, leukocytosis, elevated ESR).

4- DX: aspiration of joint.

5- TX: antibiotics.

LYME ARTHRITIS: is a tick-borne bacterial infection caused by Borrelia burgdorferi, leading to arthritis and is more prevalent in the northeastern United States.



CRYSTAL-INDUCED ARTHRITIS:

1-Crystals deposited in joints causing disease.

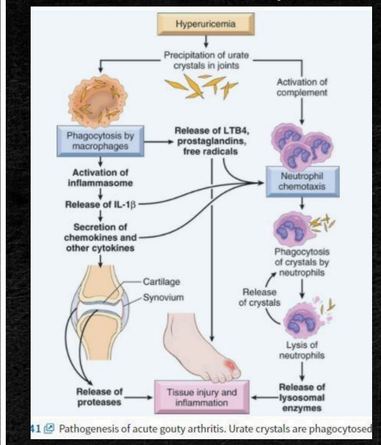
2-Crystals triggers inflammatory reaction that destroys cartilage.

3-two types: 1-GOUT(Monosodium urate, MSU).

2- PSEUDOGOUT(Calcium pyrophosphate dehydrate)

GOUT:

1- Transient attacks of arthritis.

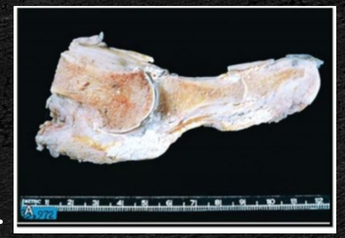


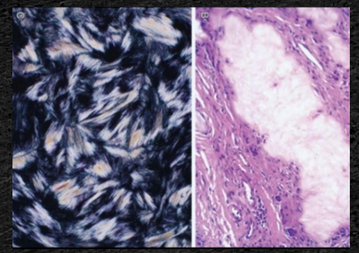
41 Pathogenesis of acute gouty arthritis. Urate crystals are phagocytosed

2- affect big toe mainly, deposition of MSU crystals.

3- Uric acid increases by : urine metabolize activity : 1- increased production. 2- decreased excretion from kidney.

4- causes: 1-hyperuricemia. 2- risk increases with age. 3-obesity. 4- alcohol. 5-genetic predisposition.





5- needle shape, negative bierfringence.

6- TX: 1- life style modifications.

2- in acute gout : NSAIDS & Colchicine.

3- in chronic and prevention : Xanthine oxidase inhibitors (Allupurinol).

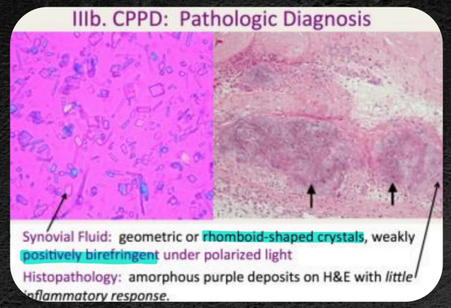
PSEUDOGOUT:

1- affect older people > 50 years.

2- caused by triggering inflammatory reaction.

3- divides into: → Idiopathic (genetic)

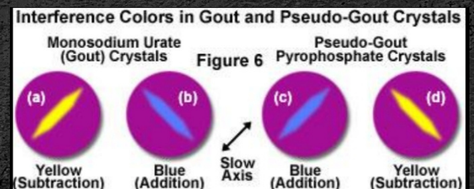
→ secondary, caused by: 1-DM. 2- previous joint damage. 3-HPTH. 4-hemochromatosis.

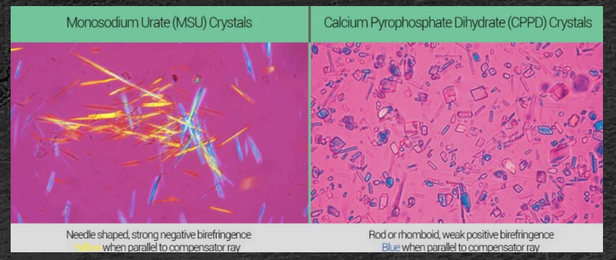


4-three forms: 1-Acute. 2-subacute. 3-chronic forms.

5- DX: harder than gout.

6- TX: supportive.





Joint tumors: Rare.

Ganglion cyst(benign):

1-common condition true cyst.

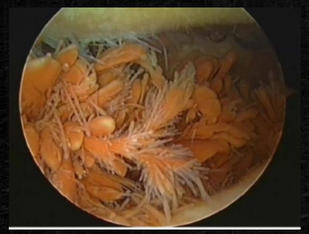
2-close to a joint.

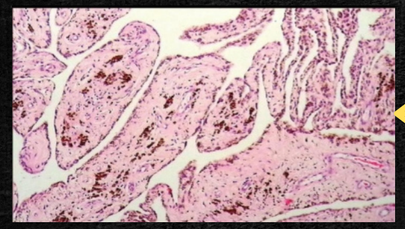
3-affect dorsum of wrist and foot.

4-no communication with synovial joint.

5-TX: surgical removal.

6-True synovial cyst(have epithelial lining)(Baker cyst around the knee): herniation process.





TENOSYNOVIAL GIANT CELL TUMOR:

1-Benign neoplasm of synovium.

2-DX: 1-Diffuse----------> pigmented villonodular synovitis, PVNS, large joints.

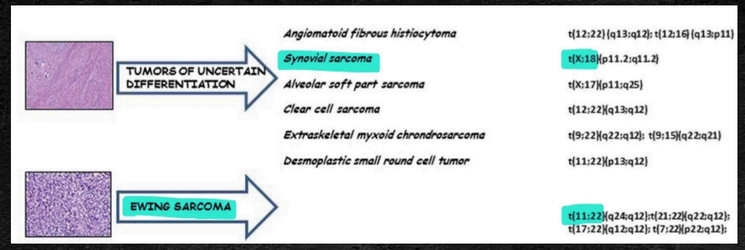
2-localized-----------> small hands tendons.

3-caused by : translocation mutation (1;2)(p13q;37); affecting type VI collagen α3.

tumors:

SOFT TISSUE TUMORS:

1-Benign is much more malignant.



2-Sarcomas are aggressive and metastasize mainly to lungs by hematogenous spread.

3-affects extremities mainly thigh.

4- caused by: 1- tumor suppressor gene mutations(NF1, Gardner syndrome, Li-Fraumeni syndrome, Osler- Webber Rendu Syndrome).

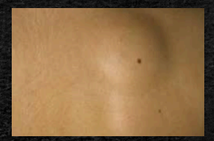
2- exposure to radiation, burns & toxins--------> secondary sarcomas.

5- divides to: 1-simple karyotype (single signature mutation)----------> Ewing and synovial sarcoma.

2-complex karyotype (genomic instability)----------> LMS and pleomor sarcoma.

6- DX,grade and stage are all important.

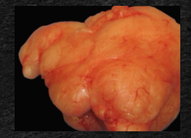
ADIPOSE TISSUE TUMORS:

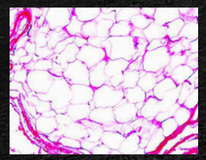


LIPOMA(benign): 1-Most common soft T tumor.

2-Mature fat cells,Well-encapsulated, subcutis.

3-Trx: excision.





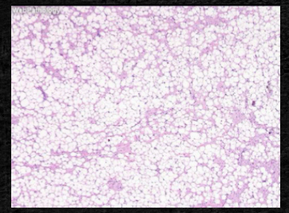
LIPOSARCOMA(malignant): 1-Most common sarcomas in adults >50 years.

2-affect extremities, thigh and retroperitoneum.

3-have 3 types:1-well differentiation (MDM2 gene chr 12).

2-Myxoid, t(12,16).

3-Pleomorphic (aggressive) : in olders, larger in size.



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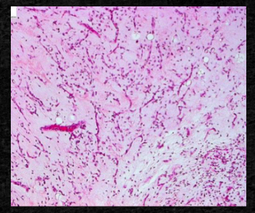

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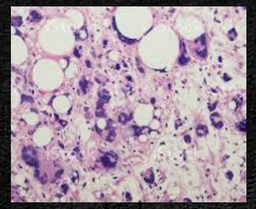

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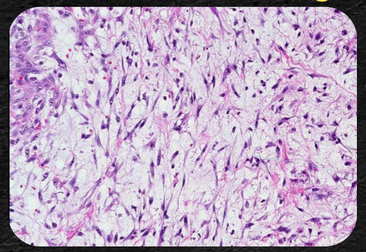
FIBROUS TUMORS:

Nodular fasciitis(benign): 1-caused by clonal, t(17;22) producing MYH9-USP6 fusion gene.



2-patients have previous trauma history, recent rapid size increase.

3- TX: self-limiting.

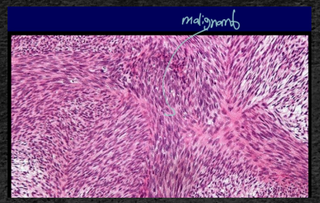
4-should not be miss diagnosed as malignant.

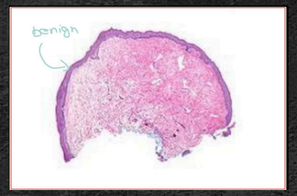
5-culture-like histology.

FIBROMAS AND FIBROSARCOMAS:

Fibromas(benign): 1- benign proliferation of fibroblasts.

2-affect skin and subcutaneous tissue.





Fibrosarcoma(malignant): 1-superficial cutaneous tumors of fibroblasts.

2- appears as cellular, storiform pattern with increased mitosis.

FIBROMATOSES:

SUPERFICIAL1-benign infiltrative fibroblastic proliferation.

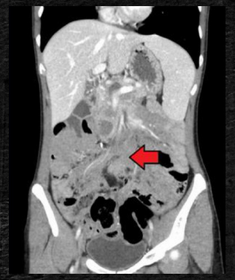
2-have three forms :

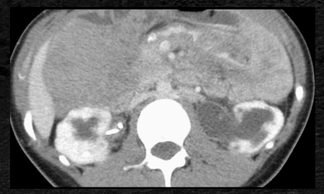
1-PALMAR (DUPUYTRENCONTRACTURE) :affects Palmar fascia.

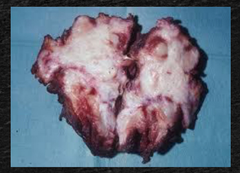
2-PLANTAR FIBROMATOSES: affects sole of foot.

3- PENILE (PEYRONIE DISEASE): affects Dorsolateral aspectof the penis.

DEEP(DESMOID TUMOR):







1- Deep infiltrative but benign fibroblastic proliferation.

2- doesn't metastasize but high rate of recurrence,kill by local infiltration

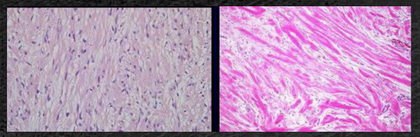
3- found in 20-30years females most commonly.

4- affects: 1-Abdominal wall. 2-mesentery. 3-limbs.

5- caused by mutations in CTNNB1 (β-catenin) or APCgenes leading to increased Wnt signaling.

6-patients with Gardner (FAP) syndrome are susceptible

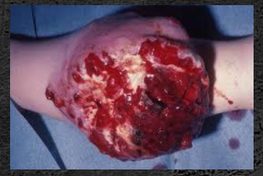
7- TX: Complete excision to prevent recurrence



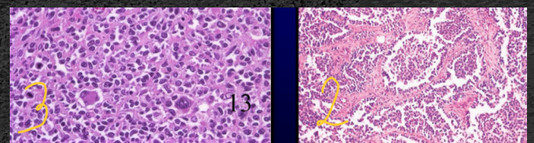
SKELETAL MUSCLE TUMORS(almost malignant):

rhabdomyoma(benign):1-occurs with patients have tuberous sclerosis.

2-afect and heart.



Rhabdomyosarcoma (RMS) (malignant):1-high grade sarcoma.



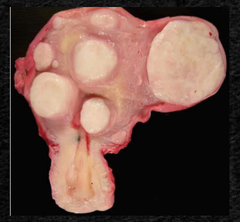
2-most common child sarcoma.

3- three types : 1-embryonal 60%. 2-alveolar 20%. 3-pleomorphic 20%.

4- TX: 1-surgery. 2- chemotherapy(CT). 3- radiotherapy(RT).

SMOOTH MUSCLE TUMORS:

Leiomyoma (benign): 1-very common, can occur any site.



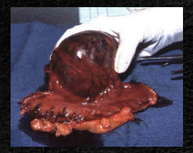
2- affects mostly uterus (fibroid).

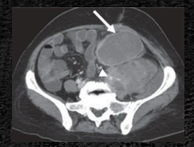
3- can cause: 1-menorrhagia. 2- infertility.

4- vary in size and location,not infiltrative,white color appearance.

5-Few can have specific mutations (Fumarate hydratase on chromosome 1q42.3)

leiomyosarcoma (malignant): 1- 10-20% of soft tissue sarcomas, more in females.





2- affects: 1-deep soft tissue. 2-extremities. 3-retroperitoneum or from great vessels•

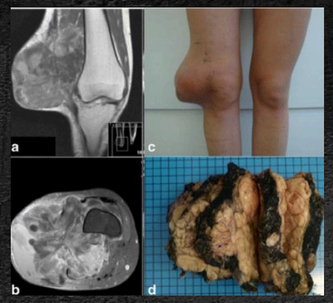
3-•DX: 1-Hemorrhage. 2- necrosis. 3-increased mitosis and infiltration

4- TX: depends on location, size and grade.

TUMORS OF UNCERTAIN ORIGIN:

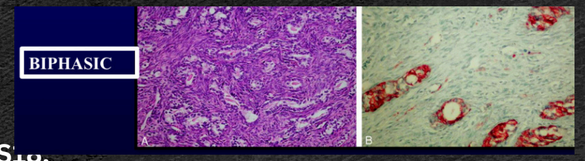
Uncertain mesenchymal lineage.

Synovial sarcoma: 1-Name is misnomer(الاسم ما اله دخل بالمرض :)).



2-present 10% of all soft tissue sarcomas at 20-40s age.

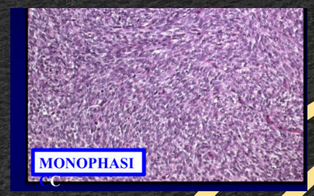
3- can occur anywhere.



4- caused by translocation mutation T(X;18)(p11;q11)----------> fusion genes SS18.

5- have two forms : 1-Monophasic----------> (only spindle cells).

2- biphasic----------> (spindle cells and glands).

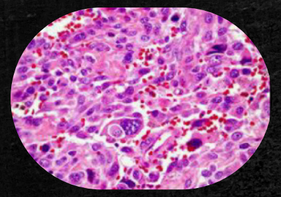


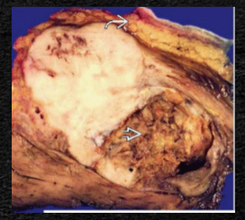
6- TX: 1-aggressive with limb sparing excision. 2- chemotherapy (CT).

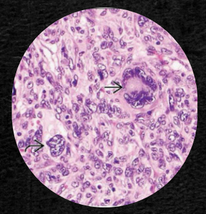
7- metastasis to lung and lymph nodes.

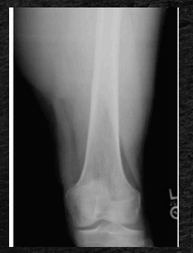
Skin Pathology

UNDIFFERENTIATED PLEOMORPHIC SARCOMA (UPS): 1- also called (MFH),high grade mesenchymal sarcomas.









2- affects : 1-Deep soft tissue. 2-xtremities.

3- caused by aneuploid and complex genetic abnormalities.

4- DX: 1-Large tumors. 2-anaplastic and pleomorphic cells. 3-abnormal mitoses, necrosis.

5- TX: 1-aggressive with surgery. 2- chemotherapy(CT). 3- radiotherapy(RT).

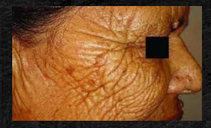
Neoplasms: 1-Inflammatory and infectious dermatosis

2-Very common lesions.

3-rarely fatal (except melanomas).

4-associated with sun damage (solar elastosis).

1- Solar (actinic) elastosis: 1-Chronic sun damage leading to thickened and yellow skin.

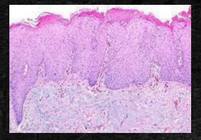


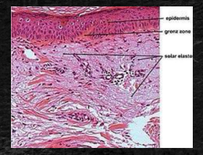
2-UV rays damage collagen and elastic fibers of the skin.

3-it will increase the risk of: 1- many skin premalignancies (Actinic keratosis).

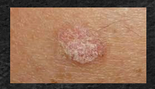
2- malignancies (melanomas, squamous cell carcinomas, basal cell carcinomas).

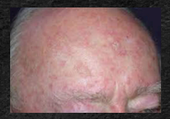
garish discoloration and degeneration of elastic fibers





2- Actinic keratosis(AK):1-Premalignant skin disease due to sun damage.

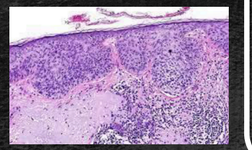




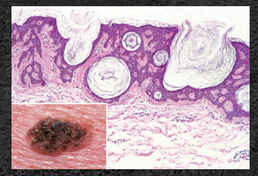
2-caused by UV light which damage the DNA via mutations in TP53.

3-They progress to squamous cell carcinoma (rate: 1-3%).

atypical keratinocytes



3-Seborrheic keratosis(SK)1-Benign, very common pigmented neoplasms.



2-affect middle age to older patients anywhere but mainly trunk.

1-caused by mutations IN FGFR3.

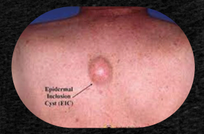
4- appearsas coin-like lesions, usually pigmented, elevated “Stuck-on”.

Cysts: 1-Benign, very common, called “Sebaceous cyst”.

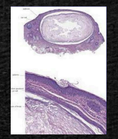
2- Malignant transformation is extremely rare.

1-Trichilemmal cyst (on the scalp).

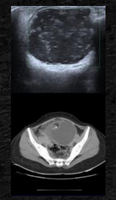
2-Epidermal (epithelial) inclusion cyst.

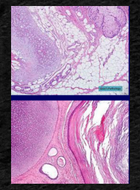


true cysts



3-Dermoid cyst: 1-growth of normal tissue in a pocket of cells called a sac.



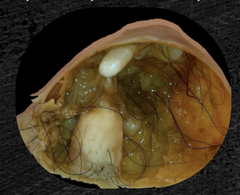


2- contains: 1)greasy yellow material. 2)mature tissues (bone, hair, muscle, teeth...etc).

3- can be anywhere on your body.

4-Rarely they can have immature or malignant.

5-affets : 1- Peri-orbital. 2-ovarian. 3-spinal.



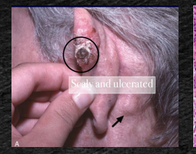
Carcinomas of the skin:

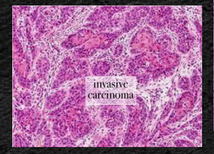
Squamous cell carcinoma: 1- Common neoplasms, due to sun damage.

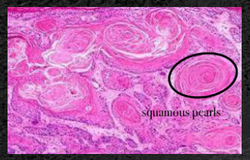
2-can be localized with rare deep infiltration or metastasis.

3- Invasive, usually keratinizing squamous cell carcinoma.

4-scaly, nodular, or ulcerated.







5- risk increases in: 1-immunosuppression (HPV). 2-prolonged sun exposure. 3-tars & oils. 4-old burns. 5-ionizing radiation.

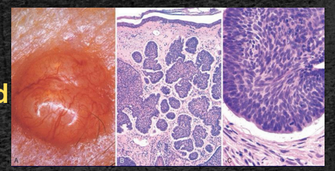
Basal cell carcinoma: 1-Arise from basal cells of epidermis, due to Sun exposure.

2- can be Localized with deep infiltration and metastasis are extremely rare.

3- caused by PTCH1 mutations and TP53 mutations.

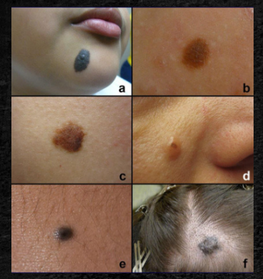
4- Gorlin syndrome: multiple basal cell carcinoma (Basal cell nevus syndrome).

Papules, slightly pigmented



Melanocytic neoplasms:

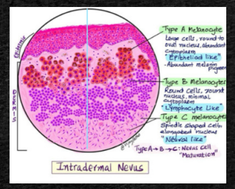
1-Nevus: 1-benign congenital melanocytic neoplasm.



2-caused by somatic gain of function mutation BRAFor RAS followed by inactivity “Senescence”.

3- appears as sharply demarcated, elevated and pigmented, Well-demarcated ,Sharp borders.

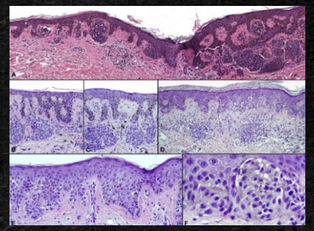
4-TX : Removed surgically for cosmetic reasons.



5-Histlogy : 1-symmetry 2-absence of atypia.

6-Types : Junctional >Compound >Intradermal.

2- DYSPLASTIC NEVUS: 1-Nevi with atypical features.



2-Occur on both sun exposed as well non sun exposed.

3-Risk of melanoma is higher than non dysplastic.

4-Familial dysplastic nevus syndrome: high lifetime risk.

5-Histopathological features:

1-Loss of symmetry.

2-Fusion of junctional nests.

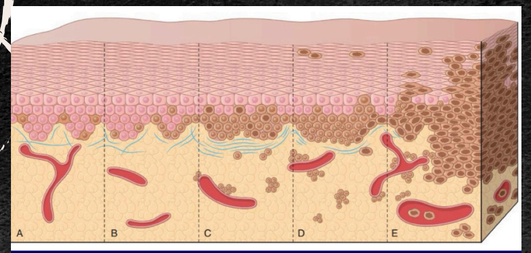
3- Cellular and nuclear atypia.

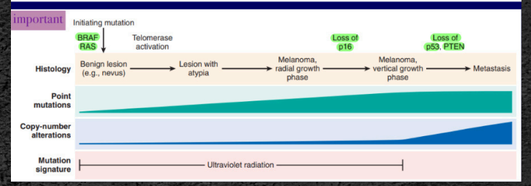
4- Superficial dermal fibrosis.

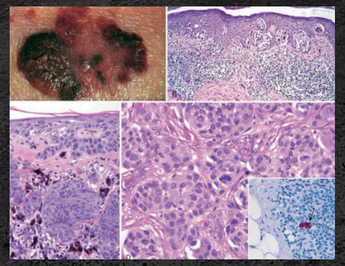
5-Lymphocytic infiltration.

6-Melanin incontinence.

3-MELANOMA(malignant): 1- less common than Squamous cell carcinoma, Basal cell carcinoma and nevi.







2- TX: 1-surgical removal. 2-Immune check point inhibitors. 3-Anti BRAF and KIT agents.

3- evolution of melanocytic neoplasm: 1-early change : loss BRAF&RAS.

2-late change : loss of p53&PTEN.

4-Pathological features: 1-Irregular borders, pigmentation and nesting with increased numbers of single cells.

2-Increased thickness (Breslow thickness) and deeper invasion.

3-Atypical larger nuclei with prominent cherryred nucleoli.

5- DX: 1-Rapid enlargement of a preexisting nevus. 2-Itching or pain. 3-Variegation of color within a pigmented lesion.

6-prognosis: 1-Stage is critical (depth of invasion).

2- Metastatic disease exhibits poor prognosis.

3- Sentinel node evaluation may help in stage determination.