Pathology

Doctor 2017 | Medicine | JU | MSS

Number >>	8
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1st system - MSS

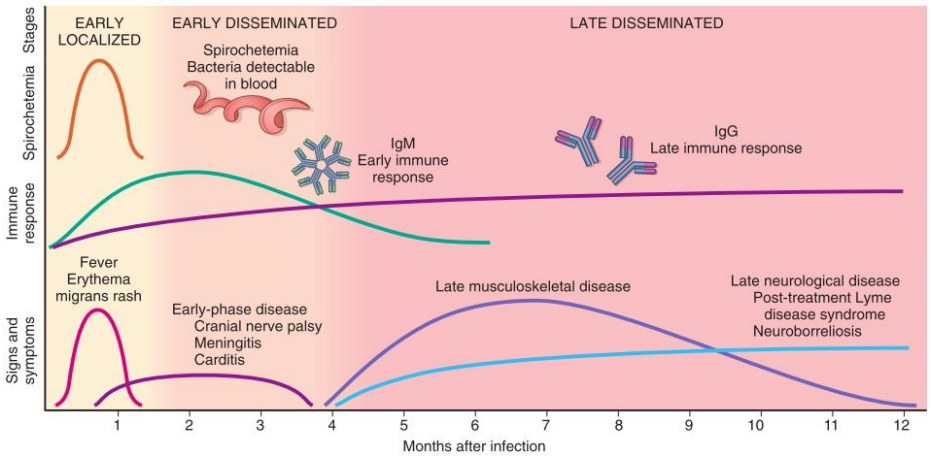
Refer first to Slides (77-84)

Suppurative Infectious Arthritis

- Bacterial infections that cause suppurative arthritis usually enter the joints from distant sites by **hematogenous** spread. It mainly affects the **joints** but could affect both the joint and the bone around it.
  - **In neonates**, contagious spread from underlying osteomyelitis causes suppurative arthritis.
  - In children younger than 2 years of age (**infants**), **H. Influenza** arthritis predominates.
  - **In older children and adults**, **S. Aureus** is the main agent.
  - **Gonococcus** is prevalent in **young adults.**
  - Patients with **Sickle cell disease** are prone to infections from **Salmonella**.
- **Appears clinically as:** Sudden acute pain, warm and swollen warm joints (mainly the knee). Systemic manifestations of fever, leukocytosis and elevated Erythrocyte Sedimentation Rate.
- **Dx:** Joint aspiration is diagnostic if it yields purulent fluid in which the causative agent can be identified.
- **Tx:** Antibiotics.

Lyme Arthritis

- Common in the west, but not in Jordan.
- It is caused by infection with the **spirochete** 'Borrelia burgdorferi', transmitted by **tick** bites.
- The figure below shows the stages of all signs, symptoms and the immune response with respect to how far the infection progresses. Notice that the bacteria spreads to the blood so it is **hematogenous**.



Immune response:

IgM (early immune response)
→ IgG (late immune response).

Signs and Symptoms:

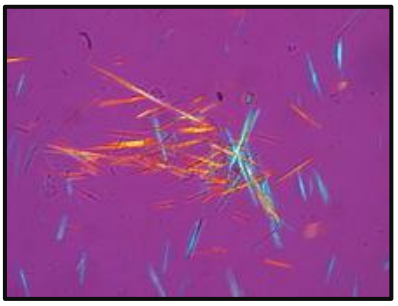
Fever, Erythema, Migraines and Rash.
→ Early-phase disease.
→ Late musculoskeletal disease.
→ Late Neurological Disease.

Crystal-Induced Arthritis

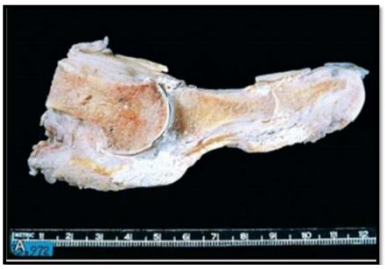
- It is a very common disease caused by **Crystals** being deposited in the **joints** triggering an **inflammatory reaction** that destroys the cartilage.
- The only way to diagnose it is to analyze a sample taken out of the joint synovial fluid.
- The crystals are made from endogenous materials:
  - Monosodium Urate (MSU) for **Gout**.
  - Calcium Pyrophosphate Dehydrogenase (CPPD) for **Pseudogout**.

1- Gout

- Gout is marked by transient attacks of acute arthritis, mainly in the **big toe** (but could be found in any synovial joint), triggered by the deposition of **MSU** crystals within the joint.
- **Elevated** uric acid (purine metabolite) levels can occur due to either increased production of it or decreased excretion from the kidney causing hyperuricemia.
- Hyperuricemia causes the deposition of the MSU crystals eventually causing gout. Risk increases with obesity, alcohol intake, 20-30 years of age, genetic predisposition and the intake of certain drugs (e.g. thiazides); meaning it's contraindicated to give thiazide to patients who have a history with gout.
- Morphologically:
  - **Acute Gout:** Could be formed within hours or a day, represented by dense inflammation of the synovium (synovial membrane) and MSU Crystals in Neutrophils. Crystals look like **needles** or toothpicks with pointed ends. **Yellow** and **negative** birefringent MSU crystals
    Tx: NSAIDs and Colchicine.



  - **Chronic Arthritis**: Repetitive transient attacks and crystal deposition in the joint, **thick synovium** and a layer of vascular fibrous tissue might extend over the surface of nearby structures (**Pannus**).
    Tx: Xanthine Oxidase Inhibitors (Allopurinol).



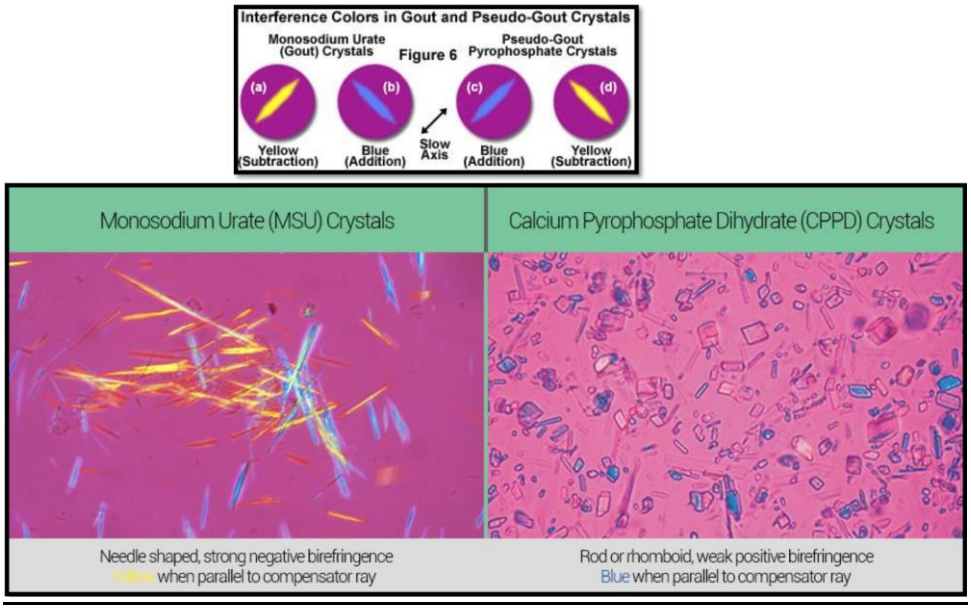
  - **Tophi**: Deposit of crystalline uric acid at various sites especially cartilage, ligaments, bursae, and tendons.

- **Gouty Nephropathy**: MSU crystals deposition in the **kidney**, nephrolithiasis (kidney stones) and pyelonephritis (inflammation in the substance of the kidney).

2- <u>Pseudogout</u>:

- In old patients (> 50 years old), becomes more common with **increasing age**.
- **Idiopathic**, **primary** in which case it is hereditary (genetic) or **secondary** manifested due to some other underlying issues, such as diabetes mellitus, previous joint damage, HPTH or Hemochromatosis *(a hereditary disorder that leads to iron salts building up in the tissues causing liver failure and diabetes mellitus).*
- Similarly, to gout, CPPD crystals induce arthritis via triggering inflammatory reactions. Could be acute, subacute (between acute and chronic) or chronic.
- It is **harder** to diagnose than gout, diagnosed by analyzing a sample of the synovial fluid, it looks like **geometric** or rhomboid-shaped crystals, having a weakly **positive** birefringence under polarized light.
- No treatment for it but only supportive treatments, and no preventive measures so far.

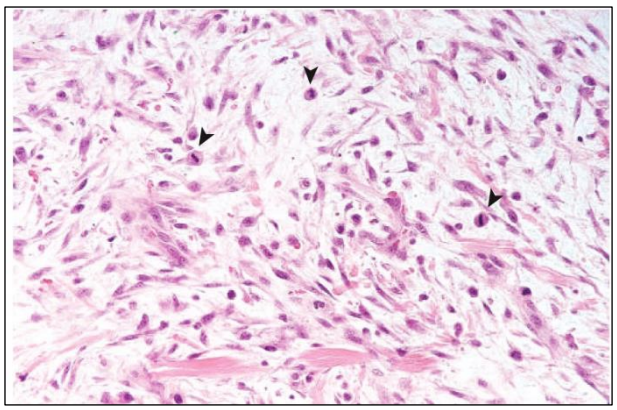
NEGATIVE VS POSITIVE BIERFRINGENCE



<u>Note: Refer to the slides for joint tumors and tumor-like conditions (96-103). Record (14:30-28:45)</u>

Fibrous Tumors

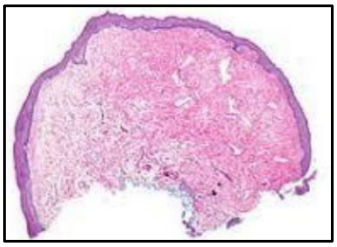
1- Nodular Fasciitis:



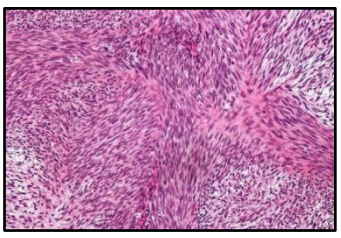
- Nodular fasciitis is a **benign self-limited** fibroblastic and myofibroblastic proliferation.
- Nodular fasciitis was considered a purely reactive lesion (not a neoplasm), until the identification of a **t(17;22) translocation** producing an *MYH9-USP6* fusion gene indicated that it is a clonal, yet self-limited, neoplasm.
- A **history of trauma** is present in some cases. The **tumor grows rapidly** during a period of several weeks or months.
- **Dx**: Don't diagnose is as malignant! It might appear malignant due to its **'culture-like' histological appearance** (not well differentiated), but unique characteristics include:
  - Recent trauma history.
  - Presence of mixed inflammatory cells (because of the persistent trauma).
- Nodular fasciitis can spontaneously regress and, if excised, rarely recurs. Malignant transformation is virtually non-existent.

2- Fibroma and Fibrosarcoma:

- **Fibroma** (لحمية): It is a very common **benign** proliferation of fibroblasts and involves the skin and subcutaneous tissue.
  'Benign' indicates that the tumor is well circumscribed, not infiltrative, no necrosis, no metastasis, no abnormal mitosis, no hemorrhage, no atypia (well differentiated).



- **Fibrosarcoma**: It is the **malignant** counterpart and is, usually, a superficial cutaneous tumor of fibroblasts. Can occur in children.
  'Malignant' indicates that the tumor is infiltrative, necrotic, hemorrhage, with increased mitosis.



Histological appearance: Very cellular; storiform pattern.

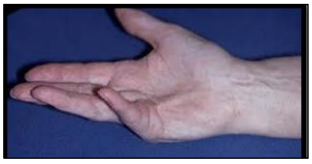
Storiform: having a cartwheel pattern. Spindle cells with elongated nuclei radiating from a center point. Irregular whorls.

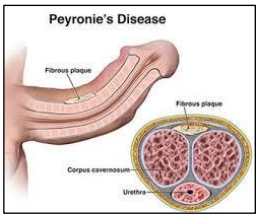
3- Fibromatoses:

They are **benign** but **locally infiltrative** fibroblastic proliferation. There are 2 types:

A- Superficial fibromatosis:

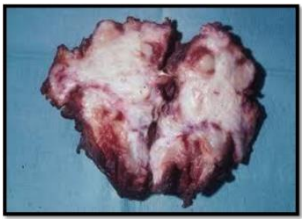
- Superficial fibromatosis is an **infiltrative benign** (not well circumscribed) fibroblastic proliferation that can cause local deformity. Local infiltration is **small** though, unlike the deep fibromatoses.
- Unknown etiology but is known to **run in families**.
- May impact function and is usually **not easy to treat**.
- Has three variations:
  - **Palmar** (*Dupuytren contracture*): involves the palmar fascia, treated by surgical release but recurs easily. Causes contracture.
  - **Plantar**: involves the sole of the foot. No contracture.
  - **Penile** (*Peyronie's disease*): involves the dorsolateral aspect of the penis, very painful and affects sexual function. Causes contracture.
- Some **recur** after excision, particularly the **plantar** variant.

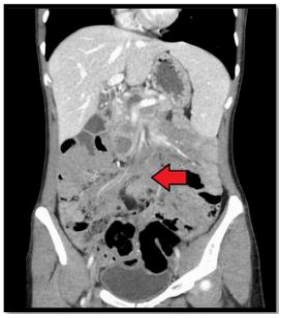


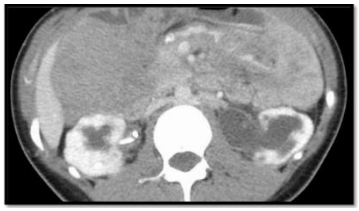


B- Deep Fibromatosis (Desmoid tumors):

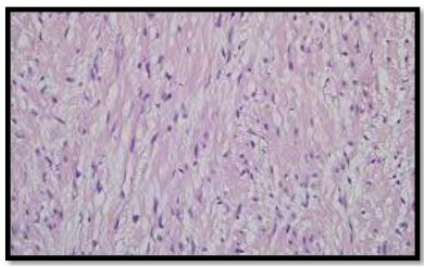
- Deep fibromatoses are **large infiltrative benign** masses that frequently **recur** but **do not metastasize**.
- Occur in **young** adults, more commonly in **women**.
- Occurs in deep tissue, in the abdominal wall, mesentery, or limbs (rare).
- Arises from mutations in the **CTNNB1 (β-catenin) or APC genes**, leading to **increased Wnt signaling**. Most tumors are sporadic, but individuals with familial adenomatous polyposis (FAP or Gardner syndrome) are at higher risk to develop deep fibromatoses.
- These tumors **kill** by **local infiltration** NOT metastasis. They envelop deep **organs** with thick fibrous tissue and lead to their **failure**.







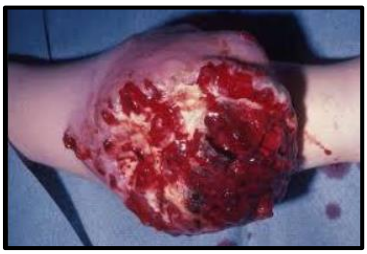
- Because of the extensively infiltrative nature, complete excision is **difficult**. Complete excision is needed to because recurrence is **very common**, therefore the best chance to treat it would be in the first surgery while being careful to take wide enough margins.
- **β-catenin** stain test gives **brown** color if the test is **positive** for **deep** fibromatosis.
- Cytologically **bland** (benign) **fibroblasts** are the characteristic histologic pattern.

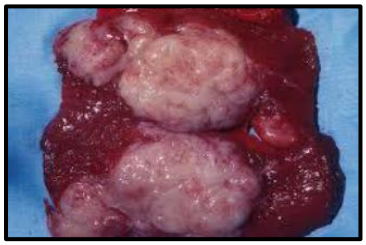


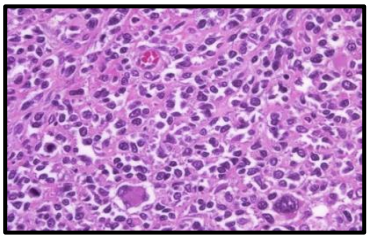
Skeletal Muscle Tumors

Skeletal muscles neoplasms are almost **always malignant**, referred to as Rhabdomyosarcoma. **Benign** skeletal muscles neoplasms are called rhabdomyomas, they are **rare** occurring more frequently in individuals with **tuberous sclerosis**. Rhabdomyomas are most commonly associated with the **heart** and **tongue**.

Rhabdomyosarcoma:







- It is a **malignant** mesenchymal tumor with skeletal muscle differentiation.
- Three main subtypes are recognized: alveolar (20%), embryonal (60%), and pleomorphic (20%).
- It is the **most common** soft tissue sarcoma of **childhood** and adolescence.
- Rhabdomyosarcomas are large, hemorrhaging, aggressive neoplasms that are usually treated with **surgery** and **chemotherapy** (CT) with or without **radiation therapy** (RT).
- Histologically, like Ewing sarcoma (recall sheet 6), **blue cells** are seen.
- Commonly occurs due to genes translocations.

Good Luck