

MSS



Sheet no.

# Pathology



**Writer:** Doctor Ol9

**Corrector:** Rahaf Turab

**Doctor:** Mousa Alabadi

## SUPPURATIVE ARTHRITIS:

❁ Suppuration means destruction of tissue, forming liquefactive necrosis, abscess, pus and this inflammatory change is usually induced by infections, mainly by **bacterial infection** and it usually reaches the joints through the blood stream (**Hematogenous spread**).

❁ There is a difference regarding which organism effects which age when a patient presents with suppurative arthritis :

**Patients who are less than 2 years: H. influenza** *Nesseria Gonorrhea*  
**older children & adults S. aureus; gonococcus young adults.**

❁ **Patients who have sickle cell disease have higher incidence of salmonella infection.** This also can occur in the abdomen causing salmonella peritonitis, so when we have patients with sickle cell disease we have to think of gram negative basili such as salmonella and we have to give strong covering antibiotics.

❁ How do these patients present clinically?

**sudden acute pain, swollen and warm joints, mainly knee with systemic manifestation: fever, leukocytosis, elevated ESR(erythrocyte sedimentation rate)**

example: if a patient came to the emergency room with knee or ankle swelling suddenly within one or two days, and you examine the joint and its swollen and warm, he has fever and you do the complete blood count you see there is probably 18000-25000 white blood count and the ESR is elevated more than 20 for example, so those are all hints and clues that this patient probably has a suppurative arthritis

❁ Dx & Rx: the diagnosis depends on the clinical picture, sometimes we do xray and it appears completely normal, MRI is more sensitive and may show you some collections, however the best way to do it is **aspiration**,

aspirate the joint and you'll see pus coming out send it for culture and microscopic analysis.

Treatment: intravenous antibiotics.

- ❁ Acute suppurative arthritis is acute medical emergency that shouldn't be missed.

### LYME ARTHRITIS:

1. It is a slightly specific type of arthritis which is a part of general systemic disease due to an infection caused by spirochetes (*Borrelia burgdorferi*), so the infection with spirochetes starts and initially the patient will have initial generalized systemic symptoms such as fever and sometimes there is a certain type of skin rash called erythema migrans rash.
2. After the initial fever and erythema migrans sometimes there is some neuritis with cranial nerve palsy, and sometimes the organism reaches the meninges and cause meningitis or reach the heart and cause carditis
3. The initial infection will induce later on a primary immune response (composed of IgM immune response)
4. After the production of IgM immune response when the spirochetes are disseminated the immunoglobulin IgG ( the late immune response) will start appearing and during that period when the primary and late immune response appear, the musculoskeletal symptoms can start appearing.

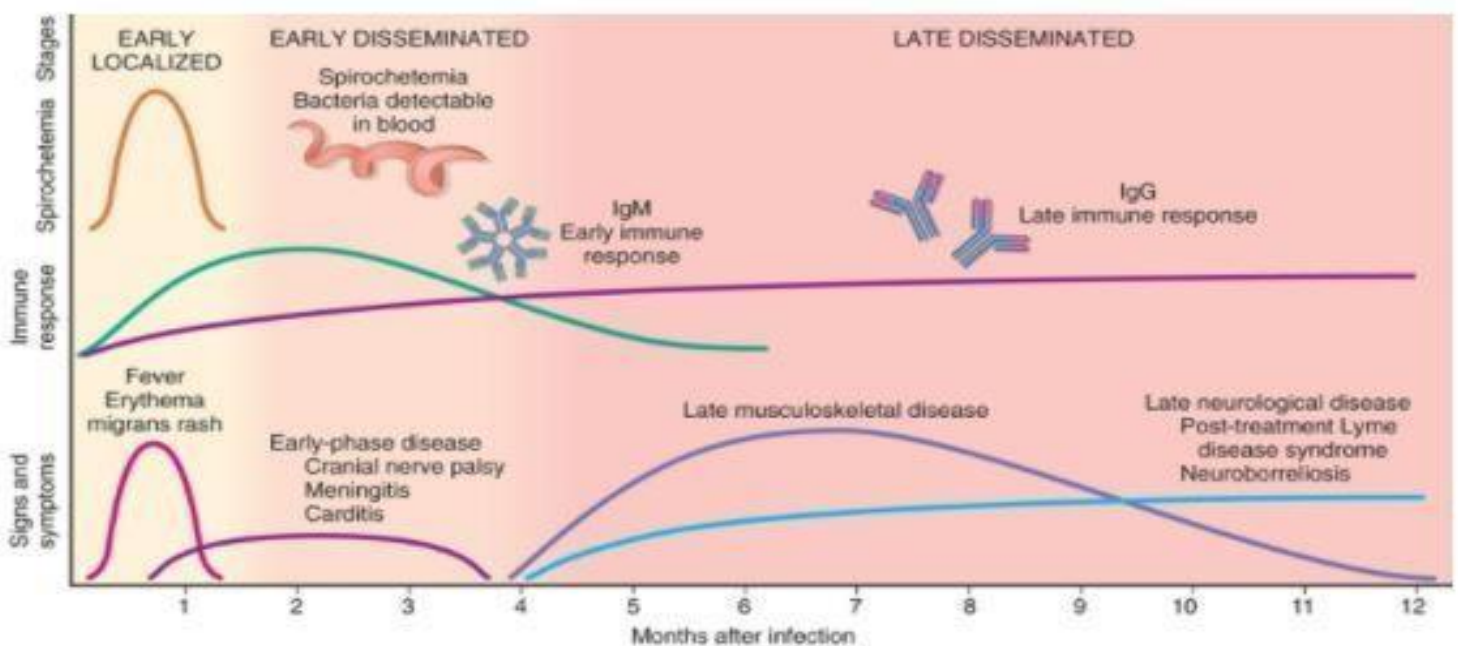


FIG. 21.40 Lyme disease progresses through three clinically recognizable phases: early...

\*continue about lyme arthritis..

\* it is sometimes self-limiting and sometimes it needs treatment, then after that later on there'll be some late neurological deficits post treatment of lyme disease syndrome or "neuroborreliosis" (because the organism is borrelia burgdorferi).

Most important things you need to know about lyme arthritis:

- \* It is an infectious arthritis, part of systemic disease.
- \* It has multiple phases and it is due to an immune response initially by IgM and then by IgG
- \* It is very rare in Jordan

**CRYSTAL-INDUCED ARTHRITIS:** (common in our region and the world)

- Crystals deposited in joints causing disease; deposition of crystals triggers inflammatory reaction which will start accumulating and destroying the cartilage.

- Can be acute and can be chronic, it can be acute and then continues to be chronic

- **the different Endogenous types of crystals:** (they are called endogenous because they are produced in your body)

- Monosodium urate, MSU , when they accumulate they are responsible for a disease called (GOUT) or gouty arthritis or acute gouty arthritis

- Calcium pyrophosphate dehydrogenase, CPPD, it is responsible for a disease which is called (PSEUDOGOUT)

\***GOUT:**

- Transient attacks of arthritis, any joint can be involved mainly big toe, triggered by deposition of MSU crystals

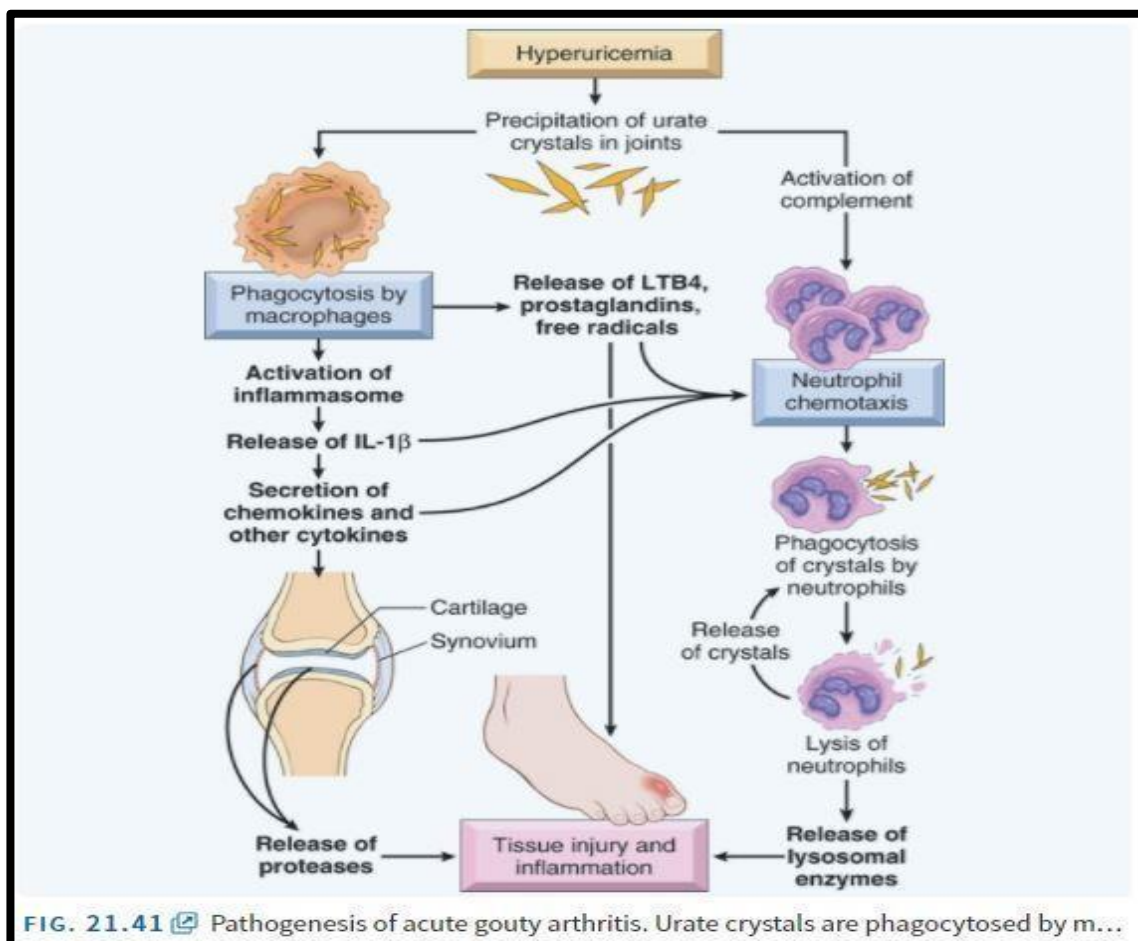
- Uric acid: is a purine metabolite; increased production of uric acid or decreased excretion from kidney cause hyperuricemia which is the major cause of gout.

- With hyperuricemia, risk increases with: 20-30 years of age, obesity, alcohol, genetic predisposition, drugs (thiazides (which are diuretics that increase uric acid in blood))

- it is usually very painful swollen toe

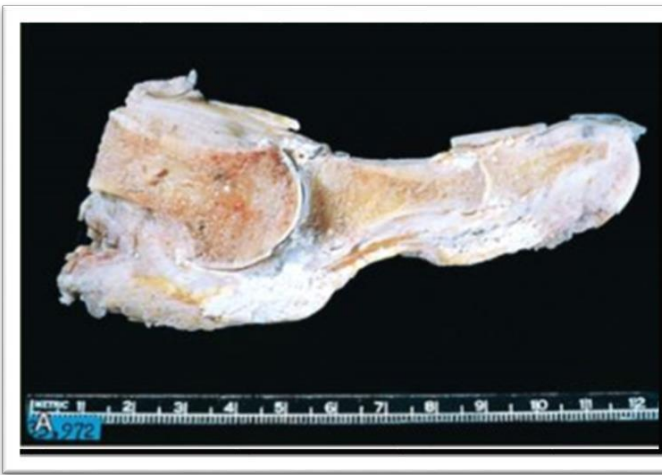
so what happens if you have any reason or any cause for hyperuricemia, the uric acid crystals will increase and they will get deposited in the joints and with deposition of those uric acid crystals there will be activation of multiple inflammatory cells, macrophages and neutrophils inducing a cascade of inflammatory reaction: (activation of a inflammasome, release of interleukin-1 beta, secretion of multiple chemokines and other cytokines), there is also a role for neutrophils where they get stimulated by chemotaxis and those will be also impacted by the phagocytosis of crystals by neutrophils causing lysis of the neutrophils and when the neutrophils are lysed they'll release also more lysosomal enzymes, more proteases leading to tissue injury and destruction in the joints. The picture here emphasizes that the big toe is probably the most common joint which is involved by the acute gouty arthritis attack.

- The major enticing event is the presence of uric acid crystals due the presence of hyperuricemia

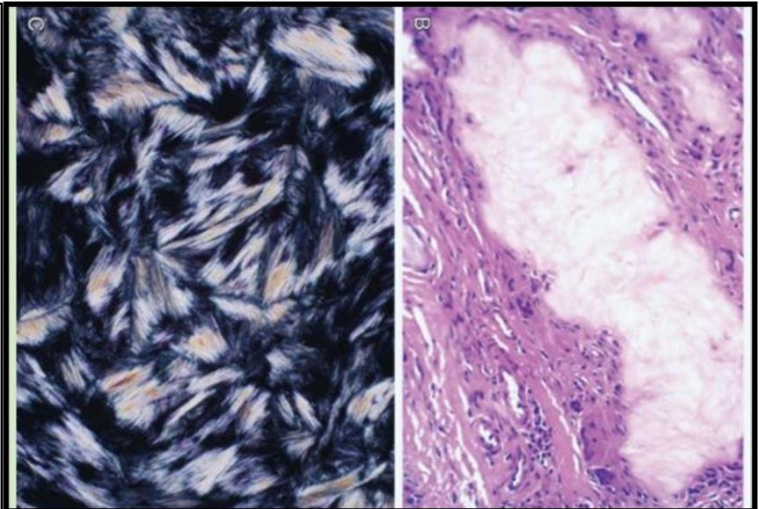


## MORPHOLOGIC CHANGES OF GOUT:

<b>Acute arthritis</b>	<b>Dense inflammation of synovium, MSU crystals in neutrophils, -ve birefringent</b>
<b>Chronic tophaceous arthritis</b>	<b>Repetitive attacks &amp; crystals deposition in the joint; thick synovium, pannus</b>
<b>Tophi in various sites</b>	<b>Cartilage, ligaments, bursae and tendons</b>
<b>Gouty nephropathy</b>	<b>MSU crystals deposition in kidney; nephrolithiasis &amp; pyelonephritis</b>



This is an amputated toe that is completely destroyed by chronic gout, all this chalky white materials are calcified monosodium urate crystals



This picture shows pannus formation that appears in chronic tophaceous arthritis

- ✿ Although the joints and mainly the big toe is the main target but the tophi (which are the crystals inducing inflammatory reaction) can be seen in many organs such as cartilage, ligaments, bursae and tendons.



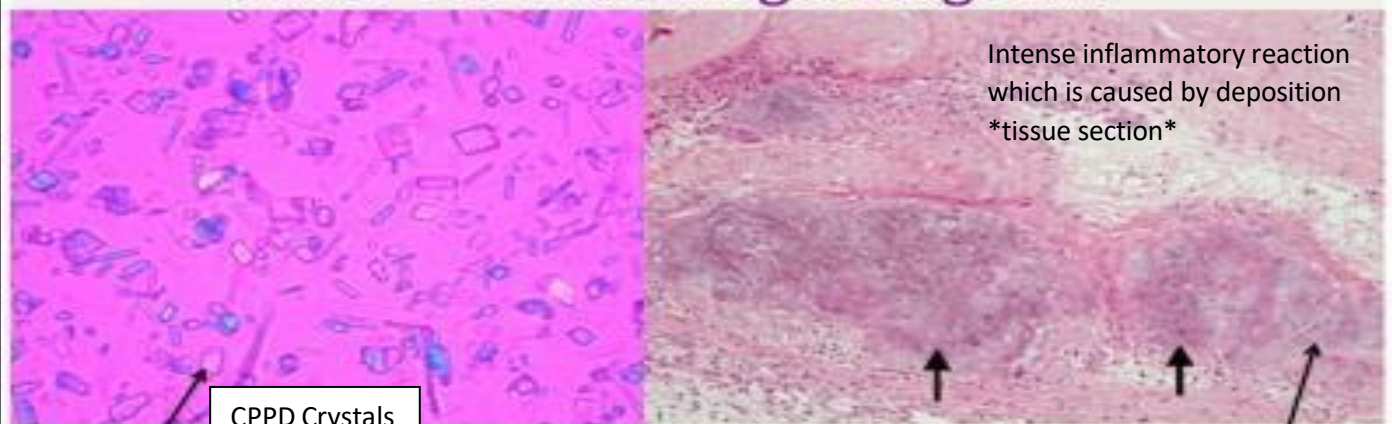
- ❁ One of the long-term complications of gouty arthritis is what we call **gouty nephropathy**, so those crystals also can be deposited in the kidney causing multiple uric acid stones, leading to sometimes big stones obstruction and recurrent attacks of upper urinary tract infection which we call pyelonephritis.

**Trx:** the treatment of gout is life style modifications ( the patients should decrease the amount of eating meat and liver because they are rich in purines and constantly they'll cause hyperuricemia leading to gout), NSAIDS (initially gout can be treated by NSAIDS in the acute attacks) & Colchicine (is the drug of choice in acute gout), Xanthine oxidase inhibitors (Allupurinol) in chronic gout and prevention.

### \*PSEUDOGOUT:

- Usually occurs in older patients > 50 years; increase with age
- Idiopathic (usually we don't know what is going on or why it happened), (genetic) or secondary to another cause.
- CPPD crystal induced arthritis via triggering inflammatory reaction (induce reaction in the same way as the msu crystals induce reaction in gout)
- In the secondary pseudogout cases: usually associated with DM, previous joint damage, HPTH (hyperparathyroidism) , hemochromatosis
- Pseudogout can be presented in Acute, subacute and chronic forms
- Trx: supportive, no preventive measures so far ( there is no curative treatment)

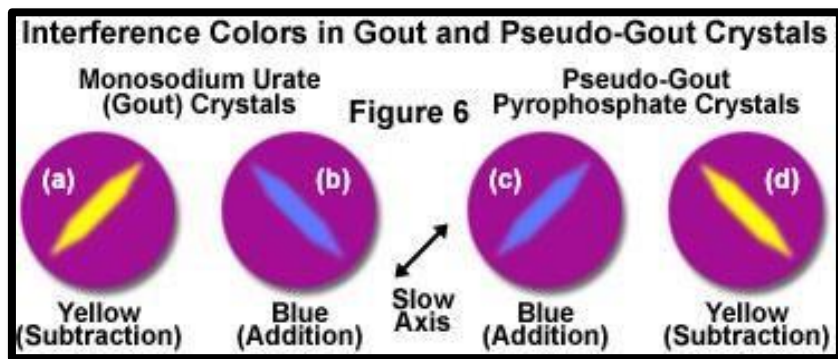
#### IIIb. CPPD: Pathologic Diagnosis



- Synovial Fluid: geometric or rhomboid-shaped crystals, weakly positively birefringent under polarized light
- Histopathology: amorphous purple deposits on H&E with *little inflammatory response*.

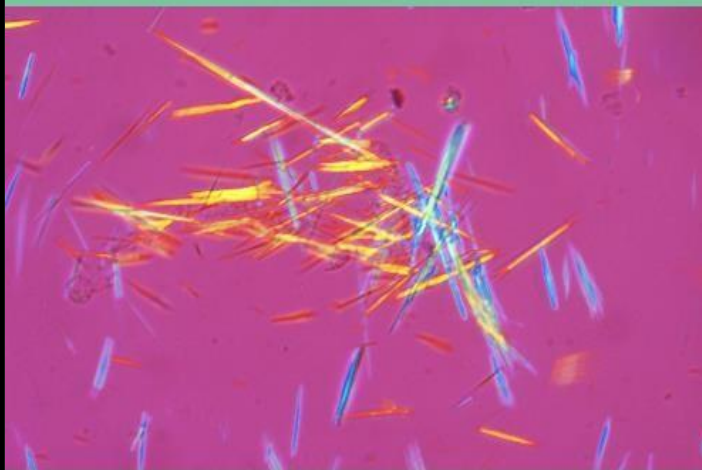
## NEGATIVE VS POSITIVE BIERFRINGENCE

- \* It depends on the polarizing angle of the microscope so if you see needle shaped crystals which are yellow perpendicular to the birefringent axis polarizing crystals so the pseudogout crystals are parallel and the monosodium gout crystals are perpendicular and yellow.
- \* MSU crystals are needle shaped, strong negative birefringence and yellow when parallel to compensatory ray.
- \* CPPD crystals are rod or rhomboid, weak positive birefringence and blue when parallel to compensatory ray.

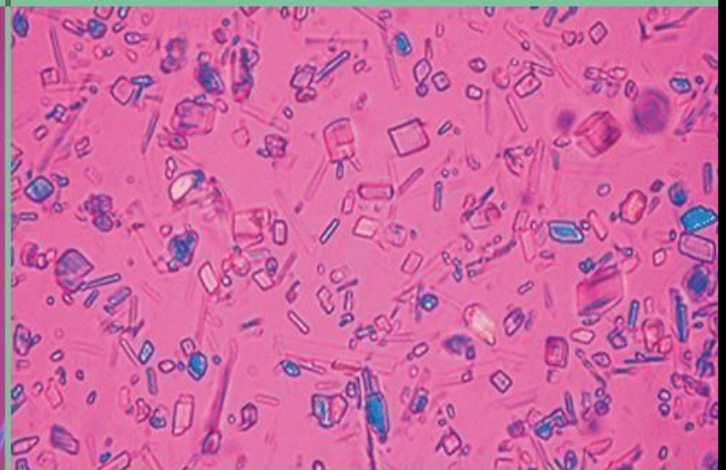


Monosodium Urate (MSU) Crystals

Calcium Pyrophosphate Dihydrate (CPPD) Crystals



Needle shaped, strong negative birefringence  
Yellow when parallel to compensator ray



Rod or rhomboid, weak positive birefringence  
Blue when parallel to compensator ray





## Summary

### Arthritis

- **Osteoarthritis (OA, degenerative joint disease)**, the most common disease of joints, is a degenerative process of articular cartilage in which matrix breakdown exceeds synthesis. Inflammation is minimal and typically secondary. Local production of inflammatory cytokines may contribute to the progression of joint degeneration.
- **Rheumatoid arthritis (RA)** is a chronic autoimmune inflammatory disease that affects mainly small joints, but can be systemic. RA is caused by a cellular and humoral immune response against self-antigens, particularly citrullinated proteins. TNF plays a central role and antagonists against TNF are of clinical benefit.
- **Seronegative spondyloarthropathies** are a heterogeneous group of likely autoimmune arthritides that preferentially involve the sacroiliac and vertebral joints and are associated with HLA-B27.
- **Suppurative arthritis** describes direct infection of a joint space by bacterial organisms.
- **Lyme disease** is a systemic infection by *Borrelia burgdorferi*, which manifests, in part, as an infectious arthritis, possibly with an autoimmune component in chronic stages.
- **Gout and pseudogout** result from inflammatory responses triggered by precipitation of urate or calcium pyrophosphate, respectively.

***GOOD LUCK***

## Test yourself

1) Rhomboid-geometric crystals were seen on joint aspirate from a 60-year old male patient who came with right ankle joint pain and swelling. The crystals exhibit weakly positive birefringence under polarizing microscope. What is the diagnosis?

- a. Pseudo gout
- b. Sero-negative arthropathy of ankle joint
- c. Acute gouty arthritis
- d. Acute exacerbation of osteoarthritis
- e. Chronic gouty arthritis

Answer: A

2) Allopurinol decreases the plasma concentration of:

- a. Hypoxanthine
- b. Xanthine
- c. Uric acid
- d. All of the mentioned
- e. Purine bases

Answer: C