# CRYSTAL DEPOSITION DISORDERS



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# INTRODUCTION



- Musculoskeletal manifestations caused by deposition of various endogenous compounds.
- Uric acid (Gout)
- Calcium pyrophosphate dihydrate (CPPD)(Pseudogout)
- Calcium hydroxyapatite (HADD)
- Calcium oxalate

# GOUT



- Characterized by abnormal deposition of monosodium urate monohydrate (MSU) crystals.
- Classification
- Primary -95%
- Secondary -5%

# Epidemiology



- Prevalence of 0.3%
- Higher prevalence in the Caucasians
- Male female ratio of ; 10:1
- Age range of 30-60years
- Kidney transplant patients have a 10% risk of gout in first 3 years.

# Clinical Manifestations



- Acute mono- or polyarthritis
- Bursitis
- Tendinitis
- Tendon calcification
- Tophaceous deposits
- Nephrolithiasis

# Etiology



- 1. Overproduction of uric acid (10%)
- 2. Under-excretion of uric acid by the kidneys (90%)

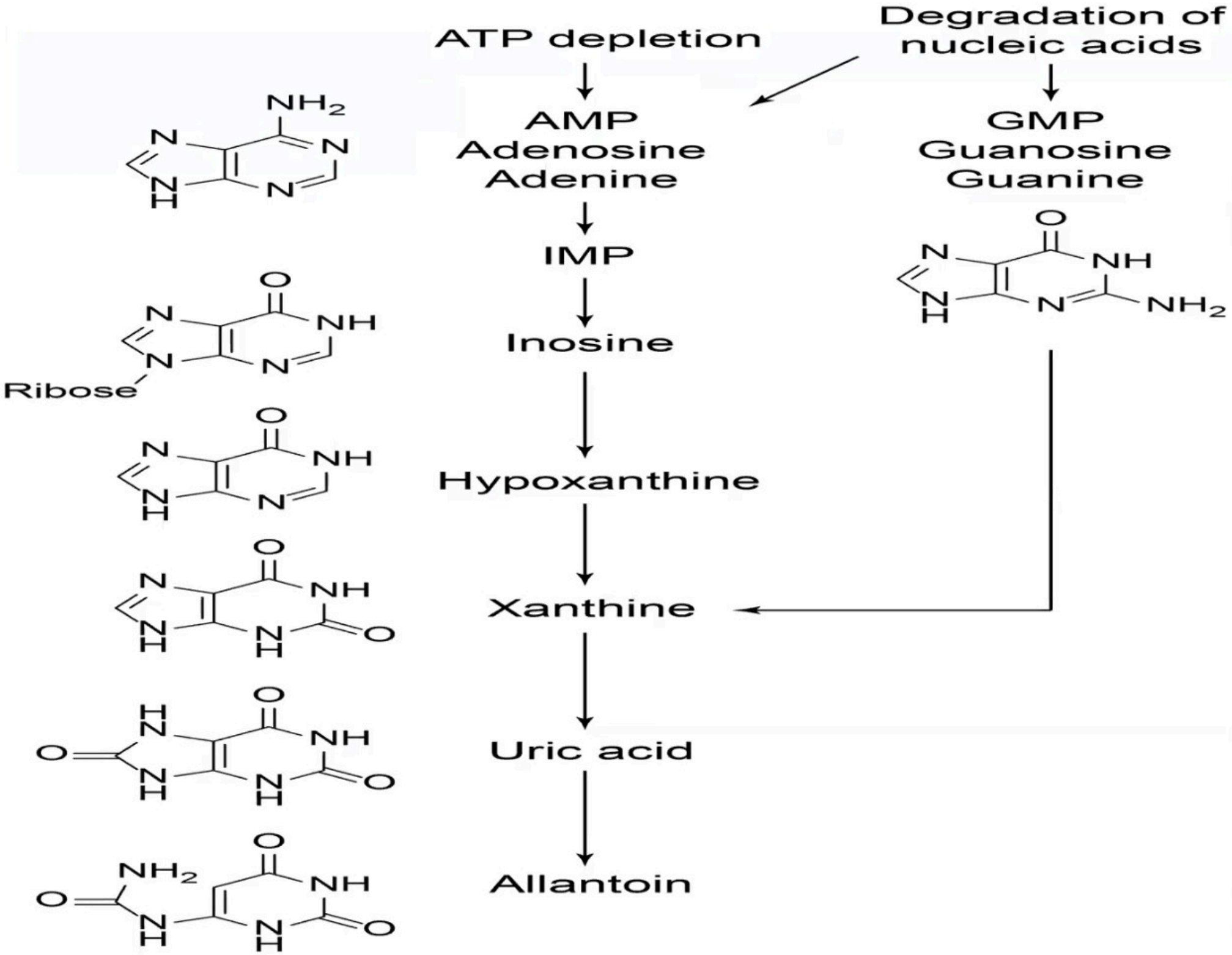
- Hyperuricaemia is not equal to gout

- Hyperuricaemia in 5% men and 1% women

# Pathophysiology



- purine metabolism problem
- Xanthine oxidase
- Normal uric acid level in blood 2-7mg/dl
- Minute crystals deposited


ATP depletion
Degradation of nucleic acids
AMP
Adenosine
Adenine
GMP
Guanosine
Guanine
IMP
Inosine
Ribose
Hypoxanthine
Xanthine
Uric acid
Allantoin

# Pathophysiology cont.



- Fluctuation in uric acid levels cause gouty attack
- Less soluble in acidic conditions and low temperatures
- 40% of patients will present with urinary stones

# Cont.

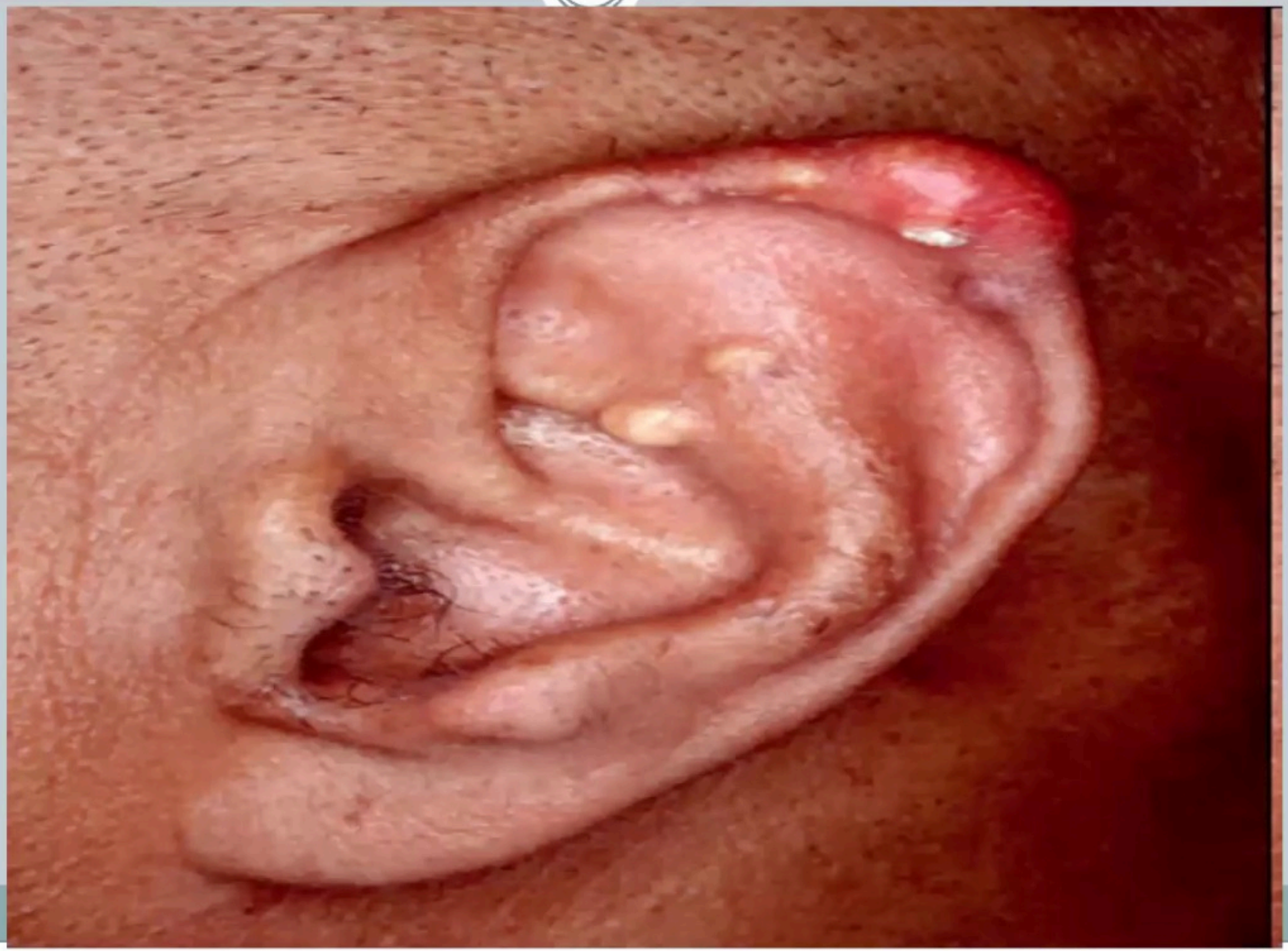


- Peripheral small joints
- Remain inert for long
- Some event cause release of needle like crystals into the joint eliciting an acute inflammatory reaction

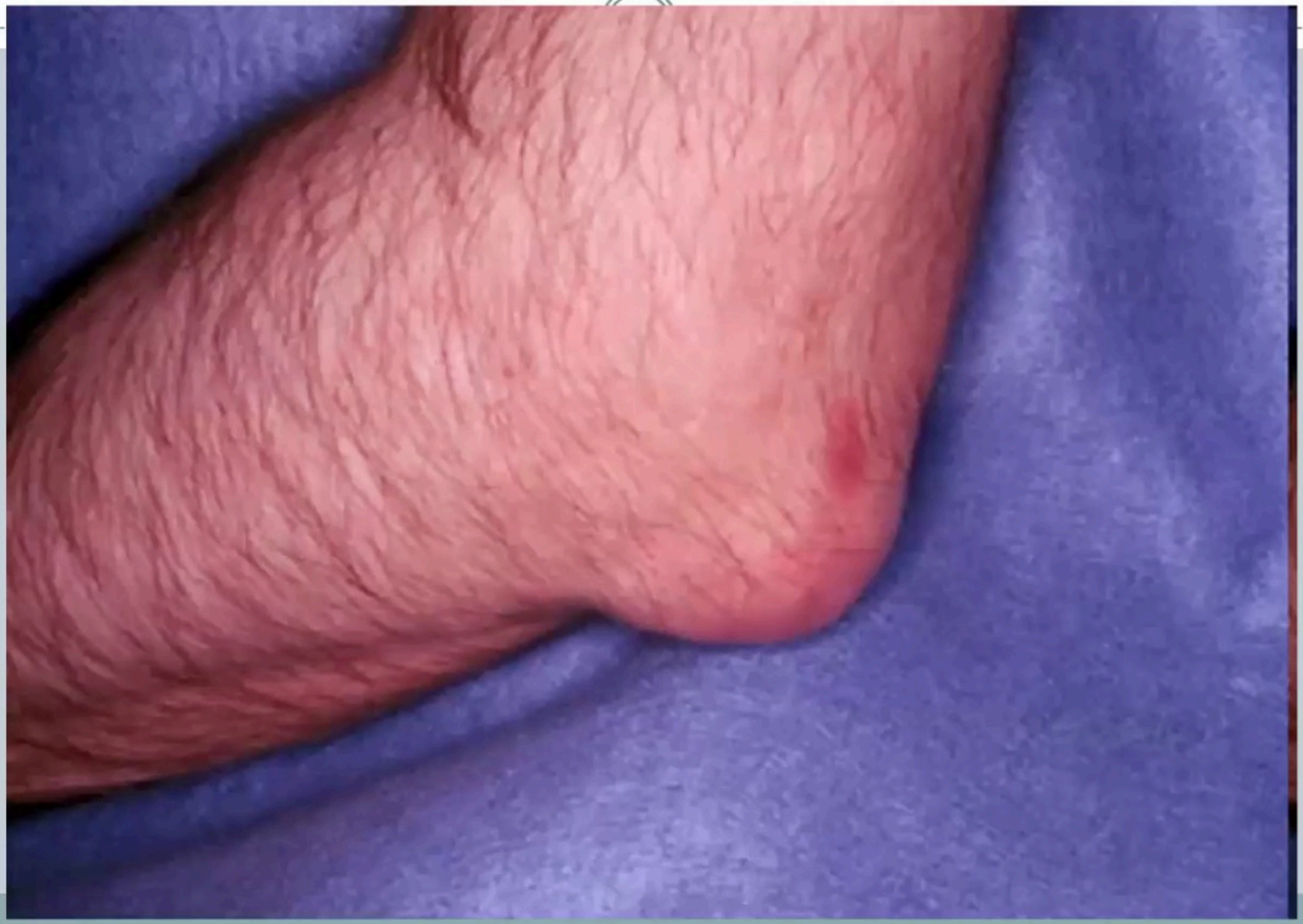
- Tophi-clumps of chalky material
- Skin ulceration
- Cartilage and bone destruction

# Ear deposition





# Elbow deposition



# Four Stages or Phases



- Asymptomatic
- Acute
- Intercritical
- Chronic

# Clinical features



- Painful swollen joint
- MP of the big toe-commonest site(50%)
- Joint is warm and tender
- History of gout

# Acute attack in the big toe

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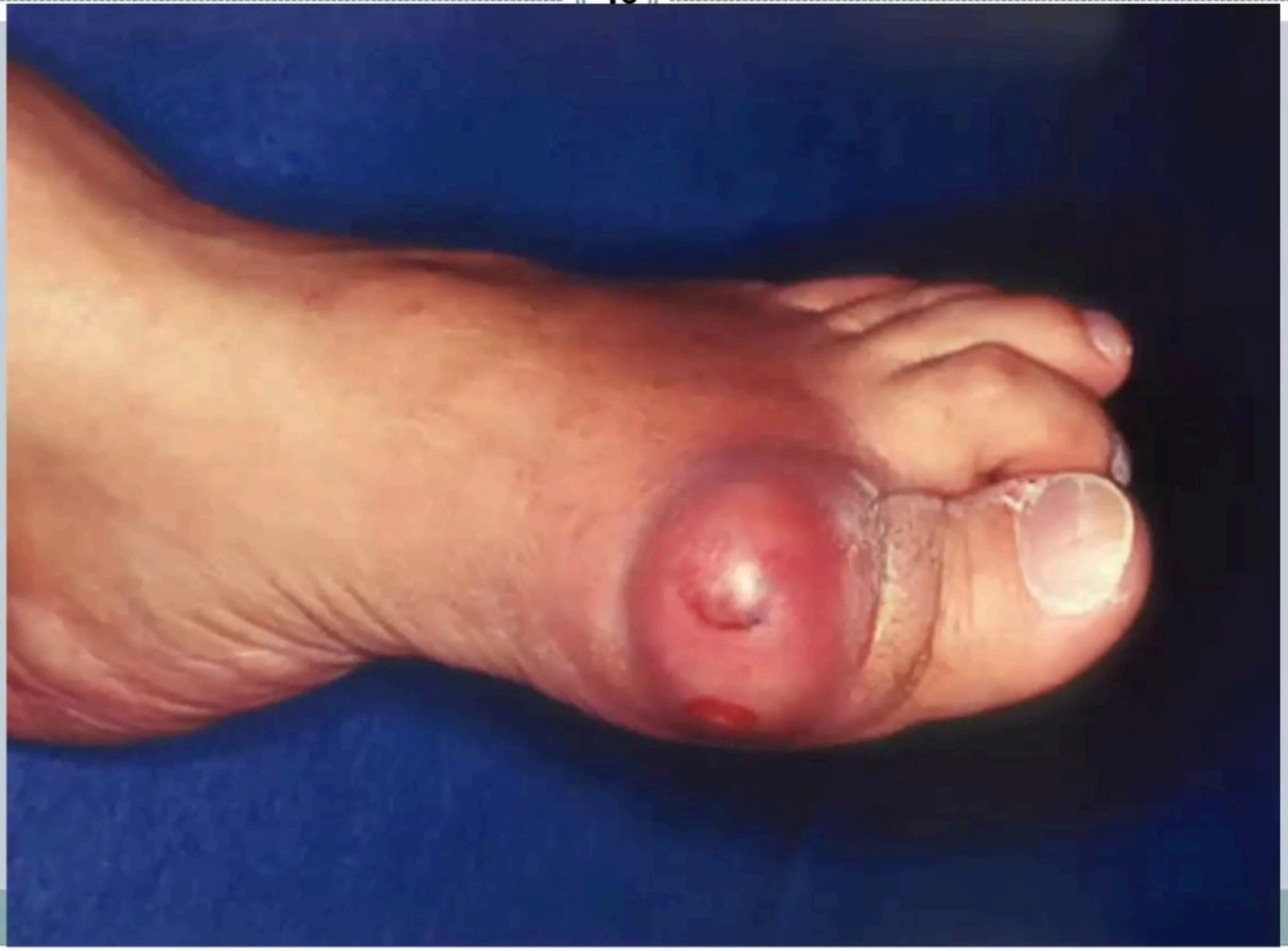


# Acute attack-Predisposing factors



- Dietary excess/ starvation
- Alcohol
- Increased fructose intake
- Diuretics
- Surgery or trauma
- Glucocorticoid withdrawal
- Hypouricemic therapy

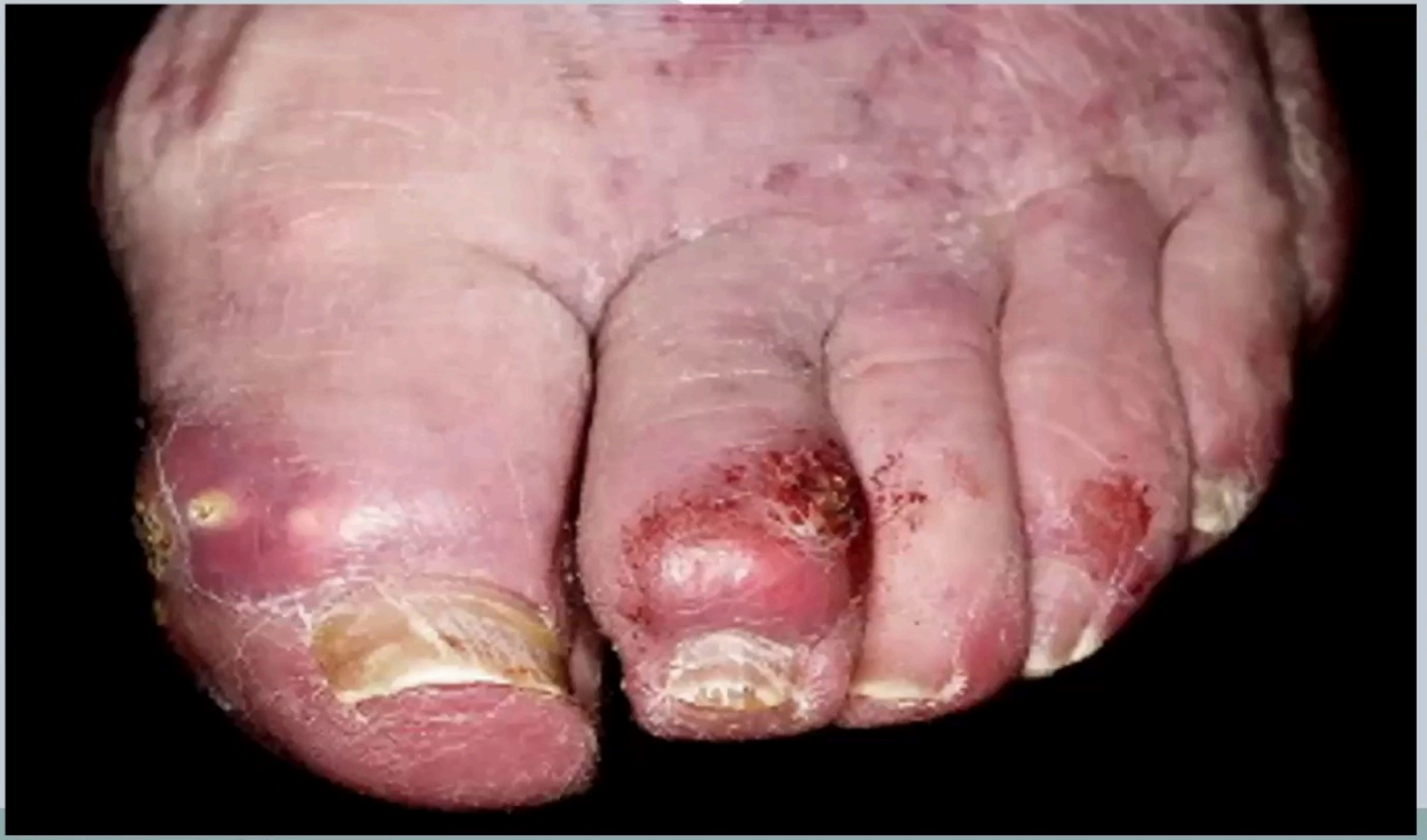
# Chronic gout



- Recurrent attacks
- Joint erosion
- Tophi
- Chronic discharging wounds
- Chronic pain,
- Stiffness  and deformity
- Renal lesions

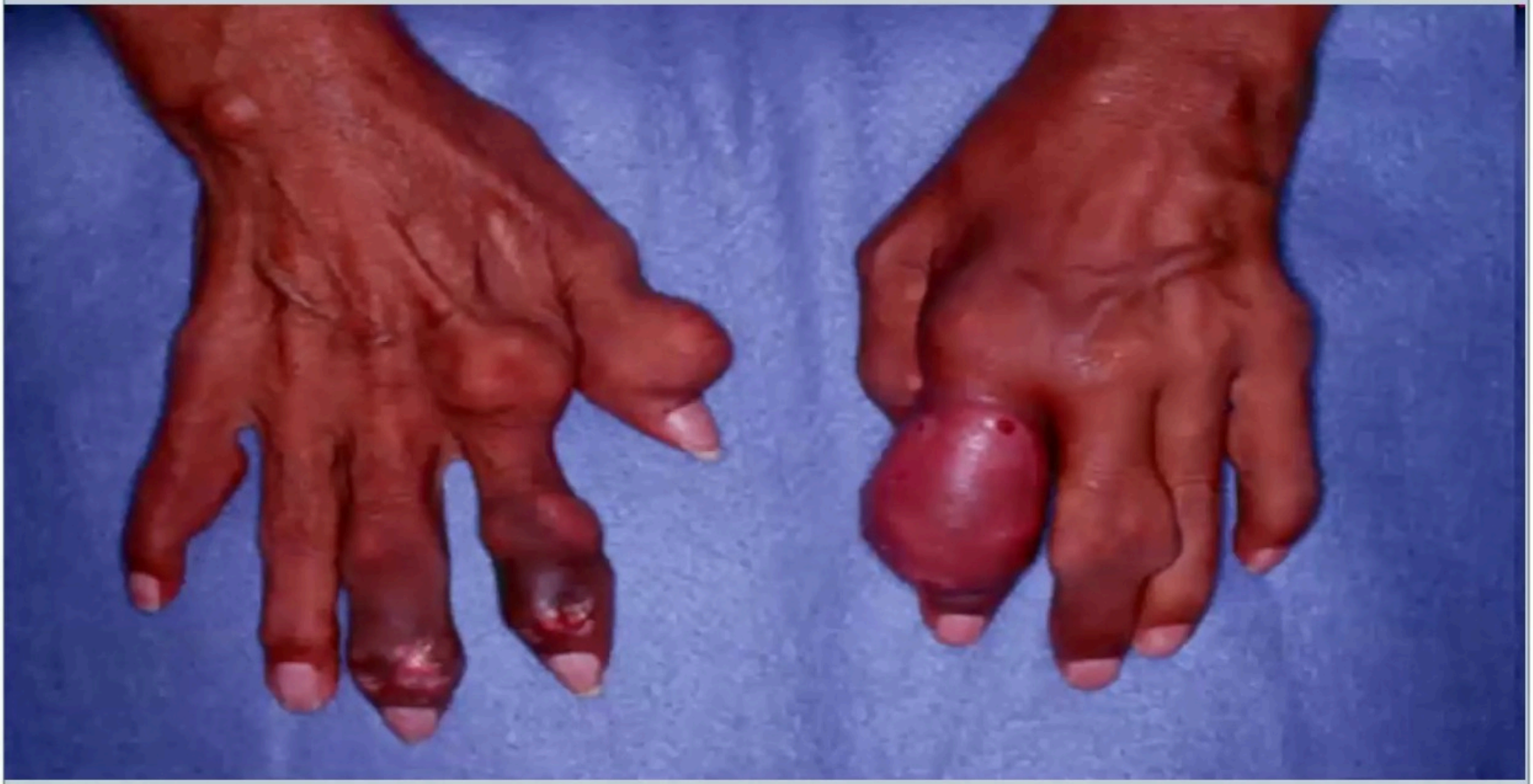
# Multiple toe involvement





# Tophaceaous deposits in the fingers





# Uric acid nephrolithiasis



- Correllates with serum uric acid levels
- 50% in patients with levels of >13gm/dl
- Or 1100mg/d in urine
- Uric acid bladder stones can occur in patients with no joint involvement.
- Nidus for other stones

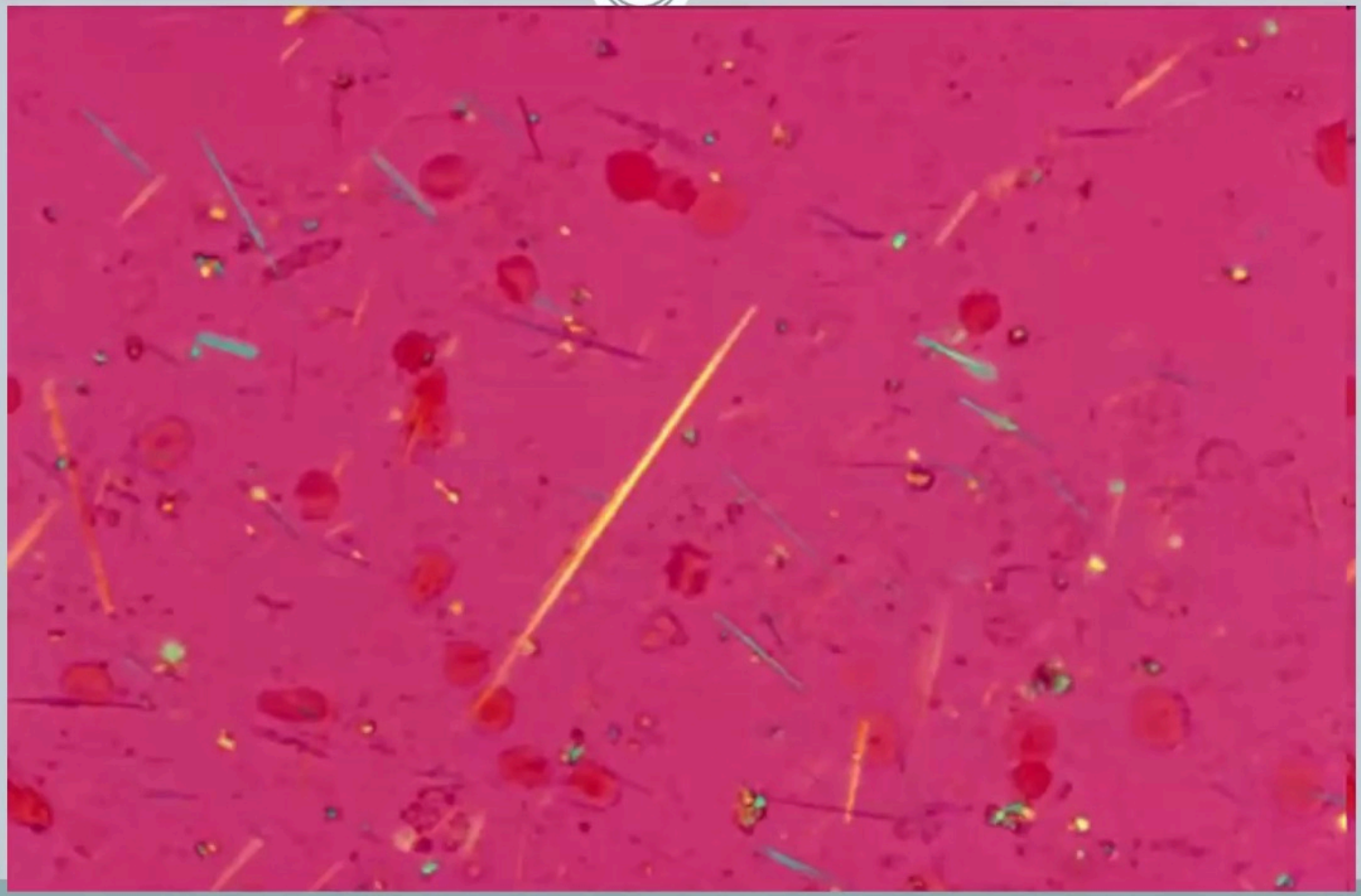
# Diagnostic Workup



- Arthrocentesis-Synovial fluid analysis
- Analysis of Tophi contents
- Uric acid levels in blood
- Uric acid in urine (250-750mg in 24hs)
- Blood tests
- Radiographs
- Ultrasound, MRI, CT-SCAN

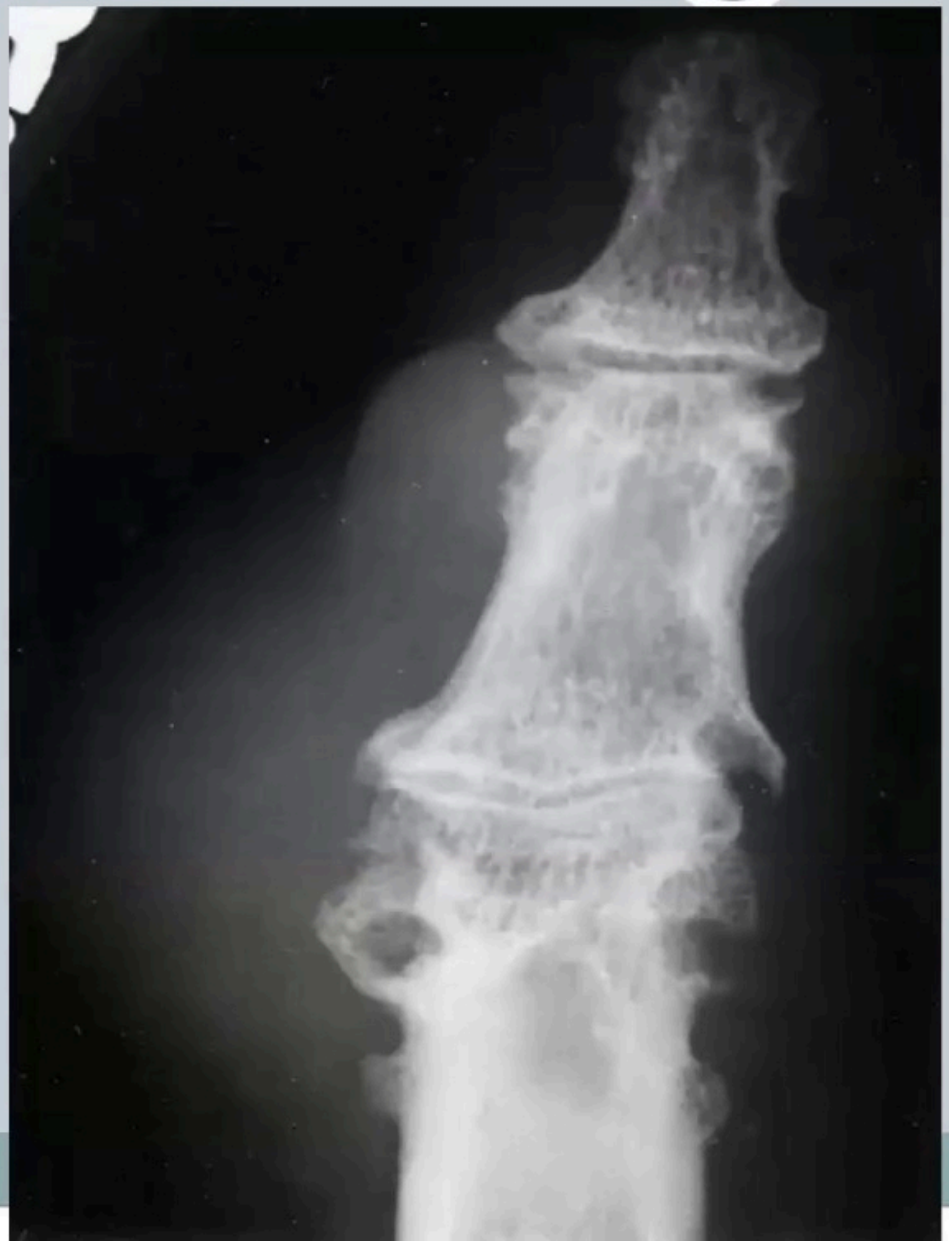
# Needle shaped negative birefrigent crystals

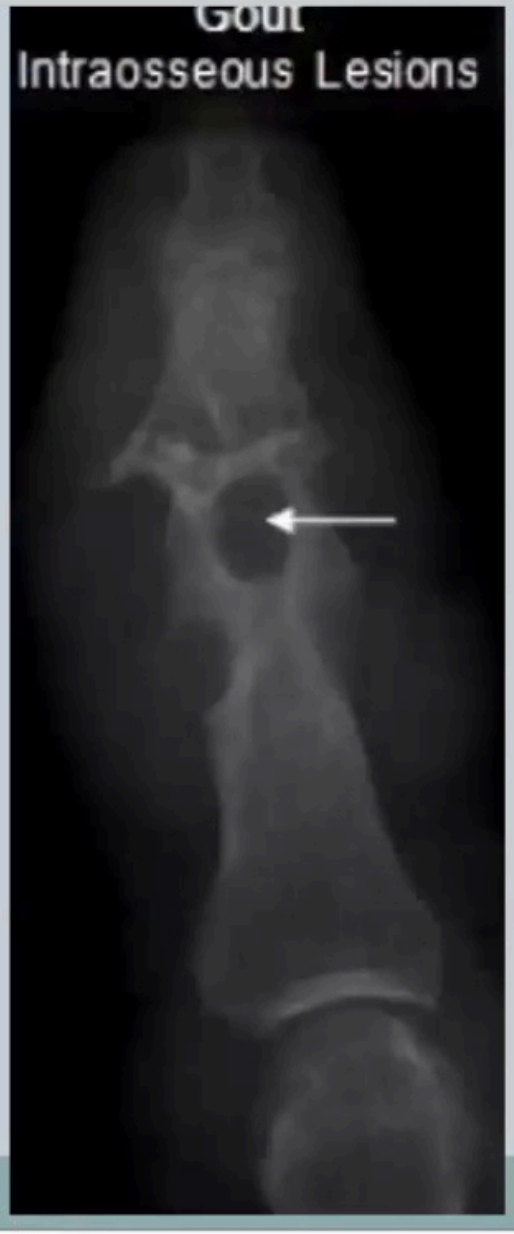


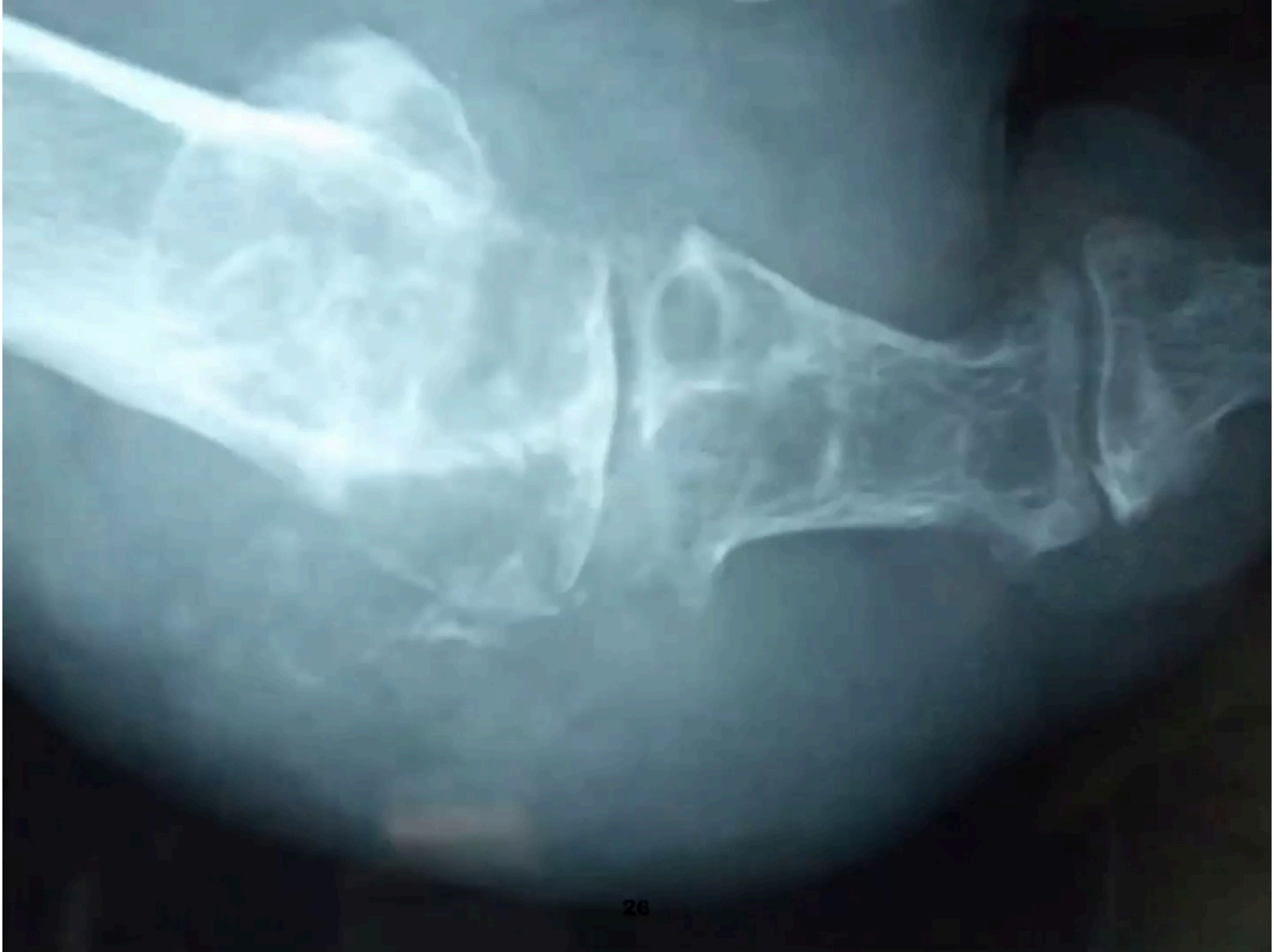


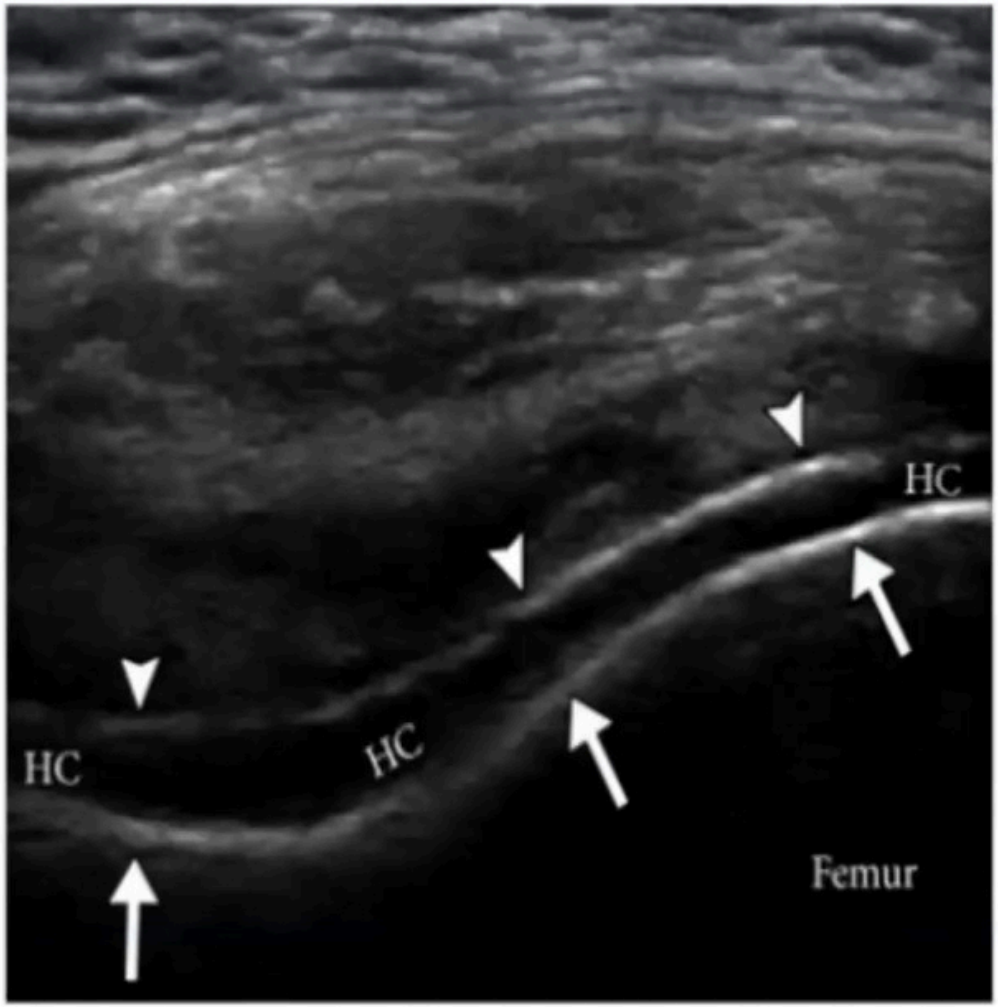
# Radiographic features






Gout
Intraosseous Lesions

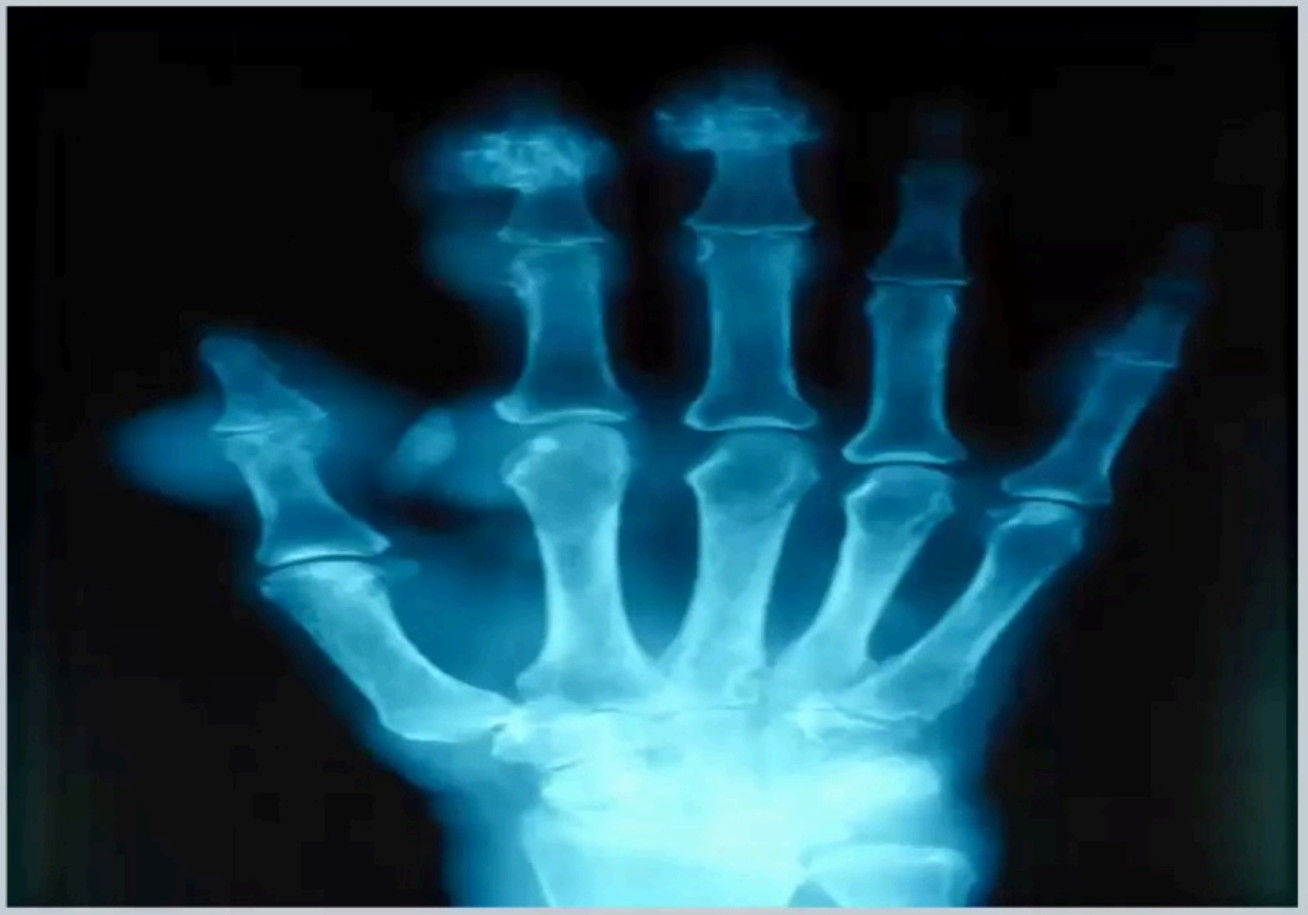





- Ultrasound double contour sign. Transverse ultrasound image of the suprapatellar knee joint demonstrates two parallel hyperechoic contours on either side of the hypoechoic hyaline cartilage (HC). The deep echogenic contour (long arrows) represents the femoral cortex, while the superficial echogenic contour (arrowheads) represents uric acid crystals accumulating on the surface of the hypoechoic hyaline cartilage (HC).

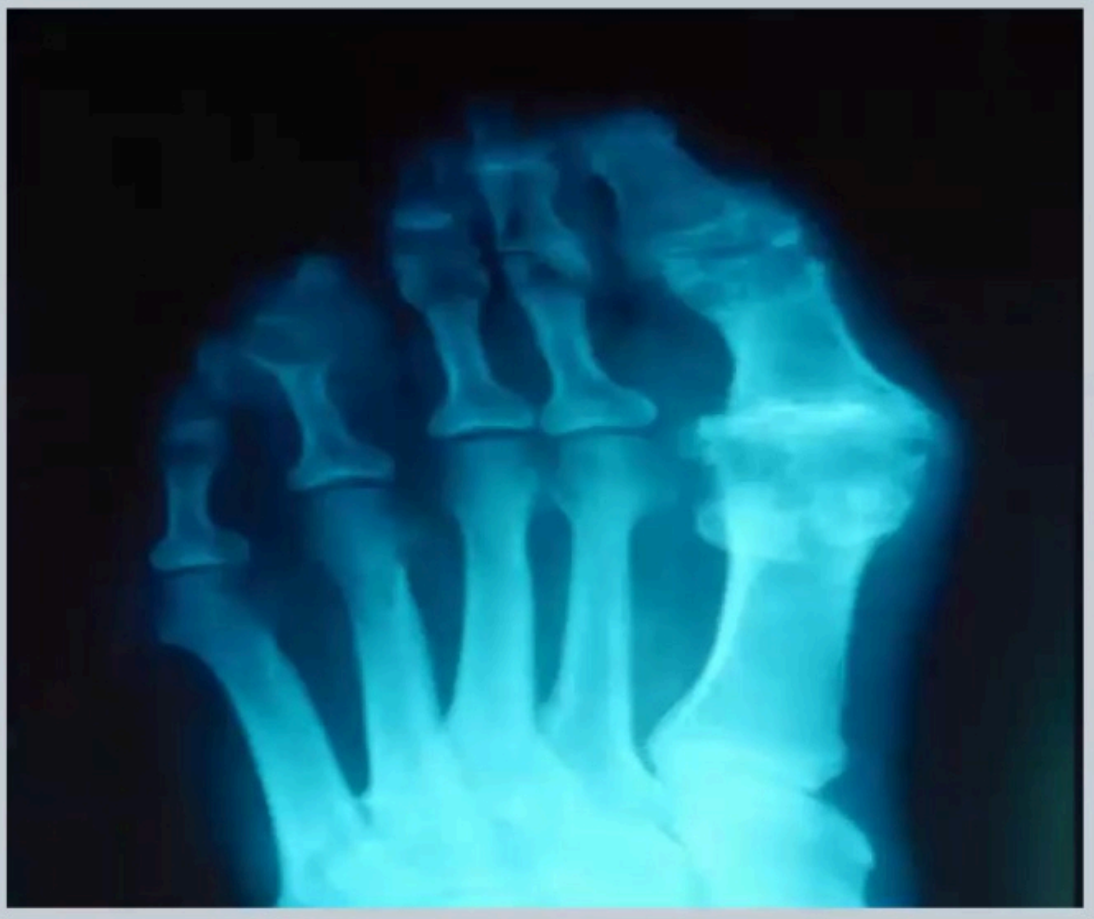
# Involvement of the fingers





# Big toe involvement





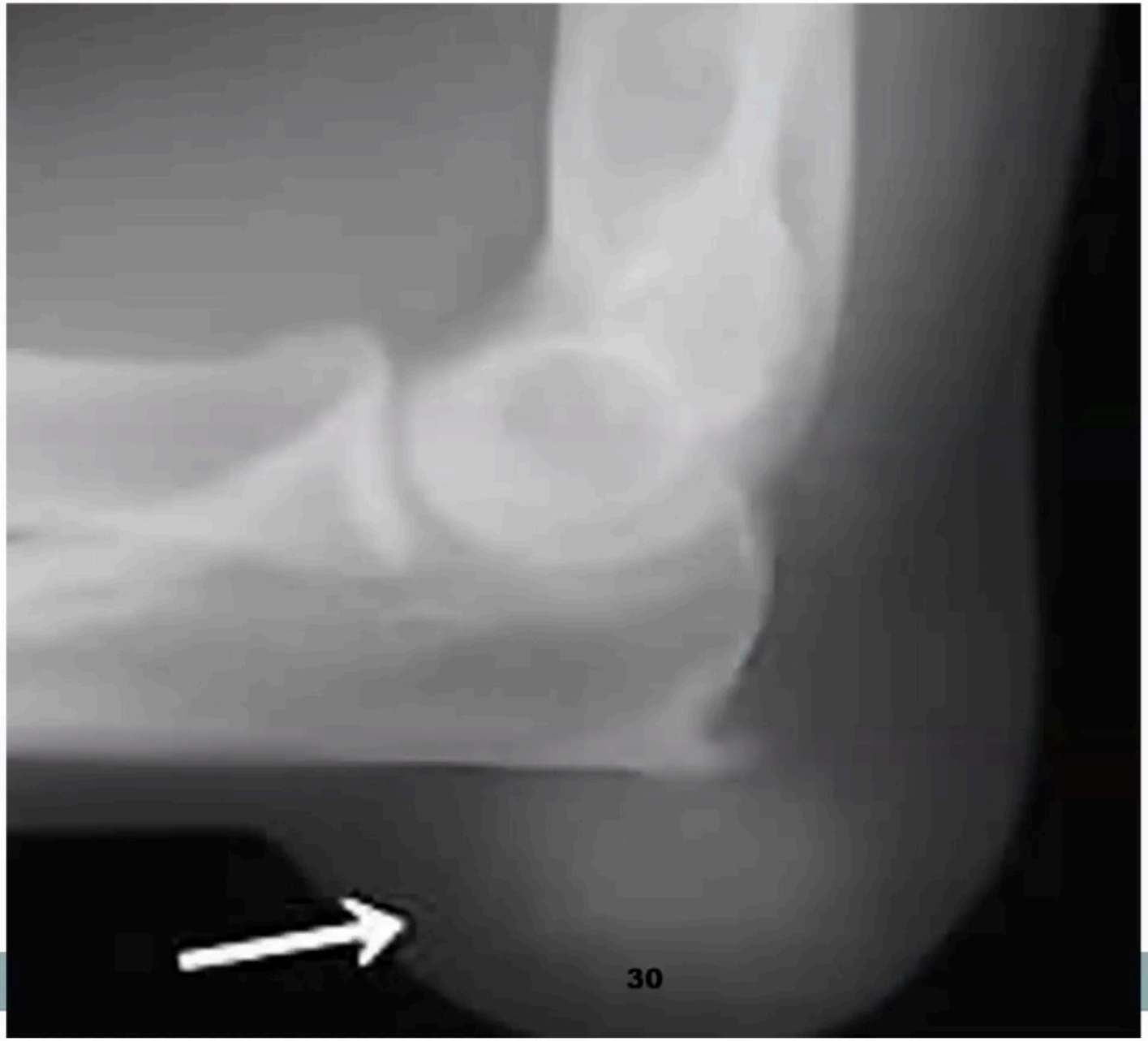


**Table 44–2.** Criteria for the diagnosis of acute gouty arthritis.

Presence of characteristic urate crystals in joint fluid, or
A tophus proved to contain urate crystals by chemical means or polarized light microscopy, or
The presence of 6 of the following 12 clinical, laboratory, and radiographic phenomena listed below:

1. More than one attack of acute arthritis
2. Maximal inflammation developed within 1 day
3. Attack of monoarticular arthritis
4. Joint redness observed
5. First metatarsophalangeal joint painful or swollen
6. Unilateral attack involving first metatarsophalangeal joint
7. Unilateral attack involving tarsal joint
8. Suspected tophus
9. Hyperuricemia
10. A symptomatic swelling within a joint (radiograph)
11. Subcortical cysts without erosions (radiograph)
12. Negative culture of joint fluids for microorganisms during attack of joint inflammation

# Principles of Treatment



- 1. Managing the acute attack
- 2. Preventing acute flares
- 3. Lowering excess stores of urate
- 4. Treating the complications

# Treatment Modalities



- 1. Non-pharmacological measures
- 2. Anti-inflammatory therapies
- 3. Control of hyperuricemia
  - Uricosuric therapy
  - Inhibit uric acid production
  - Degrade urate
- 4. Surgical interventions

# Non-pharmacological measures



- Rest the joint
- Increased fluid intake
- Loose weight
- Stop alcohol
- Decrease meat or purine rich foods  intake
- Avoid diuretic use
- Vitamin C intake
- Topical ice application

# Anti-inflammatory therapy



- 1- NSAIDS; indomethacin, diclofenac, Ibuprofen
- Give the higher doses for 3-5days
- 2-Colchicine  dose is 0.5mg 2-4times daily
- 3- Anakinra- IL1 receptor antagonist
- 4- Rilonacept- bind to IL1
- 5-Canakinumab- monoclonal Antibody against IL1B

# Anti-inflammatory therapy



- 3. Glucocorticoids eg oral prednisolone or Intra-articular steroid

- 4. Anakinra:- IL-1 receptor antagonist

- 5. Corticotropin (ACTH)

# Treating hyperuricemia

- Target Uric acid< 6 mg/dL.
- the duration of treatment is indefinite and must be long-term to be effective
- Choices:
  1. Xanthine oxidase inhibitors (allopurinol, febuxostat)
  2. Uricosuric drugs ( probencid, sulfyperazone)
  3. Uricases ( raspburicase, Pegloticase).
- Indications:
  1. Chronic Gouty arthritis.
  2. Tophi
  3. Gouty nephropathy.
  4. Recurrent kidney stones
  5. Frequent and disabling gouty attacks, often defined as two or three flares annually

# Uricosuric therapy



- Mechanism of action:- Inhibit the proximal renal tubule epithelial cell re-absorption of the urate anion
- Probenecid
- Benzbromarone
- Losartan
- Fenofibrate

# Xanthine oxidase inhibitors



- Allopurinol
- Target urate levels of <6mg/dl
- Febuxostat 40-120mg daily
- Add an anti-inflammatory agent for first 6-12months
- NB- do not initiate during an acute attack

# Degradation of urates by oxidation (uricase therapy)



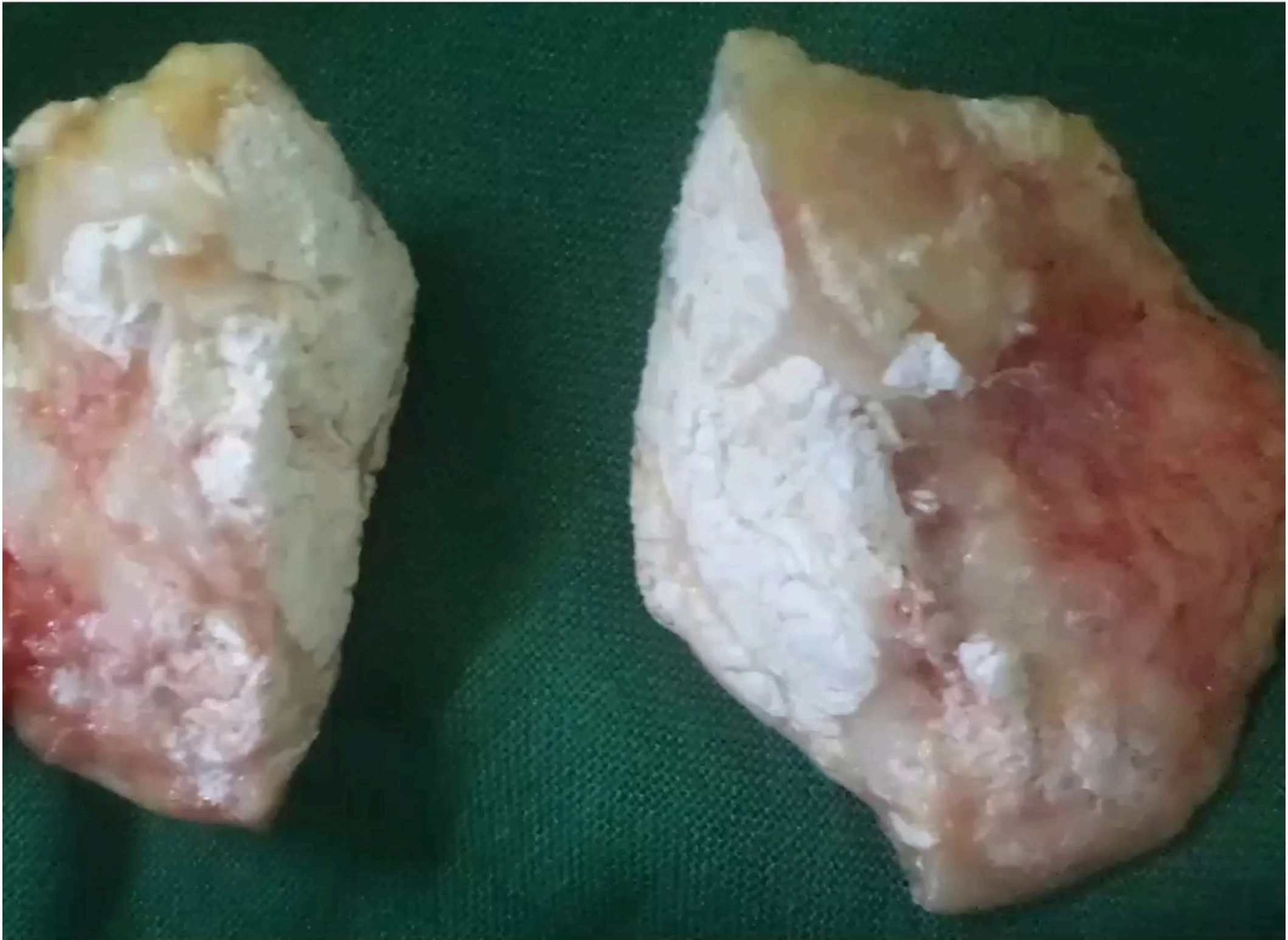
- Rasburicase :- a recombinant enzyme
- Pegloticase :- 8mg every 2 weeks

- Oxidation of uric acid to highly soluble product allantoin.

# Surgical



- Ulcerating tophi- Curretage and heal with secondary intention.
- Excision of tophi
- Tendon repair
- Joint splintage
- Arthrodesis
- Arthroplasty



# CPPD (Pseudogout) deposition disease



- Disease of elderly
- Cartilage changes favour crystal nucleation
- Increased inorganic pyrophosphate
- Combine with calcium to form CPPD
- Diminution of glycosaminoglycans in the cartilage
- CPPD crystal released into the joint is phagocytosed by neutophils which release inflammatory mediators

# Clinical features



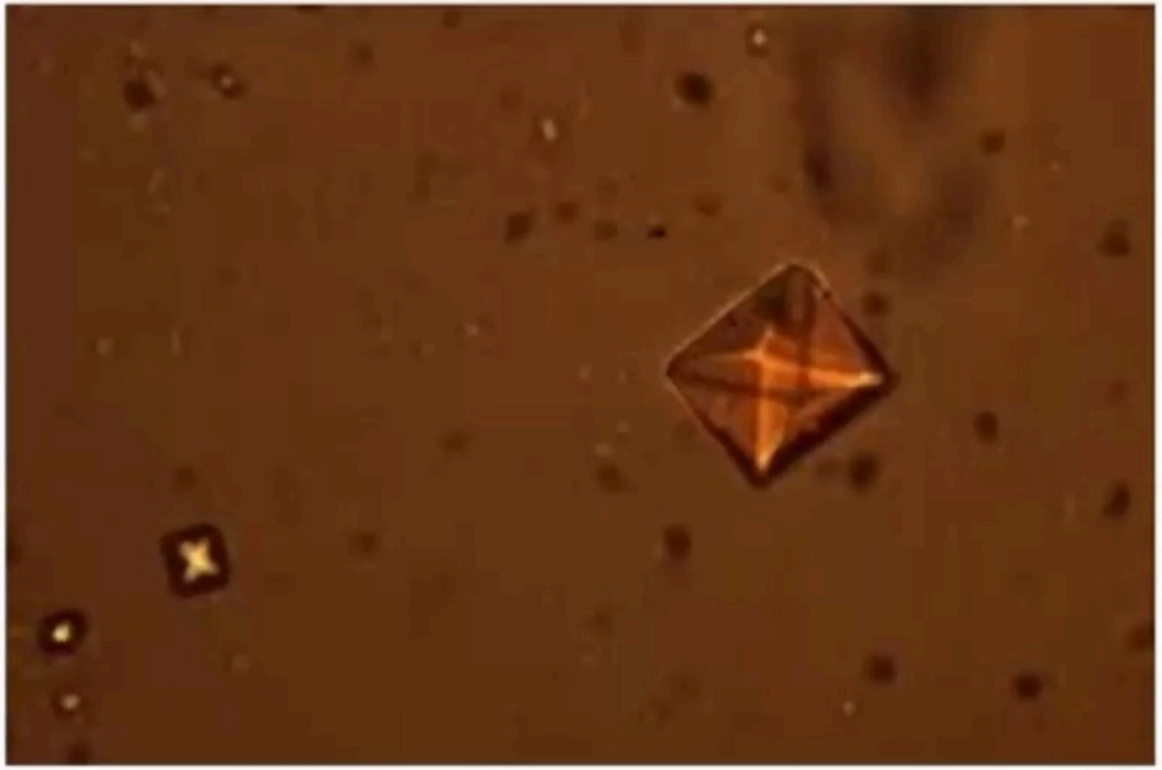
- Maybe asymptomatic, acute, subacute or chronic
- Knee most affected
- Polyarticular disease in 2/3

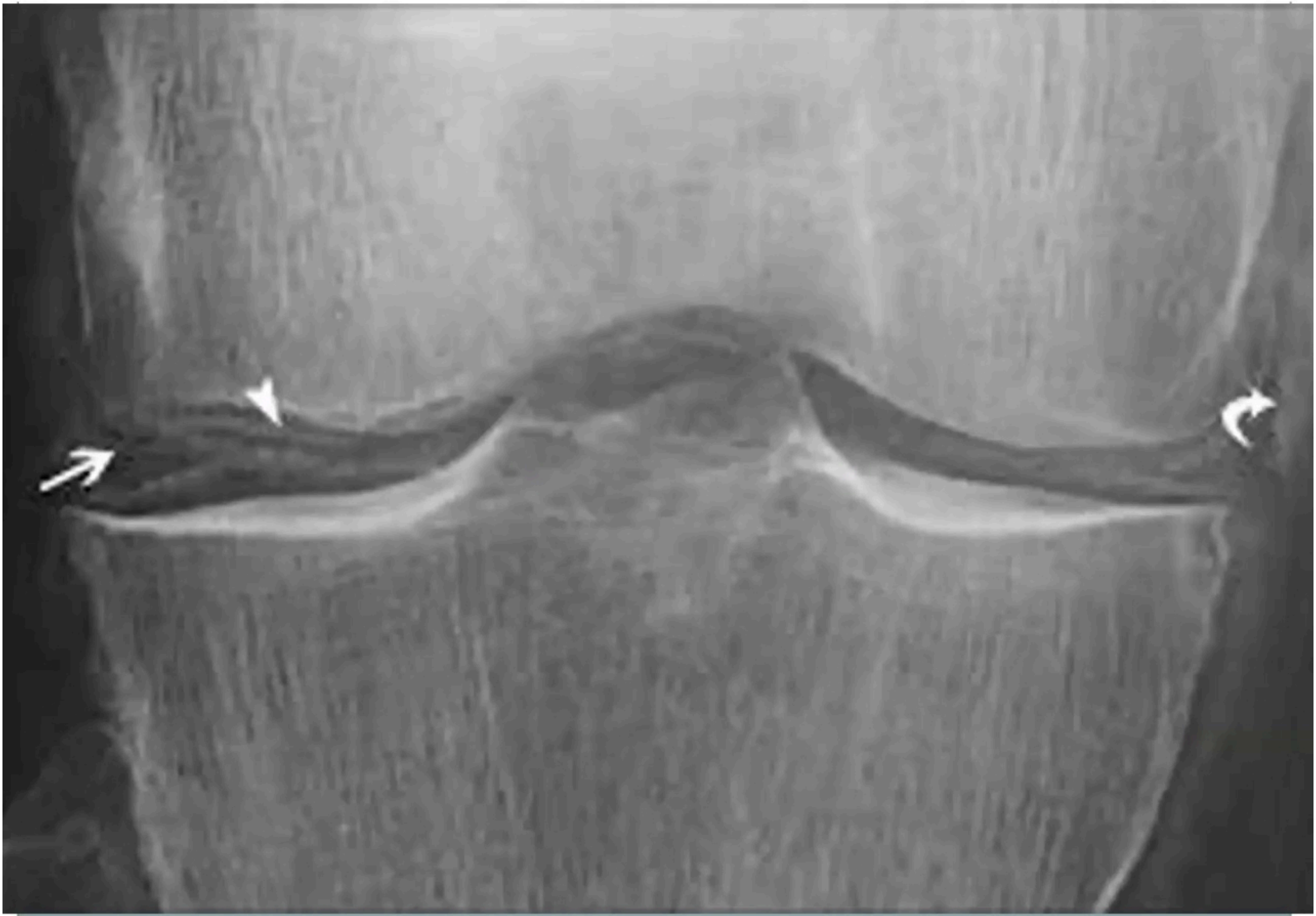
# Diagnosis

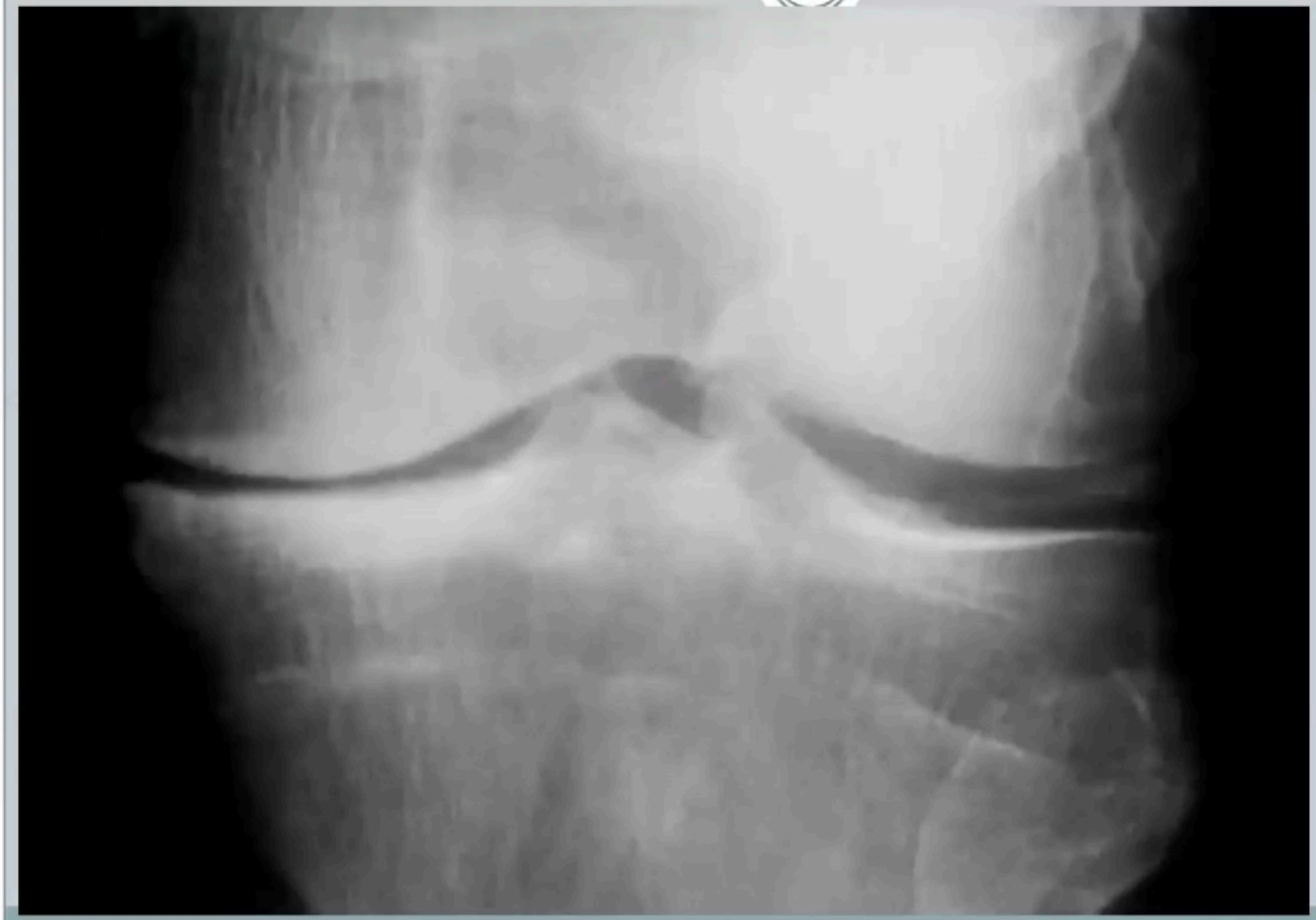


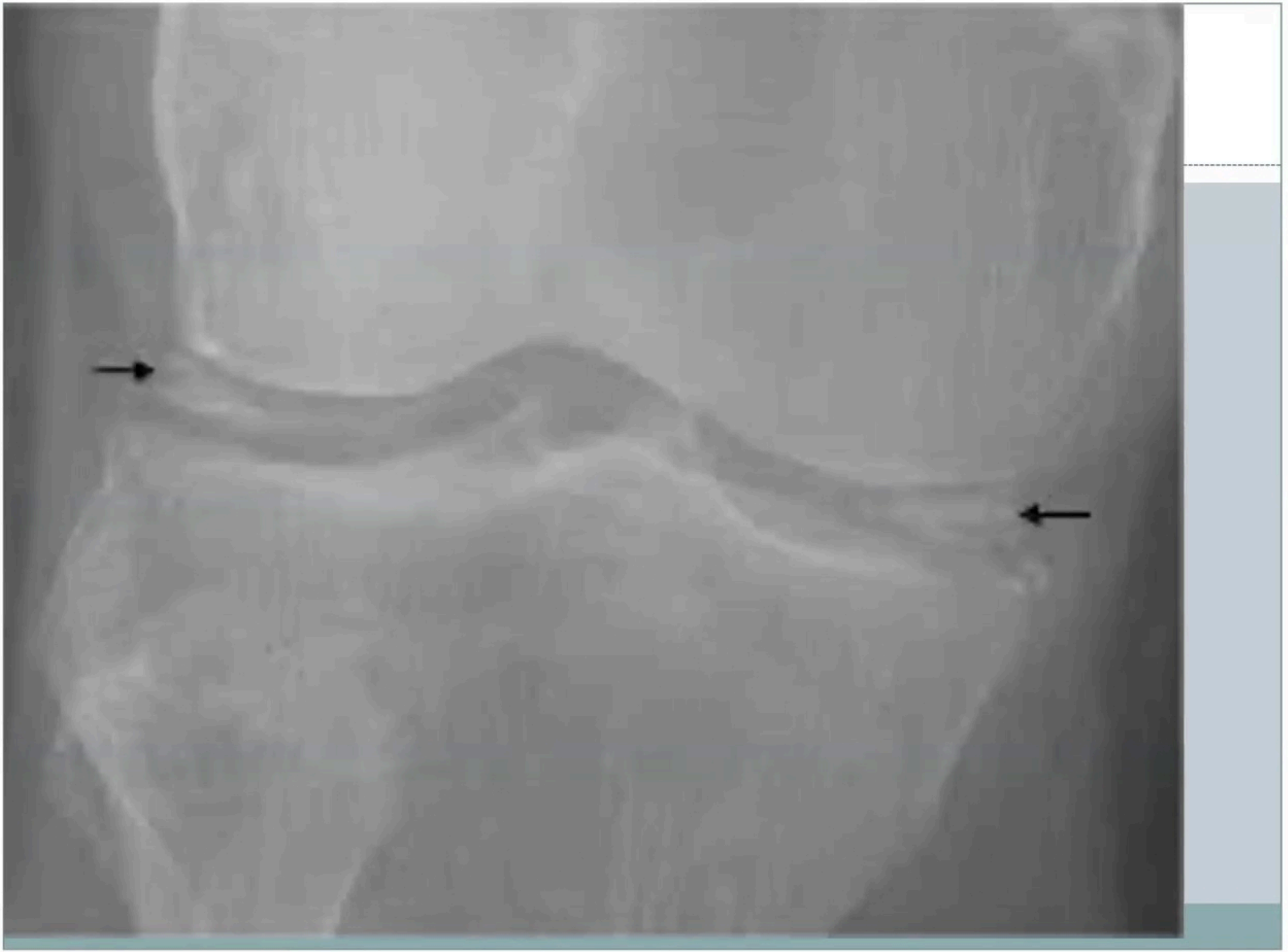
- Typical crystals in synovial fluid:- rectangular, rhomboid and rod shaped weakly positive birefrigent crystals under polarized light microscopy
- Increased WBC in joint fluid
- Radiographs- puntacte or linear radiodense deposits in fibrocartilage tissue and hyaline cartilage

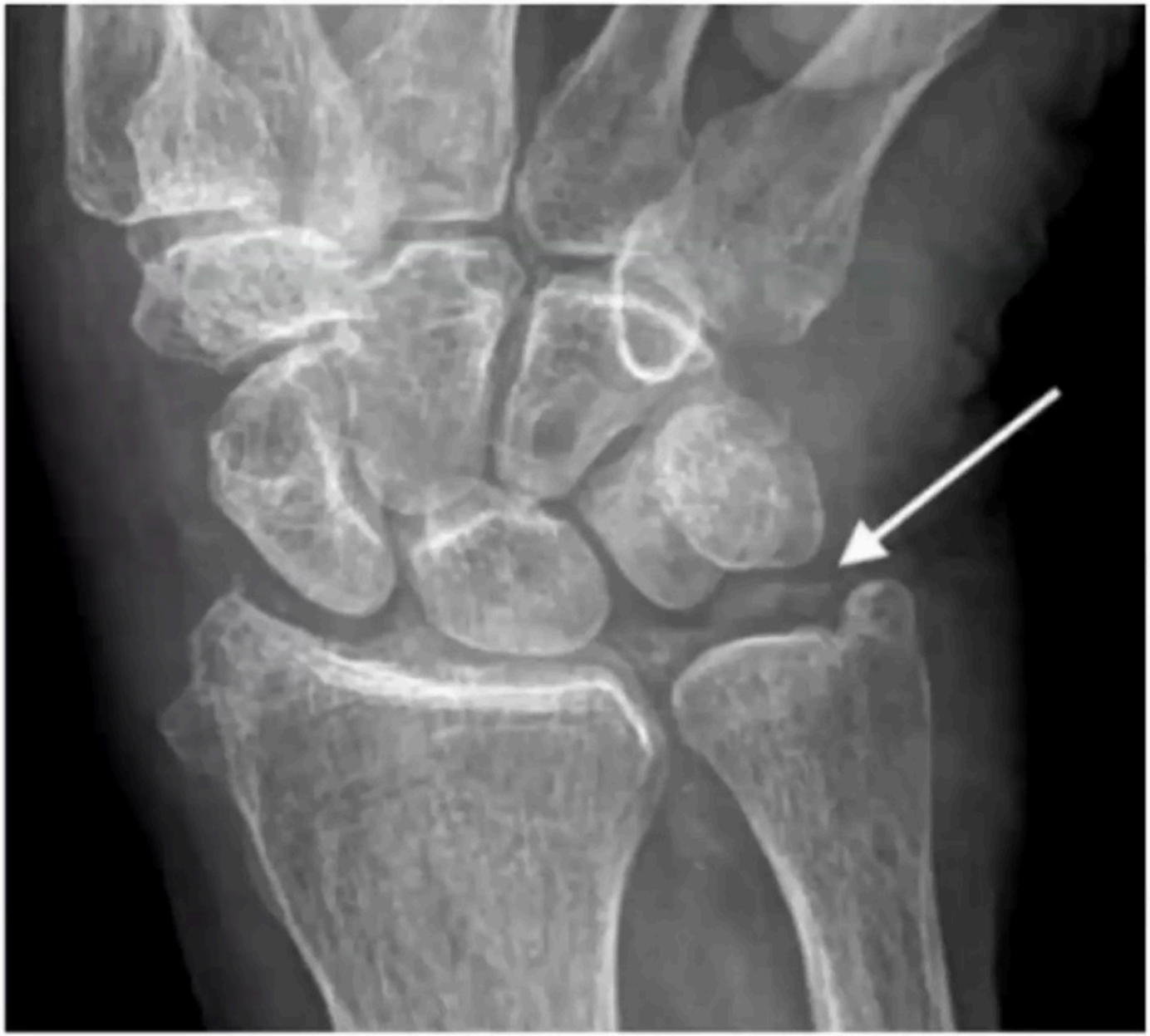
- birefringent bipyramidal structures

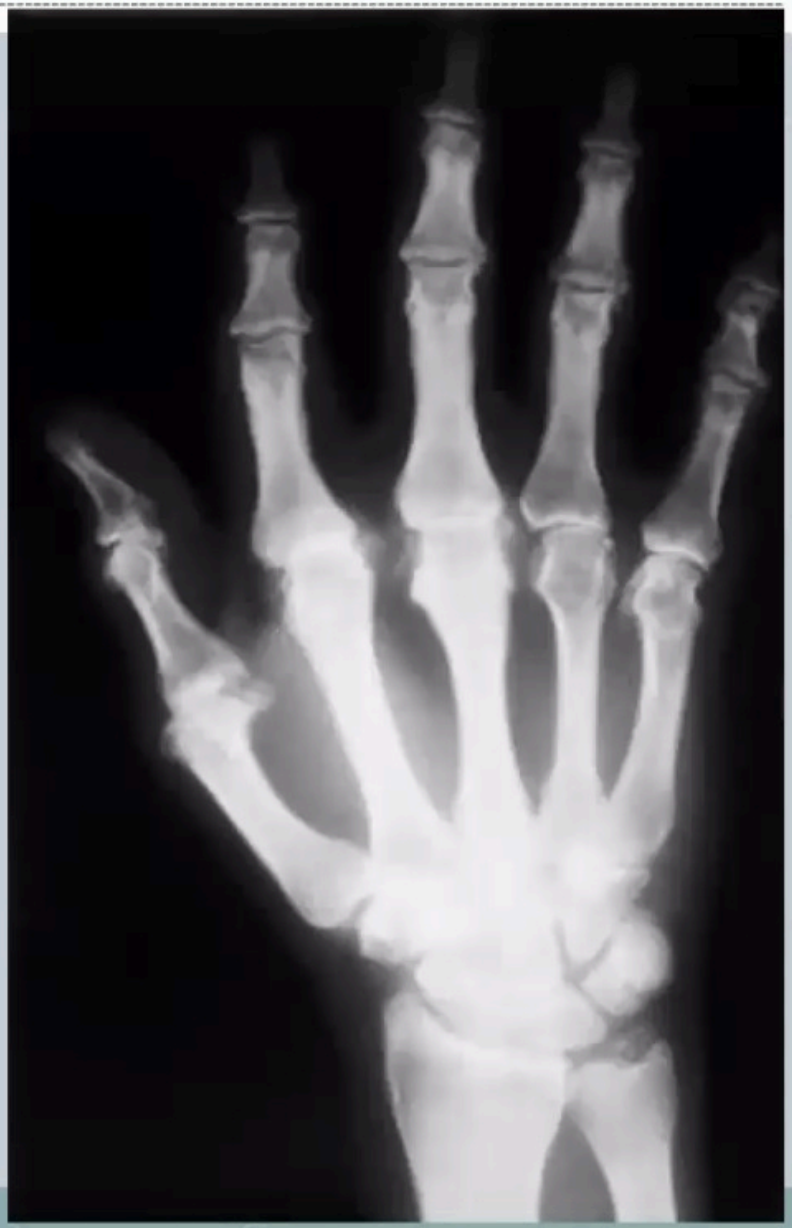












# Treatment



- Anti-inflammatory drugs
- Hydoxychloroquine- For long term control
- No known method to eliminate the CPPD crystals from the joints

# Calcium hydroxyapatite deposition disease



- Mostly is secondary to injury.
- Leading  to an acute reaction:-
- synovitis or tendinitis
- OR a chronic destructive arthropathy
- Range from mild to severe forms

# Clinical manifestations

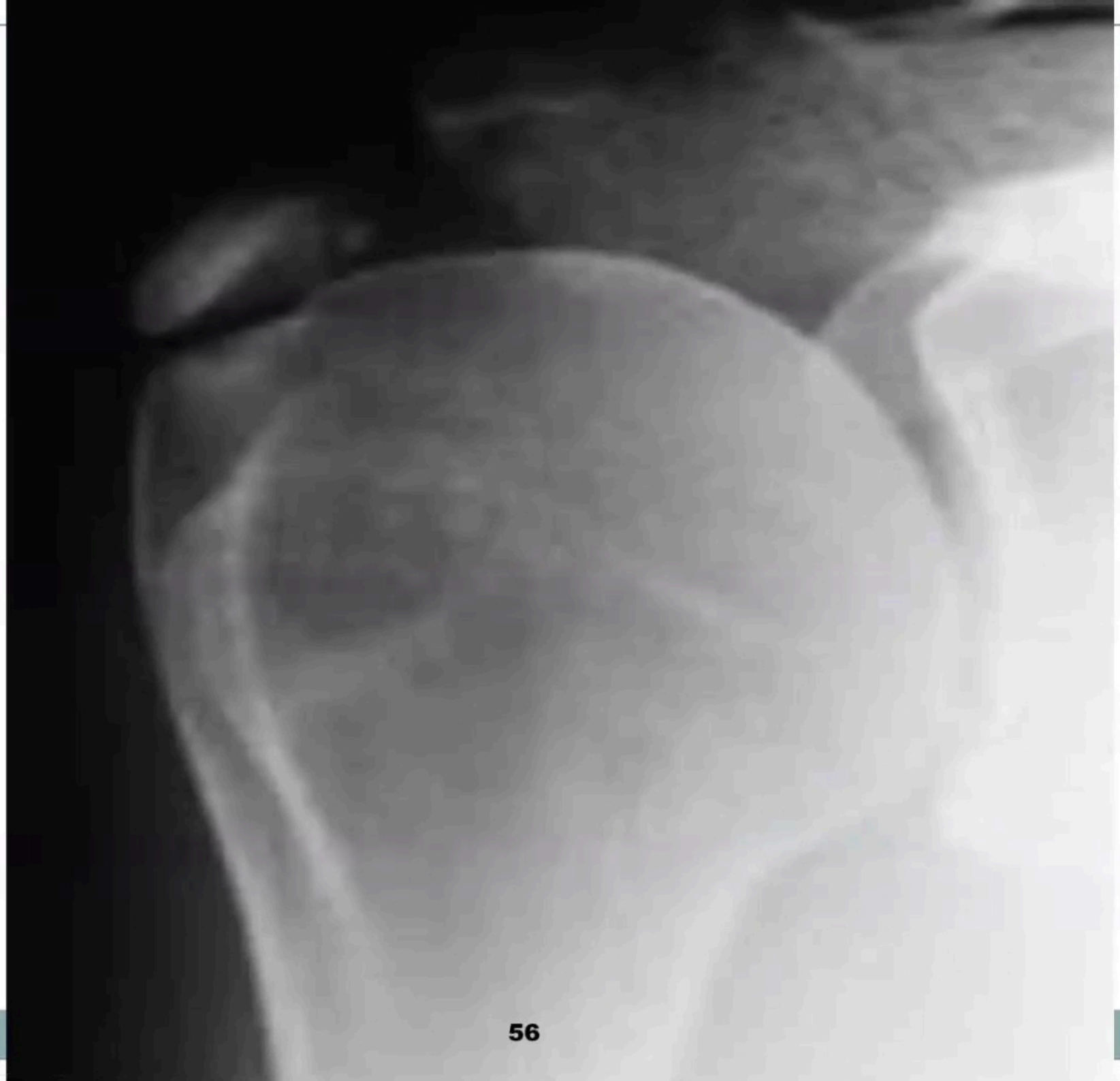


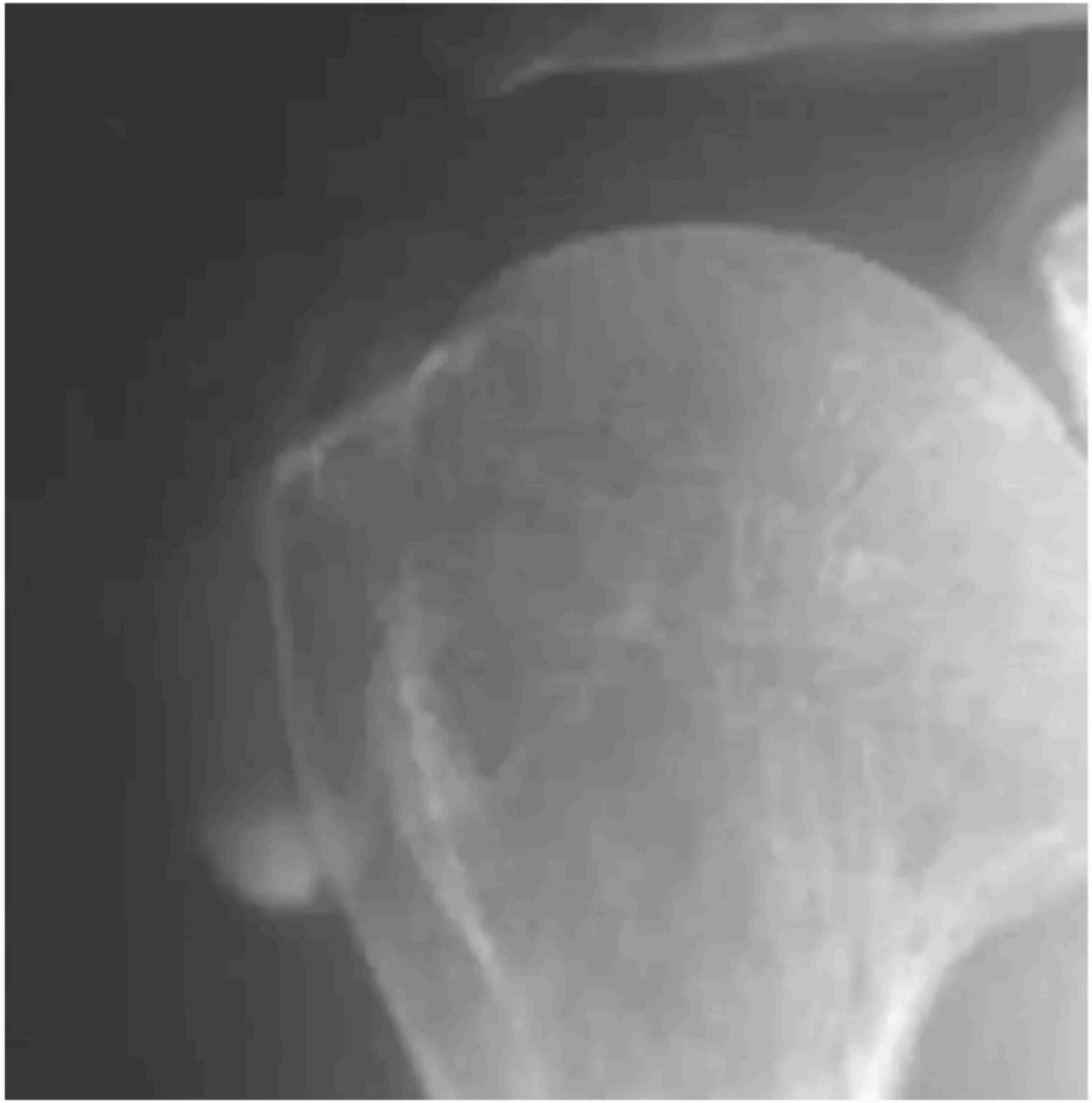
- Pain
- Swelling
- Tenderness
- Limitation of motion

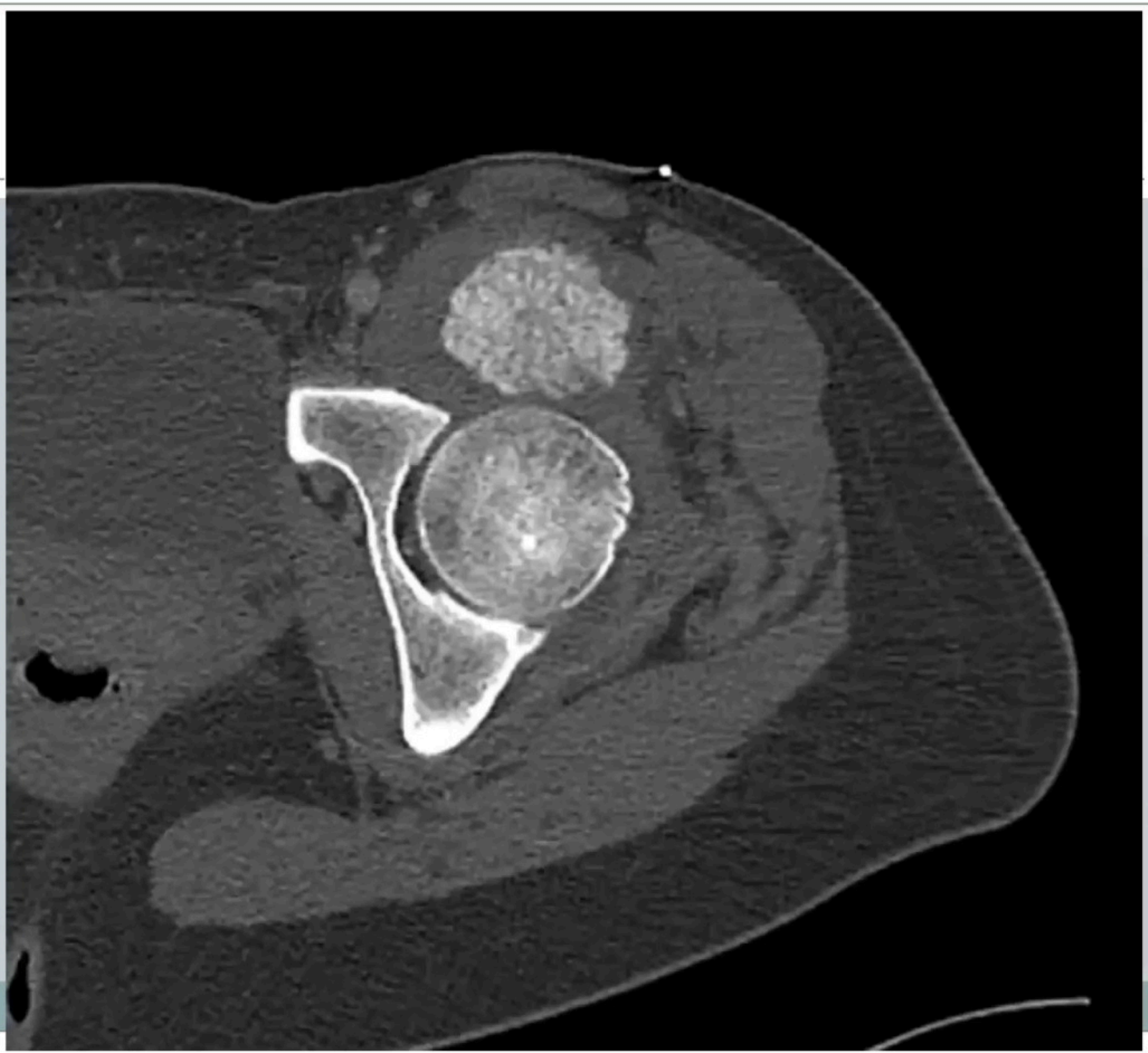
# Diagnosis



- Identification of HA crystals from synovial fluid or tissue, small nonbirefrigent using an electron microscope.
- Calcifications
- Erosion
- Destructive
- Hypertrophic changes







# Treatment



- Rest/Splint
- NSAIDS or Colchicine for 2 weeks
- Intra or Periarticular glucocorticoids
- Ultrasound ablation
- Surgical removal of calcific deposit
- Soft tissue repair

# Calcium oxalate deposition disease



- Primary or secondary
- Primary oxalosis- rare hereditary metabolic disorder. Enhanced production of oxalic acid due to enzyme defects.
- Deposition in many organs. Arthritic changes occur in later years. Nephrocalcinosis, renal failure and death occurs before age 20years.

# Secondary oxalosis



- Metabolic complications of ESRD
- Noted in vessels, bone, cartilage and visceral organs.
- Elucidated in 1982
- Ascorbic acid is metabolized to oxalate which is poorly cleared in uraemia and by dialysis

# Clinical manifestation and diagnosis



CaOx -found in bone, cartilage & synovium

Progessive articular destruction

Painful, swollen joint

Chondrocalcinosis

Effusions are non-inflammatory

Crystals- bipyramidal and positive birefrigence

# Questions

# Conclusion



- Crystal deposition diseases are caused by endogenous compounds eliciting inflammation in tissues.
- Gout is the commonest and is due to uric acid deposition, followed by pseudogout.
- Calcium Hydroxyapatite deposition do occur; but calcium oxalate deposition is rare.