

CRYSTAL-INDUCED ARTHRITIS

CRYSTAL-INDUCED INFLAMMATION

- Supersaturation of body fluids with a variety of solutes may result in the deposition of different forms of crystals and calculi.
 - Monosodium salt of uric acid (MSU)
 - Calcium pyrophosphate dihydrate [CPPD]
 - Hydroxyapatite [HA]
 - Oxalate crystal deposition, calcium oxalate (CaOx)

Musculoskeletal Manifestations of Crystal-Induced Arthritis

Acute mono- or polyarthrititis

Destructive arthropathies

Bursitis

Pseudo-rheumatoid arthritis

Tendinitis

Pseudo-ankylosing spondylitis

Enthesitis

Spinal stenosis

Tophaceous deposits

Crown dens syndrome

Peculiar type of osteoarthritis

Carpal tunnel syndrome

Synovial osteochondromatosis

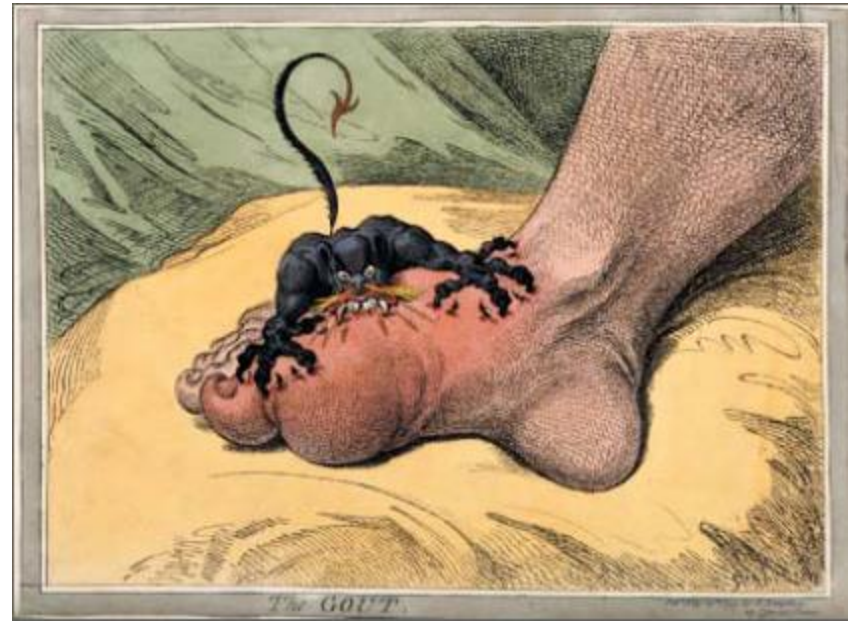
Tendon rupture

**Monosodium salt of
uric acid (MSU)
Gout**

GOUT

The term *gout* is derived from the Latin *gutta*, which means **a drop**.

In the 13th century, it was thought that gout resulted from **a drop of evil humor** affecting a vulnerable joint.



GOUT AND HYPERURICEMIA

- Gout is a clinical disease associated with hyperuricemia and caused by the deposition of monosodium urate (MSU) crystals in and around the tissues of joints.
 - Inflammatory arthritis
 - Chronic destructive arthropathy
 - Soft tissue accumulation of MSU crystals (tophi)
 - Renal disease involving glomerular, tubular, and interstitial tissues and blood vessels
 - Uric acid nephrolithiasis

Uric Acid Metabolism

- Plasma is saturated with monosodium urate at a concentration of 415 mol/L (6.8 mg/dL) at 37°C.
- Urine, pH 5.0, saturated with uric acid at 360–900 mol/L
- Urine, pH 7.0, saturation reached at 9480 and 12,000 mol/L
- Clinical point: urine alkalization is important in renal uric acid excretion in uric acid overload .

Classification of Hyperuricemia by Pathophysiology

Urate Overproduction

- Primary idiopathic
- HPRT deficiency
- PRPP synthetase overactivity
- Hemolytic processes
- Lymphoproliferative diseases
- Myeloproliferative diseases
- Polycythemia vera
- Psoriasis
- Paget's disease
- Glycogenosis III, V, and VII
- Rhabdomyolysis
- Exercise
- Alcohol
- Obesity
- Purine-rich diet

Decreased Uric Acid Excretion 90%

- Primary idiopathic
- Renal insufficiency
- Polycystic kidney disease
- Diabetes insipidus
- Hypertension
- Acidosis
- Lactic acidosis
- Diabetic ketoacidosis
- Starvation ketosis
- Berylliosis
- Sarcoidosis
- Lead intoxication
- Hyperparathyroidism
- Hypothyroidism
- Toxemia of pregnancy
- Bartter's syndrome
- Down syndrome

Classification of Hyperuricemia by Pathophysiology

Combined Mechanism

- Glucose-6-phosphatase deficiency
- Fructose-1-phosphate
- aldolase deficiency
- Alcohol
- Shock

Decreased Uric Acid Excretion

- Drug ingestion **CAN'T LEAP**
 - **C**yclosporine
 - **A**lcohol
 - **N**icotinic acid
 - **T**hiazides
 - **L**asix (furosemide)
(and other loop diuretics)
 - **E**thambutol
 - **A**spirin (low dose)
 - **P**yrazinamide

Medications with Uricosuric Activity

- Acetohexamide
- Azauridine
- Chlorprothixene Citrate
- Estrogens
- Glyceryl guaiacolate
- Losartan
- Phenolsulfonphthalein
- Radiographic contrast agents
- Salicylates (>2 g/d)
- Tetracycline that is outdated
- ACTH
- Benzbromarone
- Dicumarol
- Fenofibrate
- Glycopyrrolate
- Meclofenamate
- Phenylbutazone
- Sulfinpyrazone
- Ascorbic acid
- Calcitonin
- Diffunisal
- Glucocorticoids
- Halofenate
- Probenecid
- Zoxazolamine

GOUT - Definition

- The course of classic gout passes through three distinct stages:
 - Asymptomatic hyperuricemia
 - Acute intermittent gout
 - **Acute gout**
 - **Intercritical gout**
 - Advanced gout
- Hyperuricemia is defined as a serum uric acid level greater than 7.0 mg/dL in adult men and 6.0 mg/dL in premenopausal women.

EPIDEMIOLOGY

- Hyperuricemia is fairly common, 2.6% and 47.2%
- Factors associated with high serum urate concentrations in adults
 - Serum creatinine
 - Urea nitrogen levels
 - Body weight
 - Height
 - Age
 - Blood pressure
 - Alcohol intake
- Gout prevalence less than 1% to 15.3%

ENVIRONMENTAL FACTORS

Increased risk for gout

- Alcohol consumption (Beer)
- Meat 41% higher risk
- Seafood 51% higher risk

Not increased risk for gout

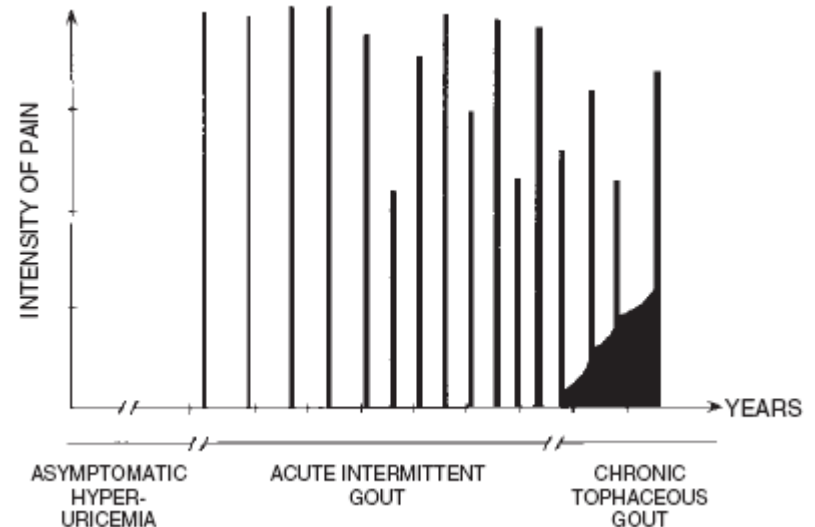
- Oatmeal
- purine-rich vegetables (e.g., peas, mushrooms, lentils, spinach, and cauliflower)
- The consumption of milk one or more times a day or yogurt consumption at least once every other day is associated with **lower serum urate levels**

CLINICAL FEATURES

Gout passes through three stages

- 1. Asymptomatic hyperuricemia**
- 2. Episodes of acute gouty arthritis separated by asymptomatic intervals (termed intercritical or interval gout)**
- 3. Chronic gouty arthritis, the period when tophi often become apparent.**

STAGES OF CLASSIC GOUT



ASYMPTOMATIC HYPERURICEMIA

- Asymptomatic hyperuricemia is a condition in which the serum urate level is high, but gout—manifested by arthritis or uric acid nephrolithiasis—has not yet occurred.
- This occurs at least 20 years of sustained hyperuricemia.
- The phase of asymptomatic hyperuricemia ends with the first attack of gouty arthritis or urolithiasis.

ACUTE GOUTY ARTHRITIS

- First attack of acute gouty arthritis
 - Between age 40 and 60 years in men
 - After age 60 in women
 - Before age 25 the possibility unusual form of gout,
 - A specific enzymatic defect that causes marked purine overproduction,
 - An inherited renal disorder
 - The use of cyclosporine.

ACUTE GOUTY ARTHRITIS

- A single joint 85% to 90% of first attacks, 1st MTP
- The initial attack is polyarticular in 3% to 14%.
- Acute gout is predominantly a disease of the lower extremities
- Ninety percent (90%) of patients experience acute attacks in the great toe, next in order of frequency are the insteps, ankles, heels, knees, wrists, fingers, and elbows.
- Acute attacks rarely affect the shoulders, hips, spine, sacroiliac joints, sternoclavicular joints, acromioclavicular joints, or temporomandibular joints.
- Acute gouty bursitis, tendinitis, or tenosynovitis can also occur.
- Early attacks tend to subside spontaneously within 3–10 days

ACUTE GOUTY ARTHRITIS

Events may precipitate acute gouty arthritis

- Dietary excess
- Trauma
- Surgery
- Excessive ethanol ingestion,
- Hypouricemic therapy
- Serious medical illnesses
 - myocardial infarction, stroke.

Podagra



ACUTE GOUTY ARTHRITIS



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INTERCRITICAL GOUT

- The periods between gouty attacks
- Some patients never have a second attack.
- Most patients suffer a second attack within 6 months to 2 years
- The frequency of gout attacks usually increases over time in untreated patients.
- Later attacks have a less explosive onset, are polyarticular, become more severe, last longer, and abate more slowly.
- Nevertheless, recovery is complete.

CHRONIC GOUTY ARTHRITIS

Tophaceous gout

- Eventually, the patient may enter a phase of chronic polyarticular gout with no pain-free intercritical periods
- Tophaceous gout is the consequence of the chronic inability to eliminate urate as rapidly as it is produced.



CHRONIC GOUTY ARTHRITIS

Tophaceous gout





Diagnosis

Needle aspiration

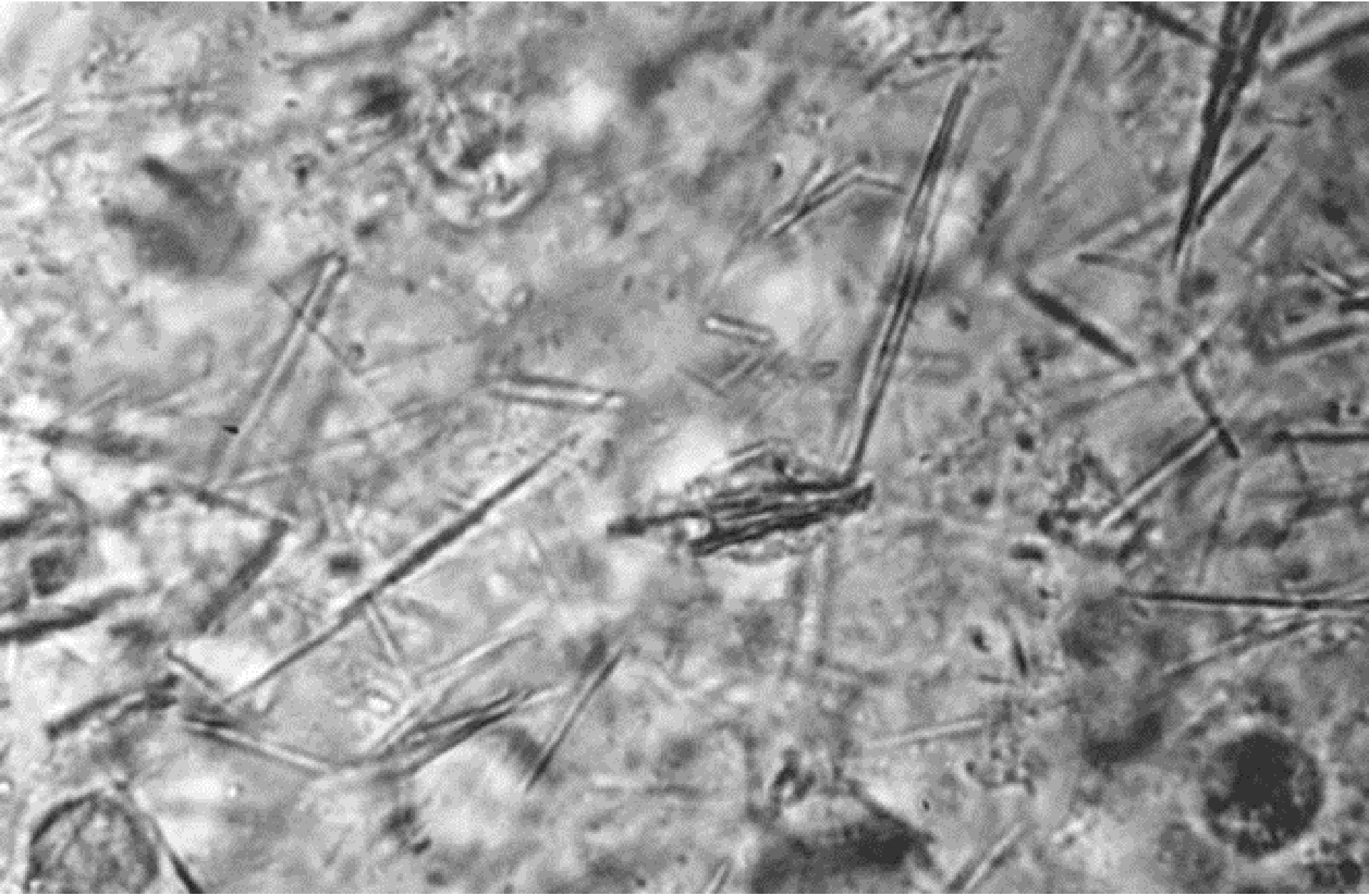
- Synovial fluid cell counts are elevated from 2000 to 60,000/L.
- Effusions appear cloudy due to the increased numbers of leukocytes.
 - strongly birefringent needle-shaped MSU crystals with negative elongation are typically seen both intracellularly and extracellularly

Extracellular and intracellular monosodium urate crystals



Serum uric acid levels can be normal or low at the time of the acute attack

Extracellular and intracellular monosodium urate crystals



Differential Diagnosis

Acute gouty arthritis

- Acute septic arthritis
- The other crystalline-associated arthropathies
- Palindromic rheumatism
- Psoriatic arthritis

Chronic tophaceous gout

- Rheumatoid Arthritis

Patient Evaluation

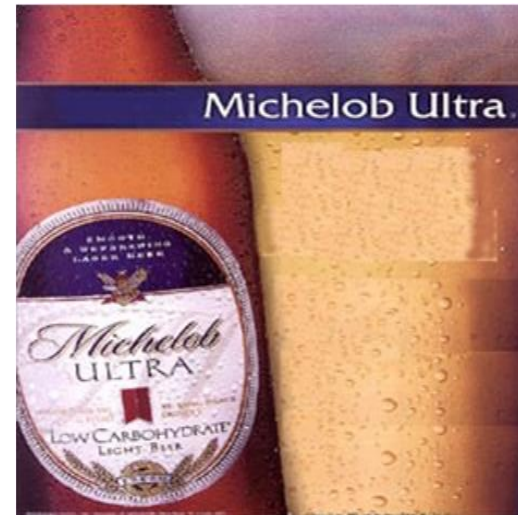
1. History of risk factors and physical Examination
2. Coexistent condition (obesity, hyperlipidemia, alcoholism, and, especially, hypertension)
3. Joint and Tophus examination
4. Uric acid level (serial control)
5. Renal function and urinary uric acid (serum Cr and uric acid and 24 hours Cr, uric acid)
6. Renal stone

Patient Evaluation

Blood Pressure



Alcohol intake



Patient Evaluation

Obesity



High purine diet



TREATMENT OF GOUT

Nonpharmacologic

- General recommendation
 - Ideal BMI
 - Healthy diet
 - Exercise
 - Smoking cessation
 - Hydration
- Diet recommendation
 - Avoid
 - Organ meat – high fructose beverage or food – Alcohol overuse -
 - Limit
 - Red meat – seafood (Sardine, Shellfish) – salt – sauces – gravy - alcohol
 - Encourage
 - Low fat or non fat dairy products – vegetables

TREATMENT OF GOUT

1. Management of Acute Gouty Attack

- NSAIDs
- Colchicine, oral
- Intraarticular steroids
- Systemic steroid therapy
- Adrenocorticotrophic Hormone

2. Management of Intercritical and Chronic Gout

3. Non-Urate-Lowering Prophylactic Therapy

4. Lifestyle Modifications and Education

5. Treatment of Hyperuricemia in Patients Without Gout

TREATMENT OF GOUT

1. Management of Acute Gouty Attack

2. Management of Intercritical and Chronic Gout

– Urate-Lowering Therapy

- Uricostatic Therapy (Allopurinol and febuxostat are XO Inhibitors)
- Uricosuric Therapy (probenecid)
- Uricolytic Therapy (Pegloticase, Rasburicase)

3. Non–Urate-Lowering Prophylactic Therapy

4. Lifestyle Modifications and Education

5. Treatment of Hyperuricemia in Patients Without Gout

TREATMENT OF GOUT

1. Management of Acute Gouty Attack
2. Management of Intercritical and Chronic Gout
3. Non-Urate-Lowering Prophylactic Therapy
 - Low-dose colchicine or NSAIDs
4. Lifestyle Modifications and Education
5. Treatment of Hyperuricemia in Patients Without Gout

TREATMENT OF GOUT

1. Management of Acute Gouty Attack
2. Management of Intercritical and Chronic Gout
3. Non-Urate-Lowering Prophylactic Therapy
4. Lifestyle Modifications and Education
 - Risk factors and associated illnesses such as obesity, hypertension, and hyperlipidemia
 - Decreased consumption of high-purine foods
 - Drugs: diuretics
5. Treatment of Hyperuricemia in Patients Without Gout

TREATMENT OF GOUT

1. Management of Acute Gouty Attack
2. Management of Intercritical and Chronic Gout
3. Non-Urate-Lowering Prophylactic Therapy
4. Lifestyle Modifications and Education
5. Treatment of Hyperuricemia in Patients Without Gout
 - There is no evidence to support their use for the routine treatment of asymptomatic hyperuricemia
 - Cancer chemotherapy

**Calcium
Pyrophosphate
Dihydrate (CPPD)
Deposition Disease**

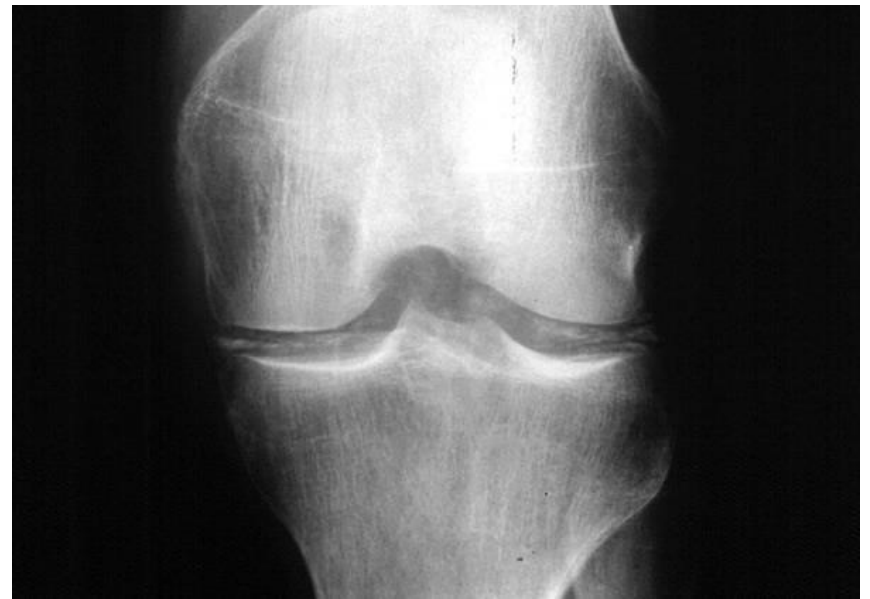
Calcium Pyrophosphate Dihydrate (CPPD) Deposition Disease

- It is characterized by the presence of intraarticular CPPD crystals.
- These crystals are deposited primarily in the cartilage.

Calcium Pyrophosphate Dihydrate (CPPD) Deposition Disease

- CPPD deposition disease typically affects the elderly population.
- Up to 50% of individuals older than 85 years of age have radiographic evidence of CPPD crystal accumulation in cartilage (chondrocalcinosis), but most are asymptomatic.
- The most commonly involved joints are the knee menisci and the triangular fibrocartilage of the wrist.

Calcium Pyrophosphate Dihydrate (CPPD) Deposition Disease



Calcium Pyrophosphate Dihydrate (CPPD) Deposition Disease

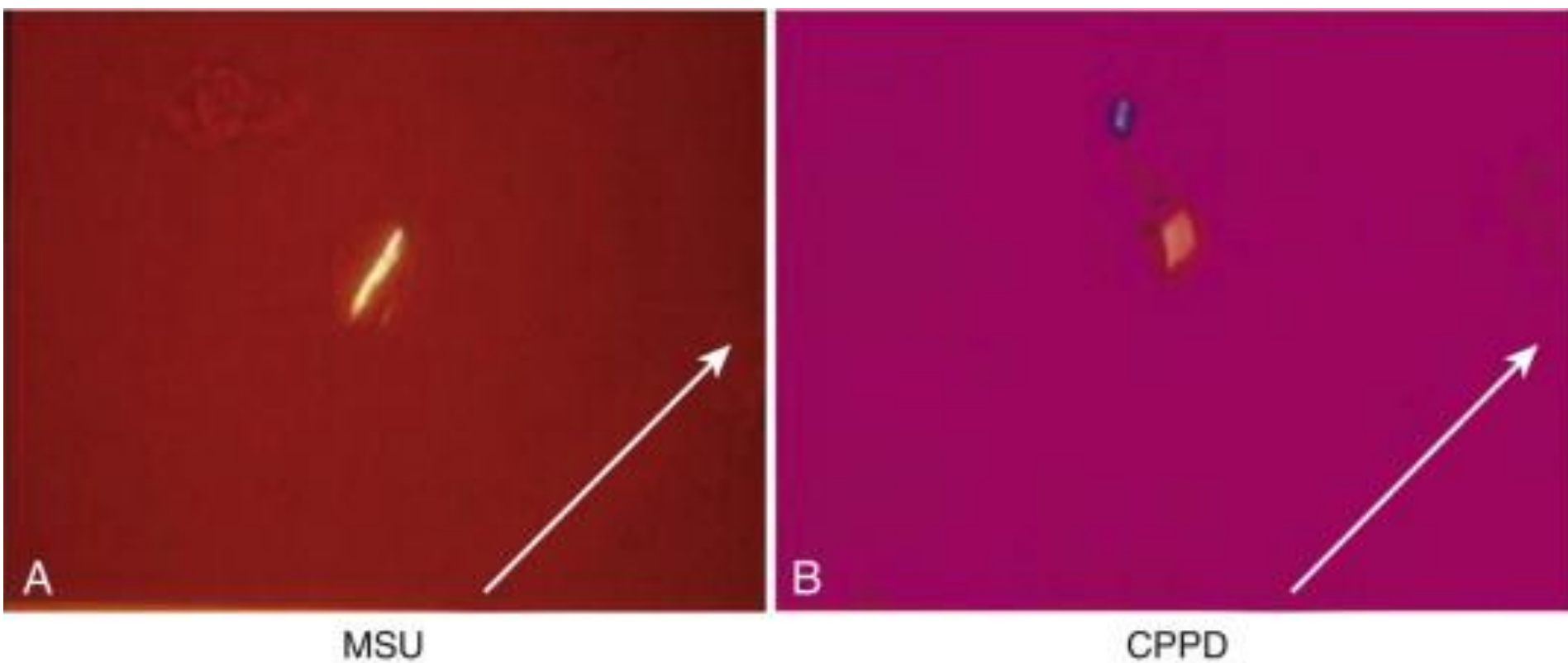


Calcium Pyrophosphate Dihydrate (CPPD) Deposition Disease

The clinical course:

- **Asymptomatic** disease may be an incidental finding on radiographs showing chondrocalcinosis.
- **Pseudogout** is an acute monoarthritis similar in presentation to the acute gouty attack.
- A **chronic symmetric polyarticular** arthritis pattern resembling rheumatoid arthritis and a severe destructive arthropathy that mimics neuropathic arthritis on radiographs may be seen.
- The **most common** clinical manifestation, (>50%) is a peculiar type of osteoarthritis called **pseudo-osteoarthritis**; it is a noninflammatory arthritis involving joints not typically affected by osteoarthritis, such as the wrist, shoulder, ankle, and metacarpophalangeal joints.

Calcium Pyrophosphate Dihydrate (CPPD) Deposition Disease



Apatite-Associated Arthropathy

Apatite-Associated Arthropathy

(Basic Calcium Phosphate, or BCP)

- Abnormal accumulation of apatite may occur in hypercalcemic states and other illnesses.
- BCP crystals are not identifiable by polarized microscopy and can be seen only by electron microscopy.
- The most common apatite-associated condition is calcific periarthritis, which typically occurs in the shoulder.

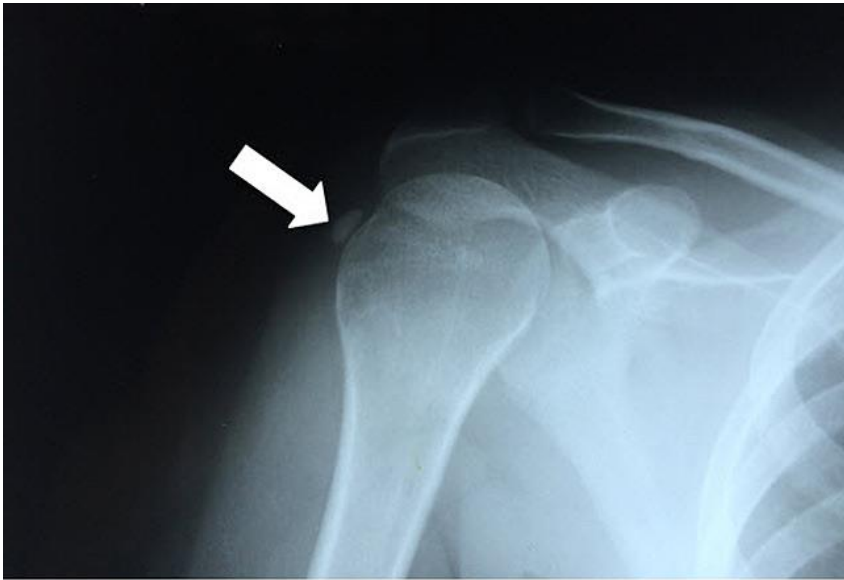
Apatite-Associated Arthropathy

(Basic Calcium Phosphate, or BCP)

- **Calcific periarthrititis**
 - Calcific deposits in tendons, bursae, joint capsules
 - Acute calcific periarthrititis
- **BCP arthropathy**
 - Acute synovitis
 - Destructive arthropathy
- **Subcutaneous/soft tissue calcifications**
 - Connective tissue diseases: SLE, SSC, MCTD, dermatomyositis
 - Metastatic calcifications: chronic renal failure with high calcium–phosphorus product (>70)
- **Tumoral calcinosis**

Apatite-Associated Arthropathy

(Basic Calcium Phosphate, or BCP)



Calcium Oxalate Deposition Disease

Calcium Oxalate Deposition Disease

- In calcium oxalate deposition disease, or oxalosis, calcium oxalate crystals are deposited in tissue.

Calcium Oxalate Deposition Disease

- **In primary oxalosis**, a hereditary metabolic disorder, this deposition leads to nephrocalcinosis, renal failure, and early mortality.
- **Secondary oxalosis** complicates long-term hemodialysis or peritoneal dialysis; crystals are deposited in bone, cartilage, synovium, and periarticular tissue.

Calcium Oxalate Deposition Disease

- Crystal shedding into the joint space may result in **inflammatory arthritis** of peripheral joints.
- **Chondrocalcinosis** or **soft tissue calcifications** can be seen on plain radiographs.