Crystal induced arthropathies

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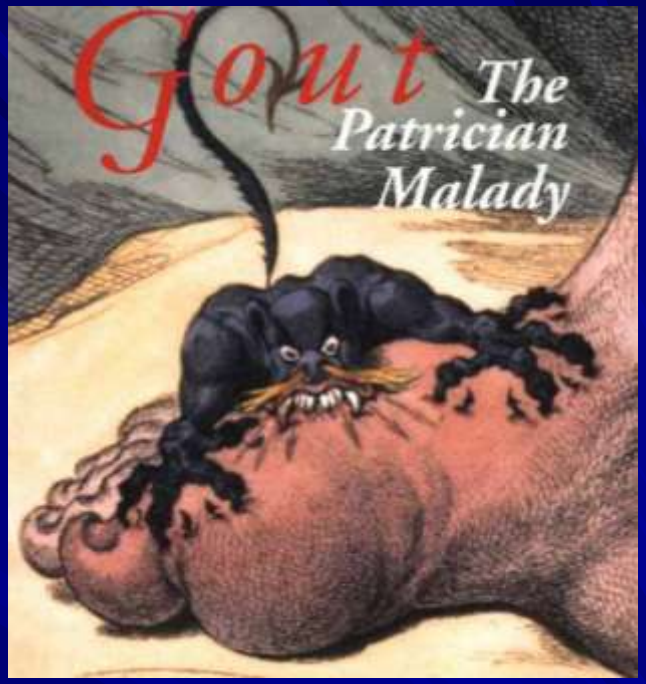
Crystal induced Arthropathies

Gout

Pseudogout

- Debilitating illnesses;
- Recurrent episodes of pain and joint inflammation;
- Formation and deposition of crystals in soft tissue & joint space

GOUT



- "Disease of Kings"
- Male predominance
- Age range is 30-60 yrs
- Uric acid levels are elevated for 20 years before the onset of gout
- Tophi are typically detectable clinically 10 years after first gout attack

ETIOLOGY

Primary gout

- Underexcretion (90%) or overproduction (10%) of uric acid

Secondary gout

- Myeloproliferative and lymphoproliferative disorders, psoriasis, hemolytic anemias, pernicious anemia, Cell lysis from chemotherapy for malignancies, excessive exercise, obesity.
- Renal insufficiency, lead nephropathy (saturnine gout), starvation or dehydration, hypothyroidism, hyperparathyroidism, drugs, chronic ethanol abuse, enzymatic defects (Lesch-Nyhan syndrome)

FLARES

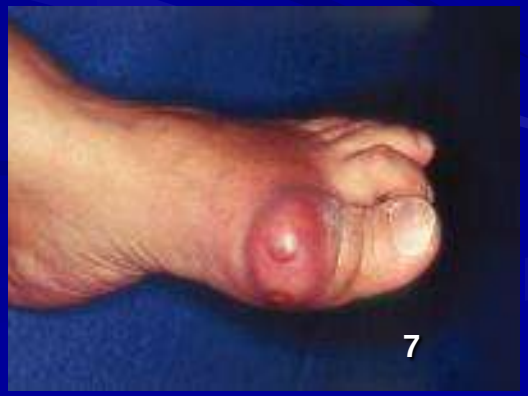
- Consumption of fructose-rich foods & beverages
- Acute alcohol ingestion
- Acute overindulgence in foods high in purines (anchovies, sardines, sweetbread, kidney, liver, meat extracts)
- Rapid weight loss
- Starvation
- Trauma & hemorrhage
- Emotional stress
- Loop or thiazide diuretics, aspirin, allopurinol, uricosurics. cyclosporine A, radiocontrast dyes

Gout and renal disease

- Chronic urate nephropathy can contribute to renal insufficiency.
- Deposition of urate crystals in the medullary interstitium and pyramids, resulting in inflammatory reaction that can lead to fibrotic changes.
- Associated with benign urinary sediment.
- Profoundly more likely to develop renal stones than healthy individuals (by X1000)

HISTORY

- Spontaneous onset of pain, edema, and inflammation in the MP joint of great toe (podagra)
- Podagra is initial joint manifestation in 50% of cases. Eventually, in 90%.
- Podagra - pseudogout, sarcoidosis, gonococcal arthritis, psoriatic arthritis, reactive arthritis.
- Other than great toe, most common sites are ankle, wrist, and knee.

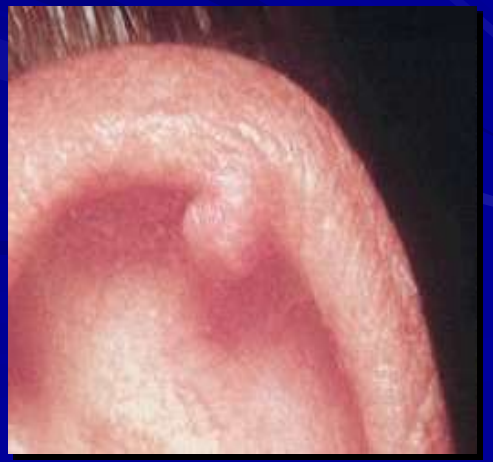


HISTORY

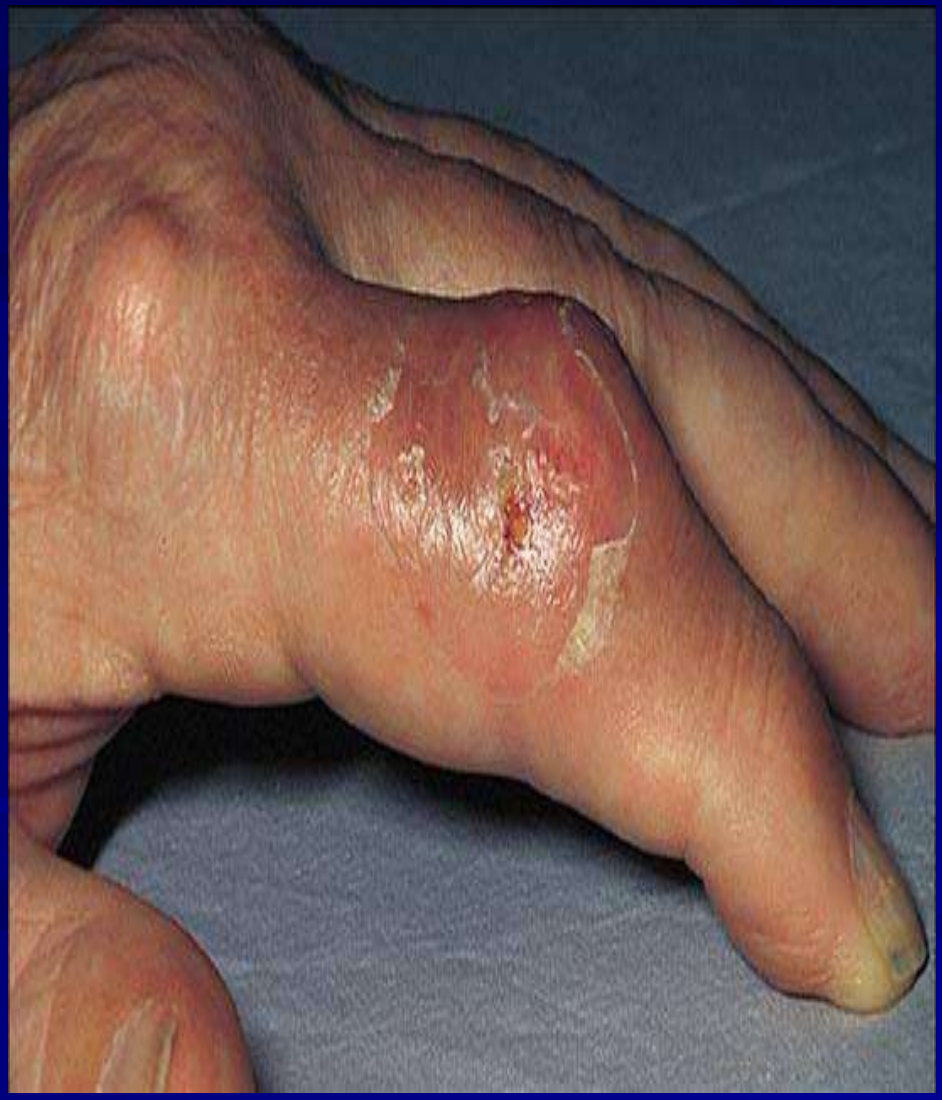
- Attacks begin abruptly and reach maximum intensity within 8-12 hours.
- Joints are red, hot, and exquisitely tender
- Untreated, first attacks resolve spontaneously in < 2 weeks.
- When oligoarticular- asymmetric
- Fever common
- Local desquamation & pruritus during recovery

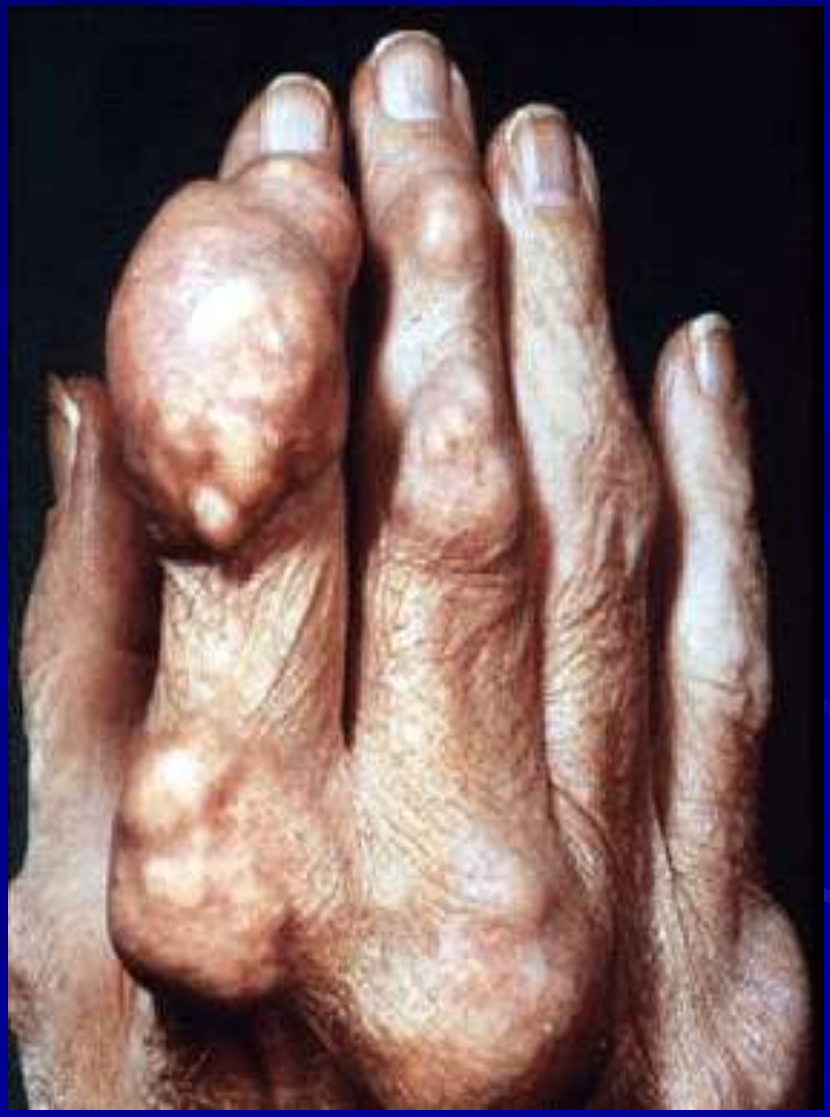
TOPHUS

- Nodular deposit of monosodium urate monohydrate crystals with associated foreign body reaction
- Classic location - helix of ear
- Other sites - fingers, toes, prepatellar bursa, olecranon
- Found in cartilage, periarticular, tendon, bone, kidney
- Late chronic stage, tophaceous of articular and periarticular tissue with structural derangement



Tophaceous gout





Complications

- Severe degenerative arthritis
- Urate or uric acid nephropathy
- Nerve or spinal cord impingement
- Increased susceptibility to infection
- Renal stones
- Fractures

Diagnostic Considerations

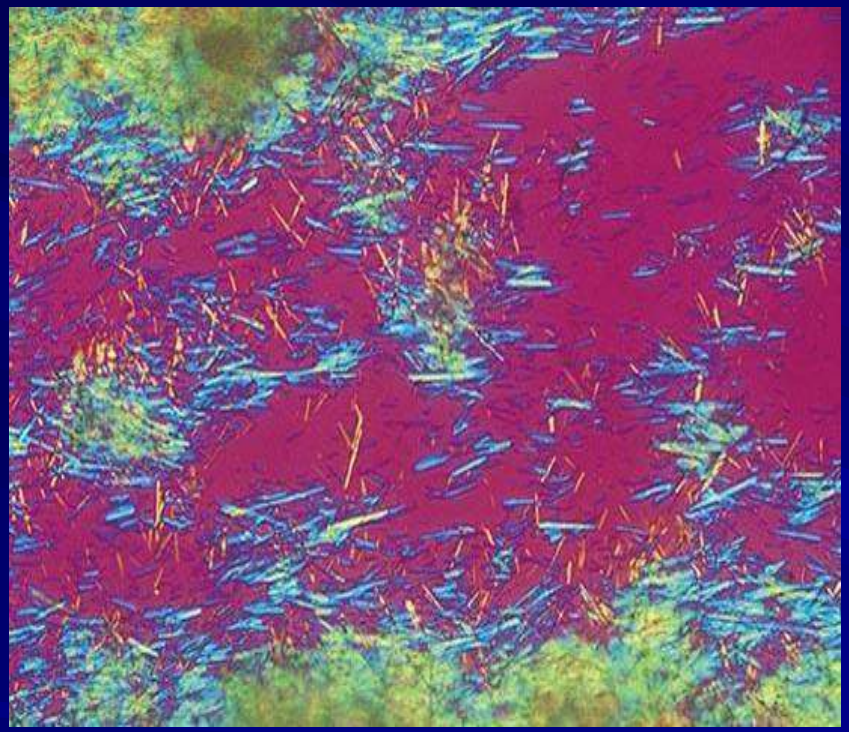
- Septic arthritis, gout, and pseudogout present in similar ways.
- Patients need to undergo arthrocentesis to exclude septic arthritis
- Diagnostic pointers:
  - Male sex
  - Previous arthritis attack
  - Onset within 1 day
  - Joint redness
  - First metatarsophalangeal joint involvement
  - Hypertension or one or more cardiovascular diseases
  - A serum uric acid level of more than 5.88 mg/dL

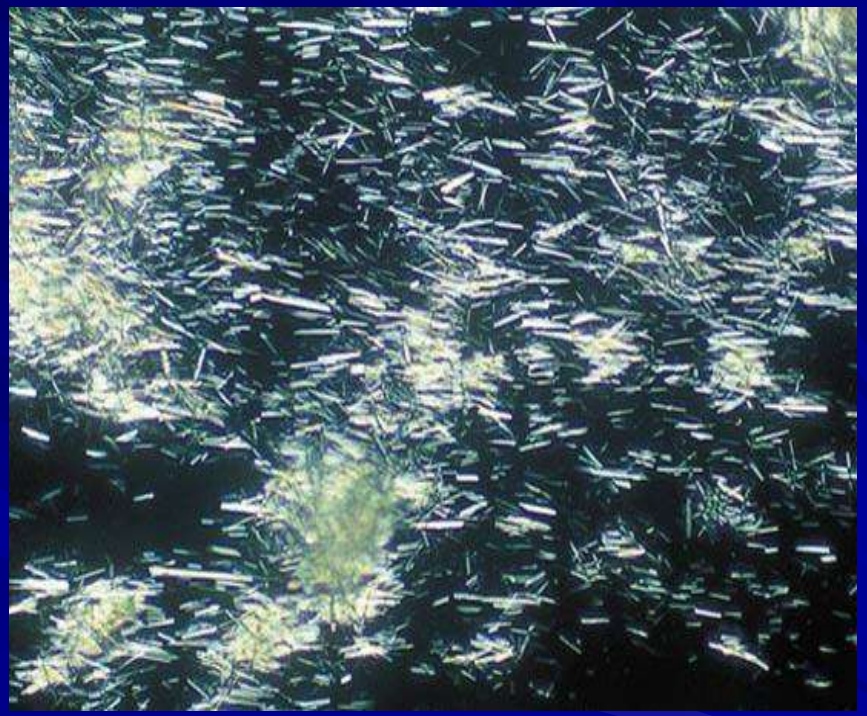
Diagnostic Considerations

- Uric acid > 7.5 in 95% (serially) normal 25% (single)
- Synovial fluid WBC count 10,000-70,000/µL
- ESR/ TLC ↑-- acute attack
- MSUM crystals on compensated polaroscopic exam

Uric acid crystal

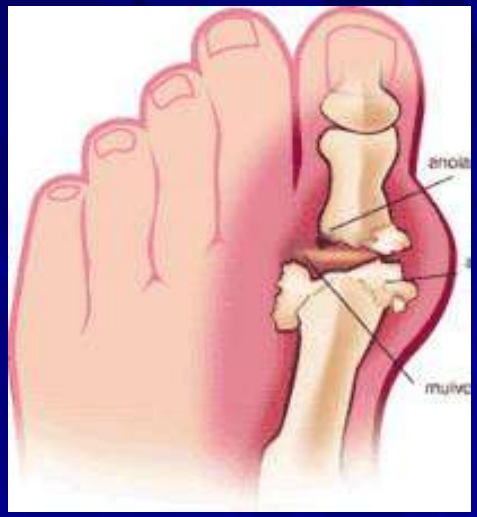
under polarized light **non-polarized light**





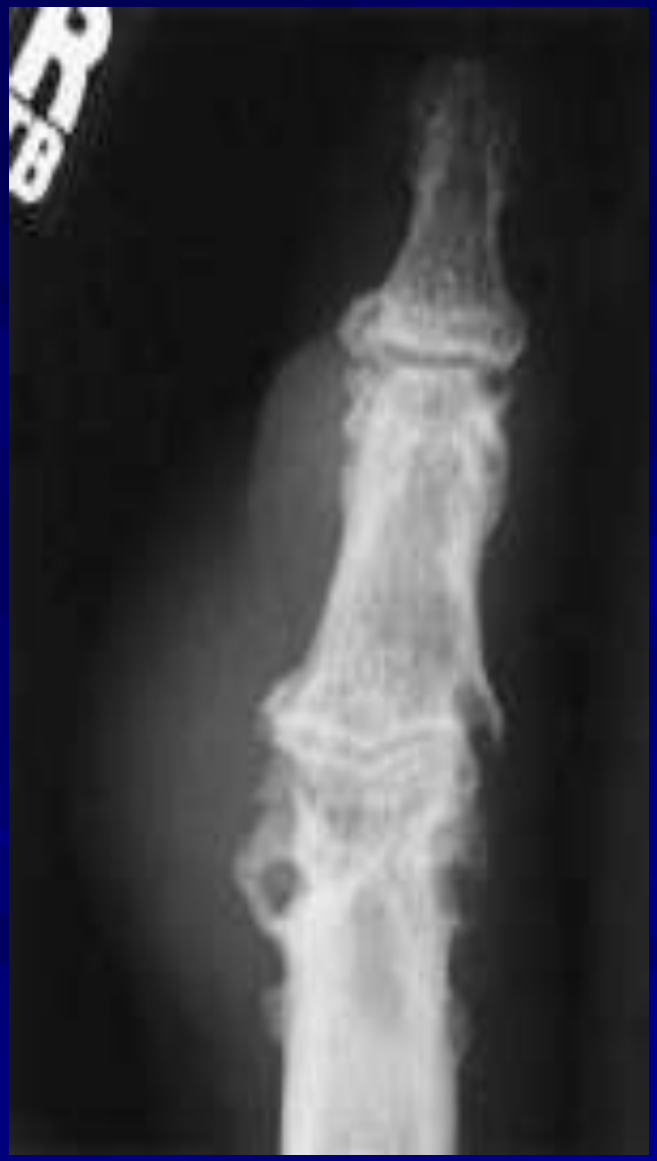
They are yellow when aligned parallel to the slow axis of the red compensator, but turn blue when aligned across the direction of polarization (negative birefringence)

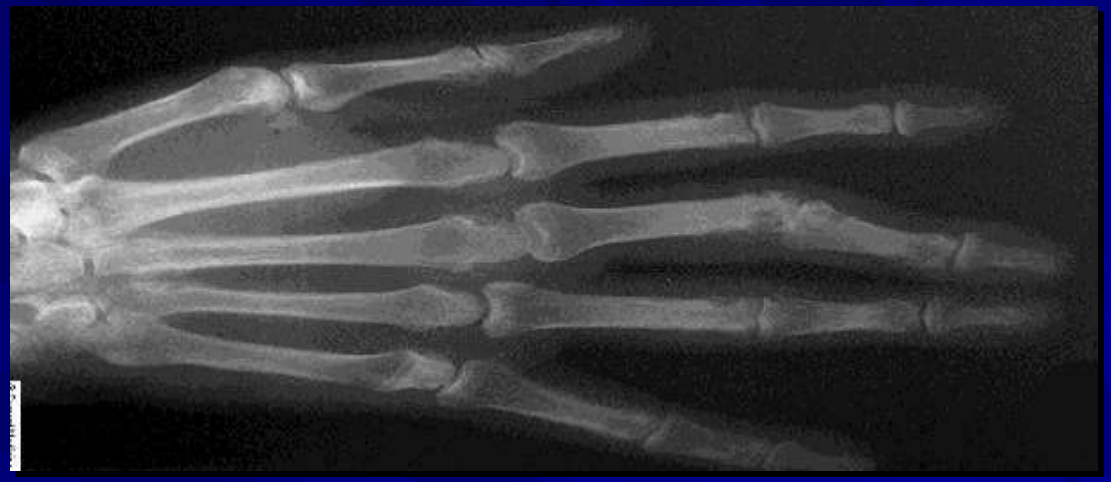
IMAGING

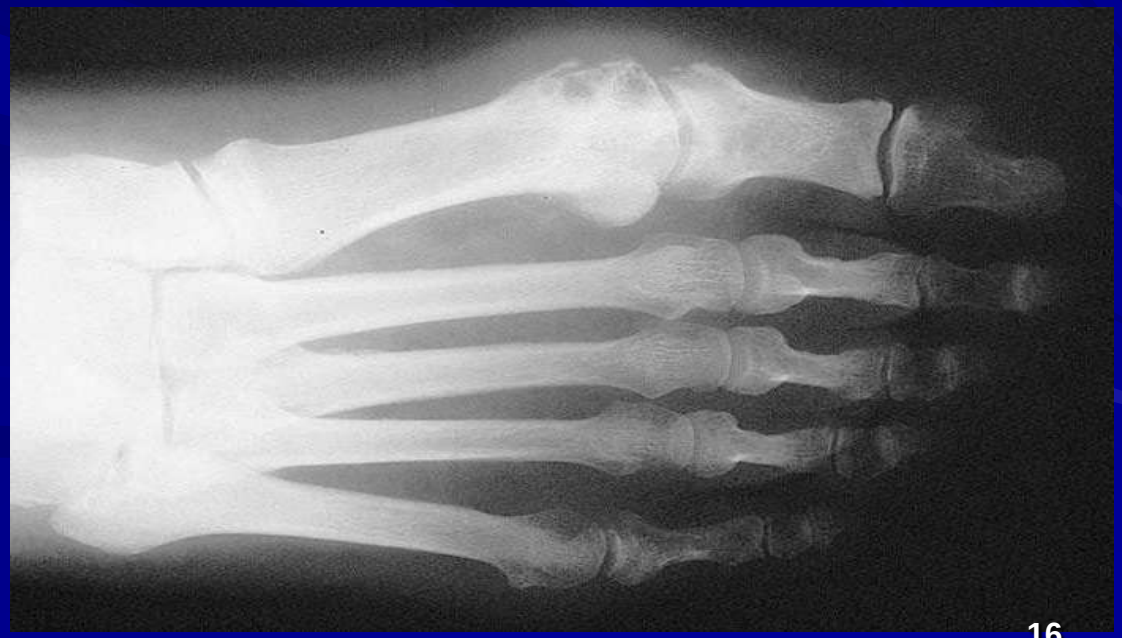


- Early—no change
- Late—punched out erosion
- Overhanging rim of cortical bone (rat bite)
- Adjacent to tophi—diagnostic
- Characteristics typical of gout but not of RA:
  - Maintenance of joint space
  - Absence of periarticular osteopenia
  - Location outside the joint capsule

Gouty erosions



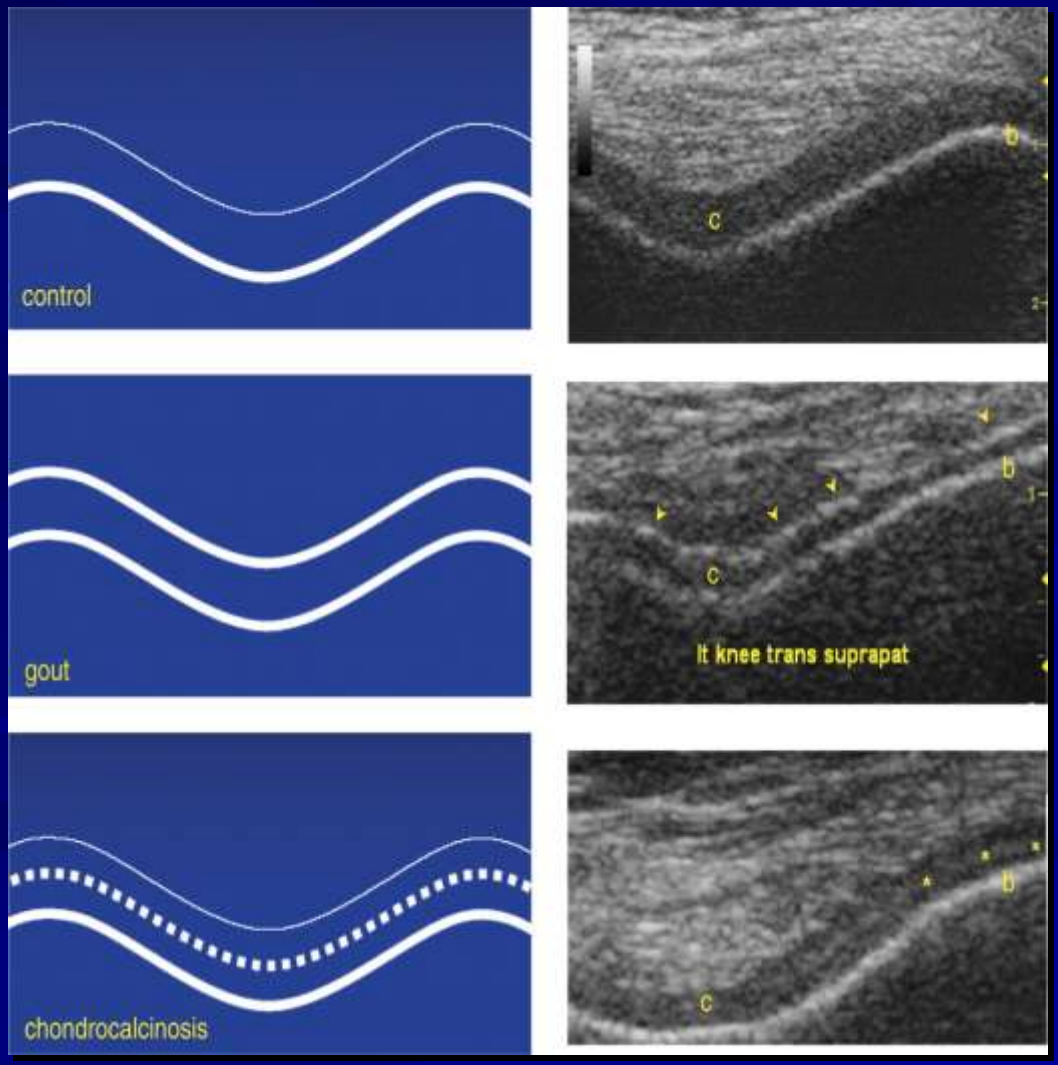


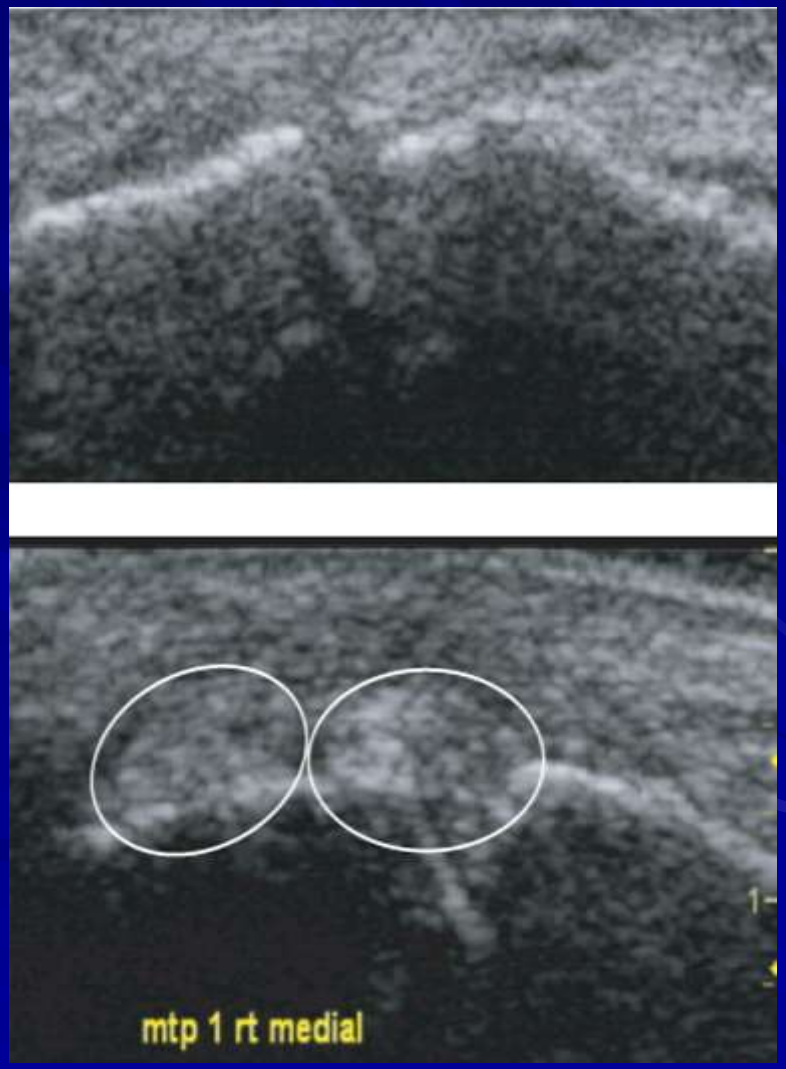


Ultrasonography

- A "double contour" sign, consisting of a hyperechoic, irregular line of MSU crystals on surface articular cartilage overlying an adjacent hyperechoic bony contour
- "Wet clumps of sugar," representing tophaceous material
- Bony erosions adjacent to tophaceous deposits

Ultrasonography





TREATMENT

Gout is managed in 3 stages:

- (1) treating the acute attack
- (2) providing prophylaxis to prevent acute flares
- (3) lowering excess stores of urate
- Surgery may be indicated for tophaceous complications, including infection, joint deformity, compression, intractable pain, ulcers related to tophaceous erosions.

Treatment of Acute Attacks

- Acute treatment - relief of pain and inflammation.
- NSAIDs - drugs of choice
- Colchicine - rarely indicated
- ACTH
- Steroids - dramatic symptomatic relief
- Therapy to control hyperuricemia generally contraindicated until acute attack is controlled
- Septic + gout can co exist

BETWEEN ATTACKS

- Low purine diet
- ↓Weight
- Stop alcohol
- ↑ dairy products
- ↑ liquid intake
- Avoid diuretics/ niacin/ low dose aspirin
- Prophylaxis: drugs (NSAIDS, Colchicine, XOI)

Treatment of Chronic Gout

- Goal - serum uric acid < 6 mg/dL
- Maintenance for 5 years is sufficient in absence of tophi to permit complete dissolution of all crystals
- Allopurinol – DOC in patients with existing renal disease
- Probenecid C/I in renal insufficiency, renal stones, use of aspirin, overproduction of uric acid, unresponsiveness to probenecid.

Reduction of uric acid

INDICATIONS

- Frequent acute arthritis
- Tophaceous deposits
- Renal damage

- 24 hr urinary uric acid excretion (>800 mg/d)

URICOSURIC

- Blocks tubular resorption of filtered urate
- Ineffective in renal insufficiency (Cr > 2 mg/dl)
- Probenecid (0.5 gm—2 gm/d)
- Sulfinpyrazone (100 mg—800 mg/d)
- Maintain urine output > 2 L/ day
- Urinary Ph > 6 (K citrate)

Xanthine oxidase inhibitor

- Allopurinol
- Febuxostat
- S/E
  - Hypersensitivity
  - Vasculitis
  - Hepatitis
- Can be administered in patients with renal insufficiency with no dosage adjustment

Uric acid oxidizers

- Facilitate conversion of urate to more soluble product, allantoin, thus preventing ARF

Pegloticase

- pegylated uric acid–specific enzyme.
- indicated for refractory to conventional therapy

Rasburicase

- recombinant form of enzyme urate oxidase
- indicated for treatment & prophylaxis of severe hyperuricemia associated with Rx of malignancy

Other therapeutic options

- ARB losartan - uricosuric
- Fenofibrate - uricosuric
- Vitamin C - uricosuric
- Rilonacept - fusion protein designed to attach to and neutralize circulating IL-1
- Shown to reduce incidence of gout flares induced by the initiation of urate-lowering drug therapy.

PSEUDOGOUT

- Calcium pyrophosphate dehydrate deposition
- Older age group (> 60yrs)
- Acute, recurrent, rarely chronic arthritis
- Large joints (Shoulder/ knee/ wrist)
- Others (MCP, hip, elbow, ankle)
- Always accompanied by chondrocalcinosis of affected joint

PSEUDOGOUT

- Pathophysiology, clinical presentation, acute-phase treatment of gout and pseudogout are very similar
- Underlying causes of 2 diseases are very different

CAUSES

- Idiopathic
- Aging
- Trauma
- Hyperparathyroidism
- Hemochromatosis.

- Acute attacks resolve within 10 days
- Onset of symptoms is usually more insidious

CHONDROCALCINOSIS

- Presence of calcium containing salts in articular cartilage
- Diagnosed radiologically

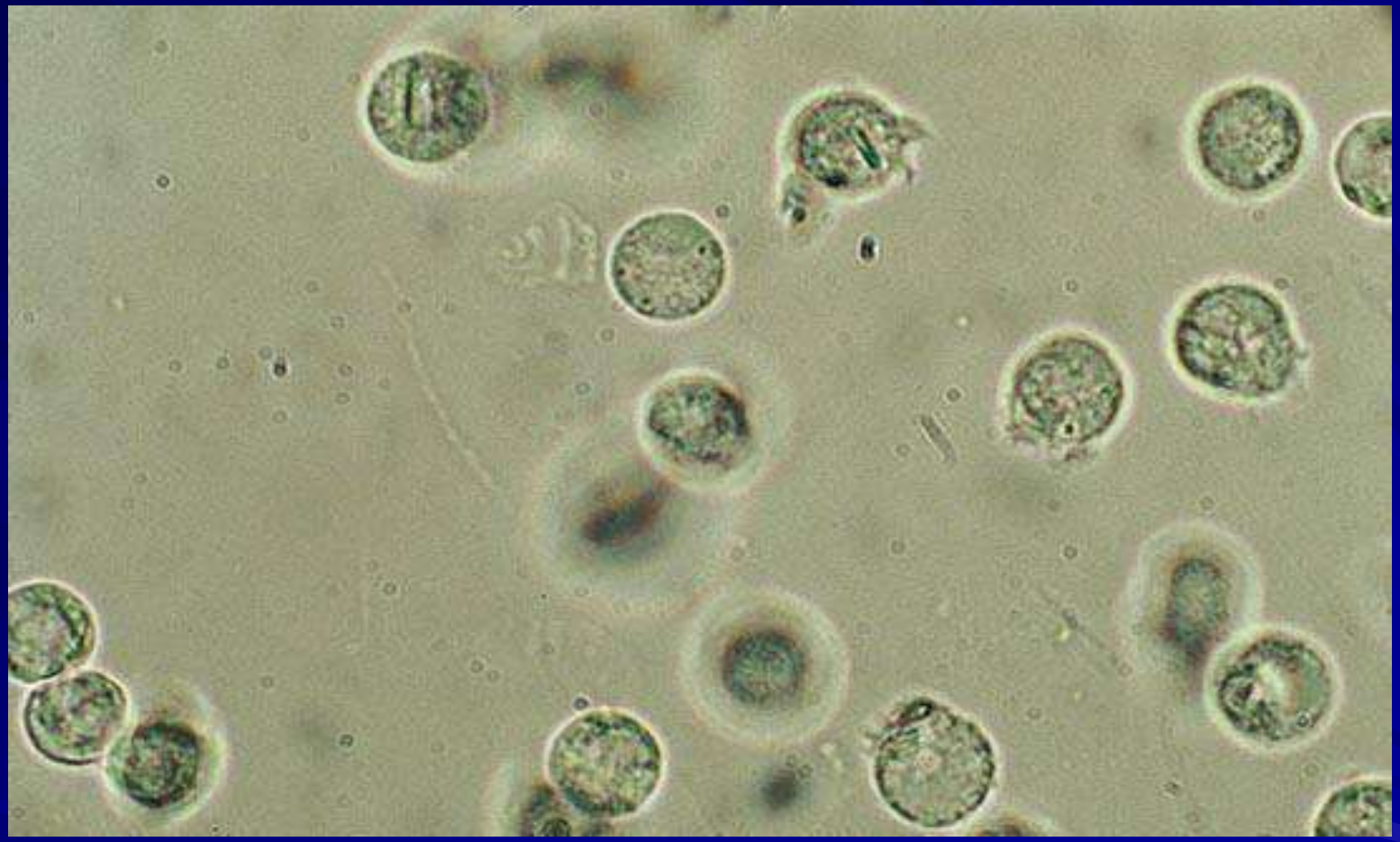
Microscopy

- Rhomboid shaped crystals
- Positive birefringence

Xray

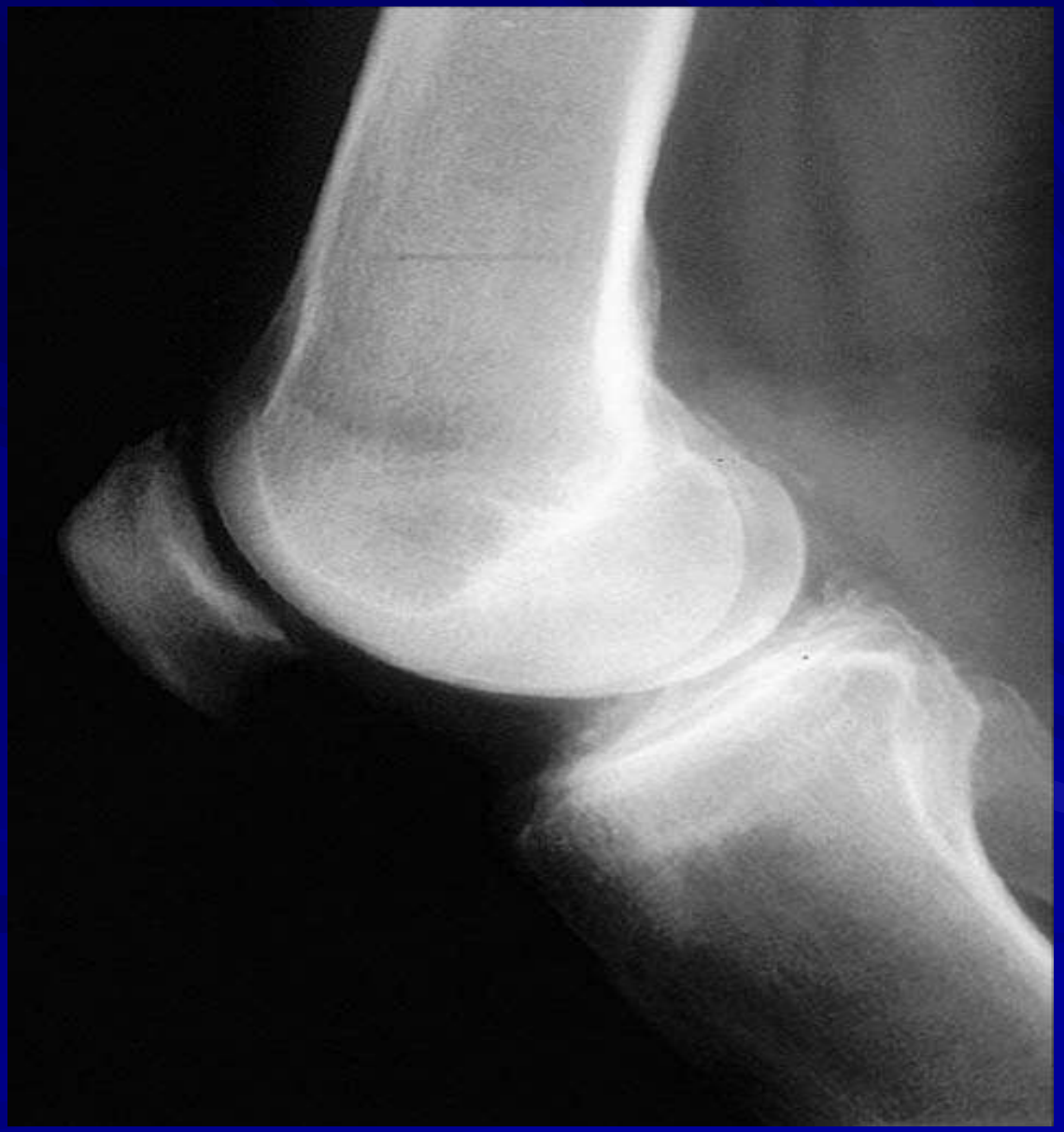
- OA, symmetrical calcification of cartilaginous tissue

Phase contrast microscopy



CPP crystals appear shorter than MSU crystals and are often rhomboidal. They are positively birefringent, appearing blue when aligned parallel with slow axis of the compensator and yellow when perpendicular.

CHONDROCALCINOSIS



- Pseudogout attacks can be triggered by many metabolic abnormalities.
- Workup includes chemistry screen; magnesium, calcium, iron levels; thyroid function tests.

TREATMENT

- Treatment of acute phase identical to gout
- Treatment of primary disease
  - Hemochromatosis
  - Hyperparathyroidism
  - Wilson's disease
  - DM
  - Hypothyroidism
- NSAID
- Colchicines & hydroxychloroquine prophylaxis
- Intra articular steroid

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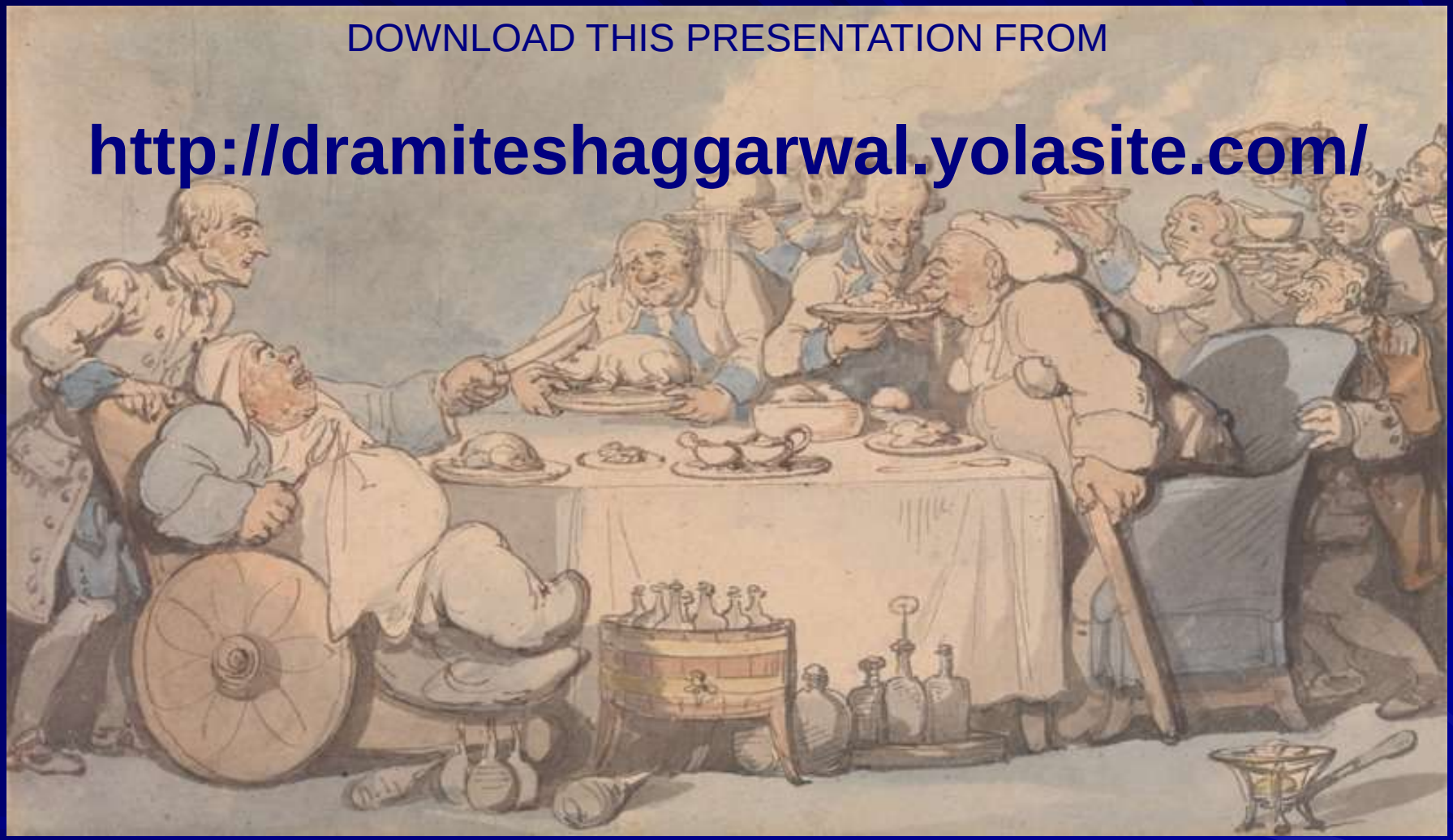

THANK YOU