CRYSTAL- INDUCED ARTHROPATHIES

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Presented by Dr Myint Myat Thway, MBBS, MD, RhMSUS, a member of MMPGA, University of Florida

Disclosure

- No disclosure
- No Financial Relationship with Med Grow
- MMPGA

Objectives

- To identify different types of Crystal- induced arthropathy
- To review etiologies and associated conditions
- To review diagnostic criteria and evaluation
- treatment options for a patient presenting with crystal induced arthropathy

Myanmar Multispecialty Physicians Global Alliance

MMPGA is a group of international multispecialty physicians who will collaborate with local Myanmar physicians to deliver international standard medical care to Myanmar people. MMPGA's main office is located in Florida, USA.

Please visit MMPGA.ORG or MMPGA Facebook page to learn more about MMPGA.

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MMPGA strives to deliver advanced medical care to people in Myanmar through collaboration with local professionals. The goal is to develop a thriving private health care system that can deliver quality medical care to the people of Myanmar.

- Volunteering at Dhamaparagu Charitity Clinic
- Clinic at GHIH
- CME at MMA and GHIH
- Donation to COVID relief in Myanmar
- Non-profit branch MMPGA Foundation

MMPGA Foundation

CRYSTALS

- MSU(mono sodium urate)
- CPPD(calcium pyrophosphate dehydrate)
- Basic Calcium phosphate (BCP)
- Oxalate crystals
- Steroid crystals
- lipid

GOUT

- Gout is a syndrome caused by the inflammatory response to tissue deposition of monosodium urate crystals (MSU) in and around the tissue of joints
- “King of the diseases” and” disease of the kings”

Prevalence

- Increasing world wide
- The prevalence of gout among US adults in 2007-2008 was 3.9%
- Man> women
- Rises with age

Zhu et al .Arthritis Rheum 2011;63(10

Pathophysiology

- Hyperuricemia

- Over production

- Under excretion

- crystal deposition

- Inflammation

Hyperuricemia

- Uric acid is the final metabolite of endogenous and dietary purine metabolism
- consumption of high purine food ;alcohol , sea food , organ meat , sea food , high fructose sweetened soft drinks
- Obesity
- Conditions of Increased Cell Turnover Promoting Hyperuricemia

Psoriasis , hemolytic anemia , tumor lysis after chemotherapy

Hyperuricemia

- 2/3 of uric acid is excreted by kidney and
  1/3 by Gastrointestinal system

- 90% of urate filtered by the kidneys is reabsorbed in proximal tubule ,mediated by specific anion transporters, including URAT1
- - Low GFR , Dehydration and alkalosis may provoke sodium or proton retention and urate retention.
- Some medications block urate excretion

Lancet. 2010 Jan 23;375(9711):3

Panel 2. Drugs that raise and lower serum urate concer

Drugs that raise serum urate concentrations

- Diuretics
- Tacrolimus
- Ciclosporin
- Ethambutol
- Pyrazinamide
- Cytotoxic chemotherapy
- Ethanol
- Salicylates (low dose)
- Levodopa
- Ribavirin and interferon
- Teriparatide

Drugs that lower serum urate concentrations

- Ascorbic acid
- Benzbromarone
- Calcitonin
- Citrate
- Oestrogens
- Fenofibrate
- Losartan
- Probenecid
- Salicylates (high dose)
- Sulfinpyrazone

Crystal Deposition

- Urate crystals begin precipitating at serum uric acid levels of about 6.8 mg/dL
- positive association between serum urate levels and a future risk for gout
- Solubility influence by temperature, pH, concentration of cations, level of articular dehydration
- The most frequent sites : cartilage, epiphyseal bone, periarticular structures and the kidney.

Hyon K. Cho et al *Ann Intern Med. 2005;*

Inflammation

- MSU crystals are potent inducer of inflammation
- Innate immune system plays a pivotal role
- neutrophil influx into the joint fluid
- Neutrophils phagocytose MSU crystals and release inflammatory mediators
- IL1 B,TNF , IL10,TGF Beta

Clinical presentation

- **Asymptomatic Hyperuricemia.**
- Acute intermittent Gout
- Intercritical Gout
- Tophaceous Gout
- Chronic Gouty Arthritis

Acute Gout

- usually begins with mono arthritis affected in the lower limbs (85–90%)
- the first metatarsophalangeal joint—is classically termed **podagra**.
- Attacks subside in 3 to 10 days.
- Recurrent attacks can involve more joints and usually persist longer

Intercritical Period

- It is the asymptomatic period between crises, but MSU crystals can still be recovered in synovial fluid
- The duration of this period varies, but untreated patients may have a second episode within two years.
- Some patients evolve to chronic polyarticular gout without pain free intercritical episodes.

Chronic Gout

- chronic destructive polyarticular involvement with low-grade joint inflammation, joint deformity, and tophi formation
- monosodium urate crystals surrounded by chronic mononuclear and giant-cell reactions.
- develops within 5 years of onset of gout in 30% of untreated patients.
- It is associated with early age of onset, long duration of untreated disease, frequent attacks, upper extremity involvement, polyarticular disease and elevated serum uric acid.

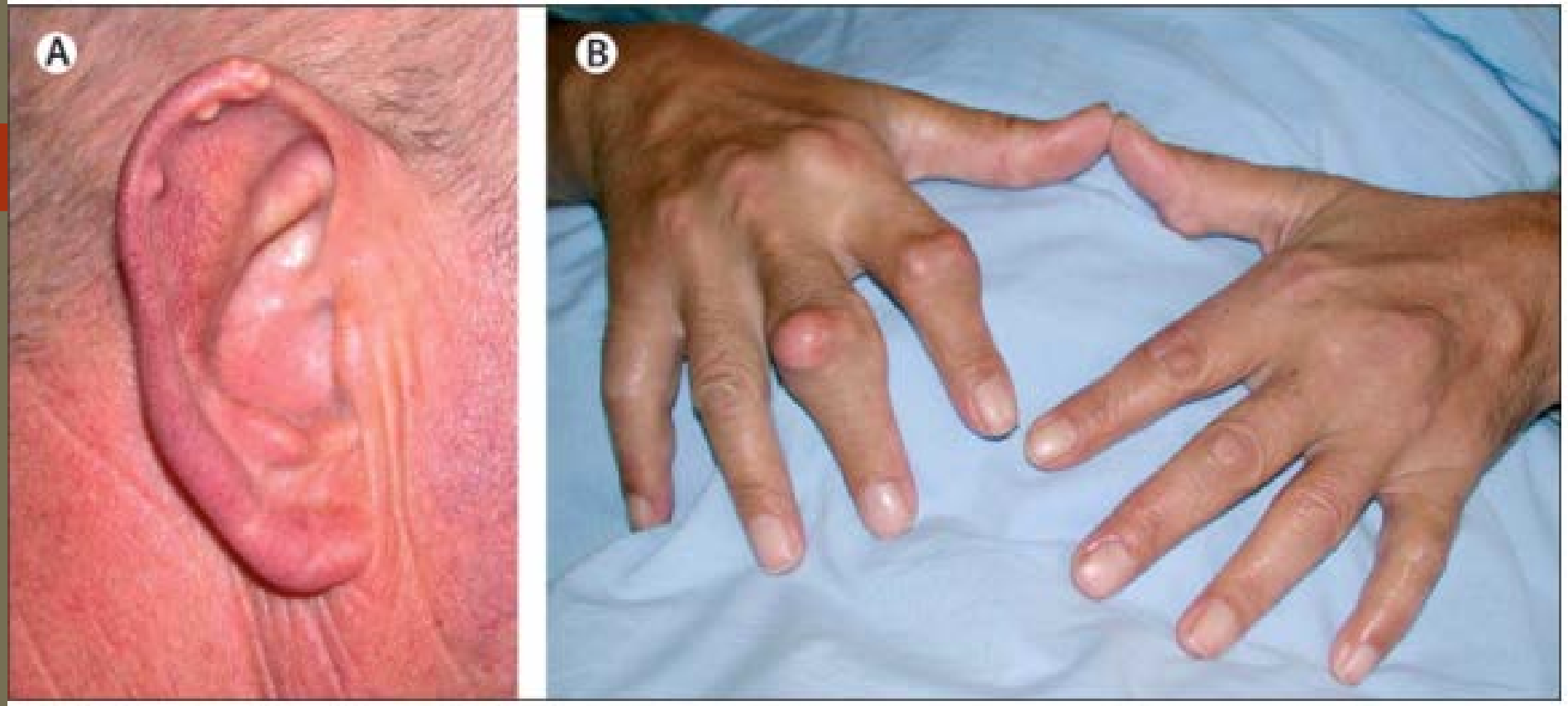


Figure 2. Deposits of uric acid (tophi) in the helix of the ear (A) and within the skin overlying the finger joints (B)

The most common sites for tophi are: the olecranon, prepatellar bursa, ulnar surface and Achilles tendon.

Diagnosis

- Careful history , Risk factors identification and Physical Exam
- Joint Aspiration and synovial fluid analysis:

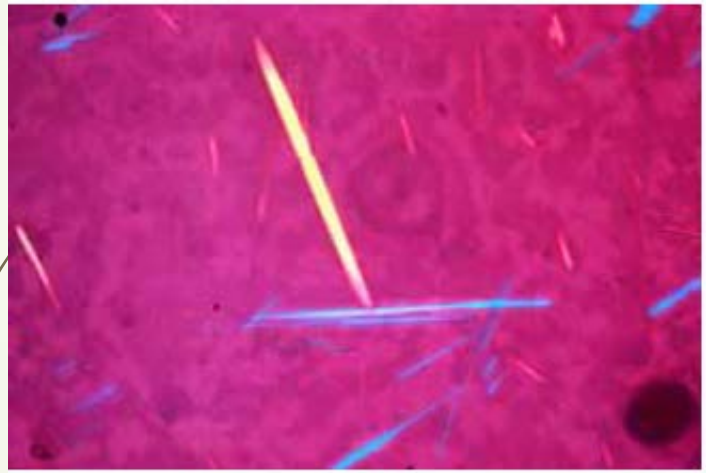
- Cell count (>3000 cells/ml) No need to do synovial protein or Glucose level
- Intracellular MSU crystals can be identified with the polarized light microscope (Sn 85%,Sp 100%).

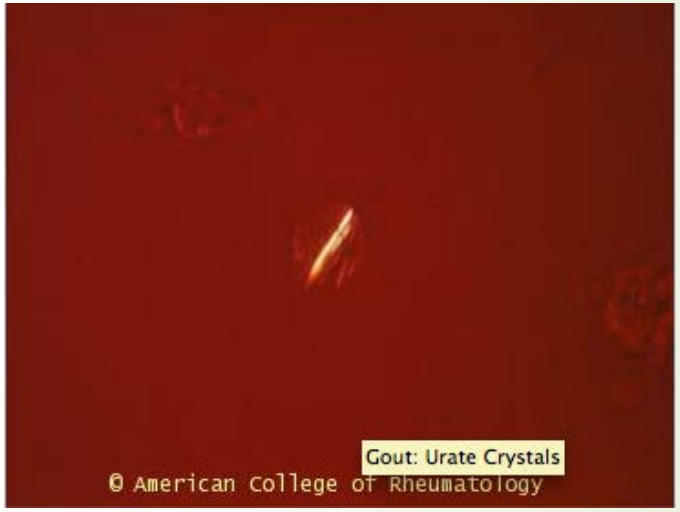
- Serum Uric Acid level

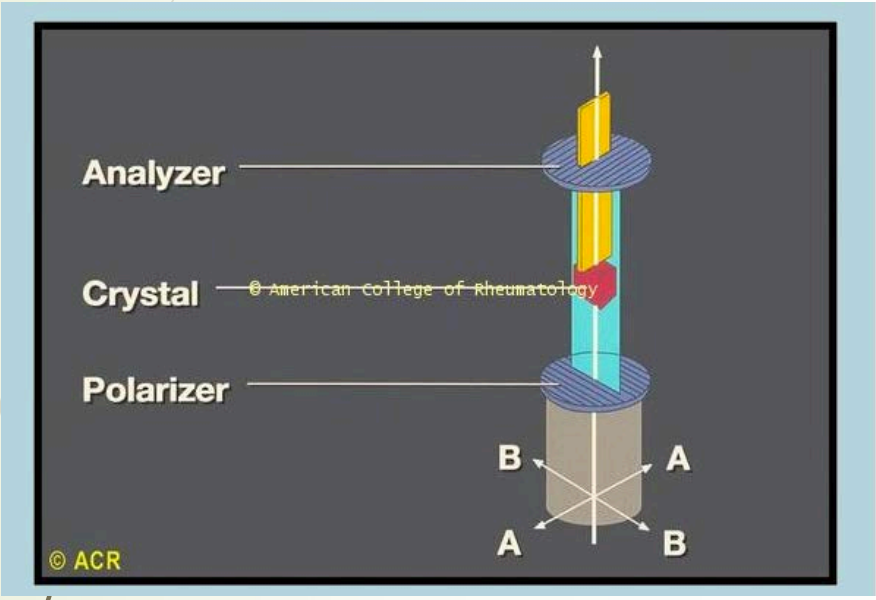
- High serum UA level support the diagnosis But Normal uric acid level doesn't exclude acute gouty attack

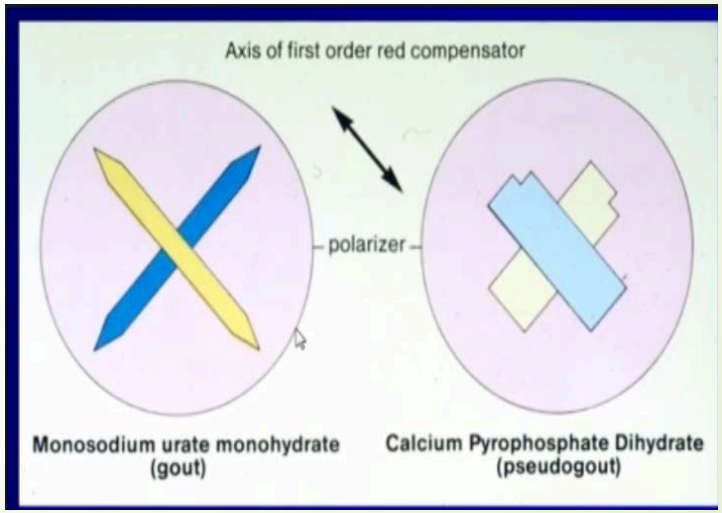
- IMAGING : X-ray , Ultrasound , DECT

The presence of needle-shaped, negatively birefringent urate crystals, viewed under polarized microscopy, supports a diagnosis of gout



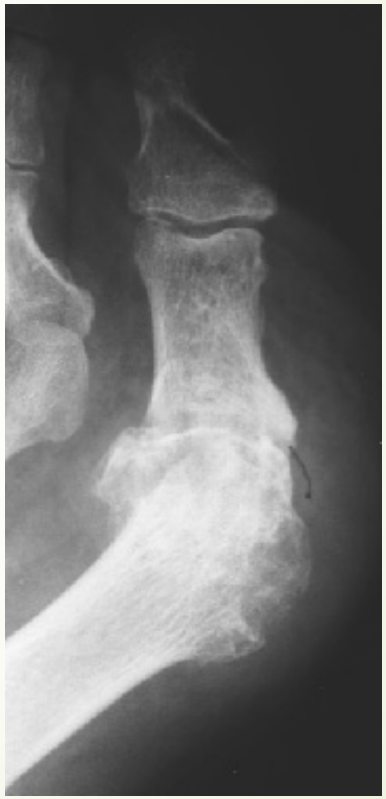



Analyzer
Crystal
Polarizer
B
A
A
B
© ACR
© American College of Rheumatology

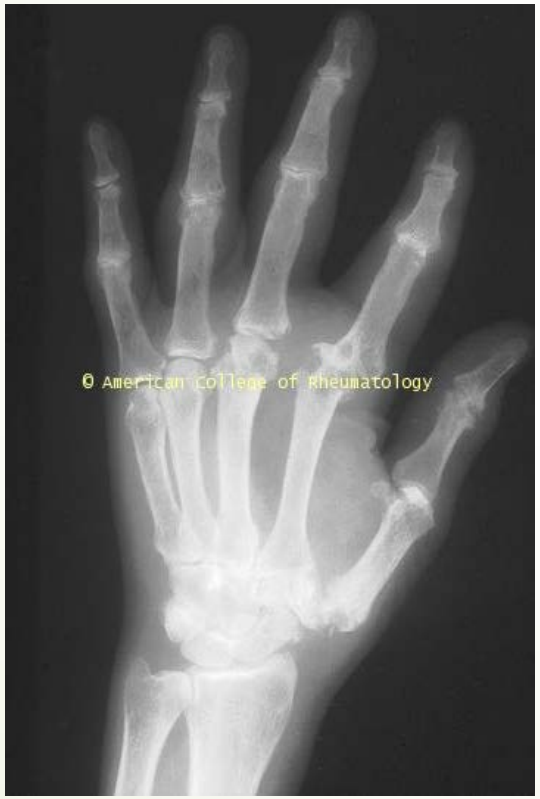

Axis of first order red compensator
polarizer
Monosodium urate monohydrate (gout)
Calcium Pyrophosphate Dihydrate (pseudogout)

Other Diagnostic Tests

- Radiological examination is helpful to exclude other kinds of arthritis. Characteristic “punched-out” erosions and “overhanging edge” of bone.



X-rays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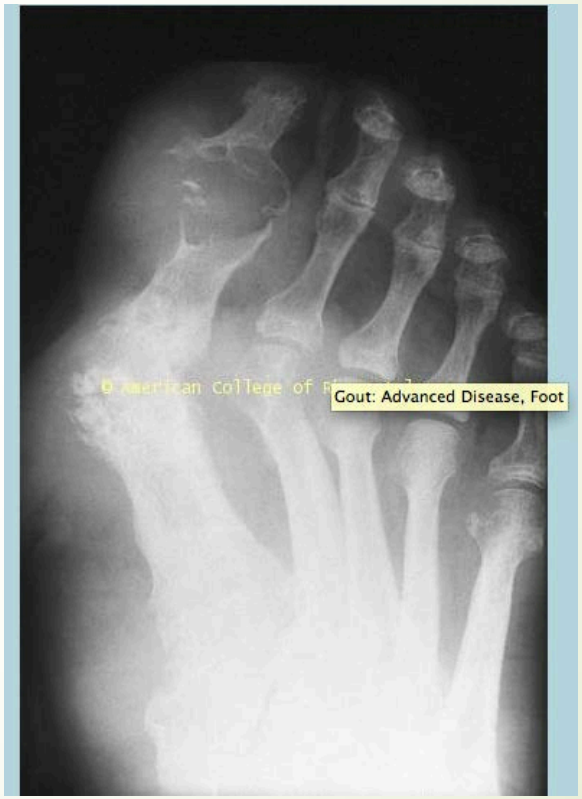

Gout: Advanced Disease, Foot

Other Diagnostic Tests

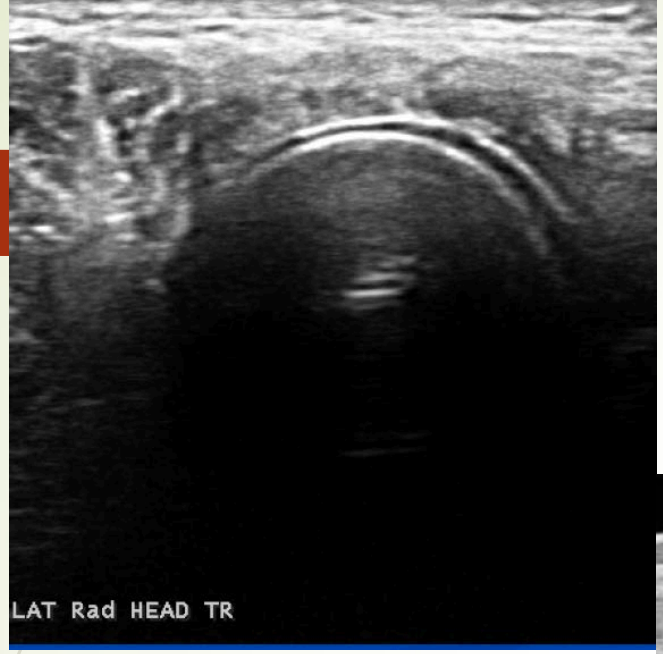
USG:

- useful in both diagnosis of acute attack as well as chronic gout
- Double contour sign ; linear density overlying the cartilage
- Snow Storm appearance
- Tophus
- Bony Erosion

Dual Energy CT(DECT)

highly sensitive and specific (sn95%, Sp 95%)

Can detect soft tissue MSU crystal and renal calculi and unusual site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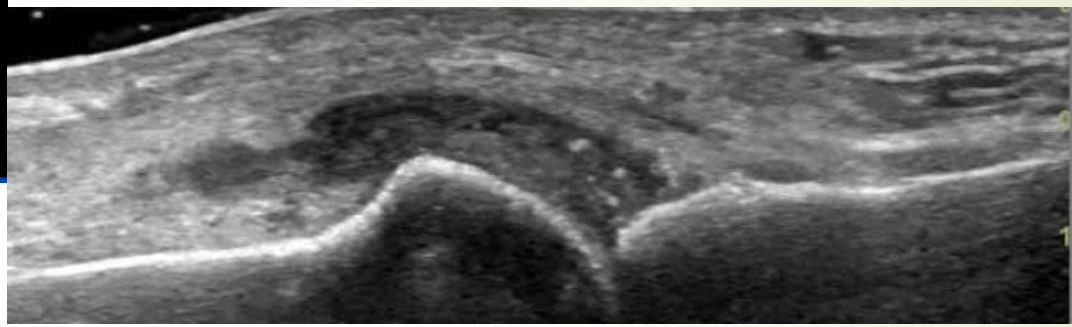

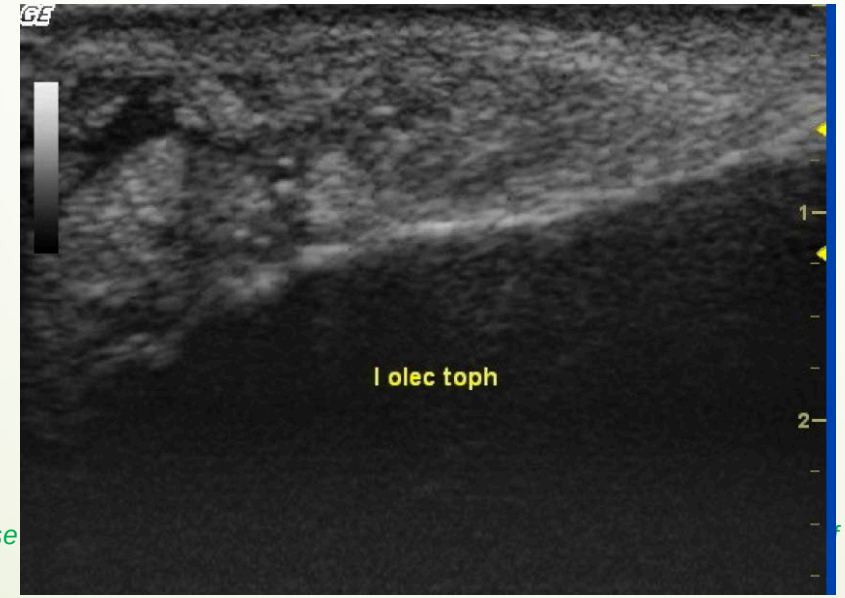
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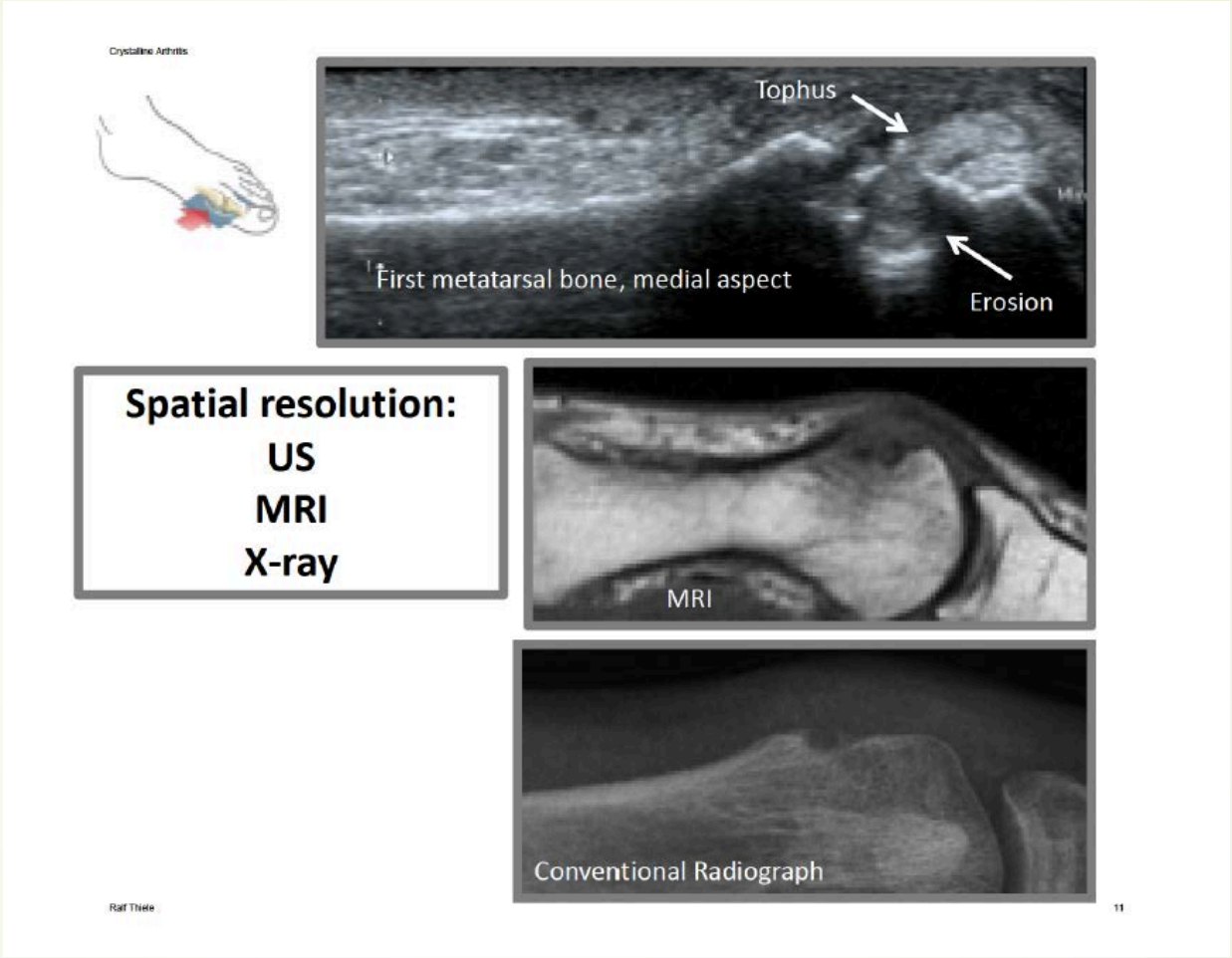
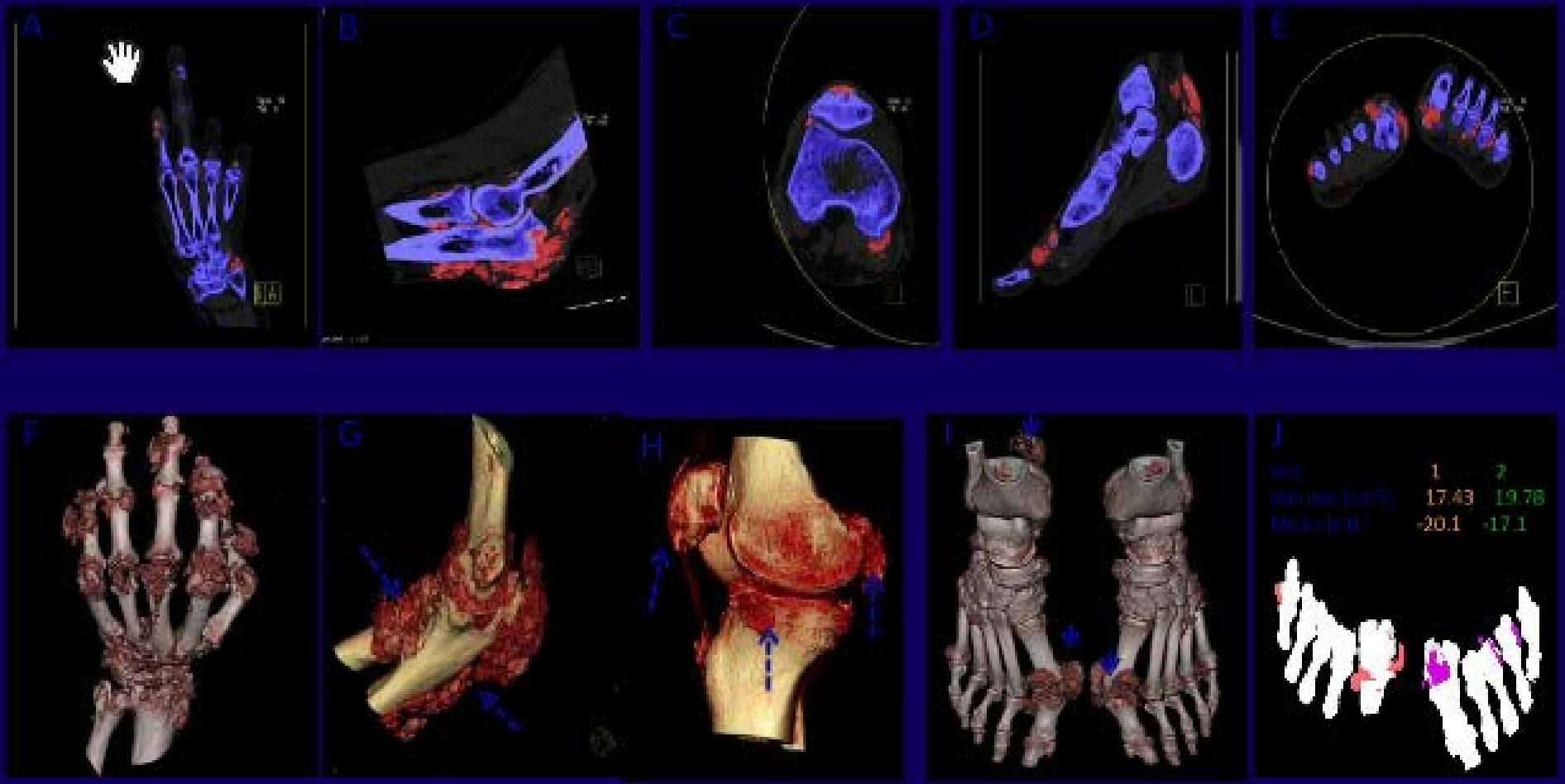
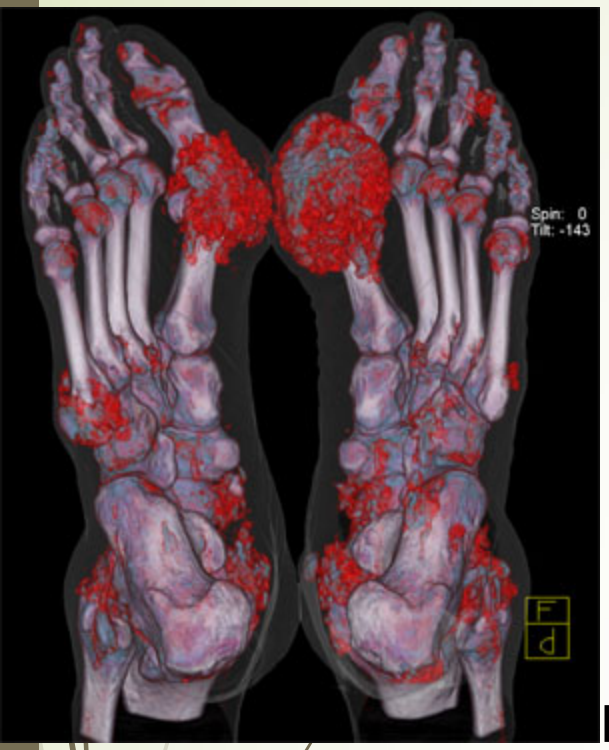


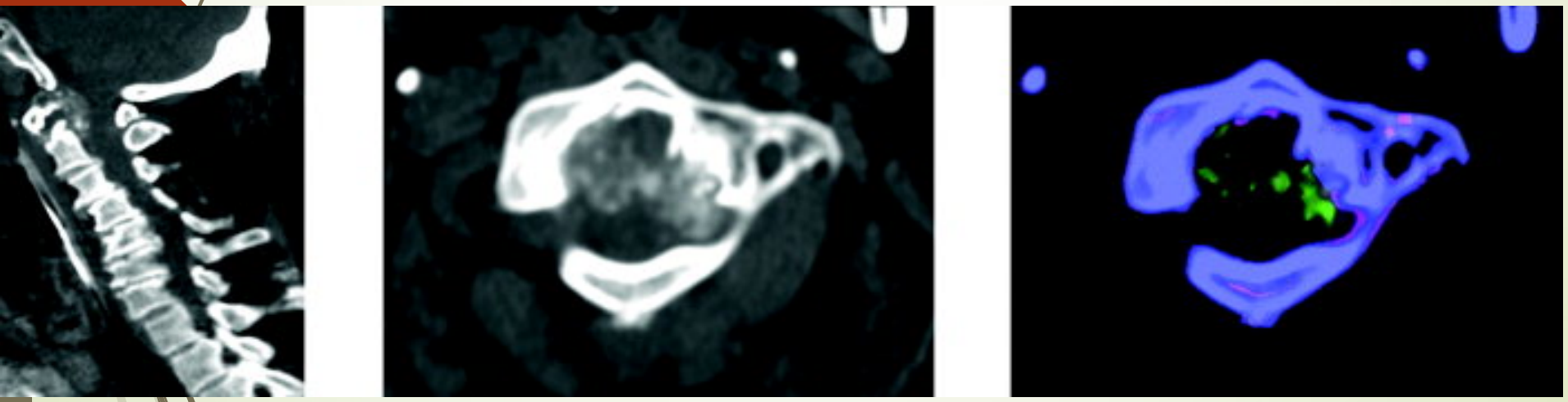
Courtesy of Dr Thiele



Choi HK, Al-Arfaj A, Eftekhari A, Munk PL Shojania, K, Reid G, Nicolaou S. Duan Energy Comuted tomography in tophaceous gout. AnnRheum Dis Dec 2008 [Pubmed ahead of print]



Detection of gouty arthritis in the atlantoaxial joint using dual-energy computed tomography



ACR/EULAR Gout Classification Criteria

Table II. Scoring algorithm for gout according to 2014 EULAR/ ACR preliminary classification criteria [46], applicable if the entry criterion is present and sufficient criterion is absent (see text). The threshold value for classifying a case as gout is 8 points.

Criteria		Categories	Score
Clinical	Pattern of joint/bursa involvement (see text for details)	Ankle or midfoot (mono-/oligo-)	1
		MTP1 (mono-/oligo-)	2
	Characteristics of episode(s) ever (see text for details)	One characteristic	1
		Two characteristics	2
		Three characteristics	3
	Time-course of episode(s) ever (see text for details)	One typical episode	1
		Recurrent typical episode	2
	Clinical evidence of tophus (see text for details)	Present	4
Laboratory	Serum Urate level (SU)	6 - < 8 mg/dl	2
		8-<10 mg/dl	3
		>10 mg/dl	4
Imaging	Imaging evidence of urate deposition	Present (US: DCS or DECT)	4
	Imaging evidence of gout-related joint damage	Present (X-ray gouty erosion)	4
If SU<4 mg/dl: take away 4 points; if MSU negative take away 2 points		Maximum Total Score	23

The threshold value for classifying a case as gout is 8 points. The performance of the criteria is significantly improved by imaging, with a sensitivity of 0.92 and a specificity of 0.89, compared with 0.85 and 0.78 respectively when applying criteria without imaging.

Neogi T, Dalbeth N, Fransen J, et al. The proposed new preliminary gout classification criteria. Arthritis Rheum 2014; 66 (11 Sup).

Differential Diagnosis

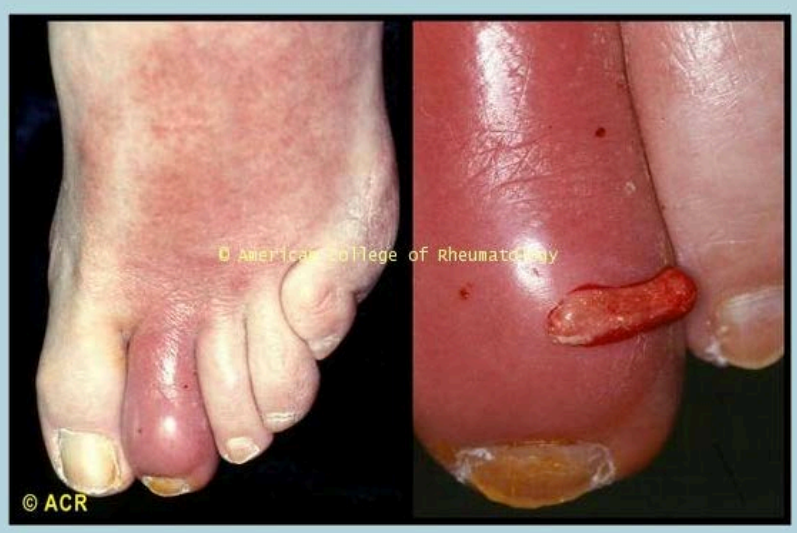
- **Acute Gout**

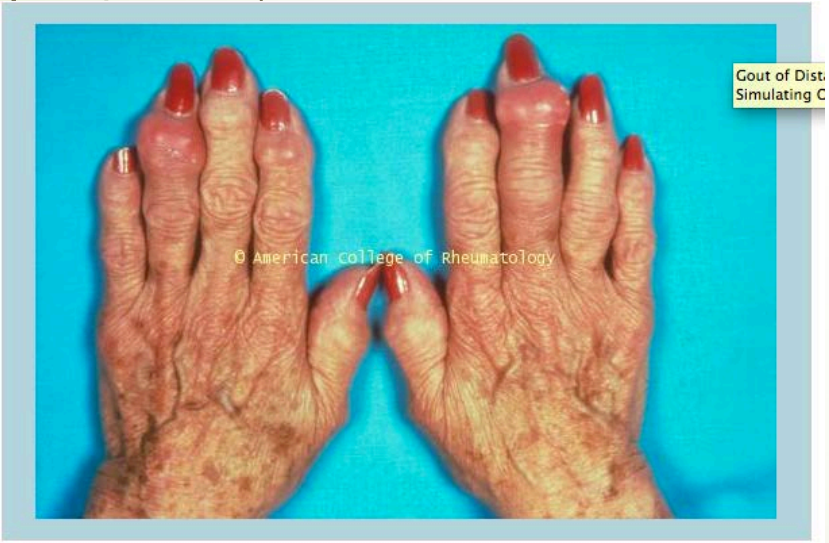
  septic arthritis, pseudo gout, OA,Reactive arthritis, acute rheumatic fever ,cellulitis

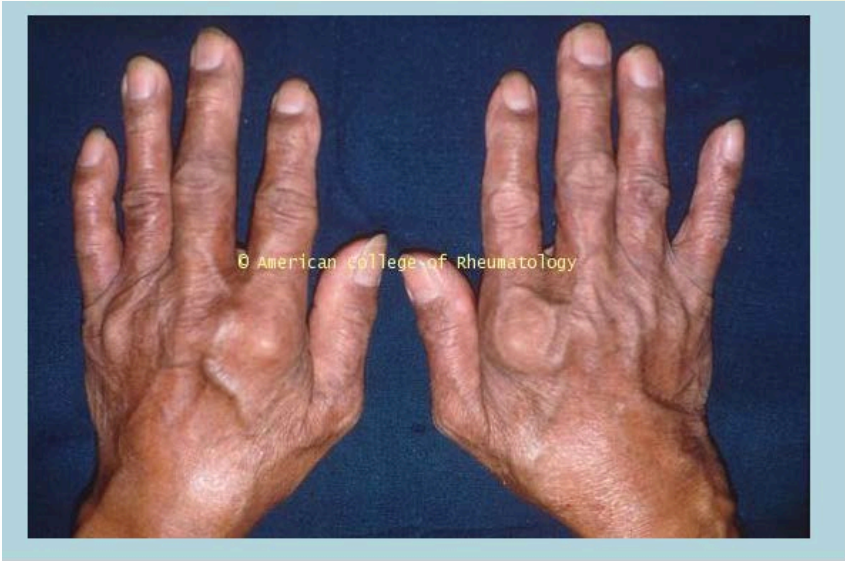
.

- **Chronic tophaceous gout**: Rheumatoid nodules, Pseudogout, seronegative spondyloarthropathies and erosive osteoarthritis.

Differential Diagnosis







Keywords: gout arthritis metacarpophalangeal joint MCP metacarpophalangeal polyarticular rheumatoid arthritis ra

Photo Details	
Title:	Gout: Hands

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Diagnostic Pearls

- The presence of MSU crystal is a GOLD STANDARD diagnostic Test for Gout
- pseudo gout and infection may each coexist with acute gout. (YOU STILL NEED TO RULE OUT)
- Synovial fluid Gram Stain and culture must do together with cell count and crystal Exam
- Consider empiric antibiotic if suspicion of infection is high
- Transient declination in serum urate level can be seen during acute attack .NORMAL URIC ACID level during attack can't exclude GOUT

Case

A 76 yr old Caucasian man, a very nice active full time design farm manager, with only past medical history of mild control hypertension, has been suffering feet and ankle pain associated with swelling for about a year.

He also has a history of chronic back pain .Dx spinal stenosis which required her surgery from in 2018.

He stated that he has neuropathy in his feet diagnosed since 2017 by neurology. He is not on any medication .

Initial visit 2/26/2020

He noted both ankles swelling sporadically about a year , worse in the afternoon , especially increase after walking .

Initially was only ankles, but in January, he has right foot swelling, the 3 days later left foot swelling, seen by primary doctor on 1/17/20 . X-ray show possible erosion on right first MTP.

It has been getting worse and consistent in past few months , ended up needing to use walker than even needed wheelchair because of the pain and swelling .

He dramatically responded to prednisone pack prescribed by PCP , back pain and swelling returned.

He was seen by podiatry 2/19/20 , prescribe meloxicam and Medrol Pak, which helped his pain significantly.

He stated that never been pain-free in the past 2 months like right now. He is on 3rd day of Medrol Pak today .

Off note he has **Abnormal creatinine off and on in the past 2 years . Last creatinine is 1.29.**

His uric acid is 6.1.

No prior History of gout. No family history of gout.

case

MUSCULOSKELETAL: No objective synovitis,

dactylitis or tenosynovitis He has bilat feet and ankle diffuse swelling without warmth , tenderness and

redness

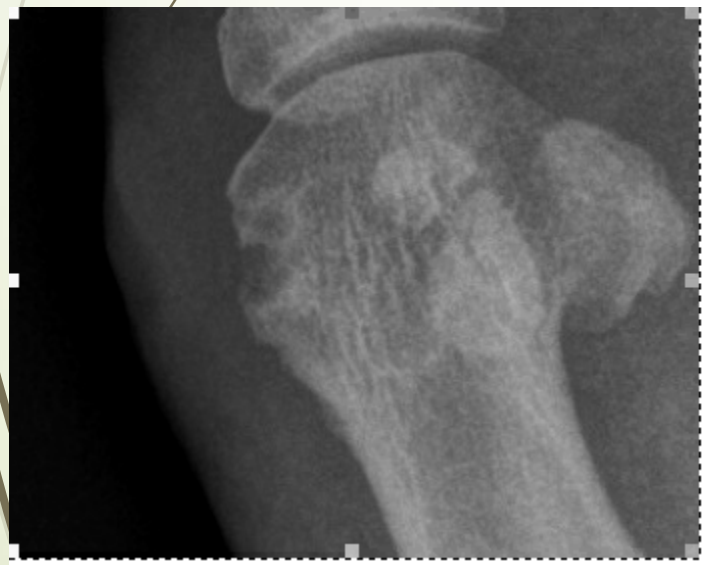
No tophi

No enthasitis

No calcanium tenderness

1/14/20

- Uric Acid - Plasma6.1 4.0 - 8.0 mg/dL)
- SEDIMENTATION RATE33 (H) < OR = 20 mm/h
- C-REACTIVE PROTEIN
- CRP 142.6 (H) <8.0 mg/L
- Rheumatoid Factor <14 <14 IU/mL
  ANA SCREEN NEGATIVE



PROCEDURE: Ultrasound report: Bilateral Lower Extremity Directed (Quadriceps Insertion, Plantar ligament attatchemets, MTP1)
INDICATION: Pain, evaluate for gout / Enthesits

Directed examination

Bilateral Quadriceps Tendons: No tophaceous deposits. Left quadriceps enthesophyte formation, no PD
Bilateral Patellar ligaments: No tophaceous depositis. No bursitis. Right distal patellar ligament bulky enthesophyte c/w osgood schlatter
Bilateral Medial and lateral paramensical areas: No Tophaceous deposits or chondrocalcinosis
Bilateral Maximal flexion - No chondrosynovial deposition

Bilateral MTP 1 Bilateral dorsal synovial hypertrophy with grade 2 PD. On the medial aspect on the right, the medial collateral ligament is thickened, ***has hypoechoic deficits and has increased vascularity. Underlying bone erosion seen correlating with plain x-rays. Plantar double contour also seen.*** On the left there is less dorsal synovitis, but on the medial side, typical heterogeneous deposits are seen with white dots c/w tophaceous deposit. Small medial erosion also seen. Medial plantar double contour seen.

Bilateral MTP 2: Bilateral dorsal grade 3 synovial hypertrophy with heterogeneous material and grade 2 PD. Double contour seen on dorsal side.

Impression:
Evidence for gout at bilateral MTP 1,2
Right knee quadriceps and patellar ligament entheosphytes
Right Achilles tendon enthesophtye but otherwise normal looking enthesis.

- What is his Diagnosis ?

2 months history of bilat feet pain and swelling

Right MTP erosion ,

Normal Uric acid .

US finding as gout

Chronic Tophaceous Gout

- What treatment will you start ?

Treatment

Arthritis Care & Research
Vol. 0, No. 0, June 2020, pp 1–17
DOI 10.1002/acr.24180

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

ACR GUIDELINE FOR MANAGEMENT OF GOUT

2020 American College of Rheumatology Guideline for the Management of Gout

John D. FitzGerald,[1] Nicola Dalbeth,[2] Ted Mikuls,[3] Romina Brignardello-Petersen,[4] Gordon Guyatt,[4] Aryeh M. Abeles,[5] Allan C. Gelber,[6] Leslie R. Harrold,[7] Dinesh Khanna,[8] Charles King,[9] Gerald Levy,[10] Caryn Libbey,[11] David Mount,[12] Michael H. Pillinger,[5] Ann Rosenthal,[13] Jasvinder A. Singh,[14] James Edward Sims,[15] Benjamin J. Smith,[16] Neil S. Wenger,[17] Sangmee Sharon Bae,[17] Abhijeet Danve,[18] Puja P. Khanna,[19] Seoyoung C. Kim,[20] Aleksander Lenert,[21] Samuel Poon,[22] Anila Qasim,[4] Shiv T. Sehra,[23] Tarun Sudhir Kumar Sharma,[24] Michael Toprover,[5] Marat Turgunbaev,[25] Linan Zeng,[4] Mary Ann Zhang,[20] Amy S. Turner,[25] and Tuhina Neogi[11]

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Treatment **Acute Gout:**

Non Pharmacological

- Rest
- Ice pack
- DIET
- Risk reduction

- Pharmacological

- NSAID : Full dose short course
- Colchicine
- Glucocorticoid

DRUGS

colchicine

- Antimitotic agent
- Best to start within 36 hours of onset of symptoms
- Peak plasma concentration-1/2 to 2 hour
- SE: GI/CNS/agranulocytosis/elevated CK
- FDA approved in 2009- total 1.8mg/day
- Acute:1.2mg stat then 0.6 mg 1 hour later then 12hr later
- prophylactic Tx –0.6mg/day continue until acute attack resolves (B)

Table 86.1 Colchicine dose adjustments

	DOSE ADJUSTMENT FOR ACUTE GOUT FLARE	DOSE ADJUSTMENT FOR GOUT PROPHYLAXIS
Strong CYP3A4 inhibitors[a]	0.6 mg × 1 dose, 0.3 mg 1 hour later Do not repeat in <3 days	0.3 mg QOD, can increase to 0.3 mg QD with monitoring
Moderate CYP3A4 inhibitors[b]	1.2 mg × 1 dose Do not repeat in <3 days	0.3 mg QD, can increase to 0.6 mg QD with monitoring
Weak CYP3AR inhibitor[c]	No dose adjustment required	No dose adjustment required
P-gp inhibitors[d]	0.6 mg × 1 dose Do not repeat in <3 days	0.3 mg QOD, can increase to 0.3 mg QD with monitoring
Severe renal impairment (CrCl <30 mL/minute)	1.2 mg × 1 dose, 0.6 mg 1 hour later Do not repeat more than once per 2 weeks	0.3 mg QD
Dialysis	0.6 mg × 1 dose Do not repeat more than once per 2 weeks	0.3 mg twice a week, monitor closely

[a]Clarithromycin, erythromycin, ketoconazole, ritonavir.
[b]Diltiazem, verapamil.
[c]Azithromycin.
[d]Cyclosporine, sunitinib, clarithromycin, erythromycin, tacrolimus (weaker P-gp inhibitor than cyclosporine) carvedilol.
Note:
Clarithromycin and erythromycin are inhibitors of both CYP3A4 and P-gp.
Cyclosporine use is especially problematic due to scheduled, chronic dosing and common use in patients with solid organ transplant (a population at risk for gout). Colchicine should be avoided if possible (elevated risk of neuromyopathy reported).
CrCl, Creatinine clearance; *QD,* every day; *QOD,* every other day.

Glucocorticoid

- Intraarticular or systemic
- Can be used as combination therapy
- 0.5mg/kg/day
- 5-10 days of full dose and stop (A)
- 2-5 days of full dose then taper 7-10 days (C)

Pearls for Treatment of acute attack

- Maximum dose of colchicine 1.8mg in 24 hours
- If a patient is already on urate-lowering therapy or it was briefly interrupted, it should be continued or restarted.
- Careful using NSAID in elderly , Renal disease
- IL-1 inhibitor (anakinra)
- In 2020 new guideline

Starting ULT during attack if patient is needed

Recommend using IV/ IM or IR steroid in NPO patient

Intercritical

The focus in this stage is prevention and prophylaxis.

- Life style modification.
- Comorbid disease management
- Low Purine Diet
- Consider elimination of non essential medication that induce hyperuricemia

e.g. thiazide and loop diuretics, niacin, and calcineurin inhibitors (evidence C).

- Time to make a Decision for using uric acid lowering agent

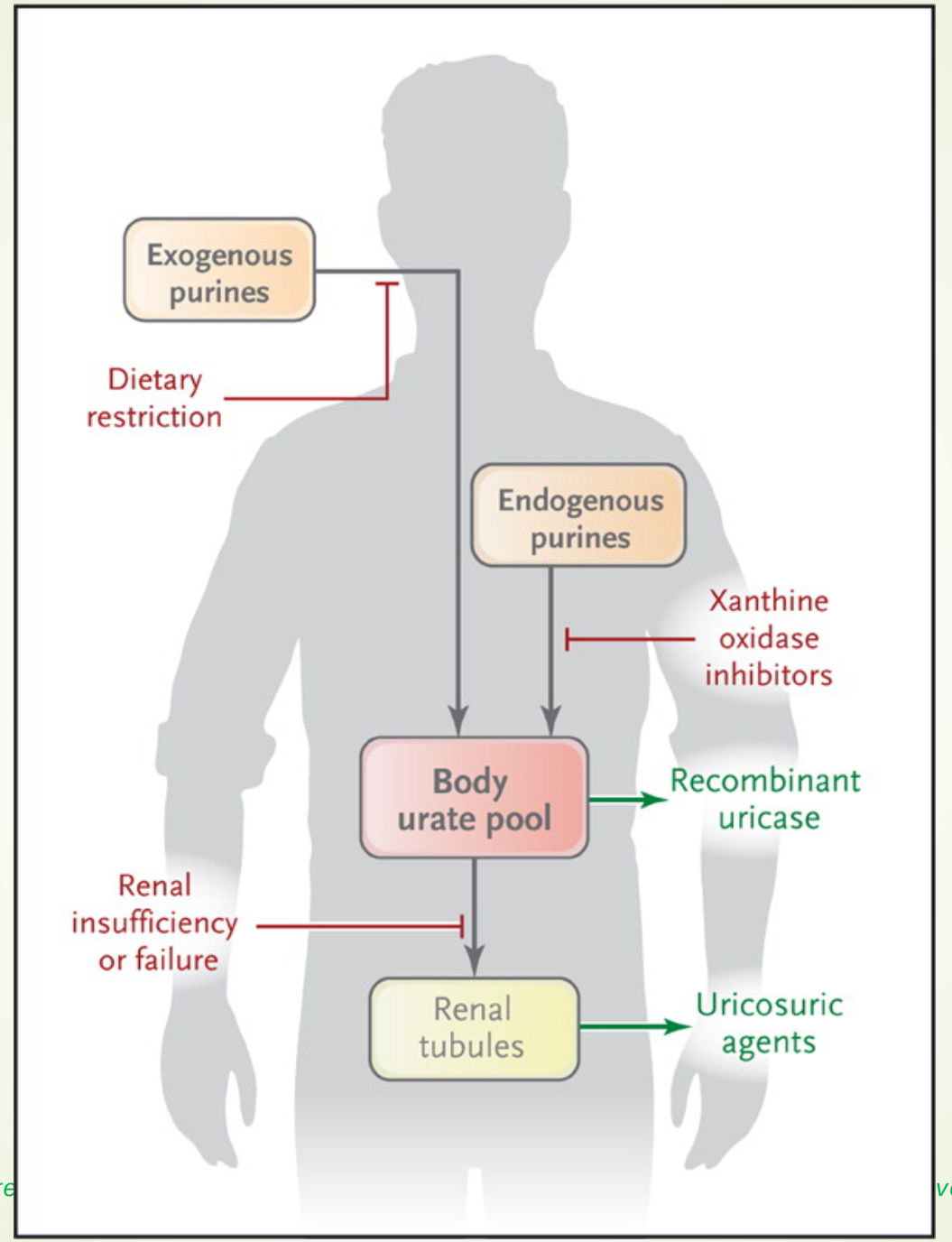
Table 7. Management of lifestyle factors*

Recommendation
For patients with gout, regardless of disease activity, we conditionally recommend limiting alcohol intake.
For patients with gout, regardless of disease activity, we conditionally recommend limiting purine intake.
For patients with gout, regardless of disease activity, we conditionally recommend limiting high-fructose corn syrup.
For overweight/obese patients with gout, regardless of disease activity, we conditionally recommend weight loss.
For patients with gout, regardless of disease activity, we conditionally recommend *against* adding vitamin C supplementation.

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

Table 8. Management of concurrent medications*

Recommendation
For patients with gout, regardless of disease activity, we conditionally recommend switching hydrochlorothiazide to an alternate antihypertensive when feasible.
We conditionally recommend choosing losartan preferentially as an antihypertensive when feasible.
We conditionally recommend *against* stopping low-dose aspirin (in those who are taking this medication for appropriate indications).
We conditionally recommend *against* adding or switching to fenofibrate.


Exogenous purines
Dietary restriction
Endogenous purines
Xanthine oxidase inhibitors
Body urate pool
Recombinant uricase
Renal insufficiency or failure
Renal tubules
Uricosuric agents

Starting Urate- lowering agent

- **Indication for therapy**

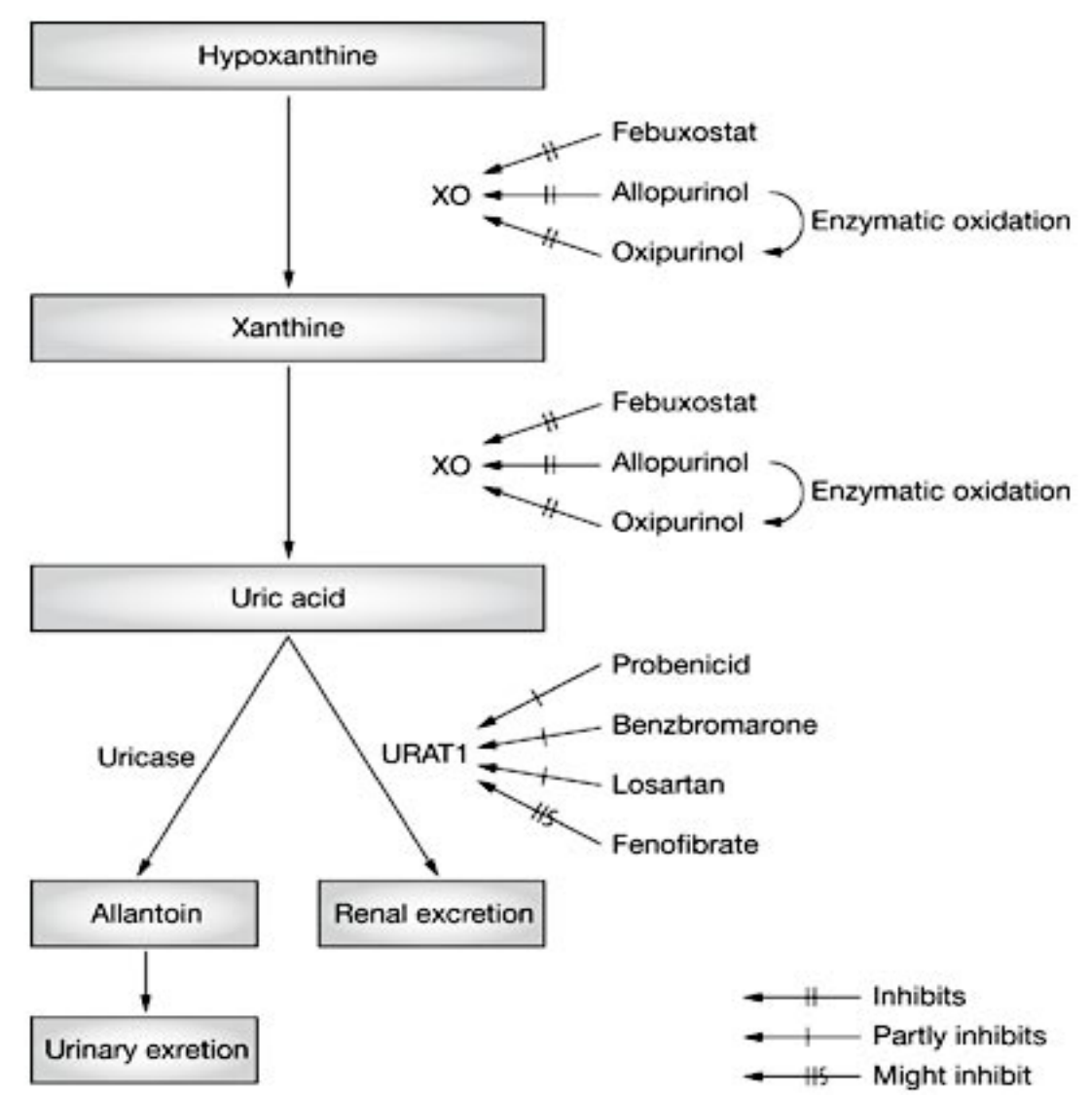
-frequent attacks (>2 attacks/year) (A)

-presence of tophus (A)

-Past urolithiasis ©

2020

- Presence of radiographic Damage
- CKD



Drugs affecting urate levels and their underlying mechanisms

URAT 1= Urate Transporter 1; XO = Xanthine Oxidase

Presented by Dr Myint Myat Thway, MBBS, MD, RhMSUS, a member of MMPGA, University of Florida

Table 1. Indications for pharmacologic urate-lowering therapy (ULT)*

Recommendation
For patients with 1 or more subcutaneous tophi, we strongly recommend initiating ULT over no ULT.
For patients with radiographic damage (any modality) attributable to gout, we strongly recommend initiating ULT over no ULT.
For patients with frequent gout flares (≥2/year), we strongly recommend initiating ULT over no ULT.
For patients who have previously experienced >1 flare but have infrequent flares (<2/year), we conditionally recommend initiating ULT over no ULT.
For patients experiencing their first flare, we conditionally recommend *against* initiating ULT over no ULT, with the following exceptions.
For patients experiencing their first flare and CKD stage ≥3, SU >9 mg/dl, or urolithiasis, we conditionally recommend initiating ULT.
For patients with asymptomatic hyperuricemia (SU >6.8 mg/dl with no prior gout flares or subcutaneous tophi), we conditionally recommend *against* initiating any pharmacologic ULT (allopurinol, febuxostat, probenecid) over initiation of pharmacologic ULT.

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

- **Conditionally recommend (level B/ C)**
- >1 flare
- 1st attack but patient has CKD 3
- Serum urate >9
- Urolithiasis

Timing of ULT initiation

- Starting ULT **during the gout flare** over starting ULT after the gout flare has resolved is conditionally recommended.
- Continuing ULT **indefinitely** over stopping ULT is conditionally recommended.

ULT Treatment

Treatment with allopurinol as the preferred first-line agent, over all other ULTs, is strongly recommended for all patients, including those with moderate-to- severe CKD (stage ≥3).

Treat to target management with dose titration

- **GOAL: serum UA < 6mg/dl,**
- **Slow reduction(1-2mg/dl/month)**
- **Pharmacologic anti-inflammatory prophylaxis when starting uric lowering therapy ; colchicine vs NSAID**
- **Continue prophylaxis for 3-6 months**

Table 2. Recommendations for choice of initial urate-lowering therapy (ULT) in patients with gout*

Recommendation
For patients starting any ULT, we strongly recommend allopurinol over all other ULT as the preferred first-line agent for all patients, including in those with CKD stage ≥3.
We strongly recommend a xanthine oxidase inhibitor over probenecid for those with CKD stage ≥3.
For allopurinol and febuxostat, we strongly recommend starting at a low dose with subsequent dose titration to target over starting at a higher dose (e.g., ≤100 mg/day [and lower in patients with CKD] for allopurinol or ≤40 mg/day for febuxostat).
For probenecid, we conditionally recommend starting at a low dose (500 mg once or twice daily) with dose titration over starting at a higher dose.
We strongly recommend initiating concomitant antiinflammatory prophylaxis therapy (e.g., colchicine, NSAIDs, prednisone/prednisolone) over no antiinflammatory prophylaxis. The choice of specific antiinflammatory prophylaxis should be based upon patient factors.
We strongly recommend continuing prophylaxis for 3–6 months rather than <3 months, with ongoing evaluation and continued prophylaxis as needed if the patient continues to experience flares.
When the decision is made that ULT is indicated while the patient is experiencing a gout flare, we conditionally recommend starting ULT during the gout flare over starting ULT after the gout flare has resolved.
We strongly recommend *against* pegloticase as first-line therapy.

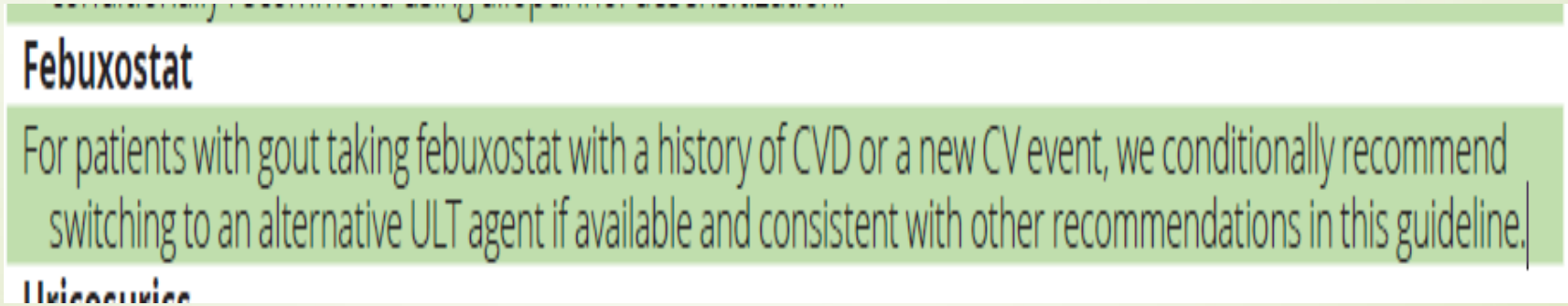
Strongly recommend	Conditionally recommend	Strongly recommend against	Conditionally recommend against

Xanthine oxidase Inhibitors Allopurinol

- Starting dose should be< 100 mg/day
- 50 mg/day in CKD stage 4
- Gradually titrate maintenance dose upward every 2–5 weeks to appropriate maximum ©
- Dose can be above 300 mg daily, even with renal impairment
- HLA–B*5801 testing **Southeast Asian descent (e.g.., Han Chinese, Korean, Thai) and for African American Patients (* 2020 new recommendation)**

Febuxostat

- FDA approved in 2009
- Only 40mg and 80mg dosing available
- Excreted from liver
- Boxed warning : Increased risk of CAD related death (2019)
- SE: nausea, arthralgia
- Expensive



Uricosuric Agent

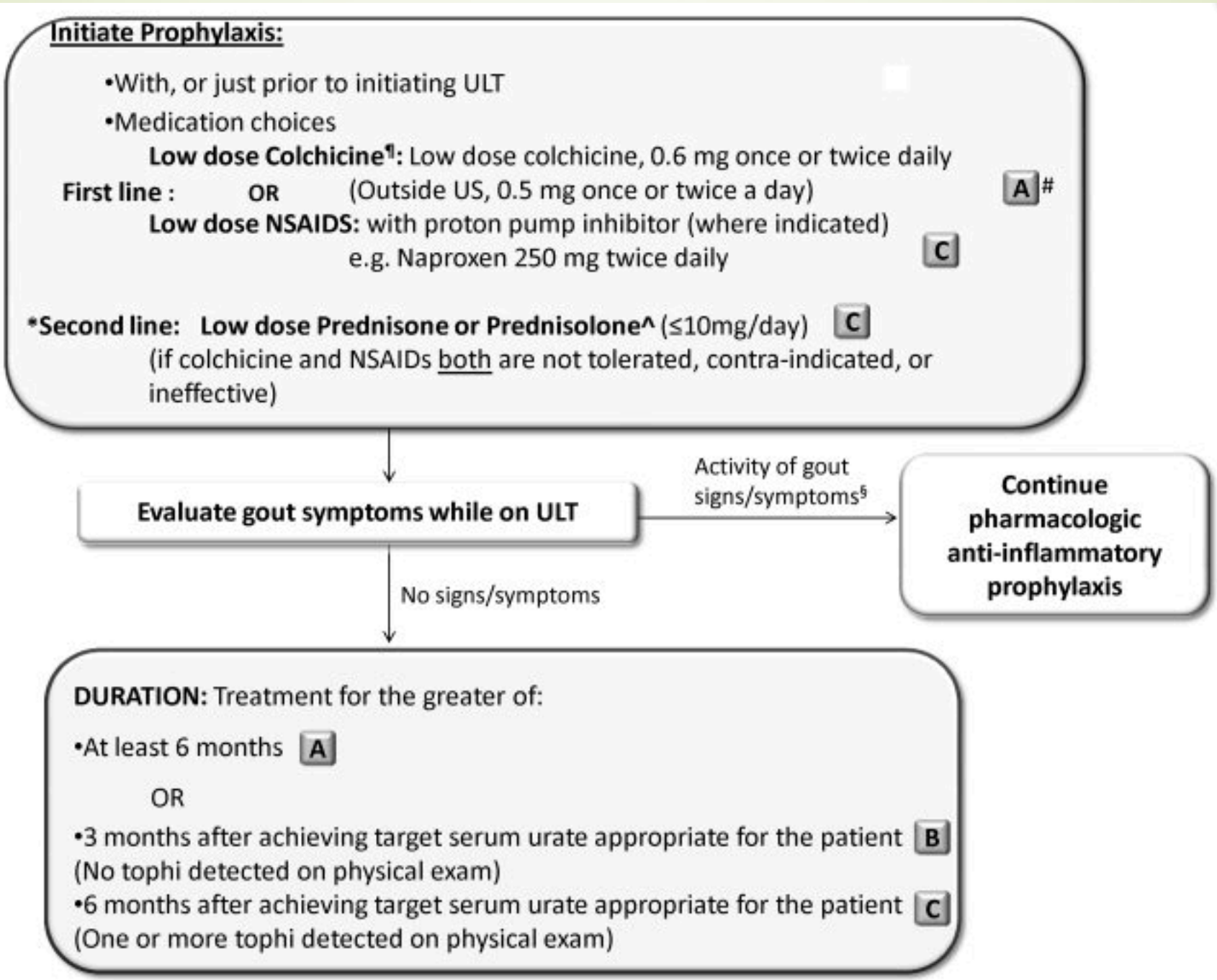
1.Probenecid(1-2g/day)

2. Sulfinpyrazone

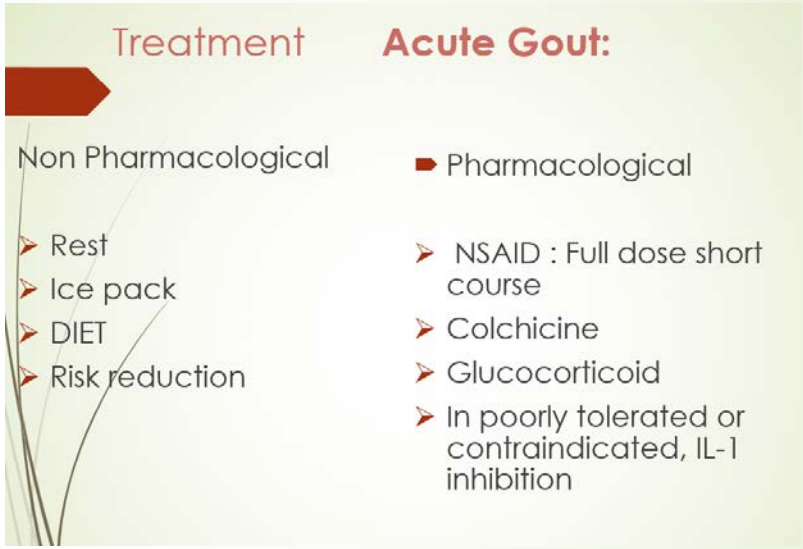
3.Benzbromarone

Others ; Losartan, fenofibrate, atrovastatin

- normal renal function,
- CI –nephrolithiasis, renal insufficiency
- Rare toxicity

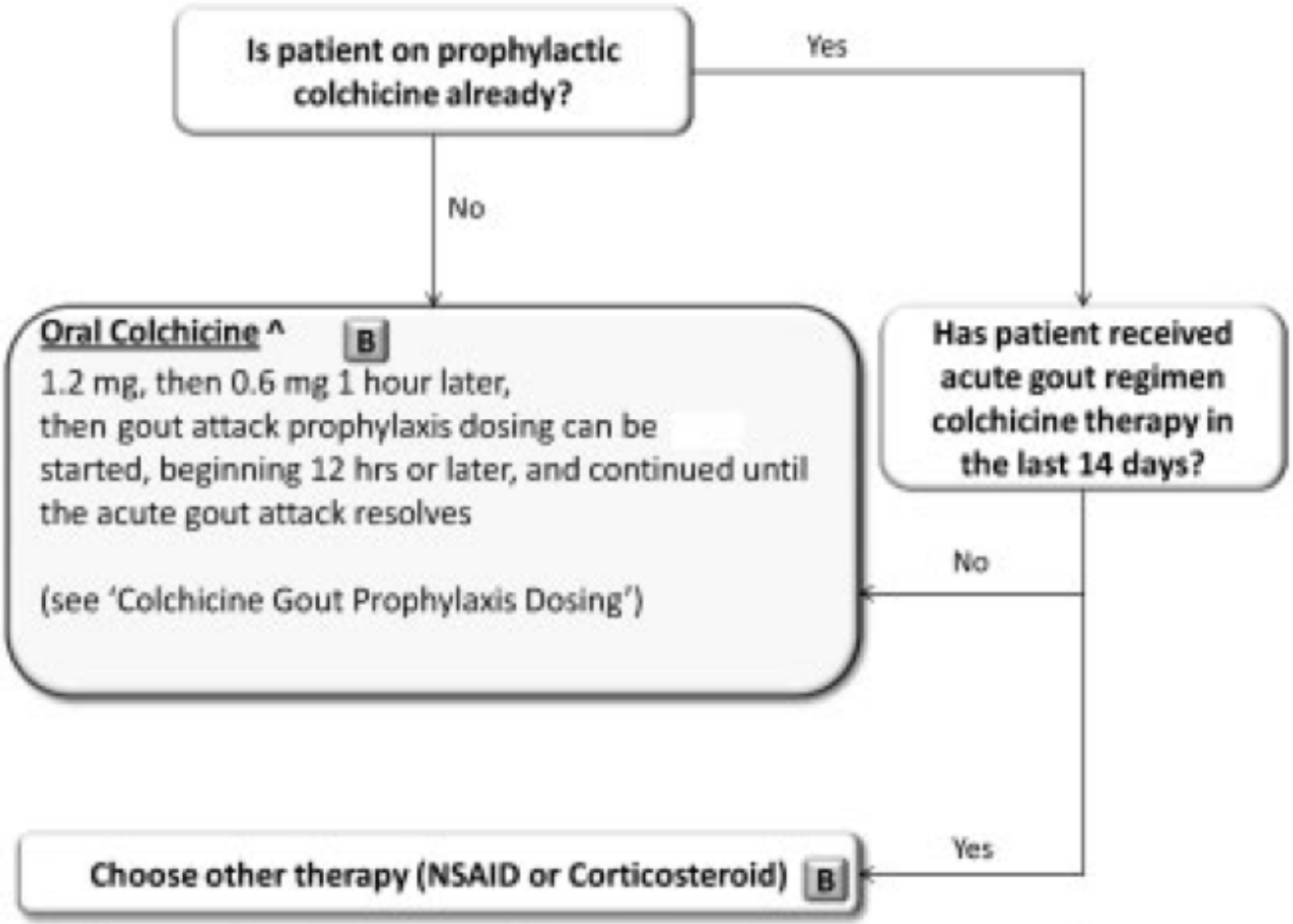

Initiate Prophylaxis:
•With, or just prior to initiating ULT
•Medication choices
Low dose Colchicine¶: Low dose colchicine, 0.6 mg once or twice daily
First line : OR (Outside US, 0.5 mg once or twice a day)
A#
Low dose NSAIDS: with proton pump inhibitor (where indicated)
e.g. Naproxen 250 mg twice daily
C
*Second line: Low dose Prednisone or Prednisolone^ (≤10mg/day) C
(if colchicine and NSAIDs both are not tolerated, contra-indicated, or ineffective)
Evaluate gout symptoms while on ULT
Activity of gout signs/symptoms§
Continue pharmacologic anti-inflammatory prophylaxis
No signs/symptoms
DURATION: Treatment for the greater of:
•At least 6 months A
OR
•3 months after achieving target serum urate appropriate for the patient B
(No tophi detected on physical exam)
•6 months after achieving target serum urate appropriate for the patient C
(One or more tophi detected on physical exam)

If Patient has an acute attack while on ULT (allopurinol , Febuxostat) what is the treatment ?



A

Oral Colchicine



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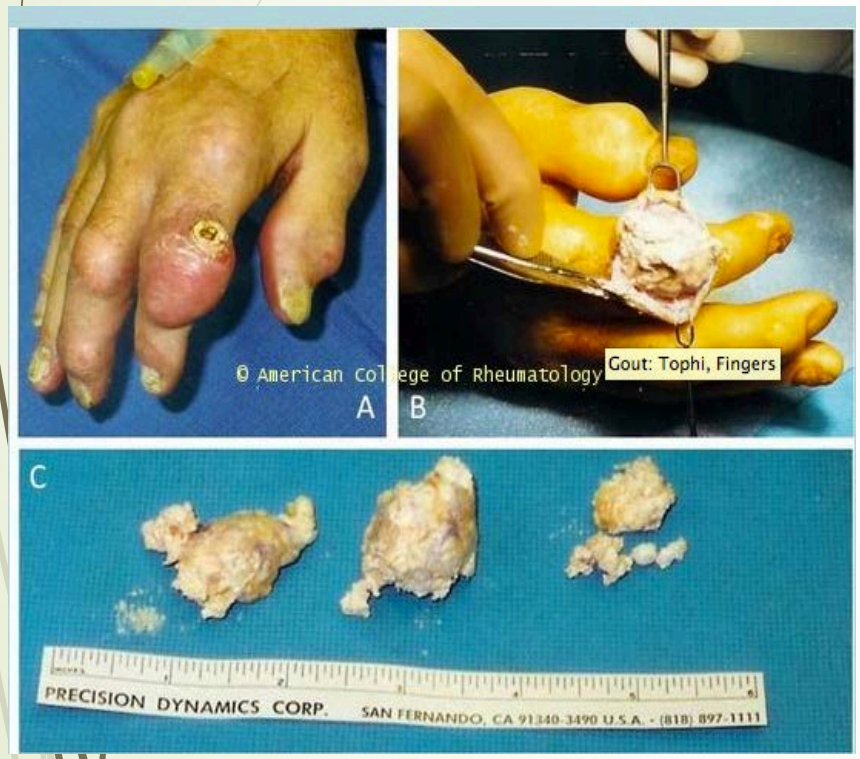
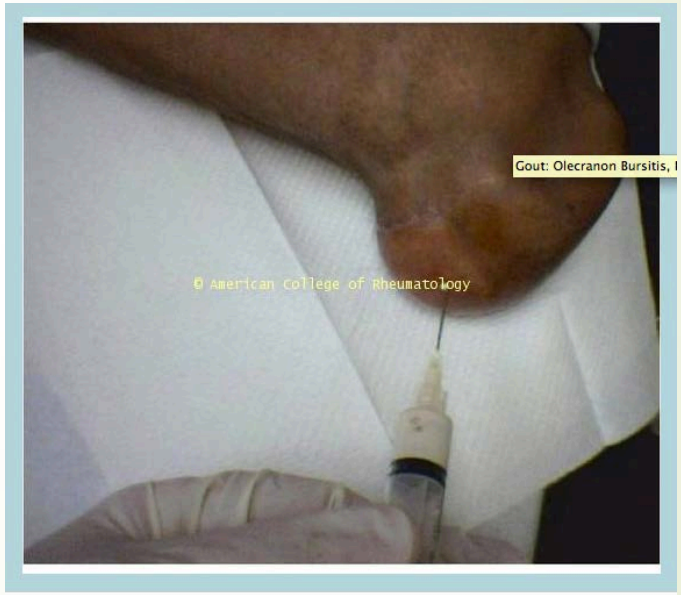




Presented by Dr Myint Myat Thway, MBBS, MD, RhMSUS, a member of MMPGA, University of Florida

Uricase(Pegloticase)

- Recombinant conjugated form of mammalian enzyme urease
  - Catalyzes the oxidation of uric acid to allantoin
  - Allantoin: 5-10 times more soluble than uric acid
  - only in the case scenarios with severe gout disease burden and refractoriness to, or intolerance of, appropriately dosed oral ULT options (evidence A)
- **Chronic tophaceous gout / resistant case**

Pegloticase rapidly degrades urates

Increase urate concentration gradient draws extravascular urates into circulation

Persistent low tissue urate concentration favor the crystals dissolution

Efficacy and Tolerability of Pegloticase for the Treatment of Chronic Gout in Patients Refractory to Conventional Treatment

Two Randomized Controlled Trials

JAMA, August 17, 2011—Vol 306, No. 7 **711**

Randomized Interventions

- Pegloticase 8mg every 2 wk (85 [43 in trial C0405 and 42 in trial C0406])
- Pegloticase 8mg every 4 wk (84 [41 in trial C0405 and 43 in trial C0406])
- Placebo every 2 wk (43 [20 in trial C0405 and 23 in trial C0406])

Result

- Responder rate : 47% and 38%respectively in 2 studies in pegloticase biweekly group compared with 0% of those given placebo (*P < .001)*
- 20% and 49% in Monthly pegloticase group (P=0.044 and < 0.001)
- Tophus Complete Response (CR) : 40% in biweekly gp and 21 % in monthly gp and 7% in placebo <P=0.002 and P=0.20>

Discussion

- Among patients with chronic gout , the use of pegloticase 8 mg either every 2 weeks

or every 4 weeks for 6 months resulted in lower uric acid levels compared with placebo.

- Tophus resolution, reduced flare frequency, reduction in TJC, and improved patient-reported outcomes in pain, physical function, and QOL
- Infusion Reaction is common and is related to high titer of antibody
- CV risk assessment and stabilization prior to treatment

Asymptomatic Hyperuricemia

- Patients who have moderately elevated serum urate levels but have never had an attack (asymptomatic hyperuricemia) have an increased risk for gout, but a low likelihood of a gout attack in the short term, and therefore do not require prophylaxis.
- Do not give allopurinol without GOUT

- hyperuricemia may contribute to several comorbidities there is not yet consensus that these risks are sufficient to warrant chronic urate-lowering therapy
- Consideration of lifestyle modifications
- dietary changes or switching from medications that promote hyperuricemia when alternatives are available

Initiating ULT is conditionally recommended
against in patients with **asymptomatic** hyperuricemia (2020)

Take Home Message

- Elevated Uric Acid Is not Gout
- Allopurinol and Febuxostat are not Benign Drugs
- If patient needs ULT, may need life long
- When you starting ULT , Use prophylaxis
- Don't forget to check Drug interaction
- Lifestyle , diet modification

My Patient

- **What treatment will you start ?**

allopurinol 50mg , colchicine 0.6mg eod (prophylaxis) , since patient is on coreg 4/24/2020

5/21/2020 : tolerating well , no acute attack , increased allopurinol to 100mg daily

7/15/2020 : Doing well , Uric acid 5.9

Creatinine normal

Stop colchicine

- **How long he will need allopurinol 100mg daily ?**

Life long

	CREATININE
Ref. Range	Latest Ref Range: 0.67 - 1.17 MG/DL
9/27/2017 1031	1.43 * ▲
5/21/2018 2115	1.33 ▲
7/20/2018 0833	1.23 ▲
7/24/2018 0946	1.14
7/25/2018 0402	1.07
10/25/2018 1451	1.24 ▲
12/11/2018 1246	1.16 *
7/23/2019 0858	1.18 *
1/8/2020 0000	1.29 * ▲
3/12/2020 1008	1.27 ▲
4/22/2020 1230	1.55 * ▲
5/22/2020 0915	1.20 ▲
7/7/2020 0955	1.07 *

Lab Results

Component	Value	Date
TSH	2.530	03/12/2020

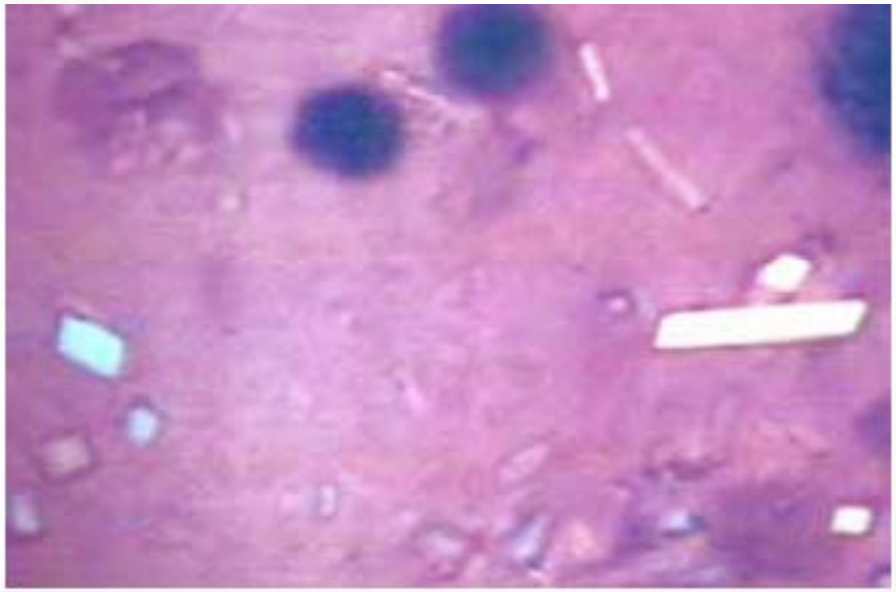
Lab Results

Component	Value	Date
SED	14	03/12/2020
SED	33 (H)	01/14/2020

	Ref. Range	1/14/2020 10:57	3/12/2020 10:08	4/22/2020 12:30	5/22/2020 09:15	7/7/2020 09:55
URIC ACID	Latest Ref Range: 3.0 - 8.2 MG/DL	6.1	8.3 (H)	8.3 (H)	6.8	5.8

CPPD

- Calcium pyrophosphate Crystal Deposition Disease (CPPD) is the syndrome secondary to the calcium pyrophosphate deposition in Hyaline and fibrocartilage as well as in periarticular structures



Etiology of CPPD

1. Post traumatic
2. Associated with Metabolic abnormality
   - Hyperparathyroidism
   - Low Mg, PO4
   - Haemochromatosis, Wilson's disease, Amyloidosis (storage disease)
   - Hypothyroid(weakly associated)
   - OA, Gout, previous joint surgery
3. Hereditary- autosomal dominant, early onset disease
   - Familial hypocalciuric hypercalcemia.
4. sporadic/idiopathic

- **Demographics:** It is predominantly a disease of the elderly, peak age 65 to 75 years old. It has female predominance (F:M, 2-7:1).
- Prevalence of chondrocalcinosis is unknown, Increasing radiogarphic chrondrocalcinosis

Clinical Manifestations

- Asymptomatic Chondrocalcinosis (radiographic deposition on cartilage)
- Acute CPPD : Pseudogout.
- Chronic CPPD Pseudo-RA
- OA with CPPD +/- acute flare
- CPPD in spine

Acute CPPD

- Usually presents with acute self-limited
- Monoarthritis resembling acute gout.
- knee is involved in 50% of the cases, followed by the wrist, shoulder, ankle, and elbow.
- Common in Post surgery, severe illness,

s/p parathyroidectomy

Pseudo OA

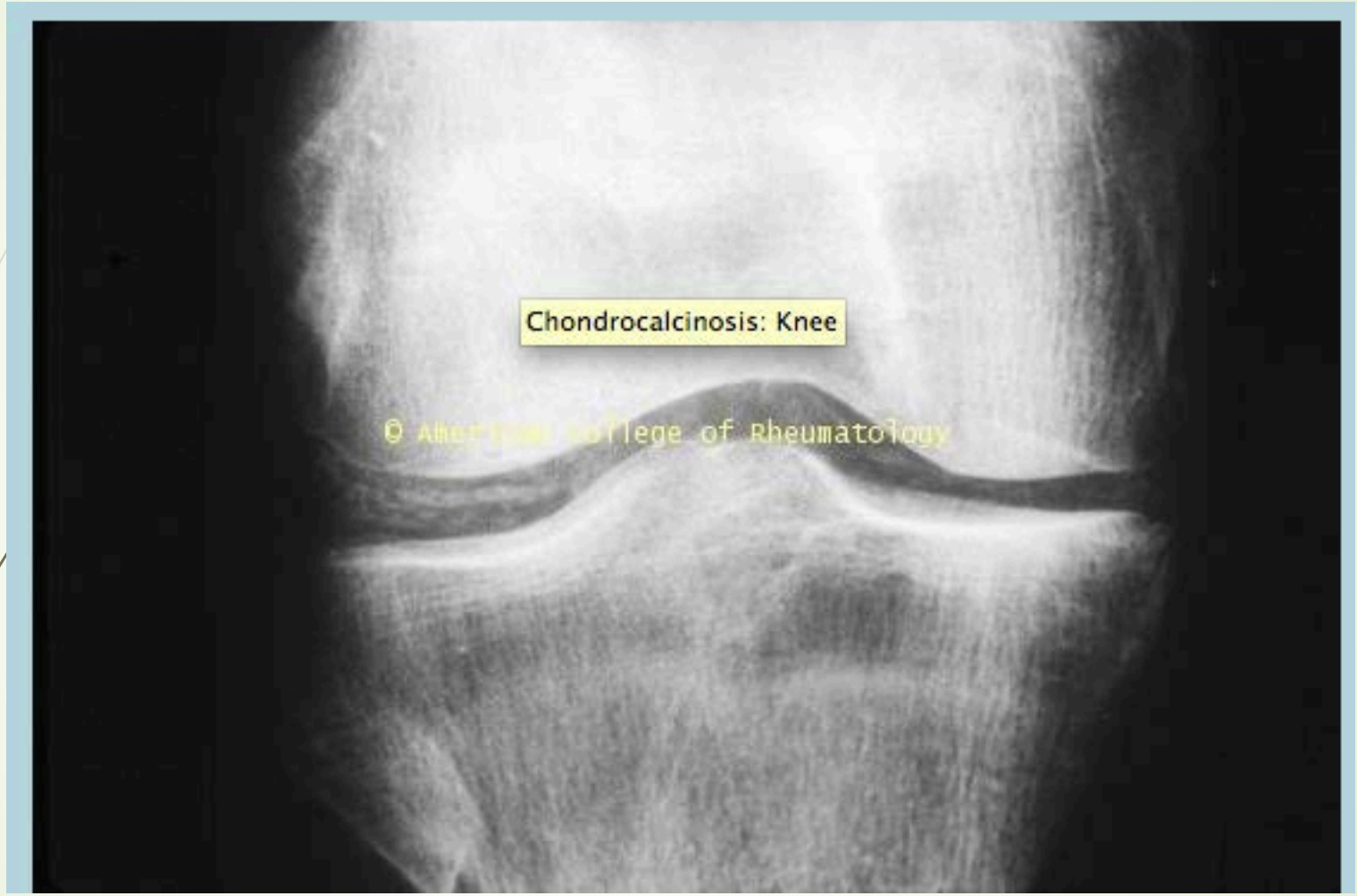
- severe, degenerative polyarthritis resembling OA.
- Gradual onset
- Most common site - knees
- second wrists, and Third in MCP
- Others hips, spine, shoulders, elbows and ankles.

Pseudo RA

- 5% CPPD
- Symmetric low grade inflammations ,stiffness
- RF can be positive in 10% (as normal population)
- No typical bony erosions like RA

Diagnostic Tests

- Synovial Analysis: Cell count>2000:
- Rhomboidal or rod like intracellular crystals.
- Imaging studies reveal chondrocalcinosis usually in the knee, but can be seen in the radial joint, symphysis pubis and intervertebral discs.
- Serum calcium, magnesium, phosphate
- Ferratin, TIBC, IRON
- TSH
- Alkaline phosphatase


Chondrocalcinosis: Knee
© American College of Rheumatology

Sonographic finding in CPPD

Presented by Dr Myint Myat Thway, MBBS, MD, RhMSUS, a member of MMPGA, University of Florida

TREATMENT

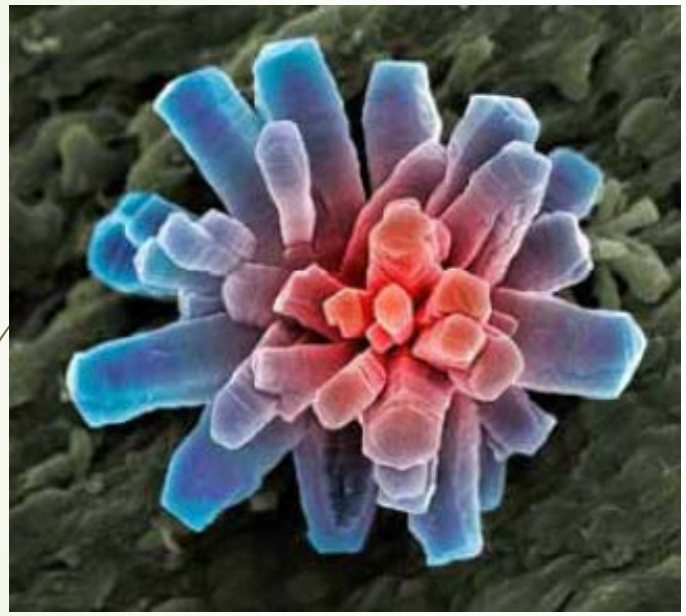
- unlike the situation with urate crystals, much of the pathogenesis of CPPD remains unclear and there are no pharmacological options to influence CPP crystal formation and dissolution, so treatment of CPPD is restricted to symptomatic control
- Joint Aspiration and fluid removal
- intraarticular corticosteroids.
- NSAID
- Colchicine can be used in acute attacks and also in prophylaxis for chronic CPPD .
- There is no specific treatment for chronic CPPD.
- It is important to treat secondary causes .

EULAR recommendations for calcium pyrophosphate deposition. Part II: Management *Ann Rheum Dis* 2011;**70**:571–575. doi:10.1136/ard.2010.139360

Table 2 LOE and SOR: order according to topic (general, acute attacks, prophylaxis and chronic CPPD management)

No	Proposition	LOE	SOR(95% CI)
1	Optimal treatment of CPPD requires both non-pharmacological and pharmacological modalities and should be tailored according to: Clinical features (isolated CC, acute, chronic CPP crystal inflammatory arthritis, OA with CPPD) General risk factors (age, comorbidities) The presence of a predisposing metabolic disorder	IV	93 (85 to 100)
2	For acute CPP crystal arthritis, optimal and safe treatment comprises application of ice or cool packs, temporary rest, joint aspiration and intra-articular injection of long-acting GCS. For many patients these approaches alone may be sufficient	IIa–IV	95 (92 to 98)
3	Both oral NSAID (with gastroprotective treatment if indicated) and low-dose oral colchicine (eg, 0.5 mg up to 3–4 times a day with or without an initial dose of 1 mg) are effective systemic treatments for acute CPP crystal arthritis, although their use is often limited by toxicity and comorbidity, especially in the older patient	Ib–IIb	79 (66 to 91)
4	A short tapering course of oral GCS, or parenteral GCS or ACTH, may be effective for acute CPP crystal arthritis that is not amenable to intra-articular GCS injection and are alternatives to colchicine and/or NSAID	IIb–III	87 (76 to 97)
5	Prophylaxis against frequent recurrent acute CPP crystal arthritis can be achieved with low-dose oral colchicine (eg, 0.5–1 mg daily) or low-dose oral NSAID (with gastroprotective treatment if indicated)	IIb–IV	81 (70 to 92)
6	The management objectives and treatment options for patients with OA and CPPD are the same as those for OA without CPPD	Ia	84 (74 to 94)
7	For chronic CPP crystal inflammatory arthritis, pharmacological options in order of preference are oral NSAID (plus gastroprotective treatment if indicated) and/or colchicine (0.5–1.0 mg daily), low-dose corticosteroid, methotrexate and hydroxychloroquine	Ib–IV	79 (67 to 91)
8	If detected, associated conditions such as hyperparathyroidism, haemochromatosis or hypomagnesaemia should be treated	Ib	89 (81 to 98)
9	Currently, no treatment modifies CPP crystal formation or dissolution and no treatment is required for asymptomatic CC	IV	90 (83 to 97)

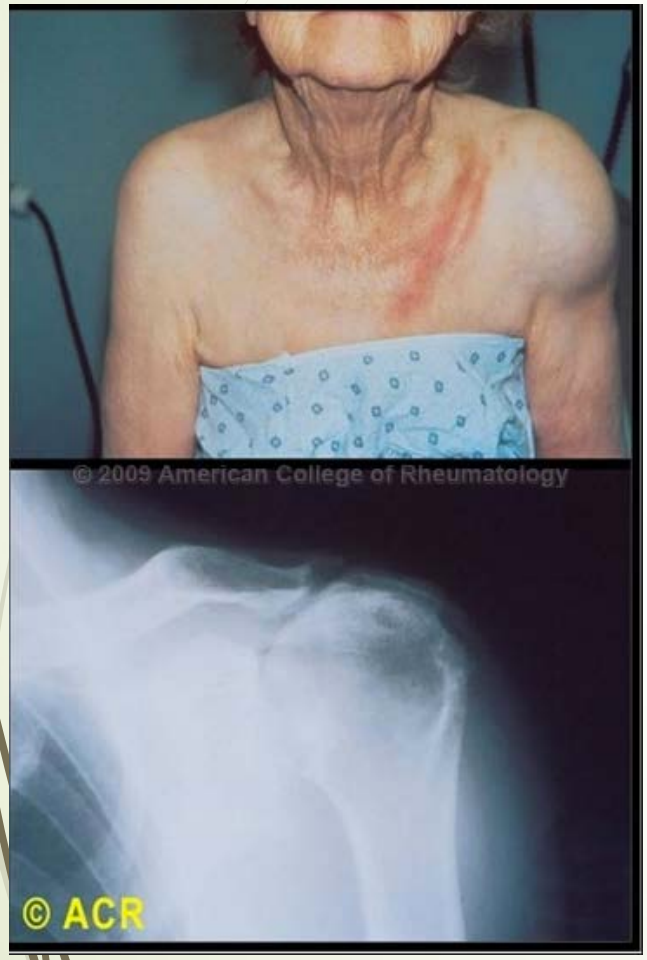
Basic Calcium Phosphate crystal Disease

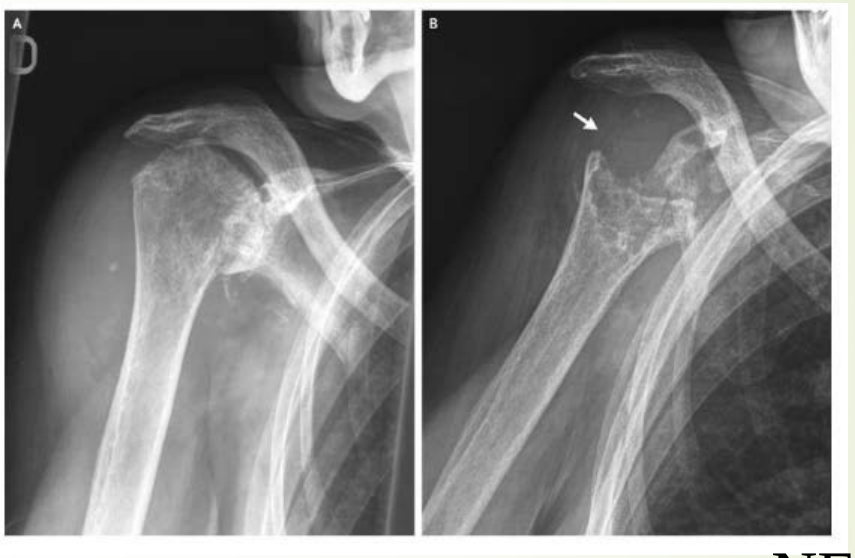


- may be asymptomatic
- BCP crystals can be found in > 50% of osteoarthritic joints
- They can cause acute arthritis or episodes or a chronic and highly destructive inflammatory arthritis (such as Milwaukee shoulder) or effect periarticular structures

- ***Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$***
- ***Carbonate apatite $Ca_{10}(PO_4)_6CO_3$***

Milwaukee Shoulder

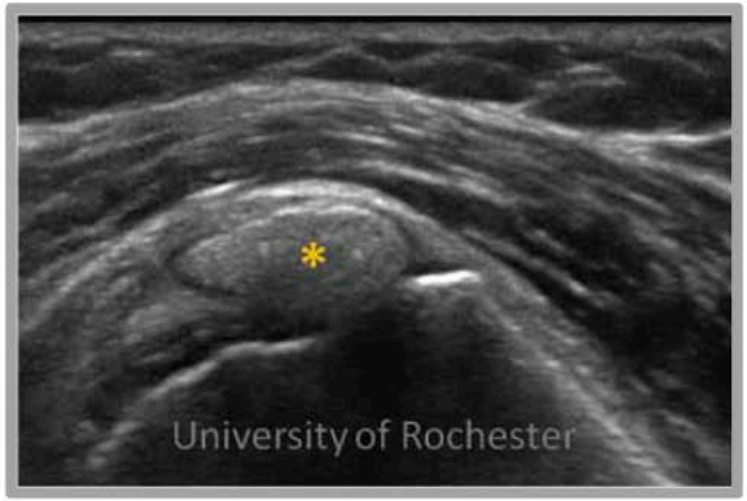


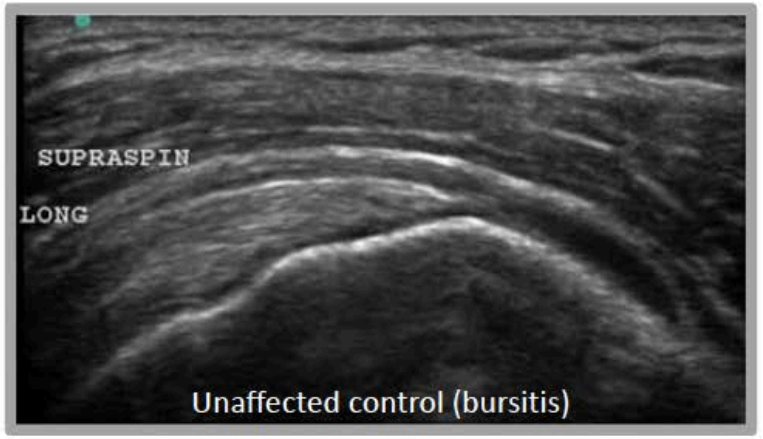


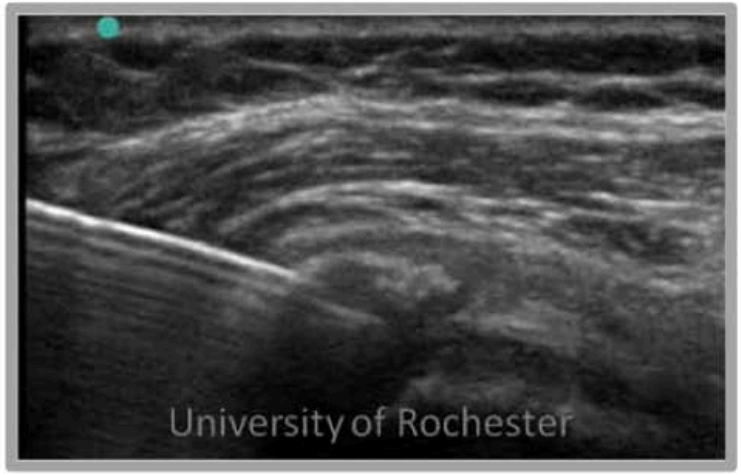
NEJ

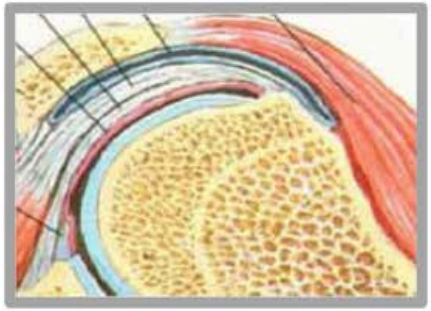
intraarticular or periarticular deposition of hydroxyapatite crystals and rapid destruction of the rotator cuff and the glenohumeral joint

Carbonate apatite disease: calcific tendinitis









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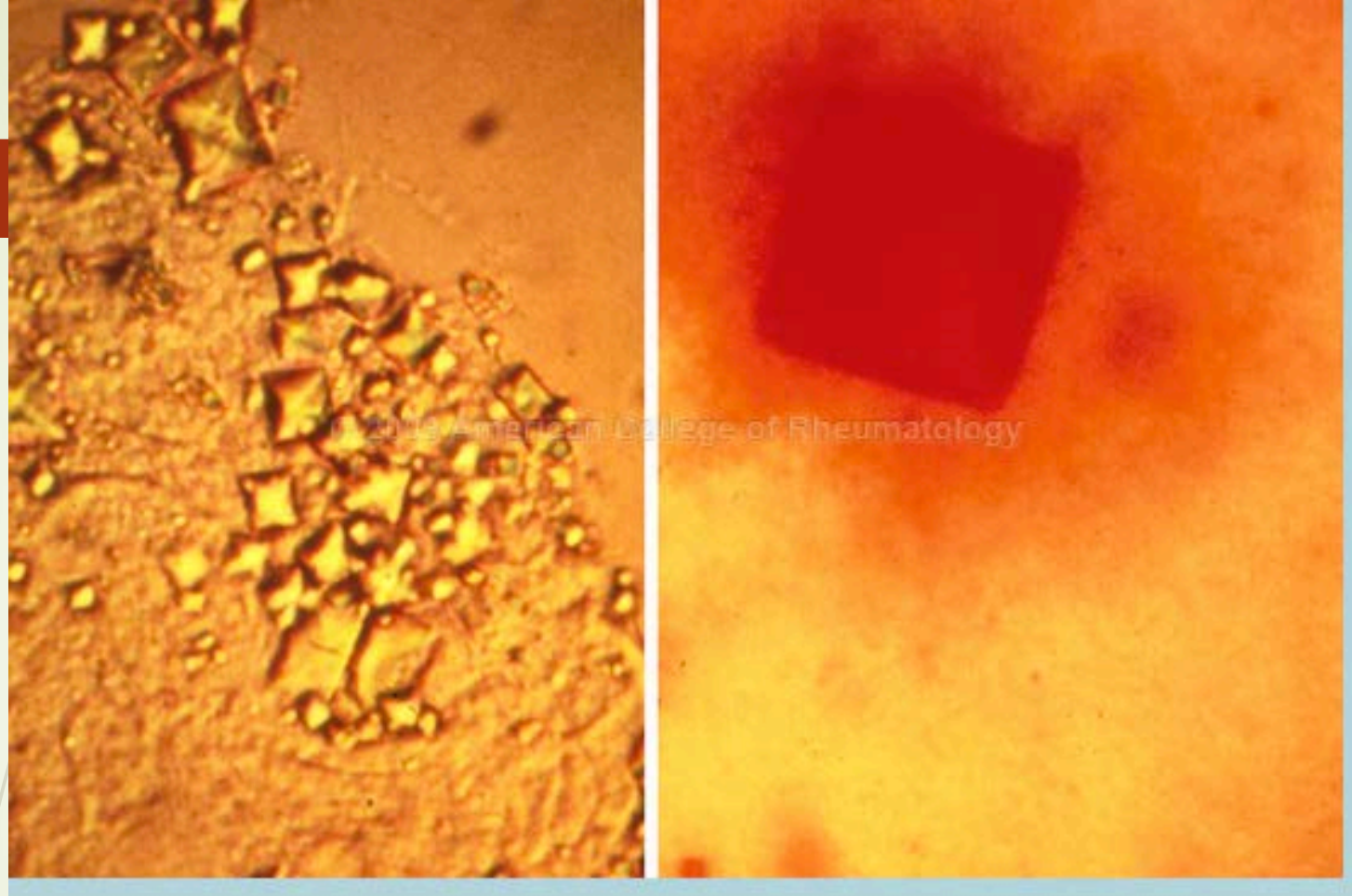
Slide ;Courtesy of Dr Thiele

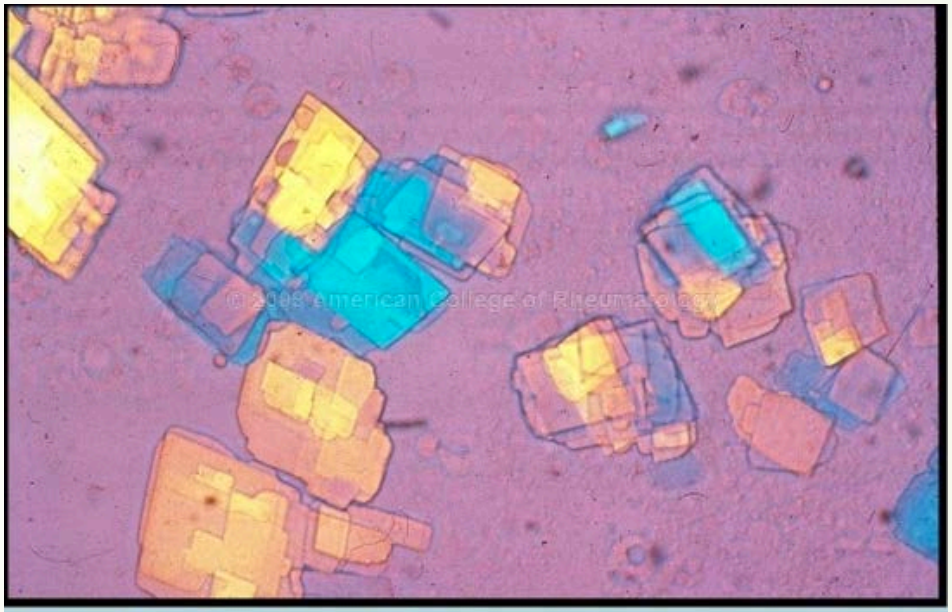


Details

Title: Calcium Oxalate Crystals

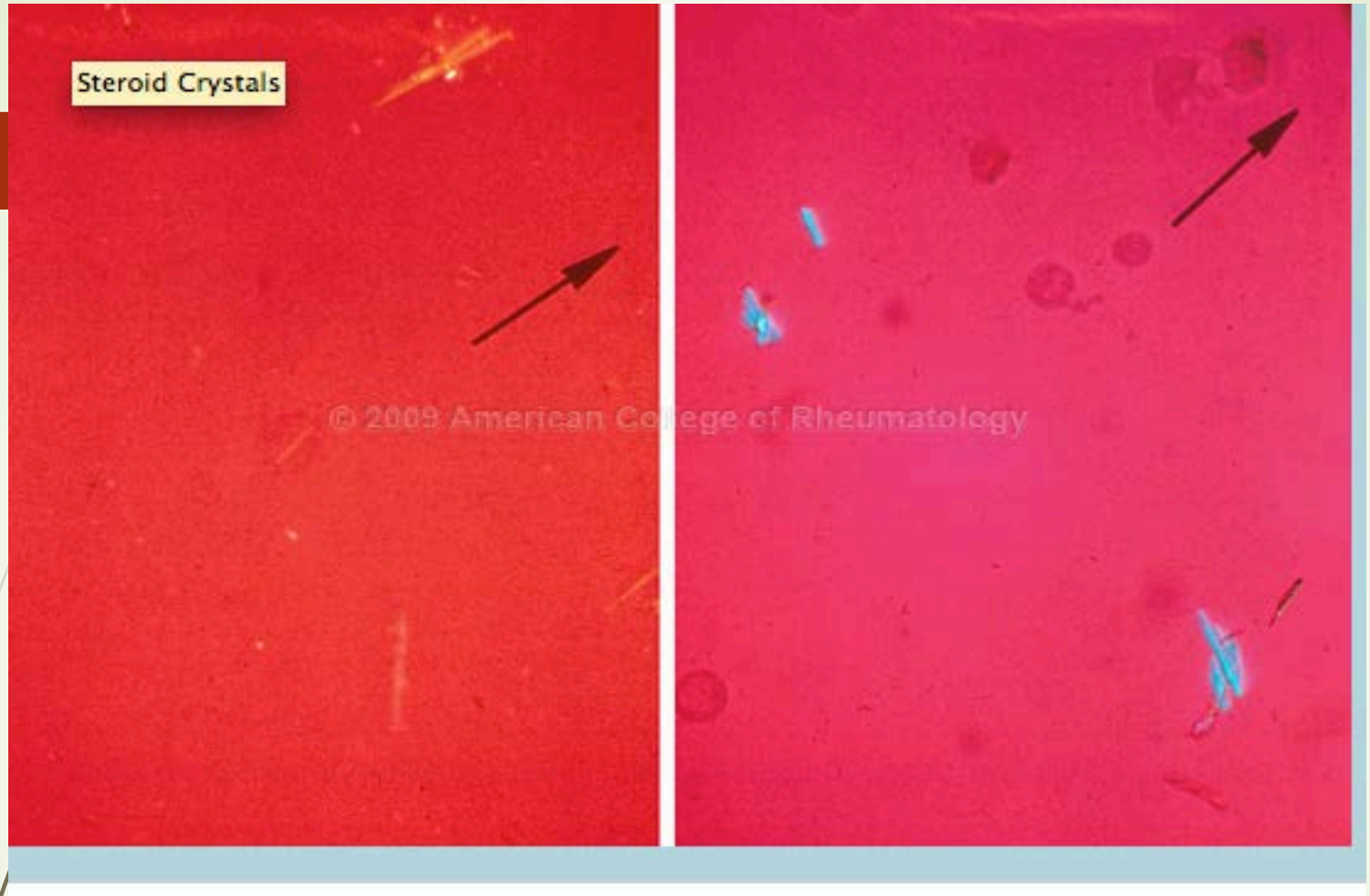
Description: Calcium oxalate crystals are seen in the synovial fluid from a patient with chronic renal failure who was receiving dialysis treatment. Left, Medium-power ordinary light microscopy shows the typical bipyramidal and envelope shapes of these crystals.

Others



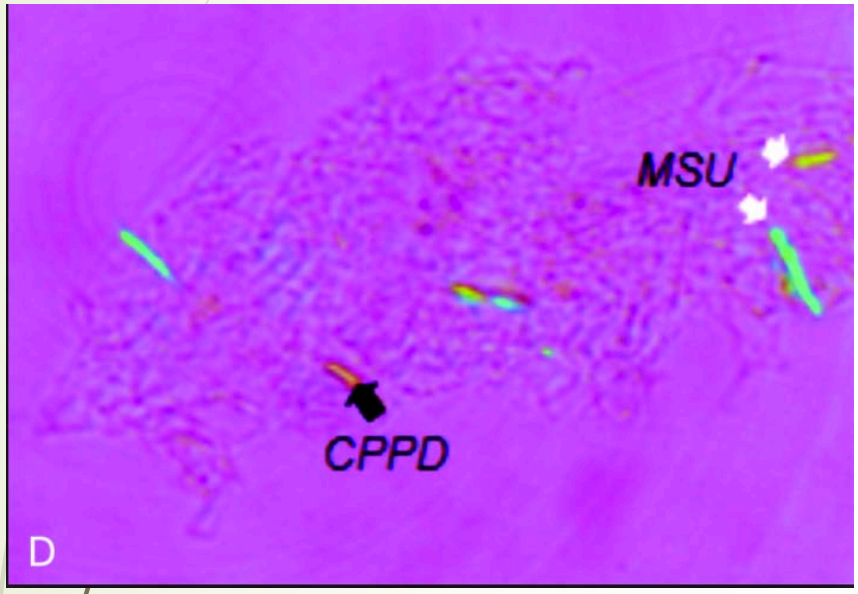
Details

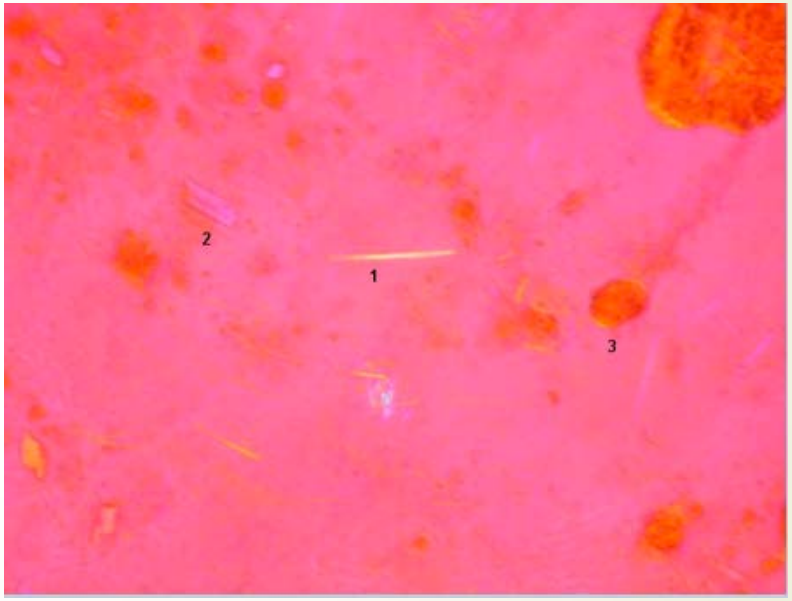
Title: Cholesterol Crystals: Synovial Fluid

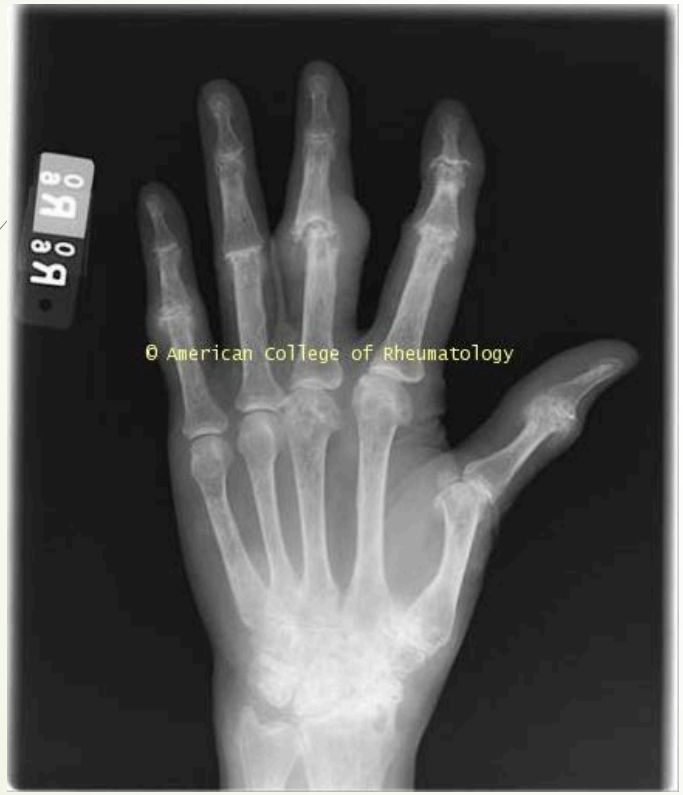


Birefringent and mimic MSU or CPPD.

One or more disease can coexist







- Triangular fibrocartilage calcification, scapholunate advanced collapse (SLAC) and narrowing of the 1st-3rd metocarpophalangeal joints with drooping osteophytes

- 3rd proximal interphalangeal joint (PIP)

  joint space loss, gull-wing deformity, and osteophyte formation.

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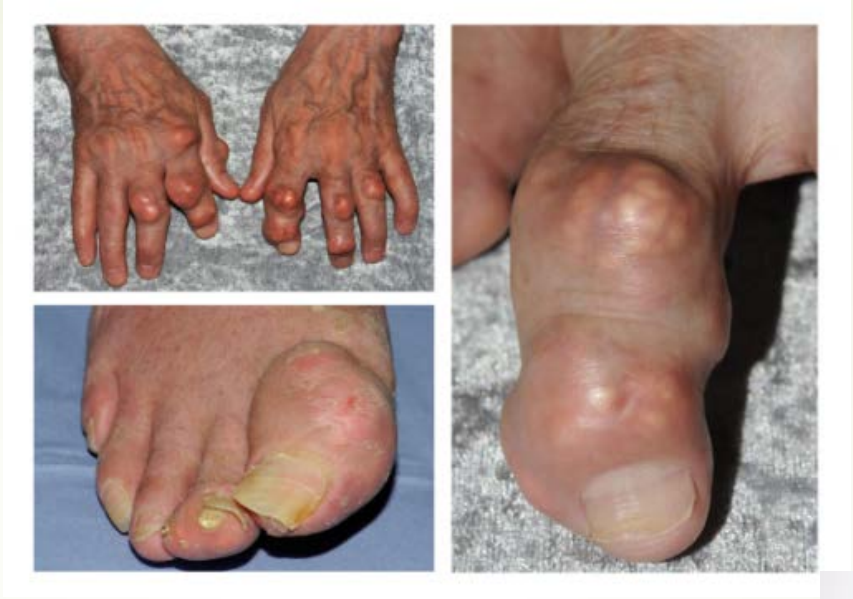

Thank you