

Gout

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Disclosures

Advisor for:

- ▶ Algorithm
- ▶ Bristol-Myer Squibb
- ▶ Janssen
- ▶ Lilly
- ▶ New bridge
- ▶ Novartis
- ▶ Pfizer
- ▶ Roche

▶ Investigator for:

- ▶ AbbVie
- ▶ Janssen
- ▶ New bridge

▶ Speaker for:

- ▶ Bristol-Myer Squibb
- ▶ Algorithm
- ▶ Janssen
- ▶ Pfizer
- ▶ Novartis
- ▶ Roche

Clinical Scenario

- ▶ Mr. Khalid is 55 year old gentleman. He presented to polyclinic with one day history of severe pain in his left big toe for one duration.





What do you want
▶ to know more?

- ▶ Fever? Other constitutional symptoms?
- ▶ Trauma ?
- ▶ Is it the first time ?
- ▶ Any history of joint pain currently?
- ▶ Any history of joint pain in the past ?

Any other questions ?

- ▶ Any history of new medication ?
- ▶ Any history of recent illness? Like diarrhea.



Case scenario

- ▶ There is no history of fever or trauma. He had a similar symptom in his other big toe last year but was not as bad.
- ▶ He has chronic low back pain for 3 years
- ▶ He has diabetes, hypertension, and dyslipidemia.
- ▶ He is a smoker and drinks alcohol occasionally when he has a chance.
- ▶ He is a retired banker and married with children.
- ▶ His current medications includes: tenoretic, Glucophage, aspirin, and Zocor. He has no drug allergies.

What do you
think he has ?



Definition

- ▶ Gout is a monosodium urate crystal deposition disease that is characterized biochemically by extracellular fluid urate saturation.

Epidemiology

- ▶ The prevalence is likely to exceed 3 percent of adults worldwide.
- ▶ The incidence rate is appreciable from age 30 in men and only after about age 50 in women.
- ▶ It affects males more than females. **In fact it rarely affect females prior to menopause.**

Risk Factors for Hyper-uricemia and Gout

Non modifiable risk factors

- ▶ Age
- ▶ Gender

Modifiable risk factors

- ▶ Obesity
- ▶ Hypertension
- ▶ Hyperlipidemia
- ▶ Ischemic cardiovascular disease
- ▶ Diabetes mellitus
- ▶ Chronic kidney disease
- ▶ Dietary factors
- ▶ Alcohol
- ▶ Medications altering urate balance

Natural History

- ▶ Hyperuricemia
- ▶ Acute gouty arthritis
- ▶ Inter-critical (or interval) gout
- ▶ Chronic articular and tophaceous gout

- ▶ The clinical manifestations of gout may include:
 - ▶ Recurrent attacks of acute inflammatory arthritis
 - ▶ Chronic arthropathy
 - ▶ Accumulation of urate crystals in the form of tophaceous deposits
 - ▶ Uric acid nephrolithiasis

Clinical manifestations

Typical Acute Attack

- ▶ Severe pain, redness, warmth, swelling, and disability.
- ▶ Maximal severity of the attack is usually reached within 12 to 24 hours.
- ▶ Complete resolution of the earliest attacks almost always occurs within a few days to several weeks, even in untreated individuals.
- ▶ Onset more often at night

Typical Acute Attack

- ▶ Lower-extremity involvement - **At least 80 %** of initial attacks (great toe or knee).
- ▶ Signs of inflammation extending beyond the confines of the joint that is primarily involved.
- ▶ sometimes accompanied by desquamation of the skin overlying the affected joint.

- ▶ The diagnosis of acute gout is most secure when supported by visualization of intracellular urate crystals by experienced examiners using compensated polarizing light microscopy in a sample of fluid aspirated from an affected joint (or bursa)

Diagnosis of Gout

- ▶ In the absence of the means to identify urate crystals or in the presence of a negative polarized light microscopic study, a tentative working diagnosis of gout may be made by a combination of clinical, historical, and laboratory criteria (Clinical diagnosis of gout). This method of diagnosis must be regarded as provisional and as much less specific. There are no validated clinical diagnostic criteria

Diagnosis of Gout

ACR-EULAR GOUT CLASSIFICATION CRITERIA#

Entry Criterion (Only apply criteria below to those meeting this entry criterion)	At least one episode of swelling, pain, or tenderness in a peripheral joint or bursa	<input type="checkbox"/> Y <input type="checkbox"/> N
Sufficient Criterion (If met, can classify as gout without applying criteria below)	Presence of MSU crystals in a symptomatic joint or bursa (i.e., in synovial fluid) or tophus	<input type="checkbox"/> Y <input type="checkbox"/> N
Criteria (to be used if Sufficient Criterion not met): <i>Score ≥8 required for classification as gout</i>	Categories	Score
Pattern of joint/bursa involvement during symptomatic* episode(s) ever	Joint(s) or bursa(e) other than ankle, midfoot or 1 st MTP (or their involvement only as part of a polyarticular presentation)	0
	Ankle OR midfoot (as part of monoarticular or oligoarticular episode without MTP1 involvement)	1
	MTP1 (as part of monoarticular or oligoarticular episode)	2
Characteristics of symptomatic episode(s) ever: i) Erythema overlying affected joint (patient-reported or physician-observed) ii) can't bear touch or pressure to affected joint iii) great difficulty with walking or inability to use affected joint	No characteristics	0
	One characteristic	1
	Two characteristics	2
	Three characteristics	3
Time-course of episode(s) ever: Presence (ever) of ≥2, irrespective of anti-inflammatory treatment: i) Time to maximal pain <24 hours ii) Resolution of symptoms in ≤14 days iii) Complete resolution (to baseline level) between symptomatic episodes	No typical episodes	0
	One typical episode	1
	Recurrent typical episodes	2
Clinical evidence of tophus: Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, located in typical locations: joints, ears, olecranon bursae, finger pads, tendons (e.g., Achilles).	Absent	0
	Present	4

CLINICAL

LAB	Serum urate: Measured by uricase method. Ideally should be scored at a time when the patient was not taking urate-lowering treatment and patient was beyond 4 weeks of the start of an episode (i.e., during intercritical period); <i>if</i> practicable, retest under those conditions. The highest value irrespective of timing should be scored.	<4mg/dL [$<0.24\text{mM}$] [†]	-4
		4-<6mg/dL [0.24-<0.36mM]	0
		6-<8mg/dL [0.36-<0.48mM]	2
		8-<10mg/dL [0.48-<0.60mM]	3
		≥10mg/dL [≥0.60mM]	4
	Synovial fluid analysis of a symptomatic (ever) joint or bursa:** Should be assessed by a trained observer.	Not done	0
		MSU negative	-2
IMAGING [‡]	Imaging evidence of urate deposition in symptomatic (ever) joint or bursa: Ultrasound evidence of double-contour sign [§] <i>or</i> DECT demonstrating urate deposition [§] .	Absent OR Not done	0
		Present (either modality)	4
	Imaging evidence of gout-related joint damage: Conventional radiography of the hands and/or feet demonstrate at least one erosion. ^{**}	Absent OR Not done	0
		Present	4

TOTAL SCORE

CLASSIFY AS GOUT? Y

(If met sufficient criterion or total score ≥8) N

* Symptomatic episodes are periods of symptoms that include any of swelling, pain, or tenderness in a peripheral joint or bursa.

† If serum urate <4mg/dL (0.24mmol/L), take away 4 points; if serum urate ≥4-<6mg/dL (≥0.24mmol/L - <0.36mmol/L), score this item as 0

**If polarizing microscopy of synovial fluid from a symptomatic (ever) joint or bursa by a trained examiner fails to show MSU crystals, take away 2 points. If synovial fluid was not assessed (not done), score this item as 0.

‡ If imaging not available, score these items 0.

§ Hyperechoic irregular enhancement over the surface of the hyaline cartilage that is independent of the insonation angle of the ultrasound beam (note: false positive DCS (artifact) may appear at the cartilage surface that should disappear with a change in the insonation angle of the probe).^{31,32}

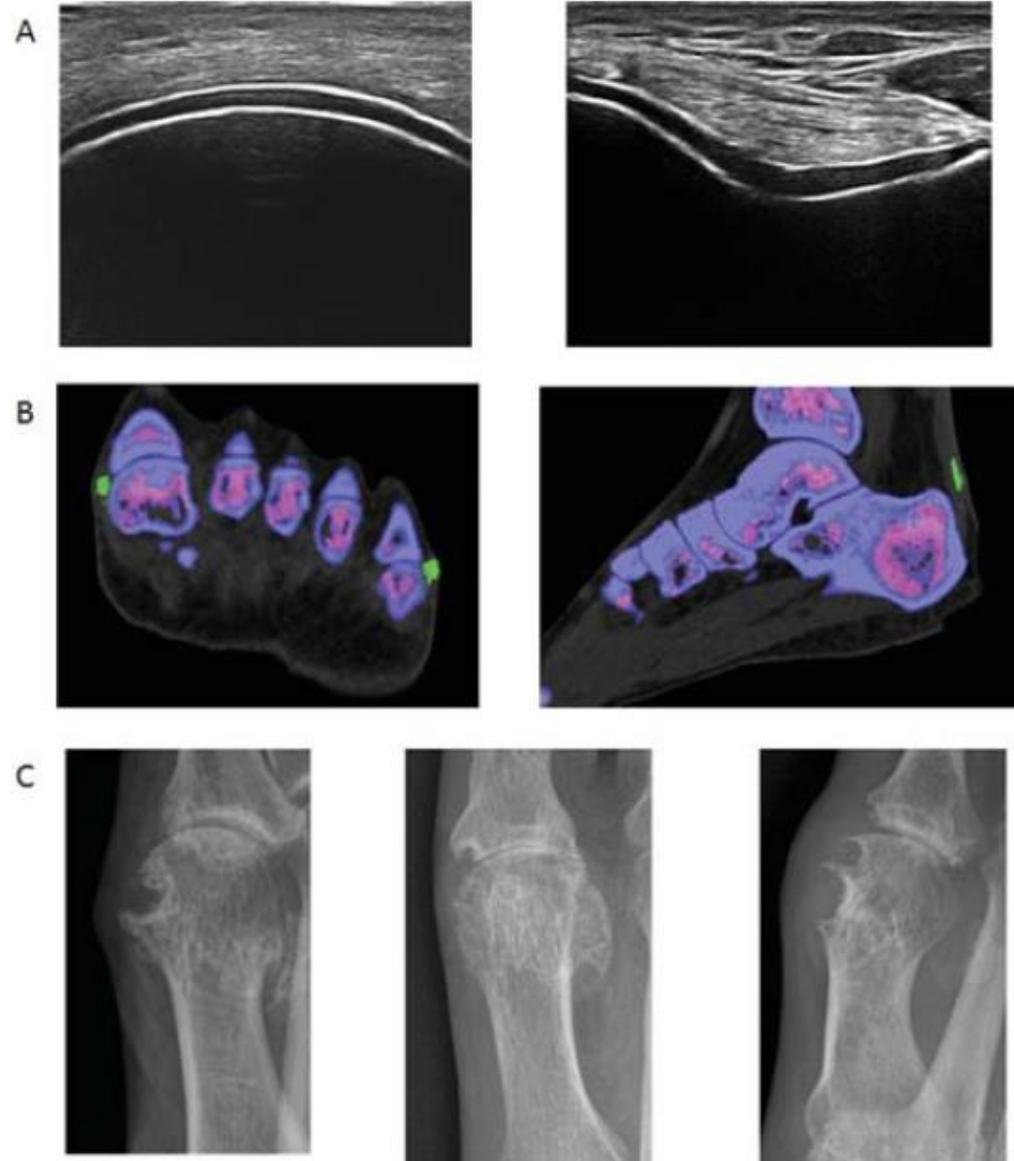
§ Presence of colour-coded urate at articular or peri-articular sites. Images should be acquired using a dual energy computed tomography scanner, with data acquired at 80 and 140 kV and analysed using gout-specific software with a two material decomposition algorithm which colour-codes urate.³³ A positive scan is defined as the presence of colour-coded urate at articular or peri-articular sites. Nailbed, submillimeter, skin, motion, beam hardening and vascular artefacts should not be interpreted as evidence of DECT urate deposition.³⁴

**Erosion is defined as a cortical break with sclerotic margin and overhanging edge; excluding DIP joints and gull wing appearance.

[#]Neogi, et al. *Arthritis & Rheumatology*. 2015;67(10):2557-2568.

Neogi, et al. *Annals of the Rheumatic Diseases*. 2015;74(10):1789-1798.

Imaging features of Gouty arthritis



Management of Gout

- ▶ General principles:
 - ▶ Treatment should start as soon as possible after the patient perceives the beginning of an attack.
 - ▶ Urate-lowering therapies are of no benefit for acute gout and should generally not be initiated during an acute attack.
 - ▶ the urate-lowering medication should be continued without interruption in patients already receiving these agents.
 - ▶ Important comorbidities (and their ongoing therapies) that are frequent among gout patients may affect drug safety or effectiveness, especially in older patients.

Treatment of acute gout

Initial Treatment Choices

- ▶ Non-steroidal anti-inflammatory drug (NSAID)
 - ▶ naproxen (500 mg Bid daily) or indomethacin (50 mg TiD)
 - ▶ the total duration of NSAID therapy for an acute attack is five to seven days
- ▶ An oral low-dose colchicine regimen
 - ▶ Colchicine 0.5 mg Tid or Bid
 - ▶ Start 0.5 mg Tid for the first day the 0.5 Bid till resolution of symptoms
- ▶ Glucocorticoids
 - ▶ Oral, intra-articular or parental
 - ▶ Prednisolone 30 mg daily (in divided doses) for 5 days.
 - ▶ Intramuscular Methylprednisolone (depo-medrol) 40 to 60 mg once and may be repeated in 48 hours.

Treatment of hyperuricemia (Prevention of recurrent gout)

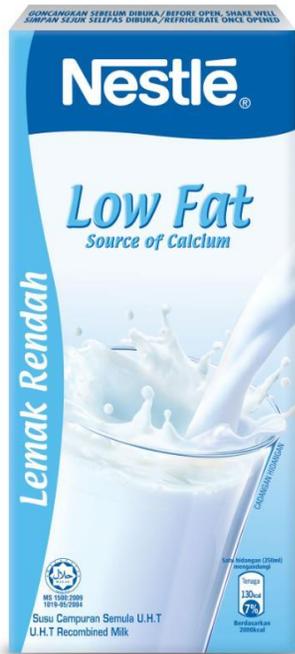
Management principles

- ▶ Identification of reversible causes of hyper-uricemia
 - ▶ dietary changes, weight loss, reduction in alcohol intake, and substitution of medications that may cause hyper-uricemia
- ▶ Management of comorbid diseases common in patients with gout
 - ▶ hypertension, chronic renal functional impairment, cardiovascular disease, and the components of the metabolic syndrome
- ▶ The need for pharmacologic urate-lowering therapy
 - ▶ Allopurinol, febuxostat, probenecid, pegloticase
- ▶ Prophylactic therapy, primarily to reduce the recurrence of acute attacks of gout during initiation of urate-lowering therapy
 - ▶ Colchicine, NSAIDS, corticosteroids

Food items rich in purine (causing hyper-uricemia)



Food items lowering serum urate.



Prophylactic treatment



This part of the management to prevent recurrent attacks of gout.



It does not lower the uric acid



Treatment options:

Colchicine 0.5 mg twice daily

NSAIDs

Low dose prednisolone (10 mg daily)

Indications for pharmacologic urate-lowering therapy in patients with a history of gout are:

- ▶ Frequent or disabling attacks of gouty arthritis
- ▶ Clinical or radiographic signs of chronic gouty joint disease (gouty arthropathy)
- ▶ Tophaceous deposits in soft tissues or subchondral bone
- ▶ Gout with renal insufficiency
- ▶ Recurrent uric acid nephrolithiasis

The background features abstract, overlapping geometric shapes in various shades of green, ranging from light lime to dark forest green. These shapes are primarily located on the left and right sides of the frame, leaving a large white central area. The shapes are layered, creating a sense of depth and movement.

Please, long story short

How treat a patient who needs treatment?

1. NSAIDs, or steroid or colchicine for 5 - 7 days (on day one)
2. Colchicine 0.5 mg twice daily for a long time (how long ??)
3. Allopurinol or febuxostat (2 weeks after resolution of the flare and start low dose (100 mg daily and titrate up every one to two weeks to target uric acid level which is 350 micromol/L or 300 micromol/L.

- ▶ Regarding colchicine prophylactic, stop treatment when you reach the target uric acid and stay on target for 3 to 6 months.

Febuxostst

- FDA and EMEA Approval: Treatment of chronic hyperuricemia in conditions where urate deposition has already occurred
- No dose adjustment required in the elderly nor in patients with mild to moderate liver or renal impairment
- Liver tests should be monitored initially
- Available as: 80mg & 120mg

Safety

- Undesirable Effects of Adenuric[®]:
 - The treatment-related events were mostly mild or moderate in severity
 - The most frequent treatment-related events were:
 - Abnormalities of liver function tests (3.5%)
 - Diarrhea (2.7%)
 - Headache (1.8%)
 - Nausea (1.7%)
 - Rash (1.5%)

Take home messages

Do not start

Do not start allopurinol for patient with acute gout.

Do not order

Do not order urate level for a young woman with joint pain.

Do not treat

Do not treat asymptomatic hyperuricemia.

Do not order

Do not order uric acid for a patient with back pain.

Refer

Refer the patient to rheumatology when you need help.

Questions ?

Thank You

The background features abstract, overlapping geometric shapes in various shades of green, ranging from light lime to dark forest green. These shapes are primarily located on the right side of the frame, creating a modern, layered effect against the white background.