The Office of Lifelong Learning, the Division of Rheumatology & the Physician Learning Program

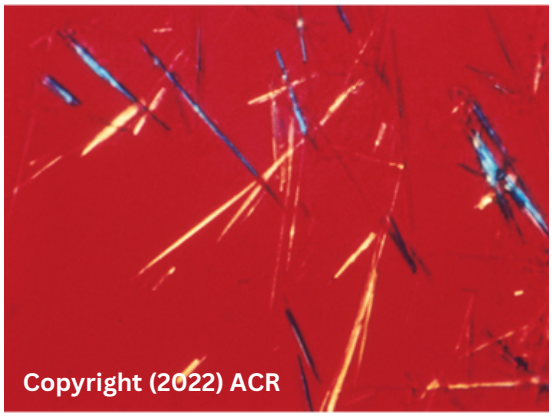
Rheumatology Revealed: Updates on Common Diseases and Referral Tips for Family Physicians | Pearls for practice

Advancing Gout Care: Latest Updates in Diagnosis, Management, and Effective Referral Practices for Family Physicians

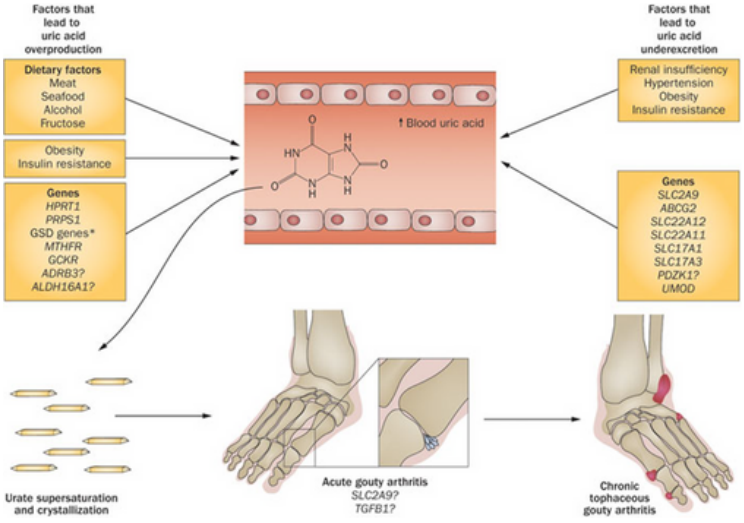
Dr. Andrea Johnson

Gout

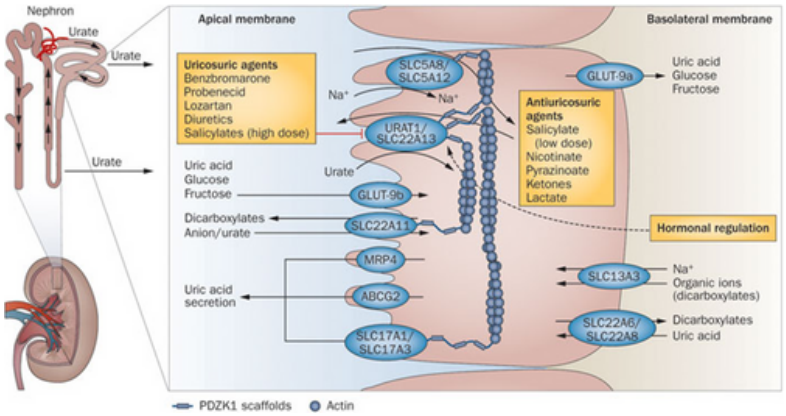
- **Monosodium urate crystal formation:**
  - **Joints (inflammatory arthritis, erosive arthropathy)**
  - **Tophaceous deposits**
  - **Kidneys (uric acid nephrolithiasis)**
- **Hyperuricemia**
  - **>360 mmol/L, solubility threshold (not lab threshold!)**
  - **Problem of overproduction, underexcretion, or combination**



Genetics of Gout and Hyperuricemia



Reginato, Anthony & Mount, David & Yang, Irene & Choi, Hyon. (2012). The genetics of hyperuricemia and gout. Nature reviews. Rheumatology. 8. 610-21. 10.1038/nrrheum.2012.144



Non-modifiable risk factors

- **Age**
- **Sex**
  - **M>F pre-menopause**
  - **M=F post-menopause**
- **Ethnicity**
  - **OR 2.62 Asian vs White individuals**
- **Genetic variants (ie inherited defects of purine metabolism or excretion)**

Modifiable risk factors

- **Comorbidities:**
  - **Obesity, hypertension, dyslipidemia, diabetes mellitus**
  - **Chronic kidney disease**
  - **Diseases associated with increased cell proliferation (ex myeloproliferative disorders, tumor lysis syndrome etc)**
- **Medications**
  - **Ex: diuretics (especially hydrochlorothiazide), ASA, calcineurin inhibitors**
- **Dietary factors**
- **Alcohol consumption**

*Yokose C, McCormick N, Lu N, Tanikella S, Lin K, Joshi AD, Raffield LM, Warner E, Merriman T, Hsu J, Saag K, Zhang Y, Choi HK. Trends in Prevalence of Gout Among US Asian Adults, 2011-2018. JAMA Netw Open. 2023 Apr 3;6(4):e239501. doi: 10.1001/jamanetworkopen.2023.9501. PMID: 37083663; PMCID: PMC10122173

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2020 American College of Rheumatology Guideline for the Management of Gout.

Asymptomatic Hyperuricemia

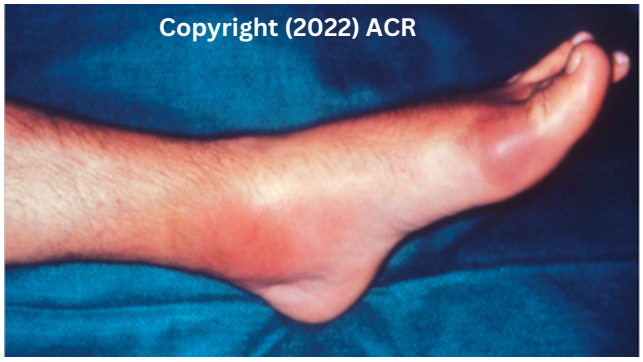
- **Recent studies have questioned treating asymptomatic hyperuricemia as it can be associated with increased CV risk, CKD risk and development of gout - ultimately this is NOT guideline based (yet!)**
- **More studies needed before this impacts clinical practice…**

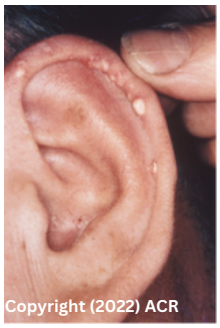
> patients with asymptomatic hyperuricemia (SU >6.8 mg/dl with no prior gout flares or subcutaneous ophi), we conditionally recommend *against* initiating any pharmacologic ULT (allopurinol, febuxostat, robenecid) over initiation of pharmacologic ULT.

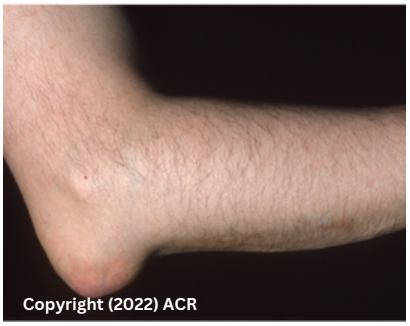
FitzGerald JD, et.al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care Res (Hoboken). 2020 Jun;72(6):744-760. doi: 10.1002/acr.24180.

Classic Gout Flare

- **Acute onset: exquisitely tender, warm, red, swollen joint**
- **Often after trigger (specific food/alcohol, fluid shifts, medication change)**
- **Typically monoarticular (~80%), although can affect periarticular area, bursae, dactylitis etc**
- **Most commonly: 1st MTP**
  - **commonly lower extremity: ankle, midfoot, knee**
  - **can involve other joints (hands, wrists, elbows etc)**
- **Flare self-limited and resolves within couple weeks, faster with treatment**
- **Typically monoarticular (~80%),**
  - **Commonly periarticular area - diffuse soft tissue swelling affecting tendons, bursae, dactylitis etc**
  - **Often can appear similar to SSTI**
  - **Oligoarticular or polyarticular also possible**
- **Migratory pattern**
- **Tophi is a great clue!**
  - **Ears, elbows, extensor surfaces**
- **Flare doesn't resolve when colchicine or abortive therapy is <u>not started soon enough</u>**





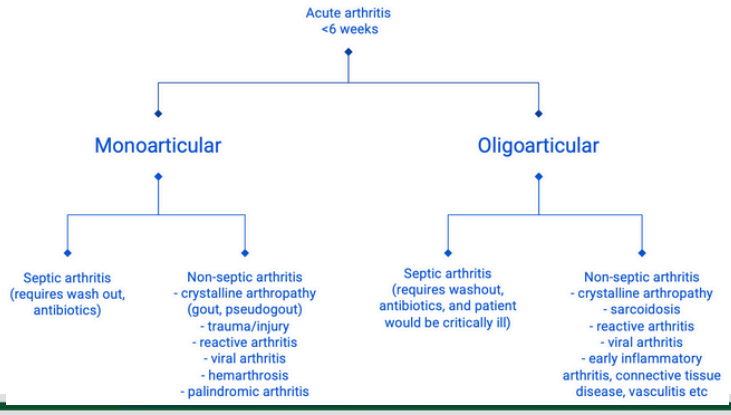


Investigations

- **Bloodwork:**
  - **Baseline: CBCd, ALT, Creatinine**
  - **Serum urate***
  - **Signs of inflammation:**
    - **elevated CRP, WBC, Plt**

***urate during flare is not reliable (often falsely LOW during gout flare)**

Acute Arthritis Differential Diagnosis



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Hot tips- URATE

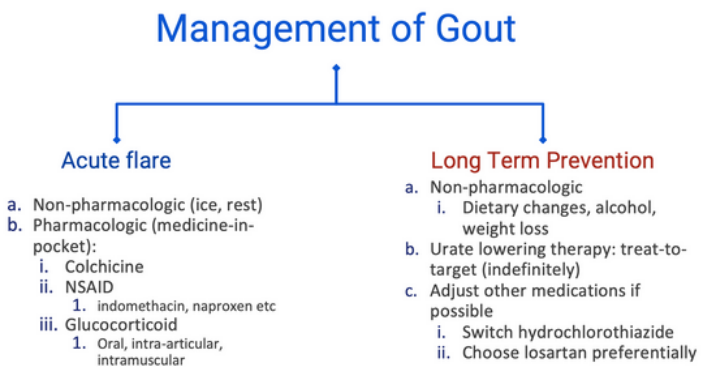
- **Urate is NOT reliable during an acute gout flare**
- **Urate often inappropriately LOW in acute gout flare - don't be fooled!**
- **Recheck urate again a couple weeks after flare has settled for more accurate picture of their "equilibrium state"**
- **Urate lab "normal value" sometimes is still not at target**
- **Urate normal value in most labs reported at <500**
  - **Note: this is higher than our goal of <350**
  - **Even a "normal" urate can sometimes be too high!**

Hot tips- JOINT ASPIRATE

- **OR of septic arthritis increases from 2.9 to 7.7 to 28 as synovial WBC increases from 25000, 50000, 100000**
- **Crystal presence does NOT exclude the possibility of CONCURRENT septic arthritis**
- **When in doubt: treat both and get a tap**

Margaretten ME, Kohlwes J, Moore D, Bent S. Does This Adult Patient Have Septic Arthritis? JAMA. 2007;297(13):1478–1488. doi:10.1001/jama.297.13.1478

Management of Gout



Investigations

- **Joint aspirate: best test to assess for active gout flare**
- **Send for: Cell count, Crystals, Culture**
  - **Inflammatory (WBC usually 10,000-60,000)**
  - **Culture negative**
  - **Crystals: monosodium urate (negatively birefringent, needle-shaped)**
    - **Within inflammatory cells particularly specific**

Investigation Summary

- **Bloodwork:**
  - **Baseline: CBCd, ALT, Creatinine**
  - **Serum urate***
  - **Inflammation: elevated CRP, WBC**
- **Joint aspirate:**
  - **Inflammatory (WBC usually 10,000-60,000)**
  - **Culture negative**
  - **Crystals: monosodium urate (negatively birefringent, needle-shaped)**
- **Imaging:**
  - **X-ray: ?erosions from chronic gout**
  - **Ultrasound (tenosynovitis, synovitis, tophi), dual energy CT…**

Acute flare management

- **Colchicine 0.6 mg po BID for duration of flare**
  - **Loading dose not necessary**
  - **Immediate abortive therapy important for first dose**
  - **Ensure it is for duration of therapy or else often rebound flare after stopping**
  - **More specific for gout, but also effective for pseudogout**
    - **Helps differentiate from other causes if absolutely no response**
- **Other NSAID ie: Indomethacin, diclofenac, naproxen**
  - **Usually higher side effects (GI, AKI, HTN etc)**
  - **But effective if unclear etiology: ie ?reactive arthritis, sarcoidosis, gout - usually treats all**
- **Glucocorticoids: for severe flare**
  - **Oral: Consider prednisone 20-30 mg daily x3-5 days, taper by 5-10 mg every 3-5 days until off**
    - **-Ie severe flare: prednisone 30 mg daily x5 days, then decrease by 10 mg every 5 days until off**
  - **IM: If oral taper is challenging: Depomedrol IM 40-80 mg IM x1 reasonable, as it would then self taper over coming weeks**
  - **Intra-articular injection:**
    - **Depomedrol 40-80 mg IA no more frequent than every 3 months into the same joint**

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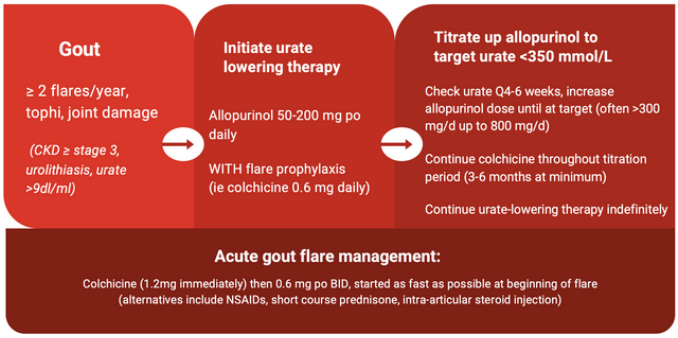
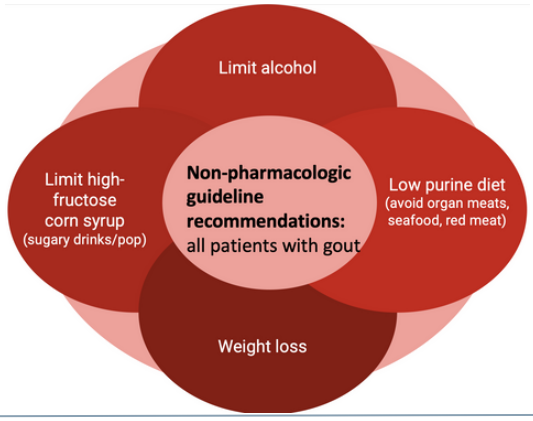
Indications to start rate-lowering therapy

- ≥ 2 flares/year
- Tophi
- Evidence of joint damage on imaging
- Conditionally recommended if:
  - CKD stage ≥ 3, Urolithiasis or urate >9dl/ml (535 µmol/L)
- First line choice: allopurinol



Referral to Rheumatology

- Not required if diagnosis is not in doubt
- Referral appropriate if:
  - Another Rheum disease is in question
  - Failed first line urate-lowering treatment (with dose escalation) or intolerance/hypersensitivity with allopurinol (other agents febuxostat etc may be considered)



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Hot tips- Allopurinol

- Allopurinol CAN be started during a flare (And often this is a great time to capitalize on starting preventative therapy)
- Always start allopurinol with prophylaxis i.e colchicine 0.6 mg daily for duration of titration (usually this is a period of 3-6 months)
- Allopurinol must be titrated up, usually Q4-6 weeks, with most patients requiring 300-500 mg daily, (max 800 mg daily)
- Risk in setting of CKD is often overstated, but be aware that patient may be at higher risk of hypersensitivity.
  - Just start at a lower dose (ie 50 mg daily), and monitor: CBCd, Cr, ALT, CRP, urate Q4W
- Allopurinol is to be continued indefinitely for ongoing control of disease, otherwise hyperuricemia will return

Clinical Pearls

- Asymptomatic hyperuricemia is an up and coming topic, but do not treat yet
- Urate lab value can be “inappropriately low”:
  - in a flare (don’t be fooled by low urate)
  - Lab value normal urate often reported normal <500. Remember the key <350 target
- Synovial aspirate interpretation to assess for septic arthritis (JAMA reference)
  - Be wary of concomitant septic arthritis with gout flare (Just because there’s crystals on aspirate doesn’t mean it isn’t septic!)
  - Other mimikers: palindromic rheumatism, sarcoidosis, pseudogout, reactive arthritis, viral arthritis
- Allopurinol initiation:
  - ok to start in a flare, requires prophylaxis with colchicine/NSAID, titration is required in most, with monthly monitoring labs, careful in CKD, but still okay to use with lower dose at first and monitoring, don’t stop allopurinol
- Colchicine trial of therapy can be helpful, but has to be started quickly to abort a flare
- Don’t pop tophi or try to express urate crystals - big nidus of infection

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