

GOUT

Pathophysiology

- At physiologic pH (7.4), most uric acid is in ionized form of urate.
- Unlike other mammals, humans lack enzyme "uricase" that converts ionized urate to soluble allantoin
- Primarily secreted by kidneys, actively and passively
- Below level of 6.8 mg/dL, crystals are unlikely to form.
- Up to 20% of population may have hyperuricemia. Only about 4% have gout. So screening for hyperuricemia is not recommended

At Risk populations

- Men after puberty
- Women after menopause
- CKD
- HTN, Diabetes

Acute Flare Presentation

- red-hot-angry joint over 12-24 hours (very fast peak time!). Pain lasts up to 14 days
- Exquisite tenderness – even touch of soft bedsheet causes pain
- After 1st MTP, other foot, ankle and knee joints are commonly involved
- Serum urate level may be low during active flare
- If redness expands beyond the involved joint, consider cellulitis in differential

Chronic recurrent / Tophaceous gout

- Long term ineffective therapy → chronic synovitis between attacks → permanent joint damage (tophi formation, bone erosions, skin ulceration, disability)

Acute Flare Management

- NSAIDs – first line – obviously avoid in CKD.
 - topical NSAIDs?
- Colchicine – doable even with CKD3 – generally less effective the longer the flare lasts
 - Has become very expensive in US for gout treatment.
 - Avoid CYP3A4 inhibitors
 - Can't use for flares if already using for prophylaxis
- Systemic Steroids – avoid in diabetics (hyperglycemia)
- Steroid injection – good for single joint therapy in patient, especially who can't tolerate other therapies
- TIP: for systemic therapies, treat for at least 10 days to prevent rebound.

Uric Acid Lowering Therapies (ULT)

- These strategies don't have strong evidence but are recommended by American college of rheumatology
- Keep uric acid below 6 for 12 months to really have a good regimen.
- Allopurinol (1st line)
 - Start with 100 mg daily. Increase to 300 mg over 4 weeks. [low starting dose helps with allopurinol hypersensitivity syndrome – associated with HLA-B5801 allele]
 - Check uric acid level after 4 weeks. Titrate dose further as needed
 - Start at 50 mg for CKD 4
- Probenecid – cheap, safe, effective. Increases urinary excretion. biggest problem is pill burden. May need 5-6 pills at a time
- Pegloticase (pegylated uricase – enzyme that we lost as species – currently 3rd line agent for tophaceous gout)
- Febxostat – similar to allopurinol. Possibly worse overall and cardiovascular mortality. Reserve for patients who can't tolerate allopurinol.
- Anti-inflammatory prophylaxis with ULT. Use NSAIDs or colchicine for 6 months. Maybe even low-dose prednisone. Don't forget about GI prophylaxis for long-term NSAID. Note: anti-inflammatory therapy is not meant for long term. This can falsely mask high uric acid levels.

Urate level in suspected acute gout flare

- Differential here would include septic and other crystal arthropathies
- While high urate level is useless (20% of people will have high levels), level less than 4 is very reassuring and can rule out gout
- However, still will probably need to tap the joint to rule out septic arthritis

Microscope

- Needle shape crystals.
- Color change of yellow to purple when turned 90 degrees.