Gout

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Case 1

- A 64 year old lady with longstanding hypertension and 2 year history of angina comes to see you for a routine visit and refill of her meds. She's a current non-smoker with a BMI of 33
- You're treating her with metoprolol 95mg/d, bendrofluazide 2.5 mg/d, aspirin 100 mg/d, quinapril 10 mg/d and simvastatin 20 mg nocte
- You've recently been to an update on Rheumatology so you check a uric acid along with her routine bloods

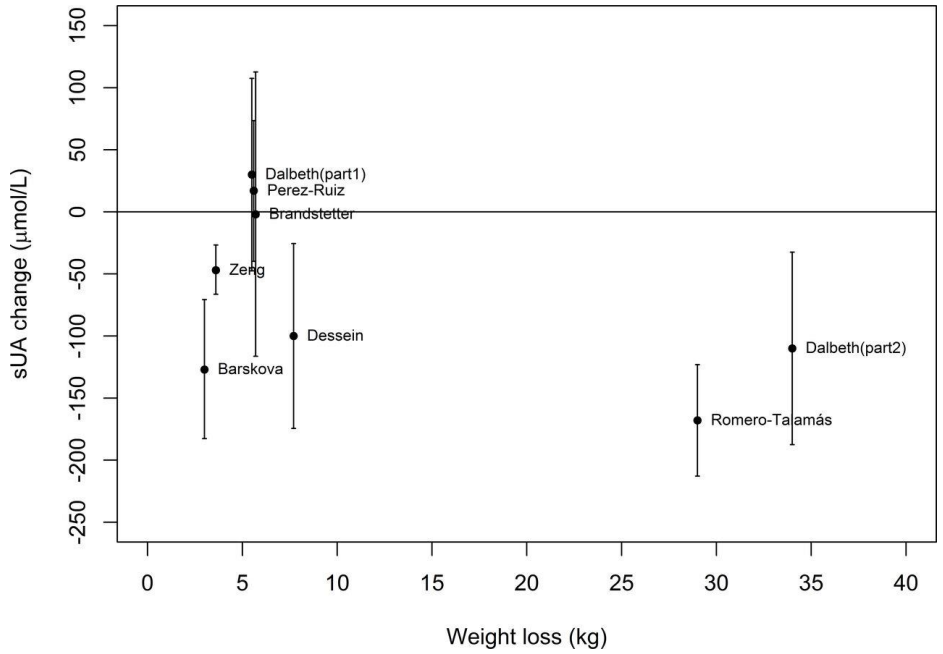
Case 1

- Her uric acid is 0.49 mmol/l. Apart from a creatinine of 112 mmol/l the rest of her bloods are normal
- So do you:
  - 1. stop her aspirin
  - 2. switch her simvastatin to atorvastatin
  - 3. observe
  - 4. Stop her bendrofluazide

Case 1 – 6 months later

- You've stopped her bendrofluazide, increased the quinapril, switched to atorvastatin and got her to drink more water and you repeat her uric acid.
- It's 0.55 mmol/l so do you
  - Refer to Rheumatology
  - Get her to lose weight
  - Start allopurinol
  - observe

What about weight loss ?



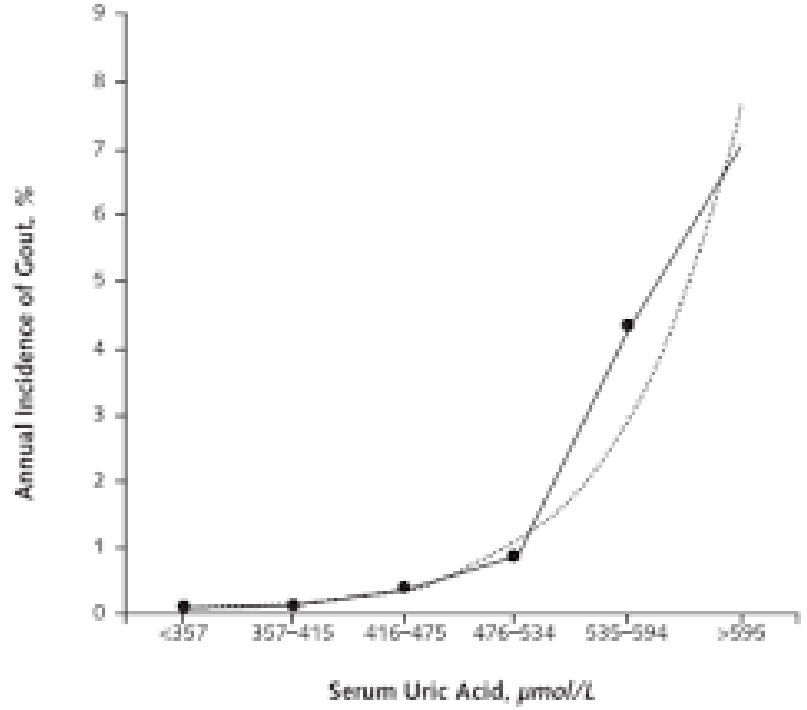
Lowers UA by 0.017 to 0.03

>10 kg weight loss → 3x higher chance of reaching target UA

Need > 7kg loss

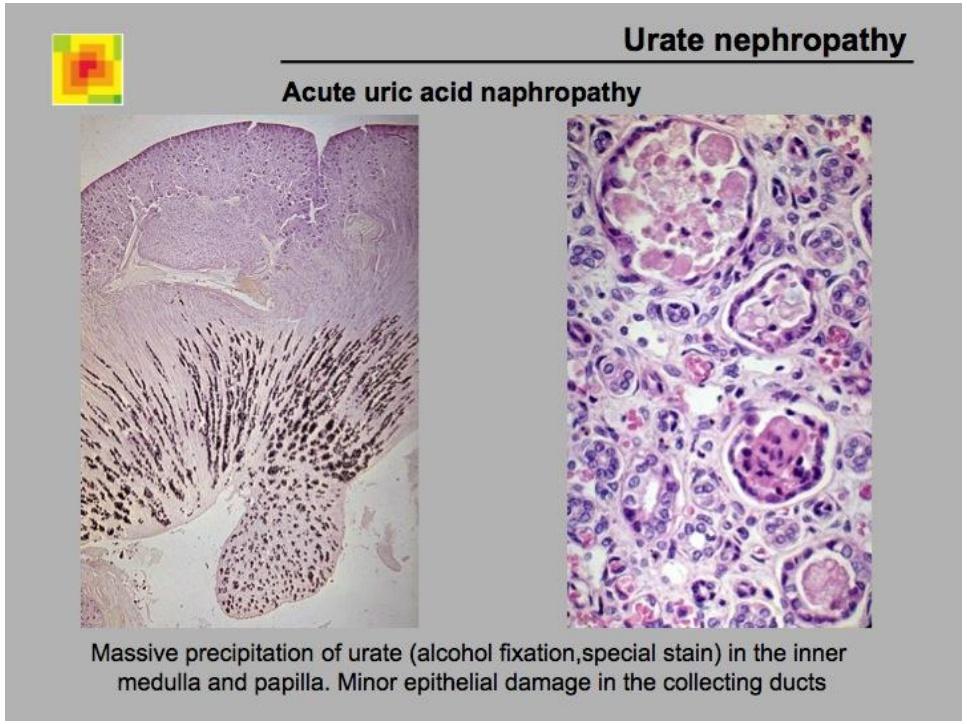
Rapid weight loss (starvation or surgery) increases UA and gout

Why lower uric acid ?



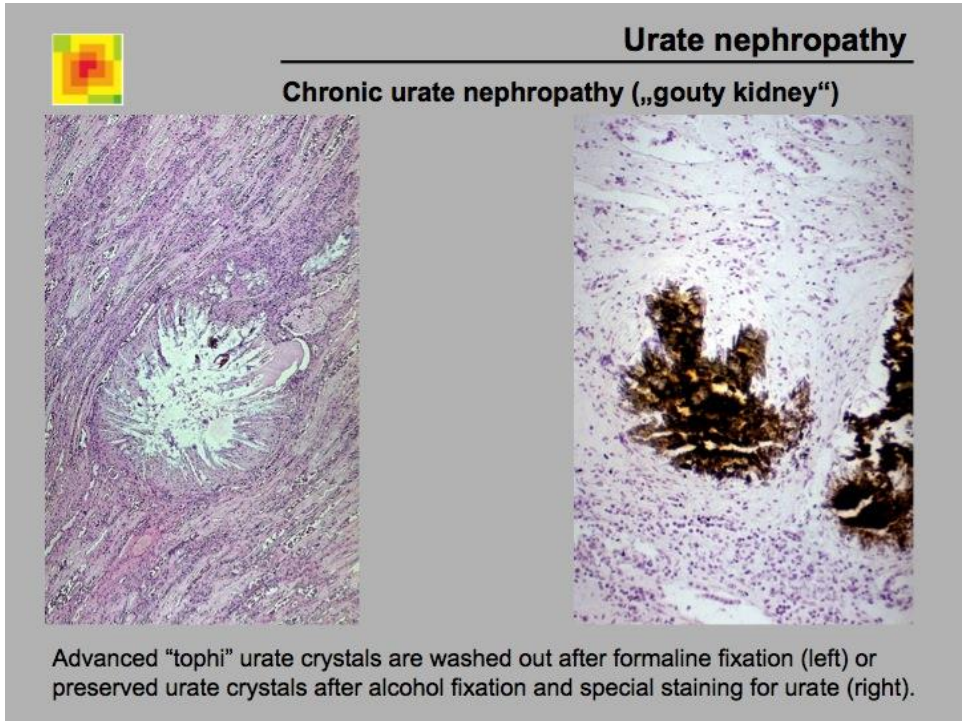
- Gout: only 20% hyperuricaemic patients will develop it
- CVD: uric acid is independent risk factor for CAD but contradictory evidence for benefit by lowering it
- Hypertension: not according to Cochrane
- Urolithiasis: after alkalinization and increased fluid intake ?
- Renal disease

kidney disease and hyperuricaemia



- acute renal failure (tumour lysis syndrome)
- Familial hyperuricaemia and renal failure syndrome
- Chronic renal failure
  - UA > 0.55 AND raised creatinine
  - Inappropriately high UA

Inappropriately high uric acid



- A uric acid level:
  - >0.53 with creat <132
  - >0.59 with creat <132-176
  - >0.70 with creat >176

Risk factors for raised uric acid - 1. genetic

- HPRT deficiency (Lesch-Nyhan)
- PRPP synthetase overactivity
- American Chinese and Filipino immigrants have higher UA than homeland relatives
- Genetics contribute 40% to UA level
- URAT1 – urate transporter
- Maori / Pacific island ethnicity
- Men

Risk factors for raised uric acid – 2. Dietary

Alcohol especially beer

Sugar and sugar sweetened drinks including fructose

High purine foods:

- **Very high** → heart, herring, meat extracts, mussels, yeast
- **High** → anchovies, bacon, liver, mutton, salmon, venison, wild fowl, cod, haddock
- **Moderately high** → asparagus, brains, chicken, beef, eel, kidney shaped beans, lentils, lobster, mushroom, peas, spinach, oysters, other fish and meat

Risk factors for raised uric acid – 3. drugs

- Low dose aspirin
- Diuretics especially thiazides
- Chemotherapy
- Anticoagulants
- Cyclosporin, tacrolimus
- Levodopa
- Pyrazinamide, ethambutol

What's good ?

- low fat dairy products
- Cherries
- Vitamin C
- coffee
- Calcium channel blockers
- losartan
- Atorvastatin
- Leflunomide

Hyperuricaemia summary

- Normal level is < 0.42 mmol/l
- The target level for gout sufferers is < 0.36
- The higher the level the greater the risk for both gout and renal impairment
- UA levels should be measured in the intercritical phase
- UA levels may be increased by drugs, diet and ethnicity
- Lowering UA can prevent gout and improve renal function

Case 2

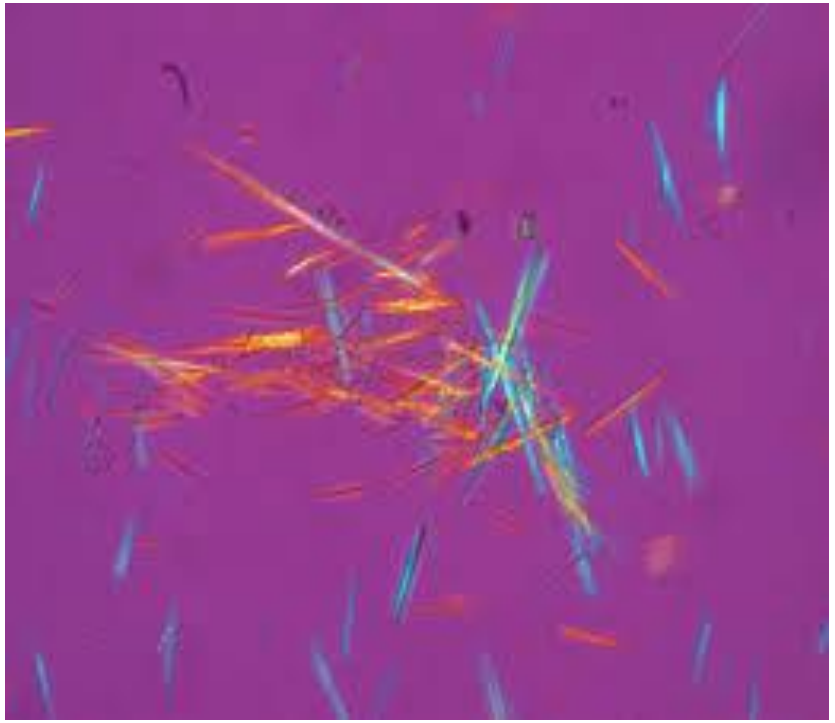
- A 49 y/o man with a history of psoriasis and hypertension but otherwise no significant PMH returns from a week in Fiji and is woken early the next morning by intense pain in the right ankle
- You're a busy GP so he can only see you the following day. Although hobbling he says it was worse the day before. The ankle is red and swollen. He had a similar episode 3 years earlier that settled without treatment in a few days.
- An urgent uric acid is 0.46 and an x-ray shows no fracture but considerable soft tissue swelling
- What's the diagnosis?

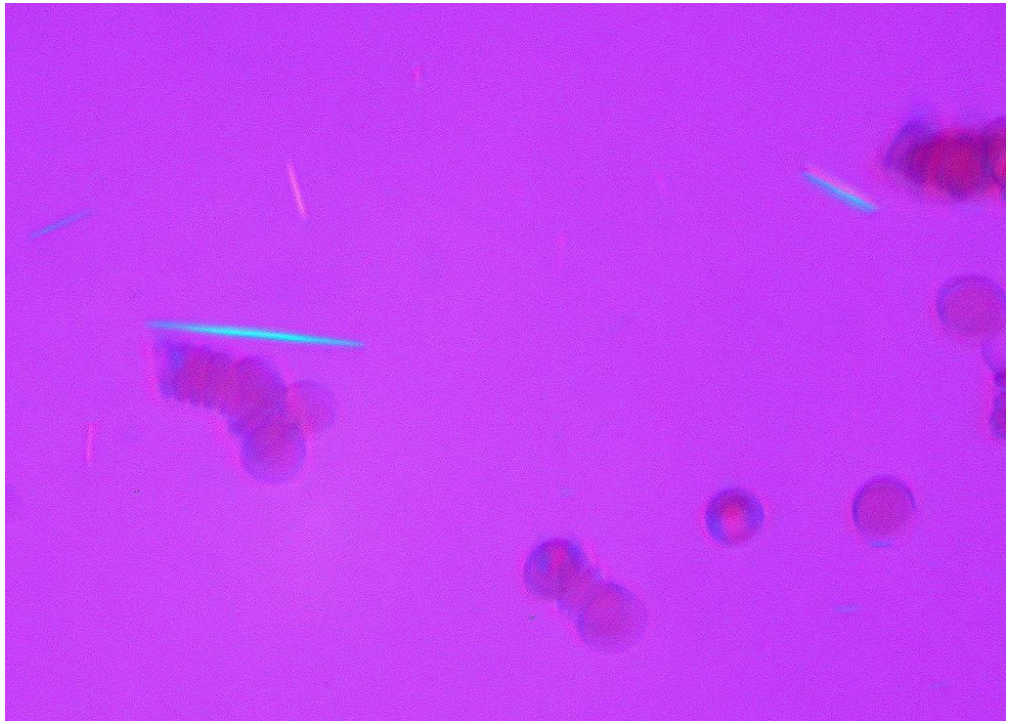
Case 2 – gout – but how do you know?

"I THINK WE'RE GOING TO HAVE TROUBLE WITH VLADIMIR."

- ACR criteria:
- 1. Demonstrate uric acid crystals in synovial fluid (sensitivity 80-90 %)
- 2. Presumed tophus contains uric acid – chemical or light microscopy
- 3. 6 of 12 clinical criteria

Diagnosing gout





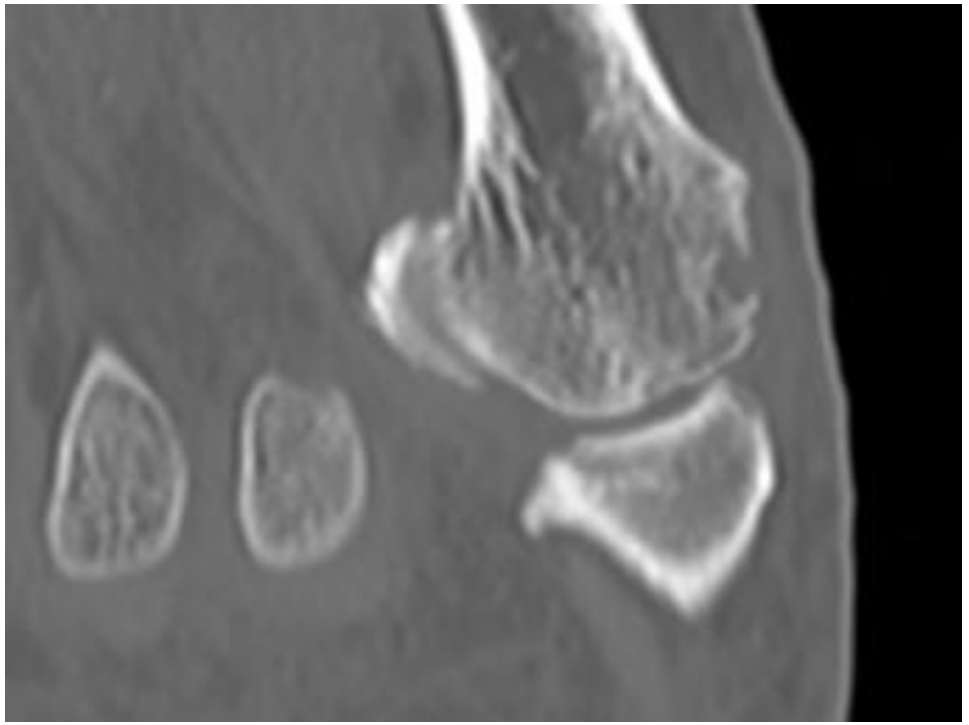
ACR clinical criteria for gout – 6 of 12

- Maximum inflammation first 24 hrs*
- More than one attack*
- Monoarticular arthritis*
- Redness over joint*
- First MTP involved
- Unilateral 1st MTP
- unilateral tarsal joint attack
- Suspected tophus
- Hyperuricaemia*
- Assymmetric swelling on x-ray of joint*
- Subcortical cysts on x-ray
- Negative culture from synovial fluid

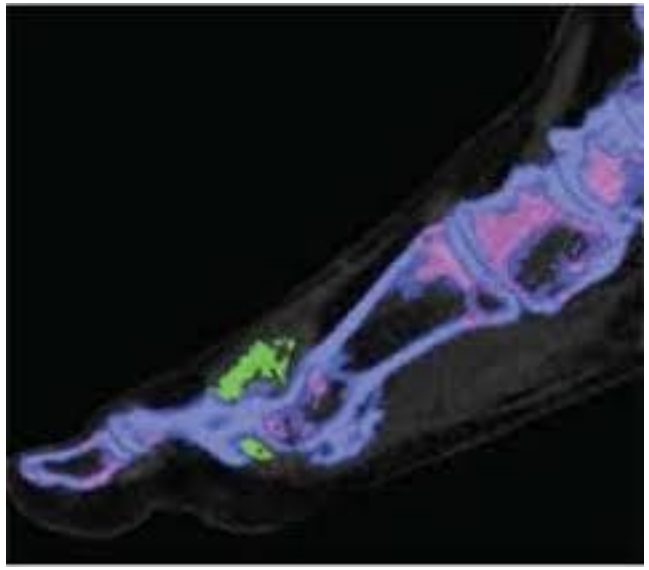
Stages of gout

- Asymptomatic hyperuricaemia
- Acute attacks
- Intercritical phase
- Chronic gout / multiple joints
- Tophaceous gout including internal organ involvement

Imaging in Gout



Imaging in Gout – dual energy CT



- Problems with sampling and with reliability of microscopy
- Hi vs low kv scans give characteristic CT numbers
- Up to 90% sensitive
- May be negative early on in disease course
- Bongartz et al Ann Rheum Dis 2014

Case 3 – 49 y/o beekeeper

- Five years previously had been kickboxing, had a few beers, took a taxi home and turned his ankle in a drain as he got out of the cab.
- Severe pain and swelling next morning. Couldn't walk. X-rays reported normal.
- 3 months later → Orthopods → MRI showed no structural damage, just effusion
- Since then 3 i-a injections to right ankle under imaging

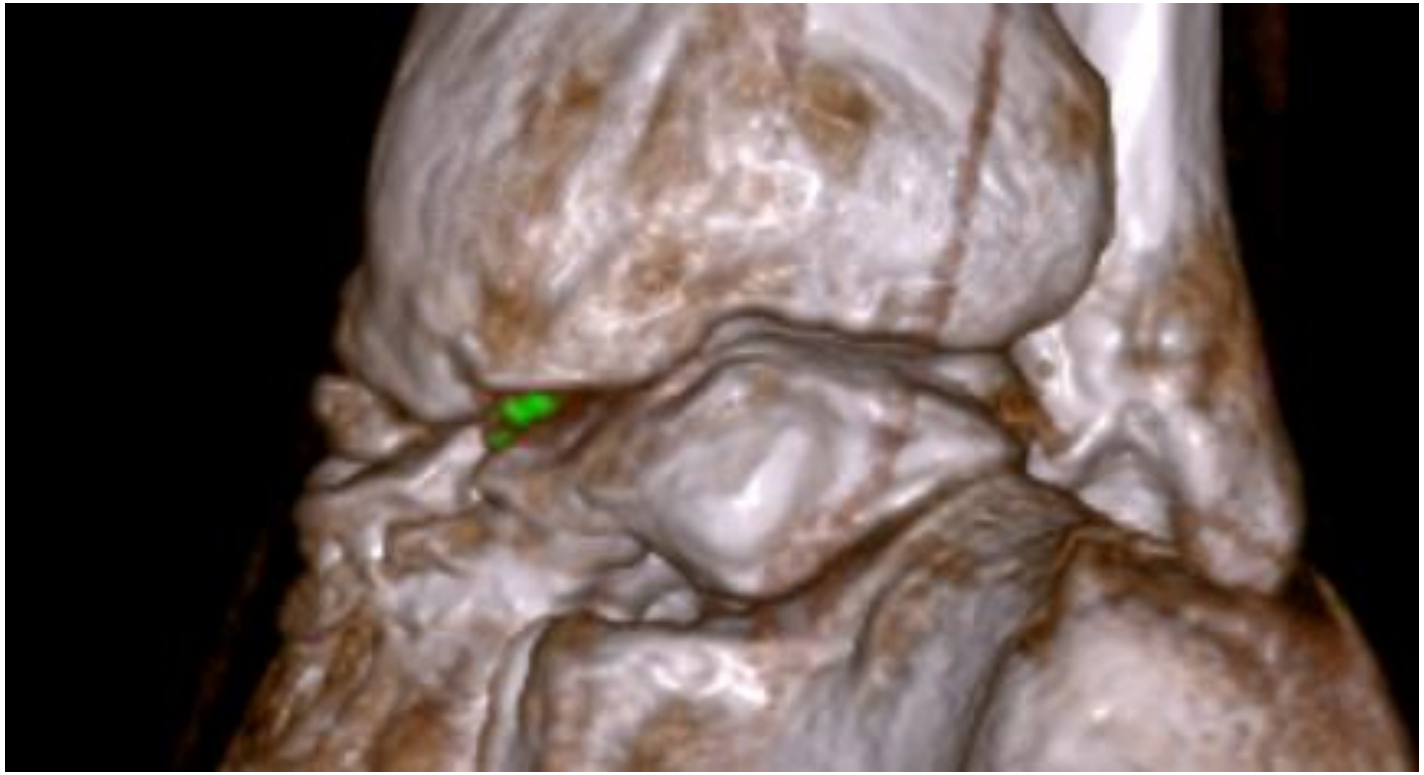
Case 3 – 49 y/o beekeeper

- Diclofenac and prednisone used episodically and helped especially the prednisone
- Dropped Hb to 102g/l in June 2018 → painful swollen left knee
- → Orthopods → MRI showed no structural damage but large effusion
- Therefore went on to an arthroscopy - no fluid analysis

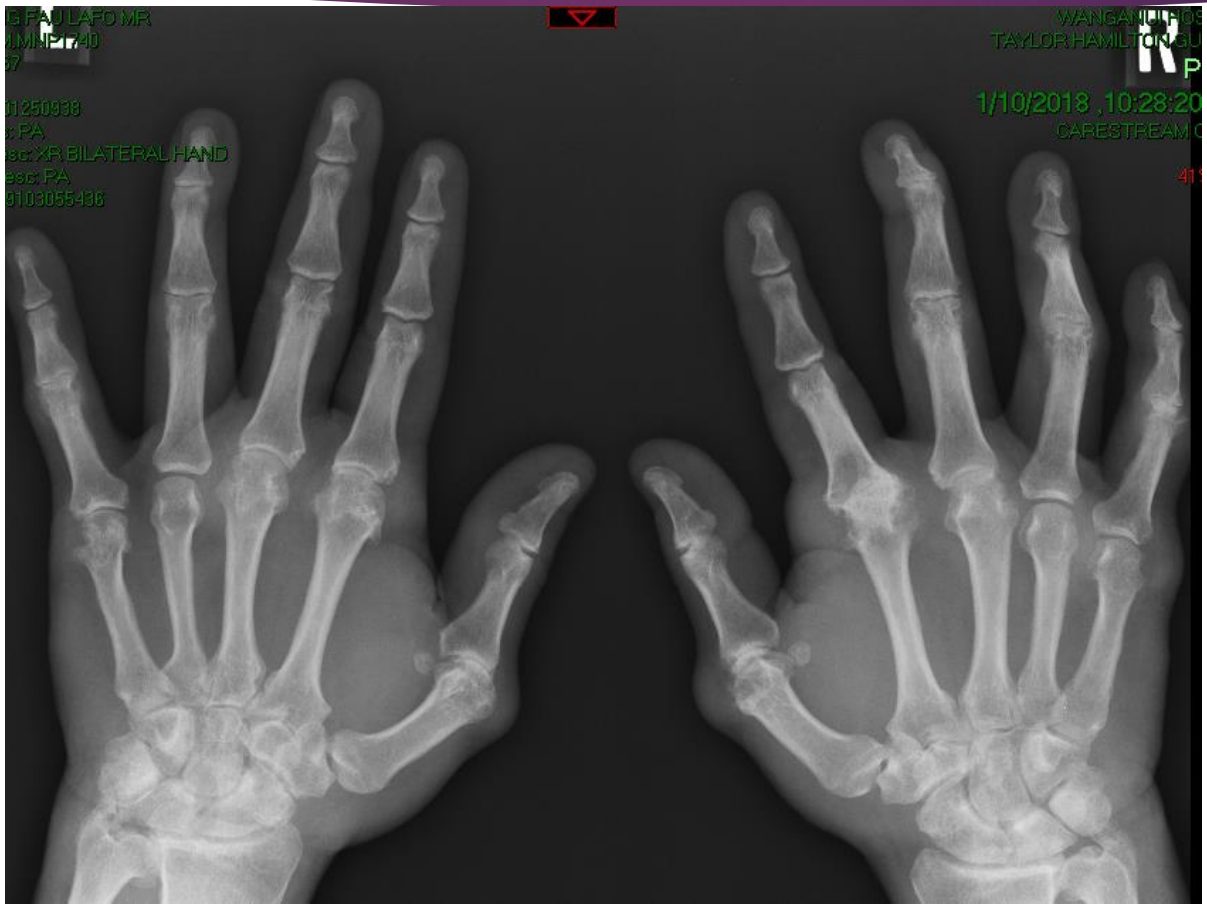
Case 3 – 49 y/o beekeeper

- Ongoing problems – refer Rheumatology
- Pt drinks 30 cans bourbon and coke / week
- Father had gout when older
- Joints have been fine for past 2 weeks
- Hb back to 157g/l on Fe supps, amoxycillin & metronidazole
- UA levels from 2013 to 2018: **0.40, 0.40, 0.41, 0.31, 0.25**
- Exam normal apart from restriction of mvt R ankle

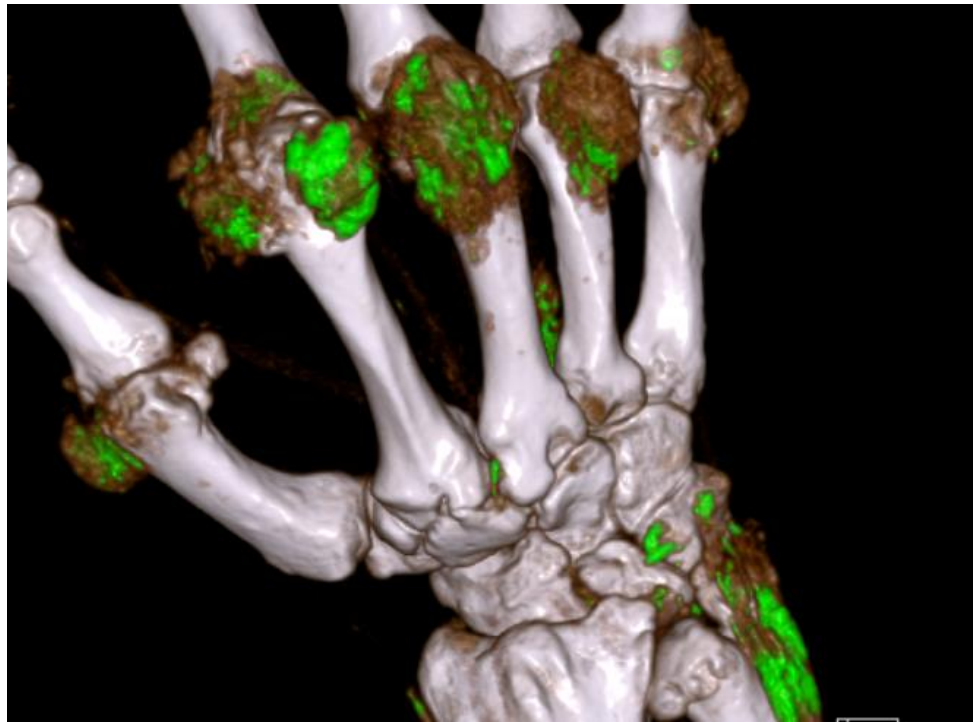
Case 3 – 49 y/o beekeeper



Case 4 – 51 y/o corrections officer



Case 4 – 51 y/o Corrections Officer



Diagnosis summary

- Demonstrate UA crystals in synovial fluid
- Demonstrate UA crystals in presumed tophus
- 6 of 12 clinical criteria (likely setting, typical symptoms)
- X-rays or CT scans can show typical changes in chronic cases
- Dual energy CT can demonstrate presence of UA
- Women can be atypical
- Exclude psoriatic arthritis, reactive arthritis, infection

Medical management of gout

- 1. Acute attacks
- 2. prophylaxis
- 3. prevention

1. Acute attacks

- Start treatment early < 12 hrs
  - i-a steroid injection
  - NSAID's
  - Colchicine
  - Prednisone
  - IL-1 blockers (canakinumab & anakinra)

1. Acute attacks

- NSAID's
  - Usually naproxen or diclofenac
  - Celebrex 800/400
  - Ibuprofen blocks aspirin
  - Caution in renal impairment, hypertension, cardiac failure, upper GI problems, older patients
- Prednisone
  - 20 – 30mg stat and daily
  - Usually 5 day course
  - 30mg/d = indomethacin
  - 35mg/d = naproxen 500mg bd

1. Acute attacks

- Colchicine
  - 1 mg stat and 0.5mg in an hour
  - 1.8mg = 4.8mg in 24hrs
  - Age, renal impairment and wt < 50kg's risks for adr's
  - 20% renally excreted
  - Reduce dose eGFR <50ml/m
  - Avoid with eGFR < 10ml/m
  - Slow excretion
- Nausea, vomiting & diarrhea initial side effects → STOP
- Also electrolyte imbalance, alopecia, blood dyscrasias, pancreatitis, renal or hepatic failure and death
- Avoid with CYP3A4 inhibitors such as cyclosporin, ketoconazole, clarithromycin, verapamil
- Increased risk of muscle toxicity with statins

2. Prophylaxis

- Colchicine 0.5mg od / bd
- Naproxen 250mg bd / diclofenac SR 75mg/d
- Prednisone 5-7.5mg/d
- 6-24 months
- 3 months at target UA with no gout

3. Prevention - urate lowering therapy (ULT)

- Who?
  - 2 or more attacks/year
  - < 40 yrs of age
  - UA > 0.48 mmol/l
  - Comorbidities – renal, hypertension, cardiac
  - < 0.36 or < 0.30 mmol/l
  - Measure UA monthly initially
- How?
  - Start low go slow
  - Allopurinol
  - Febuxostat
  - probenecid
  - Benzbromarone
  - Combination
  - pegloticase

3a. ULT – allopurinol

- 50 – 100 mg/d to 600mg/d
- 1.5 x eGFR in CRF
- Not > 200mg/d if eGFR 10-20
- Not > 100mg if eGFR <10
- Can increase monthly
- Start when you see the patient
- Never stop

- ADR's > with high doses & with renal impairment
- 10% mac-pap rash
- SCARs 0.7/1000 pt yrs – can be fatal (first 2 months)
- DRESS
- GI upset, blood dyscrasias
- Avoid with azathioprine, MP

3b. ULT - febuxostat

- More effective than allopurinol 300mg/d
- Hepatic metabolism but not recommended at <30mls/m
- Start at 80mg/d, increase to 120mg
- 3rd line after allopurinol & probenecid or allopurinol in CRF and eGFR > 30mls/m
- ADR's – d, n, headache, rash, LFT abnormalities common
- SCARs/DRESS rare
- ? Increased cardiovascular events
- Hypothyroidism with long term use
- Avoid with azathioprine & MP

3c. ULT - probenecid

- uricosuric
- Start 250mg bd increasing to 1 to 2 G/d
- Maintain good hydration
- Aspirin interferes with effect
- Needs eGFR > 30mls/m

- Upper GI symptoms may indicate excessive dose
- Increases levels of mtx, many NSAIDs, B lactams, rifampicin, acyclovir, Sulphur drugs and others
- Headache, dizziness, upper GI sx's, anaphylaxis, S-J Syndrome, anaemia (G-6PD)

3d. ULT - benzbromarone

- Uricosuric
- 50 – 200mg/d
- Good hydration
- Regular LFT's
- Avoid in liver disease
- eGFR > 20 mls/m
- Spec authority – 3rd choice after allopurinol & probenecid
- Risk of nephrolithiasis
- Occasional severe liver toxicity
- Potentiates warfarin (CYP2C9)

Treatment summary

- Education of patient:
  - Importance of uric acid levels
  - What different medications are for
  - ‘pill in the pocket’ for acute attacks
- Frequent supervision – possibly with practice nurse
- Focus on uric acid levels – monthly measurement
- Screen for associated comorbidities and cardiovascular risk factors
- Adjust non-gout medications where appropriate