



Rheumatology for GP Trainees:

Gout

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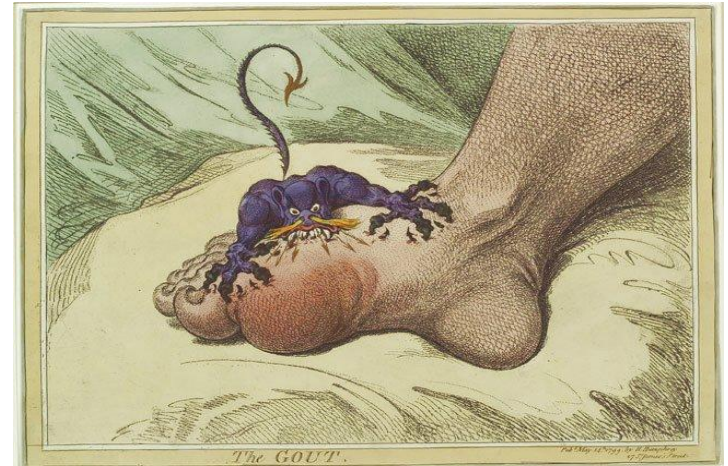
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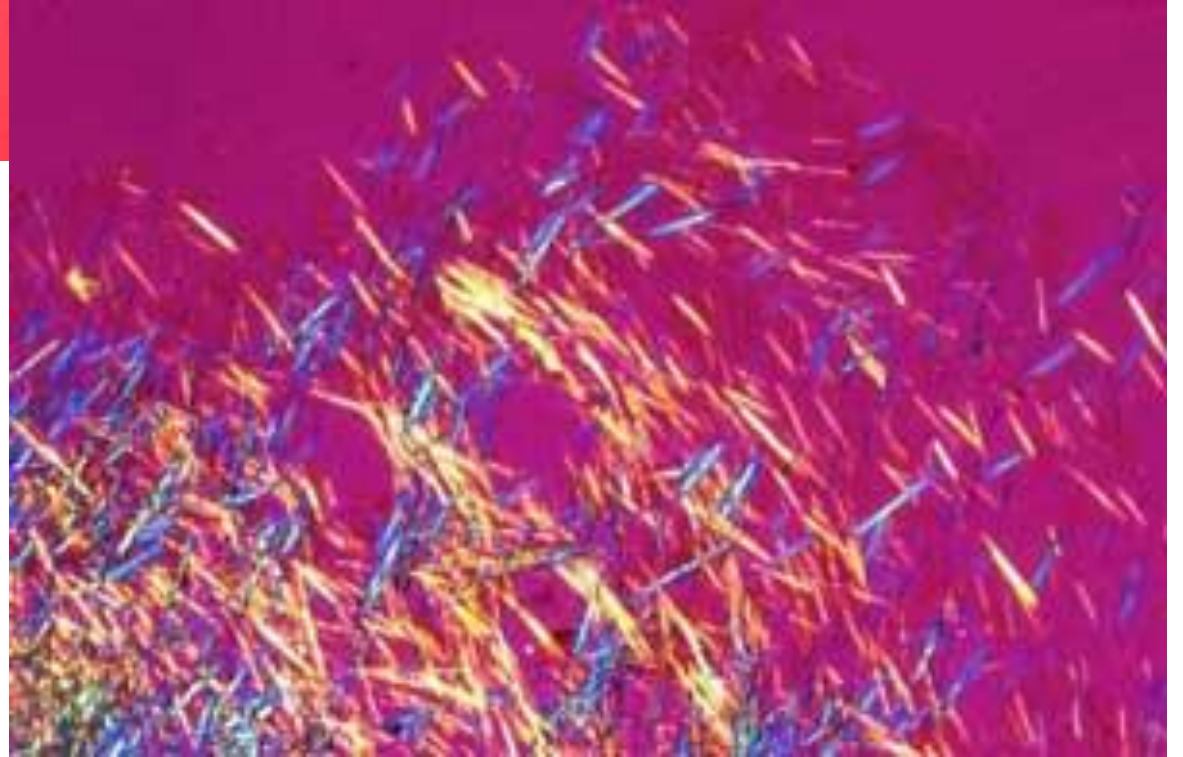
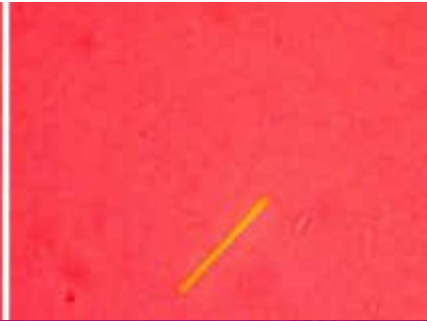
Gout - Perceptions

- Gout is not considered a serious form of arthritis and flares are the main concept
- Gout is quite humorous?!? (compare to RA/JIA)
 - “Wife’s revenge”
 - “Women love it because it causes men to cry”
 - “Well deserved and self inflicted by food and alcohol abuse”

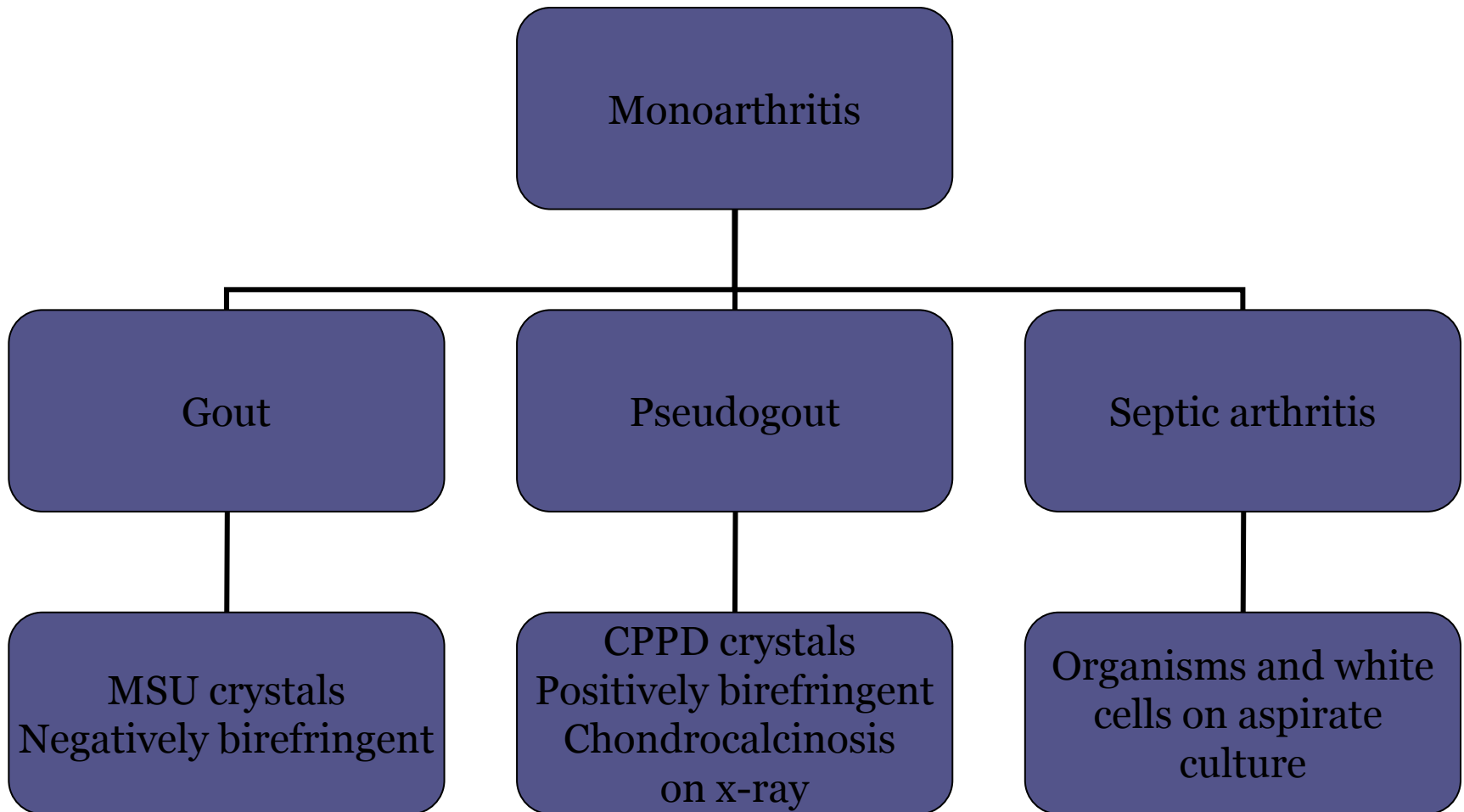
Gout - Introduction

- Gutta
 - Latin word for a drop of liquid (NB. guttate psoriasis)
 - Bad humours dropping into foot
- Gouty attacks relate to the presence of MSU crystals in joints and soft tissues (following the chronic elevation of uricaemia above the saturation point of MSU)





Differential Diagnosis





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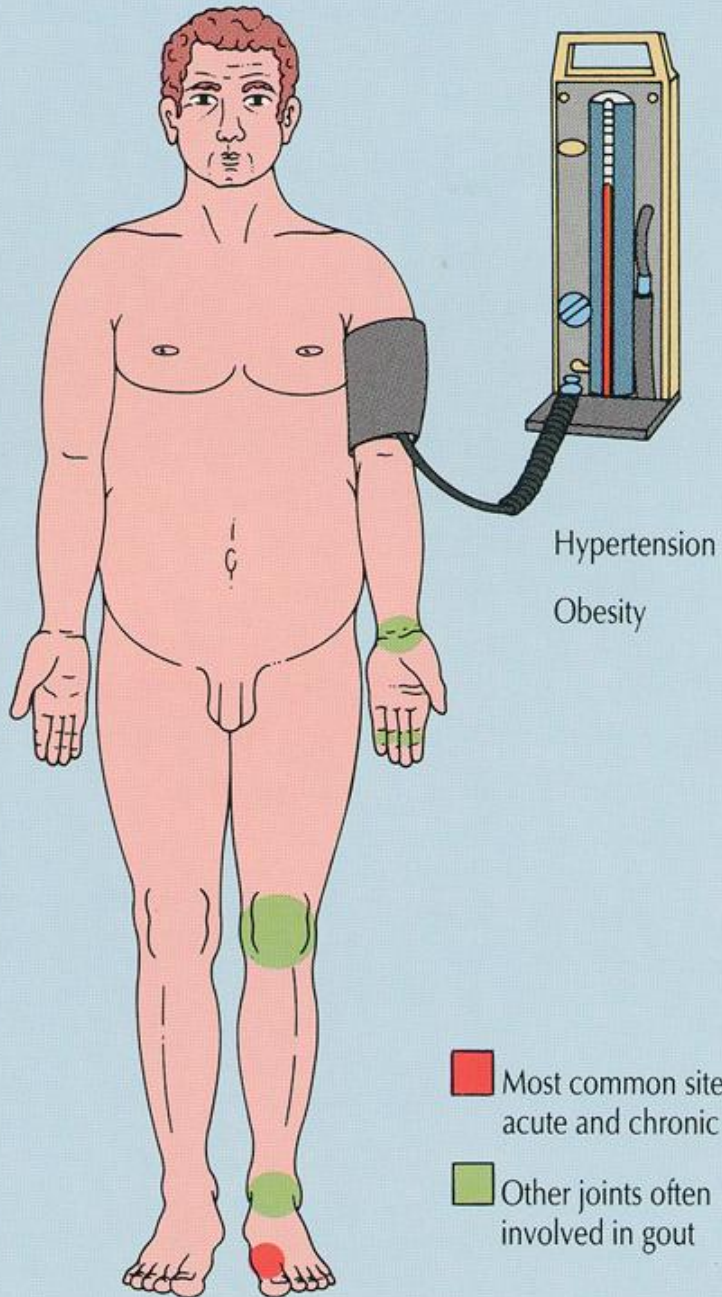


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GOUT: JOINT INVOLVEMENT AND ASSOCIATIONS



- Most common site of acute and chronic gout
- Other joints often involved in gout

Causes of Gout - Mnemonic

- D Dehydration, Diuretics (furosemide, thiazide)
- R Rash (psoriasis)
- I Idiopathic
- N Nicotinic acid
- K Killing cells (cytolytic therapies)

- N Nephron failure (renal failure)
- O Obesity (risk factor for primary gout)

- A Acidosis (DKA, lactic acidosis, starvation), Alcohol, Aspirin (low-dose)
- L Lead poisoning, Lesch-Nyhan syndrome
- C Cyclosporine
- O Over-exercising (extreme exercise)
- H High purine diet
- O Other drugs (ethambutol, pyrazinamide)
- L Lymphoproliferative or Myeloproliferative disorders

Gout - Introduction

- Gout has become more common worldwide (increase in metabolic syndrome, lifestyle, living longer)
- Most common inflammatory arthritis UK & worldwide (prevalence 1.4% in UK)
- Only chronic arthropathy where one of the aims of treatment is 'cure'

Gout - What is happening in primary care?

- Increasing prevalence
- >1 million of UK population has gout (probably more)
- 250,000 consultations/year in GP (probably more)
- Each GP about 7 consultations per year (probably more) (50% acute gout)

Gout - What is happening in primary care?

- Is this gout?
- What investigations?
- Should I exclude secondary causes?
- Important diagnosis to exclude (sepsis)?
- How should I treat gout (allopurinol for all or allopurinol only after 3 attacks per year)?
- What about allopurinol in CKD?
- How do I monitor gout (reduce serum UA or reduce attacks)?
- Management of acute gout vs hyperuricaemia?

Management of Gout - EBM

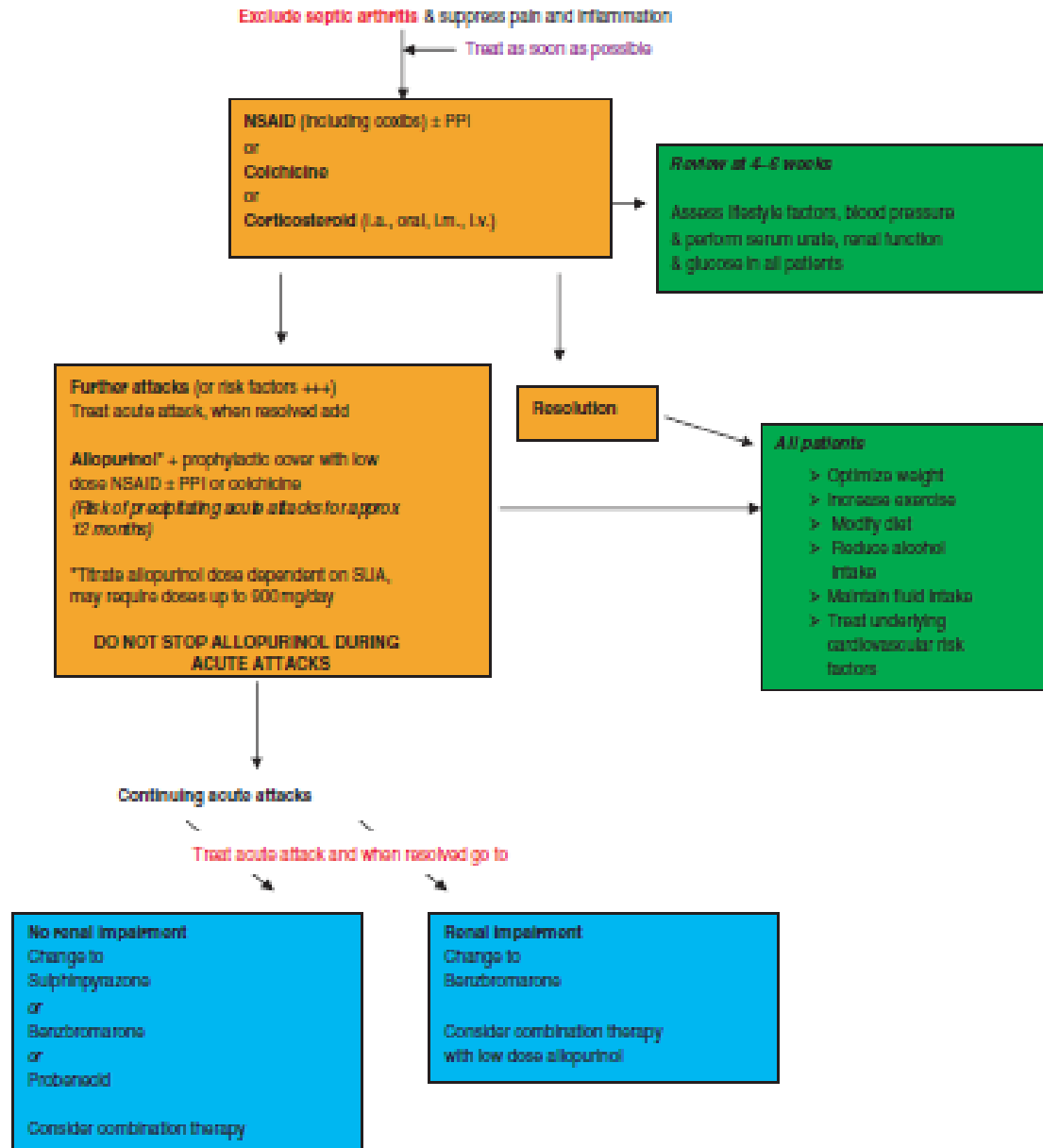
- EULAR

- Evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee For International Clinical Studies Including Therapeutics (ESCSIT)
- Zhang et al. Ann Rheum Dis 2006

- BSR

- BSR and BHPR Guideline for the Management of Gout
- Jordan et al. Rheumatology 2007

GOUT: MANAGEMENT PATHWAY



Gout - Acute treatment

- Rest
- NSAIDs
- COX₂ Inhibitors
- Glucocorticoids
 - Oral (30mg/day)
 - Intra-articular

Gout - Acute treatment

- Colchicine
 - 500mcg BD or TDS
 - Caution in renal impairment
- Time taken for crystals to disappear depends on duration of gout

Gout - Further management

- Modifiable risk factors (can be difficult):
 - Obesity (decreased renal clearance of urate, avoid crash diets)
 - High purine intake (beer, red meat, liver, kidneys, shellfish, pulses and certain seafood)
 - Alcohol (reduce clearance of uric acid, beer contains purines)
 - Soft drinks (contain fructose)
 - Maintain fluid intake
 - Moderate exercise
- Only have a modest effect (10% reduction in serum UA)

Gout - Further management

- Assess drugs:
 - Can a uricosuric drug be used? ie. amlodipine
 - Can diuretics be stopped?

Gout - Further management

- Lifestyle
 - Gout is frequently associated with the metabolic syndrome (and therefore hypertension and morbidity related to arteriosclerosis)
 - Gout is an independent risk factor for cardiovascular disease

Gout - Who needs further therapy?

- Aims of uric acid lowering therapy:
 - Dissolve crystals and prevent further crystal formation
 - Prevent acute attacks
 - Resolve tophi
 - Prevent tissue damage / bony erosions

Gout - Who needs further therapy?

- Further attack of gout within 1 year
 - After a single attack?? (NB. microtophi, benefit vs risks, CV risks, patient choice)
- Evidence of gouty tophi / tissue damage
- Renal insufficiency
- Uric acid stones and gout
- Patients who remain on diuretics

Gout - Prophylaxis (reduce serum UA levels)

- Initiation of uric acid lowering drugs can provoke gout arthritis
- Start with low doses with step-wise increments together with prophylactic therapy
- Uric acid lowering drugs should not be initiated during gout arthritis
- If gout arthritis occurs in patients on uric acid lowering drug therapy, this therapy should not be stopped
- It can take several months to eliminate the crystals from the joint, so attacks may occur for months after initiation of the uric acid lowering therapy

Gout - Prophylaxis

- Allopurinol
 - Xanthine-oxidase inhibitor (reduces amount of uric acid being produced)
 - 100mg daily with prophylactic therapy increasing to max 900mg (NB. 300mg)
 - Reduce dose in renal impairment (reduced renal excretion)
 - Effective and well tolerated in majority of patients (GI upset / hypersensitivity rash in 3-5%)
 - Rare SE (toxic epidermal necrolysis, SJ syndrome, acute haemolytic syndrome)
 - Interacts with AZA, warfarin

Gout - Prophylaxis

- Uricosurics
 - Increase renal clearance of urate (may induce calculi)
 - Benzbromarone (useful in renal impairment, withdrawn from many European countries due to occasional severe hepatic toxicity)
 - Probenecid and Sulfinpyrazone (less effective than benzbromarone and increased incidence of side effects)
 - Losartan, Amlodipine, Fenofibrate (have a modest uricosuric effect)

Gout - Prophylaxis

- Uricolytics:
 - Uricase enzyme ie. Rasburicase
 - Not routinely used (IV, expensive, antibody formation)
 - Tumour lysis syndrome

Gout - Prophylaxis

- Febuxostat (Adenuric)
 - Selective xanthine-oxidase inhibitor
 - Hepatic degradation (max 80mg in mild hepatic impairment)
 - Appears safe in renal impairment
 - No dose adjustment required in mild-to-moderate renal impairment (not investigated in severe RF, NB. ACR)
 - 80mg OD (40 - 120mg)
 - Appears to have good safety profile*
 - NOT recommended in patients with IHD or congestive heart failure (or patients being treated with azathioprine)

*Becker MA et al. Clinical efficacy and safety of successful long-term urate lowering with febuxostat or allopurinol in subjects with gout. J Rheumatol. 2009; 36: 1273-82.

Febuxostat: NICE TAG 164

- Febuxostat is a non-purine selective inhibitor of xanthine oxidase
- Febuxostat is recommended as an option for the management of chronic hyperuricaemia in gout only for people who are intolerant of allopurinol, or in whom allopurinol is contraindicated (NB mild to moderate renal impairment)
- Intolerance of allopurinol is defined as adverse effects that are sufficiently severe to warrant its discontinuation, or to prevent full dose escalation for optimal effectiveness as appropriate

Febuxostat: NICE TAG 164

- The most common side effects are diarrhoea, nausea, headache, liver function test abnormalities and rash
- The summary of product characteristics states that treatment is not recommended for people with ischaemic heart disease or congestive heart failure
- The recommended dose of febuxostat is 80 mg OD
- If a person's serum uric acid concentration is above 360 $\mu\text{mol/l}$ after 2–4 weeks of treatment, 120 mg OD may be considered
- The price for febuxostat 80 mg and 120 mg is £0.87 per tablet (annual treatment costs are approximately £318)

Febuxostat: NICE TAG 164

- FACT Trial, APEX Trial, TMX-00-004 Trial
- Pooled analysis (by manufacturer) suggested that febuxostat 80 mg/day and 120 mg/day was significantly more effective ($p \leq 0.05$) than fixed-dose allopurinol (300 or 100 mg/day) at lowering the serum uric acid concentration to target therapeutic levels
- No statistically significant differences were observed with febuxostat 80 mg/day compared with allopurinol (300 or 100 mg/day) in the proportion of patients requiring treatment for gout flares

Gout -

What should not be happening (but is)

What should be happening (but isn't)

- Is gout being optimally managed?
 - Acute gout – probably yes
 - Chronic gout – probably no

Gout -

What should not be happening (but is)

What should be happening (but isn't)

- **Barriers:**

- Not in QOF Quality Outcomes Frame
- Acute gout fitted in as an extra and no plans made for follow-up
- Investigations done at the time of acute attack (normal serum UA falsely reassuring)
- Diagnostic uncertainty unless clinical podagra (?abscess, sepsis, OA knee, olecranon bursitis – ASPIRATE)
- Gout can cause confusion and pyrexia
- Normal laboratory levels for serum UA may be unhelpful (ie. 200–420 μ mol/l for males, 140-340 μ mol/l for females)
- Confusion over target levels
- Hesitancy to prescribe allopurinol as can precipitate attacks
- How long to co-prescribe NSAIDs or colchicine with allopurinol

Gout -

What should not be happening (but is)

What should be happening (but isn't)

- BSR (2007) /EULAR (2006) Guidelines (pre febuxostat)
- Evidence based multidisciplinary guidelines:
 - Lifestyle modifications
 - Management of acute gout
 - Target serum UA levels
 - Prophylaxis when initiating UA lowering therapy

Gout -

What should not be happening (but is)

What should be happening (but isn't)

- Long-term management aims:
 - Reduce serum UA
 - Dissolve crystals
 - Cure gout
 - Prevent tophi / joint damage
 - Prevent MSK disability
- Target serum UA:
 - EULAR $< 360 \mu\text{mol/l}$
 - BSR $< 300 \mu\text{mol/l}$

Gout -

What should not be happening (but is)

What should be happening (but isn't)

- Allopurinol not increased to 900mg (treat to target serum UA levels)
- Allopurinol achieves serum UA goal in <50% of patients when prescribed at 300mg/day
- Allopurinol should not be discontinued during a flare
- Need to recheck serum UA levels (NB. failure to maintain subsaturating serum UA levels)
- Prophylaxis with colchicine for flares when initiating UA lowering therapy (6/52 – 3/12) (EB data for 6/52)
- Patient education encourages adherence

Gout -

What should not be happening (but is)

What should be happening (but isn't)

- Problems in management:
 - Poor compliance (males with metabolic syndrome are poor attenders)
 - Co-morbidities often CKD $3/4$
 - Multiple meds (ACEI, warfarin, diuretics, statins)
 - Usually NSAIDs CI
 - Need to co-prescribe PPI (allopurinol, NSAID, PPI = £22/month)

How would you treat a...

- 70-year-old male with chronic renal impairment. He is intolerant of allopurinol (failed desensitisation) and colchicine causes intractable diarrhoea?

How would you treat a...

- 70-year-old male with chronic renal impairment and a previous CABG. He is intolerant of allopurinol (failed desensitisation) and colchicine causes intractable diarrhoea?

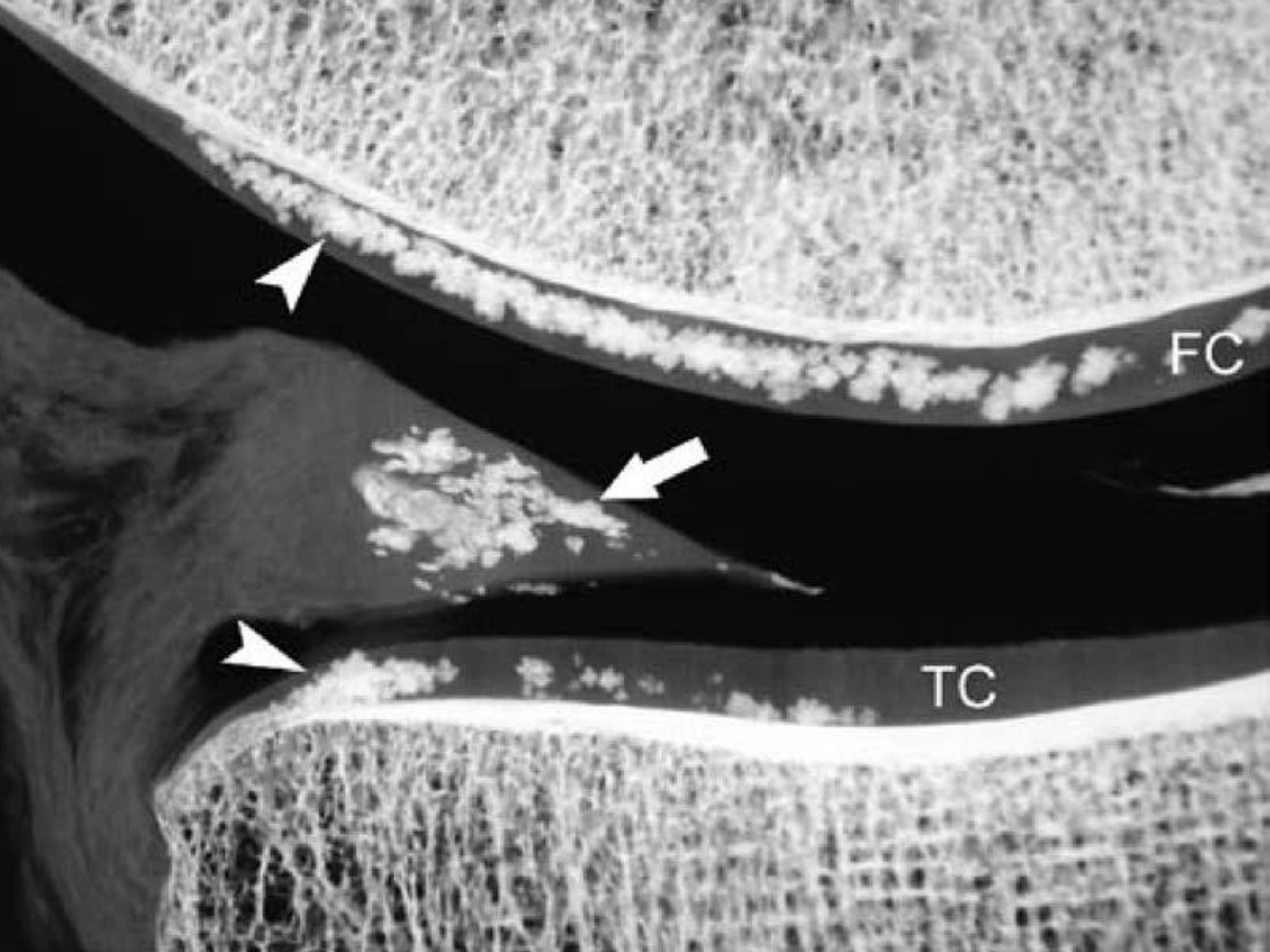
Treatment of hyperuricaemia for CV risk

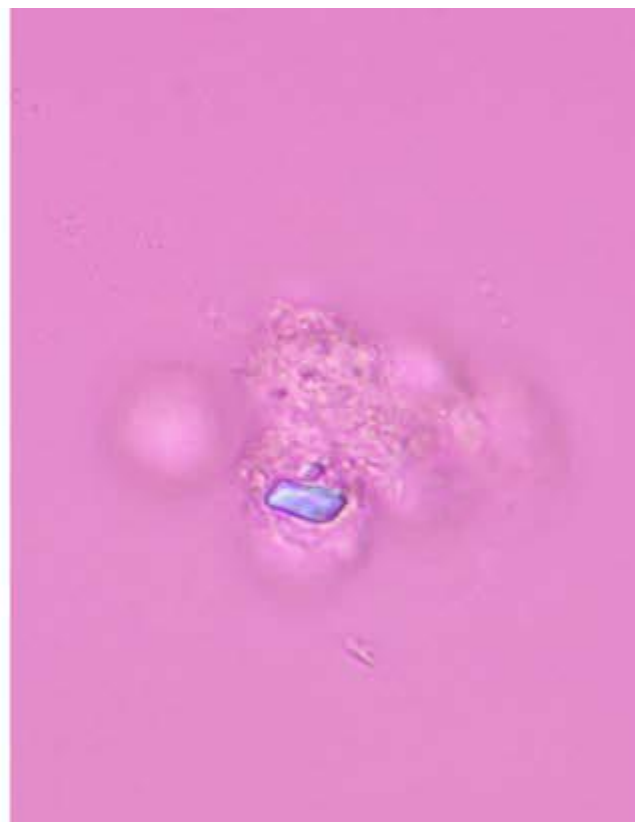
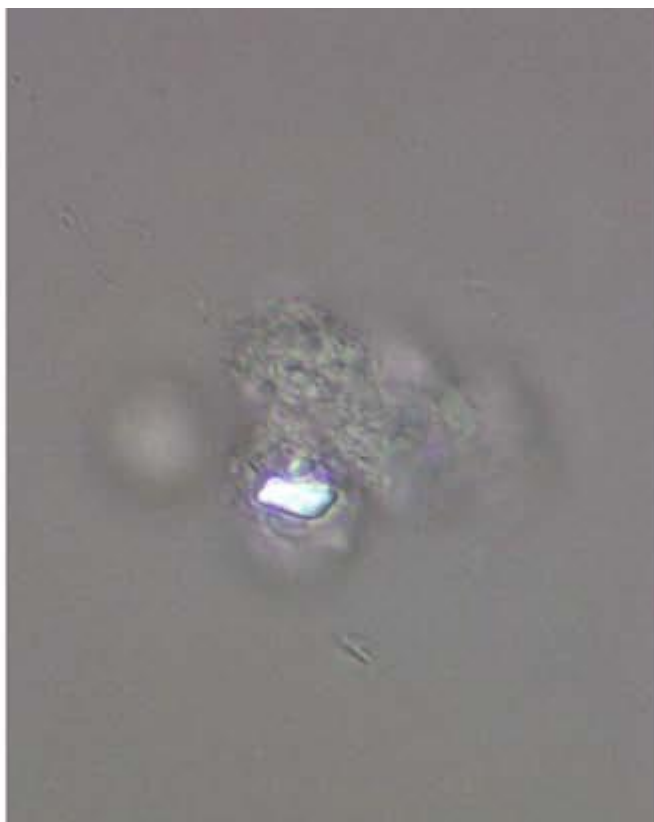
- Association between hyperuricaemia, hypertension, renal disease and CV events (association vs causation)
- UA is an antioxidant but stimulates vascular smooth muscle proliferation and endothelial dysfunction (reduction in NO)
- In animal studies hyperuricaemia causes renal hypertension and renal impairment
- Studies from Scotland and US suggest that treating hyperuricaemia with allopurinol reduces CV risk

Calcium Pyrophosphate Deposition Disease

- Calcium pyrophosphate deposition can occur:
 - In otherwise normal cartilage (radiographic chondrocalcinosis)
 - In association with structural changes and clinical arthropathy (pyrophosphate arthropathy / pseudogout)







Calcium Pyrophosphate Deposition Disease

- **Mimics of CPPD:**
 - Acute monoarthritis (gout, septic arthritis, reactive arthritis)
 - Chronic polyarthritis (RA)
 - OA
 - Bursitis, tenosynovitis, tendonitis
 - PMR
 - Cervical myelopathy
 - PUO

Calcium Pyrophosphate Deposition Disease

- Associations:
 - Hyperparathyroidism
 - Hypophosphataemia
 - Hypomagnesaemia
 - Haemochromatosis
- A screen for metabolic disease may be warranted in certain cases (ie. patients with early onset, florid polyarticular chondrocalcinosis) and should include serum calcium, alkaline phosphatase, magnesium, ferritin, and liver function

The Acute Hot Swollen Joint

- A 70 year old woman with diabetes is febrile and has a 1 day history of right knee pain. What diagnosis should be considered most likely until excluded?
- A: Acute gout
- B: Osteoarthritis
- C: Acute pseudogout
- D: Reactive arthritis
- E: Septic arthritis

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KEY POINTS

Remember to think about, look for....



....and don't miss Septic Arthritis

Joint Aspiration & Injection: Indications

- Diagnostic
- Therapeutic aspiration
- Corticosteroid injection
- Hyaluronan viscosupplementation

Joint Injection: Contraindications

- Suspected septic joint or septicaemia
- Overlying cellulitis
- Prosthetic joint
- Severe bleeding disorder

Joint Injection: What preparation to use?

- Methylprednisolone (ie. Depomedrone 40mg/ml) or Triamcinolone
- Triamcinolone is less soluble and more potent than Depomedrone (longer length of action)
- Local anaesthetic (ie. Lignocaine 1%)
- Avoid local anaesthetic in carpal tunnel syndrome

Joint Injection: Complications 1

- May be more painful once local anaesthetic wears off
- Infection
 - Risk of septic arthritis is very small (1 in 20,000 procedures) but if joint becomes hot and inflamed then patient must return.

Joint Injection: Complications 2

- Local tissue atrophy
 - Lipodystrophy if steroid is injected subcutaneously
 - Skin atrophy and/or hypopigmentation in superficial infiltrations and more potent steroid use
- Tendon rupture
 - Small risk
 - Increased in repeated injections
 - Achilles tendon, bicipital tendon, palmar flexors
- Rest joint for 24 – 48 hours

Joint Injection: How Often To Inject

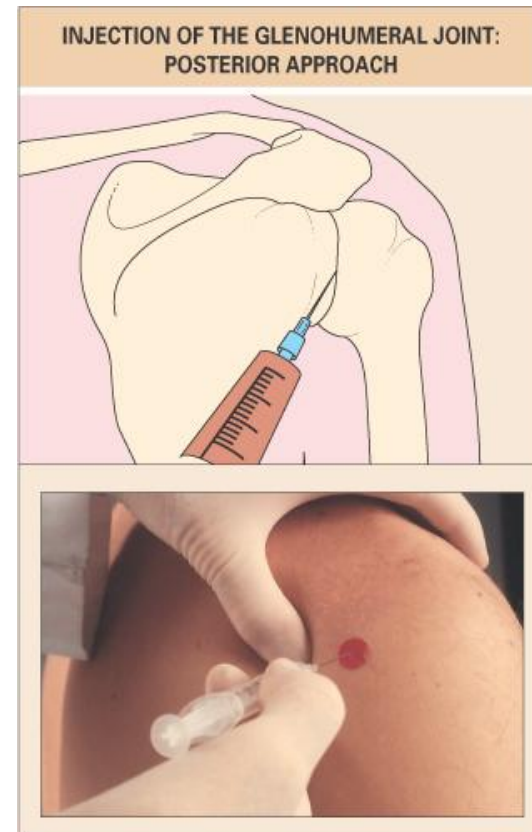
- If successful, a joint injection should last several months
- Small joint injections may last a year
- 3-4 injections/joint/year

Joint Injection: Technique

- Aseptic technique:
 - Mark area with end of pen or needle cover
 - Sterilise area thoroughly
 - Use 'no touch technique'
 - Wear gloves
- Aspirate synovial fluid if possible before injecting
- Injection should be with little resistance (except lateral and medial epicondylitis)

Posterior Approach to Glenohumeral Joint

- Feel for the spine of the scapula
- Move laterally until you feel the acromion
- Inject about 1cm below and medial to this aiming towards the middle of the clavicle

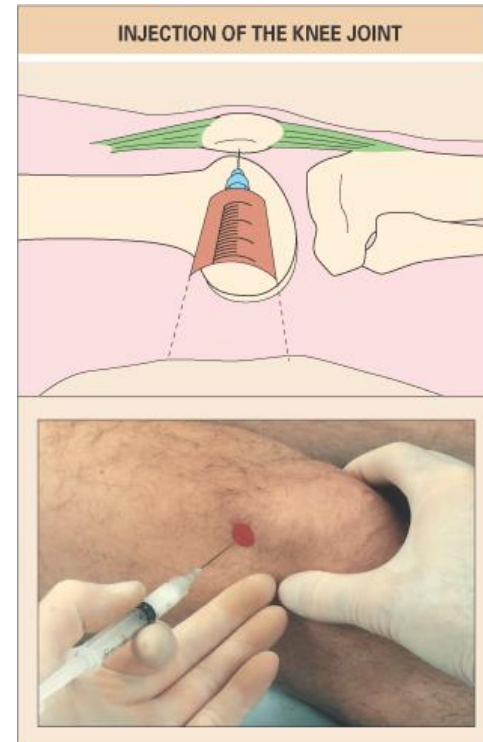


INJECTION OF THE GLENOHUMERAL JOINT: POSTERIOR APPROACH



Injection of the Knee

- Can be medial or lateral
- Palpate for the upper and lower poles of the patella
- Injection site is about 1/3 of the way down the patella
- Use left hand to compress suprapatellar pouch and open up a jaw to inject into



INJECTION OF THE KNEE JOINT

