Gout - Aetiology, Clinical Features and Management
• Inflammatory arthritis associated with hyperuricaemia

• Deposition of urate crystals causing joint pain
Purine Degradation to Uric Acid

- **Xanthine oxidase** catalyzes the final conversions to uric acid

![Diagram showing the degradation process from purine nucleotides to uric acid through Hypoxanthine and Xanthine]

- Purine nucleotides
- Purine nucleosides
- Hypoxanthine
- Xanthine
- Uric acid
Renal Elimination of Uric Acid
Operationally Defined 4 Component Model of Renal Uric Acid Handling

The multiple reabsorptive and secretory mechanisms may be regulated by a recently identified gene product of URAT-1 (Enomoto et al., Nature, 2002)
Pathogenesis of Acute Gouty Inflammation

Hyperuricemia

Complement Activation

Urate Crystals

Activation of Mast Cells

Activation of Endothelium

Chemotactic Factors

Synovial Lining Cell Activation

Synovitis

Neutrophil Influx

Amplification of Synovitis by Neutrophil Activation

• Increased Urate Formation:
  - Nutritional
  - Drugs
  - Haematological
  - Others

■ Decreased Urate Excretion:
  - Drugs
  - Renal impairment
  - Metabolic
  - Others
Clinical Features
• Urate > 416μmol/L

• Treatment not usually indicated

• Modify lifestyle/meds/underlying acquired causes
High Levels of Uric Acid Increase the Risk of Clinically Apparent Gout

The Normative Aging Study
2048 previously healthy men (initial average age 42) followed for 14.9 years

<table>
<thead>
<tr>
<th>Initial Serum Urate Level</th>
<th>Annual Incidence of Gout (in previously healthy men)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥9 mg/dL* (n=141)</td>
<td>4.9%</td>
</tr>
<tr>
<td>7-8.9 mg/dL (n=1642)</td>
<td>0.5%</td>
</tr>
<tr>
<td>&lt;7 mg/dL (n=5249)</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

*With urate levels ≥9 mg/dL, cumulative incidence of acute flares reached 22% after 5 years from enrollment

• Sudden onset agonising pain, erythema, swelling, decreased ROM

• Often fever and raised WCC

• Typically 1st metatarsophalangeal joint

• Others-instep, ankle, knee, wrist, fingers

• Precipitated by- excess food/alcohol
  - dehydration
• Asymptomatic phase
• Tophi- chalky deposit of urate in skin and around joints
  - large enough to be seen on xray

Classically-ear, olecranon bursa, achilles tendon

Often associated with renal impairment and/or longterm diuretics
• Unusual except in
  - elderly on longterm diuretics
  - allopurinol started soon after acute attack

• May mimic Rheumatoid Arthritis
Treatment
• NSAIDs are drug of choice

• Eg Indomethacin, Naproxen, Diclofenac

• Maximum dose immediately and continue for 24hrs after complete resolution of attack then taper quickly over 2-3 days
• Colchicine:

• MOA-binds to tubulin in leucocytes, prevents their migration to areas of urate deposition

• Big GI side effects

• Normally PO. Can be given IV but narrow therapeutic window.
- Steroids:
  Intra-articular e.g. Triamcinolone
  Systemically
  Useful in the elderly
• Risk Modification:

Dietary Education

Decrease alcohol intake

Lose weight

Avoid drugs that affect urate excretion

  e.g. aspirin, thiazide diuretics, pyrazinamide
• Decrease Urate - decrease formation
  - increase excretion

24 hour urine collection if ? Under excretor
  or Overproducer

Only start if
  -attacks are frequent, severe, renal impairment
ALLOPURINOL

MOA-inhibits xanthine oxidase

Start at low dose and titrate up

DO NOT USE FOR ACUTE ATTACK

If after acute attack, need colchicine/NSAIDs for at least 3 months
• Probenecid

MOA: Works at the proximal tubule, blocks reabsorption of filtered urate

Inhibited by low dose aspirin

Can precipitate acute attack/ renal stones

DO NOT USE IN ACUTE ATTACK

Contra-indicated with hx renal stones, renal impairment
- Sulpinpyrazone-added antiplatelet effect

Both less effective and more toxic than allopurinol

Allopurinol and Probenicid can be used together in severe tophaceous gout with high urate loads
• Increased risk of gout-co-morbidities, meds
• Acute tx-NSAIDs contra-indicated in many
• SE more pronounced
• Colchicine poorly tolerated
• Allopurinol-SE more pronounced
• Probenicid-contra-indicated with aspirin
- Gout and Hyperuricaemia
  
  Harris, Siegel, Alloway. American Family Physician. Vol.59/No.4. Feb 1999

- The influence of temperature on the solubility of monosodium urate
  

  
  Am J Med 1987;82:421-426

- ABC of Rheumatology: Gout, hyperuricaemia and crystal arthritis
  
  BMJ 1995;310:521-524