Hyperuricaemia and Gout

Uric Acid, Hyperuricaemia and Gout

- **URIC ACID (URATE)** - end product of purine degradation in humans
- **HYPERURICAEMIA** – is a serum urate concentration that is in excess of the solubility of urate
  - This can be due to overproduction or underexcretion of uric acid
  - **GOUT** is a disease resulting from deposition of monosodium urate crystals in tissues

Purine conversion to Uric Acid

- **XANTHINE OXIDASE** (depicted below by *) catalyzes the final conversion to uric acid
What causes hyperuricaemia and gout?

- There is a species wide deficiency of uricase (urate oxidase) activity
- There is limited solubility of uric acid and monosodium urate in body fluids
- There is a net renal absorption of about 90% of filtered uric acid

Causes of Impaired Uric Acid Excretion

- Primary or idiopathic hyperuricaemia
- Secondary hyperuricaemia
  - Diminished renal function
  - Inhibition of tubular urate secretion
    - Competitive anions (eg keto and lactic acidosis)
  - Enhanced tubular urate reabsorption
    - Dehydration, diuretics, insulin resistance (metabolic syndrome)
  - Mechanisms incompletely defined
    - Hypertension, hyperparathyroidism, certain drugs, lead nephropathy
Causes of Uric Acid Overproduction

- Primary hyperuricaemia
  - Idiopathic
  - Accelerated purine nucleotide synthesis
- Secondary hyperuricaemia
  - Excessive dietary purine intake
  - Increased purine nucleotide turnover (e.g., myelo and lymphoproliferative diseases, psoriasis)
  - Accelerated ATP degradation (e.g., glycogen storage diseases, hypoxia and tissue underperfusion, ethanol abuse)

Hyperuricaemia

- High levels of urate in extracellular fluids
- Crystals precipitate in joints and soft tissues

Deposition of urate crystals

- Decreased solubility of urate
  - Low temperature
  - Low pH
- Disturbances to the joint or soft tissue
  - Trauma or tissue injury or altered connective tissue matrix
- Reabsorption of water resulting in supersaturation
  - Lack of joint activity during sleep
Causes of acute flares

- Precipitating factors occur with acute flares
  - Local trauma
  - Alcohol, fasting or overeating
  - Acute medical or surgical illness
  - Significant change (increase or decrease) in serum uric acid
  - Seasonal factors

The 4 stages of gout

1. Assymptomatic hyperuricaemia
2. Acute gout or acute gouty arthritis
3. Interval or intercritical gout
4. Chronic tophaceous gout

See
www.niams.nih.gov/Health_Info/Gout/#acid

Pseudogout

- The crystals are calcium phosphate crystals not uric acid.
Treatment

• Non Steroidal Anti Inflammatory Drugs (NSAIDS)
• Corticosteroids
• Colchicine

Analytical Methods

• 1. Colorimetric – formation of chromogen (Tungsten blue) 650-750nm, when phosphotungstic acid is reduced by urate in alkaline solution.
• 2. Enzymic – Uricase is used to oxidise urate to allantoin, hydrogen peroxide and carbon dioxide – requires narrow bandwidth spectrophotometer to measure decrease in absorbance due to urate at 293 nm.
• Automated methods use peroxidase system to link hydrogen peroxide to an oxygen acceptor (e.g. 4-aminophenazone and a substituted phenol) to generate a chromogen.

• Association of Clinical Biochemistry 2012

Conclusion

• Uric Acid is the byproduct of purine metabolism in humans
• Hyperuricaemia and resultant disease may be on the rise
• Hyperuricaemia can result from overproduction or underexcretion of uric acid
• Increased serum concentrations of uric acid can cause crystallisation and deposition in joints and other connective tissues.
Questions

1. What is uric acid?
2. What causes gout?
3. Who is likely to develop gout?
4. How is gout diagnosed?
5. What are the signs and symptoms of gout?
6. How is gout treated?
7. What analytical methods are available for the measurement of uric acid?