10.1.6

Gout

Watch this video on Gout

Gout involves recurrent attacks of severe articular and periarticular inflammation of the joints. Gout is caused by elevated **uric acid** levels in the plasma leading to the development of uric acid crystals in the synovial fluid of the joints. Uric acid comes from the breakdown of genetic material. When DNA/RNA is broken down, purines like adenine and guanine are released. These purines are then converted to uric acid by the enzyme **xanthine oxidase** so they can be more readily excreted by the kidney. If levels of uric acid are high, it can crystallize in the joints and cause gout. Hard nodules made of crystalline uric acid known as **tophi** may form at the surface of joints and tissues including the skin. The pain associated with an acute gout attack can be quite severe; patients describe even the weight of a bedsheet making the pain worse. A gout attack may last for days or weeks.

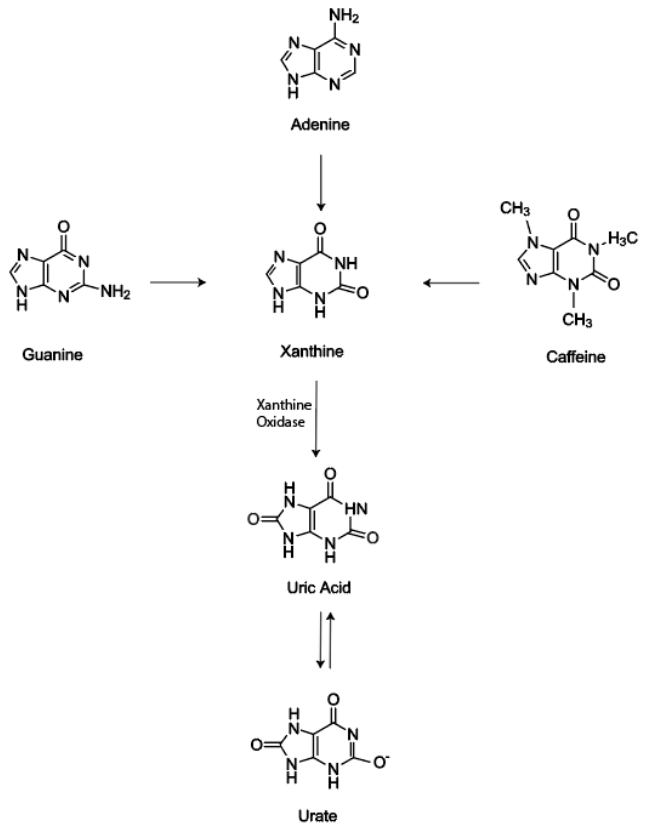

Image by Becky T. BYU-I W20

Common causes of hyperuricemia include enzyme defects (i.e. overactive xanthine oxidase), a diet high in purines, increased cell turnover (dead cells release their genetic material which must be metabolized) and chronic kidney

disease (difficulty excreting uric acid). Foods considered high in purines are meats (especially organ meats like liver), seafood (especially anchovies, shellfish, sardines and tuna), and alcohol (especially distilled liquors like beer). Caffeine is another common example of a purine that may be found in our diet. Diabetes mellitus also increases the risk of developing gout, but the exact mechanism is not well understood and probably involves the convergence of multiple biochemical pathways.

Once formed, uric acid is more likely to precipitate in the joints than other areas because synovial fluid is not as good of a solvent as blood. In addition, the temperature of synovial fluid is lower than blood, making solubility even more difficult. The first metatarsal phalangeal joint of the great toe is often the first and sometimes the only joint affected. Joints of the foot are at particular risk given how far they are away from the heart and the decreased body temperature. The precipitated uric acid crystals in the joints act as a chemoattractant to white blood cells, particularly neutrophils. The neutrophils attempt to phagocytose the crystals and die in the process, resulting in the release of hydrogen ions and lysosomal enzymes. These substances cause further damage to the joints and subchondral bone. The immune cells attracted to the joints also release cytokines that promote inflammation.

Nonsteroidal anti-inflammatories (e.g., indomethacin, ibuprofen) and colchicine are useful for the treatment of acute gout attacks because they decrease pain and inflammation. Allopurinol (Zylorim), a hypouricemic agent, lowers blood levels of uric acid by inhibiting the enzyme xanthine oxidase. Probenecid, a uricosuric agent, acts to lower uric acid levels by blocking the reabsorption of uric acid in the proximal convoluted tubules of the kidneys. Probenecid has the potential to have a lot of interactions with other drugs that the patient may be taking because the transporter that it blocks in the PCT is also used to reabsorb many other anion molecules.