

- **Cardinal manifestations of Gout that are induced by excess of uric acid :**
 - 1- Tophi (deposition of monosodium crystals, can be anywhere, e.g : on the ear helix)
 - 2- Arthritis (can be acute or chronic)

The mechanism how the inflammation is induced :
Hyperuricemia → crystal deposition → protein binding → receptor binding → cytokines release → influx of polymorphonuclear leukocytes → engulfment of the crystals → inflammation .
 - 3- Nephrolithiasis and nephropathy.
- Uric acid is a product of purine metabolism, there must be a balance between the rate of production and that of secretion of it, and gout is the condition in which this balance is broken , by increasing the production or decreasing secretion.
- **Symptoms of gouty arthritis :**
 - 1- Sudden onset.
 - 2- Middle aged males.
 - 3- Distal joints (e.g : MTP joint)
 - 4- Intense inflammation.
 - 5- Recurrent episodes.
 - 6- Hyperuricemia.
 - 7- Bony erosion of X-ray.
 - 8- Affected by diet.
 - 9- Severe pain.
- Uric acid is excreted by kidneys , both glomerular filtration and tubular excretion work to increase its secretion , while tubular re-absorption and post-secretory re-absorption send it back to the blood.

- **Drugs used to treat Gout :**

- **⊙ Acute arthritis drugs :**

- 1- **Colchicine (a plant alkaloid) :**

- Only used when it's gouty arthritis ,and has nothing to do with the uric acid , not an analgesic and only works to inhibit the inflammatory response by binding to tubulin protein → inhibits microtubules formation → PMN cells are unable to migrate and phagocytose the crystals → no inflammatory response to the deposited crystals .
 - High doses → acute gouty arthritis , Low → prevention of recurrent gouty arthritis(here it's more useful).
 - It can be toxic , this is dose dependent and more severe with patients of renal and hepatic diseases, signs of toxicity are:
 - 1- GIT symptoms (nausea , vomiting , diarrhea , cramps and pain)
 - 2- Hematologic (aplastic anemia , agranulocytosis and thrombocytopenia)
 - 3- Muscular weakness.

- 2- **NSAIDS :**

Indomethacin ,naproxen, ibuprofen, sulindac and ketoprofen ,how to memorize?

An **Indian kid** called **sulindac** took a **nap** after swallowing 2 **ibuprofen** tablets.

- 3- **Steroids**

- 4- **Rest ,analgesia,and time.**

- **⊙ Urate lowering drugs :**

- Work to block uric acid production or enhance secretion → net reduction in total uric acid level → prevent arthritis and tophi deposition.
 - Not indicated after the first attack , no role in managing acute gout and initiating the therapy with them can worsen the situation and bring on acute gouty arthritis.
 - Purine bases are either products of cell breakdown or dietary constituents.
 - Purine bases → **hypoxanthine** → **xanthine** → **uric acid**
 - Xanthine oxidase is the enzyme that catalyzes the reactions in blue .

