

Pharmacology Team 3

Our notes are in orange



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TREATMENT OF GOUT

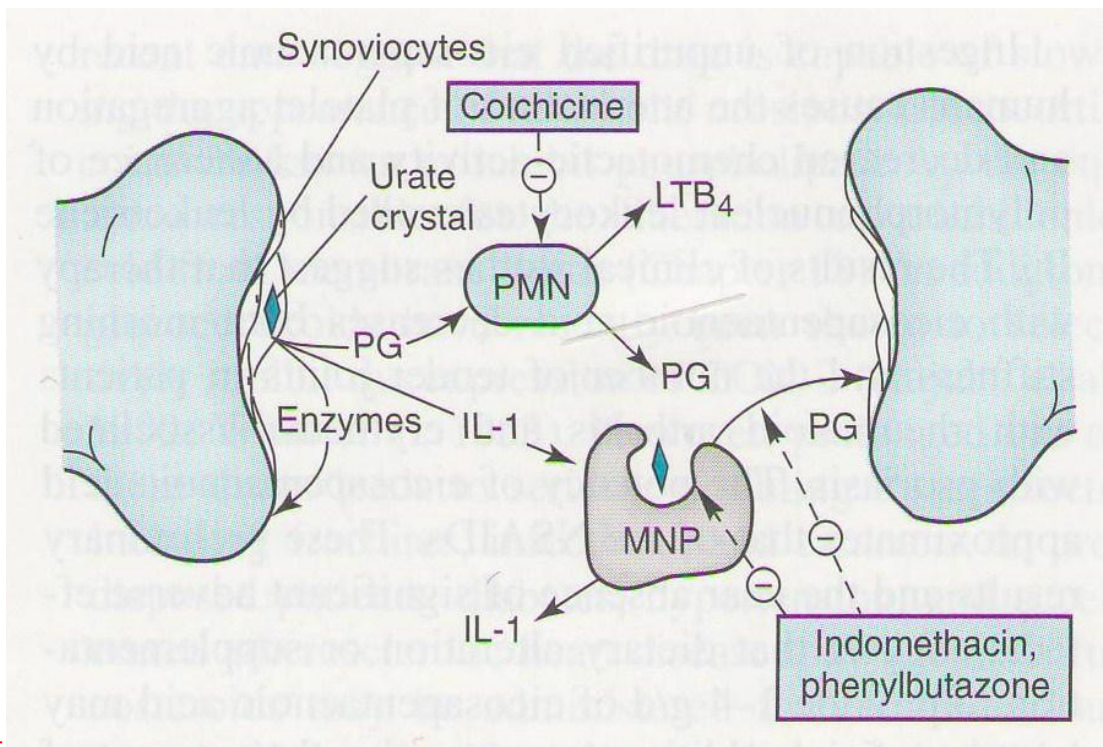
BY

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GOUT

—**Familial metabolic disease Characterized by :**

- + Acute arthritis
- + Uric stones in the kidneys
- + Hyperuricemia



Pathophysiologic events in a gouty joint

—**TREATMENT OF GOUT**

—**ACUTE GOUT :**

- + NONSTERIODAL ANTIINFLAMMATORY DRUGS (NSAIDs).
- + COLCHICINE

+ Nonsteroidal Antiinflammatory Drugs

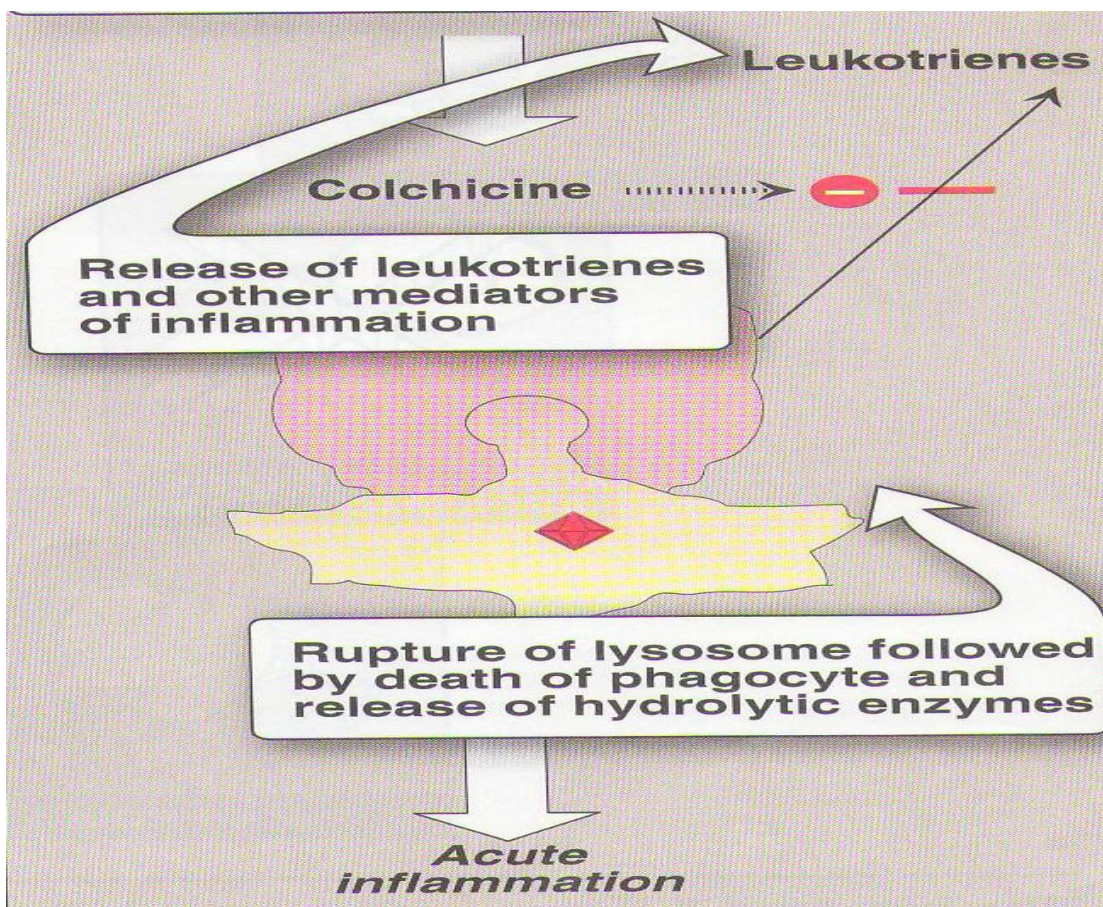
— Analgesic & Anti-inflammatory

— (Aspirin in therapeutic doses is contraindicated in acute attack)

+ COLCHICINE

—MECHANISM OF ACTION :

- Selective drug in acute gouty arthritis
- Inhibits leukocytes migration to the inflammatory site & phagocytosis



Pharmacokinetics

- Given orally
- Metabolized in liver & GIT

Excreted in urine & bile

Clinical uses

- Selective for acute gouty arthritis

Prevention of acute gout , in the early stages of anti-hyperuricemic therapy.

(patients with chronic gout and treated with anti-hyperuricem they also could be given Colchicine to decrease the incidence of another acute attack)

Colchicine

- Relief pain & inflammation of gouty arthritis within 12-24 hours .
- Has no analgesic effect

Adverse Effects

- Diarrhea is common (NSAIDs is preferred) **that's why NSAID's is the first drug of choice in acute gout**
- Nausea , vomiting , abdominal pain
- Alopecia **spot baldness** **ثعلبه**, bone marrow depression , peripheral neuritis (are rare)

Contraindication & Precautions

- Contraindicated in pregnancy
- Used with caution in hepatic, renal or gastrointestinal diseases

CHRONIC GOUT :

✚ URICOSURIC DRUGS

✚ ALLOPURINOL

✚ URICOSURIC DRUGS

Are drugs used to increase the excretion of uric acid

—Large dose of aspirin

—Probenecid

MECHANISM OF ACTION

— Block the active transport sites of the proximal tubules (middle segment); decreased reabsorption of uric acid

CLINICAL USES

Chronic gout

(urine volume should be kept at a high level & urinary pH must be kept alkaline)

Probenecid is used clinically to increase plasma level of penicillin

Ps: the probenecid decreases the Uric Acid reabsorption

But it increase the reabsorption of the other organic acid like “penicillin”

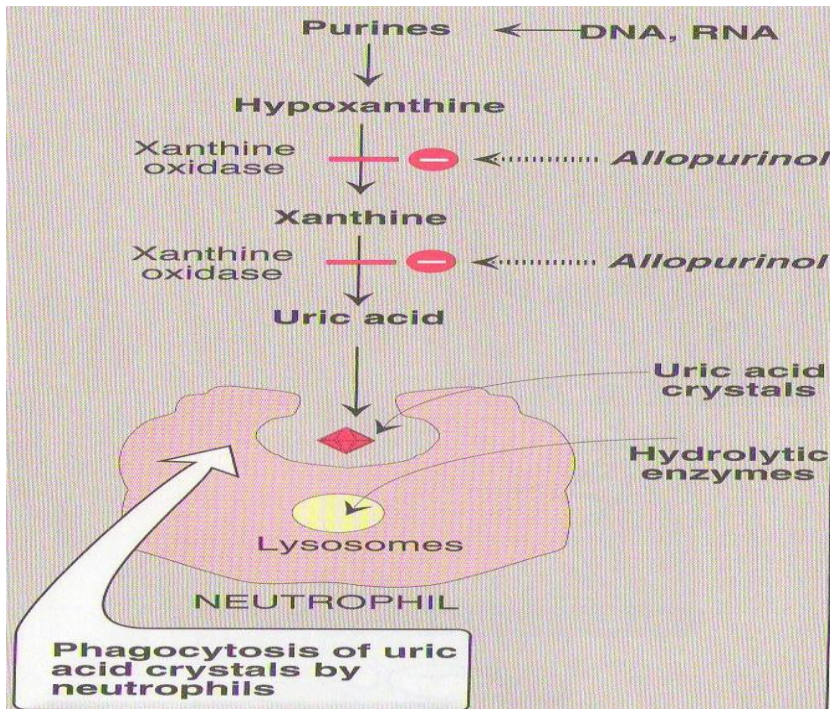
Probenecid : ADVERSE EFFECTS

- Gastrointestinal irritation
- Allergic dermatitis
- Nephrotic syndrome

ALLOPURINOL

Inhibits the synthesis of uric acid from hypoxanthine and xanthine by inhibiting xanthine oxidase enzyme. (lowering serum uric acid level)

Since hypoxanthine and xanthine are more soluble in water and can be easily excreted so, the inhibition of xanthine oxidase doesn't cause accumulation of uric acid's precursor



PHARMACOKINETICS

Well absorbed orally

Metabolized to an active metabolite (alloxanthine) which causes its long half life

Taken once daily

Excreted in urine & feces

CLINICAL USES

Primary hyperuricemia unknown etiology

Secondary hyperuricemia e.g: cancer or chemotherapeutic drugs

Recurrent renal stones

When serum urate levels are greatly increased

ADVERSE EFFECTS

— Acute attacks of gouty arthritis during the first weeks of therapy (NSAIDs, or colchicine is given) due to compensation of uric acid levels

- Gastrointestinal upset
- Peripheral neuritis
- Hypersensitivity reactions
- Hepatic toxicity & Interstitial nephritis (rare)

DRUG INTERACTIONS (MCQ)

Allopurinol inhibits the metabolism of :

- 1- Chemotherapeutic agents, such as : 6- mercaptopurine, azathioprine .
This requires reduction of the dosage of these drugs by 75%
(high doses of Chemotherapeutic agents not given with Allopurinol)
- 2- Oral anticoagulants
warfarin