

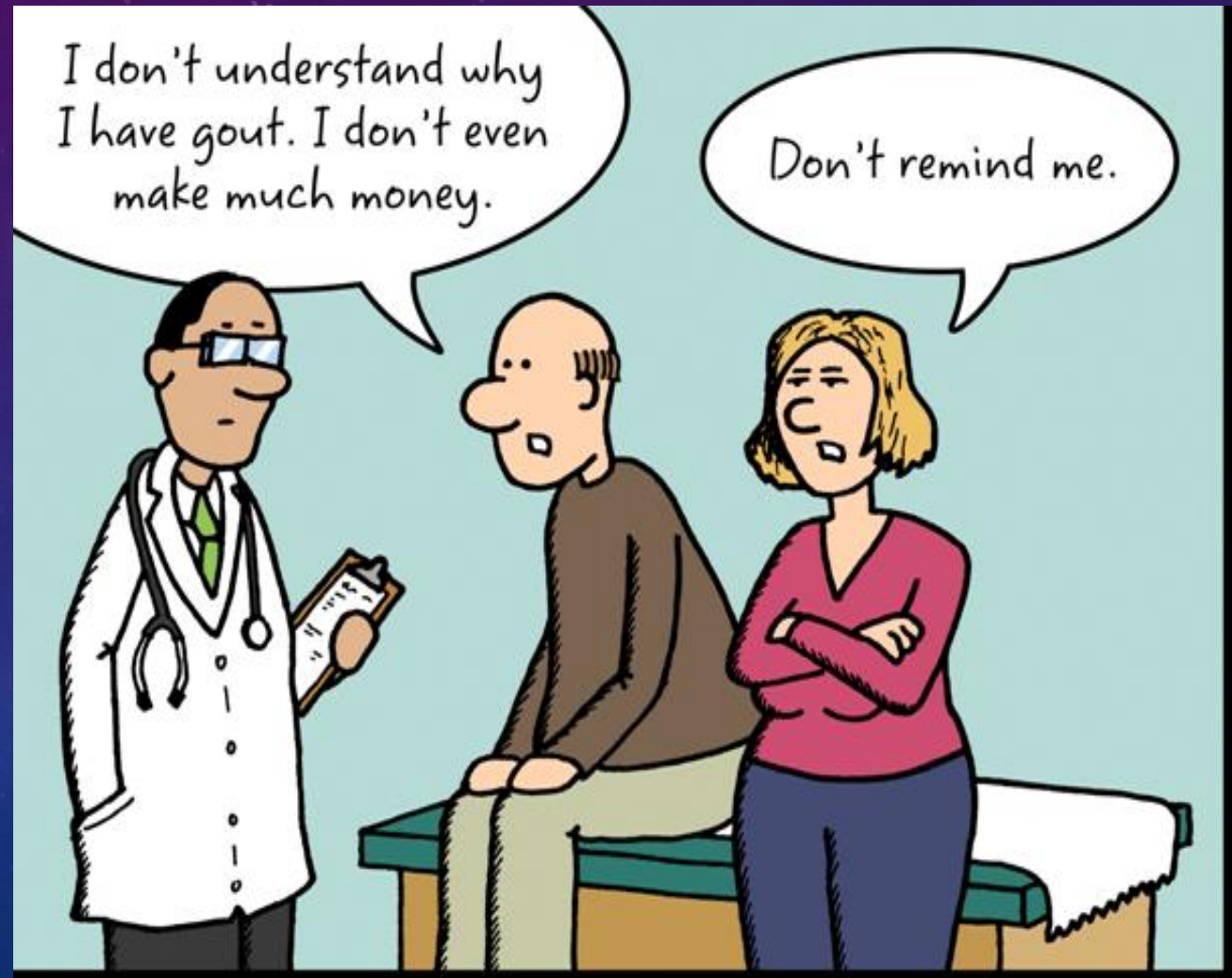
DRUGS IN GOUT

EPIDEMIOLOGY

Prevalence of hyperuricemia 5%

Prevalence of gout 0.2%

Male to female ratio 10:1



DRUGS IN GOUT

ILOS

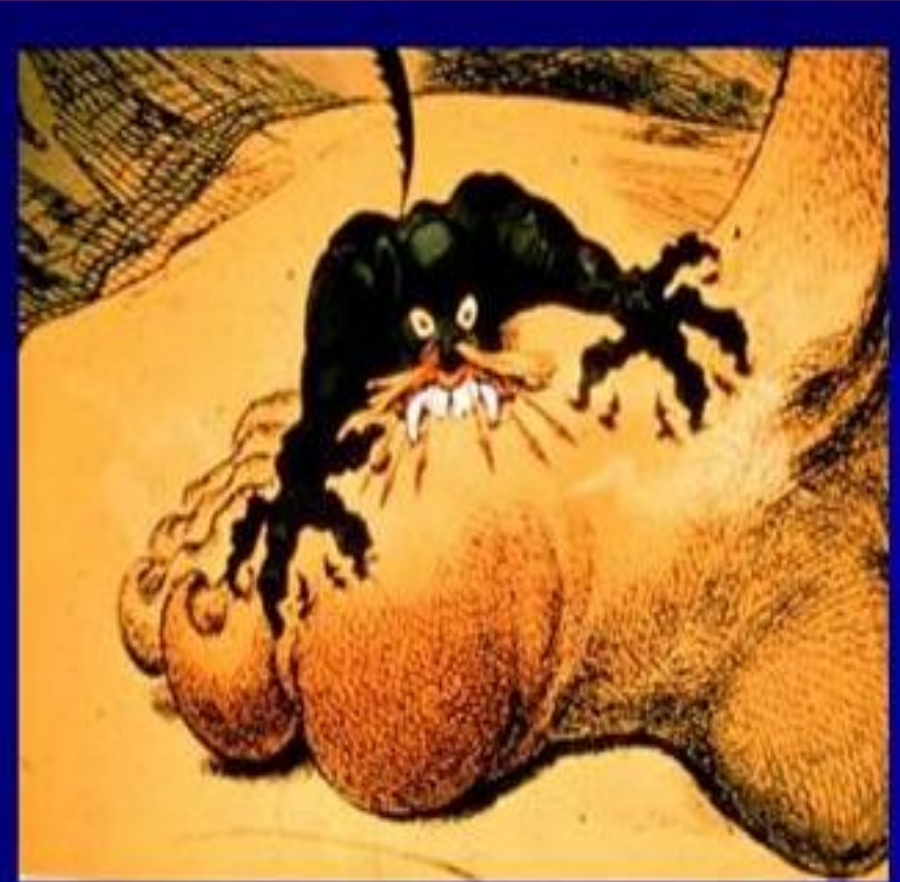
Describe drug and non drug treatment of gout

Outline the stages of gout and the therapeutic objectives in each stage

Identify the mechanism of action of drugs used for treatment of gout

Classify drugs used for treatment of gout

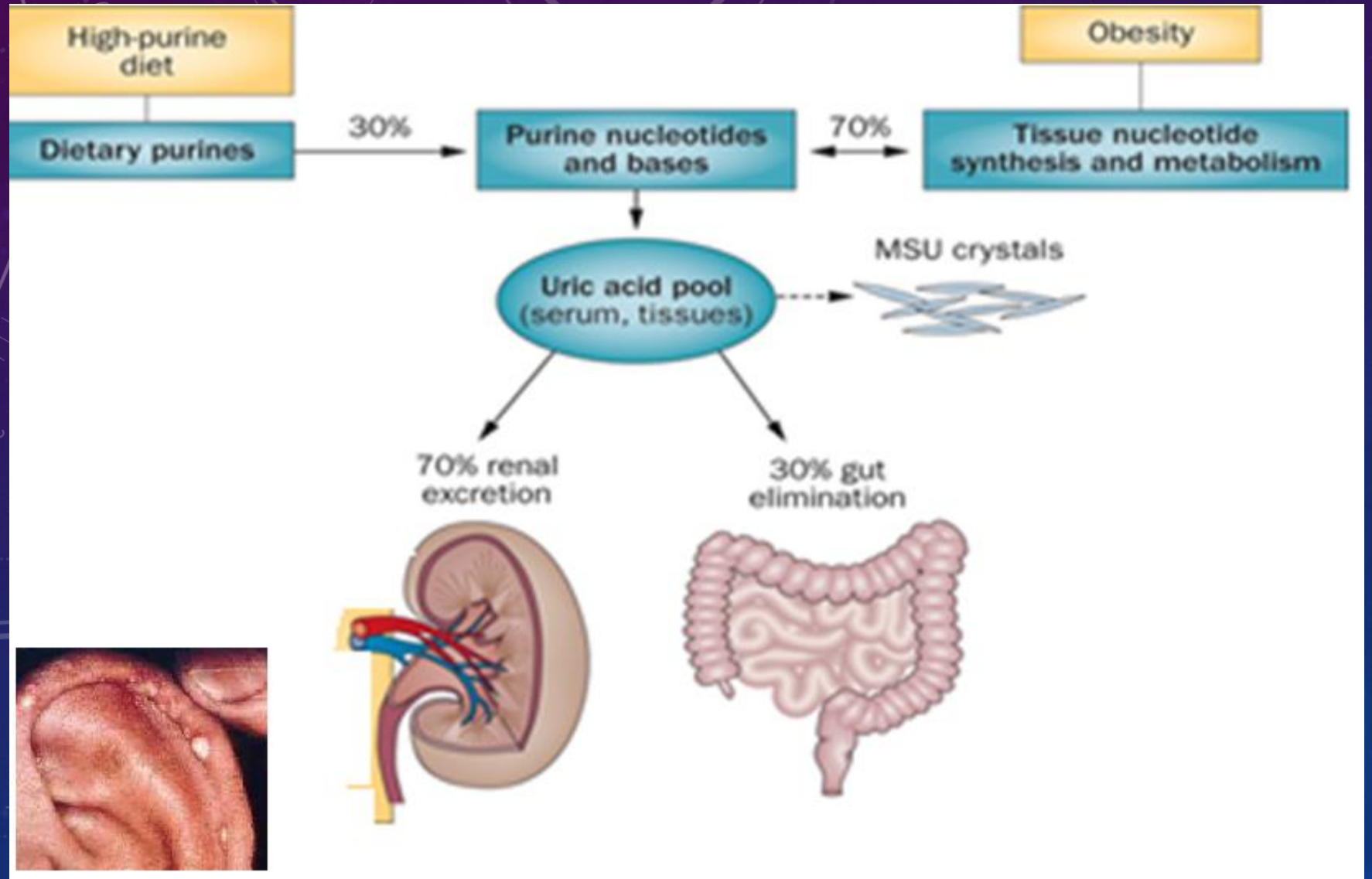
Study in details the pharmacology of drugs used for treatment of gout



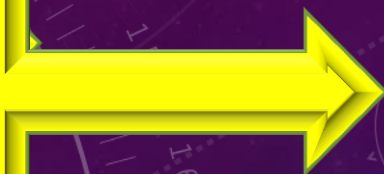
WHAT IS

GOUT?

DRUGS IN GOUT

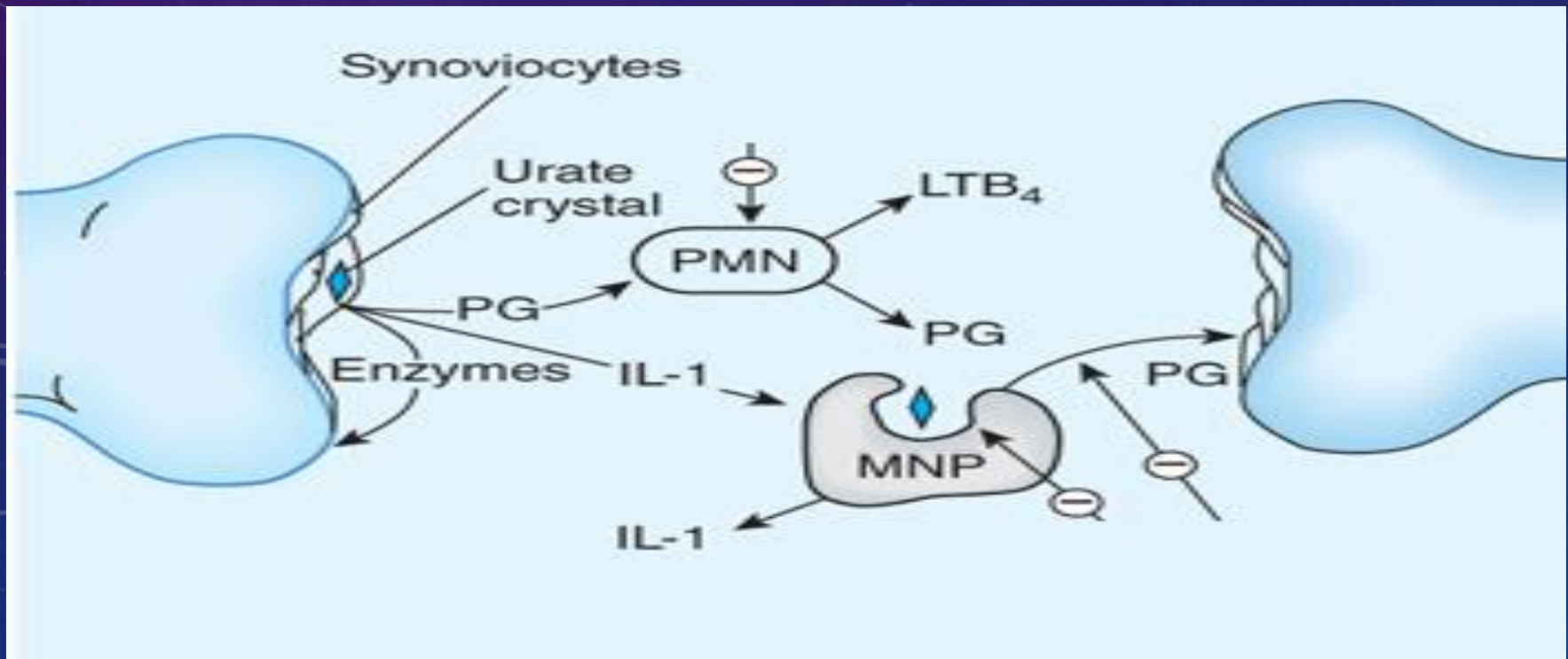


Pathophysiology



Over production

Under excretion



DRUGS IN GOUT

Uricosstatic

Allopurinol,
Febuxostat

Uricosuric

Probenecid,
Sulfinpyrazone

Anti- inflammatory

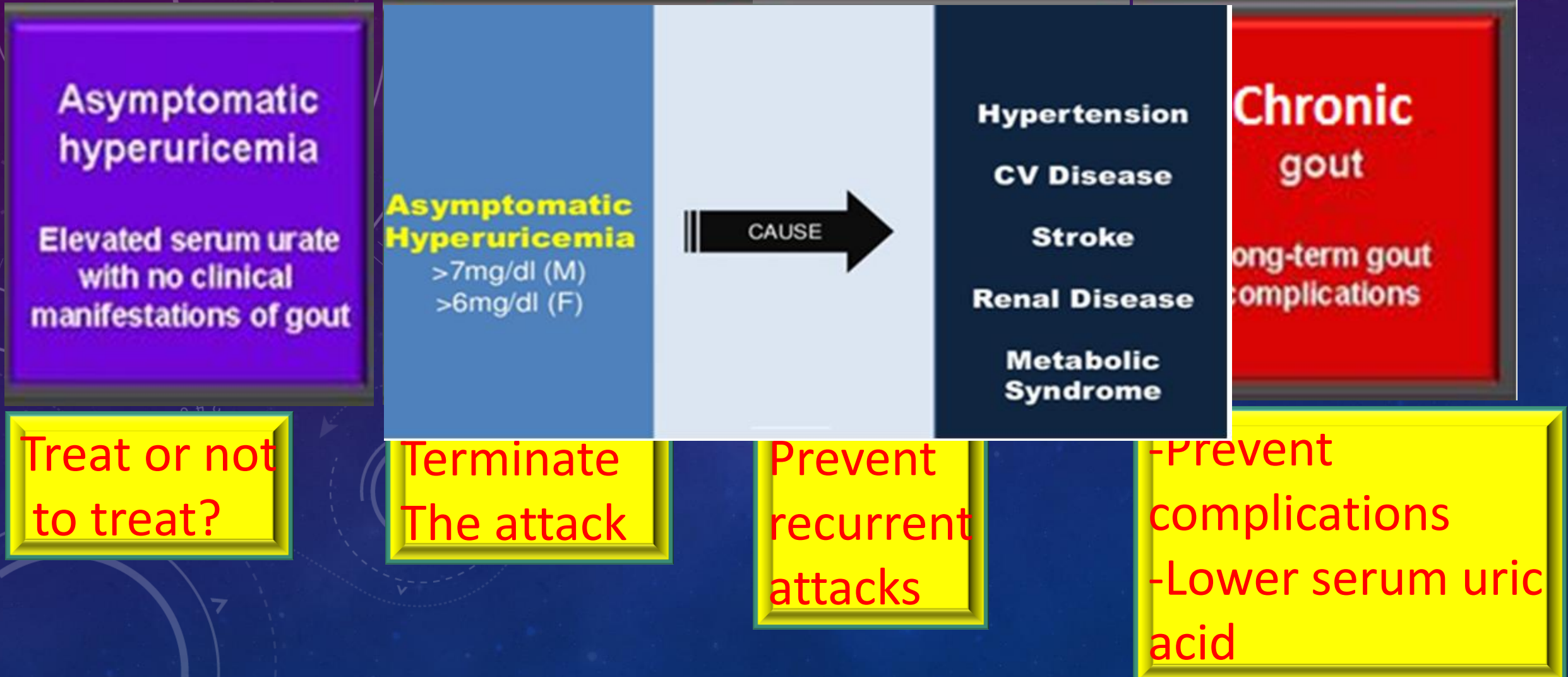
NSAIDs, Steroids

Tubulin inhibitors

Colchicine



STAGES OF GOUT & GOAL OF THERAPY



DRUGS IN GOUT



**Treatment
of gout**



**Non-
pharmacologic**

Pharmacologic

NON-PHARMACOLOGIC THERAPY

LIFESTYLE MODIFICATIONS

Loss of weight

Exercise

Diet control

Smoking cessation

Drink plenty of fluids, especially water.



Choose low-fat or fat-free dairy products.



Consume complex carbohydrates.



Reduce saturated fat consumption.



Limit fish, meat, and poultry.



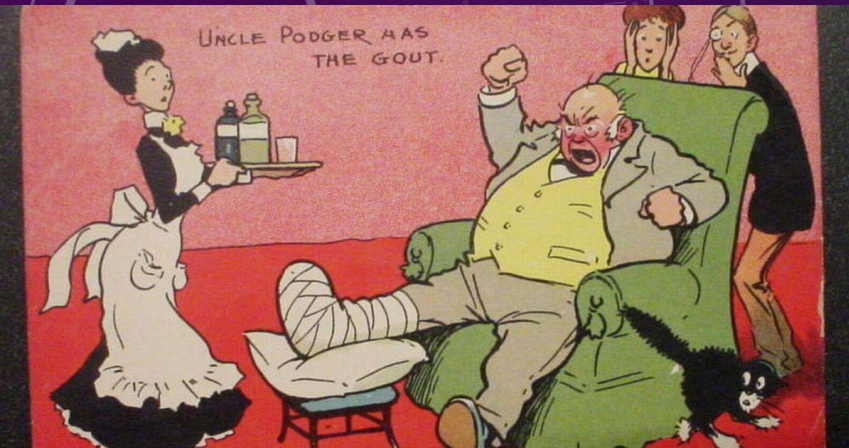
Avoid eatables sweetened with high-fructose corn syrup.



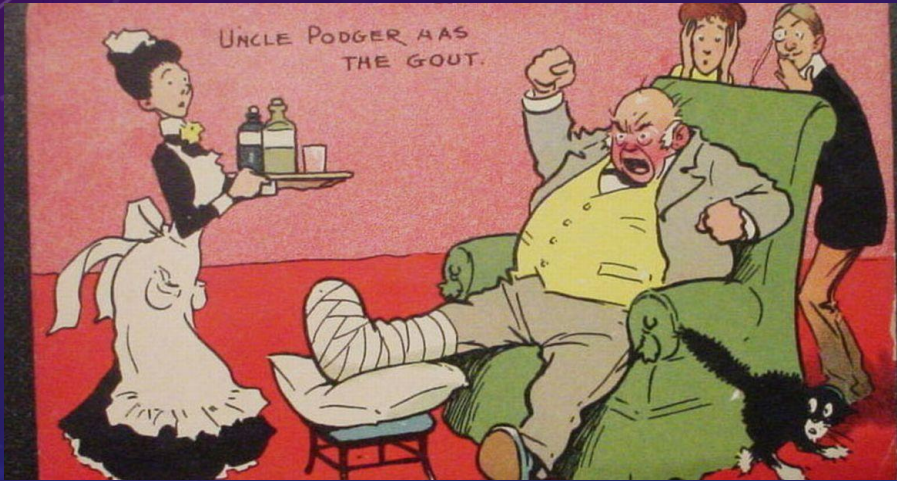
Avoid alcohol.



TREATMENT OF ACUTE GOUT



Acute gouty arthritis



Colchicine

NSAIDs

Corticosteroids

NSAIDS

NSAIDs are the most commonly used first-line treatment

Head-to-head studies show few differences between drugs

Full doses of NSAID should be initiated immediately and tapered after resolution of symptoms

Avoid NSAIDs:

- G-I ulcer
- Bleeding or perforation
- Renal insufficiency
- Heart failure
- Use of oral anticoagulants



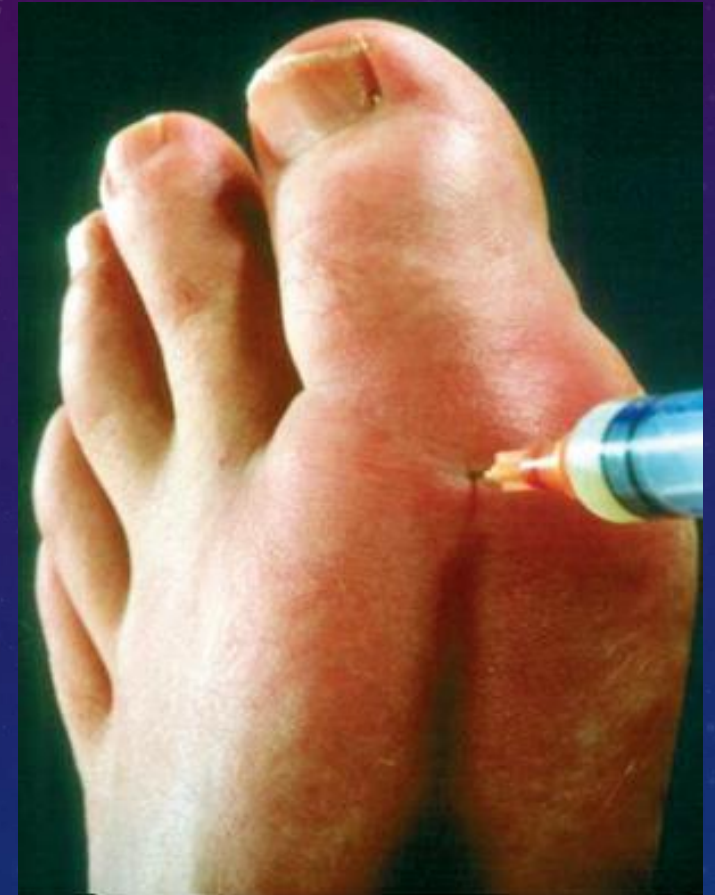
STEROIDS

Corticosteroids are a good alternative where NSAID and colchicine cannot be used or in refractory cases

Studies showed equal efficacy between corticosteroid and NSAIDs, with no reported side-effects with short-term use of corticosteroid

In elderly people, patients with kidney or hepatic impairment, IHD, PUD, hypersensitivity to NSAIDs

- Intra articularly (preferred route if one or two joints affected)
- Orally
- Intramuscularly or intravenously.



COLCHICINE

Alkaloid obtained from autumn crocus (*Colchicum autumnale*)

Minimal effect on uric acid synthesis , excretion & is not analgesic



DRUGS IN GOUT

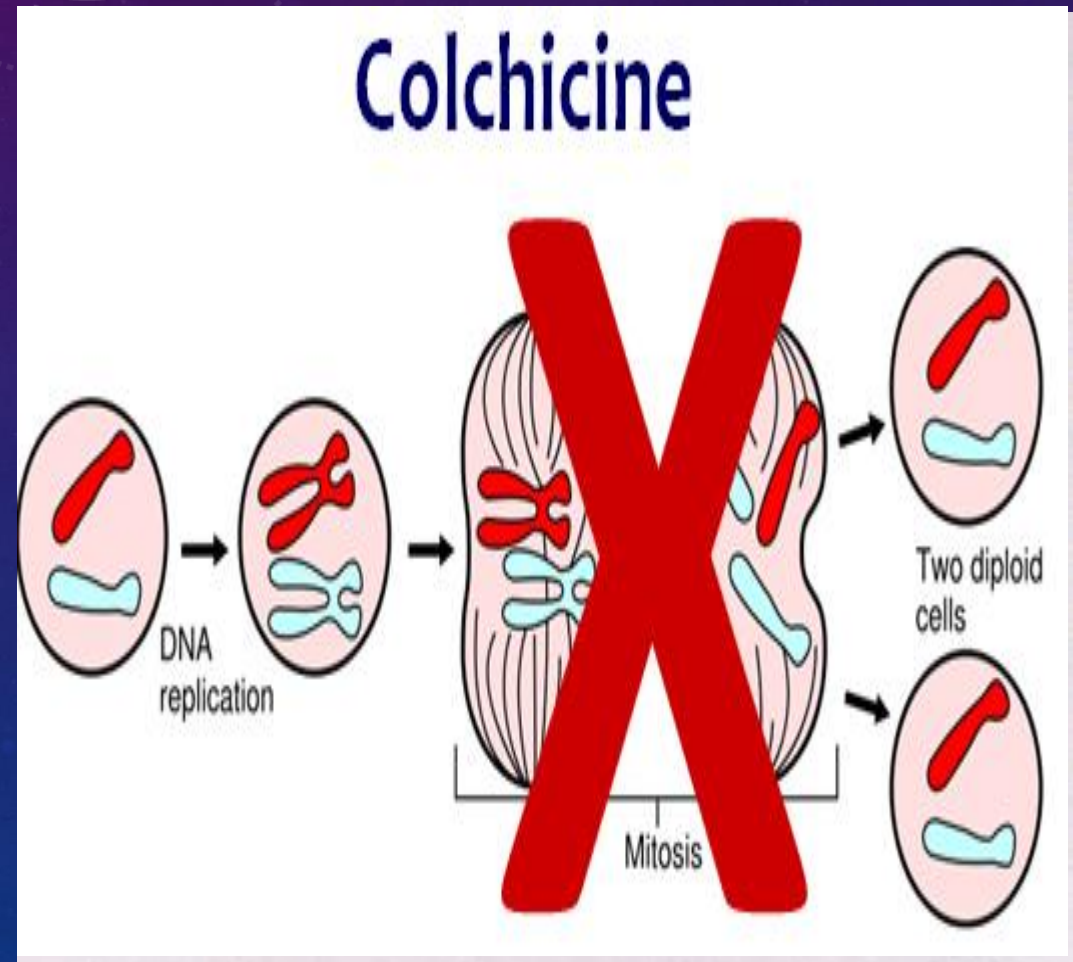
MECHANISM

Binds to microtubules in neutrophils

Inhibits cell division

Inhibits chemotactic factors

Inhibits inflammasomes & IL-1 production



COLCHICINE

PHARMACOKINETICS

Administered orally, rapid absorption from the GI tract

Reaches peak plasma levels within 2 hours

Recycled in the bile and is excreted unchanged in the faeces or urine

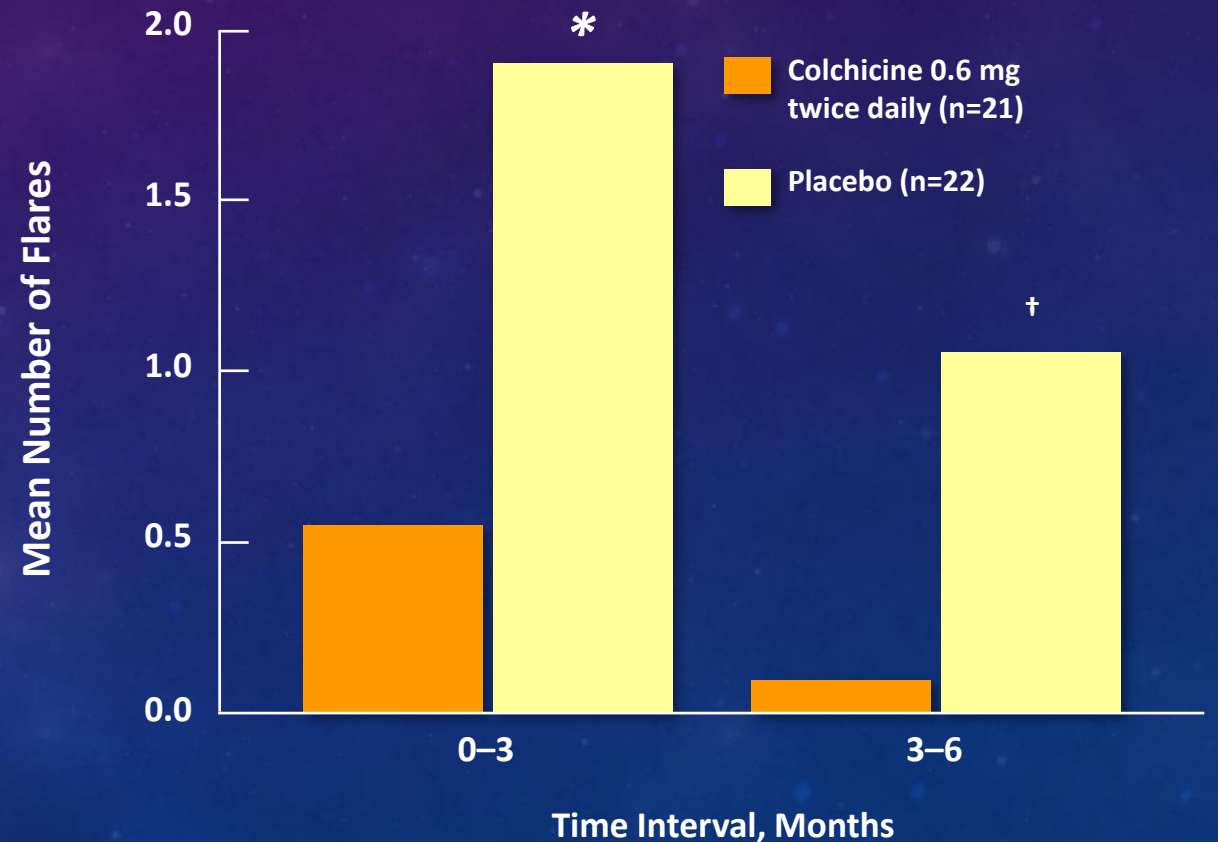
Use should be avoided in patients with a creatinine clearance of less than 50 mL/min



COLCHICINE

CLINICAL USES

- Treatment of gout flares
- Prophylaxis of gout flares
- Treatment of Mediterranean fever



ADRS

-Diarrhea (sometimes severe)

-Nausea

-Vomiting

-Abdominal cramps

-Dehydration

Bone marrow depression:
nadir at 7 days

-Less frequent:-

-Cardiac toxicity ,Arrhythmia

-Vascular collapse

Hepatotoxicity , Alopecia



Prevention of recurrent attack

Inhibition of uric acid synthesis

- Allopurinol
- Febuxostat

Uricosuric drugs

- Probenecid
- Sulfinpyrazone

Mamalian Uricase

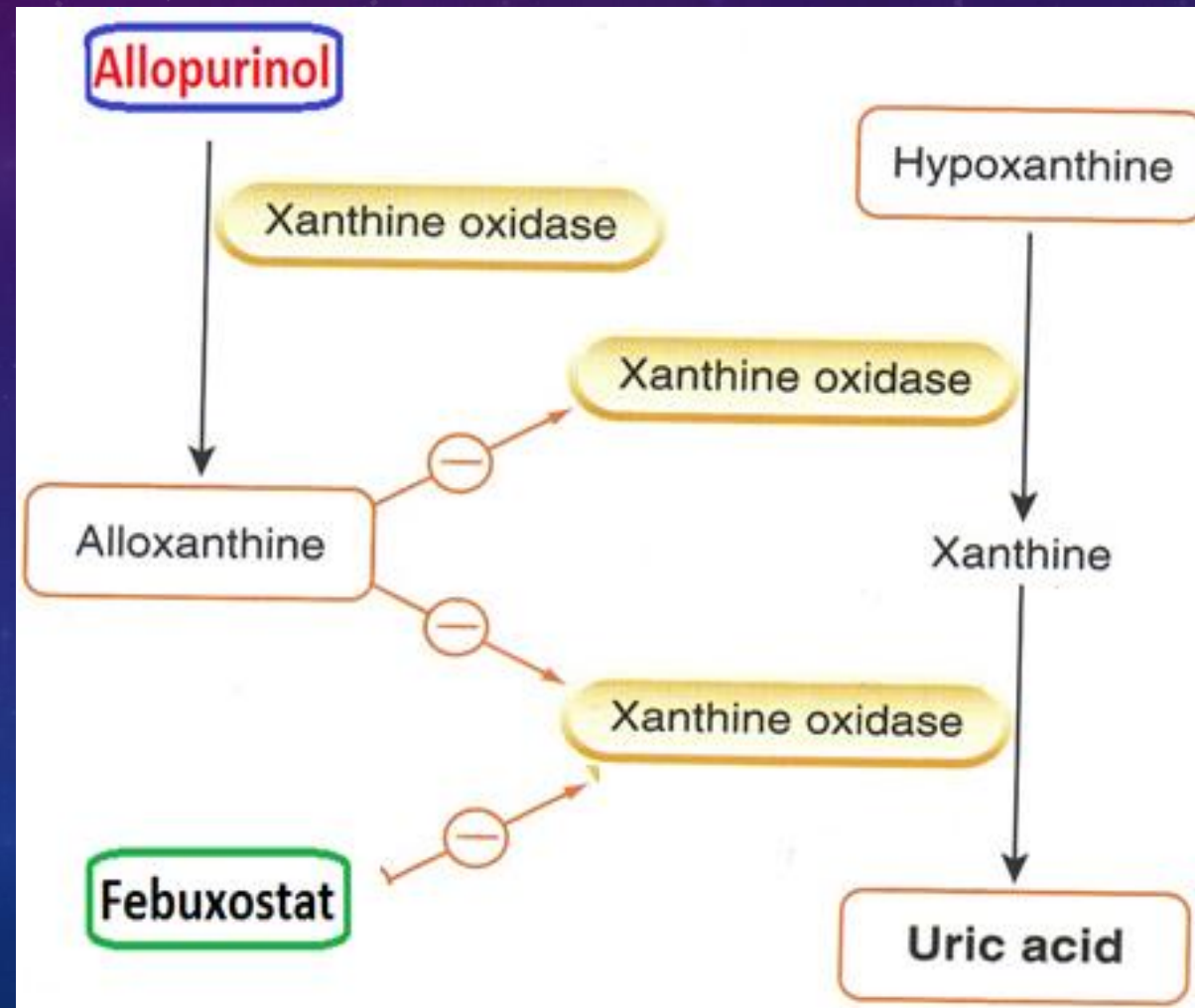


INHIBITORS OF URIC ACID SYNTHESIS

Inhibit xanthine oxidase

Include allopurinol & febuxostat

Allopurinol is metabolized by xanthine oxidase into alloxanthine (oxypurinol) which is pharmacologically active



ALLOPURINOL

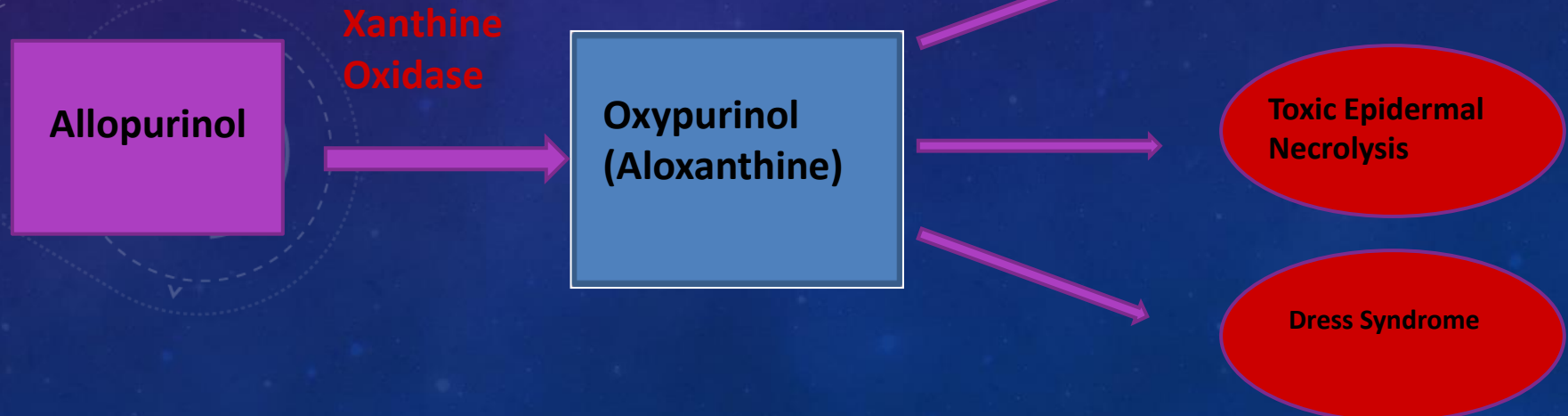
PHARMACOKINETICS

Absorption 70%

Protein binding negligible, 5%

Hepatic metabolism, 70% converted to active metabolite(oxypurinol)

Oxypurinol is eliminated unchanged in urine



ALLOPURINOL

CLINICAL USES

Management of hyperuricemia of gout

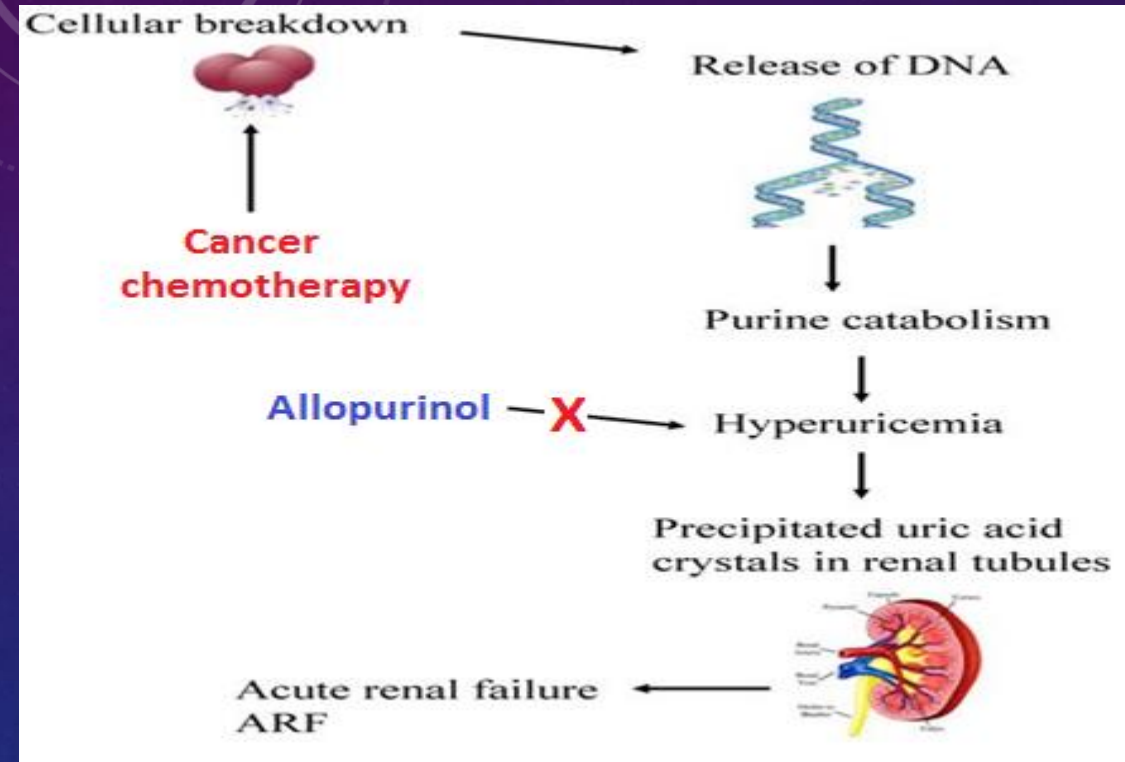
Uric acid stones or nephropathy

It is a drug of choice in patients with both gout & ischemic heart disease

Severe tophaceous deposits (uric acid deposits in tissues)

Management of hyperuricemia associated with chemotherapy

Prevention of recurrent calcium oxalate kidney stones



ADRS

Diarrhea, nausea, abnormal liver tests

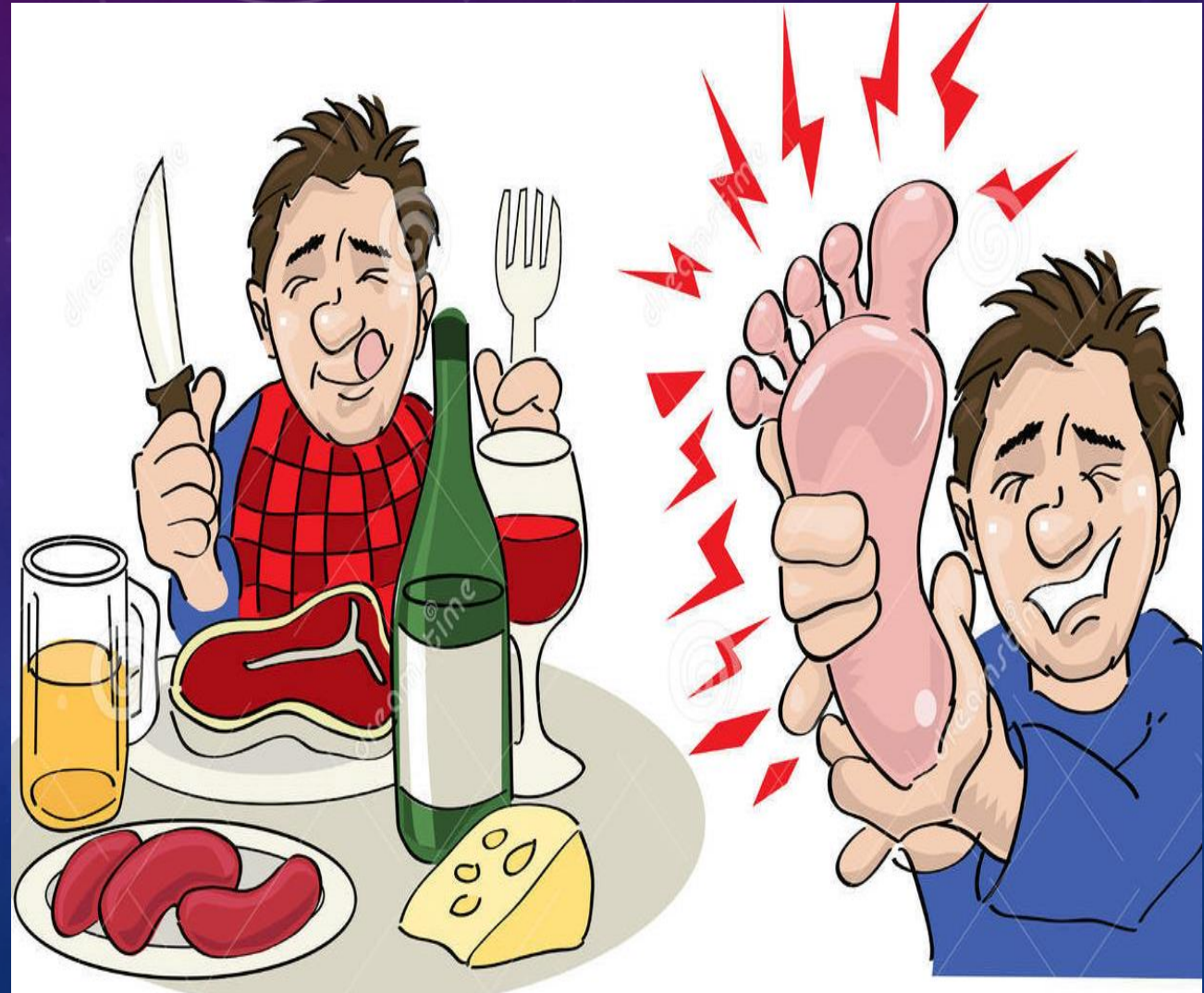
Acute attacks of gout

Fever, rash, toxic epidermal necrolysis, hepatotoxicity, marrow suppression, vasculitis

DRESS syndrome

Drug Reaction, Eosinophilia,
Systemic Symptoms

20% mortality rate

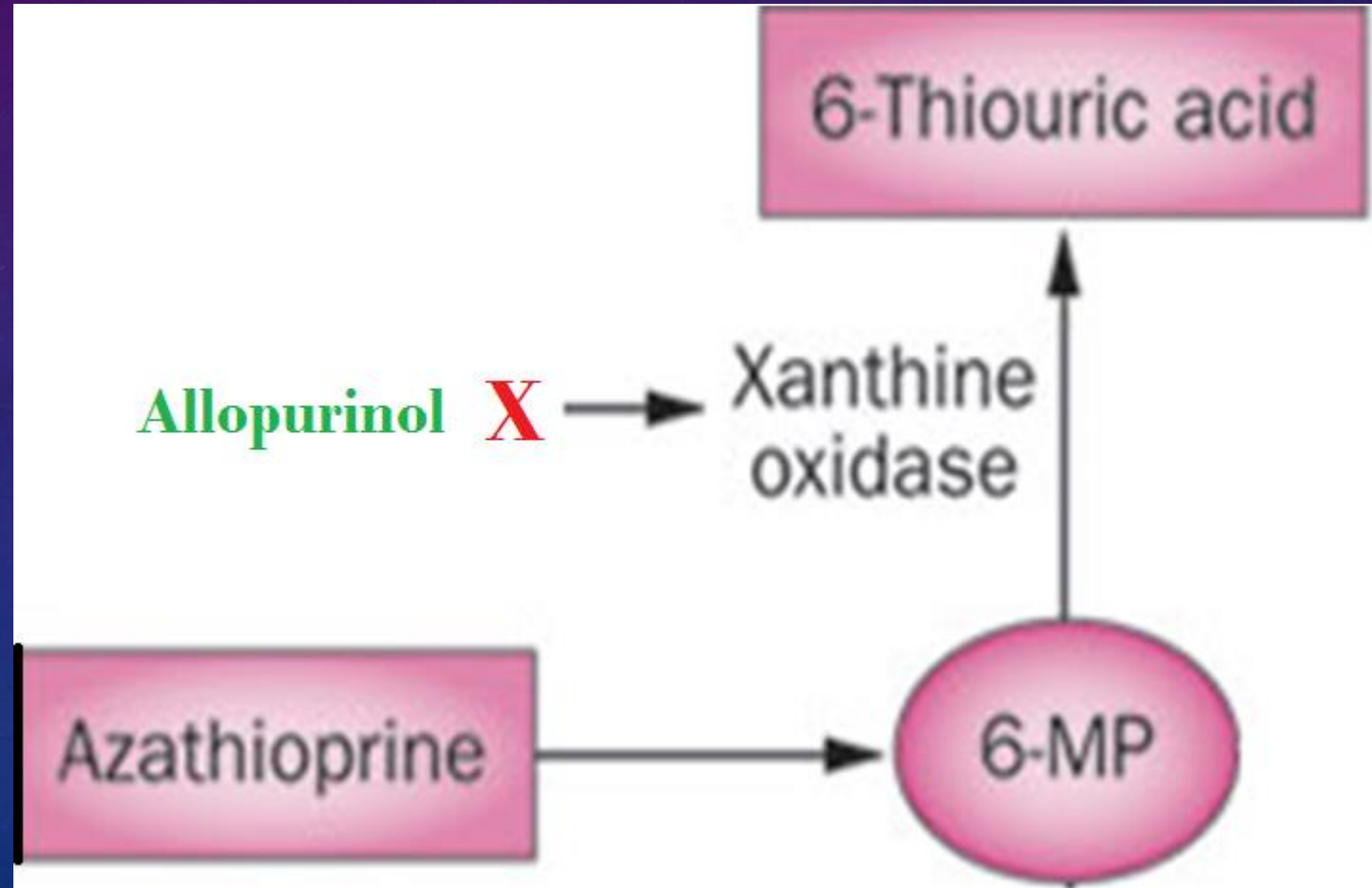


Drug Interactions

Inhibits metabolism of Warfarin & dicumarol

Reduce the metabolism of 6-mercaptopurine and azathioprine

With ampicillin : Increases frequency of skin rash



FEBUXOSTAT

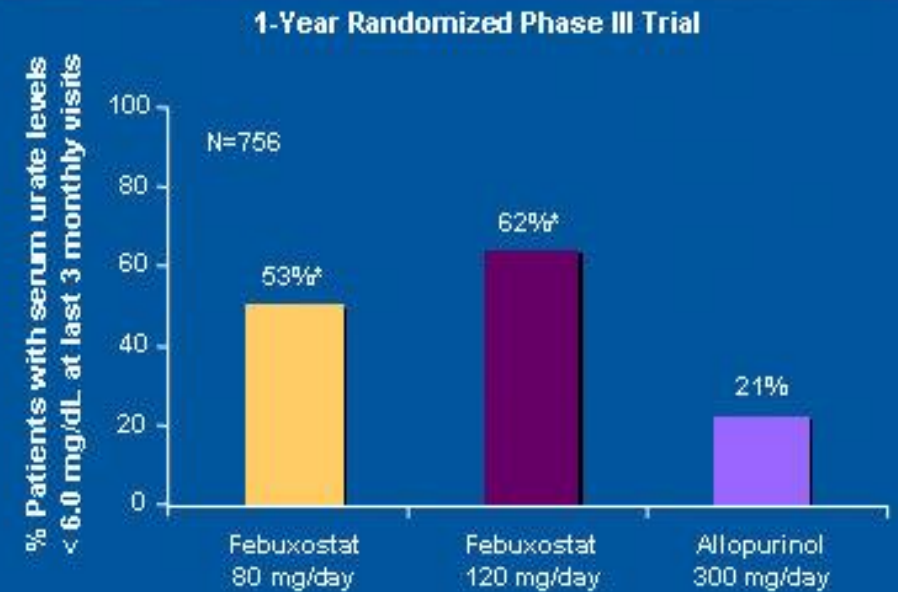
Oral specific xanthine oxidase inhibitor

Indicated for the chronic management of hyperuricemia in patients with gout

Chemically distinct from allopurinol (non purine)

Can be used in patients with renal disease

Febuxostat vs Allopurinol: Serum Urate



*P<0.001 vs allopurinol

Becker MA et al. *N Engl J Med*. 2005;353:2460-2461.

FEBUXOSTAT

PHARMACOKINETICS

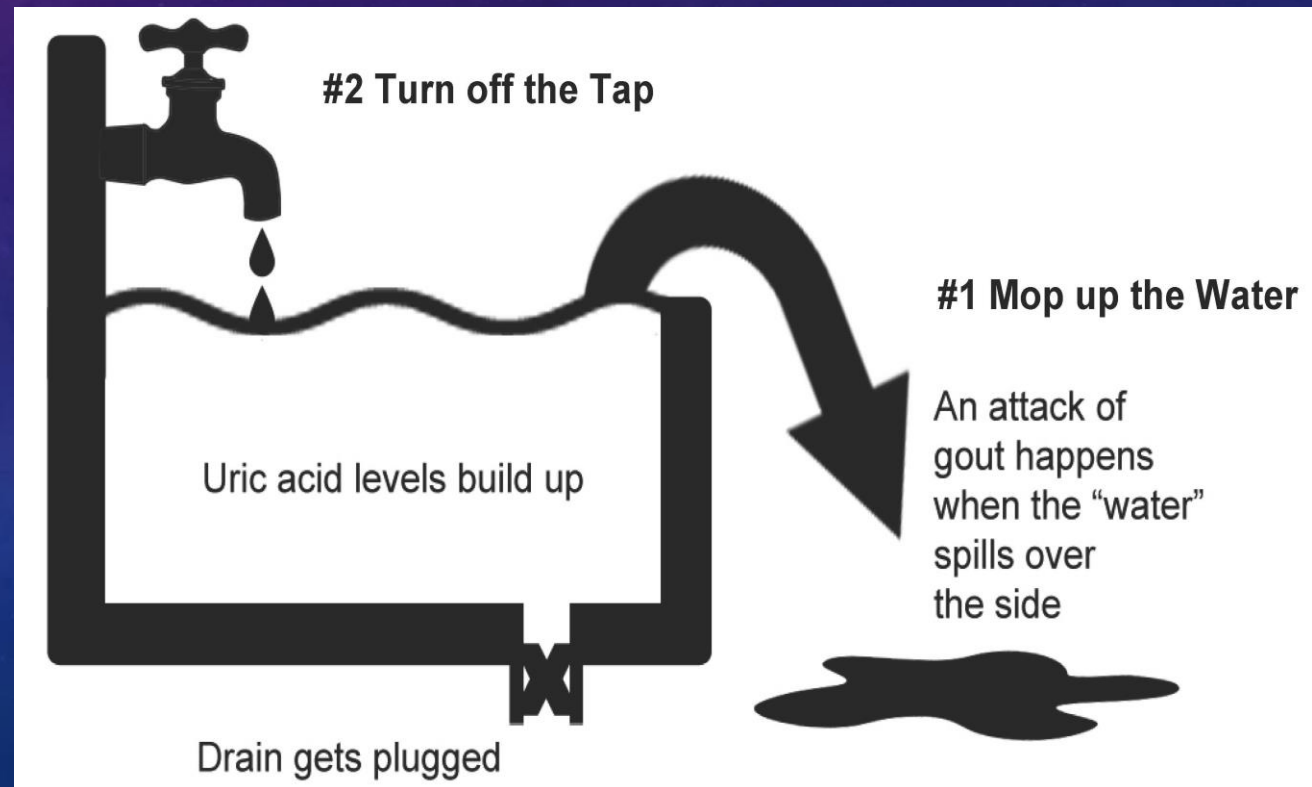
Given orally once daily, well absorbed(85%)

Metabolized in liver , mainly conjugated to glucouronic acid

Given to patients who do not tolerate allopurinol

99% protein bound

$t_{1/2}$ 4-18hours



FEBUXOSTAT

ADRS

Increase number of gout attacks during the first few months of treatment

Increase level of liver enzymes

Nausea, Diarrhea

Headache

Numbness of arm or leg



URICOSURIC DRUGS

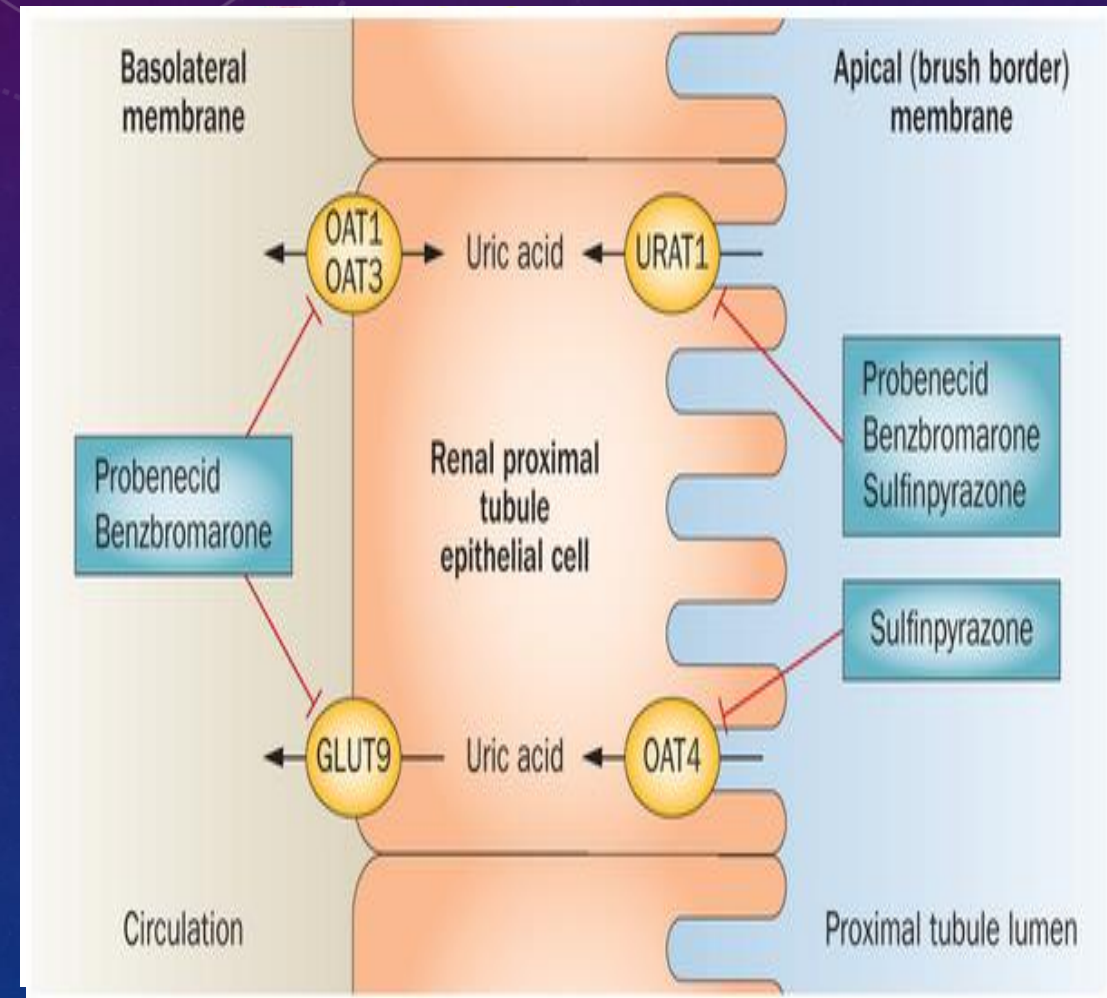
Mechanism

Blocks tubular reabsorption of uric acid & enhances urine uric acid excretion

Probenecid inhibits Urate Transporters (URAT1) in the apical membrane of the proximal tubule

It also inhibits organic acid transporter (OAT) → ↑ plasma concentration of penicillin

Sulfinpyrazol inhibits URAT1 & OAT4



URICOSURIC DRUGS

Control hyperuricemia and prevent tophus formation

Probenecid moderately effective

Increases risk of nephrolithiasis

Not used in patients with renal disease

Some drugs reduce efficacy (e.g. aspirin)



Gout is the most common type of inflammatory arthritis, but 7 in 10 adults don't know that gout is a form of arthritis.

ADRS

PROBENECID

Exacerbation of acute attack

Risk of uric acid stone

GIT upset

Allergic rash



CONTRA-INDICATIONS

History of nephrolithiasis

Recent acute gout

Existing renal disease

Less effective in elderly patients



DRUGS IN GOUT

SULFINPYRAZONE

Sulfinpyrazone can aggravate peptic ulcer disease

Aspirin reduces efficacy of sulfinpyrazone

Sulfinpyrazone enhances the action of certain antidiabetic drugs

Typical Tophaceous Manifestations



Helix of the ear



Hands, fingers, and wrists

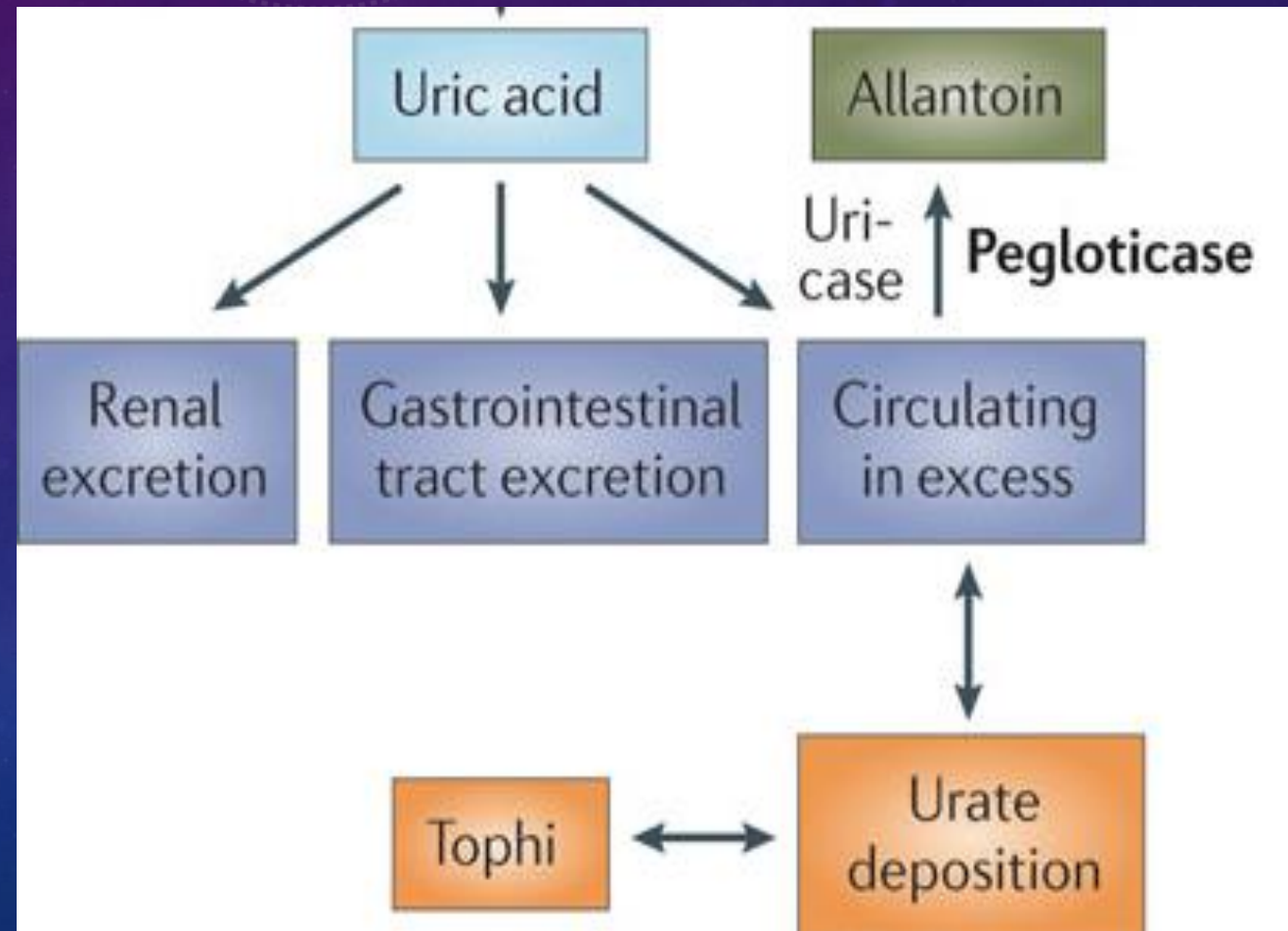
RECOMBINANT MAMMALIAN URICASE

PEGLOTICASE

A uric acid specific enzyme which is a recombinant modified mammalian uricase enzyme

Converts uric acid to allantoin

Given I.V. → peak decline in uric acid level within 24-72 hours



PEGLOTICASE

Used for the treatment of chronic gout in adult patients refractory to conventional therapy

ADRS

Infusion reactions

Anaphylaxis

Gout flare

Arthralgia, muscle spasm

Nephrolithiasis

