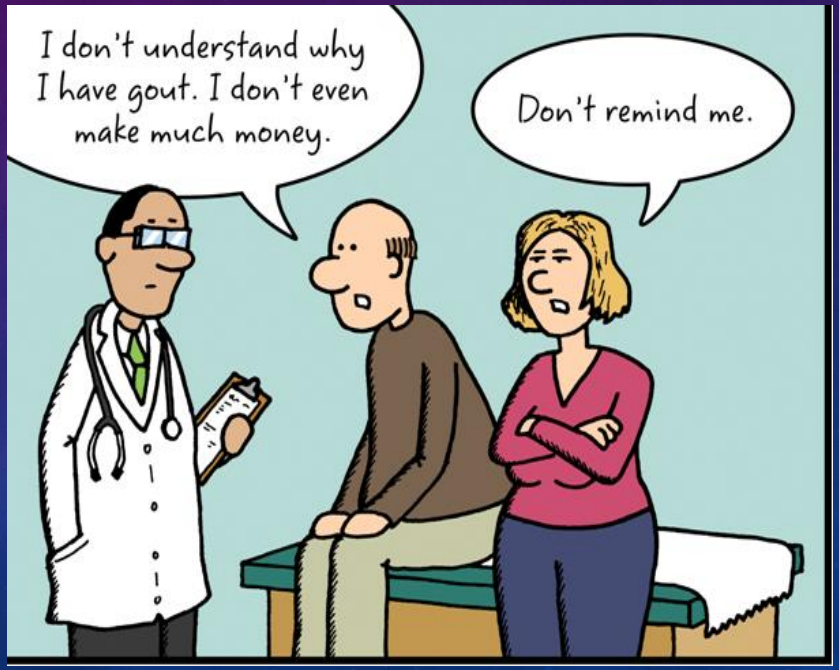
DRUGS IN GOUT

EPIDEMIOLOGY

Prevalence of hyperuricemia 5%

Prevalence of gout 0.2%

Male to female ratio 10:1



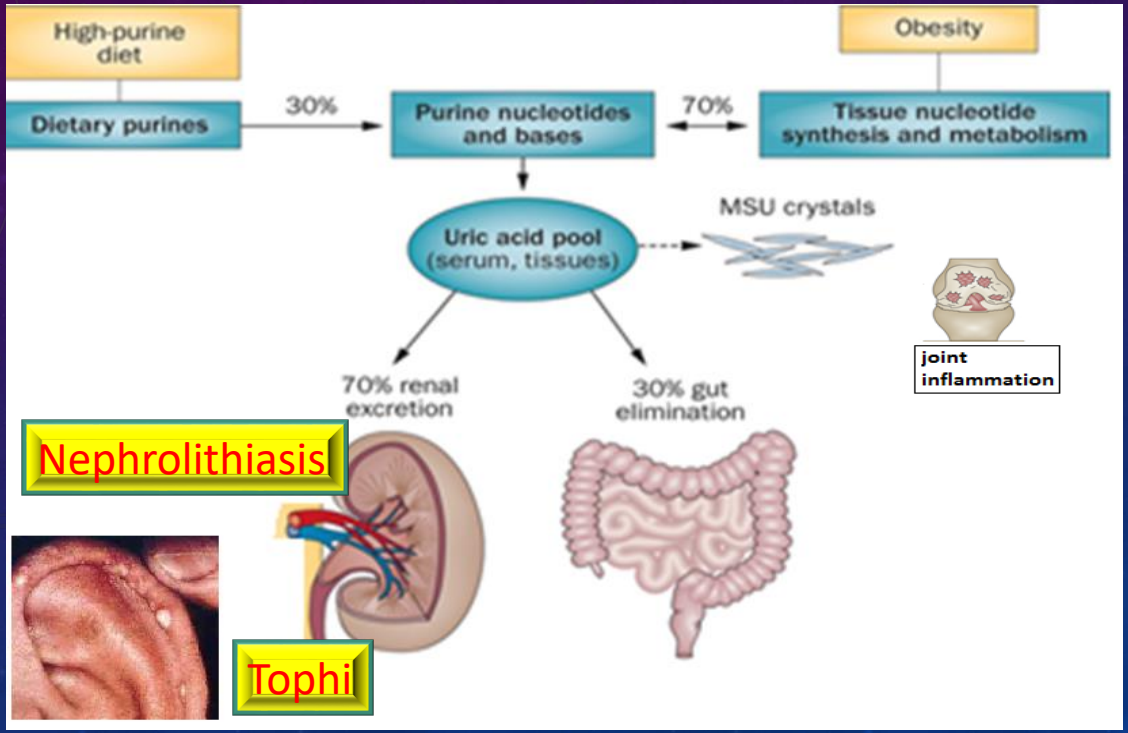
DRUGS IN GOUT

ILOS

- Identify the mechanism of action of drugs used for treatment of gout
- Classify drugs used for treatment of gout
- Outline the stages of gout and the therapeutic objectives in each stage
- Describe drug and non drug treatment of gout
- Study in details the pharmacology of drugs used for treatment of gout

WHAT IS GOUT?

DRUGS IN GOUT



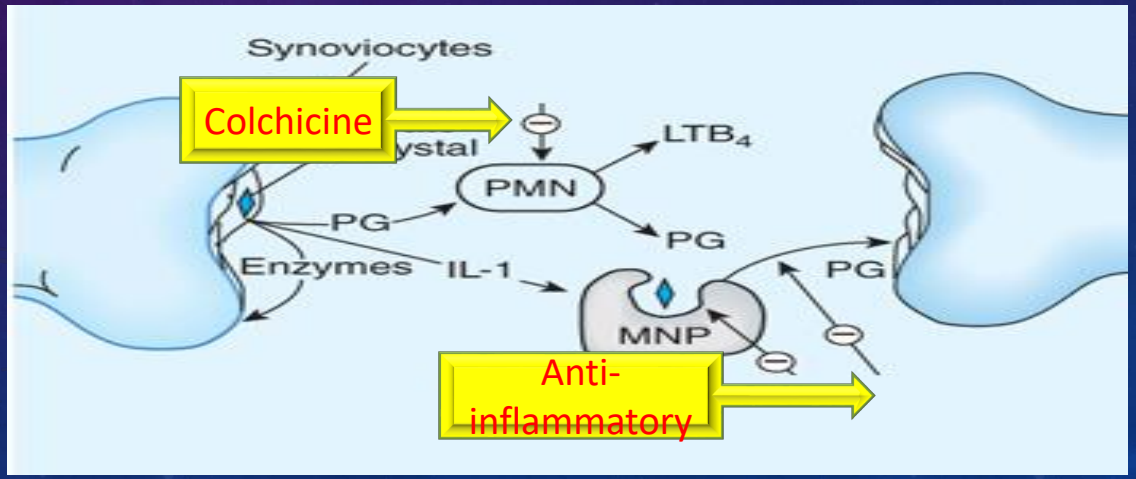
Pathophsiology

Uricostatic

Over production

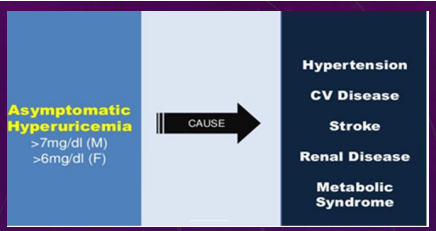
Uricosuric

Under excretion



DRUGS IN GOUT

Uricostatic	Allopurinol, Febuxostat
Uricosuric	Probenecid, Sulfinpyrazone
Anti- inflammatory	NSAIDs, Steroids
Tubulin inhibitors	Colchicine



STAGES OF GOUT & GOAL OF THERAPY

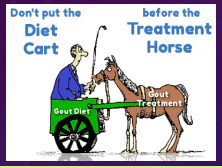
Asymptomatic hyperuricemia	Acute flares	Intercritical gout	Chronic gout
Elevated serum urate with no clinical manifestations of gout	Acute inflammation in joint caused by free urate crystals	The intervals Between acute flares	Long-term gout complications
Treat or not to treat?	Terminate The attack	Prevent recurrent attacks	-Prevent complications -Lower serum uric acid

DRUGS IN GOUT

Treatment of gout

- Non-pharmacologic
- Pharmacologic

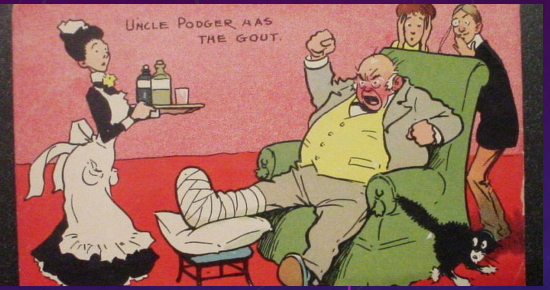
NON-PHARMACOLOGIC THERAPY



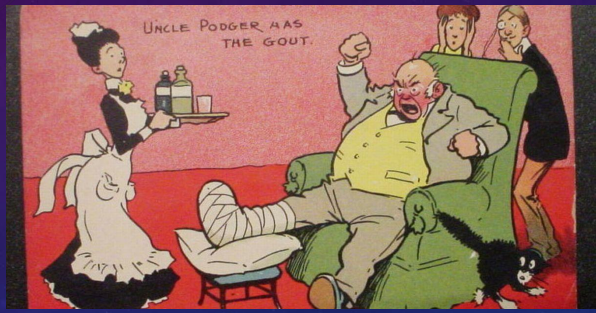
LIFESTYLE MODIFICATIONS

- Loss of weight
- Excercise
- Diet control
- Smoking cessation

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:

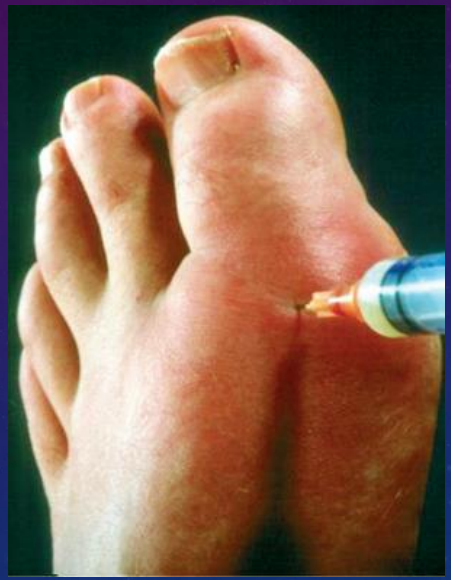
- G-I ulcer
- Bleeding or perforation
- Renal insufficiency
- Heart failure
- Use of oral anticoagulants

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

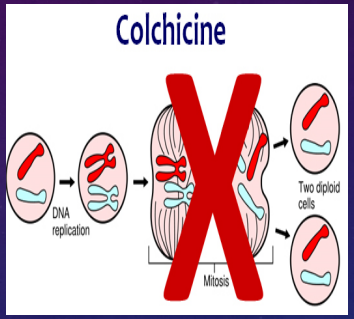
Alkaloid obtained from autumn crocus (*Colchicum autumnale*)

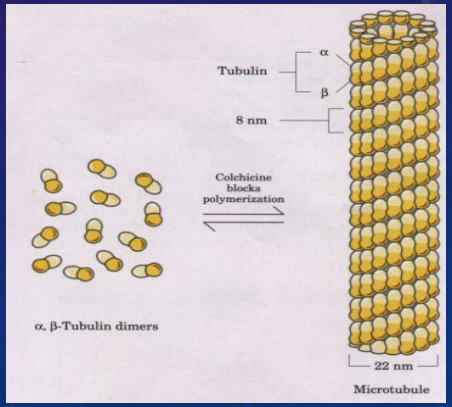
Minimal effect on uric acid synthesis , excretion & is not analgesic

DRUGS IN GOUT

MECHANISM

- Binds to microtubules in neutrophils
- Inhibits cell division
- Inhibits chemotactic factors
- Inhibits inflamosomes & 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

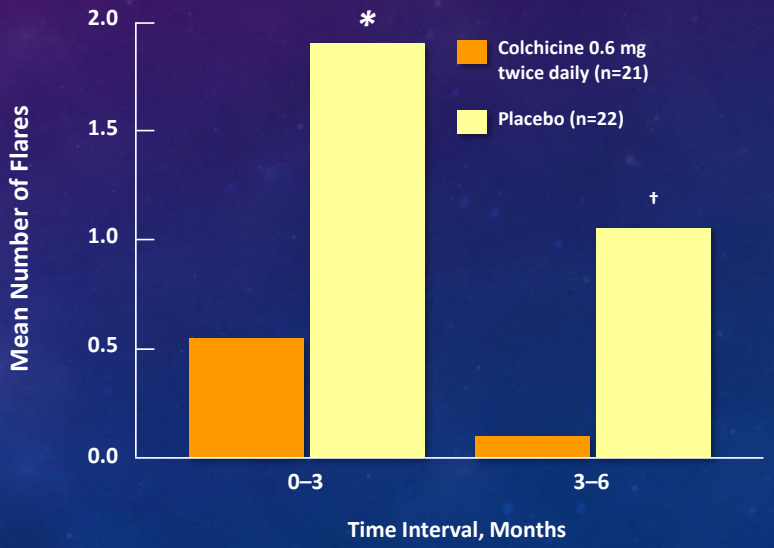
Use should be avoided in patients with a creatinine clearance of less than 50 mL/min

Gout most commonly affects the big toe, but it can also affect various other joints.

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

Uricostatic Drugs

-Allopurinol

-Febuxostat

Uricosuric Drugs

-Probenecid

-Sulfinpyrazone

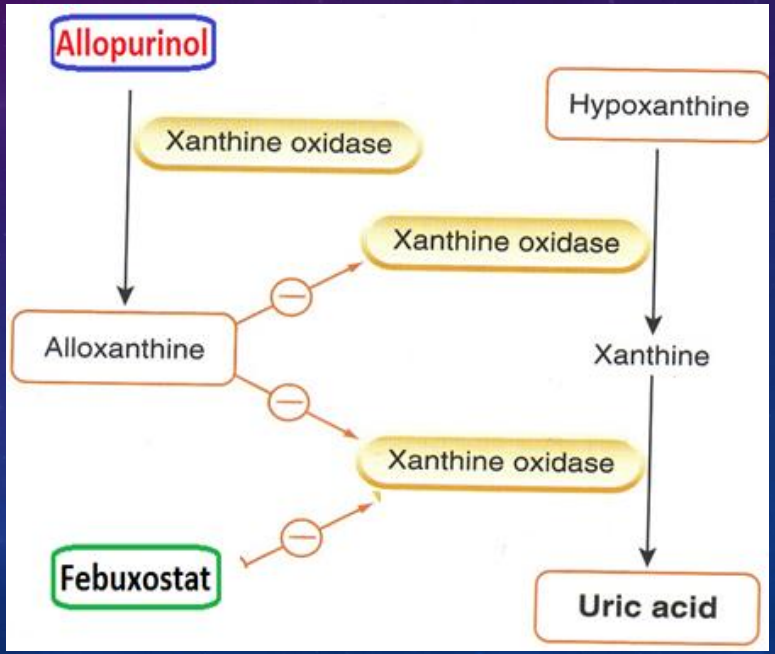
Mamalian Uricase

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

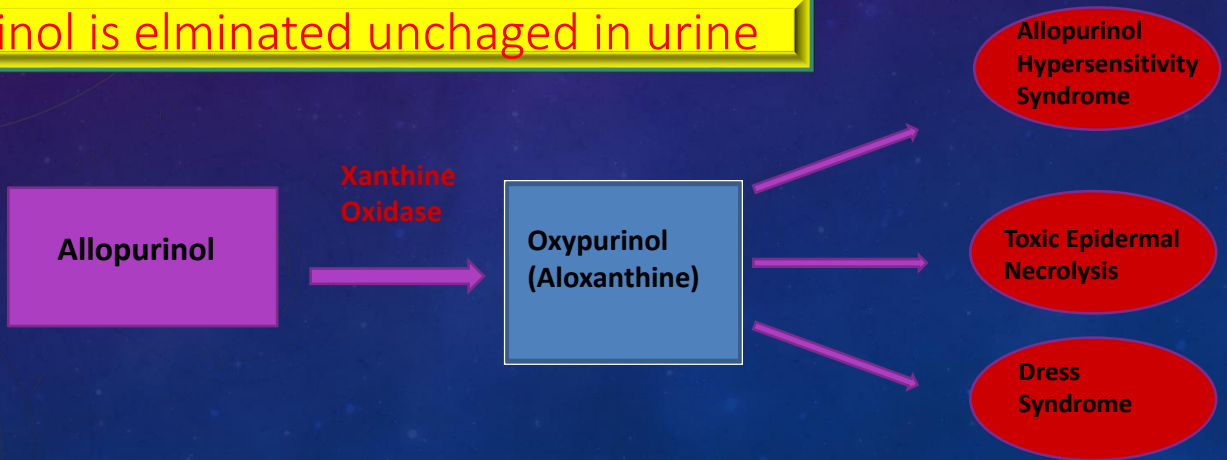
PHARMACOKINETICS

Absorption 70%

Protein binding negligble, 5%

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

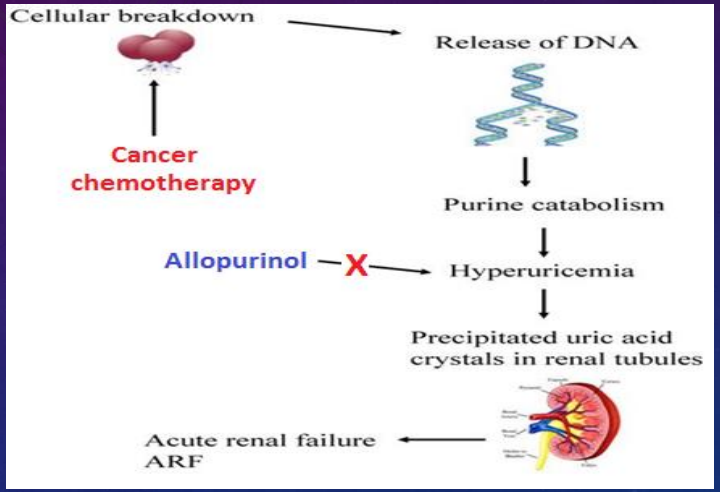
Oxypurinol is elminated unchaged in urine



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



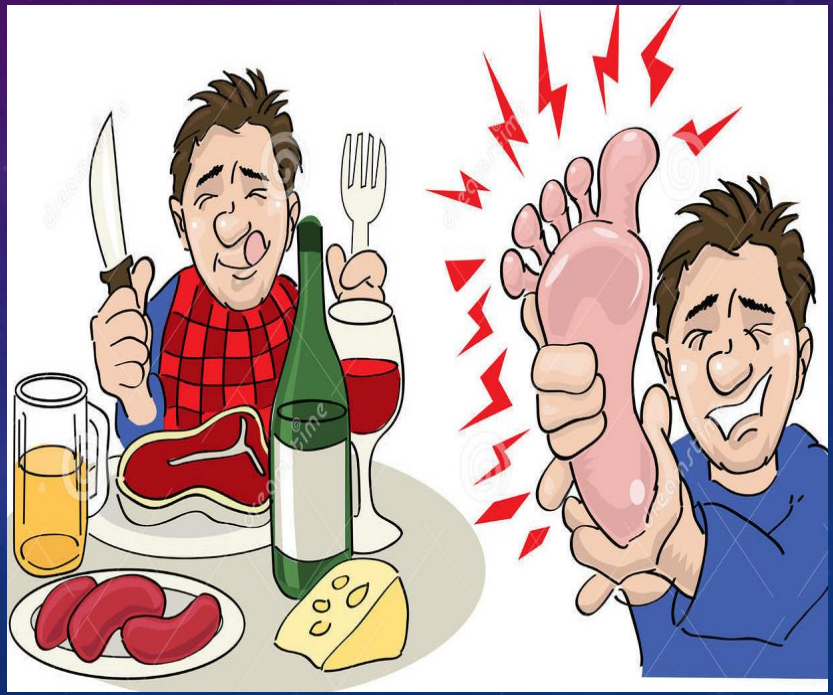
ADRS

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

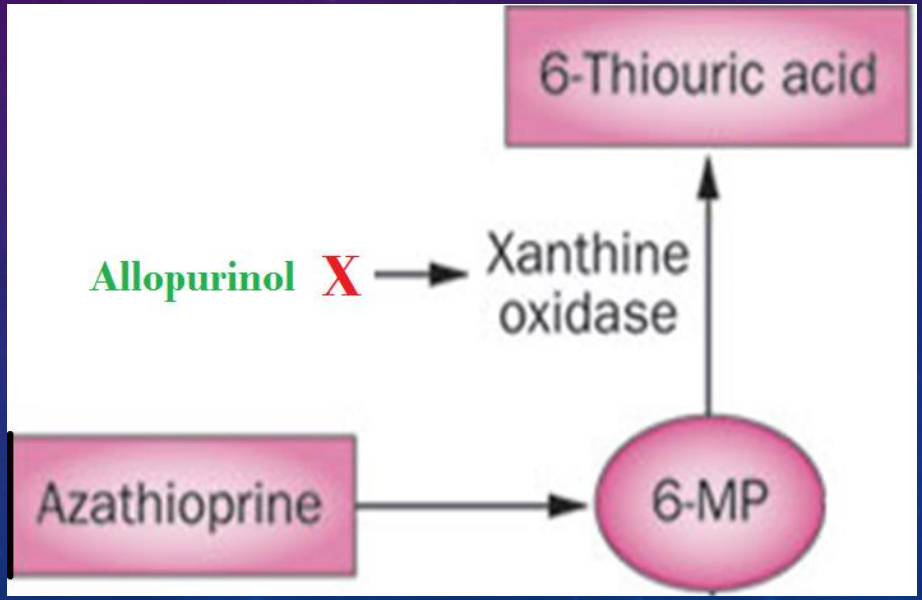


Drug Interactions

Inhibits metabolism of Warfarin & dicumarol

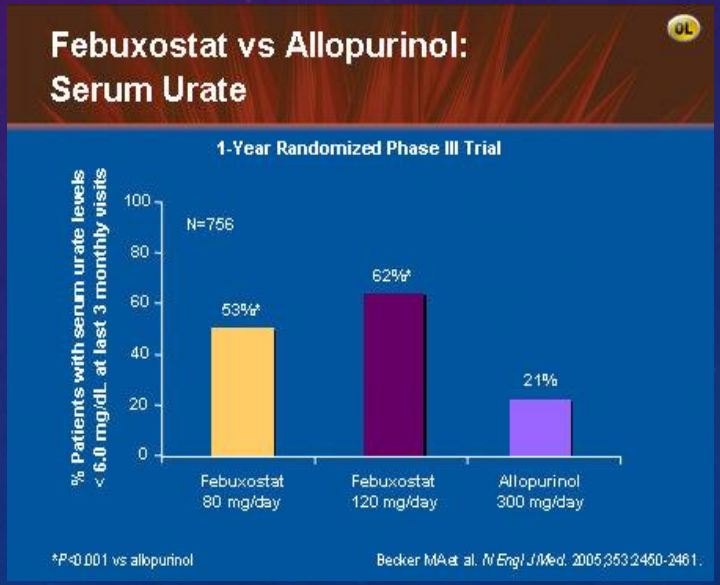
Reduce the metabolism of **6-mercaptopurine** and **azathioprine**

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

PHARMACOKINETICS

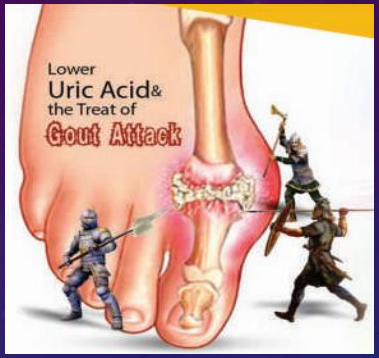
Given orally once daily, well absorbed(85%)

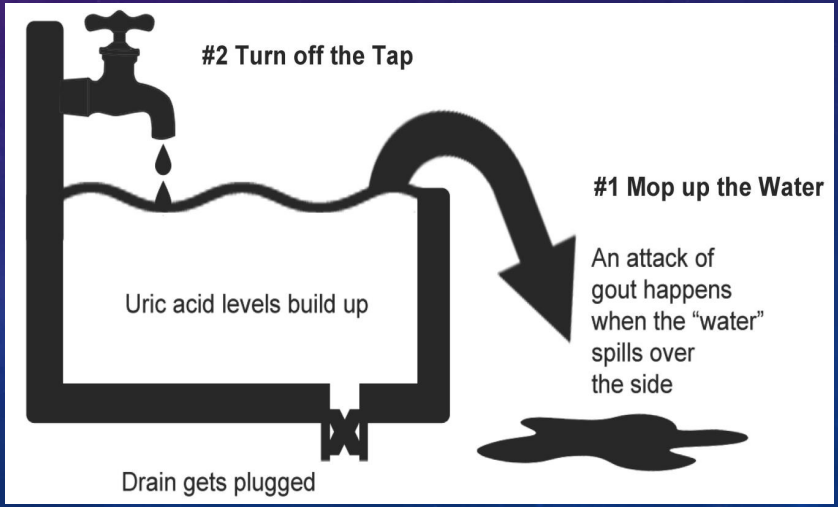
Metabolized in liver , mainly conjugated to glucouronic acid

Given to patients who do not tolerate allopurinol

99% protein bound

t½ 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

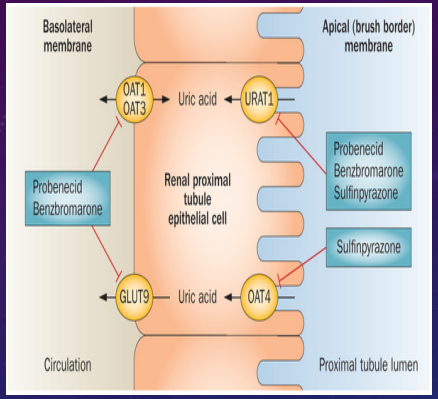
Mechanism

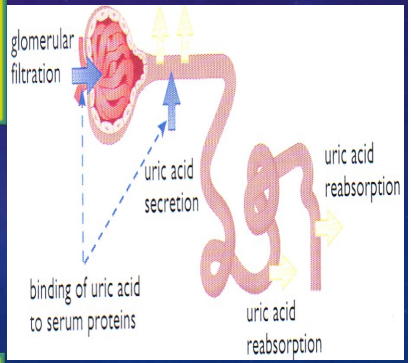
Blocks tubular reabsorption of uric acid & enhances urine uric acid excretion

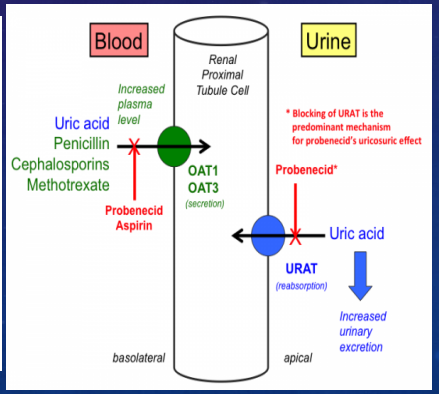
Probenecid inhibits Urate Transporters (URAT1) in the apical membrane of the proximal tubule

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

Sulfinpyrazol inhibits URAT1 & OAT4







URICOSURIC DRUGS

Control hyperuricemia and prevent tophus formation

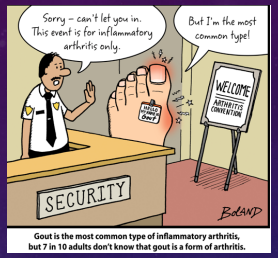
PROBENECID

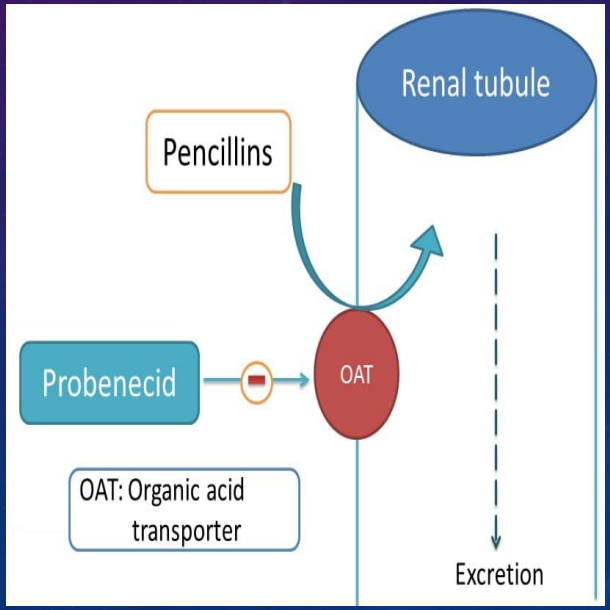
Moderately effective

Increases risk of nephrolithiasis

Not used in patients with renal disease

Some drugs reduce efficacy (e.g. aspirin)

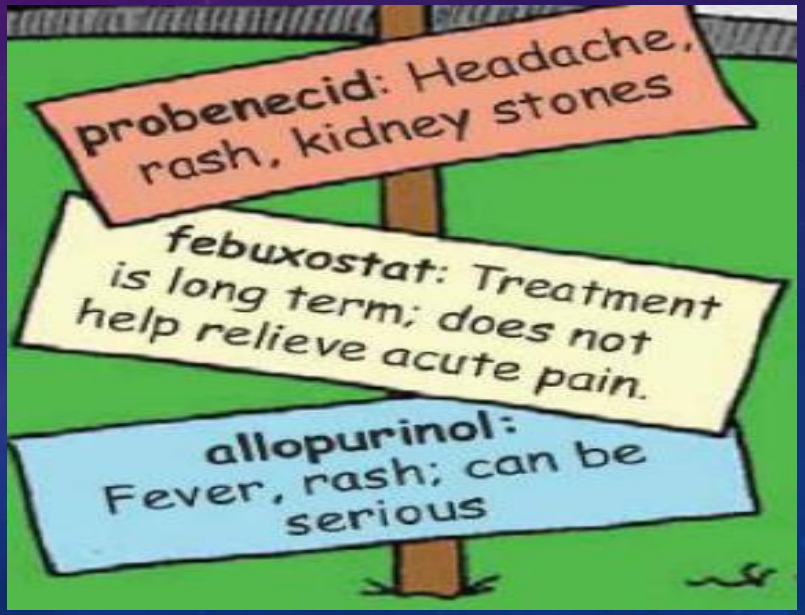




ADRS

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

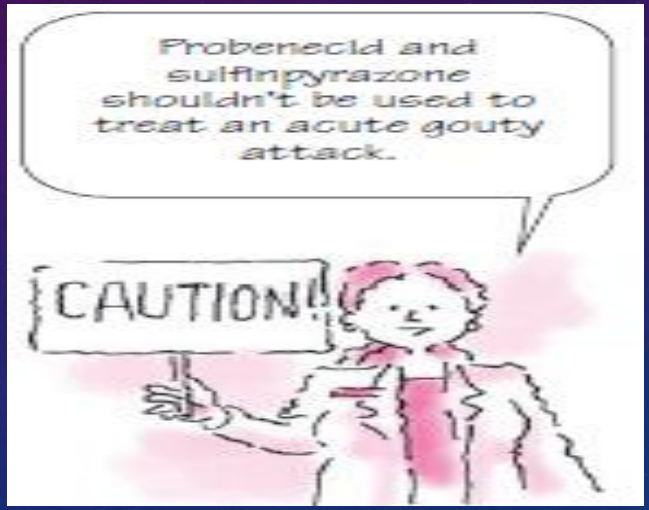
DRUGS IN GOUT

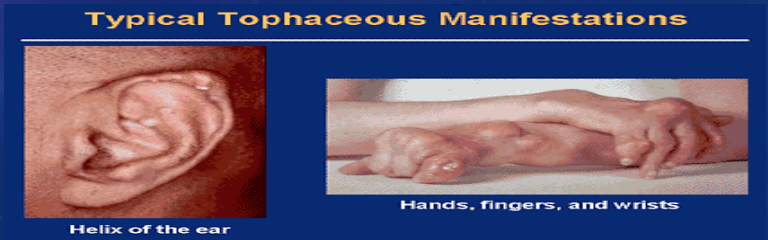
SULFINPYRAZONE

Sulfinpyrazone can aggravate peptic ulcer disease

Aspirin reduces efficacy of sulfinpyrazone

Sulfinpyrazone enhances the action of certain antidiabetic drugs





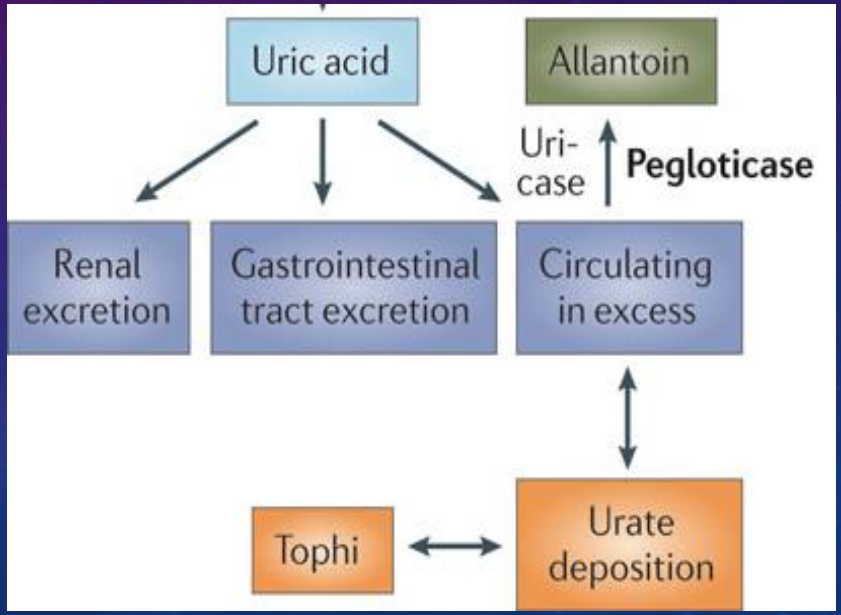
RECOMBINANT MAMMALIAN URICASE

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