GOUT

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special features about GOUT:

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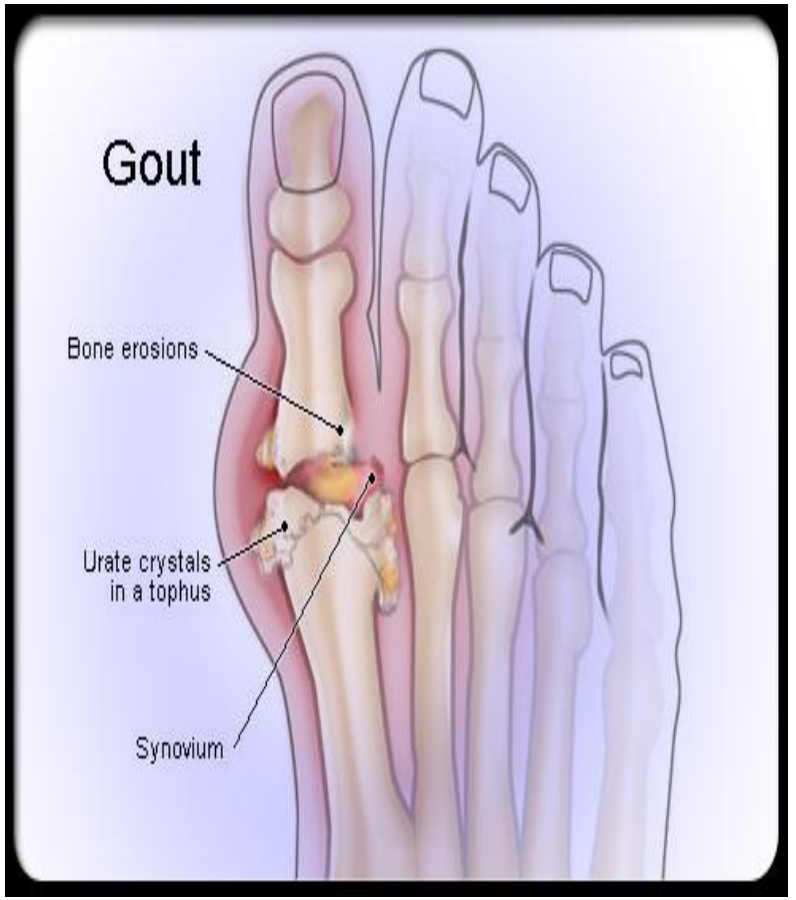
High blood uric acid level (shown through examination)

Acute arthritis

monosodium urate stone in kidney

♂>♀ (female more than male)

Familial metabolic disease



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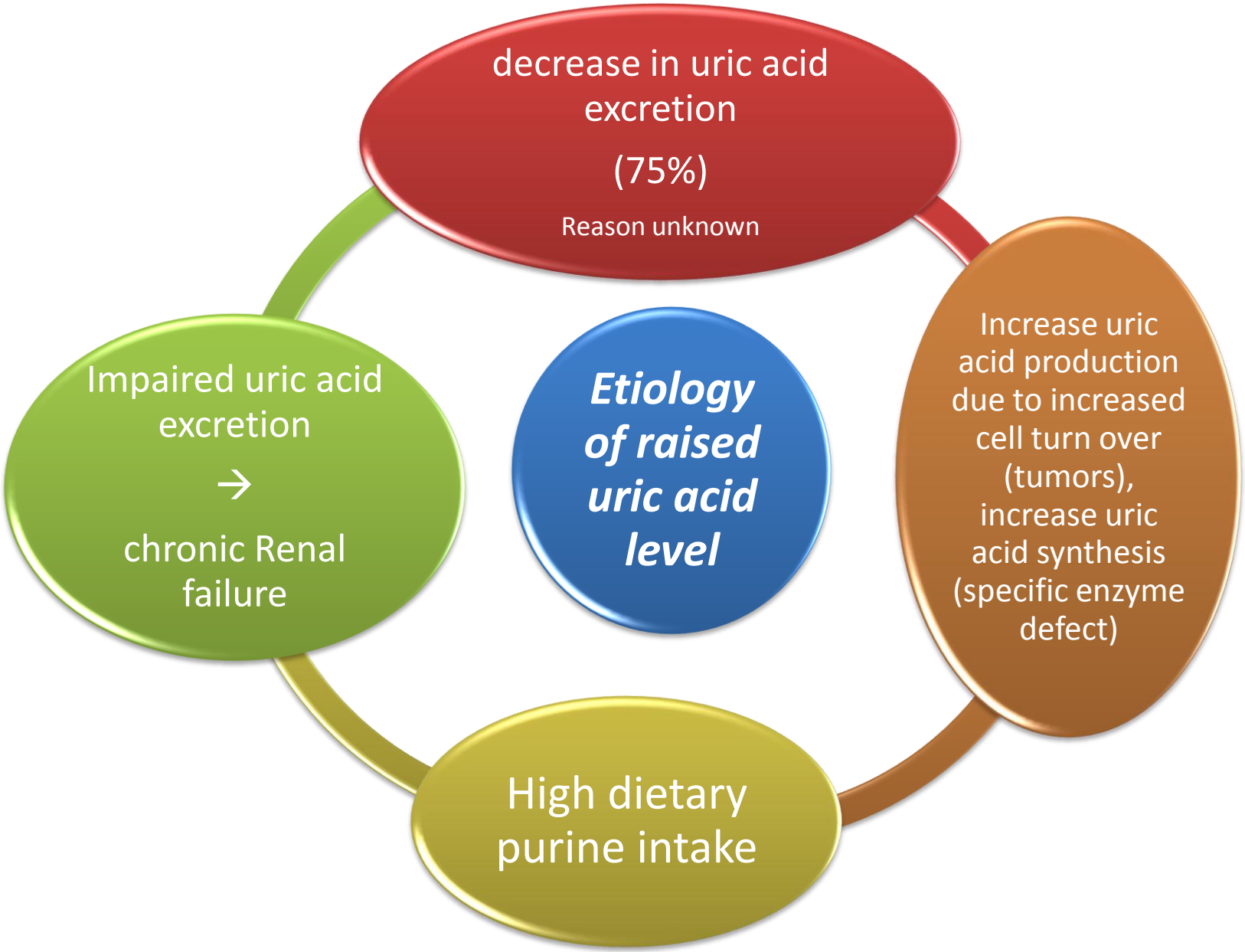


** What we need to know regarding pharmacology:

DRUGS USED IN TREATMENT OF GOUT

The main purpose from taking these drugs is to:
1-Lower the uric acid level below the saturation point. (<6 mg/dL)
2-Prevent the deposition of urate crystals.

→→ This can be accomplished by :
1*-interfering with uric acid synthesis with *allopurinol.
2*-increasing uric acid excretion with *probenecid* or *sulfinpyrazone*, *large doses of aspirin.
3*-inhibiting leukocyte entry into the affected joint with *colchicine.
***4*-administration of NSAIDs**

Stages of the Disease

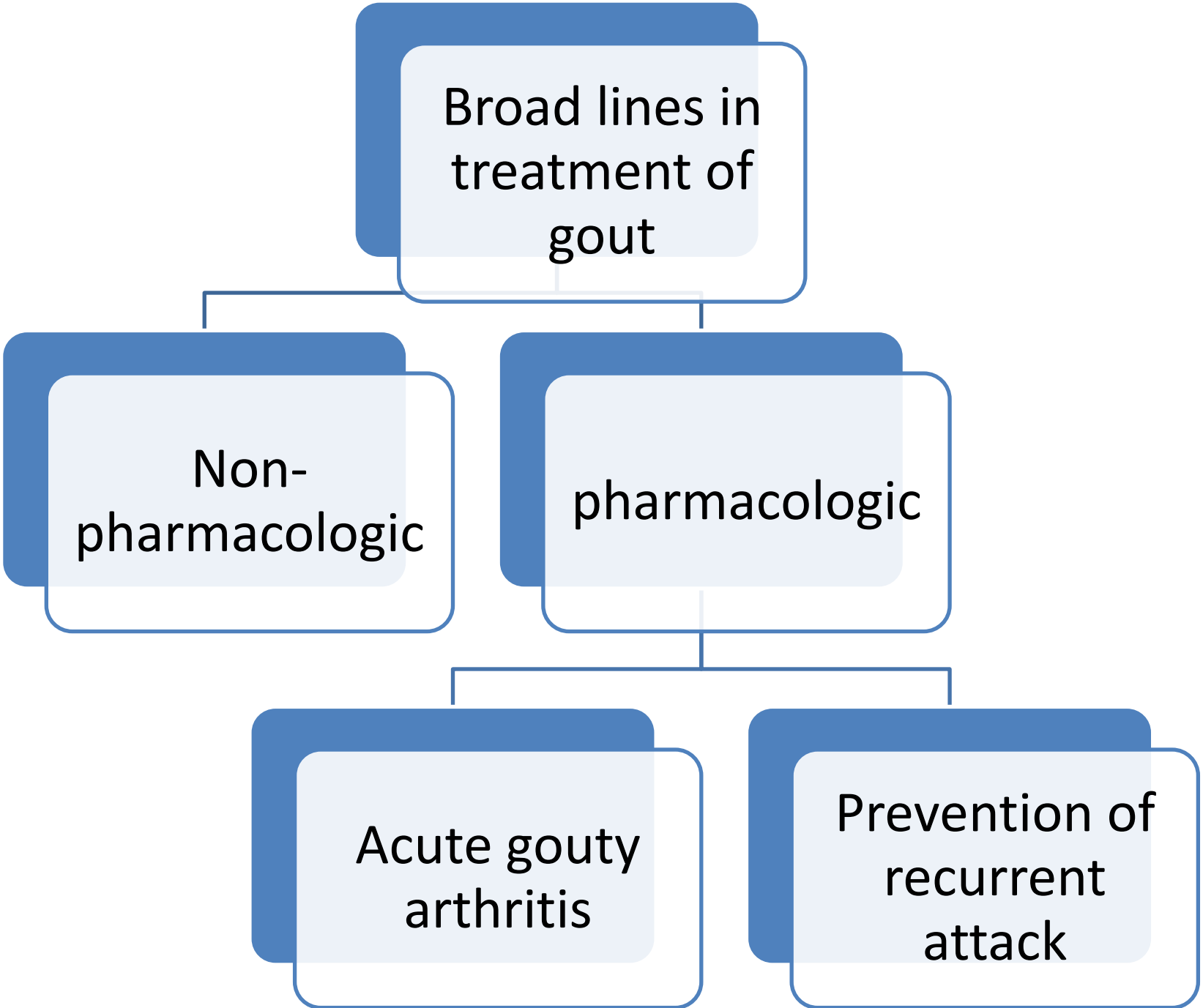
*For your Knowledge

1. • **Asymptomatic Stage:** urate levels rise in the blood, but produces no symptoms.

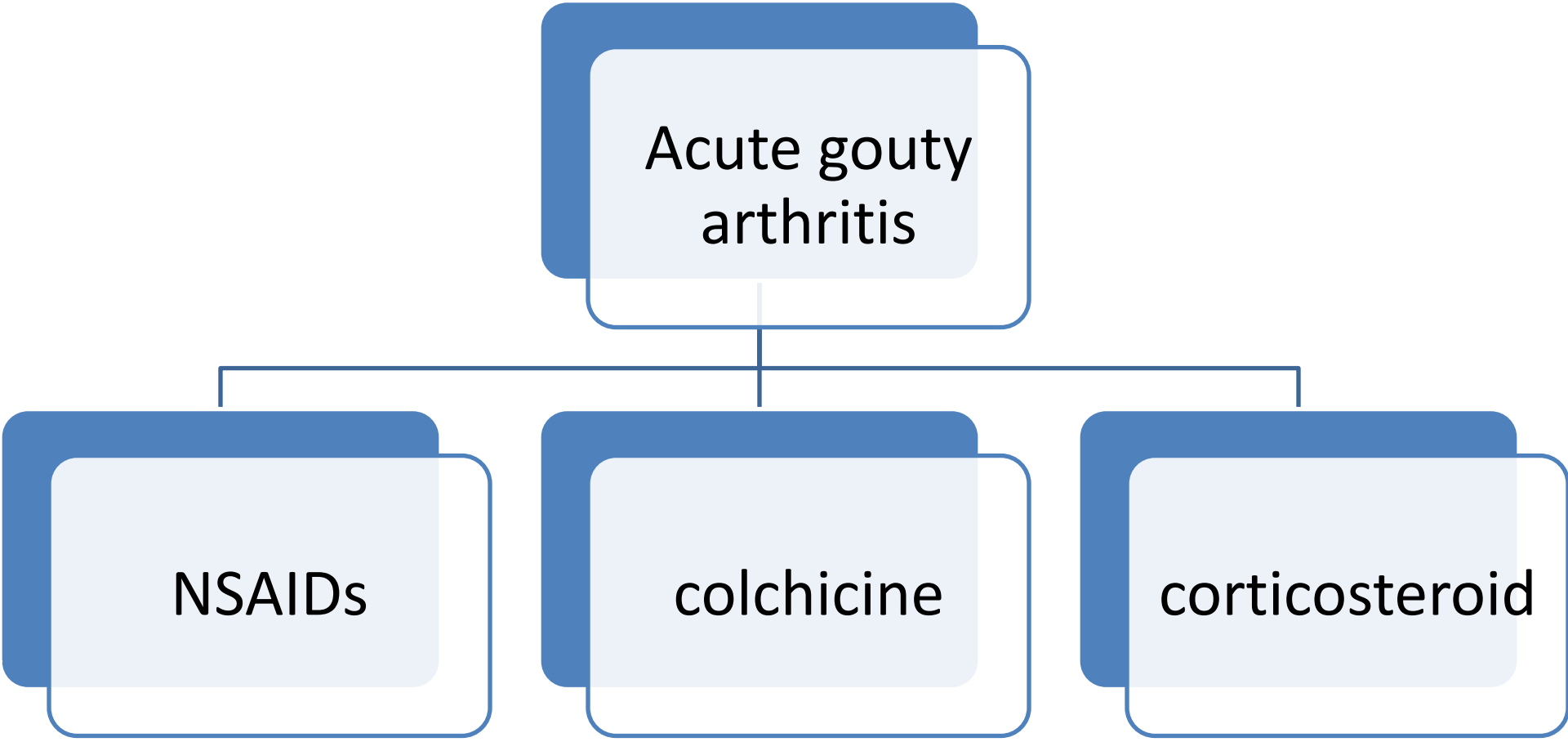
2. • **Acute stage:** the first stage when the symptoms begin showing. The symptoms are first observed as an acute pain in some of the joints.

3. • **Intercritical stage:** a transition stage from the acute stage to the more dangerous chronic stage. Most people have a second attack from six months to two years.

4. • **Chronic stage:** This is the most severe of all the stages. Large tophi make their appearance, and there is tremendous pain in the affected joints.


Broad lines in treatment of gout
Non-pharmacologic
pharmacologic
Acute gouty arthritis
Prevention of recurrent attack

Pharmacologic Therapy



Non-pharmacologic Therapy

*for your knowledge

Includes

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lifestyle

dietary changes

weight management

reduced alcohol intake

consumption of high purine foods

maintenance of blood pressure

lipid control

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1-NSAIDs

The first line of treating gouty arthritis is NSAIDs

NSAIDs (Selective or non- selective)
((commonly used))

-Inhibit pain & inflammation.
-Inhibit urate crystal phagocytosis by decreasing the migration of granulocytes into the inflammatory area.
-Aspirin in small doses is contraindicated.
(use ASPIRIN in LARGE DOSE ONLY)

2-Colchicine

A plant alkaloid

What comes in the second place is Colchicine but it is ONLY used in acute gouty arthritis usually alleviating the pain of acute gout within 12 hours

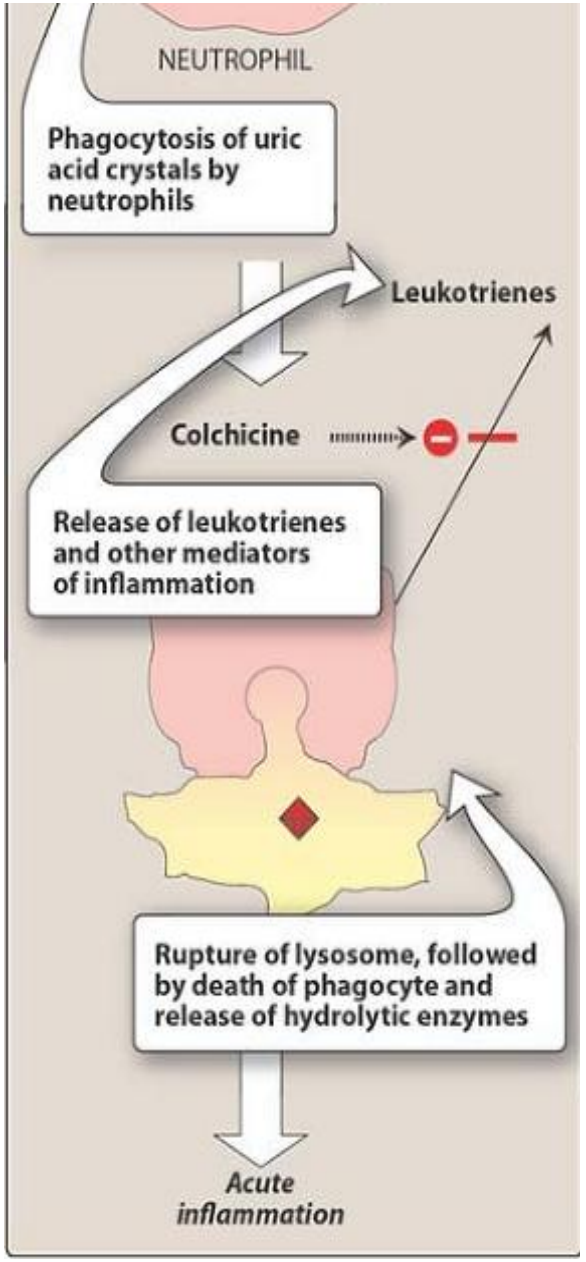
Colchicine has NO analgesic effect. It is anti-inflammatory ONLY.
Used as prophylaxis (reduces the frequency of acute attacks)

1- Administered orally, followed by rapid absorption from the GI tract.
2- Reaches peak plasma levels within 2 hours.
3- Also available combined with *probenecid.*
4- Recycled in the bile and is excreted unchanged in the faeces or urine.
5- should be used with caution in patients with renal dysfunction.

Also used for Mediterranean Fever

Mechanism of Action :

1- Prevent migration of granulocyte which leads to prevention of Phagocytosis when it bind to Tubulin.
2- Inhibits the synthesis and release of the leukotrienes.
3- Decrease production of TNF-α by macrophages.



Adverse effects:

1-Diarrhea is a common adverse effect. May cause nausea, vomiting ,abdominal
cramps.
2-Chronic use may cause, alopecia, bone marrow depression, peripheral neuritis, myopathy.
3-Also affect fertility

Acute intoxication:

Burning throat pain.
Bloody diarrhea.
Shock.
Hematuria.
C.N.S.depression

Contraindication & Precaution:

Contraindicated in pregnancy
Should be used with caution in hepatic , renal or cardiovascular diseases.

3- Corticosteroids

Prevention of recurrent attack

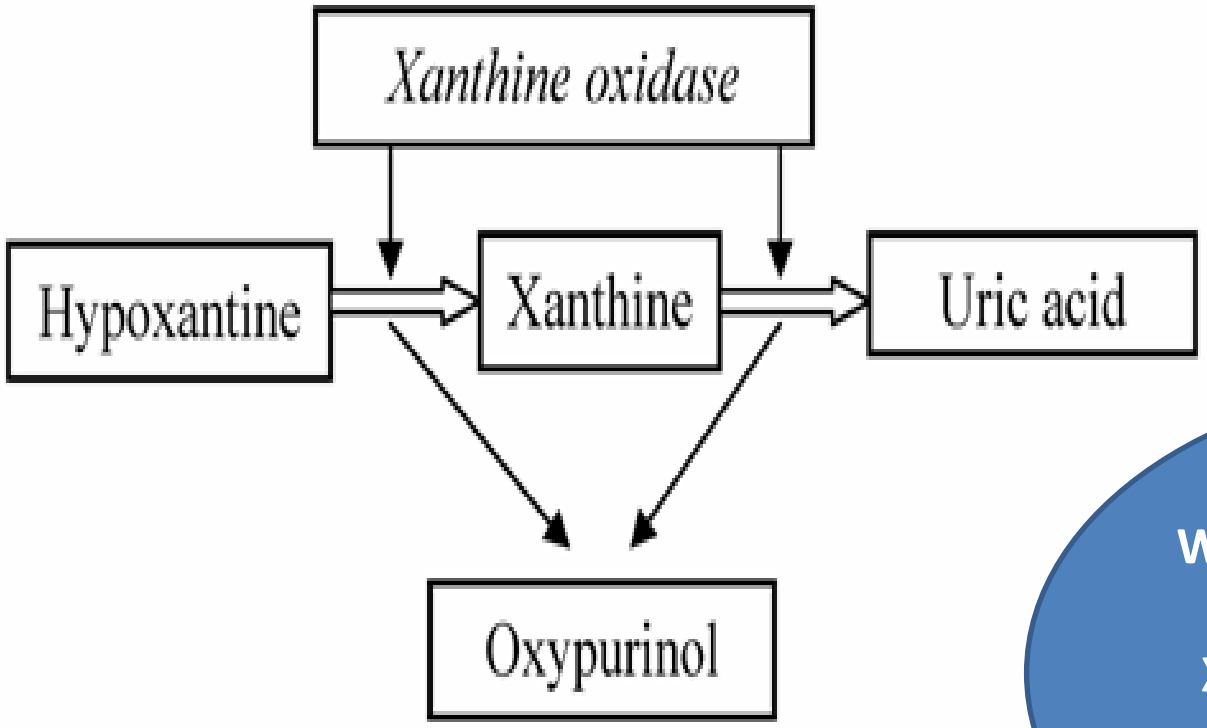
Inhibition of uric acid synthesis Allopurinol

Uricosuric drugs

- Probenacid
- Sulfinpyrazone
- Large doses of aspirin

1- Inhibition of uric acid synthesis by Allopurinol:

Mechanism of action:



Xanthine oxidase converts Xanthine to uric acid.

When using Alloperanol it works on inhibiting Xanthine oxidase which stops the formation of uric acid.

Pharmacokinetics:

-80% absorbed after oral administration.
-Metabolized in the liver to active metabolite alloxanthine.
-Given once daily.
-Drug & its metabolite are excreted in the feces & urine.

N.B: Alloxanthine is the active form of Alloperonol.

-If there is a renal dysfunction → give Alloperanol cause it doesn't work on kidneys.
-we can use it if the patient develop a tophi
-All cancer drugs and chemotherapy increase the uric acid we give Alloperanol.

Therapeutic Uses:

1-Chronic tophaceous deposits (reabsorptionis more rapid).
2- High serum uric acid in patients with impaired renal functions.
3-uric acid stones or nephropathy.
4- used to prevent increased uric acid levels in patients receiving cancer chemotherapy.

Side Effect

(more common)

1-xacerbation of an acute attack of gout.
2-Maculopopular skin rash
3-nausea and diarrhea

At the beginning of taking Alloperanol it will extract the uric acid from the tissues to blood and it may cause acute attack so we should use it with Colchicine or NSAIDs.

Side Effect

(less common)

-CVS : vasculitis
-Body : fever, headache
-Thrombocytopenia
-Epistaxis (nose bleeding)

Drug Interactions

1-With oral nticoagulant:
Potentiates **warfarin**
and **dicumarol**
•inhibits their metabolism
in liver .

2-With anticancer :
6-mercaptopurine
and **azathioprine**
• inhibits their metabolism
(doses are reduced
up to 75%).8

3-With ampicillin :
Increases frequency
of **skin rash**

4-Prolongs half life of
Chlorpropamide
• both compete for
excretion in
renal tubule

Sulfinpyrazone

-Sulfinpyrazone is a metabolite of phenylbutazone

-Metabolized into an active metabolite in the liver.

-One of the **Uricosuric drugs**

-Should not be started until 2-3 weeks after an acute attack.

Probenecid

Mechanism of action:

Uricosuric drugs:
(probenecid, sulfinpyrazone, large dose of aspirin)
block the active transport sites of the proximal tubules.
→ The reabsorption of uric acid is decreased

Clinical uses:

(for all Uricosuric drugs)

-**Chronic gout** when :
Evidence of tophi appears
And Plasma levels of uric acid are so high that may cause tissue damage (urine volume should be maintained at a high level,and urinary pH kept alkaline).

-**Probenecid** is used to prolong the action of some antibiotics e.g. penicillin

Drug Interaction:

Probenecid prolong the action of some antibiotics as: penicillin and cephalosporins

N.B: Aspirin can prevent probenecid from being fully effective

Side Effects:

-Acute attack of gout
-Risk of uric acid stone
-GIT upset
-Allergic rash
-Nephrotic syndrome (probenecid)
-Aplastic anemia (not common)

Contra-indications:

-History of urinary tract stone
-Impaired renal function
-Recent acute gouty attack
-Co-Administration of low doses of aspirin

N.B:

-Sulfinpyrazone can aggravate peptic ulcer disease
- Aspirin products can interfere with sulfinpyrazone's effects
- Sulfinpyrazone can enhance the action of certain diabetes medicines