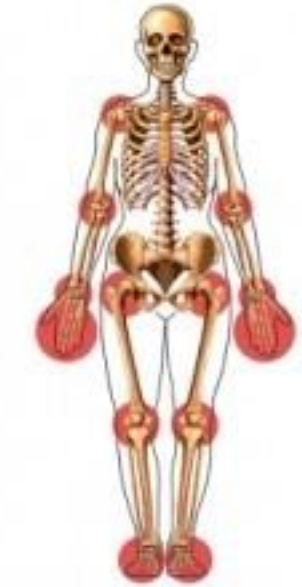
Drugs used in Rheumatoid Arthritis

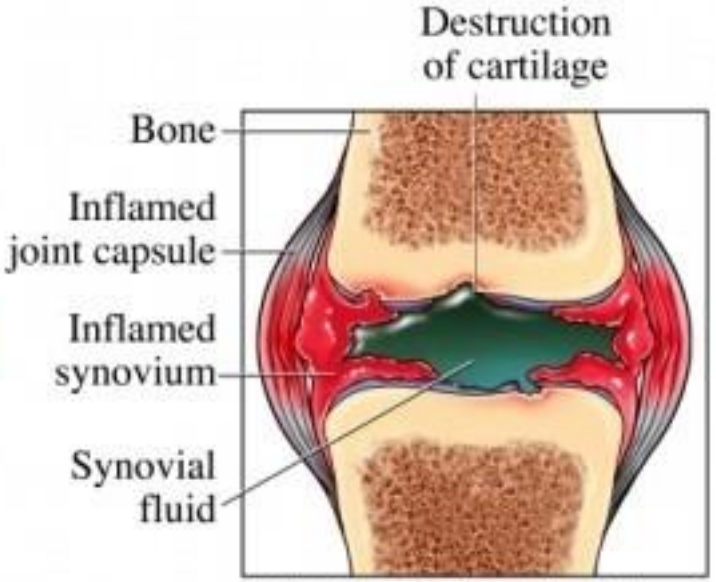
(Pharmacology)
Unit-5(4)

Rheumatoid arthritis

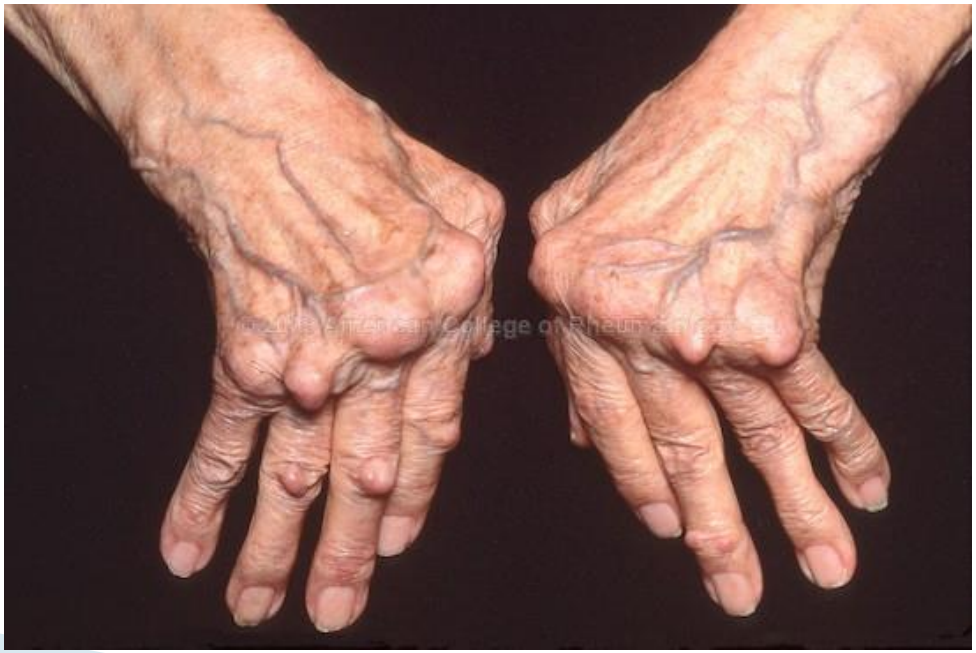
- Auto immune disease
- Joint inflammation, synovial proliferation and destruction of articular cartilage
- IgM activates compliment and release cytokines
- Attracts neutrophils – lysosomal destruction



Joint pain occurring in various joints



Enlarged view of a joint



DMARDs

Non biologics

- Immunosupressants – methotrexate
- Sulfasalazine
- Chloroquine
- Leflunomide

Biologics

- TNF inhibitors – infliximab, adalimumab
- IL-1 antagonist – Anakinra

Others – prednisolone, gold salts

NSAIDs

- Afford symptomatic relief
  - Reduce inflammation, pain, swelling and morning stiffness
  - Improve joint function
- Do not halt the disease progression

Methotrexate:

DMARD of 1st choice

- Folate antagonist

- Potent immunosuppressant and anti-inflammatory action
- Inhibits: proliferation of activated T-cells
  cytokine production
  chemotaxis of neutrophils

- Stimulates apoptosis in immune-inflammatory cells

- AE: oral ulceration and g.i upset, dose dependent progressive liver damage
- Contraindications: pregnancy, breastfeeding, liver disease

Sulfasalazine

- Sulfapyridine + 5ASA – antiinflammatory
- Suppress superoxide radicals and cytokine production
- Limited effect – main effect in IBD
- AE: neutropenia, thrombocytopenia and hepatitis

Chloroquine

- Remission in RA – 3-6 months
- Low toxicity – efficacy is also low

- Reduce monocyte IL1, antigen processing, lysosomal stabilization

- Used when few joints involved

- Corneal opacity and retinal damage

Biologics

- TNF α inhibitors
- Suppress macrophage and T cell function
- Quick response – depress joint erosion
- Effective monotherapy
- Usually combined to MTX

- Gold salts:
- Depresses CMI
- Aurothiomalate (i.v.)and auranofin (oral)
- More AE – no longer used

Glucocorticoids

- Immunosuppressant and anti-inflammatory
- Decreases the production of inflammatory cytokines viz. TNF-α, IFN-γ, IL-1
- Rapid symptomatic relief; slows the rate of joint destruction
- Relieves the severe systemic manifestations of RA – pericarditis, vasculitis, scleral nodules

- Used on a short-term basis – immediate relief /acute exacerbations/ to control systemic manifestations

- Intrarticular injection – triamcinolone, hydrocortisone, prednisolone ◊involvement of 1 or 2 major joints

- Oral prednisolone

- Low doses and gradual withdrawal of steroids - recommended

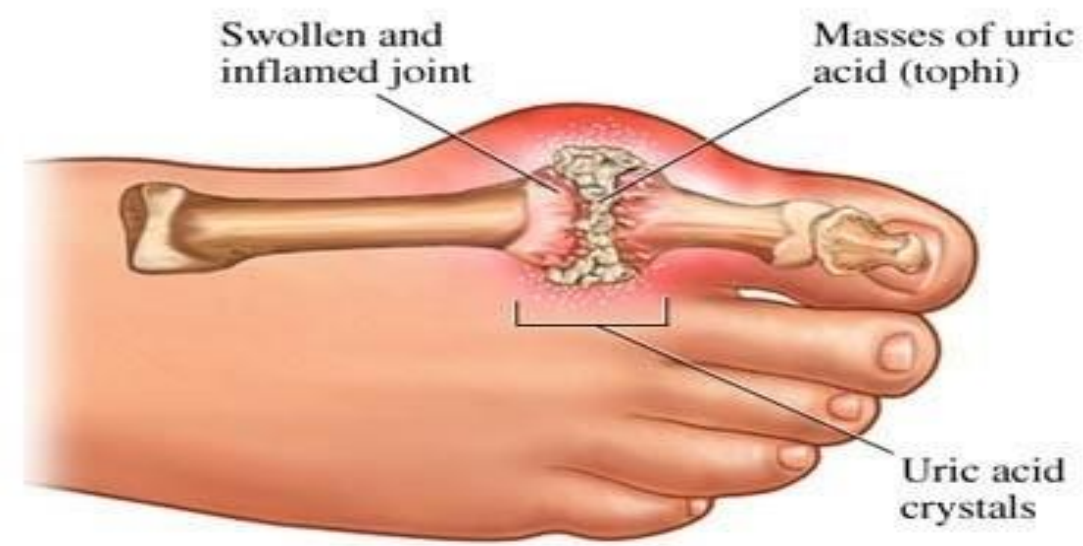
Drugs used in Gout

GOUT

- Metabolic disorder – recurrent episodes of acute and chronic arthritis
- Abnormal amounts of urates in the body
- Deposition of monosodium urate crystals in joints and cartilages
- Hyperuricemia

Acute gout:

- Sudden onset following rapid fluctuations in plasma uric acid level
- Metatarsophalangeal joint of the great toe
- Tars



Drugs used in Acute gout

1. NSAIDs
2. Colchicine
3. Corticosteroids

1. NSAIDs

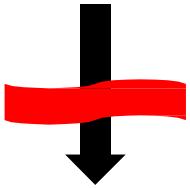
- Indomethacin, piroxicam, diclofenac, etoricoxib

- High and repeated doses

- Inhibit
  - urate crystal phagocytosis
  - Chemotactic migration of leukocytes into the inflammed joints

2. Colchicine: Antimitotic drug

MOA: depolymerization of microtubules in granulocytes



granulocyte migration and phagocytosis

- Inhibits the release of glycoprotein ◊ reduces inflammation and joint destruction

Uses:

- Relieves acute attacks of gout
- Used for the prophylaxis of recurrent episodes of gouty arthritis

A/E:

- Diarrhea, nausea, vomiting
- Hepatic necrosis
- Rarely, bone marrow suppression
- **Overdoses:** bloody diarrhoea, hematuria, shock, CNS depression and respiratory failure

Corticosteroids

- Intraarticular injection

- Refractory cases not responding to NSAIDs/ colchicine

Chronic gout:

Chronic hyperuricaemia ◊ development of tophi in the synovia ◊ joint deformities

- Pain and stiffness in the joints

Drug treatment of chronic gout

A. Uricosuric drugs: probenecid, sulfinpyrazone

B. Uric acid synthesis inhibitors : allopurinol

Uricosuric agents

Probenecid

- Inhibits the active renal tubular reabsorption of uric acid → promotes its excretion
- Prevents formation of new tophi
- **Plenty of fluid intake** – to prevent formation of renal urate calculi
- **A/E:** gastric irritation, dyspepsia, allergic dermatitis

Toxicity: convulsions, nephrotic syndrome

Drug interactions

- **Probenecid x penicillins :**

  Inhibits urinary excretion of penicillins

  ⇓

  prolonged action of penicillins.

- Sulfinpyrazone

Prevents reabsorption of uric acid

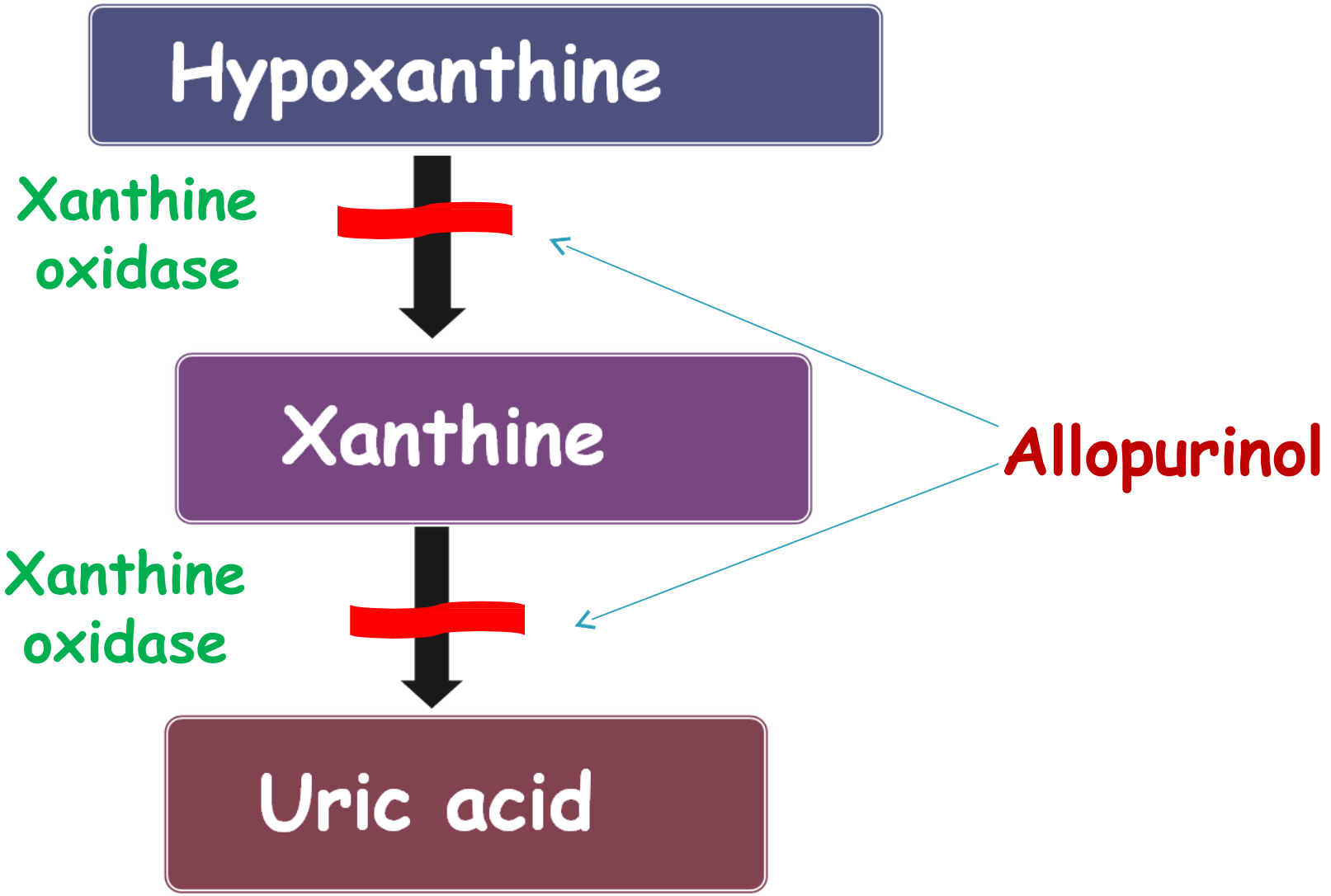
- Gastric irritation
- C/I: peptic ulcer

URIC ACID SYNTHESIS INHIBITORS

Allopurinol:

Reduces uric acid synthesis by competitively inhibiting xanthine oxidase

Allopurinol◊ Alloxanthine ◊ noncompetitive inhibitor of xanthine oxidase


Hypoxanthine
Xanthine oxidase
Xanthine
Allopurinol
Xanthine oxidase
Uric acid

Uses:

- Chronic tophaceous gout
- Recurrent renal urate stones
- Secondary hyperuricemia - cancer chemotherapy/ thiazides
- During treatment of blood dyscrasias
- As antiprotozoal agent – kala-azar

A/E:

- Hypersensitivity reactions
- GIT upset
- CNS: headache, dizziness, peripheral neuritis

<u>May precipitate acute attack of gout</u>

Prevented ◊ colchicine, indomethacin

C/I: pregnancy and lactation
hypersensitive patients

Thank you