Gout

Definition
Gout is a recurrent arthritis that result from deposition in or about the joint of sodium urate crystals from supersaturarated hyperuricemic body fluids

Drugs used in the treatment of gout
1--Anti-inflammatory drugs used for gout - (NSAIDs.......Steroids.....Colchicine)
2--Uricousuric agents ( Probencid..... Sulfinpyrazone)
3--Uric acid synthesis inhibitors (Allopurinol )

1- Anti-inflammatory drugs used for gout

A- NSAIDs=Non-steroidal anti-inflammatory drugs
...NSAIDs as indomethacin are used in acute gouty arthritis .NSAIDs reduce inflammation by inhibiting prostaglandins synthesis via inhibition of cyclooxygenase 2.

B- Steroids ( Glucocorticoids as prednisone )
...Steroids ( Glucocorticoids as prednisone) are used in acute gout to reduce inflammation by reducing prostaglandins and leukotrienes synthesis via inhibition of phospholipase A 2.

C- Colchicine
...Cholchicine is useful in acute gout but the possible severe diarhoea and gastric irritation limit its use. Cholchicine reduces inflammation by reducing leukocyte migration to the site of inflammation because it is a selective inhibitor of microtubule assembly.

Toxicity of anti-inflammatory antigout (side effects)

...NSAIDs toxicity.......( Renal damage ......Bone marrow toxicity )

...Steroids..... ( Behavioral changes.....Impaired glucose tolerance )

...Colchicine.....( Diarhoea.....Liver damage ......Renal damage )
2- Uricousuric agents

Drugs
...A- Probenecid
...B - Sulfinpyrazone

Mechanism of uricousuric agents action
They act by competing with uric acid reabsorption which is achieved by the weak acid transport mechanism in the proximal convoluted tubules of the kidney.
(At low doses, probenecid and sulfinpyrazone being acids may increase uric acid concentration in the blood but here by competing with uric acid secretion .....Aspirin , another weak acid, can do that in every dose, so aspirin is not useful in gout ).

Clinical indications of uricosuric agents
1. Chronic gout
2. Not useful in acute gout

Toxicity of uricosuric agents (side effects)
1- Precipitation of acute gouty arthritis during early phase of treatment because reduction of the level of uric acid in the blood by the uricosuric agents leads to shifting of the uric acid, which was accumulated in other tissues, shifting it to the blood and precipitation in the joints. This can be avoided by simultaneous use of an anti-inflammatory drug as indomethacin or colchicine.

2- Being sulfonamides, they can cause allergenicity like other sulfonamides.

3 - Uric acid synthesis inhibitors ( Allopurinol )
Mechanism of action
Allopurinol is an isomer for hypoxanthine. Hypoxanthine originates from DNA & RNA metabolism. Hypoxanthine is converted to xanthine by xanthine oxidase. Xanthine is then converted to uric acid by the same enzyme. Allopurinol is converted to alloxanthine by xanthine
oxidase (allopurinol is an irreversible inhibitor of this enzyme). Inhibition of xanthine oxidase increases the concentration of the more soluble hypoxanthine and xanthine and decreases the concentration of the less soluble uric acid. As a result there is less likelihood of precipitation of uric acid crystals in the joints & tissues.

Clinical use of allopurinol

1- Allopurinol is given orally in the management of chronic gout. It is usually withheld for 2 weeks after acute gouty arthritis.
2- Cancer chemotherapy: to decrease the formation of uric acid from purines released by the death of neoplastic cells.

Toxicity of allopurinol (side effects)

1- Precipitation of acute gouty arthritis during early face of treatment (because reduction of the level of uric acid in the blood by allopurinol leads to shifting of the uric acid, which was accumulated in other tissues, shifting it to the blood and its precipitation in the joints).
2- GIT disturbances.
3- Rash
4- Rare adverse effects --- peripheral neuritis --- vasculitis --- bone marrow depression

Drug interactions with allopurinol
Allopurinol inhibits the metabolism of mercaptopurine & azathioprine -drugs which depend on xanthine oxidase for their elimination-. 