GOUT

GRG.

- there is uric acid elevated in blood.
- uric acid will deposit in joints & go to joints ↑
- U.A is not water soluble.
- so it will form precipitates.
- Neutrophils will come to eat these precipitates
- ↓
- Inflammation
- painful → due to accumulation of sharp, needle-like crystals of uric acid.
- there will be intense swelling & inflammation (Neutrophils).
- Inflammation puts pressure on nerve endings.
- ↓
- Extreme pain.
- Sudden attacks can occur.
- → burning, throbbing pain.

acute Gout

↓

- pain
- inflammation

so we use.

↓

(1) NSAIDs - aspirin etc.

DOC → Indomethacin

- if not working.

↓

(2) use steroids.

- steroids can be given as Intraarticular injections.

(if few joints are involved).

if None is working we use.

"ULTIMATE DECOY"

↓

COLCHICINE

- most effective drug
- will cure Gout 100%
- if not cured, it means the disease is not gout it's that effective.
- so... most effective! But why not DOC?
- Cause of the side effect

Colchicine

SE

↙ Intractable diarrhea

↘ myopathy.

↓

Severe diarrhea 2-4 weeks, doesn't respond to normal therapeutics.

Even though colchicine is most effective- it's kept as reserve cause of its side effects

- Uric acid → normally soluble in blood warm ✓ temp.
- in synovial fluid, cooler area

↓

crystals ✓.

Mechanism of action

. when uric acid Lvl increases in blood.

↓

it causes low grade inflammation of synovium

↓

permeability of synovium increases

↓

Uric acid enters joint cavity

↓

forms urate crystals in cooler synovial fluid containing joints where solubility is less

↓

eg: 1st meta carpo phalangeal MTP joint

↓

Big toe.

Uric acid crystals once ppt are engulfed by synovial fluid cells

↓

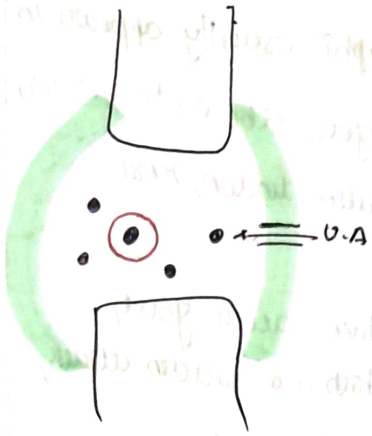
~~& they release a glycoprotein~~

↓

~~(9) Neutrophils.~~

↓

~~inflammation.~~



~~Colchicine prevents Neutrophil migration to joints.~~

↓

~~⊖ chemotaxis~~

~~⊖ granulocyte migration~~

↓

~~no~~

Colchicine binds to tubulin and prevent polymerization into microtubules.

↓

cytoskeletal dynamics ✗

cell movement ✗.

↓

⊖ Neutrophil migration to joints.

⊖ chemotaxis.

↓

⊖ Inflammation.

. they also ↓ IL-1 release from Neutrophil

& ⊖ phagocytosis

MoA

1. ⊖ microtubule formation any thereby

⊖ chemotaxis

Neutrophil migration

2. ⊖ IL-1 release from neutrophil.

3. ⊖ phagocytosis.

- Colchicine is actually anticancer drug.

- ⊖ microtubules

also

⊖ cell division

⊖ cell movement.

other uses of colchicine.

U - uric acid (gout)

C - cirrhosis

M - acute mediterranean fever

S - sarcoidosis

A - amyloidosis

SUMAC

chronic gout

- in C.G there is elevated blood uric acid level for a longer duration...

↳ body has kinda tolerated it...
so there will be gradual deposition of crystals

But doesn't cause acute attacks all the time.

- Sometimes, certain triggers can cause sudden deposition ↳ pain. {could happen}.

- Tophi

Tophi are lumps or nodules made of crystallized uric acid. that get's deposited in joints, soft tissue, organs etc..

Tophi usually appears in fingers, elbow, toes, ears, Achilles tendon, knee

- Unlike acute gout, which is a sudden attack, chronic gout

↓

tophi develops slowly over years due to gradual deposition.

↓

Tophi can become painful, disfiguring & even erode bone if not treated.

~~or~~

No tophi
Acute → sudden uric acid deposition in joints

Chronic → Long term accumulation of uric acid leading to tophi formation.
Tophi ✓

acute → Severe, sudden, excruciating pain.

Chronic → milder but persistent joint pain.
↓
(no NSAID etc).

what is the aim in treatment of chronic gout?

- It is to lower uric acid LVl

↓

so as to prevent further slow deposition and occassional acute attacks. Risk.

↓

Rx

↓

↓ URIC ACID.

- Chronic gout → ↓ uric acid is ↑ aim

- acut gout → uric acid ↓ will worsen it

✗ not to be done

Y? ↳ uric acid level should not be decreased in acute gout.

in acute gout there is suaden crystal deposition in joints.

↓

if we ↓ uric acid levels in blood.

- larger crystals will destabilize
- they breaks to smaller ones
- smaller ones - act like new crystals
- ⊕ further inflammation.

- also, uric acid ↓ in blood can cause remobilization from organ deposits and all these will move back to bloodstream.
- more likely to irritate joints
- free-floating crystals can enter joint spaces.
- new attack.

acute → never ↓ uric acid. give drugs that can → manage pain & inflammation

How to.

↓ URIC ACID.

↓ excretion

- uricosuric drugs
- ⊖ reabsorption of uric acid
- pump ⊖.
- probenecid.
- Sulfinpyrazone
- Benzbromarone
- LESINURAD.

Should always take Large amount of FLUIDS to dilute urine to ⊖ kidney deposits

or else, will deposit in kidney.

↓ formation

purine/protein

xanthine.

xanthine oxidase ⊖

Uric acid.

xanthine oxidase ⊖

↓ ALLOPURINOL. (1)

use.

- ↓ protein rich diet

DOC in chronic gout

ALLOPURINOL

Since uricosuric drugs act by ⊖ reabsorption from kidney.

if there is kidney failure.

Drug wont be effective.

Cancer cells →

↑ production

these all will have their own nucleic material.

anti cancer drug

protein, purine = released out.

Anti cancer drugs ⇒ ↑ uric acid

ALLOPURINOL

use

- anticancer induced ↑ uric acid.
- Kala azar.

anticancer drug destroy cancer cell

destroyed cell release purine/protein

↑ uric acid.

Allopurinol

Shouldn't be used in acute gout

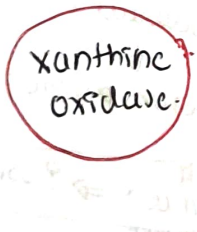
Impt Drug Interactions:

6-mercaptopurine {anti cancer drug}

and

Azathioprine (immunosuppressant)

both | metabolised by



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