



Doctor 021

MSS

PHARMACOLOGY

#6



WRITER: Hala Ajlouni

CORRECTOR: Malak Khalid

DOCTOR: Alia shatanawi

Drug Therapy of Gout

* Hyperuricemia
is the most important
characteristic of
gout.

* production
of uric
acid >>> excretion

* We work mainly on 3 gout's characteristics
to treat gout:

1. inflammation
2. PMNs
3. Hyperuricemia

Treating acute gouty arthritis

- colchicine →

prevents tubulin → monomer that
polymerization will be polymerized
to microtubules

↳ Important for inflammatory
cells (PMNs, macrophages)
movement to the site of
infection.

- NSAID's → Reduces PG production
(less pain, swelling, etc)
inflammatory signs.

- steroids

- rest, analgesia, ice, time

Aspirin is not recommended
for gout patients?



① Aspirin & uric acid have the same site of excretion
in the kidney, so aspirin will compete
with uric acid resulting in decreased
excretion

② Aspirin is used in
high doses which
leads to GI
irritation

Drugs used to treat gout

Acute Arthritis Drugs

colchicine

steroids

NSAID's

Urate Lowering Drugs

allopurinol

probenecid

febuxostat?

*if a new drug that
was under study but
now it is approved*

rest + analgesia + time

Drugs used to treat gout

For NSAIDs:

* Doses for antiinflammatory effect are usually higher than the analgesic dose.

NSAID's

they have analgesic effect in addition to the antiinflammatory effect

- Indomethacin (Indocin) 25 to 50 mg four times daily
- Naproxen (Naprosyn) 500 mg two times daily
- Ibuprofen (Motrin) 800 mg four times daily
- Sulindac (Clinoril) 200 mg two times daily
- Ketoprofen (Orudis) 75 mg four times daily

only be familiar with the names

* don't memorize the doses

Colchicine - plant alkaloid

its not an analgesic

colchicum

autumnale

الزعفران البري

)autumn crocus or
meadow saffron(



Colchicine

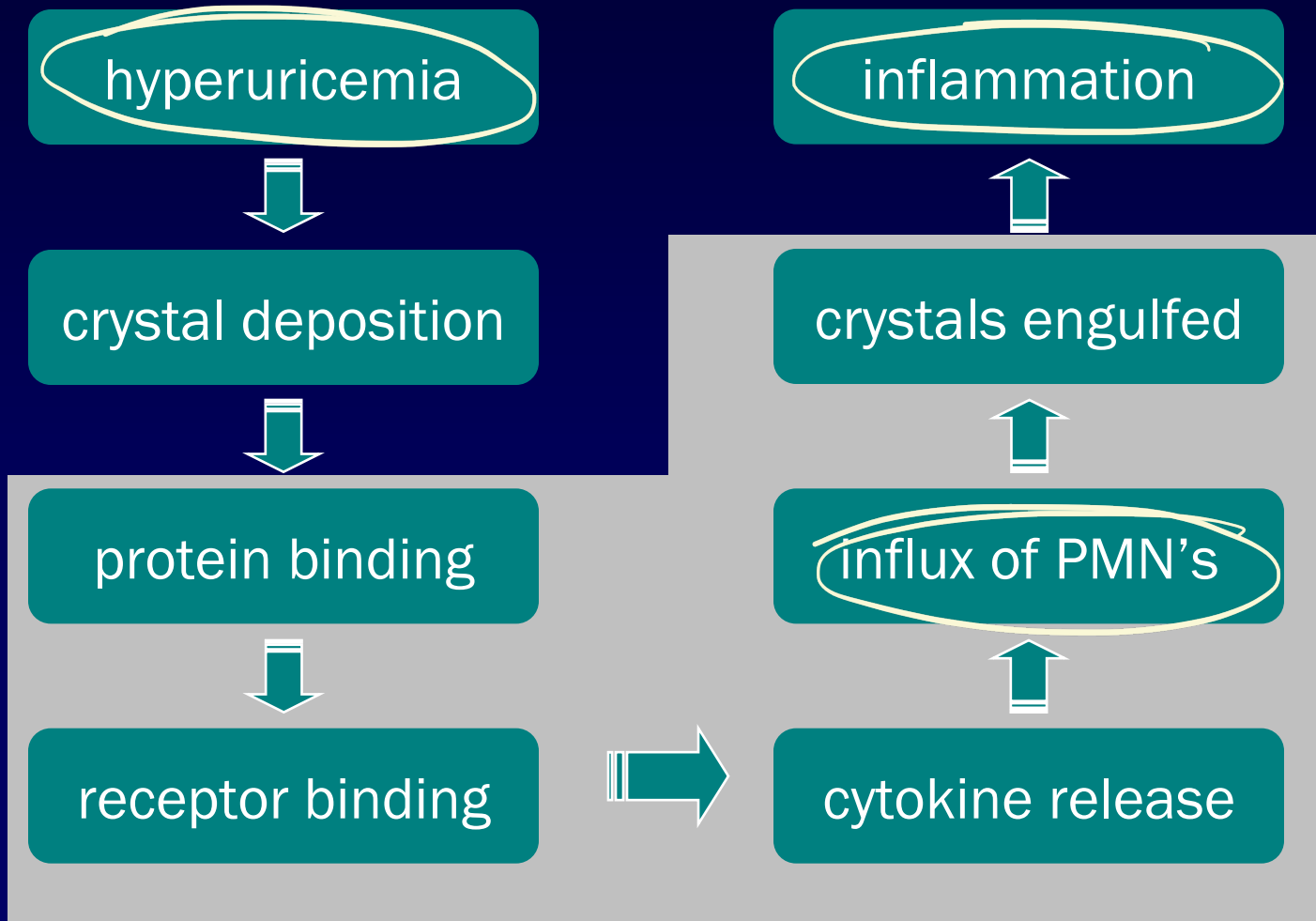
- “only effective in gouty arthritis”
- not an analgesic
- does not affect renal excretion of uric acid
- does not alter plasma solubility of uric acid
- neither raises nor lowers serum uric acid

Colchicine

- Colchicine inhibits microtubule polymerization by binding to tubulin, one of the main constituents of microtubules
- reduces inflammatory response to deposited crystals
- diminishes (PMN) phagocytosis of crystals
- blocks cellular response to deposited crystals

*very important for
the development
of inflammatory
cascade*

Crystal-induced inflammation



PMN is critical component of crystal-induced inflammation

Colchicine - indications

Dose

Indication

high

treatment of acute gouty arthritis

low

used for longer time so low dose is administered.
(prevention) of recurrent gouty arthritis to avoid side effects.

Colchicine - toxicity

- gastrointestinal (nausea, vomiting, cramping, diarrhea, abdominal pain)
- hematologic (agranulocytosis, aplastic anemia, thrombocytopenia) →
- muscular weakness

Because it affects the division of cells.

(mainly → rapidly dividing cells like those in the bone marrow).

adverse effects dose-related & more common when patient has renal or hepatic disease

Gout - colchicine therapy

- more useful for daily prophylaxis (low dose)

prevents recurrent attacks

colchicine 0.6 mg qd - bid

*do not memorize
numbers*

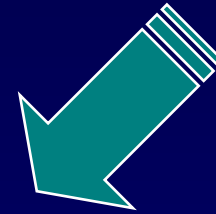
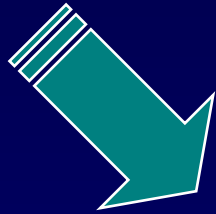
- declining use in acute gout (high dose)

because of its high toxicity

Hyperuricemia - mechanisms

excessive
production

inadequate
excretion

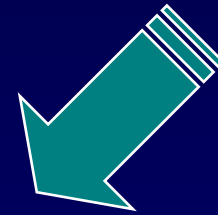
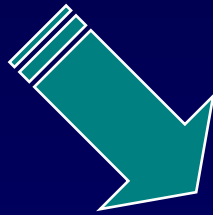


hyperuricemia

Urate-lowering drugs

block production

enhance
excretion



net reduction in total body pool of
uric acid

Gout - urate-lowering therapy

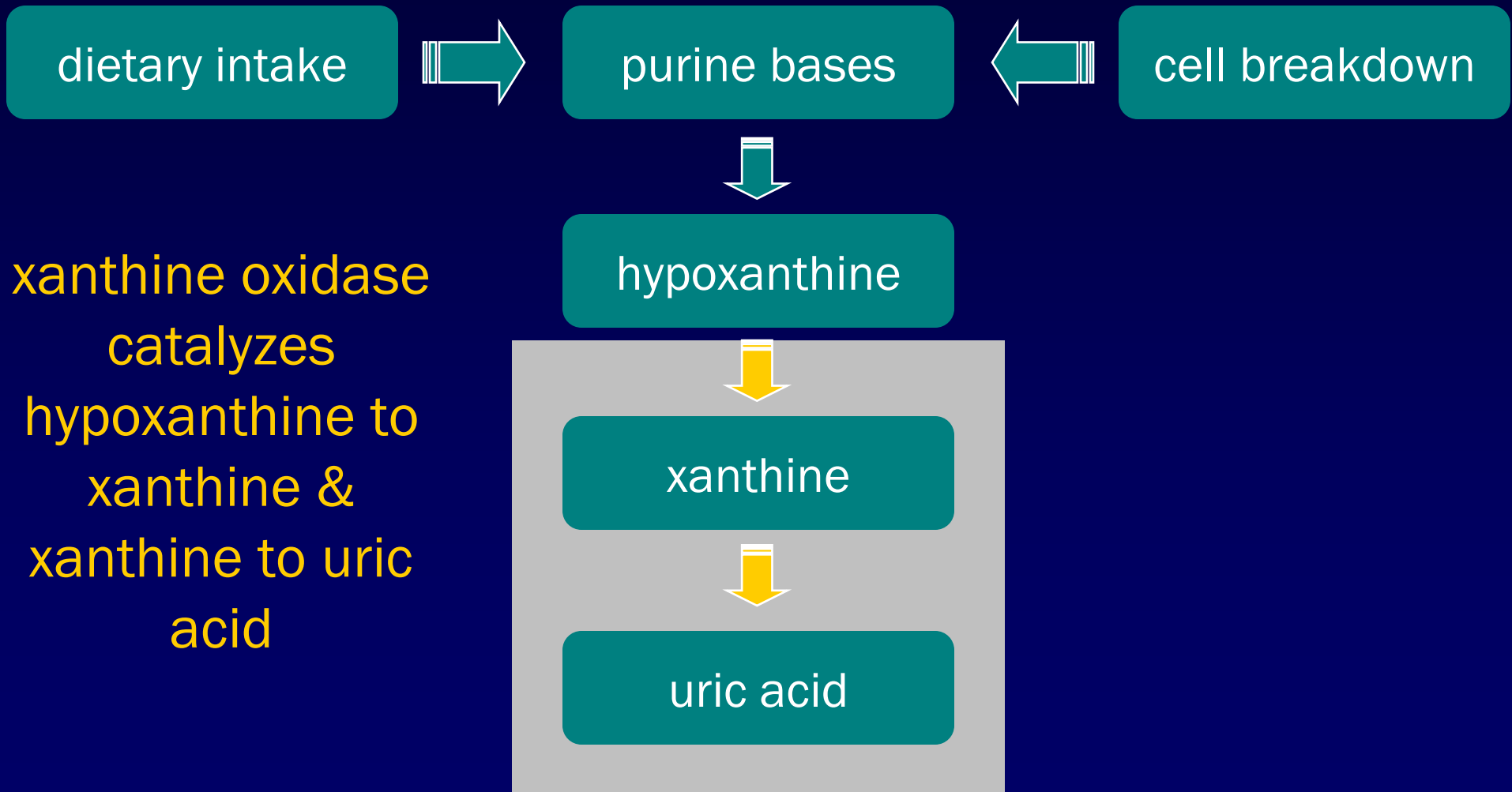
- prevents arthritis, tophi & stones by lowering total body pool of uric acid
- not indicated after first attack
- initiation of therapy can worsen or bring on acute gouty arthritis
- no role to play in managing acute gout

it lowers uric acid conc. in the blood and causes mobilization of it from the joints and thus high risk of reposition in a near joint or worsen the previous attacked joint

Drug therapy of gout

*Drugs That Block
Production of Uric Acid*

Uric acid metabolism



Allopurinol (Zyloprim™)

- inhibitor of xanthine oxidase
- effectively blocks formation of uric acid
- how supplied - 100 mg & 300 mg tablets
- pregnancy category (C) → *studies on animals approve risk on animal fetus but no enough studies on humans.*

(its up to the physician)

allopurinol



Allopurinol - usage indications

- management of hyperuricemia of gout
- management of hyperuricemia associated with (chemotherapy) *cancerous cells die
↳ more purines
more uric acid.*
- prevention of recurrent calcium oxalate kidney stones

side effects.

Allopurinol - common reactions

- diarrhea, nausea, abnormal liver tests
- acute attacks of gout
- rash

(Rare)

Allopurinol - serious reactions

similar to Stevens-Johnson Syndrome

- fever, rash, toxic epidermal necrolysis
- hepatotoxicity, marrow suppression
- vasculitis → *induction of inflammation*
- drug interactions (ampicillin, thiazides, mercaptopurine, azathioprine)
- death

Stevens-Johnson syndrome

autoimmune disease
when antibodies target the
epidermal layer under the
mucous membrane

target skin lesions

mucous membrane
erosions

epidermal necrosis with
skin detachment

target
skin
lesion 





Allopurinol hypersensitivity

- extremely serious problem
- prompt recognition required
- first sign usually skin rash
- more common with impaired renal function
- progression to toxic epidermal necrolysis & death

Febuxostat (Uloric / Adenuric)

- approved by FDA ((2008
- oral xanthine oxidase inhibitor
- chemically distinct from allopurinol
- minimal adverse events
- can be used in patients with renal disease

pegylated

PEG-uricase

→ able to degrade uric acid.

initially from animal resource (pigs)
but now we use recombinant DNA

- approved in the United States in 2010
- PEG-conjugate of recombinant porcine uricase (urate oxidase)
- it metabolises uric acid to allantoin
- severe, treatment-refractory, chronic gout.
- uricase speeds resolution of tophi
- it lowers uric acid levels
- glucose-6-phosphate dehydrogenase deficiency, pegloticase may precipitate a severe, life-threatening hemolysis

↳ means from pigs

PEG → (pegylated)
polyethylene glycol is added to increase the half-life and stability of the drug and to reduce immunogenicity against uricase.

* Its an enzyme so its administered IV to avoid degradation by the stomach

Drug therapy of gout

*Drugs That Enhance
Excretion of Uric Acid*

increase the excretion of
uric acid

Uricosuric therapy

- probenecid ↘
- blocks tubular reabsorption of uric acid
- enhances urine uric acid excretion ←
- increases urine uric acid level
- decreases serum uric acid level

Urine ↑
Blood ↓

Uricosuric therapy

- moderately effective
- increases risk of nephrolithiasis
kidney stones
- not used in patients with renal disease
- frequent, but mild, side effects

Because it lowers uric acid conc. in the serum and that leads to its mobilization and precipitation in different sites (kidney)

Uricosuric therapy

- contra-indications

 - history of nephrolithiasis

 - elevated urine uric acid level

 - existing renal disease

- less effective in elderly patients



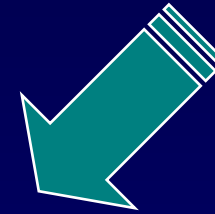
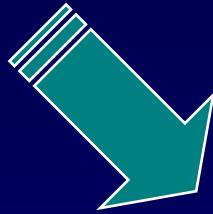
kidney function
deteriorates with age
(different kinetics
and eliminating
rate)

Choosing a urate-lowering drug

excessive
production

inadequate
excretion

xanthine
oxidase
inhibitor



uricosuric
agent

hyperuricemia