

PASSION ACADEMIC TEAM

YU - MEDICINE

MUSCULOSKELETAL SYSTEM

Sheet#5 - Pharmacology

Lec. Title : Drug Therapy of Gout

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If you come by any mistake , please
kindly report it to
shaghafbatch@gmail.com



Drug Therapy of Gout

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بداية يعطيكم الف عافية يا رب واي استفسار للمحاضرة لا
تدخلوا وسموا بالله هيك وسوا قولوا اللهم اني اسالك فهم
النبيين وحفظ الملائكة المقربين وعلى بركة الله , نبداً

الدكتور بداية المحاضرة نوه لشغلة بسيطة على انها خطأ
وهي انه في ناس بتسمي مرض النقرس بداء الملوك
والامراء بسبب اكلهم اللحمة بشكل مفرط بس حتى لمن
نوكل بقوليات بشكل مفرط مثل الفول والعدس والفاصوليا
ممکن يسبب لنا نقرس فالخلاصة مرض النقرس بصير عند
الفقراء وعند الأغنياء

Gouty arthritis - characteristics

- sudden onset
- middle aged males
- severe pain
- distal joints
- intense inflammation
- recurrent episodes
- influenced by diet
- bony erosions on Xray
- hyperuricemia

Chronic tophaceous gout



tophus = localized deposit of
monosodium urate crystals

هسة بالنسبة للصورة ف اسمحولي اشرحها بالعربي عشان تفهموا
الدكتور وصف العدوى المزمنة بمصطلح حكاانا كثير مهم بالنسبة النا
ك أطباء تسأل عنه المرض وهو **in between** ووسماه مرض مزمن
وهسة ال **gout** بنتج بشكل أساسي من تفاعل اليوريك مع
ال **neutrophils** بالمفاصل اللي على وجه الخصوص بالمفاصل
الصغيرة وهاض التفاعل وصفه الدكتور بالحرب اللي بنتج من ارتفاع
نسبة اليوريك لاعلى من الطبيعي (3-7مليغرام) وترسبه بالمفاصل
وبسبب خسارة ال **neutrophils** الحرب بصير عنا مرض
chronic tophaceous gout ال

معلومة هيك سريعة لو في عنا دوا بوقف اطلاق الجهاز المناعي
ال **neutrophils** ما بصير عنا مرض ال **chronic tophaceous**
gout

Gout - X-ray changes

DIP joint destruction

phalangeal bone cysts

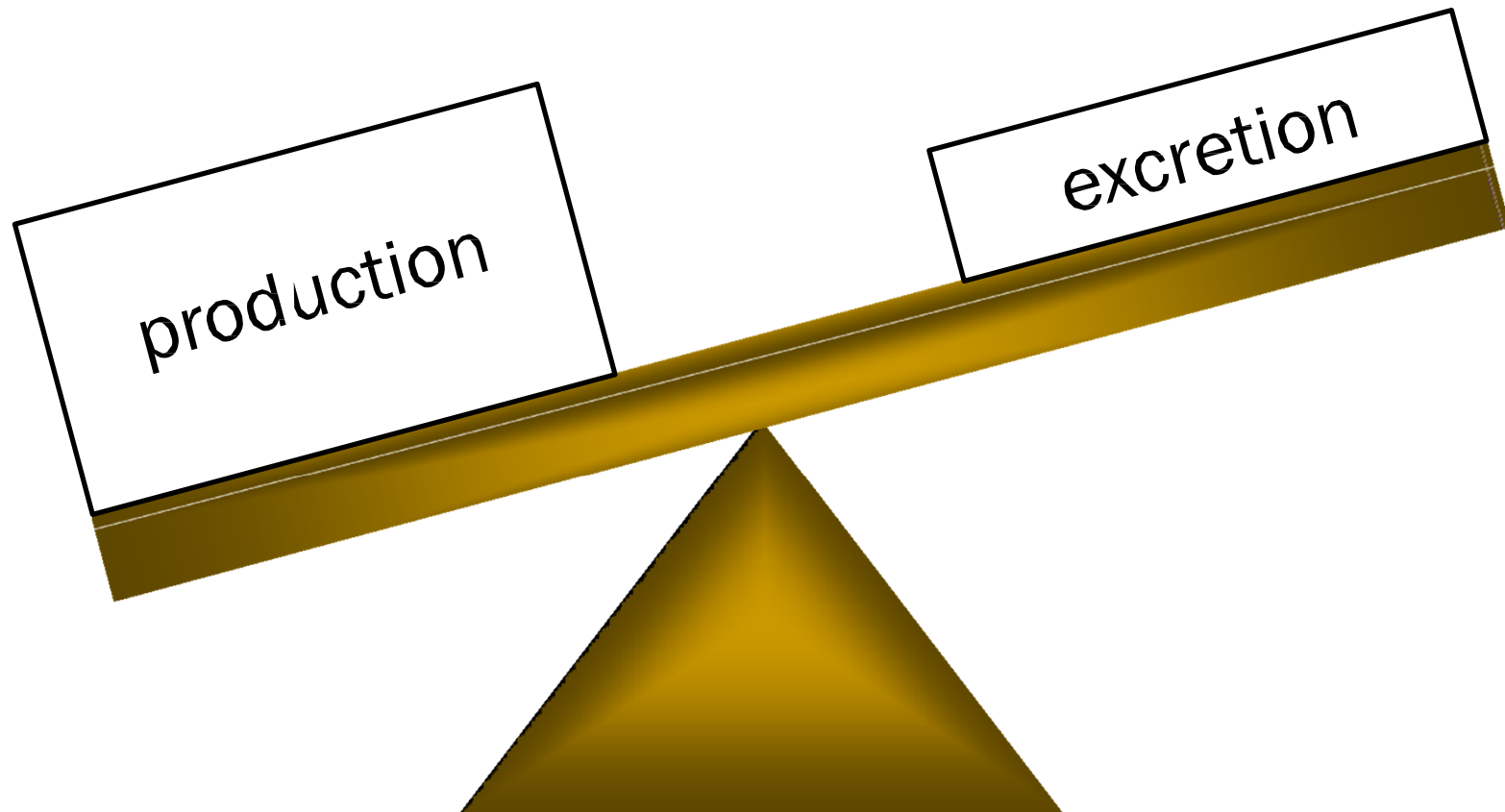


Gout - X-ray changes

bony erosions

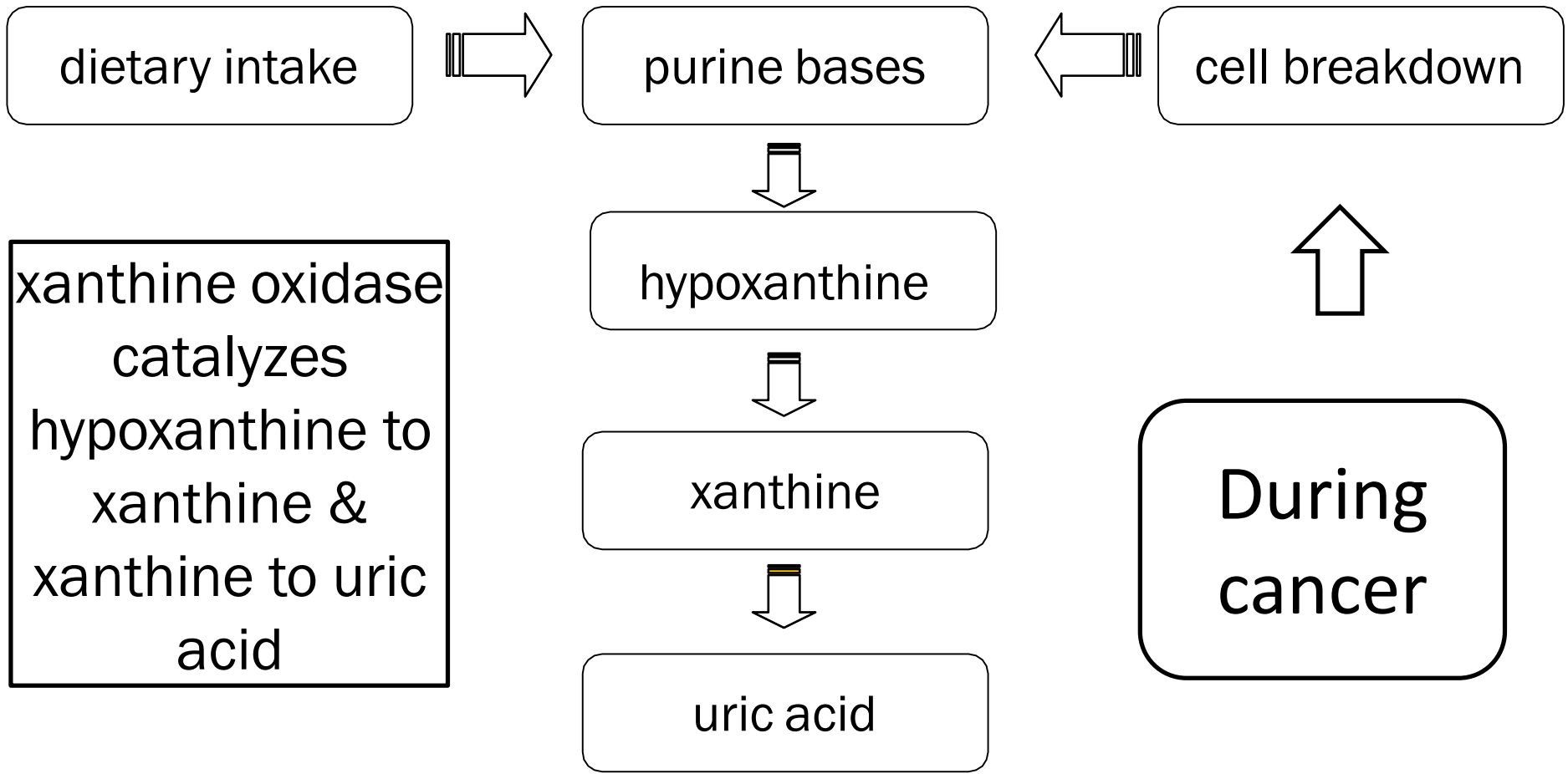


Hyperuricemia



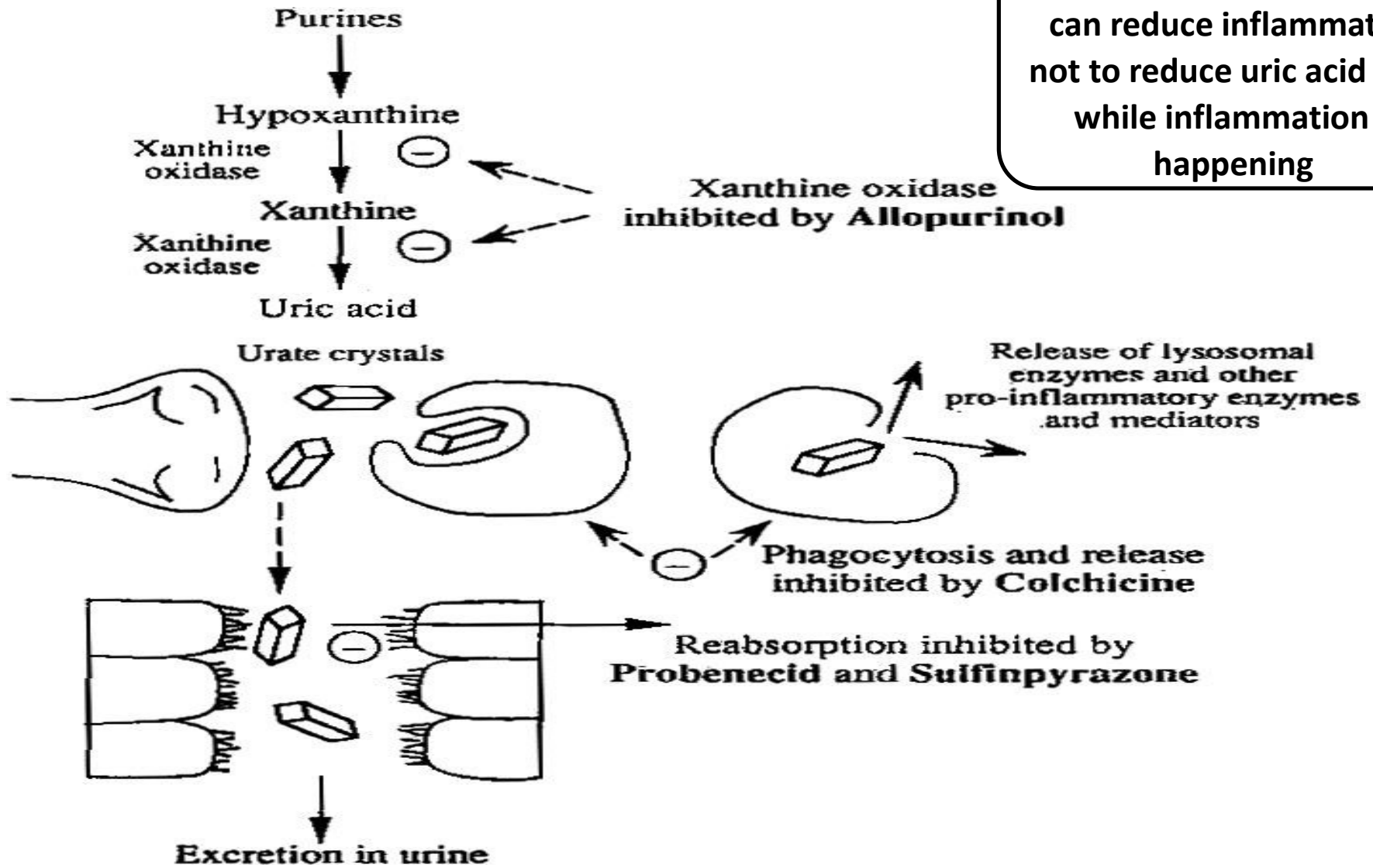
hyperuricemia results when production exceeds excretion

Uric acid metabolism



Treatment of Gout

With acute gout => drugs can reduce inflammation not to reduce uric acid level while inflammation is happening



Drugs used to treat gout

Acute Arthritis Drugs

colchicine

steroids

NSAID's

Urate Lowering Drugs

allopurinol

probenecid

febuxostat?

best

rest + analgesia + time

Non-steroidal anti-inflammatory drugs (NSAIDs)

- FDA approval for this indication
 - Indomethacin: 25–50 mg four times a day for 3 days, then taper to twice daily for 4–7 days
 - Naproxen: 500 mg twice daily for 3 days, then 250–500 mg daily for 4–7 days
 - Sulindac: 200 mg twice daily for 7–10 days
- Aspirin is **contraindicated**, because it competes with uric acid for the organic acid secretion mechanism in the proximal tubule of the kidney??

الدكتور حكا مش مطالبين بالجرعات بس حكا انو معظم
الادوية اللي فاتت بتتاخذ غالبا من أسبوع لعشر أيام وبعد
العشر أيام بنوخذ دوا لمدة شهرين يقلل نسبة اليوريك مع
الNSAIDs يعني هيك بتصير عنا القصة عشر أيام بأحد
ادوية الNSAIDs وبعد هيك لمدة شهرين دوا يقلل نسبة
اليوريك وبعد الشهرين بنوقف الNSAIDs وعلى مدى طويل
بنستمر بالدوا الثاني

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

- mechanism of action poorly understood
- reduces inflammatory response to deposited crystals
- diminishes PMN phagocytosis of crystals
- blocks cellular response to deposited crystals

Colchicine - indications

<i>Dose</i>	<i>Indication</i>
high	treatment of acute gouty arthritis
low	prevention of recurrent gouty arthritis

Colchicine - toxicity

- Gastrointestinal (nausea, vomiting, cramping, diarrhea, abdominal pain)
- Hematologic (agranulocytosis, aplastic anemia, thrombocytopenia)
- muscular weakness

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
- declining use in acute gout (high dose)

Corticosteroids

- Corticosteroids may be used to treat acute attacks of gouty arthritis, but they are reserved primarily for patients:
 - with a contraindication or who are unresponsive to NSAID or colchicine therapy.
 - Patients with multiple-joint involvement may also benefit.

Drugs used to treat gout

Acute Arthritis Drugs

colchicine

steroids

NSAID's

Urate Lowering Drugs

allopurinol

probenecid

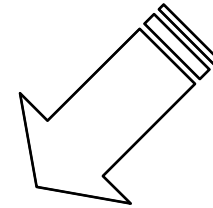
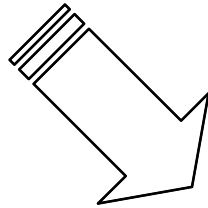
febuxostat?

rest + analgesia + time

Urate-lowering drugs

block
production

enhance
excretion



net reduction in total body pool of
uric acid

Gout - urate-lowering therapy

- It is not used with the acute gout
- 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

Allopurinol

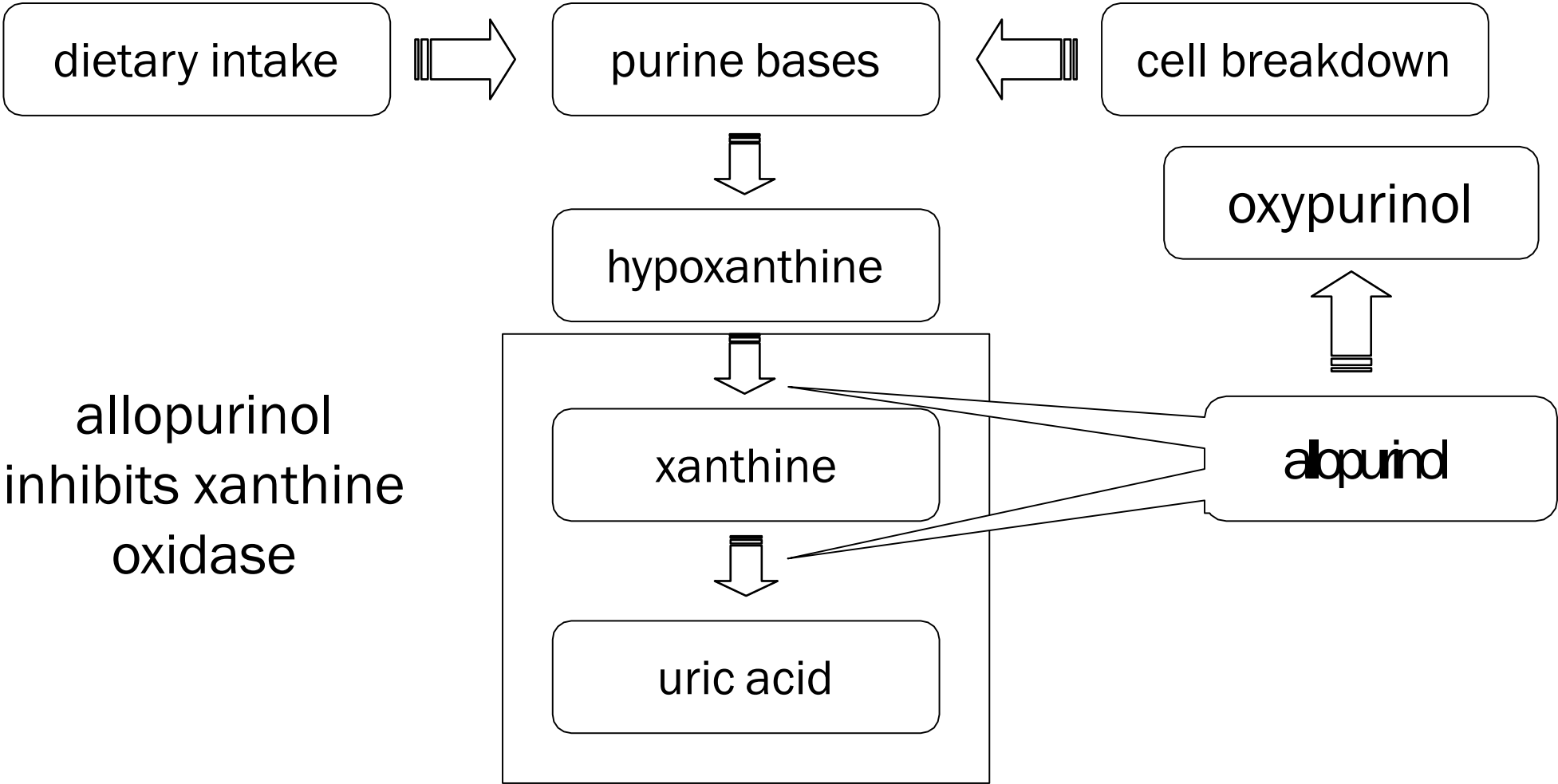
- inhibitor of xanthine oxidase
- effectively blocks formation of uric acid
- how supplied - 100 mg & 300 mg tablets
- pregnancy category C



Allopurinol

- 90% absorption from the gut
- metabolized to oxypurinol
- **once daily dosing**
- **lowers serum uric acid levels**
- **lowers urine uric acid levels**
- side effects rare, but potentially lethal

Uric acid metabolism



Allopurinol - usage indications

- management of hyperuricemia of gout
- management of hyperuricemia associated with chemotherapy
- prevention of recurrent calcium oxalate kidney stones

Allopurinol - common reactions

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

Allopurinol - serious reactions

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

Stevens-Johnson syndrome

Toxic epidermal
necrosis

target skin lesions

mucous membrane
erosions

epidermal necrosis with
skin detachment



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

- recently approved by FDA
- oral xanthine oxidase inhibitor
- chemically distinct from allopurinol
- 94% of patients reached urate < 6.0 mg/dl
- minimal adverse events
- can be used in patients with renal disease

Uricosuric therapy

probenecid

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

Uricosuric therapy

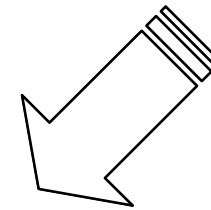
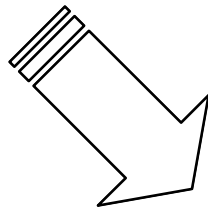
- contra-indications
 - ✓ history of nephrolithiasis
 - ✓ elevated urine uric acid level
 - ✓ existing renal disease
- less effective in elderly patients

Choosing a urate-lowering drug

excessive
production

inadequate
excretion

xanthine
oxidase
inhibitor



uricosuric
agent

hyperuricemia

Urate-lowering therapy

- no anti-inflammatory activity
- can precipitate acute gout
- can prolong attack of gout

Prophylactic Therapy Of Gout

- Patients are candidates for **prophylactic therapy** :
 - if they have had more than two of gouty arthritis per year,
 - the first attack is severe or complicated with kidney stones,
 - serum urate is greater than 10 mg/ dL
- **Colchicine given in low oral doses (0.5 to 0.6 mg twice daily)** **may be** effective in patients with no evidence of visible tophi and a normal or slightly elevated serum urate concentration

Case presentation - therapy

NSAID

NSAID

steroid

colchicine (low-dose)

allopurinol

days 1-10

days 11-365

days 365+

Pegloticase

- الدكتور حكا عن هذا الدواء انه بكسر نسبة اليوريك بالمفصل ويستخدم في حالة استخدام جميع الادوية السابقة بس بدون فائدة
- Pegloticase is approved for the treatment of hyperuricemia in patients with treatment-refractory gout.
- Pegloticase achieves its therapeutic effect by enzymatically converting uric acid to the more soluble metabolite allantoin.

Clinical case

A patient presented with an attack of acute gout.
He was treated with a 10 day course of NSAID.
His blood uric acid level is high.

What future line of treatment ???????????

عيب بعد كل هاض ما تكونوا عارفين الإجابة

The answer: allopurinol for ten days with NSAIDs and
then allopurinol only with the long term

Select the first choice drug for acute gout:

- a. Cochicine
- b. Indomethacin**
- c. Allopurinol
- d. Dexamethasone

Select the drug which is used in chronic gout but is not uricosuric:

- a. Probenecid
- b. Phenylbutazone
- c. Sulfipyrazone
- d. Allopurinol**

Best
Wishes

