



# Drug Therapy of Gout

# Drug therapy of gout

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*What Is Gout?*

# Case presentation

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- 55 y/o male
- 12 hours “pain in my big toe & ankle”
- went to bed last night feeling fine
- felt as if had broken toe this morning
- PMH of similar problems in right ankle & left wrist

# Gout - acute arthritis

acute synovitis,  
ankle & first MTP  
joints



The metatarsophalangeal articulations are the joints between the metatarsal bones of the foot and the proximal bones

# Gout - acute bursitis

acute olecranon bursitis



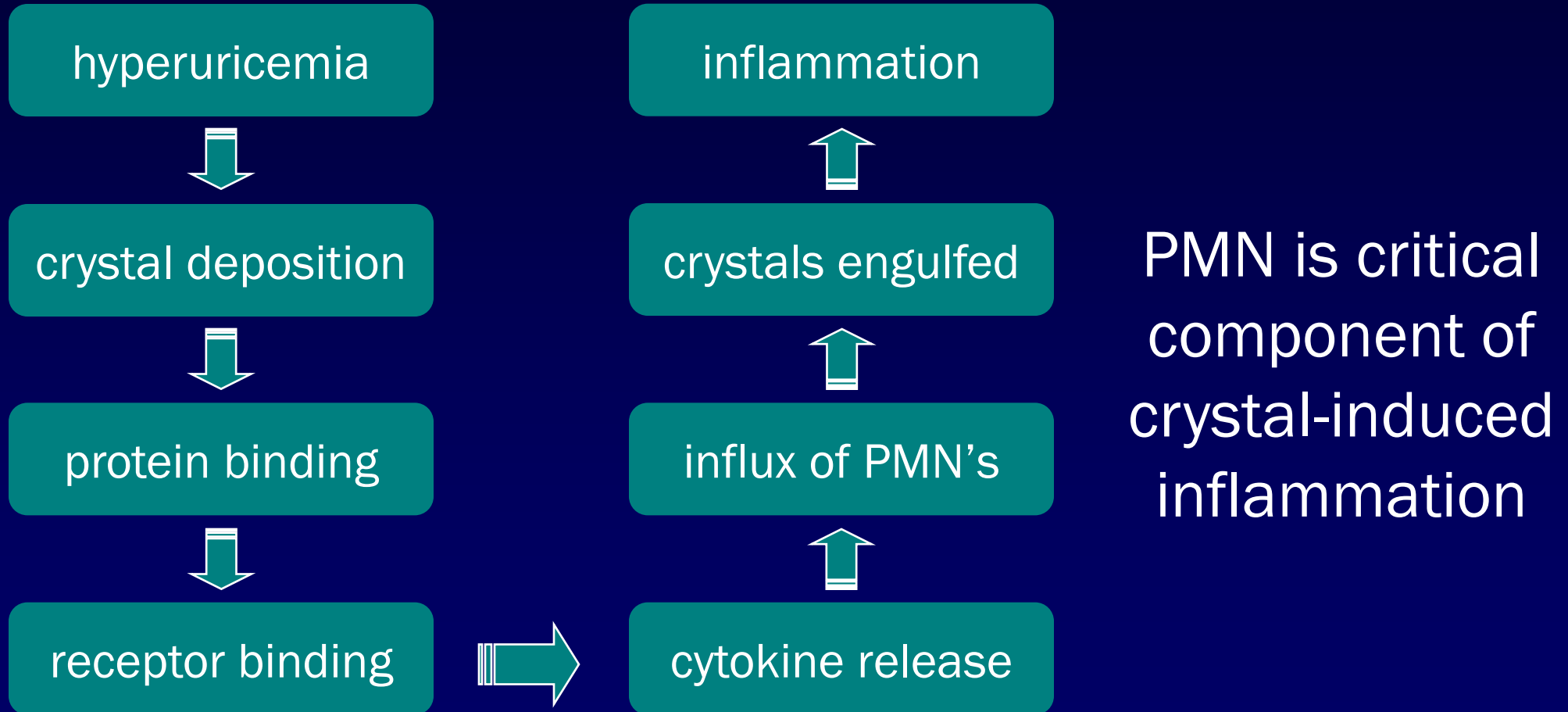
Bursitis is inflammation of the fluid-filled sac (bursa) that lies between a tendon and skin, or between a tendon and bone

# Gouty arthritis - characteristics

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

# Crystal-induced inflammation



# Gouty arthritis - characteristics

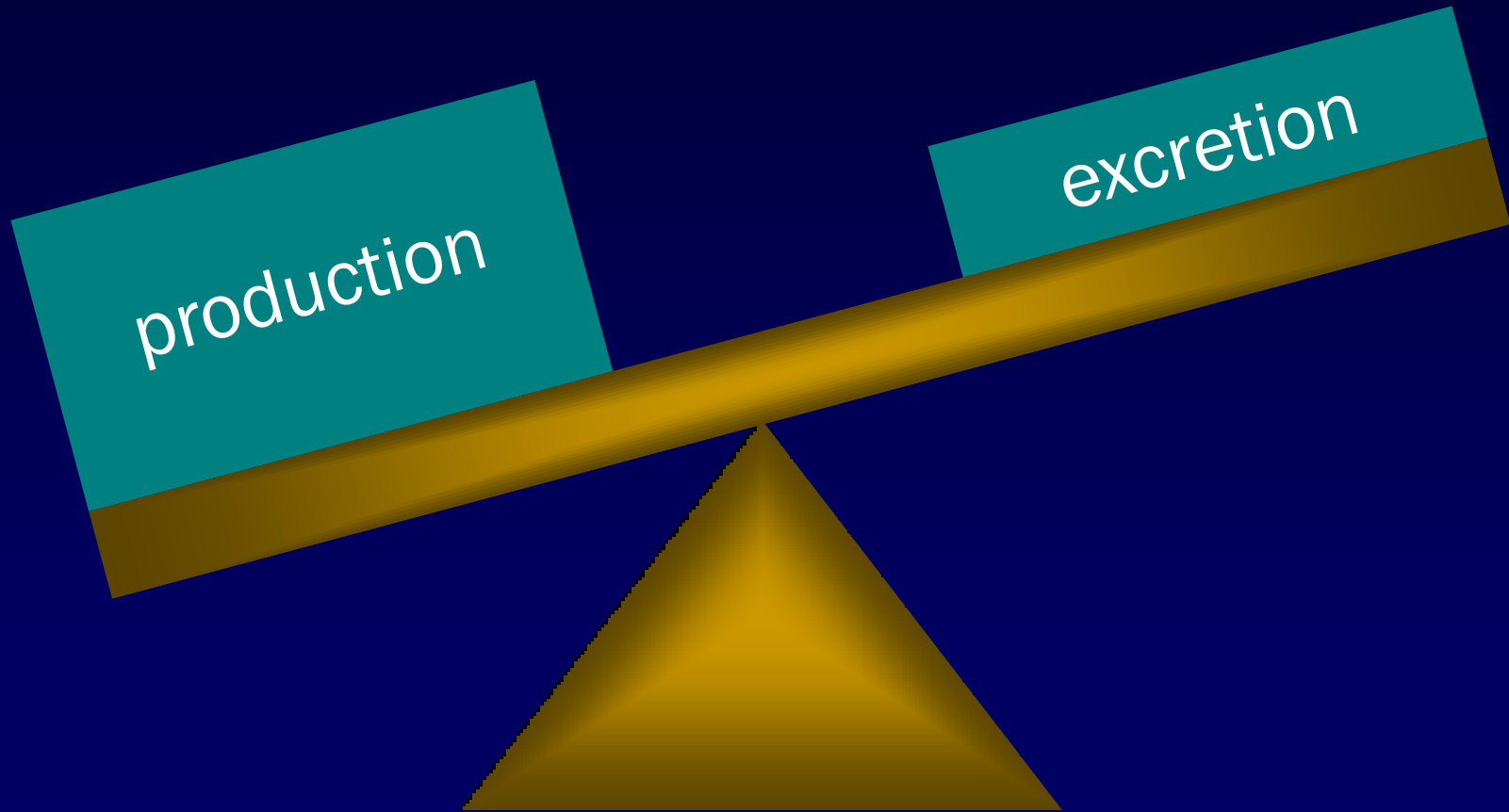
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- sudden onset
- middle aged males
- severe pain
- distal joints
- intense inflammation
- recurrent episodes
- influenced by diet
- bony erosions on Xray
- hyperuricemia



# Hyperuricemia

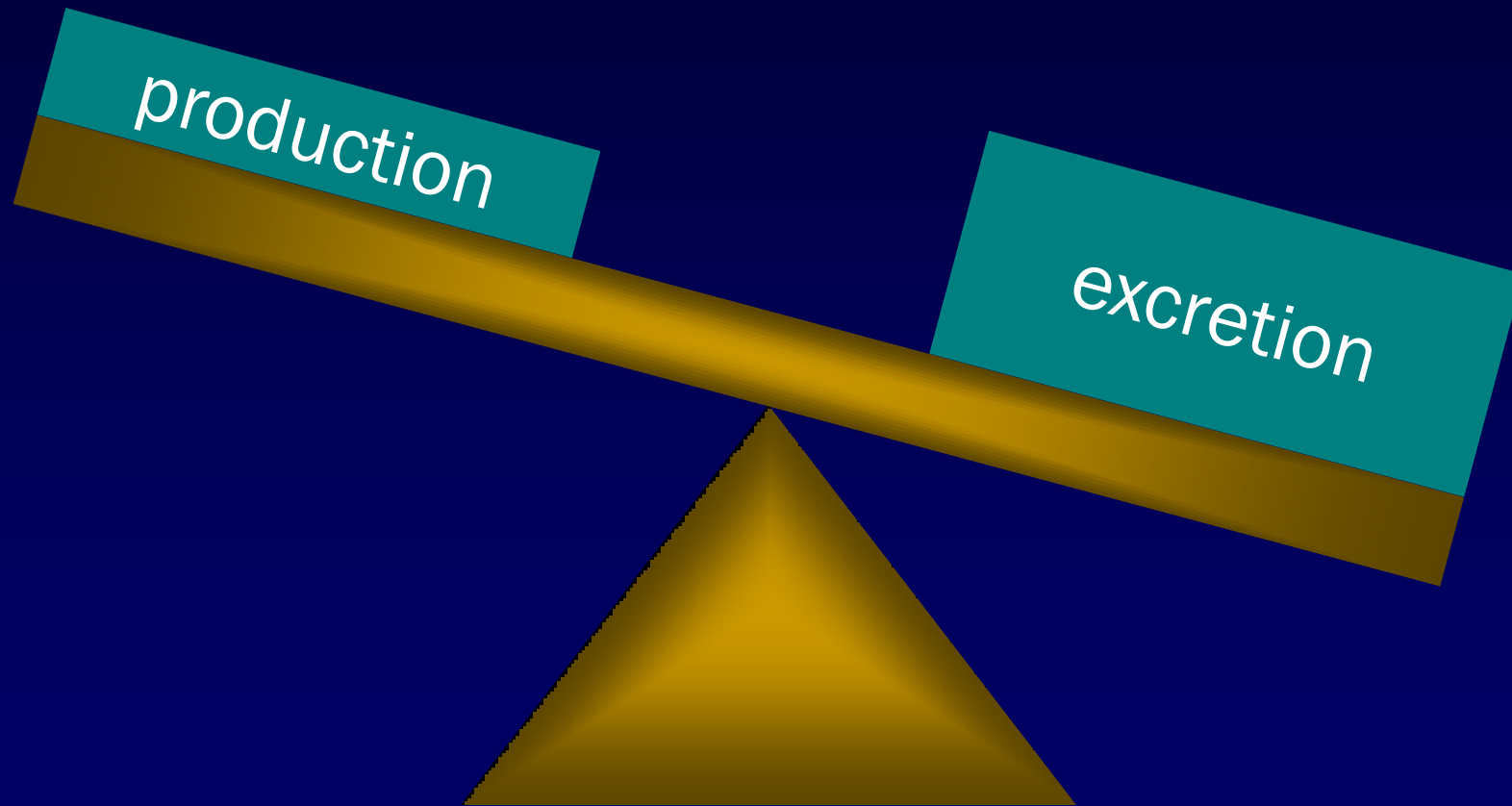
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hyperuricemia results when production exceeds excretion

# Hyperuricemia

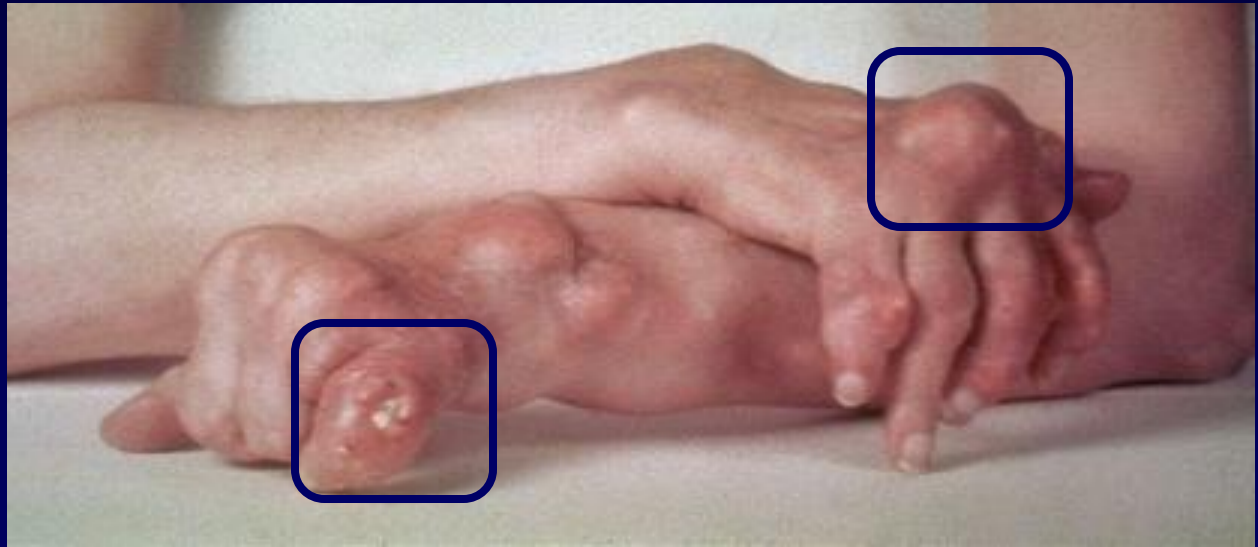
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net uric acid loss results when excretion exceeds production

# Chronic tophaceous gout

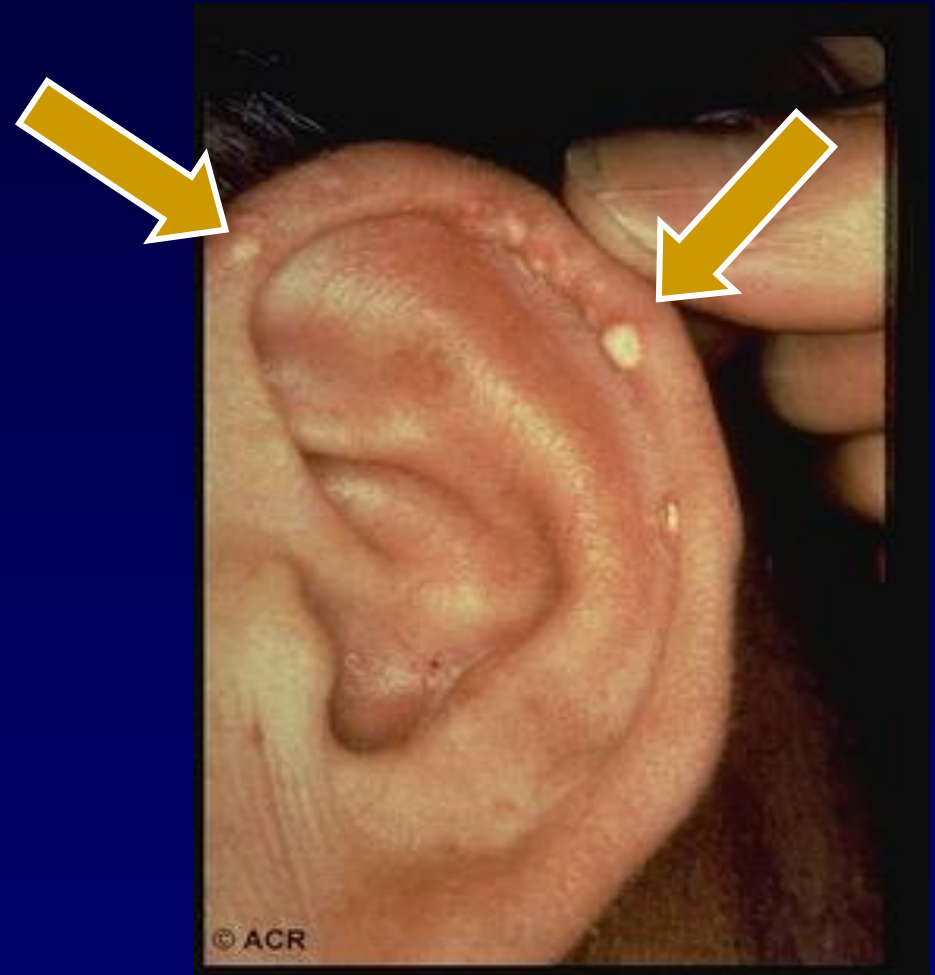
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tophus = localized deposit of  
monosodium urate crystals

# Gout - tophus

classic location of  
tophi on helix of ear



# Gout - X-ray changes

DIP (*Distal  
interphalangeal joint*)

joint destruction

phalangeal bone cysts

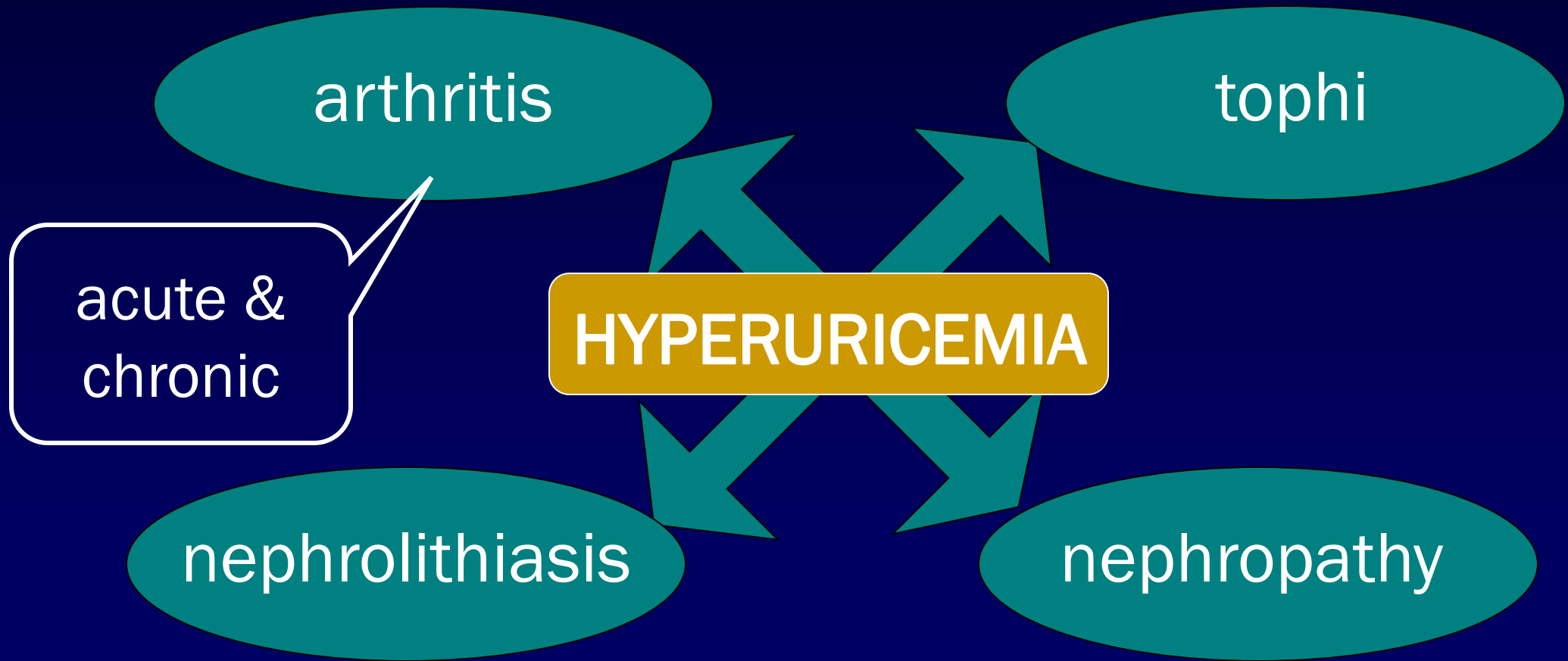


# Gout - X-ray changes

bony erosions



# Gout - cardinal manifestations



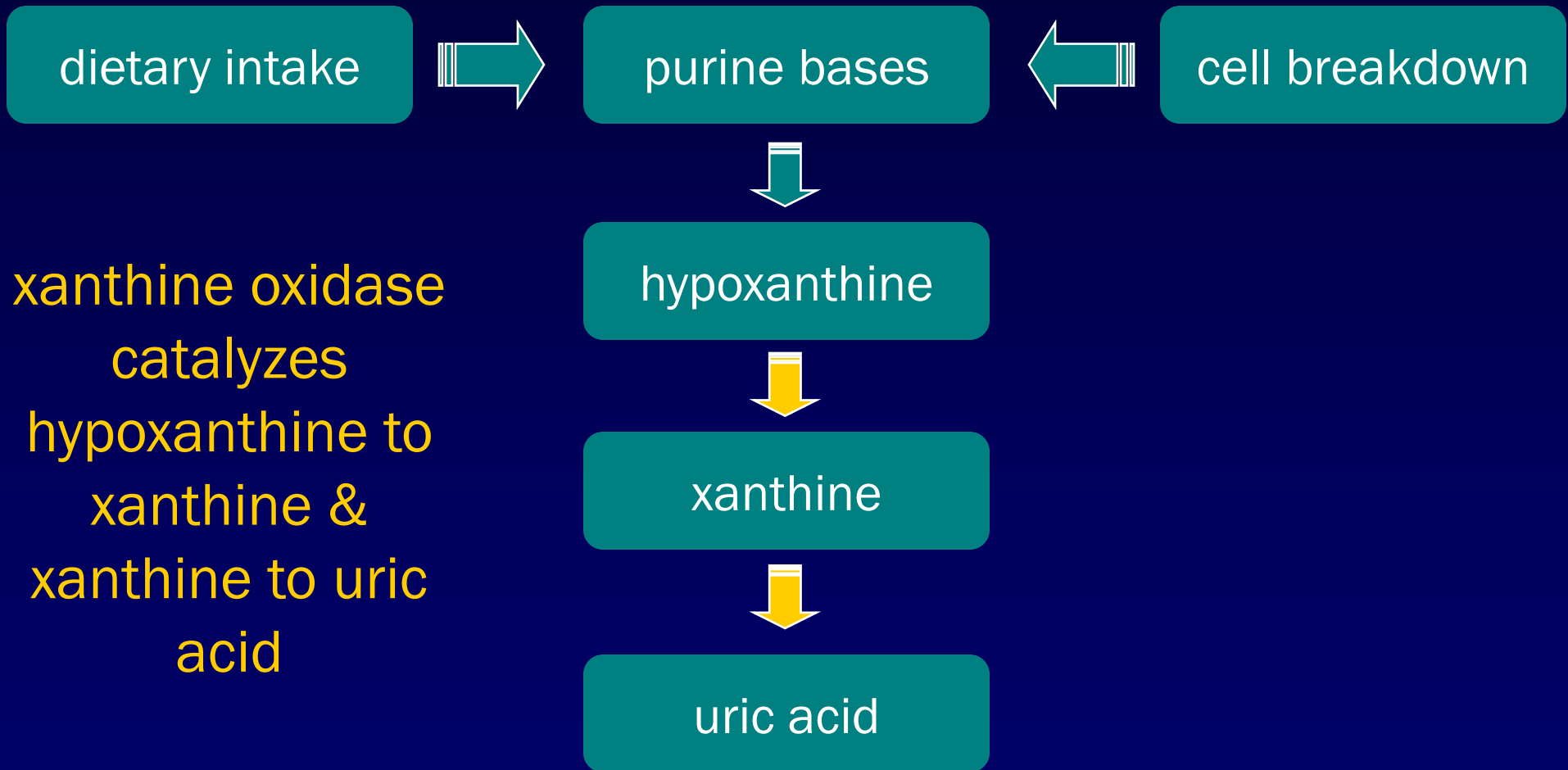
# Drug therapy of gout

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*The Role of Uric  
Acid in Gout*

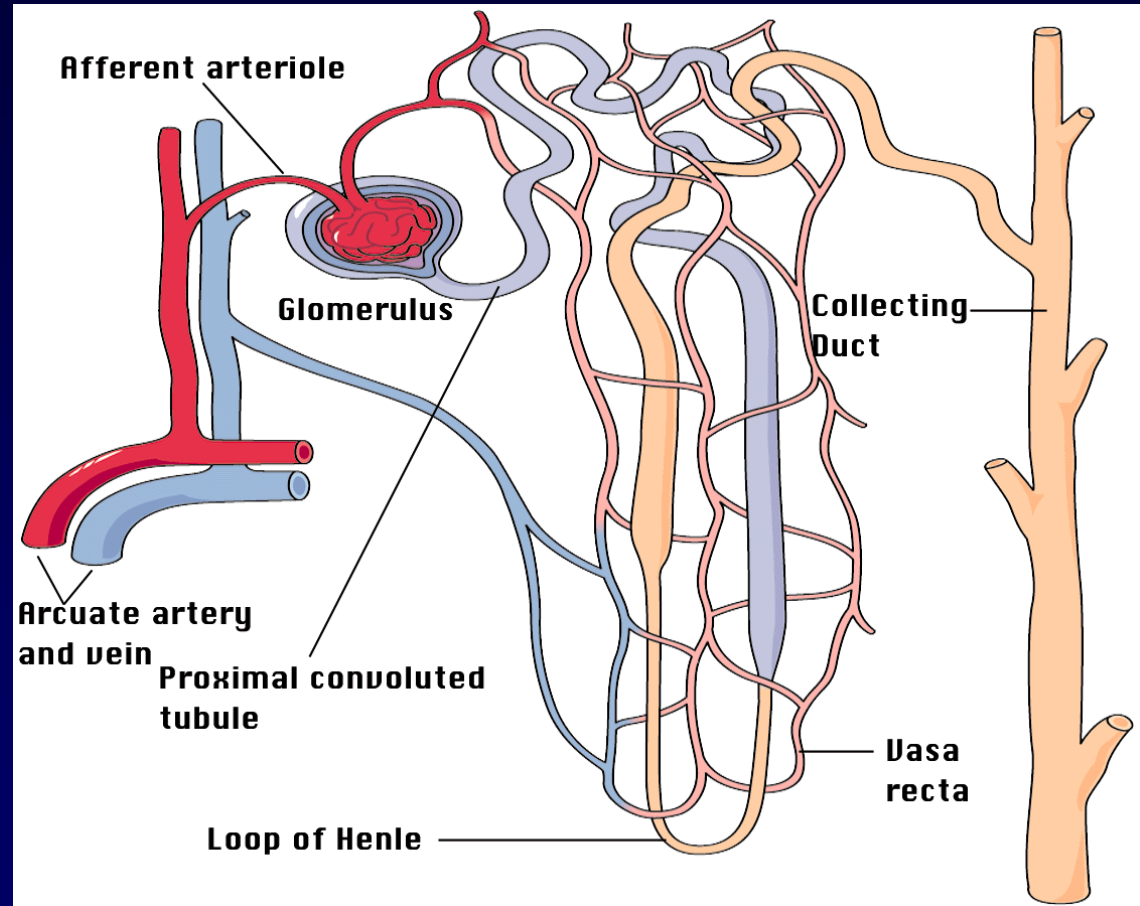


# Uric acid metabolism



# Renal handling of uric acid

- glomerular filtration
- tubular reabsorption
- tubular excretion
- post-secretory reabsorption
- net excretion



# Gout - problems

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- excessive total body levels of uric acid
- deposition of monosodium urate crystals in joints & other tissues
- crystal-induced inflammation

# Treating acute gouty arthritis

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- colchicine
- NSAID's
- steroids
- rest, analgesia, ice, time

# Drugs used to treat gout

## *Acute Arthritis Drugs*

colchicine

steroids

NSAID's

## *Urate Lowering Drugs*

allopurinol

probenecid

febuxostat?

*rest + analgesia + time*

# Drugs used to treat gout

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## NSAID's

- 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

# Colchicine - plant alkaloid

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*colchicum*  
*autumnale*

(autumn crocus or  
meadow saffron)



# Colchicine

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- “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

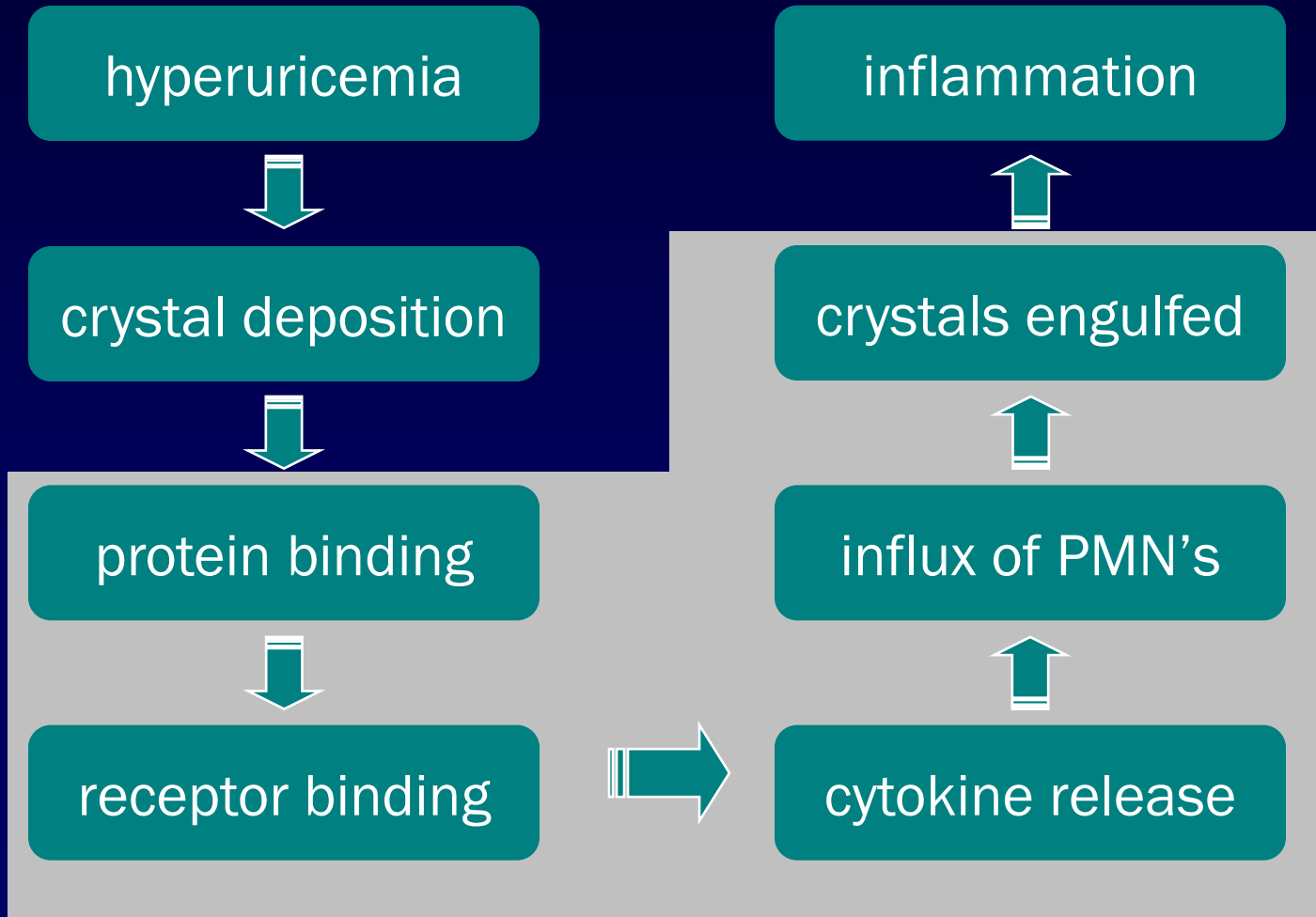


# Colchicine

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- 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

# Crystal-induced inflammation



PMN is critical component of crystal-induced inflammation

# Colchicine - indications

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*Dose*

*Indication*

high

treatment of acute gouty arthritis

low

prevention of recurrent gouty arthritis

# Colchicine - toxicity

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- 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

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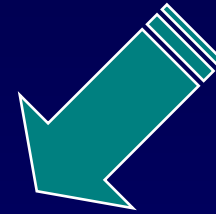
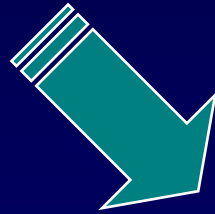
- more useful for daily prophylaxis (low dose)
  - ✓ prevents recurrent attacks
  - ✓ colchicine 0.6 mg qd - bid
- declining use in acute gout (high dose)

# Hyperuricemia - mechanisms

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excessive  
production

inadequate  
excretion



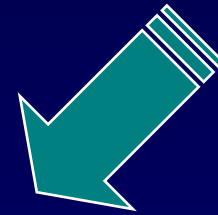
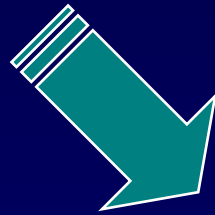
hyperuricemia

# Urate-lowering drugs

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block  
production

enhance  
excretion



net reduction in total body pool of  
uric acid

# Gout - urate-lowering therapy

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- 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

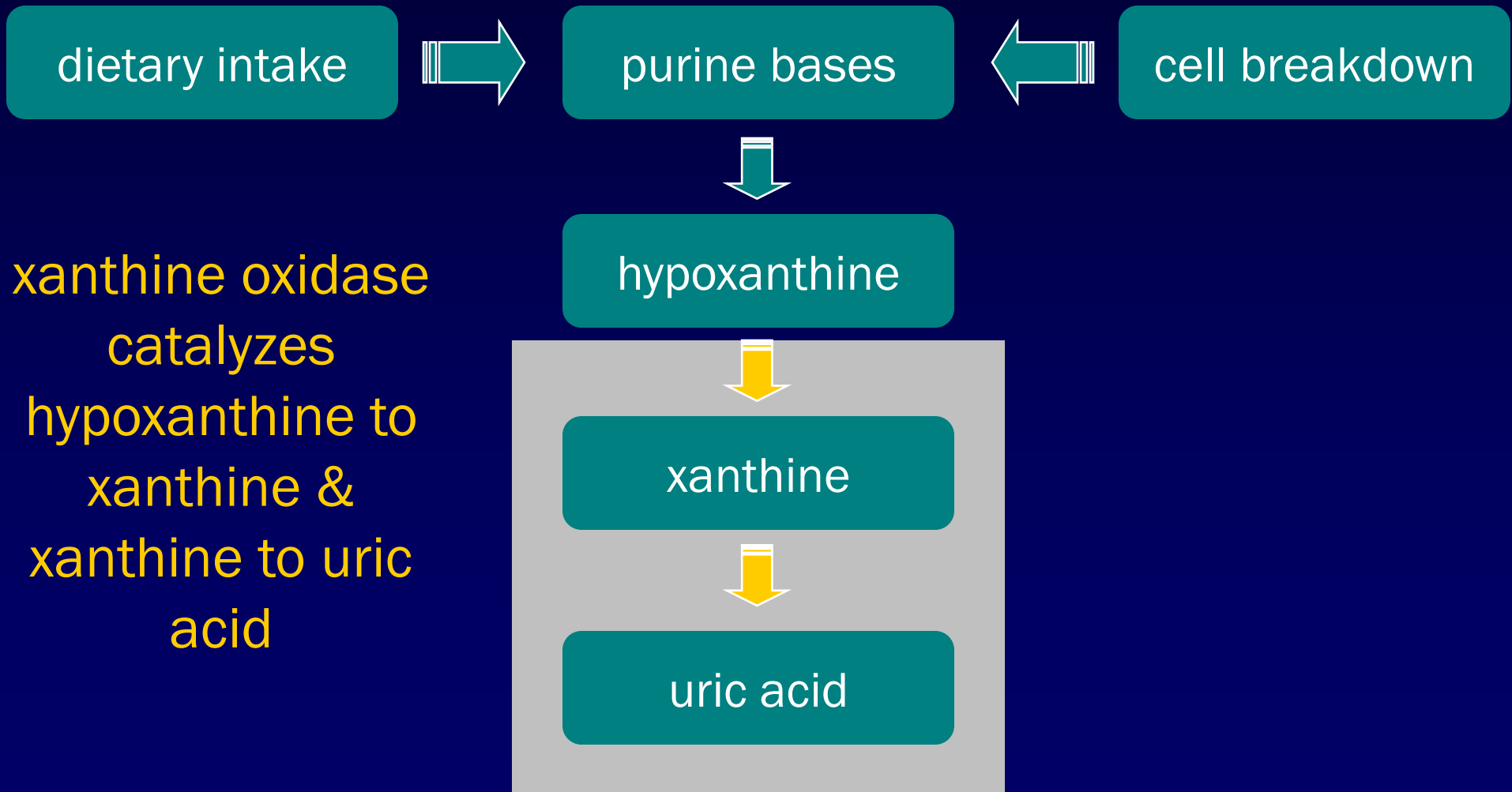


# Drug therapy of gout

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## *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

allopurinol



# Allopurinol - usage indications

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

# Allopurinol - common reactions

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

# Allopurinol - serious reactions

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

# Stevens-Johnson syndrome

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target skin lesions

mucous membrane  
erosions

epidermal necrosis with  
skin detachment



# Allopurinol hypersensitivity

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- 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)

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

# PEG-uricase

- 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

# Drug therapy of gout

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*Drugs That Enhance  
Excretion of Uric Acid*

# Uricosuric therapy

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

# Uricosuric therapy

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

# Uricosuric therapy

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

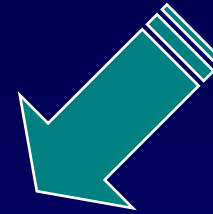
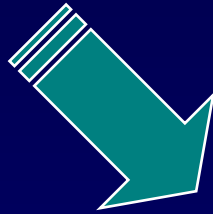
# Choosing a urate-lowering drug

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excessive  
production

inadequate  
excretion

xanthine  
oxidase  
inhibitor



uricosuric  
agent

hyperuricemia