



# Drug Therapy of Gout

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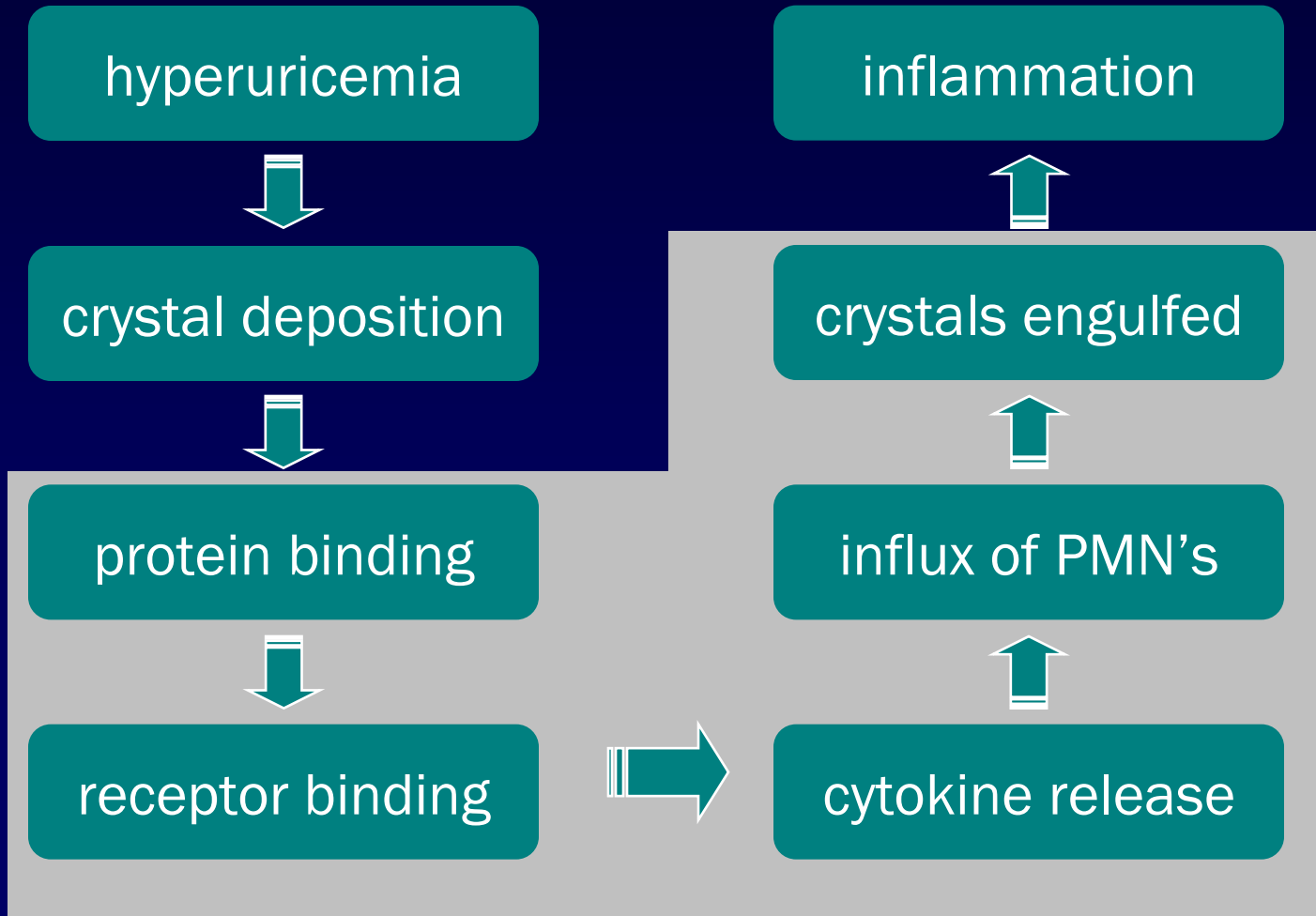
- “only effective in gouty arthritis”
- not an analgesic
- does not affect renal excretion of uric acid
- does not alter plasma solubility of uric acid
- neither raises nor lowers serum uric acid

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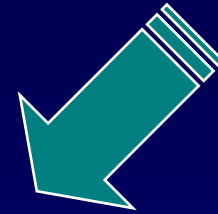
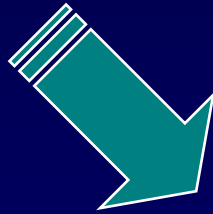
- more useful for daily prophylaxis (low dose)
  - prevents recurrent attacks
  - colchicine 0.6 mg qd - bid
- declining use in acute gout (high dose)

# Hyperuricemia - mechanisms

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excessive  
production

inadequate  
excretion



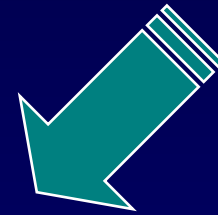
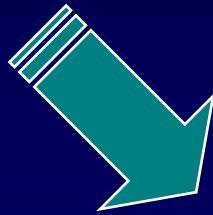
hyperuricemia

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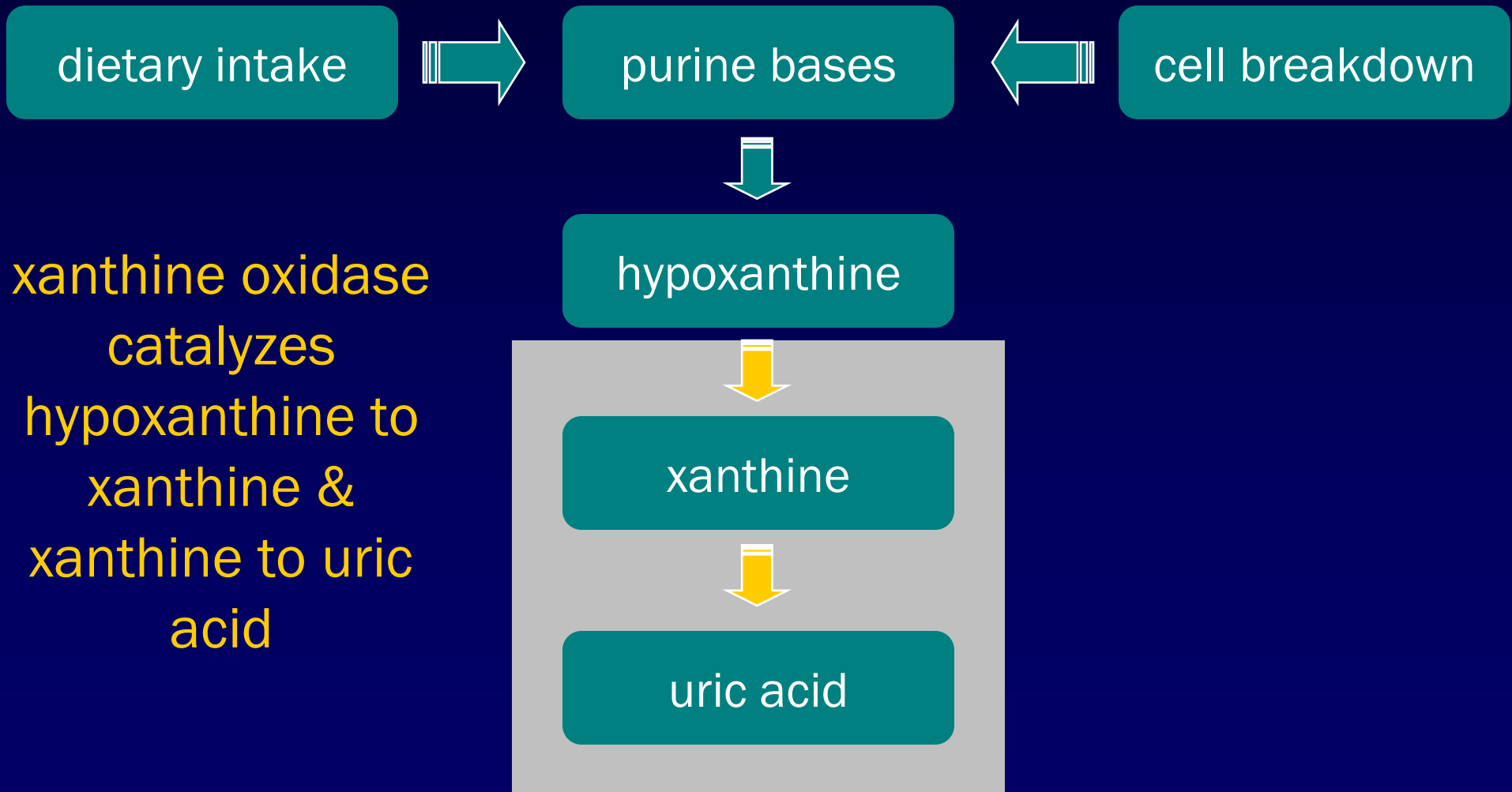
- prevents arthritis, tophi & stones by lowering total body pool of uric acid
- not indicated after first attack
- initiation of therapy can worsen or bring on acute gouty arthritis
- no role to play in managing acute gout

# 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



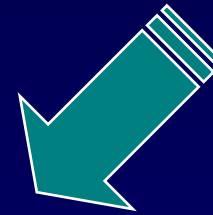
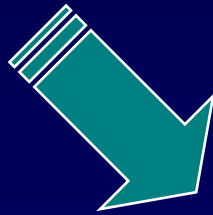
- **contra-indications**
  - history of nephrolithiasis
  - elevated urine uric acid level
  - existing renal disease
- **less effective in elderly patients**

# Choosing a urate-lowering drug

excessive  
production

inadequate  
excretion

xanthine  
oxidase  
inhibitor



uricosuric  
agent

hyperuricemia