

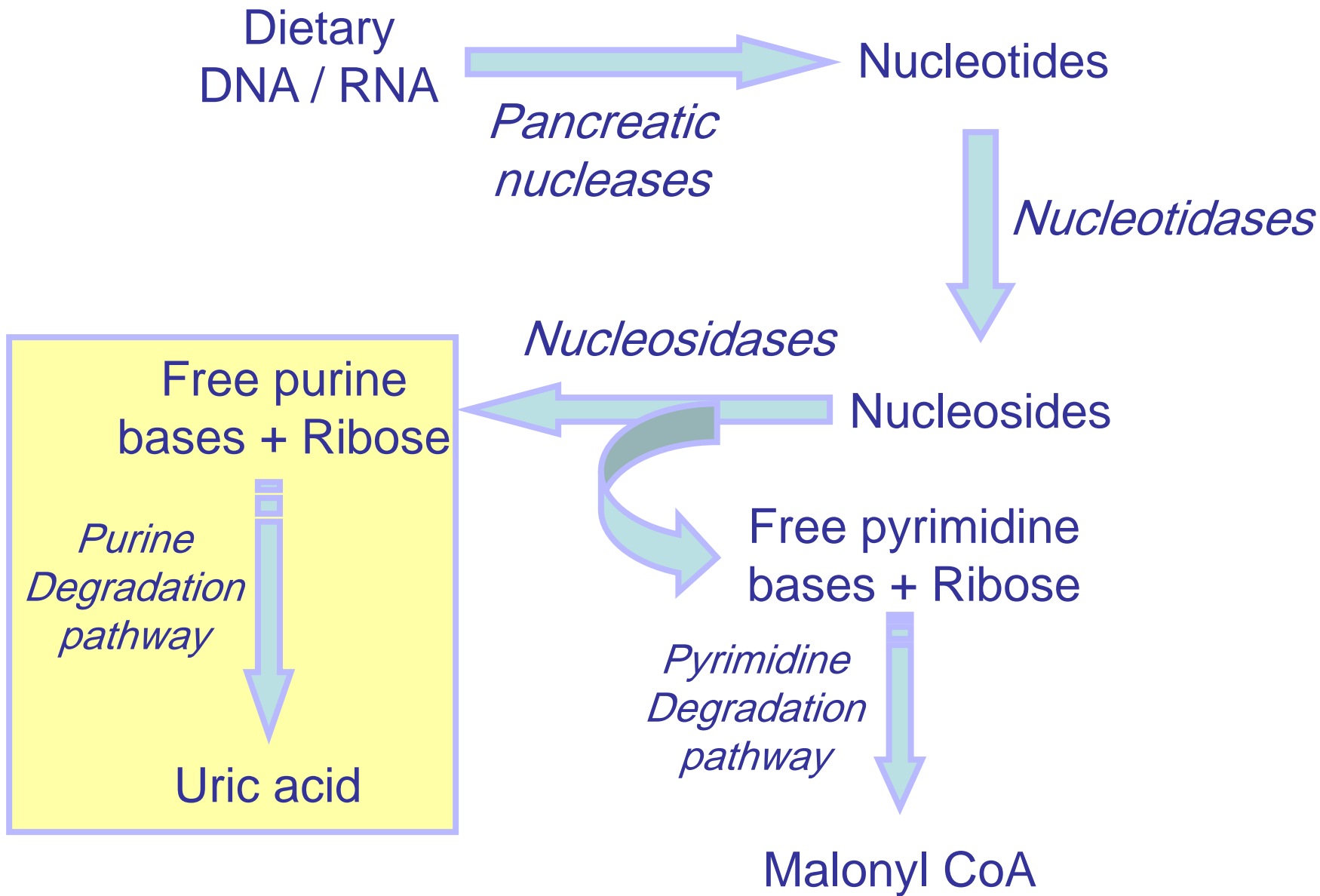
# Purine Degradation & Gout (Musculoskeletal Block)

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- Purine degradation pathway
- Fate of uric acid in humans
- Gout and hyperuricemia:
  - Biochemistry
  - Types
  - Treatment

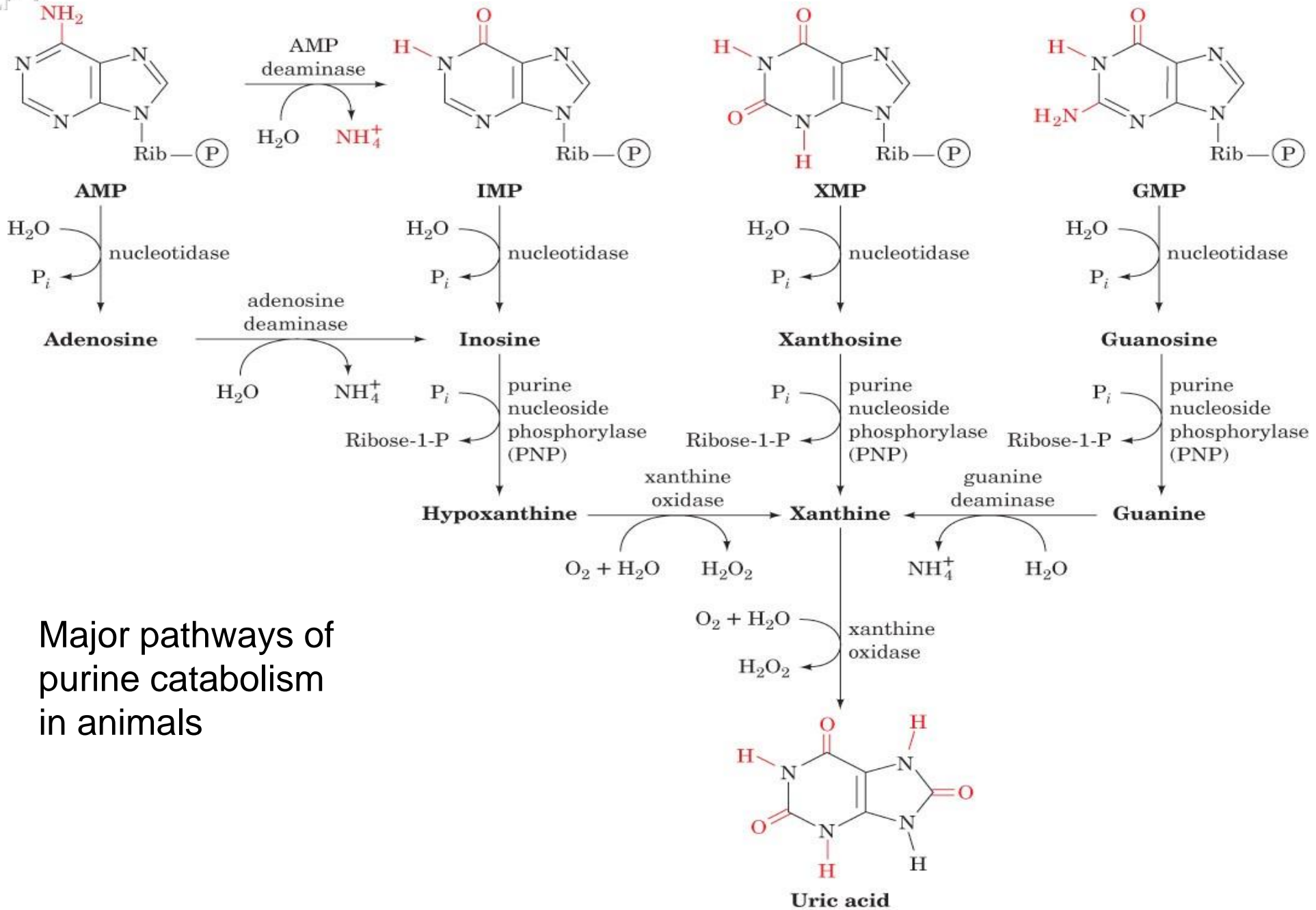
# Purine degradation pathway

- The major source of dietary nucleic acids (purines and pyrimidines) is meat
- Purine and pyrimidine bases are absorbed by the intestine
- The ingested bases are mostly degraded into different products by degradation pathways
- These products are then excreted by the body



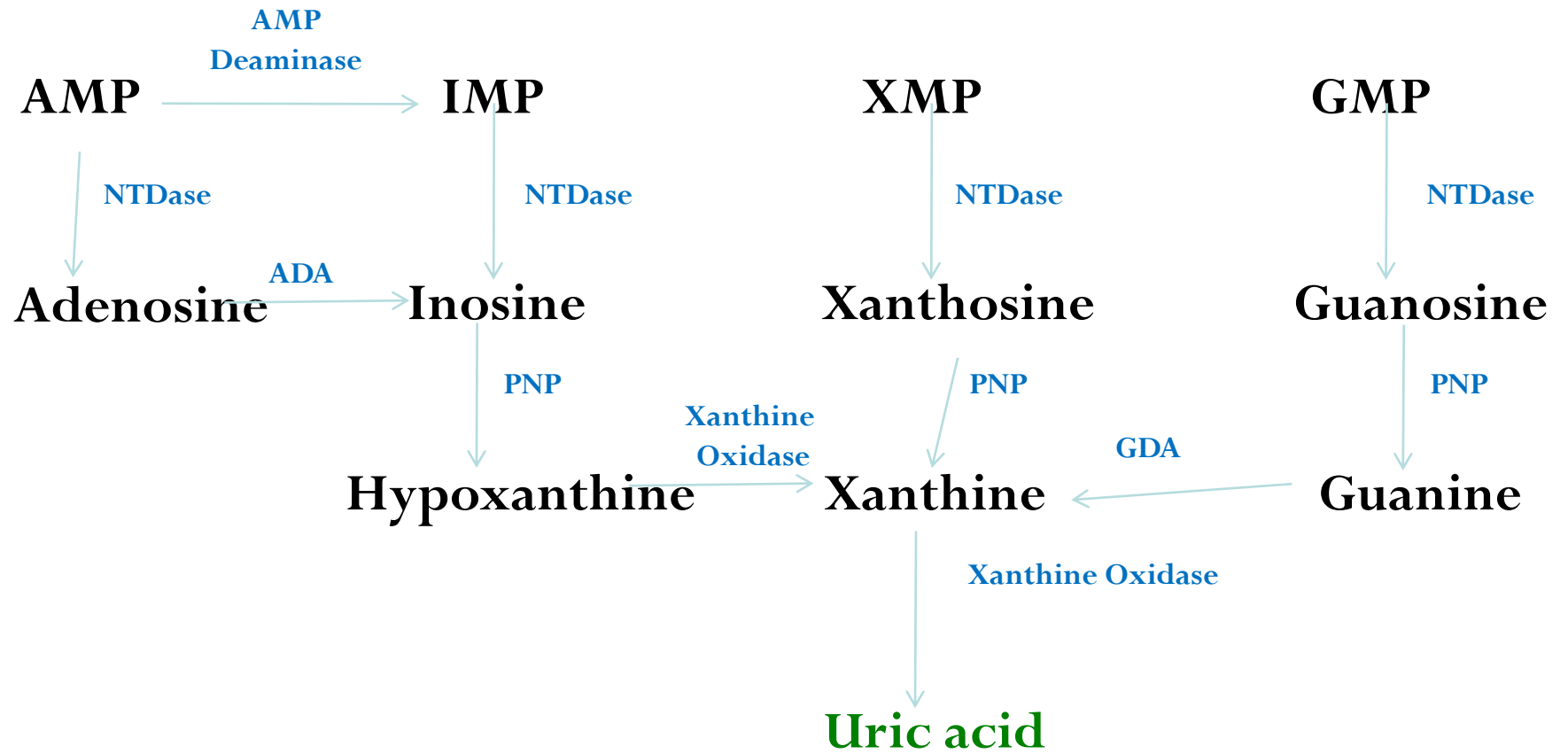
# Purine degradation pathway

- Adenosine and guanosine (purines) are finally degraded to uric acid by:
  - ◆ Purine degradation pathway



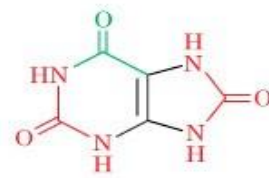
Major pathways of purine catabolism in animals

# CATABOLISM OF PURINES



# Fate of uric acid in humans

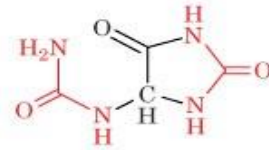
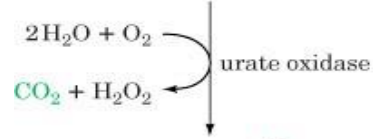
- In humans, primates, birds and reptiles the final product of purine degradation is **uric acid**
- Uric acid is excreted in the urine
- Some animals convert uric acid to other products:
  - ◆ Allantoin
  - ◆ Allantoic acid
  - ◆ Urea
  - ◆ Ammonia



Uric acid

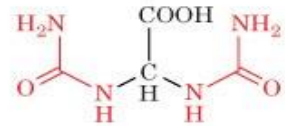
Excreted by

- Primates
- Birds
- Reptiles
- Insects



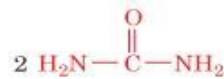
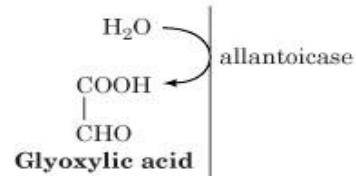
Allantoin

- Other mammals



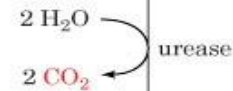
Allantoic acid

- Teleost fish



Urea

- Cartilaginous fish
- Amphibia

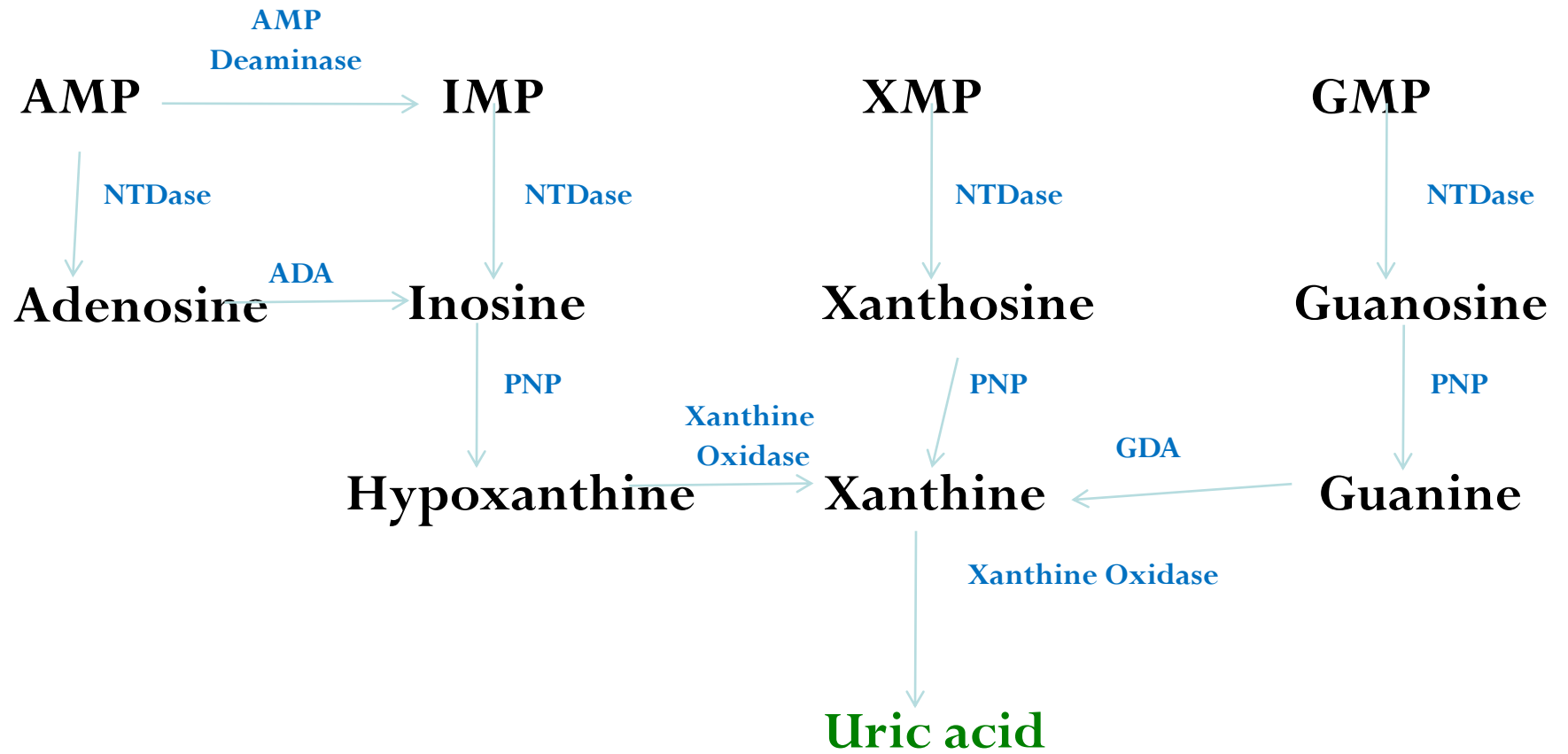


- Marine invertebrates

## Degradation of uric acid to ammonia in some animals



# CATABOLISM OF PURINES



# Fate of uric acid in humans

- Uric acid is less soluble in water
- Reptiles, insects and birds excrete uric acid as a paste of crystals
- To save water
- Humans excrete uric acid in urine

# Fate of uric acid in humans

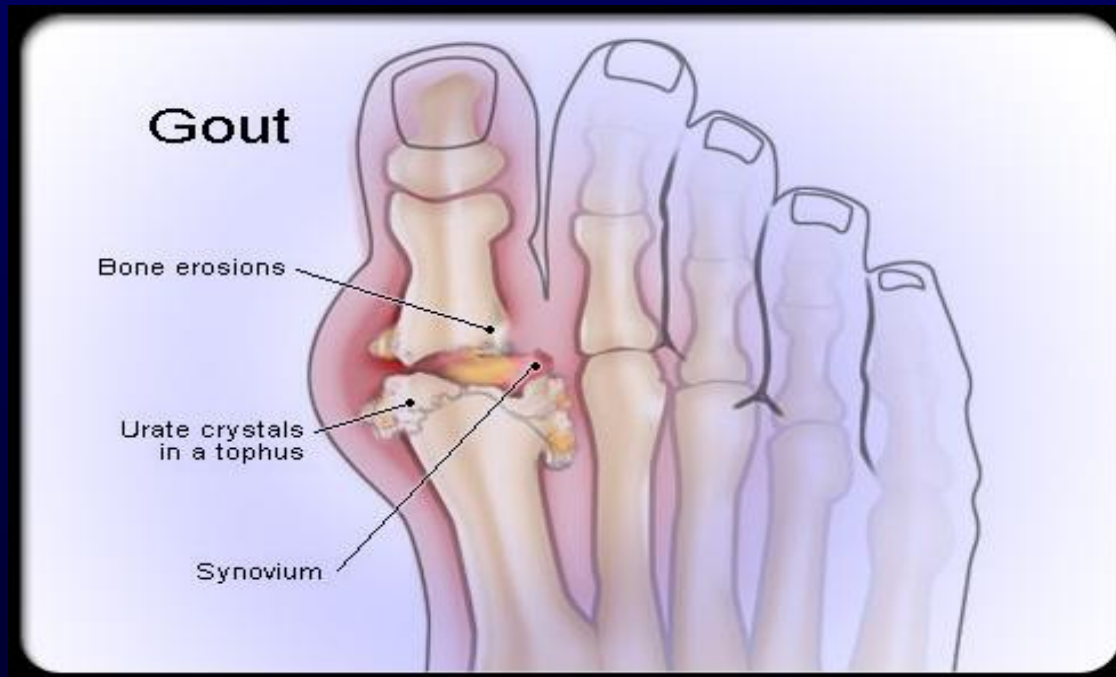
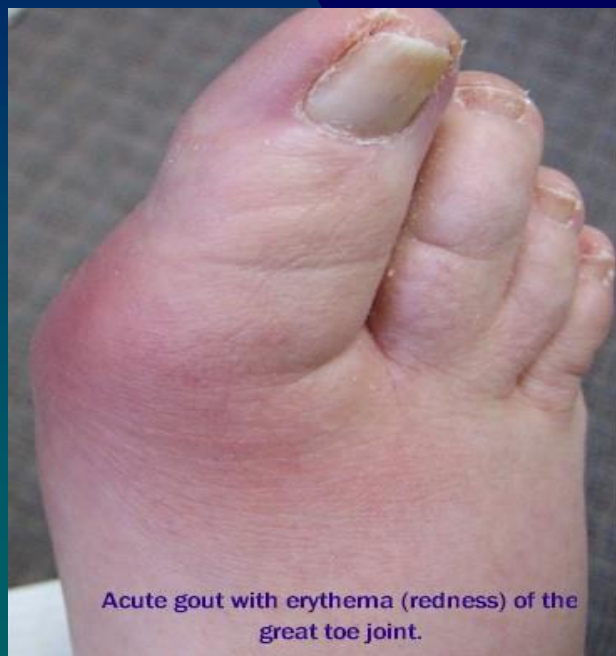
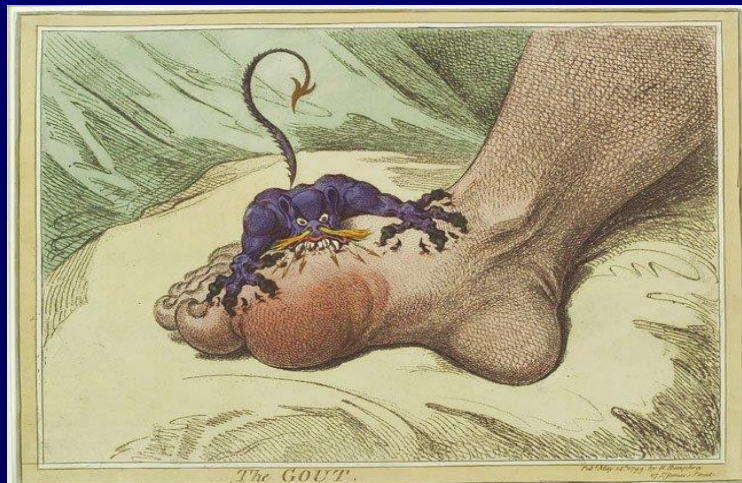
- Humans do not have enzymes to further degrade uric acid
- Excessive production of uric acid causes deposition of uric acid crystals in the joints leading to:
  - ◆ Gout
  - ◆ Hyperuricemia

# Gout

- Gout is a disease due to high levels of uric acid in body fluids
- 7.0 mg/dL and above
- Uric acid accumulates because of:
  - ◆ Overproduction or
  - ◆ Underexcretion

# Gout

- Painful arthritic joint inflammation due to deposits of insoluble sodium urate crystals (especially big toe)
- *Affects 3 per 1000 persons*
- Sodium urate crystals accumulate in kidneys, ureter, joints leading to chronic gouty arthritis





Sodium urate crystals in urine





# Gout

- Inaccurately associated with overeating and drinking
- Alcohol used to be contaminated with lead during manufacture and storage
- Lead decreases excretion of uric acid from kidneys causing hyperuricemia and gout
- Excessive meat consumption increases uric acid production in some individuals

# Gout

- Two main causes
- Overproduction of uric acid
- Underexcretion of uric acid

# Primary Gout

- Due to overproduction of uric acid
- Genetic abnormality in the enzymes of purine degradation
- Excessive production and degradation of purine bases (adenine, guanine, hypoxanthine)

# Secondary hyperuricemia

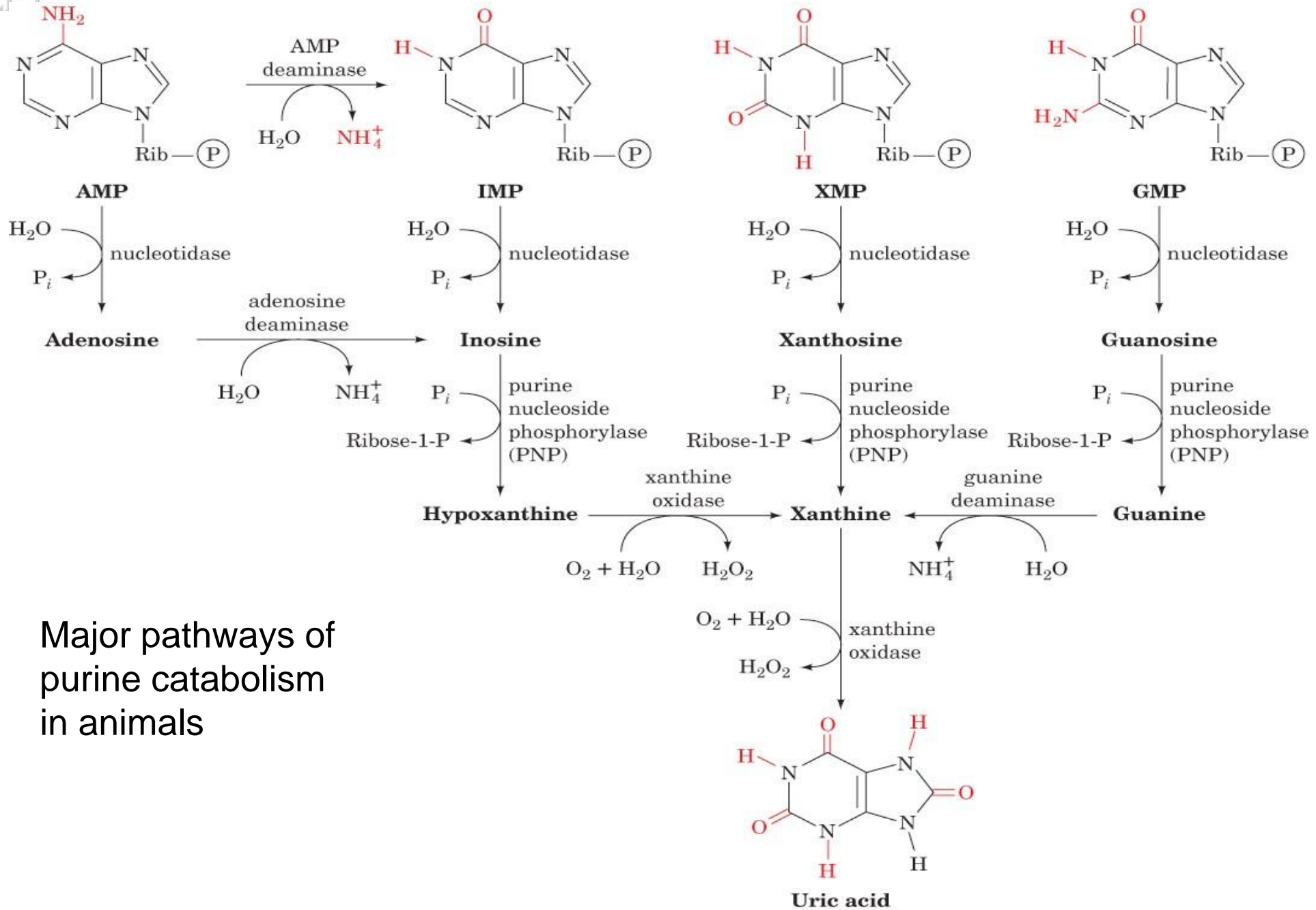
- A variety of disorders and lifestyles cause secondary hyperuricemia
- Underexcretion of uric acid due to chronic renal disease
- Chemotherapy
- Excessive consumption of purine-rich foods such as meat
- Excessive alcohol intake

# Secondary hyperuricemia

- Hyperuricemia does not always cause gout

# Treatment

- To reduce pain and inflammation (analgesics, anti-inflammatory drugs)
- To increase uric acid excretion (uricosuric agents)
- To reduce uric acid production
  - ◆ xanthine oxidase inhibitors (Allopurinol and febuxostat)



Major pathways of purine catabolism in animals

# **SUPPLEMENTARY SLIDES**



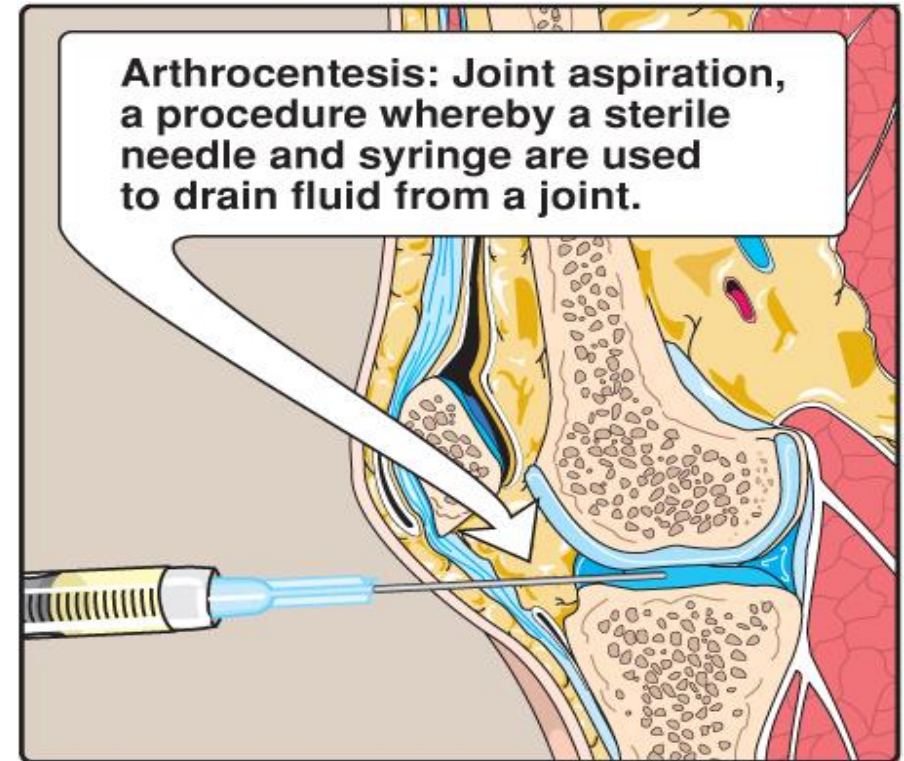
## Diagnostic features

- usually affect joints in the lower extremities (95%)
- onset is fast and sudden
- pain is usually severe; joint may be swollen, red and hot
- attack may be accompanied by fever, leukocytosis and an elevated ESR



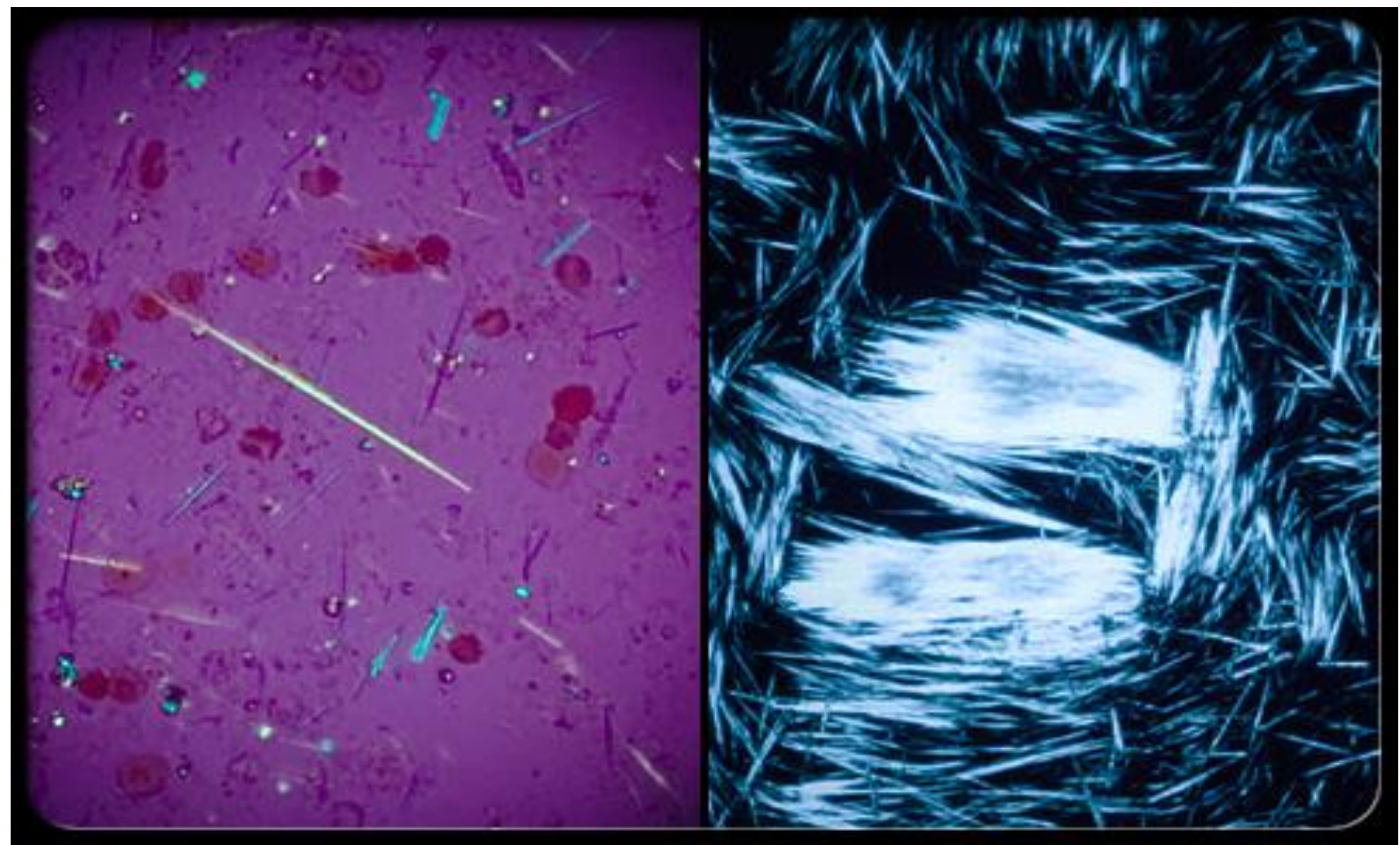
## Diagnosis

- The definitive diagnosis of gout requires aspiration and examination of synovial fluid from an affected joint (or material from a tophus) using polarized light microscopy to confirm the presence of needle-shaped monosodium urate crystals





# Monosodium urate crystals



# CLASSIFICATION OF THE CAUSES OF HYPERURICEMIA AND GOUT

## **Hyperuricemia**

may be caused by:

Dietary excess

Overproduction of urate

Undersecretion of urate

## **Gout**

may be:

### **Primary**

Most are undersecretors, a few are overproducers

### **Secondary**

Undersecretion:

eg. renal failure,  
diuretic therapy

Overproduction:

eg. myeloproliferative  
diseases

## Treatment of gout- **Acute attacks**

- Acute attacks of gout are treated with anti-inflammatory agents. **Colchicine**, steroidal drugs such as **prednisone**, and nonsteroidal drugs such as **indomethacin** are used
- Colchicine depolymerizes microtubules and inhibits the movement of neutrophils into the affected area.





## Treatment - Long term

- Involves lowering the uric acid level below the saturation point, thereby preventing the deposition of urate crystals
  - **Uricosuric agents**- probenecid or sulfinpyrazone, that increase renal excretion of uric acid
  - **Allopurinol**, an inhibitor of uric acid synthesis
- Allopurinol is converted in the body to oxypurinol, which inhibits xanthine oxidase, resulting in an accumulation of hypoxanthine and xanthine—compounds more soluble than uric acid and, therefore, less likely to initiate an inflammatory response

- Lippincott 4<sup>th</sup> Edition
- Voet & Voet

References

