

Purine Degradation & Gout (Musculoskeletal Block)

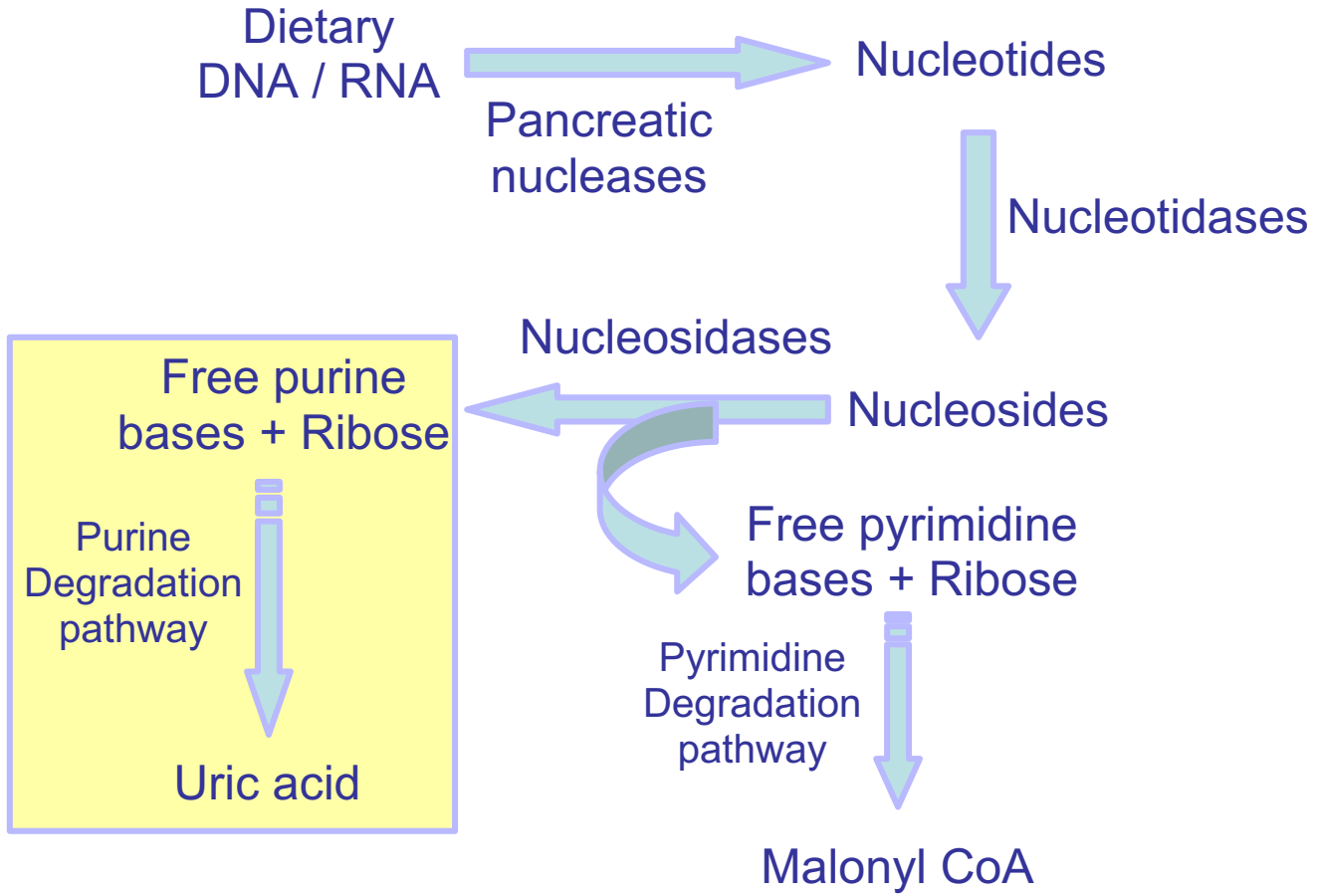
Objectives

By the end of this lecture, students should be familiar with:

- ❑ Purine degradation, uric acid formation and its association with gout.
- ❑ Fate of uric acid in humans.
- ❑ Recognize the importance of uric acid in the pathogenesis of gout.
- ❑ Overview of Gout classification and treatment.

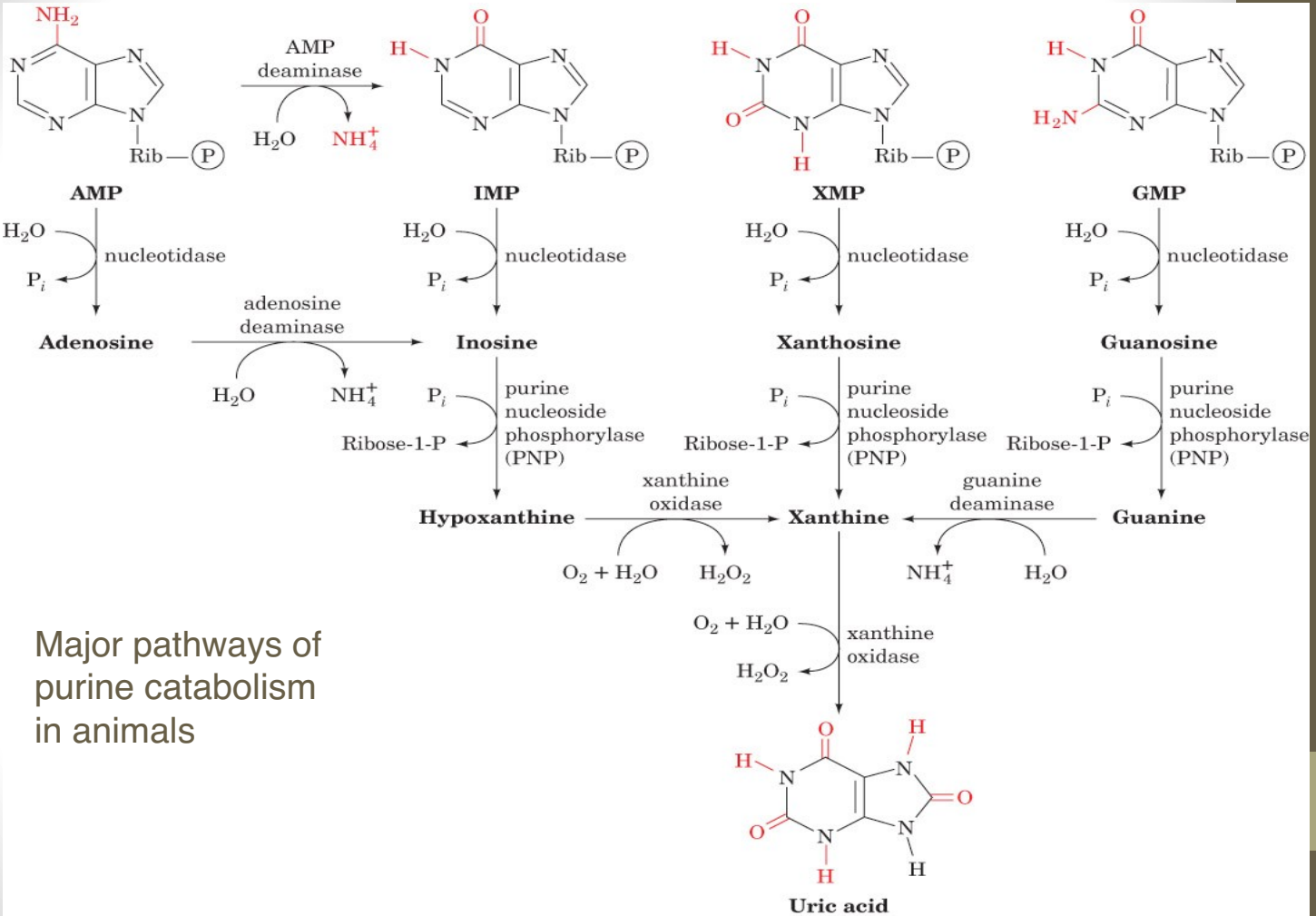
Purine degradation pathway

- 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

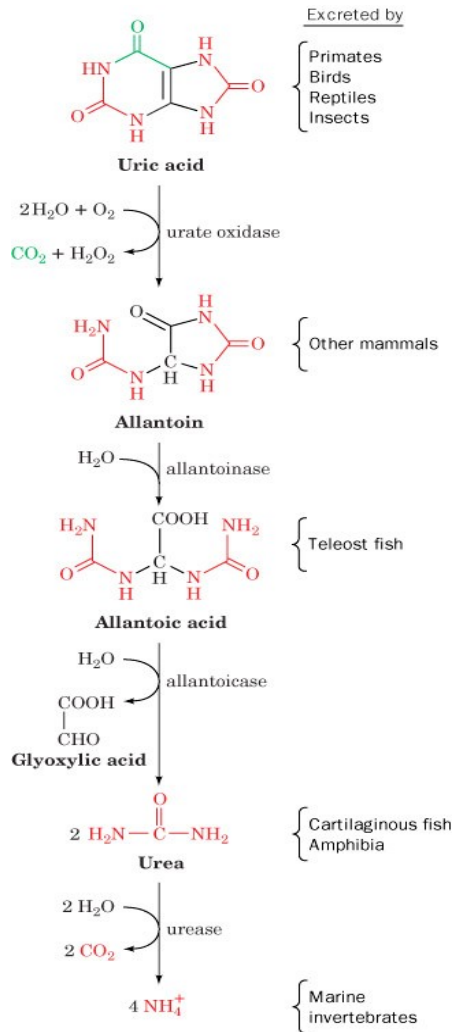


Major pathways of purine catabolism in animals

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

Degradation of uric acid to ammonia in some animals



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



Yale University Medical Historical Library

The Goat, a cartoon by James
Gilroy (1799)

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

Classification of Gout

Clinical Category	Metabolic defect
Primary Gout (90% of cases)	
Enzyme defects-Unknown (85% to 90% of cases)	<ul style="list-style-type: none"> □ Overproduction of uric acid <ul style="list-style-type: none"> -Normal excretion (Majority) -Increased excretion (Minority) □ Underexcretion of uric acid with normal production
Known enzyme defects – e.g., Partial HGPRT deficiency (rare)	Overproduction of uric acid
Secondary Gout (10% of cases)	
Associated with increase nucleic acid turnover – e.g. Leukaemia	Overproduction of uric acid with increase urinary excretion
Chronic renal disease	Reduced excretion of uric acid with normal production
Inborn errors of metabolism – e.g complete HGPRT deficiency (Lesch-nyhan syndrome)	Overproduction of uric acid with increased urinary excretion

Hypoxanthine-guanine phosphoribosyltransferase (HGPRT)

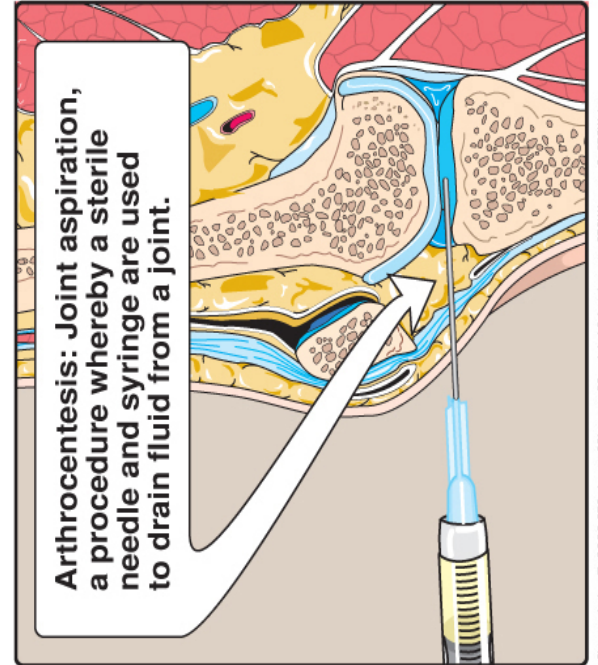
Biochemical Diagnosis

❑ Joint fluid test

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.

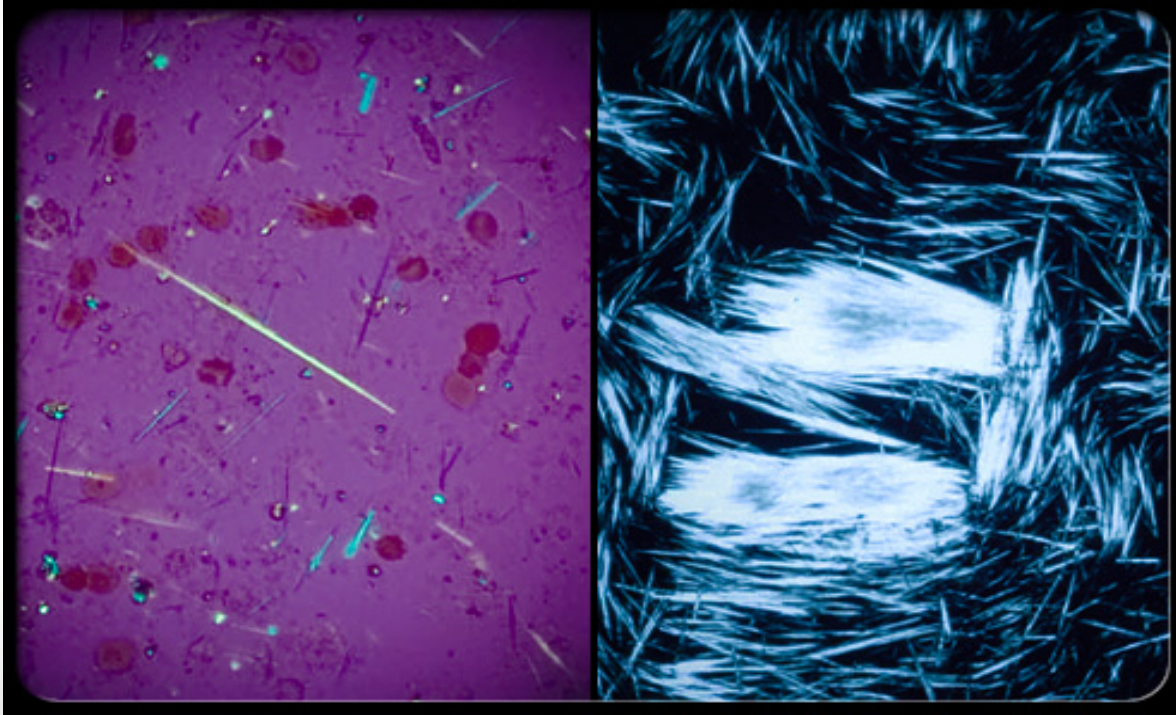
❑ Blood test

It uses to measure the levels of uric acid



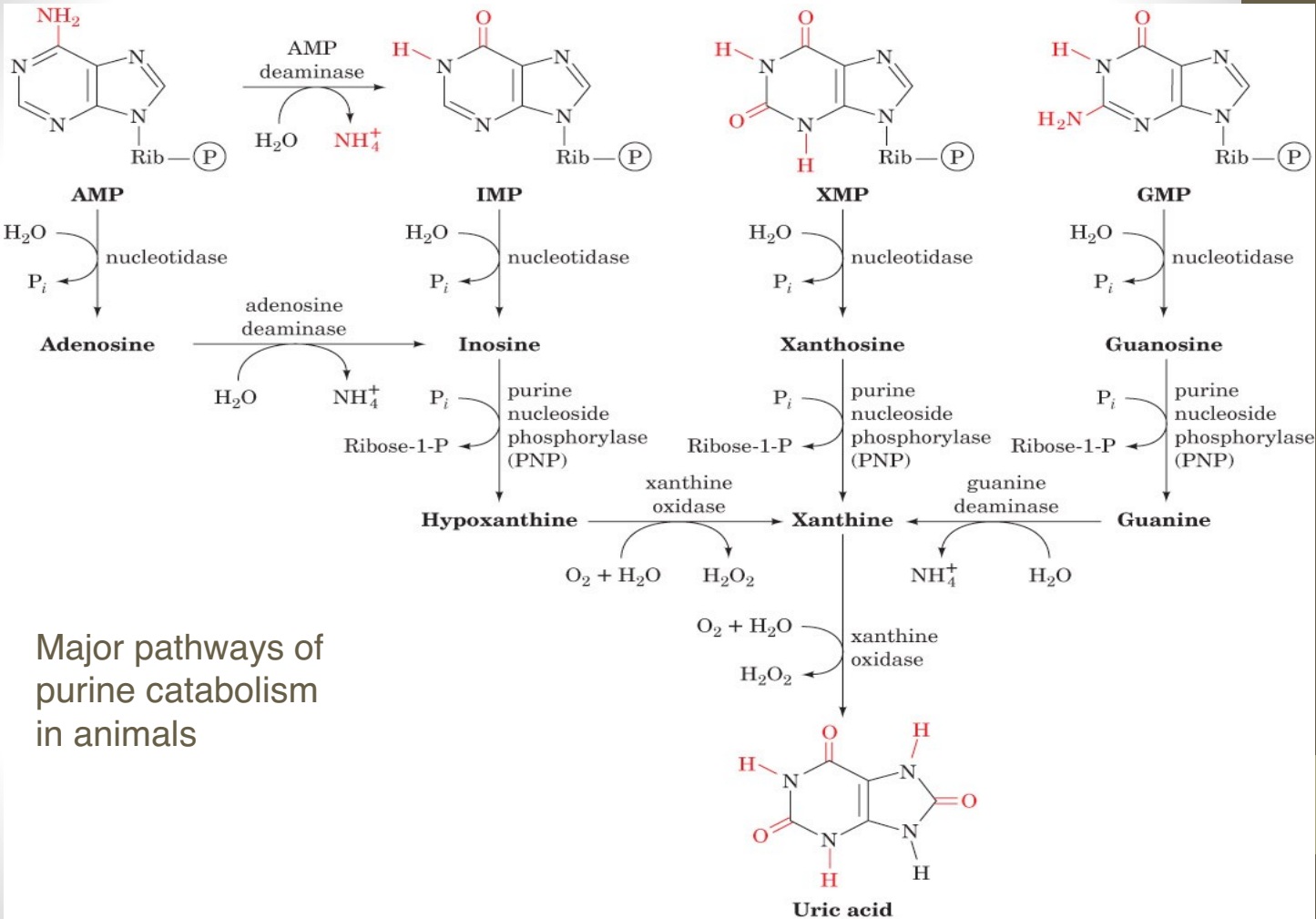


Monosodium urate crystals



Treatment

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



Major pathways of purine catabolism in animals

Take home message

- ❑ The biochemical causes that contribute to the development of gout and hyperuricemia are defects in purine degradation pathway and impaired excretion of uric acid.
- ❑ Hyperuricemia does not always cause gout.