Purine Degradation & Gout (Musculoskeletal Block)

1 Lecture

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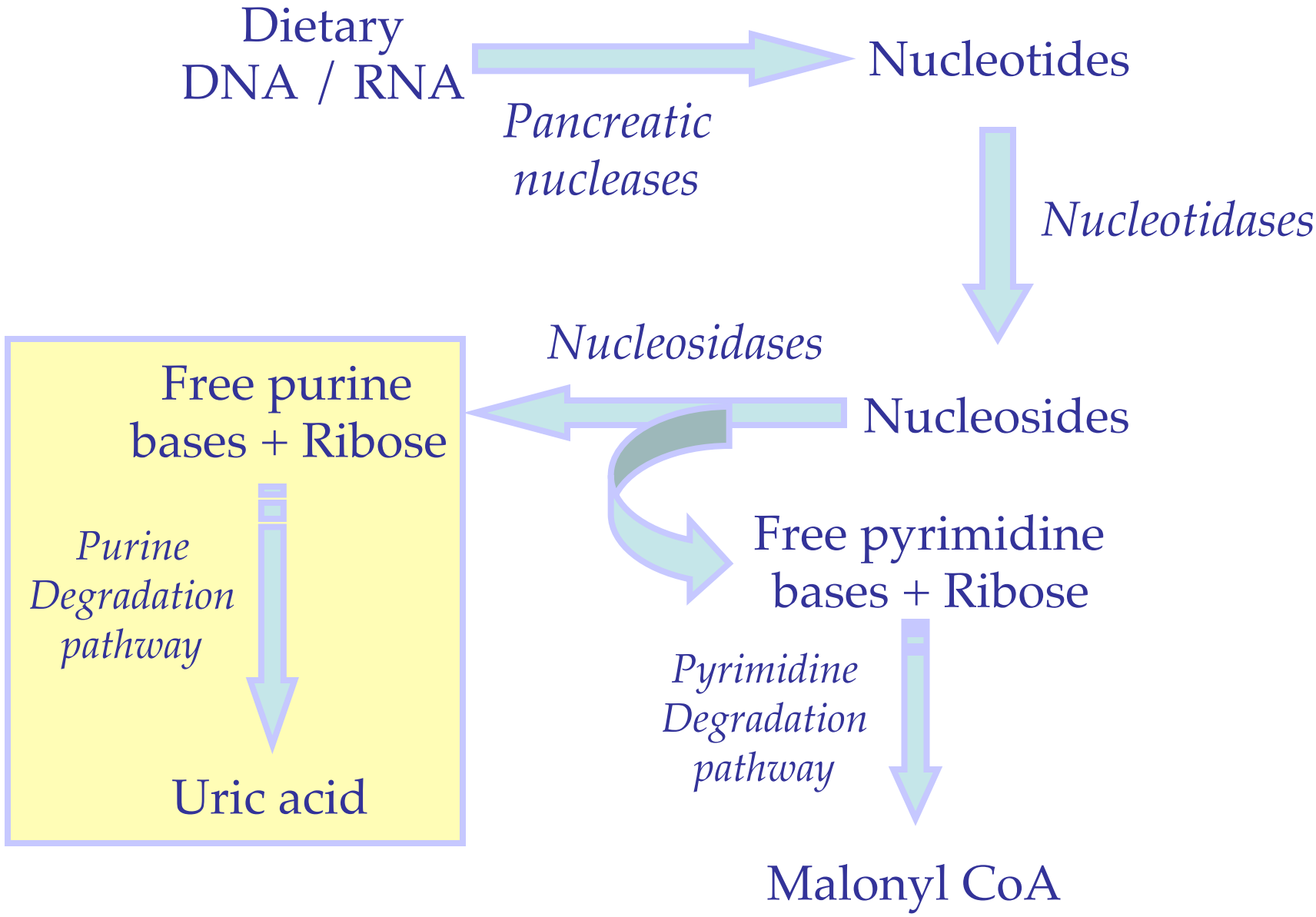
- **Purine degradation pathway**
- **Fate of uric acid in humans**
- **Gout and hyperuricemia:**
  - **Biochemistry**
  - **Types**
  - **Treatment**

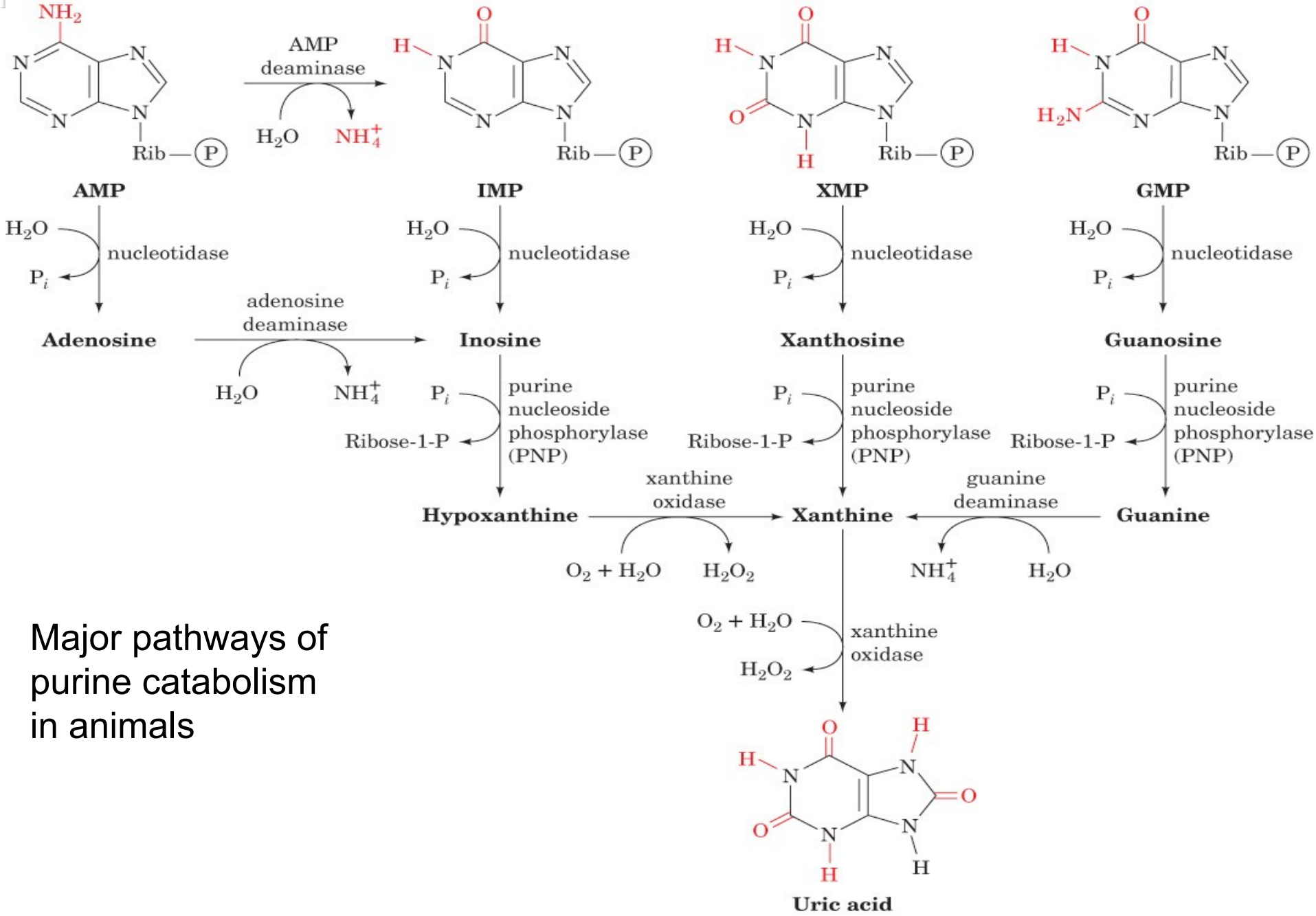
Purine degradation pathway

- 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


Dietary
DNA / RNA
Pancreatic
nucleases
Nucleotides
Nucleotidases
Nucleosidases
Nucleosides
Free purine
bases + Ribose
Purine
Degradation
pathway
Uric acid
Free pyrimidine
bases + Ribose
Pyrimidine
Degradation
pathway
Malonyl CoA

Purine degradation pathway

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

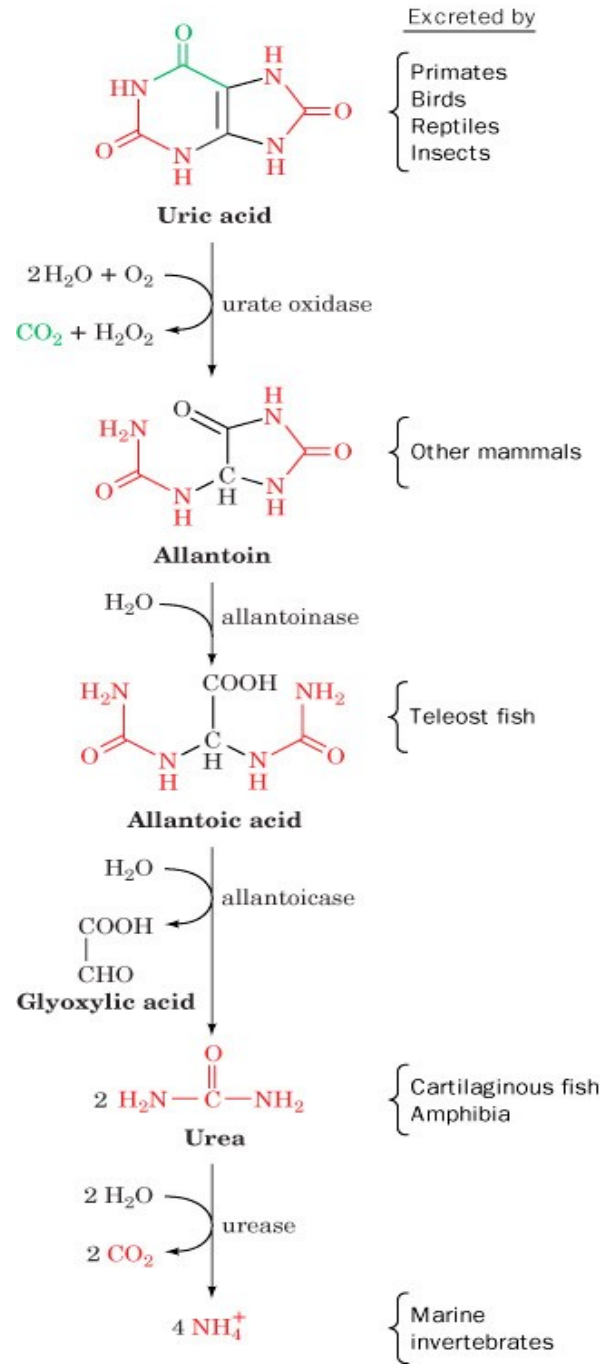


Major pathways of purine catabolism in animals

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

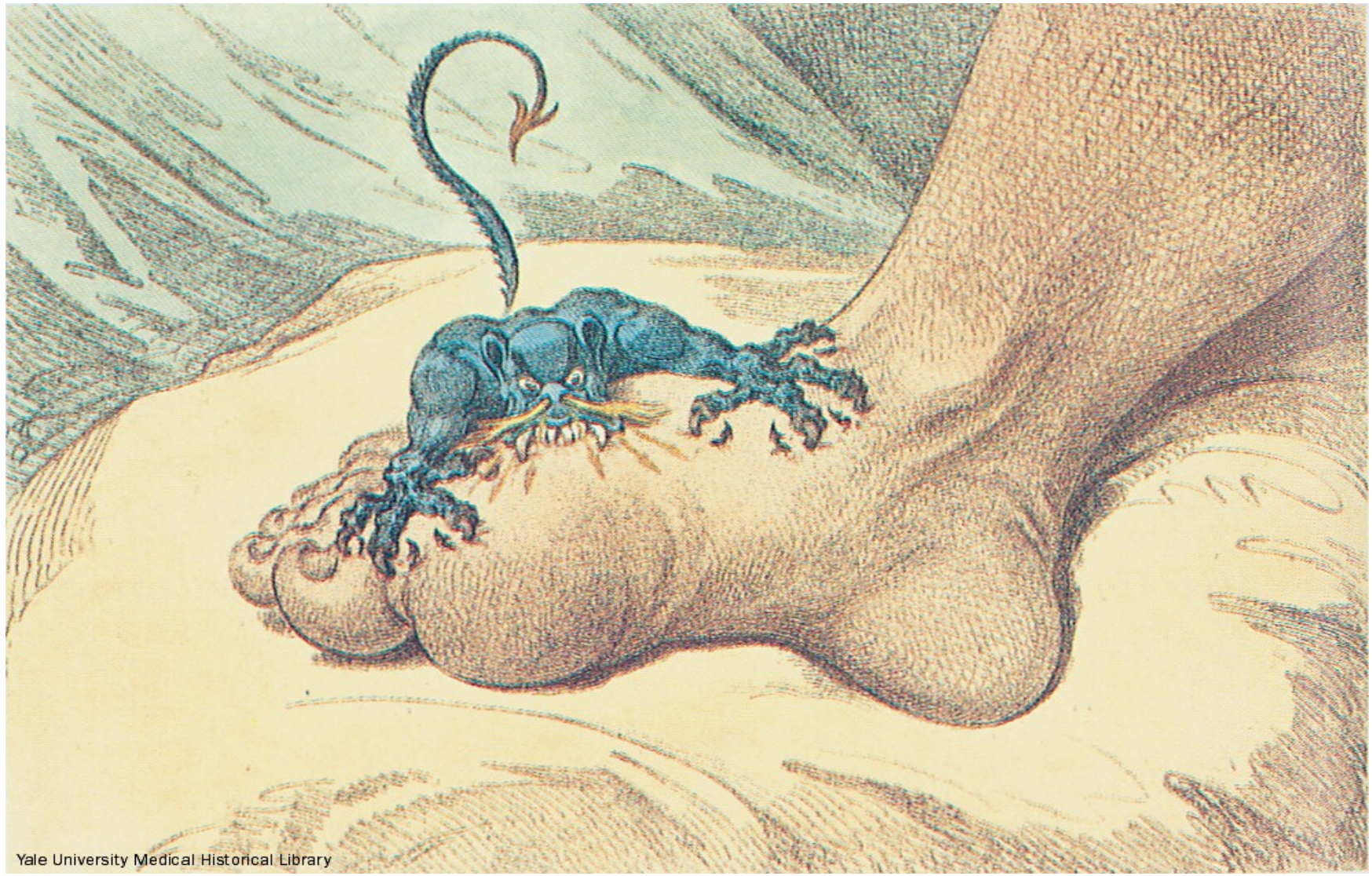


Fate of uric acid in humans

- 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



The Gout, a cartoon by James Gilroy (1799)

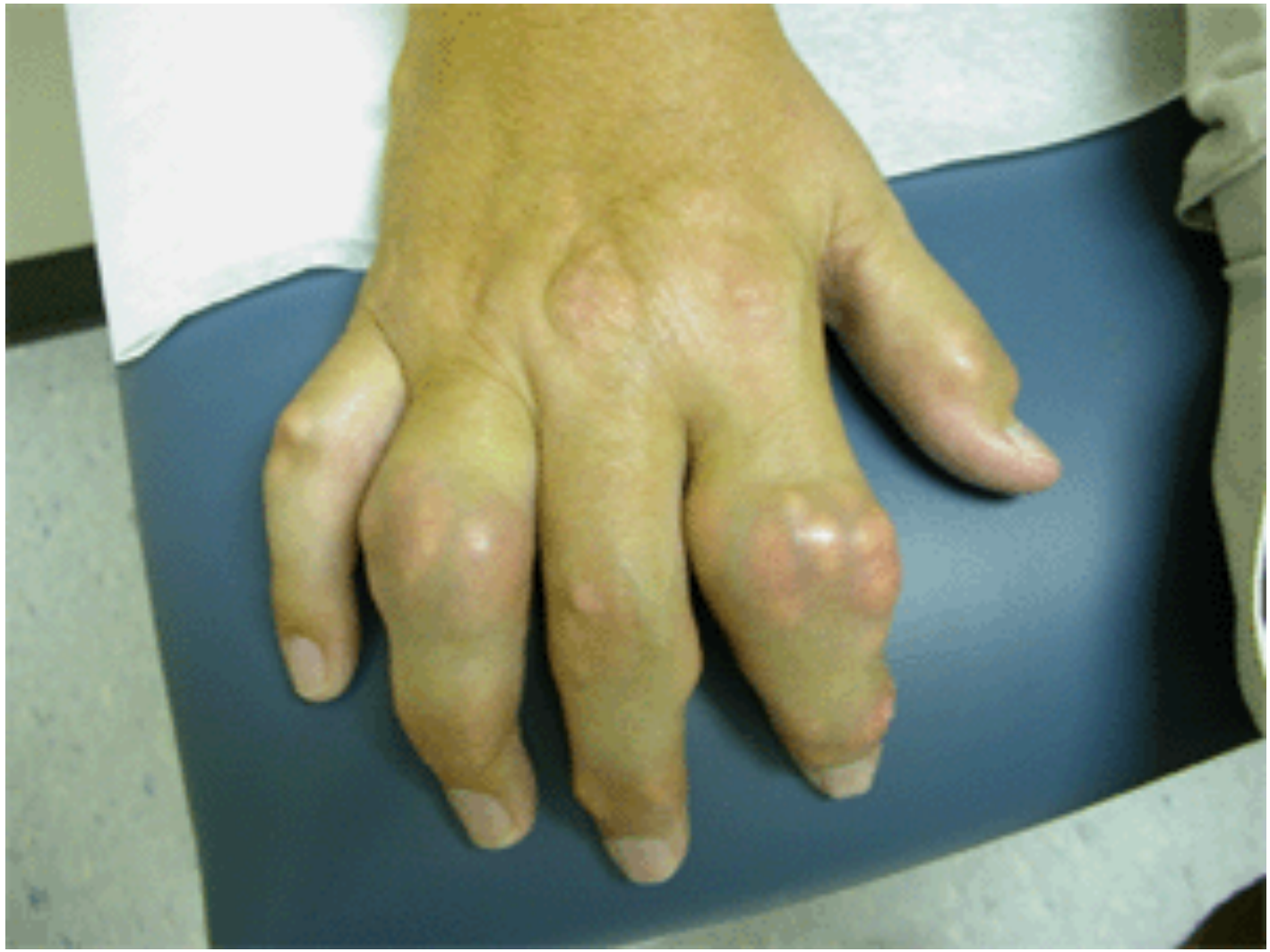
Gout

- 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 comsumption 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

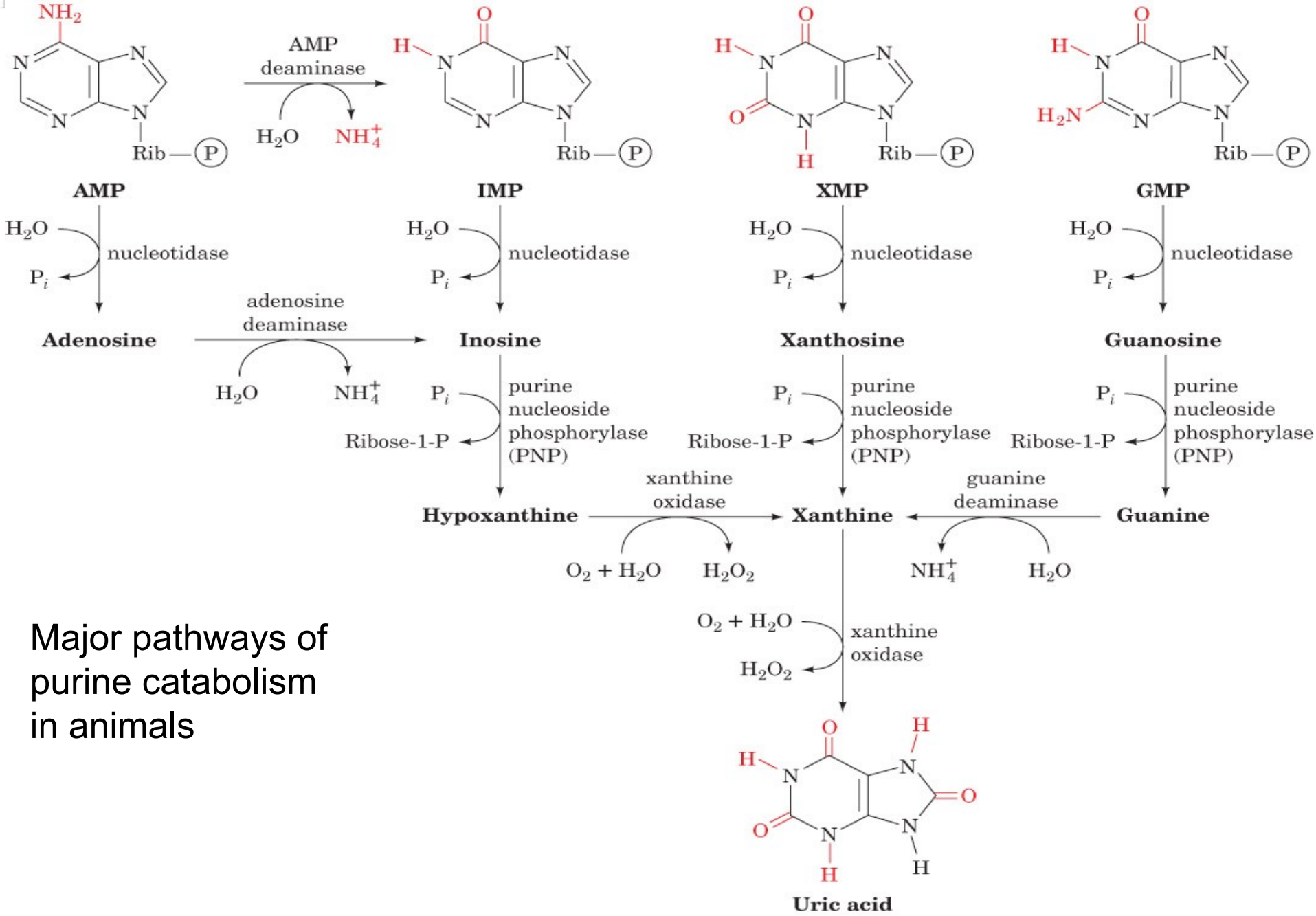
- A variety of disorders and lifestyles cause secondary hyperuricemia
- Underexcretion of uric acid due to chronic renal disease
- Chemotherapy
- Excessive consumption of purine-rich foods such as meat
- Excessive alcohol intake

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
  - Allopurinol (xanthine oxidase inhibitor)



Major pathways of purine catabolism in animals