Biochemistry Team

MEDICAL STUDENTS 432

Purine Degradation & Gout

objective:

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

أحمر = مهم

أسود = مثل ماهو موجود بالسلايدات

أزرق = مذكور عند الأولاد فقط

برتقالي = توضيح

بنفسجي = شرح اضافي مو مطلوب بالمقرر

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 (mononucleotides)

Nucleotides → (Nucleosidases) → Nucleosides

Nuclease is an enzyme capable of cleaving the phosphodiester bonds between the nucleotide subunit of nucleic acids. Also named polynucleotidase or nucleodepolymerase

Nucleosides → (Nucleotidases) → Free purine bases + Ribose

Free purine bases + Ribose → *Purine Degradation pathway* → Uric acid

Nucleosides → Free pyrimidine bases + Ribose → Pyrimidine Degradation pathway → Malonyl CoA

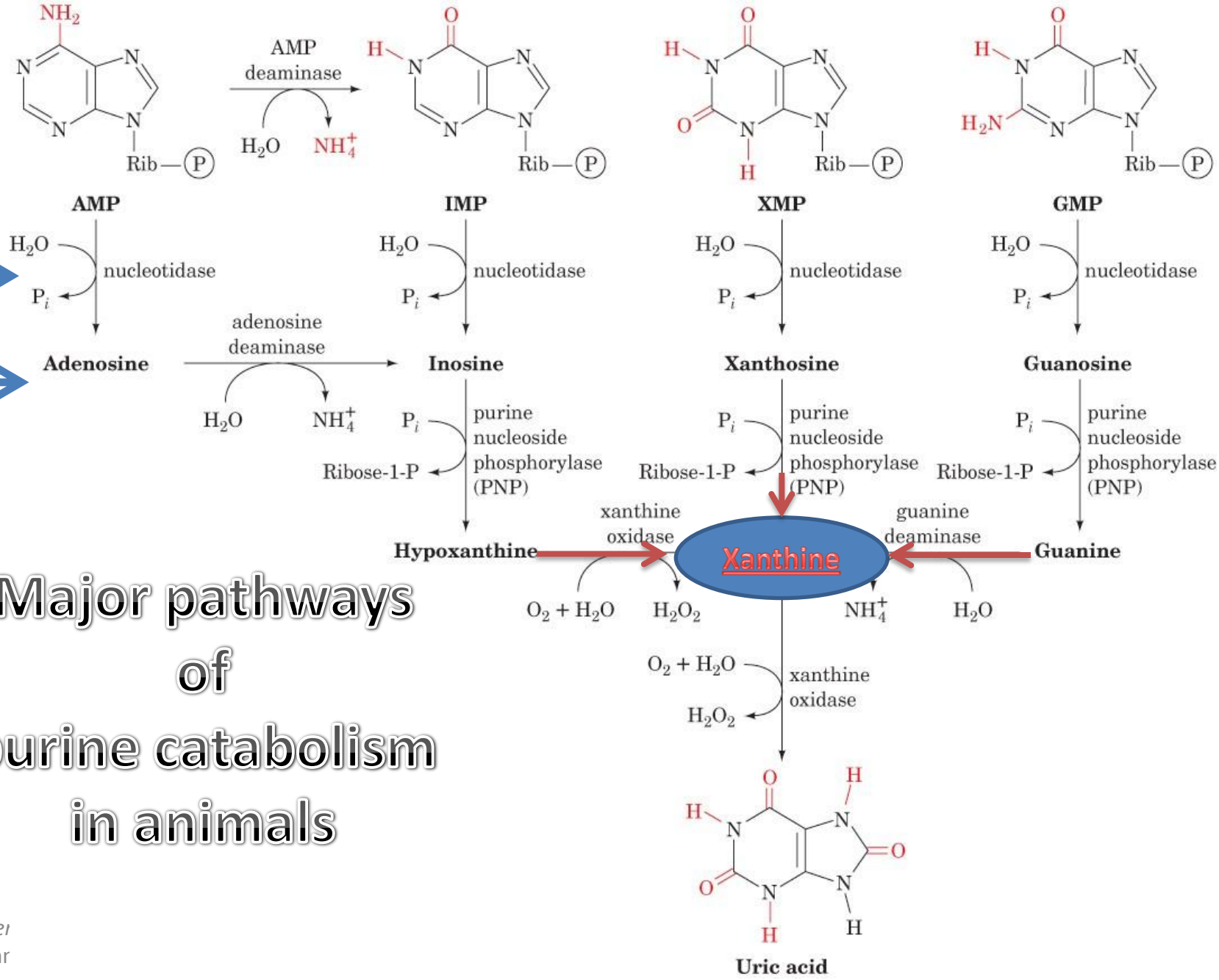
1- Broken down by obligonucleotides and further more to mononucleotides
2- nucleotides : " sugar + base + phosphate "
3- nucleosides : " sugar + base "

Purine degradation pathway

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

Nucleotides

Nucleosides



Major pathways of purine catabolism in animals

Fate of uric acid in humans

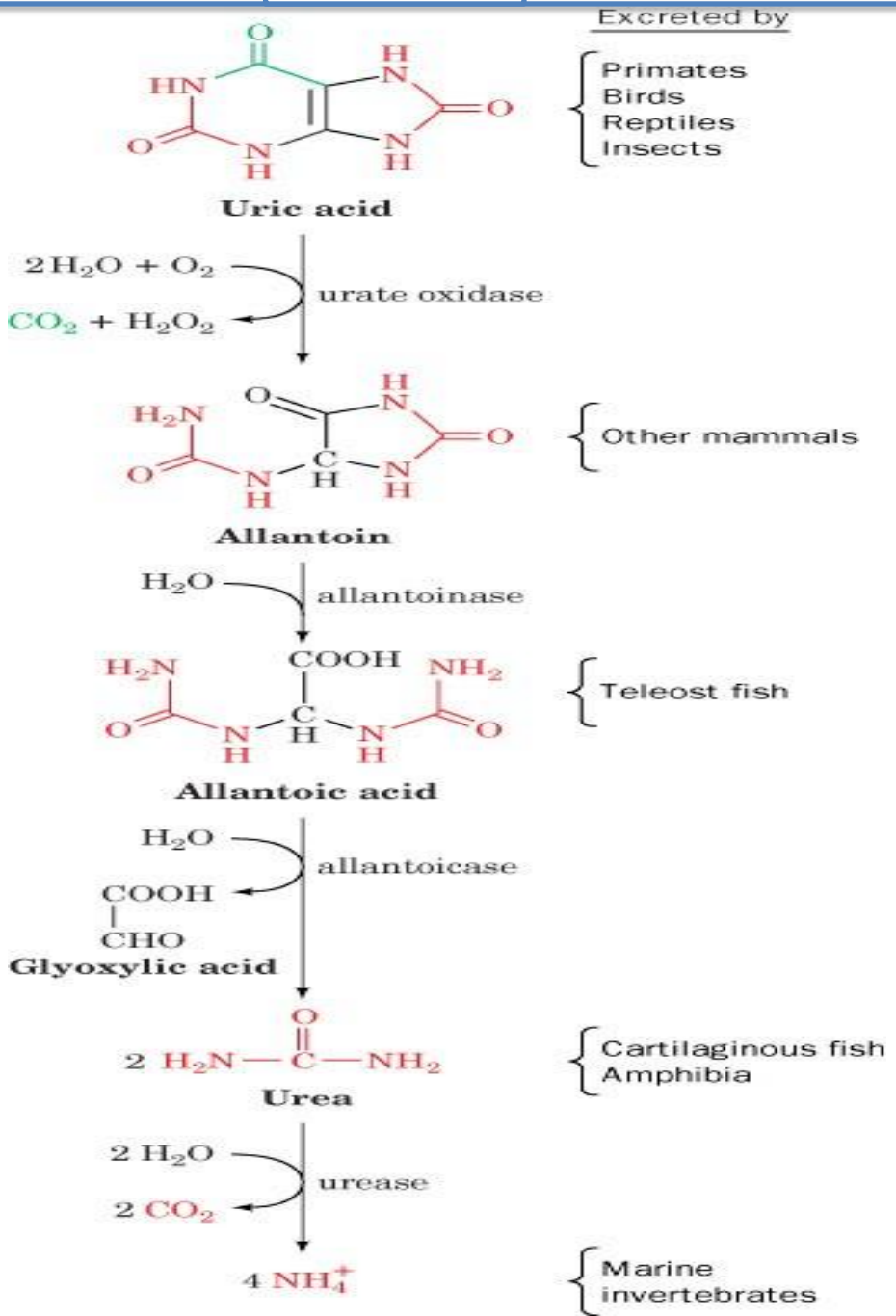
- In humans, primates, birds and reptiles the final product of purine degradation is uric acid
- **Uric acid is excreted in the urine**
- **Some animals convert uric acid to other**

" because animals have uric oxidase enzyme that convert the uric acid to other compound , human have not the enzyme "

- products:
  - Allantoin
  - Allantoic acid
  - Urea
  - Ammonia

Degradation of uric acid to ammonia in some animals

You need to know only the products from previous slide



Fate of uric acid in humans

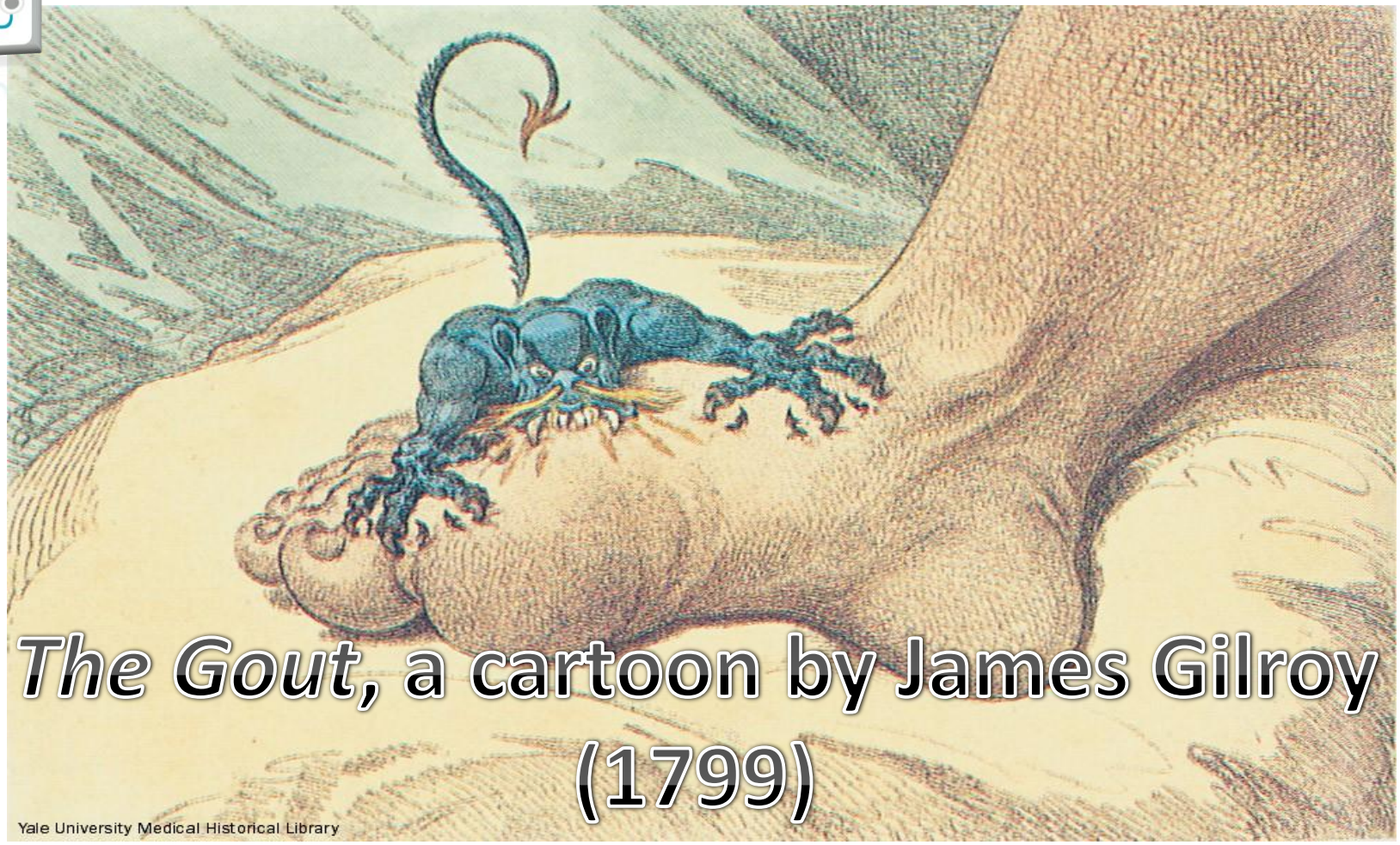
- Uric acid is less soluble in water
- Reptiles, insects and birds excrete uric acid as a paste of crystals
- **To save water**
- Humans excrete uric acid in urine

الحشرات والزواحف والطيور تخرج حمض اليوريك كـ Crystals لحفظ اكبر قدر من الماء، بينما الانسان يخرج حمض اليوريك مباشرة

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 **"disease"**
  - Hyperuricemia **"high uric acid in blood"**

" hyperuricemia is not a disease . It os a condition of elevated uric acid in the blood . It can be referred as a disease once it show symptoms or cause other disease such as gout "



The Gout, a cartoon by James Gilroy (1799)

USUALLY THE FIRST TO GET AFFECTED IS THE BIG TOE (THE EXTREMITIES IN GENERAL) DEPOSITS OF URIC ACID DEVELOP IN THE EXTREMITIES WHERE THE PH FACTOR AND A LOWER BODY TEMPERATURE ARE PRESENT. SINCE URIC ACID IS HIGHLY INSOLUBLE, A PH FACTOR OF 7.4 AND ABOVE AND ALSO A LOWER BODY TEMPERATURE WILL INCREASE THE RISK FACTOR.

Gout

- Gout is a disease due to high levels of uric acid in body fluids
- 7.0 mg/dL and above (normal: 2.5-5 mg/dL)
- Uric acid accumulates because of:
  - Overproduction or
  - Underexcretion

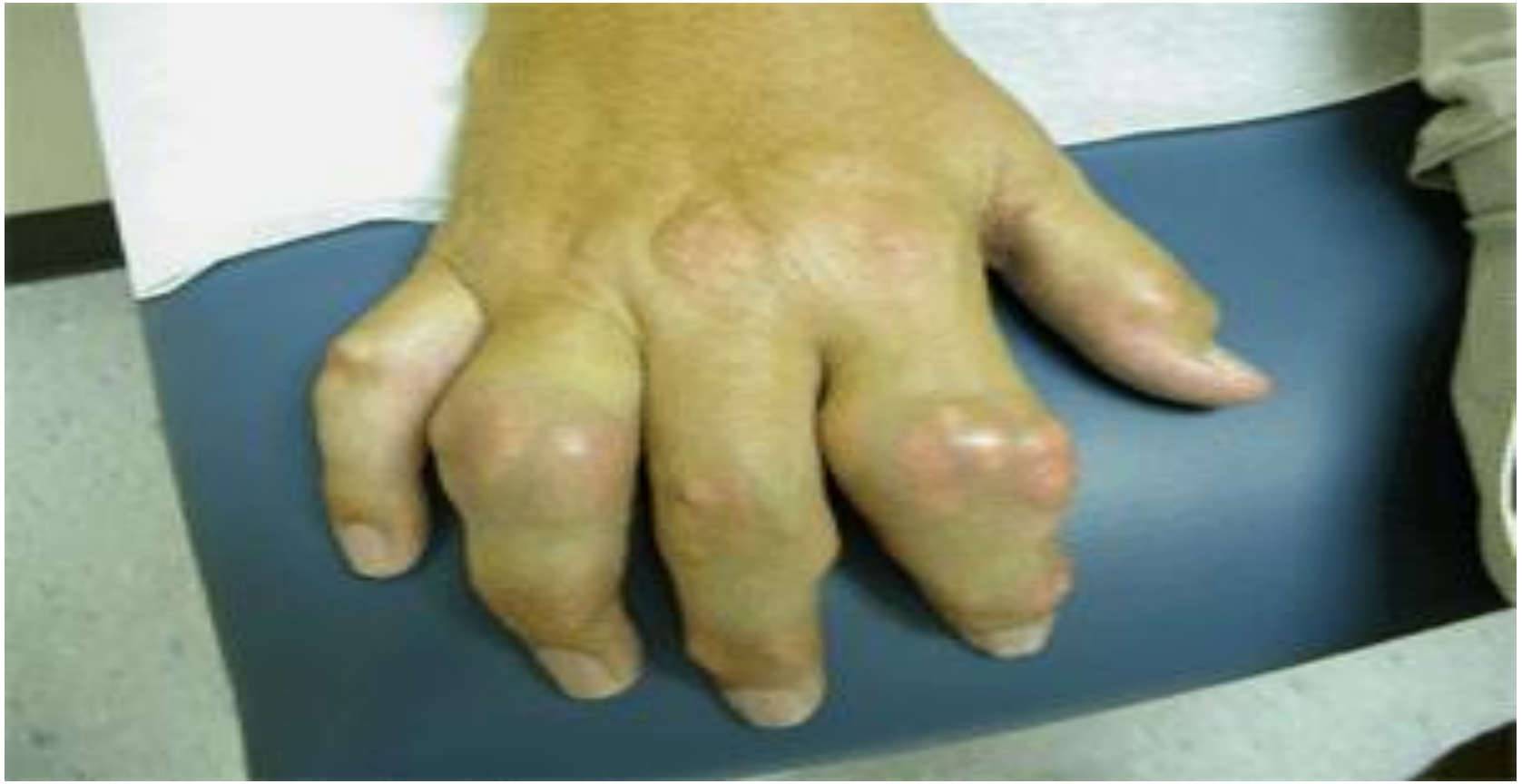
The Gout is depend on how you body deal with uric acid my production is normal but excretion is slow or production is high with normal excretion, may both high production with slow excretion" more dangers .

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

Voet *Biochemistry*



Crystals accumulate in the synovial fluid first then progress to around the joints

These are called: tophi –singular tophus-

What happens is that leukocytes gather by chemotaxis because of the inflammation and try to phagocytose the crystals but burst and send out cytokines and enzymes which have further inflammatory effects

Gout

- Inaccurately associated with overeating and drinking
- Alcohol used to be contaminated with lead «الرصاص» 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

Alcohol decreases excretion of uric acid
Meat increases production of uric acid

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)

Primary always means that it is idiopathic (unknown cause)

Secondary has a known cause.

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

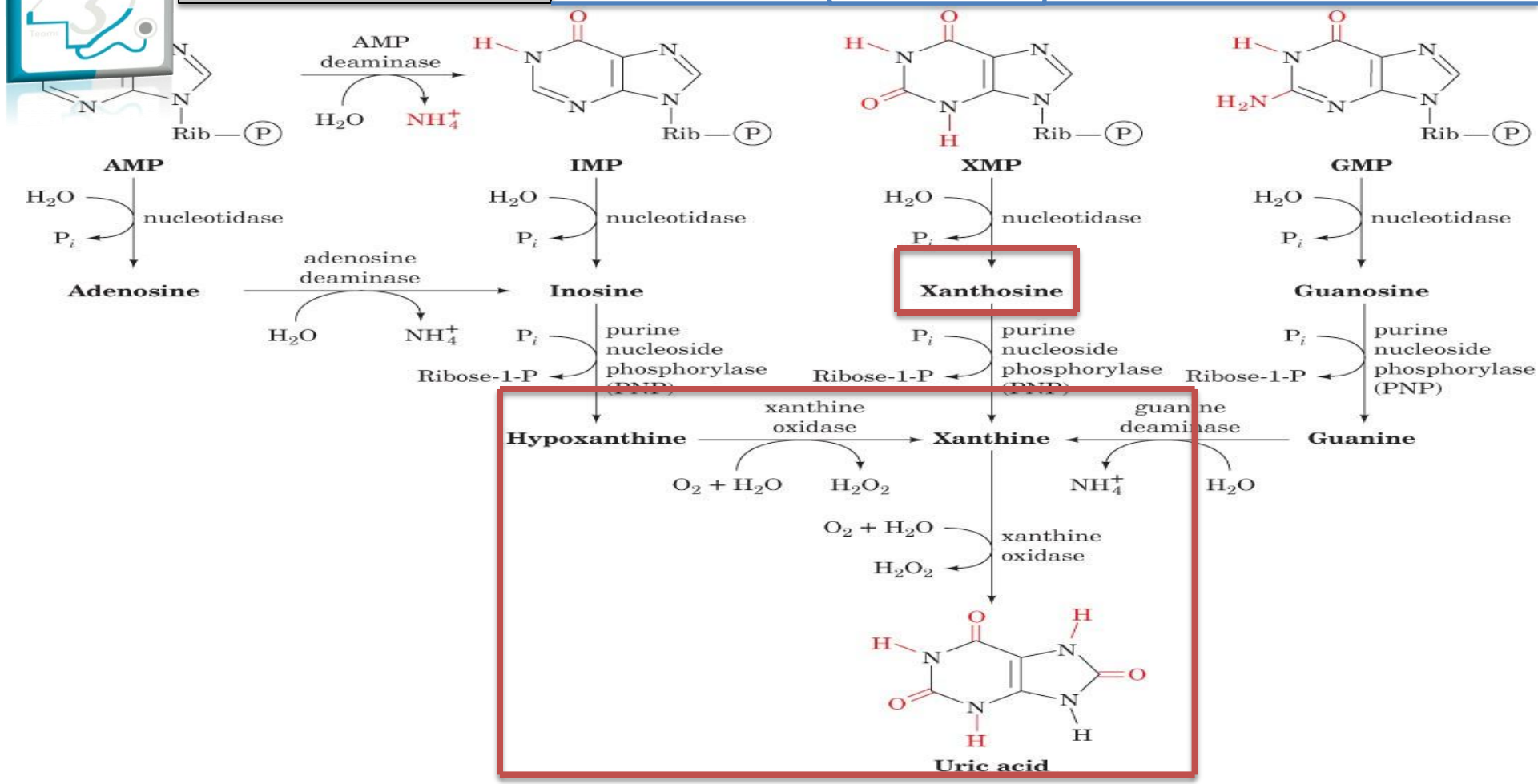
Secondary hyperuricemia

- Hyperuricemia does not always cause gout.

- Gout always accompanied with hyperuricemia.

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)



If Xanthine oxidase is inhibited then hypoxanthine will not be oxidized to xanthine and xanthine (from xanthosine) will not be oxidized to uric acid. This leads to accumulation of these 2 bases in the blood. The advantage of this drug use is that these 2 bases are highly soluble and can be readily excreted in the urine

Questions for review

Q1) Enzyme convert the uric acid to other compounds like Allantoin ,Allantoic acid in the animals but human not have this enzyme is

A. uric oxidase enzyme
B. Polynucleotidase

Q2) Alcohol ……. excretion of uric acid

A. increases
B. decreases

Q3) Meat ……. production of uric acid

A. increases
B. Decreases

Q4) To reduce uric acid production We use

A. uricosuric agents
B. Allopurinol

Q5) to aviod gout:

A. Gain weight
B. Avoid purine-rich diets

QUESTION	ANSWER
1	A
2	B
3	A
4	B
5	B

Biochemistry Team

Thank You

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