جامعة الملك سعود
King Saud University

بِسْم الله الرحمن الرحيم

MED437 KING SAUD UNIVERSITY

BIO TEAM

Purine Degradation & Gout (Musculoskeletal Block)

437 Biochemistry Team

Color index:
Doctors slides
Notes and explanations
Extra information
Highlights

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.

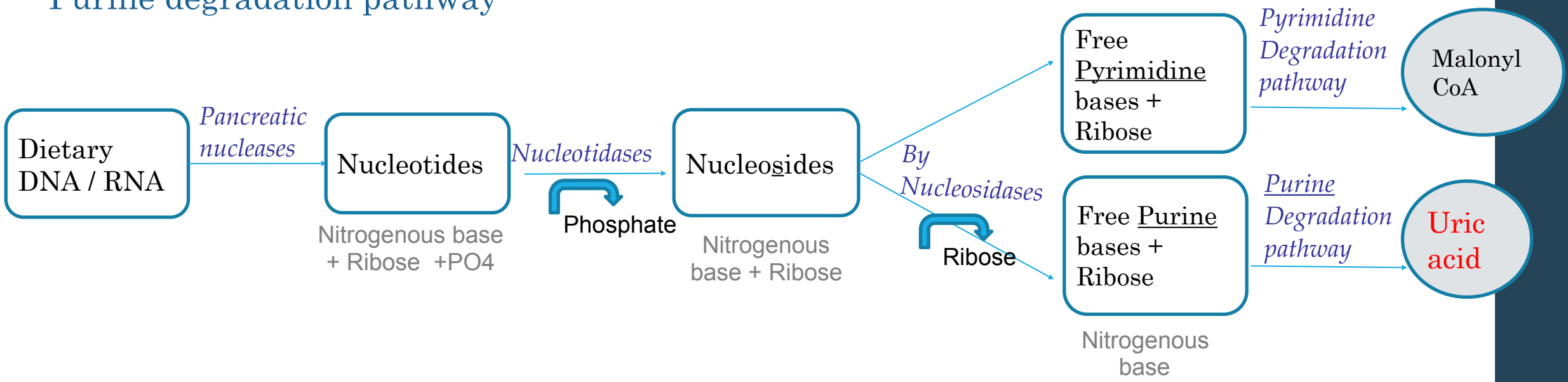
Purine degradation pathway

Purines are nitrogen basses

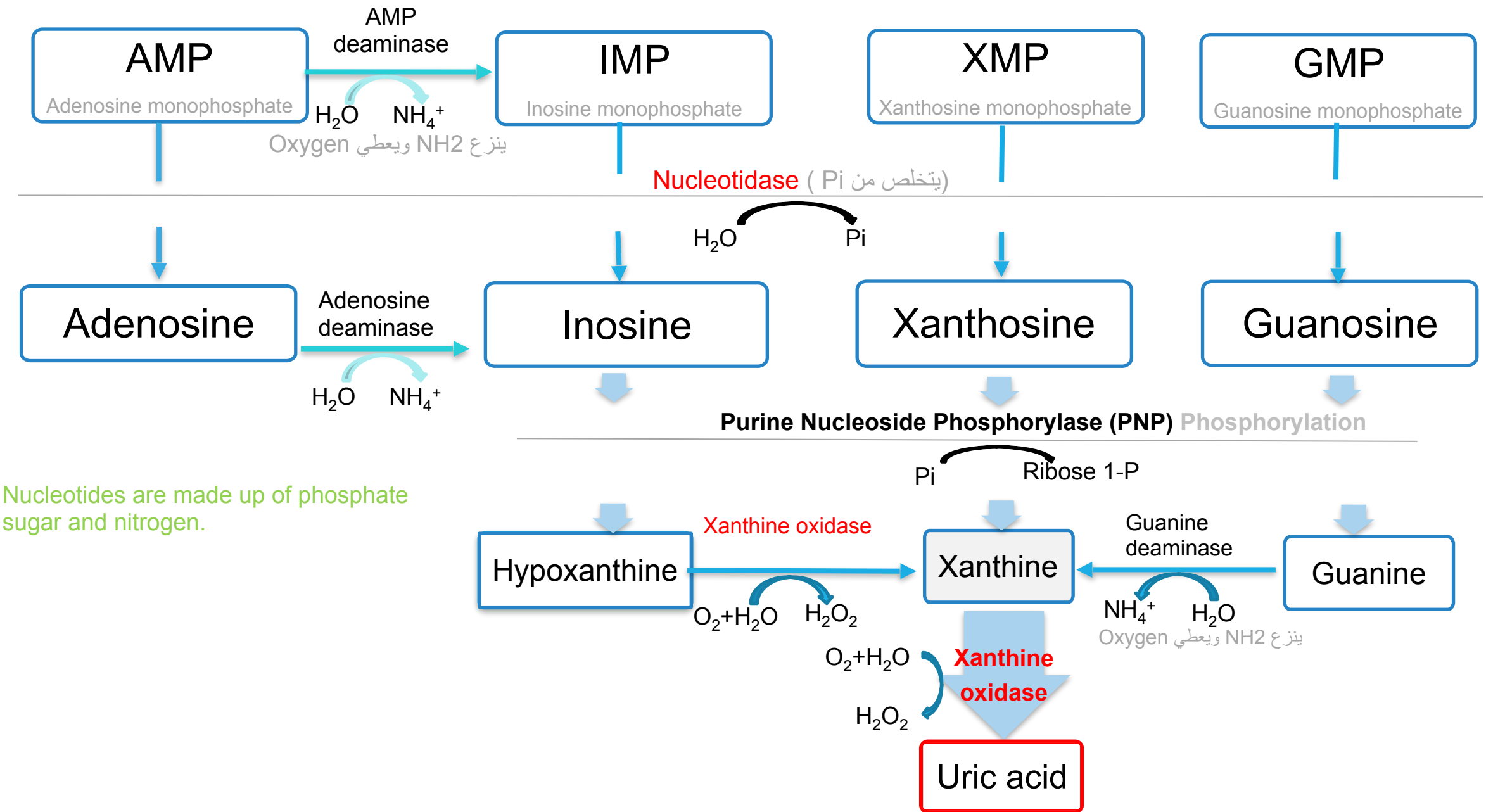
The major source of nucleic acid is meat but the amount differ from a type to another sea food and internal organs like the liver have more nucleic acid

- The major source of dietary nucleic acids (purines and pyrimidines) is meat
- Purine and pyrimidine bases are absorbed by the intestine. (small intestine)
- The ingested bases are mostly degraded into different products by degradation pathways
- These products are then excreted by the body. (small intestine). (product for purine degradation = uric acid)
- Adenosine and guanosine (purines) are finally degraded to uric acid by: Purine degradation pathway

Remember:
Nucleoside= Nitrogenous base + Ribose
Nucleotide= Nitrogenous base + Ribose + PO_4

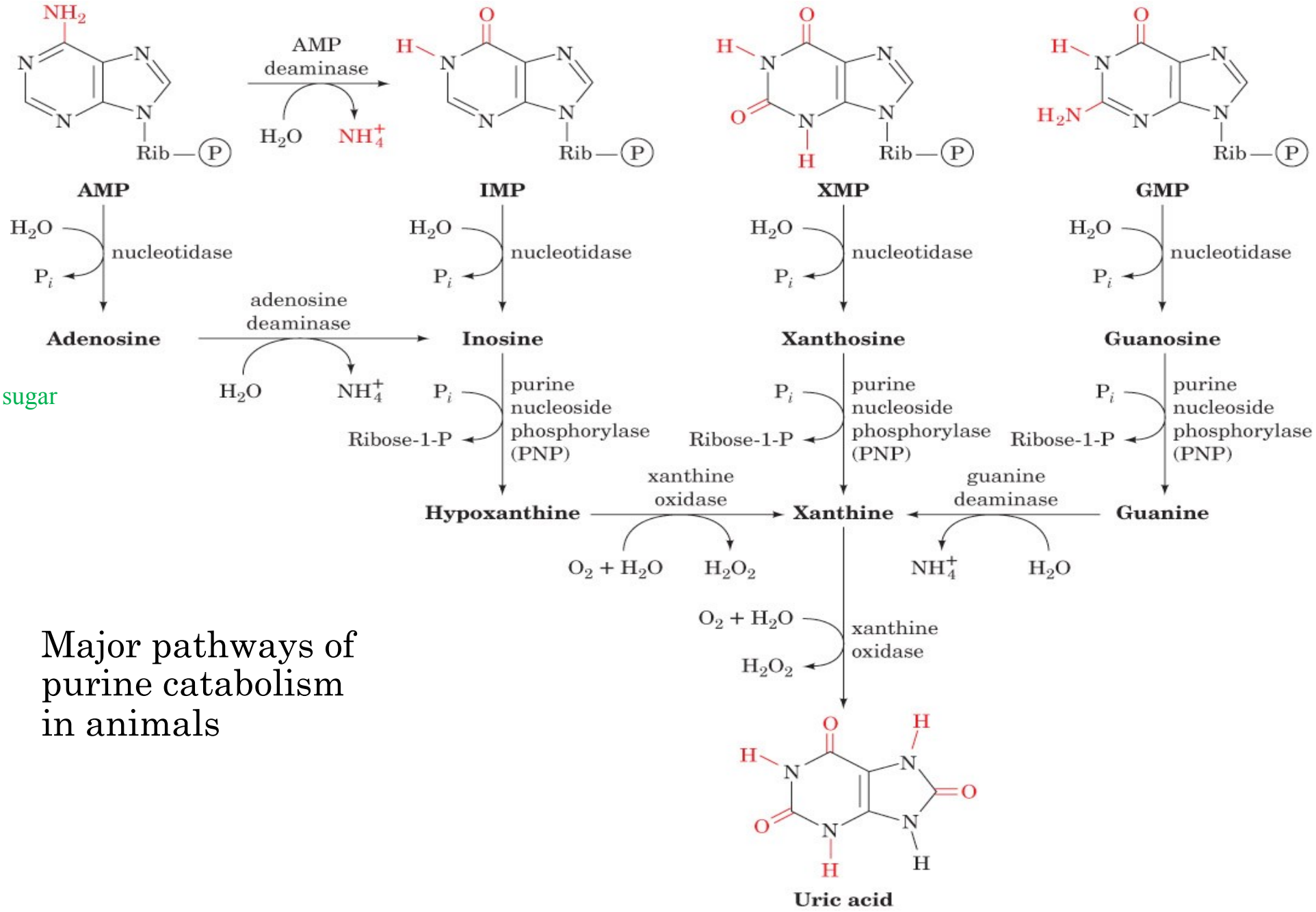


Major pathways of purine catabolism in animals



Nucleotides are made up of phosphate sugar and nitrogen.

Sine in adenosine means sugar



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

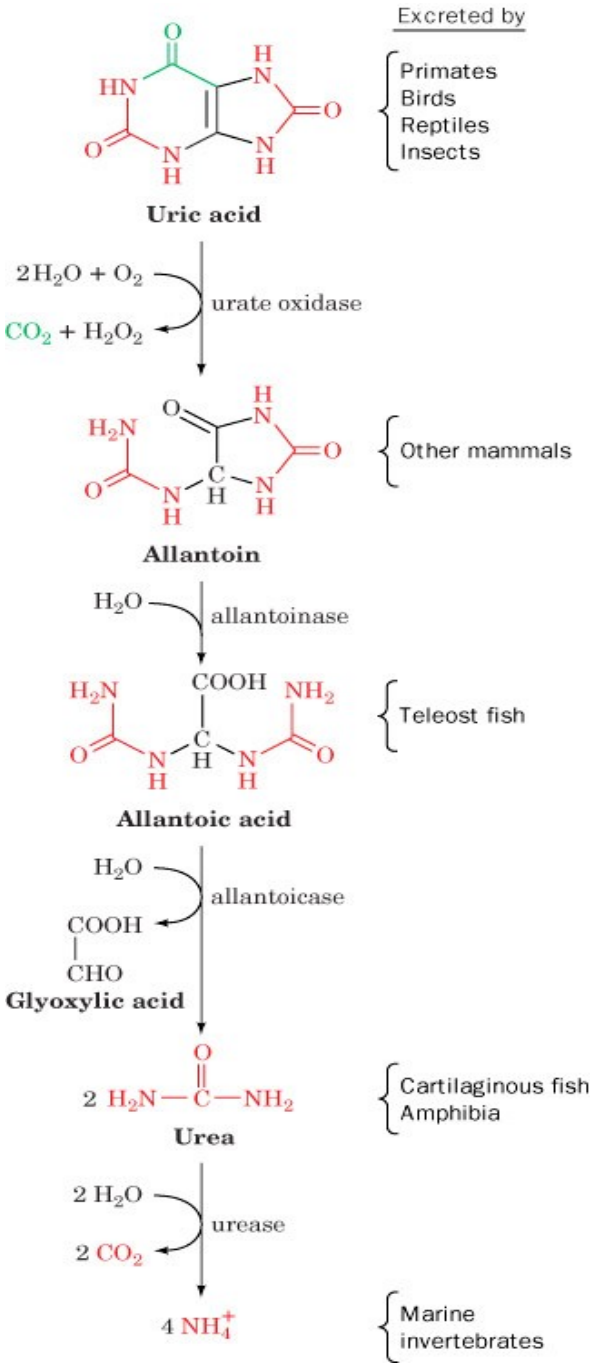
- Uric acid is excreted in the urine

- Some animals convert uric acid to other products:

(because they have the enzymes that humans lack that enable them to convert uric acid to other products)

1. Allantoin
2. Allantoic acid
3. Urea
4. Ammonia

Degradation of uric acid to ammonia in some animals



You don't need to memorize this slide, it is only to show that uric acid degradation is different depending on the enzymes found in the creature

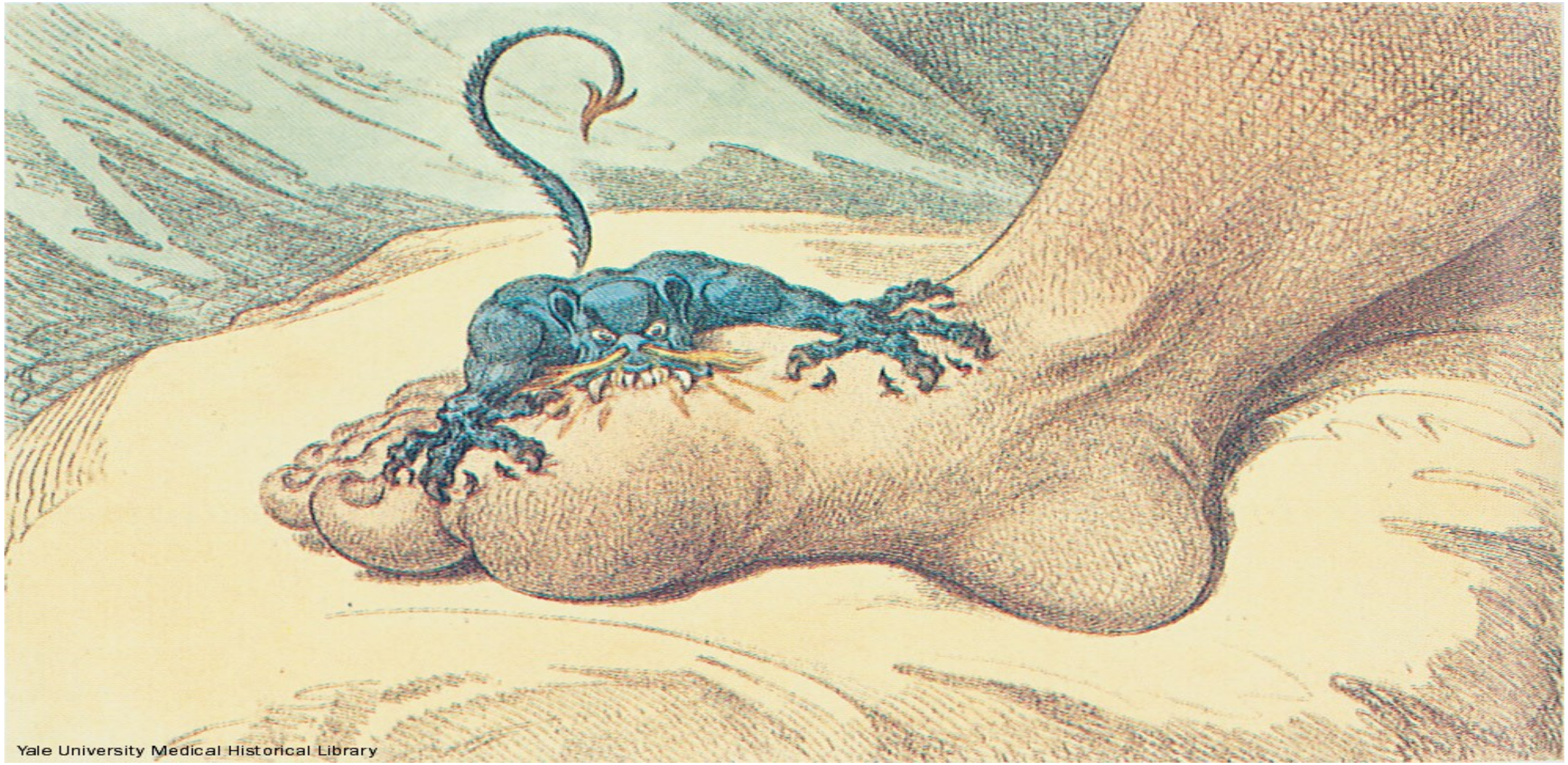
Some animals convert uric acid in to other products by special enzymes that are not found in humans

- Humans can't convert uric acid to other products Because they don't have Urate Oxidase enzyme
- This enzyme is used in treatment of Gout

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***.
- 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 *(Hyperuricemia is not a disease. It is a condition of elevated uric acid in the blood.* It can be referred as a disease once it shows symptoms or causes other diseases such as gout.*)*
    (hyperuricemia doesn't always lead to gout)

The Gout, a cartoon by James Gilroy (1799)



Gout

disease due to high levels of uric acid in body fluids .

Uric acid accumulates because of

Underexcretixon

Overproduction

Affects 3 per 1000 persons .

7.0 mg/dL and above (normal 6.8)

Sodium urate crystals accumulate in kidneys, ureter, joints leading to chronic gouty arthritis .

Painful arthritic joint inflammation due to deposits of insoluble sodium urate crystals (especially big toe)

٩٨ ٪ من - uric acid يتحد مع +Na . لأنه يمتلك شحنة ve–

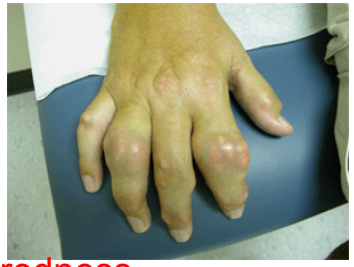
< Sodium-urate (Poorly soluble product) < accumulation of crystals

- Excessive production of uric acid causes deposition of uric acid crystals in the joints

leading to:

- (2) Gout
- (1) Hyperuricemia (increase of uric acid in blood)
- Hyperuricemia doesn't always develop to Gout

Gout



redness
Swelling
Loss of function

Some reasons that which lead to increase the uric acid:

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 affect Big Toe joints because:
It's a big joint
Weak blood circulation]

Two main causes of gout

- Overproduction of uric acid
- Underexcretion of uric acid

Sodium urate crystals in urine this is under microscope from urine

Underexcretion (due to damage in kidney)

Classification of Gout

Clinical Category	Metabolic defect
Primary Gout (90% of cases)	
Enzyme defects-Unknown (85% to 90% of cases)	❑ **Overproduction of uric acid** -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**

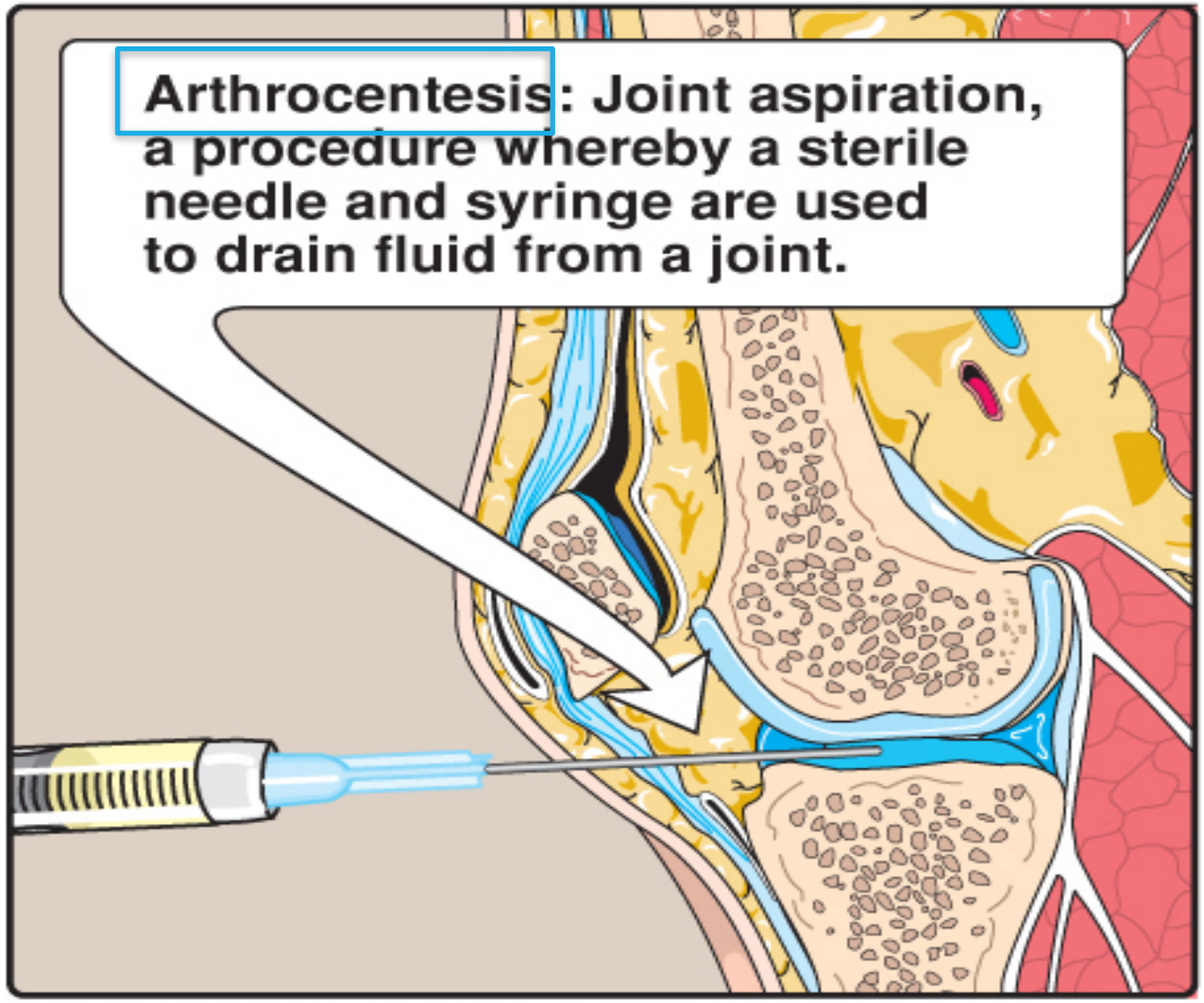
Biochemical Diagnosis

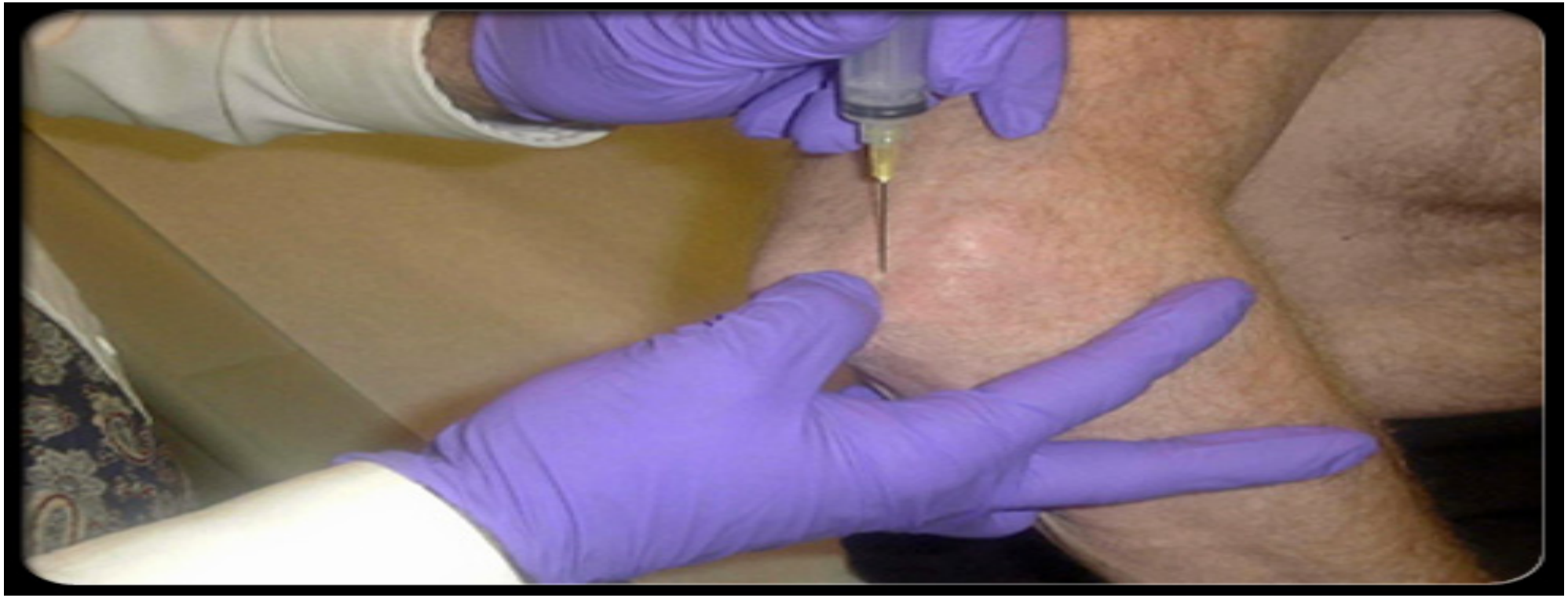
❑Joint fluid test

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

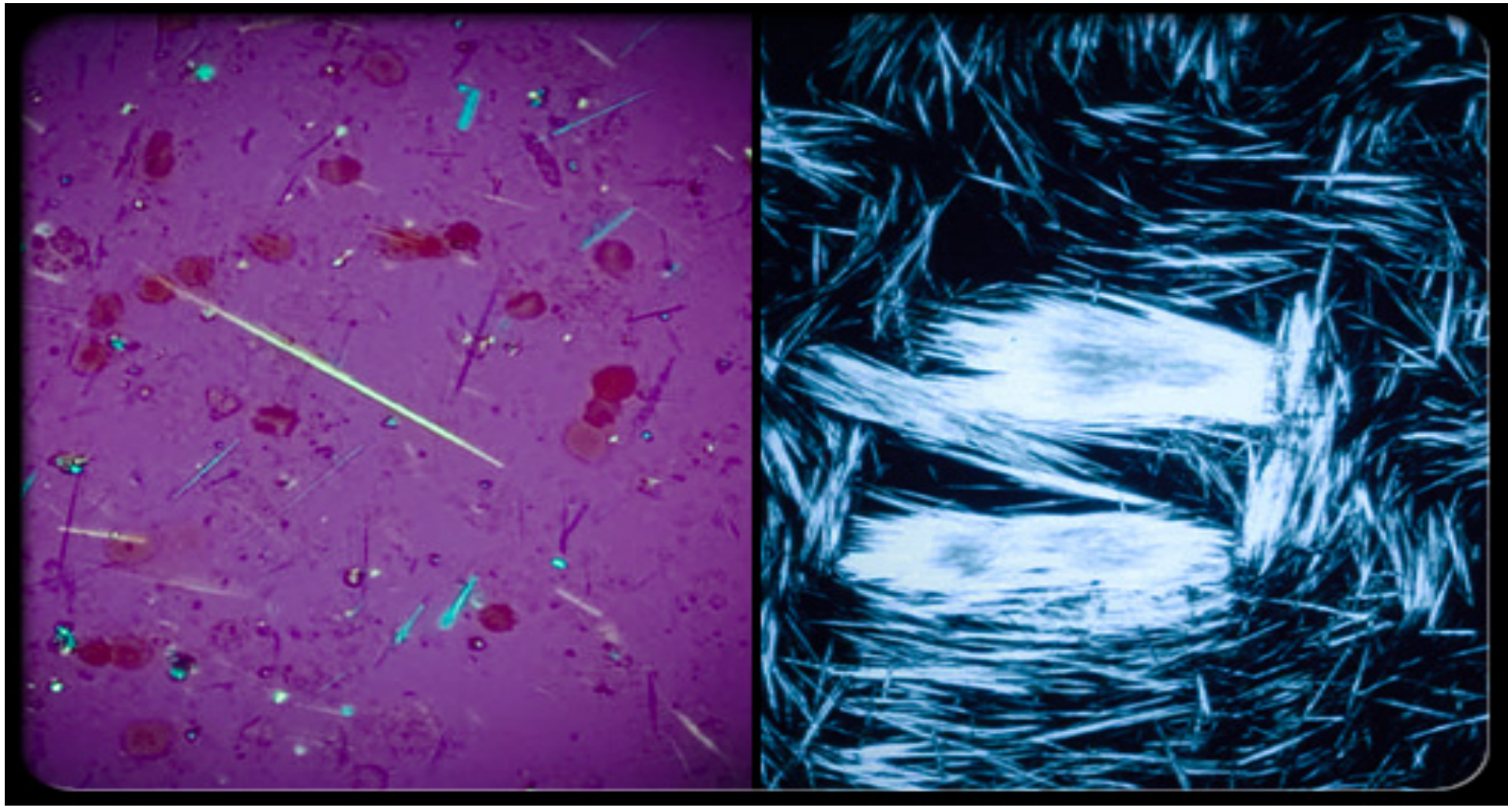




*Color of synovial fluid is yellow

* It is sticky

Monosodium urate crystals

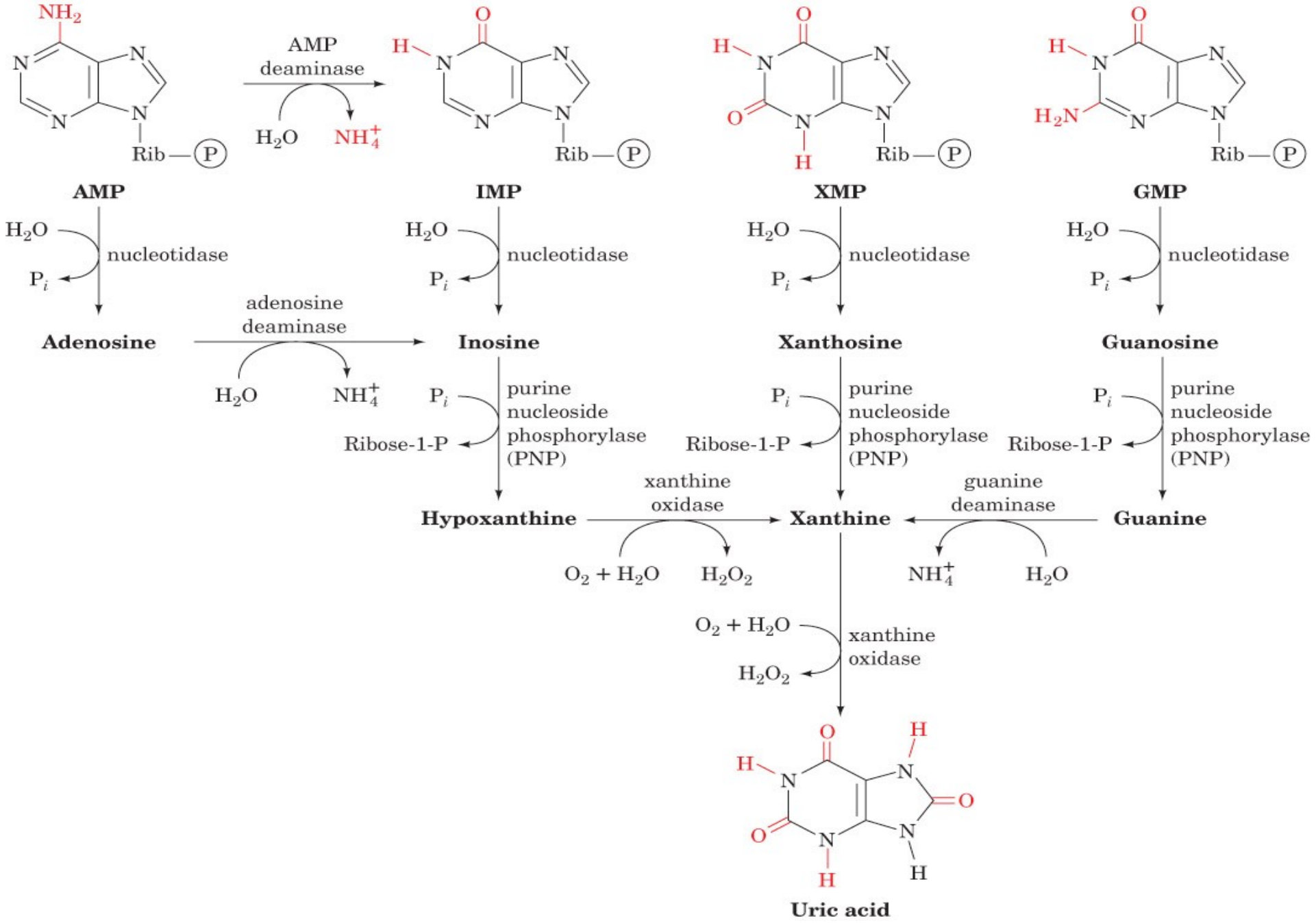


Treatment

- 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.**

Test your self

- ***1- gout is a disease due to high levels of:***
- A-uric acid B- lactic acid C- purine
- ***2- uric acids is …… soluble in water:***
- A- more B- less C- same
- ***3- which one of the following can cause gout :***
- A- Excessive vegetables consumption B- Excessive fat consumption C- Excessive meat consumption
- ***4-which of the following enzymes use to converts Guanine to Xanthine :***
- A-Guanine synthase B – Guanine convetsae C- Guanine deaminase
- ***5- 4-which of the following enzymes use to converts Hypoxanthine to Xanthine:***
- A- Xanthine oxidase B- AMP deaminase C- Adenosine deaminase

Answers

GIRLS TEAM:

- الهنوف الجلعود
- رهف الشنيبر
- شهد الجبرين
- لينا الرحمة
- منيرة المسعد
- ليلى الصّباغ
- العنود المنصور
- أرجوانة العقيل
- ريناد الغريبي
- مجد البراك
- رزان الزهراني
- ليان المانع
- مشاعل القحطاني
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- احمد ابراهيم العريفي
- سعيد آل سرار
- عبدالرحمن التركي
- سلطان بن عبيد
- صالح المعيقل
- صالح الوكيل
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For editing file:
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