Biochemistry Team 435

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King Saud University 1957

PURINE DEGRADATION & GOUT

Color index:
- Important
- Extra explanation

"IT IS OKAY TO LOSE PEOPLE BUT NEVER LOSE YOUR SELF"

Recall: difference between nucleosides and nucleotides:

***Nucleic Acids (DNA and RNA) :**

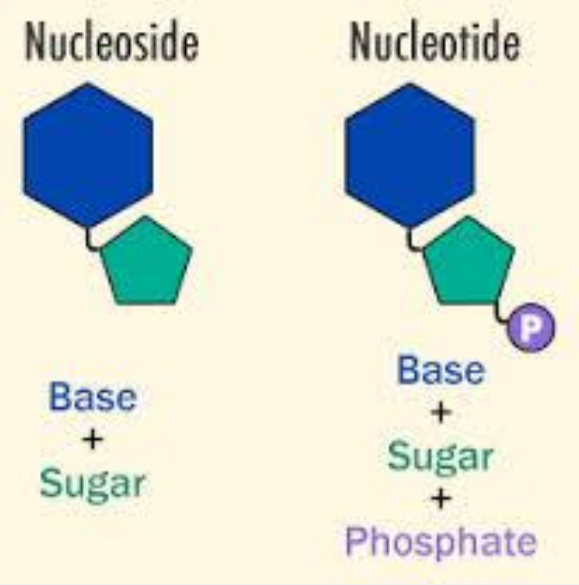
-Building blocks of Nucleic acid are nucleoside triphosphates (nucleotides).

-Difference between Nucleotides and Nucleosides :

Nucleosides: consists of a nitrogenous base covalently attached to a sugar (ribose or deoxyribose) but without phosphate group.

Nucleotides : consists of a nitrogenous base, sugar (ribose or deoxyribose) and one to three phosphate groups.

Note:
Nucleoside=Base+sugar
Nucleotide=Base+sugar + phosphate group



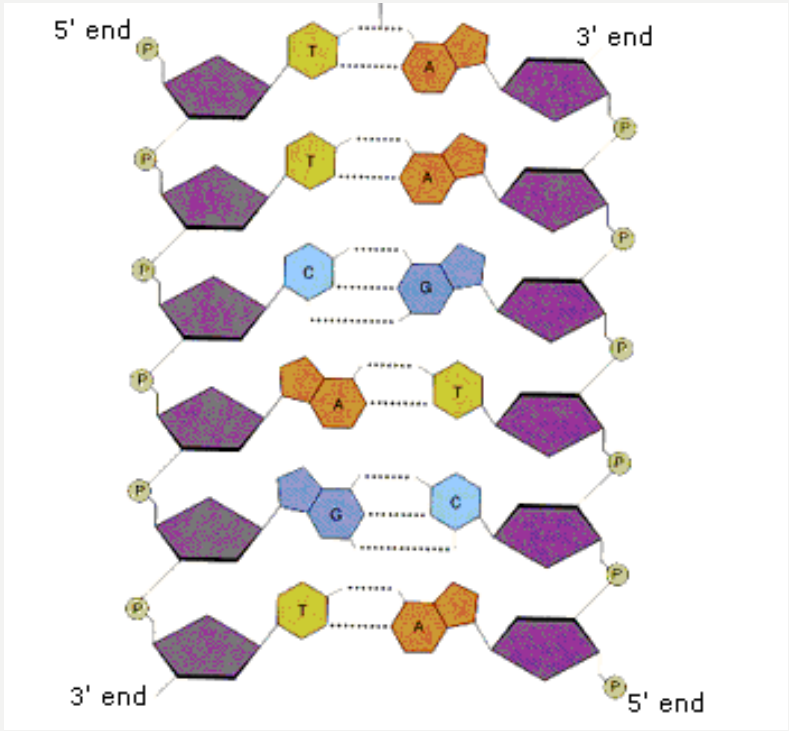
Recall: Structure of nucleotides

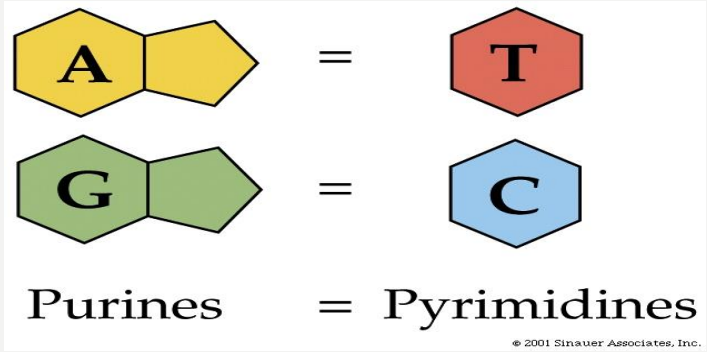
Nucleotides are composed of:

1-Nitrogenous base:
Purines: Adenine (A) and Guanine (G)
Pyrimidines: Cytosine (C), Thymine (T) and Uracil (U).

2-Sugar:
pentose with 5 carbon ring:
Ribose (In RNA)
Deoxyribose. (In DNA)

3-Phosphate group.





Extra : GOUT "THE KING'S DISEASE"

gout or gouty arthritis, has a long and colorful history with some of the earliest descriptions dating back as far as the 5th century. Historically, gout has been called "the disease of kings" due to its association with rich foods and alcohol consumption also heredity and overweight.

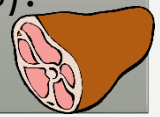
OBJECTIVES:

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

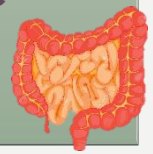
Purine degradation pathway

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

meat and fish are the **major source of dietary nucleic acids** (purines and pyrimidines).



the Purine and pyrimidine bases get **absorbed by the intestine**



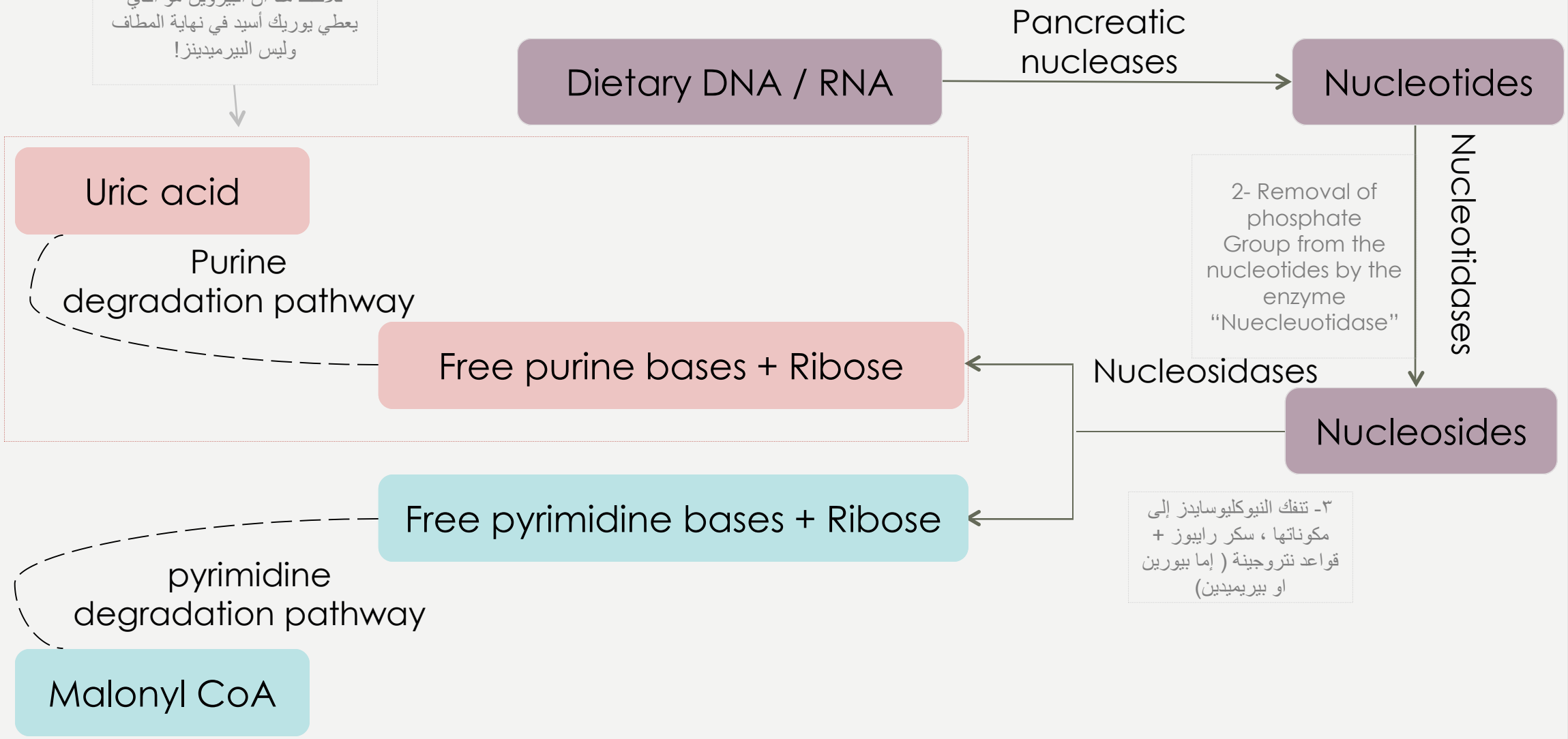
The ingested bases are mostly **degraded** into **different products** by degradation pathways.

These products are then **excreted by the body**.

Purine degradation pathway

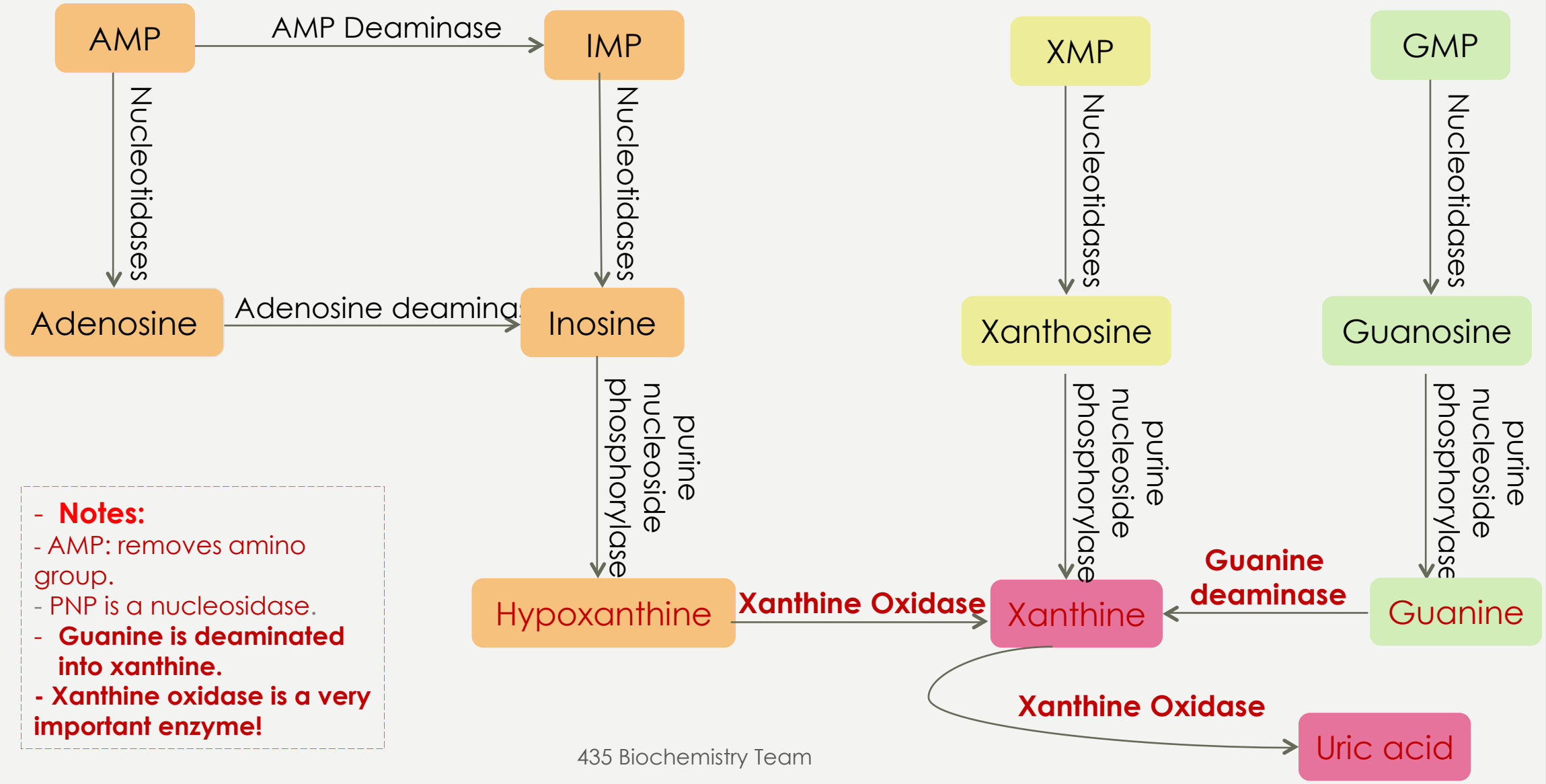
1- Degradation of the nucleic acid into its building blocks "nucleotides"

نلاحظ هنا أن البيروين هو الذي يعطي يوريك أسيد في نهاية المطاف وليس البيرميدينز!



٣- تنفك النيوكليوسايدز إلى مكوناتها ، سكر رايبوز + قواعد نتروجينة (إما بيورين او بيريميدين)

Purine degradation pathway



- **Notes:**
- AMP: removes amino group.
- PNP is a nucleosidase.
- **Guanine is deaminated into xanthine.**
- **Xanthine oxidase is a very important enzyme!**

Fate of uric acid

In human, birds and reptiles

- The final product of purine degradation : uric acid. (Why?)

- Human don't have enzymes to further degrade uric acid.

{ Uric acid is less soluble in water. -

- Excretion:

- **Some animals (birds and reptiles)** excrete uric acid as **paste of crystals** to save water.

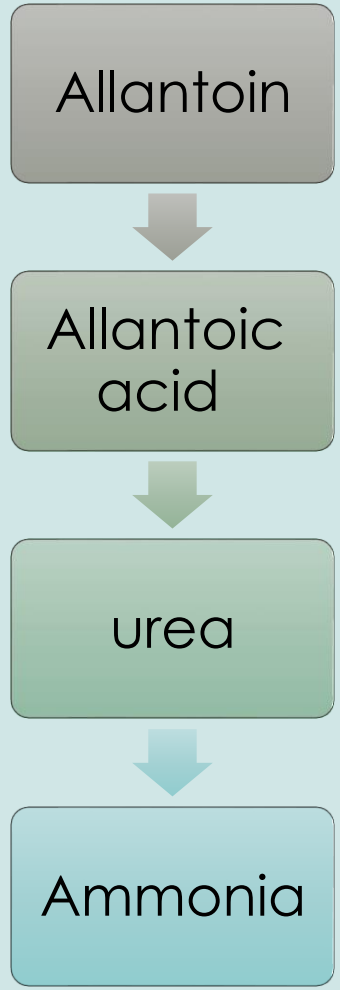
- **humans** excrete it in **urine**.

Excessive production of uric acid causes deposition of uric acid crystals in the joints leading to :

- hyperuricemia.
- Gout.

In Some animals

They Convert uric acid to More soluble products :



Gout

What is "Gout"?

-It is a disease that happens due to high level of uric acid in body fluids.
- Painful arthritic joint inflammation due to deposition of insoluble sodium urate crystals that happens especially to the big toe.
- Sodium urate crystals accumulate in : kidneys, ureter, joint leading to chorionic arthritis.

High level:

7.0 mg\dL and above

القاوت هو مرض يحدث بسبب تراكم حمض اليوريك في الجسم بكميات عالية تفوق ٧ ملغم لكل دكلي ليتر ، التراكم قد يكون سببه إنتاج كبير لحمض اليوريك وقد يكون سببه عدم إستخراجه بالجسم (إذا لم يستخرج سيتراكم) ، العادات الغذائية قد تؤثر علينا ، فمثلا تناول اللحم قد يزيد من عملية إنتاج حمض اليوريك بينما شرب الكحول الذي يحتوب على الرصاص قد يقلل من عملية إستخراجه من الكليه ، تتعدد الطرق والنتيجة واحدة.

Uric acid accumulation causes:

-Overproduction of the uric acid.

- Under-excretion of the uric acid.

Excessive meat consumption increases uric acid production in some individuals

Alcohol used to be contaminated with lead (during manufacturing and storage), will decrease the excretion of uric acid causing hyperuricemia

Note: Hyperuricemia → high level of uric acid in the blood → occurs before gout and sometimes can cause it
- It affects 3 per 1000 persons

Gout

Primary hyperuricemia

- **Due to overproduction of uric acid.**
Genetic abnormality in the enzymes of purine degradation.

- Excessive production and degradation of purine bases(Adenine ,Guinine, hypoxanthine).

(Secondary hyperuricemia)

- What is it?

A variety of **disorders** and **lifestyles** cause Secondary hyperuricemia.

- Under-excretion of uric acid due to :

1- Chronic renal diseases

2-Chemotherapy

3- excessive consumption of purine-rich foods such as meat.

4- Excessive alcohol intake

Note: 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)

Note: xanthine oxidase inhibitors are competitive inhibitors

PHARMACOLOGY 435

all about the treatment of gout, in lecture 5 pharmacology

VIDEOS:

Gout: Treatment, Causes, Massage Therapy, Prevention:
https://www.youtube.com/watch?v=QOa7TLnwFXs&spfreload=10

Gout Treatment Tips and Advice:
https://www.youtube.com/watch?v=btuhyPTwD7Q

Recall:
https://www.youtube.com/watch?v=MA-ouz1LtpM

Gout:
https://www.youtube.com/watch?v=1O3F-b8FfDY

CLICK HERE FOR THE LECTURE SUMMARY:

MCQ'S

1-Chronic renal diseases can be a cause of primary gout. (T or F)

2-When patient have Secondary hyperuricemia that means they have gout. (T or F)

3-Genetic abnormality in the enzymes of purine degradation cause:

A- primary gout B- Secondary hyperuricemia .

4-What is the correct sequence of appearance of intermediates in the degradation of adenosine?

A- Adenosine --> hypoxanthine -->xanthine --> inosine --> uric acid

B-Adenosine --> inosine --> hypoxanthine --> xanthine --> uric acid

C-Adenosine --> xanthine --> hypoxanthine --> inosine --> uric acid

D- none of the above are correct

5-A patient with acute gout wanted to reduce the pain and inflammation he's suffering from, he should take:

A- Analgesics, anti-inflammatory drugs

B- Uricosuric agents

C-xanthine oxidase inhibitors

D- all the above

6-The mechanism of uricosuric agents in treating gout is?

A- reducing pain and inflammation

B- increasing uric acid excretion

C- reducing uric acid production

D- none of the above

7-Allopurinol and febuxostat are?

A- used to reduce pain and inflammation

B- xanthine oxidase inhibitors (Allopurinol and febuxostat)

C- used to reduce uric acid production

D- both B and C are correct

7- D
6- B
5- A
4-B
3-A
2-F
1-F

MCQ'S

8-Human have enzymes to degrade uric acid.

A. True B. false

9-humans excrete uric acid in stool.

A. True B. false

10-Gout is a form of:

a. Diabetic
b. Tumor
c. Inflammatory arthritis

11- gout affect:

a.Heart
b.Big toe and joints
c.Kidney

12- Gout is more common at a younger age in what group?

a.Men
b.Women
c.both

13-Purines are converted to hypoxanthine and xanthine via what enzyme?

a. Xanthine peroxidase
b. Xanthine oxidase
c. Oxypurinol

14-Mutations in the HGPRT gene lead to (leading to high levels of uric acid in he blood, gouty arthritis, uric acid stones)

a. Hyperuricemia
b. Hypouricemia
c. Hypocalcemia

15-Which of the following is impaired in a case of gout?

A. Protein metabolism
B. Ketone metabolism
C. Purine metabolism
D. Pyrimidine metabolism

8-B
9-B
10-C
11-B
12-A
13-B
14-A
15-C

SAQs:

1- A man came to the clinic complaining of pain in his big toe, he mentioned he loved eating meat and he involved it in every meal. A laboratory examination was done. From the information you have.

A. what is the disease?
B. what is the mechanism of the disease?
C. What could be used as treatment?
D. What could the laboratory examination find?

2- A man came to the clinic complaining of pain in his joints, he mentioned he is going through chemotherapy.

A. What is the disease?
B. What could be used as treatment?
C. After doing a laboratory examination, what could we find?

SAQs Answers:

1-

A- Gout (accumulation of uric acid).

B- Excessive meat consumption → uric acid overproduction → accumulation of the uric acid in his big toe.

C- xanthine oxidase inhibitors (Allopurinol and febuxostate) to reduse the production of uric acid

D- high level of uric acid (overproduction of uric acid).

2-

A-Secondary hyperuricemia

B- uricosuric agents (to increase the excretion of the uric acid) .

C- high level of uric acid (Underproduction of uric acid)

- **They can ask us about the purine degradation pathway - so go back to slide 8**

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- علا النهير.
- أفنان المالكي.
- نوف التويجري.
- لولوه الصغير.
- خوله العريني.
- دلال الحزيمي.
- وضحى العتيبي.
- رزان السبتي.
- دانيا الهنداوي.
- رهف بن عباد.
- غاده القصيمي.
- أسماء العمار.
- مهند الزهراني .
- خالد النعيم .
- إبراهيم الشايع.
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- محمد الصهيل.
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