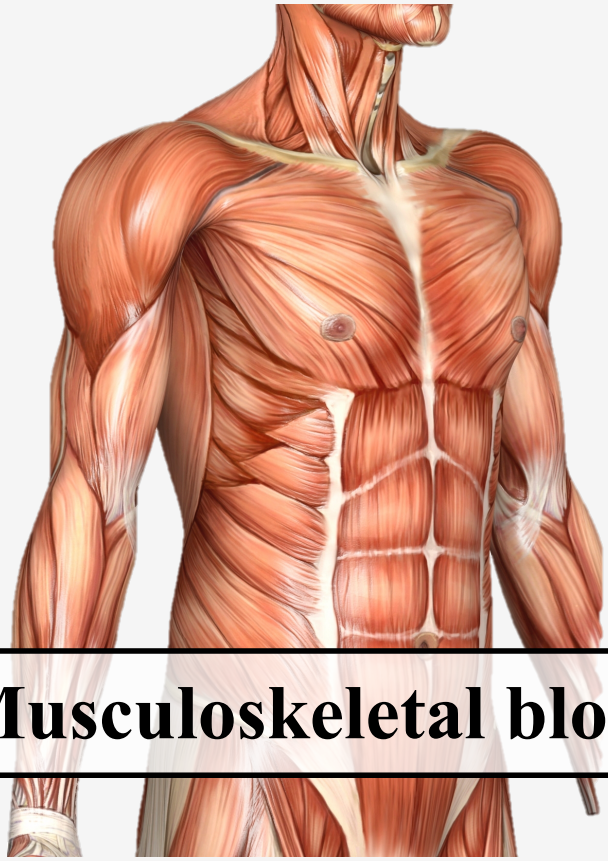

Musculoskeletal block

Purine Degradation and Gout

Lecture 4

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433 Biochemistry Team

Color index:

Red= important

Purple = addition

Orange = Explanation

Objectives:

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

Keywords:

- Purine.
- Gout.

Abbreviations:

- GMP = guanosine monophosphate.
- IMP = inosine monophosphate.
- AMP = adenosine monophosphate.
- XMP = xanthosine monophosphate.
- PNP = Purine nucleoside phosphlyrase.
- ADA = adenosine deaminase.
- GDA = guanine deaminase.
- NTDase = nucleotidase.

The major source of nucleic acids (pyrimidines and purines) is :

Meat

Absorbed in : Intestine

mostly degraded into different products by degradation pathways

Excreted

Purine degradation pathway

Dietary DNA / RNA —*Pancreatic nucleases*→ Nucleotides —*Nucleotidase*→ Nucleosides —*Nucleosidase*→ Free purine bases + Ribose —*Purine degradation pathway*→ Uric acid

Adenosine and guanosine (purines) are finally degraded to uric acid.

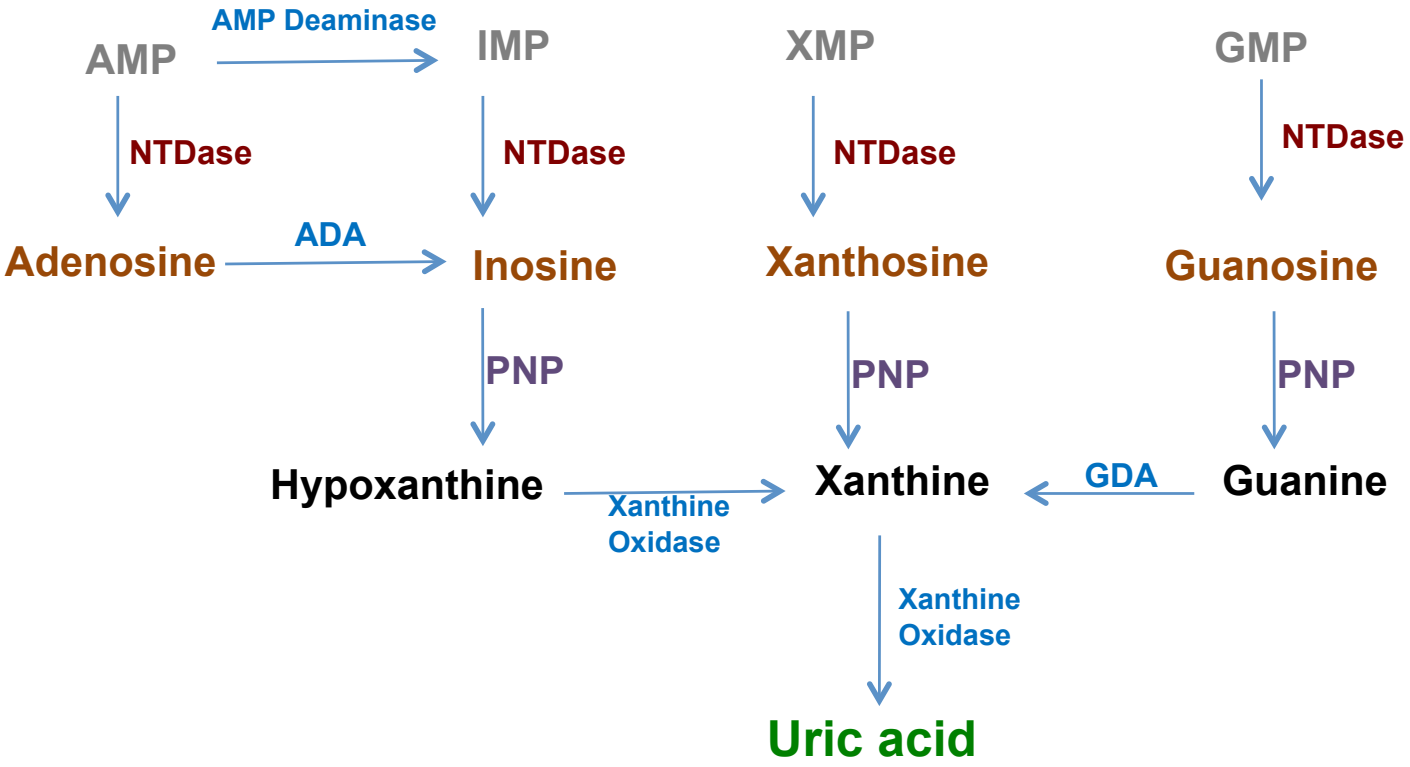
Nucleotides → (Sugar+Base+Phosphate)
Nucleosides → (Sugar+Base)

- In humans, primates, birds and reptiles the final product of purine degradation is uric acid.
- Reptiles, insects and birds excrete uric acid as a paste of crystals To save water.
- Excreted in urine in humans because of the lack of enzymes to further degrade it.
- Less soluble in water.
- Some animals convert uric acid to other products: Allantoin, Allantoic acid, Urea, Ammonia.

Color index:
Nucleotides
Nucleosides
Purine bases

Purine catabolism

AMP deaminase and **xanthine oxidase** are the most important enzymes that you should know



Fate of purine

- Uric Acid → Primates, Birds, Reptiles and insects
- Allantoin → Other mammals
- Allantoic acid → Teleost Fish
- Urea → Cartilagenous fish and Amphibia
- Ammonia → Marine invertebrates

•Not a disease.
•Nodular masses of monosodium urate crystals (tophi) may be deposited in the soft tissues, resulting in chronic tophaceous gout.
•Hyperuricemia is typically asymptomatic and does not lead to gout, but gout is preceded by hyperuricemia.

• Primary disease → a disease arising spontaneously.
• Secondary disease → acquired.

Excessive production or under secretion of uric acid causes deposition of uric acid crystals in the joints leading to **HYPERURICEMIA** **Gout**

OVER PRODUCTION OF UA:

•Primary mostly idiopathic (having no known cause).

•Secondary typically the consequence of increased availability of purines, for example, in patients with myeloproliferative disorders or who are undergoing chemotherapy and so they have a high rate of cell turnover.

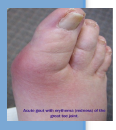
UNDER EXCRETION OF UA:

•Primary- due to as-yet-unidentified inherent excretory defects

•secondary to known disease processes that affect how the kidney handles urate, for example lactic acidosis, and to environmental factors such as the use of drugs, for example, thiazide diuretics.

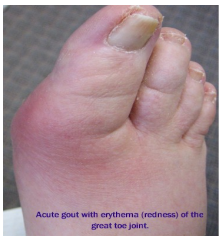
Crystals accumulate in the synovial fluid first then progress to around the joints
These are called: tophi –singular tophus-
What happens is that leukocytes gather by chemotaxis because of the inflammation and try to phagocytose the crystals but burst and send out cytokines and enzymes which have further inflammatory effects

•Disease of the rich (fashionable to associate gout with intelligence because many famous figures had it).
• a disease due to high levels of uric acid in body fluids (7.0 mg/dL and above).
•Normal range is between 2-6 mg/dl.
•prevails mainly in adult males.
•rarely encountered in premenopausal women.
•Sodium urate/uric acid may also precipitate in the kidneys and ureters as stones, resulting in renal damage and urinary tract obstruction.
•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.



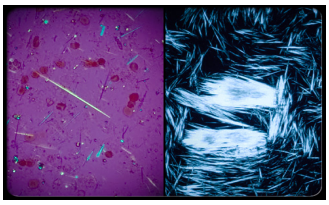
• excessive meat consumption or contaminated alcohol with lead leads to gout.
•Primary gout could be primary overproduction (more common) or primary under excretion (less common).
•Secondary gout could be secondary overproduction or under excretion (more common).

Diagnostic features



- usually affect joints in the lower extremities (pH factor of 7.4 and above and also a lower body temperature will increase the risk factor which applies on these areas).
- fast and sudden.
- Severe pain; joint may be swollen, red and hot.
- fever, leukocytosis and an elevated ESR

Diagnosis



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.

Treatment

- anti-inflammatory agents.
- Colchicine, steroidal drugs such as prednisone, and nonsteroidal drugs such as indomethacin

Colchicine depolymerizes microtubules, thus decreasing the movement of neutrophils into the affected area.

- Uricosuric agents- probenecid or sulfinpyrazone, that increase renal excretion of uric acid.
- Allopurinol, an inhibitor of uric acid synthesis. It is converted in the body to oxypurinol, which inhibits xanthine oxidase, resulting in an accumulation of hypoxanthine and xanthine —compounds more soluble than uric acid and, therefore, less likely to initiate an inflammatory response.

Preventions

•Avoid purine rich food. •Weight loss. •Control alcohol consumption.

Quiz yourself

1- an enzyme that converts the uric acid to other compounds like Allantoin and Allantoic acid in animals but human do not have this enzyme

A) uric oxidase enzyme
B) Polynucleotidase

2- contaminated alcohol with lead ..... excretion of uric acid.

A) Increases
B) Decreases
C) Has no effect.

To reduce uric acid production we use

A) uricosuric agents
B) Allopurinol

ANSWERS:
1-A
2-B
3-B

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