



Biochemistry
Team 434



PURINE DEGRADATION AND GOUT

Musculoskeletal Block

Color index

Red= Important

Purple= Addition

Orange= Explanation

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❖ Objectives:

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

◆ Purine degradation pathway

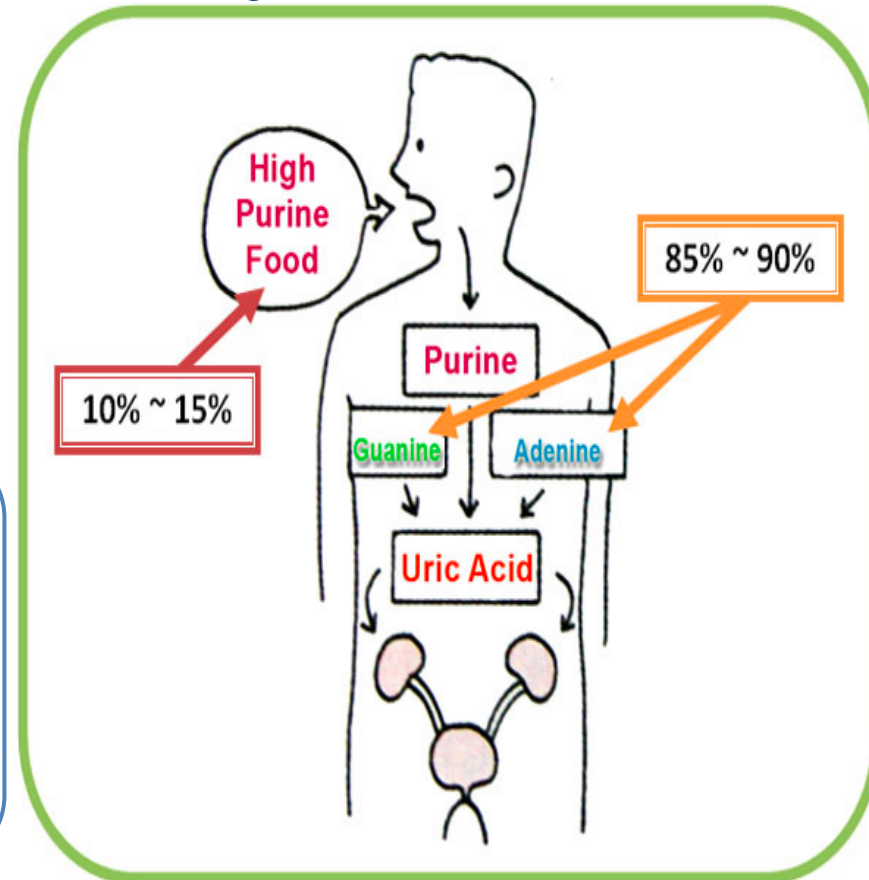
The major source of dietary nucleic acids (purines and pyrimidines) is **meat**



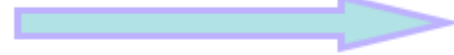
The ingested bases are mostly degraded into **different products** by degradation pathways

These products are then excreted by the body

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



Dietary
DNA / RNA



*Pancreatic
nucleases*

Nucleotides



Nucleotidases



Nucleosidases

Nucleosides



Free pyrimidine
bases + Ribose

*Pyrimidine
Degradation
pathway*



β -alanine, β -aminobutyric
acid, NH_3 and CO_2

NOTE: free purine
are not very
soluble



Free purine
bases + Ribose

*Purine
Degradation
pathway*

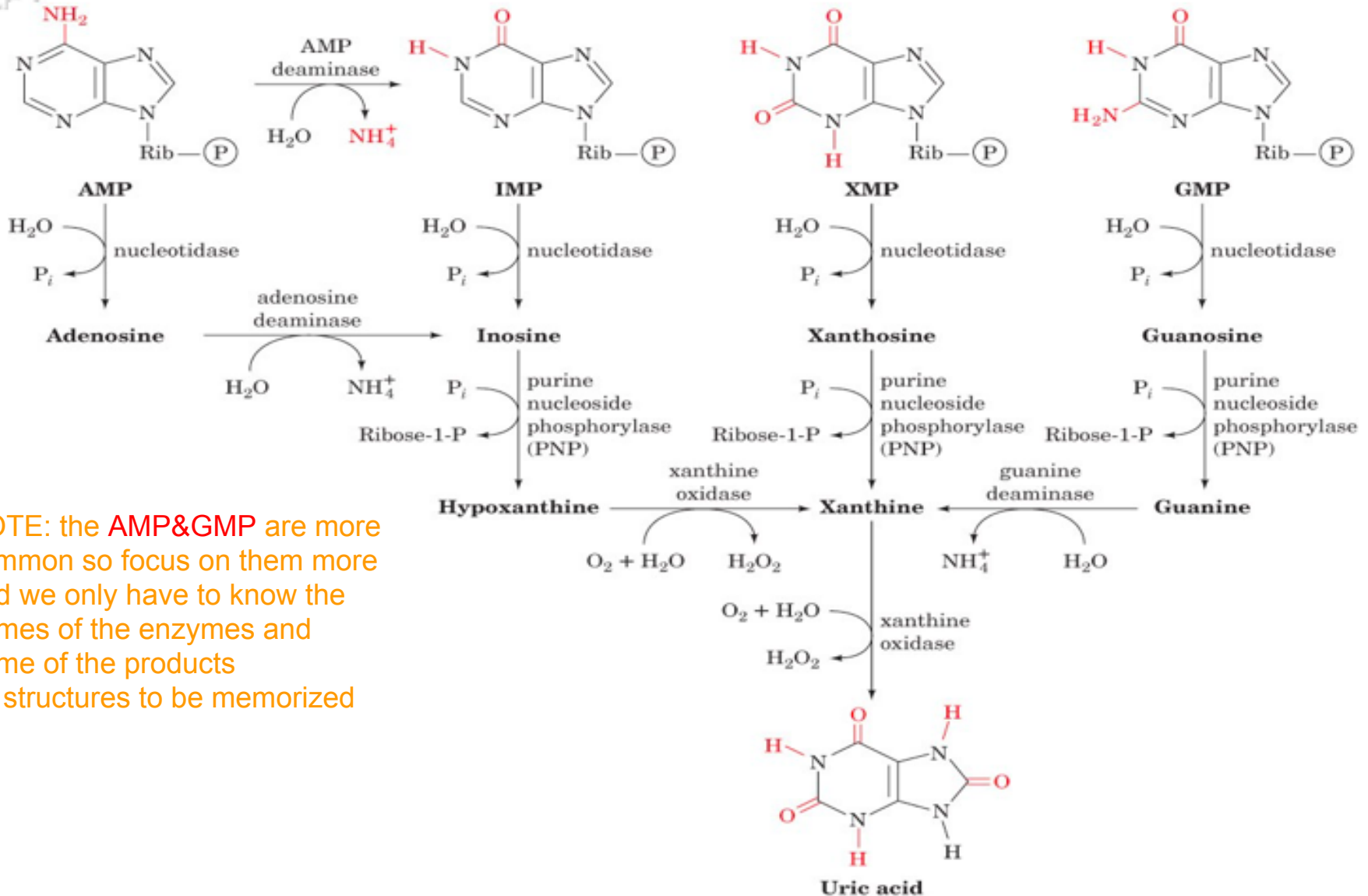


Uric acid

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

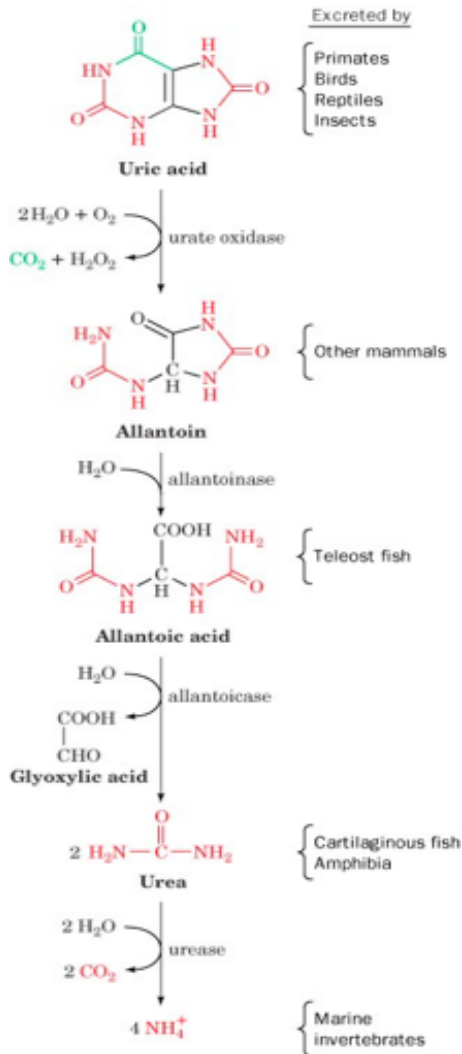
Purine degradation pathway

Major pathways of purine catabolism in animals



NOTE: the AMP&GMP are more common so focus on them more and we only have to know the names of the enzymes and name of the products no structures to be memorized

Degradation of uric acid to ammonia in some animals



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

NOTE: IF URINE WAS ACIDIC URIC ACID WILL NOT BE EXCRETED

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

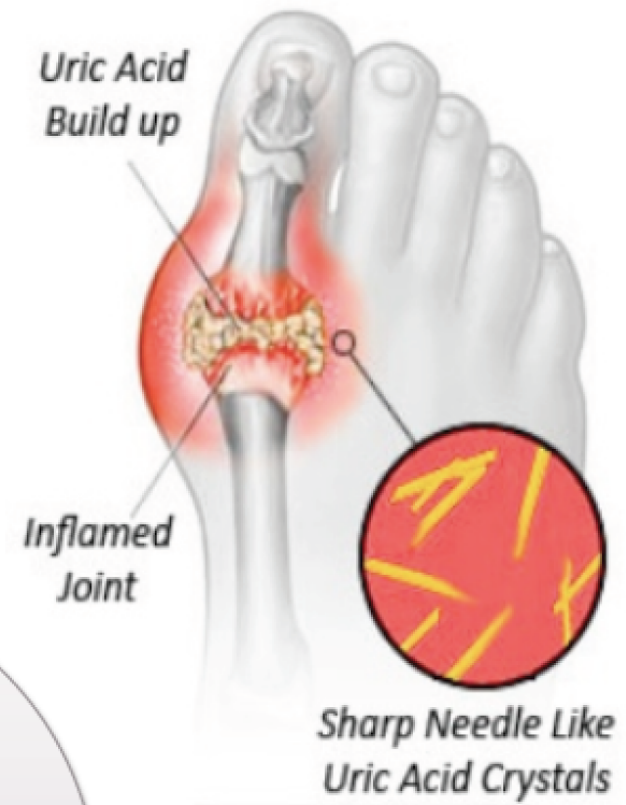
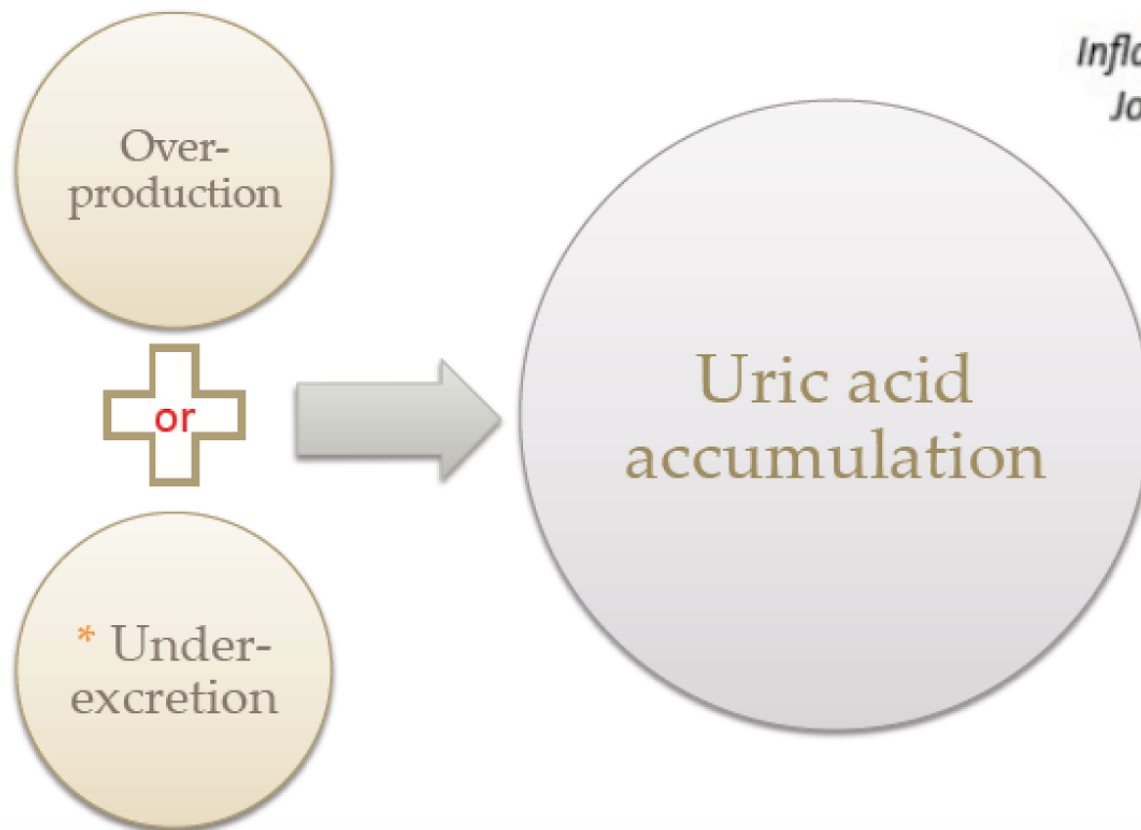
In humans, primates, birds and reptiles the final product of purine degradation is uric acid
 Uric acid is excreted in the urine
 Some animals convert uric acid to other products:

NOTE: we do NOT have to know the enzymes for the animal degradation "YAY" we only should know the products names

- Allantoin
- Allantoic acid
- Urea
- Ammonia

Gout

- Gout is a disease due to **high levels of uric acid** in body fluids.
- **7.0 mg/dL and above.**



*It is decreasing in excretion of uric acid

- Painful arthritic joint inflammation due to **deposits of insoluble** sodium urate crystals (especially big toe)
- Sodium urate crystals accumulate in kidneys, ureter, joints leading to chronic gouty arthritis

Affects 3 per
1000 persons



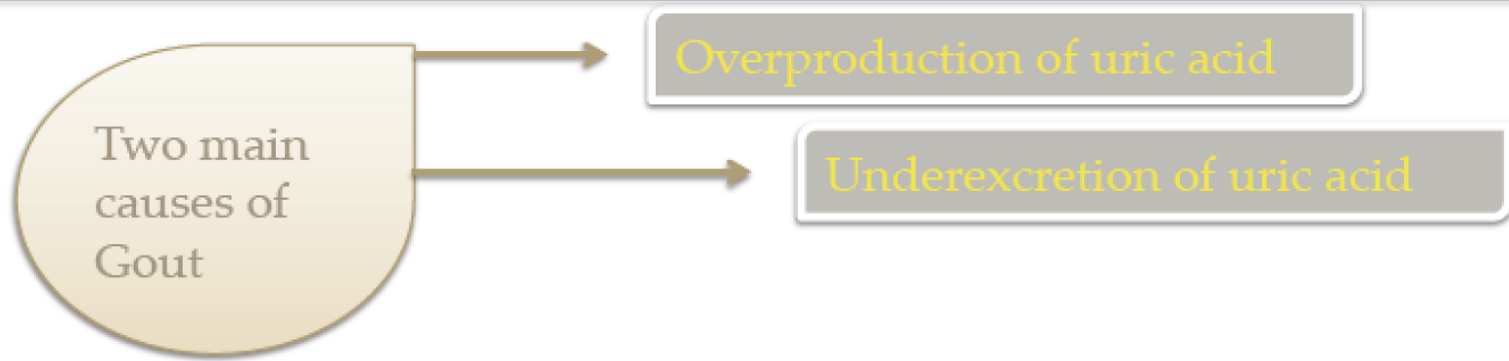
Sodium urate crystals in urine

- **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

Main
reason

Excessive meat consumption
increases uric acid production
in some individuals





Types of Gout:

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
- Hyperuricemia does not always cause gout

Hyperuricemia is an abnormally high level of uric acid in the blood and is typically asymptomatic and does not lead to gout, but gout is preceded by hyperuricemia

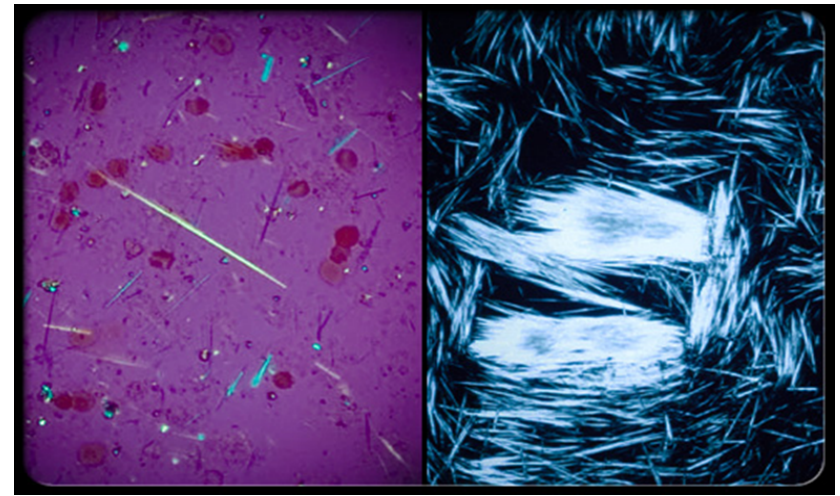
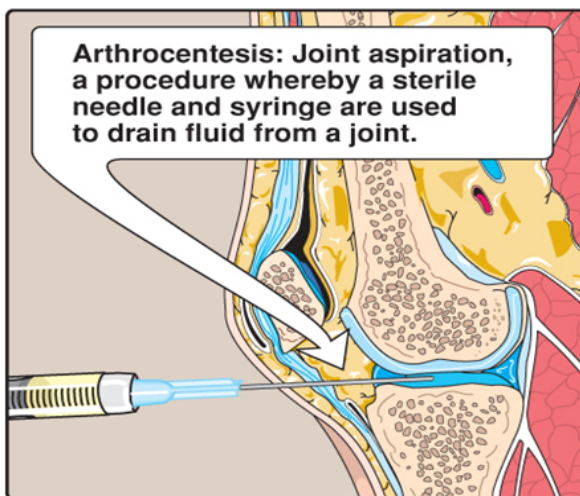
chronic tophaceous gout

Nodular masses of monosodium urate crystals (tophi) may be deposited in the soft tissues.

Diagnostic features : - —usually affect joints in the **lower extremities (95%)** - —onset is fast and sudden

—**pain is usually severe** - joint may be swollen, red and hot— - attack may be accompanied by fever, leukocytosis and an elevated ESR

Diagnosis : 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



aspiration of synovial fluid

Monosodium urate crystal



Treatment



Non pharmacological

- **Avoid purine rich foods:**
 - red meat and organ meat (liver, kidneys)
 - shellfish, anchovies, mackerel, herring
 - meat extracts and gravies
 - peas and beans, asparagus, lentils
 - alcoholic beverages
- **Weight loss**
- **Control alcohol**

Pharmacological

- 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**)

❖ Quiz:

1- The major source of dietary nucleic acid (purines and pyrimidines) is:

- A. Meat
- B. Milk
- C. Beans
- D. Fish

2- Purine and pyrimidine bases are absorbed by the:

- A. Kidney
- B. Stomach
- C. Intestine
- D. Liver

3- The final product of purine degradation is:

- A. Adenosine
- B. Uric acid
- C. Xanthine
- D. Guanine

4- Uric acid accumulates because of:

- A. Overproduction
- B. Underexcretion
- C. Both A & B
- D. Non of the above

5- Hyperuricemia always cause gout:

- A. T
- B. F

6- Gout usually affect joints in the:

- A. Lower extremities
- B. Upper extremities
- C. Both A & B
- D. Non of the above

7- Which of the following is a treatment for gout:

- A. Analgesics
- B. Uricosuric agents
- C. Allopurinol
- D. All of the above

1- A

2- C

3- B

4- C

5- B

6- A

7- D

◆ Some videos about Purine degradation and gout



Uric Acid and Gout: Foods, Symptoms, Causes, and Prevention

<http://www.youtube.com/watch?v=RNSIVCkwIIO>

What Is Uric Acid ? Foods High In Uric Acid - Uric Acid Level Blood Test

<http://www.youtube.com/watch?v=IOePUM6mRyU>

Purine metabolic pathway

http://www.youtube.com/watch?v=mIJVb_HXUQk

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