NUCLEIC ACIDS METABOLISM

Functions of nucleic acids

Nitrogenous bases purines pyrimidines

Primary structure of DNA

Purines and pyrimidines catabolism

Gout disease

Adenosine deaminase deficiency (ADA)

Functions of nucleic acids

I. Nucleic acids are responsible for the direction of metabolism throughout the life of a cell.

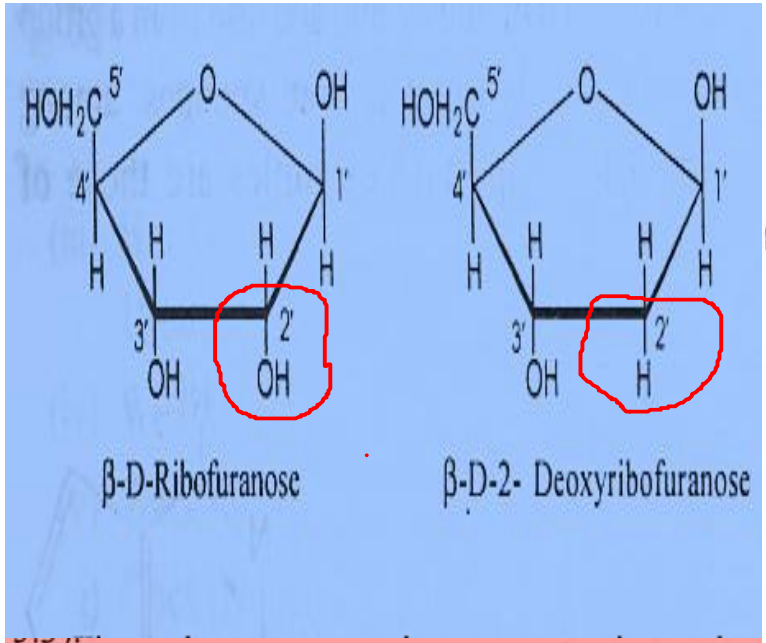
II. They direct the synthesis of proteins.

III. They control the synthesis of enzymes.

IV. They are responsible for the transfer of genetic information from one offspring to another.

V. For clinician, they are of major interest as they are undoubtedly involved in the causation of cancers (**malignancies**).

Pentose sugar Nitrogenous bases
purines Pyrimidines



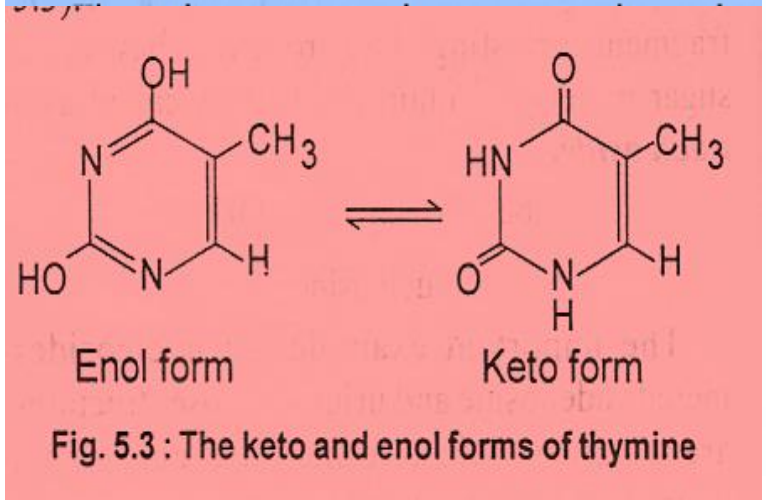
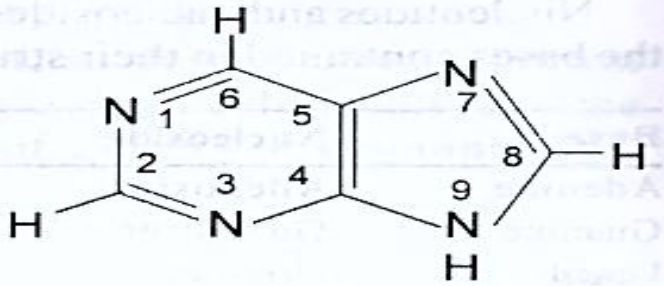
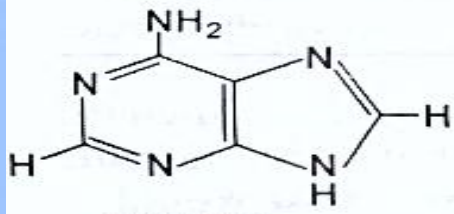
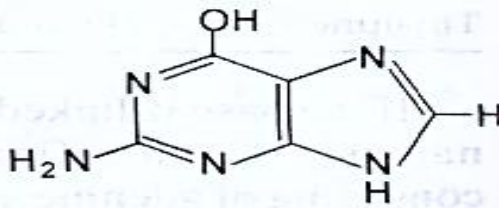


Fig. 5.3 : The keto and enol forms of thymine

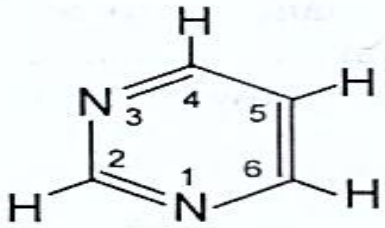
Purines

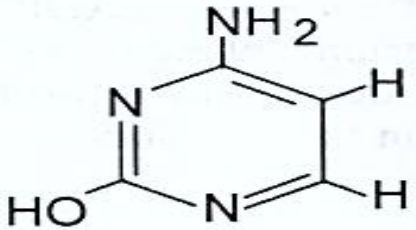


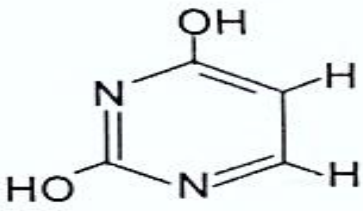


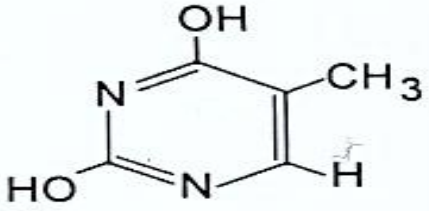


Pyrimidines

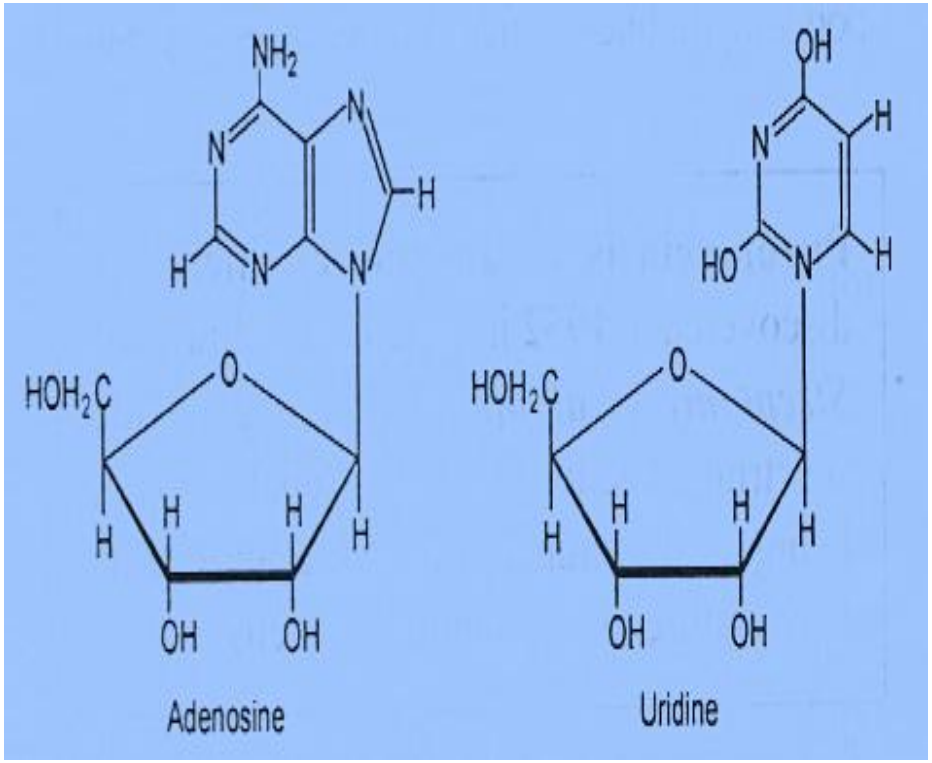


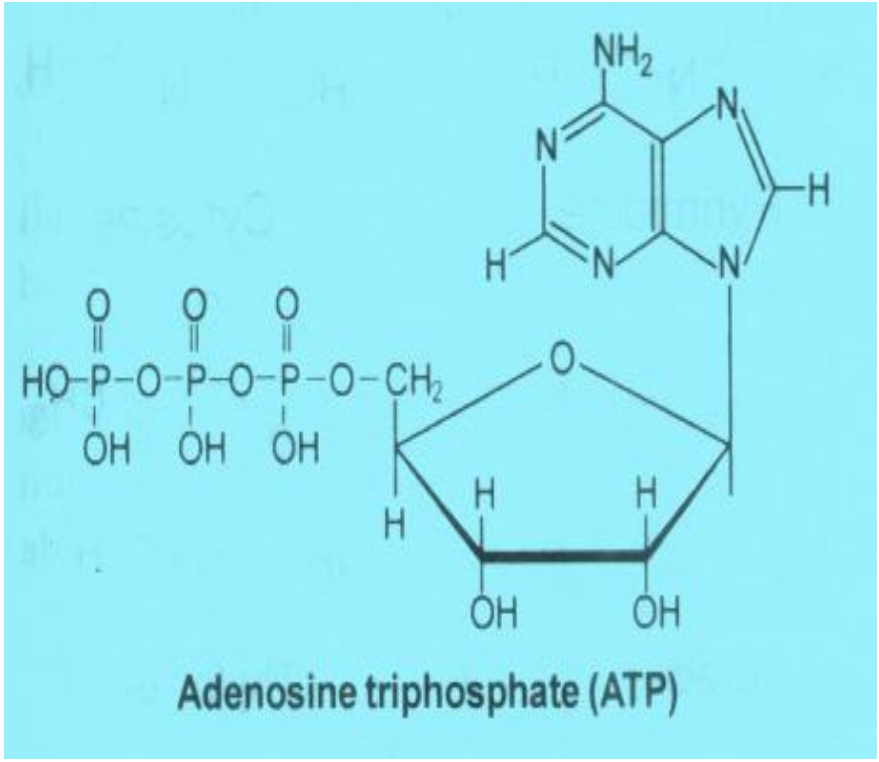






Base	Nucleoside	Nucleotide
Adenine	Adenosine	Adenylic acid
Guanine	Guanosine	Guanylic acid
Uracil	Uridine	Uridylic acid
Cytosine	Cytidine	Cytidylic acid
Thymine	Thymidine	Thymidylic acid





Hydrogen bonds between the bases

DAN is very complicated molecule which consists of two chain of polynucleotides which interwoven in the form of **aspiral structure** which stabilized by hydrogen bonding between particular base pairs.

The stereochemistry of the bases is such that **adenine pairs with thymine** and **guanine with cytosine** so that the ratio of A/T and G/C is unity.

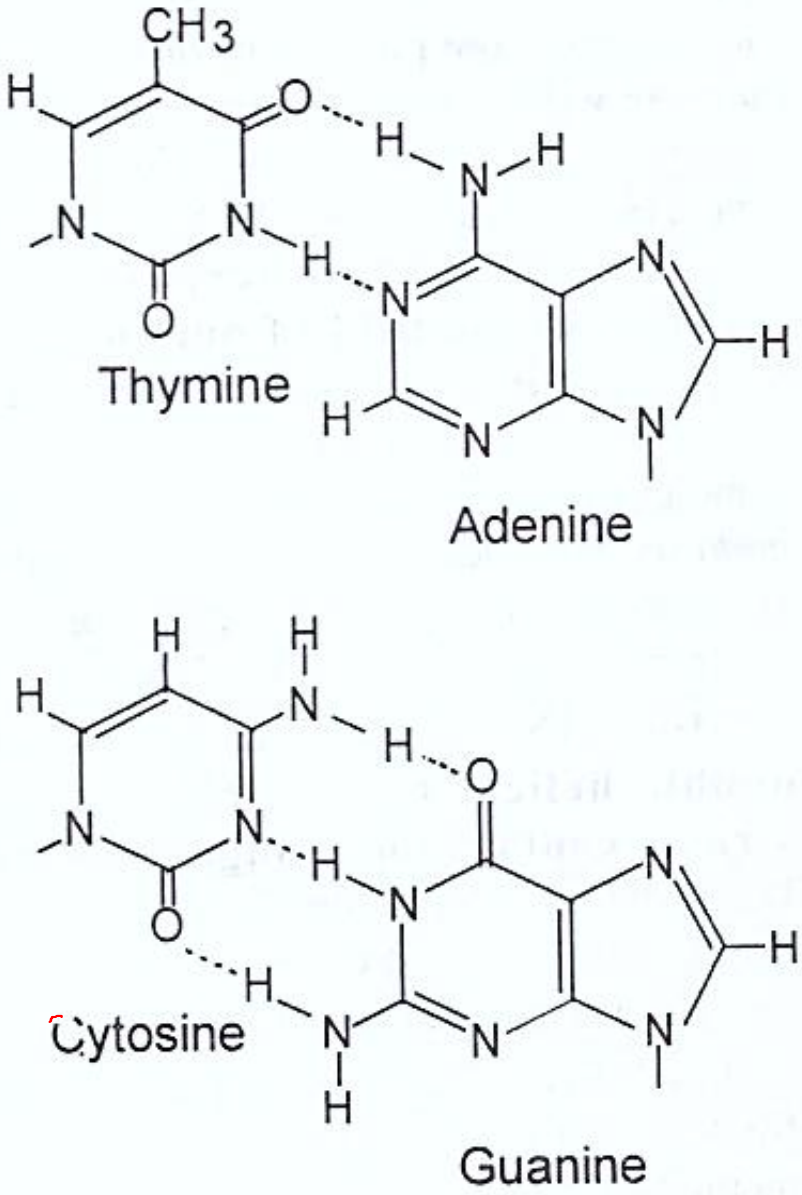


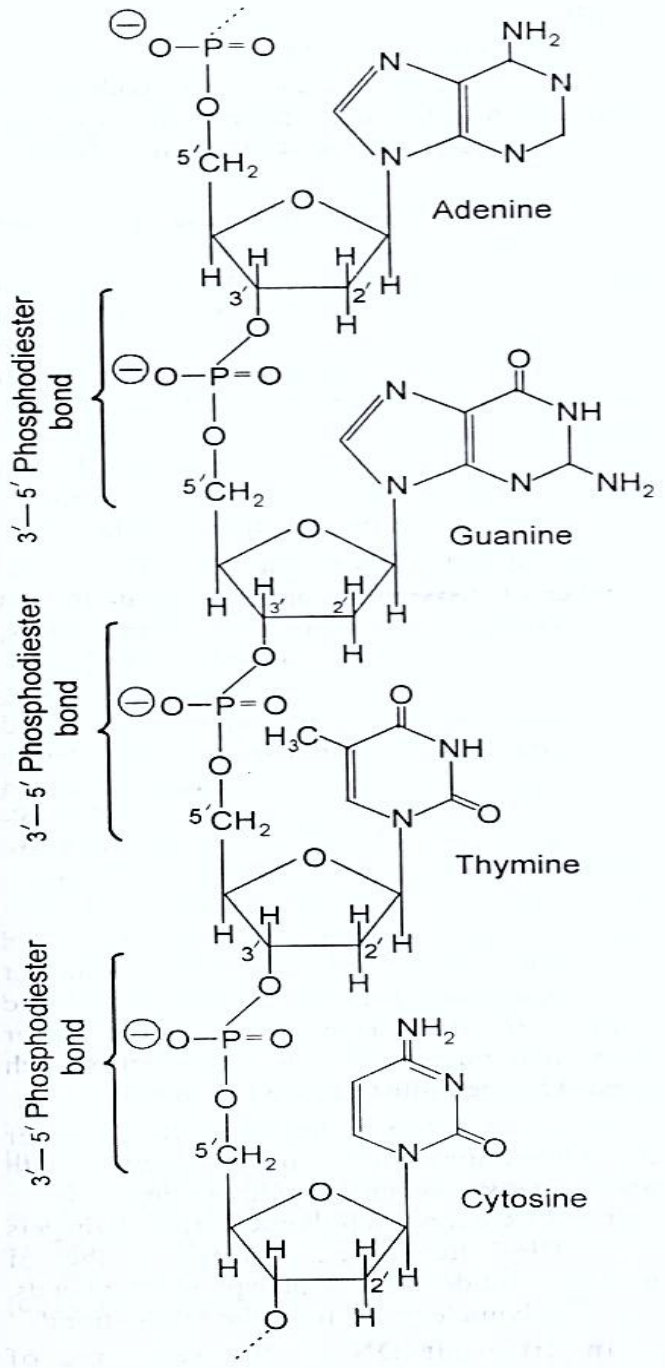
Fig. 5.6 : The pairing of bases by hydrogen bonding (- . - - - - -) as in DNA

Primary structure of DNA

- **DNA** is a linear polymer (double strand in its native state of 21-deoxynucleotide residues which remain linked to each other by **phosphodiester** bonds between**3'and 5'**positions of the 2'–deoxyribosyl moieties.

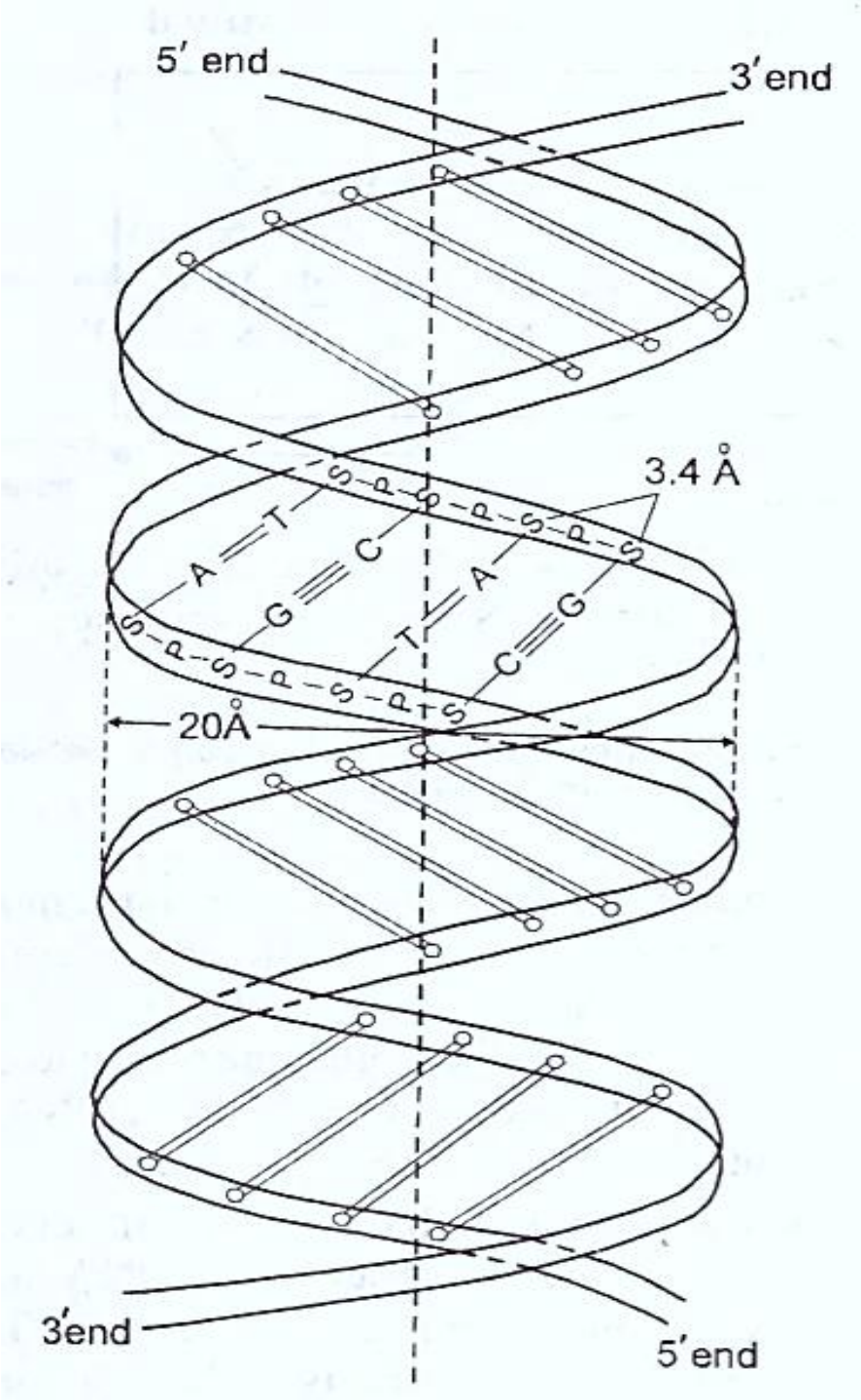
- The most common bases in DNA are

1. Adenine
2. Thymine
3. Guanine
4. Cytosine



DNA

- Most DNA molecules are of the double helical type .
- Some viruses contain only one single stranded DNA.
- DNA in the bacteriophage Φx174 is even more unusual as it is circular in shape.



Where: (i) P means phosphate diester
(ii) S means deoxyribose sugar
(iii) A = T is the adenine thymine pairing
(iv) G = C is the guanine cytosine pairing

Fig. 5.9 : Double helical structure of DNA

Purines catabolism

- Purine nucleotides are degraded by pathway in which they lose their phosphate through the action of **5ʻ-nucleotidase**.
- Adenylate yields adenosine, which is deamination to **inosine** by the action of **adenosine deaminase**.
- **Inosine** is hydrolyzed to **hypoxanthine** and D-ribose.
- **Hypoxanthine** is oxidized successively to **xanthine** and then **uric acid** by **xanthine oxidase** .
- GMP catabolism also yields uric acid as end product.

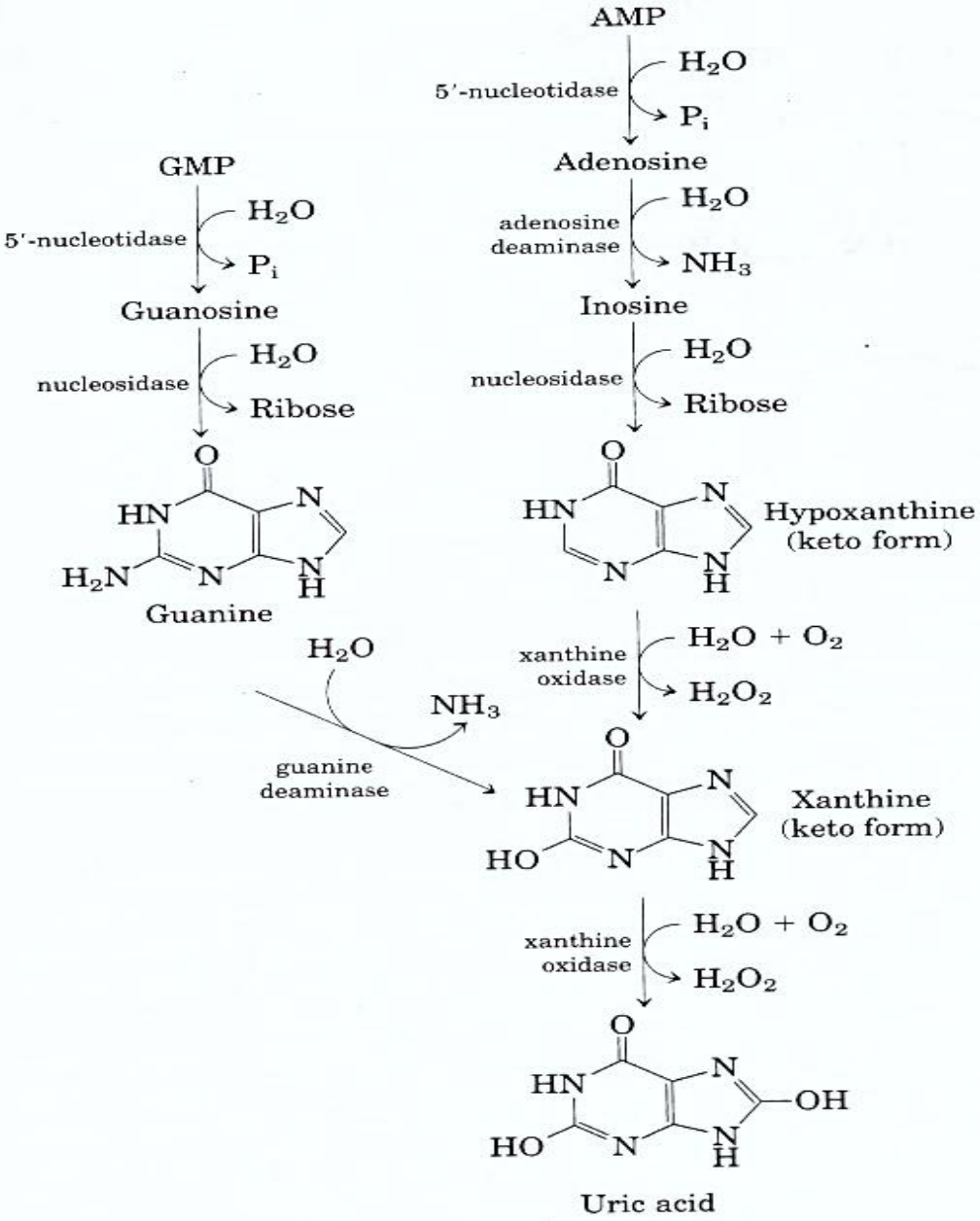
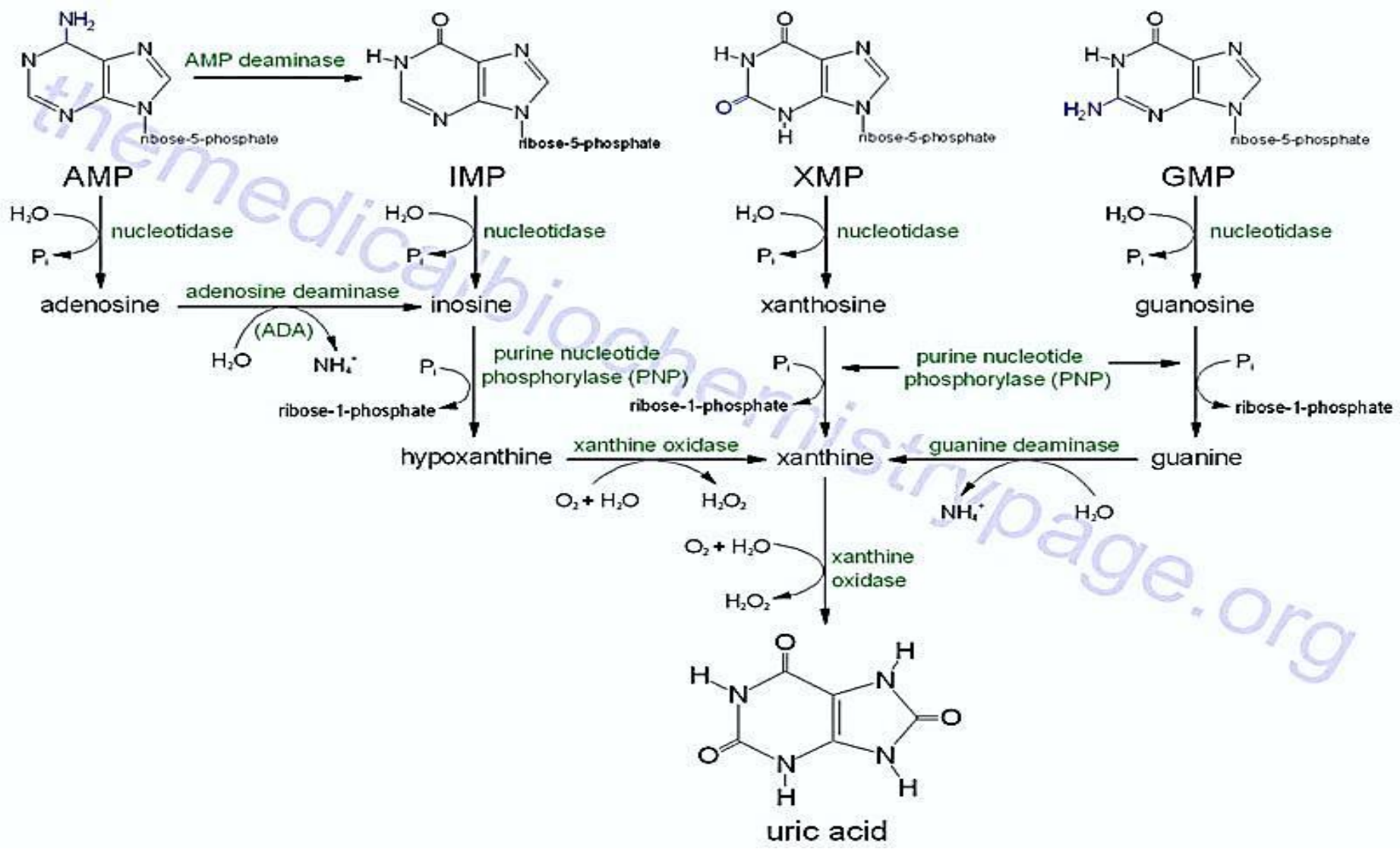
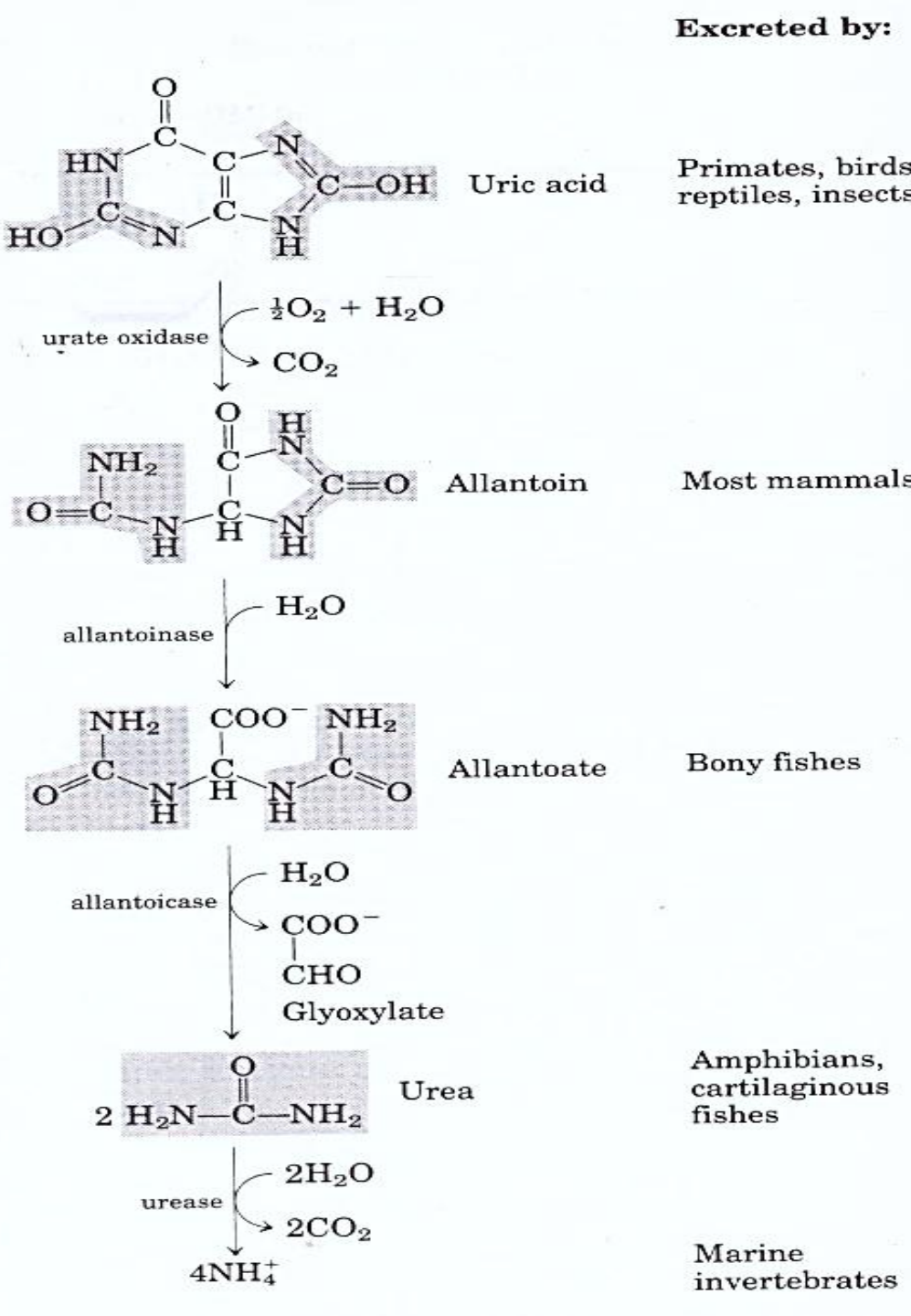


Illustration of uric acid pathway



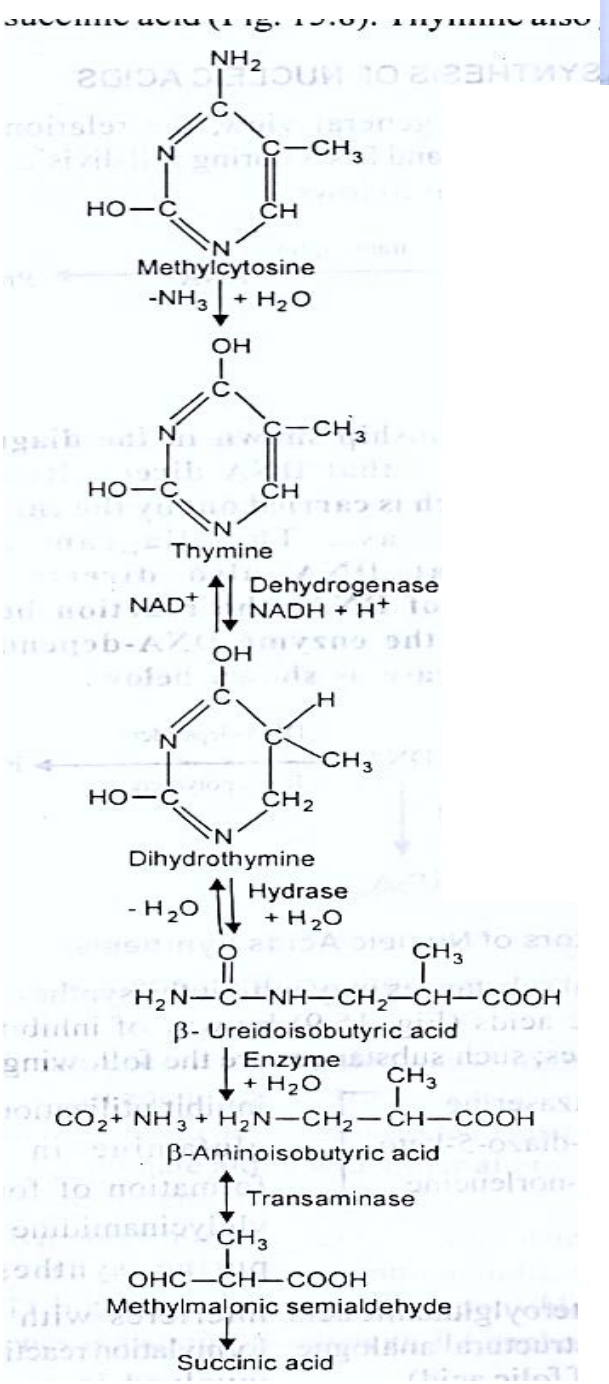
Purines catabolism in other organisms

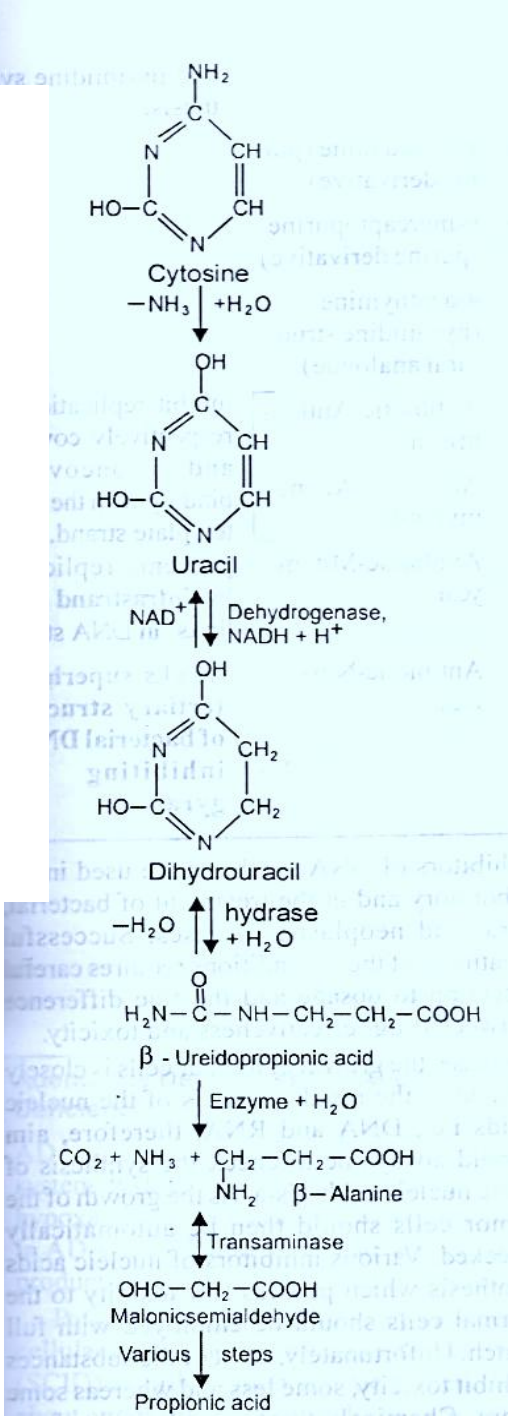
- **Uric acid** is the excreted end product of purine catabolism in primates, birds, and some other animals.
- In most mammals and many other vertebrates , uric acid is further degraded to **allantoin** by the action of **urate oxidase**.
- In other organisms the pathway is further extended as shown



Pyrimidine catabolism

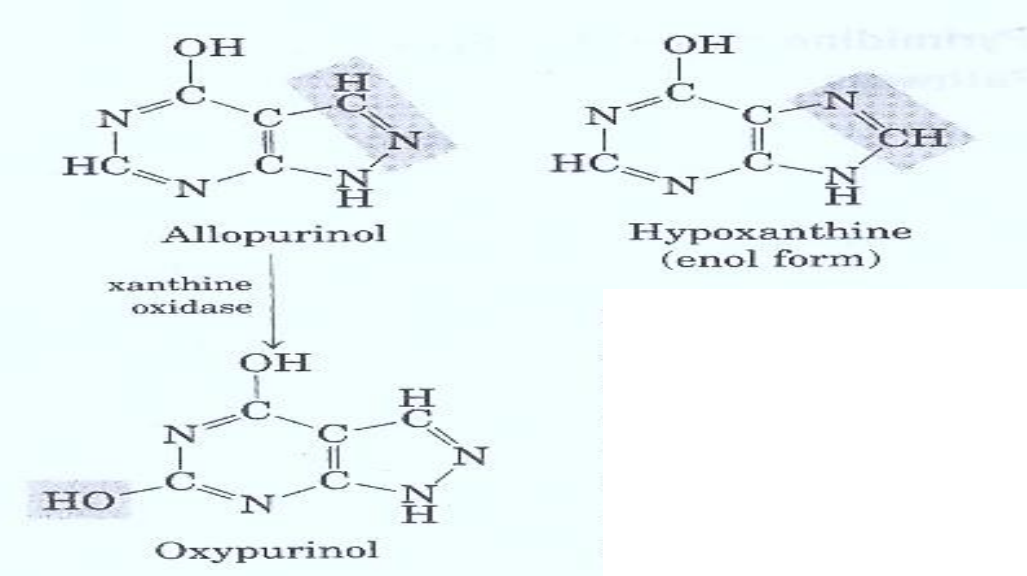
- The pathways of degradation of pyrimidine generally lead to NH^+_4 production and thus **urea** synthesis.
- **Thymine** is degraded to **methyl-malonylsemialdehyde**, an intermediate of valine catabolism.
- It is further degraded through **propionyl-CoA** and **methylmalonyl-CoA** to **succinyl-CoA.**





Excess uric acid causes GOUT

- Long thought, erroneously, to be due to “high living”
- Gout is a disease of joints caused by an elevated concentration of uric acid in the blood and tissue.
- The joints become inflamed, painful, and arthritic, owing to the abnormal deposition of sodium urate crystal.
- The kidney also affected as excess of uric acid is deposited in kidney tubules.
- Gout is predominantly in males. The precise cause is not known, but it often involves underexcretion of urate .
- A genetic deficiency of one or another enzyme of purine metabolism may also be factor in some cases.
- Gout is effectively treated by a combination of nutritional and drug therapies.



- Food especially rich in nucleotides and nucleic acids, such as liver or glandular products are withheld from the diet.

- Major alleviation of the symptoms is provided by drug **allopurinol**.

- Allopurinol inhibits xanthine oxidase, the enzyme that catalyzes the conversion of purine to uric acid.

- Xanthine oxidase converts allopurinol to oxypuriol.

- When xanthine oxidase is inhibited, the excreted products of purine metabolism are xanthine and hypoxanthine, which are more water soluble than uric acid and less likely to form crystalline deposits.

Adenosine deaminase deficiency (ADA)

- Genetic aberrations in human purine metabolism have been found, some with serious consequences . For example, **adenosine deaminase** (**ADA**) **deficiency** lead to sever immunodeficiency disease in which **T lymphocytes** and **B lymphocytes** do not developed properly.

- Lack of ADA leads to 100-fold increase in the cellular concentration of dATP, a strong inhibitor of ribonucteotide reductase.

- High level of dATP produce a general deficiency of others dNTPs in T lymphocytes. The basis toxicity of B lymphocytes is less clear.

- Individual with ADA deficiency lack an effective immune system and **do not survive** unless isolated in sterile “bubble” environment.