

Chemistry of Purines, Pyrimidines and Their Biological Significance



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Objectives

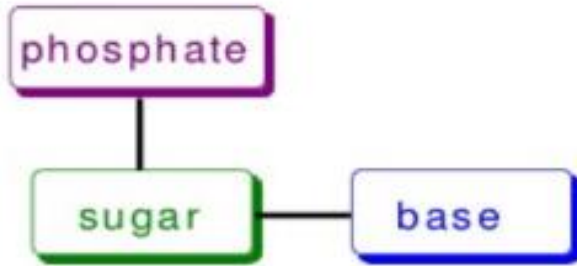
- What are Purines and Pyrimidines?- Chemistry
- What is their role in human body?- Functions
- How do we get them or get rid of them?- Metabolism
- Will there be any pathology if the metabolism is defective?- Diseases
- Can this knowledge be utilized to develop drugs?-Chemo drugs

Q1. What are Purines and Pyrimidines? Chemistry

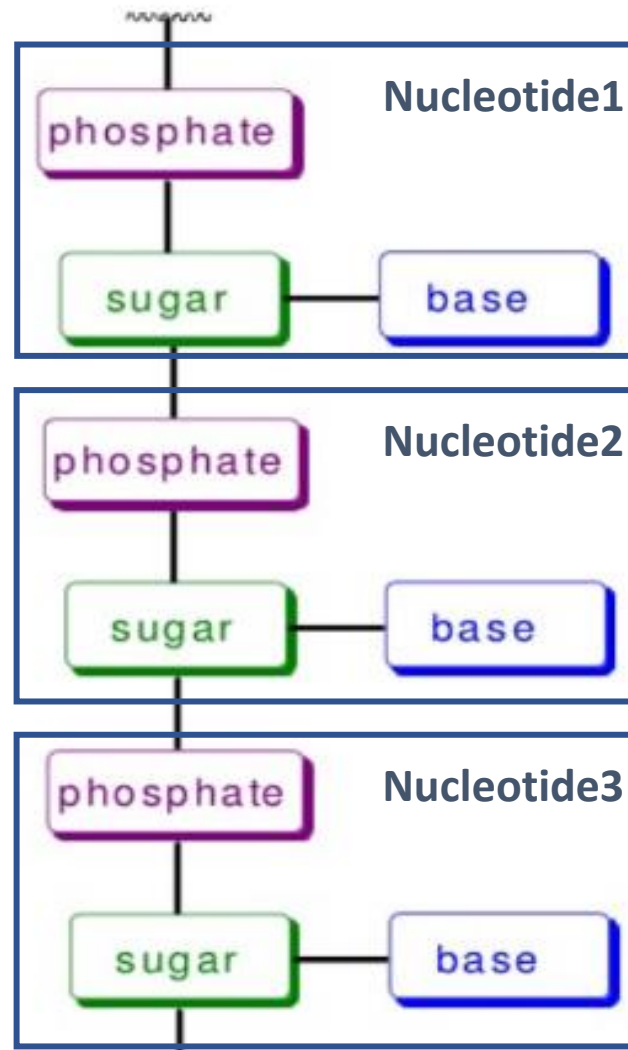
Nucleic acids are polynucleotides

- Polysaccharides
- Polypeptides
- Polynucleotides

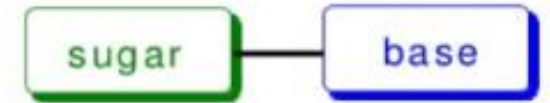
Nucleoside, Nucleotide & Nucleic acid



nucleotides

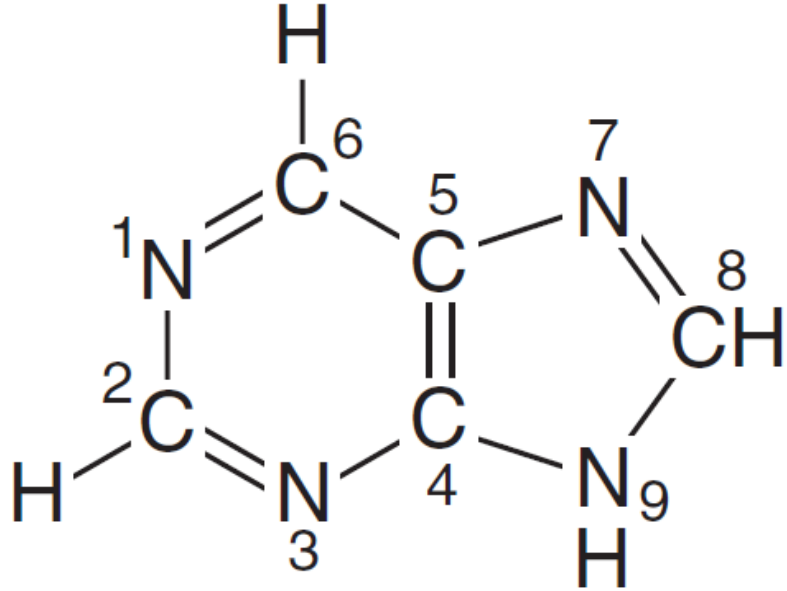


nucleic acids

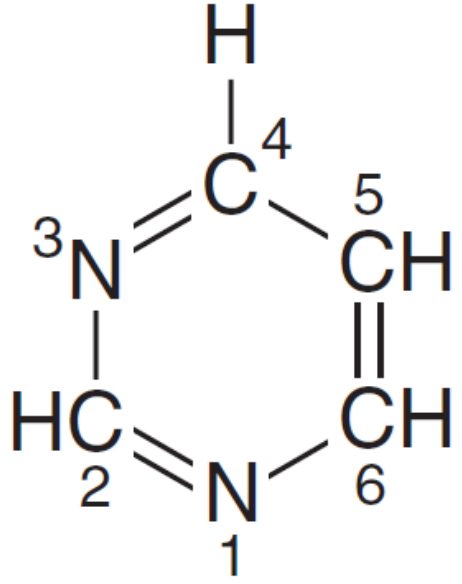


nucleoside

Base: Purines, Pyrimidines



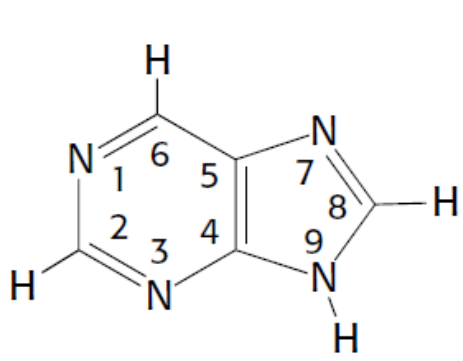
Purine



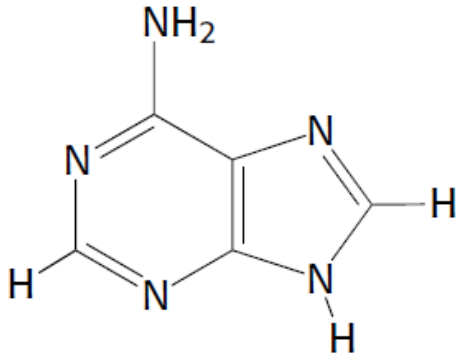
Pyrimidine

Base: Purines, Pyrimidines

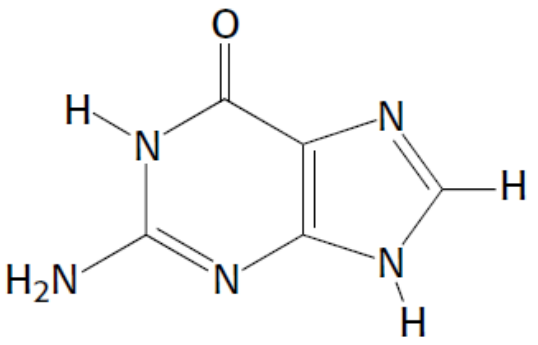
PURINES



Purine

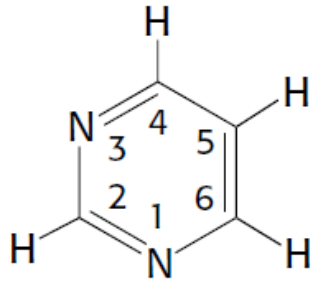


Adenine

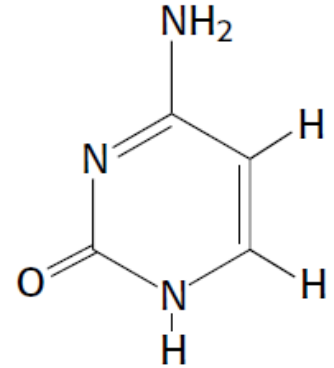


Guanine

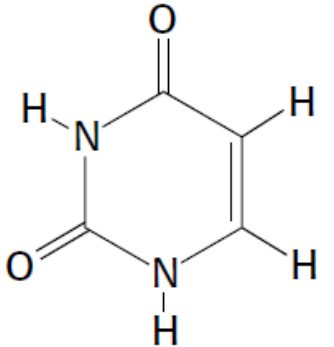
PYRIMIDINES



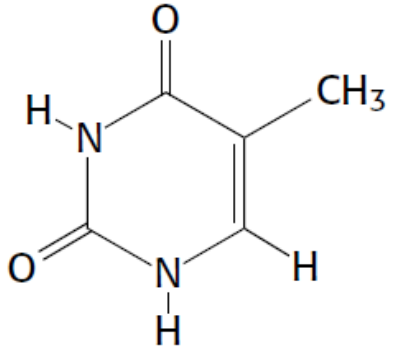
Pyrimidine



Cytosine

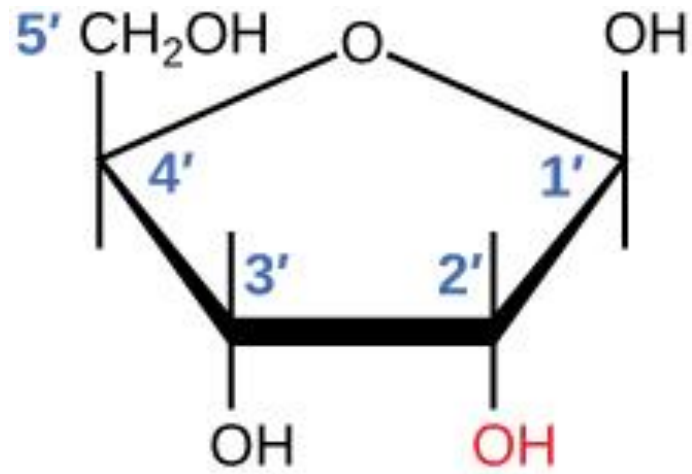


Uracil

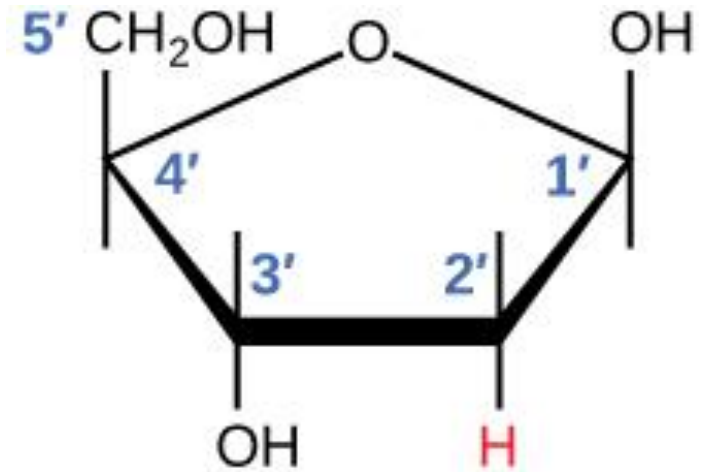


Thymine

Sugar: Ribose, Deoxy ribose

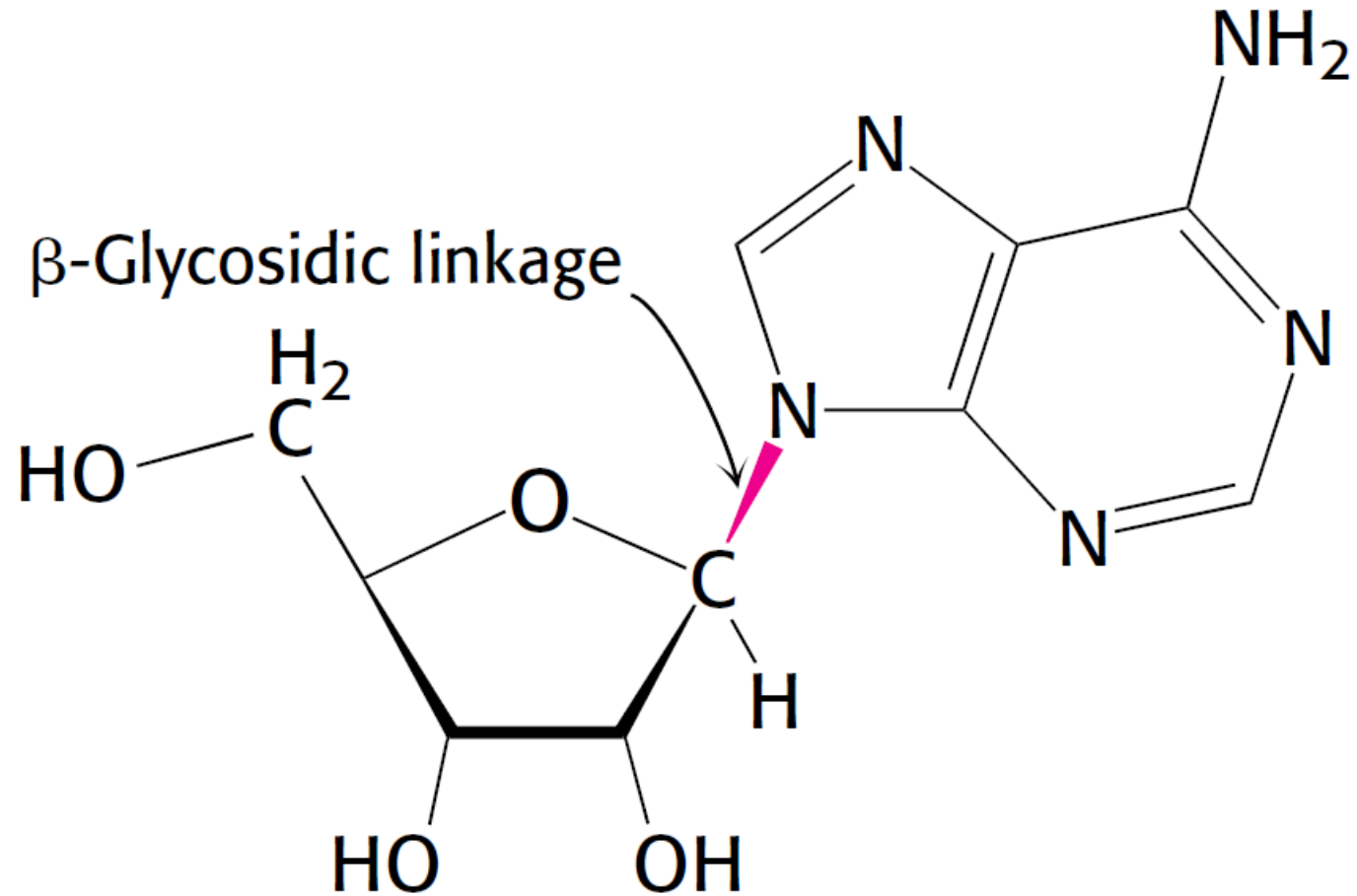


Ribose

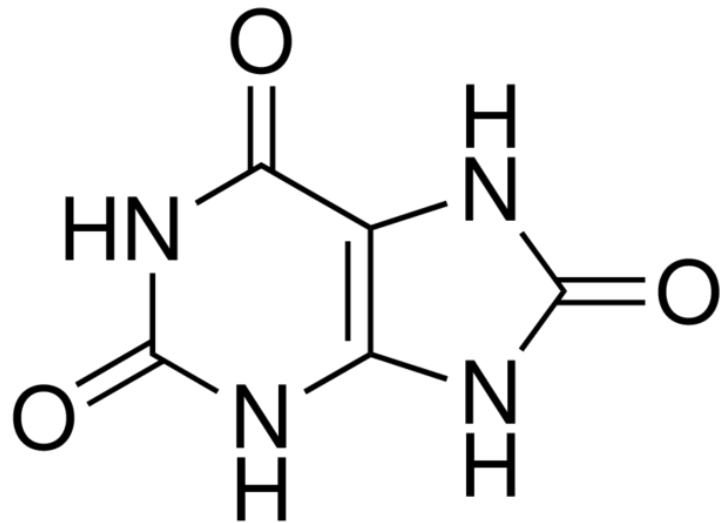


Deoxyribose

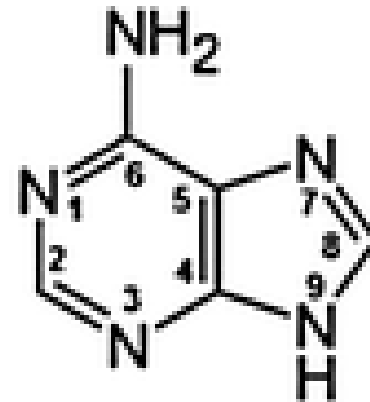
Nucleosides:



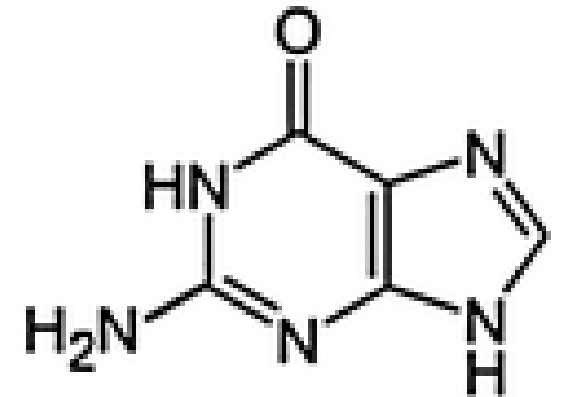
Purine Bases



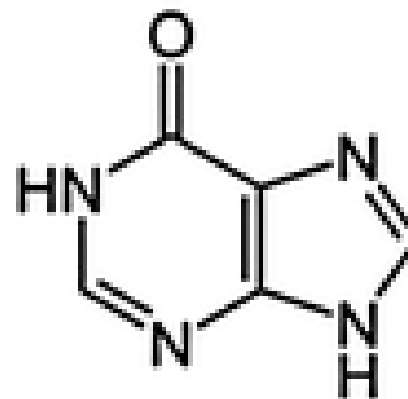
Uric acid



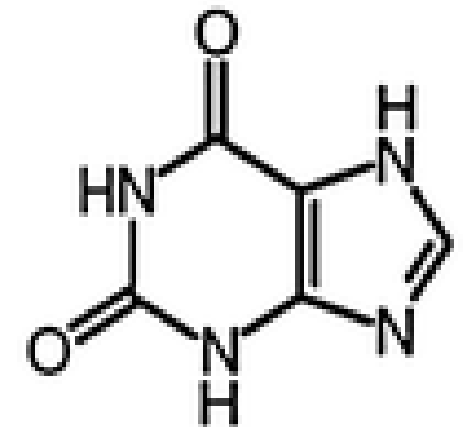
Adenine



Guanine



Hypoxanthine



Xanthine

What is their role in human body?
Functions

Role of nucleotides:

1. Monomers of nucleic acids - DNA & RNA
2. Used to activate substrates for biosynthetic reactions
 - UDP-glucose → glycogen
 - UDP-glucuronic acid → conjugation reactions
 - CDP-diacylglycerol → phosphatidyl inositol synthesis
 - CDP-ethanolamine → phosphatidyl ethanolamine synthesis
 - S-adenosylmethionine → methyl donor
 - GDP-L-fucose → Glycoproteins

3. ATP is the universal currency of energy. Thermodynamically unfavored reactions are made favorable by coupling of ATP hydrolysis.
4. Adenine nucleotides are components of the coenzymes, NAD^+ , NADP^+ , FAD & CoA
5. c-AMP, c-GMP are 2nd messengers in signal transduction
6. ATP and AMP are allosteric regulators for many enzymes
7. ATP dependent phosphorylation regulates the action of enzymes & membrane transporters.

How do we get them or get rid of them?
Metabolism

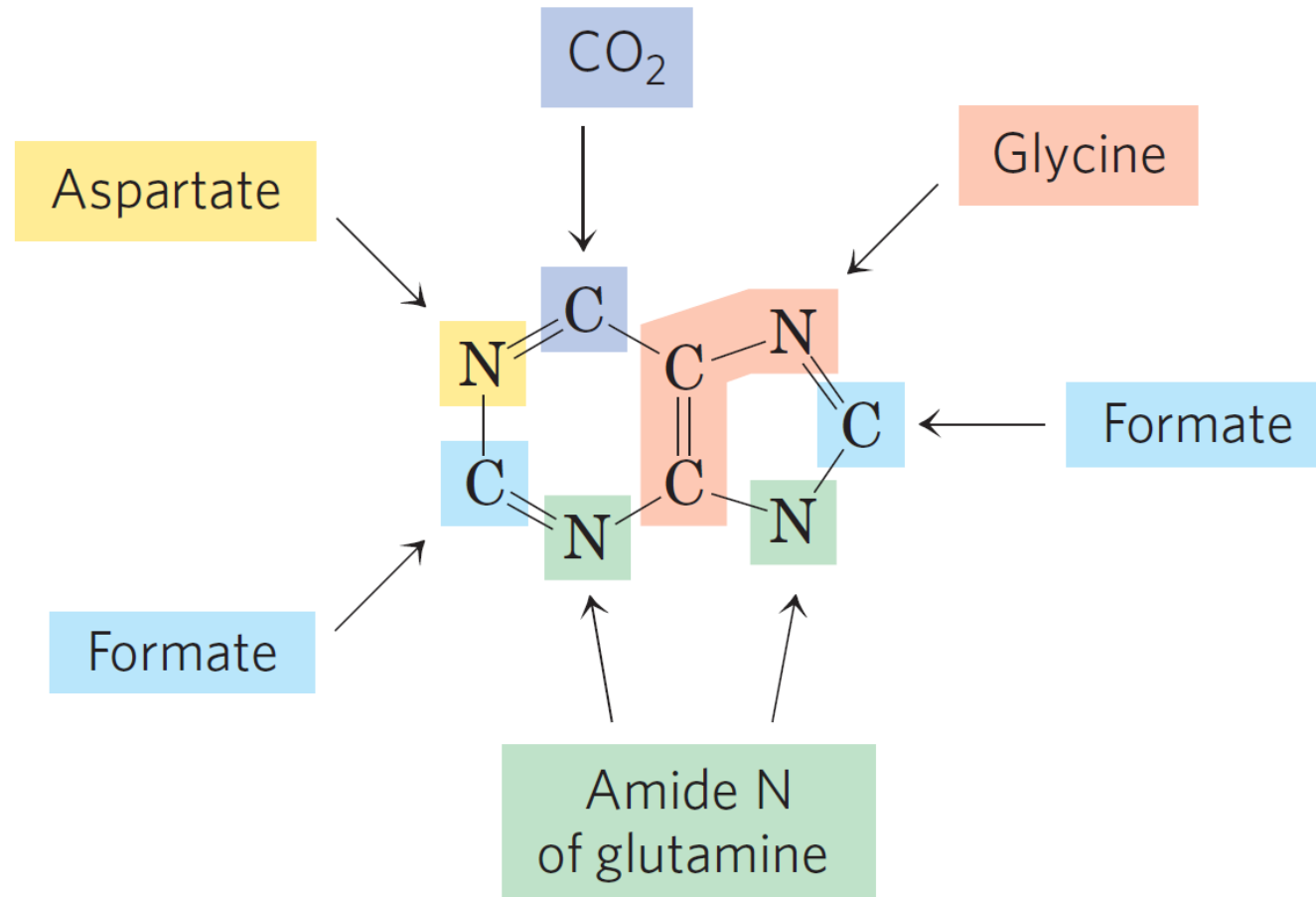
Dietary Nucleic acid

- Broken down to nucleotides
- Further, Base is released
- Purine/pyrimidine transporters in enterocytes
- Enters circulation

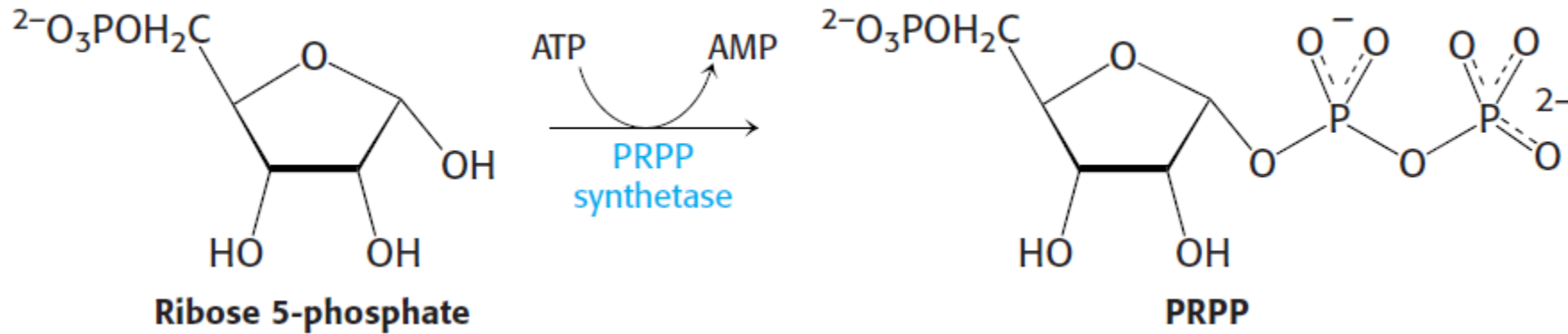
Purine/Pyrimidine Nucleotide Synthesis:

- De Novo Pathway
- Salvage Pathway

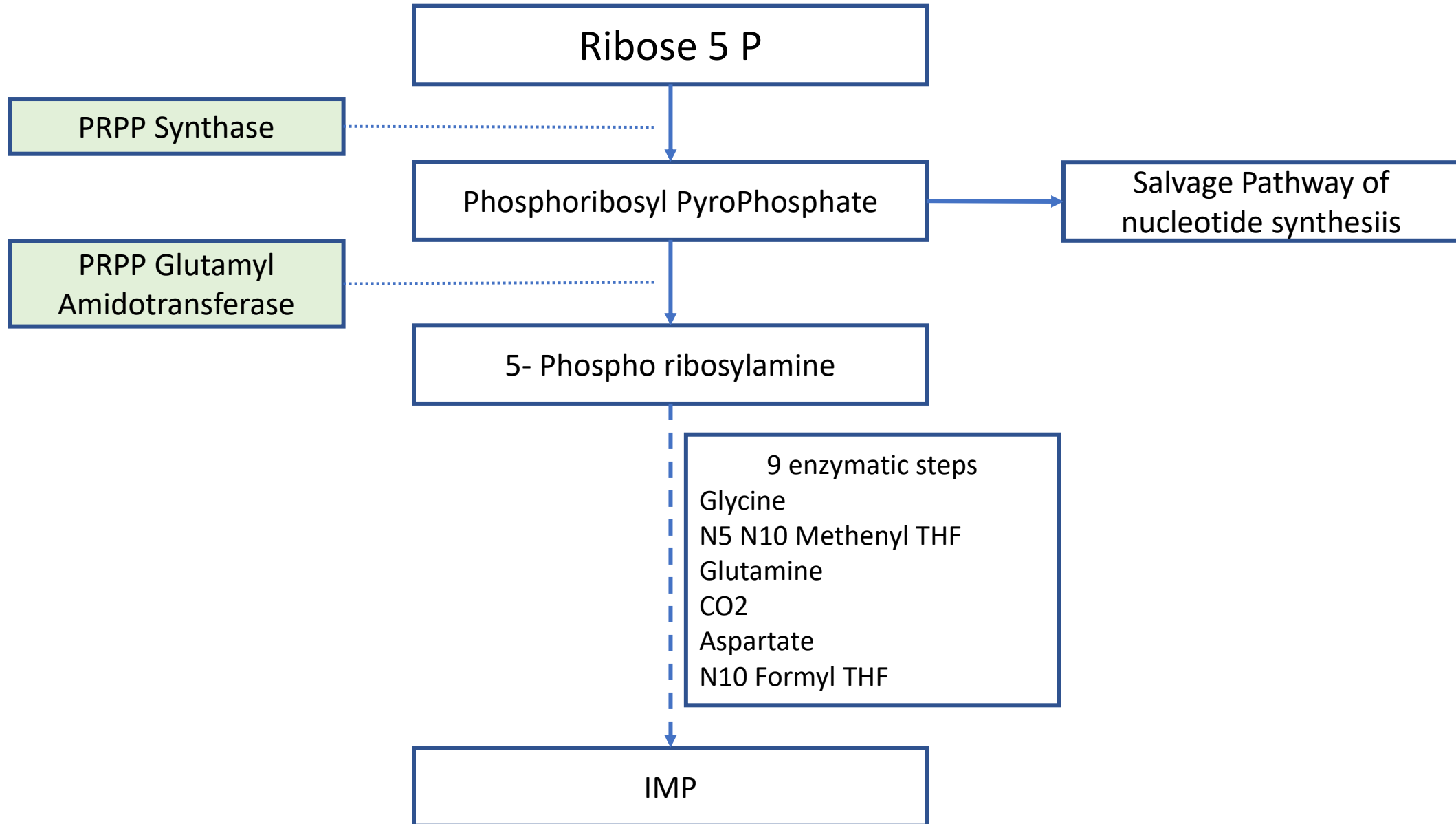
Sources of purine ring atoms



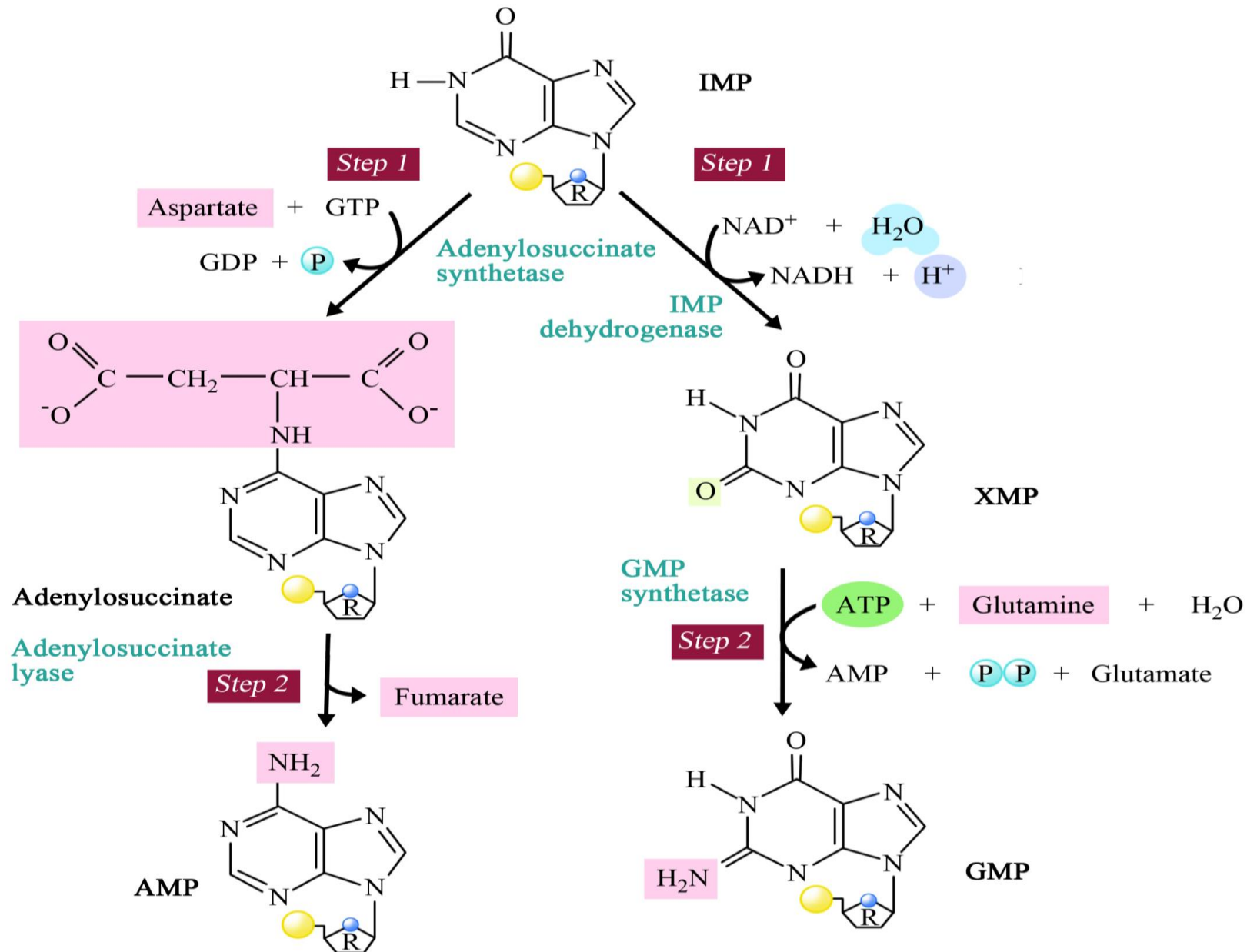
Phosphoribosyl Pyrophosphate:



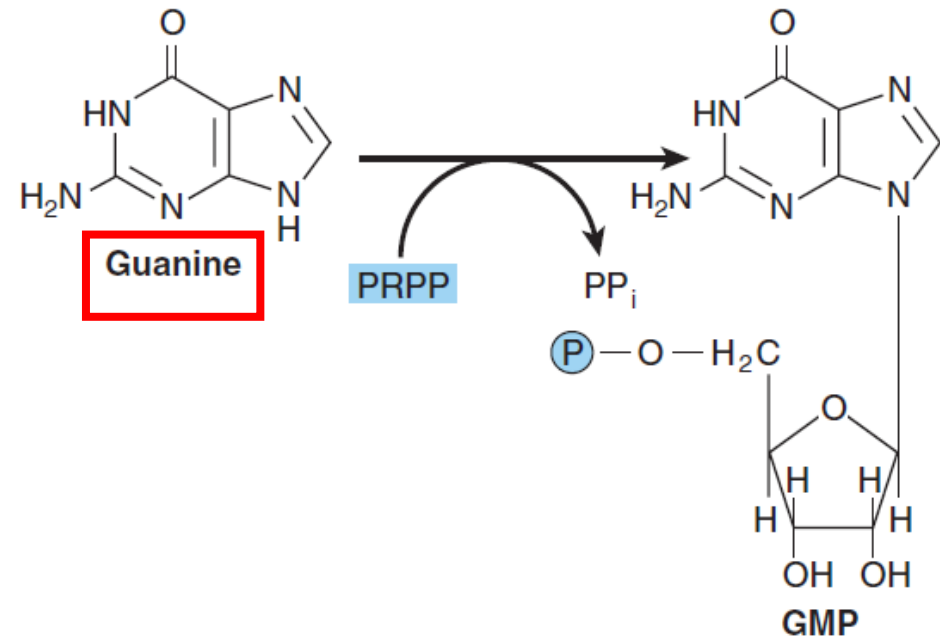
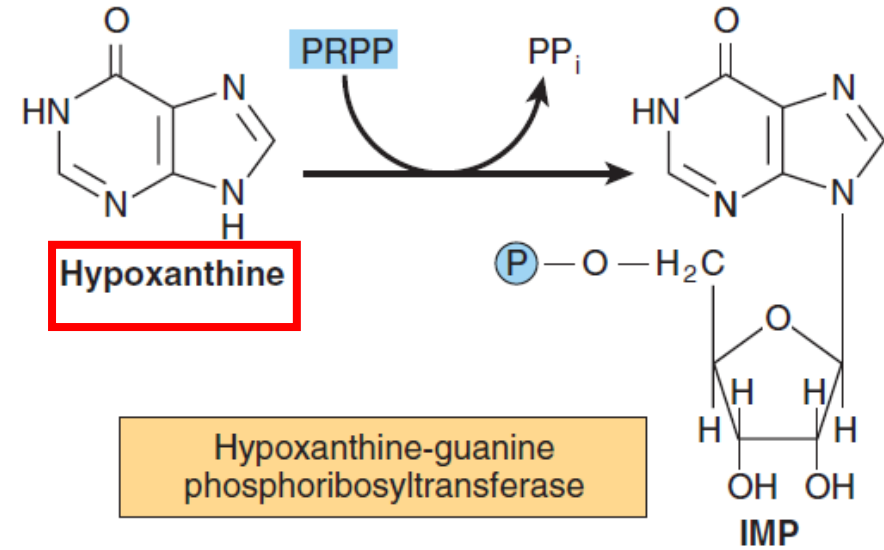
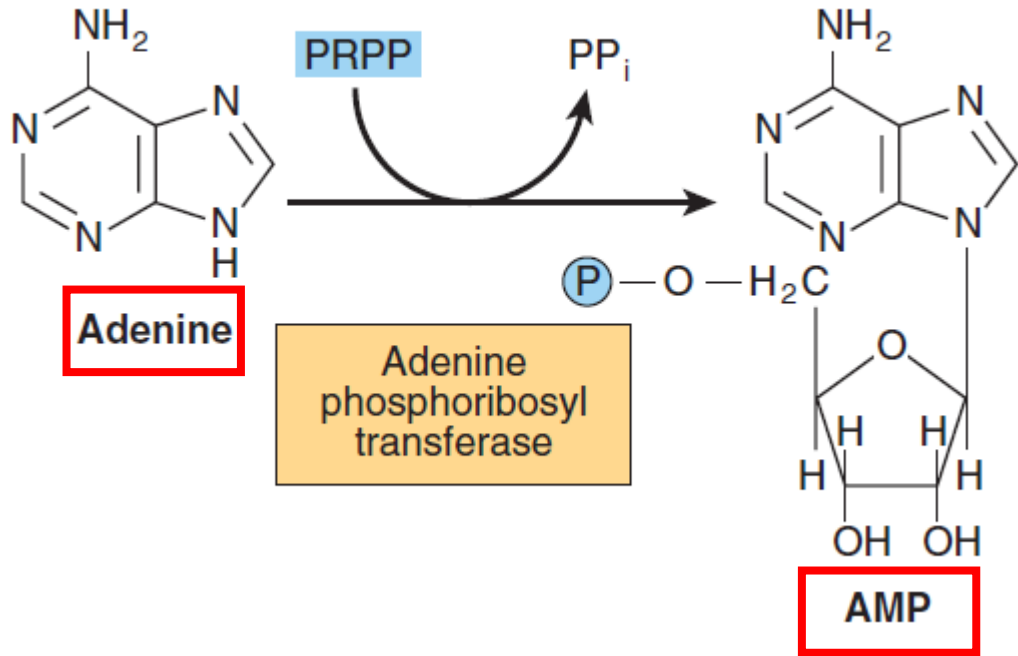
Purine Synthesis: De Novo Pathway



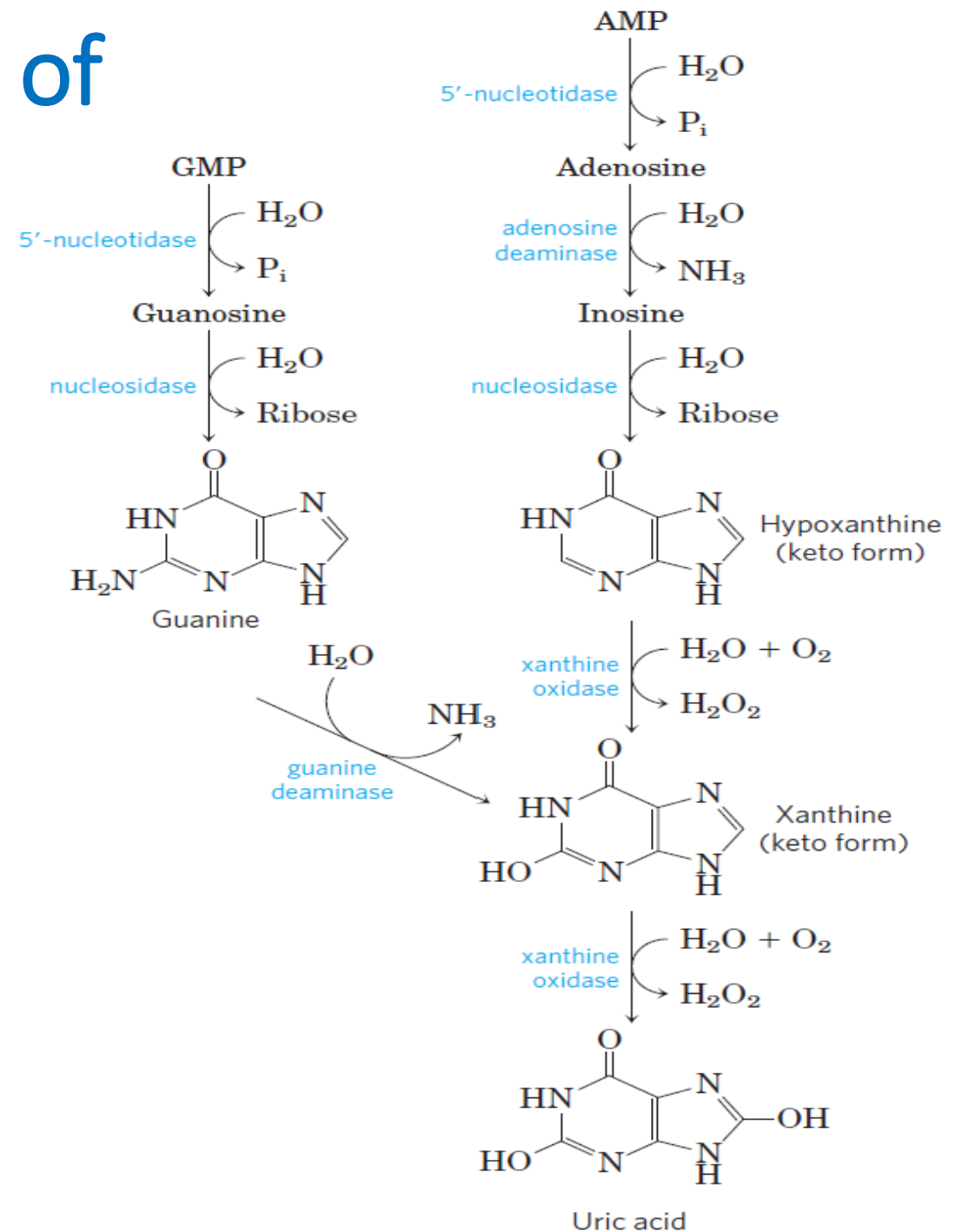
Purine Synthesis: De Novo Pathway



Purine Synthesis: Salvage Pathway



Uric Acid is the End Product of Purine Degradation



Disorders Associated with Purine Metabolism

- Gout
- Lesch-Nyhan's syndrome
- Adenosine Deaminase deficiency
- Xanthinuria

Gout is the Manifestation of Hyperuricemia

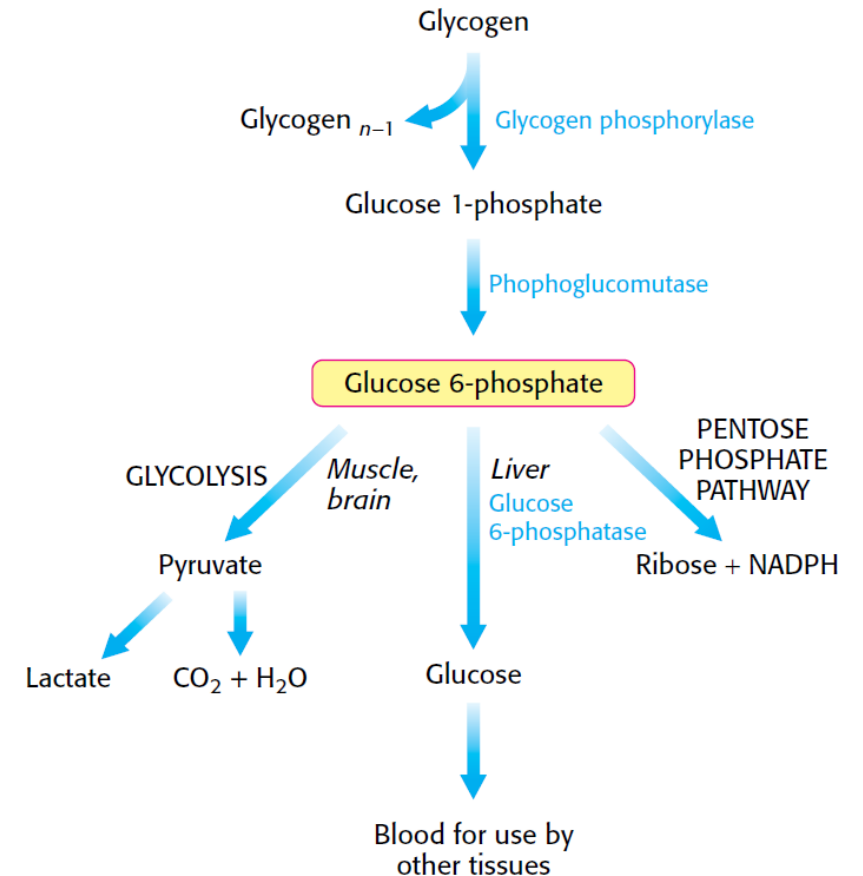
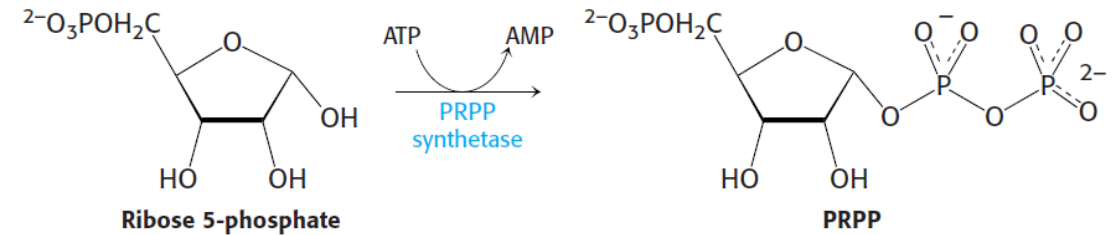
Hyperuricemia:

Increased production of uric acid

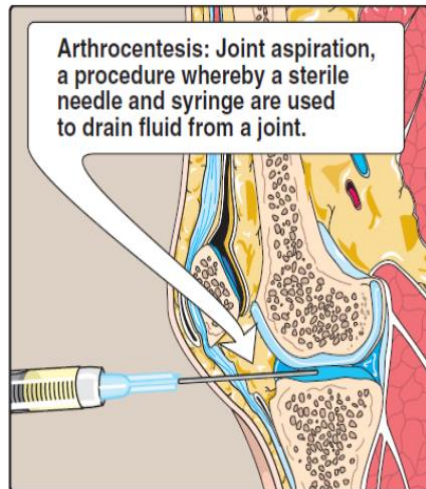
- PRPP Synthetase overactivity
- Von-Gierke's disease
- Purine rich diet
- Alcoholism
- Malignancy

Decreased excretion of uric acid

- Renal failure
- Lactic acidosis

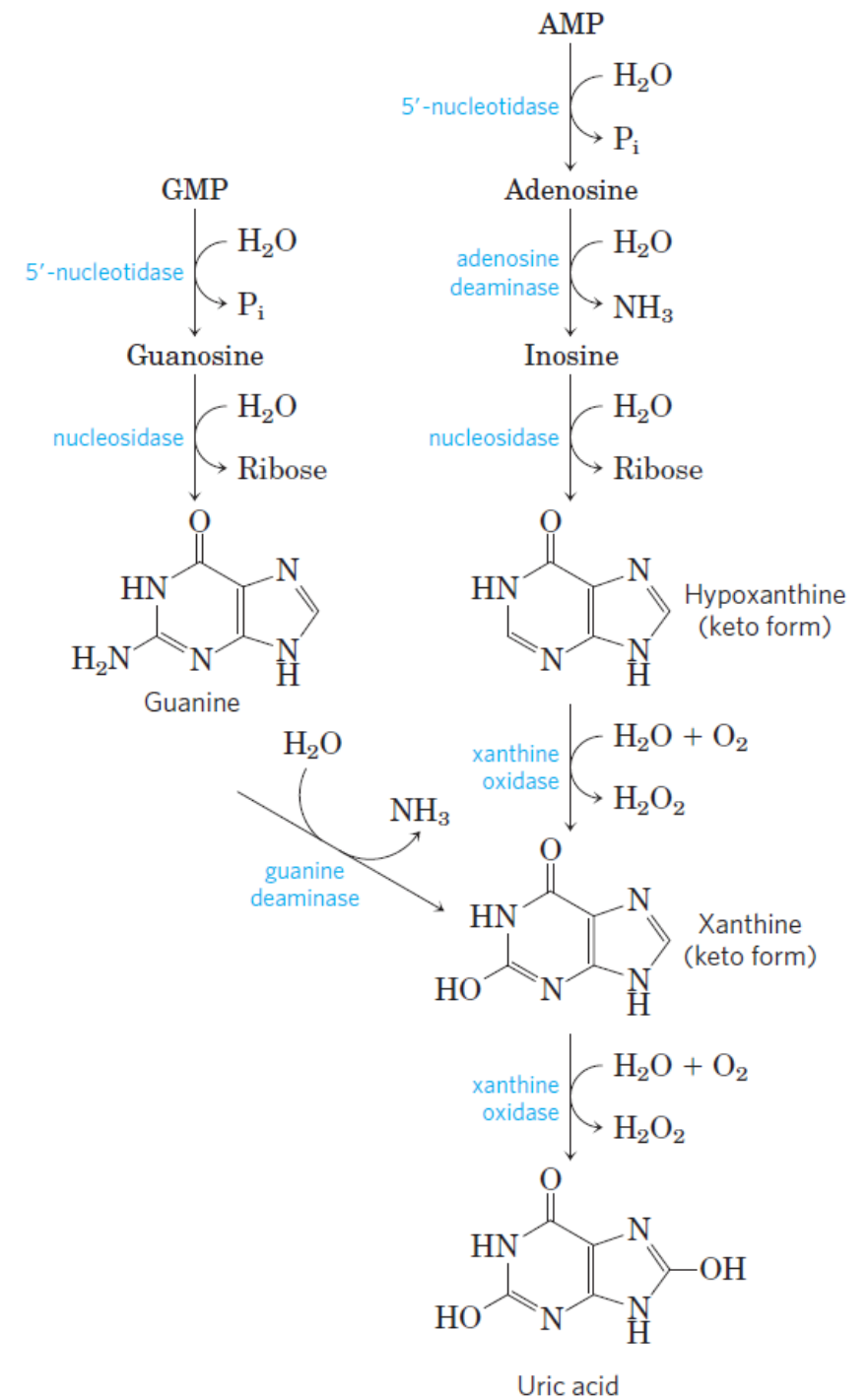


Gout:



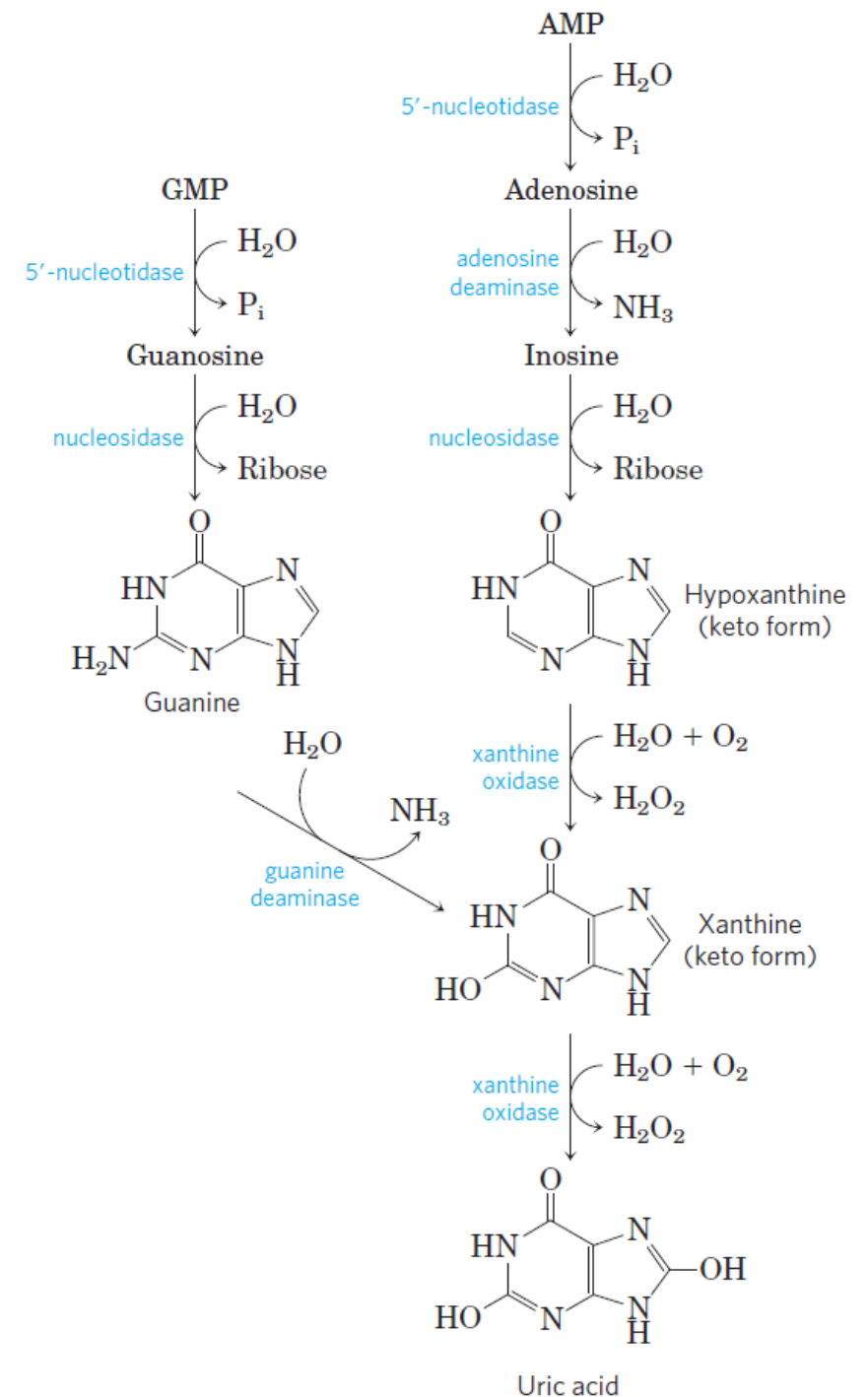
Treatment of Gout

- Low purine diet
- Avoid alcohol
- Increased water intake
- Anti-inflammatory drugs
- Allopurinol: Xanthine Oxidase Inhibitor
- Uricosuric drugs



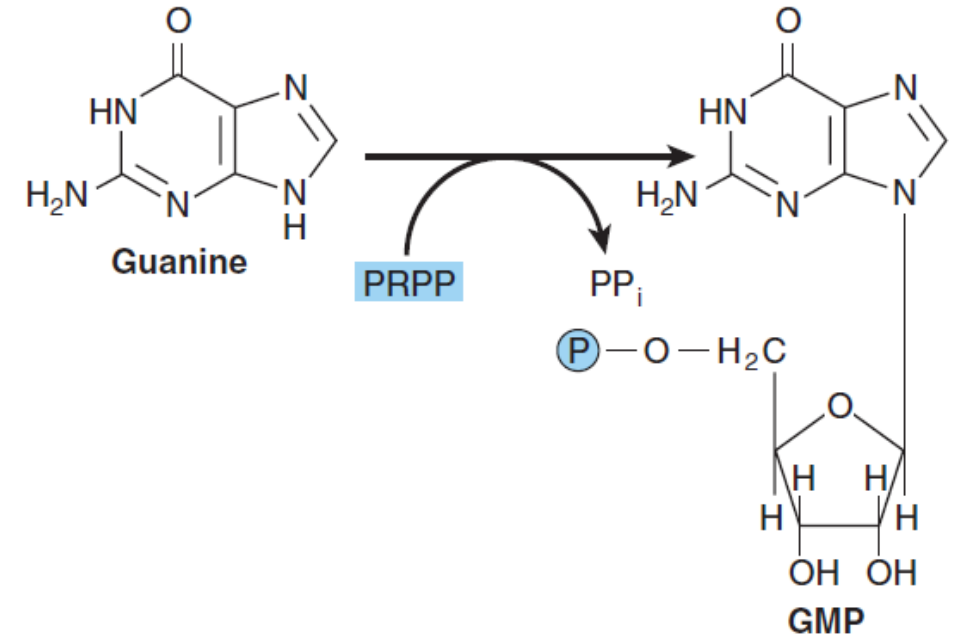
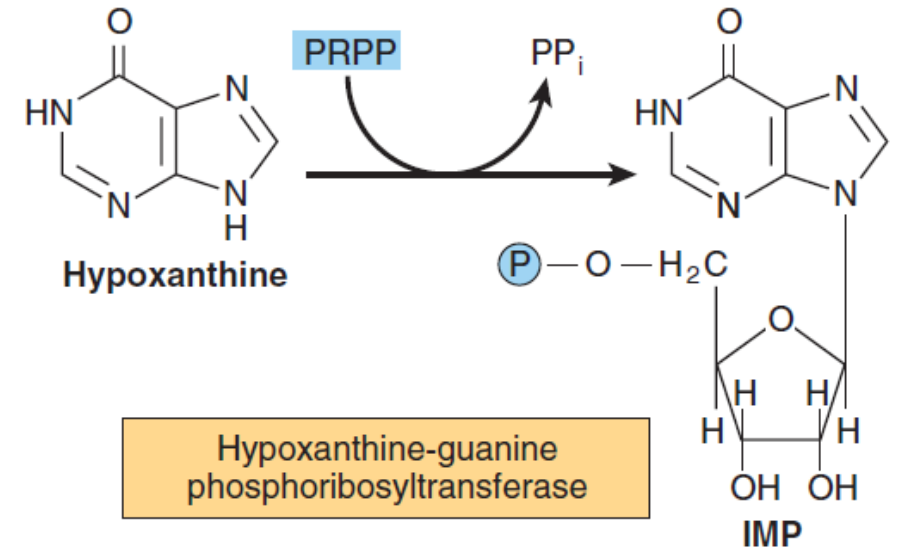
Adenosine deaminase deficiency

- Severe combined immunodeficiency
- B and T lymphocytes are affected
- First gene therapy



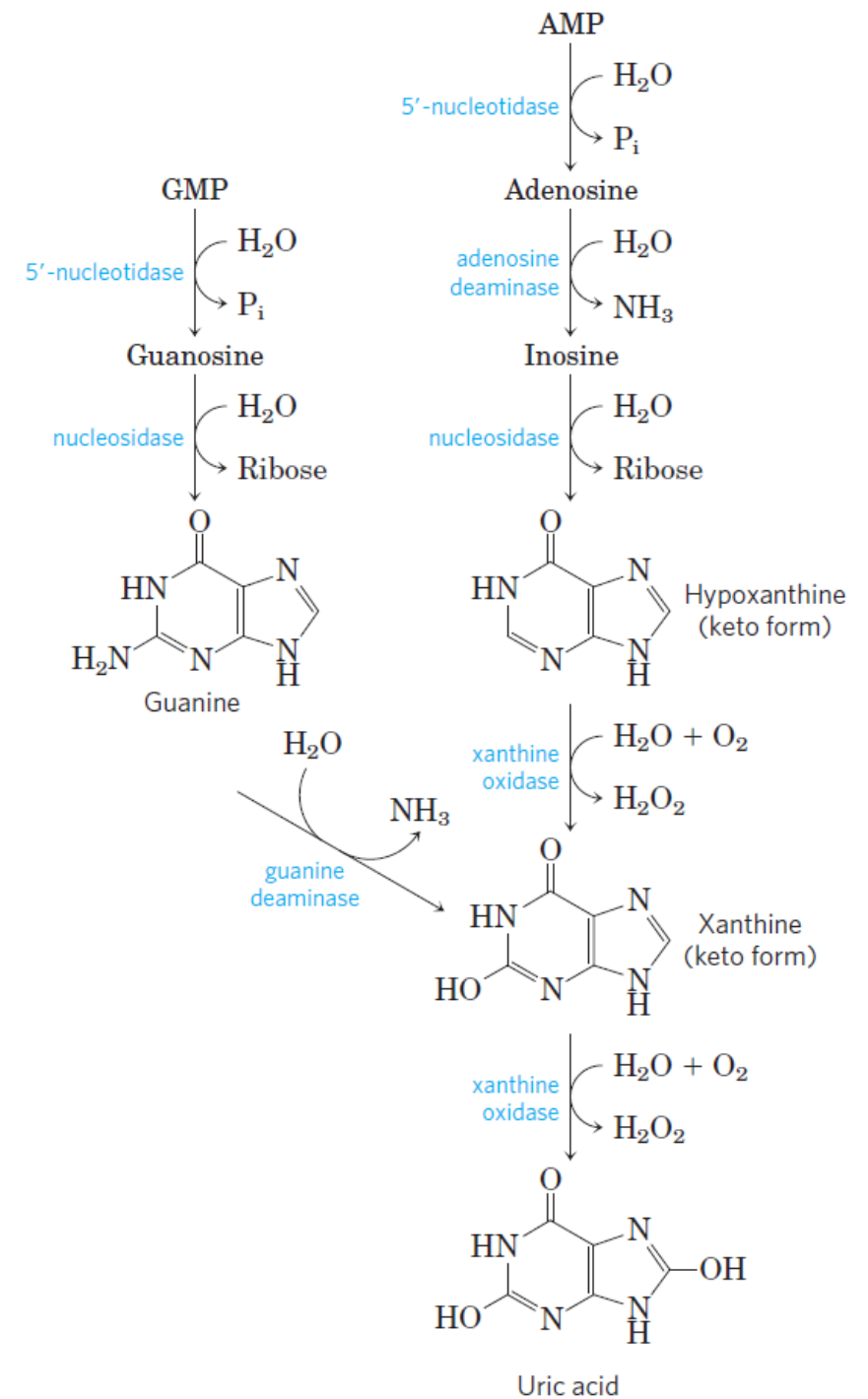
Lesch-Nyhan's syndrome

- HGPRTase deficiency
- Purine Salvage Pathway is affected
- Hyperuricemia, self-destructive behavior, mental retardation

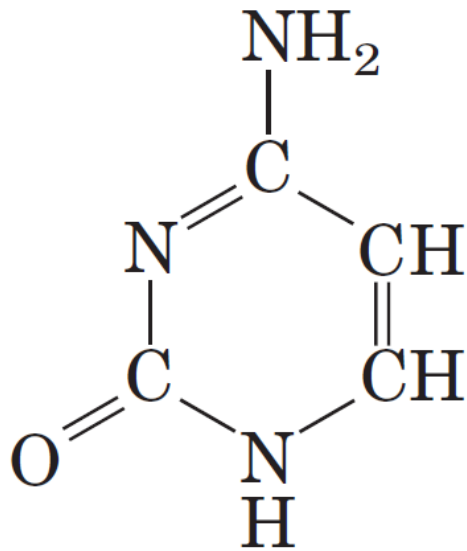


Xanthinuria

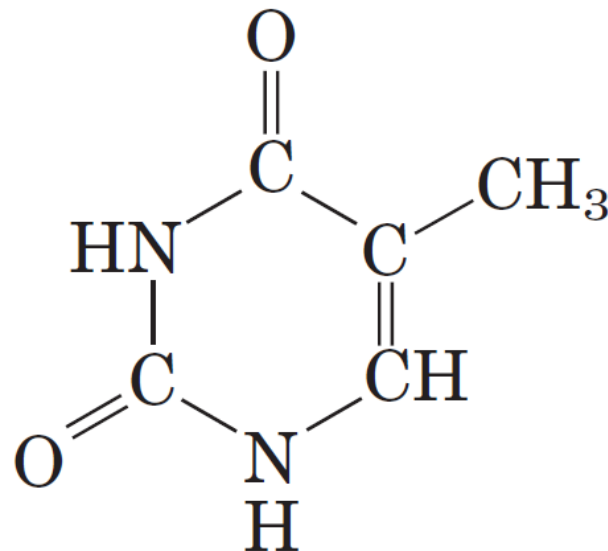
- Rare
- Xanthine stones
- Hypouricemia
- Xanthine oxidase deficiency



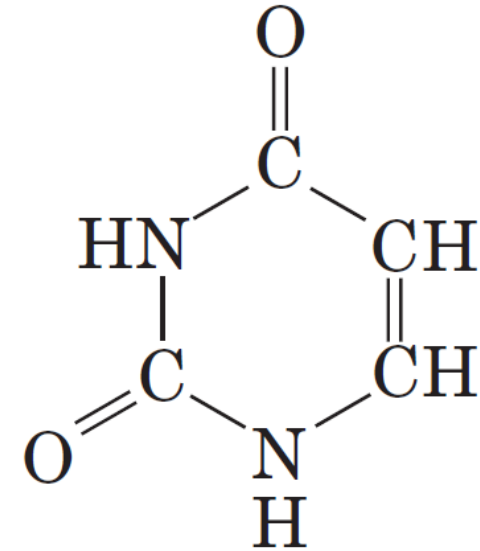
Pyrimidine Bases



Cytosine



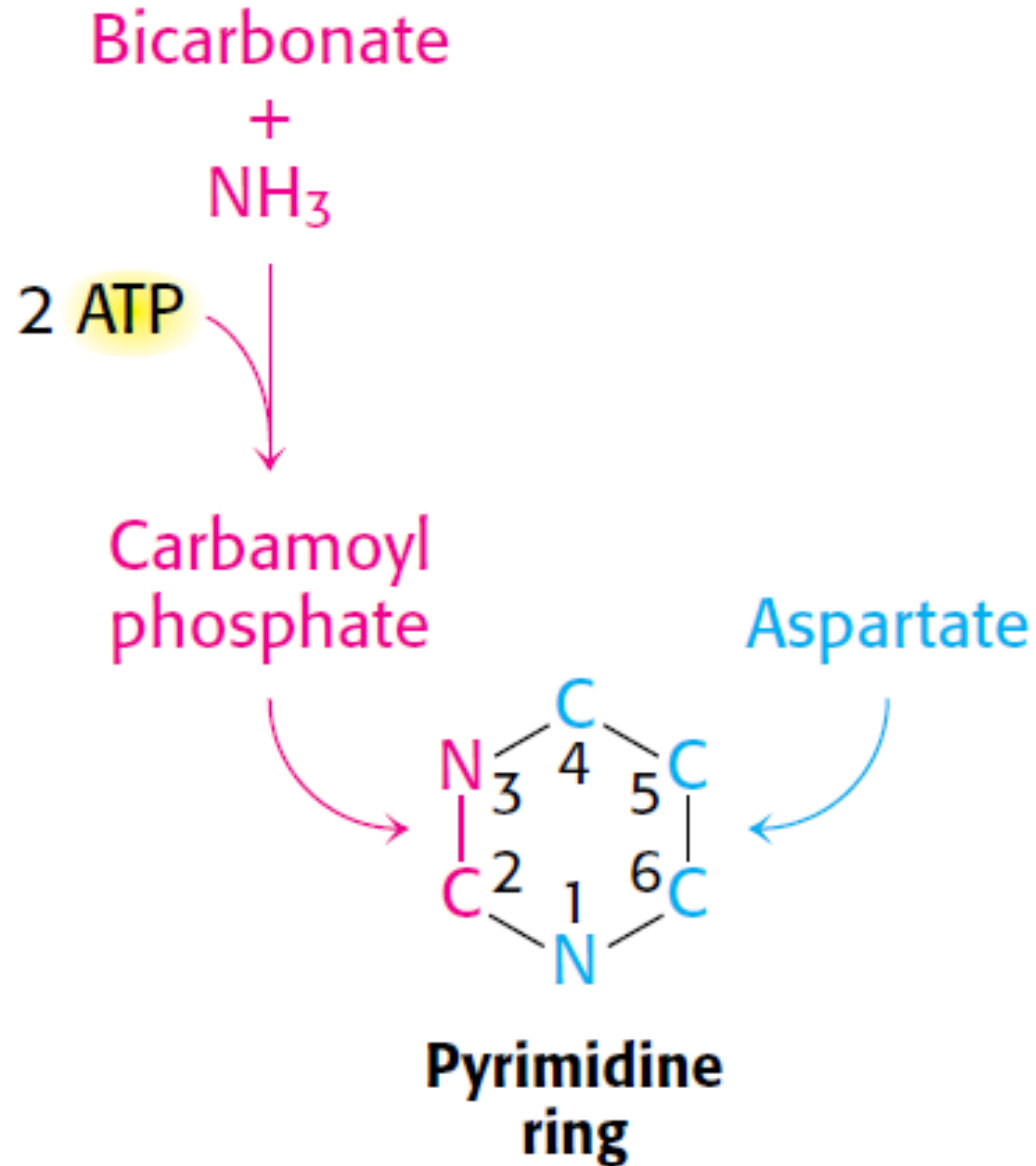
Thymine
(DNA)



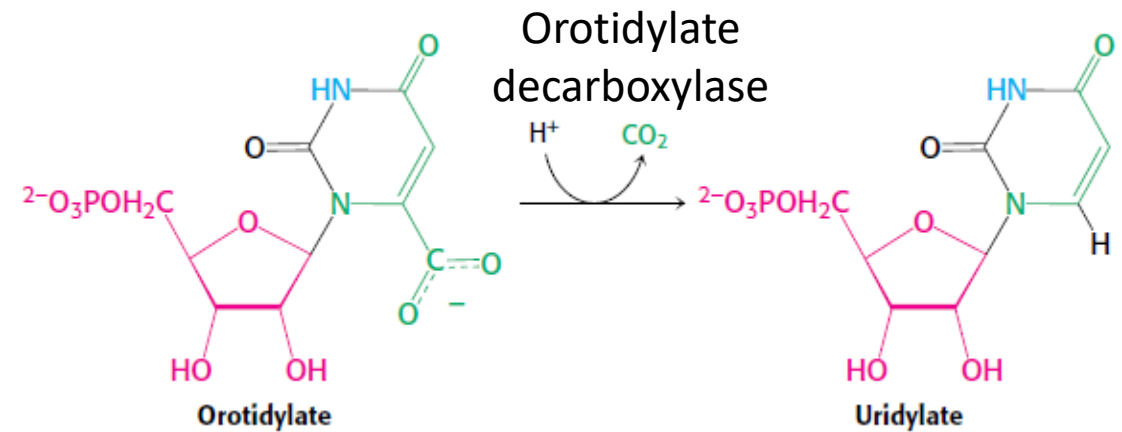
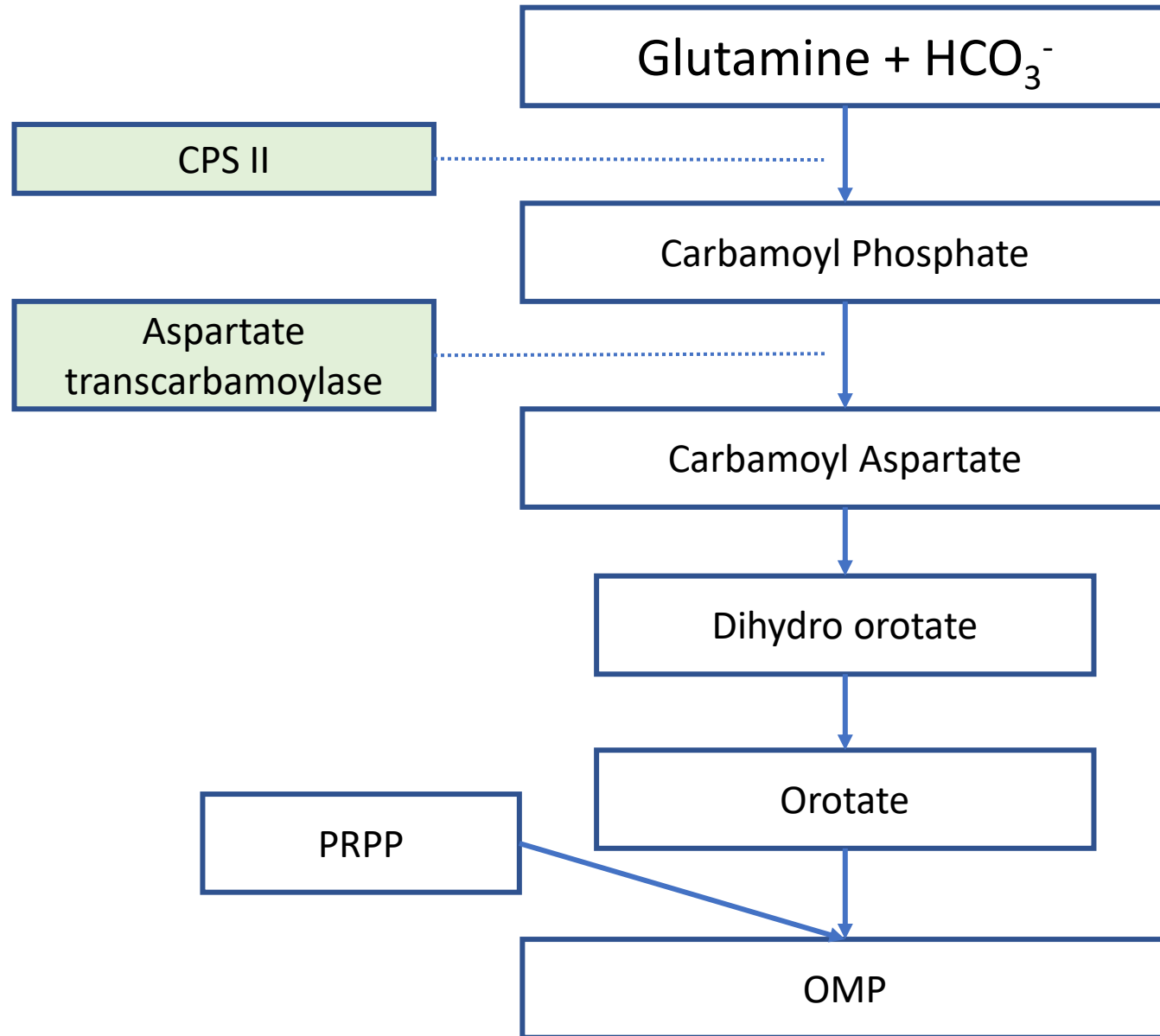
Uracil
(RNA)

Pyrimidines

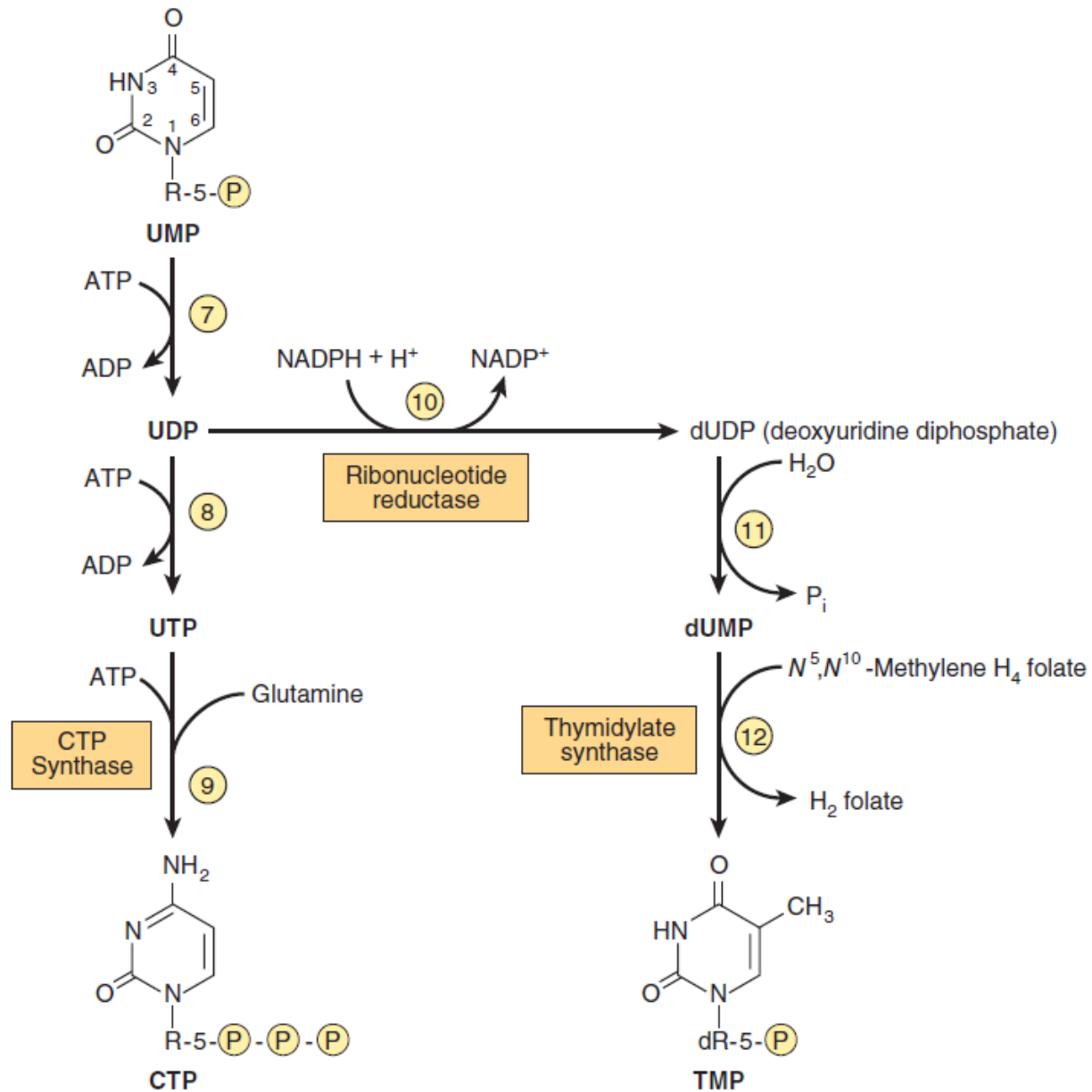
Sources of Pyrimidine Ring Atoms



Pyrimidine Synthesis: De Novo Pathway

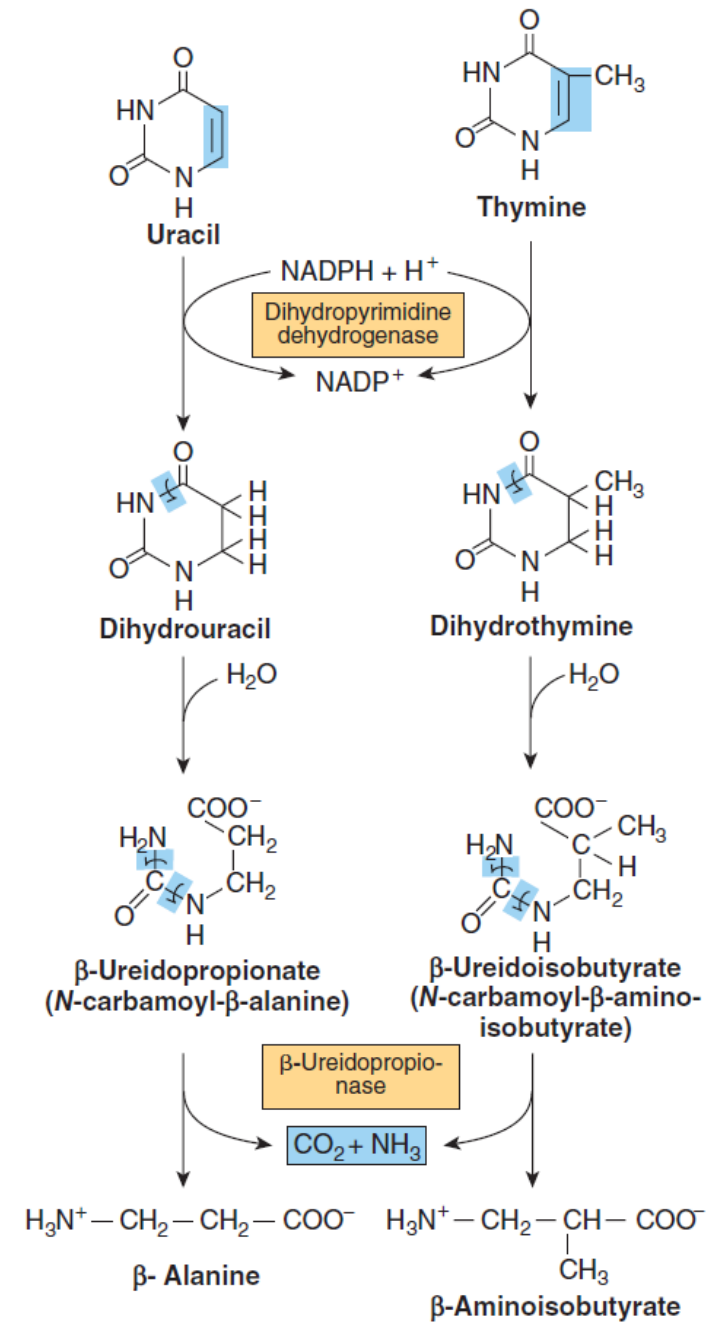


Pyrimidine Synthesis



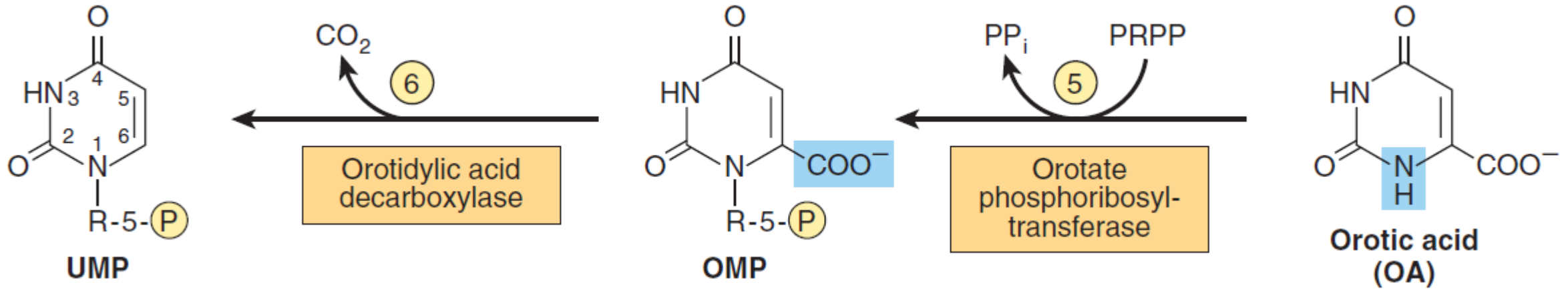
Pyrimidine Catabolism

- Water soluble products



Disorders of Pyrimidine Metabolism

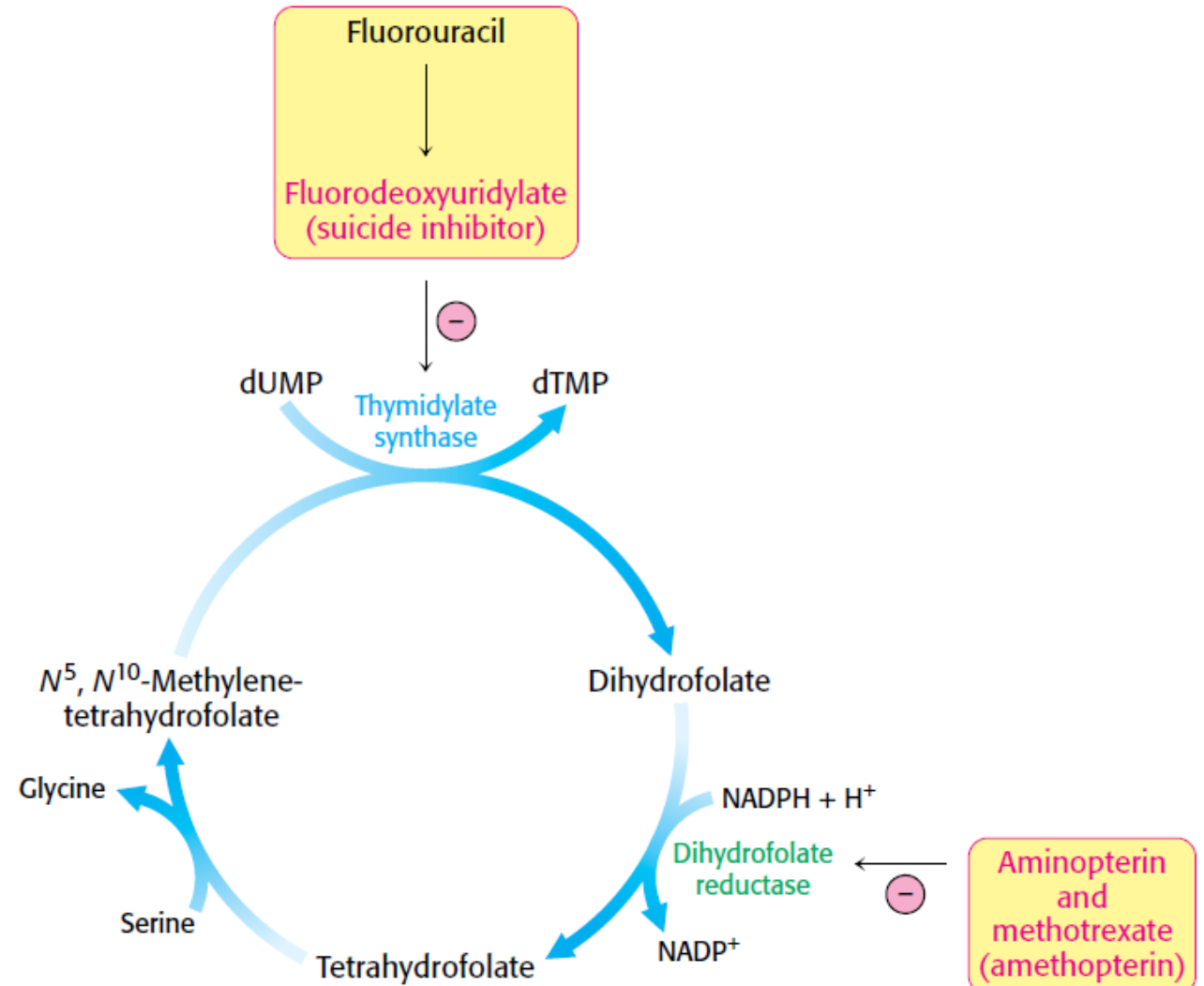
- Orotic aciduria



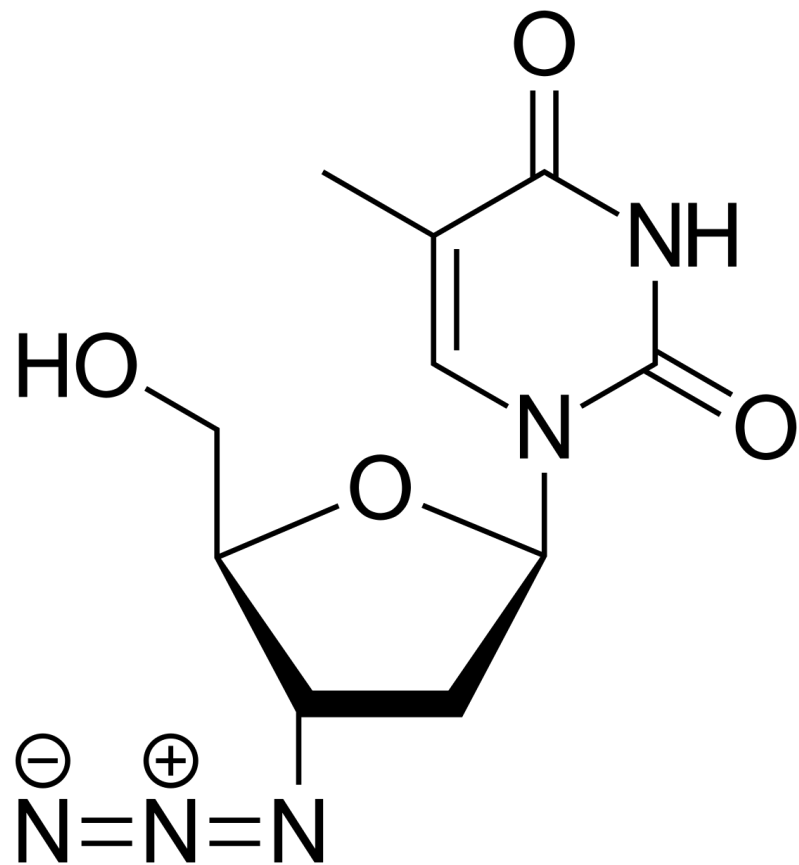
Can this knowledge be utilized to develop drugs? -
Chemo drugs

Anticancer Drugs can Target Purine and Pyrimidine Synthesis Pathways

- Methotrexate and 5-Fluorouracil



ART- Zidovudine



Adenosine

- Acts via Purinergic receptors
- Cardiac arrhythmias

Questions?

Thank you