

## CHAPTER V: ANABOLISM and PRODUCTION of BIOMASS and METABOLITES

### 3. SYNTHESIS of PURINES, PYRIMIDINES, and NUCLEOTIDES

#### 1. Introduction

Purine and pyrimidine biosynthesis is critical for all cells because these molecules are used in the synthesis of ATP, several cofactors, ribonucleic acid (RNA), deoxyribonucleic acid (DNA), and other important cell components. Nearly all microorganisms can synthesize their own purines and pyrimidines as these are so crucial to cell function. **Purines** and **pyrimidines** are cyclic nitrogenous bases with several double bonds and pronounced aromatic properties. Purines consist of two joined rings, whereas pyrimidines have only one. The purines **adenine** and **guanine** and the pyrimidines **uracil**, **cytosine**, and **thymine** are commonly found in microorganisms. A purine or pyrimidine base joined with a pentose sugar, either ribose or deoxyribose, is a **nucleoside**. A **nucleotide** is a nucleoside with one or more phosphate groups attached to the sugar.

#### 2. Phosphorus assimilation

In addition to nucleic acids, phosphorus is found in proteins, phospholipids, ATP, and coenzymes like NADP. The most common phosphorus sources are inorganic phosphate and organic phosphate esters. Inorganic phosphate is incorporated through the formation of ATP in one of three ways: by (1) photophosphorylation, (2) oxidative phosphorylation, and (3) substrate-level phosphorylation.

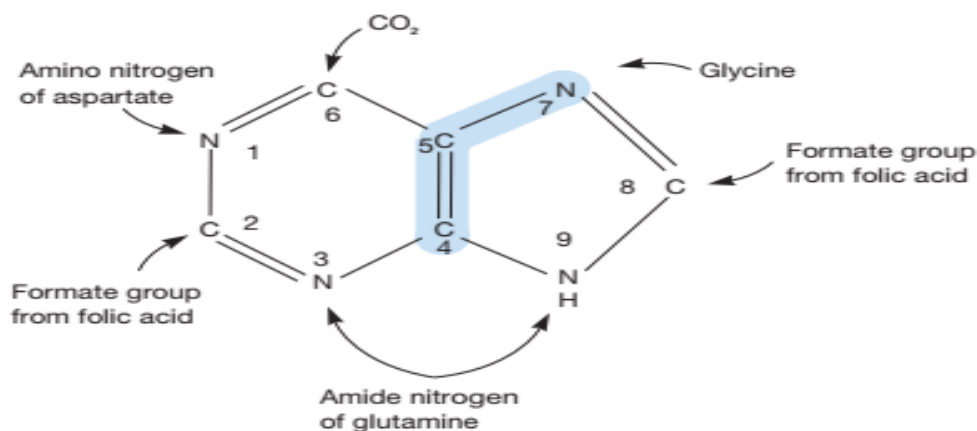
Microorganisms may obtain organic phosphates from their surroundings in dissolved or particulate form. **Phosphatases** very often hydrolyze organic phosphate esters to release inorganic phosphate. Gram-negative bacteria have phosphatases in the periplasmic space, which allows phosphate to be taken up immediately after release.

#### 3. Purine biosynthesis

The biosynthetic pathway for purines is a complex, 11-step sequence in which seven different molecules contribute parts to the final purine skeleton (**Fig. 01**). Because the pathway begins with ribose 5-phosphate and the purine skeleton is constructed on this sugar, the first purine product of the

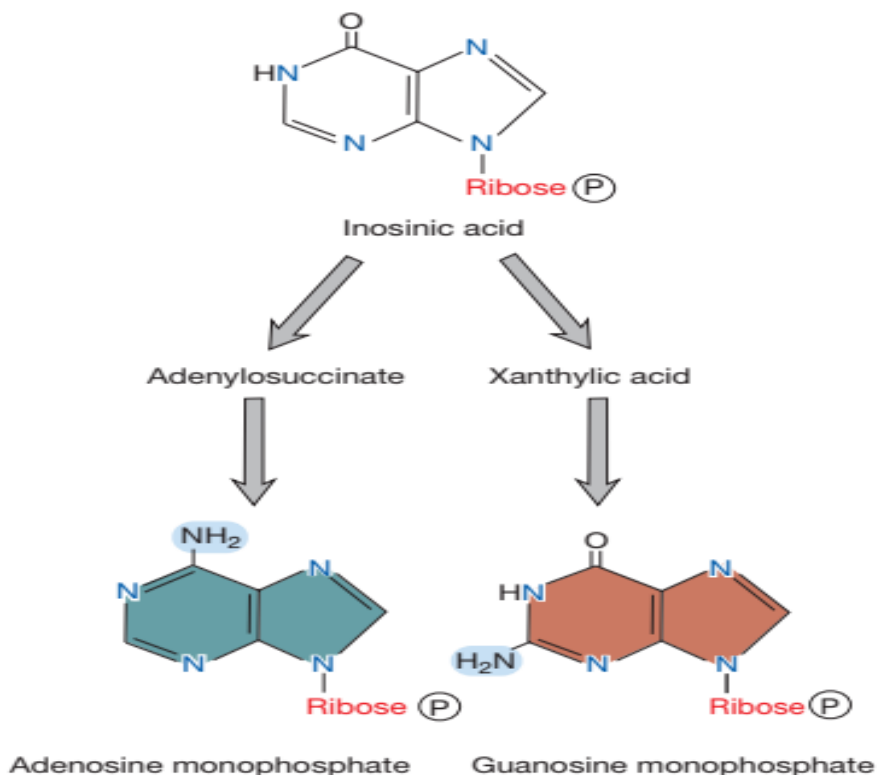
pathway is the nucleotide **inosinic acid**, not a free purine base. The cofactor folic acid is very important in purine biosynthesis. Folic acid derivatives contribute carbons two and eight to the purine skeleton. In fact, the **drug sulfonamide** inhibits bacterial growth by blocking folic acid synthesis. This interferes with purine biosynthesis and other processes that require folic acid.

Once inosinic acid has been formed, relatively short pathways synthesize *adenosine monophosphate* and *guanosine monophosphate* (**Fig. 02**).



**Figure 01:** Purine biosynthesis.

[The sources of purine skeleton nitrogen and carbon are indicated. The contribution of glycine is shaded in blue].

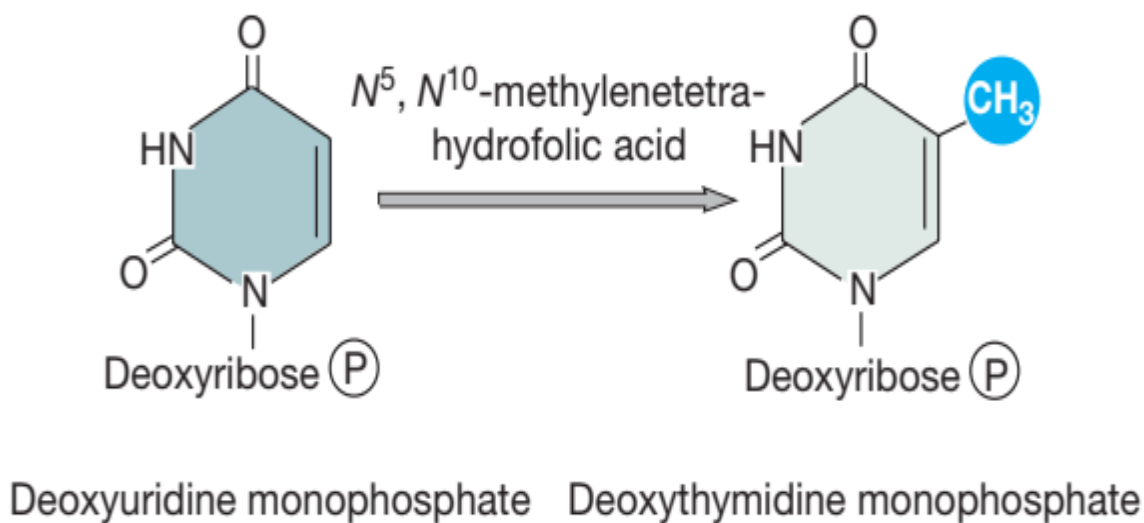


**Figure 02:** Synthesis of Adenosine Monophosphate and Guanosine Monophosphate.

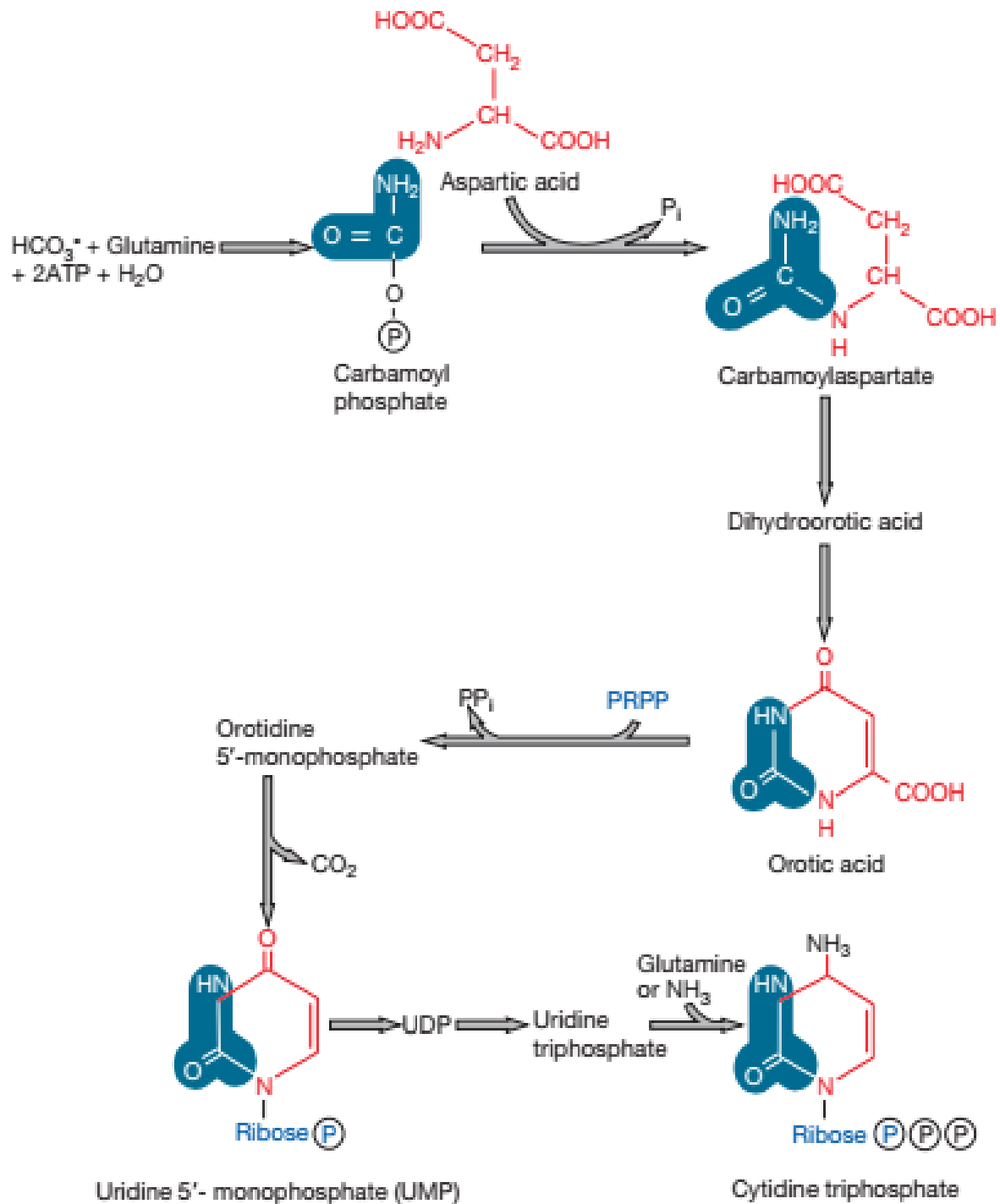
[The highlighted groups are the ones differing from those in inosinic acid].

#### 4. Pyrimidine biosynthesis

Pyrimidine biosynthesis begins with aspartic acid and carbamoyl phosphate, a high-energy molecule synthesized from CO<sub>2</sub> and ammonia (**Fig. 03**). *Aspartate carbamoyltransferase* catalyzes the condensation of these two substrates to form carbamoylaspartate, which is then converted to the initial pyrimidine product, *orotic acid*. After synthesis of the pyrimidine skeleton, a nucleotide is produced by the addition of ribose 5-phosphate, using the high energy intermediate 5-phosphoribosyl 1-pyrophosphate. Thus, construction of the pyrimidine ring is completed before ribose is added, in contrast with purine ring synthesis, which begins with ribose 5-phosphate. Decarboxylation of orotidine monophosphate yields uridine monophosphate and eventually uridine triphosphate and cytidine triphosphate. The third common pyrimidine is thymine, a constituent of DNA. The ribose in pyrimidine nucleotides is reduced in the same way as it is in purine nucleotides. Then, deoxyuridine monophosphate is methylated with a folic acid derivative to form deoxythymidine monophosphate (**Fig. 04**).



**Figure 04:** Deoxythymidine monophosphate synthesis.  
[Deoxythymidine differs from deoxyuridine in having the shaded methyl group].



**Figure 03:** Pyrimidine synthesis.

[PRPP stands for 5-phosphoribosyl 1-pyrophosphoric acid, which provides the ribose 5-phosphate chain. The part derived from carbamoyl phosphate is shaded in turquoise].