· C H A P T E R · 20 ·

PYRIMIDINE METABOLISM

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Pyrimidine Synthesis

Pyrimidine Salvage

Pyrimidine Degradation

PYRIMIDINE SYNTHESIS

Function: To make pyrimidine nucleotides (U, T, C) for DNA and RNA synthesis.
Location: Cytoplasm of most cells.
Connections: To amino acid metabolism by the requirement for glutamine and aspartate.
Regulation: UTP inhibits synthesis of carbamoylphosphate.
Equation:

$$\text{Gln} + CO_2 + \text{Asp} + \text{PRPP} + \text{some ATP} \longrightarrow \text{UTP} + \text{CTP}$$

The major difference between purine and pyrimidine *de novo* biosynthesis is that the pyrimidine ring is assembled and then added to PRPP (Fig. 20-1). With purines, the purine ring is built directly on the PRPP.

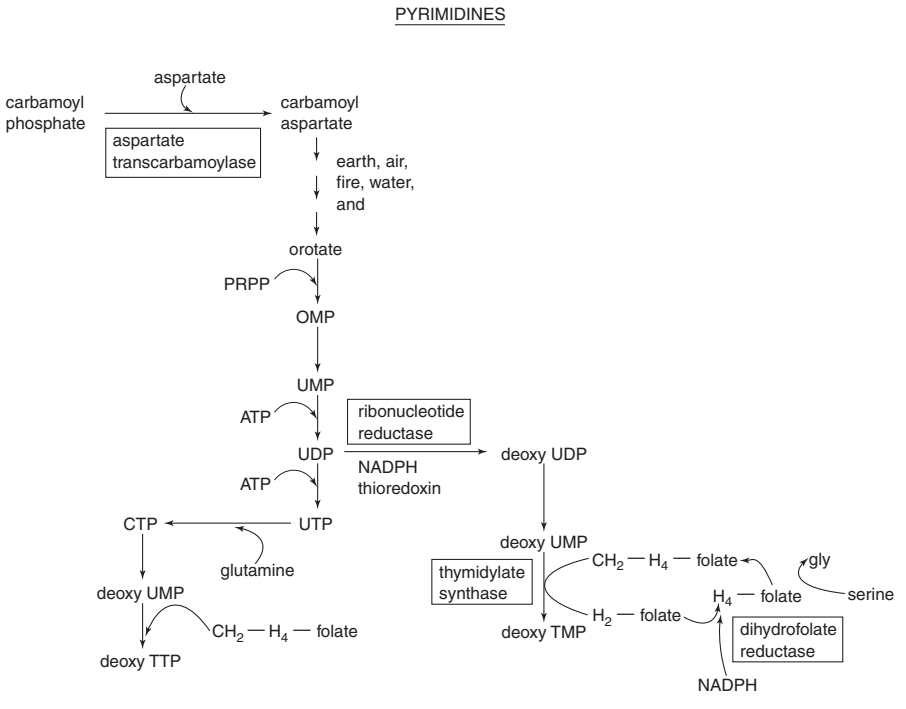

Figure 20-1 Pyrimidine Synthesis and Salvage

PYRIMIDINE SALVAGE

$$\text{Uracil} + \text{PRPP} \longrightarrow \text{UMP} + \text{PP}_i \text{ (only uracil)}$$

Nucleoside phosphorylase:

$$\text{U, C, T} + \text{ribose 1-phosphate} \longrightarrow \text{nucleosides} + \text{P}_i$$

There are basically two types of salvage. The first involves attachment of the base to PRPP with the formation of pyrophosphate. This pathway is available for salvage of purines and uracil but not for cytosine or thymine. The other pathway involves attachment of the base to ribose 1-phosphate, which occurs to some extent for most of the purines and pyrimidines. This second pathway requires the presence of specific

kinases to convert the nucleoside to the monophosphate. Except for thymidine kinase, these kinases do not exist in most cells.

PYRIMIDINE DEGRADATION

CMP ⟶ cytidine ⟶ uridine ⟶ uracil ⟶ ⟶
β-alanine ⟶ malonate semialdehyde ⟶ CO_2

Thymidine ⟶ thymine ⟶ β-aminobutyrate ⟶
methylmalonate semialdehyde ⟶ CO_2

After removal of the phosphates by various phosphatases, the nucleosides are cleaved to the base by the same nucleoside phosphorylase that catalyzes the salvage reaction. The equilibrium constant for this reaction is near 1, so that it can go in either direction depending on the relative levels of the substrates and products.

$$\text{Base–ribose} + P_i \rightleftharpoons \text{base} + \text{ribose 1-phosphate}$$

The nitrogen from the pyrimidine bases is removed by transamination and dumped onto glutamate. The carbon skeleton ends up as CO_2.