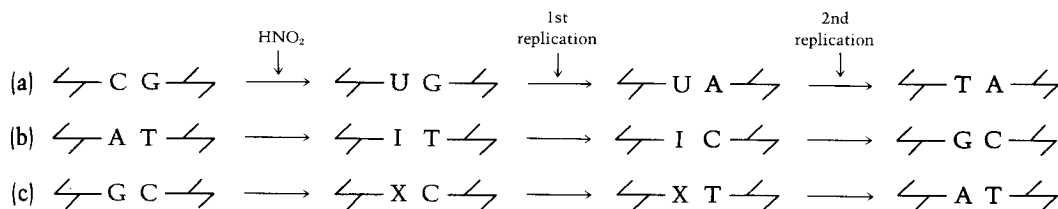
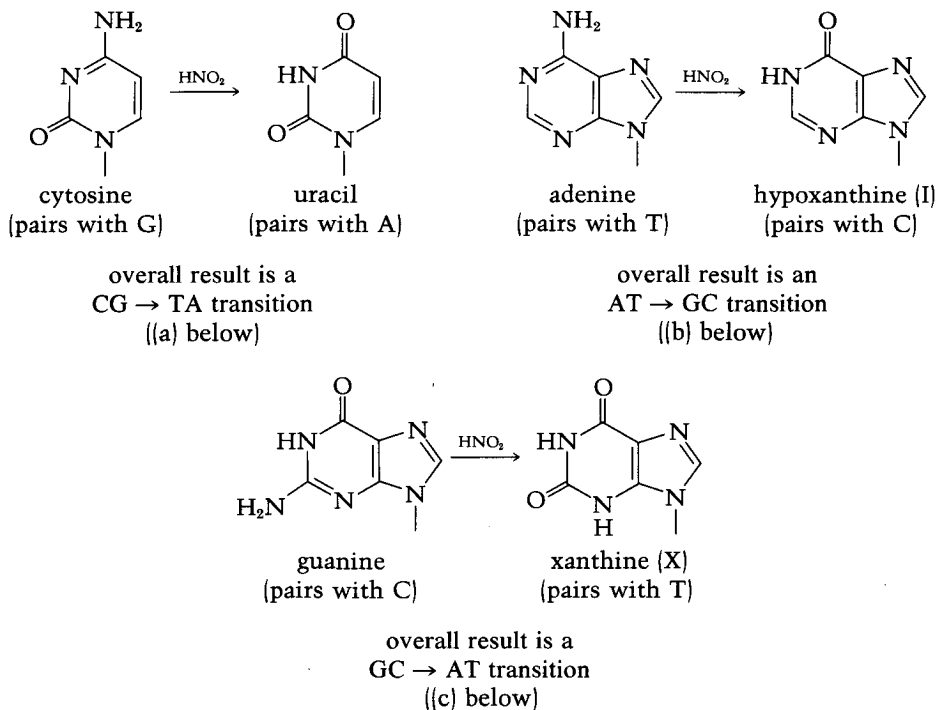


POLYPEPTIDE (PROTEIN) BIOSYNTHESIS—GENE TRANSLATION

The assembly of a polypeptide chain from its constituent amino acids is one of the most fascinating life processes. It is also a very complex process. Merely listing the substances that participate is sufficient indication of the complexity. The list includes amino acids, ATP, GTP, transfer-RNAs, aminoacyl-tRNA synthetases, ribosomes, messenger-RNA, K^+ , peptide synthetase, and various noncatalytic proteins. Although our current understanding of the process is extensive, various aspects are still under active in-

FIGURE 8-7 A summary of the mutagenic effect of HNO_2 .

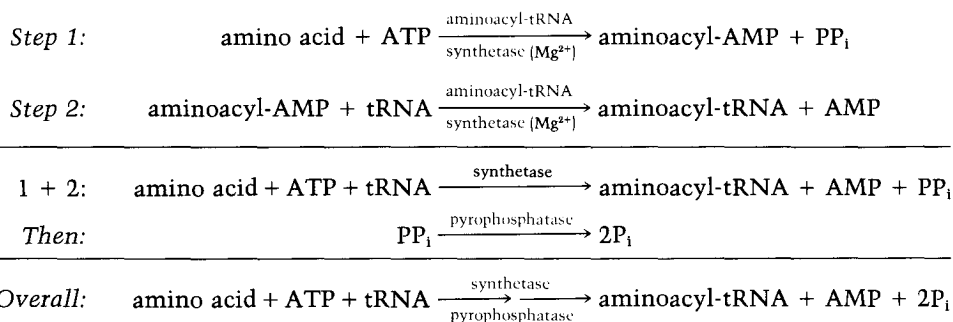


vestigation. The following description of the important highlights is necessarily brief.

It is useful to consider the process as occurring in four stages, namely:

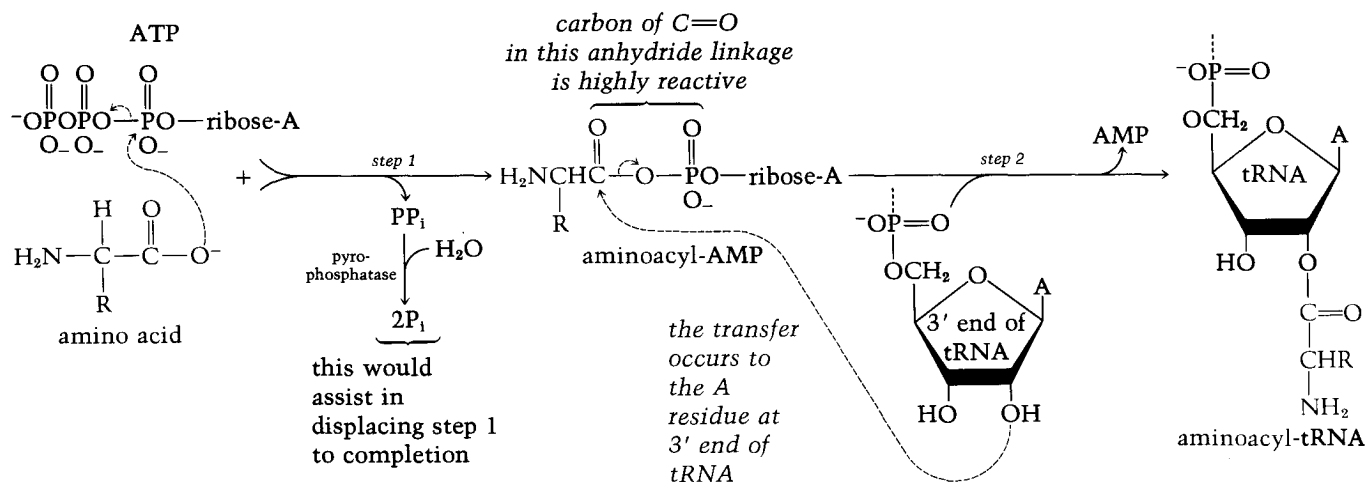
1. *Activation and selection* of amino acids (ATP-dependent).
2. *Initiation* of polypeptide chain formation (GTP-dependent).
3. *Elongation* of the polypeptide chain (GTP-dependent).
4. *Termination* of polypeptide chain formation.

Activation and selection. In all types of cells the first event of translation is the enzyme-catalyzed conversion of each amino acid to an *aminoacyl-tRNA* species. This accomplishes two things: (1) the reactivity of the amino acid for peptide bond formation is enhanced (activation); and (2) the amino acid is matched with a specific transfer-RNA (selection). The enzyme is termed an *aminoacyl-tRNA synthetase* and operates in two steps (see below). Mg^{2+} is required for optimal activity. The involvement of pyrophosphatase is also shown because it can assist the overall process.

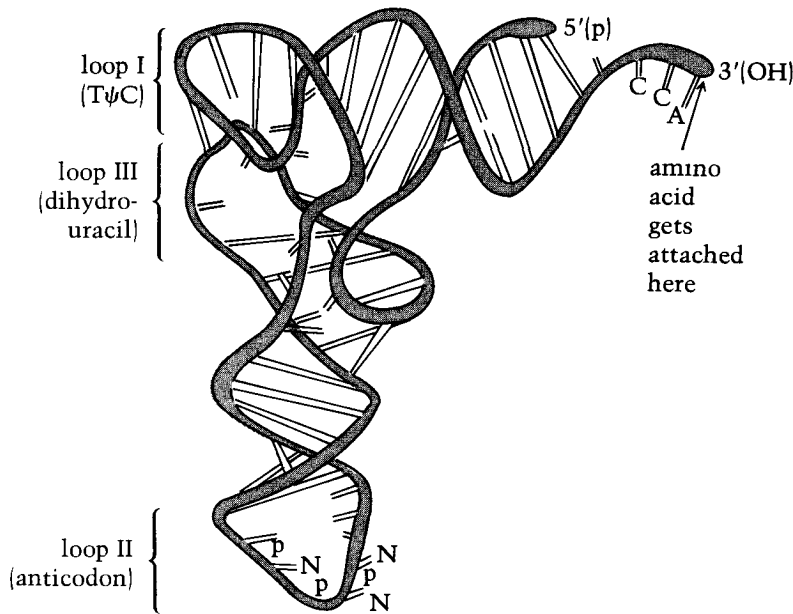


The formation of an aminoacyl-AMP species in step 1 represents the initial activation of the amino acid. Since ATP is consumed, the reaction would be labeled as *energy-requiring*. The carbonyl carbon of the carboxyl group in the free amino acid becomes (see below) a carbonyl carbon of a mixed anhydride in aminoacyl-AMP, which increases its reactivity. In step 2 a terminal OH of transfer-RNA attacks the carbonyl carbon (displacing AMP) to yield the aminoacyl-tRNA product. Since this is an ester, the increased reactivity of the aminoacyl carbonyl group is conserved.

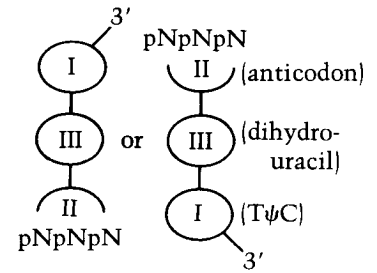
In addition to the chemistry it catalyzes, the synthetase enzyme is also



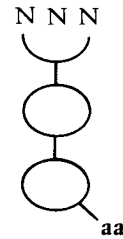
a review of
transfer-RNA structure



in this section on translation the transfer-RNA structure will be symbolized in a shorthand representation as follows:

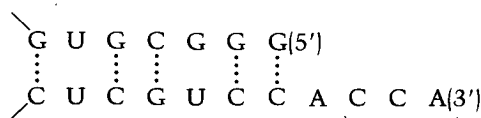


and aminoacyl-tRNA as



distinct in one other important way. It is *highly specific in its recognition of both amino acid and transfer-RNA*. One might expect then that a living cell would consist of several synthetase enzymes, each having different recognition properties. In fact 20 different synthetases are believed to exist—one for each of the 20 amino acids. The number of different tRNA molecules per cell is even greater—there are perhaps as many as 60—since most of the amino acids can be matched with at least two different tRNA molecules and some with three.

The basis of this enzyme specificity is, of course, the highly ordered recognition of the active site for a particular combination of amino acid and transfer-RNA. A logical question in this regard is, what is the feature of tRNA structure that is recognized for binding by the synthetase? Each amino acid, of course, has its own unique structure, conferred by the side chain. With transfer-RNA, the selection appears to be based on the ability of the synthetase to recognize (and hence prefer for binding) unique features of the open stem region.



individual synthetases appear to discriminate among tRNAs on the basis of the base pair sequence in this segment *universal in all tRNAs*

Initiation. Polypeptide chains are assembled one amino acid at a time from the N terminus to the C terminus. Obviously then, this stepwise process