AMINO ACID BIOSYNTHESIS

All amino acids are derived from intermediates in glycolysis, the citric acid cycle, or the pentose phosphate pathway. Nitrogen enters these pathways by way of glutamate and glutamine.

Mammals can synthesize only about half of them—generally those with simple pathways. These are the **nonessential amino acids**, not needed in the diet. The remainder, the **essential amino acids**, must be obtained from food.

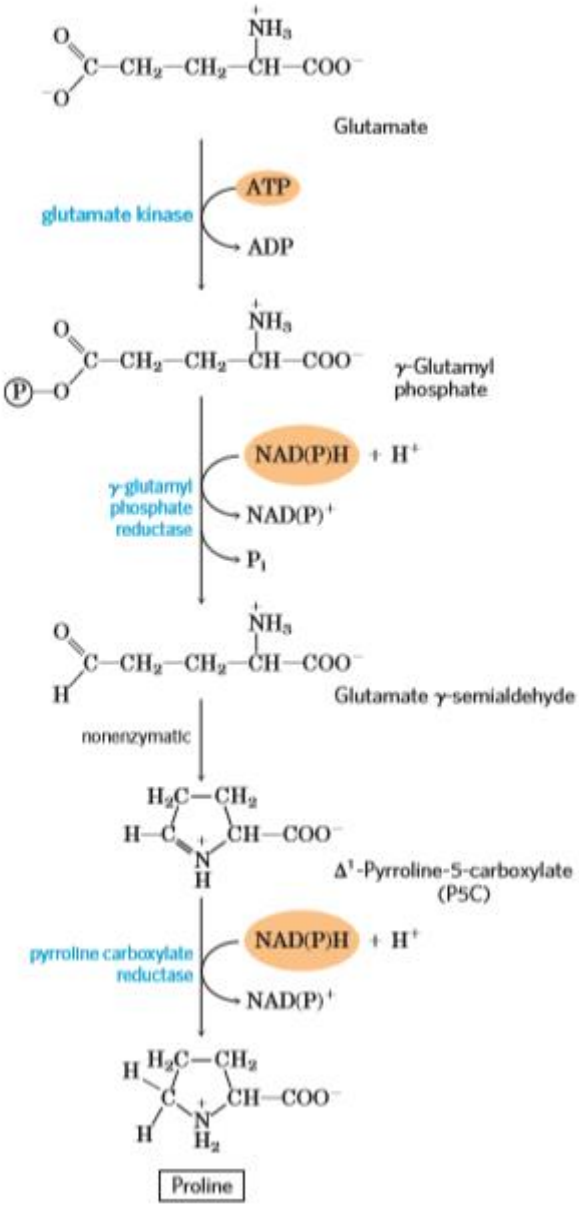
TABLE 22–1 Amino Acid Biosynthetic Families, Grouped by Metabolic Precursor

α-Ketoglutarate	**Pyruvate**
Glutamate	Alanine
Glutamine	Valine*
Proline	Leucine*
Arginine	Isoleucine*
3-Phosphoglycerate	**Phosphoenolpyruvate and erythrose 4-phosphate**
Serine	
Glycine	
Cysteine	Tryptophan*
Oxaloacetate	Phenylalanine*
Aspartate	Tyrosine†
Asparagine	**Ribose 5-phosphate**
Methionine*	Histidine*
Threonine*	
Lysine*	

In addition to these six precursors, there is a notable intermediate in several pathways of amino acid and nucleotide synthesis: 5-phosphoribosyl-1-pyrophosphate (PRPP): PRPP is synthesized from ribose 5-phosphate derived from the pentose phosphate pathway, in a reaction catalyzed by ribose phosphate pyrophosphokinase. This enzyme is allosterically regulated by many of the biomolecules for which PRPP is a precursor.

α-Ketoglutarate Gives Rise to Glutamate, Glutamine, Proline, and Arginine

Proline is a cyclized derivative of glutamate. In the first step of proline synthesis, ATP reacts with the side chain carboxyl group of glutamate to form an acyl phosphate, which is reduced by NADPH or NADH to glutamate γ-semialdehyde. This intermediate undergoes rapid spontaneous cyclization and is then reduced further to yield proline.



Arginine is synthesized from glutamate via ornithine and the urea cycle in animals. The pathways to proline and arginine are somewhat different in mammals. Proline can be synthesized by the pathway shown in Figure above, but it is also formed from arginine obtained from dietary or tissue protein. Arginase, a urea cycle enzyme, converts arginine to ornithine and urea. The ornithine is converted to glutamate γ-semialdehyde by the enzyme ornithine γ-aminotransferase. The semialdehyde cyclizes, which is then converted to proline. The pathway for arginine synthesis is different in mammals. When arginine from dietary intake or protein turnover is insufficient for protein synthesis, the ornithine γ-aminotransferase reaction operates in the direction of ornithine formation. Ornithine is then converted to citrulline and arginine in the urea cycle figures are given below.

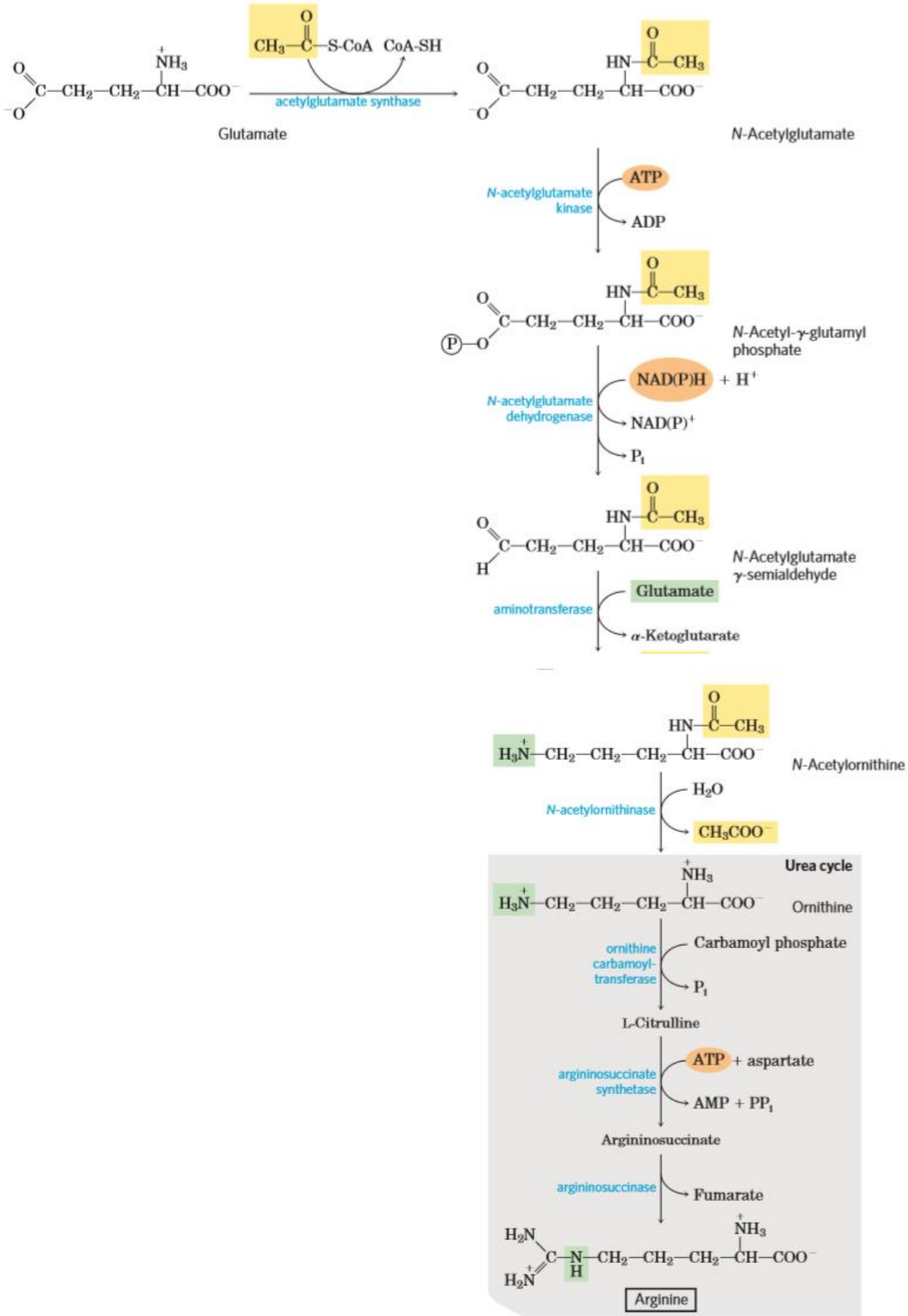
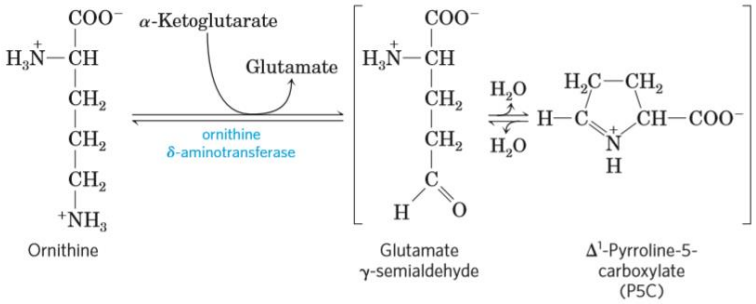
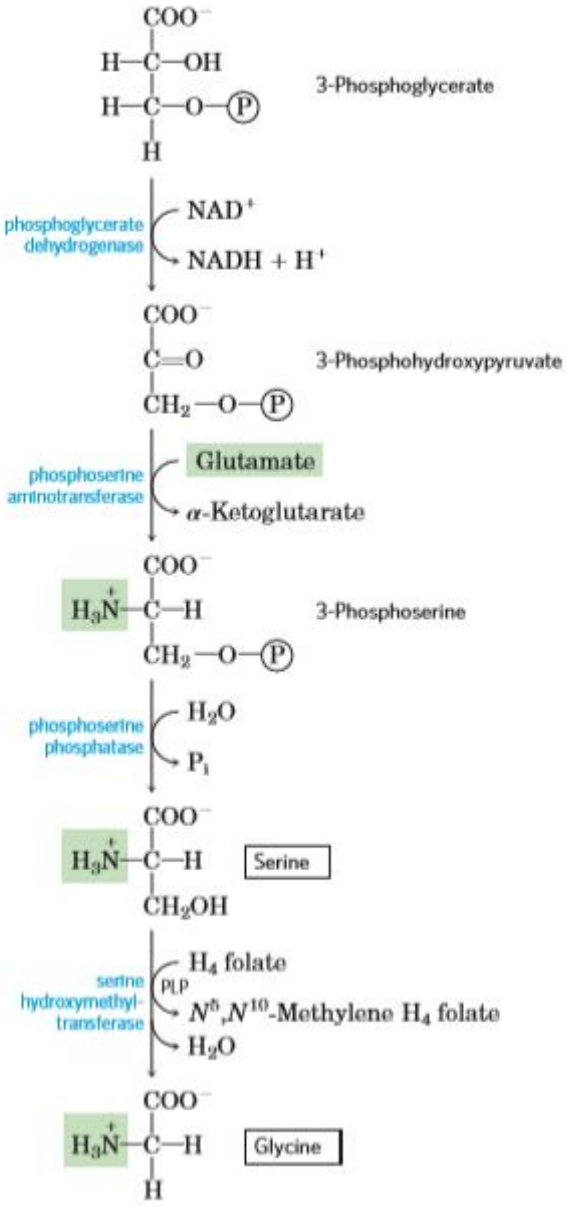


Figure: Arginine synthesis pathway taking place in animals.

FIGURE 22–13 Ornithine δ-aminotransferase reaction: a step in the mammalian pathway to proline. This enzyme is found in the mitochondrial matrix of most tissues. Although the equilibrium favors P5C formation, the reverse reaction is the only mammalian pathway for synthesis of ornithine (and thus arginine) when arginine levels are insufficient for protein synthesis.



Serine, Glycine and Cysteine are derived from 3-Phosphoglycerate



The major pathway for the formation of serine is the same in all organisms (Figure given below). In the first step, the hydroxyl group of 3-phosphoglycerate is oxidized by a dehydrogenase (using NAD) to yield 3-phosphohydroxypyruvate. Transamination from glutamate yields 3-phosphoserine, which is hydrolyzed to free serine by phosphoserine phosphatase.

Serine (three carbons) is the precursor of glycine (two carbons) through removal of a carbon atom by serine hydroxymethyltransferase. The overall reaction, which is reversible, also requires pyridoxal phosphate. In the liver of vertebrates, glycine can be made by another route: the reverse of the reaction shown in Figure 18–20c of Chapter 18, catalyzed by glycine synthase (also called glycine cleavage enzyme)

Plants and bacteria produce the reduced sulfur required for the synthesis of cysteine (and methionine, described later) from environmental sulfates; the pathway is shown on the right side of Figure 22–15. Sulfate is activated in two steps to produce PAPS, which undergoes an eight-electron reduction to sulfide. The sulfide is then used in the formation of cysteine from serine in a two-step pathway.

Mammals synthesize cysteine from two amino acids: methionine furnishes the sulfur atom, and serine furnishes the carbon skeleton. Methionine is first converted to S-adenosylmethionine, which can lose its methyl group to any of a number of acceptors to form S-adenosylhomocysteine (adoHcy). This demethylated product is hydrolyzed to free homocysteine, which undergoes a reaction with serine, catalyzed by cystathionine β-synthase, to yield cystathionine (Fig. 22–16). Finally, cystathionine γ-lyase, a PLP-requiring enzyme, catalyzes removal of ammonia and cleavage of cystathionine to yield free cysteine.

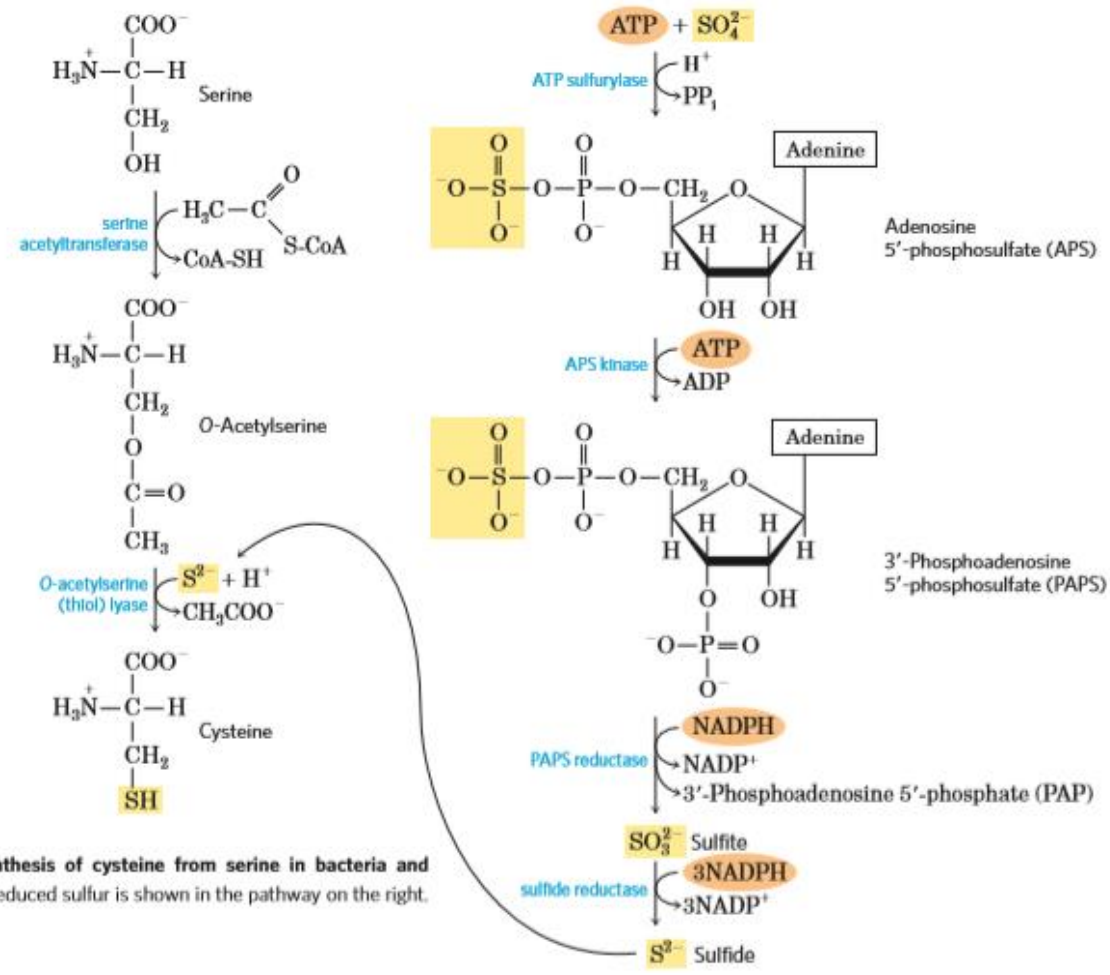


FIGURE 22–15 Biosynthesis of cysteine from serine in bacteria and plants. The origin of reduced sulfur is shown in the pathway on the right.

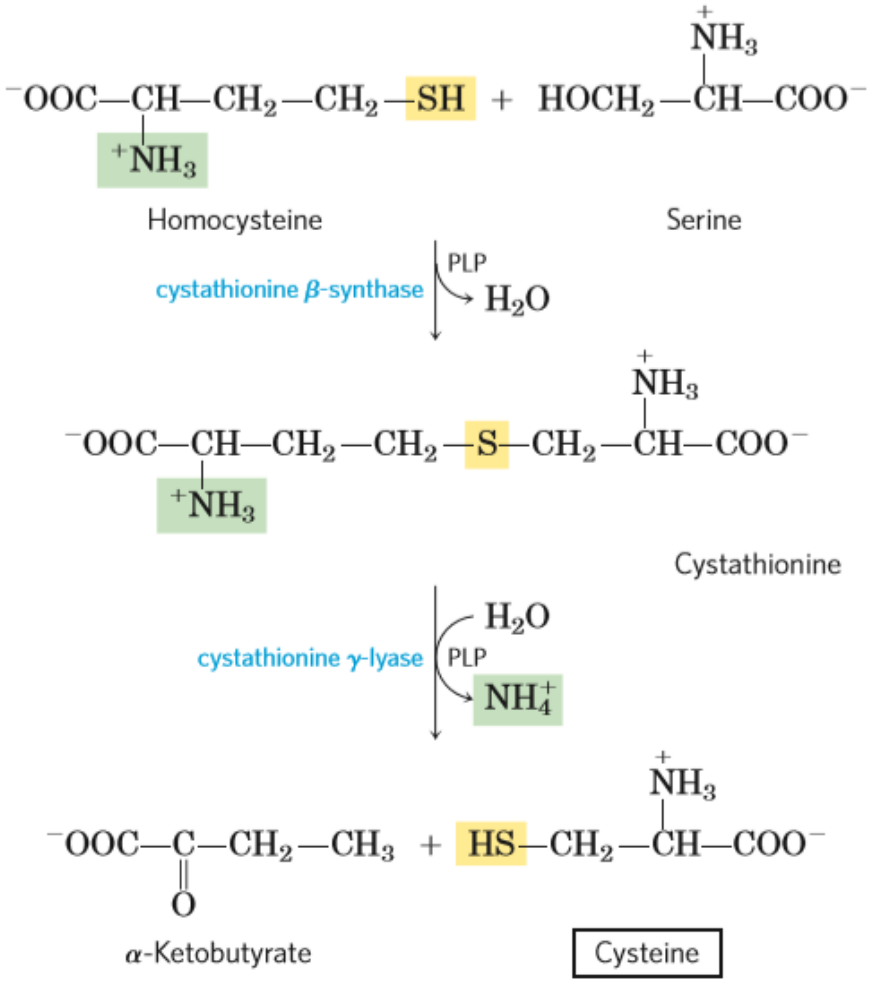


FIGURE 22–16 **Biosynthesis of cysteine from homocysteine and serine in mammals.** The homocysteine is formed from methionine as

Reference:

Lehninger, Principles of Biochemistry, 6th edition