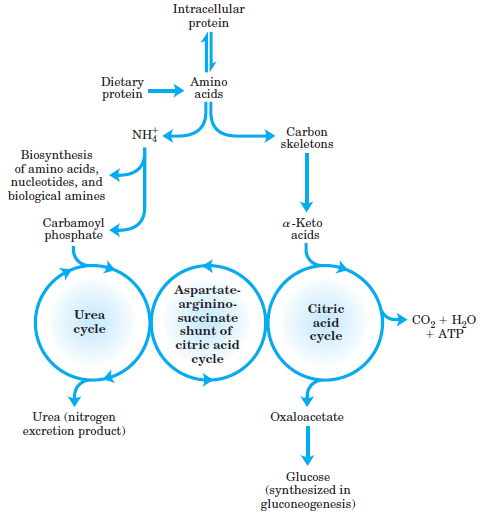
**Chapter 18**

**Amino Acid Oxidation and the Production of Urea**

* Oxidative degradation of amino acids makes a significant contribution to the generation of metabolic energy.
* Overview of amino acid catabolism in mammals. The amino groups and the carbon skeleton take separate but interconnected pathways **(Fig. 18-1)**.



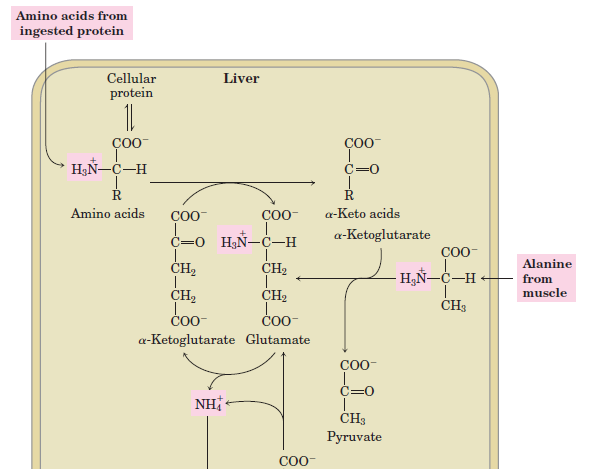


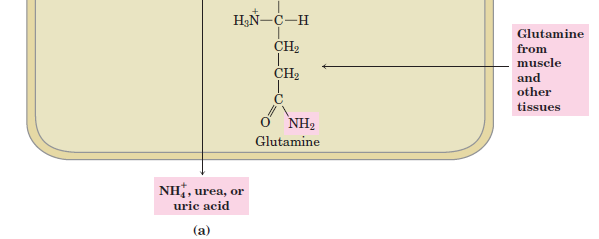
**18.1 Metabolic Fates of Amino Acids**

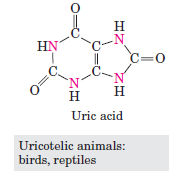
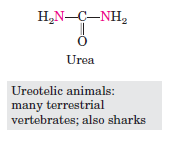
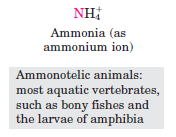
* Nitrogen, N2, is abundant in the atmosphere but is too inert for use in most biochemical processes.
* Because only a few microorganisms can convert N2 to biologically useful forms such as NH3, amino groups are carefully husbanded in biological systems.
* An overview of the catabolic pathways of ammonia and amino groups in vertebrates **(Fig. 18-2 a)**.
* Most amino acids are metabolized in the liver.
* Some of the ammonia generated in this process is recycled and used in a variety of biosynthetic pathways; the excess is either excreted directly or converted to urea or uric acid for excretion, depending on the organism **(Fig. 18-2 b)**.
* Four amino acids play central roles in nitrogen metabolism: glutamate, glutamine, alanine and aspartate.

**Dietary Protein Is Enzymatically Degraded to Amino Acids**

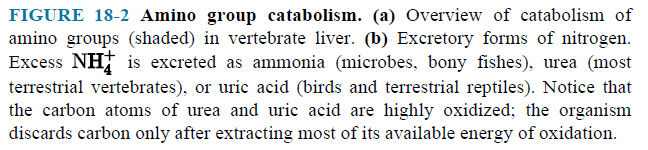
* In the stomach, **pepsin** hydrolyzes ingested proteins at peptide bonds on the amino-terminal side of the aromatic amino acid residues Phe, Trp, and Tyr, cleaving long polypeptide chains into a mixture of smaller peptides.
* The digestion of proteins continues in the small intestine by **trypsin**, **chymotrypsin**, **carboxypeptidases A** and **B** and **aminopeptidase** having different amino acid specificities.
* The free amino acids enter the blood and travel to the liver.







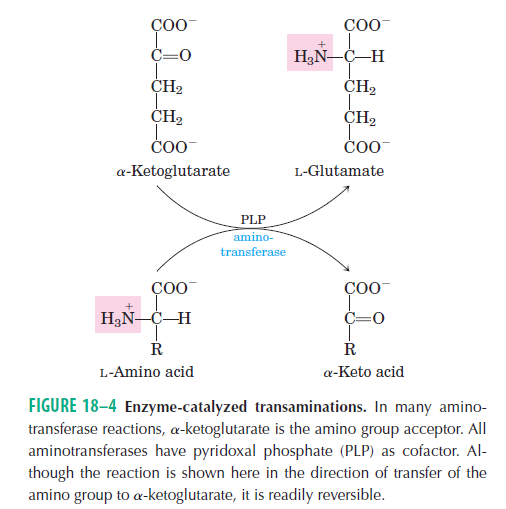
**(b)**



**Pyridoxal Phosphate (PLP) Participates in the Transfer of**

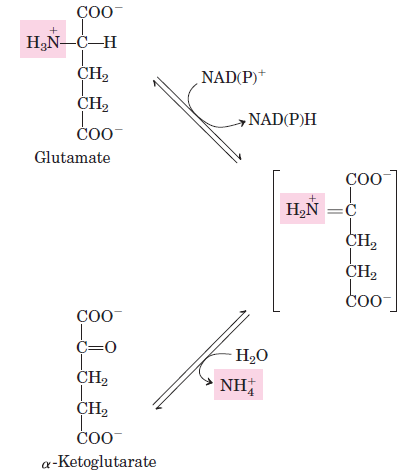
**-Amino Groups to -Ketoglutarate**

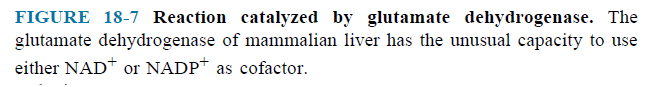
* The first step in the catabolism of most amino acids is removal of the -amino groups, promoted by enzymes called **aminotransferases** or **transaminases**.
* The effect of transamination reactions is to collect the amino groups from many different amino acids in the form of glutamate **(Fig. 18-4)**.



**Glutamate Releases Its Amino Group as Ammonia in the Liver**

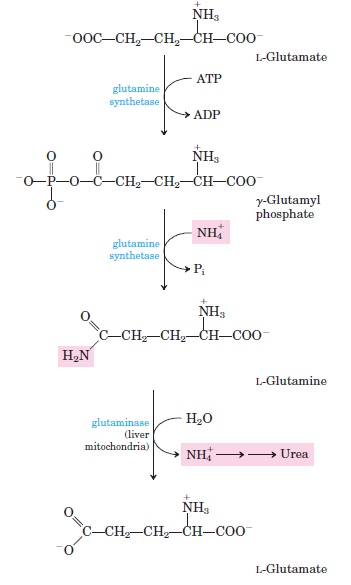
* Glutamate is transported from the cytosol into the mitochondrial matrix.
* Glutamate undergoes **oxidative deamination** catalyzed by **glutamate dehydrogenase (Fig. 18-7)**.
* The -ketoglutarate formed from glutamate deamination can be used in the citric acid cycle and for glucose synthesis.

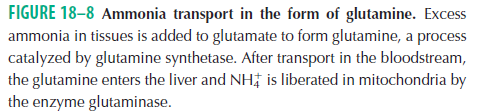




**Glutamine Transports Ammonia in the Blood**

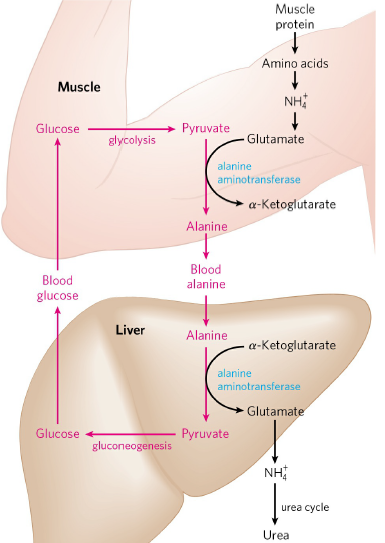
* Ammonia is toxic to animal tissues.
* In most animals, much of the free ammonia is converted to a nontoxic compound.
* The free ammonia is combined with glutamate to yield glutamine by the action of **glutamine synthetase** **(Fig. 18-8)**.

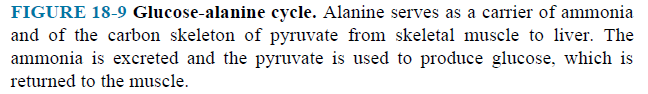




**Alanine Transports Ammonia from Skeletal Muscles to the Liver**

* Alanine plays a special role in transporting amino groups to the liver in a nontoxic form, via a pathway called the **glucose-alanine cycle (Fig. 18–9)**.

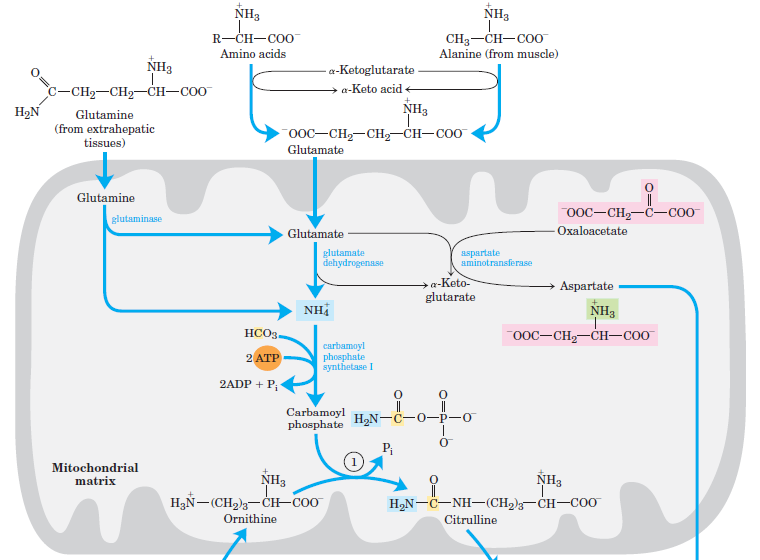
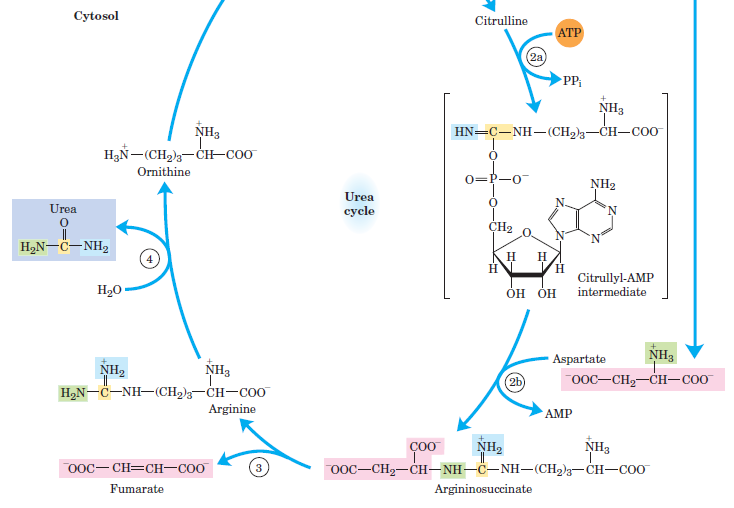




* In muscle, amino acids are degraded for fuel. Amino groups are collected in the form of glutamate.
* Glutamate can transfer its -amino group to pyruvate. Alanine is formed.
* The alanine passes into the blood and travels to the liver.
* The amino group is transferred from alanine to -ketoglutarate, forming pyruvate and glutamate.
* The pyruvate, in the liver, is converted to glucose, which is transported back to muscle as part of the glucose alanine cycle.
* Glutamate can enter mitochondria, where the glutamate dehydrogenase reaction releases NH4+. NH4+ is converted to urea by urea cycle.
* Glutamate can undergo transamination with oxaloacetate to form aspartate.
  1. **Nitrogen Excretion and the Urea Cycle**
* In ureotelic organisms, the ammonia deposited in the mitochondria of liver is converted to urea in the **urea cycle**.
* The urea passes into the blood and thus to the kidneys and is excreted into the urine.

**Urea Is Produced from Ammonia in Five Enzymatic Steps**

* The urea cycle begins inside liver mitochondria, but three of the subsequent steps take place in the cytosol (**Fig. 18-10)**.
* NH4 and CO2 (as HCO3-) are converted to carbamoyl phosphate by **carbamoyl phosphate synthetase I**.
* The cycle has four enzymatic steps.
* Carbamoyl phosphate and ornithine are converted to citrulline by **ornithine transcarbamoylase**. The citrulline passes into the cytosol.
* The second amino group now enters from aspartate. Citrulline and aspartate are converted to argininosuccinate by **argininosuccinate synthetase**.
* The argininosuccinate is then cleaved by **argininosuccinase** to form free arginine and fumarate.

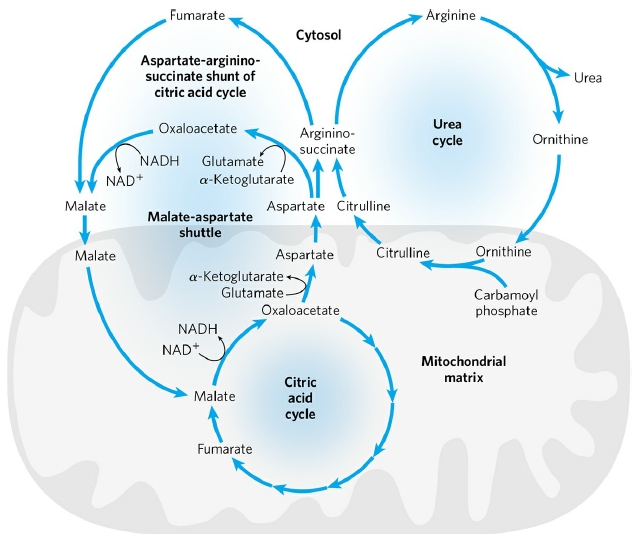
 

**FIGURE 18-10** The urea cycle and reactions that feed amino groups into the cycle.

* **Arginase** cleaves arginine to yield **urea** and ornithine.
* Ornithine is transported into the mitochondrion to initiate another round of the urea cycle.

**The Citric Acid and Urea Cycles Can Be Linked**

* Fumarate produced in the urea cycle is also an intermediate of the citric acid cycle.
* These two cycles are interconnected by fumarate (**Fig. 18-12)**.
* Several enzymes of the citric acid cycle, including fumarase and malat dehydrogenase, are also present as isozymes in the cytosol.

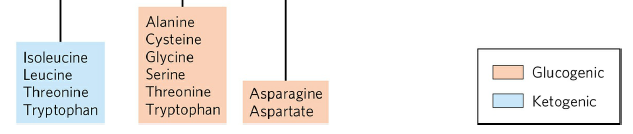
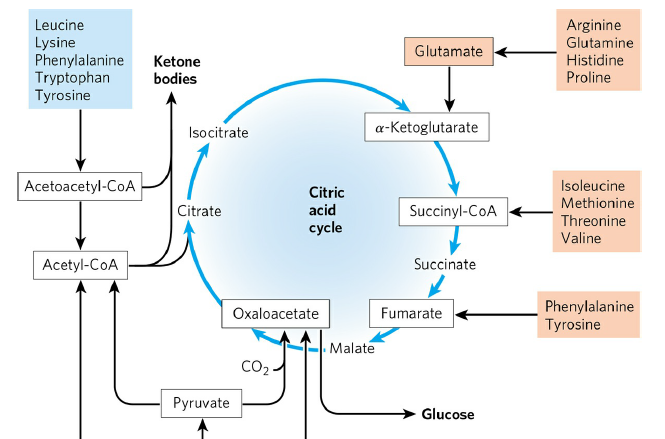


**FIGURE 18-12** Links between the urea cycle and citric acid cycle.

* The fumarate can be converted to malate in the cytosol. The malate can be transported into mitochondria for use in the citric acid cycle.
* Aspartate formed in mitochondria by transamination between oxaloacetate and glutamate can be transported to the cytosol.
* Aspartate serves as nitrogen donor in the urea cycle reaction.
* These reactions provide metabolic links between the separate pathways. It is called **aspartate-argininosuccinate shunt**.

**18.3 Pathways of Amino Acid Degradation**

* The pathways of amino acid catabolism normally account for only 10% to 15% of the human body’s energy production; these pathways are not nearly as active as glycolysis and fatty acid oxidation.
* The 20 catabolic pathways converge to form only six major products.
* They are -ketoglutarate, succinyl-CoA, fumarate, oxaloacetate, pyruvate and acetyl-CoA. All of them enter the citric acid cycle (**Fig. 18-15)**.
* Some amino acids can be converted to glucose. They are called glucogenic amino acids.
* Some amino acids can be converted to ketone bodies. They are called ketogenic amino acids.
* Some amino acids (tryptophan, phenylalanine, tyrosine, threonine, and isoleucine) can be converted to both glucose and ketone bodies.
* Remember. Catabolism of both carbohydrates and lipids produces NADH and FADH2.
* The degradation of amino acids also results NADH and FADH2 through the action of the citric acid cycle.



**FIGURE 18-15** Summary of amino acid catabolism.