Paper: Metabolism of Amino Acids and Nucleotides (SEM IV)
Unit 2

Five amino acids are converted to α-Ketoglutarate

Proline, Glutamate, Glutamine, Arginine and Histidine enter the citric acid cycle as α-Ketoglutarate.

Arg and His contain five adjacent carbons and a sixth carbon attached through a nitrogen atom. The catabolic conversion of these amino acids to glutamate is therefore slightly more complex than the path from proline or glutamine. Refer the figure given below.

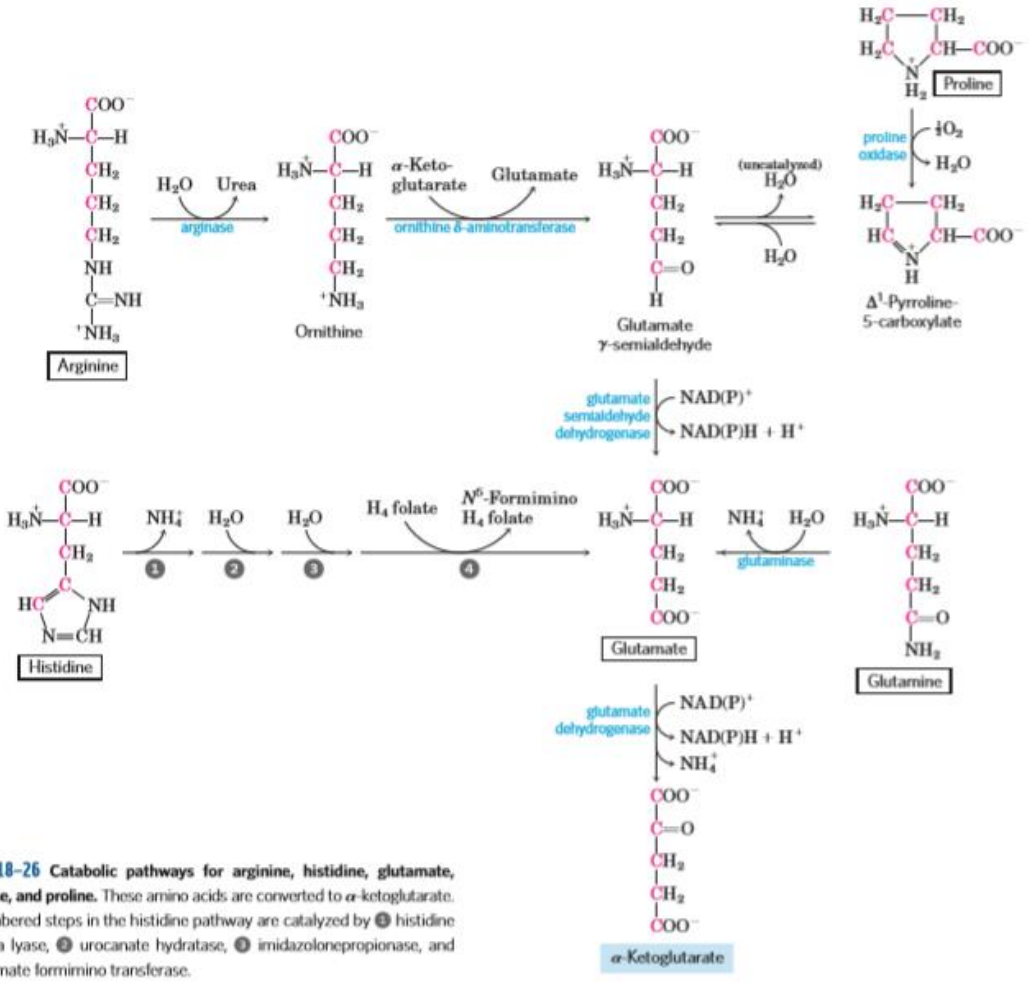

FIGURE 18–26 Catabolic pathways for arginine, histidine, glutamate, glutamine, and proline. These amino acids are converted to α-ketoglutarate. The numbered steps in the histidine pathway are catalyzed by ❶ histidine ammonia lyase, ❷ urocanate hydratase, ❸ imidazolonepropionase, and ❹ glutamate formimino transferase.

Four amino acids are converted to Succinyl-CoA

Carbon skeletons of methionine, isoleucine, threonine and valine are degraded by pathways that yield succinyl-CoA. In human tissues, threonine is converted to propionyl CoA in two steps. Refer the figure given below.

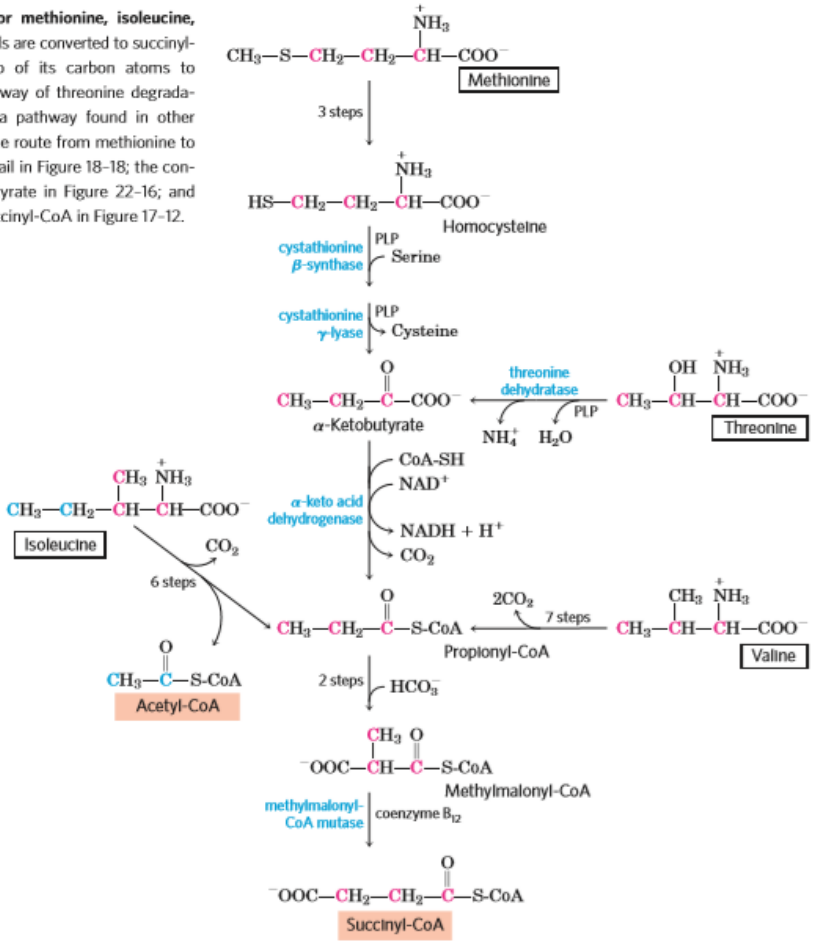

FIGURE 18–27 Catabolic pathways for methionine, isoleucine, threonine, and valine. These amino acids are converted to succinyl-CoA; isoleucine also contributes two of its carbon atoms to acetyl-CoA (see Fig. 18–21). The pathway of threonine degradation shown here occurs in humans; a pathway found in other organisms is shown in Figure 18–19. The route from methionine to homocysteine is described in more detail in Figure 18–18; the conversion of homocysteine to α-ketobutyrate in Figure 22–16; and the conversion of propionyl-CoA to succinyl-CoA in Figure 17–12.

Methylmalonic acidemia- Rare genetic disease due to lack of methylmalonyl-CoA mutase, leading to serious metabolic consequences. An example is given in Box 18-2, where the kids had died due to accumulation of methylmalonic acid in tissues, blood and urine which was initially misunderstood for ethylene glycol. Refer table 18-2 (Lehninger).

Most of the breakdown of the amino acids takes place in liver but three amino acids with branched side chains (Leucine, Isoleucine and Valine) are oxidized as fuels primarily in muscle, adipose, kidney and brain tissue. These extrahepatic tissues contain an aminotransferase, absent in liver that acts on all three branched chain amino acids to produce the corresponding α-keto acids.

Maple Syrup Urine Disease- rare genetic disease in which three branched chain α-keto acids accumulate in the blood and spill over in the urine. Named so because of the characteristic odor imparted to the urine by the α-keto acids, results from a defective branched chain α-keto acid dehydrogenase complex. Disease results in abnormal development of the brain, mental retardation and death in early infancy. Treatment includes controlled diet, limiting the intake of valine, isoleucine and leucine to the minimum required to permit normal growth.

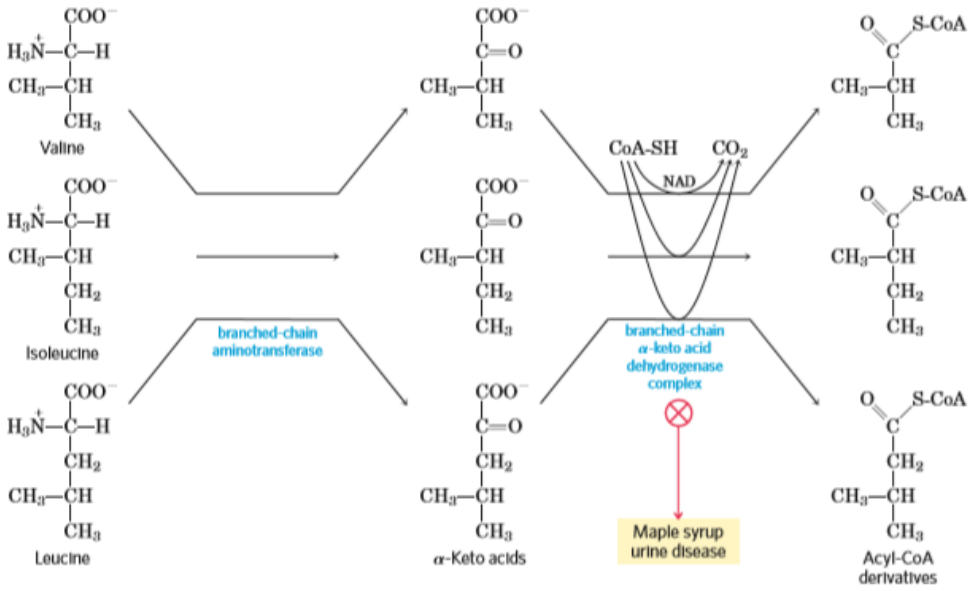

FIGURE 18–28 Catabolic pathways for the three branched-chain amino acids: valine, isoleucine, and leucine. All three pathways occur in extrahepatic tissues and share the first two enzymes, as shown here. The branched-chain α-keto acid dehydrogenase complex is analogous to the pyruvate and α-ketoglutarate dehydrogenase complexes and requires the same five cofactors (some not shown here). This enzyme is defective in people with maple syrup urine disease.

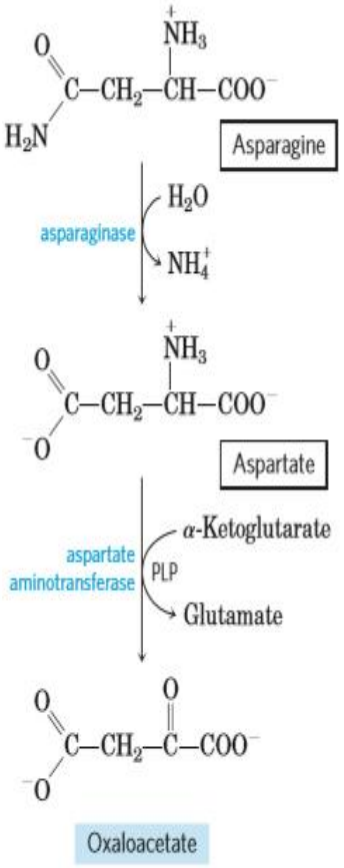

FIGURE 18–29 Catabolic pathway for asparagine and aspartate. Both amino acids are converted to oxaloacetate.

Asparagine and Aspartate are degraded to oxaloacetate

Carbon skeletons of asparagine and aspartate enter TCA cycle as malate in mammals and oxaloacetate in bacteria.

Mammals- the enzyme asparaginase catalyzes the hydrolysis of asparagine to aspartate which undergoes transamination with α-ketoglutarate to yield glutamate and oxaloacetate. Oxaloacetate is converted to malate in the cytosol and then transported into the mitochondrial matrix through malate-α-ketoglutarate transporter.

Bacteria- Oxaloacetate produced in the transamination reaction can be used directly in the citric acid cycle.