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Amino Acids 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. Ten of the amino acids are only one or a few enzymatic steps removed from their precursors. The pathways for others, such as the aromatic amino acids, are more complicated.

Different organisms vary greatly in their ability to synthesize the 20 amino acids. Whereas most bacteria and plants can synthesize all 20, mammals can synthesize only about half of them.

Those that are synthesized in mammals are generally those with simple pathways. These are called the nonessential amino acids to denote the fact that they are not needed in the diet. The remaining, the essential amino acids, must be obtained from the diet.

Essential amino acids (EAA)	EAA (%)
Arginine	1.2
Histidine	1.08
Isoleucine	12.3
Leucine	5.63
Lysine	13.42
Methionine	13.06
Phenylalanine	1.27
Tryptophan	1.3
Valine	23.72
Total	72.98

Non essential amino acids (NEAA)	NEAA (%)
Alanine	1
Asparagine	0.056
Aspartic acid	1.46
Cystine	5.56
Glutamic acid	2.51
Glycine	9.8
Proline	4.26
Serine	2.66
Tyrosine	2.51
Total	29.816

Intermediates of glycolysis serve as precursors for serine, glycine, cysteine, and alanine. Serine can be synthesized from the glycolytic intermediate 3-phosphoglycerate, which is oxidized, transaminated by glutamate, and dephosphorylated.

Glycine and cysteine can be derived from serine.

Glycine can be produced from serine by a reaction in which a methylene group is transferred to tetrahydrofolate (FH4).

Cysteine derives its carbon and nitrogen from serine. The essential amino acid methionine supplies the sulfur.

Alanine can be derived by transamination of pyruvate.

Amino acids derived from TCA cycle intermediates

Aspartate can be derived from oxaloacetate by transamination.

Asparagine is produced from aspartate by amidation.

Glutamate is derived from α-ketoglutarate by the addition of NH_4^+ via the glutamate dehydrogenase reaction or by transamination. Glutamine, proline, and arginine can be derived from glutamate.

Glutamine is produced by amidation of glutamate.

Proline and arginine can be derived from glutamate semialdehyde, which is formed by reduction of glutamate.

Proline can be produced by cyclization of glutamate semialdehyde.

Arginine, via three reactions of the urea cycle, can be derived from ornithine, which is produced by transamination of glutamate semialdehyde.

Tyrosine, the 11^{th} nonessential amino acid, is synthesized by hydroxylation of the essential amino acid phenylalanine in a reaction that requires tetrahydrobiopterin.

Degradation of amino acids

Occures in the liver. These pathways are mainly glucogenic (or gluconeogenic) which provide carbon for the synthesis of glucose.

Amino acids that form acetyl CoA or acetoacetate are ketogenic; which form ketone bodies.

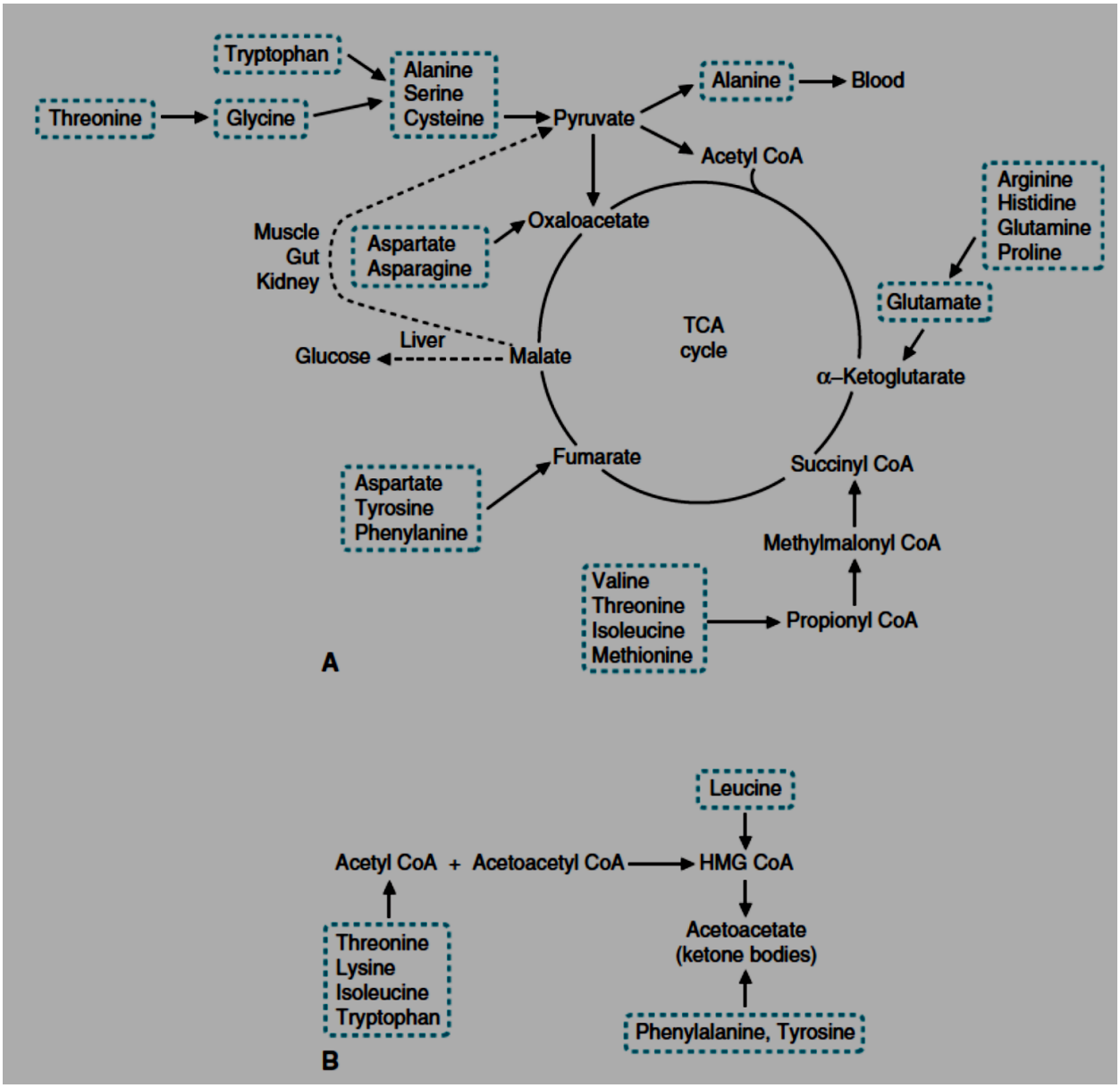
Isoleucine, tryptophan, phenylalanine, and tyrosine are glucogenic and ketogenic in the same time.

Amino acids that are converted to pyruvate

Occures in the liver. These pathways are mainly glucogenic (or gluconeogenic) which provide carbon for the synthesis of glucose. Amino acids that are synthesized from intermediates of glycolysis (serine, glycine, cysteine, and alanine) are degraded to form pyruvate.

Serine is converted to 2-phosphoglycerate, an intermediate of glycolysis, or directly to pyruvate and NH_4^+ by serine dehydratase, which is an enzyme that requires PLP.

Glycine reacts with methylene FH_4 to form serine.



Cysteine forms pyruvate. Its sulfur, which was derived from methionine, is converted to sulfuric acid (H_2SO_4), which is excreted by the kidneys.

Alanine can be transaminated to pyruvate.

Amino acids that are converted to intermediates of the TCA cycle

Carbons from four groups of amino acids form the TCA cycle intermediates α-ketoglutarate, succinyl CoA, fumarate, and oxaloacetate.

Amino acids that form α-ketoglutarate:

(1) Glutamate can be deaminated by glutamate dehydrogenase or transaminated to form α-ketoglutarate.

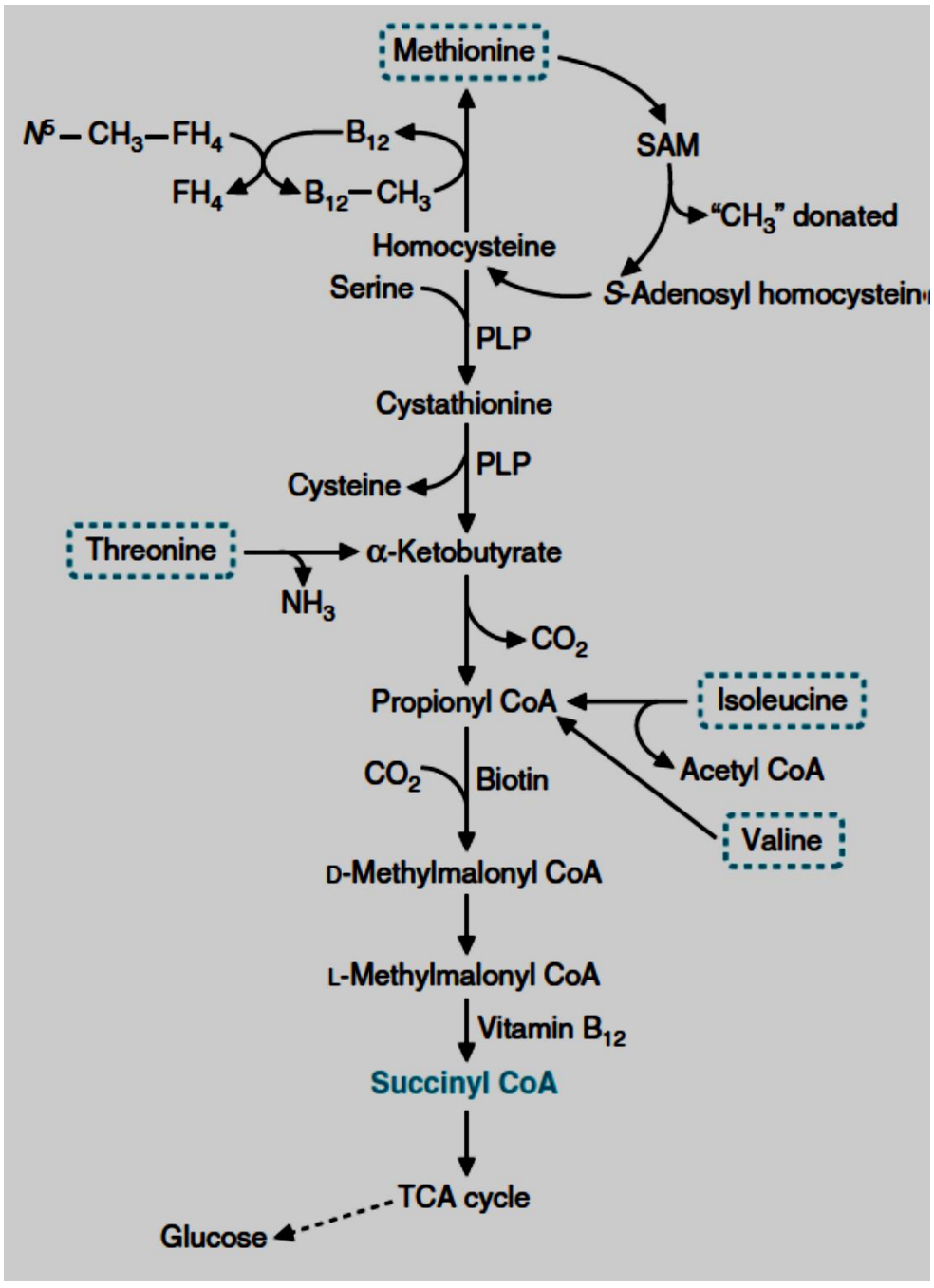
(2) Glutamine is converted by glutaminase to glutamate with the release of its amide nitrogen as NH_4^+.

(3) Proline is oxidized so that its ring opens, forming glutamate semialdehyde, which is reduced to glutamate.

(4) Arginine is cleaved by arginase in the liver to form urea and ornithine. Ornithine is transaminated to glutamate semialdehyde, which is oxidized to glutamate.

(5) Histidine is converted to formiminoglutamate (FIGLU). The formimino group is transferred to FH_4, and the remaining five carbons form glutamate.

Amino acids that form succinyl CoA



Threonine, methionine, valine, and isoleucine are converted to succinyl CoA which utilizes vitamin B12.

In a different set of reactions, threonine is converted to glycine and acetyl CoA.

Methionine provides methyl groups for the synthesis of various compounds; its sulfur is incorporated into cysteine; and the remaining carbons form succinyl CoA.

Valine and isoleucine, two of the three branched-chain amino acids, form succinyl CoA.

Degradation of all three branched-chain amino acids begins with a transamination, ketoacid dehydrogenase complex. This enzyme, like pyruvate dehydrogenase and α-ketoglutarate dehydrogenase, requires thiamine pyrophosphate, lipoic acid, CoA, flavin adenine dinucleotide (FAD), and NAD^+.

Amino acids that form fumarate

Phenylalanine, tyrosine, and aspartate are converted to fumarate.

(1) Phenylalanine is converted to tyrosine by phenylalanine hydroxylase in a reaction requiring tetrahydrobiopterin and O_2.

(2) Tyrosine, which is obtained from the diet or by hydroxylation of phenylalanine, is converted to homogentisic acid. The aromatic ring is opened and cleaved, forming fumarate and acetoacetate.

(3) Aspartate is converted to fumarate through reactions of the urea cycle and the purine nucleotide cycle. Aspartate reacts with IMP to form AMP and fumarate in the purine nucleotide cycle.

Amino acids that form oxaloacetate

(1) Aspartate is transaminated to form oxaloacetate.

(2) Asparagine loses its amide nitrogen as NH_4^+, forming aspartate in a reaction catalyzed by asparaginase.

Amino acids that are converted to acetyl CoA or acetoacetate

Lysine, threonine, isoleucine, and tryptophan can form acetyl CoA.

Phenylalanine and tyrosine form acetoacetate.

Leucine is degraded to form both acetyl CoA and acetoacetate.