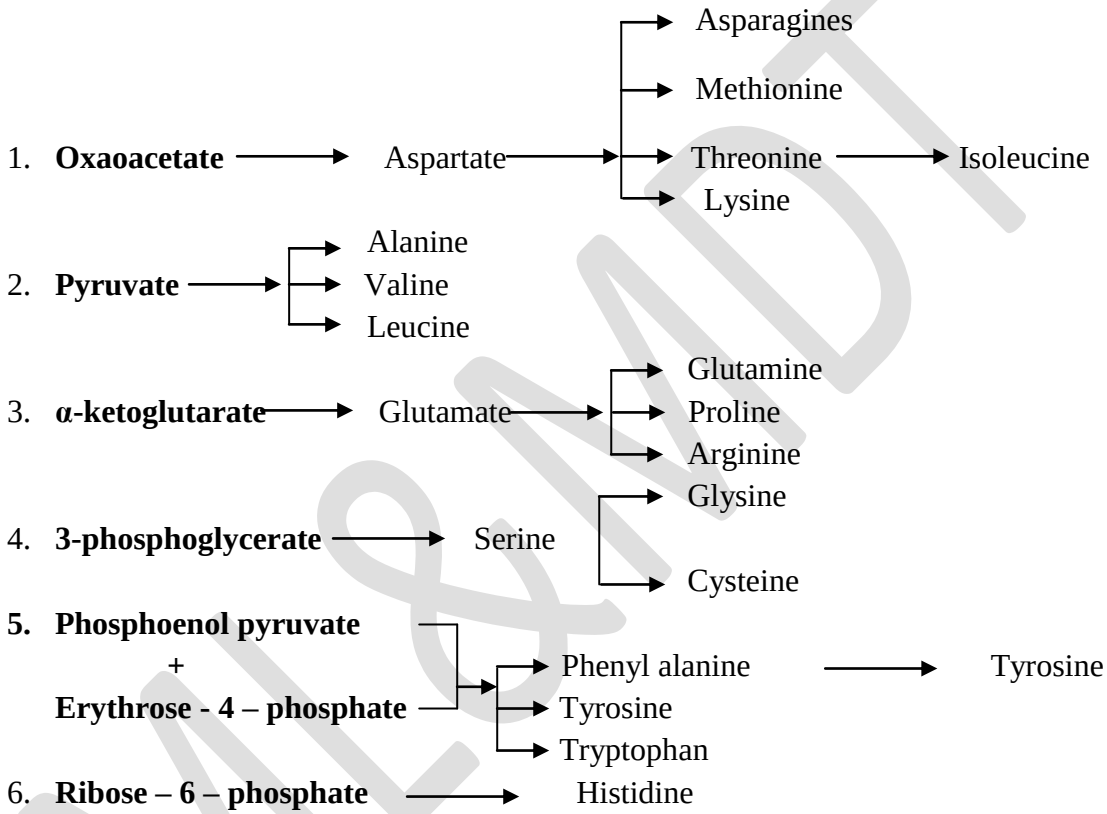
Those amino acids which can be synthesized through simple pathways are non-essential, while those which are not synthesized or synthesized with complicated pathways are essential.

Amino acids Biosynthesis:

All amino acids are synthesized by transamination of some keto acids, which are derived from intermediates of glycolysis, pentose-phosphate pathway and TCA cycle. On the basis of their precursors, the different pathways of amino acid biosynthesis could be recognized in to six groups.



Regulation of amino acid biosynthesis:

The biosynthesis of bio molecules could be controlled in two ways-

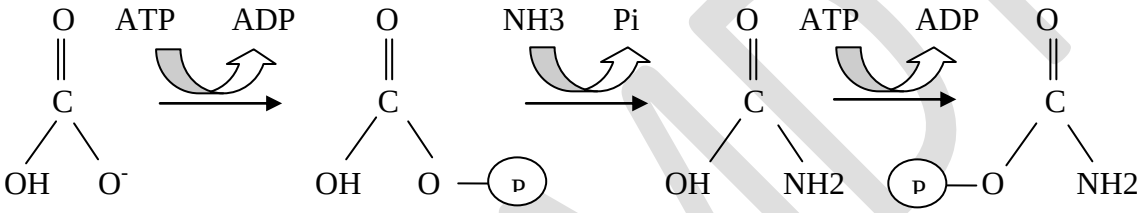
1. By controlling the synthesis of enzymes and finally the amount of enzyme.
2. By controlling the activity of enzymes. The activity could further be controlled in two ways-
   a) Allosteric modification of the enzyme which usually includes activation by substrate concentration and inactivation by product concentration.
   b) Covalent modification includes activation / inactivation of the enzymes by some molecules which are not an intermediate in metabolic pathway.

Urea cycle:

The urea cycle is the first cyclic metabolic pathway discovered (Hans Krebs and Kurt Henseleit in 1932). The cycle starts with the coupling of free ammonia (NH_4^+) with bicarbonates (HCO_3^-) resulting in the formation of carbamoyl phosphate.

In the first step of the reaction bicarbonate is phosphorelated by ATP to carboxyphosphate. Ammonia now replaces phosphate in the carboxyphosphate to produce carbamic acid and an orthophosphate. Carbamic acid is than phosphorylated by ATP to form carbamoyl phosphate. The reaction consumes two ATP molecules.

The overall reaction is:

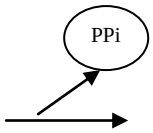


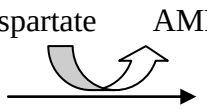
The urea cycle is mostly cytosolic but also passes through the mitochondrial matrix to accept the carbamoyl phosphate.

A non-protein amino acid ornithine enters the mitochondrial matrix and combines with the carbamoyl phosphate to form a molecule of citrulline, another non protein amino acid and inorganic phosphate. The reaction is catalyzed by the enzyme ornithine transcarbamoylase.

Ornithine transcarbamoylase

1. The citrulline is then exported to the cytosol, where ATP transfers its AMP to citrulline to form a citrullyl-AMP intermediate complex.
   The intermediate complex condenses with aspartate to form arginino succinate and releases AMP. The whole reaction is catalysed by arginino-succinate synthase.
2. In the next step arginino-succinate is split into arginine and fumarate by the enzyme arginino-succinase. Fumarate goes to mitochondria to join TCA cycle.
3. In the last step arginine is hydrolysed by the enzyme arginase to generate ornithine and urea. The urea is excreted and the ornithine enters the cycle again.
   Human beings excrete about 10 kg of urea every year.

1) Citrulline + ATP 

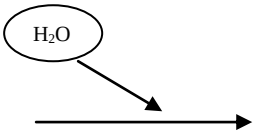
Citrullyl-AMP 

Arginino-succinate

Arginino-succinate synthase

2) Arginino-succinate ⟶ Arginine + Fumarate

Arginino-succinase

3) Arginine 

Ornithine + Urea

Arginase

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