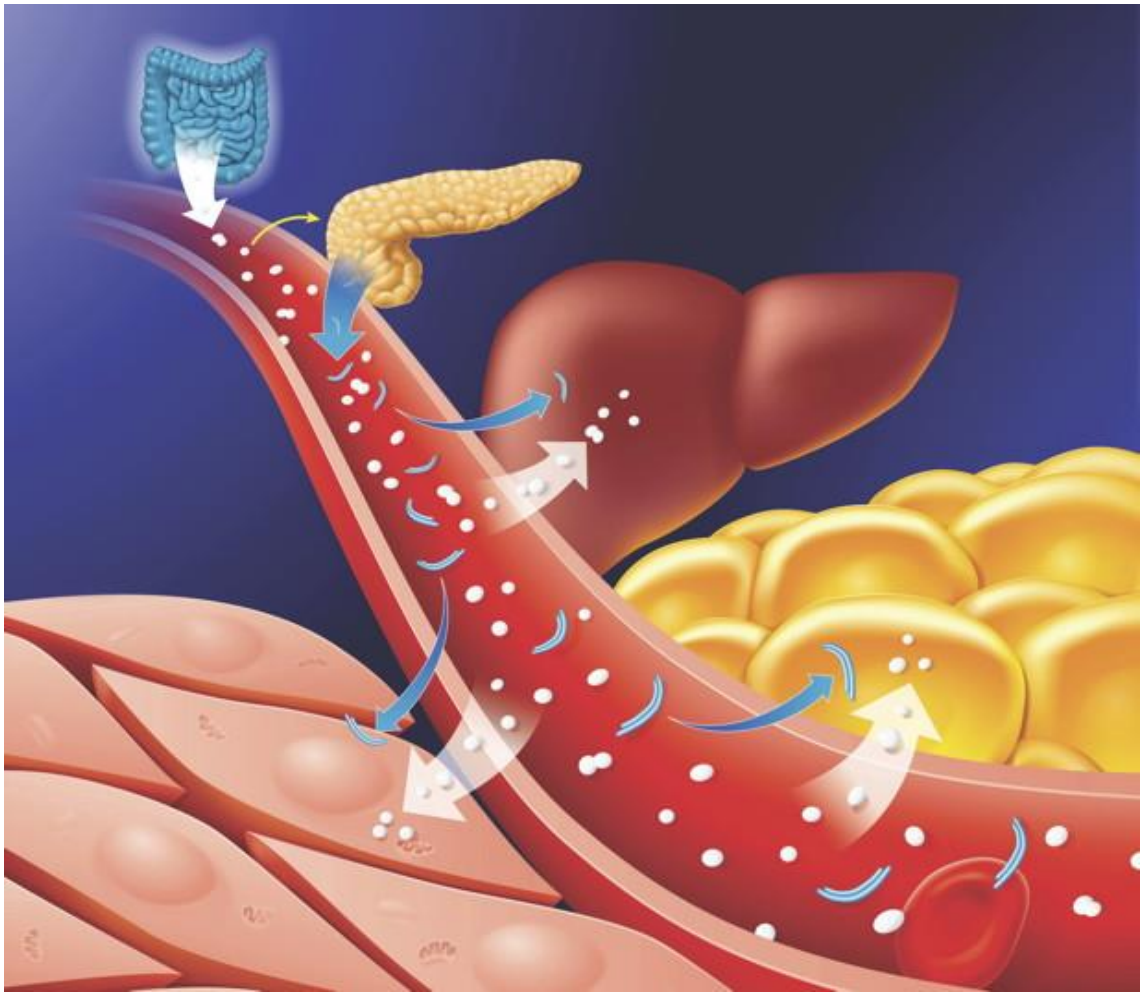
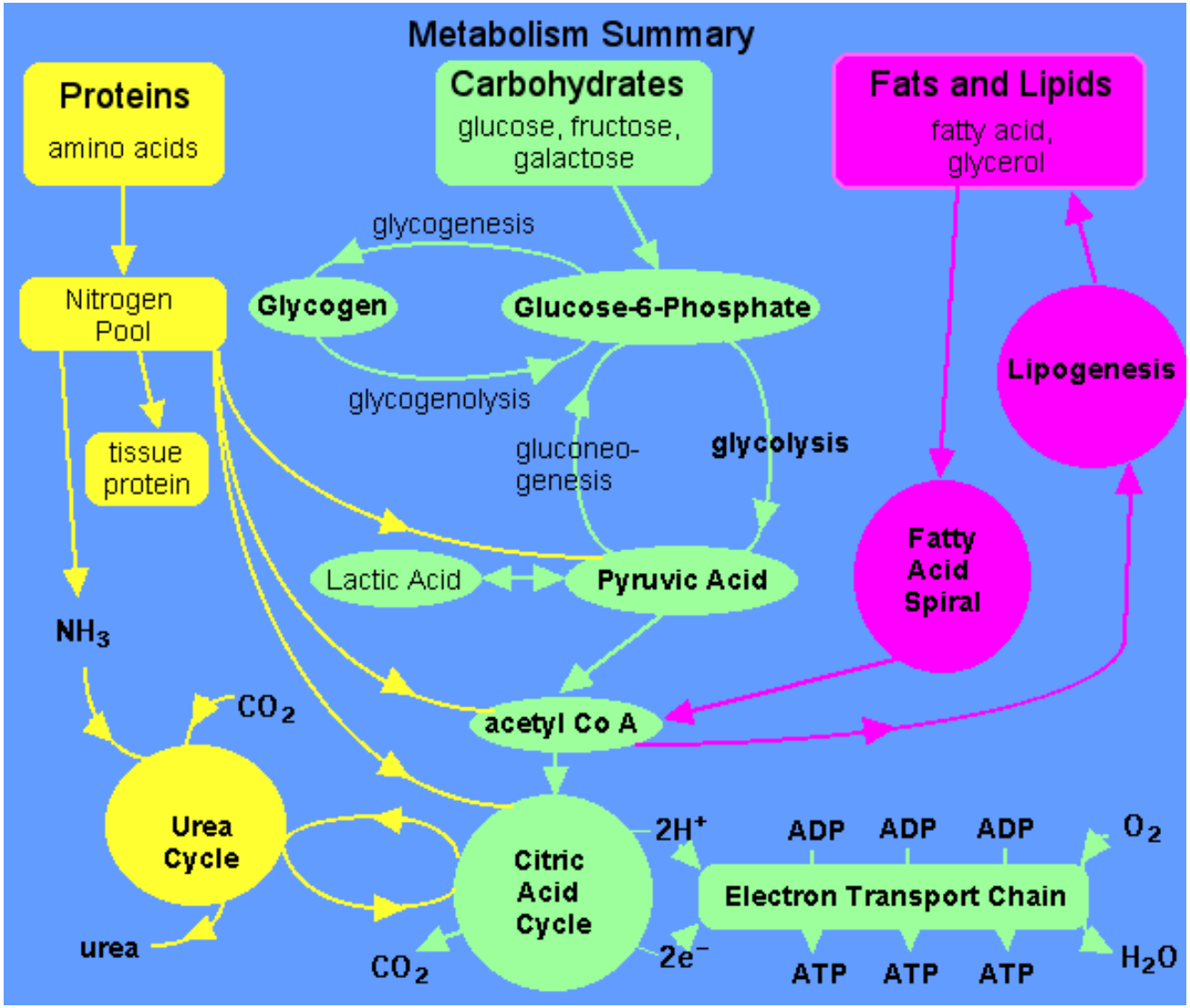
Chapter 14
Lipid and Amino Acid Metabolism

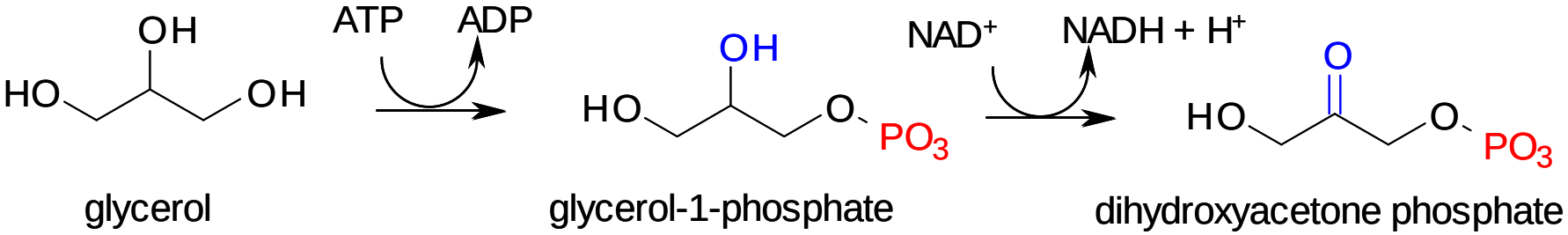


Metabolism of Foods



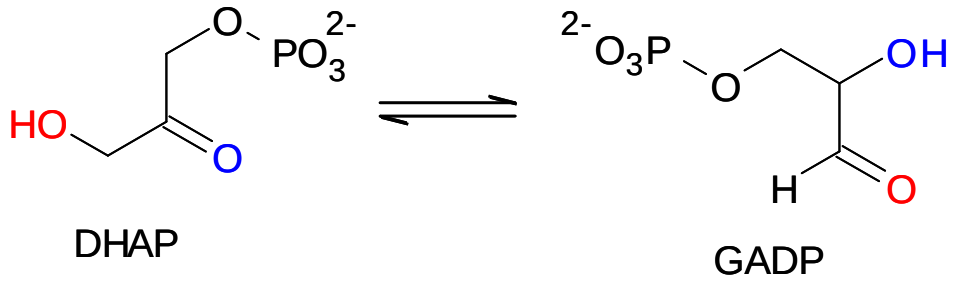
Glycerol Catabolism

Hydrolysis of triglycerides → fatty acids + glycerol



glycerol | glycerol-1-phosphate | dihydroxyacetone phosphate

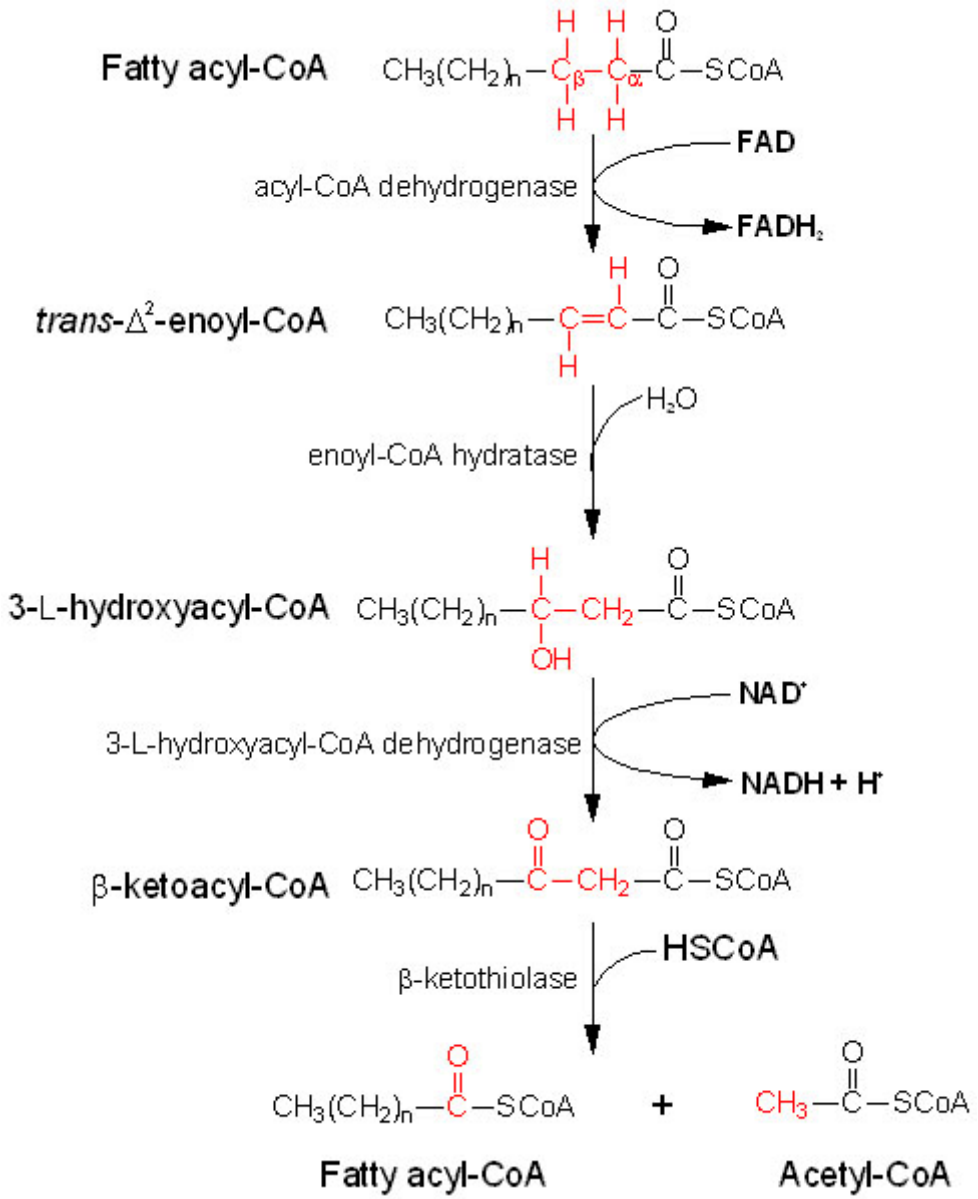
GADP can enter glycolysis.



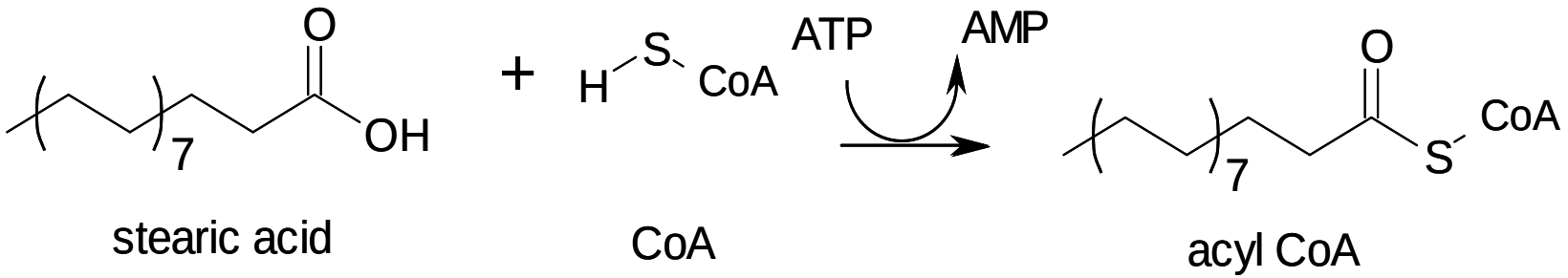
DHAP | GADP

TOTAL ENERGY GAIN: 20 ATP molecules/1 glycerol
(6.7 ATP per carbon)

β-oxidation of Fatty Acids



Step 1: Formation of acyl CoA

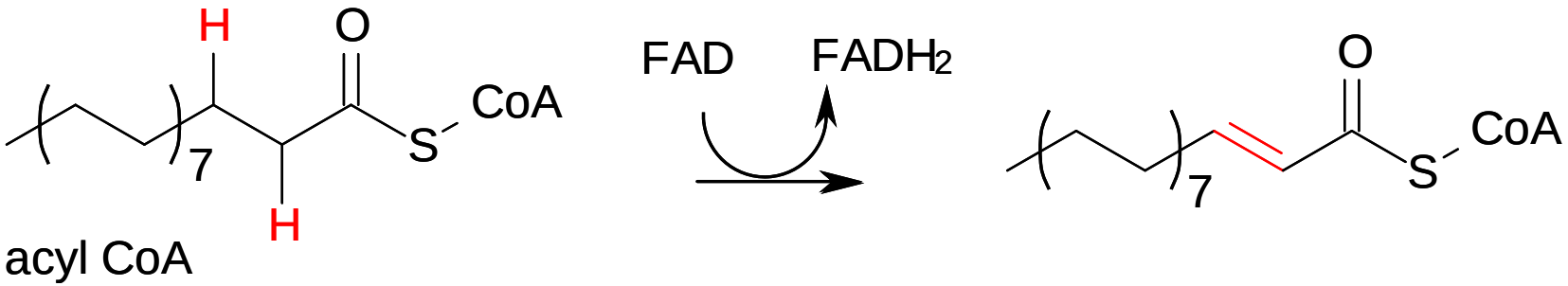


Catalyzed by carnitine acyltransferase.

The newly-formed acyl CoA now is transported to the mitochondrion via carnitine.

Step 2: Dehydrogenation

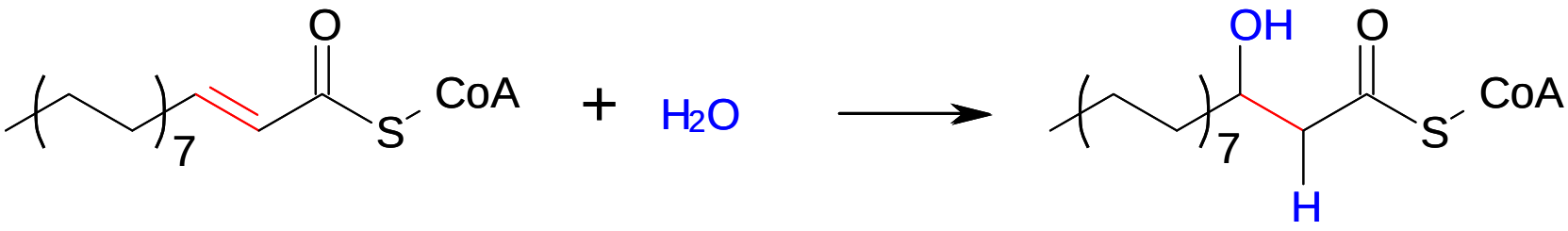
Hydrogens are removed and are picked up by FAD.



Catalyzed by *trans*-enoyl-CoA hydratase.

Step 3: Hydration

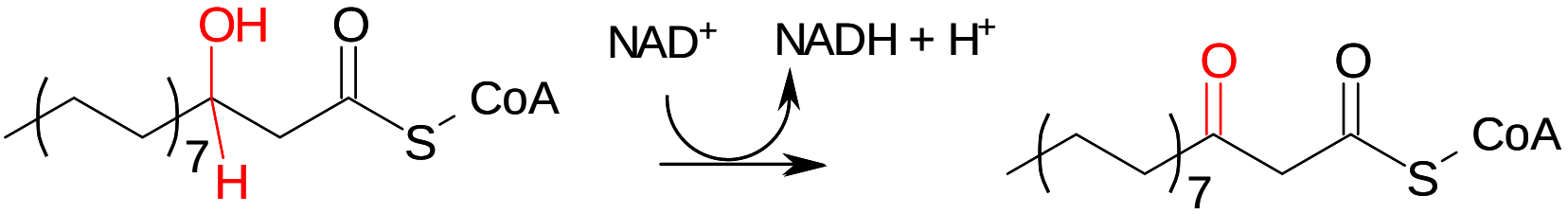
The β-carbon gains an alcohol.



Catalyzed by hydroxyacyldehydrogenase.

Step 4: Oxidation

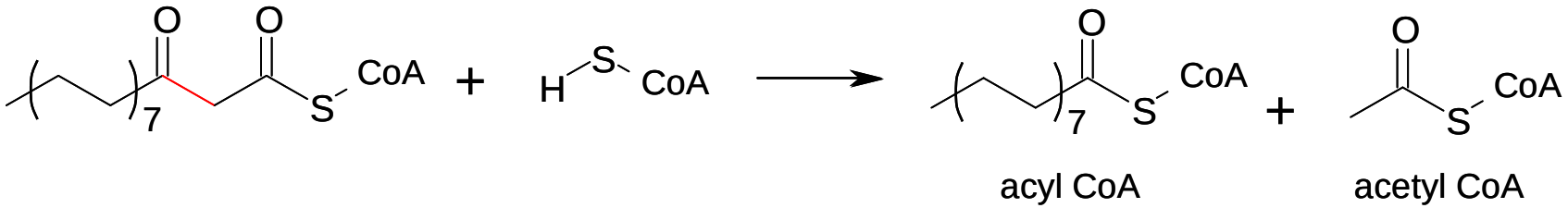
NAD^+ enters as a coenzyme to remove the hydrogens.



Catalyzed by hydroxyacyldehydrogenase.

Step 5: Cleavage of Acetyl CoA

Another equivalent of CoA enters and produces an acyl CoA and an acetyl CoA.



Catalyzed by thiolase.

The acetyl CoA can now enter the citric acid cycle.
The acyl CoA is now two carbons shorter.

Summary of β-Oxidation

Unsaturated fatty acids have to isomerize from the *cis* to the *trans* isomer.

Energy Gain:

- 2 ATP (only once)
+ 1 $FADH_2$ (2 ATP)
+ 1 NADH + H^+ (3 ATP)
+ 1 acetyl CoA (12 ATP through Citric Acid)

TOTAL: 17 ATP per 2 carbon fragments (-2 for initiation)

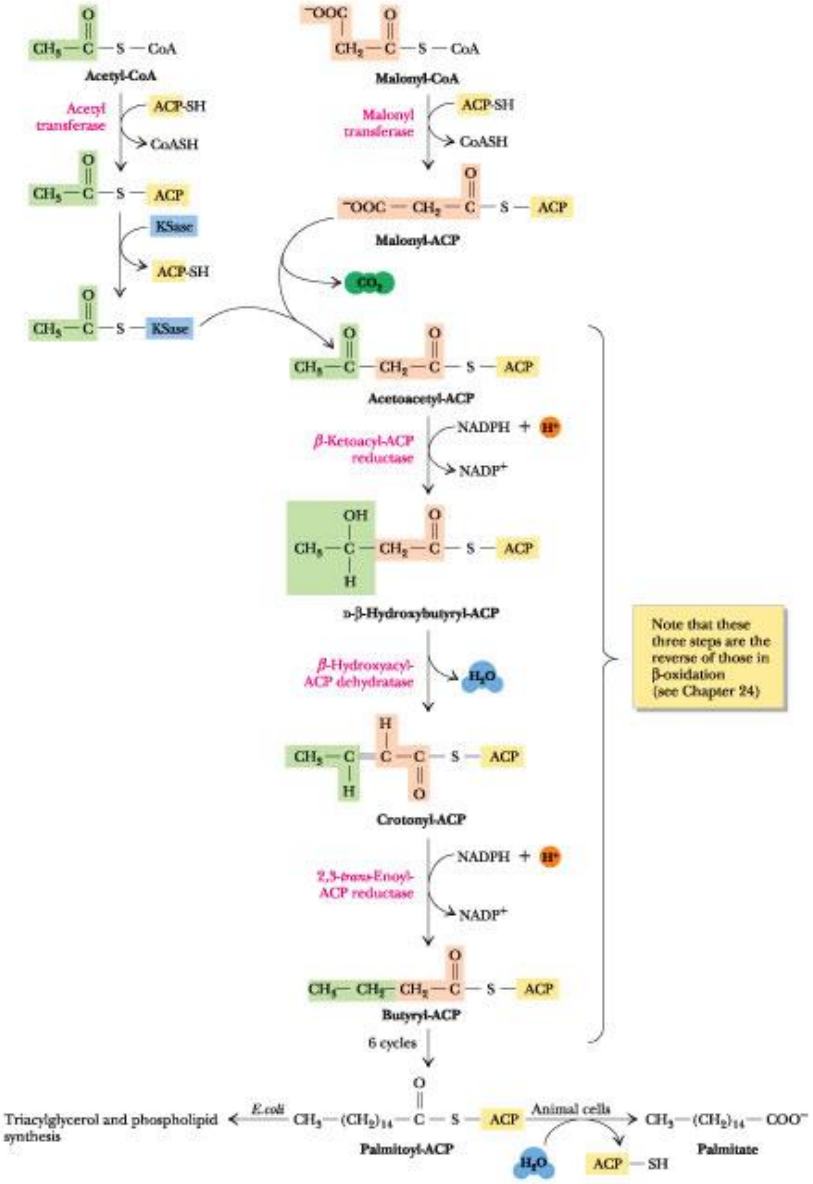
Example: stearic acid (18 carbons)

= 8 cycles x 17 – 2 + 12 ATP = 146 ATP

Biosynthesis of Fatty Acids

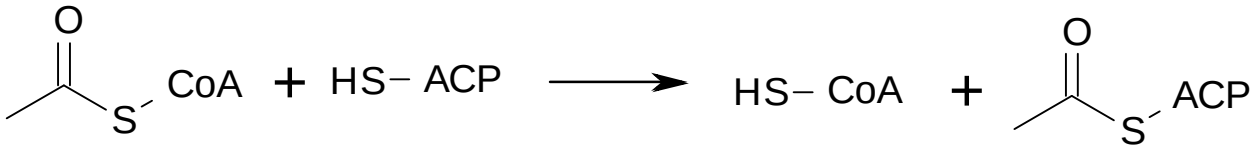
Fatty acids are synthesized from acetyl CoA in two-carbon fragments.

Excess acetyl CoA is converted into fatty acids and stored in the cells.

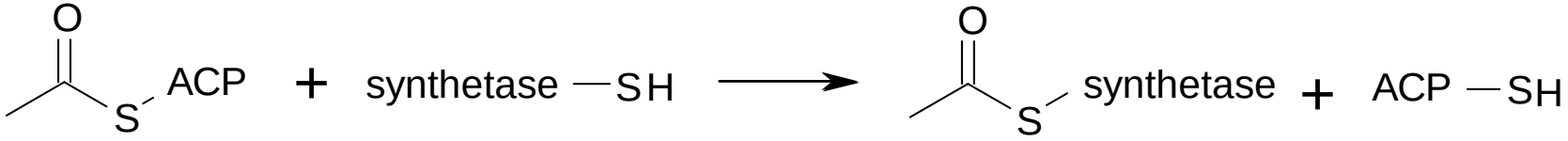


Fatty Acid Biosynthesis

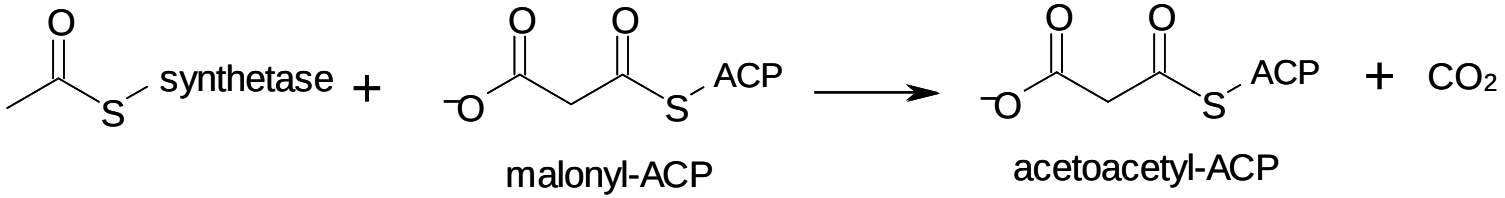
Step 1: ACP picks up an acetyl group from acetyl CoA.



Step 2: ACP delivers the acetyl to the fatty acid synthetase.



Step 3: Synthetase combines fragments.



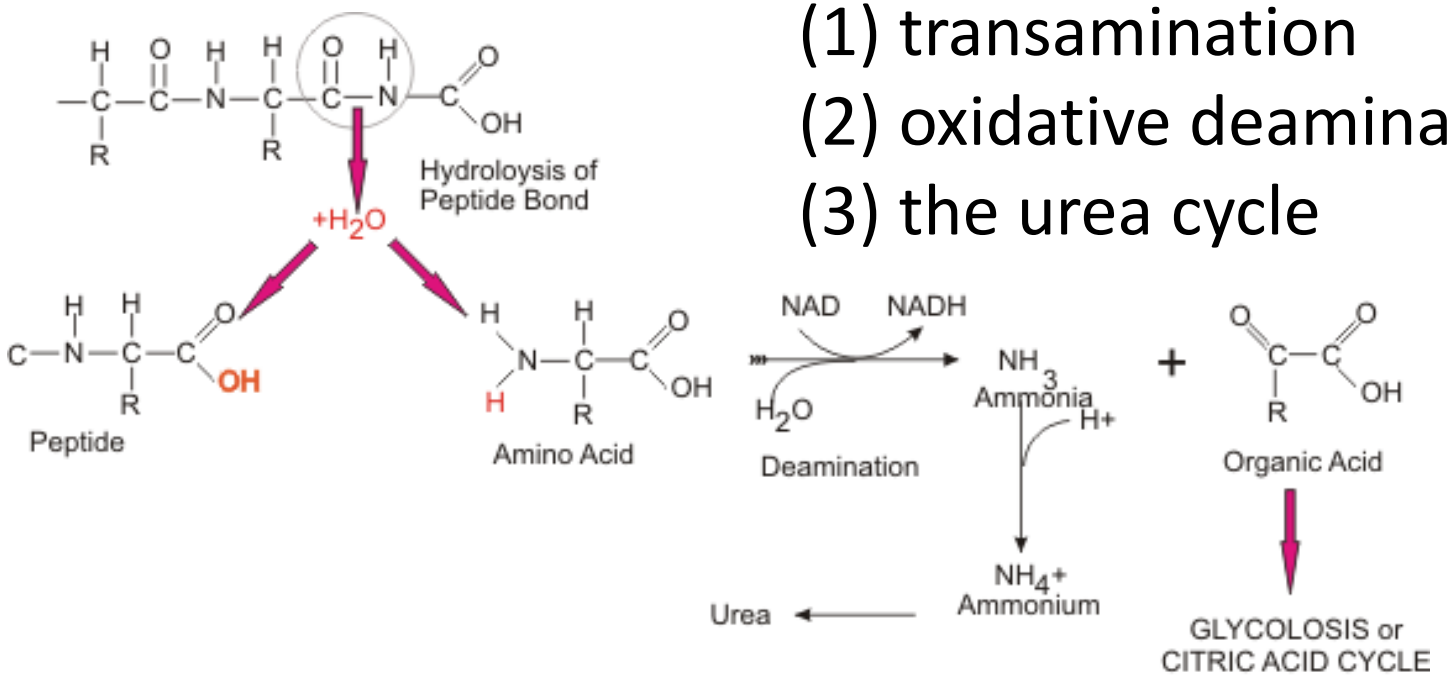
The cycle continues adding C_4 fragments together.

Catabolism of Amino Acids (N)

Proteins are hydrolyzed to amino acids to synthesize new proteins. Amino acids cannot be stored.

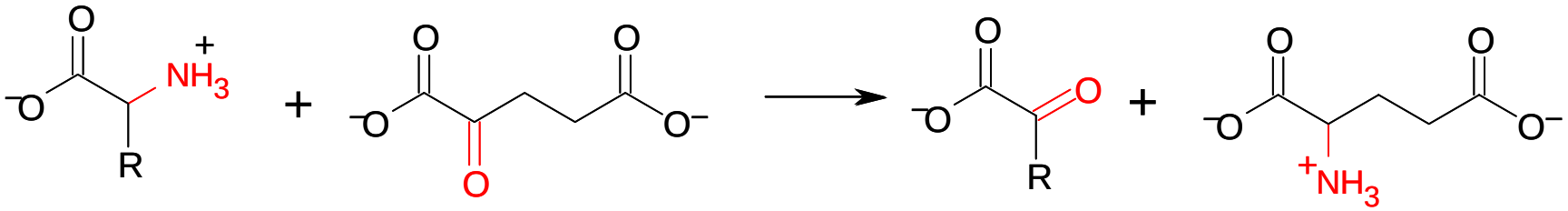
Catabolism of proteins follows three steps:

(1) transamination
(2) oxidative deamination
(3) the urea cycle

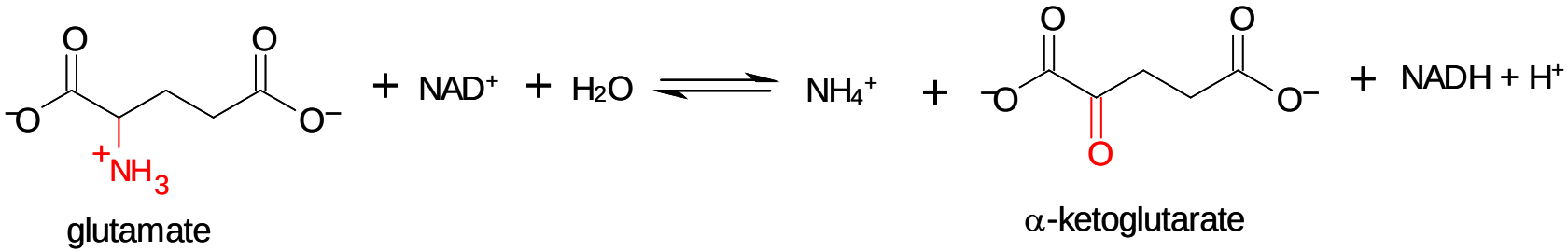


Stage 1: Transamination

Transamination moves the amino groups from amino acids to α-ketoglutarate.



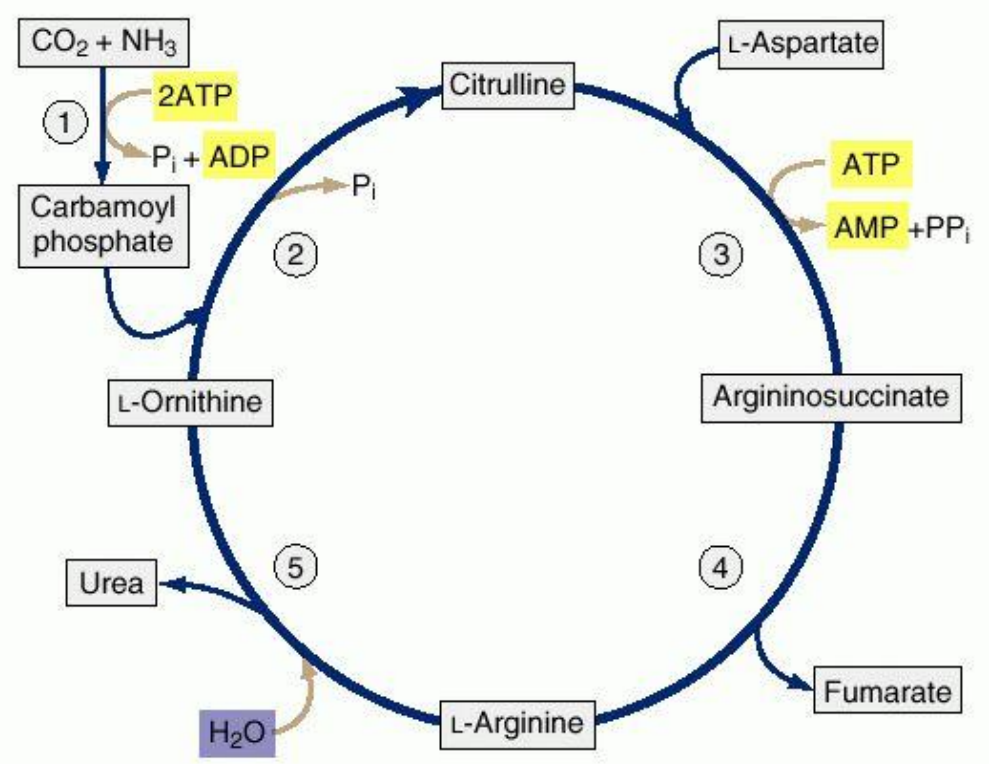
Step 2: Deamination



Oxidative deamination removes the amino group from glutamate via NAD^+ and H_2O. The regenerated α-ketoglutarate that can rejoin Stage 1.

The NADH + H^+ can join oxidative phosphorylation to produce 3 ATP.

Stage 3: Urea Cycle



KEY TO ENZYMES (Circled Numbers)

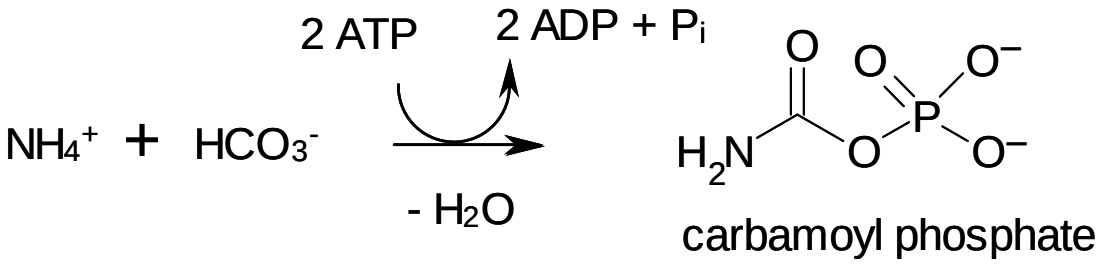
1. Carbamoyl-phosphate synthase (ammonia)
2. Ornithine carbamoyltransferase
3. Argininosuccinate synthase
4. Argininosuccinate lyase
5. Arginase

NH_4^+ and NH_3 are toxic to the body and are immediately metabolized via the urea cycle.

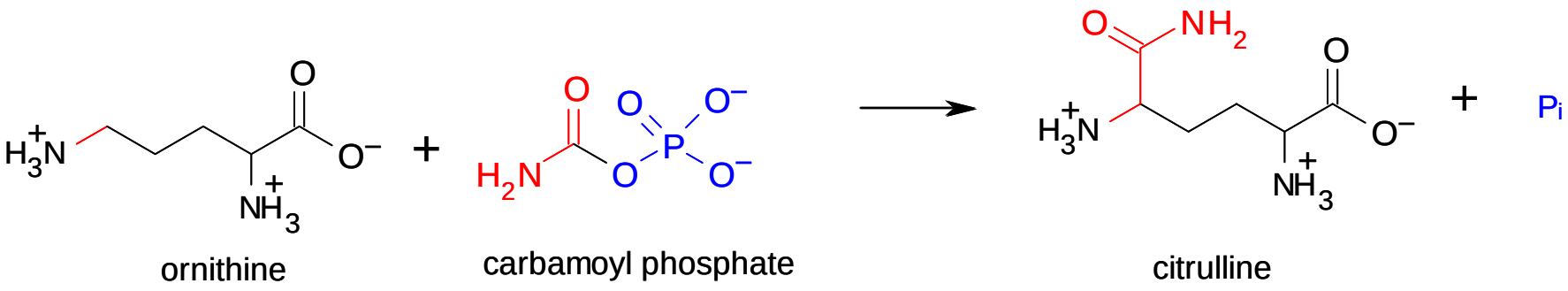
Any disorders or inhibition of the urea cycle can lead to liver failure due to a build-up of ammonia.

Step 1/2: Condensation

Step 1: Ammonium and bicarbonate are condensed with a phosphate.

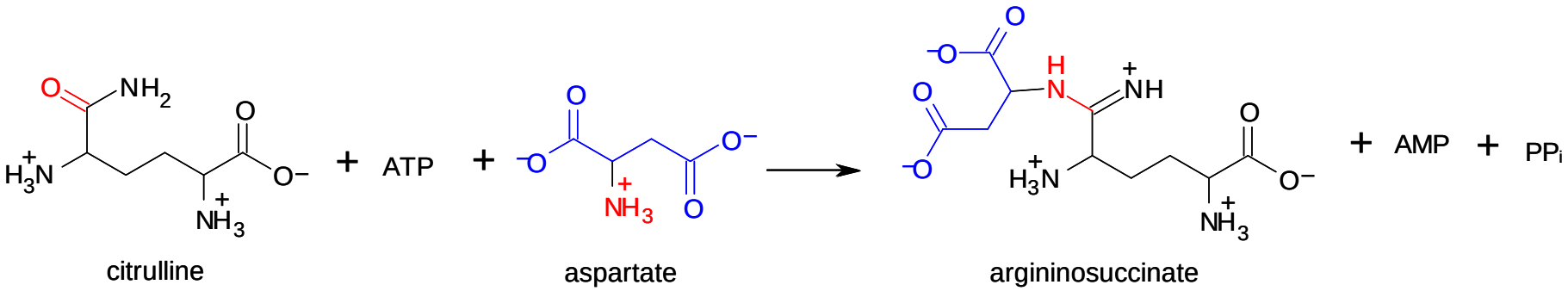


Step 2: Carbamoyl phosphate combines with ornithine to produce citrulline and releases a phosphate.



Step 3: Condensation

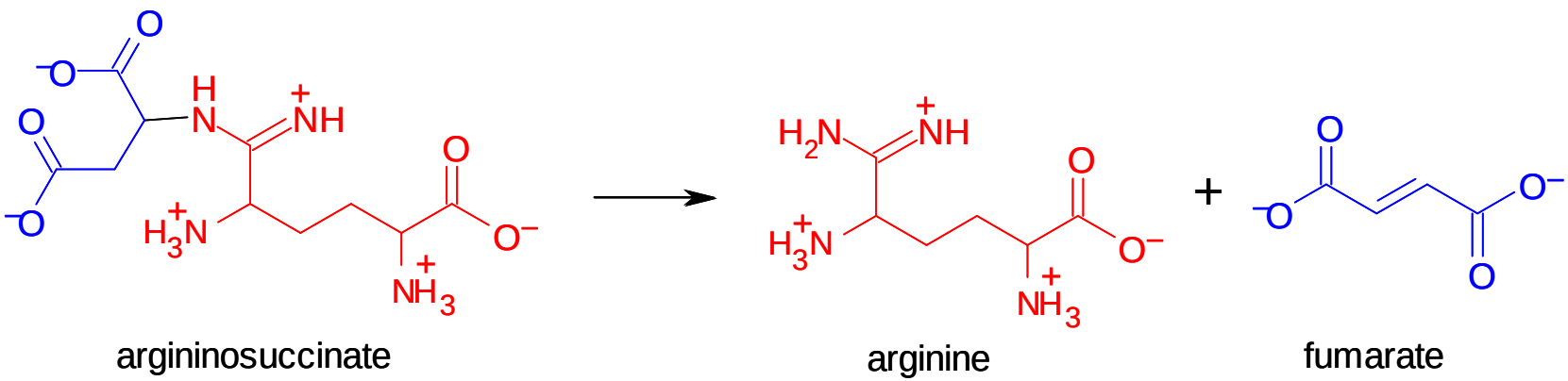
Citrulline and aspartate are condensed to form an amine linker, forming argininosuccinate.



Catalyzed by arginosuccinate synthase.
One molecule of ATP is hydrolyzed, forming AMP and pyrophosphate (free two-phosphate group).

Step 4: Cleavage of Argininosuccinate

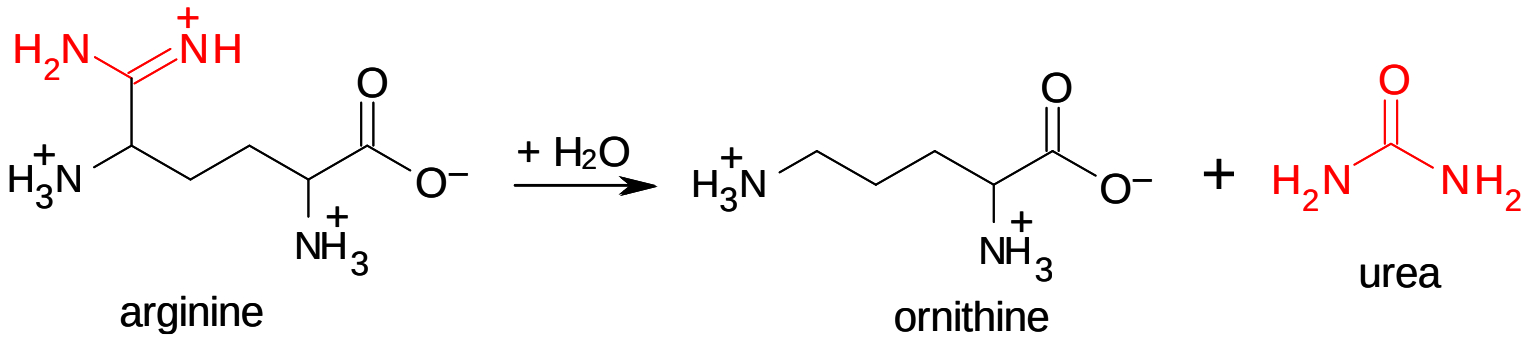
Argininosuccinate is split into arginine and fumarate. A double bond is formed in fumarate from the loss of the bond to the amino linker.



Catalyzed by arginosuccinate lyase.

Step 5: Hydrolysis

Arginine is hydrolyzed to urea and regenerates orithine that can begin the urea cycle again.



Catalyzed by arginase.

Urea is then excreted in urine while orinithine picks up another carbamoyl phosphate.

Carbamoyl phosphate can synthesize nucleotide bases. Fumarate is also used in the citric acid cycle.

Catabolism of Amino Acids (C)

glucogenic: amino acids whose products upon degradation can go on to convert to glucose.

ketogenic: amino acids whose products upon degradation are acetyl CoA and acetoacetic acid, but cannot convert to glucose.

Terms are *not* mutually exclusive.

Both glucogenic and ketogenic amino acids enter the citric acid cycle later.

Biosynthesis of Amino Acids

Nonessential amino acids are typically synthesized from intermediates from glycolysis or the citric acid cycle.