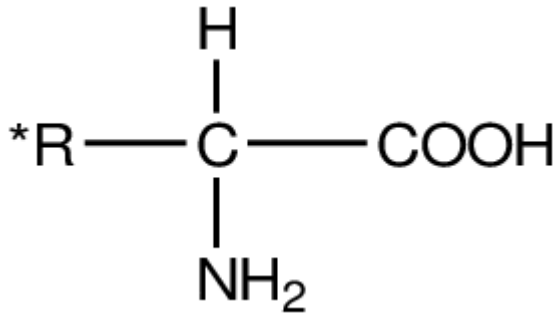
PROTEINS

Proteins are composed of carbon, hydrogen, oxygen and nitrogen. Sulfur and phosphorus may also included. Proteins is an important constituent of protoplasm (the cytoplasm and nucleus of a cell). It is broken down into amino acids by digestion. In mammals the protein requirement is continues because they do not store it to a large extent. The requirements of amino acids are variable in different mammals. Although more than 300 different amino acids have been described in nature, only 20 are commonly found as constituents of mammalian proteins (which are: Glycine, Alanine, Valine, Leucine, Isoleucine, Serine, Threonine, Cysteine, Cystine, Methionine, Glutamic acid, Aspartic acid, Lysine, Arginine, Histidine, Phenilalanine, Tyrosine, Tryptophan, Proline and Hydroxyproline).

The animal proteins are better than the vegetable proteins because the animal proteins contain most of the 20 essential amino acids. The animal proteins are found in meat (chicken, buffalo, fish, …), eggs and milk, while the vegetable proteins are found in cereals, vegetables and pulses. The minimum protein intake for body maintenance is 40 g/day.

The general formula of naturally occurring amino acids can be represented as:



The carboxyl group (-COOH) and the amino group (-NH2) are present in a molecule, hence the amino acid behaves both like an acid and a base; it is an amphoteric molecule.

The amino acids of a protein molecule are attached with each other by peptide bonds (-CO-NH-). The combination of two amino acids gives a dipeptide and similarly tripeptides and polypeptides are formed. The **peptides** form more complex **peptones**, which in turn, by their combination, form **proteoses** and **proteins**.

A. Classification of proteins based on nutritional value:

1. **Nutritionally rich proteins:** They are also called complete proteins or first-class proteins. They contain all the essential amino acids in the required proportion. On supplying these proteins in the diet, children will grow satisfactorily. A good example is the casein of milk.
2. **Incomplete proteins:** They lack one essential amino acid. They cannot promote body growth in children; but may be able to sustain the body weight in adults. Proteins from pulses are deficient in methionine, while proteins of cereals lack lysine. If both of them are combined in the diet, adequate growth may be obtained.
3. **Poor proteins:** They lack in many essential amino acids and a diet based on these proteins will not even sustain the original body weight.

B. Classification of proteins based on composition:

1. **Simple proteins**: which on hydrolysis yield only amino acids. Albumin and globulin are simple proteins. They are present in eggs, milk, and blood. They are proteins of high biological value i.e. contain all essential amino acids and are easily digested. Albumin is a protein made by the liver. It makes up about 60% of

the total protein in the blood and plays many roles. Albumin keeps fluid from leaking out of blood vessels and transports hormones, vitamins, drugs, and substances like calcium throughout the body.

2. **Conjugated proteins:** which the protein molecule is attached with other molecules Like: lipoproteins (protein combined with lipids) e.g. cell membrane, glycoproteins or mucoproteins (protein combined with carbohydrates) e.g. heparin and nucleoproteins (proteins combined with ribonucleic acid RNA or deoxyribonucleic acid DNA).
3. **Derived proteins**: which are formed by the breakdown of an original protein molecule either by acids or enzymes or by the effect of heat. Examples of derived proteins are proteases, peptones, and peptides.

Functions of proteins:

1- Proteins are important in building up processes e.g. growth and repairing.

2- Some hormones and enzymes are proteins and also hemoglobin.

3- Proteins balance the water contents of the body.

4- Plasma proteins and hemoglobin act for acid-base balance of blood.

5- Antibodies are formed of proteins.

6- The blood coagulation is formed of proteins.

7- Proteins (mucin) make the mucous secretions that help in swallowing food and protect the epithelium of the alimentary canal.

8- Many structures are essentially proteins e.g. hair, nails, fibers (collagen).

9- Provide energy but less than that provided by carbohydrates and fats (4 kcal/ g).

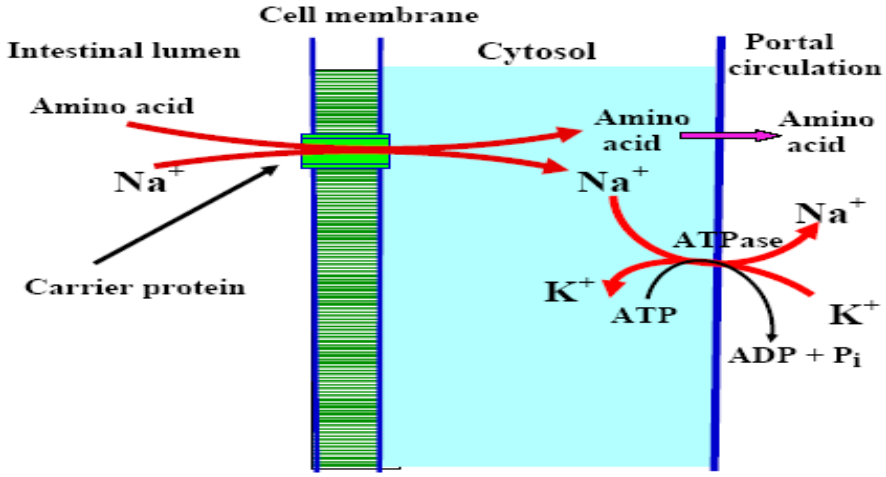
10 - Proteins may be transformed into fats or carbohydrates after deamination.

Protein Metabolism

Digestion: Dietary proteins must be digested to small simple molecules (amino acids), which are easily absorbed from the intestine. Protein digestion begins in the stomach by gastric juice, pepsin, and rennin. Digestion of proteins is completed in the small intestine by proteolytic enzymes (as trypsin, chymotrypsin, and aminopeptidase) present in pancreatic and intestinal juices.

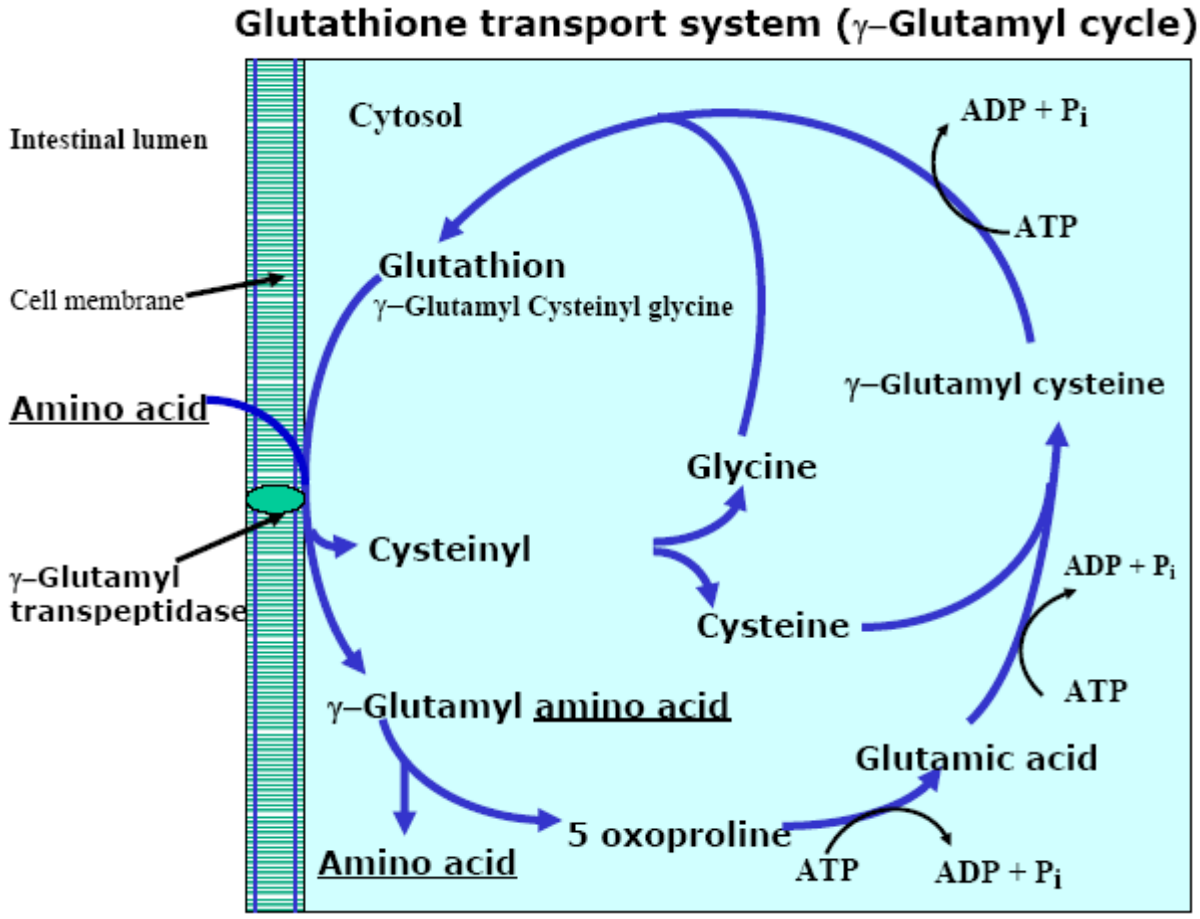
Absorption: It occurs in the small intestine. Absorption of amino acids is rapid in the duodenum and jejunum but slow in the ileum. There are two mechanisms for amino acids absorption.

1- **Carrier proteins transport system**: It is the main system for amino acid absorption. Absorption of one amino acid molecule needs one ATP molecule. There are seven carrier proteins, one for each group of amino acids. Each carrier protein has to sites one for amino acid and one for Na^+. It co-transports amino acid and Na^+ from intestinal lumen to cytosol of intestinal mucosa cells. The absorbed amino acid passes to the portal circulation, while Na^+ is extruded out of the cell in exchange with K^+ by sodium potassium pump.



Carrier Protein Transport System

2- **Glutathione transport system (γ−Glutamyl cycle):** Glutathione is used to transport amino acids from intestinal lumen to cytosol of intestinal mucosa cells. Absorption of one amino acid molecule needs 3 ATP molecules. Glutathione reacts with the amino acid in the presence of γ−glutamyl transpeptidase to form γ−glutamyl amino acid. γ−glutamyl amino acid releases amino acid in the cytosol of intestinal mucosa cells with formation of 5-oxoproline that is used for regeneration of glutathione to begin another turn of the cycle.



Sources of amino acid:

1- Dietary protein.

2- Breakdown of tissue proteins.

3- Biosynthesis of nonessential amino acids.

The fate of amino acid:

1- Biosynthesis of structural proteins e.g. tissue proteins

2- Biosynthesis of functional proteins e.g. hemoglobin, myoglobin, protein hormones and enzymes.

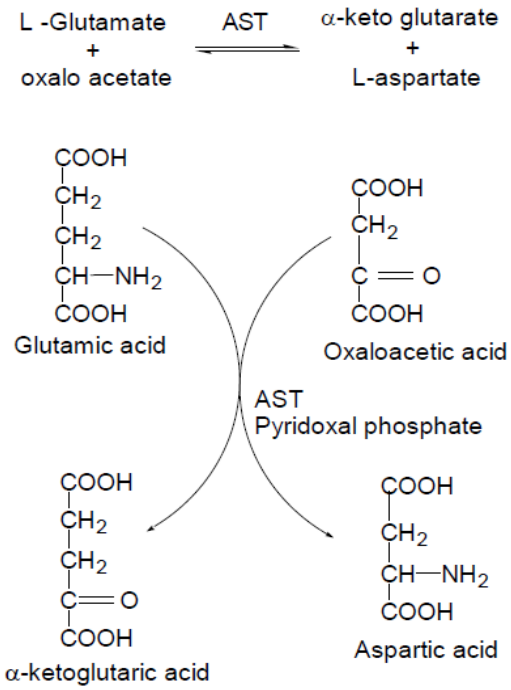
3- Biosynthesis of small peptides of biological importance e.g. glutathione.

4- Biosynthesis of non-protein nitrogenous compounds (NPN) as urea, uric acid, creatine, creatinine, and ammonia.

5- Catabolism of amino acids to give α-keto acids and ammonia. The α- keto acids that remain after removal of ammonia from amino acids are called the carbon skeleton. Ammonia is transformed mainly into urea.

The fate of carbon skeleton:

1- Biosynthesis of nonessential amino acids by transamination with glutamic acid.



2- Some amino acids give acetyl CoA are Ketogenic amino acids. Leucine and lysine are the only pure ketogenic amino acids.

3- Some amino acids give rise to pyruvic acid or one of the intermediates of Krebs cycle are glucogenic e.g. glycine, alanine, and cysteine.

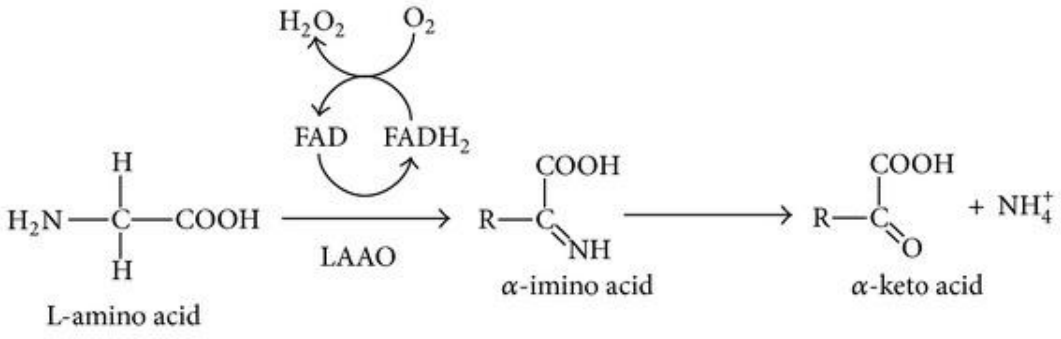
4- Oxidation via the Krebs cycle to give carbon dioxide, water, and energy.

Ammonia

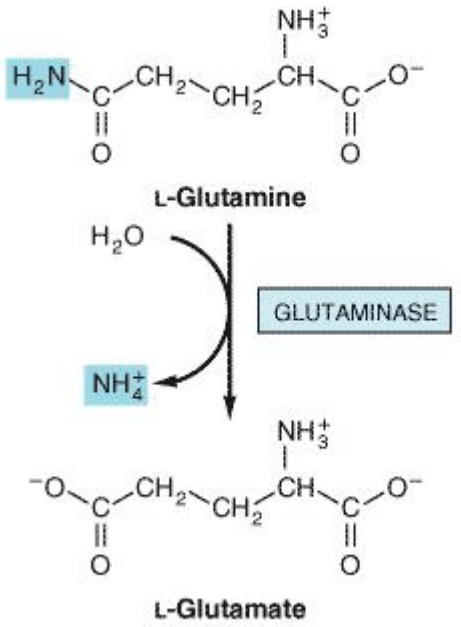
Ammonia is toxic to the central nervous system and its accumulation in the body is fatal. Once formed in the body, ammonia must be removed from the blood**.** It is removed by the liver that converts it to urea, which is less toxic, water-soluble and easily excreted in the urine.

Sources of ammonia:

1- Deamination of amino acids with the formation of α-keto acids and ammonia.

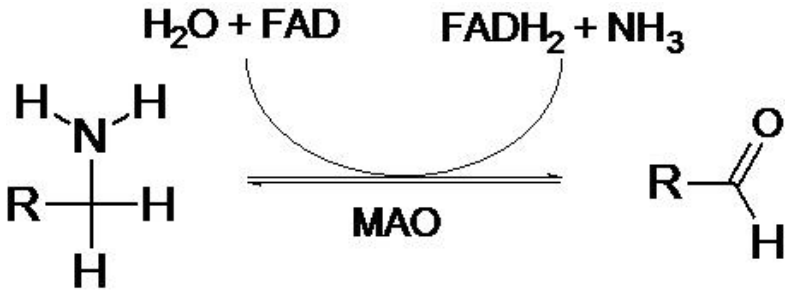


2- Glutamine in the kidney by glutaminase enzyme gives glutamic acid and ammonia which is used by the kidney to regulate the acid-base balance



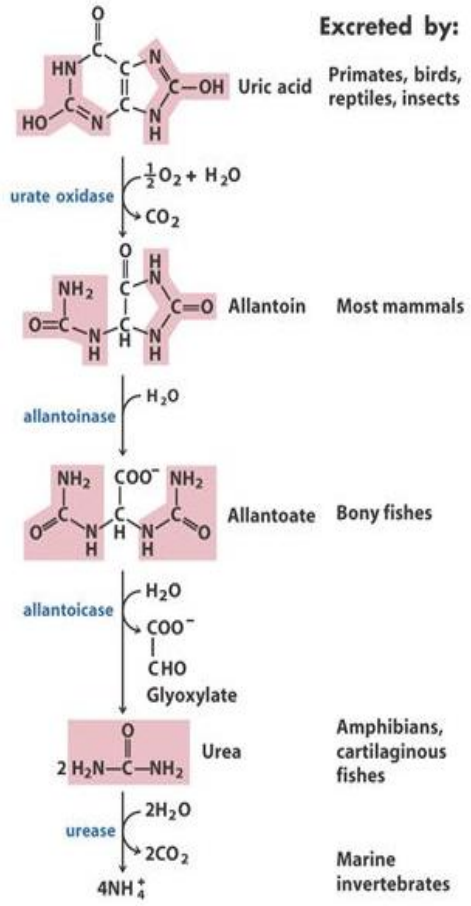
3-Ammonia produced by the action of intestinal bacteria on the non-absorbed dietary amino acids.

4-Ammonia is released from monoamines (e.g. epinephrine, norepinephrine, and dopamine) by the action of monoamine oxidase (MAO) enzyme.

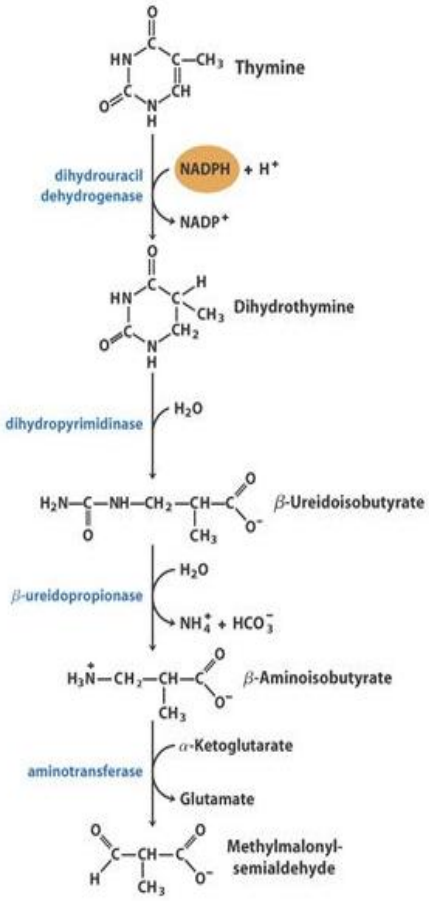


5- Ammonia is released during purine and pyrimidine catabolism.

Purine Catabolism



Pyrimidine Catabolism



The fate of ammonia:

1- Biosynthesis of urea is the main fate of ammonia.

2- Small amounts of ammonia are excreted in urine.

3- Biosynthesis of glutamic acid, nonessential amino acids and glutamine.

Urea Biosynthesis

Ammonia is highly toxic to the central nervous system. It is converted to urea, which is much less toxic, water soluble and easily excreted in urine. The liver is the site of urea biosynthesis. Urea biosynthesis occurs by urea cycle.

Steps of urea biosynthesis:

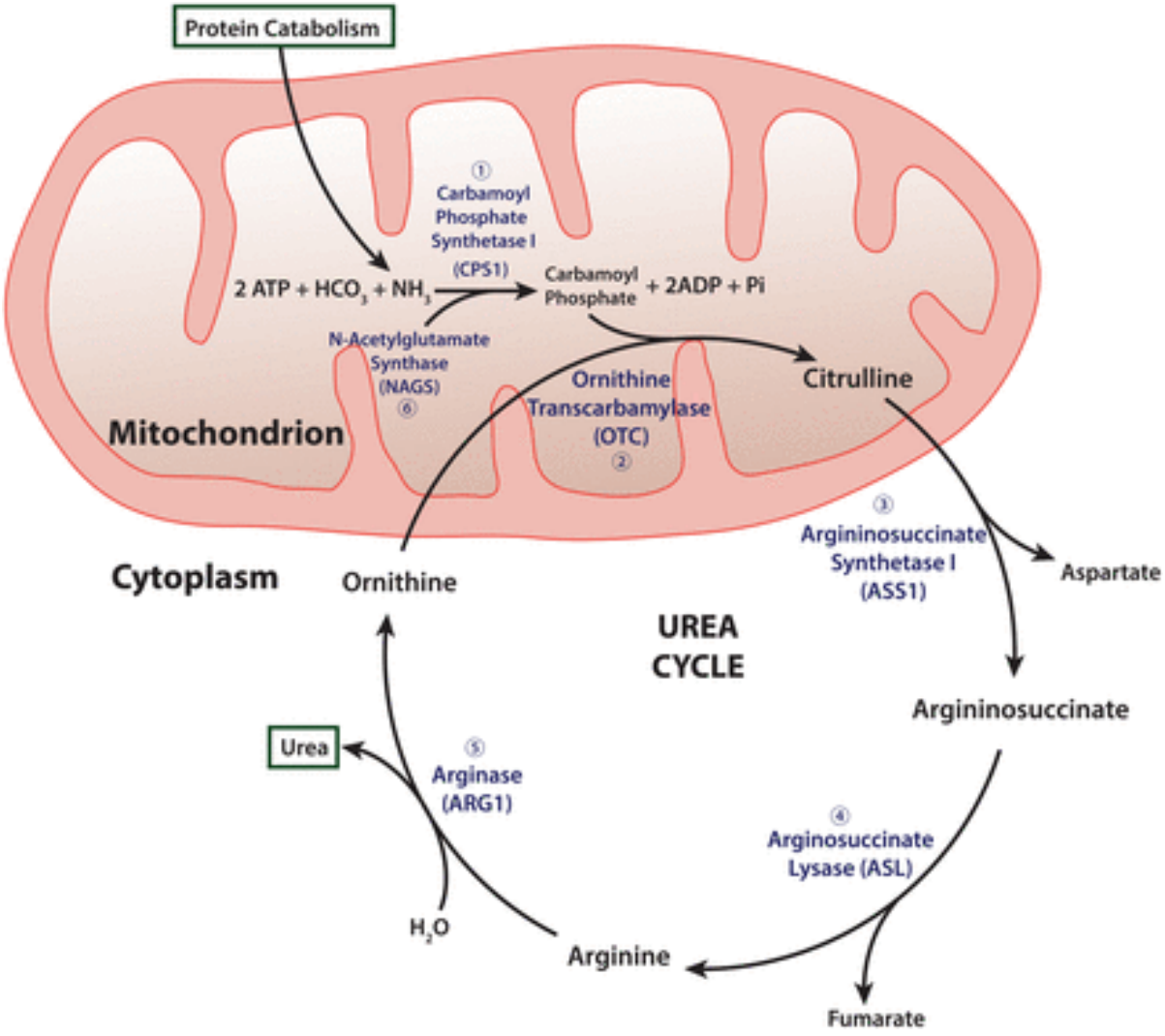
The conversion from ammonia to urea happens in five main steps: a)The first 2 steps occur in mitochondria, b) The last 3 steps occur in the cytoplasm.

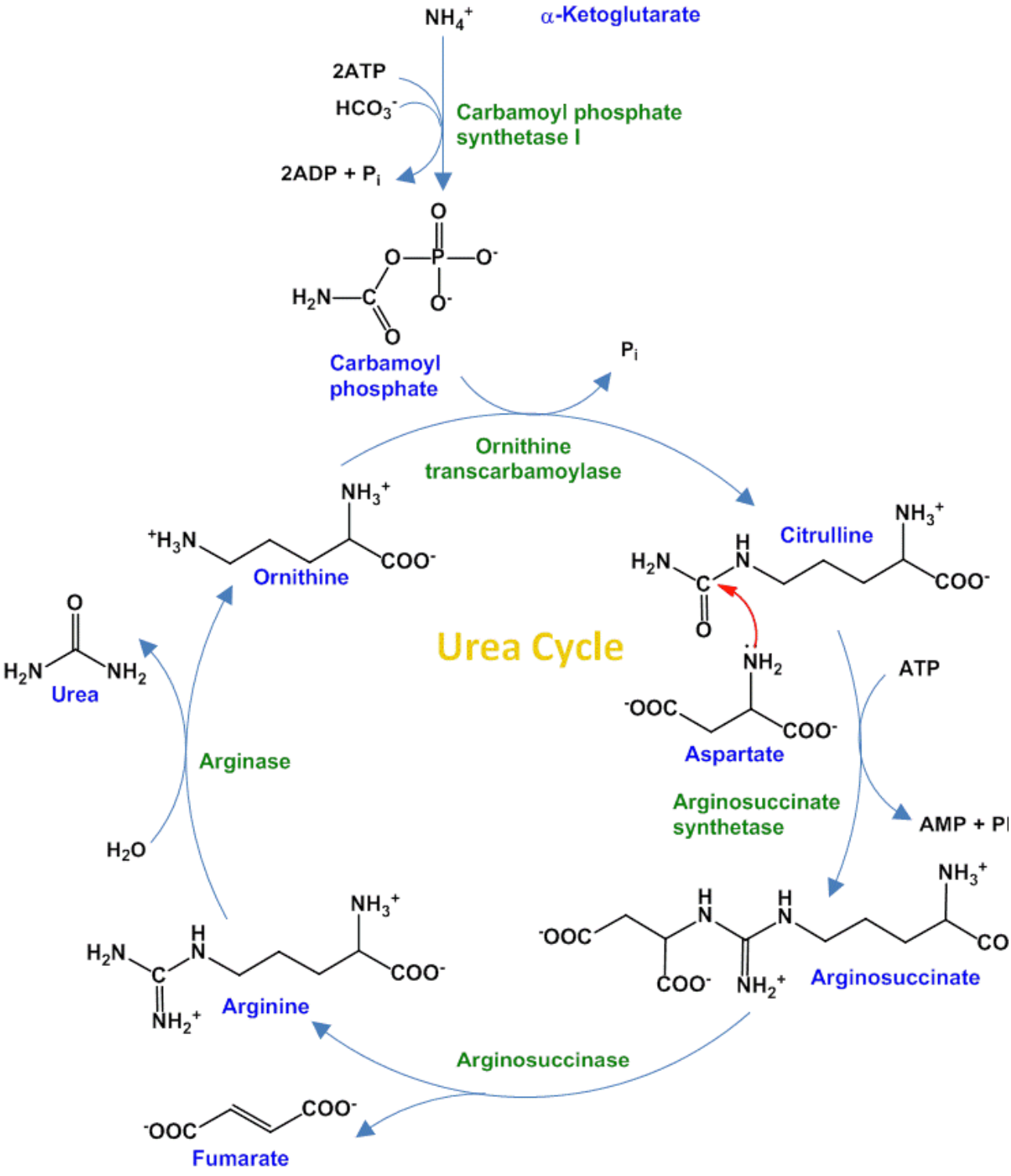
Reactions of the urea cycle

Step	Reactants	Products	Catalyzed by	Location
1	$NH_3 + HCO_3^- + 2ATP$	carbamoyl phosphate + 2ADP + P_i	CPS1	mitochondria
2	carbamoyl phosphate + ornithine	citrulline + P_i	OTC, zinc, biotin	mitochondria
3	citrulline + aspartate + ATP	argininosuccinate + AMP + PP_i	ASS	cytosol
4	argininosuccinate	arginine + fumarate	ASL	cytosol
5	arginine + H_2O	ornithine + urea	ARG1, manganese	cytosol

The entire process converts two amino groups, one from NH_4^+ and one from aspartate, and a carbon atom from HCO_3^-, to the relatively nontoxic excretion product urea at the cost of four "high-energy" phosphate bonds (3 ATP hydrolyzed to 2 ADP and one AMP).

$2NH_4^+ + HCO_3^- + H_2O + 3ATP + Aspartate \rightarrow Urea + 2ADP + 4Pi + AMP + 2H^+ +$ Fumarate


Protein Catabolism
① Carbamoyl Phosphate Synthetase I (CPS1)
2 ATP + HCO3 + NH3
Carbamoyl Phosphate
+ 2ADP + Pi
N-Acetylglutamate Synthase (NAGS) ⑥
Ornithine Transcarbamylase (OTC) ②
Citrulline
Mitochondrion
Cytoplasm
Ornithine
③ Argininosuccinate Synthetase I (ASS1)
Aspartate
UREA CYCLE
Argininosuccinate
Urea
⑤ Arginase (ARG1)
④ Arginosuccinate Lysase (ASL)
H2O
Arginine
Fumarate


NH4+
α-Ketoglutarate
2ATP
HCO3-
Carbamoyl phosphate synthetase I
2ADP + Pi
Carbamoyl phosphate
Pi
Ornithine transcarbamoylase
Ornithine
Citrulline
Urea Cycle
Urea
Aspartate
ATP
Arginase
Arginosuccinate synthetase
AMP + PI
H2O
Arginine
Arginosuccinate
Arginosuccinase
Fumarate