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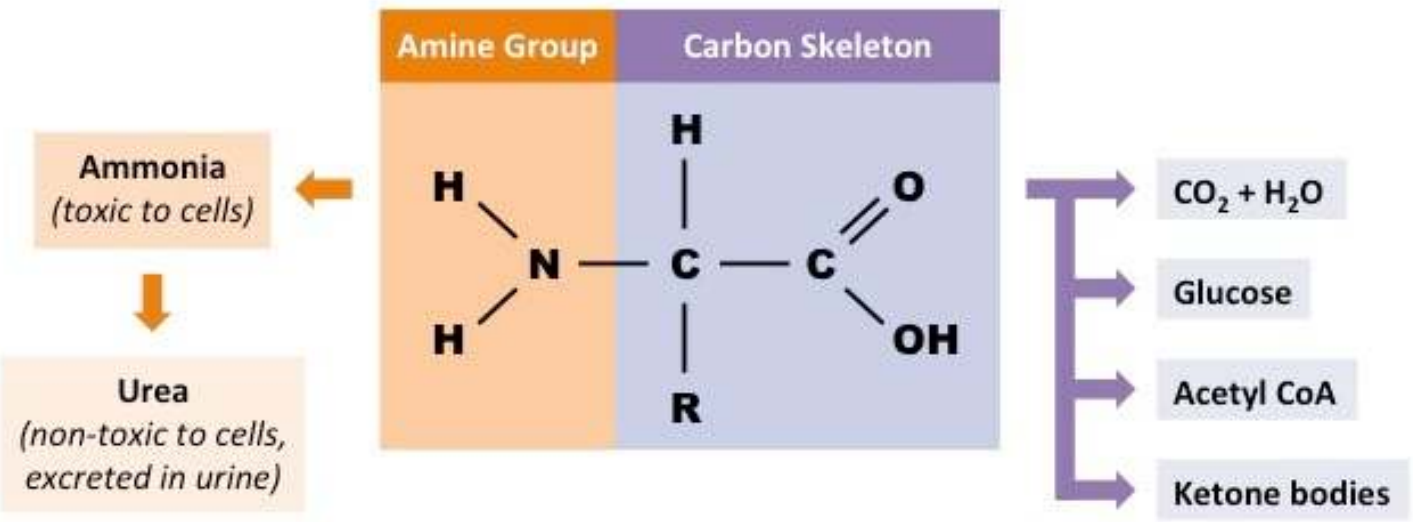
Deamination

Fate of Amino acid



- **Deamination** is the removal of an **α amino group** from a molecule. Amino group is converted into ammonia while the amino acid itself converts into its corresponding keto acid.
- Enzymes that catalyse this reaction are called **deaminases.**
- In the human body, deamination takes place primarily in the **liver, however it is also deaminated in the kidney.**

Oxidative deamination

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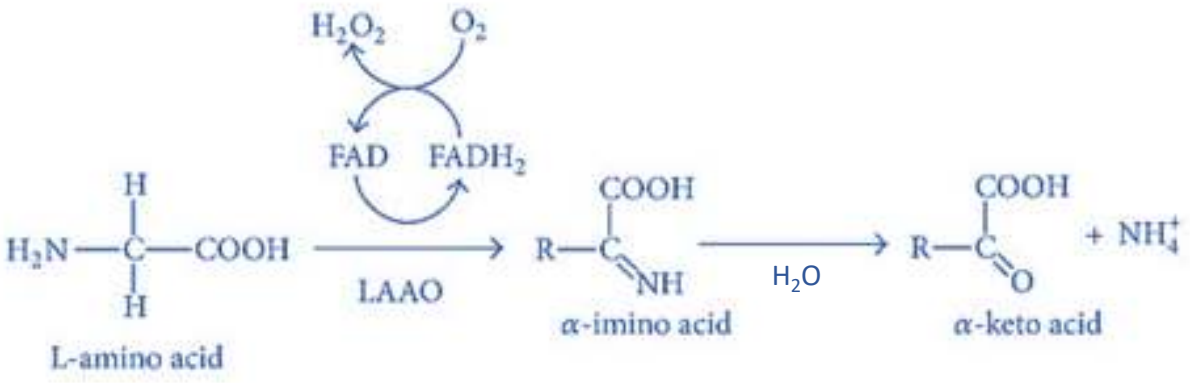
Oxidative deamination is stereospecific and is catalyzed by L- or D-amino acid oxidase. The initial step is removal of two hydrogen atoms by the flavin coenzyme, with formation of an unstable α-amino acid intermediate. This intermediate undergoes decomposition by addition of water and forms the ammonium ion and the corresponding α-keto acid. Presence of O_2 is essential.

By the help of

L-amino acid oxidase (LAAO)

- **Enzyme present in mitochondria, peroxisomes and ER of mammalian kidneys and liver only.**
- **It contains FMN/FAD as the prosthetic group.**
- **It can't act on glycine and L-isomers basic amino acids.**

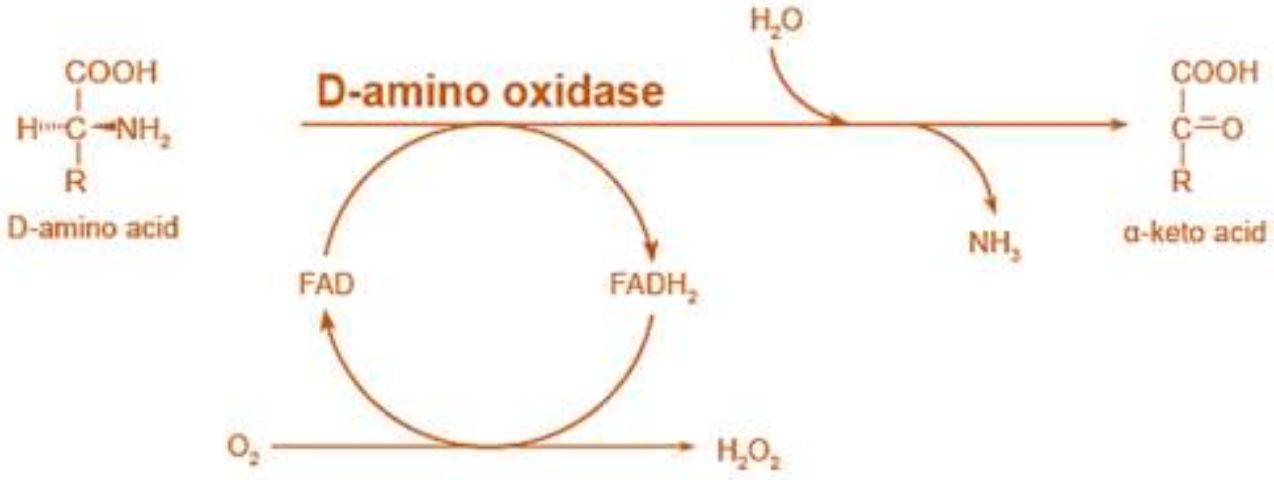


By the help of
D-amino acid oxidase (DAO)

It occurs in peroxisomes of mammalian liver and kidneys.

It can't act on D-isomers of glutamic acid, asparagine, dicarboxylic acid and basic amino acids.

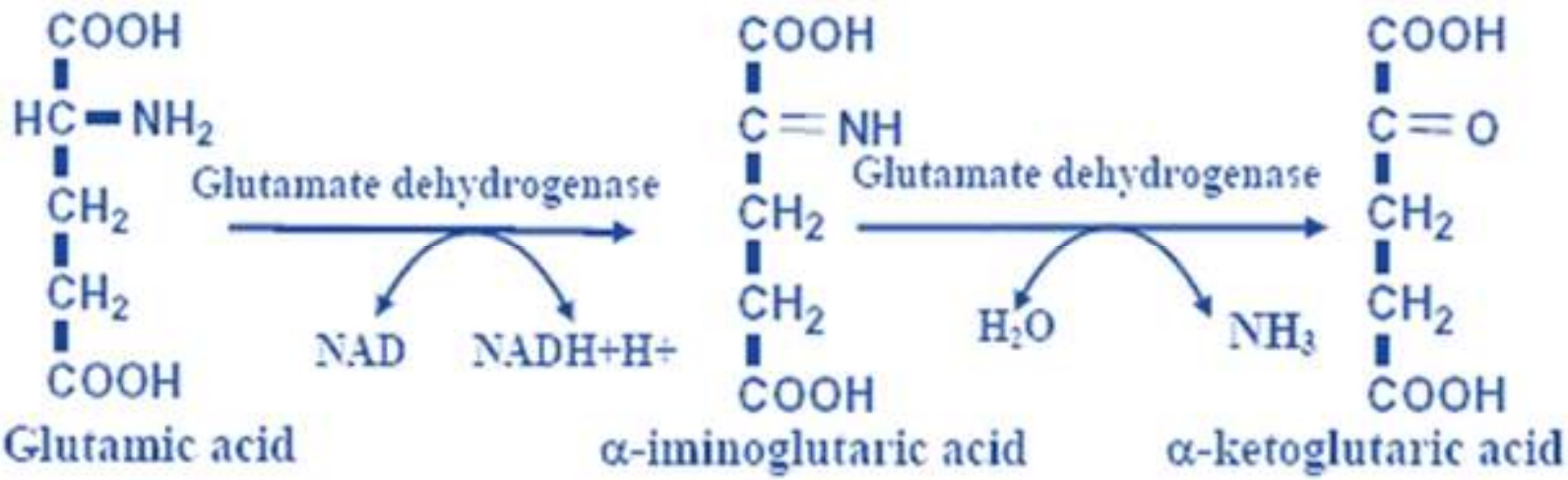
It contains FAD as prosthetic group.



By the help of

Glutamate dehydrogenase

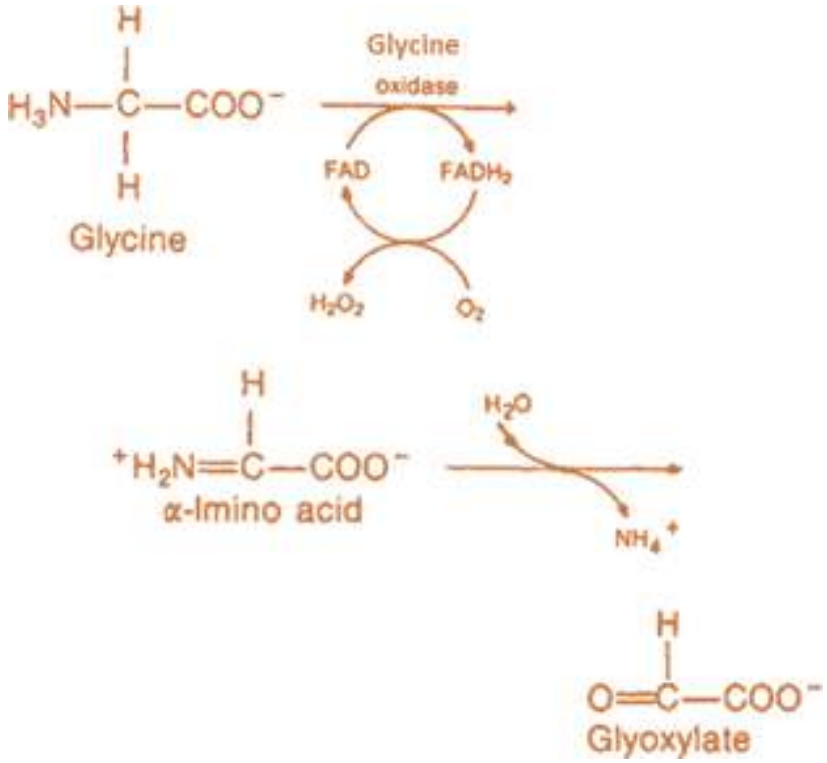
- **It is present in all tissue.**
- **It needs NAD or NADP as coenzyme.**



By the help of

Glycine oxidase

- FAD as a prosthetic group.
- Act on glycine.



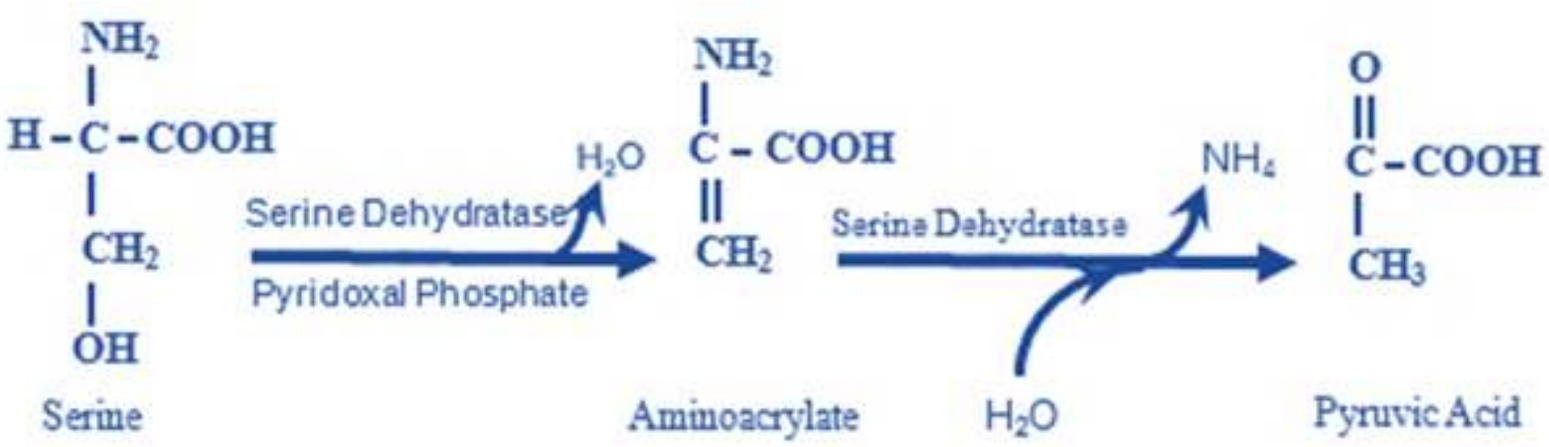
Non-oxidative deamination

Molecular O_2 is non essential.

Occurs mainly in liver.

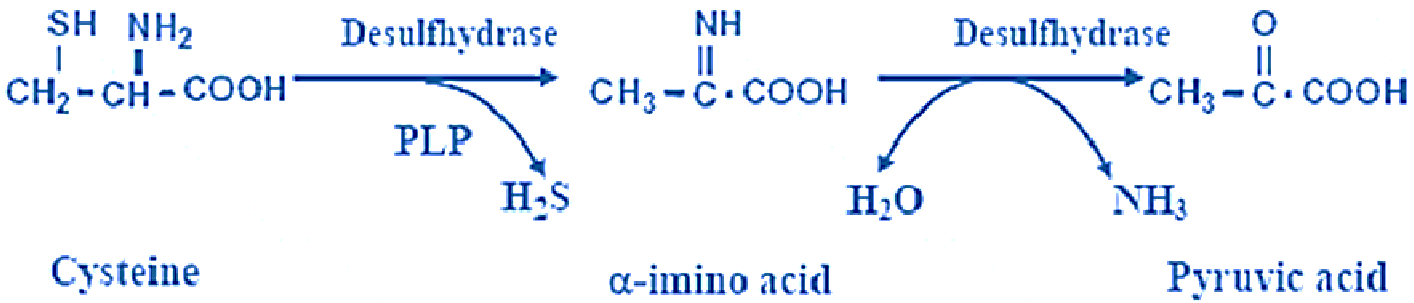
By the help of amino acid dehydratase (serine and threonine), amino acid lyase (histidine and aspartic acid), amino acid desulfhydrase (cysteine), trans-sulfurase (partial deamination, cysteine), amide hydrolase (aspargine).

By the help of
Amino acid dehydratase



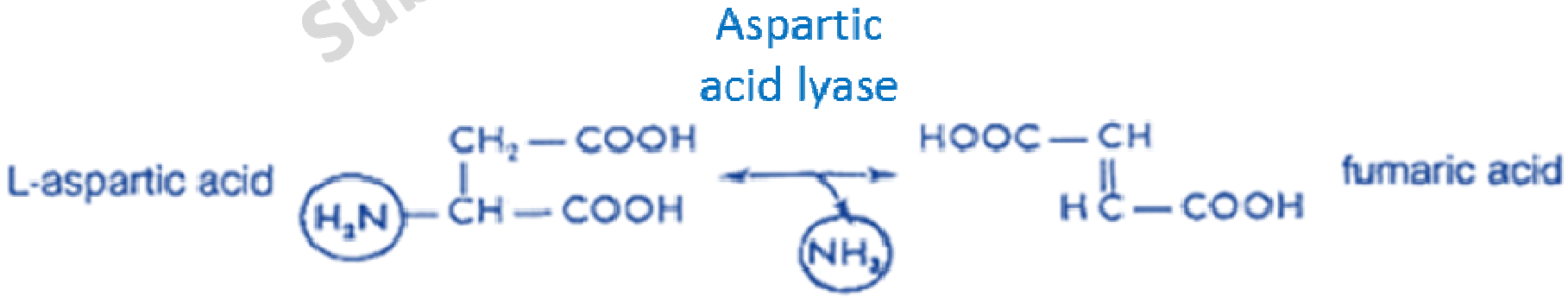
By the help of

Desulfhydrase



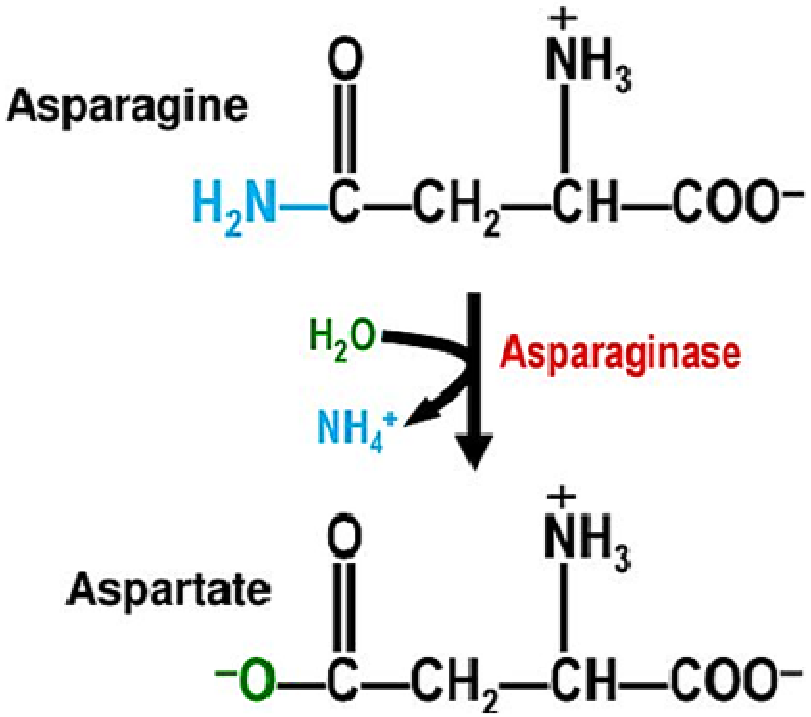
By the help of

Amino acid lyase



By the help of

Amide hydrolase/asparginase



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OXIDATIVE DEAMINATION VERSUS NONOXIDATIVE DEAMINATION

OXIDATIVE DEAMINATION	NONOXIDATIVE DEAMINATION
A form of deamination, which generates α-keto acids and other oxidized products from amine-containing compounds	A form of deamination, which liberates ammonia without undergoing oxidation
Only occurs in the liver and kidney	Occurs in other types of organisms
Enzyme: Glutamate dehydrogenase	Main form of enzymes: amino acid dehydratases
Primary type of amino acid: glutamic acid	Hydroxy amino acids including serine, homoserine, and threonine
Coenzymes are responsible for the oxidation reactions	No oxidizing agents

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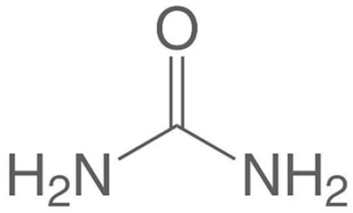
UREA CYCLE



What is urea cycle??

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- **Deamination of amino acids** produce large amounts of NH_3 which is toxic for a animal body.
- The urea cycle mediates the **removal of ammonia as urea** in the amount of 10 to 20 g per day in the healthy adult.
- When this process is not working efficiently, toxic ammonia (NH_3) **accumulates within the body** and may elicit clinical manifestations such as **lethargy, slurred speech, cerebral edema, and asterixis.**
- **Teleost** are **ammonotelic** and directly **excrete NH_3 through the gills**.
- **Reptiles and birds** convert ammonia into uric acid for excretion through kidneys and they are **uricotelic.**
- **Mammals amphibians and elasmobranch** fishes **convert NH_3 into urea** for renal excretion and they are called **ureotelic.**
- Urea is formed **mainly in liver** and very small extent in kidneys and brain.
- This **energy-dependent process** occurs only within the **liver's mitochondria and cytoplasm.**

Also known as **arginine urea pathway** or **Krebs-Hanseleit ornithine cycle.**

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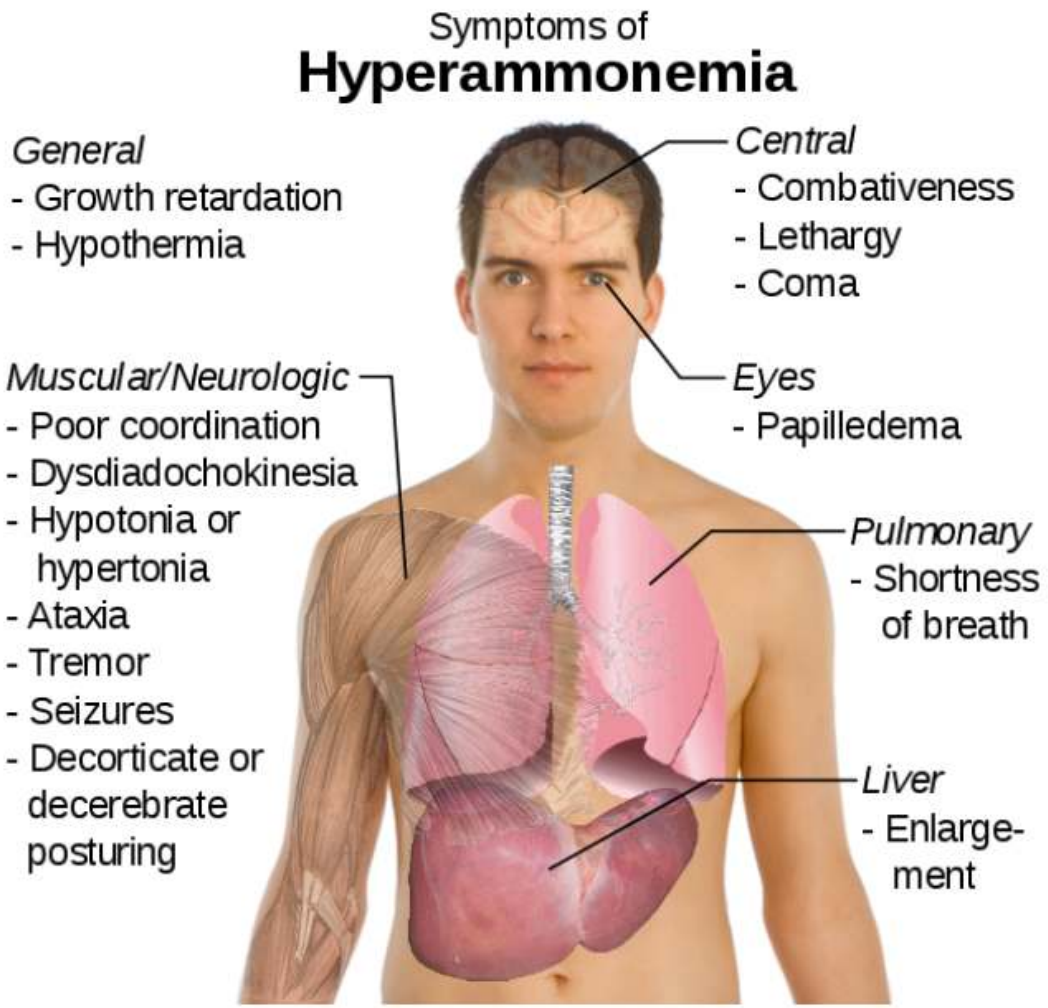

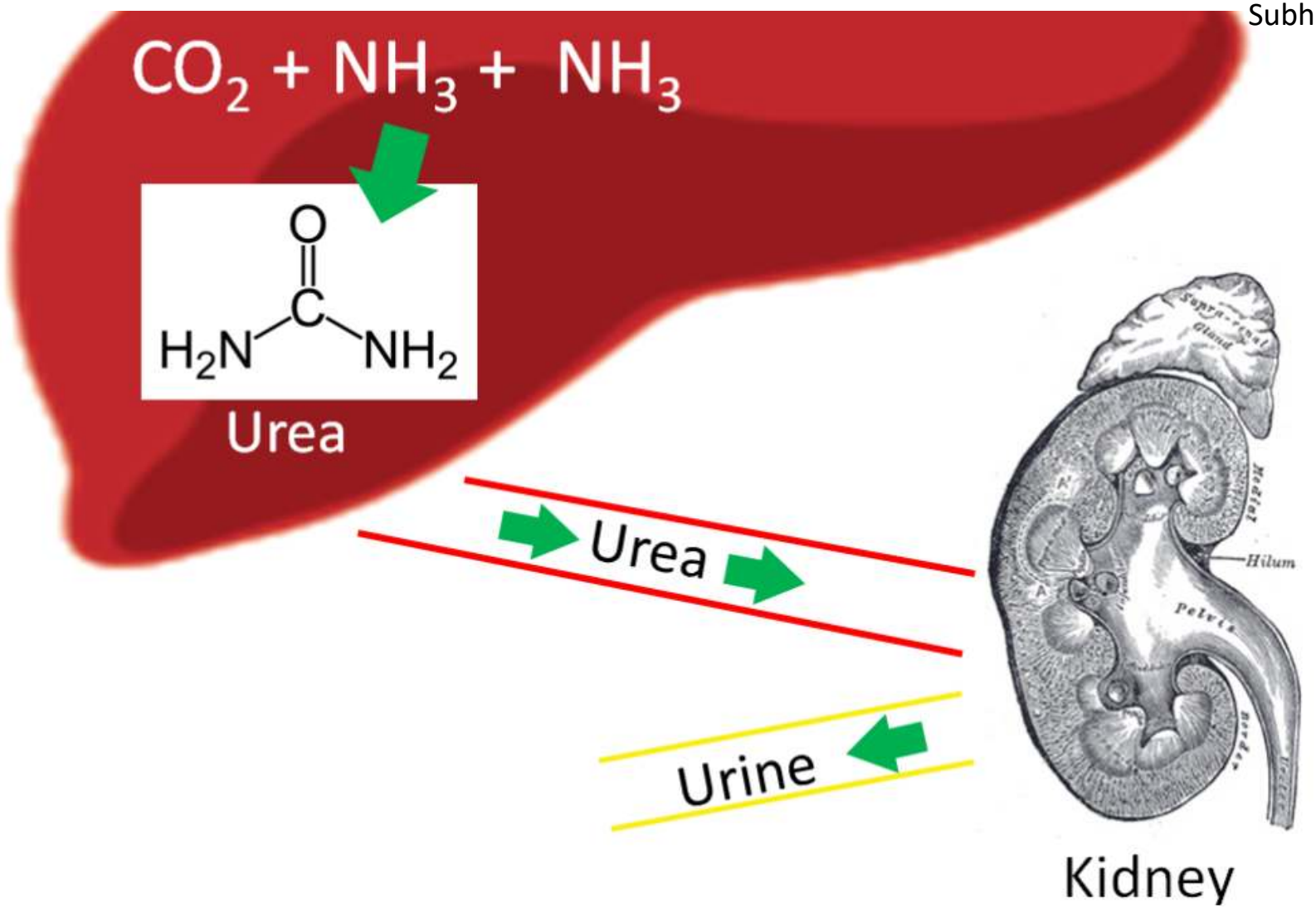
$CO_2 + NH_3 + NH_3$
O
C
H_2N
NH_2
Urea
Urea
Urine
Hilum
Pelvis
Kidney

The net reaction

$$CO_2 + NH_4^+ + \text{aspartate} + 3ATP + 2H_2O \rightarrow \text{urea} + 2ADP + 2P_i + AMP + PP_i + \text{fumarate}$$

Summary of the Steps in the Urea Cycle

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The mitochondrial stage

Carbamoyl phosphate is formed from ammonia and bicarbonate, by CPS.

OTC condenses carbamoyl phosphate and ornithine to form citrulline.

Citrulline is then transported to the cytosol by SLC25A15.

The cytosolic stage

AS condenses citrulline and aspartate to form argininosuccinate.

Argininosuccinate is broken down into arginine and fumarate by AL.

Arginine is broken down into urea and ornithine by arginase.

Ornithine translocase transports ornithine into the mitochondria.

Pathway of Urea Cycle

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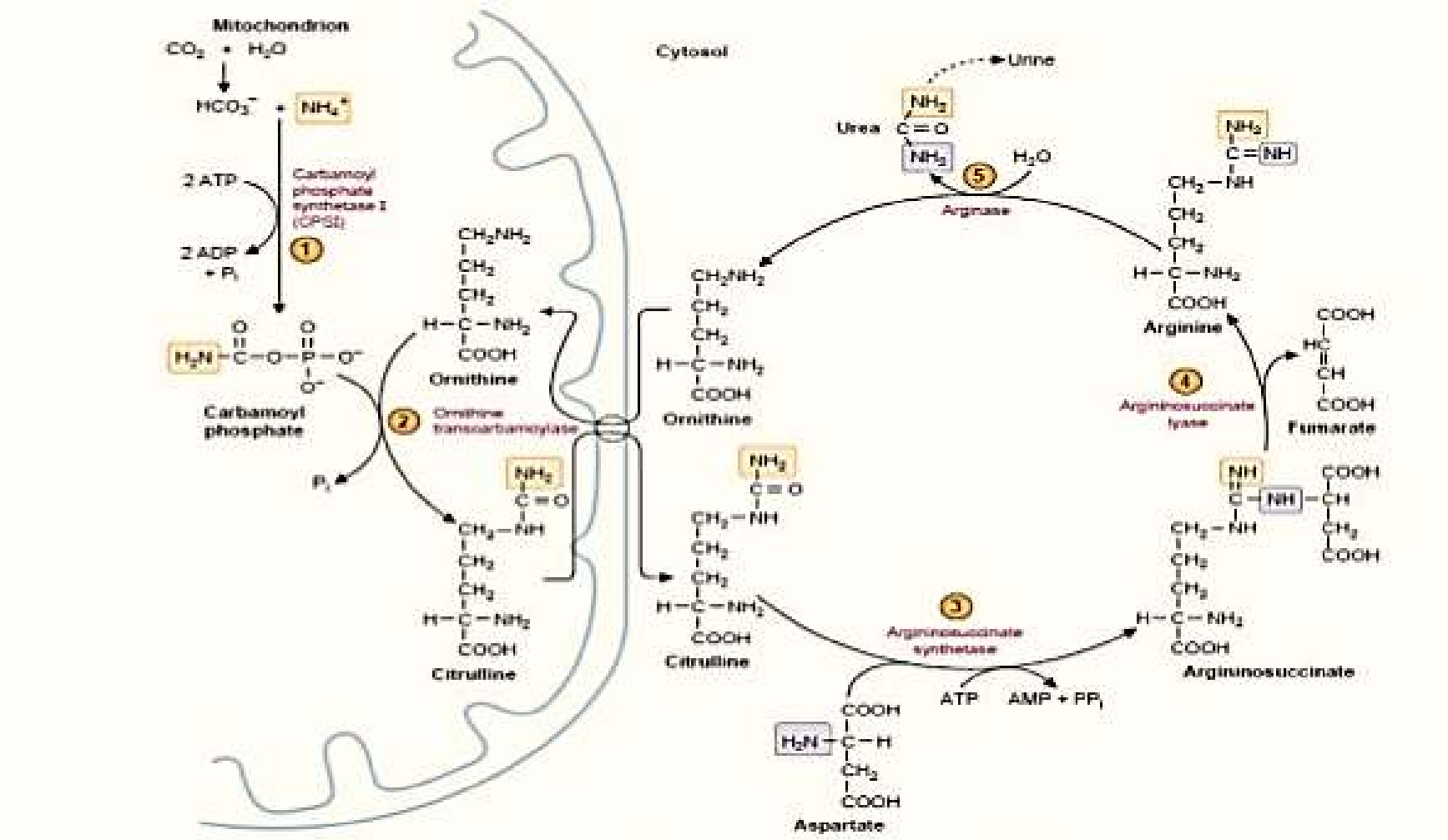

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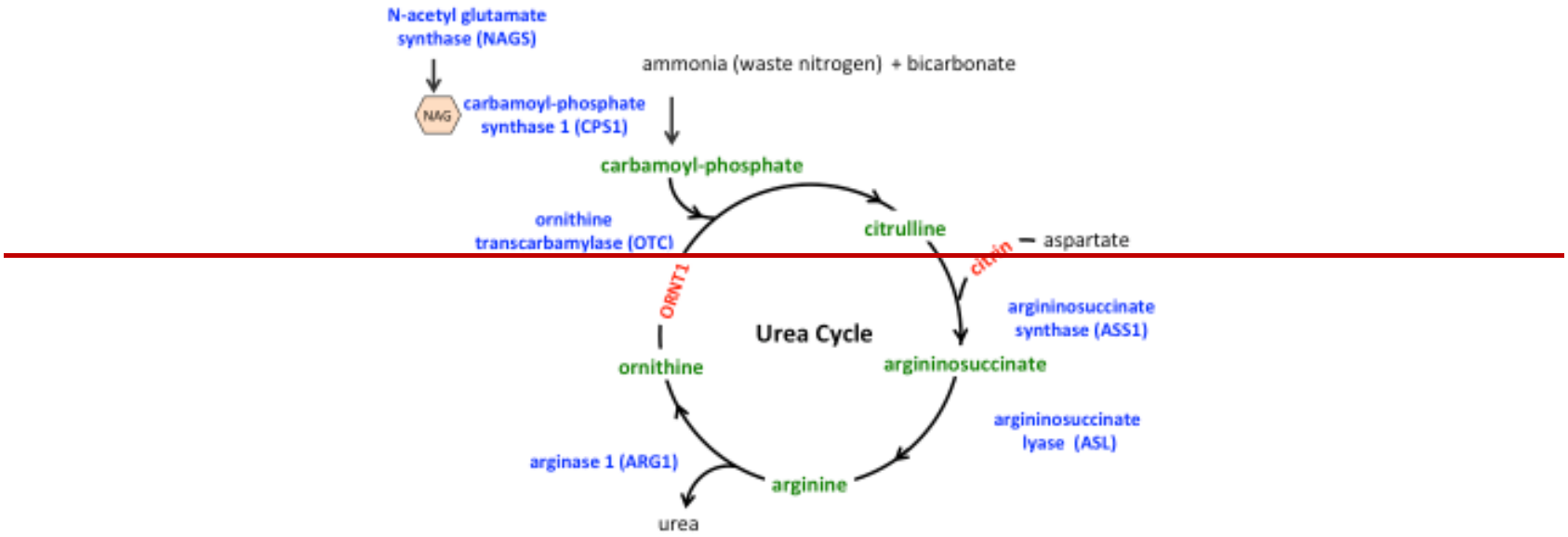
The Mitochondrial Stage



First, the enzyme **carbamoyl phosphate synthetase (CPS)** takes ammonia and bicarbonate, and forms carbamoyl phosphate with the **use of ATP.** This is the step in the cycle which determines how fast the cycle progresses. ***N*-acetylglucosamine is also required for CPS to function, and functions as a regulator for the formation of urea.**

Ornithine transcarbamoylase (OTC) then condenses carbamoyl phosphate and ornithine, which forms citrulline.

This **citrulline is then moved out of the mitochondria into the cytosol** of the cell by the **transporter SLC25A15.**

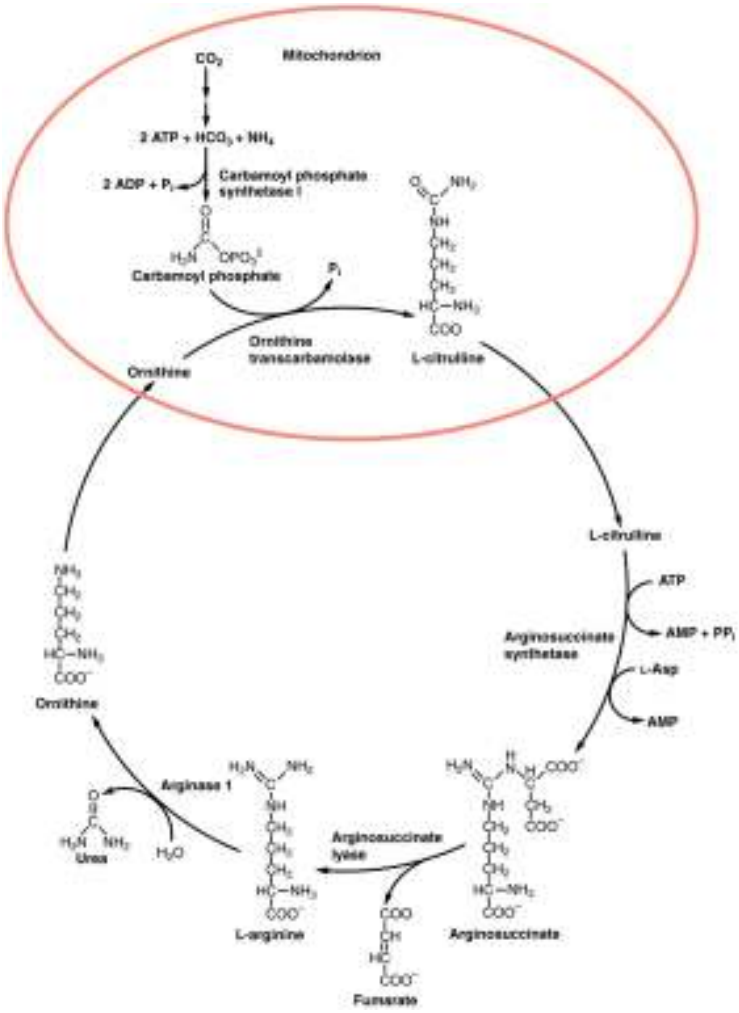
The Cytosolic Stage

- **Argininosuccinate synthetase (AS) takes the citrulline formed in the mitochondrial stage,** and condenses it with aspartate to form argininosuccinate. This occurs by the formation of an intermediate, citrulline-AMP.

- Argininosuccinate is then **broken into arginine and fumarate by argininosuccinate lyase (AL).** Fumarate is then incorporated into another metabolic cycle, the TCA cycle. The TCA cycle can then reform aspartate, which is used by AS.

- **Arginine is then further broken down into urea and ornithine by arginase.** Arginine can also be acquired from the diet, and this can also be taken in by the liver cells and broken down into urea and ornithine by arginase.

- **The ornithine is then transported into the mitochondria by ornithine translocase. There, it is used by OTC again**, to form citrulline. The citrulline is then processed to form urea and ornithine again, and the cycle continues. During the cycle, urea is the only new product which is formed, while all other molecules used in the cycle are recycled.



Significance

- The toxic ammonia is converted into nontoxic urea. It disposes off two waste products, ammonia and CO2.
- It forms semi essential amino acid, arginine. It participates in the regulation of blood pH, which is depends upon the ratio of dissolved CO2, e.g H2CO3toHCO3.
- Ornithine is a precursor for the formation of polyamines like, spermidine and spermin .

Regulation

- Carbamoyl phosphate synthetase-I is an allosteric regulatory enzyme of urea cycle, which is activated by N-acetylglutamate (NAG). NAG is synthesized from acetyl-CoA and glutamate by NAG-synthase to activate CPS-I.