

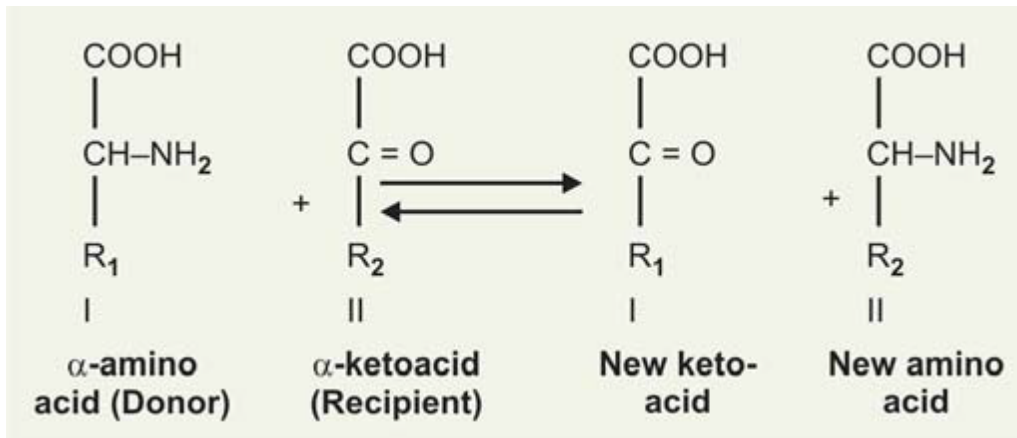
## Dissimilation of Amino Acid (N-Catabolism of Amino Acid)

$\alpha$ -NH<sub>2</sub> group of amino acid is converted first to NH<sub>3</sub> and then to urea and is excreted in the urine. The formation of NH<sub>3</sub> and urea can be discussed under the following heads: -

- \*transamination
- \* Deamination (oxidative or nonoxidative deamination)
- \*Transdeamination
- \* NH<sub>3</sub> transport
- \*formation of urea.

### Transamination

Transamination means transfer of amino group from  $\alpha$ -amino acid to  $\alpha$ -keto acid with formation of a new  $\alpha$ -amino acid and a new  $\alpha$ -keto acid. The liver is the main site for transamination. The enzymes catalyzing the reaction as a group are known as **amino transferases**. These enzymes have **pyridoxal phosphate** as prosthetic group. The reaction is readily reversible.



### Role of pyridoxal phosphate in transamination

Pyridoxal phosphate acts as an intermediate carrier for amino group( accepts the amino group from amino acid to form pyridoxamine phosphate, which in turn gives the amino group to  $\alpha$ -keto acid).

### **Examples of transaminases**

- A. Alanine transaminase (ALT)
- B. Aspartate transaminase (AST)

### **Clinical significance of serum transaminases**

Transaminases are intracellular enzymes. Their levels in blood plasma are low under normal conditions. ALT (glutamate pyruvate transaminase (GPT) is present mainly in liver cells.

AST (Glutamic – Oxaloacetic. Transaminas GOT) is present in liver, heart and skeletal muscles.

Any damage to these organs will increase the level of transaminases in blood

In liver diseases, there is an increase in both serum ALT (SGPT) and AST (SGOT) levels. In acute liver diseases, e.g. acute viral hepatitis, the increase is more in SGPT

In chronic liver diseases, e.g. liver cirrhosis the increase is more in SGOT.

In heart diseases, e.g. myocardial infarction, there is an increase in SGOT only.

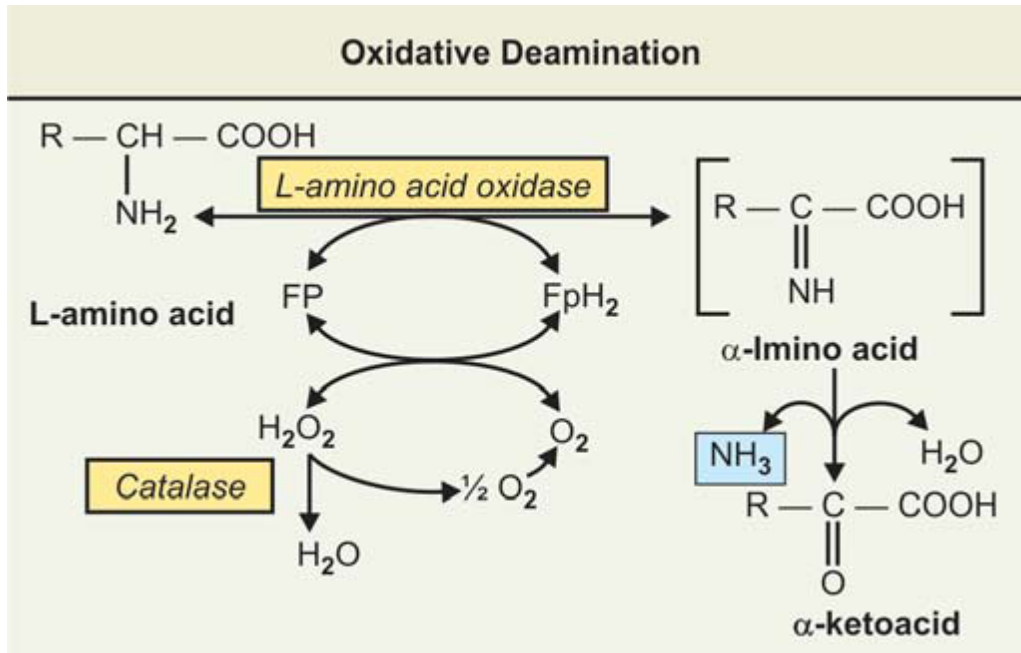
In skeletal muscle diseases, e.g. myasthenia gravis, there is an increase in SGOT only.

## **Deamination**

Deamination means the removal of amino group from  $\alpha$ -amino acid in the form of ammonia with formation of  $\alpha$ -keto acid. The liver and kidney are the main sites for deamination .Deamination may be oxidative or non-oxidative

### ***A-Oxidative deamination***

It is catalyzed by L-amino acid oxidases

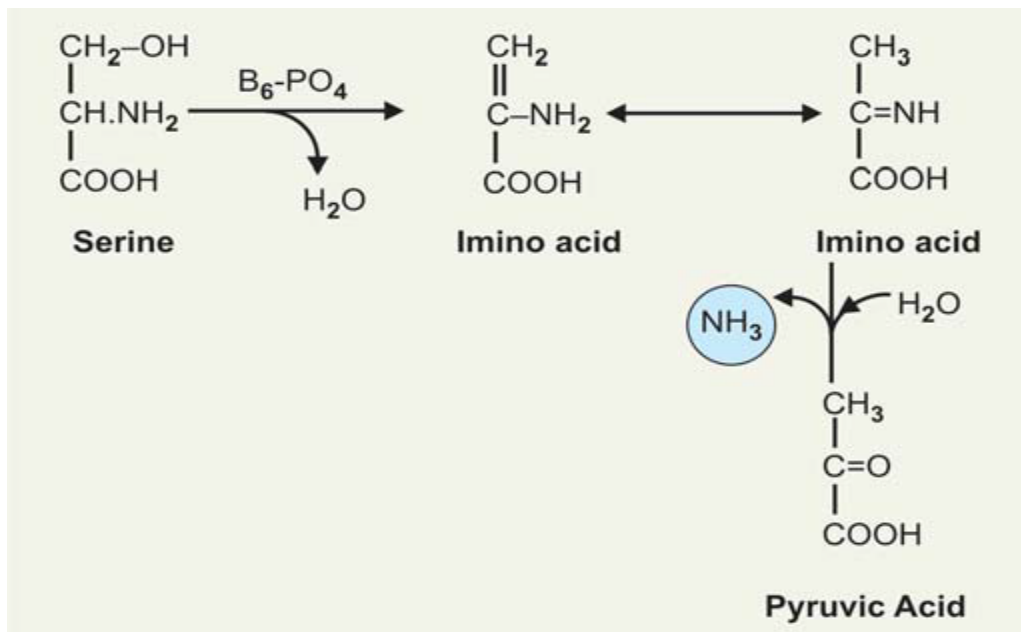


### A. Non-oxidative deamination

It is catalyzed by one of the following enzymes:

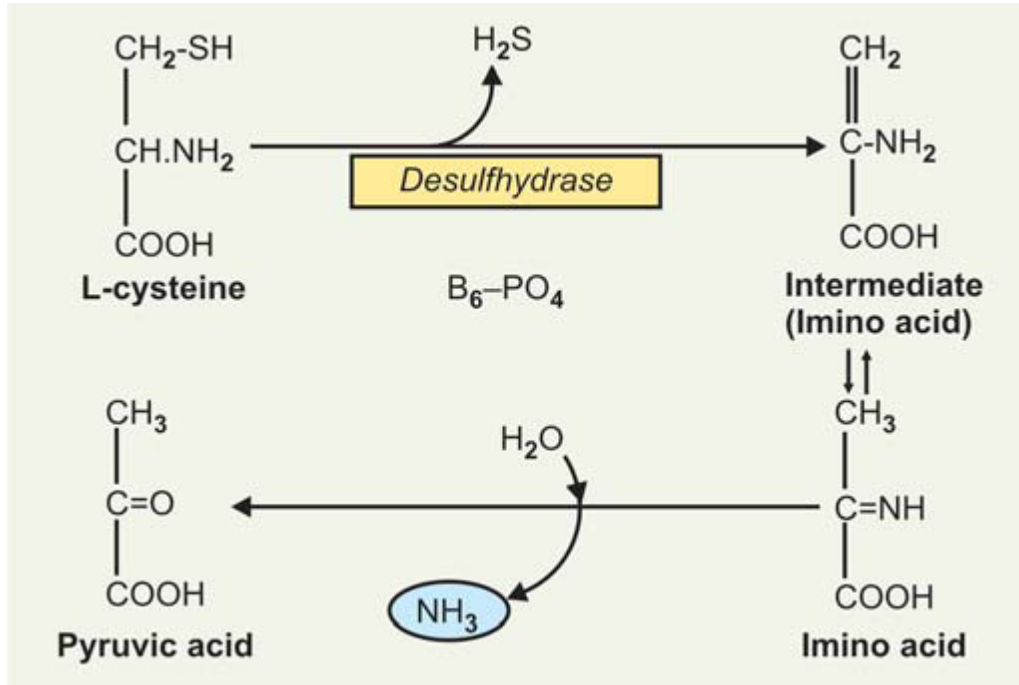
#### 1- Dehydrases

This enzyme deaminates amino acids containing hydroxyl group e.g. serine, homoserine and threonine. It needs pyridoxal phosphate as coenzyme.

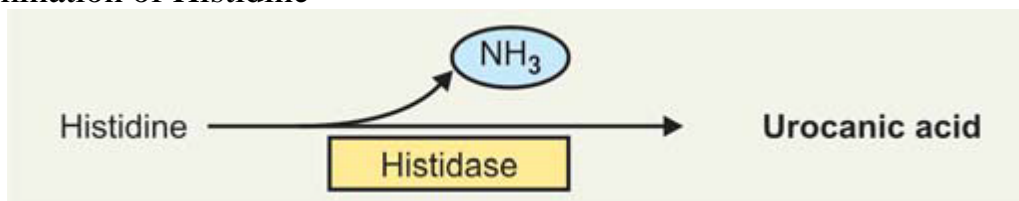


## 2- Desulfhydrases

This enzyme deaminates sulphur containing amino acids e.g. cysteine and cystine. It needs pyridoxal phosphate as a coenzyme.



## 3-Deamination of Histidine

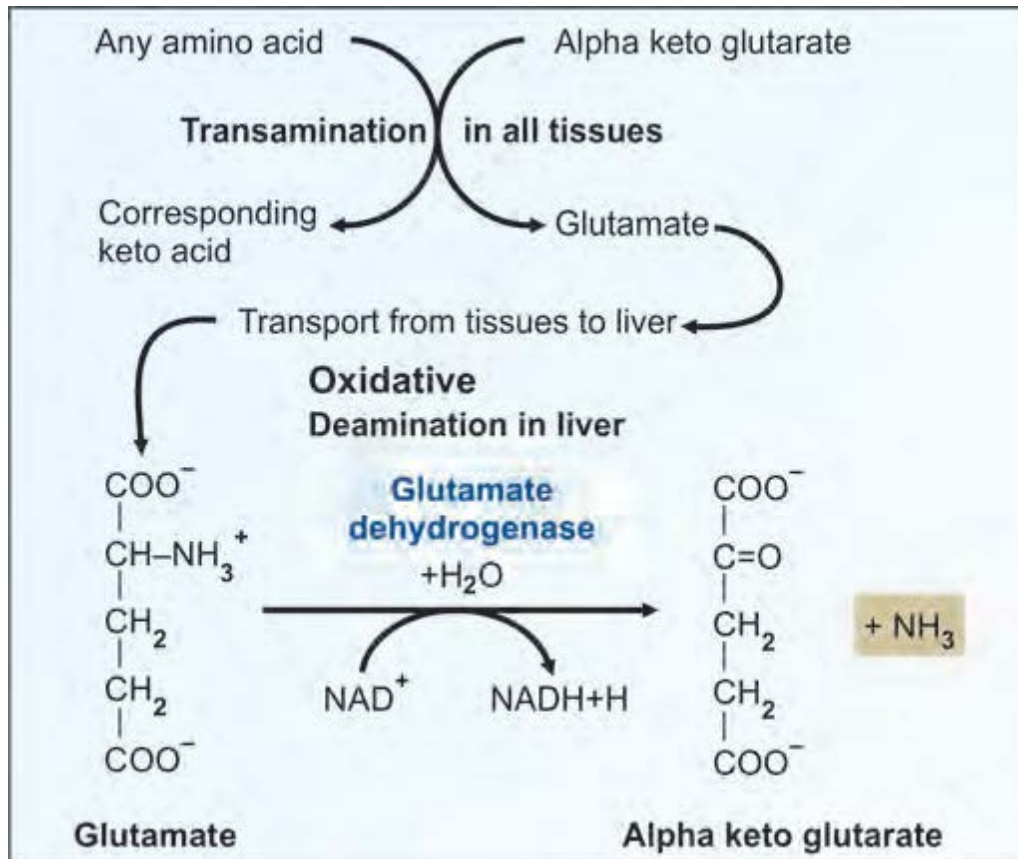


## Transdeamination

### (Deamination of L-Glutamic Acid)

The amino group of most of the amino acids is released by a coupled reaction, transdeamination, that is **transamination followed by oxidative deamination**. Transamination takes place in the cytoplasm of all the cells of the body; the amino group is transported to liver as **glutamic acid**, which is finally

oxidatively deaminated in the mitochondria of hepatocytes. The enzyme L-glutamate dehydrogenase catalyzes the deamination of L-glutamate to forms  $\text{NH}_3$  and  $\alpha$ -keto glutarate.



## DETOXIFICATION OF AMMONIA

### First Line of Defense (Trapping of Ammonia)

Being highly toxic, ammonia should be eliminated or detoxified, as and when it is formed. Even very minute quantity of ammonia may produce toxicity in central nervous system. But, ammonia is always produced by almost all cells, including neurons. The intracellular ammonia is immediately trapped by glutamic acid to form **glutamine**, especially in brain cells. The glutamine is then transported to liver,

where the reaction is reversed by the enzyme **glutaminase**. The ammonia thus generated is immediately detoxified into urea.

### Transportation of Ammonia

Inside the cells of almost all tissues, the transamination of amino acids produce glutamic acid. However, glutamate dehydrogenase is available only in the liver. Therefore, the final deamination and production of ammonia is taking place in the liver. Thus, **glutamic acid** acts as the link between amino groups of amino acids and ammonia. The concentration of glutamic acid in blood is 10 times more than other amino acids. **Glutamine** is the transport form of ammonia from brain and intestine to liver; while alanine is the transport form from muscle.

### Final Disposal

The ammonia from all over the body thus reaches liver. It is then **detoxified to urea by liver** cells, and then excreted through kidneys. **Urea is the end product of protein metabolism.**

### Why NH<sub>3</sub> is toxic?

- \* Increased NH<sub>3</sub> concentration enhances amination of  $\alpha$ -ketoglutarate, an intermediate in TCA cycle to form glutamate in brain. This reduces mitochondrial pool of  $\alpha$ -ketoglutarate consequently depressing the TCA cycle, affecting the cellular respiration.
- \* Increased NH<sub>3</sub> concentration enhances "glutamine" reduces" brain-cell" pool of Glutamic acid. Hence there is decreased formation of inhibitory neurotransmitter "GABA"(  $\gamma$ - amino butyric acid) .
- \* Rise in brain glutamine level enhances the outflow of glutamine from brain cells. Glutamine is carried "out" by the same "transporter" which allows the entry of "tryptophan" into brain cells. Hence "tryptophan" concentration in brain cells increases which leads to abnormal increases in synthesis of "serotonin", a neurotransmitter.

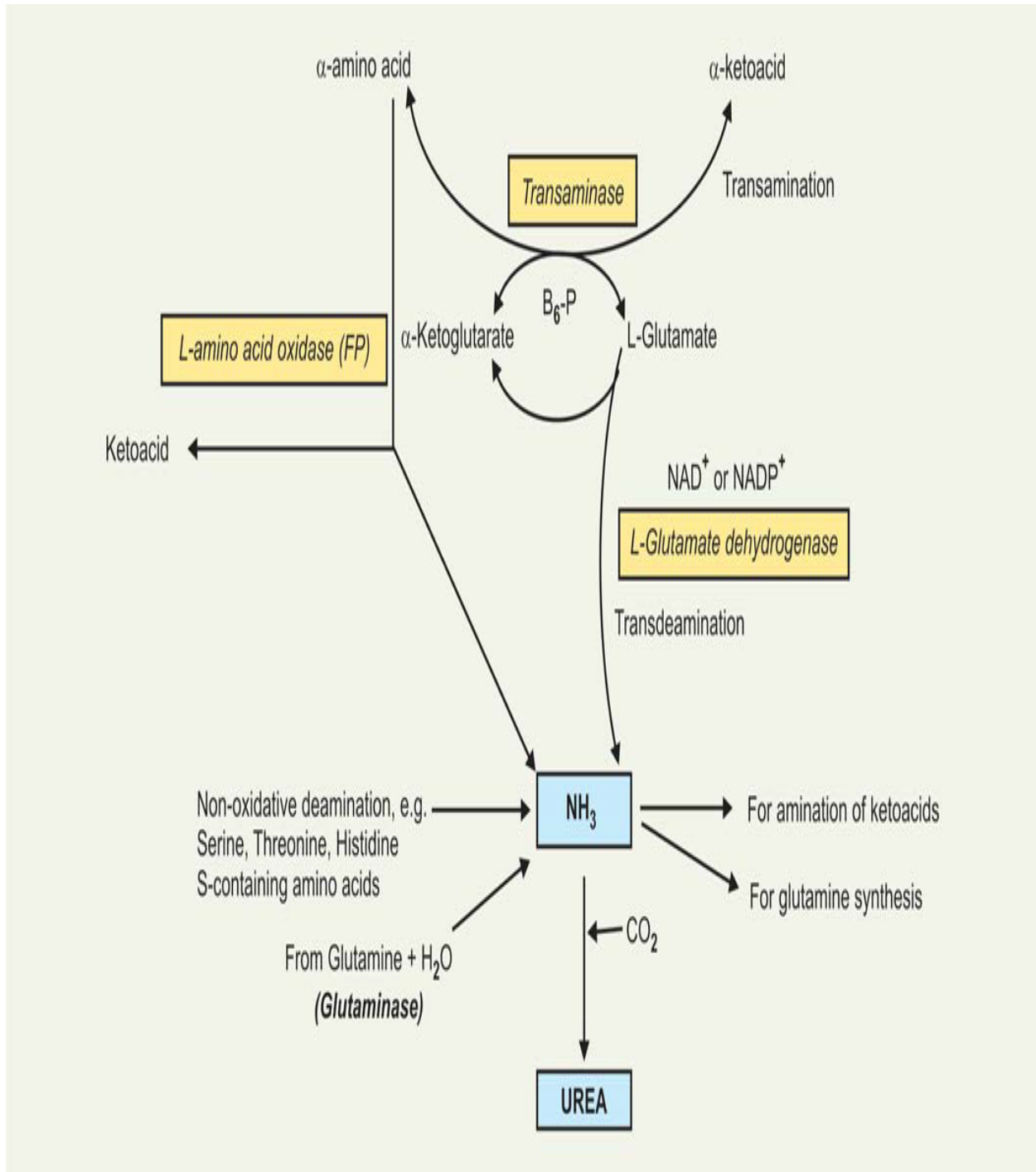


Figure: Overall pattern of N-removal from an L-amino acid

## Hyperammonaemia

Two type:

1- *Acquired hyperammonaemia*: the result of Cirrhosis of the liver.

2- *Inherited hyperammonaemia*: results from genetic defects in the urea cycle enzyme

**Features of NH<sub>3</sub> intoxication:** The symptoms of NH<sub>3</sub> intoxication include:

- a peculiar flapping tremor
- slurring of speech
- blurring of vision
- and in severe cases follows to coma and death.

These resemble those of syndrome of hepatic coma, where blood and brain NH<sub>3</sub> levels are elevated.