AMINO ACID METABOLISM
CONTENTS

- General reactions of amino acid metabolism: Transamination, deamination & decarboxylation
- Urea cycle and its disorders
- Catabolism of phenylalanine and tyrosine and their metabolic disorders (Phenyketonuria, Albinism, alkeptonuria, tyrosinemia)
- Synthesis and significance of biological substances; 5-HT, melatonin, dopamine, noradrenaline, adrenaline
- Catabolism of heme
- Hyperbilirubinemia and jaundice
The amino group of the amino acids is utilized for the formation of urea which is an excretory end product of protein metabolism.

The carbon skeleton of the amino acids is first converted to keto acids (by transamination) which meet one or more of the following fates.

1. Utilized to generate energy.
2. Used for the synthesis of glucose.
3. Diverted for the formation of fat or ketone bodies.
4. Involved in the production of non-essential amino acids.
Transamination

- The transfer of an amino (-NH$_2$) group from an amino acid to a keto acid.
- It involves the interconversion of a pair of amino acids and a pair of keto acids, catalysed by a group of enzymes called transaminases.
- All transaminases require pyridoxal phosphate (PLP), a coenzyme derived from vitamin B6.
- Aspartate transaminase and Alanine transaminase make a significant contribution for transamination.
- Only transfer of amino group occurs (free NH$_3$ is not liberated).
- Transamination is reversible.
Transaminitation is very important for the redistribution of amino groups and production of non essential amino acids, as per the requirement of the cell. Transaminitation diverts the excess amino acids towards energy generation. The amino acids undergo transamination to finally concentrate nitrogen in glutamate. All amino acids except lysine, threonine, proline and hydroxyproline participate in transamination. Transaminitation is not restricted to α-amino groups only. Serum transaminases are important for diagnostic and
Deamination

The removal of amino group from the amino acids as NH$_3$ is deamination.

Deamination may be either oxidative or non-oxidative. **Oxidative deamination** is the liberation of free ammonia from the amino group of amino acids coupled with oxidation.

This takes place mostly in liver and kidney.

The purpose of oxidative deamination is to provide NH$_3$ for urea synthesis and α-keto acids for a variety of reactions, including energy generation.
Non-oxidative deamination:
- Some of the amino acids can be deaminated to liberate NH₃ without undergoing oxidation.

Amino acid dehydrases:
- Serine, threonine and homoserine are the hydroxy amino acids undergo non-oxidative deamination.

Amino acid desulphhydrases:
- The sulfur amino acids (cysteine and homocysteine) undergo deamination coupled with desulphhydration to give keto acids.

Deamination of histidine:
- The enzyme histidase acts on histidine to liberate NH₃.
Decarboxylation

- The decarboxylation of amino acids or their derivatives results in the formation of **amines**.
- This is carried out by a group of enzymes called **decarboxylases**.
- Examples:
  - Tryptophan → 5-**Hydroxytry**P<sub>L</sub>o**phan** → 5-**Hydroxytryptamine**.
  - Histidine → **Histamine**
Urea cycle

- **Urea** is the end product of protein metabolism.
- The nitrogen of amino acids, converted to ammonia, is toxic to the body.
- It is converted to urea and detoxified.
- Urea is synthesized in liver and transported to kidneys for excretion in urine.

**Steps involved in urea cycle:**

2. Formation of citrulline.
4. Cleavage of arginosuccinate
5. Formation of urea.
Disorders of urea cycle

- All the disorders invariably lead to a build-up in blood ammonia (hyperammonemia), leading to toxicity.
- The clinical symptoms associated with defect in urea cycle enzymes include vomiting, lethargy, irritability, ataxia and mental retardation.

<table>
<thead>
<tr>
<th>Defect</th>
<th>Enzyme involved</th>
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<tbody>
<tr>
<td>Hyperammonemia type I</td>
<td>Carbamoyl phosphate synthase I</td>
</tr>
<tr>
<td>Hyperammonemia type II</td>
<td>Ornithine transcarbamoylase</td>
</tr>
<tr>
<td>Citrullinemia</td>
<td>Arginosuccinate synthase</td>
</tr>
<tr>
<td>Arginosuccinic aciduria</td>
<td>Arginosuccinase</td>
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<tr>
<td>Hyperargininemia</td>
<td>Arginase</td>
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