SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF CARDIO PULMONARY PERFUSION CARE TECHNOLOGY

COURSE NAME : BIOCHEMISTRY

TOPIC : AMINO ACIDS - INBORN ERRORS OF AMINO ACIDS METABOLISM

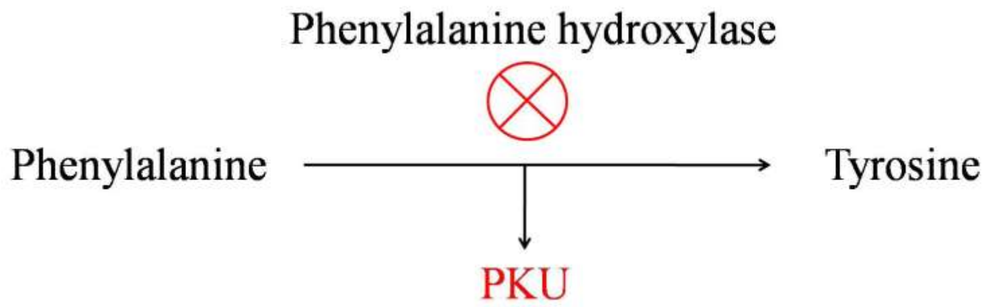
Inborn Errors of Amino acid Metabolism

- Inborn errors of metabolism (IEM) - inherited metabolic disorders leading to enzymatic defects in the human metabolism.
- Hence, it is called Inborn errors of metabolism or inherited metabolic disorders.
- IEM can appear at birth or later in life such as phenylketonuria, albinism, lactose intolerance, gaucher disease, fabry disease etc.
- The cause of IEM is mutations in a gene that code for an enzyme leading to synthesis of defective enzyme activity or deficiency of an enzyme that affects the normal function of a metabolic pathway.
- Amino acid metabolic disorders are defined by accumulation of metabolic intermediates that cause specific tissue and organ damage.

Phenylketonuria (PKU)

- Phenylketonuria is a common autosomal recessive inborn error of phenylalanine leads to intellectual disability if untreated.
- The estimated incidence of PKU 1 in 10,000 newborns.
- Phenylalanine is an essential amino acid which means it cannot synthesize in the body and must be taken from the diet.
- In PKU, the first step of phenylalanine catabolism is affected due to the defective catalytic activity of phenylalanine hydroxylase enzyme.

- **Cause**
  - The primary cause of PKU is deficient of phenylalanine hydroxylase, enzyme of phenylalanine catabolism which converts phenylalanine into tyrosine in cells.
  - Phenylalanine cannot convert to tyrosine resulting in accumulation of phenylalanine in tissues.
  - Decreasing the concentration of phenylalanine in which it converts to phenylpyruvate which further is reduced or oxidized to form phenyllactate and phenylacetate.
  - Both phenylalanine and phenylacetate accumulate in tissues and blood which can excrete in urine. Hence, the name phenylketonuria.



- **Clinical symptoms**
- Irreversible biochemical abnormalities such as mental retardation and neurological dysfunctions, eczema in the early life of infants.
- Few babies may exhibit epilepsy, Parkinson like features and decreased skin and hair pigmentation.
- **Diagnosis**
- The estimation of phenylalanine level in the blood (usually above 600 µmol/L) is primarily used to detect PKU.
- Increased level of Phenylalanine and phenylpyruvate in blood and urine are analyzed to confirm the PKU using Gas chromatography-mass spectrometry

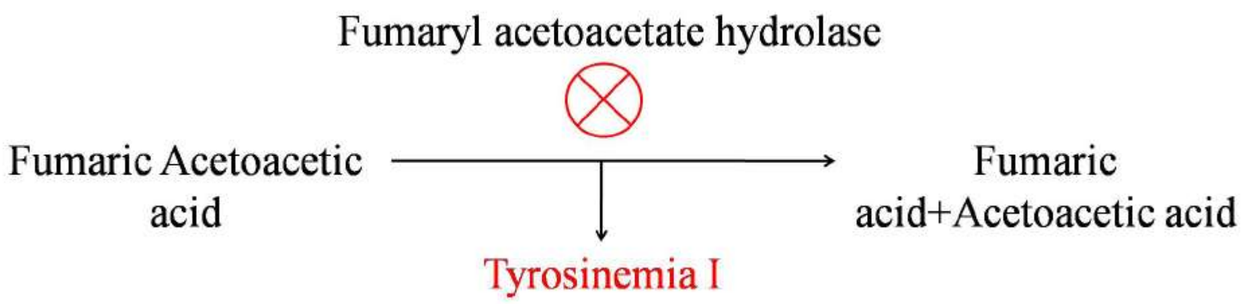
- **Treatment**
- Early diagnosis of PKU in affected person is beneficial for the treatment.
- People with PKU may recommend restricting the intake of phenylalanine in diet for reducing the toxic effects of phenylalanine accumulation and maintain the level of phenylalanine (2-6 mg/dL) in plasma.
- The adjuvant therapy with sapropterin is also helpful for PKU treatment.

Tyrosinemia

- Tyrosinemia is also metabolic genetic disorders of phenylalanine catabolism, occur usually in newborns.
- This disorder results due to the absence or deficiency of enzymes involved in the multiple steps of phenylalanine and tyrosine catabolism.

- **Tyrosinemia I**
- Lack of fumarylacetoacetate hydrolase (FAH) enzyme with inherited genetic defect results in tyrosinemia disease.
- This enzyme involves in tyrosine metabolism which converts fumaryl acetoacetic acid into fumaric and acetoacetic acids.

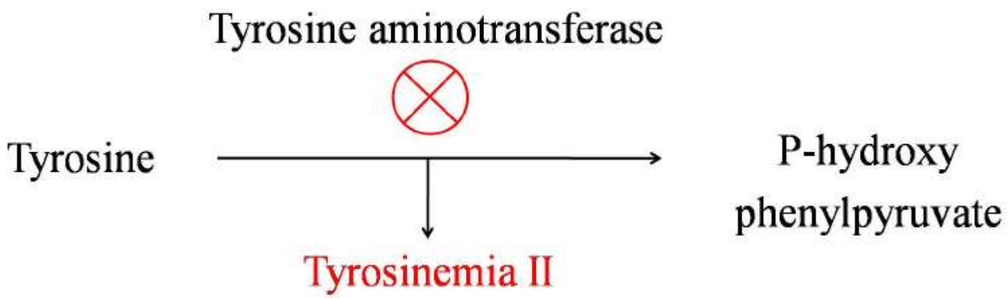
- Deficiency of this enzyme, fumaryl acetoacetic acid and other intermediate precursors accumulate in the tissue and organ cause liver and renal diseases. Hence, it is also called hepatorenal tyrosinemia.



- **Clinical symptoms**
- Diarrhoea, vomiting, renal tubular dysfunction, vitamin D-resistant rickets, acute intermittent porphyria-like symptoms (abdominal pain, neuropsychiatric findings and sensitive to light), hypertension, Progressive liver and renal failure.

Tyrosinemia II

- Nails and dorsum of hands showing bluish-colored discolorationin affected people with alkaptonuria.
- This disorder is caused by the deficiency of tyrosine aminotransferase enzyme, which catalyzes the first step in the catabolism of tyrosine forming the corresponding keto acid, p-hydroxyphenyl pyruvic acid.
- Deficiency of this enzyme leads to accumulation of the tyrosine in cells and blood.



- **Clinical symptoms**
- Accumulation of tyrosine can affect on eyes, skin, and mental development. This disease begins in early childhood. Persistent keratitis and hyperkeratosis occur on the fingers, palms of hands and soles of feet, moderate mental retardation.
- **Types:** Both acute and chronic forms are known.
- **1. In acute tyrosinosis:** Infants exhibit diarrhoea, vomiting, a “cabbage”-like odour, there is usually associated Liver damage, Liver failure.
- Untreated acute tyrosinosis do not survive and death within 6 to 8 months.
- **. In chronic tyrosinosis:** Clinical features are similar but milder symptoms and course. Children survive and in untreated cases leads to death by the age of 10 years. In both types plasma tyrosine levels are elevated: 6 to 12 mg/dl. There also occurs increase in plasma methionine level.

Hartnup disease

- Various enzymes or products of the tryptophan metabolic process are extremely closely related to neurological disorders
- (Alzheimer's disease, Parkinson's disease, Huntington's disease, Multiple sclerosis) and psychiatric disorders (Depression, Schizophrenia, Bipolar disorder, Anxiety)
- Hartnup disease is caused by a mutation of the gene that controls your body's amino acid absorption and reabsorption.
- It's an autosomal recessive trait.
- Hartnup disease is also referred to as Hartnup disorder.
- It's a hereditary metabolic disorder. It makes it difficult for your body to absorb certain amino acids from your intestine and reabsorb them from your kidneys

- Among other amino acids, Hartnup disease affects your ability to absorb tryptophan.
- This is an important building block for proteins and vitamins.
- Without enough tryptophan, your body can’t produce enough niacin.
- A niacin deficiency can cause you to develop a sun-sensitive rash. It can also lead to dementia.
- A skin rash called “pellagra” is a common symptom.
- It usually results from exposure to sunlight.
- It’s an intermittent red and scaly rash that typically appears over your face, neck, hands, and legs.
- It’s initially red, but over time it can progress to an eczematous-like rash.
- With prolonged sun exposure, the changes in your skin pigmentation can become permanent.

Assessment

1. What is inborn errors of amino acid metabolism?

2. What is Phenylketonuria?

3. What is Tyrosinemia?

4. What is Hartnup disease?

THANK YOU