Que 60

Biochemical Basis of etiology, Clinical feature, diagnosis and treatment of Various hyperphenylalaninemia.

- **Phenylketonuria**

→ Biochemical Abnormalities In PKU

Phenylalanine

↓ Phenyl Alanine Hydroxylase

Tyrosine

- Deficieny of Phenylalanine Hydroxylase is the cause for this Disease.
- So phenylalanine could not be converted to tyrosine, so phenylalanine accumulates and level elevated In Blood

→ Alternate Minor Pathway of Phenylalaine opened

Phenylalanine —(Transaminase, α-KG → Glutamate)→ Phenyl Pyruvate —(Reduction, NADH + H+ → NAD+)→ Phenyl lactate

Phenyl Pyruvate —(Decarboxylation, ↑ $CO_2$)→ Phenylacetate

Phenylacetate —(Conjugation, Glutamine, ↑ $H_2O$)→ Phenylacetylglutamine

→ 5 Types of PKU

- Type 1 is classical one described above Phenylalaine Hydroxylase deficiency
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→ Type II & III — Deficiency of Dihydrobiopterin Reductase
- Type IV & V are due to deficiency of enzyme Synthesizing biopterin
- Tetrahydrobiopterin is the coenzyme required for serotonin and dopamine, the decreased level of these neurotransmitter may also result in the neurological symptoms.

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- Mental Retardation Ig - 50 %.
- Agitation, hyperactivity, tremors and convulsions because phenylalanine interferes with neuro-transmitter synthesis
- Hypopigmentation → Due to decreased tyrosine
- Incidence is 1 in 10,000 births in India lesser than western countries ; only 1 in 25,000 births.
- It is recessive condition

## Laboratory finding

- Blood Phenylalanine - Normal level is 1mg/dl
In PKU, the level >20mg/dl
demonstrated by chromatography

- Tandem mass spectroscopy

→ **Guthrie test** rapid screening test
- Spot of blood on a filter paper disc is placed on the surface of an agar plate, which contain a substance that inhibits bacterial growth, high phenylalaine can overcome this inhibition.
- after overnight incubation bacterial growth is compared with a control disc by measuring the diameter of growth zone.
- The amount of phenylalaine in blood of the patient can be thus estimated.

→ **DNA Probes** are now available to diagnose the defects in phenylalanine hydroxylase and dihydrobiopterin deficiency.

→ **Ferric Chloride Test** - Urine of patient contain phenyl ketones about 500-3000 mg/day, this could be detected by adding drop of ferric chloride to the Urine.
A transient blue-green color is a positive test

**Treatment** - Low phenylalaine containing diet
- Low Protein diet grains, sprouts,
- Food based on tapioca (cassava).

## Phenyl Ketonuria Carrier State

- Disease is manifested only in Homozygous state
- In heterozygous state · Phenylalanine Hydroxylase enzyme is sufficient to metabolize normal level of Phenylalanine.

- But when Phenylalaine (1g) is injected intravenously, the carriers will show increased level in the blood.