VITAMIN B₆

History

- Gyorgy demonstrated a characteristic type of dermatitis in rats – produced by a factor different from known vitamins
- 1937: He showed that the factor was present in yeast & liver and named it ‘B₆’
- Chemical structure & isolation of the compound was done by Richard Kuhn
  - Nobel Prize in 1938
Chemistry

- Three compounds belong to the class of vitamin $\text{B}_6$
- Pyridoxine (Pyrridoxol), Pyridoxal, Pyridoxamine
- All three compounds are pyridine derivatives
- Difference is confined to ‘$R$’ group on C4 molecule
- $R$ – Group of Pyridoxine contains primary alcohol group, Pyridoxal contains corresponding aldehyde group & Pyridoxamine contains aminomethyl group
- Pyridoxol is usually found in plants & pyridoxal and pyridoxamine are found in animal foods
- $\text{B}_6$ is a white, crystalline, having salty taste, water soluble compound, also soluble in alcohol & fat solvents
Sources

🌟 Rich Sources: Yeast, rice polishings, cereals, pulses, vegetables & egg
🌟 Fair Sources: Liver, kidney, muscle, fish, fruits
🌟 Poor Source: Milk
🌟 Intestinal flora can also synthesise pyridoxine
**Recommended Dietary Allowance**

- Adults: 1.5 to 2.0 mg/day
- Infants & Children: 1.5 to 1.8 mg/day
- Pregnancy, Lactation & Elderly: 2.0 to 2.5 mg/day
- RDA is dependent on protein intake
Absorption, Storage, Transport & Excretion

- $B_6$ is readily absorbed from the small intestine
- It is transported all the tissues by general circulation
- It is distributed throughout the body
- Pyridoxine is readily converted to pyridoxal & pyridoxamine in the body
- Excess is excreted in urine and also some part is metabolised to 4-pyridoxic acid & excreted in urine
- Normal serum riboflavin levels is 0.5 - 3 $\mu$g/dl
Functions

Biologically active coenzyme forms of $B_6$ are:
- Pyridoxal – 5 – phosphate
- Pyridoxamine – 5 – phosphate

Phosphate group gets attached to hydroxymethyl group at position 5 of pyridine ring

The reaction takes place in the liver castalysed by the enzyme ‘pyridoxal kinase’ utilising ATP
Pyridoxal – 5 – phosphate is a versatile enzyme participating in several important reactions including amino acid metabolism.

- Pyridoxal phosphate is loosely bound as a Schiff’s base to the ε- amino group of lysine residue in all the enzymes involving PLP.

- In amino acid metabolism, it is required for transamination, decarboxylation, racemization, deamination reactions.
Transamination
- catalysed by ‘transaminases’ or ‘aminotransferases’
- converts amino acids to keto acids
- Alanine combines with $\alpha$-ketoglutarate to form Pyruvate & Glutamate, reaction catalysed by ‘alanine aminotransferase’
- Aspartate combines with $\alpha$-ketoglutarate to form Oxaloacetate & Glutamate, reaction catalysed by ‘aspartate aminotransferase’
- Keto acids enters the TCA cycle and gets oxidised to yield energy
- $B_6$ integrates carbohydrate & amino acid metabolism
Functions (Contd)

- **Decarboxylation**
  - The reaction is catalysed by the enzyme ‘α - decarboxylase’
  - α-amino acids are converted to their respective amines
  - The reaction helps to form many biogenic amines such as γ-amino butyric acid (GABA), Histamine, Serotonin, Dopamine; and other important compounds like taurine & ethanolamine
Functions (Contd)

- Racemisation
  - This reaction helps in the conversion of L-amino acids to D-amino acids

- Non-oxidative Deamination
  - Deamination of hydroxyl group containing amino acids Serine & Threonine by the enzyme ‘dehydratase’ requires PLP

- Heme synthesis
  - PLP is required for the enzyme ‘ALA synthase’ in synthesis of $\delta$ - amino levulenic acid from glycine & succinyl CoA, the first & the rate limiting step in heme biosynthesis
Functions (Contd)

- **Trans-sulfuration**
  - PLP plays an important role in the metabolism of sulphur containing amino acids
  - It acts as a coenzyme for the enzymes ‘Cystathionine synthase’ & ‘Cystathionase’

- **Formation of Serine from Glycine**
  - PLP is required for the enzyme ‘hydroxymethyl transferase’ for the synthesis of serine from glycine

- **Synthesis of Niacin from tryptophan**
  - The enzyme ‘Kynureninase’ required PLP in the pathway for the synthesis of niacin from tryptophan
Functions (Contd)

- Glycogenolysis
  - PLP is required for the enzyme ‘glycogen phosphorylase’, prime enzyme in the breakdown of glycogen

- Formation of Myelin
  - PLP is required for the synthesis of sphingolipids & formation of myelin

- Formation of Coenzyme A
  - Formation of Coenzyme A from pantothenic acid requires PLP

- PLP plays an important role in the absorption of amino acids, utilisation of unsaturated fatty acids and in promoting immune functions
Deficiency Manifestations

☆ Deficiency of B₆ can occur due to –
  - Lack of Vitamin in the diet
  - Diseases of the intestines
  - Drugs like Isoniazid, Cycloserine & Penicillamine
  - Enzyme deficiency for conversion in to active forms
  - Use of Oral contraceptives & alcohol

☆ Neurological manifestations are commonly seen due to lack of formation of biogenic amines

☆ Symptoms includes – hyperirritability, convulsions, peripheral neuritis, depression & anaemia along with pellagra like symptoms may also been seen
Deficiency Manifestations

☆ Assessment -
- Tryptophan load test – measurement of xanthurenic acid in urine
- Measurement of urinary homocysteine & cystathionine
- Measurement of urinary 4-pyridoxic acid
- Transaminase activity in RBCs

☆ Prompt administration of Vitamin B6 along with Niacin will reverse the symptoms
Therapeutic Uses

- Nausea & Vomiting in pregnancy – ‘Morning sickness’
- Radiation sickness
- Muscular dystrophies
- Hyperoxaluria & Oxalate stones in kidneys