VITAMIN B₁ (THIAMINE)

History

- Old literature: Thiamine was called ‘Aneurine’ – can relieve neuritis
- Also called ‘Anti – beri beri factor’
- 1900: Eijkman produced beri beri in chicks by feeding them with polished rice
- Batavia isolated the vitamin & named it as ‘Thiamine’
- Structure was elucidated by Adolf Windaus – Nobel prize in 1928
Chemistry

- Sulphur containing vitamin
- Thiamine is composed of -
  - Thiazole ring
  - Pyrimidine ring
- Two rings are linked by ‘Methylene bridge’
- Thiazole ring: 4-methyl-5-hydroxyethylthiazole
- Pyrimidine ring: 2,5-dimethyl-4-aminopyrimidine
- White, needle shaped, water soluble crystals having a characteristic odour
- Destroyed by heat, oxidising & reducing agents
Sources

- **Rich sources:** Rice polishings, wheat germ, yeast
- **Good sources:** Cereals, pulses, nuts, oil seeds
- **Fair source:** Meat, liver, fish, eggs, milk, legumes & fruits
- **Poor source:** Polished rice
Recommended Dietary Allowances

- Adults: 1.2 to 1.4 mg/day
- Children: 0.6 to 1.3 mg/day
- Pregnancy & Lactation: 1.2 to 1.5 mg/day
- RDA is dependent on calorie intake
  - 0.5 mg / 1000 cals
  - predominantly involved in carbohydrate metabolism
Absorption, Transport Storage & Excretion

- Thiamine is readily absorbed from small intestine
- It is distributed throughout the body after absorption
- Thiamine is not stored in appreciable amounts in the body but relatively high concentration is seen in heart, liver & kidneys
- Excess thiamine is excreted in urine & some of it is also metabolised
- Normal thiamine levels in serum: 0.5 to 1 μg/dl
Functions

- Thiamine is essential for growth & development
- Thiamine is essential for the maintenance of nervous tissue

**Physiological Role**

**Metabolic role**

- Thiamine is converted into its active coenzyme form ‘Thiamine pyrophosphate’
- Reaction takes place in the liver & intestinal mucosa
- Catalysed by the enzyme ‘Thiamine pyrophosphokinase’ requiring ATP
Functions (Contd)

✓ Oxidative Decarboxylation reactions

(a) Pyruvate dehydrogenase reaction
- TPP acts as a coenzyme for ‘Pyruvate carboxylase’, a component of pyruvate dehydrogenase complex
- It catalyses the breakdown of pyruvate to acetyl CoA & CO₂

(b) α-ketoglutarate dehydrogenase reaction
- TPP acts as a coenzyme for ‘α-ketoglutarate dehydrogenase’ enzyme in the citric acid cycle
- It is involved in the conversion of α-ketoglutarate to succinyl CoA & CO₂
(c) Branched chain $\alpha$-ketoacid dehydrogenase reaction

- TPP acts as a coenzyme for ‘branched chain $\alpha$-ketoacid dehydrogenase’ degrading $\alpha$-ketoacids of branched chain aminoacids Valine, Leucine & Isoleucine

✓ Transketolase Reactions

- TPP acts as a coenzyme for transketolase reactions forming $\alpha$-ketol derivatives in pentose phosphate pathway

✓ In ‘Tryptophan metabolism’, activity of the enzyme ‘Tryptophan pyrrolase’ is dependent on thiamine
Deficiency Manifestations

Thiamine deficiency causes a disease called ‘Beri Beri’

Pathophysiology

- Increased accumulation of pyruvate & lactate in blood & tissues → Vasodilation & oedema
- Increased accumulation of branched chain ketoacids in blood & urine
- Increased pentose levels in tissues, RBCs, blood & urine
- Decreased energy production due to decreased oxidation of pyruvate & non-regeneration of oxaloacetate in citric acid cycle
- Particularly affects nerve tissue & heart
Types of Beri Beri

- Wet Beri Beri
  - Cardiovascular manifestations are prominent
  - Important manifestation: Presence of Oedema
  - Oedema develops rapidly in legs, face, trunk & serous cavities
  - Pulse becomes rapid along with palpitations & breathlessness
  - Neck veins become enlarged with visible pulsations
  - Heart becomes weak & goes in for cardiac failure
  - Death occurs due to cardiac complications
Types of Beri Beri (Contd)

- Dry Beri Beri
  - Nervous tissue manifestations are predominant
  - Important manifestation: Presence of Neuromuscular lesions
  - Muscles shows wasting & becomes progressively weak
  - Walking becomes difficult
  - Peripheral neuritis occurs which may progress to complete paralysis
  - Oedema is *not* a prominent feature
Types of Beri Beri (Contd)

- Infantile Beri Beri
  - Beri Beri seen in infants
  - It manifests in infants born to thiamine deficit mothers
  - Inadequate intake of thiamine during pregnancy is the cause → decreased thiamine content in breast milk
  - Symptoms includes: sleeplessness, restlessness, vomiting & breathlessness
  - It’s a mixed type of beri beri involving both cardiovascular & nervous system
  - If untreated, death occurs due to congestive cardiac failure
Other Diseases related to Thiamine deficiency

- Wernike – Korsakoff’s syndrome
  - Also called as cerebral beri beri
  - Severe nutritional deficiency of thiamine leads to this disease
  - It mainly affects brain & CNS
  - Manifestations includes: Opthalmoplegia, nystagmus, cerebellar ataxia, encephalopathy in addition to psychosis
Other Diseases related to Thiamine deficiency

- Alcoholic Polyneuritis
  - Seen in chronic alcoholics
  - It is due to increased requirement as alcohol utilisation needs large doses of thiamine
  - Also TPP is not formed in adequate amounts due to liver dysfunction
  - Main Symptoms includes polyneuritis with motor & sensory defects
  - They may have mild symptoms of beri beri
Assessment of Thiamine Deficiency

- Serum thiamine levels will be decreased
- Decreased transketolase activity in RBCs
- Abnormal Lactic acid/Pyruvate ration in blood

Treatment & Prevention

- Prompt administration of thiamine & supplementation of thiamine rich foods