PYRIDOXINE (VITAMIN B₆)

*Synonyms:* Rat antidermatitis factor.

- It occurs in association, perhaps in equilibrium, with an aldehyde-*Pyridoxal* and an amine *Pyridoxamine* form. **All three forms exhibit vitamin B6 activity.**

**Biological ‘Active’ Forms**

- **Pyridoxal-PO₄**, and **Pyridoxamine-PO₄**

*Formation of pyridoxal-P:* Phosphorylation takes place in Liver, Brain and other tissues with the help of ATP, Zn++ and an enzyme *Pyridoxal kinase.*
**Biosynthesis:** Vitamin B6 can be formed by many microorganisms and probably also by plants. *Human beings cannot synthesize the vitamin, hence has to be provided in the diet. Intestinal bacteria can synthesise the vitamin.*

**Metabolism**

**Absorption:** Dietary vitamin B6 is readily absorbed by the intestine.

**Excretion:**
- Pyridoxal and pyridoxamine are excreted in urine in small amounts 0.5 to 0.7 mg daily.
- Major urinary metabolite, about 3 mg daily is the biologically inactive form 4-pyridoxic acid.

**Occurrence and food sources:** The vitamin is distributed widely in animal and plant tissues. Rich sources of the vitamin are yeast, rice polishings, germinal portion of various seeds and cereal grains and egg-yolk. Moderate amounts are present in liver, kidney, muscle, fish. *Milk is a poor source.* Highest concentration occurs in royal jelly (bee).

**Metabolic Role**

Pyridoxal P acts as a coenzyme, it is *principally involved with metabolism of amino acids.*

1. **Co-transaminase:** It acts as a coenzyme for the enzyme transaminases (aminotransferases) in transamination reaction.

2. **Co-decarboxylase:** It acts as coenzyme for the enzyme decarboxylases in decarboxylation reaction. Amino acids are decarboxylated to form corresponding amines.

**Examples:**
- Tyrosine → Tyramine + CO2
- Histidine → Histamine + CO2
- Glutamic acid → GABA + CO2.
3- **In porphyrin synthesis**: Pyridoxal-P is required for conversion of \( \alpha \)-amino-\( \beta \)-ketoadipic acid to \( \delta \)-ALA, an important step in haem synthesis. **In B6-deficiency haem synthesis suffers and leads to anaemia.**

4- **Hypercholesterolaemia**: Relationship of B6-deficiency, hypercholesterolaemia and atherosclerosis has received considerable attention, although the exact role of vitamin B6 is not clear.

5- **Immune response**: In vitamin B6 deficiency, immune response is impaired.

6- **Oxaluria**: Vitamin B6 deficiency has been observed to produce oxaluria in experimental animals.

---

**CLINICAL ASPECT**

**Deficiency Manifestations**

No deficiency disease has been described. But following clinical manifestations are attributed to vitamin B6 deficiency.

1- **Epileptiform convulsions in infants**: have been attributed to pyridoxine deficiency. It is related to lowered activity of Glutamic acid decarboxylase, for which pyridoxal P is a coenzyme. As a result there occurs lowering of \( \gamma \)-amino butyric acid (GABA) in the brain which causes convulsions.

2- Pyridoxal-P is required as a coenzyme in the reaction of heme synthesis. **In B6-deficiency heme synthesis suffers and Fe cannot be utilized leads to anemia.**

3- **Isonicotinic acid hydrazide treatment in tuberculosis**: A syndrome resembling vitamin B6 deficiency has been observed in humans during the treatment of tuberculosis with high doses of tuberculostatic drug **Isonicotinic acid hydrazide** or **Isoniazid (INH)**.

4- Tryptophan metabolism was also altered, there was increased Xanthurenic acid excretion in urine. Signs and symptoms were alleviated by administration of pyridoxine to these patients. 50 mg of pyridoxine per day completely prevented the development of neuritis and neuropathies.

**Therapeutic uses**: Vitamin B6 has been found empirically to be of value in treatment of:

1- Nausea and vomiting of pregnancy (“morning sickness”).
2- Radiation sickness.
3- Muscular dystrophies.
3- Hyperoxaluria, and recurring oxalate stones of kidney.
LIPOIC ACID (THIOCTIC ACID)

*Synonyms:* Protogen, Acetate replacement factor (ARF), Pyruvate oxidation factor (POF).

Deficiency manifestations: Not known. Lipoic acid occurs in a wide variety of natural materials.

Metabolic Role of Lipoic Acid
It is recognised as an essential component in metabolism although it is active in extremely minute amounts.

1- **As a coenzyme of pyruvate dehydrogenase complex (PDH):** It is required alongwith other coenzymes in oxidative decarboxylation of pyruvic acid to acetyl-CoA.

2- **As a coenzyme of α-oxoglutarate dehydrogenase complex:** Required alongwith other coenzymes in oxidative decarboxylation of α-oxoglutarate to succinyl CoA.

3- **Lipoic acid is also required for the action of the enzyme sulphite oxidase:** Required for conversion of SO2 – to SO4=.

CLINICAL ASPECT
1- **Antioxidant Property:** Recently it has been shown that lipoic acid/or dihydrolipoic acid in large dosage 100 to 500 mg/day can act as an antioxidant. This property has been utilised in treatment of certain diseases (therapeutic uses).

2- useful in prevention of myocardial infarction and stroke.

3- Can mop up “free” radicals in brain tissue and thus can prevent conditions like multiple sclerosis, Alzheimer’s disease, etc.

4- Helps in reducing the plasma low density lipoproteins (LDL).

5- Stimulates production of glutathione (G-SH).
PANTOTHENIC ACID (VITAMIN B5)

Synonyms: Filtrate factor, Chick antidermatitis factor.

Biological “Active” Form:
Active form is coenzyme A. In tissues, this vitamin is present almost entirely in the form of the coenzyme (coenzyme A is also known as Coacetylase) and largely bound to proteins (apoenzyme).

Biosynthesis and Metabolism
I. Biosynthesis Pantothenic acid
(a) In many microorganisms, including yeast pantothenic acid is synthesized by direct coupling of β-alanine and pantoic acid. β-Alanine is formed from decarboxylation of Aspartic acid and pantoic acid from α-ketoisovalerate.
(b) Human tissues cannot synthesize pantothenic acid hence it has to be obtained from diet. In addition to dietary source, synthesis by intestinal bacteria supply fair amount of pantothenic acid.

II. Synthesis of Coenzyme A: Human tissues as well as plants and bacteria can synthesise CoASH.

Whole blood level: The concentration of pantothenic acid in whole blood is 15–45 μg/100 ml (average 30 μg%).

Excretion: Catabolic products of pantothenic acid are not known.
• Urine: Under ordinary dietary conditions about 2.5 to 5 mg are excreted daily in the urine.
**Metabolic Role**

Only demonstrated metabolic function of pantothenic acid is as a constituent of coenzyme A. As a constituent of CoA, pantothenic acid is essential to several fundamental metabolic reactions.

1. **Formation of active acetate:** In the form of active acetate, it participates in a number of important metabolic reactions, e.g. • Acetylcholine formation.

2. **Formation of active succinate (Succinyl-CoA):** Succinyl-CoA is involved in certain important metabolic reactions as follows:
   • Haem synthesis.
   • Degradation of ketone bodies by extrahepatic tissues.
   • Role in lipid metabolism.
   • Role in Adrenocortical function.
   • Activation of some amino acids may also involve CoASH.

**Deficiency Manifestations:** No deficiency disease has been recognised in man. This may be due to: Its widespread distribution in food stuffs and supply from synthesis by bacterial flora of intestines.

**Deficiency manifestations observed in experimental animals are:**
Dermatitis, Loss of hair (alopecia), GI manifestations, Nervous system manifestations.

**Daily requirement:** The human requirement of pantothenic acid is not known due to its widespread distribution.

**For adults** it is recommended, a daily intake of 5 to 12 mg per 2500 cal.

• **In infants:** 1 to 2 mg

**Requirement Increases in:**
Presence of severe stress, e.g. acute illness, burns, severe injury, etc, oral administration of broad spectrum antibiotics, in pregnancy and lactation, in growing children, and in convalescence.
BIOTIN (VITAMIN B7)


Excretion: Excreted in urine, faeces and milk. Normal adult on an adequate diet excretes 10 to 180 μg daily in the urine and 15 to 200 μg daily in the faeces. Faecal excretion probably represents unabsorbed biotin synthesized by intestinal bacteria.

Occurrence and food sources: Widely distributed in plants and animal tissues. Occurs chiefly as:

- **Water-soluble** form in most plant materials, except cereals and nuts,
- Mainly in a **water-insoluble** form in animal tissues. Foods rich in biotin include:
- **Animal sources**: They are liver, kidney, milk and milk products and egg-yolk.

Note: Human beings cannot synthesise the vitamin and hence it has to be supplied in diet. But **bacterial flora in intestine can synthesise** the vitamin and is a good source.

Metabolic Role

Biotin is the prosthetic group of certain enzymes that catalyse CO2-transfer reaction (CO2-fixation reaction). In biologic system, **biotin functions as the coenzyme for the enzyme called carboxylases, which catalyse the CO2-fixation (Carboxylation).**

Deficiency manifestations: Biotin deficiency may be induced in experimental animals: By

1- inclusion of large amounts of raw-egg white in the diet.
2- using sulphonamide drugs or broad spectrum oral antibiotics for prolonged periods.

The features include:

Dermatitis, **Spectacle-eyed**, appearance, due to circumocular alopecia, thinning or loss of fur/and hairs, graying of hairs/fur of black or brown colours, paralysis of hind legs.