

# FAT SOLUBLE VITAMINS

Vitamins are organic compounds occurring in small quantities in different natural foods and are necessary for the growth and maintenance of good health.

## Fat-Soluble Vitamins

Vitamin A, D, E, K

### Vitamin A

#### Sources of Vitamin A

- Animal food (mainly As retinol)
- Plant food as Carotene
- Animal sources: Fish liver oils, Halibut liver oil, Cod liver oil
- Other animal sources are liver, egg, butter, cheese, whole milk, fish and meat.
- Plant sources: Richest source is carrot
- Other sources are spinach, Amaranth, Green and yellow fruits like papaya, Mango, and Pumpkin.

#### RDA (Required daily allowance)

- Adults - 750 micrograms
- Children - 500- 750 micrograms
- Pregnancy & lactation - 1200 micrograms

#### Forms of vitamin A

- Retinol (vitamin A alcohol)
- Retinal (vitamin A aldehyde)
- Retinoic acid (vitamin A acid)
- Beta-Carotene (provitamin A)
- Beta-carotene or provitamin A is found in plant foods. It is cleaved in the intestine to produce two moles of retinal, which is nothing but an aldehyde form of vitamin A.

## Properties

- Vitamin A is required for tooth development and calcification
- Antioxidant vitamins
- Vitamin A helps in wound health

## Importance

- Plays an important role in the rhodopsin cycle or Wald's visual cycle.
- Rods are involved in dim Light vision. Cones are involved in bright Light and colour vision.
- Rhodopsin is a conjugated protein present in rods. It contains **11-cis retinal**, which is one of the vitamers of vitamin A.
- **Dark adaptation time is increased** in vitamin A-deficient individuals.

## Storage of Vitamin A

Stored in the **Liver Perisinusoidal Stellate (Ito) cells** as Retinyl Ester (Retinol Palmitate).

## Transport of Vitamin A from the Liver to Target Organs

Carried to target sites in the plasma as trimolecular complex bound to Retinol Binding Protein (RBP) and Transthyretin.

## Deficiency of vitamin A

### Eyes

- Loss of sensitivity to green light is the earliest manifestation
- All the ocular manifestations are collectively called Xerophthalmia
- Impairment to adapt in dim light, i.e. night blindness or Nyctalopia is the earliest symptom
- Conjunctival Xerosis (Dryness of Conjunctiva)
- Bitot's spots (white patches of keratinized epithelium appearing on the sclera)
- Blinding corneal ulceration and necrosis
- Keratomalacia (softening of the cornea)
- Corneal scarring that causes blindness.

### Skin and Mucosa

- **Epithelial metaplasia and keratinization**

- Hyperplasia and hyperkeratinization of the epidermis with plugging of ducts of the adnexal gland produce **Follicular Hyperkeratosis** or Papular dermatosis. This is called **Phrynoderma** or Toad Skin
- Squamous Metaplasia in the mucus-secreting epithelium of the upper respiratory tract and urinary tract
- Loss of taste sensation.

### **Oral manifestations of deficiency**

- Keratinising metaplasia of epithelium results in increased keratin formation.
- Occlusion of salivary gland ducts with keratin.
- Enamel hypoplasia, atypical dentin formation and epithelial invasion of pulpal tissue are characteristic features.
- Enamel is more severely affected than dentine.
- Delayed eruption of teeth

### **Assay of vitamin A**

- Dark adaptation time
- Serum Vitamin A by **Carr and Price reaction**.

### **Treatment of Vitamin A deficiency**

- 200000 IU or 110 mg of Retinol Palmitate orally in two successive days.

### **Prevention of Vitamin A deficiency**

- A single massive dose of 200000 IU to children (1–6 years) once in 6 months.
- A single massive dose of 100000 IU to children (6 months - 1 year) once in 6 months.

### **Hypervitaminosis A**

- Common for Arctic explorers who eat polar bear liver.
- Organelle damaged in hypervitaminosis is **Lysosomes**
- Acute toxicity: Pseudotumor cerebri and exfoliative dermatitis. In the liver, hepatomegaly and hyperlipidemia.
- Chronic toxicity: If intake of > 50,000 IU/day for > 3 months

- Weight loss, anorexia, nausea, vomiting, bony exostosis, bone and joint pain, decreased cognition, hepatomegaly progresses to cirrhosis.

## Vitamin D

### Sources of vitamin D

- Sunlight
- **Foods: Only animal sources Liver, Egg yolk, butter and liver oils. Out of the food sources Fish liver oils are the richest source**
- The richest source of Vitamin D is also Halibut Liver oil.

### RDA (Required daily allowance)

- Adults - 2.5 micrograms or 100 units
- Children - 1 microgram or 400 units

### Forms of vitamin D

- 1, 25 - dihydroxy chole calciferol or calcitriol is active form
- Ergocalciferol (Vit D2): Commercial Vitamin D obtained from the fungus, ergot
- Cholecalciferol (Vit D3): Endogenous synthesis from 7-Dehydrocholesterol.

### Properties

- Antirachitic vitamin
- Vitamins required for tooth development and calcification.
- Enamel hypoplasia is seen in association with deficiency.
- The vitamin that cannot cross the placenta
- Vitamin with its action similar to a hormone
- The vitamin that is synthesized in the skin
- Vitamin stored in fat, liver
- The vitamin that is present in animal food only
- Vitamin necessary for the absorption of bile salts

### Importance

Calcitriol increases serum calcium and phosphorous level by increasing intestinal absorption and by reducing renal excretion.

## **Functions**

- Regulation of calcium and phosphorus homeostasis
- Action on intestine - Vitamin D increases  $\text{Ca}^{2+}$  absorption.
- Action on kidney - Vitamin D increases  $\text{Ca}^{2+}$  and Phosphorus reabsorption.
- Action on bones - 1, 25-dihydroxy vitamin D and parathyroid hormone, enhance the expression of RANKL (receptor activator of NF- $\kappa$ B ligand) on osteoblasts.
- Immunomodulatory and antiproliferative effects - Prevent infection by Mycobacterium tuberculosis.
- Mineralization of bones - Vitamin D contributes to the mineralization of osteoid matrix and epiphyseal cartilage in both flat and long bones.

## **Deficiency**

- The normal reference range for circulating 25-(OH) D is 20 to 100 ng/mL
- The concentration circulating 25-(OH) D < 20 ng/mL is called Vitamin D deficiency.
- Chronic renal failure

## **Rickets**

- Rickets in children
- Osteomalacia in adults
- Vitamin D–dependent rickets type 1 (Pseudo-vitamin D–resistant rickets)
- Vitamin D–dependent rickets type 2 (True vitamin D– resistant rickets)
- The pigeon chest is one of the important features of rickets
- Renal rickets or renal osteodystrophy is seen in patients with chronic renal failure. Renal rickets is mainly due to decreased synthesis of calcitriol in the kidney.
- In rickets, the plasma calcitriol is decreased and alkaline phosphatase activity is elevated.

## **Oral Manifestations**

- Delayed eruption of primary and permanent teeth.
- Mal-alignment of the teeth in the jaws.
- Developmental anomalies of dentin and enamel. The teeth show a wide predentin zone with much interglobular dentin.
- The pulp horns are elongated and extend high, reaching the dentinoenamel junction.

## **Assay of Vitamin D**

- The release into the circulation of osteocalcin provides an index of vitamin D status
- 25(OH) Vitamin D level is measured in the serum to indicate Vitamin D status.

## **Toxicity**

- The upper limit of Vitamin D intake has been set at 4000 IU/day
- Some infants are sensitive to intakes of vitamin D as low as 50 µg/day, resulting in an elevated plasma concentration of calcium
- This can lead to the contraction of blood vessels, high blood pressure, and **calcinosis**—the calcification of soft tissues.

## **Vitamin E**

### **Sources of vitamin E**

Vegetable oils like Wheat germ oil, sunflower oil, and Cotton seed oil.

### **RDA (Required daily allowance)**

- Males 10 mg/day
- Females 8 mg/day
- Pregnancy 10 mg/day
- Lactation 12 mg/day

### **Forms of Vitamin E**

α -tocopherol is the active form.

### **Properties**

- Antioxidant vitamins
- Antisterility vitamin
- Vitamin associated with peripheral neuritis

- The vitamin that causes Encephalomalacia
- Selenium decreases the requirement for Vitamin E

### **Importance**

- Its antioxidant property protects polyunsaturated fatty acids (PUFA) from peroxidation reactions.
- Protects the liver from toxic compounds.
- Preserves and maintains the germinal epithelium of gonads.
- Prevents heart disease by preventing the oxidation of LDL.
- Vit. E in association with Vitamin A and C delays the onset of cataracts.
- Protects RBC from hemolysis by oxidizing agents.

### **Deficiency**

- Decreased male fertility
- Impaired fetal-maternal vascular relationships
- Encephalomalacia
- Nutritional muscular dystrophy
- Axonal degeneration
- Hemolytic anaemia
- Peripheral neuropathy
- Spinocerebellar ataxia
- Skeletal myopathy
- Pigmented retinopathy
- Ophthalmoplegia.

### **High Doses of Vitamin E**

**Vitamin E in high doses may protect against**

Oxygen-induced retrolental fibroplasia

Bronchopulmonary dysplasia

Intraventricular haemorrhage of prematurity

Treat intermittent claudication

Slow the ageing process

### **Toxicity of Vitamin E**

Reduce platelet aggregation and interfere with Vitamin K.

## Vitamin K

Coagulation vitamin

### Sources of vitamin K

- Green vegetables
- Synthesized by bacteria in the gut

### RDA (Recommended Daily allowance)

- 50-100 micrograms

### Forms of Vitamin K

- Vitamin K1: Phylloquinone from dietary sources
- Vitamin K2: Menaquinone Synthesized by Bacterial Flora
- Vitamin K3: Menadione (and Menadiol diacetate) Synthetic, Water Soluble.

All three forms of vitamins are naphthoquinones derivatives.

### Properties

- Vitamins involved in electron transfer
- Heat-stable and light-sensitive vitamins
- Vitamins stored in the liver
- The vitamin that is associated with neonatal jaundice
- Vitamin necessary for the absorption of bile salts
- Clotting factors II (prothrombin), VII (proconvertin), IX (Christmas factor), and X (Stuart power factor) are vitamin K-dependent factors. They are synthesized in the liver.

### Deficiency

#### **Drugs causing Vitamin K deficiency**

- Warfarin and Dicoumoral inhibit  $\gamma$  carboxylation by competitively inhibiting the enzyme that converts vitamin K to its active hydroquinone form
- Antiobesity drug orlistat.

#### **Vitamin K Deficiency**

- Elevated prothrombin time, bleeding time
- Newborns, especially premature infants are particularly susceptible to Vitamin K deficiency because of low fat stores, low breast milk levels of vitamin K, sterility of the infantile intestinal tract, liver immaturity, and poor placental transport.



## **Oral Manifestations**

- Prothrombin levels below 35% result in gingival bleeding after tooth brushing.
- Spontaneous gingival haemorrhages occur when the prothrombin levels fall below 20%.

## **Hypervitaminosis K**

- Hemolysis
- Hyperbilirubinemia
- Kernicterus and brain damage.