

FAT-SOLUBLE VITAMINS

INTRODUCTION

- ✗ Vitamins are organic nutrients that are required in small quantities for a variety of biochemical functions and which generally cannot be synthesized by the body and must be supplied by the diet
- ✗ They are classified into fat-soluble and water-soluble vitamins
- ✗ The fat-soluble vitamins are vitamins A, D, E and K
- ✗ They are stored in the body for long periods of time

VITAMIN A (RETINOL)

Introduction/Structure

- ✗ The active form is present only in animal tissues
- ✗ Carotenoids (e.g. β -carotene) are provitamins that are converted to active forms of vitamin A
- ✗ β -carotene is present in plant tissues
- ✗ The β -carotene is oxidized to two molecules of retinal
- ✗ All the compounds with vitamin A activity are referred to as **retinoids**.
- ✗ They have polyisoprenoid compounds having beta-ionone ring system
- ✗ Three different compounds with vitamin A activity are;
 - ✗ Retinol (vitamin A alcohol)
 - ✗ Retinal (vitamin A aldehyde)
 - ✗ Retinoic acid (vitamin A acid)
- ✗ The retinal may be reduced to retinol by retinal reductase. This reaction is readily reversible
- ✗ Retinal is oxidized to retinoic acid, which cannot be converted back to other forms

Sources

- ✗ Retinoids are from animals
- ✗ Retinol (especially retinol palmitate) is mostly what is ingested from animal products
- ✗ The retinoid forms of vitamin A are supplied primarily by foods of animal origin such as;
 - ✗ Dairy products
 - ✗ Fish; and
 - ✗ Liver
- ✗ Carotenoids are from plants
- ✗ Some foods of plant origin contain the antioxidant, β -carotene, which the body converts to vitamin A
- ✗ The β -carotene comes from fruits and vegetables especially those that are orange or dark green in colour;
 - ✗ Carrots
 - ✗ Pumpkin
 - ✗ Winter squash

- ✍ Dark green leafy vegetables
- ✍ Apricots
- ✍ In natural sources, vitamin A is present as esters of fatty acids
- ✍ These, as well as their precursors are readily absorbed from the intestines

Metabolism, Absorption & Storage

- ✍ Pre-albumin and specific binding proteins on cell surface membranes are involved in the uptake of Vitamin A esters from the plasma into the tissues
- ✍ Carotenoids (e.g. β -carotene) are provitamins that are converted to retinal and retinol, which are the forms used by the body
- ✍ Carotenoids may be directly absorbed, but most are cleaved to retinal and then converted to retinol, which is absorbed
- ✍ Their transport is effected by specific proteins such as;
 - ✍ Serum retinol binding protein (SRBP)
 - ✍ Cytosolic retinol binding protein (CRBP)
 - ✍ Specific retinoic acid binding protein (RABP)
 - ✍ Albumin
- ✍ β carotene is cleaved by a di-oxygenase to form retinal
- ✍ The retinal is reduced to retinol by an NADH or NADPH dependent retinal reductase present in the intestinal mucosa [**intestine is the major site of absorption**]
- ✍ The absorption is along with other fats and requires bile salts. [**in biliary tract obstruction and steatorrhea, vitamin A absorption is reduced**]
- ✍ Within the mucosal cells, retinol is re-esterified with palmitate, incorporated into chylomicrons and transported to the liver [**where 90% of the body's vitamin A is stored**]
- ✍ It is stored in the liver stellate cells mainly as its ester, retinol palmitate

Recommended Dietary Allowance (RDA)

The Recommended Dietary Allowance for vitamin A for an;

- ✍ Adult male – 750-1000 $\mu\text{g/day}$
- ✍ Adult female – 750 $\mu\text{g/day}$
- ✍ Pregnancy – 1000 $\mu\text{g/day}$













Functions

- ✍ It helps the eyes to adjust to light changes
- ✍ It plays an important role in;
 - ✍ Bone growth
 - ✍ Tooth development
 - ✍ Reproduction
 - ✍ Cell division

- ✍ Gene expression; and
- ✍ Regulation of the immune system
- ✍ It is necessary for the moistening of;
 - ✍ The skin
 - ✍ The eyes; and
 - ✍ Mucous membranes of;
 - ✓ The mouth
 - ✓ Nose
 - ✓ Throat; and
 - ✓ Lungs
- ✍ Vitamin A is also an important oxidant that may play a role in the prevention of certain cancers

Clinical Correlates

Vitamin A deficiency

- ✍ It is rare in developed nations
- ✍ It most commonly occurs in developing nations usually due to malnutrition
- ✍ Vitamin A deficiency can result in the following conditions;
 -  Night blindness (Nyctalopia): inability to see well in dim light
 -  Xerophthalmia: the conjunctiva and cornea becomes abnormally dry and keratinized. Without treatment, it may progress to keratomalacia
 -  Keratomalacia: occurs when Xerophthalmia persists for a long time. There is degeneration of corneal epithelium and the cornea becomes opaque, ulcerated and perforated leading to blindness
 -  Bitot's spots: greyish-white triangular plaques on the conjunctiva due to the buildup of keratin
 -  Preventable blindness
 -  Skin and mucous membrane lesions
 -  Growth retardation: slower bone growth. May be due to defective synthesis in chondroitin sulfate
 -  Decreased protein synthesis
 -  Decreased protein synthesis
 -  Lowered glycoprotein content of cell
 -  Reduced immunity against infections
 -  Gonadal dysfunction in males and miscarriage in females

Vitamin A Toxicity: Hypervitaminosis A

- ✍ In developed countries, toxic or excess levels of vitamin A are more of a concern than deficiencies
- ✍ Food alone does not normally give this level of toxicity except when taken with some multivitamin supplements, which contain high doses of vitamin A, over time

Symptoms

- ✗ Anorexia (loss of appetite)
- ✗ Dry, itchy skin
- ✗ Peeling of the skin
- ✗ Headache
- ✗ Nausea

VITAMIN D (CHOLECALCIFEROL)

Introduction/Structure

- ✗ Vitamin D is a group of fat-soluble secosteroids
- ✗ It is the only vitamin that is usually most required in the diet
- ✗ Dietary intake is required under the conditions of inadequate exposure to sunlight

Metabolism, Absorption & Storage

- ✗ Vitamin D is derived either from 7-dehydrocholesterol or ergosterol by the action of ultraviolet radiations
- ✗ 7-dehydrocholesterol is present in the Malpighian layer of epidermis
- ✗ UV light converts this sterol to secosterol, a provitamin, which is then isomerized to produce cholecalciferol (vitamin D₃)

Activation

- ✗ Vitamin D is a prohormone
- ✗ Cholecalciferol is first transported to the liver where it is hydroxylated at C₂₅ to form 25 (OH)-cholecalciferol
- ✗ In the plasma, 25-hydroxyvitamin D₃ is bound to vitamin D binding protein (VDBP)
- ✗ A significant proportion of 25 (OH)-D₃ is excreted in the bile
- ✗ In the kidney, it is further hydroxylated at C₁ to form 1,25-dihydroxyvitamin D₃ (1,25-dihydroxycholecalciferol) also known as calcitriol
- ✗ Calcitriol is the active form of vitamin D. It is a hormone
- ✗ Commercially the vitamin is derived from the fungus, ergot
- ✗ Ergosterol is treated with UV light and ergocalciferol (or vitamin D₂) is formed

Sources

- ✗ Exposure to ultraviolet light is necessary for the body to produce the active form of vitamin D
- ✗ Vitamin D is also found in the diets
- ✗ The primary food sources of vitamin D are;
 - ✗ Milk and other dairy products fortified with vitamin D
 - ✗ Oily fish, e.g.
 - ✓ Salmon

- ✓ Sardines
- ✓ Cod liver oil

Recommended Dietary Allowance (RDA)

- ✗ Children – 10 µg/day
- ✗ Adults – 5 µg/day
- ✗ Pregnancy/Lactation – 10 µg/day
- ✗ Above the age of 60 – 15 µg/day

Functions

- ✗ It is responsible for enhancing intestinal absorption of;
 - ✗ Calcium
 - ✗ Iron
 - ✗ Magnesium
 - ✗ Phosphate; and
 - ✗ Zinc
- ✗ 1,25-dihydroxyvitamin D₃ is responsible for the maintenance of calcium balance in the body
- ✗ Vitamin D plays a crucial role in the body's use of calcium and phosphorus
- ✗ It works by increasing the amount of calcium absorbed from the small intestine
- ✗ Calcitriol increases the reabsorption of calcium and phosphorus by renal tubules
- ✗ Helping to form and maintain bones
- ✗ Vitamin D plays a role in immunity
- ✗ It also plays a role in controlling cell growth
- ✗ Children especially need adequate amounts of vitamin D to develop strong bones and healthy teeth

Clinical Correlates

Vitamin D Deficiency

The deficiency diseases are;

- ✗ Rickets in children
- ✗ Osteomalacia in adults

Causes of deficiency

- ✗ Insufficient exposure to sunlight
- ✗ Malabsorption of vitamin (obstructive jaundice and steatorrhoea)
- ✗ Abnormality of vitamin D activation
- ✗ Nutritional deficiency of calcium or phosphate
- ✗ Deficient renal absorption of phosphates

Symptoms

- ✍ Flattening of the back of the skull
- ✍ In children;
 - ✍ Rickets – long, soft bowed legs
- ✍ In adults;
 - ✍ Osteomalacia – muscle and bone weakness
 - ✍ Osteoporosis – loss of bone mass

Hypervitaminosis D

- ✍ High doses of supplements coupled with large amounts of fortified foods may cause accumulations in the liver and produce signs of poisoning
- ✍ Excess vitamin D levels enhances calcium absorption leading to;
 - ✍ Hypercalcaemia; and
 - ✍ Metastatic calcium deposits
- ✍ There is a tendency to develop kidney stones from hypercalciuria, secondary to hypercalcaemia
[Although vitamin D is toxic in high doses, excessive exposure to sunlight does not result in vitamin D toxicity because excess D₃ is destroyed by sunlight itself]

VITAMIN E (TOCOPHEROL)

Introduction/Structure

- ✍ Vitamin E (tocopherol) is required in the human diet
- ✍ It exists in the diet as a mixture of eight closely related compounds called Tocopherols
- ✍ The most potent is α -tocopherol

Sources

- ✍ About 60% of vitamin E in the diet comes from vegetable oil including products made with vegetable oil e.g.;
 - ✍ Margarine; and
 - ✍ Salad dressing
- ✍ Vitamin E sources also include;
 - ✍ Fruits
 - ✍ Vegetables
 - ✍ Grains
 - ✍ Nuts
 - ✍ Seeds; and
 - ✍ Fortified cereals

Metabolism, Absorption & Storage

- ✍ Absorption is dependent on appropriate fat absorption with the help of bile salts
- ✍ Tocopherol is absorbed and transported as chylomicrons

- ✗ It is stored in adipose tissue

Recommended Dietary Allowance (RDA)

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

Functions

- ✗ Vitamin E is the most powerful antioxidant **[It is a scavenger of potentially damaging free radicals]**
- ✗ It protects vitamins A and C, red blood cells and essential fatty acids from destruction
- ✗ It boosts immune response
- ✗ It reduces the risk of atherosclerosis by reducing oxidation of LDL
- ✗ It can depress leukocyte oxidative bactericidal activity
- ✗ It prevents oxidation and peroxidation of polyunsaturated fatty acids, thus preventing membrane dysfunction and altered lipoprotein metabolism

Clinical Correlates

Vitamin E Deficiency

Deficiency is rare except in;

- ✗ Pregnancy
- ✗ Newborn
- ✗ Premature infants; and
- ✗ In those unable to absorb fats

Where it is associated with;

- ✗ Hemolytic anaemia due to lack of protection against peroxides
- ✗ Creatinuria due to increased muscle breakdown

Hypervitaminosis E

- ✗ Occurs at very high doses of vitamin E
- ✗ It may cause tendency to haemorrhage, as it is a mild anticoagulant

VITAMIN K

Introduction/Structure

- ✍ It refers to a group of **naphthoquinone** derivatives with varying number of isoprenoid units in its side chain
 - ✍ Vitamin K₁ (Phylloquinone) – 20C side chain
 - ✍ Vitamin K₂ (Menquinine) – 30C side chain
 - ✍ Menadione – a water soluble synthetic vitamin used in clinical practice

Sources

- ✍ Menquinine is present in animals
- ✍ Phylloquinone is present in plants
- ✍ Menadione is a synthetic water-soluble vitamin available for treatment
- ✍ **Vitamin K is naturally produced by bacteria in the intestines**

Good food sources of vitamin K are;

- ✍ Green, leafy vegetables such as;
 - ✍ Spinach
 - ✍ Cabbage; and
 - ✍ Certain vegetable oils
- ✍ **Animal foods, in general, contain limited amounts of vitamin K**

Metabolism, Absorption & Storage

- ✍ Like vitamin E, absorption is dependent on appropriate fat absorption
- ✍ It occurs in the intestine along with chylomicrons
- ✍ Bile salts are required for normal absorption
- ✍ It is stored in the liver and transported in plasma along with beta lipoproteins

Recommended Dietary Allowance (RDA)

- ✍ 50-100 mg/day
- ✍ This is usually available in a normal diet

Functions

- ✍ Normal blood clotting
- ✍ Promoting bone health
- ✍ Helping to produce proteins for blood, bones and kidneys
- ✍ It is also required for post translational modifications of several proteins required in the coagulation cascade such as factors II, VII, IX and X

Clinical Correlates

Vitamin K Deficiency

- ✍ Vitamin K deficiency may appear in infants due to lack of intestinal bacteria to produce vitamin K
- ✍ It may also appear in people who take anticoagulants such as Coumadin or antibiotic drugs because intestinal bacteria are sometimes killed as a result of long-term use of antibiotics
- ✍ Without sufficient amounts of vitamin K, haemorrhaging can occur

Hypervitaminosis K

- ✍ Administration of large quantities of menadione may result in toxicity
- ✍ Excessive amounts of vitamin K can cause;
 - ✍ Haemolysis of red blood cells
 - ✍ Liver damage
 - ✍ Hyperbilirubinaemia
 - ✍ Kernicterus
 - ✍ Brain damage