

FAT SOLUBLE VITAMINS: A, D, E, and K

Fat soluble vitamins: A, D, E, and K

- require bile for their absorption
- travel through lymphatic system within chylomicrons, then enter bloodstream
 - in bloodstream uses protein carrier, **retinol binding protein (RBP)**, for transport
- excess stored in liver and adipose tissue, and released as needed by the body
- risk of toxicity because these vitamins are not regularly excreted

I. VITAMIN A and BETA-CAROTENE

1. OVERVIEW

Carotenoids – pigments found in plants and animals, some of which have vitamin A activity.

Beta-Carotene – carotenoid with the greatest vitamin A activity; an orange pigment found in plants

- a. *vitamin A precursor.*
- b. Beta-carotene is cleaved in the intestine and liver yielding 2 Vit A molecules

Retinoids - These compounds are three different active forms of vitamin A in the body.

- a. retinol- the alcohol form.
 - i. Supports reproduction.
 - ii. Is the major transport and storage form.
- b. retinal- the aldehyde form. Participates in vision.
- c. and retinoid acid - the acid form. Regulates growth

Retinal Esters –found in food derived from animals. Easily converted to retinol in the body.

Vitamin A- all naturally occurring compounds with the biological activity of retinol, the alcohol form of vitamin A. Absorption of Vit A in the body is greater than beta-carotene.

Conversion of vitamin A compounds—significant due to specific function of each form of vitamin A

- a. retinal esters convert into retinol
- b. beta-carotene converts into retinal
- c. retinol and retinal convert reversibly into each other
- d. retinal converts into retinoid acid irreversibly

2. ROLES OF VITAMIN A IN THE BODY

A. Vision (retinal)

1. Maintains clarity of cornea
2. Converts light energy into nerve impulses at the retina
 - a. Rhodopsin – pigment molecule of cells of retina composed of protein opsin and retinal
 - i. light changes conformation of **retinal**, causing it to dissociate from opsin
 - ii. opsin then changes shape causing a change in the membrane potential of the cell and sends an electrical impulse to the nerve cell, which is subsequently sent to the brain
 - iii. dissociated retinal and opsin recombine after signal is sent, but there are small losses in retinal, thus requiring constant replenishment from food

B. Protein synthesis and cell differentiation (retinoic acid)

1. Cell differentiation – process by which immature cells develop specific functions characteristic of a mature cell type
2. Vitamin A maintains the integrity of epithelial cells and mucous membranes

a. Promotes differentiation of epithelial cells and goblet cells (mucus secreting cells)

C. Reproduction and growth (retinol)

1. Men –promotes sperm development
2. Women- supports normal fetal development
3. Growth of bones. Vitamin A aids osteoclast activity in bone remodeling
3. Deficiency of retinol in children causes failure to grow

D. Beta Carotene as an Antioxidant

1. Beta-carotene that is not converted into vit A serves a protective barrier against disease

3. VITAMIN A DEFICIENCY

Vitamin A utilized in the body is dependent on

1. Quantity stored in liver
 - a. Deficiency symptoms appear in 1-2 years due to high amounts stored in liver
2. Protein status/effectiveness (because of dependency on RPB)

Deficiency rare in US, but common in developing nations

A. Infectious diseases

1. Measles- severity in developing countries correlated with Vitamin A deficiency.
 - a. Death ensues from associated symptoms: pneumonia or diarrhea
 - b. Severity can be avoided by treating with large amounts of vit A
2. Vit A supplements also protect against complications associated with malaria, lung disease, and HIV

B. Night Blindness – one of the first detectable signs of vit A deficiency

1. Insufficient retinal to regenerate visual pigments in retina that causes a slow recovery after flashes of bright light at night or an inability to see in dim light

C. Blindness

1. Lack of vitamin A in the cornea causes cornea to become dry and hard (xerosis) which progresses to softening of cornea (keratomalacia) and irreversible blindness
2. Major cause of childhood blindness

D. Keratinization

1. Mucous membranes
 - a. Lack of vit a causes goblet cells to not form properly, causing less mucous to be secreted which can hinder nutrient absorption
 - b. Weakens immune defenses of epithelial tissues
2. Skin – epithelial cells secrete keratin causing skin to become dry rough and scaly

4. VITAMIN A TOXICITY

-Toxicity occurs when RBP are saturated with vit A, and free unbound Vit A begins to destroy cells.

-Toxicity is possible by consuming active vitamin A from animal derived foods, (especially liver, since it stores Vit A), fortified foods, or supplements

Arctic persons who eat an abundance of polar bear livers were found to have Hypervitaminosis A (Vit A toxicity). Dr. Dise said this was a “quirky” question that has appeared on the boards.

-Occurs more in children because they require lower doses

Pediatric correlation from Dr. Dise: In babies aged 6-18 months, it is common to see hypercarotenemia, because relatively speaking, they eat so much fruit and vegetables that are orange. The child’s skin turns yellow (Not the whites of their eyes, though). This is a pediatric thing to know about. It is benign.

-RDA of Vit A is 700µg for women and 900µg for men

-Over consumption of Beta-carotene from foods is not harmful, but turns the skin yellow due to storage in the skin. Beta carotene from supplements is harmful, however, by acting as a prooxidant.

A. Bone defects

1. Excessive Vit A weakens bones, contributes to osteoporosis, higher incidence of hip injury

B. Birth defects

1. Birth defects associated with high doses of Vit A before the 7th week of fetal development

C. Acne- High doses of active Vit A do not help acne

1. Accutane- Vit A *derivative* that acts on deep skin lesions
 - a. detrimental to growth and to fetuses
2. Retin A – another vit A derivative that is used topically

5. VITAMIN A RECOMMENDATIONS

-**Retinol activity equivalents (RAE)**- measure of vitamin A activity

-1 RAE = 1 µg retinol = 12 µg beta carotene

6. VITAMIN A IN FOODS

-Animal derived foods are richest sources: liver, fish liver oil, milk and dairy, butter, eggs

1. Liver- stores vit A, can cause toxicity if overeaten

-Skim milk – Vit A is lost, but added in as supplements (margarine is also supplemented)

-Vegetables contain Vit A precursors (carotenoids) that give the red and yellow color to plants

1. Dark leafy greens, rich yellow, deep orange fruits and vegetables (spinach, cantaloupe, etc)

II. VITAMIN D

1. OVERVIEW

Vitamin D (also called calciferol) – Is actually a hormone (produced by the body, used by the body). Different forms include plant version, vitamin D₂ (ergocalciferol) and the animal version Vitamin D₃ (cholecalciferol)

1. With sunlight, the body synthesizes Vit D from a cholesterol derived precursor
 - a. Vit D is *not* an essential nutrient

-Cholesterol derived precursor uses UV light to convert to Previtamin D₃, which is then converted to Vitamin D₃ (inactive form. Also the form obtained from foods) using body heat. Vit D₃ is then hydroxylated in the liver and then hydroxylated in the kidneys to make active Vit. D

2. ROLES IN THE BODY

A. Bone growth – bone maintenance and growth by maintaining blood concentrations of Ca and P

1. Enhances Ca and P absorption from GI tract, reabsorption from kidney, and mobilization from bones into blood

B. Other- targets include immune system cells, brain and nervous system, pancreas, skin, muscles, cartilage, reproductive organs.

3. VITAMIN D DEFICIENCY

-Causes: Dark skin, breast feeding, lack of sunlight, sunscreen, consumption of non fortified milk

1. Results in lower production of calcium binding protein, creating a calcium deficiency

Another quote from Dr. Dise: “The book says "breastfeeding without supplementation causes Deficiency”, but that's a very simplistic summation. The truth is, that in very sunny areas of the world, it is rare to see Vit D deficiency in breastfed children, and the cases that are seen in northern climes also have other variables complicating the picture. The best example in the USA is Muslim women who use the burka, who exclusively breastfeed, and don't let their babies go in the sun either. I usually don't recommend Vit D supplements in my practice in breast feeders. However, on a test, you should probably know they will want you to say breastfeeding is linked to Vit D deficiency. I just think that my students need to know the whole story.”

- A. Rickets- failure of bones to calcify in children, causing growth retardation
- B. Osteomalacia – adult form of rickets, causes softening of bones, bending of spine and bowed legs.
- C. Osteoporosis – Loss of calcium from bones, can result in fractures
- D. Elderly – with age, skin, liver and kidney cannot make active Vit D as readily

4. VITAMIN D TOXICITY

-Excess Vit D raises blood calcium, and the blood calcium precipitates in soft tissue (kidney stones) and hardens blood vessels.

5. VITAMIN D RECOMMENDATIONS AND SOURCES

- A. Sources: Sunlight, fortified milk and dairy
- B. RDA: 5-15 µg/day (increases with age)

III. VITAMIN E

Tocopherol – class of compounds found in vegetable oil. Only one of this class of compounds, Alpha-tocopherol, contains active Vitamin E

1. VITAMIN E AS AN ANTIOXIDANT

- Stops the chain reaction of free radicals producing more free radicals, thus protecting cells and membranes and preventing oxidation of polyunsaturated fats
- Reduces risk of heart disease by preventing oxidation of LDL

2. VITAMIN E DEFICIENCY

- Deficiency is rare, but usually associated with disease of fat malabsorption (cystic fibrosis)
- A. Erythrocyte hemolysis – breaking open of red blood cells due to oxidation of cell membranes
- B. Neuromuscular dysfunction of spinal cord and retina – loss of muscle coordination and reflexes, impaired vision and speech

3. VITAMIN E TOXICITY

-Rare, but high levels may interfere with Vitamin K actions in blood clotting and anticoagulants

4. VITAMIN E RECOMMENDATIONS

-RDA 15 mg/day, upper level of 1000mg/day

5. VITAMIN E IN FOODS

- Vegetable oils and their products, seeds, and nuts
- Destroyed by heat and oxidation

IV. VITAMIN K

Vitamin K – derived from foods and intestinal bacteria. Acts in blood clotting

1. ROLES OF VITAMIN K

- A. Activation of mineral calcium and proteins involved in clotting, including prothrombin conversion to thrombin
- B. Synthesis of bone proteins – Vit K helps produce a protein necessary for the binding of minerals to form bone

2. VITAMIN K DEFICIENCY

- A. Secondary deficiency (deficiency due to reasons other than poor intake), can be fatal (lack of clotting)
 - 1. Vit K absorption decreases when fat absorption fails (eg, when bile secretion fails)
 - 2. Drugs disrupt Vit K synthesis and action
 - 3. Antibiotics kill bacteria in GI that synthesize bacteria
 - 4. Anticoagulants interfere with Vit K metabolism
- B. Newborns- born w/o bacteria in GI to tract to produce Vit K, and prothrombin concentrations are low
 - 1. Newborns given Vit K dose at birth to prevent hemorrhage

3. VITAMIN K TOXICITY

-Uncommon, but high doses may reduce the effectiveness of anticoagulant drugs

4. VITAMIN K RECOMMENDATIONS AND SOURCES

RDA: Men 120 µg/day. Women 90 µg/day

- A. GI tract bacteria. Vit K stored in liver
- B. Leafy green vegetables and cabbage (major sources), milk, meats, eggs, cereal, fruits, vegetables.

HIGHLIGHT: ANTIOXIDANT NUTRIENTS AND DISEASE PREVENTION

1. FREE RADICALS AND DISEASE

-Free Radicals – unstable molecules that have one or more unpaired electrons in the outer orbital.

Form after oxygen reacts with body compounds, or form from UV radiation, air pollution, and tobacco smoke.

- 1. Act by damaging polyunsaturated fatty acids in lipoproteins of cell membranes, damaging cell proteins, and causing DNA mutations
- 2. body has natural defenses against free radicals that loses effectiveness with age

-Oxidant – compounds that oxidize other compounds

-Antioxidants – Neutralize free radicals by donating electrons to a free radical to stabilize it

-Oxidative stress – production of free radicals and oxidants exceeds the body's ability to defend itself

2. DEFENDING AGAINST FREE RADICALS

- Limit free-radical formation
- Destroy free radicals and precursors
- Stimulate antioxidant enzyme activity
- Repair oxidative damage
- Stimulate repair enzyme activity

A. Enzymes

- 1. Disarm oxidants with the help of minerals (Selenium, copper, manganese, zinc)
- 2. Lack of minerals in diet decrease enzyme effectiveness

B. Vitamins

- 1. Vit.E defends cell membrane lipids and lipoproteins

2. Vit C defends water based fluid compartments, including blood fluid, and neutralizes polluted air and cigarette smoke

3. DEFENDING AGAINST CANCER

- DNA damage by free radicals causes cancer
- Diets high in antioxidants (fruits and vegetables) have lower incidence of cancer
- Vit C protects against cancer of mouth, pharynx, esophagus, stomach
- Low Vit E counts associated with higher incidence of cancer

4. DEFENDING AGAINST HEART DISEASE

- Free radicals oxidize LDL, which then accelerates the formation of plaques
- Oxidation of polyunsaturated fatty acids of cell membrane cause damage to arterial walls
- Vit E – consumption lowers rate and slows progression of heart disease
 1. defends against LDL oxidation, inflammation, arterial injuries, blood clotting
- Vit C – Protect against LDL oxidation, raises HDL, lowers total cholesterol, improve blood pressure

5. FOOD AND SUPPLEMENTS AS ANTIOXIDANTS

- Food as opposed to supplements is found to be superior in supplying beneficial antioxidants
- High supplemental doses have varying effects. Don't have as much variety of nutrients

A. Recommendations:

1. Use unsaturated fats, not trans or saturated fats
2. Consume Omega-3 fatty acids
3. Diet high in veggies, fruits, whole grains, nuts