VITAMINS

- Name “vitamins” meaning vital amines (first vitamins discovered contained nitrogen)
- Considered noncaloric **micronutrients** or accessory food factors.
- Organic molecules needed in small amounts in the diets for normal growth, functioning & reproduction of cells.; Must be supplied in our diet as our body tissue cannot synthesize them in adequate amounts.

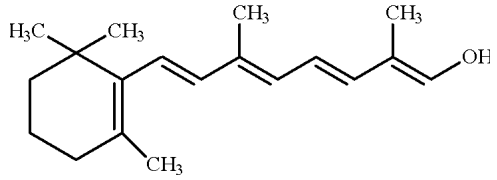
	Water-Soluble Vitamins: B Vitamins and Vitamin C	Fat-Soluble Vitamins: Vitamins A, D, E, and K
Absorption	Directly into the blood.	First into the lymph, then the blood.
Transport	Travel freely.	Many require protein carriers.
Storage	Circulate freely in water-filled parts of the body.	Stored in the cells associated with fat.
Excretion	Kidneys detect and remove excess in urine.	Less readily excreted; tend to remain in fat-storage sites.
Toxicity	Possible to reach toxic levels when consumed from supplements.	Likely to reach toxic levels when consumed from supplements.
Requirements	Needed in frequent doses (perhaps 1 to 3 days).	Needed in periodic doses (perhaps weeks or even months).

Avitaminosis: Vitamin deficiencies are capable of causing a variety of pathological conditions. However, many of the same symptoms can result from conditions other than lack of a vitamin. Deficiency of vitamins causes deficiency diseases or **avitaminosis.**

Hypervitaminosis:

- Water Soluble Vitamins: Unusual, reach renal threshold;High enough doses can be pharmocologic
- Fat Soluble Vitamins – A & D--TOXIC

(1) VITAMIN A (RETINOL)



- Can exist in 3 forms: as an alcohol (retinol), an aldehyde (retinal) or a carboxylic acid (retinoic acid)
- Vitamin A does not occur in plants but rather as its precursor, carotene, or carotenoid pigments.

Provitamins include α-, β- & γ- carotene & cryptoxanthin. Most important is β-carotene. Conversion of β-carotene to Vit A occurs in liver & intestinal wall & and possibly in kidney & lung.

- Note: Vit A is stored in liver. Zinc is required for mobilization of vit A. It is released in plasma as & when required.
- **Dietary sources:** Animal fats (fish liver oil, egg-yolk, milk, butter, cheese); palm oils, dark green leafy vegetables (spinach,cabbage), yellow vegetables (carrot, pumpkin) and yellow fruits (mango, papaya).Note grains, except corn, are low or devoid of Vit A activity.

Roles of Vitamin A

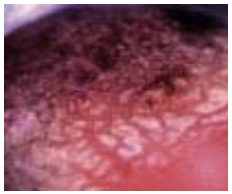
- **Good vision** : Molecular mechanism through which Vit A functions in visual system is known as **Rhodopsin cycle** or Wald's visual cycle for which George Wald was awarded Nobel Prize.

✓Rhodopsin is a photosensitive pigment present in rod cells responsible for dim light vision (night vision).It is a complex between opsin & retinine or 11-cis-retinal form of vitamin A.

✓When light falls on rhodopsin,it splits to form opsin & all-trans retinal after series of changes.

✓All-trans retinal is inactive to resynthesize rhodopsin. It has to be converted to 11-cis retinal (the active form).Retina picks up cis-retinal from blood which is converted into 11 cis retinal by the enzyme retinine reductase.11-cis retinal +opsin→rhodopsin regenerated in the dark & sensitivity of the retina is restored (Dark adaptation) ;hence a constant supply of vit A is needed in the diet.

▪Essential for integrity of mucous secreting cells of epithelial tissue.In absence of Vit A, they become keratinized & susceptible to infection.
▪Maintenance of myelin sheath on nerves require the presence of Vit A.
▪Most important role of vit A is in the control of cell differentiation **&** turnover**. Retinoic acid** serves as a signal molecule & activates the transcription of specific genes that mediate growth & development.
▪Provitamin A (β-carotene)is a vital antioxidant-Prevents initiation of fatty acid peroxidation chain reactions; possible roles in atherosclerosis & cancer prevention.
▪Vit A is required for synthesis of iron transport protein transferrin.



Vitamin A Deficiency

▪ Earliest sign of deficiency is a loss of sensitivity to green light, followed by impairment of adaptation to dim light, followed by night blindness.
▪**Night blindness (nyctalopia):** Inability to see in dimlight. When Vit A is deficient, rhodopsin formation is impaired. Both time taken to adapt to darkness & ability to see in poor or dim light are impaired.
▪**Xerophthalmia** (‘**dry eye**’)**:** Cells of lachrymal glands become keratinized.External surface of cornea becomes dry with dull appearance. Eyelids, swells & becomes sticky resulting in severe eye infection. It may lead to corneal ulcers (keratomalacia) & blindness.

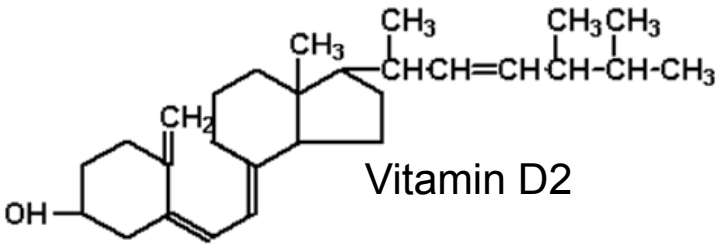
▪Hyperkeratosis (scaly skin) or toad skin.
▪Anemia caused by impaired mobilization of iron from the liver.
▪Role in differentiation of immune system cells, and mild deficiency leads to increased susceptibility to infectious diseases.
▪Urolithiasis which leads to formation of urinary calculi.
▪Increased risk of cancer in vitamin deficiency is thought to be the result of depletion in beta-carotene.

- Geneticists Ingo Potrykus and Peter Beyer wanted to help impoverished people by improving the nutritional value of rice. They genetically modified rice plants to make betacarotene in their seeds—in the grains of Golden Rice→**Genetically modified organisms (GMOs)**

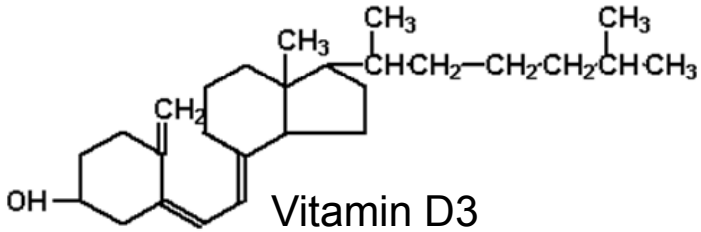
Vitamin A is toxic in excess

- There is only a limited capacity to metabolize Vit A, and excessive intakes lead to accumulation beyond the capacity of binding proteins, so that unbound vitamin A causes tissue damage→Hypervitaminosis A syndrome.
- Symptoms of toxicity affect the central nervous system (headache, nausea, ataxia, & anorexia, all associated with increased cerebrospinal fluid pressure), liver (hepatomegaly with histologic changes & hyperlipidemia), calcium homeostasis (thickening of long bones, hypercalcemia & calcification of soft tissues), & skin (excessive dryness, desquamation & alopecia).
- **Carotenemia**: Yellowing of skin due to excessive beta-carotene intake; may occur in infants who eat too much orange/yellow or dark green baby foods: carrots, apricots, winter squash, sweet potatoes, peas, green beans, etc.

(2) VITAMIN D (CALCIFEROL): SUNSHINE VITAMIN



Vitamin D2



Vitamin D3

- Vitamin D is not strictly a vitamin since it can be synthesized in the skin, & under most conditions that is its major source. Only when sunlight is inadequate is a dietary source required.
- There are 2 forms of vitamin D.
- **Vitamin D_2** : Plant form is ergocalciferol (D_2). Vit D_2 is produced by irradiation (sunlight) of plant sterols called ergosterol.
- **Vitamin D_3** : Animal form is chole-calciferol (D_3). D_3 is produced in human skin by irradiation (sunrays) of animal sterol (7 dehydrocholesterol).
- In humans, Vit D can be ingested as vitamin D_3 or D_2. Vitamin D_3 or D_2 is absorbed from intestinal tract & requires presence of bile salts, after absorption it is transported to liver bound to a specific vitamin D-binding protein (alpha-2 globulin).
- **Dietary sources**: Cod & fish-liver oils, liver, egg yolk, fresh milk, butter, cheese, margarine,infant formula.
- **Vitamin D Is Synthesized in the Skin:** 7-Dehydrocholesterol (intermediate in synthesis of cholesterol that accumulates in **skin**) undergoes a nonenzymic reaction on exposure to UV light, yielding previtamin (vitamin D_3). Vitamin D3 is converted to 25-hydroxycholecalciferol, or 25-hydroxyvitamin D (Calcidiol) in LIVER. Part of calcidiol is converted to 1, 25- dihydroxy vitamin D3 (Calcitriol), the biologically active form of vitamin D in kidney. Note: The 25-hydroxy vitamin D test is the most accurate way to measure vitamin D level.

Role of Vitamin D

▪Main function of vitamin D is in the control of calcium Homeostasis.Main role of calcitriol is to maintain the plasma calcium concentration. Calcitriol achieves this in 3 ways:

- increases intestinal absorption of calcium.

NB: Synthesis of the intracellular calcium binding protein, calbindin, required for calcium absorption is also induced by vitamin D.

- reduces excretion of calcium (by stimulating reabsorption in the distal renal tubules)
- mobilizes bone mineral, promoting healthy growth & remodeling of bone.

▪ Calcitriol is also involved in insulin secretion, synthesis & secretion of parathyroid & thyroid hormones.

▪ Calcitriol functions in the inhibition of production of interleukin by activated T lymphocytes and of immunoglobulin by activated B lymphocytes, differentiation of monocyte precursor cells, and modulation of cell proliferation.

▪Vit D influences the growth and differentiation of cells, and may be implicated in cancer. In fact, vit D deficiency has been shown to correlate with increased risk for many types of cancer.

Vitamin D is toxic in excess

•Some infants are sensitive to intakes of Vit D as low as 50 µg/d, resulting in an elevated plasma Ca concentration.

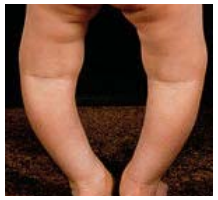
•Increased Ca absorption from gut leading to elevated Ca in plasma (hypercalcemia).

•Deposition of Ca in many soft tissues such as kidney & arteries contraction of blood vessels-calcinosis (calcification of soft tissues); Formation of stones in kidney (renal calculi)

•High blood pressure, loss of appetite, nausea, increased thirst, polyuria,diarrhea, loss of weight.

Vit D Deficiency

Rickets:



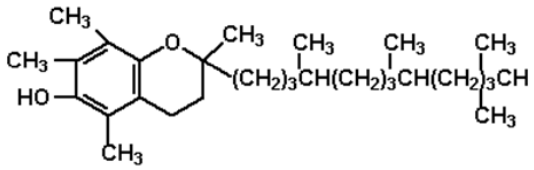
•Occurs in children; poor mineralization of bone as a result of poor absorption of calcium.
•If affected in the first year of life→ widening on cranial sutures, frontal bossing, enlarged swollen epiphyses: particularly wrists; bow legs & knock knees; bulging of costo-chondral joints (Rachitic Rosary); Rickets after the first year:; dentition with enamel hypoplasia; bone pain, proximal myopathy.

Osteomalacia:

▪Occurs in adults, especially in women who have little exposure to sunlight or during pregnancy & lactation when there is extra demand for the vitamin & the drain of Vit D due to secretion in milk,& people with darker skin (eg: people of African, South Asian origin).
▪Bone demineralization (softening of bones). This increases the susceptibility to fracture.
▪Bones specially of pelvic girdle,ribs become soft, painful & deformed.
▪Malabsorption (Coeliac disease), Renal disease (low 1,25 dihydroxy vit D- the most active form), liver Disease.

- ▪Vitamin D Deficiency has been implicated in increased cancer susceptibility
  - ▪Prostate Cancer (more common in Northern latitudes)
  - ▪Colon Cancer (more common in Northern latitudes)
- ▪Immune dysfunction/Autoimmune disease
  - ▪Tuberculosis treatment with sunlight
  - ▪Multiple Sclerosis (more common in Northern latitudes)
- ▪Diabetes susceptibility
- ▪Anxiety and Depression in Fibromyalgia: Vitamin D deficiency is associated with anxiety and depression in fibromyalgia .

(3) VITAMIN E (TOCOPHEROL):ANTI-STERILITY FACTOR



- Tocopherols; different types are α, β, γ & δ tocopherol. α-tocopherol is the most active Vit E.
- Major site of Vit E storage is adipose tissue.
- **Dietary sources** : Vegetable oils ; wheat germ oil, corn oil, cotton seed oil, pea nut oil, also whole grains, egg-yolk, green leafy vegetables, tomato, nuts, milk , butter.
- Intake of Vit E is directly related to consumption of PUFA. Requirement of Vit E increases with increased intake of PUFA.

Roles of Vitamin E

▪Acts as powerful **antioxidant.** It prevents the nonenzymatic oxidation of cell components & unsaturated fatty acids by molecular oxygen & free radicals such as superoxide & hydrogen peroxide.Vit E is a **chain-breaking, free radical trapping antioxidant.**

▪Vit E reacts with lipid peroxide radicals formed by peroxidation of PUFA before they can establish a chain reaction. T**ocopheroxyl free radical product** is relatively unreactive & ultimately forms nonradical compounds. Usually, the tocopheroxyl radical is reduced back to tocopherol by reaction with vitamin C from plasma.

▪Acts synergistically with selenium as antioxidant. Vit E & selenium prevent hepatic necrosis.

▪Improves vitamin A absorption

▪Maintains nervous system and immune system function; Enhances phagocytic role of neutrophils, macrophages, NK cells. Possible roles in atherosclerosis & cancer prevention.

▪Prevents muscle, liver and blood vessel degeneration.

▪Vit E is necessary for normal reproduction, muscular development & resistance of erythrocytes to hemolysis.

Vitamin E Deficiency

- In experimental animals, Vit E deficiency results in resorption of fetus, testicular atrophy & possible inhibition of sperm production.
- Premature infants are born with inadequate reserves of Vit E. Their RBCs are abnormally fragile due to oxidation of polyunsaturated fatty acids in erythrocyte membranes. This leads to to **hemolytic or macrolytic anemia**.
- Any fat malabsorption diseases can lead to deficiencies in Vit E intake. Neurological disorders have been associated with Vit E deficiencies associated with fat malabsorptive disorders.
- Muscular dystrophy-degenerative changes in muscles; Hepatic necrosis

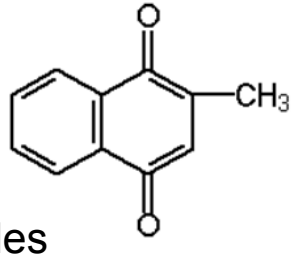
Excess of Vitamin E

•Among the fat soluble vitamins, Vit E is the least toxic. No severe toxic effect has been reported as such.

•Some data suggest a possible increase in mortality & in incidence of heart failure with long-term use of Vit E, especially in patients with chronic diseases.

▪New medical research suggests that high doses of vitamin E can cause "bone-stripping", or loss of bone mass. So people taking supplements are potentially exposing themselves to increased risk of fracture.

(4) VITAMIN K (COAGULATION VITAMIN)



- Naphthoquinone derivative.
- Three compounds have the biologic activity of Vit K:

✓**Vit K1: phylloquinone,** the normal dietary source, found in green leafy vegetables

✓**Vit K2: menaquinone,** synthesized by intestinal bacterial flora. (So Vit K deficiency is rare)

✓**Vit K3:** synthetic analogue of Vit K. **menadione, menadiol & menadiol diacetate** are synthetic compounds that can be metabolized to phylloquinone.

- **Dietary sources:** liver, meat, egg yolk, fresh green leafy vegetables (spinach, cabbage, broccoli, cauliflower), soyabean.

Roles of Vitamin K

- Needed for production of vitK-dependent coagulation factors (eg: synthesis of prothrombin**)** in liver..Prothrombin & several other proteins of blood clotting system (Factors VII, IX & X, proteins C & S) contain **γ-carboxy glutamate residues**. Vit K-dependent carboxylation reaction converts glutamate, a weak chelator of Ca^{2+} into γ-carboxy glutamate, a stronger chelator. Prothrombin is thus able to bind Ca^{2+} that helps to anchor the zymogen to phospholipid membranes derived from platelets after injury.Binding of prothrombin to phospholipid surfaces brings prothrombin into close proximity to other clotting proteins that catalyze its conversion into thrombin.
- Vit K is also important in synthesis of bone calcium-binding proteins like Osteocalcin & bone matrix Gla protein that contain γ-carboxyglutamate.
- Gas6 is Vit K-dependent protein identified in 1993. It is important for neuronal function.

- **Excess of Vitamin K:**
- Hemolytic anaemia & jaundice are the toxic effects, noticed particularly in infants due to the administration of large doses of Vit K. This is due to increased breakdown of RBC.

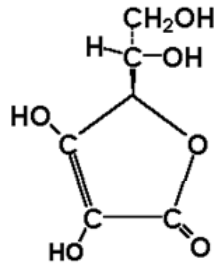
Vit K Deficiency

- Vit K deficiency is quite uncommon as it is sufficiently found in diet & adequately synthesized by intestinal bacteria. However, deficiency can occur due to its faulty absorption (lack of bile salts), sterilisation of gut (long term use of broad spectrum antibiotics).
- In Vit K deficiency, there is insufficient carboxylation of glutamate in prothrombin. This results in abnormal precursor of prothrombin (preprothrombin) containing little or no γ-carboxyglutamate & incapable of chelating calcium ; hence it is released into the circulation.
- Subdermal **hemorrhaging or bleeding** (specially in new-born infants who has not ye t developed own gut flora).Extended bleeding from small cuts & increased bruising;

Water-Soluble Vitamins Function As Coenzymes

- Most function as components of specific coenzymes.
- Ascorbate(ionized form of ascorbic acid) serves as a reducing agent (antioxidant). Vit B series comprises components of coenzymes.
- In all cases except Vit C, the vitamin must be modified before it can serve its function.

VITAMIN C (ASCORBIC ACID)



- Powerful reducing agent.Reducing property of Vit C depends on the release of hydrogen atoms from the enediol –OH groups on C2 & C3.In this action,the ascorbic acid is oxidised to dehydroascorbic acid. Both the forms are biologically active.
- Vit C is destroyed by cooking.**Sources:** citrus fruits (oranges, lime, lemon), grapes, broccoli, tomatoes,green leafy vegetables (cabbage, cauliflower).

Roles of Vitamin C:

▪Vital for collagen biosynthesis-hydroxyproline from proline & hydroxylysine from lysine (ascorbate serves here as a specific antioxidant**).**Collagen is initially synthesized as a larger precursor polypeptide, procollagen. Hydroxyprolyl & hydroxylysyl residues (addition of hydroxyl groups) provide additional hydrogen bonding capability that stabilizes the mature protein-the collagen triple helix.

▪A prominent role of vitamin C is its immune-stimulating effect, e.g., important for defence against infections such as common colds. It also acts as an inhibitor of histamine, a compound that is released during allergic reactions.

▪Improves iron absorption from the diet.

▪Necessay for the hydroxylation reactions in the synthesis of corticosteroid hormones.

▪Tryptophan metabolism: vitamin C is essential for hydroxylation of tryptophan to hydroxytryptophan in synthesis of serotonin.

▪Tyrosine metabolism: ascorbic acid is required for oxidation of p-hydroxyphenylpyruvate to homogentisic acid in tyrosine metabolism.

▪Keeps nervous system healthy; Promotes healthy gums and tissues, wound healing and iron absorption