

Nutrition: Nutrition: Vitamin Replacements

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Introduction

4 Major Nutrient Types:

1. **Macronutrients** (Carbohydrate, protein, lipid)

→ to supply energy for body

2. **Vitamins**

→ help to use the macronutrients & maintain body's tissues

3. **Minerals & Electrolytes**

→ to maintain the homeostasis

4. **Water**

→ as a solvent in the body, media of body's chemical reaction, & distribute the nutrients to tissues

HEALTHY BALANCED DIET

■ **BALANCED**

■ **VARIATION**

■ **MODERATION**

VITAMIN

- The organic chemical substances are essential for life.
- Work as a **regulator or modulator** to keep biological reactions in the body functioning normally
- Vitamins act as **coenzymes** for enzymes so that nutrients such as amino acids and glucose are enzymatically utilized for muscle growth or energy.
- Vital for **growth, maintenance and reproduction**

VITAMIN

- An exception vitamin D, our bodies cannot synthesize vitamins → all vitamins must be consumed daily as a part of the diet.
- The body **only need a small amount** of vitamin daily, which can be easily obtained through one's diet.
- The **intake of vitamins should be increased:**
 - during periods of rapid body growth,
 - by who are pregnant or are breastfeeding,
 - by those with inadequate diet (ex: alcoholic, geriatrics)
 - by children who have poor nutrient or are malnourished

VITAMIN

- Vitamin deficiencies can cause cellular and organ dysfunction that may result in a slow recovery from illness
- When there is lack of these in diet ⇒ replacement drug therapy
- For those who maintain a nutritionally balanced daily diet ⇒ vitamin replacements are not necessary

Justification for Vitamin Supplement

Categories	Deficiencies
Inadequate absorption	Malabsorption, diarrhea, infectious & inflammatory diseases
Inability to utilize vitamins	Liver disease, renal disease, certain hereditary deficiencies
Increased vitamin losses	Fever from infection process, hyperthyroidism, hemodialysis, cancer, starvation, crash diet
Increased vitamin requirements	Early childhood, pregnancy, debilitating disease (cancer, alcoholism), gastrointestinal surgery, special diets

VITAMIN

- Two groups of Vitamins : fat-soluble and water-soluble.
- Fat-soluble vitamins are vitamins A, D, E and K.
- Water-soluble vitamins are vitamins B1, B2, B6, B12, C, niacin, pantothenic acid, folic acid and biotin
- Based on solubility, some vitamins are absorbed differently. Ex: fat is required for vitamins A, D, E and K and is an intrinsic factor for vitamin B12.

VITAMIN

- Some vitamins are **labile during food processing and cooking**, ways of consuming and timing must be considered for proper nutrition.
- Unlike proteins, carbohydrates or fats, vitamins are **not metabolized** to build tissues or organs.

Fat-soluble Vitamin

- Vitamin A, D, E, & K
- Pharmacokinetics
 - 1) Are absorbed easily
 - 2) Are metabolized slowly
 - 3) Can be stored in fatty tissue, liver, & muscle in significant amounts
 - 4) Are excreted in the urine at a slow rate
- Vitamin A & D are toxic if taken in excess amounts over time.
- Vitamin A can be store in the liver up to 2 years
- Vitamin E & K are less toxic than vitamin A & D

Vitamin A

- A family includes retinol, retinal or retinaldehyde, retinyl esters, retinoic acid, and provitamin carotenoids such as β -carotene.
- Vitamin A is essential for growth and life, taking part not only in vision but also in developmental processes that begin early in embryogenesis.
- Vitamin A continues to be necessary to maintain normal cellular differentiation throughout life.
- Preformed vitamin A comes from animal origin, such as liver and egg yolk, while the provitamin β -carotene is found only in foods of plant origin, particularly carrots and dark leafy vegetables.

Vitamin A

- The human body stores only limited amounts of vitamin A, mostly in the liver, making dietary intake essential.
- The liver stores 50 – 80% of body vitamin A. Small amounts are also found in lungs, body fat and kidneys.
- **Carotenoids** are deposited more widely throughout the body than retinoids and are found in adipose tissues, adrenals, and the liver.
- Excess and deficiency of vitamin A in the mother's diet during pregnancy has been shown to cause **malformations of fetal brain** and **hydrocephalus**.

Function of Vitamin A

- Night vision, due to its involvement in photochemical reactions in the retina.
- Growth and maintenance of epithelial tissue including the cornea, all mucous membranes of gastrointestinal tract, lungs, vagina, urinary tract, bladder and skin.
- Reproductive function in humans.
- Nerve formation and function.

Function of Vitamin A

- Epithelial cell proliferation and epidermal differentiation. Natural and synthetic retinoids have been used increasingly as systemic or topical agents in the treatment of hyperkeratotic disorders, acne, and certain skin cancers.
- **Antioxidants** may play a preventive role in heart disease and epithelial cancers.
- Both cell-mediated and antibody-mediated immune response.
- Signal transduction, via retinoic acid's hormonal action.

Deficiency Symptoms of Vitamin A

- The symptoms of vitamin A deficiency ~ skin, bone, and dental health and immune function. The earliest symptom → the inability to see in dim light, called night blindness or nyctalopia. Other symptoms → rough, scaly skin (called follicular hyperkeratosis), sinus infection, chronic sore throat and abscesses in the mouth and ears.

Deficiency Symptoms of Vitamin A

- In children, deficiency → growth retardation, impaired bone and tooth formation.
- Both a deficiency and an excess of vitamin A → fetal malformations.
- Vitamin A deficiency → the cessation of spermatogenesis and interrupts the estrus cycle.

Requirements and Recommendations of Vitamin A

	mcg/day	Tolerable Upper Intake Levels (UL)
Infants		
1 to 6 months	400	600
7 to 12 months	500	600
Children		
1-3 years	300	600
4-8 years	400	900
9-13 years	600	1700
Females		
14-> 70 years	700	3000
Males		
14-> 70 years	900	3000
Pregnancy		
\leq 18 years	750	2800
19-50 years	770	3000
Lactation		
\leq 18 years	1200	2800
19-50 years	1300	3000

Toxicity of Vitamin A

- **Symptoms:** loss of appetite, headache, blurred vision, irritability, hair loss, drying and flaking of the skin, swelling in the extremities, drowsiness, diarrhea, nausea, and enlargement of the spleen and liver.
- Since vitamin A stores increase with age, the elderly are at particular risk for toxicity.

Toxicity of Vitamin A

- Vitamin A excess during the first trimester of pregnancy can result in **severe craniofacial and oral clefts and limb defects of the fetus.**
- High doses of vitamin A (retinol and retinyl esters) during pregnancy have been associated with **birth defects.** It is recommended that women who are pregnant or may become pregnant consume no more than 2667 IU/day of vitamin A.

Dietary Sources of Vitamin A

- Rich sources of vitamin A are liver and cod liver oil.
- The major source of vitamin A in the diet is from carotene; provitamin A. They are yellow and green leafy vegetables such as carrots, spinach, sweet potatoes, squash, and yellow fruits.

Indication, Contraindication, Side effects & Adverse reactions

- Indication: deficiency of Vitamin A, prevent night blindness, skin disorders, promote bone development
- Contraindication: hypervitaminosis A, pregnancy (massive doses)
- Side effects: headache, fatigue, drowsiness, irritability, anorexia, vomiting, diarrhea, dry skin, visual changes
- Adverse reactions: evident only with toxicity: leucopenia, aplastic anemia, papilledema, increased intracranial pressure, hypervitaminosis A

Pharmacokinetic & Pharmacodynamic of Vitamin A

- Pharmacokinetics:

A: per oral 1 h; is absorbed faster than if there is no deficiency or intestinal obstruction

D: protein-binding

M: half-life: weeks-months

E: urine & feces

- Pharmacodynamics:

Per oral : Onset: 1-2 h; Peak: 4-5 h;
duration: unknown (is stored in the liver)

Drug-vitamin Interaction

- **Warfarin**, an anticoagulant, increases the risk of abnormal bleeding
- **Cholestyramine** are used to lower cholesterol concentrations by preventing reabsorption of bile acids from the digestive system and by preventing micelle formation in gastrointestinal (GI) lumen. Fat-soluble vitamin A requires the presence of bile for absorption, deficiency may occur if these drugs are used for a long period of time.
- Oral antibiotics such as **neomycin** decrease the absorption
- **Orlistat**, a weight loss GI agent, may decrease GI absorption of fat-soluble vitamins.

Vitamin D

- Vitamin D consists of a group of similar molecules that are involved in calcium absorption and metabolism and bone formation and that also act as a human hormone.
- the two are equally useful to humans: Vitamin D2 (ergocalciferol) is produced by plants, while vitamin D3 (cholecalciferol) is made by animals:
- Human skin can synthesize it when exposed to sunlight and is only essential in the diet if we do not have enough exposure to sunlight.
- Vitamin D is a hormone precursor that can be manufactured by the body, therefore it is not an essential nutrient.

Function of Vitamin D

- Maintenance of bone health. It is essential for calcium absorption and it regulates parathyroid hormone (PTH).

Vitamin D deficiency \rightarrow Ca absorption \downarrow & PTH concentrations \uparrow \rightarrow \uparrow bone resorption; \uparrow bone resorption without sufficient vitamin D and calcium \Rightarrow bone loss and osteoporosis.

- Helps regulate excretion of calcium from the kidney and maintains normal blood Ca concentrations
- Vitamin D receptors are found in variety of other tissues in the body \rightarrow the rate of cell growth and differentiation.

Deficiency of Vitamin D

A vitamin D deficiency can result from:

1. Inadequate dietary intake,
2. Reduced endogenous production due to limited exposure to sunlight,
3. Kidney and/or liver dysfunctions, which inhibit conversion of vitamin D to its metabolically active forms,
4. Fat-malabsorption syndromes, such as cystic fibrosis and cholestatic liver diseases.

Deficiency Symptoms of Vitamin D

- Rickets in children: skeletal deformities and muscular weakness
- Osteomalacia in adults; develops in women with closely spaced, multiple pregnancies or in people confined indoors with no exposure to sunlight. Symptoms in adults: painful softening and bending of bones, low serum ca concentrations and tetany.
- Less severe vitamin D deficiency can result in **hyperparathyroidism** and \uparrow bone turnover \rightarrow bone loss and **osteoporosis**.
- Osteoporosis: The disease results in fractures of the vertebra, hip and wrist that occur either spontaneously or with minimal daily activities such as opening a window.

Requirements and Recommendations of Vitamin D

	mcg/d	IU/d	Tolerable Upper Intake Levels (mcg/d)
Infants			
0 to 6 months	5	200	25
7 to 12 months	5	200	25
Children			
1 to 3 years	5	200	50
4 to 8 years	5	200	50
Males/Females			
9 to 18 years	5	200	50
19 to 70 years	5	200	50
51 to 70 years	10	400	50
> 70 years	15	600	50
Pregnancy			
</= 18 years	5	200	50
19 to 50 years	5	200	50
Lactation			
</= 18 years	5	200	50
19 to 50 years	5	200	50

Values are Adequate Intakes (AI).

Toxicity of Vitamin D

- Prolonged exposure to sunlight does not cause vitamin D toxicity.
- The NOAEL (the No Observed Adverse Effect Level) is 50 mcg (2000 IU).
- The majority of dietary supplements include 400 IU of vitamin D. There are no reports of adverse effects at this concentration of intake.
- There is no evidence of any benefit in taking more than 800 IU.
- The effects of excessive vitamin D intake include hypercalcemia and hypercalciuria → deposition of calcium in soft tissue and irreversible renal and cardiovascular damage.
- Symptoms of toxicity: loss of appetite, excessive thirst, nausea, vomiting, irritability, weakness and weight loss.

Dietary Sources of Vitamin D

- The only frequently consumed dietary source of vitamin D is vitamin D-fortified milk. Muscle meat, milk (nonfortified), fruits and vegetables are negligible sources of vitamin D. Liver, butter, cream, mushrooms, fatty fish oil and egg yolk contains varying amounts of vitamin D, and some ready-to-eat cereals are fortified with the vitamin.
- Cod liver oil and fatty fish oils are excellent sources of vitamin D.

Indication of Vitamin D

- Deficiency of Vitamin D → ricketsia & osteomalacia;
- Elderly (> 70 years old) → capacity of skin to synthesize vitamin D₃ in the elderly is approximately half that of younger people;
- in people with AIDS: vitamin D deficiency → hypocalcemia;
- infants who are breastfed without supplemental vitamin D or exposure to sunlight are at an increased risk for deficiency;
- vegetarians; low fat, high fiber diets of vegetarians → reduce the absorption of dietary vitamin D;
- alcoholism;
- smoker → ↑ the rate of bone turnover → ↑ requirement of vitamin D.

Contraindication & Adverse reactions of Vitamin D

- Contraindication: hypervitaminosis D
→ hypercalcemia ⇒ nephrolithiasis
- Adverse reactions: evident only with toxicity: anorexia, nausea, vomiting (early symptoms of vitamin D toxicity)

Pharmacokinetic of Vitamin D

- Pharmacokinetics:

A: in intestine need bile → calcifediol in the liver
→ calcitriol (active form) in kidneys

D: protein-binding

E: primarily in bile, only a small amounts in
urine

Drug-vitamin Interaction

- Warfarin → ↓ absorption of vitamin D → osteoporosis (a loss of bone tissue) or osteopenia (a decrease of bone density).
- Laxatives that contain mineral oil → ↓ the intestinal absorption of many nutrients, including vitamin D.
- Cholestyramine, colestipol and mineral oil → ↓ absorption of vitamin D.
- Thiazide diuretics → hypercalcemia.
- Anticonvulsant drugs: phenobarbital and phenytoin → ↓ plasma vitamin D concentrations by inhibiting enzyme activity in the liver and by preventing the conversion of the vitamin to its active form.

Drug-vitamin Interaction

- The concentrations of magnesium-containing antacids → ↑ hypomagnesemia in patients on chronic renal dialysis. To minimize potential problems, take these antacids 2 to 3 hours apart from meals or mineral supplements.
- Vitamin D may → hypocalcemia in patients on digitalis → cardiac arrhythmias.
- Ketoconazole, an antifungal agent, may inhibit vitamin D synthetic and catabolic enzymes
- Long-term therapy (longer than 2 weeks) with corticosteroids, anti-inflammatory drugs, → ↓ the body's ability to activate vitamin D → ↑ the risk of bone loss.

Drug-vitamin Interaction

- Vitamin D may interfere with the effectiveness of verapamil, a calcium-channel blocker
- Orlistat, a weight loss agent, →↓ gastrointestinal absorption of fat-soluble vitamins such as vitamin D. An interval of at least two hours (before or after) between Orlistat and vitamin D analog administration is recommended. However, taking multivitamins including fat-soluble vitamins did not decrease drug concentrations in clinical studies.

Vitamin E

- Is a fat-soluble vitamin and a powerful antioxidant
- Divided into two major groups: tocopherol (have saturated side chains) and tocotrienols (have unsaturated chains); natural vitamin E (d- α -tocopherol) is the most potent.
- Natural and synthetic forms of α -tocopherol: to be absorbed equally well \Rightarrow both of them are as effective inhibiting the oxidation of LDL-C in humans

Function of Vitamin E

- Tocopherols act as antioxidants and prevent the peroxidation of phospholipids of the cellular membranes → maintains membrane activity.
- To prevent membranes from destruction by oxidation → maintenance of intracellular membrane integrity
- Vitamin E located in cell membranes → break the chain of radical attack by reacting with the peroxide radical
- Vitamin E and selenoenzyme glutathione peroxidase protect against peroxidation of membrane lipids → preventing cellular damage.
- To prevent LDL oxidation → ↓ the risk of cardiovascular diseases.

Deficiency Symptoms of Vitamin E

- Red blood cell hemolysis, shorter red blood cell life
- Creatinuria, and deposits of ceroid in muscle;
- Neurologic changes of cerebellar ataxia, demyelination of the peripheral nerves → posterior column dysfunction, and possibly peripheral, neuropathy; progressive loss of proprioceptive and vibratory sensation, areflexia and gaze paresis
- Retinopathy of prematurity in neonates
- Edema and flaky dermatitis
- ↑ risk of cardiovascular disease.

Requirements & Recommendations of Vitamin E

	mg/day [†]	Tolerable Upper Intake Levels (UL)
Infants		
0 to 6 months	4	ND*
7 to 12 months	5	ND*
Children		
1 to 3 years	6	200
4 to 8 years	7	300
Males		
9 to 13 years	11	600
14 to 18 years	15	800
19+ years	15	1000
Females		
9 to 13 years	11	600
14 to 18 years	15	800
19+ years	15	1000
Pregnancy		
</= 18 years	15	800
19 to 50 years	15	1000
Lactation		
</= 18 years	19	800
19 to 50 years	19	1000

Toxicity of Vitamin E

- Relatively large doses of vitamin E (up to 3200 mg) have been taken for months to years with no significant side effects.
- At doses > 800 mg \rightarrow muscle weakness, nausea, fatigue, diarrhea and most commonly gastrointestinal disturbances.
- High doses of vitamin E in animals \rightarrow interfere with intestinal absorption of vitamins A and K.
- Doses > 1 g/d \rightarrow \uparrow effect of anticoagulant medications. Vitamin E or its quinone may inhibit the function of vitamin K in the formation of prothrombin \Rightarrow haemorrhage
- Large doses of vitamin E (100 mg/kg/day) in low-birth-weight infants \rightarrow \uparrow necrotizing enterocolitis and sepsis.

Dietary Sources of Vitamin E

- Spinach Bean sprouts
- Green peas; Blackeyed peas
- Sweet potatoes
- Almonds
- Cashews
- Peanuts
- Sunflower seeds
- Mayonnaise

Indication of Vitamin E

- Primary deficiency may occur in early infancy, particularly in formulas high in unsaturated oils.
- Protein-energy malnourished children may have low vitamin E concentrations.
- A secondary deficiency may be seen in malabsorption syndrome, steatorrhea (sprue, celiac disease, cystic fibrosis, or biliary atresia), cholestasis, and in abetalipoproteinemia.

Pharmacokinetics of Vitamin E

- Optimal vitamin E absorption requires presence of bile salts and pancreatic juice in the intestine.
- Absorbed tocopherol is incorporated into chylomicrons and transported through the lymph into circulation and blood where it is equilibrated with other plasma lipoproteins.
- Tocopherol is distributed to body tissues mainly by the low-density lipoproteins (LDL).
- The largest storage area for vitamin E is in adipose tissue. Tocopherol in the liver is depleted rapidly, whereas in deficiency loss of vitamin E in the fatty tissue is slow.

Drug-vitamin Interaction

- Vitamin E → ↑ absorption, utilization and storage of vitamin A
- Intake of > 10 IU/kg daily → delay the response to iron therapy in children with iron-deficiency anemia and lowbirth weight infants treated with iron supplements → vitamin E-deficiency hemolytic anemia.
- Vitamin E + aspirin, an antiplatelet agent, and nonsteroidal antiinflammatory drugs (NSAIDs), → ↑ risk of bleeding.
- A large dose of vitamin E (>4000 IU) → anti-vitamin K effects; with oral anticoagulants, warfarin → ↑ at risk of hemorrhage
- Cisplatin, a chemotherapeutic → oral mucositis, an inflammation of the membranes lining the inside of the mouth. Vitamin E → ↓ the duration of this condition

Vitamin K

- Vitamin K is known as the **anti-hemorrhagic** vitamin that is necessary for the synthesis of four of the 13 cofactors required for the normal coagulation of blood.
- Two **naturally** occurring forms of vitamin K exist: vitamin K1 (phylloquinone or phytylmenaquinone) and K2 (menaquinone or multiprenyl-menaquinone) are **fat soluble and stable during cooking**. Vitamin K1 is **not stable under sunlight**. Vitamin K1 and K2 are found in green plants and in microorganisms, respectively.
- **Synthetic forms** of vitamin K, one of which is **menadione**; watersoluble and destroyed to a great degree during cooking.
- Natural vitamin K (K1 and K2) requires bile and pancreatic juice for absorption in the small intestine.
- Vitamin K2 is synthesized by microflora in the small and large intestine. § Menadione is converted to vitamin K2 in the body.
- Synthesis of osteocalcin that promotes mineral deposition in bone is dependent on vitamin K.

Function of Vitamin K

- For **synthesis of blood clotting factors** in the liver; factor II or prothrombin; factor VII or proconuvertin; factor IX or Christmas factor and factor X or Stuart-Power.
- Vitamin K has **hemostatic activity** and is used to treat anticoagulant-induced prothrombin deficiency.
- Vitamin K may have **anti-osteoporotic activity**; vitamin K2 has been shown *in vitro* and *in vivo* to inhibit bone resorption substances such as prostaglandin E2 and interleukin-6 and enhance human osteoblast-induced mineralization.
- Vitamin K may have **antioxidant activity**. Vitamin K-hydroquinone is a potent reactive oxygen species scavenger and has been found to inhibit lipid peroxidation.
- Synthetic vitamin K menadione has shown to have **anti-tumor activity** *in vitro* and *in vivo*. Vitamin K2 was shown to induce *in vitro* differentiation of myeloid leukemic cell lines.

Deficiency Symptoms of Vitamin K

- Hypoprothrombinemia manifested by defective coagulation of the blood and hemorrhage.
- Lack of intestinal bacterial flora might explain part of the hypoprothrombinemia observed during the first 3 to 5 days of life in neonates. Low concentrations for plasma clotting protein factors: II, VII, IX, and X may reflect hepatic immaturity.
- Malabsorption → secondary deficiency of vitamin K
- Severe liver disease → ↓ prothrombin synthesis and may be unresponsive to vitamin K therapy.
- In obstructive jaundice, hemorrhage usually begins after the 4th or 5th day. Hemorrhage may ooze slowly from wounds, gums, nose, GI mucosa or may be a massive bleed into the GI tract.
- Some infants may have intracranial hemorrhages at birth or within the first days of life. Breast-fed infants who have not received vitamin K at birth are susceptible to deficiency because human milk is a poor source of vitamin K.

Requirements & Recommendation of Vitamin K

	mcg/day
Infants	
0 to 6 months	2.0
7 to 12 months	2.5
Children	
1 to 3 years	30
4 to 8 years	55
Males	
9 to 13 years	60
14 to 18 years	75
19+ years	120
Females	
9 to 13 years	60
14 to 18 years	75
19+ years	90
Pregnancy	
</= 18 years	75
19 to 30 years	90
31 to 50 years	90
Lactation	
</= 18 years	75
19 to 30 years	90
31 to 50 years	90

Toxicity of Vitamin K

- Natural forms of vitamin K have caused **no symptoms of toxicity**, even when supplemented in large amounts.
- The **synthetic product**, menadione, has an unsubstituted carbon 3 that can combine with tissue sulfhydryl groups → the **oxidation of membrane phospholipids**.
- Toxic effects such as **hemolytic anemia**, **hyperbilirubinemia**, and **kernicterus**, have been reported in infants supplemented with menadione.

Indication of Vitamin K

- Newborn infants
- Persons who have been injured, have renal insufficiency and/or are being treated chronically with antibiotics are at risk for vitamin K deficiency.
- Malabsorption: obstructive jaundice, Celiac sprue, Steatorrhea, Crohn's disease, Chronic diarrhea, Liver disease, Intestinal bypass, Chronic pancreatitis, prolonged sulfa and antibiotic drug therapy
- Haemorrhage

Drug-Vitamin Interaction

- With non-absorbable sulfonamides or oral antibiotics → interfere vitamin K synthesis in the intestines.
- Warfarin for anticoagulant therapy should not consume large amounts of vitamin K supplements or vitamin
- Mineral oil → ↓ the gastrointestinal absorption of vitamin K
- Anticonvulsant agents, phenytoin, → ↑ the normal breakdown of vitamin K into its inactive byproduct → ↑ osteoporosis, and vitamin K deficiency (resulting in bleeding disorders or facial bone abnormalities) in babies born to mothers taking the drugs. Mothers on these medications may need to take vitamin K supplementation during pregnancy to prevent these problems.