



The Role of Vitamins in Health and Disease

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Disclosures

I, do not have a vested interest in or affiliation with any corporate organization offering financial support or grant money for this continuing education program, or any affiliation with an organization whose philosophy could potentially bias my presentation.

Objectives for Pharmacists

- 1. Assess the role of vitamins in disease prevention and management.
- 2. Evaluate the clinical evidence behind supplementation.
- 3. Identify high-risk populations and recommend interventions.

Objectives for Technicians

- 1. Recognize the role of vitamins in health.
- 2. Identify strengths/weaknesses of vitamin use.
- 3. Assist pharmacists with patient supplementation needs.



Fat-soluble vitamins

- DEKA
- Stored in the liver and fatty tissues
- Requires dietary fats and bile for absorption
- Excessive intake can lead to toxicity

Key characteristics of fat-soluble vitamins:

- Vitamin D: Critical for bone health and calcium metabolism
- Vitamin E: Antioxidant that protects cell from oxidative damage
- Vitamin K: Essential for blood clotting and bone health
- Vitamin A: Involved in vision, immune function, and cellular growth

Water-soluble vitamins

- B vitamins and vitamin C
- Not stored in the body- excess is excreted in urine
- Absorbs directly into bloodstream from GI tract
- Toxicity is less common

Key characteristics of water-soluble vitamins:

- B vitamins: important for energy production, metabolism, and red blood cell formation.
- Folate (B9): DNA synthesis and neural tube development during pregnancy
- Vitamin C: Antioxidant, essential for collagen synthesis and immune function



Vitamin D

Vitamin D - Introduction

- Also referred to as calciferol
- Natural sources: fatty fish (salmon, mackerel, sardines), fish liver oils, egg yolks, mushrooms
- Supplements: D2 (ergocalciferol) and D3 (cholecalciferol)
- Sunlight exposure: UVB rays stimulate vitamin D3 synthesis in skin



Vitamin D - Basic Functions and Role

- Facilitates calcium and phosphorus absorption
- Essential for bone growth and remodeling
- Supports immune function and decreases inflammation
- May have roles in cell growth and neuromuscular function

Vitamin D - D2 vs D3

- Differ in their side-chain structure
- Both absorbed through small intestine
- Presence of fat enhances vitamin D absorption
- Aging and obesity does NOT alter absorption



Vitamin D - D2 vs D3

- Vitamin D2 is produced from yeast
- Vitamin D3 is produced from lanolin obtained from sheep wool
- Evidence suggests that vitamin D3 increases serum concentration better

Vitamin D - Serum Concentration

• 25(OH)D

- Main indicator with circulating half-life of 15 days
- Reflects vitamin D from intake and endogenous production

• 1,25(OH)2D

- Not a good indicator with half-life measured in hours
- Levels are regulated by parathyroid hormone, calcium, and phosphate
- Does not change unless deficiency is severe

Vitamin D - 25(OH)D

- Although a biomarker, health status relationship is unclear
 - Endocrine Society does not recommend routine testing in healthy individuals
- Food and Nutrition Board
 - < 12 ng/mL: Associated with vitamin D deficiency
 - 12 to <20 ng/mL: Considered inadequate for healthy individuals
 - $\circ \geq 20$ ng/mL: Considered adequate for healthy individuals
 - > 50 ng/mL: Linked to adverse effects

Vitamin D - Daily Requirements

Recommended Dietary Allowances:

- 0-12 months: 400 IU (10 mcg)
- 1-70 years: 600 IU (15 mcg)
- > 70 years: 800 IU (20 mcg)
- Pregnancy/Lactation: 600 IU (15 mcg)

Tolerable Upper Intake Level for adults: 4,000 IU (100 mcg)

Needs may be higher for those with limited sun exposure or certain medical conditions

Vitamin D - OTC Products







Vitamin D - Food Sources



1,360 IU/34 mcg per serving



645 IU/16.2 mcg per serving



570 IU/14.2 mcg per serving



44 IU/1.1 mcg per serving

Vitamin D - Sunlight Exposure

- Type B UV (UVB) radiation converts 7-dehydrocholesterol to previtamin D3
- Older people and people with dark skin are less able to produce vitamin D3 from sunlight
- UVB radiation does not penetrate glass

Vitamin D - Deficiency

• Signs of deficiency: bone pain, muscle weakness, increased fracture risk

- Children: manifested as rickets
- o Adolescents and adults: can lead to osteomalacia
- Groups at risk
 - o Breastfed infants
 - Older adults
 - Limited sun exposure
 - People with dark skin
 - Limited fat absorption

Vitamin D - Toxicity and Drug Interactions

- Toxicity (usually from excessive supplementation)
 - Symptoms: hypercalcemia (> 11.1 mg/dL), nausea, weakness, kidney stones
- Drug interactions:
 - Corticosteroids: reduce calcium absorption, impair vitamin D metabolism
 - Orlistat and cholestyramine: reduce fat-soluble vitamin absorption
 - Thiazide diuretics: hypercalcemia

Vitamin D - Supplementation Evidence

- Most studies evaluating vitamin D's bone benefits also included calcium
- Isolating vitamin D's individual effect is challenging
- Trials vary in dosage and schedules, limiting conclusive findings

Vitamin D - Clinical Trials

USPSTF - **Inadequate evidence** that vitamin D w/ calcium prevented fractures in community-dwelling men and postmenopausal women.

VITAL - Supplementation **did not lower** the risk of total fractures, hip fractures, or nonvertebral fractures.

Aloia JF, et al - **No association** between 25(OH)D levels or vitamin D dose and risk of falling.

Vitamin D3 raises serum 25(OH)D levels more effectively than vitamin D2.

A. True B. False Which of the following is the primary circulating form used to assess vitamin D status?

A. 1,25(OH)₂D

B. 25(OH)D

C. D2

D. Calcitriol



Vitamin E

Vitamin E - Introduction

- Naturally found in food and available as a supplement
- Eight chemical forms, but alpha-tocopherol is relevant to humans
- Serum concentration depend on liver

Vitamin E - Basic Functions and Role

- Acts as an antioxidant, protecting cell membranes from oxidative damage
- Helps maintain immune function
- Prevents oxidation of LDL cholesterol
- May contribute to skin and eye health

Vitamin E - Tocopherols & Tocotrienols

Toco**pher**ols

- α-Tocopherol (most biologically active form in humans)
- β-Tocopherol
- γ-Tocopherol (common in U.S. diet; found in corn and soybean oil)
- δ-Tocopherol

Toco**trien**ols

- α-Tocotrienol
- β-Tocotrienol
- γ-Tocotrienol
- δ-Tocotrienol

Vitamin E - Tocotrienols

Tocotrienols

- α-Tocotrienol
- β-Tocotrienol
- γ-Tocotrienol
- δ-Tocotrienol

Vitamin E - Chemical Structure



Vitamin E - Daily Requirements

Recommended Dietary Allowances (RDA) for vitamin E

- Adults (≥ 14 years): 15 mg/day
- Pregnancy: 15 mg/day
- Lactating women: 19 mg/day
- Based on serum levels in a test measuring survival of erythrocytes when exposed to hydrogen peroxide
- Tolerable Upper Intake Level: 1,000 mg/day (1,500 IU for natural, 1,100 IU for synthetic)
- Higher doses may be used therapeutically but should be monitored

Vitamin E - OTC Products





Vitamin E - Natural vs Synthetic

- 1 IU of natural form = 0.67 mg of alpha-tocopherol
- 1 IU of synthetic form = 0.45 mg of alpha-tocopherol
Vitamin E - Food Sources





7.4 mg per 1 ounce



2.2 mg per 2 tablespoons

20.3 mg per 1 tablespoon

Vitamin E - Deficiency and At-Risk Populations

- Rare in healthy individuals; symptoms include:
 - Neuromuscular problems (e.g., ataxia, muscle weakness)
 - Peripheral neuropathy
 - Retinopathy and immune dysfunction
- At-Risk Populations:
 - Individuals with fat-malabsorption disorders (e.g., cystic fibrosis, Crohn's)
 - Premature infants with low birth weight

Vitamin E - Toxicity and Drug Interactions

- Toxicity: Generally low risk from food; high doses from supplements may increase risk of:
 - Bleeding (especially with anticoagulants like warfarin)
 - Hemorrhagic stroke (in very high doses)
- Drug interactions:
 - May potentiate the effects of anticoagulants
 - Statins and chemotherapy drugs may have reduced effectiveness with high doses

Vitamin E - Clinical Trials

HOPE & HOPE-TOO Trial:

- Studied in high-risk populations
- No benefit for CVD or cancer prevention
- High doses may increase risk

Evidence so far **do not support** routine high-dose supplementation for chronic disease prevention

Which of the following is the most biologically active form of vitamin E in humans?

A. γ-Tocopherol

B. α -Tocopherol

C. β-Tocotrienol

D. δ -Tocopherol

Which medication increases bleeding risk when combined with high doses of vitamin E?

A. Metformin

B. Atorvastatin

C. Warfarin

D. Omeprazole



Vitamin K

Vitamin K - Introduction

• Two forms

- Phylloquinone (Vitamin K1)
- Menaquinones (Vitamin K2, MK-4 to MK-13)
- Requires bile and pancreatic enzymes for absorption
- Monitored via prothrombin time

Vitamin K - Clotting cascade



Vitamin K - Basic Functions and Role

- Essential for blood clotting: activates clotting factors II, VII, IX, X
- Supports bone health through activation of osteocalcin
- Vitamin K1 from plants; K2 from fermented foods and gut bacteria

Vitamin K - Daily Requirements

• Recommended Dietary Allowance (19 years+):

- Men: 120 mcg/day
- Women: 90 mcg/day
- Pregnancy: 90 mcg/day
- Lactation: 90 mcg/day
- No Tolerable Upper Intake Level established due to low toxicity risk

Vitamin K - OTC Products







Vitamin K - Phylloquinone vs Menaquinones

- Phylloquinone: green leafy vegetables (spinach, kale), vegetable oils
 - From plant foods, tightly bound to chloroplasts
- Menaquinones: fermented food (natto), cheese, meats, egg yolks
 - Limited research suggests that long-chain MKs have higher absorption rate
- Phytonadione: synthetic form of vitamin K

Vitamin K - Food Sources







145 mcg per 1 cup



530 mcg per 1/2 cup

Vitamin K - Deficiency and At-Risk Populations

- Deficiency symptoms:
 - Easy bruising, excessive bleeding
 - In newborns: vitamin K deficiency bleeding
- At-Risk Populations:
 - People on long-term antibiotic therapy
 - Individuals with fat-malabsorption conditions
 - Newborns (low placental transfer and sterile gut)

Vitamin K - Toxicity and Drug Interactions

- Toxicity: No known adverse effects from high dietary or supplemental intake of vitamin K
- Drug Interactions:
 - Warfarin antagonizes vitamin K patients must maintain consistent intake
 - Antibiotics can deplete gut flora, reducing vitamin K2 synthesis
 - Bile acid sequestrants and Orlistat

Vitamin K - Clinical Trials

Multiple studies indicating that higher vitamin K intake **linked to** better bone mineral density

Beulens JW et al: K2 intake **associated** with reduced arterial calcification and cardiovascular risk

Limited RCTs; **more evidence needed** for supplementation benefits in nondeficient populations

Which of the following patients is at the highest risk for vitamin K deficiency?

A. An athlete taking a multivitamin

B. A newborn baby

C. A patient eating lots of kale

D. A healthy adult

Patients on warfarin should avoid all sources of vitamin K.

A. True B. False



Vitamin A

Vitamin A - Introduction

- Exists in multiple forms:
 - Preformed Vitamin A from animal sources
 - Provitamin A carotenoids from plant sources
- Absorbed through the duodenum
- Liver stores 90% as retinyl esters

Vitamin A - Activation Cycle



Vitamin A - Basic Functions and Role

- Essential for vision, especially for low-light conditions
- Supports immune system function and epithelial cell integrity
- Aids in reproduction and embryonic development
- Functions in cellular communication and gene expression

Vitamin A - Serum Concentration

- Typically measured in plasma or serum
 - Not reliable indicators because they don't decline until levels in liver and other sites are depleted
- Liver measures is the best way
- Clinical practice = plasma retinol levels are used to document deficiency

Vitamin A - Daily Requirements

• Recommended Dietary Allowances (14 years+):

- Men: 900 mcg RAE/day
- Women: 700 mcg RAE/day
- Pregnancy: 750-770 mcg RAE/day
- Lactation: 1,200-1,300 mcg RAE/day
- Tolerable Upper Intake Level for adults: 3,000 mcg RAE/day
- 1 RAE = 1 mcg retinol, 12 mcg beta-carotene from food

Vitamin A - Conversions

• 1 mcg RAE is:

- 1 mcg retinol
- 2 mcg supplemental beta-carotene
- o 12 mcg dietary beta-carotene
- 24 mcg dietary alpha-carotene/beta-cryptoxanthin
- 1 IU retinol = 0.3 mcg RAE
- 1 IU supplemental beta-carotene = 0.3 mcg RAE
- 1 IU dietary beta-carotene = 0.05 mcg RAE
- 1 IU dietary alpha-carotene/beta-cryptoxanthin = 0.025 mcg RAE

Vitamin A - OTC Products







Vitamin A - Food Sources



6,582 mcg RAE per serving





573 mcg RAE per serving

1,403 mcg RAE per serving

Vitamin A - Deficiency and At-Risk Populations

• Very common in developing countries

- Deficiency Symptoms:
 - Night blindness
 - Xerophthalmia (dry eyes)
 - Abnormal lung development
- At-Risk Populations
 - Children in developing countries
 - Individuals with fat-malabsorption disorders
 - People with chronic alcoholism

Vitamin A - Toxicity & Drug Interactions

- Acute Hypervitaminosis A
 - Severe headache
 - Blurred vision
 - o Nausea
 - o Dizziness
- Chronic Hypervitaminosis A
 - Dry skin
 - Fatigue
 - Depression
 - o Abnormal liver test results

- Orlistat decrease absorption
- Retinoids concomitant use can lead to hypervitaminosis A

Vitamin A - Clinical Trials

Sommer et al: High-dose vitamin A supplementation **reduced** child mortality by up to 34% in vitamin A-deficient populations.

West et al: Found 45% **reduction** in maternal mortality with vitamin A or beta-carotene supplementation in women of reproductive age.

Klemm et al: Newborn vitamin A supplementation **reduced** infant mortality in rural Bangladesh.

High-dose vitamin A is **not routinely recommended** during pregnancy due to teratogenic risk

High-dose vitamin A is recommended for all pregnant women to prevent deficiency.

A. True B. False The provitamin A carotenoid most commonly found in carrots and converted to active vitamin A in the body is .



Clinical Application

A 68-year-old woman with osteoporosis is taking calcium but has limited sun exposure and lives in a northern climate. **Question:** Which vitamin should be evaluated or supplemented?



A patient on long-term warfarin therapy reports changes in diet, especially more leafy greens. Question: Which vitamin is relevant to monitor in this situation?



A patient with cystic fibrosis has symptoms of peripheral neuropathy and muscle weakness. Question: Which fat-soluble vitamin deficiency is likely?



A pregnant woman in a developing country reports dry eyes and night blindness. **Question:** Which vitamin might be deficient, and what is the risk of excessive supplementation?



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Any questions?

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