The Fat-Soluble Vitamins: A, D, E, and K

Chapter 11
Introduction

- Fat-soluble vitamins differ from water-soluble vitamins
  - Require bile for digestion and absorption
  - Travel through lymphatic system
  - Many require transport proteins in bloodstream
  - Excesses stored in liver and adipose tissue
  - Not readily excreted
    - Risk of toxicity is greater
Vitamin A and Beta-Carotene

- **Vitamin A**
  - First fat-soluble vitamin recognized
  - Precursor: beta-carotene
- **Three different forms**
  - Retinol, retinal, and retinoic acid
    - Conversion to other forms
- **Absorption and conversion**
  - Beta-carotene
Forms of Vitamin A

Retinol, the alcohol form

Retinal, the aldehyde form

Retinoic acid, the acid form

Beta-carotene, a precursor

*Cleavage at this point can yield two molecules of vitamin A.*

Sometimes cleavage occurs at other points as well, so that one molecule of beta-carotene may yield only one molecule of vitamin A. Furthermore, not all beta-carotene is converted to vitamin A, and absorption of beta-carotene is not as efficient as that of vitamin A. For these reasons, 12 μg of beta-carotene are equivalent to 1 μg of vitamin A. Conversion of other carotenoids to vitamin A is even less efficient.
Vitamin A Roles in the Body

- Regulates expression of more than 100 genes
- Retinal
  - Active in vision
- Retinoic acid
  - Regulates cell differentiation, growth, and embryonic development
- Retinol
  - Supports reproduction
  - Major transport and storage form
Conversion of Vitamin A Compounds

IN FOODS:
- Retinyl esters (in animal foods)
  - Retinol (supports reproduction)
  - Beta-carotene (in plant foods)

IN THE BODY:
- Retinal (participates in vision)
  - Retinoic acid (regulates growth)
Vitamin A and Vision

- Helps maintain clear cornea
- Helps convert light energy to nerve impulses in the retina
  - Photosensitive cells contain rhodopsin
- Repeated small losses of retinal
  - Need for replenishment
Vitamin A’s Role in Vision

As light enters the eye, the cells of the retina convert images into electrical impulses.

The cells of the retina contain rhodopsin, a molecule composed of opsin (a protein) and cis-retinal (vitamin A).

As rhodopsin absorbs light, retinal changes from cis to trans, which triggers an electrical impulse that carries visual information to the brain through the optic nerve.
Vitamin A and Cell Differentiation

- Epithelial cells
  - Skin
  - Mucous membrane integrity
- Goblet cells
Vitamin A maintains healthy cells in the mucous membranes. Without vitamin A, the normal structure and function of the cells in the mucous membranes are impaired.

- Mucus
- Goblet cells
Vitamin A’s Role in Reproduction and Growth

- Sperm development
- Normal fetal development
- Growth of children
  - Bone remodeling
- Antioxidant
  - Beta-carotene
Vitamin A Deficiency

- Large problem in developing countries
- Vitamin A status
  - Adequacy of stores
    - Liver
  - Protein status
- Consequences of deficiency
  - Risk of infectious diseases
  - Night blindness and blindness
  - Death
Keratinization

- Change in shape and size of epithelial cells
  - Skin becomes dry, rough, and scaly
- Disrupts normal digestion and absorption of nutrients from GI tract
- Weakens defenses in respiratory tract, vagina, inner ear, and urinary tract
In vitamin A deficiency, the epithelial cells secrete the protein keratin in a process known as keratinization. (Keratinization doesn't occur in the GI tract, but mucus-producing cells dwindle and mucus production declines.) The extreme of this condition is hyperkeratinization or hyperkeratosis. When keratin accumulates around hair follicles, the condition is known as follicular hyperkeratosis.
Vitamin A Toxicity

- Develops when binding proteins are loaded
  - Vitamin A free to damage cells
- Toxicity is a real possibility
  - Preformed vitamin A from animal sources
  - Fortified foods
  - Supplements
  - Children most vulnerable
- Bone defects
- No effect on acne
Vitamin A and Beta-Carotene

- Recommendations
  - Expressed as retinol activity equivalents (RAE)
  - Supplements measured in International Units (IU)

- Food sources
  - Animal sources
  - Plant sources
  - Golden rice
### Vitamin A in Selected Foods

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<th>Food</th>
<th>Serving size (kcalories)</th>
<th>Micrograms RAE</th>
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<td>Chicken breast</td>
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<tr>
<td>Egg</td>
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<td><strong>Excellent, and sometimes unusual, sources:</strong></td>
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<tr>
<td>Beef liver</td>
<td>3 oz fried (184 kcal)</td>
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<td>Sweet potatoes</td>
<td>½ c cooked (116 kcal)</td>
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<tr>
<td>Mango</td>
<td>1 (135 kcal)</td>
<td>80</td>
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</table>

**VITAMIN A**

Dark green and deep orange vegetables (green) and fruits (purple) and fortified foods such as milk contribute large quantities of vitamin A. Some foods are rich enough in vitamin A to provide the RDA and more in a single serving.

**Key:**
- **Grains**
- **Vegetables**
- **Fruits**
- **Milk and milk products**
- **Legumes, nuts, seeds**
- **Meats, poultry, seafood**

**Best sources per calorie**
Vitamin D

- Not an essential nutrient
  - Body synthesizes
    - Sunlight
    - Precursor from cholesterol

- Activation of vitamin D
  - Two hydroxylation reactions
    - Liver
    - Kidneys
Vitamin D Synthesis and Activation

**Synthesis**
- In the skin: 7-dehydrocholesterol (a precursor made in the liver from cholesterol)
  - Ultraviolet light from the sun
  - Previtamin D₃
  - Heat from the body

**Activation**
- In the liver: Hydroxylation
  - Calcidiol
- In the kidneys: Hydroxylation
  - Calcitriol

**From the diet:**
- Vitamin D₂ (plants)
- Vitamin D₃ (animals)
In the skin:
7-dehydrocholesterol (a precursor made in the liver from cholesterol)

UV light from the sun
Previtamin D₃

Heat from the body
Vitamin D₃ (Calciol)

From the diet:
Vitamin D₂ (plants)
Vitamin D₃ (animals)

In the liver:
Calcidiol

Hydroxylation
Calcitriol

In the kidneys:
Calcitriol

Hydroxylation

From the diet:
Vitamin D₂ (plants)
Vitamin D₃ (animals)
Vitamin D’s Roles in the Body

• Active form of vitamin D is a hormone
  • Binding protein carries it to target organs

• Bone growth
  • Calcium and phosphorus absorption
    • Enhances absorption
    • Provides minerals from other sources

• Other roles
  • Enhances or suppresses gene activity
  • Protects against cognitive decline
Vitamin D Deficiency

- Overt signs are relatively rare
  - Insufficiency is quite common
- Contributory factors
  - Dark skin
  - Breastfeeding without supplementation
  - Lack of sunlight
  - Not drinking fortified milk
- Creates a calcium deficiency
Diseases Associated with Vitamin D Deficiency

• **Rickets**
  - Bones fail to calcify normally
    - Bones bend
  - Affects children

• **Osteomalacia**
  - Poor mineralization of bones
  - Affects adults
  - Bones are soft, flexible, brittle, and deformed
Vitamin D Deficiency Symptoms

Bowed legs. In rickets, the poorly formed long bones of the legs bend outward as weight-bearing activities such as walking begin.

Beaded ribs. In rickets, a series of “beads” develop where the cartilages and bones attach.
Other Effects of Vitamin D Deficiency

- Osteoporosis
  - Loss of calcium from bones
    - Results in fractures
- Vitamin D deficiency especially likely in elderly
  - Reduced ability to make and activate vitamin D
  - Drink less milk
  - Spend much of day indoors
Vitamin D Toxicity

- Most likely of the vitamins to have toxic effects
  - When consumed in excessive amounts
- Raises blood calcium concentrations
  - Forms stones in soft tissues
  - May harden blood vessels
    - Can cause death
Vitamin D Recommendations

- Few food sources
  - Oily fish and egg yolks
  - Fortified milk
  - Recommendations difficult to meet without sunlight and supplementation or fortification

- Recommendations may be insufficient

- Sun exposure: no risk of toxicity
  - Vitamin D production varies with skin color, latitude, season, and time of day
Vitamin D Synthesis and Latitude

Above 40° north latitude (and below 40° south latitude in the southern hemisphere), vitamin D synthesis essentially ceases for the 4 months of winter. Synthesis increases as spring approaches, peaking in summer, and declines again in the fall. People living in regions of extreme northern (or extreme southern) latitudes may miss as much as 6 months of vitamin D production.
Vitamin E

- Two subgroups: tocopherols and tocotrienols
  - Each contains four compounds: alpha, beta, gamma, and delta
    - Position of methyl group
  - Only alpha-tocopherol maintained in the body
- Antioxidant
  - Stops chain reaction of free radicals
    - Protects cells and their membranes
    - Heart disease and protection of LDLs
Vitamin E Deficiency

- Primary deficiency is rare
- Secondary deficiency
  - Fat malabsorption
- Effects of deficiency
  - Red blood cells break open
    - Erythrocyte hemolysis
  - Neuromuscular dysfunction
- Other conditions and vitamin E treatment
Vitamin E Toxicity

- Liver regulates vitamin E concentrations
  - Toxicity is rare
- UL is 65 times greater than recommended intake for adults
- Extremely high doses of vitamin E
  - May interfere with vitamin K activity
    - Hemorrhage
Vitamin E Recommendations

- RDA based on alpha-tocopherol only
- Widespread in foods
  - Destroyed by heat and oxidation
  - Fresh foods preferred source
**Vitamin K**

- **Primary action:** blood clotting
  - Prothrombin
- **Metabolism of bone proteins**
  - Osteocalcin
    - Low bone density
- **Other possible roles of vitamin K in the body**
Blood-Clotting Process

1. Vitamin K
2. Calcium and thromboplastin (a phospholipid) from blood platelets
3. Prothrombin (an inactive protein)
4. Thrombin (an active enzyme)
5. Fibrinogen (a soluble protein)
6. Fibrin (active protein that forms a solid clot)

Several precursors earlier in the series depend on vitamin K.
Vitamin K Deficiency

- Primary deficiency is rare
- Secondary deficiency
  - Fat absorption falters
  - Some drugs disrupt vitamin K’s synthesis and action
- Newborn infants
  - Sterile intestinal tract
  - Single dose of vitamin K given at birth
Vitamin K Toxicity

- Not common
  - No adverse effects with high intakes
- No UL
- High doses can reduce effectiveness of anticoagulant drugs
Vitamin K Sources

• Nonfood source: GI tract
  • Synthesized by bacteria
  • Amount insufficient

• Food sources
  • Green vegetables
    • Spinach, kale
  • Green fruits
    • Avocado, kiwi
  • Some vegetable oils
The Fat-Soluble Vitamins: A Summary

- Toxicities are possible
- Functions of fat-soluble vitamins together
  - Vitamins E and A
    - Oxidation, absorption, and storage
  - Vitamins A, D, and K
    - Bone growth and remodeling
  - Vitamins E and K
    - Blood clotting
Antioxidant Nutrients in Disease Prevention

Highlight 11
Free Radicals

- Compound with one or more unpaired electrons
  - Predisposed to steal electron from vulnerable compound
    - Electron-snatching chain reaction

- Free radical production
  - Normal bodily functions
  - Environmental factors
Antioxidants

• Neutralize free radicals
  • Stable in various forms
• Defend body against oxidative stress
Free Radical Damage

- Free radical attacks
  - Occasionally helpful
  - Most cause damage
- Contribute to cell damage, disease progression, and aging
  - Polyunsaturated fatty acids in lipoproteins and membranes
  - Alter DNA, RNA, and proteins
  - Elicit inflammatory response
Free Radical Damage Illustrated

Free radical
Polyunsaturated fatty acids → Lipid radicals

Free radical
DNA and RNA → Altered DNA and RNA → Absence of specific proteins, Excess of specific proteins → Cell damage, Diseases, Aging

Free radical
Proteins → Altered proteins → Impaired cell function, Inflammatory response
Some Effects of Oxidative Stress

- Oxidative stress causative factor in:
  - Reduced cognitive performance
  - Cancer and heart disease
  - Arthritis and cataracts
  - Diabetes
- Body’s natural defenses and repair systems
  - Not 100 percent effective
  - Less effective with age
The Body’s Defenses Against Free Radicals

- System of enzymes against oxidants
  - Uses copper, selenium, manganese, and zinc
- Antioxidant vitamins
  - Vitamin E
    - Defends body lipids
  - Beta-carotene
    - Defends lipid membranes
  - Vitamin C
    - Protects skin and blood fluid
Defending Against Cancer

- Damage to cellular DNA
  - Antioxidants may protect DNA from this damage
  - Inverse relationship with vegetable intake
  - Direct relationship with beef and pork intake
- Healthy diet with abundant fruits and vegetables
  - Protect against certain types of cancer
- Vitamin E
Defending Against Heart Disease

- Oxidized LDL scenario
  - Accelerate formation of artery-clogging plaques
  - Additional changes in arterial walls
- Vitamin E
  - Defends against LDL oxidation
  - No evidence it slows progression of heart disease
Foods, Supplements, or Both?

• Most effective dietary strategies for preventing heart disease
  • Use unsaturated fats instead of saturated
  • Select foods rich in omega-3 fatty acids
  • High consumption of fruits, vegetables, nuts, and whole grains
    • Low consumption of refined grain products

• Supplement use
  • Research outcome: provides no benefit
    • May increase risk

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# Antioxidants and Chronic Disease Risk

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