



# 9

## Fat-Soluble Vitamins

### Learning Outcomes

After reading this chapter, you will be able to:

- 9.1** Explain the characteristics of vitamins, and classify vitamins according to their solubility.
- 9.2** Compare and contrast the absorption and storage of fat-soluble and water-soluble vitamins.
- 9.3** Define the term “antioxidant” and explain which vitamins perform this function.
- 9.4** Describe the best sources of vitamins and the factors that affect the vitamin content of foods.
- 9.5** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin A.
- 9.6** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin D.
- 9.7** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin E.
- 9.8** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin K.
- 9.9** Explain the role of dietary supplements in maintaining a healthy diet.

### True or False?

1. Vitamins provide the body with energy. **T/F**
  2. Fat-soluble vitamins are found in fatty foods. **T/F**
  3. Taking vitamin supplements is *never* harmful. **T/F**
  4. Most people can meet their vitamin needs through food, so supplements are unnecessary. **T/F**
  5. Steaming is the best cooking method to retain the vitamins in vegetables. **T/F**
  6. Carrots, winter squash, and broccoli are good sources of vitamin A. **T/F**
  7. The body makes vitamin D with the help of sunlight. **T/F**
  8. Vitamin K is an anticoagulant. **T/F**
  9. Vitamin E helps keep bones strong. **T/F**
  10. Antioxidants are a magic pill that will prevent aging. **T/F**
- See page 355 for the answers.

**V**itamins remained nameless and undiscovered substances until the early part of the twentieth century, when scientists sought substances to cure diseases such as beriberi, scurvy, and rickets. These may sound like the names of rock bands, but they are actually devastating diseases caused by deficiencies of thiamin (for beriberi), vitamin C (for scurvy), and vitamin D (for rickets). Throughout the twentieth century, scientists discovered the vitamins that cured these and other diseases. By the 1940s, the U.S. government mandated the addition of specific vitamins to grains and milk to improve the nation's health.

In the latter part of the twentieth century, improved diets meant that vitamin deficiencies were less of an issue for most Americans. Scientists shifted their focus from using vitamins to cure disease to using them to prevent disease. Today, researchers seek to find out how vitamins affect and prevent everything from birth defects to heart disease and cancer.

In this chapter, we begin with an overview of vitamins, followed by a discussion of differences between the fat-soluble and water-soluble vitamins. We then cover the four fat-soluble vitamins in detail, including their functions, recommended intakes, food sources, and the deficiency and toxicity effects. (We cover water-soluble vitamins in Chapter 10.)

---

## What Are Vitamins?

**LO 9.1** Explain the characteristics of vitamins, and classify vitamins according to their solubility.

**Vitamins** are tasteless organic compounds the body requires in small amounts for normal metabolic functions. Vitamins act as coenzymes to regulate metabolism; assist the body to convert the energy in fat, carbohydrates, and protein into ATP; and promote growth and reproduction. Vitamins do not provide energy themselves, but a deficiency of any vitamin can cause serious symptoms.

### Vitamins Were Discovered about One Hundred Years Ago

During the eighteenth century alone, an estimated 2 million sailors died of scurvy, the deficiency disease caused by a lack of vitamin C. The mottled skin and spongy gums that are symptomatic of the disease frequently occurred among men on long sea voyages, during which supplies of fresh foods would be depleted before the end of the trip. Eventually, the acid in citrus fruit was recognized as a curative factor, and British sailors came to be known as “Limeys” because of the British Navy’s policy of issuing lime juice on board its ships to prevent scurvy. What they didn’t recognize was that the citrus fruit provides vitamin C, which is the vitamin needed to ward off scurvy.

In the early part of the twentieth century, scientists searching for substances to cure diseases such as beriberi and rickets<sup>1</sup> eventually identified thiamin as the curative vitamin for beriberi, and vitamin D as the cure for rickets. As they associated additional vitamins with other diseases and conditions, scientists realized their value in promoting public health.

As each new vitamin was discovered, it was given a temporary name until its structure was isolated. Researchers started at the beginning of the alphabet with vitamins A, B, C, D, E, and K. The letters F, G, and H were dropped once those substances were found not to exist.

This nomenclature changed after vitamin B was found to have more than one physiological function, and chemists began adding a subscript number to each newly isolated role. Together, these vitamins became known as the B complex, with

**vitamins** Thirteen essential, organic micronutrients that are needed by the body for normal functions, such as regulating metabolism and assisting in energy production, growth, reproduction, and overall health.

individual vitamins labeled B<sub>1</sub>, B<sub>2</sub>, and so forth. While vitamins B<sub>6</sub> and B<sub>12</sub> still retain their numeric names, most of the B vitamins are now better known by their chemical names, such as thiamin (for B<sub>1</sub>) and riboflavin (for B<sub>2</sub>).

## There Are Criteria for Classifying Vitamins

Vitamins are unique nutrients in that they are not alike in their chemical structure nor do they have similar functions. Whereas, as you learned from earlier chapters, amino acids each have a basic structure but differ in their side groups, this is not the case with vitamins. How, then, are vitamins classified?

An organic, non-energy-providing nutrient is classified as a vitamin when it cannot be synthesized in ample amounts in the body. For instance, vitamin K and two of the B vitamins (niacin and biotin) can be made in the body, but not in amounts sufficient to meet the body's metabolic needs, so they must also be consumed in the diet. A second requirement for a compound to be called a vitamin is that a chronic deficiency of the compound is likely to cause physical symptoms, from fatigue or confusion to scaly skin or blindness. The symptoms disappear once the vitamin has been sufficiently restored to the diet and absorbed into the body, provided the deficiency has not caused permanent damage.

Based on these criteria, 13 compounds are classified as vitamins. The vitamins are further organized according to their solubility. There are four fat-soluble (hydrophobic) vitamins: A, D, E, and K, and nine water-soluble (hydrophilic) vitamins, including the B vitamin complex and vitamin C (see **Figure 9.1**). The distinction in solubility is important because it influences how the body digests, absorbs, transports, stores, and excretes these essential nutrients.

## All Vitamins Are Organic, but Differ in Structure and Function

All vitamins are organic because they contain carbon. Vitamins also contain hydrogen and oxygen and, in some cases, nitrogen or sulfur. The chemical structure of each vitamin is unique. That is, unlike proteins, which consist of and vary by chains of amino acids, vitamins are singular units. There are no bonds for the body to hydrolyze during digestion, and vitamins are absorbed intact into the intestinal wall.

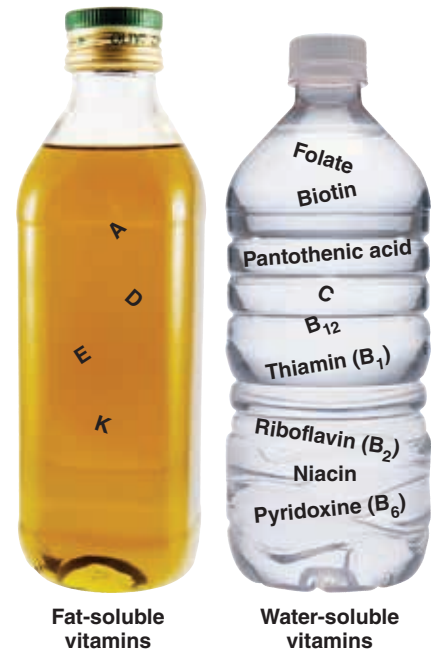
Vitamins perform numerous essential functions in the body. Some, including thiamin, riboflavin, and niacin, participate in releasing energy from the macronutrients. Vitamin D helps regulate bone metabolism, while vitamins E and C donate or accept electrons as antioxidants. Several vitamins play more than one role in metabolism. **Table 9.1** illustrates the variety of functions vitamins play in maintaining health.

## Provitamins Can Be Converted to Active Vitamins by the Body

**Provitamins** are substances found in foods that are not in a form directly usable by the body, but that can be converted into an active form once they are absorbed. The most well-known example of this is beta-carotene, which is split into two molecules of vitamin A in the small intestinal cell wall or in the liver cells. Vitamins found in foods that are already in the active form, called **preformed vitamins**, do not undergo conversion.

## Overconsumption of Some Vitamins Can Be Toxic

Vitamin **toxicity**, or **hypervitaminosis**, results when a person ingests more of a vitamin than the body needs, to the point where tissues become saturated. The



▲ **Figure 9.1** Categorizing the Vitamins: Fat Soluble and Water Soluble

A vitamin is either fat soluble or water soluble, depending on how it is absorbed and handled in the body. Fat-soluble vitamins need dietary fat to be properly absorbed, while water-soluble vitamins are absorbed with water.

**provitamin** A vitamin precursor that is converted to a vitamin in the body.

**preformed vitamins** Vitamins found in food.

**toxicity** The accumulation of a substance to a harmful level.

**hypervitaminosis** A condition resulting from the presence of excessive amounts of vitamins in the body; also referred to as *vitamin toxicity*.

**TABLE 9.1** The Many Roles of Vitamins in Maintaining Health

Metabolic Function	Vitamins That Play a Role
Antioxidants	Vitamin C, vitamin E, beta-carotene
Blood clotting and red blood cell synthesis	Folate, vitamin B <sub>6</sub> , vitamin B <sub>12</sub> , vitamin K
Bone health	Vitamin A, vitamin C, vitamin D, vitamin K
Energy production	Biotin, niacin (B <sub>3</sub> ), pantothenic acid, riboflavin (B <sub>2</sub> ), thiamin (B <sub>1</sub> ), vitamin B <sub>6</sub> , vitamin B <sub>12</sub>
Growth and reproduction	Vitamin A, vitamin D
Immune function	Vitamin A, vitamin C, vitamin D
Protein metabolism and synthesis	Folate, vitamin B <sub>6</sub> , vitamin B <sub>12</sub>

excess vitamin can damage cells, sometimes permanently. Vitamin toxicity does not occur by eating a normal balanced diet. While rare, vitamin toxicity can result when individuals consume **megadose** levels of vitamin supplements, usually in the false belief that “more is better.” Many individuals, for example, overload on vitamin C tablets to ward off a cold, despite the fact that there is no evidence that vitamin C prevents the common cold, and they may suffer unpleasant side effects, including diarrhea. In general, water-soluble vitamins do not cause toxicity because the excess is excreted in the urine. Some water-soluble vitamins, such as vitamin B<sub>6</sub>, and the fat-soluble vitamins, A, D, and E, which are stored, can be toxic in megadose amounts.

To prevent excessive intake, the Dietary Reference Intakes include a tolerable upper intake level for most vitamins. Even though sufficient evidence to establish a UL is lacking for some vitamins, there still may be risks in taking them in megadose amounts.

**LO 9.1: THE TAKE-HOME MESSAGE** Vitamins are essential nutrients needed in small amounts for growth, reproduction, and overall good health. All vitamins are either fat soluble or water soluble. Provitamins are converted to their active form before they can be directly used in the body. Most water-soluble vitamins are not toxic. Vitamins A, D, and E can be toxic if taken in megadose amounts.

## How Do Vitamins Differ in Their Absorption and Storage?

**LO 9.2** Compare and contrast the absorption and storage of fat-soluble and water-soluble vitamins.

All vitamins are absorbed in the small intestine, but they differ in their bioavailability from foods. Also, fat-soluble vitamins are absorbed differently from water-soluble vitamins. Let’s take a closer look at these differences.

### Vitamins Differ in Bioavailability

Not all of the vitamins consumed in foods are completely absorbed. The **bioavailability** of individual vitamins varies according to several factors, including the amount of the vitamin in the food; whether the food is cooked, raw, or refined;

**megadose** An amount of a vitamin or mineral that’s at least 10 times the amount recommended in the DRI.

**bioavailability** The degree to which a nutrient is absorbed from foods and used in the body.

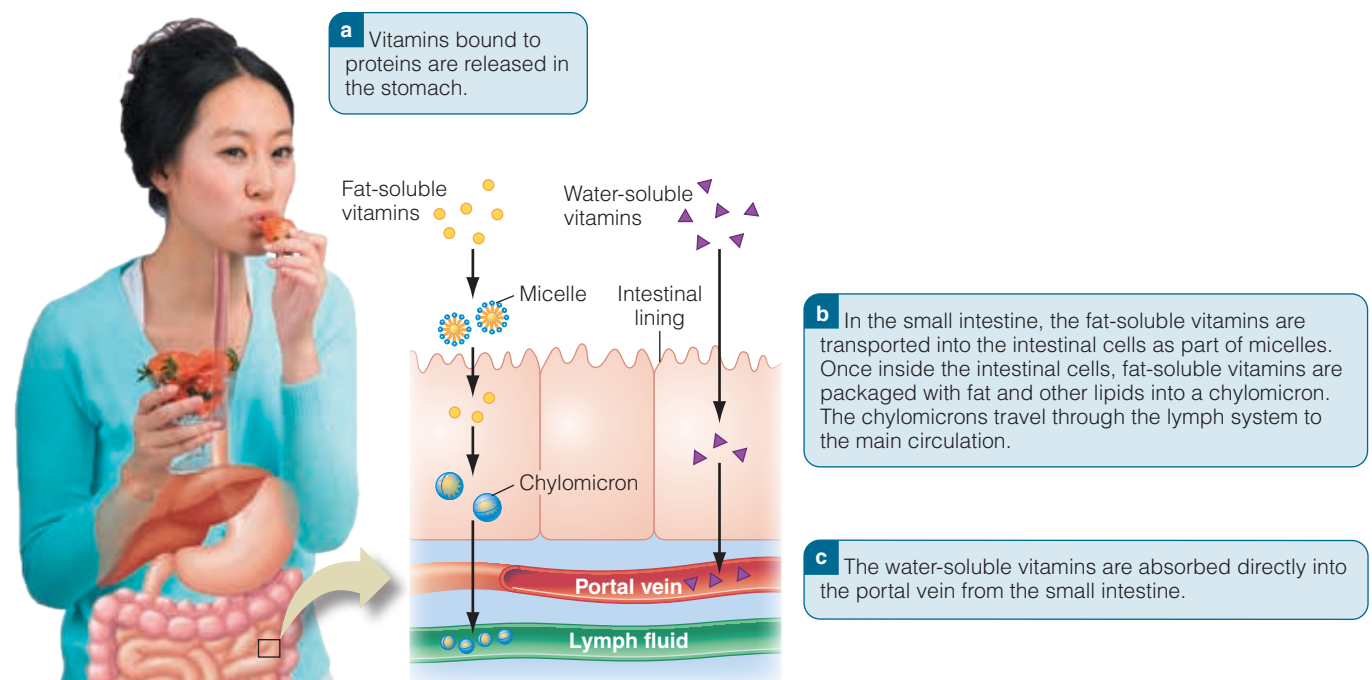
how efficiently the food is digested and absorbed; the individual's nutritional status and general health; and whether or not the vitamin is natural or synthetic. In general, if the body needs more of a certain vitamin, a greater percentage is absorbed. For example, a young child or pregnant woman absorbs a higher percentage of ingested vitamins than does a nonpregnant adult.

The bioavailability of vitamins differs based on their solubility and the type of food. Fat-soluble vitamins are usually less bioavailable than water-soluble vitamins because fat-soluble vitamins require bile and the formation of a micelle in order to be absorbed. Vitamins in plant foods are typically less bioavailable than those in animal foods because plant fiber can trap vitamins.

## Fat-Soluble Vitamins Are Stored after They Are Absorbed

Fat-soluble vitamins are often attached to food components, usually protein, in foods. To be absorbed, the vitamin must be released from the protein with the help of pepsin and hydrochloric acid (refer to Chapter 3). The freed fat-soluble vitamins are then ready to be absorbed, primarily in the duodenum (Figure 9.2). They are packaged with fatty acids and bile in micelles that transport them close to the intestinal mucosa. Once there, the fat-soluble vitamins travel through the cells in the intestinal wall, and are repackaged with fat and other lipids into chylomicrons. The vitamins then travel through the lymph system before they enter the bloodstream. Note that absorption of fat-soluble vitamins can be compromised in the absence of adequate fatty acids or bile. This is why having some fat in the diet is absolutely necessary to avoid fat-soluble vitamin deficiencies.

Fat-soluble vitamins are stored in the body and used as needed when dietary intake falls short of the body's needs. The liver is the main storage depot for vitamin A and to a lesser extent vitamins K and E, whereas vitamin D is mainly stored in fat and muscle tissues. Because they are stored in the body, large quantities of some of the fat-soluble vitamins, particularly A, can build up to the point of toxicity, causing harmful symptoms and conditions.



▲ Figure 9.2 Digesting and Absorbing Vitamins

## Water-Soluble Vitamins Are Not Stored after Absorption

Water-soluble vitamins are absorbed with water and enter the bloodstream directly from the small intestine. Most water-soluble vitamins are absorbed in the duodenum and jejunum, although vitamin B<sub>12</sub> is absorbed in the ileum. Water-soluble vitamins are not stored in the body, and excess amounts are excreted, so it's important to consume adequate amounts of them every day. Note that even though most water-soluble vitamins aren't stored, dietary excesses can still be harmful.

**LO 9.2: THE TAKE-HOME MESSAGE** Bioavailability of individual vitamins varies based on the amount of the vitamin in the food, whether the food is cooked, raw, or refined, the digestibility of the food, an individual's nutrition status, and whether the vitamin is in natural or synthetic form. Fat-soluble vitamins—A, D, E, and K—are not as bioavailable as water-soluble vitamins. They need dietary fat to be absorbed and are stored in the body. Because they are stored, overconsumption of fat-soluble vitamins can be toxic. The water-soluble B and C vitamins are absorbed with water. Excess water-soluble vitamins are excreted through the urine, and generally aren't stored.

## What Are Antioxidants?

**LO 9.3** Define the term “antioxidant” and explain which vitamins perform this function.

**Antioxidants** (*anti* = against, *oxidants* = oxygen-containing substances) are a group of compounds that include vitamins E and C, the mineral selenium, **flavonoids** (colorful pigments found in fruits and vegetables), and carotenoids (such as beta-carotene, zeaxanthin, lutein, and lycopene). Just as their name implies, antioxidants counteract the **oxidation** that takes place in cells. Recall that oxidation reactions are essential chemical reactions that are part of metabolism, such as energy production (discussed in Chapter 8). However, in some reactions, oxidation can be damaging, such as when free radicals are formed.

During oxidation, harmful oxygen-containing **free radicals** are created as by-products of the body's metabolic reactions. Free radicals are molecules with an unpaired electron, which makes them very unstable. They can also result from exposure to chemicals in the environment (such as cigarette smoke and air pollution) or from the damaging effects of the sun's ultraviolet rays. The unpaired electron in free radicals enables them to damage cells by altering cell structure, body proteins, and even DNA.<sup>2</sup>

Free radicals are formed in a series of chain reactions. The first free radical is formed when energy, in the form of heat or ultraviolet light, is added to a reaction. Free radicals seek stability, so the newly formed free radical will search for an electron to steal from another molecule. Once the theft occurs, a new free radical is created, and it becomes a thief in pursuit of another molecule to attack. A free radical can also become stable by depositing its unpaired electron onto another molecule. This causes the molecule that takes on the electron to become a new free radical. The chain reaction stops when two free radicals collide to form a new molecule and the number of free radicals is reduced. **Figure 9.3** illustrates free radicals in action in the body.

Antioxidants are part of the body's natural defense system to neutralize free radicals and stop them from damaging cells. If free radicals accumulate faster than the body can neutralize them, causing **oxidative stress**, their damaging effects can

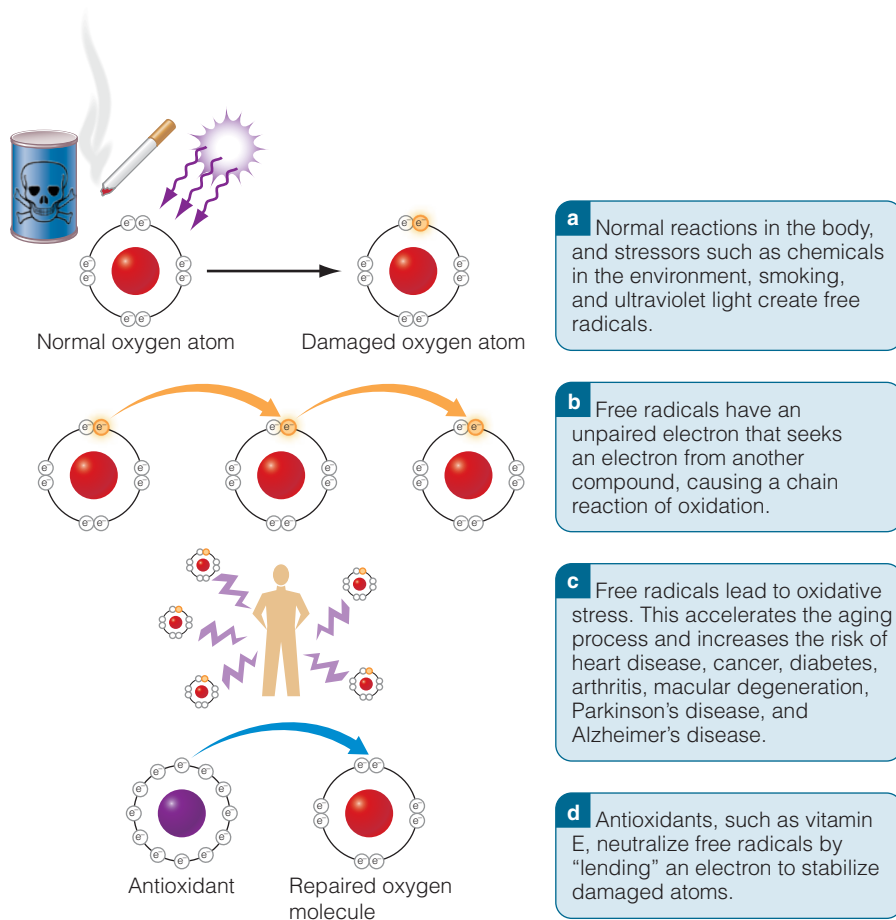
**antioxidants** Substances that neutralize harmful oxygen-containing free radicals that can cause cell damage. Vitamins A, C, and E and beta-carotene are antioxidants.

**flavonoids** Food pigments that act as antioxidants and may help reduce the risk of chronic diseases; flavonoids are found in many fruits, vegetables, tea, and wine.

**oxidation** A chemical reaction in which oxygen combines with other substances, resulting in the loss of an electron.

**free radicals** Unstable molecules that contain an unpaired electron; free radicals can damage the cells of the body and possibly contribute to the increased risk of chronic diseases.

**oxidative stress** A condition whereby free radicals are being produced in the body faster than they are neutralized.



▲ **Figure 9.3 Antioxidants Neutralize Free Radicals**

contribute to various chronic diseases and conditions, including heart disease, cancer, aging, diabetes mellitus, arthritis, Parkinson's disease, and Alzheimer's disease.<sup>3</sup>

Free radicals can also damage eyes, contributing to **age-related macular degeneration (AMD)** and cataracts. AMD affects over 1.8 million Americans<sup>4</sup> and results from damage to the macula, a tiny area of the eye that is needed for central vision (the ability to see things that are directly in front of you). The macula is shown in the eye illustrated in the vitamin A section on page 330. AMD can make activities such as reading, driving, and watching television impossible (**Figure 9.4**). AMD is the most common cause of permanent impairment for reading and other activities requiring close-up vision in Americans 60 years of age and older.<sup>5</sup> In the early stages of AMD, there are few symptoms or vision loss. As the disease progresses, images become blurred, or a dark, empty area can appear in the center of your vision. Colors can also become less vivid as AMD progresses. While there is no cure for AMD, there are certain vitamins and minerals that may reduce the risk of developing AMD or improve vision in those who already have AMD. A number of well-designed studies have indicated that vitamin A, beta-carotene, vitamin C, and vitamin E, along with the minerals zinc and copper, may be effective in reducing the risk of AMD as well as the loss of vision in individuals with advanced stages of AMD.<sup>6</sup>

Some studies have also suggested that specific antioxidants—namely vitamins C and E and the carotenoids lutein and zeaxanthin—may help lower the risk of cataracts.<sup>7</sup> A **cataract** is a common eye condition among older adults in which the lens of the eye becomes cloudy, resulting in blurred vision, as shown in **Figure 9.4c**. More than 20 million Americans over the age of 40 (17.5 percent)



**a** Normal vision and the ability to clearly see the world around you is often taken for granted.



**b** People with age-related macular degeneration (AMD) have difficulty seeing things directly in front of them.



**c** Cataracts cause vision to become cloudy.

▲ **Figure 9.4 Normal and Impaired Vision**

Source: National Institutes of Health, National Eye Institute.

**age-related macular degeneration (AMD)** A disease that affects the macula of the retina, causing blurry vision and, potentially, blindness.

**cataract** A common eye disorder that occurs when the lens of the eye becomes cloudy.

have cataracts in at least one or both eyes.<sup>8</sup> The National Eye Institute recommends consuming antioxidant- and carotenoid-rich vegetables and fruits, such as citrus fruits, broccoli, and dark green leafy vegetables, for the health of the eyes.<sup>9</sup>

The antioxidants carotenoids and flavonoids are part of a larger group of **phytochemicals** (*phyto* = plant), naturally occurring plant compounds that have many beneficial functions in the body, such as acting as antioxidants, stimulating the immune system, and interacting with hormones that may help prevent certain cancers.<sup>10, 11</sup> Some phytochemicals, including carotenoids, are also responsible for the vibrant colors of many fruits and vegetables. **Table 9.2** emphasizes the importance of consuming a colorful diet so as to take in an abundance of phytochemicals.

The big question that remains is if antioxidant *supplements* provide the same health protection as antioxidants consumed in foods. Studies are currently under way exploring the role of antioxidant supplements in fighting disease. At this time, the American Heart Association, National Cancer Institute, and United States Preventive Services Task Force do not advocate taking supplements to reduce the risk of specific diseases, but encourage eating a phytochemical- and antioxidant-rich, well-balanced diet.<sup>12, 13</sup>

**LO 9.3: THE TAKE-HOME MESSAGE** Antioxidants, such as vitamins E and C, the mineral selenium, flavonoids, and carotenoids, help counteract the damaging effects of oxygen-containing molecules called free radicals. If free radicals accumulate faster than the body can neutralize them, the damaging effects of oxidative stress can contribute to chronic diseases and conditions. Fruits, vegetables, and whole grains are excellent sources of antioxidants and other phytochemicals.

**phytochemicals** Naturally occurring substances in fruits, vegetables, and whole grains that protect against certain chronic diseases.

**TABLE 9.2** The Phytochemical Color Guide

The National Cancer Institute recommends eating a variety of colorful fruits and vegetables daily to provide your body with valuable vitamins, minerals, fiber, and disease-fighting phytochemicals. Whole grains also have phytochemicals and have been added to this list.

Color	Phytochemical	Found in
<b>Red</b>	Anthocyanins	Apples, beets, cabbage, cherries, cranberries, red cabbage, red onions, red beans
<b>Yellow/Orange</b>	Beta-carotene	Apricots, butternut squash, cantaloupe, carrots, mangoes, peaches, pumpkin, sweet potatoes
	Flavonoids	Apricots, clementines, grapefruits, lemons, papaya, pears, pineapple, yellow raisins
<b>White</b>	Alliums/allicin	Chives, garlic, leeks, onions, scallions
<b>Green</b>	Lutein, zeaxanthin	Broccoli, collard greens, honeydew melon, kale, kiwi, lettuce, mustard greens, peas, spinach
	Indoles	Arugula, broccoli, bok choy, brussels sprouts, cabbage, cauliflower, kale, Swiss chard, turnips
<b>Blue/Purple</b>	Anthocyanins	Blackberries, black currants, elderberries, purple grapes
	Phenolics	Eggplant, plums, prunes, raisins
<b>Brown</b>	Beta-glucan, lignans, phenols, plant sterols, phytoestrogens, saponins, tocotrienols	Barley, brown rice, oats, oatmeal, whole grains, whole-grain cereals, whole wheat

Source: Adapted from Fruits & Veggies—More Matters. 2012. Available at [www.fruitsandveggiesmorematters.org](http://www.fruitsandveggiesmorematters.org).

# What's the Best Source of Vitamins?

**LO 9.4** Describe the best sources of vitamins and the factors that affect the vitamin content of foods.

Eating whole foods, including fruits, vegetables, and whole grains, remains the best way to meet vitamin needs: They provide more than just vitamins because they are also rich in disease-fighting phytochemicals, antioxidants, and fiber. The *Dietary Guidelines for Americans* recommends eating a wide variety of foods from each food group, with ample amounts of vitamin-rich fruits, vegetables, whole grains, and dairy foods. **Figure 9.5** illustrates each food group and the vitamins it contributes to the diet.

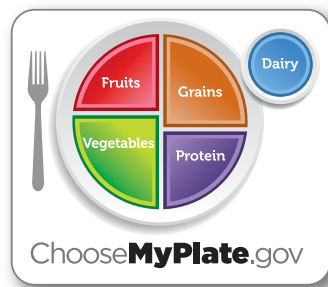
**Table 9.3** shows the estimated intake for each nutrient that a 2,000-kilocalorie diet based on the *Dietary Guidelines* provides. As shown in the table, vitamins D and E are the only nutrients in which Americans typically fall short. Add some margarine on toast, a few nuts to yogurt, and a little salad dressing on a dinner salad to increase overall intake of both vitamins D and E. Refer to the Table Tips for vitamin D (on page 342) and vitamin E (on page 344) for more suggestions.

## Vitamins Can Be Destroyed during Cooking or Storage

How you prepare and store fresh foods once you obtain them can affect their nutritional content. Water-soluble vitamins can be destroyed by exposure to air, ultraviolet (UV) light, water, changes in pH, or heat. In fact, vegetables and fruits begin to lose their vitamins almost immediately after being harvested, and some preparation and storage methods can accelerate vitamin loss. Though the fat-soluble vitamins tend to be more stable than water-soluble vitamins, some food preparation techniques can cause the loss of these vitamins as well.

### Exposure to Oxygen

Air—or, more specifically, exposure to oxygen—can destroy the water-soluble vitamins and the fat-soluble vitamins A, E, and K. Thus, fresh vegetables and fruits should be stored in airtight, covered containers and used soon after being purchased.



◀ **Figure 9.5 Vitamins Found Widely in the Food Groups**

Eating a wide variety of foods from all food groups ensures that you meet your vitamin needs.

Vegetables	Fruits	Grains	Protein	Dairy
Folate	Folate	Folic acid	Niacin	Riboflavin
Vitamin A	Vitamin C	Niacin	Thiamin	Vitamin A
Vitamin C	Vitamin A	Vitamin B <sub>6</sub>	Vitamin B <sub>6</sub>	Vitamin B <sub>12</sub>
Vitamin E		Vitamin B <sub>12</sub> (if fortified)	Vitamin B <sub>12</sub>	Vitamin D
Vitamin K		Riboflavin		
		Thiamin		

**TABLE 9.3** Meeting the Dietary Reference Intakes with Healthy Food Choices

Nutrient	Estimated Vitamin Intake Based on 2,000 Kilocalories*	Institute of Medicine Recommendations, Nutrient RDA/AI
Vitamin A, $\mu\text{g}$ RAE	851	700–900
Vitamin D, IU	258	600
Vitamin E, mg	8.3	15.0
Vitamin K, $\mu\text{g}$	140	90–120
Thiamin, mg	1.8	1.1–1.2
Riboflavin, mg	2.2	1.1–1.3
Niacin, mg	23.0	14.0–16.0
Vitamin B <sub>6</sub> , mg	2.3	1.3–1.7
Vitamin B <sub>12</sub> , $\mu\text{g}$	6.5	2.4
Folate, $\mu\text{g}$	628	400
Vitamin C, mg	126	75–90
Choline, mg	340	425–550

\*The highest intake level for young adult men or women is stated.

RDA = Recommended Dietary Allowance; AI = Adequate Intakes; RAE = retinol activity equivalents; mg = milligrams;  $\mu\text{g}$  = micrograms.

Data from U.S. Department of Agriculture. 2010. *Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2010*. Available at [www.cnpp.usda.gov](http://www.cnpp.usda.gov); Food and Nutrition Board, Institute of Medicine, National Academies. *Dietary Reference Intakes Series*. Available at [www.iom.edu](http://www.iom.edu). Accessed March 2014.

**TABLE TIPS****Preserve Your Vitamins!**

Cook vegetables in a small amount of already boiling water—not cold water brought to a boil. Use any leftover cooking liquid as a soup or gravy base.

Don't rinse rice before cooking it or pasta after cooking it. You'll wash away water-soluble vitamins.

Microwave or stir-fry vegetables instead of boiling or frying them. These methods reduce the amount of time vegetables are exposed to heat and therefore the amount of vitamins that are lost.

Store produce in a refrigerator and eat it soon after purchasing.

Cut vegetables and fruits in larger pieces to reduce the surface area exposed to oxygen. Prepare vegetables close to the time that they are going to be cooked and/or served.

Source: Adapted from U.S. Department of Agriculture Food and Nutrition Services. 2002. *Chapter 5, Quality Meals in Building Blocks for Fun and Healthy Meals—A Menu Planner for the Child and Adult Care Food Program*. USDA Team Nutrition Resources. Available at [www.fns.usda.gov/tl/Resources/buildingblocks.html](http://www.fns.usda.gov/tl/Resources/buildingblocks.html). Accessed March 2014.

**Exposure to Light**

Light, especially ultraviolet light (UV), can destroy vitamins. Foods stored in glass containers, such as milk or grains, or sun-dried fruits and vegetables, can lose vitamins. For example, up to 80 percent of the riboflavin content of milk in glass containers can be destroyed by sunlight.<sup>14</sup> For this reason, milk is sold in opaque containers. The traditional methods of sun-drying fruits and vegetables destroy susceptible vitamins such as beta-carotene and vitamin C. However, new advances in solar drying have shown some promise.<sup>15</sup>

**Exposure to Water**

Water-soluble vitamins leach out of foods when soaked or cooked in liquids, so cooking foods in as little water as possible is recommended.<sup>16</sup> Water should be boiling before vegetables are added even if you use a steamer basket. Some enzymes naturally found in the food oxidize specific vitamins, changing them to forms that are not metabolically active. Boiling water inactivates these enzymes. For instance, potatoes are a good source of vitamin C but they also contain an enzyme, ascorbic oxidase, that changes the chemical structure of vitamin C to an inactive form. Potatoes added to boiling water retain more vitamin C than if they are added to cold water and brought to a boil.

**Changes in pH**

Changes in pH can destroy some vitamins, especially thiamin and vitamin C. Most vitamins are stable in acid, but adding ingredients such as baking soda to foods increases the pH and destroys pH-sensitive vitamins. For instance, adding baking soda to shorten the cooking time of beans or other legumes destroys the thiamin content.

## Exposure to Heat

Heat, especially prolonged heat from cooking, also destroys water-soluble vitamins, especially vitamin C. Because they are exposed to less heat, vegetables cooked by microwaving, steaming, or stir-frying can have approximately one-and-a-half times more vitamin C after cooking than if they were boiled, which involves longer heat exposure.<sup>17</sup> Whereas heat reduces the vitamin content of foods, cooler temperatures help preserve them. For this reason, produce should be stored in the refrigerator rather than on a counter or in a pantry. A package of fresh spinach left at room temperature loses over half of its folate, a B vitamin, after four days. Refrigeration delays that loss to eight days.<sup>18</sup> See the Table Tips for more ways to preserve the vitamins in foods.



Cooking foods in the microwave allows for a shorter cooking time, which means fewer vitamins are lost.

## Some Foods Are Fortified with Vitamins

When you pour a glass of orange juice, you know that you are getting a significant intake of vitamin C. However, depending on the brand of orange juice, you may also be meeting the recommendations for vitamin E and vitamin D—two nutrients that are not naturally found in oranges. This is due to the process called fortification. **Fortified foods** are becoming more popular with the American consumer. For example, sales of foods fortified with one popular nutrient, omega-3 fatty acids, approached \$4 billion in 2010.<sup>19</sup>

Food fortification is the voluntary addition of nutrients by manufacturers to enhance the nutrient quality of the food and to prevent or correct dietary deficiencies. Vitamins and minerals are the most commonly used nutrients in fortified foods, but fiber, amino acids, essential fatty acids, and other bioactive ingredients are also sometimes added. Based on current Food and Drug Administration (FDA) regulations, all 13 vitamins and 20 minerals can be added to foods.<sup>20</sup>

Enrichment of foods is a form of fortification. Foods that are enriched, such as rice, bread, flour, pasta, and other refined grains, have levels of nutrients added that may bring the nutritional value closer to its state before the grain was processed. Four water-soluble B vitamins (thiamin, riboflavin, niacin, and folate) and the mineral iron are required by law to be added to refined grains.

## Fortified Foods Can Help Ensure Adequate Intake for Some Individuals

Fortified foods can be a valuable option for individuals whose diet falls short of some nutrients. For instance, an adult on a very low-kilocalorie diet may not be getting adequate vitamins and minerals from food and would benefit from fortified cereals. Strict vegans or individuals who are lactose intolerant and do not consume dairy products would benefit from drinking vitamin D- and calcium-fortified soy milk. Older adults who are inactive and thus have lower kilocalorie needs may choose fortified foods to add vitamin E to their limited dietary selections. Women in their childbearing years may look to folic acid-fortified cereals to help them meet their daily needs for this B vitamin.

## Fortified Foods Can Contribute to Health Risks

Because overconsumption of a vitamin or mineral can result in nutrient toxicity, individuals who consume high amounts of some fortified foods may be at risk for health problems. If a heavily fortified food, like some cereals, snack bars, and beverages, claims to contain “100% of the vitamins needed daily,” then eating several servings of the food or a combination of several fortified foods is similar to taking several multivitamin supplements. Individuals are more likely to overconsume vitamins from fortified foods than from whole foods.

Fortified foods can also do a disservice in the diet if they displace other vitamin- and mineral-rich foods. For example, a sugary orange drink that has

**fortified foods** Foods with added vitamins and minerals; fortified foods often contain nutrients that are not naturally present in the food or that are in higher amounts than the food contains naturally.

► **Figure 9.6 The Nutritional Value of Juices versus Fruit Drinks**

While both of these beverages are a good source of vitamin C, they are worlds apart in nutrient content. Pure orange juice (**a**) is also an excellent source of the mineral potassium and doesn't contain any added sugar. Orange drink (**b**) is basically sugar water fortified with vitamin C. A glass of it contains the equivalent of 8 teaspoons of added sugar.



vitamin C added to it should not replace vitamin C-rich orange juice. The beverages may have the same vitamin C content, but the orange-flavored drink doesn't provide the nutrients and phytochemicals that the juice does. As you can see in **Figure 9.6**, the orange drink is basically orange-flavored water sweetened heavily with added sugar and fortified with vitamin C. Even though the sugar content is similar for each beverage, the orange-flavored drink is sweetened with corn syrup, whereas the pure orange juice is sweetened naturally with sugars found in the orange.

Now that we've discussed the general characteristics of vitamins, let's survey the individual fat-soluble vitamins presented in **Table 9.4**. Before we begin, take the Self-Assessment to see if your diet is rich in foods that contain these important nutrients.

**LO 9.4: THE TAKE-HOME MESSAGE** A well-balanced diet rich in whole foods that provides adequate kilocalories can meet many individuals' daily vitamin needs. Proper handling, storage, and cooking of fresh foods can retain vitamins. Vitamins in foods can be destroyed or lost by exposure to air, water, UV light, changes in pH, and heat. Fortified foods can add nutrients to a low-kilocalorie diet. Fortified foods can also contribute to overconsumption of individual nutrients and may lead to toxicity.

**TABLE 9.4** Functions, Daily Needs, Food Sources, and Symptoms of Toxicity and Deficiency of the Fat-Soluble Vitamins

Fat-Soluble Vitamin	Metabolic Function	Daily Needs (19 years +)	Food Sources	Toxicity Symptoms/UL	Deficiency Symptoms
Vitamin A	Vision, protein synthesis, growth, immune function, bone health	Males: 900 $\mu\text{g}$ RAE/day Females: 700 $\mu\text{g}$ RAE/day	<ul style="list-style-type: none"> <li>■ Beef liver</li> <li>■ Fortified dairy products</li> </ul>	Compromised bone health; birth defects during pregnancy UL: 3,000 $\mu\text{g}/\text{day}$	Night blindness, xerophthalmia, keratinization
Beta-carotenes			<ul style="list-style-type: none"> <li>■ Sweet potatoes</li> <li>■ Carrots</li> <li>■ Squash</li> </ul>		
Vitamin D	Calcium balance, bone health, cell differentiation, immune system	Males and females: 15 $\mu\text{g}/\text{day}$	<ul style="list-style-type: none"> <li>■ Fatty fish such as salmon, tuna, sardines</li> <li>■ Fortified foods, such as dairy products, orange juice, and cereals</li> </ul>	Hypercalcemia UL: 100 $\mu\text{g}/\text{day}$	Rickets and osteomalacia
Vitamin E	Antioxidant, health of cell membranes, heart health	Males and females: 15 mg alpha-tocopherol/day	<ul style="list-style-type: none"> <li>■ Vegetable and seed oils</li> <li>■ Nuts, seeds</li> <li>■ Fortified cereals</li> <li>■ Green leafy vegetables</li> </ul>	Nerve problems, muscle weakness, and uncontrolled movement of body parts UL: 1,000 mg/day	Hemolysis of RBCs
Vitamin K	Carboxylation, blood clotting, and bone health	Males: 120 $\mu\text{g}/\text{day}$ Females: 90 $\mu\text{g}/\text{day}$	<ul style="list-style-type: none"> <li>■ Green leafy vegetables</li> <li>■ Soybeans</li> <li>■ Canola and soybean oils</li> <li>■ Beef liver</li> </ul>	None known UL: none established	Excessive bleeding

### Self-Assessment

## Are You Getting Enough Fat-Soluble Vitamins in Your Diet?

Take this brief self-assessment to see if your diet contains enough food sources of the four fat-soluble vitamins.

1. Do you eat at least 1 cup of deep yellow or orange vegetables, such as carrots and sweet potatoes, or dark green vegetables, such as spinach, every day?  
**Yes**  **No**
2. Do you consume at least 2 glasses (8 ounces each) of milk daily?  
**Yes**  **No**
3. Do you eat a tablespoon of vegetable oil, such as corn or olive oil, daily?  
(Tip: Salad dressings, unless they are fat free, count!)  
**Yes**  **No**
4. Do you eat at least 1 cup of leafy green vegetables in your salad and/or put lettuce in your sandwich every day?  
**Yes**  **No**

### Answers

If you answered yes to all four questions, your diet is close to meeting your fat-soluble vitamin needs! If you answered no to any one of the questions, your diet needs some fine-tuning. Deep orange and dark green vegetables are excellent sources of vitamin A, and milk is an excellent choice for vitamin D. Adding small amounts of vegetable oils to a vitamin K-rich leafy green salad improves the vitamin E content.

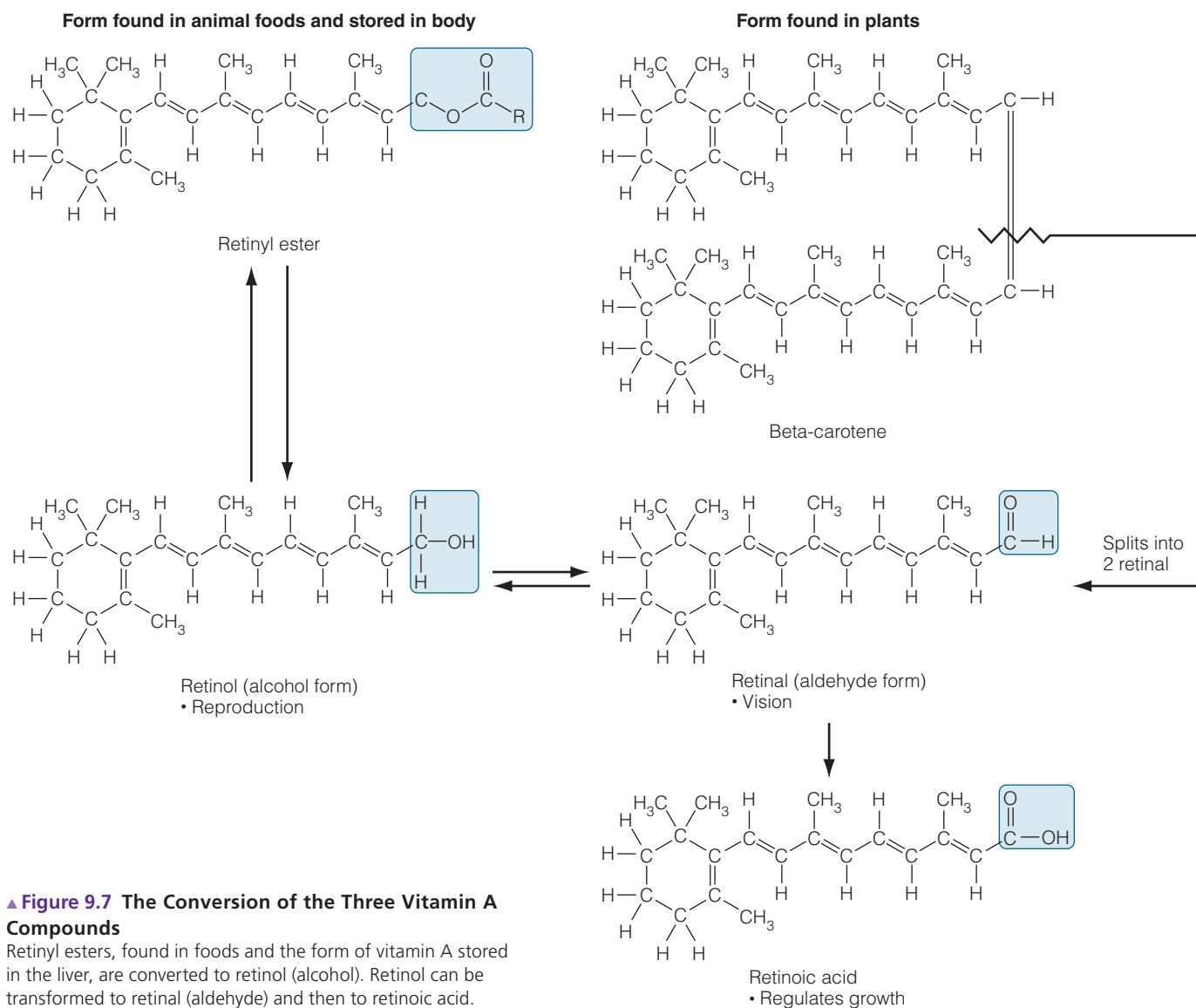
# Exploring Vitamin A

**LO 9.5** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin A.

## What Is Vitamin A?

The term vitamin A refers to a family of fat-soluble **retinoids** that include **retinol**, **retinal**, and **retinoic acid** (Figure 9.7). These compounds are similar in their chemical structure. They each contain a ring with a polyunsaturated fatty acid tail. Attached at the end of the fatty acid tail is either an alcohol group (retinol),

an aldehyde group (retinal), or an acid group (retinoic acid). Whereas retinol, retinal, and retinoic acid all participate in essential functions in the body, retinol, the alcohol form, is the most usable. In foods, vitamin A is found as retinol or as a **retinyl ester**, which has an ester group attached at the fatty acid tail. The body also stores vitamin A as a retinyl ester in the liver. Retinol can be reversibly converted to retinal, the aldehyde.



**▲ Figure 9.7 The Conversion of the Three Vitamin A Compounds**

Retinyl esters, found in foods and the form of vitamin A stored in the liver, are converted to retinol (alcohol). Retinol can be transformed to retinal (aldehyde) and then to retinoic acid. Beta-carotene is split during digestion to yield two molecules of retinal.

Retinal can be transformed into the acidic form called retinoic acid, but the process is irreversible. Retinoids are preformed vitamin A, which means they are in a form that the body can use immediately without first being activated. Preformed sources of vitamin A are found primarily in animal foods.

On the right side of Figure 9.7 is the structure of one of the family of provitamin A compounds called **carotenoids**. The provitamin A compounds found in plants are precursors to retinol in the body. Three such compounds—**beta-carotene** ( $\beta$ -carotene), beta-cryptoxanthin ( $\beta$ -cryptoxanthin), and alpha-carotene ( $\alpha$ -carotene)—are the most common carotenoids, the yellow-red pigments that give carrots, butternut squash, and cantaloupe their vibrant, deep orange color. For vegans, these carotenoids are the only dietary source of vitamin A. Almost 25 to 35 percent of the dietary vitamin A consumed by adults in the United States comes from carotenoids, especially beta-carotene.<sup>21</sup>

### Vitamin A Absorption and Transport

All forms of preformed vitamin A are absorbed by active transport in the small intestine with the help of bile salts and micelles. The rate of absorption of preformed vitamin A is high, ranging from 70 to 90 percent as long as the diet contains some fat. Beta-carotene, in contrast, is absorbed via passive diffusion at a much lower rate of 5 percent to up to 60 percent.<sup>22</sup> Fat in the diet enhances the absorption of vitamin A, but diarrhea or an infection in the GI tract reduces vitamin A absorption. Beta-carotene absorption is reduced with high fiber intakes and improved when foods are cooked. For example, the amount of beta-carotene absorbed from cooked carrots is much higher than that from raw carrots.

Most forms of vitamin A are packaged as a chylomicron along with other dietary lipids, and absorbed into the lymph fluid. Retinoic acid doesn't need a chylomicron, but rather is attached to a protein called albumin and absorbed into the portal vein. Carotenes are converted to vitamin A in the intestine before absorption.



Vitamin A is stored in the liver until needed by the body. Retinol binding protein transports the retinol from storage through the bloodstream to the receptor sites located on the cells.

Vitamin A is difficult to excrete from the body. When the liver becomes saturated with vitamin A, some is excreted through the bile to prevent toxicity.

### Metabolic Functions of Vitamin A

Each form of retinoid plays a specific role in the body. Retinal (the aldehyde form) participates in vision. The hormone-like action of retinoic acid (the acid form) is essential for growth and development of cells, including bone development. Retinol (the alcohol form) supports reproduction and a healthy immune system. In addition to these critical roles, vitamin A may help prevent cancer.

**retinoids** The term used to describe the family of preformed vitamin A compounds.

**retinol** The alcohol form of preformed vitamin A.

**retinal** The aldehyde form of preformed vitamin A.

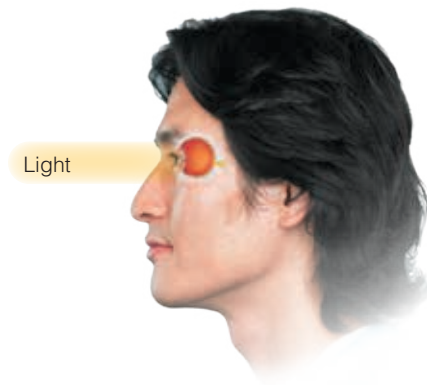
**retinoic acid** The acid form of preformed vitamin A.

**retinyl ester** The ester form of preformed vitamin A found in foods and stored in the body.

**carotenoids** The family of provitamin compounds that includes beta-carotene. Also a group of yellow, red, and orange pigments found in plants; three of them are precursors to vitamin A. The body stores carotenoids in the liver and in fat cells.

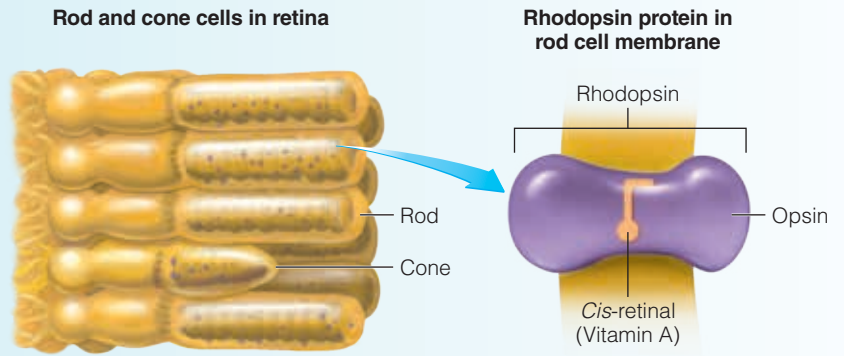
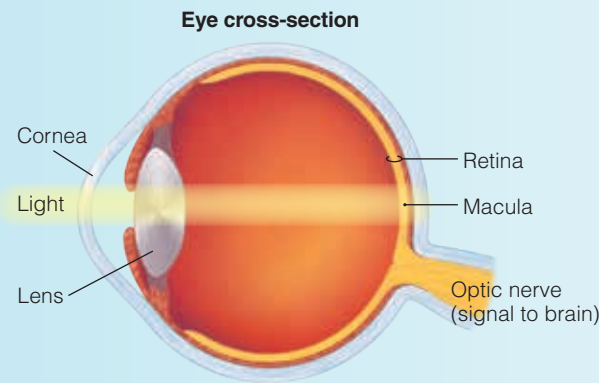
**beta-carotene** One of the provitamin A carotenoids.

*continued*



Vitamin A is a component of two light-sensitive proteins, rhodopsin and iodopsin, that are essential for vision. Here we examine rhodopsin's role in vision. Although the breakdown of iodopsin is similar, rhodopsin is more sensitive to light than iodopsin and is more likely to become bleached.

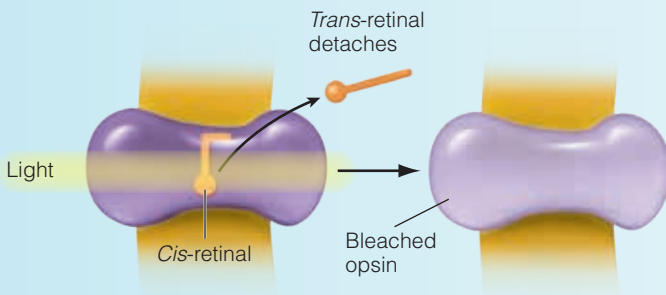
EYE STRUCTURE



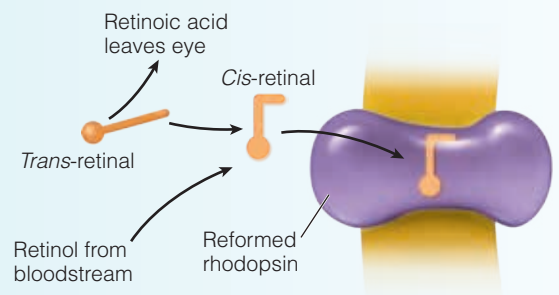
**1** After light enters your eye through the cornea, it travels to the back of your eye to the macula, which is located in the retina. The macula allows you to see fine details and things that are straight in front of you.

**2** Inside the retina are two types of light-absorbing cells, rods and cones. Rods are responsible for black-and-white vision and contain the protein rhodopsin. Cones are responsible for color vision and contain the protein iodopsin. Both proteins contain vitamin A in the form of *cis*-retinal.

EFFECT OF LIGHT ON RHODOPSIN



**1** As light interacts with rhodopsin, it transforms the *cis*-retinal to *trans*-retinal, separating it from the protein opsin. This process, called bleaching, causes a cascade of events that transmits visual messages through the optic nerve to the brain.



**2** *Trans*-retinal is converted back to *cis*-retinal and binds with opsin to reform rhodopsin, regenerating the eye's light-absorbing capabilities. Some *trans*-retinal is irreversibly converted to retinoic acid and leaves the eye tissue. Retinol from the blood is converted to retinal to replenish what is lost.

## Vitamin A in Vision

One of the most well-known functions of vitamin A is the role it plays in vision. Light that passes into the eyes and hits the retina is translated into visual images with the help of two vitamin A-dependent proteins, **rhodopsin** and **iodopsin**. These proteins are found in the tips of light-absorbing cells in the retina called **rods** and **cones**, respectively. Rhodopsin, which contains *cis*-retinal (the aldehyde form of vitamin A), absorbs the light entering the rods. The light changes the shape of *cis*-retinal to *trans*-retinal, detaching it from the protein opsin. This change in shape is referred to as **bleaching**. When rhodopsin is bleached, it transmits a signal through the optic nerve to the part of the brain involved in vision.

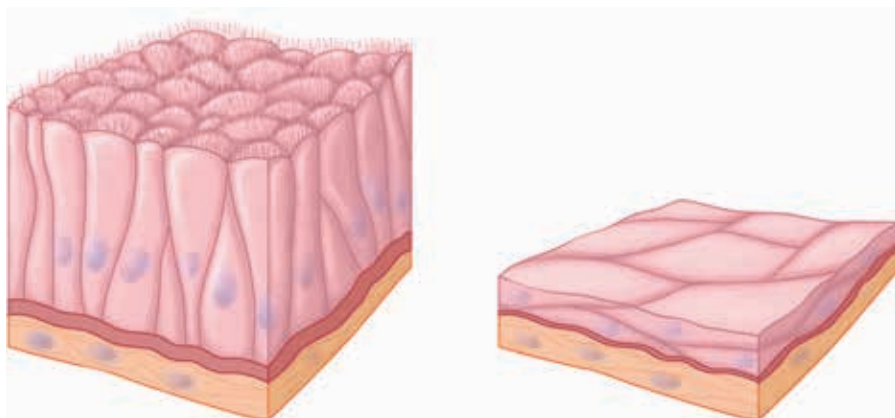
After rhodopsin is bleached, most of the *trans*-retinal returns to its *cis* shape. This form is now able to bind with opsin, which regenerates rhodopsin and the eye's light-absorbing capabilities. This reaction is illustrated in **Focus Figure 9.8**.

Walking into a dark building after being in the sun without sunglasses may require taking time to adjust to the dimmer light. This adjustment period occurs because the reformation of *trans*- to *cis*-retinal takes time. Fortunately, there is a pool of vitamin A in the retina to help with this conversion.

In order for vitamin A to participate in the visual cycle, it must first be metabolized in the retina. Retinol attaches to **retinol binding protein (RBP)** and is transported through the blood to the eye. Once inside the retina, retinol is converted to retinal before moving into the photoreceptor cells of the rods.

## Vitamin A in Protein Synthesis and Cell Differentiation

Vitamin A is important for keeping the epithelial cells moist and structurally sound. **Epithelial cells** in the skin protect the body from damage from the sun. The epithelial cells that line the lungs, nose, eyes, and urinary tract are round, moist, secrete a thick mucus, and are lined with microscopic hairlike structures called cilia. The mucus coats the cells and protects them from bacteria and viruses that can infiltrate the body and cause infection. In the respiratory



**a** Healthy epithelial cells are rounded, moist, and contain mucus-secreting cells and cilia lining the surface.

**b** A vitamin A deficiency can lead to unhealthy epithelial cells that are flat, hard, lacking cilia, and unable to produce mucus.

▲ **Figure 9.9** Healthy and Vitamin A-Deficient Epithelial Cells

tract, the cilia sweep away dust and germs trapped in the mucus. Vitamin A deficiency can cause these cells to become flattened, hard, and unable to produce mucus (**Figure 9.9**). Vitamin A also works with the immune system to create white blood cells (*lymphocytes*) and antibodies that fight foreign invaders should they enter the bloodstream.

Vitamin A stimulates **cell division** and **cell differentiation** of the epithelial cells as they grow and develop. Retinoic acid prompts gene expression, a process that uses genetic information to make the proteins needed to begin cell division. As cells divide and cluster together, changes occur that cause them to become different from their initiating cells. This differentiation determines what cells become in the body. For immature skin cells to differentiate into mature skin cells, for example, vitamin A acts as a signal to turn on the genes to create the proteins needed to make healthy skin.

This role of vitamin A is one reason dermatologists prescribe retinoid-containing medications, such as Retin-A or tretinoin, to treat acne (**Figure 9.10**). Retin-A is a topical medication that works by enhancing the turnover of skin cells and inhibiting the formation of acne.<sup>23</sup> Accutane, or isotretinoin, is a medication taken orally that manipulates cell differentiation through gene expression of acne-producing cells to alter their development in the skin.<sup>24</sup>

## Vitamin A in Growth and Reproduction

In addition to its role in cell differentiation, vitamin A plays several critical roles in growth and reproduction. Both retinol and retinoic acid participate in growth, although the mechanism is still unknown. What is known is that without vitamin A, embryonic and fetal development is impaired, especially in the development of the limbs, heart, eyes, and ears.<sup>25</sup>

**rhodopsin** A compound found in the rods of the eye that is needed for night vision. It is comprised of *cis*-retinal and the protein opsin.

**iodopsin** The compound found in the cones of the eye that is needed for color vision.

**rods** Light-absorbing cells responsible for black-and-white vision and night vision.

**cones** Light-absorbing cells responsible for color vision.

**bleaching** When light enters the eye and interacts with rhodopsin, splitting it into *trans*-retinal and opsin.

**retinol binding protein (RBP)** A protein made in the liver that transports retinol through the blood to the cells.

**epithelial cells** Cells that line the cavities in the body and cover flat surfaces such as the skin.

**cell division** The process of dividing one cell into two separate cells with the same genetic material.

**cell differentiation** The process of a less specialized immature cell becoming a specialized mature cell.

*continued*



▲ **Figure 9.10** Vitamin A Derivatives Can Help Treat Acne

Children fail to grow when their diets lack vitamin A, but when either retinol or retinoic acid are given, growth is enhanced.

Retinol, but not retinoic acid, is essential for reproduction. Normal levels of retinol are required for sperm production in males and normal menstrual cycles in females.

#### Vitamin A and Bone Health

All three forms of vitamin A may help regulate the cells involved in bone growth. Too much vitamin A stimulates bone resorption—breaking down bone—and inhibits bone formation, which can negatively affect healthy bones and may be a risk factor for developing osteoporosis.<sup>26</sup> Both excessive intake and insufficient intake of vitamin A have negative impacts on bone density. Research reports that retinol intakes of less than 510  $\mu\text{g}$  RAE (1,700 IU) and more than 2,030  $\mu\text{g}$  RAE (6,700 IU) per day may increase fracture risk (beta-carotene has no effect).<sup>27</sup> A diet closer to 600 to 850  $\mu\text{g}$  RAE (2,000 to 2,800 IU) per day of vitamin A is most likely to improve the bone mineral density of elderly men and women.<sup>28</sup>

#### Carotenoids as Antioxidants

Provitamin A compounds are able to quench free radical reactions and

**retinol activity equivalents (RAE)** The unit of measure used to describe the total amount of all forms of preformed vitamin A and provitamin A carotenoids in food.

**international units (IU)** A system of measurement of a biologically active ingredient such as a vitamin that produces a certain effect.



The carotenoid lycopene, found in tomatoes and tomato products, functions as an antioxidant in the body.

protect cells from damage. Lycopene, which is the form of carotenoid that gives red tomatoes their dark red color, is especially effective in quenching free radicals. Two other carotenoids, lutein and zeaxanthin (found in corn and dark green leafy vegetables), protect the eyes from free radical damage.<sup>29</sup>

#### Daily Needs for Vitamin A

The Recommended Dietary Allowance (RDA) for vitamin A is based on maintaining sufficient storage of the vitamin in the liver. Vitamin A in foods

and supplements can be measured in two ways: in micrograms ( $\mu\text{g}$ ) of **retinol activity equivalents (RAE)** and in **international units (IU)**.

Because retinol is the most usable form of vitamin A and because provitamin A carotenoids can be converted to retinol, the preferred way to measure vitamin A in foods is to include all forms as RAE. However, some vitamin supplements and food labels show the older measure, IU, on their products. (Note: 1  $\mu\text{g}$  RAE is the equivalent of 3.3 IU.) The Calculation Corner provides more detail on the conversion from IU to micrograms RAE.

Adult females need 700  $\mu\text{g}$  RAE (2,310 IU) of vitamin A daily, whereas adult males need 900  $\mu\text{g}$  RAE (3,000 IU) daily. This is the average amount needed to maintain adequate stores in the body.<sup>30</sup> The daily recommendation for beta-carotene hasn't been established, but the Institute of Medicine suggests consuming 3 to 6 milligrams of beta-carotene every day from foods.<sup>31</sup> This can easily be obtained by consuming five or more servings of fruits and vegetables. This amount of beta-carotene also provides about 50 percent of the recommended vitamin A intake. Hence, eating beta-carotene-rich foods adds not only antioxidants to the diet, but also vitamin A.

Vegetarians who eat no animal foods, including vitamin A-rich milk and eggs, need to be especially conscientious about eating carotenoids and beta-carotene-rich foods to meet their daily vitamin A needs.

#### Food Sources of Vitamin A

Milk, cereals, cheese, egg yolks, and organ meats (such as liver) are the most popular sources of preformed vitamin A in the U.S. diet. Liver is especially abundant in vitamin A but can cause toxicity if consumed too often. For example, 1 ounce of beef liver contains 2 milligrams of retinol, or more than 100 percent of the RDA of vitamin A for adults.

Carrots, spinach, and sweet potatoes are American favorites for provitamin A carotenoids, including beta-carotene. Similar to vitamin A and other fat-soluble vitamins, carotenoids are absorbed more efficiently when fat is



## Calculation Corner

### Converting International Units for Vitamin A

International units (IU) are a system of measurement of the biologic activity or potency of a substance, such as a vitamin, that produces a particular effect. Because each vitamin differs in potency per milligram, the conversion factors from IU to milligrams also differ.

(a) Vitamin A is measured in retinol activity equivalents, or RAE. Use the following conversion factors to determine the micrograms retinol activity equivalents ( $\mu\text{g}$  RAE) found in 1 IU:

**1 IU retinol is the biological equivalent of 0.3  $\mu\text{g}$  retinol or 0.3  $\mu\text{g}$  RAE or 0.6  $\mu\text{g}$  beta-carotene**

**Example:** A vitamin supplement contains 25,000 IU of retinol. How many  $\mu\text{g}$  RAE does it contain?

**Answer:**  $0.3 \mu\text{g} \times 25,000 \text{ IU} = 7,500 \mu\text{g}$  RAE

(b) The requirements for vitamin A are expressed as RAE. To determine the amount of RAE in micrograms in a meal, you have to convert the various forms of vitamin A equivalents. For example:

**1  $\mu\text{g}$  RAE = 1  $\mu\text{g}$  retinol and 12  $\mu\text{g}$  beta-carotene.**

The first step is to divide the amount of beta-carotene by 12 to convert to RAE. Next, add that number to the preformed vitamin A in the meal.

**Example:** If a meal contains 500  $\mu\text{g}$  retinol and 1,800  $\mu\text{g}$  beta-carotene, how many  $\mu\text{g}$  RAE does the meal contain?

**Answer:**  $500 \mu\text{g}$  retinol +  $(1,800 \mu\text{g}$  beta-carotene  $\div$  12) = 650  $\mu\text{g}$  RAE

present in the GI tract. Adding as little as 1 tablespoon of vegetable oil to the diet daily can increase the absorption of carotenoids by as much as 25 percent.<sup>32</sup>

**Figure 9.11** shows the vitamin A content in  $\mu\text{g}$  RAE, and includes both retinoid- and carotenoid-rich sources.

### Vitamin A Toxicity

Vitamin A toxicity is caused by ingesting too much preformed vitamin A, not carotenoids. Consuming more than 15,000  $\mu\text{g}$  of preformed vitamin A at one time or over a short period of time can lead to nausea, vomiting, headaches, dizziness, and blurred vision. Overconsumption of preformed vitamin A is usually due to taking supplements and is less likely to occur from

overeating vitamin A in foods. Vitamin A supplements do not improve acne. Only specially formulated vitamin A-containing drugs such as Retin-A or Accutane are effective for preventing



and treating acne. Because 90 percent of vitamin A is stored in the liver, chronic daily consumption of more than 30,000 micrograms of preformed vitamin A (more than 300 times the RDA for adults) can lead to **hypervitaminosis A** (*hyper* = over, *osis* = condition), an extremely serious condition in which the liver accumulates toxic levels of vitamin A. Hypervitaminosis A can lead to deterioration and scarring of the liver and even death. To prevent toxicity, the tolerable upper intake level (UL) of preformed vitamin A for adults has been set at 3,000  $\mu\text{g}$  (10,000 IU) daily.<sup>33</sup>

Higher intake of preformed vitamin A during pregnancy, particularly in the first trimester, can cause birth defects in the face and skull and damage the child's central nervous system. All women of childbearing age who are using retinoids for acne or other skin conditions should take the proper steps to avoid becoming pregnant.<sup>34</sup>

### Vitamin A and Osteoporosis

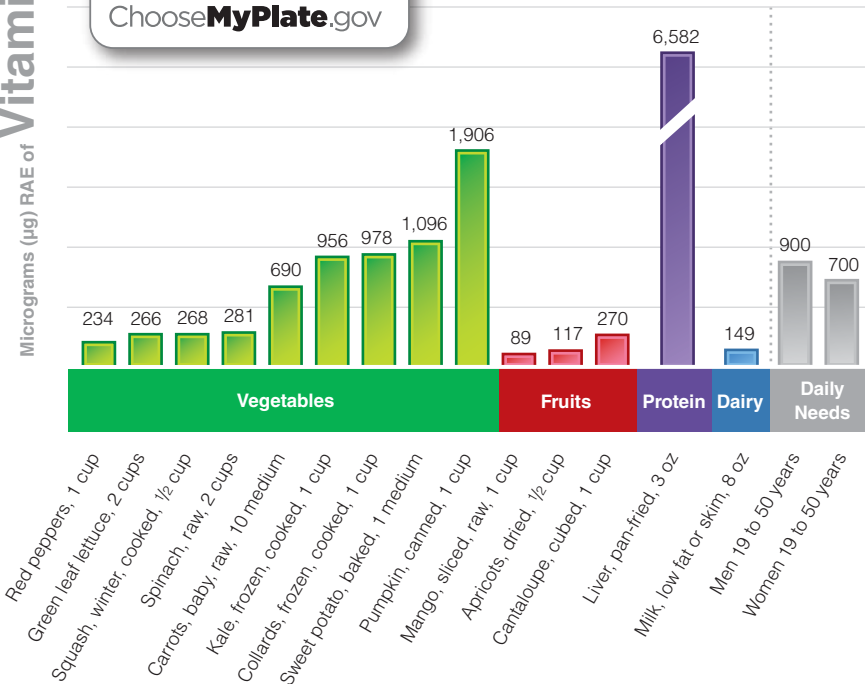
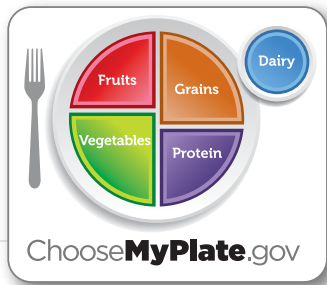
While vitamin A is needed for bone health, some research suggests that consuming too much may lead to **osteoporosis**, which in turn increases the risk of fractures. Osteoporosis-related hip fractures appear to be prevalent in Swedes and Norwegians, who tend to have high consumption of vitamin A-rich cod-liver oil and specialty dairy products that have been heavily fortified with vitamin A.<sup>35</sup>

Additional studies involving both women and men have shown similar associations between high vitamin A intake and increased risk of fractures. As little as 1,500 micrograms (3,000 IU) of retinol, which is slightly more than twice the RDA recommended for women, can be unhealthy for bones.<sup>36</sup> This amount can be quickly reached when taking a supplement and eating a diet rich in vitamin A-fortified foods. The Daily Value (DV) for vitamin A used in the Nutrition Facts panel on food labels is 5,000 IU.

**hypervitaminosis A** The serious condition in which the liver accumulates toxic levels of vitamin A.

**osteoporosis** A condition in which bones become brittle and porous, making them fragile due to depletion of calcium and bone proteins.

*continued*



▲ Figure 9.11 Vitamin A Content in Selected Foods

Recall from Chapter 2 that the DVs used on food labels are based on older recommendations, not the current recommended intakes. Consuming a serving of a food that provides a large percentage of the DV for vitamin A may mean consuming more than the upper limit.

**Overconsuming Carotenoids**

The upper levels apply only to preformed vitamin A from foods, fortified foods, and supplements. Provitamin A carotenoids in foods are not toxic and do not pose serious health problems. The body has a built-in safeguard to prevent provitamin A carotenoids from contributing to vitamin A toxicity, birth defects, or bone damage. If individuals consume more carotenoids than necessary to meet vitamin A needs, the body decreases their conversion to retinol. Extra

**carotenodermia** The presence of excess carotene in the blood, resulting in an orange color to the skin due to excessive intake of carrots or other carotene-rich vegetables.

amounts of carotenoids are stored in the liver and in the subcutaneous fat.

Eating too many carotenoids can, however, cause the nonthreatening

condition **carotenodermia** (*carotene* = carotene, *dermia* = skin), which results in orange-tinged skin, particularly in the palms of the hands and soles of the feet (Figure 9.12). Because these areas are cushioned with fat, they become more concentrated with the pigments and more visibly orange in color (right hand in photo). Cutting back on carotenoid-rich foods reverses carotenodermia.

**Overconsuming Beta-Carotene Supplements**

Although a diet abundant in carotenoid-rich foods is not dangerous, carotenoid supplements may be. In a study of adult male smokers, those who consumed beta-carotene supplements were shown to have significantly higher rates of lung cancer than those who didn't take the supplements.<sup>37</sup> While some earlier studies suggested alcohol may contribute to the effects of beta-carotene supplements on lung cancer risk, more recent research shows consistent evidence that beta-carotene supplements alone increase a smoker's risk of lung cancer and mortality.<sup>38</sup>

**Vitamin A Deficiency**

Vitamin A deficiency is uncommon in the United States but is a serious problem in developing countries. Signs of vitamin A deficiency, such as vision problems and increased infections, begin to develop after the liver stores of vitamin A are depleted.



▲ Figure 9.12 Carotenodermia  
The hand on the right exhibits the orange-tinged skin characteristic of carotenodermia.

## TABLE TIPS

## Score an A

Dunk baby carrots in a tablespoon of low-fat ranch dressing for a healthy snack.

Keep dried apricots in your backpack for a sweet treat.

Add baby spinach to a lunchtime salad.

Bake sweet potatoes rather than white potatoes at dinner.

Buy frozen mango chunks for a ready-to-thaw beta-carotene-rich addition to cottage cheese or yogurt.

**Vitamin A and Blindness**

If the diet is deficient in vitamin A, an insufficient pool of retinal in the retina can result in **night blindness**, or the inability to see in the dark. Individuals with night blindness have difficulty seeing at dusk, because they can't adjust from daylight to dark, and may not be able to drive a car during this time of the day. If diagnosed early, night blindness can be reversed by taking vitamin A.

A prolonged vitamin A deficiency can lead to complete blindness. A severe

deficiency of vitamin A results in dryness and permanent damage to the cornea, a condition called **xerophthalmia** (*xero* = dry, *ophthalm* = eye). Up to 10 million children, mostly in developing countries, suffer from xerophthalmia annually, and as many as 500,000 of these children go blind every year because they don't consume enough vitamin A.<sup>39</sup> Vitamin A deficiency is the number-one cause of preventable blindness in children.<sup>40</sup>

**Vitamin A and Immunity**

**Keratinization** of the epithelial tissues throughout the body occurs with vitamin A deficiency. The epithelial cells secrete keratin, which creates a hard, dry epithelial cell. Such a cell is unable to secrete the protective layer of mucus. Without mucus, the cells are unable to function properly, and they become

**night blindness** The inability to see in dim light or at night due to a deficiency of retinal in the retina.

**xerophthalmia** Permanent damage to the cornea causing blindness due to a prolonged vitamin A deficiency.

**keratinization** The accumulation of the protein keratin in epithelial cells, forming hard, dry cells unable to secrete mucus due to vitamin A deficiency.

susceptible to infection, especially in the nasal passages and the urinary and respiratory tracts. Keratinization also occurs in the skin.

**LO 9.5: THE TAKE-HOME MESSAGE**

Vitamin A refers to a family of retinoids, which are essential for cell growth and development, reproduction, and a healthy immune system. Retinol is the most usable form of vitamin A in the body; retinal is essential for eye health and vision and retinoic acid regulates growth. Retinyl ester is found in foods and the form of vitamin A stored in the liver. Vitamin A is not excreted. Three carotenoids, including beta-carotene, are provitamins that must be converted to vitamin A to be used in the body. Most of the preformed dietary vitamin A, measured as retinol activity equivalents (RAE), is absorbed. Preformed vitamin A is found in milk, cereals, cheese, egg yolks, and organ meats, especially liver. Provitamin A is found in carrots, spinach, and sweet potatoes. Vitamin A deficiencies can result in vision problems and increased infections. Toxic amounts of vitamin A can compromise bone health and lead to birth defects during pregnancy.

## Exploring Vitamin D

**LO 9.6** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin D.

**What Is Vitamin D?**

Vitamin D (**calciferol**) is called the “sunshine vitamin” because it is derived from the reaction between ultraviolet (UV) rays and a form of cholesterol found in the skin. Exposure to sunlight can synthesize up to 100 percent of the vitamin D the body needs.<sup>41</sup> For this reason, vitamin D is often considered a

conditionally essential nutrient. However, it still fits the criteria of a vitamin because a deficiency of this compound can cause symptoms that are cured once adequate intake is restored. Because of its function, vitamin D is also considered a **prohormone**, an inactive precursor, that is activated inside the body. Vitamin D is found in two forms. **Cholecalciferol** or **vitamin D<sub>3</sub>** is the form produced in the skin and found in animal foods. **Ergocalciferol** or **vitamin D<sub>2</sub>** is found in plants and dietary supplements.

Ergocalciferol and cholecalciferol differ chemically in the structure of their side chains, as illustrated in **Figure 9.13**.

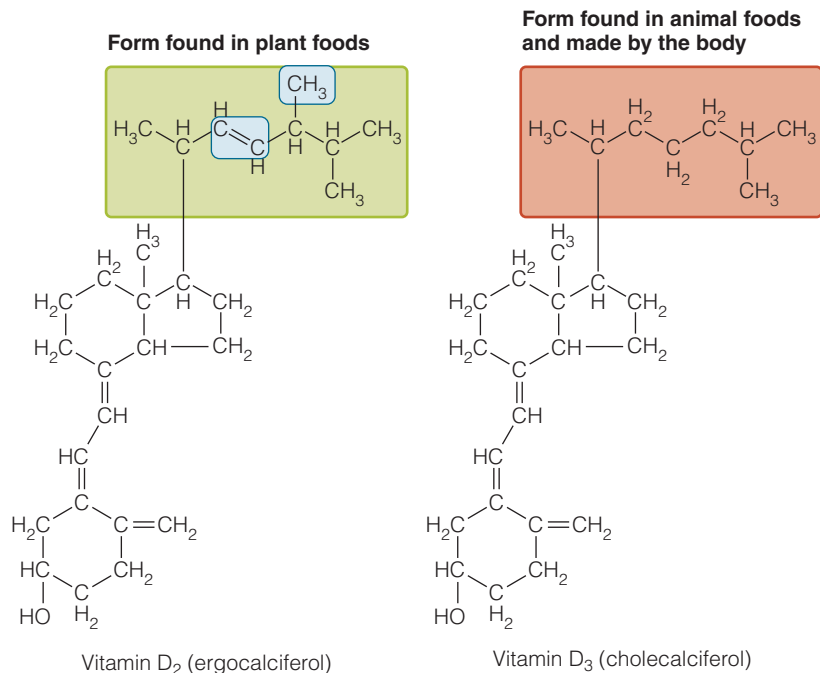
**calciferol** The family of vitamin D compounds.

**prohormone** A physiologically inactive precursor to a hormone.

**cholecalciferol (vitamin D<sub>3</sub>)** The form of vitamin D found in animal foods and formed from precalciferol in the skin. This is the form absorbed through the skin into the blood.

**ergocalciferol (vitamin D<sub>2</sub>)** The form of vitamin D found in plants and dietary supplements.

*continued*



▲ **Figure 9.13 The Chemical Structure of Vitamin D**

Vitamin D is found in the ergocalciferol (vitamin D<sub>2</sub>) form in plants and the cholecalciferol (vitamin D<sub>3</sub>) form in animal foods.

Ergocalciferol or D<sub>2</sub> contains a double bond in the side chain between carbons 22 and 23 and a methyl group on carbon 24. Cholecalciferol or D<sub>3</sub> has a single bond in the place of the double bond and a hydrogen on carbon 24. Even though their structure is different, they still function in the body.

**7-dehydrocholesterol (provitamin D<sub>3</sub>)** The compound in the skin that is converted to precalciferol by UV light from the sun; synthesized in the liver from cholesterol.

**provitamin D<sub>3</sub> (precalciferol)** The compound that is formed from 7-dehydrocholesterol when sunlight hits the skin.

**vitamin D<sub>3</sub> binding protein (DBP)** A protein made in the liver that transports vitamin D through the blood to the cells.

**25-hydroxycholecalciferol** The compound formed in the liver by adding a hydroxyl group to the 25th carbon of cholecalciferol.

**1,25-dihydroxycholecalciferol** The active form of vitamin D, also called calcitriol, that is formed in the kidney by adding a second hydroxyl group on the first carbon to 25-dihydroxycholecalciferol.

**calcitriol** The active form of vitamin D, also referred to as 1,25-dihydroxycholecalciferol.

**parathyroid hormone (PTH)** The hormone secreted from the parathyroid glands that activates vitamin D formation in the kidney.

### Vitamin D Metabolism

Whether from food or sunlight, vitamin D enters the body in an inactive form. In the skin, a compound called **7-dehydrocholesterol** or **provitamin D<sub>3</sub>** (which is made in the liver from cholesterol) is converted to **provitamin D<sub>3</sub>** or **precalciferol** when UV rays hit the skin (see **Figure 9.14**). Precalciferol is changed to cholecalciferol, which slowly diffuses through the skin into the blood attached to a protein called **vitamin D<sub>3</sub> binding protein (DBP)**. Cholecalciferol is then taken up by the liver to begin the activation process.

Once cholecalciferol reaches the liver, a two-step activation process begins. First, liver enzymes add a hydroxyl group on the twenty-fifth carbon of cholecalciferol, forming **25-hydroxycholecalciferol** (see step 3 in **Figure 9.12**). This newly formed compound circulates in the blood transported by DBP. In the kidneys a second hydroxyl group is added on the first carbon, forming **1,25-dihydroxycholecalciferol**. This is the active form of vitamin D, also called **calcitriol** (see step 4 in **Figure 9.14**), that leaves the kidney and enters the cells.

Vitamin D<sub>2</sub> and vitamin D<sub>3</sub> consumed in the diet are absorbed into



the small intestine as part of a micelle along with other dietary lipids. Each is repackaged into a chylomicron and circulates through the lymph system before arriving at the liver for storage.

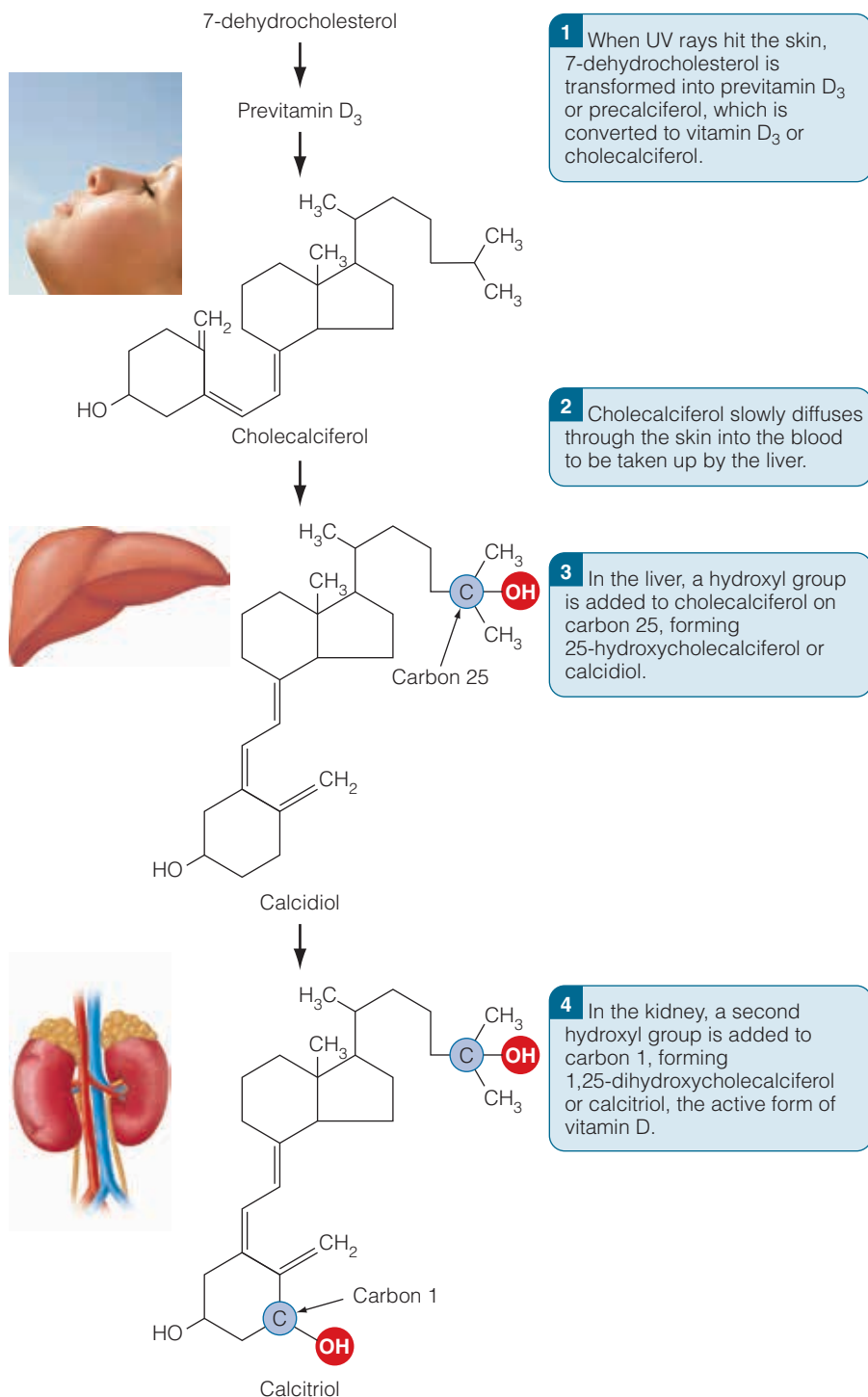
Blood calcium levels influence the metabolism of vitamin D (see **Figure 9.15**). When blood calcium levels drop, **parathyroid hormone (PTH)** is secreted from the parathyroid gland and travels to the kidney to activate vitamin D or 25-hydroxycholecalciferol. This boost in the levels of active vitamin D enhances the intestinal absorption of calcium, increases the amount of calcium reabsorbed through the kidneys, and mobilizes calcium from the bone. The result is that blood calcium levels return to normal.

### Metabolic Functions of Vitamin D

Vitamin D regulates two important bone minerals, calcium and phosphorus. Vitamin D also participates in several other functions, including cell differentiation, stimulation of the immune system, blood pressure regulation, and insulin secretion.

### The Role of Vitamin D in Bone Growth

Calcitriol functions as a hormone to stimulate the absorption of calcium and phosphorus in the intestinal tract. It also functions to maintain a healthy ratio of



▲ **Figure 9.14** The Metabolism of Vitamin D

calcium and phosphorus levels in the blood, which promotes uptake of these two minerals in the bone. As calcium levels in the blood rise, more calcium is deposited in the bone. Vitamin D controls the interaction between *osteoblasts* and *osteoclasts*, the two specialized bone cells involved in remodeling bone.

Because of its role in regulating calcium and phosphorus, vitamin D helps to build and maintain bone mass.

#### Vitamin D Helps Regulate the Growth of Cells

Research studies have shown that the incidence of breast, colon, and prostate

cancers is greater among individuals living in sun-poor areas of the world than among those living in sunny regions.<sup>42</sup> Vitamin D helps regulate the growth and differentiation of certain cells. Researchers speculate that a deficiency of vitamin D in the body may reduce the proliferation of healthy cells and allow cancer cells to flourish.<sup>43</sup>

#### Vitamin D May Regulate the Immune System

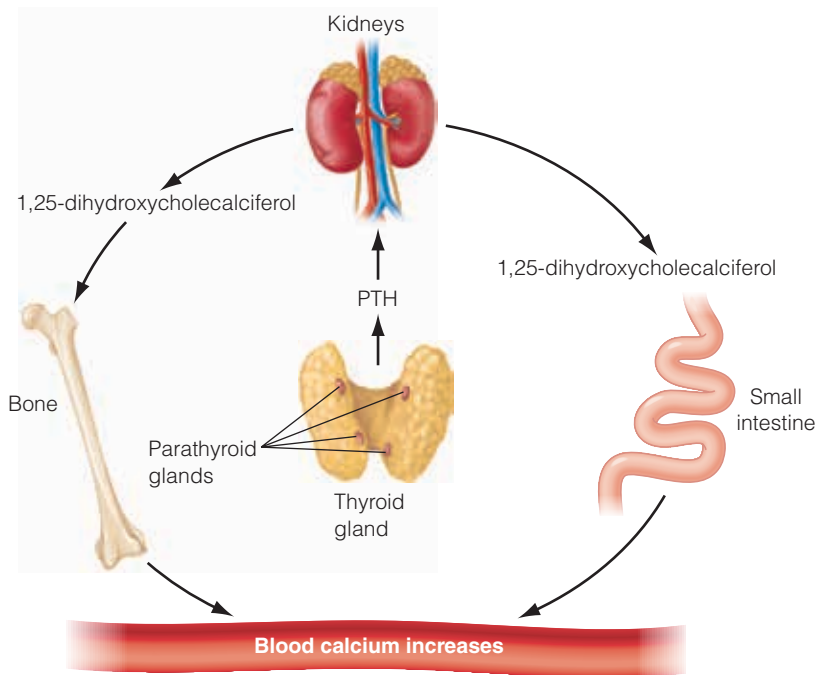
The active form of vitamin D may reduce the risk of developing certain autoimmune disorders, such as inflammatory bowel syndrome (which is not the same thing as irritable bowel syndrome). Most cells in the immune system, such as T cells and macrophages, have a receptor for vitamin D. The role of vitamin D in immune system function is still not understood, but some researchers suggest that it may affect the function of the immune system and inhibit the development of autoimmunity.<sup>44</sup>

Vitamin D may also help reduce the risk of type 1 diabetes mellitus by up to 50 percent in adults.<sup>45</sup> Type 1 diabetes mellitus is an autoimmune disease in which the insulin-producing cells of the pancreas are attacked and destroyed by the body's own immune system. A large prospective study of military personnel reported that the risk of developing type 1 diabetes mellitus was highest when blood levels of 25-hydroxycholecalciferol fell below 20 percent of normal.<sup>46</sup> But no change in risk was noted above 20 percent of normal. The researchers proposed that low levels of 25-hydroxycholecalciferol may contribute to the autoimmune process. Although not an autoimmune disorder, similar results have been reported that individuals who have been diagnosed with type 2 diabetes mellitus also have low blood levels of vitamin D.<sup>47</sup> One study revealed that insulin resistance, or the inability of the cells to use insulin in the blood, was more pronounced in people with low levels of vitamin D in the blood, perhaps due to a genetic polymorphism.<sup>48</sup>

#### Vitamin D May Help Regulate Blood Pressure

Vitamin D reduces hypertension by acting on the gene that regulates the

*continued*



▲ **Figure 9.15** The Relationship of Blood Calcium to Parathyroid Hormone and Vitamin D

Low blood levels of calcium stimulate the parathyroid glands to release parathyroid hormone (PTH). PTH stimulates the kidneys to increase the amount of active vitamin D, which in turn increases calcium absorption from the intestines, stimulates the reabsorption of calcium through the kidneys, and releases calcium from the bone. These actions help raise blood calcium back to normal levels.

renin-angiotensin system, the system that regulates blood pressure.<sup>49</sup> Vitamin D appears to reduce the activity of this gene, which results in less renin being produced. Renin is an enzyme that balances sodium and potassium levels in the blood, which controls blood pressure (we discuss the relationship of renin to hypertension in Chapter 11). Further evidence for the role of vitamin D in regulating blood pressure is the fact that blood pressure readings tend to be higher during the winter, when people are exposed to less sunlight, than in the summer. People with mild hypertension may be able to lower their blood pressure by spending a little time in the sun.

### Daily Needs for Vitamin D

Not everyone can rely on the sun to meet his or her daily vitamin D needs. There are a number of limiting factors that influence vitamin D synthesis from sun:



melanin content of the skin, whether it is cloudy or smoggy, and use of sunscreen. There is new positive evidence, however, that even during the winter months sun exposure is strong enough to synthesize adequate vitamin D in the skin.<sup>50</sup>

Individuals with darker skin, such as African-Americans, have a higher amount of the skin pigment melanin, which reduces vitamin D production from sunlight. To derive the same amount of vitamin D as people with less melanin, these individuals need a longer period of sun exposure. A cloudy day can reduce the synthesis of vitamin D by 50 percent, and by 60 percent if it is smoggy or you sit in the shade.<sup>51</sup> And the use of sunscreen

## Calculation Corner

### Converting International Units for Vitamin D

Vitamin D content in dietary supplements and fortified foods is often listed in international units (IU), while vitamin D found in food is measured in  $\mu\text{g}$  cholecalciferol. Use the following conversion factor to determine the  $\mu\text{g}$  cholecalciferol in 1 IU.

**1 IU of cholecalciferol is equivalent to 0.025  $\mu\text{g}$  cholecalciferol**

**Example:** A vitamin supplement contains 1,000 IU of cholecalciferol. How many  $\mu\text{g}$  cholecalciferol does it contain?

**Answer:**  $0.025 \mu\text{g}$  cholecalciferol  $\times$  1,000 IU = 25  $\mu\text{g}$  cholecalciferol

Scan this QR code with your mobile device to access practice math activities. You can also access the activities in **MasteringNutrition™**.



can block the body's ability to synthesize vitamin D by more than 95 percent.<sup>52</sup> Because of these variables involving sun exposure, daily vitamin D needs are based on the amount in foods and are not based on the synthesis of vitamin D in the skin from exposure to sunlight.

The RDA for adults is 15 to 20 micrograms (600 to 800 IU) of vitamin D daily, depending on your age. These recommendations are listed in both micrograms and international units.<sup>53</sup> Learn how to convert micrograms to IUs in the Calculation Corner.

The RDA for children has been set at 15 micrograms (600 IU) of vitamin D per day for children aged 1 to 13. This is an increase in vitamin D from 5 micrograms due to newly reported research suggesting that the previous RDA was too low. Vitamin D supplementation as high as 2,500 IUs is safe for children aged 1 to 3 and up to 3,000 IUs for children 4 to 8 years old.<sup>54</sup>

When reading labels to assess the amount of vitamin D in foods, keep in mind that the Daily Value (DV) on the Nutrition Facts panel is set at 400 IU, a recommendation based on the older

RDA for vitamin D. This means that the amount of vitamin D in a serving of a packaged food does not reflect the new, higher recommendations for children and adults.<sup>55</sup>

### Food Sources of Vitamin D

One of the easiest ways to get vitamin D from food is to drink fortified milk, which provides 100 IU, or 2.5 micrograms, of vitamin D per 8 fluid ounces. Other than fortified milk, breakfast cereals, yogurt, and fatty fish (such as sardines and salmon), very few foods provide ample amounts of vitamin D (see **Figure 9.16**). With this scarcity of naturally occurring food sources, it isn't surprising that many Americans are not meeting their daily vitamin D needs.<sup>56</sup>

### Vitamin D Toxicity

The tolerable upper limit (UL) for vitamin D has been set at 100 micrograms (4,000 IU) for individuals nine years or older. This upper limit is over six times higher than the recommended daily amount. Consuming too much vitamin D can cause loss of appetite, nausea, vomiting, and constipation.

As with the other fat-soluble vitamins, excess amounts of vitamin D are stored in the adipocytes, and an accumulation can reach toxic levels, causing **hypervitaminosis D**. This condition causes overabsorption of calcium from the intestines as well as calcium loss from bones. When both of these symptoms occur, blood calcium levels can become dangerously high.

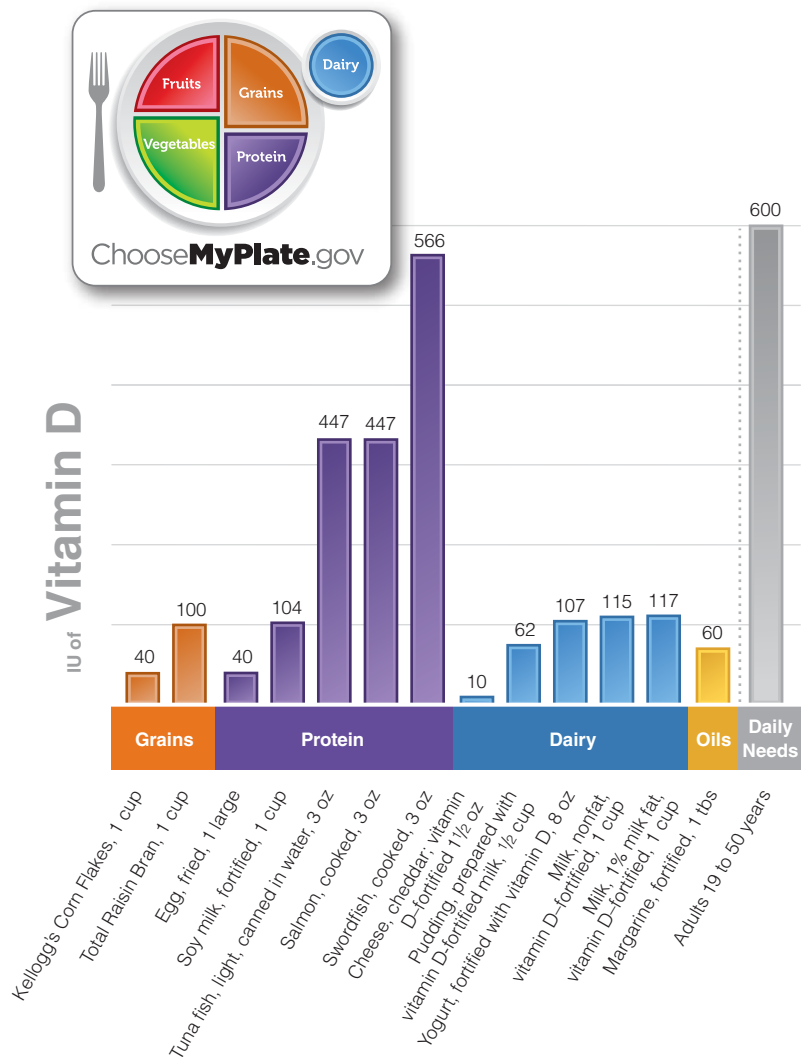
A chronically high amount of calcium in the blood, or **hypercalcemia** (*hyper* = over, *calc* = calcium, *emia* = blood), can cause damaging calcium deposits in the tissues of the kidneys, lungs, blood vessels, and heart. Excess vitamin D can also affect the nervous system and cause severe depression.<sup>57</sup>

Hypervitaminosis D rarely occurs as a result of consuming too much vitamin D from foods, even fortified foods. The only exception is fish oils, specifically cod-liver oil, which provides 34 micrograms (1,360 IU) of vitamin D per tablespoon. Luckily, the less-than-pleasant taste of cod-liver oil is a safeguard against overconsumption. A more likely culprit behind hypervitaminosis D is the overuse of vitamin D supplements.

Sun worshippers don't have to worry about hypervitaminosis D from the sun (although they should be concerned about the risk of skin cancer). Overexposing the skin to UV rays eventually destroys the inactive form of vitamin D in the skin, causing the body to shut down production of vitamin D. It is estimated that about 10 to 20 minutes of sun exposure two to three times per week is sufficient to obtain adequate vitamin D.<sup>58</sup>

### Vitamin D Deficiency

Vitamin D deficiencies are increasing worldwide, most likely due to individuals' misunderstanding of the critical role of sunshine as a source of vitamin D. **Rickets** is one of the consequences of a lack of sunshine and insufficient dietary intake of vitamin D in children (**Figure 9.17**). The bones of children with rickets aren't adequately mineralized with calcium and phosphorus, and this causes them to weaken. Because of their "soft bones," these children cannot hold up their own body weight, and develop bowed legs.<sup>59</sup> Babies with rickets also



▲ **Figure 9.16** Vitamin D Content in Selected Foods

**hypervitaminosis D** A condition resulting from excessive amounts of vitamin D in the body.

**hypercalcemia** A chronically high amount of calcium in the blood.

**rickets** A vitamin D deficiency in children resulting in soft bones.

*continued*



▲ **Figure 9.17 Rickets**

Rickets can cause bowed legs in children.

have a delayed closure of the anterior fontanel or “soft spot” in the skull.<sup>60, 61</sup>

Since fortification of milk with vitamin D began in the 1930s, rickets has been considered a rare disease among children in the United States. However, the disease has resurfaced as a public health concern. In the late 1990s, a review of hospital records in Georgia suggested that as many as five out of every 1 million children between 6 months and 5 years of age in that state were hospitalized with vitamin D–related rickets.<sup>62</sup> Similarly, more than 20 percent of over 300 adolescents at a Boston-based hospital clinic in 2004 were reported to be deficient in vitamin D.<sup>63</sup> Whether the increase in rickets is due to a rise in the incidence of rickets or an increased awareness is not clear. The majority of cases of rickets in the United States have been African-American infants who were solely breast-fed. In Canada,

**osteomalacia** The adult equivalent of rickets, causing muscle and bone weakness, and pain.

the incidence of rickets was reported as 2.9 per 100,000 infants, almost all of whom were breast-fed.<sup>64</sup>

Because the vitamin D content of breast milk is affected by the vitamin D status of the mother, the American Academy of Pediatrics recommends that all breast-fed infants receive a supplement of 10 micrograms (400 IU) per day until they are also consuming 32 ounces of vitamin D–fortified formula or whole milk daily.<sup>65</sup>

The *Dietary Guidelines for Americans, 2010* and the Academy of Pediatrics recommends that all children 2 years and older drink low-fat milk to promote bone health. A National Health and Nutrition Examination Survey (NHANES) of children 2 to 19 years of age conducted from 2007 to 2008 reported that an average of 70 percent of children are drinking milk daily, most of which was 2 percent milk.<sup>66</sup> Children should be encouraged to drink low-fat milk to lower kilocaloric intake but at the same time consume a good source of vitamin D and calcium.

Increased concern over skin cancer may be a factor in the rise of rickets among American children. Skin cancer is the most common form of cancer in the United States, and childhood sun exposure appears to increase the risk of skin cancer in later years.<sup>67</sup> Because of this, organizations such as the Centers for Disease Control and the American Cancer Society have run campaigns that recommend limiting exposure to ultraviolet light. People are encouraged to use sunscreen, wear protective clothing when outdoors,



Most milk sold in the United States today has been fortified with vitamin D.

and minimize activities in the sun. The American Academy of Pediatrics also recommends that infants younger than 6 months not be exposed to direct sunlight. With less exposure to UV light, many children aren’t able to synthesize vitamin D in adequate amounts to meet their needs, thereby increasing their risk of developing rickets. The increased use of child day-care facilities, which may limit outdoor activities during the day, may also play a role in this increased prevalence of rickets.

**Osteomalacia** is the adult equivalent of rickets and can cause muscle and bone weakness and pain. The bones can’t mineralize properly because there isn’t enough calcium and phosphorus available in the blood. Although there may be adequate amounts of these minerals in the diet, the deficiency of vitamin D hampers their absorption. Explore the Nutrition in Practice on page 341. How can Abby



# Nutrition in Practice: Abby

Abby's mom is a cosmetologist, so she knows the effect of sunlight exposure and its impact on the aging of skin. Even though she grew up in Wisconsin, her mother lathered her up with a sunscreen with SPF of 30 every day before leaving for school or going outside to play, and always dressed her in hats and light cotton, long-sleeved shirts and pants in the summer. To Abby, putting on sunscreen and covering her skin from hat to toe before leaving the house is as routine as brushing her teeth.

For her college admission, Abby needed to get a complete physical. When taking a family history, the doctor uncovered that her mom has osteomalacia. When the doctor got her blood laboratory report back, he called Abby to tell her that her blood level of vitamin D was on the low side of normal and suggested she visit a dietitian.



### Abby's Stats:

- Age: 17
- Height: 5 feet 5 inches
- Weight: 128 pounds

## Abby's Food Log

Food/Beverage	Time Consumed	Hunger Rating*	Location
Nothing	6 AM	3	
Bagel with cream cheese	9:30 AM	5	High school cafeteria
Turkey and Swiss cheese sandwich, chips, cola	12:30 PM	5	High school cafeteria
Cheese and crackers	3:30 PM	3	Kitchen
Pizza, 2 slices	6:30 PM	4	With friends in a restaurant

\*Hunger Rating (1–5): 1 = not hungry; 5 = super hungry.

### Critical Thinking Questions

1. What symptoms might Abby expect to have if her levels of vitamin D continue to decline?
2. Why does Abby's avoidance of sunlight increase her potential deficiency of vitamin D?
3. Based on her food record, why do you think that she is deficient in vitamin D?

### Dietitian's Observation and Plan for Abby:

- Discuss the need to add vitamin D–fortified foods to her diet to meet her daily needs. Explain why cheese is a good source of calcium, but it does not contain vitamin D.
- Abby agrees to eat cereal with skim milk for breakfast prior to leaving for school, having a vitamin D–fortified yogurt as a daily afternoon snack, and to consume a large glass of skim milk with dinner.

A month later, Abby returns to the dietitian. Because she often eats dinner with her friends at the local pizzeria, she is having a difficult time routinely having a glass of milk with dinner. The dietitian recommends that Abby consume a glass of milk or a mug of hot cocoa made with milk daily when she gets home in the evening.

*continued*

## TABLE TIPS

## Ways to Get Vitamin D

Use vitamin D–fortified low-fat milk, not cream, in hot or iced coffee.

Buy vitamin D–fortified low-fat yogurts and have one daily as a snack. Top it with a vitamin D–fortified cereal for another boost of D.

Start the morning with vitamin D–fortified cereal and low-fat or skim milk.

Flake canned salmon over a lunchtime salad.

Make instant hot cocoa with hot milk rather than water.

Drink vitamin D–fortified orange juice with breakfast.

improve her vitamin D intake to reverse osteomalacia?

Vitamin D deficiency and its subsequent effect on decreased calcium absorption can lead to osteoporosis, a condition in which the bones can mineralize properly, but there isn't enough calcium in the diet to maximize the bone density or mass.

Muscle weakness and pain is also associated with low levels of serum vitamin D concentrations. One study found that a vitamin D supplement of 20 micrograms (800 IU) per day plus calcium was more effective in increasing muscle strength and reducing the number of falls reported by elderly women than just calcium alone.<sup>68</sup>

## LO 9.6: THE TAKE-HOME MESSAGE

Vitamin D can be made in the skin from exposure to ultraviolet rays from the sun. The active form of vitamin D is calcitriol. Vitamin D regulates blood calcium, enhances the absorption of calcium and phosphorus from the small intestine, and maintains healthy bones. It may also help regulate blood pressure and the immune system, and it may prevent diabetes and some cancers. Milk and fortified yogurts are excellent food sources of vitamin D. A deficiency of vitamin D can cause rickets in children and osteomalacia in adults. Hypervitaminosis D can result in hypercalcemia, affect the nervous system, and cause severe depression.

## Exploring Vitamin E

**LO 9.7** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin E.

## What Is Vitamin E?

There are eight different forms of naturally occurring vitamin E, but one form, **alpha-tocopherol (α-tocopherol)**, is most active in the body with a side

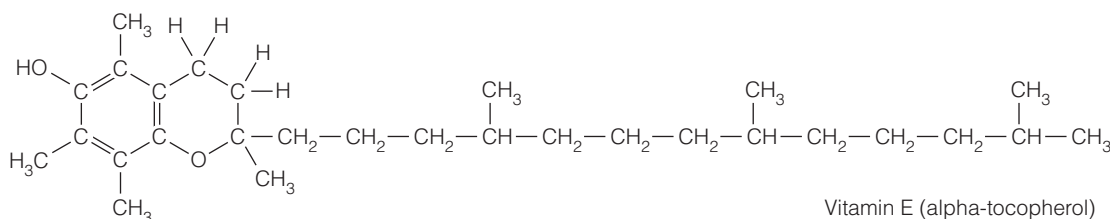
**alpha-tocopherol (α-tocopherol)** The most active form of vitamin E in the body.

chain of saturated carbons (**Figure 9.18**). The synthetic form of vitamin E found in dietary supplements is only half as active as the natural form. Alpha-tocopherol is the only form of vitamin E that is reflected in the Dietary Reference Intakes.

## Vitamin E Absorption and Transport

Vitamin E is absorbed with the aid of bile salts and micelles into the cells of the small intestinal lining. Once absorbed,

vitamin E is transported as part of a chylomicron through the lymph fluid into the blood, where it eventually arrives at the liver. Some researchers have suggested that vitamin E is transported through the cells of the small intestine attached to a protein, but so far a transport protein has not been discovered. More than 90 percent of the vitamin E is stored in the adipose tissue. Excess vitamin E is excreted through the bile, urine, feces, and the pores in the skin.



## ▲ Figure 9.18 The Structure of Alpha-Tocopherol

There are eight different types of vitamin E compounds (or tocopherols), but alpha-tocopherol is the most active and is the form reflected in the Dietary Reference Intakes.

## Metabolic Functions of Vitamin E

Vitamin E is sometimes referred to as the vitamin in search of a disease to cure. For almost 40 years after its discovery, scientists searched unsuccessfully for a curative role for vitamin E. They now have shifted their focus and begun valuing the vitamin's importance as an effective antioxidant and in maintaining healthy cell membranes. Vitamin E also plays an important function in blood clotting. The role of vitamin E in preventing cardiovascular disease is still unclear. Even though vitamin E was thought to show promise in preventing other diseases such as cancer or cataracts, researchers have not been able to provide conclusive evidence supporting this.

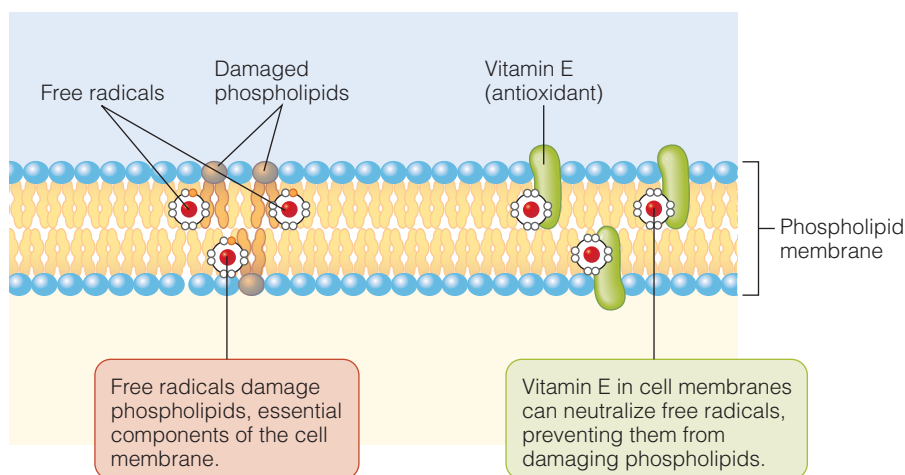
### Vitamin E as an Antioxidant

Vitamin E's nutritional claim to fame is its role as a powerful antioxidant, particularly in cell membranes. Recall from Chapter 5 that phospholipids are critical components of cell membranes. Many phospholipids contain unsaturated fatty acids, which are vulnerable to the damaging effects of free radicals. Vitamin E is unique in its ability to neutralize free radicals before they can harm cell membranes (see **Figure 9.19**). The hydrogen ions in vitamin E quickly react with the free radical and stop the chain reaction. In doing so, vitamin E itself is altered and loses its antioxidant abilities.

Oxidation of the LDL cholesterol carrier in the blood is also harmful, as it contributes to the buildup of artery-clogging plaque. Antioxidants, including vitamin E, help protect the LDL cholesterol carrier from being oxidized and reduce the risk of atherosclerosis in the arteries.<sup>69</sup>

### Vitamin E as an Anticoagulant

Vitamin E is an anticoagulant (*anti* = against, *coagulant* = causes clotting), which means that it inhibits platelets from unnecessarily clumping together and creating a damaging clot in the bloodstream. Vitamin E also lessens the stickiness of the cells that line the lymph and blood vessels. This reduces plaque buildup that clogs the passageways, reducing the risk of heart attack or stroke. Although this function clearly helps maintain the health of the cardiovascular system, studies are still under



▲ **Figure 9.19** Vitamin E as an Antioxidant in Cell Membranes

## Calculation Corner

### Converting International Units for Vitamin E

Vitamin E content in dietary supplements and fortified foods is often listed in international units (IU), while vitamin E found naturally in food is measured in milligrams of alpha-tocopherol (mg  $\alpha$ -tocopherol). Use the following conversion factors to determine the alpha-tocopherol equivalents in mg  $\alpha$ -tocopherol found in 1 IU.

1 IU of alpha-tocopherol is equivalent to 0.67 mg alpha-tocopherol

1 IU of alpha-tocopherol is equivalent to 0.45 mg of synthetic alpha-tocopherol

**Example:** A vitamin supplement contains 400 IU of alpha-tocopherol. How many mg  $\alpha$ -tocopherol does it contain?

**Answer:**  $0.67 \text{ mg} \times 400 \text{ IU} = 268 \text{ mg}$   $\alpha$ -tocopherol

or

$0.45 \text{ mg} \times 400 \text{ IU} = 180 \text{ mg}$   $\alpha$ -tocopherol (synthetic  $\alpha$ -tocopherol)

way to assess if the long-term use of vitamin E supplements could play a protective role against heart disease.

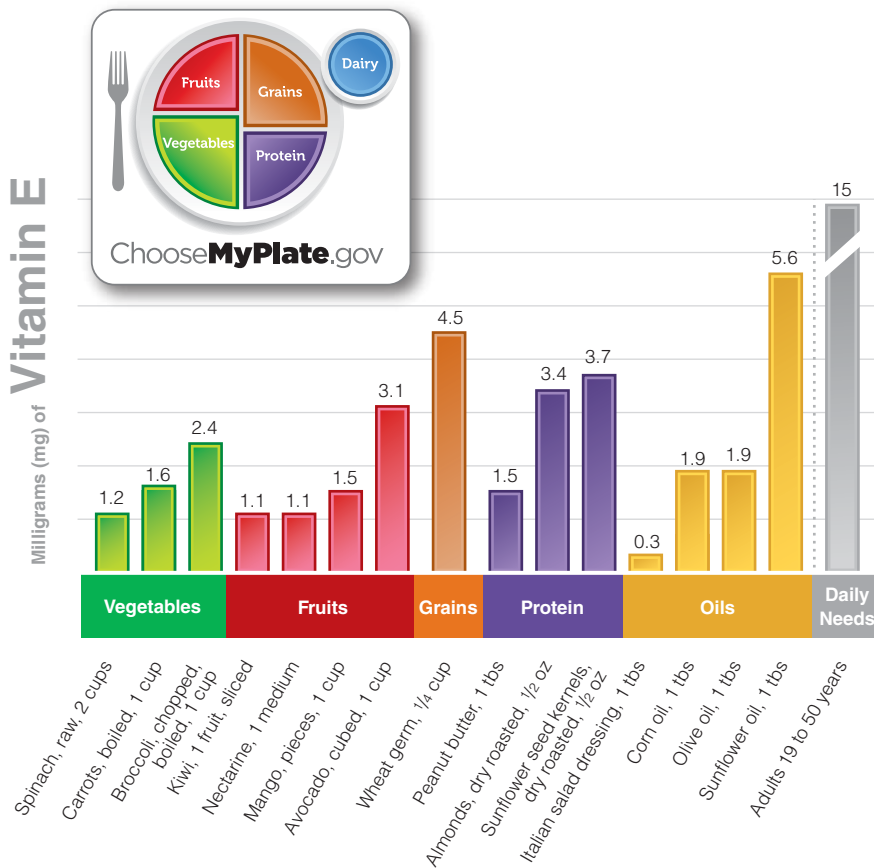
### Daily Needs of Vitamin E

Adults should consume 15 milligrams (22.4 IU) of vitamin E daily (see the Calculation Corner to learn how to convert vitamin E in milligrams to international units) as an Adequate Intake (AI). Because alpha-tocopherol is the most active form of vitamin E in the body, vitamin E requirements are presented in alpha-tocopherol equivalents. Researchers speculate that healthy Americans are not consuming adequate amounts of vitamin E.<sup>70</sup>

### Food Sources of Vitamin E

Vegetable oils (and foods that contain them), avocados, nuts, and seeds are good food sources of vitamin E. The *Dietary Guidelines for Americans* specifically recommend consuming vegetable

*continued*



▲ Figure 9.20 Vitamin E Content in Selected Foods

oils daily to meet vitamin E needs. Some green leafy vegetables and fortified cereals can also contribute to daily needs (see Figure 9.20).

### Vitamin E Toxicity

There isn't any known risk of consuming too much vitamin E from natural food sources. However, overconsumption of the synthetic form that is found in supplements and/or fortified foods could pose risks.

Because vitamin E can act as an anticoagulant and interfere with blood clotting, excess amounts in the body increase the risk of **hemorrhage**. To prevent hemorrhage, the upper limit from

**hemorrhage** Excessive bleeding or loss of blood.



supplements and/or fortified foods is 1,000 milligrams for adults. This applies only to healthy individuals consuming adequate amounts of vitamin K. (Vitamin K also plays a role in blood clotting.) Individuals taking anticoagulant medication and vitamin E supplements should be monitored by their physician to avoid the serious situation in which the blood can't clot quickly enough to stop the bleeding from a wound.

The upper level of 1,000 milligrams may actually be too high. Research has shown that those at risk of heart disease who took 265 milligrams (400 IU) or more of vitamin E daily for at least one year had an overall higher risk of dying.<sup>71</sup> One theory is that too much vitamin E may disrupt

### TABLE TIPS

#### Enjoying Your Es

Add fresh spinach and broccoli to salad.

Add a slice of avocado, or use guacamole as a spread, on sandwiches.

Spread peanut butter on apple slices.

Top low-fat yogurt with wheat germ.

Pack a handful of almonds in a zip-closed bag for a snack.

the balance of other antioxidants in the body, causing more harm than good.

### Vitamin E Deficiency

Though rare, a chronic vitamin E deficiency can cause nerve problems, muscle weakness, and uncontrolled movement of body parts. Because vitamin E is an antioxidant and is found in the membranes of red blood cells, a deficiency can also increase the susceptibility of cell membranes to damage by free radicals. Individuals who can't absorb fat properly may fall short of their vitamin E needs.

### LO 9.7: THE TAKE-HOME MESSAGE

There are several forms of naturally occurring vitamin E but alpha-tocopherol is the most active form in the body. Vitamin E is transported via the chylomicron and stored in the adipose tissue. Vitamin E is an antioxidant that protects the cells' membranes and an anticoagulant that inhibits clot formation. Vitamin E may help prevent the oxidation of LDL cholesterol. Vegetable oils, avocados, nuts, and seeds are good sources of vitamin E. Green leafy vegetables and fortified cereals also contribute to daily intake. The recommended intake for vitamin E is presented in alpha-tocopherol equivalents. Too little vitamin E, although rare, may result in nerve problems and muscle weakness, and increase susceptibility to free radical damage. Excess amounts of vitamin E from supplements may cause hemorrhage.

# Exploring Vitamin K

**LO 9.8** Describe the functions, recommended intakes, food sources, and the deficiency and toxicity effects of vitamin K.

## What Is Vitamin K?

Vitamin K is found naturally in two forms. Some plants manufacture **phylloquinone**, or **vitamin K<sub>1</sub>**. Phylloquinone, shown in **Figure 9.21**, has a long chain of carbons with methyl groups attached at every fourth carbon. This is the primary source of vitamin K in the diet. In animals, bacteria that reside naturally in the colon synthesize **menaquinone**, also referred to as **vitamin K<sub>2</sub>**. A third form of vitamin K, called **menadione**, or **vitamin K<sub>3</sub>**, is synthetic and formulated

for use in animal feed and vitamin supplements.

## Vitamin K Absorption and Transport

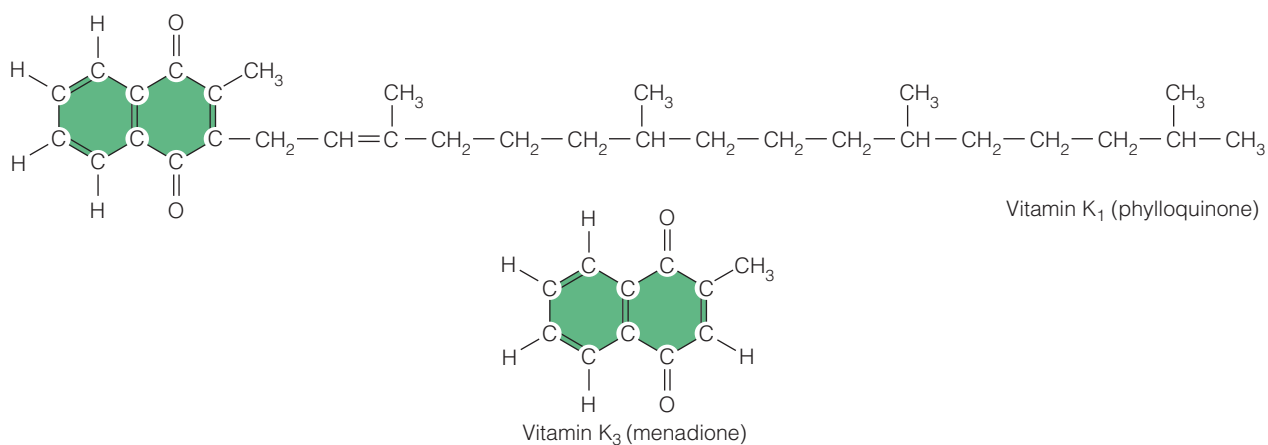
About 80 percent of dietary vitamin K is absorbed, mostly in the jejunum. In contrast, only 10 percent of the vitamin K produced by bacteria in the large intestine is absorbed. Both forms of vitamin K are incorporated into chylomicrons and transported to the liver, where they are stored for future use. When the diet is deficient in vitamin K, the storage forms are transported by the lipoproteins VLDL, LDL, and HDL. Excess vitamin K is excreted, mostly bound to bile. It can also be eliminated through the urine. Vitamin K is stored in small amounts, mostly in the liver.

## Metabolic Functions of Vitamin K

Vitamin K is so named because of its role in *koagulation*, the Danish word for **coagulation**, or blood clotting.<sup>72</sup> It also functions as a cofactor in several key roles in the body, and is essential for strengthening the bones.

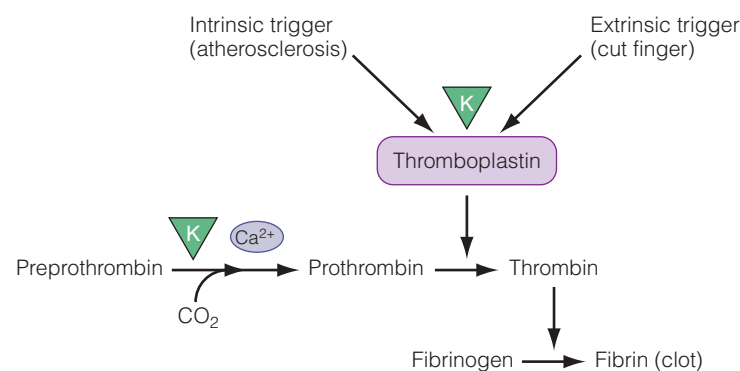
## Vitamin K Promotes Blood Clotting

A series of reactions, referred to as a cascade, must happen before the blood coagulates and forms a blood clot (**Figure 9.22**). At step seven in the cascade, a carboxyl group is added to a protein, which enables the protein to bind calcium ions. The reaction, called **carboxylation** (see the Chemistry Boost for an illustration), is catalyzed by a



▲ **Figure 9.21** The Structure of Vitamin K

Vitamin K occurs naturally in plants as phylloquinone. Menadione is the synthetic form of vitamin K.



▲ **Figure 9.22** The Role of Vitamin K in Blood Clotting

Vitamin K is a coenzyme involved in carboxylation reactions of several proteins during blood clotting.

**phylloquinone (vitamin K<sub>1</sub>)** The form of vitamin K found in plants.

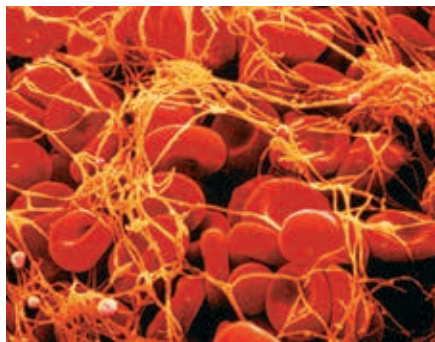
**menaquinone (vitamin K<sub>2</sub>)** The form of vitamin K produced by bacteria in the colon.

**menadione (vitamin K<sub>3</sub>)** The synthetic form of vitamin K used in animal feed and dietary supplements.

**coagulation** The process of blood clotting.

**carboxylation** The chemical reaction in which a carboxyl group is added to a molecule.

*continued*



▲ **Figure 9.23 Blood Clot**  
(SEM, magnified 1,900×)

carboxylase enzyme that is dependent on vitamin K as a coenzyme. Four of these vitamin K–dependent proteins are known as **clotting factors**: II (prothrombin), VII, IX, and X. Once calcium is bound to the clotting factors, the clotting process continues with the conversion of prothrombin to thrombin. Thrombin converts fibrinogen to fibrin, which holds together red blood cells to form the actual blood clot (**Figure 9.23**). As soon as vitamin K has completed its role in activating the carboxylase enzyme, it is released and the enzyme must be activated again. Without vitamin K, a simple nick or cut could quickly result in hemorrhage.

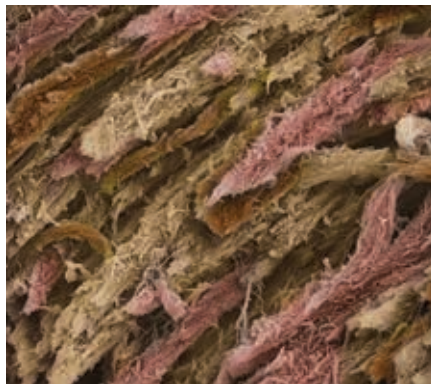
Anticoagulants (anticlotting medications) such as Coumadin (also known as **warfarin**) decrease vitamin K activity, resulting in thinner blood. Severe liver disease also results in lower blood levels of the vitamin K–dependent clotting factors and increases the risk of hemorrhage.

### Vitamin K Promotes Strong Bones

Vitamin K participates in the carboxylation of other proteins. Two of these proteins are essential components in bone formation: *osteocalcin* and *matrix Gla protein*. Osteocalcin is a type of Gla protein secreted by bone-forming osteoblasts. Matrix Gla protein is found

**clotting factors** Substances involved in the process of blood clotting, such as prothrombin and fibrinogen.

**warfarin** An anticoagulant drug given to prevent blood from clotting.



▲ **Figure 9.24 Bone Matrix**  
(colored SEM, magnified 2,000×).

in the bone matrix (**Figure 9.24**), blood vessels, and cartilage. The carboxylation of osteocalcin and matrix Gla protein is necessary for calcium ions to bind to the bone matrix, which strengthens the bone and improves bone mass.<sup>73</sup> Matrix Gla protein may also provide protection against atherosclerosis.<sup>74</sup>

### Daily Needs for Vitamin K

Currently, the amount of vitamin K made from bacteria in the intestinal tract that contributes to meeting daily needs is not known. Because of this, it is hard to determine an Estimated



Average Requirement (EAR), so an Adequate Intake (AI) is reported instead. Therefore, the AI for dietary vitamin K is based on the average amount consumed by healthy Americans.<sup>75</sup> Adult women need 90 micrograms (1,000 IU) of vitamin K per day, and men need 120 micrograms (1,300 IU) daily.

### Food Sources of Vitamin K

To meet vitamin K needs, think green. Green vegetables like broccoli, asparagus, spinach, salad greens, brussels sprouts, and green cabbage are all rich in vitamin K. Vegetable oils and margarine are the second largest source of vitamin K in the diet (see **Figure 9.25**). A green salad with oil-and-vinegar dressing at lunch and three-quarters of a cup of broccoli at dinner will meet an individual's vitamin K needs for the entire day.

### Vitamin K Toxicity and Deficiency

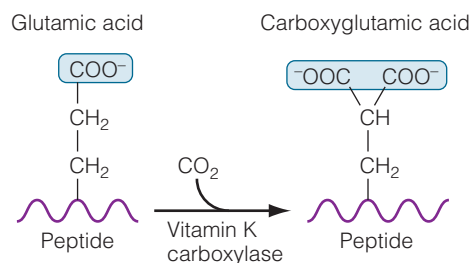
There are no known adverse effects of consuming too much vitamin K from foods or supplements, so an upper intake level hasn't been set for healthy people.

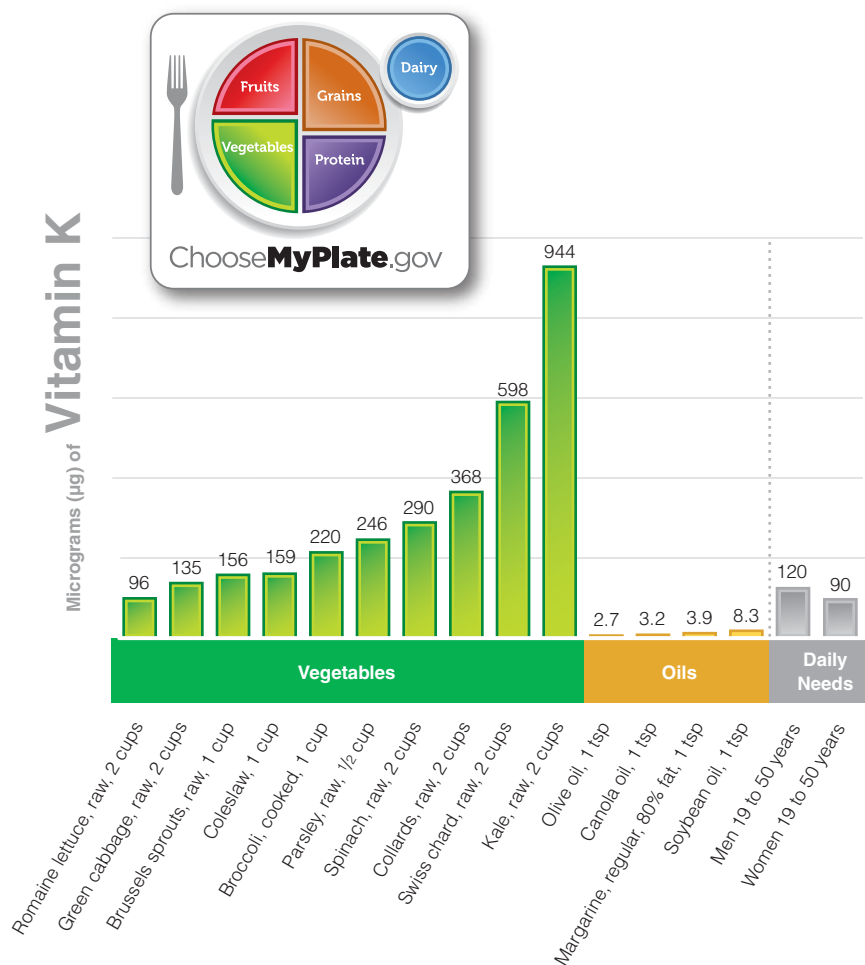
Individuals taking anticoagulant medications such as Coumadin need to maintain a consistent intake of vitamin K. This medication decreases the activity of vitamin K and prolongs the time it takes

## Chemistry Boost

### Carboxylation Reactions

Carboxylation is a chemical reaction that occurs when a carboxyl group (COOH) is added to a protein, such as during the blood-clotting reaction. As illustrated, the glutamic acid molecule is converted to carboxyglutamic acid with the aid of vitamin K. The carboxyl group in this illustration is shown as COO<sup>-</sup>.





▲ **Figure 9.25** Vitamin K Content in Selected Foods

for blood to clot. If individuals taking Coumadin suddenly increase the vitamin K in their diets, the vitamin can override the effect of the drug, enabling the blood to clot too quickly. In contrast, a sudden decline in dietary vitamin K can enhance the effectiveness of the drug and increase the risk of bleeding.<sup>76</sup>

Babies are born with low levels of vitamin K in their bodies. This is because little vitamin K passes through the placenta and newborns have sterile intestinal tracts with few bacteria to produce vitamin K. In addition, breast milk is low in vitamin K. For this reason,



## TABLE TIPS

### Getting Your Ks

Have a green salad daily.

Cook with soybean oil.

Add shredded green cabbage to salad, or top a salad with a scoop of coleslaw.

Add a small amount of margarine to steamed spinach. Both provide some vitamin K.

Dunk raw broccoli florets in salad dressing for two sources of vitamin K.

newborns are routinely given vitamin K soon after birth, either as an injection or by mouth, to enable blood clotting until the bacteria in the intestinal tract can begin to produce vitamin K.<sup>77</sup>

A vitamin K deficiency severe enough to affect blood clotting is extremely rare in healthy individuals.<sup>78</sup> People with conditions such as gallbladder disease, which reduces the absorption of fat and fat-soluble vitamins in the intestinal tract, may be at risk for not meeting their vitamin K needs.

Though the exact mechanism is unknown, a chronic dietary deficiency of vitamin K may be a factor in increased hip fractures in older men and women. A diet rich in phylloquinone (vitamin K<sub>1</sub>) has been shown to improve bone mineral content in older women.<sup>79</sup>

### LO 9.8: THE TAKE-HOME MESSAGE

Vitamin K is found in plants as phylloquinone and as menaquinone in the colon manufactured by bacteria. Vitamin K functions as a carboxylation coenzyme in blood clotting and bone formation. Leafy greens, vegetable oils, and margarine are good dietary sources of vitamin K. While there are no known toxicity problems for vitamin K, a deficiency may result in hemorrhage and bone fractures. Individuals taking anticoagulant medications such as Coumadin should monitor their vitamin K intake.

# Are Vitamin Supplements Necessary for Good Health?

**LO 9.9** Explain the role of dietary supplements in maintaining a healthy diet.

Sales of dietary supplements in the United States have increased markedly in the last several decades. More than 30 percent of Americans spent over \$12 billion in 2012 on dietary supplements as single vitamins or minerals, or in the most popular form of a multivitamin and mineral combination.<sup>80</sup> One in three Americans reports taking a multivitamin and mineral supplement daily.<sup>81</sup> To encourage supplement use, manufacturers are developing new chewable forms, including chocolate, gummies, and soft gels alongside the pills, powders, and liquids. Are vitamin supplements worth the money? Are they harmful or essential to be healthy?



Some of the most popular forms of vitamin supplements sold today are in chewable, candylike forms.

## Vitamin Supplements and Aging

The aging population appears to be one of the forces driving this increase in the use of supplements: Older people may use vitamin supplements in an attempt to mitigate ongoing medical issues or prevent chronic diseases,<sup>82</sup> especially cardiovascular disease, cancer, and cognitive decline in later years.

A staggering number of studies have examined the association between ingesting specific individual vitamins or combinations of vitamins to prevent cardiovascular disease and cancer, including the antioxidant vitamins A, C, E, beta-carotene, and folic acid. A recent review found that any single vitamin or combination of vitamins had no benefit in preventing cardiovascular disease or cancer. In the case of beta-carotene and vitamin E supplements, the risks outweighed any benefits. The researchers concluded that ingesting beta-carotene in supplement form might increase the risk of developing cancer in people who smoke. Vitamin E supplements do not impact the risk of developing cardiovascular disease or cancer,<sup>83</sup> nor did a daily multivitamin prevent heart attacks, stroke, or death

from a cardiovascular event even after 10 years of supplementation.<sup>84</sup>

In addition to cardiovascular disease and cancer, middle-aged Americans are fearful that as they age, cognitive decline will rob them of their independence and quality of life. Does a daily multivitamin supplement help maintain mental sharpness and prevent cognitive decline? The research says no. The cognitive decline in men over a 13-year study found no benefit of taking a multivitamin supplement on four different cognitive tests.<sup>85</sup> Researchers suggest that the results could be due to the fact that the subjects were already too well nourished to benefit from a daily supplement.

While the idea that a multivitamin pill daily can ward off cardiovascular disease, cancer, and even cognitive decline is appealing, it's best to save your money. The current research doesn't support dietary supplements as a cure for aging or to prevent the chronic diseases that accompany aging.

## Vitamin Supplements Are Not a Substitute for Healthy Eating

Consumers often choose supplements because they are unwilling to improve



Unlike synthetic supplements, whole fruits and vegetables contain fiber and phytochemicals that provide health benefits beyond those of the vitamin content.

their diets. However, supplements should never be used to replace a healthy diet. The Academy of Nutrition and Dietetics maintains that an unhealthy diet of nonnutritious foods cannot be transformed into a healthy diet by simply ingesting a daily supplement. There is little scientific evidence to promote the use of dietary supplements in place of eating a healthy, balanced diet. Remember that disease-fighting phytochemicals, fiber, and other substances that the body needs are all missing from a bottle of supplements.

Further, supplement use may have adverse side effects. In fact, supplement use, not food, is responsible for most of the reported problems associated with vitamin toxicity. Any individual who is considering taking supplements should consult a credible source of nutrition information, such as a Registered Dietitian Nutritionist, before purchasing or consuming supplements.

## Supplements May Be Helpful for Some Individuals

Whereas many healthy individuals do not need to consume supplements, some supplements are useful for people who cannot meet their nutrient needs through a regular, varied diet. Others may have been advised by their physician to consume supplements to correct a vitamin or mineral deficiency.

Among those who may benefit from taking a dietary supplement are:<sup>86</sup>

- Women of childbearing age who may become pregnant, as they need to consume adequate synthetic folic acid (a B vitamin) to prevent certain birth defects
- Pregnant and lactating women who can't meet their increased nutrient needs with foods
- Older individuals, who need adequate amounts of synthetic vitamin B<sub>12</sub>
- Individuals who do not drink enough milk and/or do not have

adequate sun exposure to meet their vitamin D needs

- Individuals on low-kilocalorie diets that limit the amount of vitamins and minerals they can consume through food
- Strict vegetarians, who have limited dietary options for vitamins D and B<sub>12</sub> and other nutrients
- Individuals with food allergies or lactose intolerance that limit food choices
- Individuals who abuse alcohol, have medical conditions such as intestinal disorders, or are taking medications that may increase their need for certain vitamins
- Individuals who are food insecure and those who are eliminating food groups from their diet
- Infants who are breast-fed should receive 400 IU of vitamin D daily unless they are also consuming at least 1 quart of vitamin D–fortified formula daily. Children aged 1 and older should receive 400 IU of vitamin D daily if they consume less than 1 quart of milk per day. Adolescents who consume less than 400 IU of vitamin D daily from their diet would also benefit from a supplement.

Supplements can interact or interfere with certain medications, so individuals should consult a doctor before consuming a supplement if they are taking prescription medications.

## Supplements Are Not Regulated Like Drugs

Another factor to keep in mind regarding the use of dietary supplements (including vitamins, minerals, and herbs) is that the FDA does not stringently regulate them. In fact, the individuals most responsible for regulating these substances are their manufacturers. Unlike drugs, dietary supplements—unless they contain a new



▲ **Figure 9.26** The U.S. Pharmacopeia Verified Mark

Source: Registered trademark of The United States Pharmacopeial Convention. Used with Permission.

ingredient—do not need approval from the FDA before they can be marketed to the public, and the FDA cannot remove a supplement from the marketplace unless it has been shown to be unsafe or harmful to the consumer.<sup>87</sup>

An option exists to help consumers choose among dietary supplements. **The United States Pharmacopeial Convention (USP)** is a nonprofit organization that sets standards for dietary supplements.<sup>88</sup> Though it does *not* endorse or validate health claims that the supplement manufacturers make, it sets standards for the identity, strength, quality, and purity of dietary supplements. Supplement manufacturers can voluntarily submit their products to the USP's staff of scientists for review. USP verifies supplements through a comprehensive testing and evaluation process and awards its USP Verified Mark (**Figure 9.26**) only after rigorous facility audits, product documentation reviews, and product testing have been completed and approved.

For individuals who choose to use supplements, the best place to start when picking a supplement is to carefully read the label. The FDA does have strict guidelines for the information that must appear on any supplement label. For example, the term “high potency” can only be used if at least two-thirds of the nutrients in the

**The United States Pharmacopeial Convention (USP)** A nonprofit organization that sets quality standards for dietary supplements.

**a** The FDA allows the term “high potency” to be used as long as at least two-thirds of the nutrients contain at least 100 percent of the daily value.

**b** All supplements must clearly identify what is in the bottle.

**c** Always look for the USP seal of approval for quality and purity. Choose the cheapest supplement with the seal to save a few dollars.

**d** The FDA disclaimer is a reminder that this product doesn't have the FDA seal of approval for effectiveness.

**e** The net quantity of contents must be listed. The Supplement Facts panel lists the serving size, the vitamins in the supplement, and the amount of the vitamin in each capsule.

**f** The structure/function claim explains that vitamin C is beneficial for your immune system.

**g** The amount of each supplement is also given as a percentage of the Daily Value. Remember, the Daily Value may be higher than you actually need.

**h** All the ingredients must be listed in descending order by weight.

**i** The name and address of the manufacturer or distributor must be provided.

**Supplement Facts**

When you need to perform your best, take vitamin C. It's a smart choice to help your immune system.

**DIRECTIONS FOR USE:** Take one capsule daily.

Serving Size 1 Capsule	%DV
<b>Amount Per Capsule</b>	
Vitamin C	60mg 100%

Other ingredients: Gelatin, water, and ascorbic acid.

XYZ Company  
Some Place, NJ 00001

▲ **Figure 9.27 Dietary Supplement Labels**

The FDA has strict guidelines for the information that must appear on any supplement label.

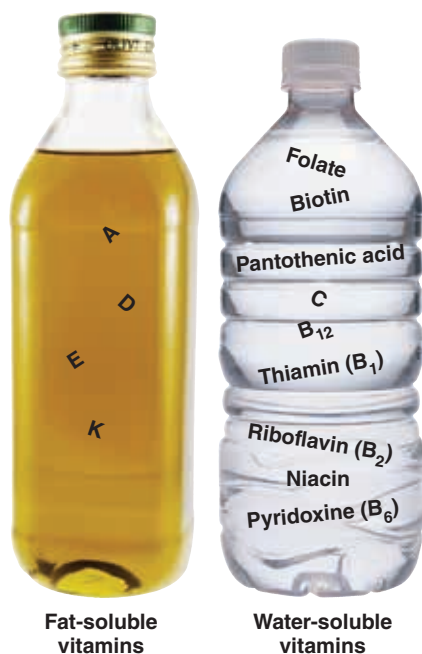
supplement contain at least 100 percent of the daily value. The label must also clearly identify the contents of the bottle. While a supplement may have the USP seal of approval for quality and purity, it doesn't have the FDA's approval, even if it makes a claim. Supplements must contain a panel that lists the serving size, the number of capsules or tablets in the bottle, the amount of the vitamin in each capsule, and the percentage of the daily value (**Figure 9.27**). All the ingredients must also be listed.

**LO 9.9: THE TAKE-HOME MESSAGE** The ingestion of a daily multivitamin supplement is on the rise in the United States, especially among older adults. The research doesn't support dietary supplements as a cure for aging or the chronic diseases that accompany aging, including cardiovascular disease, cancer, or cognitive decline. A well-balanced diet that provides adequate kilocalories can meet most individuals' daily vitamin needs without a vitamin supplement. A vitamin supplement is an option for individuals unable to meet their daily vitamin needs. The FDA does not strictly regulate vitamin supplements. Each supplement bottle contains a label and if the U.S. Pharmacopoeia (USP) has tested the supplement to determine if it meets the criteria for purity and accuracy, it will carry the USP seal. Consumers should seek guidance from a qualified health professional before taking a dietary supplement.

# Visual Chapter Summary

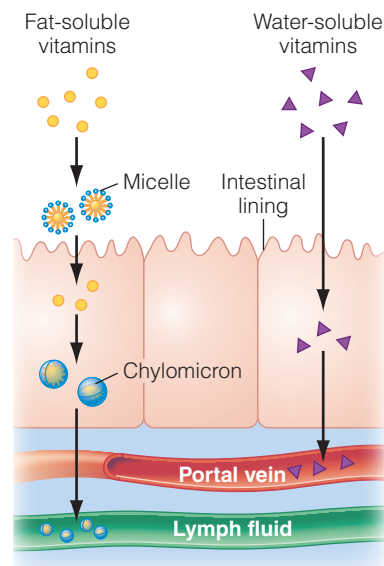
## Lo 9.1 Vitamins Are Essential Organic Compounds

Vitamins are essential, organic compounds the body requires in small amounts for normal metabolic functions. There are 13 different vitamins found naturally in foods, added to foods through fortification, or concentrated in dietary supplements. These 13 vitamins are classified as either water soluble or fat soluble. The water-soluble vitamins include the B-complex vitamins and vitamin C. The fat-soluble vitamins are vitamins A, D, E, and K. Provitamins, such as the carotenoids, are converted to their active form before they can be directly used in the body. Most water-soluble vitamins are not toxic except vitamin B<sub>6</sub>. Vitamins A, D, and E can be toxic if taken in megadose amounts.



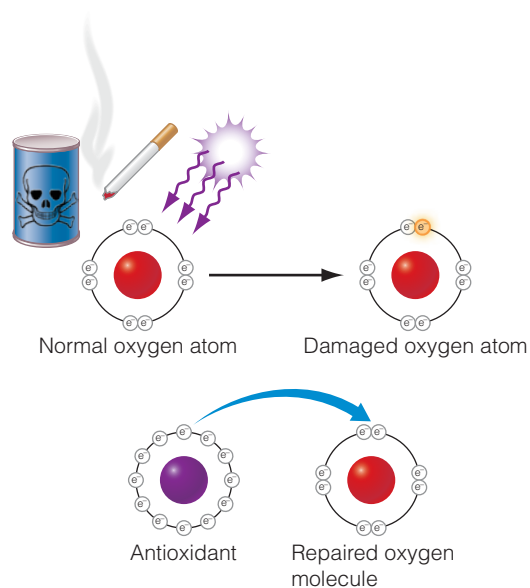
## Lo 9.2 Vitamins Differ in Their Absorption and Storage

Bioavailability of individual vitamins varies based on the amount of the vitamin in the food, whether the food is cooked, raw, or refined, the food's digestibility, an individual's nutrition status, and whether the vitamin is a natural or synthetic form. Vitamins are often attached to proteins in food and must be released in the stomach to be absorbed. Once freed, fat-soluble vitamins are transported as part of micelles and absorbed through the lymph system as part of chylomicrons. Fat-soluble vitamins are stored in the body and need fat to be absorbed. Water-soluble vitamins are absorbed with water and typically aren't stored in the body for extended periods. Fat-soluble vitamins are less bioavailable than water-soluble vitamins.



## Lo 9.3 Antioxidants Suppress Free Radicals

Antioxidants, such as vitamins E and C and beta-carotene, neutralize harmful oxygen-containing molecules called free radicals that can damage cells by lending them an electron. Free radicals can contribute to chronic diseases such as cancer and heart disease and accelerate the aging process. Diets abundant in antioxidant-rich fruits, vegetables, and whole grains are associated with a lower incidence of many diseases. Carotenoids and flavonoids that give fruits and vegetables their vivid colors are referred to as phytochemicals and have antioxidant properties.



## Lo 9.4 Vitamins Are Found in Every Food Group

Whole foods, including fruits, vegetables, whole grains, legumes, dairy foods, and meats, provide phytochemicals, antioxidants, and fiber in addition to vitamins. Food handling and preparation techniques such as exposure to air, water, UV light, changes in pH, and heat can cause the loss of vitamins. Fortified foods

Vegetables	Fruits	Grains	Protein	Dairy
Folate	Folate	Folic acid	Niacin	Riboflavin
Vitamin A	Vitamin C	Niacin	Thiamin	Vitamin A
Vitamin C	Vitamin A	Vitamin B <sub>6</sub>	Vitamin B <sub>6</sub>	Vitamin B <sub>12</sub>
Vitamin E		Vitamin B <sub>12</sub> (if fortified)	Vitamin B <sub>12</sub>	Vitamin D
Vitamin K		Riboflavin		
		Thiamin		

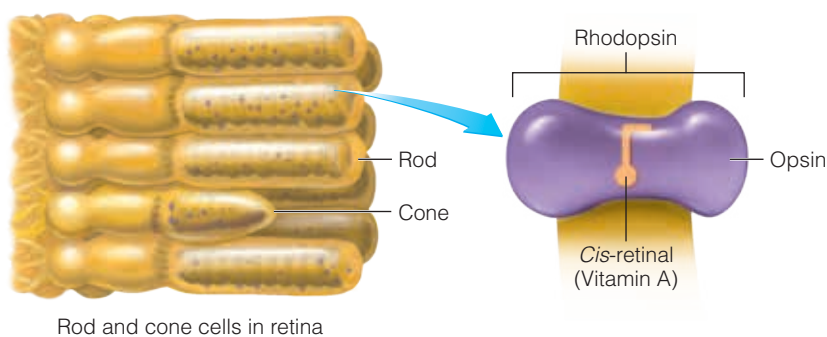
and vitamin supplements can help individuals with inadequate diets meet their nutrient needs. However, there are health risks associated with the overconsumption of vitamins in fortified foods.

## Lo 9.5 Vitamin A

Vitamin A refers to a family of retinoids, which include retinol, retinal, and retinoic acid. Retinol is most usable in the body. Retinal is essential for eye health and vision. The retinoids are also essential for cell growth and development, reproduction, and a healthy immune system. Three carotenoids, alpha-carotene, beta-carotene, and beta-cryptoxanthin, are provitamins that can be converted to vitamin A in the body; beta-carotene is the most commonly consumed. Vitamin A is stored in the liver until needed, and is not easily excreted from the body.

Most of the dietary, preformed vitamin A consumed (70 to 90 percent) is absorbed; absorption occurs via active transport in the small intestine. Beta-carotene is absorbed at a much lower rate. Vitamin A in foods is measured in retinol activity equivalents (RAE). Preformed vitamin A is found in milk, cereals, cheese, egg yolks, and organ meats, especially liver. Provitamin A sources include carrots, spinach, and sweet potatoes.

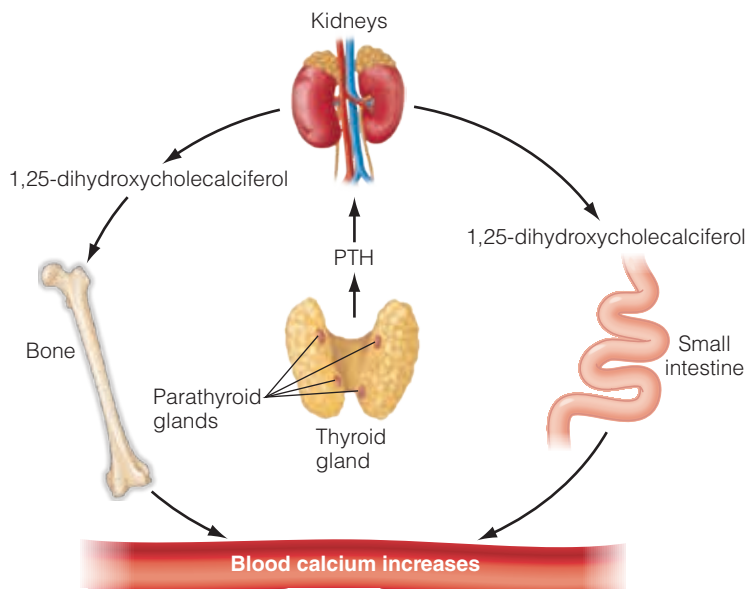
Vitamin A deficiencies can result in vision problems and increased infections. Toxic amounts of vitamin A can compromise bone health and can lead to birth defects during pregnancy.



## Lo 9.6 Vitamin D

Although vitamin D (the “sunshine vitamin”) can be made in the body with the help of ultraviolet rays from the sun, some individuals are not exposed to enough sunlight to meet their needs. The active form of vitamin D, called calcitriol, regulates blood calcium, enhances the absorption of calcium and phosphorus from the small intestine, and maintains healthy bones. It may also help regulate blood pressure and the immune system, and it may prevent diabetes and some cancers.

Milk and fortified yogurts are excellent food sources of vitamin D. A deficiency of vitamin D can cause rickets in children and osteomalacia in adults. Hypervitaminosis D can result in hypercalcemia, affect the nervous system, and cause severe depression.

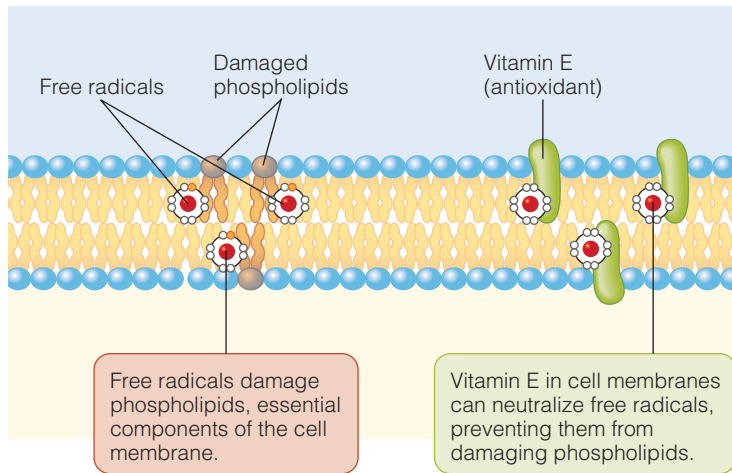


## Lo 9.7 Vitamin E

Alpha-tocopherol is the most active form of vitamin E in the body. Vitamin E is an antioxidant that protects the cells' membranes. It plays an important role as an anticoagulant and may help prevent the oxidation of LDL cholesterol.

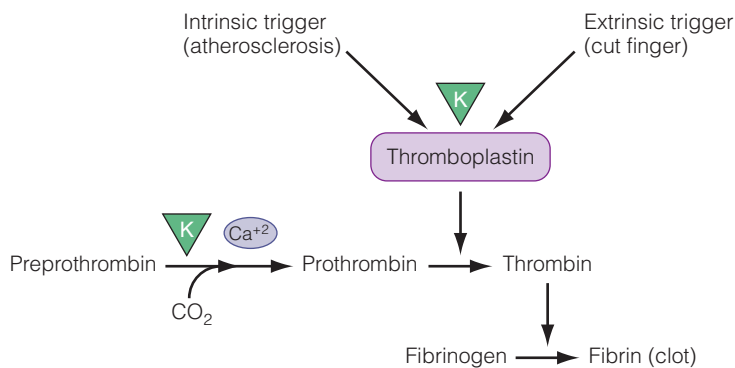
Vegetable oils, avocados, nuts, and seeds are good sources of vitamin E. Green leafy vegetables and fortified cereals also contribute to daily intake. The recommended intake for vitamin E is presented in alpha-tocopherol equivalents.

Vitamin E deficiencies, although rare, may result in nerve problems, muscle weakness, and increased susceptibility to free radical damage. Excess amounts of vitamin E from supplements may cause hemorrhage.



## Lo 9.8 Vitamin K

Vitamin K is a fat-soluble vitamin found naturally as phylloquinone in plants, and as menaquinone (manufactured by bacteria) in the colons of animals. Menadione is the synthetic form of vitamin K used in vitamin supplements. Vitamin K is a coenzyme for the carboxylation of factors involved in blood clotting and two proteins involved in bone formation. Dietary sources include leafy greens, vegetable oils, and margarine. A deficiency of vitamin K may result in hemorrhage and bone fractures. Individuals taking anticoagulant medications need to carefully monitor their vitamin K intake. There are no known toxicity problems.



## Lo 9.9 Vitamin Supplements Are Not a Substitute for Healthy Eating

Individuals often take daily vitamin supplements to prevent chronic disease without scientific research that supports their use. Vitamin supplements should never replace a healthy diet. A vitamin supplement is an option for individuals unable to meet their daily vitamin needs, such as during pregnancy, lactation, solely breast-fed infants, older individuals, strict vegetarians, people with allergies, or people who are on strict weight-loss diets or who eliminate certain food groups.

Vitamin supplement standards are not strictly enforced by the FDA. Each vitamin supplement bottle carries a nutrition label consumers can use to compare products. The U.S. Pharmacopoeia (USP) seal on a supplement label indicates that the supplement has been tested and meets the criteria for purity and accuracy. It does not ensure safety. Consumers should seek guidance from a qualified health professional before taking a dietary supplement.



## Terms to Know

- vitamins
- provitamins
- preformed vitamins
- toxicity
- hypervitaminosis
- megadose
- bioavailability
- antioxidants
- flavonoids
- oxidation
- free radicals
- oxidative stress
- age-related macular degeneration (AMD)
- cataract
- phytochemicals
- fortified foods
- retinoids
- retinol
- retinal
- retinoic acid
- retinyl ester
- carotenoids
- beta-carotene
- rhodopsin
- iodopsin
- rods
- cones
- bleaching
- retinol binding protein (RBP)
- epithelial cells
- cell division
- cell differentiation
- retinol activity equivalents (RAE)
- international units (IU)
- hypervitaminosis A
- osteoporosis
- carotenoderma
- night blindness
- xerophthalmia
- keratinization
- calciferol
- prohormone
- cholecalciferol (vitamin D<sub>3</sub>)
- ergocalciferol (vitamin D<sub>2</sub>)
- 7-dehydrocholesterol (provitamin D<sub>3</sub>)
- previtamin D<sub>3</sub> (precalciferol)
- vitamin D<sub>3</sub> binding protein (DBP)
- 25-hydroxycholecalciferol
- 1,25-dihydroxycholecalciferol
- calcitriol
- parathyroid hormone (PTH)
- hypervitaminosis D
- hypercalcemia
- rickets
- osteomalacia
- alpha-tocopherol (α-tocopherol)
- hemorrhage
- phyloquinone (vitamin K<sub>1</sub>)
- menaquinone (vitamin K<sub>2</sub>)
- menadione (vitamin K<sub>3</sub>)
- coagulation
- carboxylation
- clotting factors
- warfarin
- U.S. Pharmacopoeia (USP)

### MasteringNutrition™

Scan this QR code with your mobile device to access practice math activities. You can also access the activities in MasteringNutrition™.



## Check Your Understanding

- Vitamins are
  - essential nutrients needed in large amounts to prevent disease.
  - classified as either water-soluble or fat-soluble nutrients.
  - defined as inorganic nutrients.
  - easily made by the body from leftover glucose.
- Vitamins can be destroyed by
  - cold.
  - ultraviolet light.
  - acid pH.
  - cooking in a microwave.
- An individual who does not produce enough bile will have difficulty absorbing
  - thiamin (B<sub>1</sub>).
  - vitamin A.
  - folate.
  - pantothenic acid.
- A megadose of a vitamin
  - occurs when you eat too much of one particular food.
  - is necessary to prevent a variety of diseases.
  - is defined as 10 times the RDA.
  - is safe because all vitamins are easily excreted from the body.
- Which of the following are considered antioxidants?
  - vitamin E and beta-carotene
  - vitamin D and vitamin K
  - vitamin E and vitamin K
  - vitamin A and vitamin D
- The most usable form of vitamin A in the body is
  - retinol.
  - retinal.
  - retinoic acid.
  - retinoids.
- Vitamin D
  - is not toxic if consumed in amounts greater than the RDA.
  - is made in the skin from 1,25-dihydroxyvitamin D<sub>3</sub> and ultraviolet light.
  - is found in whole milk, but not in skim milk.
  - is found in fruits.
- The role of vitamin E in the body is to
  - prevent oxidative damage to cell membranes.
  - serve as a coenzyme.
  - enhance the absorption of calcium and phosphorus.
  - participate in blood clotting.
- Vitamin K is necessary for the synthesis of
  - glycogen.
  - rhodopsin.
  - prothrombin.
  - cholecalciferol.
- Which of the following statements is NOT true regarding the USP seal on the vitamin supplement label?
  - The dietary supplement contains the amount of the substance that is stated on the label.
  - The dietary supplement is good quality.
  - The dietary supplement is free of any contaminants.
  - The dietary supplement meets your daily needs for that vitamin.

## Answers

1. (b) Vitamins are classified by their solubility, as either fat-soluble or water-soluble nutrients. They are organic nutrients needed in small amounts in the diet because the body cannot synthesize sufficient amounts to maintain health.
2. (b) Some vitamins, especially vitamin B<sub>12</sub>, are destroyed by exposure to ultraviolet light, heat (such as during cooking), and when prepared in an alkaline pH (adding baking soda, for example). Cold temperatures do not destroy vitamins. Microwave cooking increases the retention of vitamins compared to steaming or boiling.
3. (b) Fat-soluble vitamins such as vitamin A are absorbed along with dietary fat, which requires bile for the process. Thiamin, folate, and pantothenic acid are water-soluble vitamins and do not need bile for absorption.
4. (c) A megadose of a vitamin is defined as 10 times or more of the RDA. Megadose levels can only be achieved by taking a supplement and can be harmful even if the vitamin is water soluble.
5. (a) Both vitamin E and beta-carotene function as antioxidants in the body. Vitamins A, D, and K perform other essential functions, but are not antioxidants.
6. (a) Retinol is the most usable form of vitamin A in the body. Retinoids include all three forms of preformed vitamin A: retinol, retinal, and retinoic acid.
7. (b) Vitamin D is a fat-soluble vitamin stored in the liver. It can be toxic if ingested in supplemental form in amounts greater than the RDA. The active form of vitamin D is 1,25-dihydroxyvitamin D<sub>3</sub> and 7-dehydrocholesterol is the compound in the skin that is converted to vitamin D from sunlight. Both whole and skim milk are usually

fortified with vitamin D but fruits do not contain vitamin D.

8. (a) Vitamin E functions as an antioxidant to prevent oxidative damage to cell membranes. Water-soluble vitamins usually serve as coenzymes, active vitamin D enhances the absorption of calcium and phosphorus, and vitamin K participates in blood clotting.
9. (c) Vitamin K is necessary for the synthesis of prothrombin, a protein that is involved in blood clotting. Rhodopsin is formed with retinal (vitamin A), and cholecalciferol is the active form of vitamin D in the body. Glycogen is the stored form of glucose found in muscles and liver.
10. (d) Manufacturers of dietary supplements can voluntarily have their products tested for the strength, quality, and purity of the supplement. It does not confirm that it will meet your daily need for the vitamin.

## Answers to True or False?

1. **False.** Although vitamins perform numerous essential functions in the body, they do not provide energy. Only the macronutrients (carbohydrates, protein, and fat) and alcohol provide kilocalories.
2. **True.** Fat-soluble vitamins are often found in foods that contain fat. For example, vitamin E is found in vegetable oils and vitamin A is found in egg yolks. However, some fat-soluble vitamins are also found in fortified foods that are low in fat, such as fortified cereals.
3. **False.** Overconsumption of vitamin supplements can result in intakes above the tolerable upper limits. Such high intakes can in turn lead to harmful toxicity symptoms.
4. **True.** Healthy individuals can meet their vitamin requirements by consuming an adequate, balanced

diet. However, some individuals, such as those with a specific vitamin deficiency, strict vegans, or those with dietary restrictions, may benefit from taking a vitamin supplement.

5. **False.** Cooking foods in a microwave helps retain more vitamins because of the reduced cooking time and exposure to heat. Foods prepared in a microwave oven also require very little cooking water; this prevents leaching of water-soluble vitamins.
6. **True.** Deep orange vegetables and some green vegetables are good sources of the vitamin A precursor beta-carotene, which is converted to vitamin A in the body.
7. **True.** In the skin is a compound called 7-dehydrocholesterol, which is converted to a previtamin D form when the ultraviolet rays of the sun alter its structure.
8. **False.** Vitamin K actually helps blood clot, as it participates in the synthesis of several proteins involved in the blood-clotting cascade.
9. **False.** The main role of vitamin E is as an antioxidant that helps protect cell membranes. However, the fat-soluble vitamins D and K are involved in bone health.
10. **False.** Antioxidants serve several beneficial functions in the body, but there is no magic pill for aging.

## Web Resources

- To learn more about the importance of fruits and vegetables to vitamin intake, visit [www.fruitsandveggiesmorematters.org](http://www.fruitsandveggiesmorematters.org)
- To learn more about the role of alternative therapies and dietary supplements in health and disease prevention, visit [www.complementarynutrition.org](http://www.complementarynutrition.org)
- To find out the latest recommendations for vitamins, visit <http://ods.od.nih.gov>

## References

- Rosenfeld, L. 1997. Vitamine-Vitamin. The Early Years of Discovery. *Clinical Chemistry* 43:680–685.
- Droge, W. 2002. Free Radicals in the Physiological Control of Cell Function. *Physiology Review* 82:47–95.
- Fiedor, J., and K. Burda. 2014. Potential Role of Carotenoids as Antioxidants in Human Health and Disease. *Nutrients* 6(2):466–488.
- Centers for Disease Control and Prevention. 2013. *Common Eye Disorders*. Available at www.cdc.gov. Accessed March 2014.
- Parmeggiani, F., M. R. Romano, C. Costagliola, F. Semeraro, C. Incorvaia, S. D'Angelo, P. Perri, et al. 2012. Mechanism of Inflammation in Age-Related Macular Degeneration. *Mediators of Inflammation* doi: 10.1155/2012/546786.
- Schleicher, M., K. Weikel, C. Garber, and A. Taylor. 2013. Diminishing Risk for Age-Related Macular Degeneration with Nutrition: A Current View. *Nutrients* 5(7):2405–2456.
- American Optometric Association. 2014. *Cataract*. Available at www.aoa.org. Accessed March 2014.
- Centers for Disease Control and Prevention. 2013. *Common Eye Disorders*.
- National Eye Institute. 2011. *Are These High Levels of Antioxidants and Zinc Right for You?* Available at www.nei.nih.gov. Accessed March 2014.
- Craig, W. J. 1997. Phytochemicals: Guardians of Our Health. *Journal of the American Dietetic Association* 97:S199–S204.
- Bilecova-Rabajdova, M., A. Birkova, P. Urban, K. Gregova, E. Durovcova, and M. Marekova. 2013. Naturally Occurring Substances and Their Role in Chemo-Protective Effects. *Central Europe Journal of Public Health* 21(4):213–219.
- Ruiz-Canela, M., and M. A. Martinez-Gonzalez. 2014. Lifestyle and Dietary Risk Factors for Peripheral Artery Disease. *Circulation Journal* 78(3):553–559.
- U.S. Department of Agriculture, U. S. Department of Health and Human Services. 2010. *Dietary Guidelines for Americans, 2010*. 7th ed. Washington, DC: U.S. Government Printing Office.
- Ross, A. C., B. Cabellero, R. J. Cousins, K. L. Tucker, and T. R. Ziegler. 2014. *Modern Nutrition in Health and Disease*. 11th ed. Philadelphia: Lippincott Williams & Wilkins.
- Santos, P. H. S., and M. A. Silva. 2008. Retention of Vitamin C in Drying Processes of Fruits and Vegetables—A Review. *Drying Technology—An International Journal* 26:1421–1437.
- Lee, S. K., and A. A. Kader. 2000. Preharvest and Postharvest Factors Influencing Vitamin C Content of Horticultural Crops. *Postharvest Biology and Technology* 20:207–220.
- Hwang, I. G., Y. J. Shin, S. Lee, J. Lee, and S. M. Yoo. 2012. Effects of Different Cooking Methods on the Antioxidant Properties of Red Pepper (*Capsicum annuum* L.). *Preventive Nutrition and Food Science* 17(4):286–292.
- Pandurangi, S., and L. E. LaBorde. 2004. Retention of Folate, Carotenoid and Other Quality Characteristics in Commercially Packaged Fresh Spinach. *Journal of Food Science* 69:C702–C707.
- Packaged Facts Project. 2011. *Omega-3 Ingredient Market to Grow 40% by 2015*. Available at www.packagedfacts.com. Accessed March 2014.
- Principles for Nutrition Labeling and Fortification*. Washington, DC: The National Academies Press.
- National Institutes of Health. 2013. *Vitamin A Fact Sheet for Health Professionals*. Available at http://ods.od.nih.gov. Accessed March 2014.
- Gropper, S. S., and J. L. Smith. 2014. *Advanced Nutrition and Metabolism*. 6th ed. Belmont, CA: Wadsworth—Cengage Learning.
- Kircik, L. H. 2014. Evaluating Tretinoin Formulations in the Treatment of Acne. *Journal of Drugs in Dermatology* 13(4):466–470.
- Rasi, A., E. Behrangi, M. Rohaninasab, and Z. M. Nahad. 2014. Efficacy of Fixed Daily 20 mg of Isotretinoin in Moderate to Severe Scar-Prone Acne. *Advanced Biomedical Research* doi: 10.4103/2277-9175.129693.
- Institute of Medicine, Food and Nutrition Board. 2001. *Dietary Reference Intakes: Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: The National Academies Press.
- Tanumihardjo, A. S. 2013. Vitamin A and Bone Health: The Balancing Act. *Journal of Clinical Densitometry* 16(4):414–419.
- Lind, T., A. Sundqvist, L. Hu, G. Pejler, G. Andersson, A. Jacobson, and H. Melhus. 2013. Vitamin A Is a Negative Regulator of Osteoblast Mineralization. *PLoS One* 8(12):e82388. doi:10.1371/journal.pone.0092388.
- Promislow, J. H., D. Goodman-Guren, D. J. Slymen, and E. Barrett-Connor. 2002. Retinol Intake and Bone Mineral Density in the Elderly: The Rancho Bernardo Study. *Journal of Bone Mineral Research* 17:1359–1362.
- Ross, et al. 2014. *Modern Nutrition*.
- Institute of Medicine, Food and Nutrition Board. 2001. *Dietary Reference Intakes: Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*.
- Ibid.
- Brown, M. J., M. G. Ferruzzi, M. L. Nguyen, D. A. Cooper, A. L. Eldridge, S. J. Swartz, and W. S. White. 2004. Carotenoid Bioavailability Is Higher from Salads Ingested with Full-Fat than with Fat-Reduced Salad Dressings as Measured with Electrochemical Detection 1'2'3. *American Journal of Clinical Nutrition* 80:396–403.
- Institute of Medicine, Food and Nutrition Board. 2001. *Dietary Reference Intakes: Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*.
- Ibid.
- Brinkley, N., and D. Krueger. 2000. Hypervitaminosis A and Bone. *Nutrition Reviews* 58:138–144.
- Feskanich, D. 2002. Vitamin A Intake and Hip Fractures among Postmenopausal Women. *Journal of the American Medical Association* 287:47–54.
- Bjelakovic, G., D. Nikolova, L. L. Gluud, R. G. Simonetti, and C. Gluud. 2007. Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention: Systematic Review and Meta-Analysis. *JAMA* 297(8):842–857.
- Virtamo, J., P. R. Taylor, J. Kontto, S. Männistö, M. Utriainen, S. T. Weinstein, J. Huttunen, and D. Albanes. 2014. Effects of  $\alpha$ -Tocopherol and  $\beta$ -Carotene Supplementation on Cancer Incidence and Mortality: 18-Year Postintervention Follow-Up of the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *International Journal of Cancer* 135(1):178–185.
- Sommer, A. 2014. Preventing Blindness and Saving Lives: The Centenary of Vitamin A. *Journal of the American Medical Association Ophthalmology* 132(1):115–117.
- Jones, G. 2014. Vitamin D. In A. C. Ross, et al., eds. *Modern Nutrition in Health and Disease*. 11th ed. Philadelphia: Lippincott Williams & Wilkins.
- Autier, P., M. Boniol, C. Pizot, and P. Mullie. 2014. Vitamin D Status and Ill Health. *Lancet Diabetes Endocrinology* 2(1):76–89.
- Holick, M. F. 2013. Vitamin D, Sunlight, and Cancer Connection. *Anticancer Agents in Medicinal Chemistry* 13(1):70–82.
- Ibid.
- Aranow, C. 2011. Vitamin D and the Immune System. *Journal of Investigative Medicine* 59(6):881–886.
- Munger, K. L., L. I. Levin, J. Massa, R. Horst, T. Orban, and A. Ascherio. 2013. Preclinical Serum 25-Hydroxyvitamin D Levels and Risk of Type 1 Diabetes in a Cohort of U.S. Military Personnel. *American Journal of Epidemiology* doi:10.1093/aje/kws243.
- Ibid.
- Chih-Chien, S., L. Min-Tser, L. Kuo-Cheng, and W. Chia-Chao. 2012. Role of Vitamin D in Insulin Resistance. *Journal of Biomedical Biotechnology* doi: 10.1155/2012/634195.

48. Stadlmayr, A., E. Aigner, U. Huber-Schönauer, D. Niederseer, et al. 2014. Relations of Vitamin D Status, Gender and Type 2 Diabetes in Middle-Aged Caucasians. *Acta Diabetologica* doi:10.1007/s00592-014-0596-9.
49. Min, B. 2013. Effects of Vitamin D on Blood Pressure and Endothelial Function. *Korean Journal of Physiology and Pharmacology* 17(5):385–392.
50. National Institutes of Health. 2011. *Vitamin D Fact Sheet for Health Professionals*. Available at <http://ods.od.nih.gov>. Accessed March 2014.
51. Ibid.
52. Ibid.
53. Institute of Medicine, Food and Nutrition Board. 2010. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington, DC: The National Academies Press.
54. Ibid.
55. Ibid.
56. Ibid.
57. Parker, G., and H. Brotchie. 2011. 'D' for Depression: Any Role for Vitamin D? *Acta Psychiatrica Scandinavica* 124(4):243–249.
58. Byrne, S. N. 2014. How Much Sunlight Is Enough? *Photochemical and Photobiological Sciences* 13:840–852.
59. Pettifor, J. M., and A. Prentice. 2011. The Role of Vitamin D in Paediatric Bone Health. *Best Practice & Research Clinical Endocrinology & Metabolism* 25(4):573–784.
60. Prentice, A. 2013. Nutritional Rickets Around the World. *The Journal of Steroid Biochemistry and Molecular Biology* 136:201–206.
61. Thacher, T. D., P. R. Fischer, P. J. Tebben, R. J. Singh, S. S. Cha., J. A. Maxon, and B. P. Yawn. 2013. Increasing Incidence of Nutritional Rickets: A Population-Based Study in Olmsted County, Minnesota. *Mayo Clinic Proceedings* 88(2):176–183.
62. Centers for Disease Control and Prevention. 2001. Severe Malnutrition among Young Children—Georgia, January 1997–1999. *Morbidity and Mortality Weekly Report*. Available at [www.cdc.gov](http://www.cdc.gov). Accessed April 2014.
63. Gordon, C. M., K. C. DePeter, H. A. Feldman, E. Grace, and S. J. Emans. 2004. Prevalence of Vitamin D Deficiency among Healthy Adolescents. *Archives of Pediatric and Adolescent Medicine* 158:531–537.
64. Ward, L. M., I. Gaboury, M. Ladhani, and S. Zlotkin. 2007. Vitamin D–Deficiency Rickets among Children in Canada. *Canadian Medical Association Journal* 177:161–166.
65. Gallos, S., K. Comeau, C. Vanstone, S. Agellon, et al. 2013. Effect of Different Dosages of Oral Vitamin D Supplementation on Vitamin D Status in Healthy, Breastfed Infants: A Randomized Trial. *Journal of the American Medical Association* 309(17):1785–1792.
66. Kit, B. K., M. D. Carroll, and C. L. Ogden. 2011. *Low-Fat Milk Consumption among Children and Adolescents in the United States, 2007–2008*. Available at [www.cdc.gov](http://www.cdc.gov). Accessed March 2014.
67. Centers for Disease Control and Prevention. 2013. *Skin Cancer Statistics*. Available at [www.cdc.gov](http://www.cdc.gov). Accessed March 2014.
68. Marantes, I., S. J. Achenbach, E. J. Atkinson, S. Khosla, L. J. Melton III, and S. Amin. Is Vitamin D a Determinant of Muscle Mass and Strength? *Journal of Bone Mineral Research* 26(12):2860–2870.
69. National Institutes of Health, Office of Dietary Supplements. 2013. *Vitamin E*. Available at <http://ods.od.nih.gov>. Accessed March 2014.
70. Ibid.
71. Miller, E. R., R. Pastor-Barriso, D. Dalal, R. A. Riemersma, L. J. Appel, and E. Vitamin E Supplementation May Increase All-Cause Mortality. *Annals of Internal Medicine* 142:37–46.
72. Almquist, H. J. 1975. The History of Vitamin K. *The American Journal of Clinical Nutrition* 28:656–659.
73. Hamidi, M. S., O. Gajic-Veljanoski, and A. M. Cheung. 2013. Vitamin K and Bone Health. *Journal of Clinical Densitometry* 16(4):409–413.
74. Shea, M. K., and R. M., Holden. 2012. Vitamin K Status and Vascular Calcification: Evidence from Observational and Clinical Studies. *Advances in Nutrition* 3:158–165.
75. Institute of Medicine. 2006. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: The National Academies Press.
76. National Institutes of Health. 2003. *Coumadin and Vitamin K*. Available at <http://ods.od.nih.gov>. Accessed March 2014.
77. Lippi, G., and M. Franchini. 2011. Vitamin K in Neonates: Facts and Myths. *Blood Transfusion* 9(1): 4–9.
78. Institute of Medicine. 2006. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*.
79. Booth, S. L., L. Martini, J. W. Peterson, E. Saltzman, G. E. Dallal, and R. J. Wood. 2003. Dietary Phylloquinone Depletion and Repletion in Older Women. *Journal of Nutrition* 133:2565–2569.
80. Gahche, J., R. Bailey, B. V. Hughes, E. Yetley, J. Dwyer, et al. 2011. *Dietary Supplement Use among U.S. Adults Has Increased Since NHANES III (1988–1994)*. NCHS Data Brief. Available at [www.cdc.gov](http://www.cdc.gov). Accessed March 2014.
81. Nutrition Business Journal. 2012. NBJ's Supplement Business Report 2012. Penton Media, Inc.
82. National Institutes of Health, Office of Dietary Supplements. 2013. *Multivitamin/Mineral Supplements*. Available at <http://ods.od.nih.gov>. Accessed March 2014.
83. Moyer, V. A. 2014. Vitamin, Mineral, and Multivitamin Supplements for the Primary Prevention of Cardiovascular Disease and Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine* doi:10.7326/M14-0198.
84. Sesso, H. D., W. G. Christen, V. Bubes, J. P. Smith, J. MacFadyen, M. Schvartz, J. E. Manson, et al. 2012. Multivitamins in the Prevention of Cardiovascular Disease in Men: The Physicians' Health Study II Randomized Controlled Trial. *Journal of the American Medical Association* 308(17):1751–1760.
85. Grodstein, F., J. O'Brien, J. H. Kang, R. Dushkes, N. R. Cook, O. Okereke, J. E. Manson, et al. 2013. Long-Term Multivitamin Supplementation and Cognitive Function in Men: A Randomized Trial. *Annals of Internal Medicine* 159(12):806–814.
86. Marra, M., and A. Boyar. 2009. Position of the American Dietetic Association: Nutrient Supplementation. *Journal of the American Dietetic Association* 109:2073–2085.
87. Van Laccck, R. 2014. *Foods and Dietary Supplements*. Available at [www.fdalawblog.net](http://www.fdalawblog.net). Accessed March 2014.
88. United States Pharmacopoeia. 2014. *USP Verified Dietary Supplements*. Available at [www.usp.org](http://www.usp.org). Accessed March 2014.