CHAPTER 7

Vitamins

KEY CONCEPTS

- Vitamins are noncaloric, essential nutrients that are necessary for many metabolic tasks.
- Certain health problems are related to inadequate or excessive vitamin intake.
- Vitamins occur in a wide variety of foods and are packaged with the energy-yielding macronutrients (i.e., carbohydrate, fat, and protein).
- The body uses vitamins to make the coenzymes that are required for some enzymes to function.
- The need for particular vitamin supplements depends on a person's vitamin status.

More than any other group of nutrients, vitamins have captured public interest and concern. This chapter answers some of the questions about vitamins: What do they do? How much of each vitamin does the human body need? What foods do they come from? Do we need to take supplements? The scientific study of nutrition, on which the Dietary Reference Intake (DRI) guidelines are based, continues to expand the body of nutrition knowledge. Thus, the answers to these questions have evolved through years of research.

This chapter looks at the vitamins both as a group and as individual nutrients. It explores general and specific vitamin needs as well as reasonable and realistic supplement use.

DIETARY REFERENCE INTAKES

The study of vitamins and minerals and their many functions in human nutrition is a subject of intense scientific investigation. As discussed in Chapter 1, the DRIs are recommendations for nutrient intake by healthy population groups. The continuing development of DRIs under the direction of the National Academy of Sciences takes place over several years and involves numerous scientists from the United States and Canada. They include recommendations for each gender and age group, and they incorporate and expand upon the well-known Recommended Dietary Allowances (RDAs).

Within the DRIs are the following four interconnected categories of recommendations, which were also defined in Chapter 1:

1. *RDA:* The daily intake that meets the needs of almost all healthy individuals in a specified group
2. *Estimated Average Requirement (EAR):* The nutrient intake that meets the needs of half of the individuals in the reference population
3. *Adequate Intake (AI):* A guideline that is used when not enough scientific data is available to establish an RDA
4. *Tolerable Upper Intake Level (UL):* A guideline that sets the maximum nutrient intake that is unlikely to pose a risk of toxicity in healthy individuals

This chapter's discussion of vitamins and the following chapters that discuss minerals, fluids, and electrolytes refer to the various DRI recommendations (especially the RDAs) whenever possible.

evolve Please refer to the Students' Resource section of this text's Evolve Web site for additional study resources.

REFERENCES

1. Food and Nutrition Board, Institute of Medicine. *Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids.* Washington, DC: National Academies Press; 2002.
2. Bosy-Westphal A, Reinecke U, Schlörke T, et al. Effect of organ and tissue masses on resting energy expenditure in underweight, normal weight and obese adults. *Int J Obes Relat Metab Disord.* 2004;28(1):72-79.
3. Frankenfield D, Roth-Yousey L, Compher C. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. *J Am Diet Assoc.* 2005;105(5):775-789.
4. Müller MJ, Bosy-Westphal A, Later W, et al. Functional body composition: insights into the regulation of energy metabolism and some clinical applications. *Eur J Clin Nutr.* 2009;63(9):1045-1056.
5. Johnstone AM, Murison SD, Duncan JS, et al. Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine, *Am J Clin Nutr.* 2005;82(5):941-948.
6. Geer EB, Shen W. Gender differences in insulin resistance, body composition, and energy balance. *Gend Med.* 2009;6 (Suppl 1):60-75.
7. Ahmed T, Haboubi N. Assessment and management of nutrition in older people and its importance to health. *Clin Interv Aging.* 2010;5:207-216.
8. St-Onge MP, Gallagher D. Body composition changes with aging: the cause or the result of alterations in metabolic rate and macronutrient oxidation? *Nutrition.* 2010;26 (2):152-155.
9. Butte NF, King JC. Energy requirements during pregnancy and lactation. *Public Health Nutr.* 2005;8(7A):1010-1027.
10. Hall KD. Computational model of in vivo human energy metabolism during semistarvation and refeeding. *Am J Physiol Endocrinol Metab.* 2006;291(1):E23-E37.
11. Landsberg L, Young JB, Leonard WR, et al. Do the obese have lower body temperatures? A new look at a forgotten variable in energy balance. *Trans Am Clin Climatol Assoc.* 2009;120:287-295.
12. Kreitschmann-Andermahr I, Suarez P, Jennings R, et al. GH/IGF-I regulation in obesity—mechanisms and practical consequences in children and adults. *Horm Res Paediatr.* 2010;73(3):153-160.
13. Martin CK, Church TS, Thompson AM, et al. Exercise dose and quality of life: a randomized controlled trial. *Arch Intern Med.* 2009;169(3):269-278.
14. U.S. Department of Agriculture, U.S. Department of Health and Human Services. *Dietary guidelines for Americans, 2010.* Washington, DC: U.S. Government Printing Office; 2010.
15. U.S. Department of Agriculture, Center for Nutrition Policy and Promotion. *USDA's MyPlate home page* (website): www.choosemyplate.gov. Accessed August 23, 2011.

FURTHER READING AND RESOURCES

The following Web sites provide methods for predicting total energy needs and for evaluating energy expenditure.

Adult energy needs and body mass index calculator. www.bcm.edu/cnrc/caloriesneed.cfm

Children's energy needs calculator. www.bcm.edu/cnrc/healthyeatingcalculator/eatingCal.html

Mayo Clinic. *Metabolism and weight loss: how you burn calories:* www.mayoclinic.com/health/metabolism/WT00006

Gardner DS, Rhodes P. Developmental origins of obesity: programming of food intake or physical activity? *Adv Exp Med Biol.* 2009;646:83-93.

This review article outlines theories regarding obesity. The authors briefly discuss the multifactorial elements that are involved in energy storage and energy expenditure.

THE NATURE OF VITAMINS

Discovery

Early Observations

Vitamins were largely discovered while searching for cures of classic diseases that were suspected to be associated with dietary deficiencies. As early as 1753, British naval surgeon Dr. James Lind observed that many sailors became ill and died on long voyages when they had to live on rations without fresh foods. When Lind provided the sailors with fresh lemons and limes, which were easily stored on a later voyage, no one became ill. Dr. Lind had discovered that scurvy, which had been the curse of sailors, was caused by a dietary deficiency and was prevented by adding lemons or limes to the diet. Because British sailors carried limes on these long voyages, they got the nickname *limeys.*

Early Animal Experiments

In 1906, Dr. Frederick Hopkins of Cambridge University performed an experiment in which he fed a group of rats a synthetic mixture of protein, fat, carbohydrate, mineral salts, and water. All of the rats became ill and died. In another experiment, he added milk to the purified ration, and all of the rats grew normally. This important discovery—that elements present in natural foods are essential to life—provided the necessary foundation for the individual vitamin discoveries that followed.

Era of Vitamin Discovery

Most of the vitamins that are known today were discovered during the first half of the 1900s. The nature of these vital molecules became more evident over time. A form of the name *vitamin* was first used in 1911, when Casimir Funk, a Polish chemist working at the Lister Institute in London, discovered a nitrogen-containing substance (in organic chemistry, known as an *amine*) that he speculated might be a common characteristic of all vital agents. He coined the word *vitamine,* meaning "vital amine." The final *e* was dropped later, when other vital substances turned out not to be amines, and the name *vitamin* was retained to designate compounds within this class of essential substances. At first scientists assigned letters of the alphabet to each vitamin in the order that they were discovered; however, as more vitamins were discovered, this practice was abandoned in favor of more specific names based on a vitamin's chemical structure or body function. Both letter designation and current name will be presented here.

Definition

As each vitamin was discovered during the first half of the 1900s, the following two characteristics that define a vitamin clearly emerged:

1. It must be a vital organic substance that is not a carbohydrate, fat, or protein, and it must be necessary to perform its specific metabolic function or to prevent its associated deficiency disease.
2. It cannot be manufactured by the body in sufficient quantities to sustain life, so it must be supplied by the diet.

Because the body only needs them in small amounts, vitamins are considered micronutrients. The total volume of vitamins that a healthy person normally requires each day would barely fill a teaspoon. Thus, the units of measure for vitamins—milligrams or micrograms—are exceedingly small and difficult to visualize (see the For Further Focus box, "Small Measures for Small Needs"). Nonetheless, all vitamins are essential to life.

Functions of Vitamins

Although each vitamin has its specific metabolic tasks, general functions of vitamins include the following: (1) as components of coenzymes; (2) as antioxidants; (3) as hormones that affect gene expression; (4) as components of cell membranes; and (5) as components of the light-sensitive rhodopsin molecule in the eyes (i.e., vitamin A).

Metabolism: Enzymes and Coenzymes

Coenzymes that are derived from vitamins are an integral part of some enzymes, without which these enzymes cannot catalyze their metabolic reactions. For example, several of the B vitamins (i.e., thiamin, niacin, and riboflavin) are part of coenzymes. These coenzymes are, in turn, integral parts of enzymes that metabolize glucose, fatty acids, and amino acids to extract energy. Enzymes act as catalysts; catalysts increase the rate at which their specific chemical reactions proceed, but they are not themselves consumed during the reactions.

scurvy a hemorrhagic disease caused by a lack of vitamin C that is characterized by diffuse tissue bleeding, painful limbs and joints, thickened bones, and skin discoloration from bleeding; bones fracture easily, wounds do not heal, gums swell and tend to bleed, and the teeth loosen.

FOR FURTHER FOCUS

SMALL MEASURES FOR SMALL NEEDS

By definition, vitamins are essential nutrients that are necessary in small amounts for human health. Just how small those amounts truly are is sometimes hard to imagine. Vitamins are measured in metric system terms such as *milligram* and *microgram,* but how much is that? Perhaps comparing these amounts with commonly used household measures will be helpful.

Early during the age of scientific development, scientists realized that they needed a common language of measures that could be understood by all nations to exchange rapidly developing scientific knowledge. Thus, the metric system was born. Like American money, it is a simple decimal system, but here it is applied to weights and measures. This system was developed in the mid-1800s by French scientists and named *Le Système International d'Unités,* which is abbreviated as *SI units.* The use of these more precise units is now widespread, especially because it is mandatory for all purposes in most countries besides the United States. The U.S. Congress passed the official Metric Conversion Act in 1975, but this country has been slower to apply the metric system to common use as compared with other countries (see Appendix E). However, the use of this system in scientific work is worldwide.

Compare the two metric measures that are used for vitamins in the United States. Below are the Recommended Dietary Allowances equated with common measures to demonstrate just how small our needs really are:

- One *milligram* (mg) is equal to one thousandth of a gram (28 g = 1 oz; 1 g is equal to approximately ¼ tsp). Recommended Dietary Allowances are measured in milligrams for vitamins B_6, C, and E and for thiamin, riboflavin, niacin, pantothenic acid, and choline.
- A *microgram* (mcg or μg) is equal to one millionth of a gram. Recommended Dietary Allowances are measured in micrograms for vitamins A (retinol equivalents), B_{12}, D, and K and for folate and biotin.

It is a small wonder that the total amount of vitamins that we need each day would scarcely fill a teaspoon; however, that small amount makes the big difference between life and death.

Tissue Structure and Protection

Some vitamins are involved in tissue or bone building. For example, vitamin C is involved in the synthesis of collagen, which is a structural protein in the skin, ligaments, and bones. In fact, the word *collagen* comes from a Greek word meaning "glue." Collagen is like glue in its capacity to add tensile strength to body structures. Vitamins (e.g., A, C, and E) also act as **antioxidants** to protect cell structures and to prevent damage caused by free radicals.

Prevention of Deficiency Diseases

When a vitamin deficiency becomes severe, the nutritional deficiency disease associated with the specific function of that vitamin becomes apparent. For example, the classic vitamin deficiency disease scurvy is caused by insufficient dietary vitamin C. Scurvy is a hemorrhagic disease that is characterized by bleeding in the joints and other tissues and by the breakdown of fragile capillaries under normal blood pressure; these are all symptoms that are related to vitamin C's role in producing the collagen in strong capillary walls. Internal membranes disintegrate and death occurs, as previously mentioned regarding British sailors of earlier centuries. The name *ascorbic acid* comes from the Latin word *scorbutus,* meaning "scurvy," and the prefix *a-* means "without"; thus, the term *ascorbic* means "without scurvy." In developed countries today, we do not see frank scurvy often, but we do see vitamin C deficiency in combination with other forms and degrees of malnutrition among low-income and poverty-stricken population groups.

Vitamin Metabolism

The way in which our bodies digest, absorb, and transport vitamins depends on the vitamin's solubility. Vitamins are traditionally classified as either fat soluble or water soluble. The fat-soluble vitamins are A, D, E, and K. The water-soluble vitamins are C and all of the B vitamins. This chapter is divided into the following sections: (1) Fat-Soluble Vitamins; (2) Water-Soluble Vitamins; (3) Phytochemicals; and (4) Vitamin Supplementation.

Fat-Soluble Vitamins

Intestinal cells absorb fat-soluble vitamins with fat as a micelle and then incorporate all fat-soluble nutrients into chylomicrons. From the intestinal cells, chylomicrons enter the lymphatic circulation and then the blood (see Chapter 3). The absorption of fat-soluble vitamins is enhanced by dietary fat. For instance, the vitamin A in a glass of vitamin-A-fortified milk is better absorbed from

antioxidant a molecule that prevents the oxidation of cellular structures by free radicals whole or 2% milk than from skim milk, because skim milk contains no fat.

Unlike water-soluble vitamins, fat-soluble vitamins can be stored the liver and adipose tissue for long periods of time. The body uses this reserve in times of inadequate daily intake. Fat-soluble vitamin accumulation in the liver and in adipose tissue is the reason that excess intake can result in toxicity over time.

Water-Soluble Vitamins

Intestinal cells easily absorb water-soluble vitamins. From these cells, the vitamins move directly into the portal blood circulation. Because blood is mostly water, the transport of water-soluble vitamins does not require the assistance of carrier proteins.

With the exception of cobalamin (vitamin B_{12}) and pyridoxine (vitamin B_6), the body does not store water-soluble vitamins to any significant extent. Therefore, the body relies on the frequent intake of foods that are rich in water-soluble vitamins. The potential toxicity of each vitamin is determined by the body's capacity to store it and the capacity of the liver and kidneys to clear it.

Fat-soluble and water-soluble vitamins are absorbed throughout the small intestines. Refer to Figure 5-8 for the general absorptive sites of all nutrients in the gastrointestinal tract.

SECTION 1 **FAT-SOLUBLE VITAMINS**

VITAMIN A (RETINOL)

Functions

Vitamin A performs the functions of aiding vision, tissue strength and immunity, and growth.

Vision

The chemical name ***retinol*** was given to vitamin A because of its major function in the retina of the eye. The aldehyde form, retinal, is part of a light-sensitive pigment in retinal cells called *rhodopsin,* which is commonly known as *visual purple.* Rhodopsin enables the eye to adjust to different amounts of available light. A mild vitamin A deficiency may cause night blindness, slow adaptation to darkness, or glare blindness. Vitamin-A–related compounds (i.e., the **carotenoids** lutein and zeaxanthin) are specifically associated with the prevention of age-related macular degeneration.[1]

Tissue Strength and Immunity

The other retinoids (i.e., retinoic acid and retinol) help to maintain healthy epithelial tissue, which is the protective tissue that covers body surfaces (i.e., the skin and the inner mucous membranes in the nose, throat, eyes, gastrointestinal tract, and genitourinary tract). These tissues are the primary barrier to infection. Vitamin A is also important as an antioxidant and in the production of immune cells that are responsible for fighting bacterial, parasitic, and viral attacks.

Growth

Retinoic acid and retinol are involved in skeletal and soft-tissue growth through their roles in protein synthesis and the stabilization of cell membranes. The constant need to replace old cells in the bone matrix, the gastrointestinal tract, and other areas requires adequate vitamin A intake.

Requirements

Vitamin A requirements are based on its two basic forms in foods (i.e., preformed vitamin A and provitamin A) and its storage in the body. The established RDA for adults is 700 mcg retinol equivalents for women and 900 mcg retinol equivalents for men.[2]

retinol the chemical name of vitamin A; the name is derived from the vitamin's visual functions related to the retina of the eye, which is the back inner lining of the eyeball that catches the light refractions of the lens to form images that are interpreted by the optic nerve and the brain and that makes the necessary light–dark adaptations.

carotenoids organic pigments that are found in plants; known to have functions such as scavenging free radicals, reducing the risk of certain types of cancer, and helping to prevent age-related eye diseases; more than 600 carotenoids have been identified, with β-carotene being the most well-known.

Food Forms and Units of Measure

Vitamin A occurs in two forms, as follows:

1. Preformed vitamin A or retinol, which is the active vitamin A found in foods that are derived from animal products.
2. Provitamin A or **β-carotene**, which is a pigment in yellow, orange, and deep green fruits or vegetables that the human body can convert to retinol. Carotenoids are a family of compounds that are similar in structure; β-carotene and lutein are the most common in foods (Box 7-1).

In the typical American diet, a significant amount of vitamin A is in the *pro*vitamin A form (i.e., β-carotene). To account for all food forms, individual carotenoids and preformed vitamin A are measured, and the amounts are converted to retinol equivalents. For the body to make 1 mcg of retinol, 12 mcg of dietary β-carotene, 2 mcg of supplemental β-carotene, or 24 mcg of either of the carotenoids (α-carotene or β-cryptoxanthin) are necessary. An older measure that is sometimes used to quantify vitamin A is the International Unit (IU). One IU of vitamin A equals 0.3 mcg of retinol or 0.6 mcg of β-carotene.

Body Storage

The liver can store large amounts of retinol. In healthy individuals, the liver stores approximately 80% of the body's total vitamin A. Thus, the liver is particularly susceptible to toxicity as a result of excessive vitamin A supplementation. The remaining vitamin A may be stored in adipose tissue, the kidneys, and the lungs.

Deficiency Disease

Adequate vitamin A intake prevents two eye conditions: (1) xerosis, which involves itching, burning, and red, inflamed eyelids; and (2) xerophthalmia, which is blindness that is caused by severe deficiency. Dietary vitamin A deficiency is the leading cause of preventable blindness in children worldwide. A recent publication by the World Health Organization reports that vitamin A deficiency that results in night blindness currently affects 5.2 million preschool-aged children and 9.8 million pregnant women globally.[3]

Deficiency symptoms are directly related to vitamin A's functions. Therefore, a lack of dietary vitamin A may also result in epithelial and immune system disorders.

Toxicity Symptoms

The condition created by excessive vitamin A intake is called *hypervitaminosis A*. Symptoms include bone pain, dry skin, loss of hair, fatigue, and anorexia. Excessive vitamin A intake may cause liver injury with portal hypertension, which is elevated blood pressure in the portal vein, and ascites, which is fluid accumulation in the abdominal cavity. Because of the potential for toxicity, the UL of retinol for adults has been set at 3000 mcg/day.[2] Although vitamin A deficiency is more common worldwide than toxicity, children in the United States may consume excess vitamin A from fortified foods alone, without added vitamin A from dietary supplements.[4] Toxicity symptoms usually result from the overconsumption of preformed vitamin A rather than of carotenoids. The absorption of dietary carotenoids is dose dependent at high intake levels. However, the prolonged excessive intake of foods that are high in β-carotene will cause a harmless orange skin tint that disappears when the excessive intakes are discontinued. Alternatively, β-carotene supplements can reach concentrations in the body that promote oxidative damage, cell division, and the destruction of other forms of vitamin A.

Food Sources

Fish liver oils, liver, egg yolks, butter, and cream are sources of preformed natural vitamin A. Preformed vitamin A occurs naturally in milk fat. Low-fat and nonfat milks and margarine are significant sources of vitamin A, because they are fortified. Some good sources of β-carotene are dark green leafy vegetables such as Swiss

BOX 7-1 CAROTENOIDS

Carotenes: orange pigments that contain no oxygen
- α-Carotene
- β-Carotene
- γ-Carotene
- δ-Carotene
- Lycopene

Xanthophylls: yellow pigments that contain some oxygen
- Lutein
- Zeaxanthin
- Neoxanthin
- Violaxanthin
- α- and β-Cryptoxanthin

carotene a group name for three red and yellow pigments (α-, β-, and γ-carotene) that are found in dark green and yellow vegetables and fruits; β-carotene is most important to human nutrition because the body can convert it to vitamin A, thus making it a primary source of the vitamin.

chard, turnip greens, kale, and spinach as well as dark-orange vegetables and fruits such as carrots, sweet potatoes or yams, pumpkins, mangoes, and apricots. Table 7-1 provides some comparative food sources of vitamin A.

β-Carotene and preformed vitamin A require emulsification by bile salts to be absorbed by the intestine. Preformed vitamin A is efficiently absorbed at a rate of 70% to 90%, whereas provitamin A (carotenoids) are less bioavailable at an absorption rate of 20% to 50%. Inside the intestinal cells, both forms are incorporated into chylomicrons with fat, and the chylomicrons pass through the lymphatic system and into the bloodstream.

Stability

Retinol is unstable when it is exposed to heat and oxygen. Quick cooking methods that use little water help to preserve vitamin A in food.

TABLE 7-1 FOOD SOURCES OF VITAMIN A

Item	Quantity	Amount (mcg of Retinol Equivalents)
Vegetables		
Beet greens, boiled	½ cup	276
Bok choy, boiled	½ cup	180
Carrots, raw	½ cup	534
Collard greens, boiled	½ cup	386
Dandelion greens, boiled	½ cup	260
Kale, raw	½ cup	258
Mustard greens, boiled	½ cup	221
Pumpkin, boiled	½ cup	306
Spinach, boiled	½ cup	472
Sweet potato, baked, in skin	1 medium (114 g)	1096
Winter squash	½ cup	268
Fruits		
Cantaloupe	1 cup, diced	264
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Beef liver, pan fried	3 oz	6582
Chicken liver, pan fried	3 oz	3652
Milk and Dairy Products		
Milk, low-fat 2%, fortified	8 oz	134
Milk, skim, fortified	8 oz	149
Ricotta cheese, whole milk	½ cup	149

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 12 2010.

VITAMIN D (CALCIFEROL)

Vitamin D was mistakenly classified as a vitamin in 1922 by its discoverers when they cured rickets with fish oil, which is a natural source of vitamin D. Today, we know that the compound produced by animals (i.e., **cholecalciferol** or vitamin D_3) and some organisms (i.e., **ergocalciferol** or vitamin D_2) is a **prohormone** rather than a vitamin. Vitamins D_2 and D_3 are both physiologically relevant to human nutrition, and they are collectively referred to as *calciferol*.

Upon exposure to ultraviolet light, humans are able to convert the precursor 7-dehydrocholesterol, a compound that is found in the epidermal layer of skin, into cholecalciferol. Similarly, organisms such as invertebrates and fungi are capable of converting the precursor ergosterol into ergocalciferol after they receive ultraviolet irradiation.

The activated and functional form of vitamin D is **calcitriol** (i.e., 1,25-dihydroxycholecalciferol). Vitamins D_2 and D_3 must be activated in two successive hydroxylation reactions to yield calcitriol. The first hydroxylation reaction occurs in the liver to produce 25-hydroxycholecalciferol. The enzyme **1-α-hydroxylase** then catalyzes the second hydroxylation reaction in the kidneys to produce the most active form of vitamin D, calcitriol. Figure 7-1 illustrates the activation process of vitamin D in the body.

cholecalciferol the chemical name for vitamin D_3 in its inactive form; it is often shortened to *calciferol.*

ergocalciferol the chemical name for vitamin D_2 in its inactive form; it is produced by some organisms (not humans) upon ultraviolet irradiation from the precursor ergosterol.

prohormone a precursor substance that the body converts to a hormone; for example, a cholesterol compound in the skin is first irradiated by sunlight and then converted through successive enzyme actions in the liver and kidney into the active vitamin D hormone, which then regulates calcium absorption and bone development.

calcitriol the activated hormone form of vitamin D.

1-α-hydroxylase the enzyme in the kidneys that catalyzes the hydroxylation reaction of 25-hydroxycholecalciferol (i.e., calcidiol) to calcitriol, which is the active form of vitamin D; 1-α-hydroxylase activity is increased by parathyroid hormone when blood calcium levels are low.

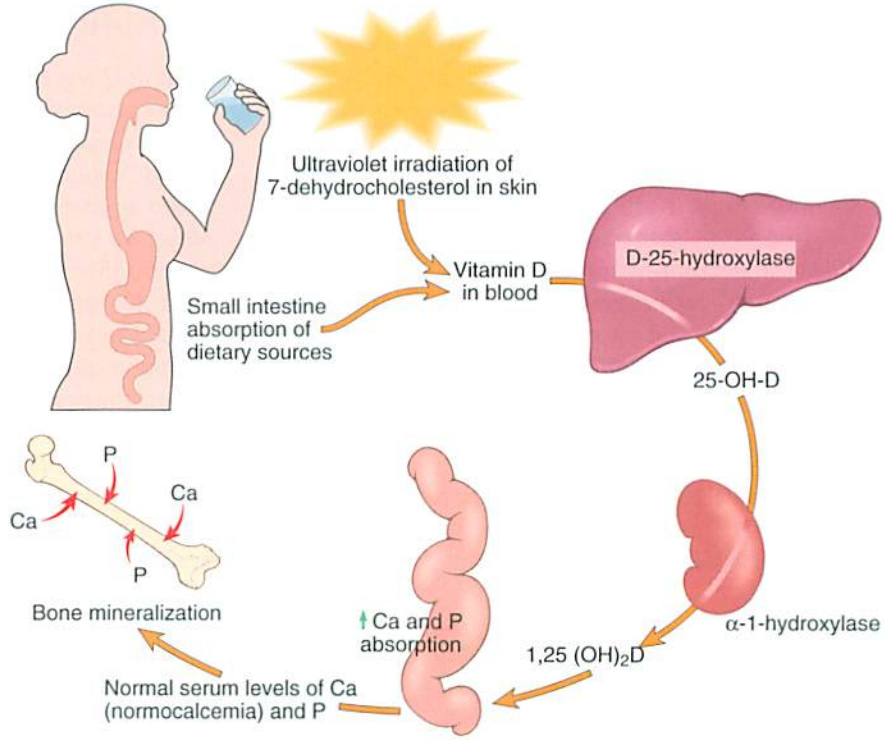


Figure 7-1 Vitamin D activation from skin synthesis and dietary sources. Normal vitamin D metabolism maintains blood calcium levels. (Reprinted from Kumar V, Abbas A, Fausto N, Mitchell R. *Robbins basic pathology*. 8th ed. Philadelphia: Saunders; 2007.)

Functions

Absorption of Calcium and Phosphorus and Bone Mineralization

Calcitriol acts physiologically with two other hormones—parathyroid hormone and the thyroid hormone calcitonin—to control calcium and phosphorus metabolism. Calcitriol stimulates the following: (1) the intestinal cell absorption of calcium and phosphorus; (2) the kidney reabsorption of calcium and phosphorus; and (3) the osteoclastic **resorption** of calcium and phosphorus from trabecular bone. All of these mechanisms maintain blood calcium and phosphorus homeostasis (see Figure 7-1).

Osteoporosis Treatment

Osteoporosis involves a loss of bone density that leads to brittle bones and spontaneous fractures. Because calcitriol regulates the rate of calcium and phosphorus resorption from bone, it has been clinically used to reduce the risk of osteoporosis.

Requirements

Establishing requirements for vitamin D is difficult because it is made in the skin by the sun's ultraviolet rays from 7-dehydrocholesterol and because the number of food sources are limited. Vitamin D requirement varies with individual exposure to sunlight, which is affected by season, the latitude at which a person resides, and even a person's skin color.

Recent research indicates that worldwide vitamin D deficiency is pandemic, with multifactorial health consequences.[5] The primary cause of inadequate circulating serum vitamin D is a lack of sun exposure. In the northern hemisphere, particularly above 40 degrees latitude, less sunlight is present during fall and winter than during spring and summer. Because the amount of vitamin D produced in the skin is relative to the intensity of the sun, significantly less vitamin D is produced during the winter and at higher latitudes. This also affects the vitamin D requirement of people with darker skin, because melanin absorbs ultraviolet B radiation in a way that is similar to that of sunscreen. Thus, less vitamin D is produced in darker-skinned people than in lighter-skinned people who receive the same sun exposure.

resorption the breaking down and releasing of minerals from bones.

A flurry of research over the past decade indicates that the dietary needs of vitamin D are higher than what was established at the time of publication of the previous DRIs in 1997. The current DRI for vitamin D is 600 IU/day for individuals who are between 1 and 70 years old and 800 IU/day for individuals who are older than 70 years of age.[6] The American Academy of Pediatrics recommends that infants receive a minimum of 400 IU of vitamin D beginning soon after birth to prevent rickets.[7]

Deficiency Disease

Calcitriol deficiency causes **rickets**, which is a condition seen in growing children that is characterized by the malformation of the bones. Children with rickets have soft long bones that bend under the child's weight (Figure 7-2). In addition to causing skeletal malformations, inadequate vitamin D intake prevents children from attaining their peak bone mass, thereby contributing to the development of osteoporosis or osteomalacia as adults. Many other chronic diseases have been linked with vitamin D deficiency, including muscle weakness, several types of cancer, coronary heart disease, hypertension, tuberculosis, and several autoimmune diseases (e.g., type 1 diabetes, multiple sclerosis, Crohn's disease, rheumatoid arthritis).[5] It is currently estimated that 77% Americans have inadequate vitamin D stores, with a disproportionate prevalence occurring among non-Hispanic blacks (97%) and Mexican Americans (90%).[8]

Figure 7-2 A child with rickets; note the bowlegs.
(Reprinted from Kumar V, Abbas A, Fausto N, Mitchell R. *Robbins basic pathology*. 8th ed. Philadelphia: Saunders; 2007.)

Toxicity Symptoms

Excessive dietary intake of vitamin D can be toxic, especially for infants and children. Symptoms of toxicity or hypervitaminosis D include the calcification of the soft tissues (e.g., kidneys, heart, lungs), fragile bones, and kidney stones. The prolonged elevated intake of cholecalciferol may produce elevated blood calcium concentrations (i.e., hypercalcemia) and calcium deposits in the kidney nephrons, which interferes with overall kidney function. The UL for vitamin D among people who are older than 9 years of age is 4000 IU/day.[9] Vitamin D intoxication cannot occur as a result of the cutaneous production of vitamin D. For most people, vitamin D intake from food and dietary supplements is not likely to exceed the UL. However, individuals who consume diets that are high in fatty fish and fortified milk in addition to dietary supplements that contain vitamin D may be at risk for toxicity.

Food Sources

Fatty fish are one of the only good natural sources of vitamin D. Therefore, a large portion of daily vitamin D intake comes from fortified foods (Table 7-2). Because it is a common food that also contains calcium and phosphorus, milk is a practical food to fortify with vitamin D. The standard commercial practice is to add 400 IU per quart. Butter substitutes such as margarines also are fortified with vitamin D. Children who are consuming vitamin-D–deficient diets (e.g., a rigid macrobiotic diet with no vitamin-D–fortified food products) are especially vulnerable to stunted bone development and rickets.

Stability

Vitamin D is relatively stable under most conditions that involve heat, aging, and storage.

rickets a disease of childhood that is characterized by the softening of the bones from an inadequate intake of vitamin D and insufficient exposure to sunlight; it is also associated with impaired calcium and phosphorus metabolism.

TABLE 7-2 FOOD SOURCES OF VITAMIN D

Item	Quantity	Amount (International Units)
Bread, Cereal, Rice, and Pasta		
All Bran, Kellogg's cereal	½ cup	50
Total Whole Grain, General Mills cereal	1 cup	53
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Herring or trout, cooked	3 oz	177
Salmon, Atlantic, cooked	3 oz	255
Salmon, canned (includes Chinook, coho, pink, and sockeye)	3 oz	689
Sardines, Pacific, canned	3 oz	408
Tuna, canned, albacore or ahi	3 oz	119
Tuna, bluefin, cooked	3 oz	782
Milk and Dairy Products		
Milk, vitamin-D fortified	1 cup (8 fl oz)	100
Soy or rice milk, vitamin-D fortified	1 cup (8 fl oz)	80
Fats, Oils, and Sugars		
Fish oil, cod liver	1 Tbsp	1360

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010; and the British Columbia Ministry of Health. *Food sources of calcium and vitamin D* (website): www.bchealthguide.org/healthfiles/hfile68e.stm#hf004. Accessed August 2007.

VITAMIN E (TOCOPHEROL)

Early vitamin studies identified a substance that was necessary for animal reproduction. This substance was named ***tocopherol*** from two Greek words: *tophos,* meaning "childbirth," and *phero,* meaning "to bring," with the *-ol* ending used to indicate its alcohol functional group. Tocopherol became known as the antisterility vitamin, but it was soon demonstrated to have this effect only in rats and a few other animals and not in people. A number of related compounds have since been discovered. Tocopherol is the generic name for this entire group of homologous fat-soluble nutrients, which are designated as α-, β-, γ-, and δ-tocopherol or tocotrienol. Of these eight, α-tocopherol is the only one that is significant in human nutrition and thus, used to calculate dietary needs.[10]

Functions

The most vital function of α-tocopherol is its antioxidant action in tissues. In addition to the potent antioxidant activity of vitamin E, it has been associated with antiproliferative effects in the eye that are seemingly protective against conditions such as cataracts and glaucoma.[11]

Antioxidant Function

α-Tocopherol is the body's most abundant fat-soluble antioxidant. The polyunsaturated fatty acids (see Chapter 3) in the phospholipids of cell and organelle membranes are particularly susceptible to free radical oxidation. α-Tocopherol intercepts this oxidation process and protects the polyunsaturated fatty acids from damage.

Relation to Selenium Metabolism

Selenium is a trace mineral that, as part of the selenium-containing enzyme glutathione peroxidase, works with α-tocopherol as an antioxidant. Glutathione peroxidase is the second line of defense for preventing free radical damage to membranes. Glutathione peroxidase spares α-tocopherol from oxidation, thereby reducing the dietary requirement for α-tocopherol. Similarly, α-tocopherol spares glutathione peroxidase from oxidation, thus reducing the dietary requirement for selenium.

Requirements

α-Tocopherol requirements are expressed in milligrams per day. The RDA for men and women who are 14 years old and older is 15 mg/day, with lesser amounts necessary during childhood. During the first year of infancy, no RDA has been determined, but the AI is 4 to 6 mg/day.[10]

Deficiency Disease

Young infants—especially premature infants who missed the final 1 to 2 months of gestation, when α-tocopherol stores are normally filled—are particularly vulnerable to hemolytic anemia. With hemolytic anemia, red blood cell membrane phospholipids and proteins are left unprotected and are easily oxidized and degraded, and the continued loss of functioning red blood cells leads to anemia.

A dietary deficiency of vitamin E is rare; the only cases occur in individuals who cannot absorb or metabolize fat. In such cases, the α-tocopherol deficiency disrupts the normal synthesis of myelin, which is the protective phospholipid-rich membrane that covers the nerve cells. The

tocopherol the chemical name for vitamin E, which was named by early investigators because their initial work with rats indicated a reproductive function; in people, vitamin E functions as a strong antioxidant that preserves structural membranes such as cell walls.

major nerves that are affected are the spinal cord fibers that affect physical activity and the retina of the eye, which affects vision.

Toxicity Symptoms

α-Tocopherol from food sources has no known toxic effects in people. Supplemental α-tocopherol intakes that exceed the UL of 1000 mg/day may interfere with vitamin K activity and blood clotting. Although the exact mechanism is unknown, this may be particularly problematic for individuals who are deficient in vitamin K or for patients who are receiving anticoagulation therapy.[12]

Food Sources

The richest sources of α-tocopherol are vegetable oils (e.g., wheat germ, soybean, safflower). Note that vegetable oils are also the richest sources of polyunsaturated fatty acids, which α-tocopherol protects. Other food sources of α-tocopherol include nuts, fortified cereals, and avocados. Table 7-3 provides a list of food sources of vitamin E.

TABLE 7-3 FOOD SOURCES OF VITAMIN E AS α-TOCOPHEROL

Item	Quantity	Amount (mg of α-tocopherol)
Bread, Cereal, Rice, and Pasta		
Total Whole Grain, General Mills cereal	1 cup	18.0
Wheat germ, toasted, plain	1 oz	4.53
Fruits		
Avocado	¼ medium	1.04
Mango, raw	½ medium	1.16
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Almonds, dried	1 oz	7.33
Hazelnuts, dried	1 oz	4.26
Sunflower seeds	2 Tbsp	6.21
Fats, Oils, and Sugars		
Corn oil	1 Tbsp	2.83
Cottonseed oil	1 Tbsp	4.80
Palm oil	1 Tbsp	2.17
Peanut oil	1 Tbsp	2.12
Safflower oil	1 Tbsp	4.64
Sunflower oil	1 Tbsp	5.59

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Stability

α-Tocopherol is unstable to heat and alkalis.

VITAMIN K

In 1929, Henrik Dam, a biochemist at the University of Copenhagen, discovered a hemorrhagic disease in chicks that were fed a diet from which all lipids had been removed. Dam hypothesized that an unidentified lipid factor had been removed from the chicks' feed. Dam called it *koagulations vitamin* or *vitamin K*, and the letter that he assigned it is still used today. Dam later succeeded in isolating the agent from alfalfa and identifying it, for which he received the Nobel Prize for physiology and medicine. As with many of the vitamins, not just one but several homologous forms of vitamin K make up the group. The major form in plants that was initially isolated from alfalfa by Dam is **phylloquinone**, which is the dietary form of vitamin K. Menaquinone, a second form, is synthesized by intestinal bacteria. Menaquinone contributes approximately half of our daily supply of vitamin K. Menadione is a synthetic precursor of vitamin K, but it has not been used as a dietary supplement since the U.S. Food and Drug Administration banned it because of its toxicity effects.

Functions

Vitamin K has two well-established functions in the body: blood clotting and bone development.

Blood Clotting

The most well-known and the earliest discovered function of vitamin K is in the blood-clotting process. Vitamin K is essential for maintaining the normal blood concentrations of four blood-clotting factors. The first of these vitamin–K-dependent blood factors to be identified and characterized was prothrombin (i.e., clotting factor II). Prothrombin, which is synthesized in the liver, is converted to thrombin, which then initiates the conversion of fibrinogen to fibrin to form the blood clot (Figure 7-3).

Phylloquinone is an antidote for the effects of excessive anticoagulant drug doses, and it is often used to control and prevent certain types of hemorrhages. Fat-soluble vitamins are more completely absorbed when bile is

phylloquinone a fat-soluble vitamin of the K group that is found primarily in green plants.

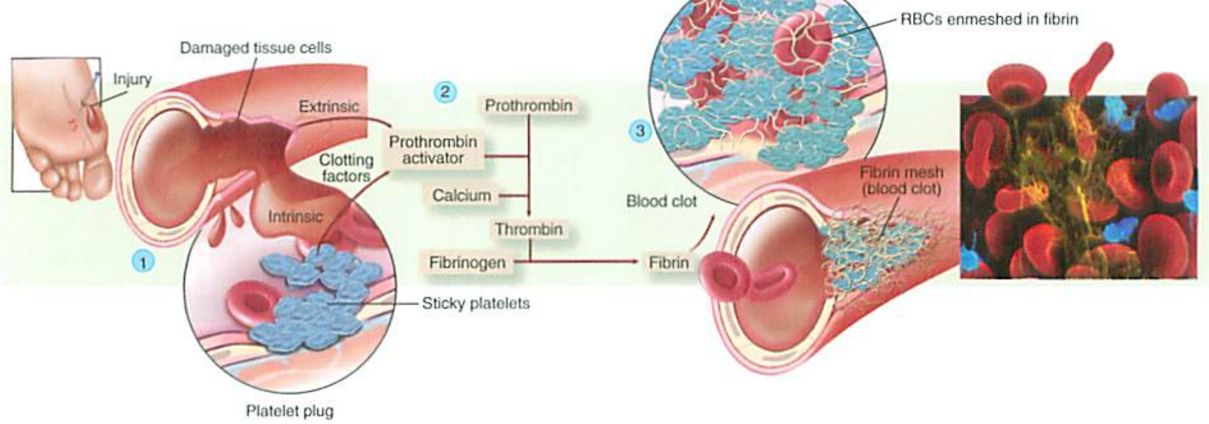


Figure 7-3 The blood-clotting mechanism. The complex clotting mechanism can be distilled into three steps: (1) the release of clotting factors from both injured tissue cells and sticky platelets at the injury site, which form a temporary platelet plug; (2) a series of chemical reactions that eventually result in the formation of thrombin; and 3) the formation of fibrin and the trapping of blood cells to form a clot. (Modified from Thibodeau GA, Patton KT. *Anatomy & physiology*. 6th ed. St. Louis: Mosby; 2007.)

DRUG-NUTRIENT INTERACTION

VITAMIN K CONSIDERATIONS WITH ANTICOAGULANT AND ANTIBIOTIC MEDICATIONS

Anticoagulation medications such as warfarin act to reduce the overall production of blood-clotting factors. Because the primary action of vitamin K is the manufacturing of these same proteins, the amount of vitamin-K-rich foods that a patient eats can affect the medication level that is needed for optimal anticoagulation. Many patients believe that they should avoid foods that are rich in vitamin K while they are taking warfarin, but this can lead to unstable anticoagulation and the restriction of the other nutrients that are found in these foods. Patients should strive to eat a consistent diet rather than limiting vitamin-K-rich foods like dark leafy greens. A dietitian can educate the patient about foods that are rich in vitamin K and help them to achieve a balance between their medication level and their desired vitamin K intake.

One form of vitamin K, menaquinone, is synthesized by healthy bacteria in the gut. This source is significant for meeting overall vitamin K needs. Therefore, the long-term use of medications that destroy gastrointestinal bacteria (e.g., antibiotics) also obliterates a valuable source of vitamin K. Patients should be advised to maintain their daily intakes of food sources of vitamin K (Table 7-4).

present. Thus, conditions that hinder the release of bile into the small intestine decrease the absorption of vitamin K and ultimately increase the length of time that is required for blood to clot. When bile salts are given with vitamin K concentrate, the blood-clotting time returns to normal. See the Drug-Nutrient Interaction box entitled "Vitamin K Considerations With Anticoagulant and Antibiotic Medications" for additional information about special medication-related considerations with vitamin K.

Bone Development

Five proteins in bone and cartilage require vitamin-K-dependent modifications to function.[13] The most abundant noncollagenous protein in bone matrix, osteocalcin, is one of the vitamin-K-dependent proteins. Vitamin K is involved in the modification of the glutamic acid residues of osteocalcin to form calcium-binding γ-carboxyglutamic acid residues. Like the blood-clotting proteins, osteocalcin binds calcium; unlike the blood-clotting proteins, it forms bone crystals.

Requirements

Because intestinal bacteria synthesize a form of vitamin K (menaquinone), a constant supply is normally available to support body needs. Currently not enough scientific evidence is available to establish an RDA. Therefore, the DRIs for vitamin K are AIs. Values gradually increase from birth to adulthood. The AI for men is 120 mcg/day; for women, it is 90 mcg/day.[2]

Deficiency Disease

Deficiency diseases related to vitamin K are not common. A deficiency (i.e., hypoprothrombinemia) may present as a secondary result of another clinical condition as opposed to a dietary deficiency. Patients who have severe malabsorption disorders (e.g., Crohn's disease) or who are treated chronically with antibiotics that kill intestinal bacteria are susceptible to blood loss induced by vitamin K deficiency.

Vitamin K is routinely given at birth to prevent hemorrhaging, because vitamin K does not efficiently transfer through the placenta during gestation, and the intestinal tract of a newborn does not yet have vitamin-K–producing gut flora. Thus, infants are deficient in vitamin K at birth.

Toxicity Symptoms

Toxicity from vitamin K—even when large amounts are taken over extended periods—has not been observed. Therefore, no UL has been established.

TABLE 7-4 FOOD SOURCES OF VITAMIN K

Item	Quantity	Amount (mcg)
Vegetables		
Broccoli, raw	½ cup, chopped	45
Brussels sprouts, cooked, drained	½ cup	109
Kale, raw	½ cup, chopped	273
Mustard greens, raw	½ cup, chopped	139
Spinach, raw	½ cup	72
Turnip greens, raw	½ cup	69

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Food Sources

Green leafy vegetables such as spinach, turnip greens, and broccoli are the best dietary sources of vitamin K, providing 40 to 80 mcg of phylloquinone per half cup of raw food. Small amounts of phylloquinone are contributed by milk, dairy products, meats, fortified cereals, fruits, and vegetables (see Table 7-4).

Stability

Phylloquinone is fairly stable, although it is sensitive to light and irradiation. Therefore, clinical preparations are kept in dark bottles.

Table 7-5 provides a summary of the fat-soluble vitamins.

SECTION 2 WATER-SOLUBLE VITAMINS

VITAMIN C (ASCORBIC ACID)

Functions

Vitamin C has several critical functions in the body. It acts as an antioxidant and a cofactor of enzymes, and it plays a role in many metabolic and immunologic activities.

Connective Tissue

Ascorbic acid is necessary to build and maintain strong tissues through its involvement in collagen synthesis. Collagen is especially important in tissues of mesodermal origin, including connective tissues (e.g., ligaments, tendons, bone matrix, other binding lattices that hold together and give tensile strength to tissues) and other tissues that contain connective tissue (e.g., cartilage, tooth dentin, capillary walls).

Each time that the amino acids proline or lysine are added during collagen synthesis, they are hydroxylated (i.e., OH is added) to form hydroxyproline and hydroxylysine by the ascorbic-acid-dependent enzymes prolyl hydroxylase and lysyl hydroxylase. Iron is a cofactor for

ascorbic acid the chemical name for vitamin C; the vitamin was named after its ability to cure scurvy.

TABLE 7-5 SUMMARY OF FAT-SOLUBLE VITAMINS

Vitamin	Functions	Recommended Intake (Adults)	Deficiency	Tolerable Upper Intake Level (UL) and Toxicity	Sources
Vitamin A (retinol, retinal, and retinoic acid) Provitamin A (carotene)	Vision cycle: adaptation to light and dark; tissue growth, especially skin and mucous membranes; reproduction; immune function	Men, 900 mcg/day; women, 700 mcg/day	Night blindness; xerosis; xerophthalmia; susceptibility to epithelial infection; dry skin; impaired immunity, growth, and reproduction	UL: 3000 mcg/day Hair loss; irritated skin; bone pain, liver damage; birth defects	Retinol (animal foods): liver, egg yolk, cream, butter or fortified margarine, fortified milk Provitamin A (plant foods): dark green and deep orange vegetables (e.g., spinach, collard greens, broccoli, pumpkin, sweet potatoes, carrots)
Vitamin D (cholecalciferol, ergocalciferol)	Absorption of calcium and phosphorus; calcification of bones and teeth; growth	Between the ages of 1 and 70 years, 600 IU/day; 70 years of age or older, 800 IU/day	Rickets and growth retardation in children; osteomalacia (soft bones) in adults	UL: 1000 to 4000 IU/day Calcification of soft tissue; kidney damage; growth retardation	Synthesized in the skin with exposure to sunlight, fortified milk, fish oils
Vitamin E (α-tocopherol)	Antioxidant (i.e., protection of materials that oxidize easily)	Adults, 15 mg/day	Breakdown of red blood cells; anemia; nerve damage; retinopathy	UL: 1000 mg/day (from supplements) Inhibition of vitamin K activity in blood clotting	Vegetable oils, vegetable greens, wheat germ, nuts, seeds
Vitamin K (phylloquinone, menaquinone)	Normal blood clotting and bone development	Men, 120 mcg/day; women, 90 mcg/day	Bleeding tendencies; hemorrhagic disease; poor bone growth	UL: Not set Interference with anticoagulation drugs	Synthesis by intestinal bacteria, dark green leafy vegetables, soybean oil

both enzymes, and ascorbic acid is required to maintain the iron atoms in these enzymes in their active ferrous (Fe^{2+}) form. Hydroxyproline and hydroxylysine form covalent bonds with other residues, which strengthen collagen's structure. When ascorbic acid is plentiful, collagen and the connective tissues in which it is integral quickly develop. Blood vessels are particularly dependent on ascorbic acid's role in collagen synthesis to help their walls resist stretching as blood is forced through them.

General Body Metabolism

The more metabolically active body tissues (e.g., adrenal glands, brain, kidney, liver, pancreas, thymus, spleen) contain greater concentrations of ascorbic acid. Ascorbic acid in the adrenal glands is drawn upon when the gland is stimulated. This use of ascorbic acid during adrenal stimulation suggests an increased need for ascorbic acid during stress. More ascorbic acid is present in a child's actively growing tissues than in adult tissues. Other enzymes that require ascorbic acid perform very diverse functions, including the following: (1) the conversion of the neurotransmitter dopamine to the neurotransmitter norepinephrine; (2) the synthesis of carnitine, a mitochondrial fatty acid transporter that is involved in extracting energy from fatty acids; (3) the oxidation of phenylalanine and tyrosine; (4) the metabolism of tryptophan and folate; and (5) the maturation of some bioactive neural and endocrine peptides. Furthermore, ascorbic acid helps the body to absorb nonheme iron by keeping it in its bioactive reduced ferrous form (Fe^{2+}), thereby making it available for hemoglobin production and helping to prevent iron-deficiency anemia.

CLINICAL APPLICATIONS

ASCORBIC ACID NEEDS IN SMOKERS

Free radicals are reactive molecules that can disrupt the normal structure of DNA, proteins, carbohydrates, and fatty acids. Such damage is linked to an increased risk of cancer and cardiovascular disease. Cigarette smoke is one environmental source of free radicals. The body fights these free radicals with antioxidants such as vitamins A, E, and C and minerals such as selenium and zinc. Antioxidants neutralize free radicals and work to protect the body from free radical damage.

As free radical production increases, antioxidant needs also increase. Cigarette smokers deplete their supply of ascorbic acid more rapidly than nonsmokers because of increased exposure to free radicals. The vitamin is needed to break down the toxic compounds found in cigarette smoke. Therefore, it is recommended that cigarette smokers consume an additional 35 mg of vitamin C per day to meet these increased needs; it is also recommended that they stop smoking.

Antioxidant Function

Similar to vitamin E in function, ascorbic acid is an antioxidant that works to protect the body from damage caused by free radicals. Free radicals lead to oxidative stress, which is associated with increased risks of inflammatory diseases, Alzheimer's disease, cancer, and heart disease.

Requirements

The DRI guidelines for ascorbic acid sets an RDA of 75 mg/day for women and 90 mg/day for men, with increases for women during pregnancy and lactation.[10] Because cigarette smoke increases oxidative stress and free radicals in body tissues, the DRI committee recommends an additional 35 mg/day for smokers (see the Clinical Applications box, "Ascorbic Acid Needs in Smokers").

Deficiency Disease

Signs of ascorbic acid deficiency include tissue bleeding (e.g., easy bruising, pinpoint skin hemorrhages), bone and joint bleeding, susceptibility to bone fracture, poor wound healing, and soft bleeding gums with loosened teeth. Extreme deficiency results in the disease scurvy.

Toxicity Symptoms

The UL for ascorbic acid is 2000 mg/day. Although most excessive intakes of water-soluble vitamins are efficiently excreted in the urine, levels of more than 2000 mg/day are cleared less efficiently and may result in gastrointestinal disturbances and osmotic diarrhea. The supplemental intake of vitamin C at 1000 mg/day is associated with increased oxalate stone (i.e., kidney stone) formation.[14] The Institute of Medicine states that further research into the toxic effects of ascorbic acid is warranted because of the popularity of high intake of the vitamin in the United States.[10]

Food Sources

The best food sources of ascorbic acid include citrus fruits, red bell peppers, and kiwis (Figure 7-4). Additional good sources include tomatoes, cabbage, berries, melons, green peppers, broccoli, potatoes, and other green and yellow vegetables (Table 7-6).

Stability

Ascorbic acid is readily oxidized upon exposure to air and heat. Therefore, care must be taken when handling its food sources. Ascorbic acid is not stable in alkaline mediums; thus, baking soda, which often is added to foods to preserve color, destroys the ascorbic acid content. Acidic fruits and vegetables retain their ascorbic acid content better than nonacidic foods, and the vitamin is also highly soluble in water. The more water added for cooking, the more ascorbic acid leaches out of the fruit or vegetable into the cooking water.

THIAMIN (VITAMIN B_1)

The name of the vitamin ***thiamin*** comes from the presence of the thiazole ring in its structure.

thiamin the chemical name of vitamin B_1; this vitamin was discovered in relation to the classic deficiency disease beriberi, and it is important in body metabolism as a coenzyme factor in many cell reactions related to energy metabolism.

Figure 7-4 Foods that are high in Vitamin C. (Copyright JupiterImages Corp.)

TABLE 7-6 **FOOD SOURCES OF VITAMIN C**

Item	Quantity	Amount (mg)
Vegetables		
Green pepper, raw	½ cup, chopped	60
Peppers, hot chili, red, raw	½ cup, chopped	108
Red pepper, sweet, raw	½ cup, chopped	95
Fruits, Raw		
Kiwi	1 medium	70.5
Lemon juice, fresh	8 fl oz	112
Orange juice, fresh	8 fl oz	124
Orange, navel	1 medium	80
Papaya	½ medium	94
Strawberries	½ cup	49

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Functions

Thiamin is a component of the coenzyme thiamin pyrophosphate, which is involved in several metabolic reactions that ultimately provide the body with energy in the form of adenosine triphosphate. Thiamin is especially necessary for the healthy function of systems that are in constant action and in need of energy, such as the gastrointestinal tract, the nervous system, and the cardiovascular system.

Requirements

The dietary requirement for thiamin is directly related to its function in energy and carbohydrate metabolism. For healthy people, the RDAs are based on average energy needs: 1.2 mg/day for men and 1.1 mg/day for women; children require less. For infants up to the age of 12 months, no RDA exists; the AI is 0.2 to 0.3 mg/day.[15] Increased thiamin intake is needed during pregnancy and lactation as well as during the treatment of infectious diseases and alcoholism.

Deficiency Disease

The gastrointestinal tract relies on glucose for muscular energy. Therefore, a lack of dietary thiamin may result in poor appetite, indigestion, and constipation. The central nervous system also depends on glucose for constant energy. Without sufficient thiamin, alertness and reflexes decrease, and apathy, fatigue, and irritability result. If the thiamin deficit continues, nerve irritation, pain, and prickly or numbing sensations may eventually progress to paralysis.

Chronic thiamin deficiency is known as **beriberi**; this paralyzing disease was especially prevalent in Asian countries that relied heavily on polished white rice as a food staple. The name describes the disease well; it is Singhalese for "I can't, I can't," because afflicted people were too ill to do anything. In industrialized societies, thiamin deficiency is largely associated with chronic alcoholism and poor diet. Alcohol inhibits the absorption of thiamin. Alcohol-induced thiamin deficiency causes a debilitating brain disorder known as *Wernicke's encephalopathy,* which affects mental alertness, short-term memory, and muscle coordination.

Toxicity Symptoms

The kidneys clear excess thiamin; therefore, there is no evidence of toxicity from oral intake, and no UL exists.

Food Sources

Although thiamin is widespread in most plant and animal tissues, the amount is usually small. Thus, thiamin deficiency is a distinct possibility when food

beriberi a disease of the peripheral nerves that is caused by a deficiency of thiamin (vitamin B_1) and is characterized by pain (neuritis) and paralysis of legs and arms, cardiovascular changes, and edema.

intake is markedly curtailed (e.g., with alcoholism or highly inadequate diets). Good food sources of thiamin include wheat germ, lean pork, beef, liver, whole or **enriched** grains (e.g., flour, bread, cereals), and legumes (Table 7-7). Eggs, fish, and a few vegetables are also fair sources. Some raw fish contain a thiamin-degrading enzyme (i.e., thiaminase) and consequently are not good sources.

Stability

Thiamin is a fairly stable vitamin, but it is destroyed by alkalis and prolonged exposure to high cooking temperatures. As with other water-soluble vitamins, prepared dishes retain more thiamin when their cooking water is used in the dish during preparation rather than discarded.

RIBOFLAVIN (VITAMIN B_2)

The name ***riboflavin*** comes from the vitamin's chemical nature. It is a yellow-green fluorescent pigment that contains ribose, which is a monosaccharide.

Functions

Riboflavin is active in its coenzyme forms: flavin adenine dinucleotide and flavin mononucleotide. These two flavin coenzymes are required for macronutrient metabolism to produce adenosine triphosphate via the Krebs cycle and the electron transport chain. Flavoproteins are involved in a number of other metabolic reactions as well. Some examples of riboflavin-dependent reactions include converting tryptophan to niacin, converting retinal to retinoic acid, and synthesizing the active form of folate.

TABLE 7-7 FOOD SOURCES OF THIAMIN

Item	Quantity	Amount (mg)
Bread, Cereal, Rice, and Pasta		
Bran flakes cereal	1 cup	0.5
Complete, Kellogg's cereal	1 cup	2.08
Product 19, Kellogg's cereal	1 cup	1.5
Quaker Oat Life, Kellogg's cereal	1 cup	0.54
Total Whole Grain, General Mills cereal	1 cup	2.0
Wheaties, General Mills cereal	1 cup	0.75
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Ham, sliced, regular (11% fat)	3 oz	0.53
Pork loin, lean, boneless, roasted	3 oz	0.75

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Requirements

Riboflavin needs are related to total energy requirements for age, level of exercise, body size, metabolic rate, and rate of growth. The RDA for adults who are 18 years old and older is 1.3 mg/day and 1.1 mg/day for men and women, respectively. The RDA is higher for women during pregnancy (1.4 mg/day) and lactation (1.6 mg/day). An AI of 0.3 to 0.4 mg/day has been established for infants who are up to 12 months old.[15]

Deficiency Disease

Areas of the body with rapid cell regeneration are most affected by riboflavin deficiency. Signs of riboflavin deficiency include cracked lips and mouth corners; a swollen, red tongue; burning, itching, or tearing eyes caused by extra blood vessels in the cornea; and a scaly, greasy dermatitis in the skin folds. Riboflavin deficiency usually occurs with other B vitamin and nutrient deficiencies (e.g., protein malnutrition) rather than by itself. No specific riboflavin deficiency disease is comparable to beriberi. A rare riboflavin deficiency condition has been given the general name *ariboflavinosis.* Its symptoms are tissue inflammation and breakdown and poor wound healing; even minor injuries become easily aggravated and do not heal well.

enriched a word that is used to describe foods to which vitamins and minerals have been added back to a food after a refining process that caused a loss of some nutrients; for example, iron may be lost during the refining process of a grain, so the final product will be enriched with additional iron.

riboflavin the chemical name for vitamin B_2; this vitamin was discovered in relation to an early vitamin deficiency syndrome called *ariboflavinosis* that is mainly evidenced in the breakdown of skin tissues and resulting infections; it also has a role as a coenzyme factor in many cell reactions related to energy and protein metabolism.

Toxicity Symptoms

No adverse effects of riboflavin intake from food or supplements have been reported. Thus, there is no UL for riboflavin.

Food Sources

The most important food source of riboflavin is milk. Each serving of milk and milk products contains 0.3 to 0.5 mg of riboflavin. Other good sources include enriched grains and animal protein sources such as meats (especially beef liver), poultry, and fish. Vegetables such as mushrooms, spinach, and avocados are good natural sources. Table 7-8 provides a summary of riboflavin food sources.

Stability

Riboflavin is destroyed by light; therefore, milk is usually sold and stored in plastic or cardboard cartons instead of glass containers to preserve the vitamin.

NIACIN (VITAMIN B_3)

Functions

Niacin is part of two coenzymes. The role of one of the niacin-containing coenzymes (nicotinamide adenine dinucleotide) is the metabolism of the macronutrients (similar to the coenzymes that contain riboflavin and thiamin). The other niacin-containing coenzyme (nicotinamide adenine dinucleotide phosphate) is involved in DNA repair and steroid hormone synthesis.

TABLE 7-8 FOOD SOURCES OF RIBOFLAVIN

Item	Quantity	Amount (mg)
Bread, Cereal, Rice, and Pasta		
Bran flakes cereal	1 cup	0.57
Complete, Kellogg's cereal	1 cup	2.28
Product 19, Kellogg's cereal	1 cup	1.7
Total Whole Grain, General Mills cereal	1 cup	2.26
Wheaties, General Mills cereal	1 cup	0.85
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Beef liver, fried	3 oz	2.9
Chicken liver, simmered	3 oz	1.7
Milk and Dairy Products		
Buttermilk, reduced fat	8 fl oz	0.51
Milk, skim or whole	8 fl oz	0.45
Yogurt, low fat	8 fl oz	0.52

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Requirements

Factors such as age, growth, pregnancy and lactation, illness, tissue trauma, body size, and physical activity—all of which affect energy needs—influence niacin requirements. Because the body can make some of its needed niacin from the essential amino acid tryptophan, the total niacin requirement is stated in terms of niacin equivalents (NE) to account for both sources. Approximately 60 mg of tryptophan can yield 1 mg of niacin; thus, 60 mg of tryptophan equals 1 NE. The DRI guidelines include an RDA for adults who are 14 years old and older of 16 mg NE/day for men and 14 mg NE/day for women. The RDA is higher during pregnancy (18 mg NE/day) and lactation (17 mg NE/day). No RDA has been determined for infants who are up to 12 months old, but the AI is 2 to 4 mg NE/day.[15]

Deficiency Disease

Symptoms of general niacin deficiency are weakness, poor appetite, indigestion, and various disorders of the skin and nervous system. Skin areas that are exposed to sunlight develop a dark, scaly dermatitis. Extended deficiency may result in central nervous system damage with resulting confusion, apathy, disorientation, and neuritis. Such signs of nervous system damage are seen in patients with chronic alcoholism. The deficiency disease that is associated with niacin is **pellagra**, which is characterized by the "four Ds": *d*ermatitis, *d*iarrhea, *d*ementia, and *d*eath (Figure 7-5). When therapeutic doses of niacin are given, pellagra symptoms improve. Pellagra was common in the United States and parts of Europe during the early twentieth century in regions where corn (which is low in niacin) was the staple food. Between 1900 and 1940 alone, more than 100,000 people living in the southern United States were estimated to have died as a result of pellagra.[16]

niacin the chemical name for vitamin B_3; this vitamin was discovered in relation to the deficiency disease pellagra, which is largely a skin disorder; it is important as a coenzyme factor in many cell reactions related to energy and protein metabolism.

pellagra the deficiency disease caused by a lack of dietary niacin and an inadequate amount of protein that contains the amino acid tryptophan, which is a precursor of niacin; pellagra is characterized by skin lesions that are aggravated by sunlight as well as by gastrointestinal, mucosal, neurologic, and mental symptoms.

Figure 7-5 **Pellagra, which results from a niacin deficiency.** (Reprinted from McLaren DS. *A colour atlas and text of diet-related disorders.* 2nd ed. London: Mosby-Year Book; 1992.)

Toxicity Symptoms

Excessive niacin intake can produce adverse physical effects, unlike high intakes of thiamin and riboflavin. The UL is 35 mg/day, which is based on the skin flushing that is caused by high supplemental intakes.[15] Although no evidence exists of adverse effects from consuming niacin that naturally occurs in foods, evidence does exist of excessive niacin consumption and adverse effects from nonprescription vitamin supplements and niacin-containing prescription medications. The primary reaction is a reddened flush on the skin of the face, arms, and chest that is accompanied by burning, tingling, and itching. This reaction also occurs in many patients who are therapeutically treated with niacin (see the Clinical Applications box, "Niacin as a Treatment for High Cholesterol").

Food Sources

Meat is a good source of niacin. Most dietary niacin in the United States comes from meat, poultry, fish, or enriched grain products. In addition, enriched and whole-grain breads and bread products and fortified ready-to-eat cereals have ample levels of niacin. Other good sources of niacin include legumes (e.g., peanuts, dried beans, peas). Table 7-9 gives the food sources of niacin.

TABLE 7-9 FOOD SOURCES OF NIACIN

Item	Quantity	Amount (mg of Niacin Equivalents)
Bread, Cereal, Rice, and Pasta		
Bran flakes cereal	1 cup	6.7
Complete, Kellogg's cereal	1 cup	26.7
Mueslix Fine Grain, Kellogg's cereal	⅔ cup	5.5
Product 19, Kellogg's cereal	1 cup	20.0
Quaker Oat Life, Kellogg's cereal	1 cup	7.32
Total Whole Grain, General Mills cereal	1 cup	26.6
Wheaties, General Mills cereal	1 cup	9.9
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts*		
Beef liver, fried	3 oz	14.9
Chicken, white meat, boneless, roasted	3 oz	10.6
Chicken liver, simmered	3 oz	9.4
Mackerel, baked	3 oz	5.8
Salmon, cooked, dry heat	3 oz	7.25
Sirloin steak, lean, broiled	3 oz	6.64
Swordfish, cooked, dry heat	3 oz	10.0

*The amino acid tryptophan can be converted into niacin. Therefore, foods that are high in tryptophan also are significant sources of niacin.

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Stability

Niacin is stable in acidic mediums and in heat, but it is lost in cooking water unless the water is retained and consumed (e.g., in soup).

VITAMIN B_6

The name ***pyridoxine*** comes from the pyridine ring in the structure of this vitamin. The term *vitamin B_6* collectively refers to a group of six related compounds: pyridoxine, pyridoxal, pyridoxamine, and their respective activated phosphate forms. Two of the phosphorylated compounds are the coenzymes pyridoxal 5′-phosphate and pyridoxamine 5′-phosphate.

pyridoxine the chemical name of vitamin B_6; in its activated phosphate form (i.e., B_2PO_4), pyridoxine functions as an important coenzyme factor in many reactions in cell metabolism that are related to amino acids, glucose, and fatty acids.

CLINICAL APPLICATIONS

NIACIN AS A TREATMENT FOR HIGH CHOLESTEROL

In addition to the many other important functions of niacin, improved blood lipid profiles are seen at supplemental doses of 1500 mg/day. At high doses, niacin decreases low-density lipoprotein cholesterol and triglyceride levels, both of which are linked with cardiovascular disease. In addition, pharmacologic doses of niacin improve high-density lipoprotein cholesterol levels; this is the "good" cholesterol. When niacin is used in this sense, it is functioning more as a drug than as a vitamin, and it should be used *only* under medical supervision. Niacin that is used in combination with other hypolipidemic agents is a common therapy regime, and it is more effective than medications that are used only to lower low-density lipoprotein cholesterol.[1]

To understand the potentially beneficial role of niacin at pharmacologic dosing, the potential side effects must also be understood. The Recommended Dietary Allowance for niacin in adult men and women is 16 mg/day and 14 mg/day, respectively. The Tolerable Upper Intake Level for niacin is 35 mg/day. Therefore, a long-term dose of 1500 mg/day has serious side effects. Adverse effects from pharmacologic dosing are the same as the toxicity effects: flushing of the skin, tingling sensation in the extremities, nausea, and vomiting. Some individuals may even experience liver damage if long-term use is continued unsupervised for months or years at a time.

1. Brooks EL, Kuvin JT, Karas RH. Niacin's role in the statin era. *Expert Opin Pharmacother* 2010;11(14):2291-3300.

Functions

Pyridoxal 5′-phosphate, which is the metabolically active form of vitamin B_6, has an essential role in protein metabolism and in many cell reactions that involve amino acids. It is involved in neurotransmitter synthesis and thus, in brain and central nervous system activity. Unlike most water-soluble vitamins, vitamin B_6 is stored in tissues throughout the body, particularly muscle. It participates in amino acid absorption, energy production, the synthesis of the heme portion of hemoglobin, and niacin formation from tryptophan. Enzymes that make use of vitamin B_6 coenzymes are also involved in carbohydrate and fat metabolism.

Requirements

Vitamin B_6 is involved in amino acid metabolism; therefore, needs vary directly in response to protein intake. The DRI guidelines set the RDA for healthy men and women up to the age of 50 years at 1.3 mg/day. For older adults, the RDA is slightly higher at 1.7 mg/day for men and 1.5 mg/day for women. The RDA is also higher for women during pregnancy (1.9 mg/day) and lactation (2.0 mg/day). The AI for infants up to 12 months old is 0.1 to 0.3 mg/day.[15]

Deficiency Disease

A vitamin B_6 deficiency is unlikely, because much more is available in a typical diet than is required. A vitamin B_6 deficiency causes abnormal central nervous system function with hyperirritability, neuritis, and possible convulsions. Vitamin B_6 deficiency is one cause of microcytic hypochromic anemia, because it is required for heme synthesis (part of the red blood cell protein hemoglobin).

Toxicity Symptoms

High vitamin B_6 intake from food does not result in adverse effects, but large supplemental doses can cause uncoordinated movement and nerve damage. Symptoms improve when supplemental overdosing is discontinued. The UL for adults is 100 mg/day on the basis of studies that related vitamin B_6 dosage to nerve damage.[15]

Food Sources

Vitamin B_6 is widespread in foods. Good sources include grains, enriched cereals, liver and kidney, and other meats. Limited amounts are in milk, eggs, and vegetables. Table 7-10 lists food sources of vitamin B_6.

Stability

Vitamin B_6 is stable to heat but sensitive to light and alkalis.

FOLATE

The given name *folate* comes from the Latin word *folium*, meaning "leaf," because it was originally discovered in dark green leafy vegetables. In nutrition, the term *folate* refers loosely to a large class of molecules that are derived from folic acid (i.e., pteroylglutamic acid) found in plants

TABLE 7-10 FOOD SOURCES OF VITAMIN B_6 (PYRIDOXINE)

Item	Quantity	Amount (mg)
Bread, Cereal, Rice, and Pasta		
Bran flakes cereal	1 cup	0.67
Complete, Kellogg's cereal	1 cup	2.71
Mueslix Fine Grain, Kellogg's cereal	⅔ cup	2.04
Quaker Oat Life, Kellogg's cereal	1 cup	0.73
Total Whole Grain, General Mills cereal	1 cup	2.66
Vegetables		
Potato, baked, with skin	1 medium (173 g)	0.54
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Beef liver, fried	3 oz	0.87
Chicken, white meat, boneless, roasted	3 oz	0.51
Chicken liver, simmered	3 oz	0.64
Sirloin steak, lean, broiled	3 oz	0.52

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

and animals. The most stable form of folate is folic acid, which is rarely found in food but which is the form that is usually used in vitamin supplements and fortified food products. In the body, folate is converted to and used as the coenzyme tetrahydrofolic acid (TH_4).

Functions

TH_4 participates in DNA synthesis (with the enzyme thymidylate synthetase) as well as cell division. TH_4 is involved in the synthesis of the amino acid glycine, which in turn is required for heme synthesis and thus hemoglobin synthesis.

TH_4 also participates in the reduction of blood homocysteine concentration and indirectly in gene expression (with the enzyme methionine synthase). Blood homocysteine concentrations are high in patients with cardiovascular disease, although whether this contributes to or is merely an effect of cardiovascular disease has not been determined. Nonetheless, adequate dietary folate is one of the important factors for the prevention of **hyperhomocysteinemia**.

Requirements

The DRI standards give a general folate RDA for both men and women 14 years old and older of 400 mcg of dietary folate equivalent (DFE) per day. DFE is used because naturally occurring food folate has a lower bioavailability than synthetic folic acid.[17] One mcg of DFE equals 1 mcg of food folate, 0.5 mcg of folic acid taken on an empty stomach, or 0.6 mcg of folic acid taken with food. As a result of the role of folate in cell division during embryogenesis, adequate prepregnancy and pregnancy intake are linked to reduced neural tube defect occurrences. Thus, the DRIs include a special recommendation that all women who are capable of becoming pregnant take 400 mcg/day of synthetic folic acid from fortified foods or supplements in addition to natural folate from a varied diet. During pregnancy, the RDA is increased to 600 mcg DFE/day to meet the elevated needs for fetal growth. A lactating mother needs 500 mcg DFE/day. For infants, the observed AI is 65 mcg DFE/day during the first 6 months and 80 mcg DFE/day from the ages of 7 to 12 months. The DRI recommendations are aimed at providing adequate safety allowances that include specific population groups that are at risk for deficiency, such as pregnant women, adolescents, and older adults.[15]

Deficiency Disease

Folate deficiency impairs DNA and RNA synthesis. Thus, rapidly dividing cells are affected quickly by folate deficiency. When red blood cells cannot divide, the result is large and immature erythrocytes (i.e., megaloblastic macrocytic anemia). If the deficiency is not corrected, symptoms may progress to poor growth in children, weakness, depression, and neuropathy. Pregnant and lactating women are particularly susceptible to diminished blood folate concentrations and anemia as a result of their higher needs.

Neural tube defects such as **spina bifida** and **anencephaly** are some of the most common birth defects in the United States; they affect approximately 1 in every 1000 pregnancies (Figure 7-6). This defect occurs within the first 28 days after conception, often before a woman realizes that she is pregnant. Although the exact causes of neural tube defects are not known, studies show that, if women had adequate stores of folic acid before

hyperhomocysteinemia the presence of high levels of homocysteine in the blood; associated with cardiovascular disease.

spina bifida a neural tube defect in which the lower end of the neural tube does not close properly and the spinal cord may protrude through the spinal column.

anencephaly a neural tube defect in which the brain does not form.

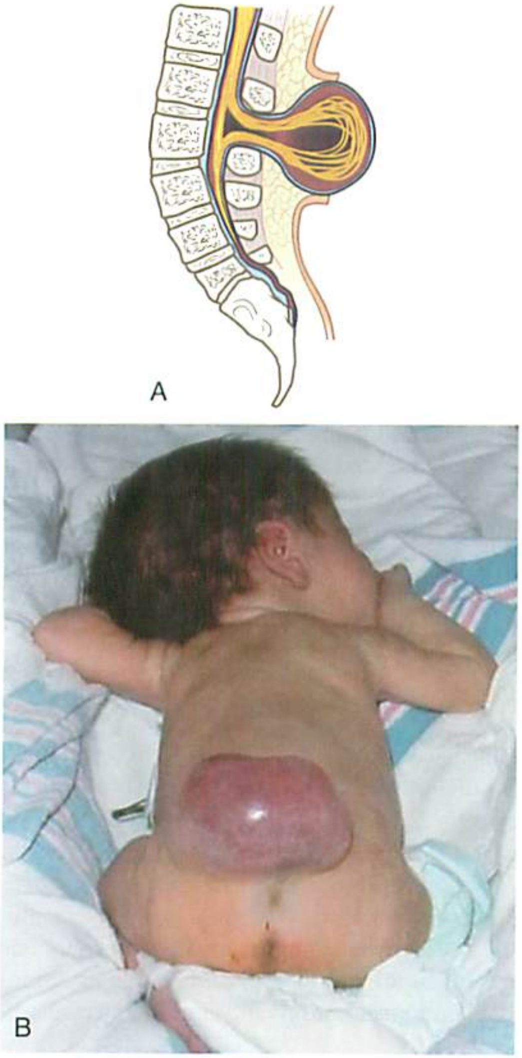


Figure 7-6 **A,** Myelomeningocele. **B,** Spina bifida in a child at birth with a cutaneous defect over the lumbar spine. (**B,** Courtesy Dr. Robert C. Dauser, Baylor College of Medicine, Houston, Texas.)

conception and during early gestation, approximately half of the neural tube defect cases could be prevented. Supplemental folic acid can significantly improve the folate status of women and improve pregnancy outcomes, including women with prior pregnancies that have been affected by neural tube defects.[18-20]

Toxicity Symptoms

No negative effects have been observed from the consumption of folate from foods. However, some evidence shows that excessive folic acid can mask biochemical indications of vitamin B_{12} deficiency. Prolonged B_{12} deficiency can result in permanent nerve damage; therefore, the UL for adults for supplemental folic acid (not DFE) has been set at 1000 mcg/day.[15]

TABLE 7-11 FOOD SOURCES OF FOLATE

Item	Quantity	Amount (mcg DFE)
Bread, Cereal, Rice, and Pasta		
Bran flakes cereal	1 cup	221
Mueslix Fine Grain, Kellogg's cereal	⅔ cup	683
Product 19, Kellogg's cereal	1 cup	673
Quaker Oat Life, Kellogg's cereal	1 cup	553
Total Whole Grain, General Mills cereal	1 cup	901
Wheat Flakes, Kellogg's All-Bran Complete cereal	1 cup	901
Wheaties, General Mills cereal	1 cup	449
Vegetables		
Collard greens, boiled	½ cup	88
Spinach, boiled	½ cup	131
Fruits		
Orange juice, fresh	1 cup, 8 oz	74
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Black beans, boiled	½ cup	128
Chicken liver, simmered	3 oz	491
Chickpeas (garbanzo beans)	½ cup	141
Kidney beans, boiled	½ cup	115

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed January 23 2012.

Food Sources

Folate is widely distributed in foods (Table 7-11). Rich sources include green leafy vegetables, orange juice, dried beans, and chicken liver. Since January 1998, as part of an effort to reduce the occurrences of neural tube defects, the U.S. Food and Drug Administration has required all manufacturers of certain grain products (e.g., enriched white flour; white rice; corn grits; cornmeal; noodles; fortified breakfast cereals, bread, rolls, and buns) to fortify with folic acid. The fortification of the general food supply has successfully reduced the prevalence of neural tube defects in the United States by 22.9%.[21] The special DRI recommendation that women who are capable of becoming pregnant consume folic acid from supplements or fortified foods is one of only two current RDAs that specifically recommend consuming vitamin sources in addition to those available in a varied diet of natural foods. (The other supplementation recommendation concerns vitamin B_{12}.)

Stability

Folate is easily destroyed by heat, and it easily leaches into cooking water, especially when the food is submerged in the water. As much as 50% to 90% of food folate may be destroyed during food processing, storage, and preparation.

COBALAMIN (VITAMIN B_{12})

Vitamin B_{12} is the B vitamin designation for cobalamin. The name ***cobalamin*** was derived from cobalt, which is the trace mineral that is the single gray atom at the center of cobalamin's corrin ring. The term *vitamin B_{12}* originally referred to the synthetic pharmaceutical molecule cyanocobalamin. In nutrition, it has become a term for all cobalamin derivatives, including the two biologically active coenzyme derivatives methylcobalamin and deoxyadenosylcobalamin.

Functions

Methylcobalamin is a coenzyme that is required for the catalytic activity of two of the same enzymes as tetrahydrofolic acid: methionine synthase and serine hydroxymethyltransferase. Thus, like tetrahydrofolic acid, methylcobalamin participates in the reduction of blood homocysteine concentration and indirectly in gene expression as well as in the synthesis of the amino acid glycine, which in turn is required for heme synthesis and therefore hemoglobin synthesis. In addition, vitamin B_{12} is essential for DNA synthesis and cell division.

Deoxyadenosylcobalamin is a coenzyme for the mitochondrial enzyme methylmalonyl-coenzyme A mutase, which is involved in the metabolism of fatty acids that have an odd number of carbon atoms.

Requirements

The amount of dietary vitamin B_{12} needed for normal human metabolism is quite small, and it consists of only a few micrograms per day. A mixed diet that includes animal foods easily provides this much and more. The DRI guidelines list an RDA for men and women who are 19 years of age and older of 2.4 mcg/day. The RDA during pregnancy is 2.6 mcg/day and during lactation is 2.8 mcg/day. An observed AI during the first year is 0.4 to 0.5 mcg/day. Evidence exists that approximately 20% of adults in industrialized countries may be deficient in cobalamin, and 60% to 70% of the cases in elderly adults are explained by poor absorption from food as opposed to inadequate intake.[22] Therefore, the DRIs include a special recommendation that both men and women who are 50 years old and older meet their RDA with vitamin-B_{12}–fortified foods or supplements.[15]

Deficiency Disease

Vitamin B_{12} deficiency usually results from malabsorption (most commonly) or inadequate intake (e.g., vegan diets). A component of the gastric digestive secretions called *intrinsic factor* is necessary for the absorption of vitamin B_{12} by intestinal cells (Figure 7-7). Gastrointestinal disorders that destroy the cells that line the stomach (e.g., atrophic gastritis) disrupt the secretion of intrinsic factor and hydrochloric acid, both of which are needed for vitamin B_{12} absorption. As mentioned previously, a significant contributor to vitamin B_{12} deficiency, especially in the elderly population, is the malabsorption of

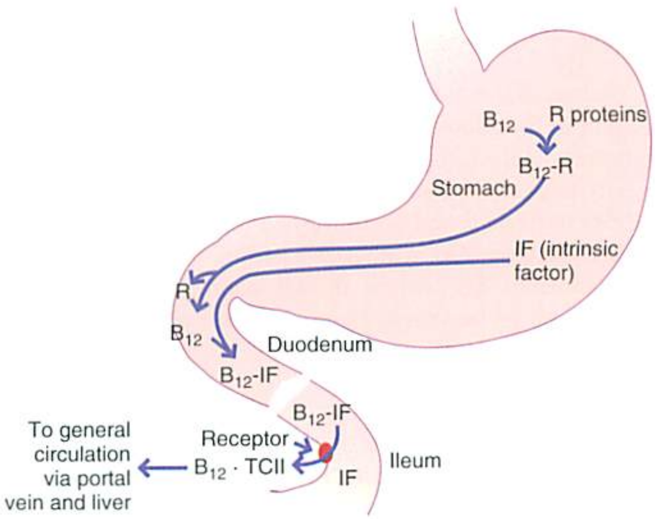


Figure 7-7 Digestion and absorption of vitamin B_{12}. (Reprinted from Mahan LK, Escott-Stump S. *Krause's food & nutrition therapy*. 12th ed. Philadelphia: Saunders; 2008.)

cobalamin the chemical name for vitamin B_{12}; this vitamin is found mainly in animal protein food sources; it is closely related to amino acid metabolism and the formation of the heme portion of hemoglobin; the absence of its necessary digestion and absorption agents in the gastric secretions, hydrochloric acid and intrinsic factor, leads to pernicious anemia and degenerative effects on the nervous system.

cobalamin in food. Other cases of vitamin B_{12} deficiency from inadequate intake have been reported in vegans (see Chapter 4); cobalamin supplements are recommended for vegans to prevent such deficiency, because their diets contain no animal foods, which are the only natural sources of vitamin B_{12}.[23]

The general symptoms of vitamin B_{12} deficiency include nonspecific symptoms such as fatigue, anorexia, and nausea. In the case of continued vitamin B_{12} deficiency, a multitude of conditions may develop, including hematologic (e.g., **pernicious anemia**), neurologic (e.g., myelosis funicularis), and digestive (e.g., glossitis) manifestations.[22] In such cases, vitamin B_{12} is most often administered via hypodermic injection to bypass the absorption defect.

Toxicity Symptoms

Vitamin B_{12} has not been shown to produce adverse effects in healthy individuals when intake from food or supplements exceeds body needs; therefore, no UL has been established.

Food Sources

Vitamin B_{12} is bound to protein in foods. All dietary vitamin B_{12} originates from bacteria that inhabit the gastrointestinal tracts of herbivorous animals. Thus, the only human food sources are of animal origin or come from bacteria found on unwashed plants. Human intestinal bacteria also synthesize vitamin B_{12}, but it is not bioavailable. The richest dietary sources are beef and chicken liver, lean meat, clams, oysters, herring, and crab (Table 7-12).

TABLE 7-12 FOOD SOURCES OF VITAMIN B_{12} (COBALAMIN)

Item	Quantity	Amount (mcg)
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts*		
Beef liver, fried	3 oz	71
Clams, cooked, moist heat	3 oz	84
Mussels, steamed	3 oz	20
Oysters, cooked, moist heat	3 oz	25

*Several vegan-friendly meat and dairy substitute products (e.g., soy milk, tofu) are fortified with vitamin B_{12}.

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Stability

Vitamin B_{12} is stable throughout ordinary cooking processes.

PANTOTHENIC ACID

The name ***pantothenic acid*** refers to this substance's widespread functions in the body and its widespread availability in foods of all types. The name is based on the Greek word *pantothen,* meaning "from every side." Pantothenic acid is present in all living things, and it is essential to all forms of life.

Functions

Pantothenic acid is part of coenzyme A (CoA), which is a carrier of acetyl moieties or larger acyl moieties. It is involved in cellular metabolism as well as both protein acetylation and protein acylation.

Acetyl CoA is involved in energy extraction from the fuel molecules: glucose, fatty acids, and amino acids. CoA also is involved in the biosynthesis of the following: (1) sphingolipids, which are found in neural tissue; (2) some amino acids; (3) isoprenoid derivatives (e.g., cholesterol, steroid hormones, vitamins A and D); (4) δ-aminolevulinic acid, which is the precursor of the porphyrin rings in hemoglobin, the cytochromes of the electron transport chain, and the corrin ring of vitamin B_{12}; (5) the neurotransmitter acetylcholine; and (6) melatonin, which is a sleep inducer that is derived from the neurotransmitter serotonin.

Requirements

No specific RDA for pantothenic acid is given in the DRI guidelines. The usual intake range of the American diet is 4 to 7 mg/day. The DRI guidelines report an AI for people

pernicious anemia a form of megaloblastic anemia that is caused by destroyed gastric parietal cells that produce intrinsic factor; without intrinsic factor, vitamin B_{12} cannot be absorbed.

pantothenic acid a B-complex vitamin that is found widely distributed in nature and that occurs throughout the body tissues; it is an essential constituent of the body's main activating agent, coenzyme A; this special compound has extensive metabolic responsibility for activating a number of compounds in many tissues, and it is a key energy metabolism substance in every cell.

14 years of age and older of 5 mg/day. The AI is slightly higher during pregnancy (6 mg/day) and lactation (7 mg/day). For infants during the first year, the observed AI is 1.7 to 1.8 mg/day.[15]

Deficiency Disease

Given its widespread natural occurrence, pantothenic acid deficiencies are unlikely. The only cases of deficiency have been in individuals who are fed synthetic diets that contain virtually no pantothenic acid.

Toxicity Symptoms

No observed adverse effects have been associated with pantothenic acid intake in people or animals. Therefore, the DRI guidelines have not established an UL for this vitamin.

Food Sources

Pantothenic acid occurs as widely in foods as in body tissues. It is found in all animal and plant cells, and it is especially abundant in animal tissues, whole-grain cereals, and legumes (Table 7-13). Smaller amounts are found in milk, vegetables, and fruits.

TABLE 7-13 FOOD SOURCES OF PANTOTHENIC ACID

Item	Quantity	Amount (mg)
Bread, Cereal, Rice, and Pasta		
All-Bran cereal	1 cup	1.34
Mueslix Fine Grain, Kellogg's cereal	⅔ cup	2.53
Total Whole Grain, General Mills cereal	1 cup	13.3
Wheat Flakes, Kellogg's Complete cereal	1 cup	13.5
Vegetables		
Corn, yellow, boiled	½ cup	0.72
Portabella mushroom, grilled	1 medium (173 g)	0.65
Potato, baked, with skin	½ cup, pieces	0.97
Fruits		
Avocado, raw	¼ medium	0.70
Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts		
Beef liver, fried	3 oz	5.90
Beef, ground, 70% fat, pan browned	3 oz	0.68
Chicken liver, simmered	3 oz	5.67
Egg, scrambled	1 large	0.61
Mackerel, baked	3 oz	0.84
Milk and Dairy Products		
Milk, skim	8 fl oz	0.88
Yogurt, low fat	8 fl oz	1.45

Data from the U.S. Department of Agriculture, Agricultural Research Service: Nutrient Data Laboratory. *USDA nutrient database for standard reference* (website): www.ars.usda.gov/ba/bhnrc/ndl. Accessed October 2010.

Stability

Pantothenic acid is stable to acid and heat, but it is sensitive to alkalis.

BIOTIN

Functions

Biotin is a coenzyme for five carboxylase enzymes. Carboxylase enzymes transfer carbon dioxide moieties from one molecule to another in the following biotin enzymes:

1. *α-Acetyl-CoA carboxylase*, which is involved in fatty acid synthesis
2. *β-Acetyl-CoA carboxylase*, which is involved in inhibiting fatty acid breakdown during the hours after starch, sucrose, or fructose is consumed
3. *Pyruvate carboxylase*, which is involved in synthesizing glucose during fasting (gluconeogenesis) or during short bursts of energy (from lactic acid)
4. *Methylcrotonyl-CoA carboxylase*, which is involved in the degradation of the amino acid leucine
5. *Propionyl-CoA carboxylase*, which is involved in the breakdown of the three-carbon fatty acid propionic acid

Requirements

The amount of biotin needed for metabolism is extremely small, and it is measured in micrograms. The DRI guidelines do not establish an RDA for biotin. An AI has been set on the basis of the intakes of healthy individuals. The AI for adults who are 18 years old and older is 30 mcg/day. For infants during the first 12 months, the observed AI is 5 to 6 mcg/day. The AI during pregnancy also is 30 mcg/day, and during lactation it is 35 mcg/day. The intestinal cells also absorb biotin, which is synthesized by the bacteria that normally inhabit the intestine.[15]

Deficiency Disease

Because the potency of biotin is great, despite the tiny microgram quantities present in the body, no known natural dietary deficiency occurs. Biotin is bound by avidin, a protein that is found in uncooked egg whites. Consequently, consuming raw eggs inhibits biotin absorption. Mice studies found that marginal biotin deficiency during gestation inhibited the availability of insulin-like growth factor (IGF-I), thereby resulting in malformations of the long bones.[24] Biotin deficiency may be teratogenic for humans as well. A rare inborn error of metabolism called *biotinidase deficiency* can result in neurologic disturbances if it is left untreated, but it is treatable with pharmacologic doses of biotin.[25]

Toxicity Symptoms

No toxicity or other adverse effects from the consumption of biotin by people or animals are known. No data currently support setting an UL for biotin.

Food Sources

Biotin is widely distributed in natural foods, but it is not equally absorbed from all of them. For example, the biotin in corn and soy meal is completely bioavailable (i.e., able to be digested and absorbed by the body). However, almost none of the biotin in wheat is bioavailable. The best food sources of biotin are liver, cooked egg yolk, soy flour, cereals (except bound forms in wheat), meats, tomatoes, and yeast.

Stability

Biotin is a stable vitamin, but it is water soluble. A summary of the water-soluble vitamins is given in Table 7-14.

CHOLINE

Choline is a water-soluble nutrient that is associated with the B-complex vitamins. The Institute of Medicine established choline as an essential nutrient for human nutrition in the 1998 DRIs.[15]

Functions

Choline is important for maintaining the structural integrity of cell membranes as a component of the phospholipid lecithin (i.e., phosphatidyl choline). Choline is also involved in lipid transport (i.e., lipoproteins), homocysteine reduction, and the neurotransmitter acetylcholine, which is involved in involuntary functions, voluntary movement, and long-term memory storage, among other things.

Requirements

The DRI guidelines provide an AI of 550 mg/day for men 14 years of age or older and of 425 mg/day for women 18 years of age or older. During pregnancy, the AI is 450 mg/day; during lactation, it is 550 mg/day, because an ample amount of choline is secreted into human milk. For infants, the observed AI is 125 to 150 mg/day during the first year of life.[15]

Deficiency Disease

Choline deficiency may cause liver and muscle damage. Other conditions associated with choline deficiency include neural tube defects, heart disease related to hyperhomocysteinemia, inflammation, and breast cancer. Some researchers conclude that suboptimal choline intake may be a public health concern and think that it warrants the attention of health professionals.[26]

Toxicity Symptoms

Very high doses of supplemental choline have caused lowered blood pressure, fishy body odor, sweating, excessive salivation, and reduced growth rate. The UL for adults is 3.5 g/day.[15]

Food Sources

Choline is found naturally in a wide variety of foods. Soybean products, milk, eggs, liver, and peanuts are especially rich sources of choline.

Stability

Choline is a relatively stable nutrient. It is water soluble, as are all of the B-complex vitamins.

SECTION 3 **PHYTOCHEMICALS**

In addition to the vitamins discussed so far in this chapter, there are other bioactive molecules called *phytochemicals* that have health benefits and that come from the plants that we eat. Phytochemicals are nonessential organic molecules. The term *phytochemical* comes from the Greek word *phyton*, meaning "plant." Scientists believe that

TABLE 7-14 SUMMARY OF VITAMIN C AND THE B-COMPLEX VITAMINS

Vitamin	Functions	Recommended Intake (Adults)	Deficiency	Tolerable Upper Intake Level (UL) and Toxicity	Sources
Vitamin C (ascorbic acid)	Antioxidant; collagen synthesis; helps prepare iron for absorption and release to tissues for red blood cell formation; metabolism	Men, 90 mg; women, 75 mg; smokers: an additional 35 mg/day	Scurvy (deficiency disease); sore gums; hemorrhages, especially around bones and joints; anemia; tendency to bruise easily; impaired wound healing and tissue formation; weakened bones	UL: 2000 mg Diarrhea	Citrus fruits, kiwi, tomatoes, melons, strawberries, dark leafy vegetables, chili peppers, cabbage, broccoli, chard, green and red peppers, potatoes
Thiamin (vitamin B_1)	Normal growth; coenzyme in carbohydrate metabolism; normal function of heart, nerves, and muscle	Men, 1.2 mg; women, 1.1 mg	Beriberi (deficiency disease); gastrointestinal: loss of appetite, gastric distress, indigestion, deficient hydrochloric acid; central nervous system: fatigue, nerve damage, paralysis; cardiovascular: heart failure, edema of the legs	UL not set; toxicity unknown	Pork, beef, liver, whole or enriched grains, legumes, wheat germ
Riboflavin	Normal growth and energy; coenzyme in protein and energy metabolism	Men, 1.3 mg; women, 1.1 mg	Ariboflavinosis; wound aggravation; cracks at the corners of the mouth; a swollen red tongue; eye irritation; skin eruptions	UL not set; toxicity unknown	Milk; meats, enriched cereals, green vegetables
Niacin (vitamin B_3, nicotinamide, nicotinic acid)	Coenzyme in energy production; normal growth; health of skin	Men, 16 mg of niacin equivalents; women: 14 mg of niacin equivalents	Pellagra (deficiency disease); weakness; loss of appetite; diarrhea; scaly dermatitis; neuritis; confusion	UL: 35 mg Skin flushing	Fortified cereals and grains
Vitamin B_6 (pyridoxine)	Coenzyme in amino acid metabolism: protein synthesis; heme formation; brain activity; carrier for amino acid absorption	Between the ages of 19 and 50 years, 1.3 mg; Men 50 years of age or older: 1.7 mg; women 50 years of age or older: 1.5 mg	Anemia; hyperirritability; convulsions; neuritis	UL: 100 mg Nerve damage	Wheat germ, legumes, meats, poultry, seafood
Folate (folic acid, folacin)	Coenzyme in DNA and RNA synthesis; amino acid metabolism; red blood cell maturation	400 mcg of dietary folate equivalents	Megaloblastic anemia (large immature red blood cells); poor growth; neural tube defects	UL: 1000 mcg Masks vitamin B_{12} deficiency	Liver, green leafy vegetables, legumes, yeast, fortified orange juice
Cobalamin (vitamin B_{12})	Coenzyme in synthesis of heme for hemoglobin; myelin sheath formation to protect nerves	2.4 mcg	Pernicious anemia; poor nerve function	UL not set; toxicity unknown	Liver; lean meats, fish, seafood
Pantothenic acid	Formation of coenzyme A; fat, cholesterol, protein, and heme formation	Adequate Intake, 5 mg	Unlikely because of widespread distribution in most foods	UL not set; toxicity unknown	Meats, eggs, milk, whole grains, legumes, vegetables
Biotin	Coenzyme A partner; synthesis of fatty acids, amino acids, and purines	Adequate Intake, 30 mcg	Natural deficiency unknown	UL not set; toxicity unknown	Liver, egg yolk, soy flour, nuts

Fortified cereals and grains

fruits, vegetables, beans, nuts, and whole grains provide thousands of phytochemicals, many of which have yet to be identified.

What prompted researchers to investigate phytochemicals were the health differences seen in people who were eating whole fruits and vegetables compared with people who were eating mostly refined foods and taking vitamin and mineral supplements. Those individuals who were obtaining their essential nutrients from a diet rich in plant foods benefited far more than those who did not.

FUNCTION

Phytochemicals have a wide variety of functions, some of which include antioxidant activity, hormonal actions, interactions with enzymes and DNA replication, and antibacterial effects. Studies show that diets that are high in phytochemicals protect against cardiovascular disease, counteract inflammatory compounds, help to prevent cancer, and increase antioxidant status.[27] The beneficial effects of phytochemicals are thought to result from the synergistic actions of multiple constituents as opposed to the actions of isolated compounds.[28]

RECOMMENDED INTAKE

There are no established DRIs for phytochemicals. Phytochemicals give fruits and vegetables their specific colors; thus, consuming a colorful variety of fruits, vegetables, whole grains, and nuts will provide a rich supply of phytochemicals. The Centers for Disease Control and Prevention (CDC) recommends consuming a combined total of five to nine servings of fruits and vegetables daily. At www.fruitsandveggiesmatter.gov, the CDC provides recommendations for the number of cups of fruits and vegetables that a person should consume daily on the basis of age, gender, and activity level. One cup of raw or cooked vegetables or vegetable juice or 2 cups of raw leafy greens are equivalent to 1 cup from the vegetable group. One cup of fruit or 100% fruit juice or half a cup of dried fruit is equivalent to 1 cup from the fruit group.[29]

This recommendation is based on the finding that consuming 400 to 600 g/day of fruits and vegetables reduces the risk of developing some forms of cancer. Current reports from the Economic Research Service of the U.S. Department of Agriculture show that the average American consumes much less than the recommendations: 0.8 servings of fruit per day and 1.7 servings of vegetables per day.[30]

FOOD SOURCES

Foods derived from animals and those that have been processed and refined are virtually devoid of phytochemicals. Phytochemicals are found in whole and unrefined foods such as vegetables, fruits, legumes, nuts, seeds, whole grains, and certain oils (e.g., olive oil).

The following is a list of seven typical fruit and vegetable colors along with the specific phytochemical (e.g., lycopene) or phytochemical class (e.g., flavonoids) that these fruits and vegetables may contain. The specified phytochemical or phytochemical class is present in fruits or vegetables of other colors, but color is one prominent indicator that a significant quantity of the specified phytochemical or phytochemical class may be present. One specific exception that is worth noting is flavonoids. Although orange-yellow foods are good sources of flavonoids, other significant sources include purple grapes, black tea, olives, onions, celery, green tea, oregano, and whole wheat, none of which have an orange-yellow color.

- *Red* foods provide lycopene.
- *Yellow-green* foods provide zeaxanthin.
- *Red-purple* foods provide anthocyanin.
- *Orange* foods provide β-carotene.
- *Orange-yellow* foods provide flavonoids.
- *Green* foods provide glucosinolate.
- *White-green* foods provide allyl sulfides.

By consuming one fruit or vegetable from each of these seven color categories daily, individuals get a variety of phytochemicals. Thousands of other phytochemicals are also widely distributed in fruits, vegetables, grains, soybeans, legumes, and nuts.

SECTION 4 VITAMIN SUPPLEMENTATION

The Dietary Supplement Health and Education Act (DSHEA) of 1994 officially defined supplements as a product (other than tobacco) that has the following characteristics:

- It is intended to supplement the diet.
- It contains one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and other substances) or their constituents.

- It is intended to be taken by mouth as a pill, capsule, tablet, or liquid.
- And it is labeled on the front panel as being a dietary supplement.

Dietary supplements are regulated in the United States by the U.S. Food and Drug Administration. The Office of Dietary Supplements (http://ods.od.nih.gov/), which is housed within the National Institutes of Health, has the following mission: "to strengthen knowledge and understanding of dietary supplements by evaluating scientific information, stimulating and supporting research, disseminating research results, and educating the public to foster an enhanced quality of life and health for the U.S. population."[31]

The use of dietary supplements is quite common in the United States. About half of the population regularly takes a dietary supplement. The most commonly used supplement is of the multivitamin or multimineral variety. It is the position of the Academy of Nutrition and Dietetics that "... the best nutrition-based strategy for promoting optimal health and reducing the risk of chronic disease is to wisely choose a wide variety of foods. Additional nutrients from supplements can help some people meet their nutritional needs ..."[32] If people ate a healthy and varied diet in accordance with the *Dietary Guidelines for Americans* and the MyPlate guidelines, adequate nutrients should be provided by whole foods. However, since only about 3% to 4% of Americans currently eat in the ways that these guidelines recommend, inadequate nutrient consumption is quite possible.[32,33] Although dietary vitamin and mineral supplements may be beneficial for bridging this gap, it is also possible to exceed the UL for certain nutrients. Of interest is that the use of dietary supplements is most common among the healthiest people rather than among those who need it the most.

RECOMMENDATIONS FOR NUTRIENT SUPPLEMENTATION

Health care professionals should be aware that people often fail to notify their health care providers about the use of dietary supplements. Drug-nutrient interactions are more common with dietary supplements than with whole foods; thus, it is important to specifically ask patients about their use of supplements. Although dietary supplements may not be necessary for everyone, there are some instances in which supplemental forms of specific nutrients are recommended on the basis of age, lifestyle, or disease state.

Life Cycle Needs

Vitamin needs fluctuate with age and with situations that occur throughout the life cycle.

Pregnancy and Lactation

The DRI guidelines explicitly establish separate recommendations for women during pregnancy and lactation that take into account the increased nutrient demands that occur during this period. To reduce the risk of neural tube defects, the DRI committee recommends that pregnant women and women who are capable of becoming pregnant increase their intake of folic acid from fortified foods and/or dietary supplements in addition to the folate that is already present in their diets. Women may find meeting the increased nutrient needs of pregnancy difficult by diet alone as a result of nutrient bioavailability, tolerances, food preferences, or other factors that can marginalize their diet (i.e., effectively decrease the nutrients that their diet provides). Supplements may then become a viable way of ensuring adequate intake to meet increased nutrient demands.

Infants, Children, and Adolescents

The American Academy of Pediatrics recommends that all breast-fed infants receive 400 IU of supplemental vitamin D daily to help prevent rickets. Infants who are not breast fed, children, and adolescents who do not consume at least 1 qt/day of vitamin-D-fortified milk or otherwise have an intake of 400 IU of vitamin D should also receive 400 IU of supplemental vitamin D daily.[7]

Older Adults

The aging process may increase the need for some vitamins because of decreased food intake and less efficient nutrient absorption, storage, and usage (see Chapter 12). The Institute of Medicine recommends that people who are 50 years of age or older take 2.4 mcg/day of supplemental vitamin B_{12}. Advancing age also decreases the ability of the skin to produce vitamin D. Thus, older adults are encouraged to consume extra vitamin D from fortified foods or dietary supplements.[32]

Lifestyle

Personal lifestyle choices also influence individual needs for nutrient supplementation.

Restricted Diets

People who habitually follow fad diets may find meeting many of the nutrient intake standards difficult, particularly if their meals provide fewer than 1200 kcal/day. Very restrictive diets are not recommended, because they may cause multiple nutrient deficiencies. A wise weight-reduction program should meet all nutrient needs. People who are following strict vegan diets need supplemental vitamin B_{12} in fortified foods or dietary supplements, because the only natural food sources of this vitamin are of animal origin.

Smoking

Smoking cigarettes adversely affects health in many ways, including reducing the body's vitamin C pool. Research shows that smokers have significantly less serum vitamin C than nonsmokers.[34] The Institute of Medicine sets the RDA of vitamin C at 35 mg/day higher for smokers to compensate for the oxidative stress that is induced by smoking. The additional vitamin C does not necessarily need to come from a dietary supplement; however, if the person chooses to not quit smoking or to not consume additional vitamin-C–rich foods, a dietary supplement may be advisable.

Alcohol

The chronic or abusive use of alcohol can interfere with the absorption of B-complex vitamins, especially thiamin, folate, and vitamin B_6. Multivitamin supplements that are rich in B vitamins may partially mitigate the effects. However, decreased alcohol use must accompany this nutrition therapy to rectify the alcohol-induced deficiency.

Disease

Evidence does not support the use of multivitamin and multimineral dietary supplements to prevent chronic disease. However, for patients with certain diseases, dietary supplements may be warranted to help combat specific nutrient deficiencies. In states of disease, malnutrition, malabsorption, debilitation, or hypermetabolic demand, each patient requires careful nutrition assessment. Nutrition support, including therapeutic supplementation as indicated, is part of the total medical therapy. A dietitian plans dietary and supplemental therapy to meet the patient's clinical requirements.

MEGADOSES

At high pharmacologic concentrations, vitamins no longer operate strictly as nutritional agents. Nutrients and drugs can do the following: (1) participate in or improve physiologic conditions or illnesses; (2) prevent diseases; or (3) relieve symptoms. However, many people are ignorant of the similarities between drugs and vitamins. Most people realize that too much of any drug can be harmful or even fatal and take care to avoid overdosing. However, too many people do not apply this same logic to nutrients and only realize the dangers of vitamin megadoses when they experience toxic side effects.

The liver can store large amounts of fat-soluble vitamins, especially vitamin A. Therefore, the potential toxicity of fat-soluble vitamin megadoses, including liver and brain damage in extreme cases, is well known.[35-37] Megadoses of one vitamin can also produce toxic effects and lead to a secondary deficiency of another nutrient. Hyperphysiologic levels of one vitamin may increase the need for other nutrients with which it works in the body, thereby effectively inducing a deficiency. Deficiencies can also occur when a person suddenly stops overdosing, which is known as a *rebound effect*. For example, infants who are born to mothers who took ascorbic acid megadoses during pregnancy may develop rebound scurvy after birth, when their high doses of ascorbic acid are cut off.

SUPPLEMENTATION PRINCIPLES

The following basic principles may help to guide nutrient supplementation decisions:

- *Read the labels carefully.* The Nutrition Labeling and Education Act of 1990 standardized and defined label terminology on food products in an effort to ensure that health claims on food packaging are clear and truthful. Consumers can make better-informed decisions knowing that a product's ingredients, toxicity levels, potential side effects, and health claims are based on significant scientific evidence.
- *Vitamins, like drugs, can be harmful in large amounts.* The only time that larger vitamin doses may be helpful is when severe deficiency exists or when nutrient absorption or metabolism is inefficient.
- *Professionally determined individual needs govern specific supplement usage.* Each person's need should be the basis for supplementing nutrients. This prevents excessive intake, which may have a cumulative effect over time.
- *All nutrients work together to promote good health.* Consuming large amounts of one vitamin often induces deficiencies of other vitamins or nutrients.
- *Food is the best source of nutrients.* Most foods are the best "package deals" in nutrition. Foods provide a wide variety of nutrients in every bite as compared with the dozen or so that are found in a vitamin bottle. In addition, by itself, a vitamin can do nothing. It is catalytic, so it must have a substrate (i.e., carbohydrate, protein, fat, or their metabolites) on which to work. With the careful selection of a wide variety

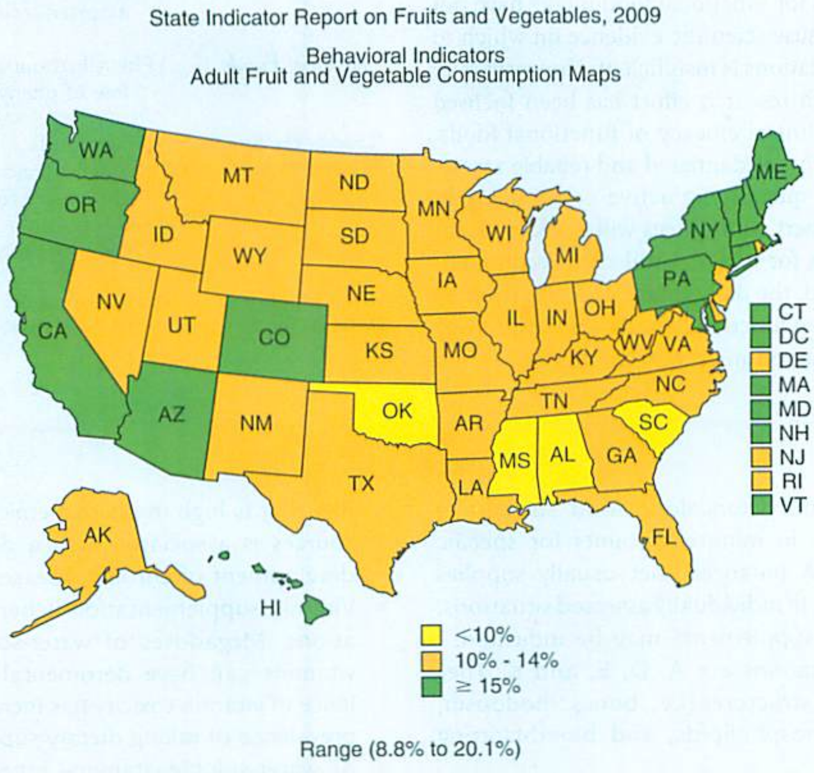
of foods and with good storage techniques, meal planning, and preparation techniques, most people can obtain ample amounts of essential nutrients from their diets (see the Cultural Considerations box, "The American Diet"). Furthermore, the evidence still overwhelmingly supports whole foods as the superior vehicles for delivering nutrients to the body.

- *Evaluate the information.* The Further Reading and Resources section at the end of the chapter provides a list of reliable organizations and resources related to dietary supplements.

CULTURAL CONSIDERATIONS

THE AMERICAN DIET

By consuming the recommended servings from each food group in accordance with the MyPlate guidelines, an individual's vitamin and mineral needs should be met. However, the average American does not consume the recommended servings per day of key vitamin-rich foods such as fruits and vegetables. Note that, in the map below, no state reported more than 20.1% of its adult population to be consuming the recommended minimum number of servings of fruits and vegetables per day.



Instead, studies show that the average American overconsumes "nutrient-empty" foods such as fats and sugars. The average daily MyPlate equivalents consumed in the United States for each food group are as follows[1]:

- Flour and cereal products 7.7 servings per day
- Vegetables 1.7 servings per day
- Fruit 0.8 servings per day
- Dairy 1.7 servings per day
- Meat, eggs, and nuts 6.6 servings per day
- Added fats and oils 71.2 servings per day
- Added sugars 28.7 servings per day

How do you measure up? What about your family and friends? The prevention of deficiency or any diseases associated with nutrient deficiency is always better than treatment.

(Data from Centers for Disease Control and Prevention. *State indicator report on fruits and vegetables,* 2009 (website): www.fruitsandveggiesmatter.gov/health_professionals/maps_adults.html. Accessed October 12 2010.)

1. U.S. Department of Agriculture Economic Research Service. *Average daily per capita MyPyramid equivalents from the U.S. food availability* (website): www.ers.usda.gov/Data/FoodConsumption/FoodGuideSpreadsheets.htm#servings. Accessed October 12 2010.

FUNCTIONAL FOODS

The term *functional food* technically has no legal definition or meaning. Generally, "functional foods" include any foods or food ingredients that may provide a health benefit beyond their basic nutritional value. Such foods are also referred to as *nutraceuticals* or *designer foods.* The position of the Academy of Nutrition and Dietetics is that such whole foods—having been fortified, enriched, or enhanced in some way—could be beneficial when regularly consumed as part of a varied diet.[38] The regulation of functional foods is complicated by the fact that they fall under different areas of federal jurisdiction, because they include conventional foods, food additives, dietary supplements, medical foods, and foods for special dietary use. Box 7-2 gives examples of functional food categories.

Recommendations for functional food intake have not been established, because scientific evidence on which to base such recommendations is insufficient. However, over the past decade, much research effort has been focused on determining the clinical efficacy of functional foods. When efficacy is clearly substantiated and reliable assessments for accurately quantifying active constituents in foods are in place, expert committees will work to establish recommendations for intake. Until such recommendations are established, the daily intake of foods from all food groups—including functional foods—is the best way to meet macronutrient and micronutrient needs.

BOX 7-2 FUNCTIONAL FOOD CATEGORIES ALONG WITH SELECTED FOOD EXAMPLES

Functional Food Category	Selected Functional Food Examples
Conventional Foods (whole foods)	Garlic Nuts Tomatoes
Modified Foods	
Fortified	Calcium-fortified orange juice Iodized salt
Enriched	Folate-enriched breads
Enhanced	Energy bars, snacks, yogurts, teas, bottled water, and other functional foods that are formulated with bioactive components such as lutein, fish oils, ginkgo biloba, St. John's wort, saw palmetto, or assorted amino acids
Medical Foods	Phenylketonuria formulas that are free of phenylalanine
Foods for Special Dietary Use	Infant foods Hypoallergenic foods such as gluten-free foods and lactose-free foods Weight-loss foods

Hasler CM, Brown AC. Position of the Academy of Nutrition and Dietetics: functional foods. *J Am Diet Assoc.* 2009; 109(4):735-746.

SUMMARY

- Vitamins are organic, noncaloric food substances that are necessary in minute amounts for specific metabolic tasks. A balanced diet usually supplies sufficient vitamins. In individually assessed situations, however, vitamin supplements may be indicated.
- The fat-soluble vitamins are A, D, E, and K. They mainly affect body structures (i.e., bones, rhodopsin, cell membrane phospholipids, and blood-clotting proteins).
- The water-soluble vitamins are vitamin C (ascorbic acid), the eight B-complex vitamins (i.e., thiamin, riboflavin, niacin, pyridoxine, folate, cobalamin, pantothenic acid, and biotin), and choline. Their major metabolic tasks relate to their roles in coenzyme factors, except for vitamin C, which is a biologic reducing agent that quenches free radicals and helps with collagen synthesis.
- Phytochemicals are compounds that are found in whole and unrefined foods derived from plants. A diet that is high in phytochemicals from a variety of sources is associated with a decreased risk of the development of chronic diseases.
- Vitamin supplementation is beneficial in some situations. Megadoses of water-soluble or fat-soluble vitamins can have detrimental effects. The prevalence of vitamin toxicity has increased along with the prevalence of taking dietary supplements.
- All water-soluble vitamins—especially vitamin C—are easily oxidized, so care must be taken to minimize the exposure of food surfaces to air or other oxidizers during storage and preparation. With few exceptions, all nutrients in foods are more bioavailable and beneficial to the body than nutrients in supplements.
- Functional foods are whole foods with added nutrients, such as vitamins, minerals, herbs, fiber, protein, or essential fatty acids that are thought to have beneficial health effects.

CRITICAL THINKING QUESTIONS

1. What are vitamins? Name them, and distinguish between fat-soluble and water-soluble vitamins.
2. Describe three general functions of vitamins, and give examples of each.
3. How would you advise a friend who was taking self-prescribed vitamin supplements? Give reasons and examples to support your answer.
4. Describe four situations in which vitamin supplements should be used. Give reasons and examples in each case.
5. What are phytochemicals? How can you incorporate them into your diet?

CHAPTER CHALLENGE QUESTIONS

True-False

Write the correct statement for each statement that is false.

1. *True or False:* A coenzyme acts alone to control a number of different types of reactions.
2. *True or False:* Carotene is preformed vitamin A that is found in animal food sources.
3. *True or False:* Exposure to sunlight produces vitamin D from a cholesterol precursor in the skin.
4. *True or False:* Extra vitamin C is stored in the liver to meet the demands of tissue infection.
5. *True or False:* Vitamin D and sufficient levels of calcium and phosphorus can prevent rickets.
6. *True or False:* Good sources of vitamin K are found in green leafy vegetables such as kale and spinach.
7. *True or False:* Dietary supplements are a necessary part of healthy living for all people.

Multiple Choice

1. Vitamin A is fat soluble and formed from carotene in plant foods, or it is consumed as a fully formed vitamin in animal foods. Which of the following supplies the greatest amount of this vitamin?
   a. Cantaloupe
   b. Collards
   c. Beef liver
   d. Carrots
2. If you wanted to increase the vitamin C content of your diet, which of the following foods would you choose in larger amounts?
   a. Liver, other organ meats, and seafood
   b. Potatoes, enriched cereals, and fortified margarine
   c. Green peppers, strawberries, and oranges
   d. Milk, cheese, and eggs
3. Which of the following statements is true about the sources of vitamin K?
   a. Vitamin K is found in a wide variety of foods, so no deficiency can occur.
   b. Vitamin K is easily absorbed without assistance, so we absorb all of the nutrient that we consume into our circulatory system.
   c. Vitamin K is rarely found in foods, so a natural deficiency can occur.
   d. A large portion of the amount of vitamin K that is required for metabolic purposes is produced by our own intestinal bacteria.
4. A food with nutrients that have been added through fortification or enrichment is considered a
   a. dietary supplement.
   b. functional food.
   c. phytochemical.
   d. None of the above
5. One of the primary functions of folate is as a(n)
   a. antioxidant.
   b. coenzyme in protein and energy metabolism.
   c. CoA partner.
   d. coenzyme in DNA and RNA synthesis.
6. Beriberi is the deficiency disorder that is associated with which vitamin?
   a. Thiamin
   b. Riboflavin
   c. Niacin
   d. Pantothenic acid
7. The formation of prothrombin for normal blood-clotting purposes is a primary function of which fat-soluble vitamin?
   a. Vitamin A
   b. Vitamin D
   c. Vitamin E
   d. Vitamin K

Evolve Please refer to the Students' Resource section of this text's Evolve Web site for additional study resources.

REFERENCES

1. Wang W, Connor SL, Johnson EJ, et al. Effect of dietary lutein and zeaxanthin on plasma carotenoids and their transport in lipoproteins in age-related macular degeneration. *Am J Clin Nutr*. 2007;85(3):762-769.
2. Food and Nutrition Board, Institute of Medicine. *Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. Washington, DC: National Academies Press; 2001.
3. World Health Organization. *Global prevalence of vitamin A deficiency in populations at risk 1995-2005*, Geneva: World Health Organization; 2009.
4. Briefel R, Hanson C, Fo MK, et al. Feeding Infants and Toddlers Study: do vitamin and mineral supplements contribute to nutrient adequacy or excess among US infants and toddlers? *J Am Diet Assoc*. 2006;106(1 Suppl 1): S52-S65.
5. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr*. 2008;87(4):1080S-1086S.
6. Ross AC, Manson JE, Abrams SA, et al. The 2011 Dietary Reference Intakes for Calcium and Vitamin D: what dietetics practitioners need to know. *J Am Diet Assoc*. 2011; 111(4):524-527.
7. Wagner CL, Greer FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics*. 2008;122(5):1142-1152.
8. Ginde AA, Liu MC, Camargo Jr CA. Demographic differences and trends of vitamin D insufficiency in the US population, 1988-2004. *Arch Intern Med*. 2009;169(6): 626-632.
9. Food and Nutrition Board, Institute of Medicine. *Dietary reference intakes for calcium and vitamin D*. Washington, DC: National Academy of Sciences; 2010.
10. Food and Nutrition Board, Institute of Medicine. *Dietary reference intakes for vitamin C, vitamin E, selenium, and carotenoids*. Washington, DC: National Academies Press; 2000.
11. Engin KN. Alpha-tocopherol: looking beyond an antioxidant. *Mol Vis*. 2009;15:855-860.
12. Traber MG. Vitamin E and K interactions—a 50-year-old problem. *Nutr Rev*. 2008;66(11):624-629.
13. Bonjour JP, Guéguen L, Palacios C, et al. Minerals and vitamins in bone health: the potential value of dietary enhancement. *Br J Nutr*. 2009;101(11):1581-1596.
14. Taylor EN, Curhan GC. Determinants of 24-hour urinary oxalate excretion. *Clin J Am Soc Nephrol*. 2008;3(5):1453-1460.
15. Food and Nutrition Board, Institute of Medicine. *Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline*, Washington, DC: National Academies Press; 2000.
16. Marks HM: Epidemiologists explain pellagra: gender, race, and political economy in the work of Edgar Sydenstricker. *J Hist Med Allied Sci*. 2003;58(1):34-55.
17. Winkels RM, Brouwer IA, Siebelink E, et al. Bioavailability of food folates is 80% of that of folic acid. *Am J Clin Nutr*. 2007;85(2):465-473.
18. Wilson RD, Johnson JA, Wyatt P, et al; Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada and The Motherrisk Program. Pre-conceptional vitamin/folic acid supplementation 2007: the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies. *J Obstet Gynaecol Can*. 2007;29(12): 1003-1026.
19. Wolff T, Wiktop CT, Miller T, et al. Folic acid supplementation for the prevention of neural tube defects: an update of the evidence for the U.S. Preventive services task force. *Ann Intern Med*. 2009;150(9):632-639.
20. Grosse SD, Collins JS. Folic acid supplementation and neural tube defect recurrence prevention. *Birth Defects Res A Clin Mol Teratol*. 2007;79(11):737-742.
21. Centers for Disease Control and Prevention. Racial/ethnic differences in the birth prevalence of spina bifida—United States, 1995-2005. *MMWR Morb Mortal Wkly Rep*. 2009; 57(53):1409-1413.
22. Dali-Youcef N, Andres E. An update on cobalamin deficiency in adults. *QJM*. 2009;102(1):17-28.
23. Elmadfa I, Singer I. Vitamin B-12 and homocysteine status among vegetarians: a global perspective. *Am J Clin Nutr*. 2009;89(5):1693S-1698S.
24. Báez-Saldaña A, Gutiérrez-Ospina G, Chimal-Monroy J, et al. Biotin deficiency in mice is associated with decreased serum availability of insulin-like growth factor-I. *Eur J Nutr*. 2009;48(3):137-144.
25. Wolf B. Clinical issues and frequent questions about biotinidase deficiency. *Mol Genet Metab*. 2010;100(1):6-13.
26. Zeisel SH, da Costa KA. Choline: an essential nutrient for public health. *Nutr Rev*. 2009;67(11):615-623.
27. Heber D. Vegetables, fruits and phytoestrogens in the prevention of diseases. *J Postgrad Med*. 2004;50(2):145-149.
28. de Kok TM, van Breda SG, Manson MM. Mechanisms of combined action of different chemopreventive dietary compounds: a review. *Eur J Nutr*. 2008;47(Suppl 2):51-59.
29. Centers for Disease Control and Prevention. *What counts as a cup?* (website): www.fruitsandveggiesmatter.gov/what/index.html. Accessed October 12 2010.
30. U.S. Department of Agriculture Economic Research Service. *Average daily per capita MyPyramid equivalents from the U.S. food availability* (website): http://www.ers.usda.gov/Data/FoodConsumption/FoodGuideSpreadsheets.htm#servings. Accessed October 12 2010.
31. Office of Dietary Supplements. *Mission statement* (website): ods.od.nih.gov/About/about_ods.aspx. Accessed October 12 2010.
32. Marra MV, Boyar AP. Position of the academy of nutrition of dietetics: nutrient supplementation. *J Am Diet Assoc*. 2009;109(12):2073-2085.
33. King JC. An evidence-based approach for establishing dietary guidelines. *J Nutr*. 2007;137(2):480-483.
34. Schleicher RL, Carroll MD, Ford ES, Lacher DA. Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003-2004 National Health and Nutrition Examination Survey (NHANES). *Am J Clin Nutr*. 2009; 90(5):1252-1263.