Chapter 8

Nutrients Important As Antioxidants

Big Idea

Eating foods such as fruits, vegetables, herbs, and spices that are high in antioxidants can help prevent cell damage and promote health.

Government trickery and greed are a big part of the history of the woody, bittersweet nutmeg people sprinkle in their eggnog and add to their pumpkin pie.

Nutmeg, which is obtained from the seed of the evergreen tree, Myristica fragrans, was once a highly coveted spice.

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Arabs originally controlled the lucrative nutmeg trade. Run Island, part of the Banda archipelago in the Maluku province of Indonesia, and (for a while) the sole source of nutmeg, remained a well-kept secret under their control. Then, in 1521, the Portuguese conquered the southern region of Malay in Indonesia and discovered the island.

Control of this nutmeg source switched hands rapidly from this point on. Although the Portuguese claimed ownership for a moment, the Spaniards were quick to take over. In the seventeenth century, the Dutch East India Company invaded the Band Islands. They then ran plantation estates on Run Island and actively patrolled the sea in war vessels to discourage the stealing of seeds from *Myristica fragrans*. They went so far as to track the movement of pigeons and other animals that might unwittingly transport the seeds elsewhere, and they burned any trees found off of Run Island.

The battles over Run Island had one important motivation: money. Trade was lucrative in the seventeenth century because nutmeg was valued as a curative for stomach ailments, as an aphrodisiac, and as a healer of the liver. The spice even had a reputation for curing the plague, which might have worked—wearing a clove of it

around the neck may have deterred fleas and other disease carriers. Buyers were also well aware of nutmeg's hallucinogenic properties and used it in high doses as a psychoactive drug. Its price was astronomically high and kept so by the Dutch, who burned their own nutmeg warehouses down to assure the laws of supply and demand did not lower the spice's value.

During the Napoleanic wars, while the Dutch were battling the French, the British slipped onto Run Island, stole *Myristica fragras* seeds, and successfully grew the tree on plantations on the island of Grenada. Today, Grenada, also known as the "Isle of Spice," produces about one-third of the world's supply, which is why its flag boasts a clove of nutmeg.

Our ancestors were probably right to value nutmeg for its curative properties. While it does not actually cure disease outright, nutmeg contains a variety of antioxidants, including phenolic compounds, lignans, and eugenol. Foods rich in antioxidants have been touted as preventative and curative, and some believe they delay certain aspects of the aging process. While we are no longer fighting over nutmeg's production and sale, we are waging a fierce debate about the lack of scientific proof of these believed benefits.

The "antioxidant hypothesis"—the educated guess that antioxidant chemicals protect against chronic disease—has existed for decades. Despite thousands of studies conducted on the health benefits of particular antioxidants, there is little evidence supporting the idea that they singularly prevent disease, reduce the effects of aging, or promote health. It is the *combination* of antioxidants, phytochemicals, and nutrient-rich foods that achieves these end goals.

Nutmeg has been shown in animal and laboratory studies to act as an antimicrobial, antifungal, and anti-inflammatory agent. It has protected against liver damage and stimulated male sexual activity in rats. However, none of these effects has been scientifically shown to occur in humans. On the other hand, nutmeg has proven effective as a psychoactive drug when taken in high doses.

In this chapter, you will learn there is no miracle food or supplement. The debate over the nutmeg's effectiveness as an antioxidant—and over the effects of antioxidants in general—is proof of this. You will also learn that plant chemicals can affect the body in many different ways, depending on the type of chemical and the dosage. Different antioxidants are believed to have different functions, and those functions are sometimes interdependent or dependent on the amount of nutrient-rich foods you eat.

You Decide

Will you increase your intake of antioxidant- and nutrient-rich foods to improve health and reduce the risk of chronic disease? Why and how?

“Shall I not have intelligence with the earth? Am I not partly leaves and vegetable mould myself?”

- Henry David Thoreau (July 12, 1817–May 6, 1862)

8.1 Generation of Free Radicals in the Body

LEARNING OBJECTIVES

1. Describe how free radicals are generated in the body.
2. Explain oxidative stress and what diseases it is associated with.

In mainstream advertising you may have heard that antioxidants can extend your life by preventing disease and slowing the aging process. But what are antioxidants? And how do they work in the body? Is there any truth to the marketers' claims? Are there better sources than supplements for antioxidants? After reading this chapter you will be able to answer these questions, and your new knowledge will assist you in making dietary decisions to optimize your health.

Keep in mind as you read there is no scientific evidence that antioxidants *singularly* provide bodily benefits, but there is evidence that certain benefits are achieved by ingesting antioxidants as part of a balanced, healthy, nutrient-rich diet. This is to say antioxidants may go a long way toward preventing damage, but other nutrients are necessary to repair damage and sustain health. No one chemical acts alone!

The Atom

Before we can talk about the nutritional value of antioxidants we must review a few chemistry basics, starting with the atom. Cells are the basic building blocks of life, but **atoms**[1] are the basic building blocks of all matter, living and nonliving.

The structural elements of an atom are protons (positively charged), neutrons (no charge), and electrons (negatively charged). Protons and neutrons are contained in the dense nucleus of the atom; the nucleus thus has a positive charge. Because opposites attract, electrons are attracted to this nucleus and move around it in the electron cloud.

Electrons contain energy, and this energy is stored within the charge and movement of electrons and the bonds atoms make with one another. However, this energy is not always stable, depending on the number of electrons within an atom.

Atoms are more stable when their electrons orbit in pairs. An atom with an odd number of electrons must have an unpaired electron. In most cases, these unpaired

1. The basic building blocks of all matter, living and nonliving.

electrons are used to create chemical bonds. A chemical bond is the attractive force between atoms and contains potential energy. By bonding, electrons find pairs and chemicals become part of a molecule.

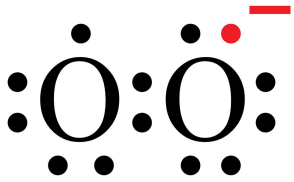
Bond formation and bond breaking are chemical reactions that involve the movement of electrons between atoms. These chemical reactions occur continuously in the body and many of them will be discussed in more detail in Chapter 10 "Nutrients Important for Metabolism and Blood Function".

In Chapter 3 "Nutrition and the Human Body" we reviewed how glucose breaks down into water and carbon dioxide as part of cellular respiration. The energy released by breaking those bonds is used to form molecules of adenosine triphosphate (ATP). Recall how during this process electrons are extracted from glucose in a stepwise manner and transferred to other molecules. Occasionally electrons "escape" and, instead of completing the cellular respiration cycle, are transferred to an oxygen molecule. Oxygen (a molecule with two atoms) with one unpaired electron is known as superoxide (Figure 8.1).

Atoms and molecules such as superoxide that have unpaired electrons are called **free radicals**[2]; those containing oxygen are more specifically referred to as **reactive oxygen species**[3]. The unpaired electron in free radicals destabilizes them, making them highly reactive. Other reactive oxygen species include hydrogen peroxide and the hydroxyl radical.

The reactivity of free radicals is what poses a threat to macromolecules such as DNA, RNA, proteins, and fatty acids. Free radicals can cause chain reactions that ultimately damage cells. For example, a superoxide molecule may react with a fatty acid and steal one of its electrons. The fatty acid then becomes a free radical that can react with another fatty acid nearby. As this chain reaction continues, the permeability and fluidity of cell membranes changes, proteins in cell membranes experience decreased activity, and receptor proteins undergo changes in structure that either alter or stop their function. If receptor proteins designed to react to insulin levels undergo a structural change it can negatively effect glucose uptake.

Figure 8.1



Superoxide: A molecule with one unpaired electron, which makes it a free radical.

Source: Wikipedia. "Superoxide." Last modified November 2, 2012.

Free radical reactions can continue unchecked unless stopped by a defense mechanism.

2. Highly reactive atoms with unpaired electrons.

3. Molecules containing oxygen that have unpaired electrons and are highly reactive.

The Body's Defense

http://en.wikipedia.org/wiki/File:Superoxide.svg.

Free radical development is unavoidable, but human bodies have adapted by setting up and maintaining defense mechanisms that reduce their impact. The body's two major defense systems are free radical detoxifying enzymes and antioxidant chemicals.

Free radical detoxifying enzyme systems are responsible for protecting the insides of cells from free radical damage. An **antioxidant**[4] is any molecule that can block free radicals from stealing electrons; antioxidants act both inside and outside of cells.

Free Radical Detoxifying Enzymes

The three major enzyme systems and the chemical reactions they catalyze are:

1. **Superoxide Dismutases (SOD).** These enzymes have either a manganese, copper, or zinc cofactor, which is essential for their free radical detoxifying activity. During SOD-mediated enzymatic catalysis, two superoxides are converted into hydrogen peroxide and oxygen. Hydrogen peroxide (H_2O_2) is still considered a reactive oxygen species, but it is markedly less reactive than a superoxide. SOD enzymes are one of the fastest enzymes known, and they are also inducible, meaning that the higher their exposure to superoxides the greater their number and detoxifying activity.
2. **Catalase.** This enzyme contains iron as a cofactor and converts hydrogen peroxide to water and oxygen, thereby finishing the detoxification reaction started by SOD. In cells, catalase enzymes are found in high numbers and continuously patrol for hydrogen peroxide molecules. Catalase is highly efficient and is capable of destroying millions of hydrogen peroxide molecules per second.
3. **Glutathione Peroxidases.** The majority of enzymes within this family are dependent on the micronutrient selenium. Similar to catalase, these enzymes convert hydrogen peroxide to water and oxygen.

Antioxidant Chemicals

Antioxidants are broadly classified as either hydrophilic (water soluble) or hydrophobic (lipid soluble) chemicals, and this classification determines where they act in the body. Hydrophilic antioxidants act in the cytosol of cells or in

4. Any molecule that can block free radicals from stealing electrons.

extracellular fluids such as blood; hydrophobic antioxidants are largely responsible for protecting cell membranes from free radical damage.

The body can synthesize some antioxidants, but others must be obtained from the diet.

Antioxidant Chemicals the Body Synthesizes

There are two antioxidant chemicals that the body synthesizes. They are:

1. **Glutathione.** This molecule is composed of three amino acids and is found in high concentrations in cells. The cysteine amino acid of glutathione contains a sulfur group that can donate an electron to a free radical, thereby stabilizing it. After glutathione has lost its electron, it is regenerated enzymatically so that it can perform its antioxidant function once again.
2. **Uric Acid.** This molecule is a metabolic intermediate in the breakdown of nucleotides such as adenine, which is found in DNA and RNA, among other macromolecules. It circulates at high concentrations in the blood and disables circulating free radicals. However, uric acid is a good example of the adage "it's the dose that makes the poison" because high concentrations in the blood can cause gout, a painful joint disorder.

Antioxidant Chemicals Obtained from the Diet

There are many different antioxidants in food, including selenium, which is one of the major antioxidants. However, the antioxidants you may be the most familiar with are vitamins. The "big three" vitamin antioxidants are vitamins E, A, and C, although it may be that they are called the "big three" only because they are the most studied.

Table 8.1 Some Antioxidants Obtained from Diet and Their Related Functions

Antioxidant	Functions Attributed to Antioxidant Capacity
Vitamin A	Protects cellular membranes, prevents glutathione depletion, maintains free radical detoxifying enzyme systems, reduces inflammation
Vitamin E	Protects cellular membranes, prevents glutathione depletion
Vitamin C	Protects DNA, RNA, proteins, and lipids, aids in regenerating vitamin E
Carotenoids	Free radical scavengers

Antioxidant	Functions Attributed to Antioxidant Capacity
Lipoic acid	Free radical scavenger, aids in regeneration of vitamins C and E
Phenolic acids	Free radical scavengers, protect cellular membranes
Selenium	Cofactor of free radical detoxifying enzymes, maintains glutathione levels, aids in regeneration of vitamins C and E

The Body's Offense

While our bodies have acquired multiple defenses against free radicals, we also use free radicals to support its functions. For example, the immune system uses the cell-damaging properties of free radicals to kill pathogens. First, immune cells engulf an invader (such as a bacterium), then they expose it to free radicals such as hydrogen peroxide, which destroys its membrane. The invader is thus neutralized.

Scientific studies also suggest hydrogen peroxide acts as a signaling molecule that calls immune cells to injury sites, meaning free radicals may aid with tissue repair when you get cut.

Free radicals are necessary for many other bodily functions as well. The thyroid gland synthesizes its own hydrogen peroxide, which is required for the production of thyroid hormone. Reactive oxygen species and reactive nitrogen species, which are free radicals containing nitrogen, have been found to interact with proteins in cells to produce signaling molecules. The free radical nitric oxide has been found to help dilate blood vessels and act as a chemical messenger in the brain.

By acting as signaling molecules, free radicals are involved in the control of their own synthesis, stress responses, regulation of cell growth and death, and metabolism.

Sources of Free Radicals in the Environment

Video 8.1

Free Radical Formation

(click to see video)

The body creates free radicals through the normal processes of metabolism. When the amount of free radicals exceeds the body's ability to eliminate or neutralize them, an oxidative imbalance results.

Substances and energy sources from the environment can add to or accelerate the production of free radicals within the body. Exposure to excessive sunlight, ozone, smoke, heavy metals, ionizing radiation, asbestos, and other toxic chemicals increase the amount of free radicals in the body. They do so by being free radicals themselves or by adding energy that provokes electrons to move between atoms. Excessive exposure to environmental sources of free radicals can contribute to disease by overwhelming the free radical detoxifying systems and those processes involved in repairing oxidative damage.

Oxidative Stress

Oxidative stress[5] refers to an imbalance in any cell, tissue, or organ between the amount of free radicals and the capablilities of the detoxifying and repair systems. Sustained oxidative damage results only under conditions of oxidative stress—when the detoxifying and repair systems are insufficient. Free radical-induced damage, when left unrepaired, destroys lipids, proteins, RNA, and DNA, and can contribute to disease. Oxidative stress has been implicated as a contributing factor to cancer, atherosclerosis (hardening of arteries), arthritis, diabetes, kidney disease, Alzheimer's disease, Parkinson's disease, schizophrenia, bipolar disorder, emphysema, and cataracts.

Aging is a process that is genetically determined but modulated by factors in the environment. In the process of aging, tissue function declines. The idea that oxidative stress is the primary contributor to age-related tissue decline has been around for decades, and it is true that tissues accumulate free radical-induced damage as we age. Recent scientific evidence slightly modifies this theory by suggesting oxidative stress is not the initial trigger for age-related decline of tissues; it is suggested that the true culprit is progressive dysfunction of metabolic processes, which leads to increases in free radical production, thus influencing the stress response of tissues as they age.

Video 8.2

Free Radicals or Oxidative Stress Will Age Our Bodies' Cells

(click to see video)

Oxidative stress occurs when there is an imbalance between free radical production and their detoxification. Sustained oxidative tissue damage that can contribute to disease occurs only when free radical detoxification systems and repair systems are overwhelmed.

5. An imbalance in any cell, tissue, or organ between the amount of free radicals and the capablilities of its detoxifying and repair systems.

KEY TAKEAWAYS

- Free radicals, unstable molecules with unpaired electrons, are an unavoidable byproduct of cellular metabolism.
- Free radicals can steal electrons from lipids, proteins, RNA, and DNA, causing them damage.
- The body has defenses against free radicals—free radical detoxifying enzymes and antioxidant chemicals.
- The body can synthesize some antioxidant molecules, but many are obtained from the diet.
- The body sometimes uses free radicals for beneficial functions such as killing pathogens and regulating cell growth and death.
- Oxidative stress is an imbalance between free radical production and detoxification and repair systems. It also plays an integral role in the development of many chronic diseases and in age-related decline of tissues.
- Excessive sunlight, ozone, smoke, heavy metals, radiation, asbestos, and other toxic chemicals increase the amount of free radicals in the body and can accelerate the progression of diseases in which oxidative stress is a contributing cause.

DISCUSSION STARTER

1. What are some ways you can prevent exposure to environmental factors that increase free radical production in your body?

8.2 Antioxidant Micronutrients

LEARNING OBJECTIVES

1. List the antioxidant nutrients.
2. Give examples of the best food sources of antioxidant nutrients.
3. Name some phytochemicals and their health benefits as backed by scientific evidence.

The market is flooded with advertisements for "super antioxidant" supplements teeming with molecules that block free radical production, stimulate the immune system, prevent cancer, and reduce the signs of aging. Based on the antioxidant-supplement industry's success, the general public appears to believe these health claims. However, these claims are not backed by scientific evidence; rather, there is some evidence suggesting supplements can actually cause harm.

While scientists have found evidence supporting the consumption of antioxidant-rich foods as a method of reducing the risk of chronic disease, there is no "miracle cure;" no pill or supplement alone can provide the same benefits as a healthy diet. Remember, it is the combination of antioxidants and other nutrients in healthy foods that is beneficial.

In this section, we will review how particular antioxidants function in the body, learn how they work together to protect the body against free radicals, and explore the best nutrient-rich dietary sources of antioxidants.

Antioxidant Vitamins

One dietary source of antioxidants is vitamins. In our discussion of antioxidant vitamins, we will focus on vitamins E, C, and A.

Vitamin E Functions and Health Benefits

Vitamin E is actually eight chemically similar substances, of which alpha-tocopherol appears to be the most potent antioxidant. Alpha-tocopherol and vitamin E's other constituents are fat-soluble and primarily responsible for protecting cell membranes against lipid destruction caused by free radicals.

After alpha-tocopherol interacts with a free radical it is no longer capable of acting as an antioxidant unless it is enzymatically regenerated. Vitamin C helps to regenerate some of the alpha-tocopherol, but the remainder is eliminated from the body. Therefore, to maintain vitamin E levels, you ingest it as part of your diet.

In addition to its antioxidant functions, vitamin E, mainly as alpha-tocopherol, can change the functions of proteins in cells, plays a role in the operations of the immune system, enhances the dilation of blood vessels, and inhibits blood clot formation. Despite vitamin E's numerous beneficial functions when taken in recommended amounts, large studies do not support the idea that taking higher doses of this vitamin will increase its power to prevent or reduce disease risk.Goodman, M., Bostlick RM, Kucuk O, Jones DP. 2011. Clinical trials of antioxidants as cancer prevention agents: past, present, and future. Free Radic Biol Med. 51(5): 1068–84.' McGinley C, Shafat A. Donnelly AE. 2009. Does antioxidant vitamin supplementation protect against muscle damage. Sports Med. 39(12): 1011–32.

Cardiovascular Disease

Recall from Chapter 5 "Lipids" that low-density lipoproteins (LDLs) transport cholesterol and other lipids from the liver to the rest of the body. LDLs are often referred to as "bad cholesterol," as an elevation in their levels in the blood is a risk factor for cardiovascular disease. Oxidation of the lipids and proteins in LDLs causes them to stick to the walls of arteries and this contributes to the development of fatty streaks and, eventually, plaque, which hardens the arteries. Hardening of the arteries, called **atherosclerosis**[6] can lead to a heart attack.

Vitamin E reduces the oxidation of LDLs, and it was therefore hypothesized that vitamin E supplements would protect against atherosclerosis. However, large clinical trials have not consistently found evidence to support this hypothesis. In fact, in the "Women's Angiographic Vitamin and Estrogen Study," postmenopausal women who took 400 international units (264 milligrams) of vitamin E and 500 milligrams of vitamin C twice per day had higher death rates from all causes.Waters, D.D. et al. "Effects of Hormone Replacement Therapy and Antioxidant Vitamin Supplements on Coronary Atherosclerosis in Postmenopausal Women: A Randomized Controlled Trial." *JAMA* 288, no. 19 (2002): 2432–40. doi: 10.1001/jama.288.19.2432

Other studies have not confirmed the association between increased vitamin E intake from supplements and increased mortality. There is more consistent evidence from observational studies that a higher intake of vitamin E from foods is linked to a decreased risk of dying from a heart attack.

6. A progressive hardening of the arteries that can lead to a heart attack.

Cancer

The large clinical trials that evaluated whether there was a link between vitamin E and cardiovascular disease risk also looked at cancer risk. These trials, called the HOPE-TOO Trial and Women's Health Study, did not find that vitamin E at doses of 400 international units (264 milligrams) per day or 600 international units (396 milligrams) every other day reduced the risk of developing any form of cancer.HOPE and HOPE-TOO Trial Investigators. "Effects of Long-Term Vitamin E Supplementation on Cardiovascular Events and Cancer." *JAMA* 293 (2005):1338–47. http://jama.ama-assn.org/content/293/11/1338.long.' Lee, I-M., et al. "Vitamin E in the Primary Prevention of Cardiovascular Disease and Cancer: The Women's Health Study." *JAMA* 294 (2005): 56–65. http://jama.ama-assn.org/content/294/1/56.long.

Eye Conditions

Oxidative stress plays a role in age-related loss of vision, called macular degeneration. **Age-related macular degeneration (AMD)**[7] primarily occurs in people over age fifty and is the progressive loss of central vision resulting from damage to the center of the retina, referred to as the macula. There are two forms of AMD, dry and wet, with wet being the more severe form.

In the dry form, deposits form in the macula; the deposits may or may not directly impair vision, at least in the early stages of the disease. In the wet form, abnormal blood vessel growth in the macula causes vision loss. Clinical trials evaluating the effects of vitamin E supplements on AMD and cataracts (clouding of the lens of an eye) did not consistently observe a decreased risk for either. However, scientists do believe vitamin E in combination with other antioxidants such as zinc and copper may slow the progression of macular degeneration in people with early-stage disease.

Dementia

The brain's high glucose consumption makes it more vulnerable than other organs to oxidative stress. Oxidative stress has been implicated as a major contributing factor to dementia and Alzheimer's disease. Some studies suggest vitamin E supplements delay the progression of Alzheimer's disease and cognitive decline, but again, not all of the studies confirm the relationship. A recent study with over five thousand participants published in the July 2010 issue of the *Archives of Neurology* demonstrated that people with the highest intakes of dietary vitamin E were 25 percent less likely to develop dementia than those with the lowest intakes of vitamin E.Devore, E. E. et al. "Dietary Antioxidants and Long-Term Risk of Dementia." *Arch Neurol* 67, no.7 (2010): 819–25. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2923546/?tool=pubmed. More studies are needed to better assess the

7. The progressive loss of central vision resulting from damage to the center of the retina, referred to as the macula.

dose and dietary requirements of vitamin E and, for that matter, whether other antioxidants lower the risk of dementia, a disease that not only devestates the mind, but also puts a substantial burden on loved ones, caretakers, and society in general.

Dietary Reference Intakes for Vitamin E

The Recommended Dietary Allowances (RDAs) and Tolerable Upper Intake Levels (ULs) for different age groups for vitamin E are given in Table 8.2 "Dietary Reference Intakes for Vitamin E". The RDAs are based on scientific evidence that these levels of vitamin E in the diet prevent conditions associated with vitamin E deficiency, which are rare (signs and symptoms of such conditions are not always evident) but are primarily the result of nerve degeneration. People with malabsorption disorders, such as Crohn's disease or cystic fibrosis, and babies born prematurely, are at higher risk for vitamin E deficiency.

Fat in the diet is required for vitamin E absorption as it is packaged into lipid-rich chylomicrons in intestinal cells and transported to the liver. The liver stores some of the vitamin E or packages it into lipoproteins, which deliver it to cells.

Table 8.2 Dietary Reference Intakes for Vitamin E

Age Group	RDA Males and Females mg/day	UL
Infants (0–6 months)	4*	–
Infants (7–12 months)	5*	–
Children (1–3 years)	6	200
Children (4–8 years)	7	300
Children (9–13 years)	11	600
Adolescents (14–18 years)	15	800
Adults (> 19 years)	15	1,000
***denotes Adequate Intake**		

Source: National Institutes of Health, Office of Dietary Supplements. "Dietary Supplement Fact Sheet: Vitamin E." Last modified October 11, 2011. http://ods.od.nih.gov/factsheets/VitaminE-QuickFacts/.

Vitamin E supplements often contain more than 400 international units, which is almost twenty times the RDA. The UL for vitamin E is set at 1,500 international units for adults. There is some evidence that taking vitamin E supplements at high doses has negative effects on health. As mentioned, vitamin E inhibits blood clotting and a few clinical trials have found that people taking vitamin E supplements have an increased risk of stroke. In contrast to vitamin E from supplements, there is no evidence that consuming foods containing vitamin E compromises health.

Dietary Sources of Vitamin E

Vitamin E is found in many foods, especially those higher in fat, such as nuts and oils. Some spices, such as paprika and red chili pepper, and herbs, such as oregano, basil, cumin, and thyme, also contain vitamin E. (Keep in mind spices and herbs are commonly used in small amounts in cooking and therefore are a lesser source of dietary vitamin E.) See Table 8.3 "Vitamin E Content of Various Foods" for a list of foods and their vitamin E contents.

Add some nuts to your salad and make your own dressing to get a healthy dietary dose of vitamin E.

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Tools for Change

To increase your dietary intake of vitamin E from plant-based foods try a spinach salad with tomatoes and sunflower seeds, and add a dressing made with sunflower oil, oregano, and basil.

Table 8.3 Vitamin E Content of Various Foods

Food	Vitamin E (mg)	Percent Daily Value
Wheat-germ oil (1 Tbsp.)	20.3	100
Sunflower seeds (1 oz.)	7.4	37
Almonds (1 oz.)	6.8	34
Sunflower oil (1 Tbsp.)	5.6	28

Food	Vitamin E (mg)	Percent Daily Value
Safflower oil (1 Tbsp.)	4.6	23
Hazelnuts (1 oz.)	4.3	22
Peanut butter (2 Tbsp.)	2.9	15
Peanuts (1 oz.)	2.2	11
Corn oil (1 Tbsp.)	1.9	10
Kiwi (1 medium)	1.1	6
Tomato (1 medium)	0.7	4
Spinach (1 c. raw)	0.6	3

Source: National Institutes of Health, Office of Dietary Supplements. "Dietary Supplement Fact Sheet: Vitamin E." Last reviewed October 11, 2011. http://ods.od.nih.gov/factsheets/VitaminE-HealthProfessional/.

Vitamin C Functions and Health Benefits

Vitamin C, also commonly called ascorbic acid, is a water-soluble micronutrient essential in the diet for humans, although most other mammals can readily synthesize it. Vitamin C's ability to easily donate electrons makes it a highly effective antioxidant. It is effective in scavenging reactive oxygen species, reactive nitrogen species, and many other free radicals. It protects lipids both by disabling free radicals and by aiding in the regeneration of vitamin E.

In addition to its role as an antioxidant, vitamin C is a required part of several enzymes involved in the synthesis of collagen, signaling molecules in the brain, some hormones, and amino acids. Vitamin C levels in the body are affected by the amount in the diet, which influences how much is absorbed and how much the kidney allows to be excreted, such that the higher the intake, the more vitamin C is excreted. Vitamin C is not stored in any significant amount in the body, but once it has reduced a free radical, it is very effectively regenerated and therefore it can exist in the body as a functioning antioxidant for many weeks.

Cardiovascular Disease

Vitamin C's ability to prevent disease has been debated for many years. Overall, higher dietary intakes of vitamin C (via food intake, not supplements), are linked to decreased disease risk. A review of multiple studies published in the April 2009 issue of the *Archives of Internal Medicine* concludes there is moderate scientific

evidence supporting the idea that higher dietary vitamin C intakes are correlated with reduced cardiovascular disease risk, but there is insufficient evidence to conclude that taking vitamin C supplements influences cardiovascular disease risk.Mente, A., et al. "A Systematic Review of the Evidence Supporting a Causal Link between Dietary Factors and Coronary Heart Disease." *Arch Intern Med* 169, no.7 (2009): 659–69. http://archinte.ama-assn.org/cgi/content/full/169/7/659.

Vitamin C levels in the body have been shown to correlate well with fruit and vegetable intake, and higher plasma vitamin C levels are linked to reduced risk of some chronic diseases. In a study involving over twenty thousand participants, people with the highest levels of circulating vitamin C had a 42 percent decreased risk for having a stroke.Myint, P.K. et al. "Plasma Vitamin C Concentrations Predict Risk of Incident Stroke Over 10 Y[ears] in 20,649 Participants of the European Prospective Investigation into Cancer, Norfolk Prospective Population Study." *Am J Clin Nutr* 87, no.1 (2008): 64–69. http://www.ajcn.org/content/87/1/64.long.

Cancer

There is some evidence that a higher vitamin C intake is linked to a reduced risk of cancers of the mouth, throat, esophagus, stomach, colon, and lung, but not all studies confirm this is true. As with the studies on cardiovascular disease, the reduced risk of cancer is the result of eating foods rich in vitamin C, such as fruits and vegetables, not from taking vitamin C supplements. In these studies, the specific protective effects of vitamin C cannot be separated from the many other beneficial chemicals in fruits and vegetables.

Immunity

Vitamin C does have several roles in the immune system, and many people increase vitamin C intake either from diet or supplements when they have a cold. Many others take vitamin C supplements routinely to prevent colds. Contrary to this popular practice, however, there is no good evidence that vitamin C prevents a cold. A review of more than fifty years of studies published in 2004 in the *Cochrane Database of Systematic Reviews* concludes that taking vitamin C routinely does not prevent colds in most people, but it does slightly reduce cold severity and duration. Moreover, taking megadoses (up to 4 grams per day) at the onset of a cold provides no benefits.Douglas, R.M. et al. "Vitamin C for Preventing and Treating the Common Cold." *Cochrane Database of Systematic Reviews* 4 (2004): CD000980. http://www.ncbi.nlm.nih.gov/pubmed/15495002?dopt=Abstract.

Gout is a disease caused by elevated circulating levels of uric acid and is characterized by recurrent attacks of tender, hot, and painful joints. There is some evidence that a higher intake of vitamin C reduces the risk of gout.

Dietary Reference Intakes for Vitamin C

The classic condition associated with vitamin C deficiency is scurvy. The signs and symptoms of scurvy include skin disorders, bleeding gums, painful joints, weakness, depression, and increased susceptibility to infections. Scurvy is prevented by having an Adequate Intake of fruits and vegetables rich in vitamin C.

The RDAs and ULs for different age groups for vitamin C are listed in Table 8.4 "Dietary Reference Intakes for Vitamin C". They are considered adequate to prevent scurvy. Vitamin C's effectiveness as a free radical scavenger motivated the Institute of Medicine (IOM) to increase the RDA for smokers by 35 milligrams, as tobacco smoke is an environmental and behavioral contributor to free radicals in the body.

Table 8.4 Dietary Reference Intakes for Vitamin C

Age Group	RDA Males and Females mg/day	UL
Infants (0–6 months)	40*	–
Infants (7–12 months)	50*	–
Children (1–3 years)	15	400
Children (4–8 years)	25	650
Children (9–13 years)	45	1200
Adolescents (14–18 years)	75 (males), 65 (females)	1800
Adults (> 19 years)	90 (males), 75 (females)	2000
***denotes Adequate Intake**		

Source: National Institutes of Health, Office of Dietary Supplements. "Dietary Supplement Fact Sheet: Vitamin C." Last reviewed June 24, 2011. http://ods.od.nih.gov/factsheets/VitaminC-QuickFacts/.

High doses of vitamin C have been reported to cause numerous problems, but the only consistently shown side effects are gastrointestinal upset and diarrhea. To prevent these discomforts the IOM has set a UL for adults at 2,000 milligrams per day (greater than twenty times the RDA).

At very high doses in combination with iron, vitamin C has sometimes been found to increase oxidative stress, reaffirming that getting your antioxidants from foods is better than getting them from supplements, as that helps regulate your intake levels. There is some evidence that taking vitamin C supplements at high doses increases the likelihood of developing kidney stones, however, this effect is most often observed in people that already have multiple risk factors for kidney stones.

Dietary Sources of Vitamin C

Citrus fruits are great sources of vitamin C and so are many vegetables. In fact, British sailors in the past were often referred to as “limeys” as they carried sacks of limes onto ships to prevent scurvy. Vitamin C is not found in significant amounts in animal-based foods.

Because vitamin C is water soluble, it leaches away from foods considerably during cooking, freezing, thawing, and canning. Up to 50 percent of vitamin C can be boiled away. Therefore, to maximize vitamin C intake from foods, you should eat fruits and vegetables raw or lightly steamed. For the vitamin C content of various foods, see Table 8.5 "Vitamin C Content of Various Foods".

Table 8.5 Vitamin C Content of Various Foods

Food	Serving	Vitamin C (mg)
Orange juice	6 oz.	62–93
Grapefruit juice	6 oz.	62–70
Orange	1 medium	70
Grapefruit	½ medium	38
Strawberries	1 c.	85
Tomato	1 medium	16
Sweet red pepper	½ c. raw	95
Broccoli	½ c. cooked	51
Asparagus	1 c. cooked	20
Romaine lettuce	2 c.	27
Kale	1 c. boiled	53
Cauliflower	1 c. boiled	55
Potato	1 medium, baked	17

Source: National Institutes of Health, Office of Dietary Supplements. "Dietary Supplement Fact Sheet: Vitamin C." Last reviewed June 24, 2011. http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/.

Vitamin A Functions and Health Benefits

Vitamin A is a generic term for a group of similar compounds called retinoids. Retinol is the form of vitamin A found in animal-derived foods, and it is converted in the body to the biologically active forms of vitamin A: retinal and retinoic acid (thus retinol is sometimes referred to as "preformed vitamin A"). About 10 percent of plant-derived carotenoids, including beta-carotene, can be converted in the body to retinoids and are another source of functional vitamin A. The retinoids are aptly named as their most notable function is in the retina of the eye where they aid in vision, particularly in seeing under low-light conditions. This is why night blindness is the most definitive sign of vitamin A deficiency.

Like vitamin E, vitamin A is fat-soluble and is packaged into chylomicrons in small intestine mucosal cells, and then transported to the liver. The liver stores and exports vitamin A as needed; it is released into the blood bound to a retinol-binding protein, which transports it to cells.

Vitamin A has several important functions in the body, including maintaining vision and a healthy immune system. Many of vitamin A's functions in the body are similar to the functions of hormones (for example, vitamin A can interact with DNA, causing a change in protein function). Vitamin A assists in maintaining healthy skin and the linings and coverings of tissues; it also regulates growth and development. As an antioxidant, vitamin A protects cellular membranes, helps in maintaining glutathione levels, and influences the amount and activity of enzymes that detoxify free radicals.

Vision

Retinol that is circulating in the blood is taken up by cells in the retina, where it is converted to retinal and is used as part of the pigment rhodopsin, which is involved in the eye's ability to see under low light conditions. A deficiency in vitamin A thus results in less rhodopsin and a decrease in the detection of low-level light, a condition referred to as nightblindness.

Insufficient intake of dietary vitamin A over time can also cause complete vision loss. In fact, vitamin A deficiency is the number one cause of preventable blindness worldwide. Vitamin A not only supports the vision function of eyes but also maintains the coverings and linings of the eyes. Vitamin A deficiency can lead to

the dysfunction of the linings and coverings of the eye, causing dryness of the eyes, a condition called xerophthalmia. This condition can progress, causing ulceration of the cornea and eventually blindness.

Immunity

The common occurrence of advanced xerophthalmia in children who died from infectious diseases led scientists to hypothesize that supplementing vitamin A in the diet for children with xerophthalmia might reduce disease-related mortality. In Asia in the late 1980s, targeted populations of children were administered vitamin A supplements, and the death rates from measles and diarrhea declined by up to 50 percent. Vitamin A supplementation in these deficient populations did not reduce the number of children who contracted these diseases, but it did decrease the severity of the diseases so that they were no longer fatal. Soon after the results of these studies were communicated to the rest of the world, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) commenced worldwide campaigns against vitamin A deficiency. UNICEF estimates that the distribution of over half a billion vitamin A capsules prevents 350,000 childhood deaths annually.Sommer, A. "Vitamin A Deficiency and Clinical Disease: An Historical Overview." *J Nutr* 138 (2008):1835–39. http://jn.nutrition.org/content/138/10/1835.long.

In the twenty-first century, science has demonstrated that vitamin A greatly affects the immune system. What we are still lacking are clinical trials investigating the proper doses of vitamin A required to help ward off infectious disease and how large of an effect vitamin A supplementation has on populations that are not deficient in this vitamin. This brings up one of our common themes in this text—micronutrient deficiencies may contribute to the development, progression, and severity of a disease, but this does not mean that an increased intake of these micronutrients will solely prevent or cure disease. The effect, as usual, is cumulative and depends on the diet as a whole, among other things.

Growth and Development

Vitamin A acts similarly to some hormones in that it is able to change the amount of proteins in cells by interacting with DNA. This is the primary way that vitamin A affects growth and development. Vitamin A deficiency in children is linked to growth retardation; however, vitamin A deficiency is often accompanied by protein malnutrition and iron deficiency, thereby confounding the investigation of vitamin A's specific effects on growth and development.

In the fetal stages of life, vitamin A is important for limb, heart, eye, and ear development and in both deficiency and excess, vitamin A causes birth defects. Furthermore, both males and females require vitamin A in the diet to effectively reproduce.

Cancer

Vitamin A's role in regulating cell growth and death, especially in tissues that line and cover organs, suggests it may be effective in treating certain cancers of the lung, neck, and liver. It has been shown in some observational studies that vitamin A-deficient populations have a higher risk for some cancers. However, vitamin A supplements have actually been found to increase the risk of lung cancer in people who are at high risk for the disease (i.e., smokers, exsmokers, workers exposed to asbestos). The Beta-Carotene and Retinol Efficacy Trial (CARET) involving over eighteen thousand participants who were at high risk for lung cancer found that people who took supplements containing very high doses of vitamin A (25,000 international units) and beta-carotene had a 28 percent higher incidence of lung cancer midway through the study, which was consequently stopped.Goodman, G.E. et al. "The Beta-Carotene and Retinol Efficacy Trial: Incidence of Lung Cancer and Cardiovascular Disease Mortality During 6-year Follow-up after Stopping Beta-Carotene and Retinol Supplements." *J Natl Cancer Inst* 96, no. 23 (2004): 1743–50. http://jnci.oxfordjournals.org/content/96/23/1743.long.

Vitamin A supplementation is a relatively common practice in treating some types of cancer patients and is thought to improve the effectiveness of some anticancer drugs, but many oncologists (physicians who treat cancer patients) do not recommend this practice as vitamin A may actually inhibit the actions of some anticancer drugs.

Vitamin A Toxicity

Vitamin A toxicity, or hypervitaminosis A, is rare. Typically it requires you to ingest ten times the RDA of preformed vitamin A in the form of supplements (it would be hard to consume such high levels from a regular diet) for a substantial amount of time, although some people may be more susceptible to vitamin A toxicity at lower doses. The signs and symptoms of vitamin A toxicity include dry, itchy skin, loss of appetite, swelling of the brain, and joint pain. In severe cases, vitamin A toxicity may cause liver damage and coma.

Vitamin A is essential during pregnancy, but doses above 3,000 micrograms per day (10,000 international units) have been linked to an increased incidence of birth defects. Pregnant women should check the amount of vitamin A contained in any

prenatal or pregnancy multivitamin she is taking to assure the amount is below the UL.

Dietary Reference Intakes for Vitamin A

There is more than one source of vitamin A in the diet. There is preformed vitamin A, which is abundant in many animal-derived foods, and there are carotenoids, which are found in high concentrations in vibrantly colored fruits and vegetables and some oils.

Some carotenoids are converted to retinol in the body by intestinal cells and liver cells. However, only miniscule amounts of certain carotenoids are converted to retinol, meaning fruits and vegetables are not necessarily good sources of vitamin A. Beta-carotene dissolved in oil is more readily converted to retinol; one-half of a microgram of beta-carotene is converted to retinol. Overall, the carotenoids do not have the same biological potency of preformed vitamin A, but as you will soon find out, they have other attributes that influence health, most notably their antioxidant activity.

The RDA for vitamin A includes all sources of vitamin A. The amount of vitamin A obtained from carotenoids—the retinol activity equivalent (RAE)—can be calculated. For example, 12 micrograms of fruit- or vegetable-based beta-carotene will yield 1 microgram of retinol, as mentioned.

The RDA for vitamin A is considered sufficient to support growth and development, reproduction, vision, and immune system function while maintaining adequate stores (good for four months) in the liver.

Table 8.6 Dietary Reference Intakes for Vitamin A

Age Group	RDA Males and Females mcg/day	UL
Infants (0–6 months)	400*	600
Infants (7–12 months)	500*	600
Children (1–3 years)	300	600
Children (4–8 years)	400	900
Children (9–13 years)	600	1,700
Adolescents (14–18 years)	Males: 900	2,800
***denotes Adequate Intake**		

Age Group	RDA Males and Females mcg/day	UL
	Females: 700	
Adults (> 19 years)	Males: 900	3,000
	Females: 700	
***denotes Adequate Intake**		

Source: Source: National Institutes of Health, Office of Dietary Supplements. "Dietary Supplement Fact Sheet: Vitamin A." Last reviewed September 5, 2012. http://ods.od.nih.gov/factsheets/VitaminA-QuickFacts/.

Dietary Sources of Vitamin A

Preformed vitamin A is found only in foods from animals, with the liver being the richest source because that's where vitamin A is stored (see Table 8.7 "Vitamin A Content of Various Foods"). The dietary sources of carotenoids will be given in the following text.

Table 8.7 Vitamin A Content of Various Foods

Food	Serving	Vitamin A (IU)	Percent Daily Value
Beef liver	3 oz.	27,185	545
Chicken liver	3 oz.	12,325	245
Milk, skim	1 c.	500	10
Milk, whole	1 c.	249	5
Cheddar cheese	1 oz.	284	6

Source: Source: National Institutes of Health, Office of Dietary Supplements. "Dietary Supplement Fact Sheet: Vitamin A." Last reviewed July 25, 2012. http://ods.od.nih.gov/factsheets/VitaminA-HealthProfessional/.

Phytochemicals

Phytochemicals[8] are chemicals in plants that may provide some health benefit. Carotenoids are one type of phytochemical. Phytochemicals also include indoles, lignans, phytoestrogens, stanols, saponins, terpenes, flavonoids, carotenoids, anthocyanidins, phenolic acids, and many more. They are found not only in fruits and vegetables, but also in grains, seeds, nuts, and legumes.

8. Chemicals in plants that may provide some health benefit.

Many phytochemicals act as antioxidants, but they have several other functions, such as mimicking hormones, altering absorption of cholesterol, inhibiting inflammatory responses, and blocking the actions of certain enzymes.

Phytochemicals are present in small amounts in the food supply, and although thousands have been and are currently being scientifically studied, their health benefits remain largely unknown. Also largely unknown is their potential for toxicity, which could be substantial if taken in large amounts in the form of supplements. Moreover, phytochemicals often act in conjunction with each other and with micronutrients. Thus, supplementing with only a few may impair the functions of other phytochemicals or micronutrients. As with the antioxidant vitamins, it is the mixture and variety of phytochemicals in foods that are linked to health benefits.

Carotenoids Function and Health Benefits

Carotenoids are pigments synthesized by plants that give them their yellow, orange, and red color. Over six hundred carotenoids have been identified and, with just a few exceptions, all are found in the plant kingdom. There are two classes of carotenoids—the xanthophylls, which contain oxygen, and the carotenes, which do not.

In plants, carotenoids absorb light for use in photosynthesis and act as antioxidants. Beta-carotene, alpha-carotene, gamma-carotene, and beta-cryptoxanthin are converted to some extent to retinol in the body. The other carotenoids, such as lycopene, are not. Many biological actions of carotenoids are attributed to their antioxidant activity, but they likely act by other mechanisms, too.

Eye Conditions

Lutein, found in green leafy vegetables, and zeaxanthin, found in peppers, corn, and saffron, act as antioxidants in the retina of the eye and protect it from ultraviolet light damage. Diets high in these carotenoids are associated with a decreased risk of AMD, and there is good evidence that supplements containing these carotenoids also provide vision benefits. A review published in the August 2010 issue of *Current Medical Research and Opinion* concludes that supplementation with lutein and zeaxanthin reduces the incidence of AMD and cataracts.Barker II, F. M. “Dietary Supplementation: Effects on Visual Performance and Occurrence of AMD and Cataracts.” *Curr Med Res Opin* 26, no. 8 (2010): 2011–23. http://informahealthcare.com/doi/abs/10.1185/03007995.2010.494549.

The data that supports that beta-carotene supplementation may delay the progression of AMD is more convincing when beta-carotene is taken in combination with other micronutrients. The Age-Related Eye Disease Study found that a supplement containing 500 milligrams of vitamin C, 400 international units of vitamin E, 15 milligrams of beta-carotene, 80 milligrams of zinc oxide, and 2 milligrams of copper as cupric oxide reduced the risk of progressing to advanced stages of AMD by 25 percent.Age-Related Eye Disease Study Research Group. "A Randomized, Placebo-Controlled, Clinical Trial of High-Dose Supplementation with Vitamins C and E, Beta-Carotene, and Zinc for Age-Related Macular Degeneration and Vision Loss." *Arch Ophthalmol* 119, no. 10 (2001): 1417–36. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1462955/. This study did not find that the formulated supplement significantly prevented the onset of disease, only that it delayed its progression specifically in people with intermediate or advanced stage AMD. Studies are ongoing to determine if other antioxidant combinations actually protect against developing AMD at all.

Cardiovascular Disease

While some studies do associate a decreased risk for atherosclerosis with higher dietary intake of carotenoids, others do not. There is a large number of studies that show total carotenoid intake is associated with improvement in blood vessel function. A smaller number of studies show that intake of specific carotenoids, such as lycopene and alpha-carotene, are also associated with improved blood vessel function. The main problems associated with linking carotenoids to a decrease in cardiovascular disease risk, or any other disease for that matter, are that they are present in foods containing many other beneficial plant chemicals, and trials evaluating the effects of specific carotenoids in the form of supplements provide inconsistent and sometimes contradictory results.

Cancer

A higher intake of some carotenoids, but not others, is linked to decreased risks for some cancers. A review of two large studies (> 120,000 men and women) published in the October 2000 issue of *The American Journal of Clinical Nutrition* reports that there is no significant association between beta-carotene intake and lung cancer risk, but men and women with the highest intakes of total carotenoids had a more than 30 percent risk reduction for developing lung cancer.Michaud, D.S. et al. "Intake of Specific Carotenoids and Risk of Lung Cancer in 2 Prospective US Cohorts." *Am J Clin Nutr* 72, no. 4 (2000): 990–97. http://www.ajcn.org/content/72/4/990.long. Other large studies conducted in Europe have confirmed the inverse relationship of total dietary carotenoid intake with lung cancer risk. There is some evidence that diets rich in lycopene, which is present in high concentrations in tomatoes, is linked to decreased prostate cancer risk, but it is not known if it is

lycopene specifically or some other component in tomatoes that protects against prostate cancer.

Carotenoid Bioavailability and Dietary Sources

Carotenoids are not absorbed as well as vitamin A, but similar to vitamin A, they do require fat in the meal for absorption. In intestinal cells, carotenoids are packaged into the lipid-containing chylomicrons inside small intestine mucosal cells and then transported to the liver. In the liver, carotenoids are repackaged into lipoproteins, which transport them to cells.

In contrast to most micronutrients, carotenoid availability is actually increased by the cooking process because cooking, along with chopping and homogenizing, releases carotenoids from the plant matrix. Thus, eating a can of tomatoes provides more lycopene than eating a raw tomato. However, overcooking transforms some of the carotenoids into inactive products, and in general it is best to chop and lightly steam vegetables containing carotenoids to maximize their availability from foods. Cooking carotenoid-containing foods in oil also enhances the bioavailability of carotenoids.

In the United States, the most consumed carotenoids are alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, and zeaxanthin. See Table 8.8 "Alpha- and Beta-Carotene Content of Various Foods" and Note 8.18 "Interactive 8.1" for the carotenoid content of various foods.

Try a variety of foods containing thousands of phytochemicals.

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Table 8.8 Alpha- and Beta-Carotene Content of Various Foods

Food	Serving	Beta-carotene (mg)	Alpha-carotene (mg)
Pumpkin, canned	1c.	17.00	11.70

Food	Serving	Beta-carotene (mg)	Alpha-carotene (mg)
Carrot juice	1c.	22.00	10.20
Carrots, cooked	1c.	13.00	5.90
Carrots, raw	1 medium	5.10	2.10
Winter squash, baked	1c.	5.70	1.40
Collards, cooked	1c.	11.60	0.20
Tomato	1 medium	0.55	0.10
Tangerine	1 medium	0.13	0.09
Peas, cooked	1c.	1.20	0.09

Source: US Department of Agriculture, Agricultural Research Service. 2010. *USDA National Nutrient Database for Standard Reference,* Release 23. http://www.ars.usda.gov/ba/bhnrc/ndl.

Interactive 8.1

Visit the USDA website and find out more about the carotenoid content of various foods.

http://www.ars.usda.gov/Services/docs.htm?docid=20958

Three Other Phytochemicals and Their Potential Health Benefits

Three classes of phytochemicals (other than carotenoids) are flavonoids, organosulfur compounds, and lignans. Their potential health benefits are discussed below.

Flavonoids

Flavonoids are a large class of chemicals including anthocyanidins (found in red, blue, and purple berries), flavanols (found in teas, chocolate, berries, apples, yellow onions, kale, and broccoli), and isoflavones (found in soy products). Flavonoids are very effective free radical scavengers, and there is some evidence that higher intakes of flavonoid-rich foods and/or beverages reduce the risk of cardiovascular disease, but this has not been consistently observed. Although flavonoids have been

shown to reduce the incidence of some tumors in animals, similar studies in humans have been inconclusive.

Organosulfur Compounds

These compounds are predominantly found in garlic, but can also be found in onions and leeks. It's suspected that the higher intake of garlic is the aspect of the Mediterranean diet that contributes to a decreased risk of cardiovascular disease. Animal and laboratory studies suggest the organosulfur compounds in garlic reduce cholesterol, are anti-inflammatory, stimulate the synthesis of glutathione, and cause death of cancer cells. There is some evidence in humans that garlic reduces cholesterol, but more recent studies did not confirm that the effect was signficant or sustained. A higher intake of garlic likely inhibits blood clot formation in humans.

Observational studies suggest diets high in organosulfur compounds decrease the risk of gastric and colorectal cancer. For other cancers, the data is less consistent.

Lignans

Lignans are a group of chemical compounds obtained from many food sources, including grains, nuts, seeds, fruits, and vegetables, and especially flax seed. Some lignans are also called phytoestrogens as they can mimic or inhibit some of the actions of the hormone estrogen in the body.

The antiestrogenic effect of some lignans suggests they may be helpful in treating hormone-dependent cancers, such as breast and ovarian cancers. However, studies are few and conflicting on whether eating foods high in lignans reduces breast or ovarian cancer.

In regard to cardiovascular disease risk, diets rich in whole grains are protective, but it remains unclear whether it is the lignans in whole grains that are responsible for the reduced risk. Whole grains contain many other beneficial phytochemicals, micronutrients, and fiber.

Interactive 8.2

To discover more about phytochemicals, visit the website for the Micronutrient Information Center of the Linus Pauling Institute at Oregon State University.

http://lpi.oregonstate.edu/infocenter/phytochemicals.html

Other Dietary Sources of Beneficial Phytochemicals

Herbs and Spices

These are the aromatic parts of plants, such as the leaves, seeds, pods, and berries. They are an additional dietary source of phytochemicals, and many have exceptional antioxidant capacity.

Throughout the ages, people have used spices and herbs not only for adding flavor to foods, but also as medicines. Curcumin, the principal component of tumeric, has been used for over two thousand years in India to treat a variety of ailments. As of 2011, over seventy clinical trials are investigating the health benefits of curcumin, which may include reducing cancer risk and delaying the progression of Alzheimer's disease.

You learned in the beginning of this chapter that nutmeg comes from the dried seed kernel of *Myristica fragrans* and has been used as an antimicrobial, antifungal, and anti-inflammatory agent, and as a pain reliever. In high doses nutmeg acts similar to a psychoactive drug in that it causes euphoria, delusions, and hallucinations. According to a study conducted on over 3,100 foods, beverages, spices, herbs, and supplements, the spices and herbs were the dietary sources most rich in antioxidants (see Note 8.20 "Interactive 8.3").

Interactive 8.3

Read the article, "The Total Antioxidant Content of More than 3,100 Foods, Beverages, Spices, Herbs, and Supplements Used Worldwide," published in the January 2010 issue of the *Nutrition Journal*. It is a useful source to find dietary sources of antioxidants.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2841576/?tool=pubmed

Tools for Change

Add some spice, flavor, and decoration to your food along with beneficial antioxidants and phytochemicals. Embracing cuisine rich in spices and herbs further enhances the health benefits of eating a diet rich in fruit and vegetables. Think spices are too hot for your palate? As little as half a teaspoon of cinnamon has been shown in scientific studies to provide health benefits, such as improving glucose homeostasis in people with Type 2 diabetes. Over fifteen clinical trials are now evaluating the effectiveness of cinnamon as a adjunct treatment for Type 2 diabetes and/or cardiovascular disease.

Tea

Tea is an aromatic beverage made from the dried parts of plants steeped in hot water. Its health benefits have been known for years, and as with coffee the benefits are not just physiological, but also mental and social. In folklore, teas are considered curatives of stomachache, diarrhea, and even the plague. In *The Book of Tea*, Okakura Kakuzo asserts that consuming a cup of tea provides "the adoration of the beautiful among the sordid facts of everyday existence."Okakura Kakuzo. *The Book of Tea*. (Berlin, Germany: Dover Publications, 1964).

Teas can contain more than seven hundred different phytochemicals. Some of them may be beneficial and others may not be, as some reduce the dietary

absorption of some micronutrients. The health claims of drinking tea—black, green, or red—number at least in the hundreds but remain mostly scientifically unsupported. There are a great number of studies showing that drinking tea is at least linked to a decreased risk of heart disease, cancer, and diabetes, but the exact phyotchemicals illiciting these health benefits are under intense scrutiny. Moreover, people who consume more tea are likely to drink fewer soft drinks and therefore, based on a "replacement theory," have a reduced likelihood of having a chronic disease.

Drinking tea can enhance physiological, mental, and social aspects of health.

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Antioxidant Minerals

In addition to the antioxidant vitamins and phytochemicals, several minerals have antioxidant function, including selenium, manganese, iron, copper, and zinc.

Selenium Functions and Health Benefits

Around twenty-five known proteins require selenium to function. Some are enzymes involved in detoxifying free radicals and include glutathione peroxidases and thioredoxin reductase. As an integral functioning part of these enzymes, selenium aids in the regeneration of glutathione and oxidized vitamin C. Selenium as part of glutathione peroxidase also protects lipids from free radicals, and, in doing so, spares vitamin E. This is just one example of how antioxidants work together to protect the body against free radical-induced damage.

Other functions of selenium-containing proteins include protecting endothelial cells that line tissues, converting the inactive thyroid hormone to the active form in cells, and mediating inflammatory and immune system responses.

Observational studies have demonstrated that selenium deficiency is linked to an increased risk of cancer. A review of forty-nine observational studies published in the May 2011 issue of the *Cochrane Database of Systematic Reviews* concludes that higher selenium exposure reduces overall cancer incidence by about 34 percent in men and 10 percent in women, but notes these studies had several limitations, including data quality, bias, and large differences among different studies.Dennert, G. et al. "Selenium for Preventing Cancer." *Cochrane Database of Systematic Reviews* 5 (2011): CD005195. http://www.ncbi.nlm.nih.gov/pubmed/21563143. Additionally, this review states that there is no convincing evidence from six clinical trials that selenium supplements reduce cancer risk.

Because of its role as a lipid protector, selenium has been suspected to prevent cardiovascular disease. In some observational studies, low levels of selenium are associated with a decreased risk of cardiovascular disease. However, other studies have not always confirmed this association and clinical trials are lacking.

Dietary Reference Intakes for Selenium

The IOM has set the RDAs for selenium based on the amount required to maximize the activity of glutathione peroxidases found in blood plasma. The RDAs for different age groups are listed in Table 8.9 "Dietary Reference Intakes for Selenium".

Table 8.9 Dietary Reference Intakes for Selenium

Age Group	RDA Males and Females mcg/day	UL
Infants (0–6 months)	15*	45
Infants (7–12 months)	20*	65
Children (1–3 years)	20	90
Children (4–8 years)	30	150
Children (9–13 years)	40	280
Adolescents (14–18 years)	55	400
Adults (> 19 years)	55	400
***denotes Adequate Intake**		

Selenium at doses several thousand times the RDA can cause acute toxicity, and when ingested in gram quantities can be fatal. Chronic exposure to foods grown in soils containing high levels of selenium (significantly above the UL) can cause brittle hair and nails, gastrointestinal discomfort, skin rashes, halitosis, fatigue, and irritability. The IOM has set the UL for selenium for adults at 400 micrograms per day.

Dietary Sources of Selenium

Organ meats, muscle meats, and seafood have the highest selenium content. Plants do not require selenium, so the selenium content in fruits and vegetables is usually low. Animals fed grains from selenium-rich soils do contain some selenium. Grains and some nuts contain selenium when grown in selenium-containing soils. See

Table 8.10 "Selenium Contents of Various Foods" for the selenium content of various foods.

Table 8.10 Selenium Contents of Various Foods

Food	Serving	mcg
Brazil nuts	1 oz.	544.0
Shrimp	3 oz.	34.0
Crab meat	3 oz.	41.0
Ricotta cheese	1 c.	41.0
Salmon	3 oz.	40.0
Pork	3 oz.	35.0
Ground beef	3 oz.	18.0
Round steak	3 oz.	28.5
Beef liver	3 oz.	28.0
Chicken	3 oz.	13.0
Whole-wheat bread	2 slices	23.0
Couscous	1 c.	43.0
Barley, cooked	1 c.	13.5
Milk, low-fat	1 c.	8.0
Walnuts, black	1 oz.	5.0

Source: US Department of Agriculture, Agricultural Research Service. 2010. *USDA National Nutrient Database for Standard Reference*, Release 23. http://www.ars.usda.gov/ba/bhnrc/ndl.

Manganese, Iron, Copper, and Zinc: Functions and Health Benefits

As with selenium, manganese, iron, copper, and zinc are essential cofactors for enzymes involved in detoxifying free radicals. In the proper doses they allow for optimal detoxification of free radicals. In excess and when not bound to proteins, manganese, iron, and copper actually accelerate the production of free radicals. This is an attribute of all antioxidants in general, although the effect is greater for certain antioxidants.

Antioxidants can become pro-oxidants when the conditions are altered. Recall from Section 8.1 "Generation of Free Radicals in the Body" of this chapter that oxidative stress results from an imbalance in free radicals with their detoxifying and repair systems. Another factor that can cause oxidative stress is a high level of antioxidants, as some will revert to acting as pro-oxidants.

KEY TAKEAWAYS

- Health claims of antioxidant supplements are not backed by scientific evidence and there is some evidence suggesting they cause harm.
- Consuming antioxidant-rich foods is scientifically supported to reduce the risk of chronic diseases.
- Antioxidants have specific functions, and they can act in concert with each other to protect against free radicals.
- Some antioxidants are involved in the regeneration of other antioxidants.
- Many phytochemicals act as antioxidants, but they perform several other functions as well.
- Dietary antioxidants and phytochemicals in the proper doses are beneficial to health but can cause harm in excess.

DISCUSSION STARTERS

1. In regard to doses, discuss why it is better to obtain antioxidants from the diet and not from supplements. When might supplements be advantageous?
2. With more scientific evidence in hand, debate whether or not the supplement industry requires more regulation.

8.3 The Whole Nutrient Package versus Disease

LEARNING OBJECTIVES

1. List some of the health-related conditions that might be mitigated by eating antioxidant- and phytochemical-rich foods regularly.
2. Explain the importance of eating a variety of fruits, vegetables, nuts, legumes, teas, and grains to obtain antioxidants and phytochemicals.

A healthy diet incorporating seven or more servings of fruits and vegetables has been shown in many scientific studies to reduce cardiovascular disease and overall deaths attributable to cancer. The WHO states that insufficient fruit and vegetable intake is linked to approximately 14 percent of gastrointestinal cancer deaths, about 11 percent of heart attack deaths, and 9 percent of stroke deaths globally.World Health Organization. "Global Strategies on Diet, Physical Activity, and Health." Accessed September 30, 2011. http://www.who.int/dietphysicalactivity/fruit/en/index.html. The WHO estimates that, overall, 2.7 million deaths could be avoided annually by increasing fruit and vegetable intake. These preventable deaths place an economic, social, and mental burden on society. This is why, in 2003, the WHO and the Food and Agricultural Organization of the United Nations launched a campaign to promote fruit and vegetable intake worldwide.

Forget the antioxidant-pill hype and get all of the health benefits from antioxidants and phytochemicals by eating a variety of fruits and vegetables.

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In the last section we reviewed the health benefits of particular antioxidants and phytochemicals obtained from fruits and vegetables and discovered that naturally incorporating them in the diet rather than taking supplements is best. Here we will consider the scientific evidence that diets rich in antioxidants actually lower chronic disease risk.

Antioxidant Variety in Food Provides Health Benefits

Not only has the several-billion-dollar supplement industry inundated us with FDA-unapproved health claims, but science is continously advancing and providing us

with a multitude of promising health benefits from particular fruits, vegetables, teas, herbs, and spices. For instance, blueberries protect against cardiovascular disease, an apple or pear a day reduces stroke risk by over 52 percent, eating more carrots significantly reduces the risk of bladder cancer, drinking tea reduces cholesterol and helps glucose homeostasis, and cinnamon blocks infection and reduces the risk of some cancers. However, recall that science also tells us that no one nutrient alone is shown to provide these effects.

What micronutrient and phytochemical sources are best at protecting against chronic disease? All of them, together. Just as there is no wonder supplement or drug, there is no superior fruit, vegetable, spice, herb, or tea that protects against all diseases. A review in the July–August 2010 issue of *Oxidative Medicine and Cellular Longevity* concludes that the plant-food benefits to health are attributed to two main factors—that nutrients and phytochemicals are present at low concentrations in general, and that the complex mixtures of nutrients and phytochemicals provides additive and synergistic effects.Bouayed, J. and T. Bohn. "Exogenous Antioxidants—Double-Edged Swords in Cellular Redox State: Health Beneficial Effects at Physiologic Doses versus Deleterious Effects at High Doses." *Oxidative Medicine and Cellular Longevity* 3, no. 4 (2010): 228–37. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2952083/?tool=pubmed. In short, don't overdo it with supplements and make sure you incorporate a wide variety of nutrients in your diet.

Eating a variety of fruits and vegetables rich in antioxidants and phytochemicals promotes health. Consider these diets:

- **Mediterranean diet.** Fresh fruit and vegetables are abundant in this diet, and the cultural identity of the diet involves multiple herbs and spices. Moreover, olive oil is the main source of fat. Fish and poultry are consumed in low amounts and red meat is consumed in very low amounts. An analysis of twelve studies involving over one million subjects published in the September 2008 issue of the *British Medical Journal* reports that people who followed the Mediterranean diet had a 9 percent decrease in overall deaths, a 9 percent decrease in cardiovascular death, a 6 percent decrease in cancer deaths, and a 13 percent reduced incidence of Parkinson's disease and Alzheimer's disease.Sofi, F. et al. "Adherence to Mediterranean Diet and Health Status: Meta-Analysis." *Br Med J* 337 (2008): a1344. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2533524/. The authors of this study concluded that the Mediterranean diet is useful as a primary prevention against some major chronic diseases.
- **Dietary Approaches to Stop Hypertension (DASH diet).** Recall from Chapter 7 "Nutrients Important to Fluid and Electrolyte Balance" that

the DASH diet is an eating plan that is low in saturated fat, cholesterol, and total fat. Fruits, vegetables, low-fat dairy foods, whole-grain foods, fish, poultry, and nuts are emphasized while red meats, sweets, and sugar-containing beverages are mostly avoided. Results from a follow-up study published in the December 2009 issue of the *Journal of Human Hypertension* suggest the low-sodium DASH diet reduces oxidative stress, which may have contributed to the improved blood vessel function observed in salt-sensitive people (between 10 to 20 percent of the population).Al-Solaiman, Y. et al. "Low-Sodium DASH Reduces Oxidative Stress and Improves Vascular Function in Salt-Sensitive Humans." *J Hum Hypertens* 12 (2009): 826–35. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2783838/?tool=pubmed.

- **Diets high in fruits and vegetables.** An analysis of The Nurses' Health Study and the Health Professionals' Follow-up Study reported that for every increased serving of fruits or vegetables per day, especially green leafy vegetables and vitamin C-rich fruits, there was a 4 percent lower risk for heart disease.Joshipura, K.J. et al. "The Effect of Fruit and Vegetable Intake on Risk for Coronary Heart Disease." *Ann Intern Med* 134, no. 12 (2001): 1106–14. http://www.ncbi.nlm.nih.gov/pubmed/11412050.

Americans Typically Eat Fewer than the Recommended Servings of Fruits and Vegetables

An article in the January 2009 issue of the *Medscape Journal of Medicine* reports that fewer than one in ten Americans consumes the recommended amount of fruits and vegetables, which is between five and thirteen servings per day.Kimmons, J. et al. "Fruit and Vegetable Intake among Adolescents and Adults in the United States: Percentage Meeting Individualized Recommendations." *Medscape Journal of Medicine* 11, no. 1 (2009): 26. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2654704/?tool=pubmed. According to this study, the largest single contributor to fruit intake was orange juice, and potatoes were the dominant vegetable.

The USDA recommends that you fill half your plate with fruits and vegetables. The number of servings of fruits and vegetables that a person should consume every day is dependent on age, sex, and level of physical activity. For example, a forty-year-old male who exercises for sixty minutes per day should consume 2 cups of fruit and 3½ cups of vegetables, while a fifteen-year-old female who exercises for thirty minutes per day should consume 1½ cups of fruit and 2½ cups of vegetables. (One cup of a fruit or vegetable is equal to one banana, one small apple, twelve baby carrots, one orange, or one large sweet potato.) To find out the amount of fruits and

vegetables the Centers for Disease Control and Prevention (CDC) recommends, see Note 8.25 "Interactive 8.4".

Interactive 8.4

The CDC provides a fruit- and vegetable-intake calculator.

http://www.fruitsandveggiesmatter.gov/form.html

Improving Fruit and Vegetable Intake at Home and in Your Community

Eating more fruits and vegetables can make you think better, too. According to a study published in 2009 in the *Journal of Alzheimer's Disease*, no matter your age, eating more fruits and vegetables improves your brain function.Polidori, M.C. et al. "High Fruit and Vegetable Intake Is Positively Correlated with Antioxidant Status and Cognitive Performance in Healthy Subjects." *Journal of Alzheimer's Disease* 17, no. 4 (2009): 921–7. http://www.ncbi.nlm.nih.gov/pubmed/19542607. Check out Note 8.26 "Interactive 8.5" for thirteen fun ways to increase your fruit and vegetable intake.

Interactive 8.5

Visit the University of Nebraska-Lincoln's website to discover thirteen fun ways to increase your fruit and vegetable intake.

http://food.unl.edu/web/fnh/freezer-bags

For individually based strategies on how to stretch your fruit and vegetable budget see Note 8.27 "Interactive 8.6".

Interactive 8.6

The Department of Health and Human Services provides “30 Ways in 30 Days to Stretch Your Fruit and Vegetable Budget.”

http://www.fruitsandveggiesmatter.gov/downloads/Stretch_FV_Budget.pdf

Tools for Change

Accept the challenge of optimizing your fruit and vegetable intake. Make it easier on your wallet by choosing five of the thirty ways (Note 8.27 "Interactive 8.6") to stretch your fruit and vegetable budget, and implement them in the next seven days.

The CDC has developed seven strategies to increase American’s intake of fruits and vegetables.Centers for Disease Control and Prevention. “The CDC Guide to Fruit and Vegetable Strategies to Increase Access, Availability, and Consumption.” March 2010. http://www.cdph.ca.gov/SiteCollectionDocuments/StratstoIncreaseFruitVegConsumption.pdf.

1. Support local and state governments in the implementation of a Food Policy Council, which develops policies and programs that increase the availability of affordable fruits and vegetables.
2. In the food system, increase the availability and affordability of high-quality fruits and vegetables in underserved populations.
3. Promote farm-to-where-you-are programs, which is the delivery of regionally grown farm produce to community institutions, farmers markets, and individuals.
4. Encourage worksites, medical centers, universities, and other community and business establishments to serve more fruits and vegetables in cafeterias and onsite eateries.
5. Support schools in developing healthy food messages to students by incorporating activities such as gardening into curricula.
6. Encourage the development and support of community and home gardens.

7. Have emergency food programs, including food banks and food rescue programs, increase their supply of fruits and vegetables.

The seven strategies developed by the CDC are based on the idea that improving access to and availability of fruits and vegetables will lead to an increase in their consumption.

KEY TAKEAWAYS

- Antioxidants and phytochemicals from fruits and vegetables are thought to reduce disease risk.
- Antioxidants and phytochemicals may be beneficial in low doses but not in high doses.
- Eat a variety of foods rich in micronutrient antioxidants and phytochemicals to promote health.
- Fewer than one in ten Americans consumes the recommended amount of fruits and vegetables, which is between five and thirteen servings per day.
- National and international campaigns aim to increase the intake of fruits and vegetables worldwide.

DISCUSSION STARTERS

1. Discuss the various strategies you use, or plan to use, to increase the amount of fruits and vegetables in your diet. Learn other interesting and fun ways to do so from your peers.
2. Share with your classmates your favorite spices, how you use them, and where you buy them.

8.4 End-of-Chapter Exercises

IT'S YOUR TURN

1. Use the fruit- and vegetable-intake calculator provided by the CDC to determine the amount of fruit and vegetables recommended for your diet, and then plan a menu for a day that incorporates the recommended amount of fruits and vegetables. http://www.fruitsandveggiesmatter.gov/form.html
2. The next time you're at the grocery store, record the number, color, and names of the fruits and vegetables available. Draw a table of them, sorted by color. Write a brief statement on whether you have access to an affordable variety of fruits and vegetables.
3. Visit the website "Nutrition-and-You" and choose three herbs and/or spices to write a brief summary on, including the plant they come from, their potential health benefits, and how they are used in foods. http://www.nutrition-and-you.com/healthy_spices.html

APPLY IT

1. Visit the Oldways website at http://www.oldwayspt.org/mediterranean-diet-pyramid and construct a pyramid of the Mediterranean diet.

EXPAND YOUR KNOWLEDGE

1. Read the article, "Antioxidant Content of Whole-Grain Breakfast Cereals, Fruits, and Vegetables" in the *Journal of the American College of Nutrition* (http://www.jacn.org/content/19/suppl_3/312S.long) and summarize in a paragraph the unique phytochemical profile and antioxidant capacity of whole grains.
2. Find out how much fruit and vegetables cost by reviewing this document published by the USDA (http://www.ers.usda.gov/Publications/EIB71/EIB71.pdf), and make a chart of the costs of your favorite fruits and vegetables.