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Vitamins

Vitamins:

- **Organic, essential nutrients required in small amounts by the body for health.**
- **Vitamins regulate body processes that support growth, maintain life and prevent diseases.**
- **vita = life**
- **amine = containing nitrogen (the first vitamins discovered contained nitrogen)**
- **Vitamins must be supplied by the food.**

The vitamins differ from carbohydrates, fats, and proteins in the following ways:

Structure: Vitamins are individual units; they are not linked together (as are molecules of glucose or amino acids). •

Function: Vitamins do not yield energy when metabolized; many of them do, however, assist the enzymes that participate in the release of energy from carbohydrates, fats, and proteins.

Food contents: **The amounts of vitamins people ingest from foods and the amounts they require daily are measured in micrograms (µg) or milligrams (mg), rather than grams (g). The vitamins are similar to the energy-yielding nutrients, though, in that they are vital to life, organic, and available from foods.**

Bioavailability: **The amount of vitamins available from foods depends not only on the quantity provided by a food but also on the amount absorbed and used by the body-referred to as the vitamins' bioavailability. The quantity of vitamins in a food can be determined relatively easily.**

Researchers analyze foods to determine the vitamin contents and publish the results in tables of food composition.

Determining the bioavailability of a vitamin is a more complex task because it depends on many factors, including:

- **Efficiency of digestion and time of transit through the GI tract**
- **Previous nutrient intake and nutrition status**
- **Method of food preparation (raw, cooked, or processed)**
- **Source of the nutrient (synthetic, fortified, or naturally occurring)**
- **Other foods consumed at the same time.**

Precursors: Some of the vitamins are available from foods in inactive forms known as precursors, or provitamins. Once inside the body, the precursor is converted to an active form of the vitamin. **For example**, beta-carotene, a red-orange pigment found in fruits and vegetables, is a precursor to vitamin A. Thus, in measuring a person's vitamin intake, it is important to count both the amount of the active vitamin and the potential amount available from its precursors.

Organic Nature: **Fresh foods naturally contain vitamins, but because they are organic, vitamins can be readily destroyed during processing. Therefore, processed foods should be used sparingly, and fresh foods should be handled with care during storage and in cooking. Prolonged heating may destroy much of the thiamin in food.**

Because riboflavin can be destroyed by the ultraviolet rays of the sun or by fluorescent light, foods stored in transparent glass containers are most likely to lose riboflavin. Oxygen destroys vitamin C, so losses occur when foods are cut, processed, and stored; these losses may be enough to reduce its action in the body.

Minimizing Nutrient Losses

- **To slow the degradation of vitamins, refrigerate (most) fruits and vegetables.**

- **To minimize the oxidation of vitamins, store fruits and vegetables that have been cut in airtight wrappers, and store juices that have been opened in closed containers (and refrigerate them).**

- **To prevent vitamin losses during washing, rinse fruits and vegetables before cutting (not after).**

- **To minimize vitamin losses during cooking, use a microwave oven or steam vegetables in small amount of water. Add vegetables after water has come to a boil. Use the cooking water in mixed dishes such as casseroles and soups. Avoid high temperatures and long cooking times**

Solubility: As you may recall, carbohydrates and proteins are hydrophilic and lipids are hydrophobic. The vitamins divide along the same lines—the hydrophilic, water-soluble ones are the B vitamins and vitamin C; the hydrophobic, fat-soluble ones are vitamins A, D, E, and K. As each vitamin was discovered, it was given a name and sometimes a letter and number as well. Many of the vitamins have multiple names, which has led to some confusion.

Water-Soluble and Fat-Soluble Vitamins

Water-soluble vitamins	Fat-Soluble Vitamins
B vitamins:	**Vitamin A**
Thiamin (B1)	**Vitamin D**
Riboflavin (B2)	**Vitamin E**
Niacin (B3)	**Vitamin K**
Pantothenic acid (B5)	
pyridoxine, pyridoxal, pyridoxamine (B6)	
Biotin (B7)	
Folate (B9)	
Cobalamins (B12)	
Vitamin C	

- **Solubility of the different vitamins affects on absorption, transport, storage, and excretion by the body.**
- **The water-soluble vitamins are found in the watery compartments of foods.**
- **The fat-soluble vitamins usually occur together in the fats and oils of foods.**
- **On being absorbed, the water-soluble vitamins move directly into the blood. Like fats, the fat-soluble vitamins must first enter the lymph, then the blood.**

- **Once in the blood, many of the water-soluble vitamins travel freely, whereas many of the fat-soluble vitamins require transport proteins.**
- **Upon reaching the cells, water-soluble vitamins freely circulate in the water-filled compartments whereas fat-soluble vitamins are held in fatty tissues and the liver until needed.**
- **The kidneys detect and remove small excesses of water-soluble vitamins.**

- **Fat soluble vitamins tend to remain in fat-storage sites in the body rather than being excreted, and so are more likely to reach toxic levels when consumed in excess.**
- **The water-soluble vitamins must be eaten more regularly than the fat-soluble vitamins, although a single day's omission from the diet does not create a deficiency.**

Toxicity

- **Many people to take vitamin supplements, assuming that "more is better." Just as an inadequate intake can cause harm, so can an excessive intake.**
- **Even some of the water-soluble vitamins have adverse effects when taken in large doses, that a vitamin can be both essential and harmful may seem surprising.**

Water-Soluble and Fat-Soluble Vitamins Compared

	Water-Soluble Vitamins: B Vitamins and Vitamin C	Fat-Soluble Vitamins: Vitamins A, D, E, and K
Absorption	Directly into the blood	First into the lymph, then the blood
Transport	Travel freely	Many require transport proteins
Storage	Circulate freely in water-filled parts of the body	Stored in the cells associated with fat
Excretion	Kidneys detect and remove excess in urine	Less readily excreted; tend to remain in fat-storage sites
Toxicity	Possible to reach toxic levels when consumed from supplements	Likely to reach toxic levels when consumed from supplements
Requirements	Needed in frequent doses (perhaps 1 to 3 days)	Needed in periodic doses (perhaps weeks or even months)

The B Vitamins

- **The vitamins do not provide the body with fuel for energy.**
- **Without B vitamins the body would lack energy.**
- **The energy-yielding nutrients; carbohydrate, fat, and protein are used for fuel; the B vitamins help the body to use that fuel.**

- **Several of the B vitamins; thiamin, riboflavin, niacin, pantothenic acid, and biotin form part of the coenzymes that assist enzymes in the release of energy from carbohydrate, fat, and protein.**
- **Other B vitamins play other indispensable roles in metabolism.**
- **Vitamin B6 assists enzymes that metabolize amino acids.**
- **Folate and vitamin B12 help cells to multiply. Among these cells are the red blood cells and the cells lining the GI tract cells that deliver energy to all the others.**

- **The vitamin portion of a coenzyme allows a chemical reaction to occur; the remaining portion of the coenzyme binds to the enzyme.**
- **Without its coenzyme, an enzyme cannot function. Thus symptoms of B vitamin deficiencies directly reflect the disturbances of metabolism caused by a lack of coenzymes.**

Thiamin

- **Thiamin is the vitamin part of the coenzyme TPP (thiamin pyrophosphate) that assists in energy metabolism.**
- **The TPP coenzyme participates in the conversion of pyruvate to acetyl CoA. The reaction removes 1 carbon from the 3-carbon pyruvate to make the 2-carbon acetyl CoA and carbon dioxide (CO_2).**
- **In a similar step in the TCA cycle, TPP helps convert a 5-carbon compound to a 4-carbon compound.**

- **Besides playing these pivotal roles in energy metabolism, thiamin occupies a special site on the membranes of nerve cells. Consequently, nerve activity and muscle activity in response to nerves depend heavily on thiamin.**

Thiamin Recommendations

- **Dietary recommendations are based primarily on thiamin's role in enzyme activity. Generally, thiamin needs will be met if a person eats enough food to meet energy needs if that energy comes from nutritious foods.**

Thiamin Deficiency and Toxicity

- **People who fail to eat enough food to meet energy needs risk nutrient deficiencies, including thiamin deficiency.**
- **Inadequate thiamin intakes have been reported among the nation's malnourished and homeless people.**
- **people who derive most of their energy from empty-kcalorie foods and beverages risk thiamin deficiency.**
- **Alcohol impairs thiamin absorption and enhances thiamin excretion in the urine, doubling the risk of deficiency.**

- **Prolonged thiamin deficiency can result in the disease beriberi.**
- **Beriberi is often described as “dry” or “wet.” Dry beriberi reflects damage to the nervous system and is characterized by muscle weakness in the arms and legs. Wet beriberi reflects damage to the cardiovascular system and is characterized by dilated blood vessels, which cause the heart to work harder and the kidneys to retain salt and water, resulting in edema.**
- **Typically, both types of beriberi appear together, with one set of symptoms predominating.**

Thiamin Food Sources

- **Thiamin occurs in small quantities in many nutritious foods.**
- **Meats in the pork family are rich in thiamin.**
- **Grains; whole grains or enriched are a reliable source of thiamin.**
- **prolonged cooking can destroy thiamin, thiamin leaches into water when foods are boiled or blanched.**
- **Cooking methods that require little or no water such as steaming and microwave heating conserve thiamin and other water-soluble vitamins.**

Riboflavin

- **It is serve as a coenzyme in many reactions in energy metabolism.**
- **The coenzyme forms of riboflavin are FMN (flavin mononucleotide) and FAD (flavin adenine dinucleotide); both can accept and then donate two hydrogens. During energy metabolism, FAD picks up two hydrogens (with their electrons) from the TCA cycle and delivers them to the electron transport chain.**

Riboflavin Recommendations

- **Riboflavin's RDA is based primarily on its role in enzyme activity.**

Riboflavin Deficiency and Toxicity

- **Riboflavin deficiency most often accompanies other nutrient deficiencies.**
- **Lack of the vitamin causes inflammation of the membranes of the mouth, skin, eyes, and GI tract. Excesses of riboflavin appear to cause no harm.**

Riboflavin Food Sources

- **The greatest contributions of riboflavin come from milk and milk products.**
- **Whole-grain or enriched grains are also valuable sources because of the quantities typically consumed.**
- **When riboflavin sources are ranked by nutrient density (per kcalorie), many dark green, leafy vegetables (such as broccoli, turnip greens, asparagus, and spinach) appear high on the list.**

- **Vegans and others who don’t use milk must rely on ample servings of dark greens and enriched grains for riboflavin. Nutritional yeast is another good source.**
- **Ultraviolet light and irradiation destroy riboflavin. For these reasons, milk is sold in cardboard or opaque plastic containers, instead of clear glass bottles. In contrast, riboflavin is stable to heat, so cooking does not destroy it.**

Niacin

- **The name niacin describes two chemical structures: nicotinic acid and nicotinamide (also known as niacinamide).**
- **The body can easily convert nicotinic acid to nicotinamide, which is the major form of niacin in the blood.**
- **The two coenzyme forms of niacin, NAD (nicotinamide adenine dinucleotide) and NADP (the phosphate form), participate in numerous metabolic reactions.**

- **They are central in energy-transfer reactions, especially the metabolism of glucose, fat, and alcohol.**
- **NAD is similar to the riboflavin coenzymes in that it carries hydrogens (and their electrons) during metabolic reactions, including the pathway from the TCA cycle to the electron transport chain. NAD also protects against neurological degeneration.**

Niacin Recommendations

- **Niacin is unique among the B vitamins in that the body can make it from the amino acid tryptophan. This use of tryptophan occurs only after protein synthesis needs have been met.**
- **Approximately 60 milligrams of dietary tryptophan is needed to make 1 milligram of niacin. For this reason, recommended**
- **intakes are stated in niacin equivalents (NE).**

- **A food containing 1 milligram of niacin and 60 milligrams of tryptophan provides the equivalent of 2 milligrams of niacin, or 2 niacin equivalents. The RDA for niacin allows for this conversion and is stated in niacin equivalents.**

Niacin Deficiency

- **The niacin-deficiency disease, pellagra, produces the symptoms of diarrhea, dermatitis, dementia, and eventually death (pellagra).**
- **In the early 1900s, pellagra caused widespread misery and some 87,000 deaths in the US South, where many people subsisted on a low-protein diet centered on corn.**

- **This diet supplied neither enough niacin nor enough tryptophan. At least 70 percent of the niacin in corn is bound to complex carbohydrates and small peptides, making it unavailable for absorption. Furthermore, corn is high in the amino acid leucine, which interferes with the tryptophan to niacin conversion, thus further contributing to the development of pellagra.**

- **Pellagra was originally believed to be caused by an infection. Medical researchers spent many years and much effort searching for infectious microbes until they realized that the problem was not what was present in the food but what was absent from it. That a disease such as pellagra could be caused by diet and not by pathogens was a ground breaking discovery.**

Niacin Toxicity

- **When a normal dose of a nutrient (levels commonly found in foods) provides a normal blood concentration, the nutrient is having a physiological effect.**
- **When a large dose (levels commonly available only from supplements) overwhelms the body and raises blood concentrations to abnormally high levels, the nutrient is acting like a drug and having a pharmacological effect.**

- **Naturally occurring niacin from foods has a physiological effect that causes no harm. Large doses of nicotinic acid from supplements or drugs, however, produce a variety of pharmacological effects, most notably "niacin flush." Niacin flush occurs when nicotinic acid is taken in doses only three to four times the RDA. It dilates the capillaries and causes a tingling sensation that can be painful. The nicotinamide form does not produce this effect.**

- **Large doses of nicotinic acid have been used to lower LDL cholesterol, raise HDL cholesterol, and increase adiponectin levels—all factors that help to protect against heart disease. Such therapy must be closely monitored. People with the following conditions may be particularly susceptible to the toxic effects of niacin: liver disease, diabetes, peptic ulcers, gout, irregular heartbeats, inflammatory bowel disease, migraine headaches, and alcoholism. The nicotinamide form does not improve blood cholesterol levels.**

Niacin Food Sources

- **Niacin can be made in the body from the amino acid tryptophan. Dietary tryptophan could meet about half the daily niacin need for most people, but the average diet easily supplies enough preformed niacin.**
- **Niacin present in selected foods. Meat, poultry, fish, legumes, and enriched and whole grains contribute about half the niacin people consume. Mushrooms, potatoes, and tomatoes are among the richest vegetable sources, and they can provide abundant niacin when eaten in generous amounts.**

- **Niacin is less vulnerable to losses during food preparation and storage than other water-soluble vitamins. Being fairly heat resistant, niacin can withstand reasonable cooking times, but like other water-soluble vitamins, it will leach into cooking water.**

Biotin

- **Biotin plays an important role in metabolism as a coenzyme that carries activated carbon dioxide. This role is critical in the TCA cycle: biotin delivers a carbon to 3-carbon pyruvate, thus replenishing oxaloacetate, the 4-carbon compound needed to combine with acetyl CoA to keep the TCA cycle turning.**
- **The biotin coenzyme also participates in gluconeogenesis, fatty acid synthesis, and the breakdown of certain fatty acids and amino acids.**

Biotin Recommendations

- **Biotin is needed in very small amounts. Because there is insufficient research on biotin requirements, an Adequate Intake (AI) has been determined, instead of an RDA.**

Biotin Deficiency and Toxicity

- **Biotin deficiencies rarely occur. Researchers can induce a biotin deficiency in animals or human beings by feeding them raw egg whites, which contain a protein that binds biotin and thus prevents its absorption.**

- **Biotin-deficiency symptoms include skin rash, hair loss, and neurological impairment. More than two dozen raw egg whites must be consumed daily for several months to produce these effects; cooking eggs denatures the binding protein.**

Biotin Food Sources

- **Biotin is widespread in foods (including egg yolks), so eating a variety of foods protects against deficiencies. Some biotin is also synthesized by GI tract bacteria, but this amount does not contribute much to the biotin absorbed.**

Pantothenic Acid

- **Pantothenic acid is part of the chemical structure of coenzyme A the same CoA that forms acetyl CoA, the "crossroads" compound in several metabolic pathways, including the TCA cycle.**
- **Coenzyme A is made up in part of pantothenic acid. As such, it is involved in more than 100 different steps in the synthesis of lipids, neurotransmitters, steroid hormones, and hemoglobin.**

Pantothenic Acid Recommendations

- **An Adequate Intake (AI) for pantothenic acid has been set. It reflects the amount needed to replace daily losses.**

Pantothenic Acid Deficiency and Toxicity

- **Pantothenic acid deficiency is rare. Its symptoms involve a general failure of all the body's systems and include fatigue, GI distress, and neurological disturbances.**
- **The "burning feet" syndrome that affected prisoners of war in Asia during World War II is thought to have been caused by pantothenic acid deficiency. No toxic effects have been reported.**

Pantothenic Acid Food Sources

- **Pantothenic acid is widespread in foods, and typical diets seem to provide adequate intakes. Beef, poultry, whole grains, potatoes, tomatoes, and broccoli are particularly good sources.**
- **Losses of pantothenic acid during food production can be substantial because it is readily destroyed by the freezing, canning, and refining processes.**

Vitamin B6

- **Vitamin B6 occurs in three forms; pyridoxal, pyridoxine, and pyridoxamine. All three can be converted to the coenzyme PLP (pyridoxal phosphate), which is active in amino acid metabolism.**
- **Because PLP can transfer amino groups (NH2) from an amino acid to a keto acid, the body can make nonessential amino acids.**

- **The ability to add and remove amino groups makes PLP valuable in protein and urea metabolism as well. The conversions of the amino acid tryptophan to niacin or to the neurotransmitter serotonin also depend on PLP.**
- **Inaddition, PLP participates in the synthesis of heme (the nonprotein portion of hemoglobin), nucleic acids (such as DNA and RNA), and lecithin (a phospholipid).**

Vitamin B6 Recommendations

- **The RDA for vitamin B6 is based on the amounts needed to maintain adequate levels of its coenzymes. Unlike other water-soluble vitamins, vitamin B6 is stored extensively in muscle tissue. The large doses of vitamin B6 enhance muscle strength or physical endurance.**

Vitamin B6 Deficiency

- **Without adequate vitamin B6, synthesis of key neurotransmitters diminishes, and abnormal compounds produced during tryptophan metabolism accumulate in the brain.**
- **Early symptoms of vitamin B6 deficiency include depression and confusion; advanced symptoms include abnormal brain wave patterns and convulsions. Low levels of vitamin B6 are associated with increased risks of some cancers and cardiovascular disease.**

- **Alcohol contributes to the destruction and loss of vitamin B6 from the body, when the body breaks down alcohol, it produces acetaldehyde. If allowed to accumulate, acetaldehyde dislodges the PLP coenzyme from its enzymes; once loose, PLP breaks down and is excreted.**
- **Another drug that acts as a vitamin B6 antagonist is isoniazid, a medication that inhibits the growth of the tuberculosis bacterium.**

- **This drug has saved countless lives, but because isoniazid binds and inactivates vitamin B6, it can induce a deficiency. Whenever isoniazid is used to treat tuberculosis, vitamin B6 supplements must be given to protect against deficiency.**

Vitamin B6 Toxicity

- **The first major report of vitamin B6 toxicity appeared in the early 1980s. Until that time, most researchers and dietitians believed that, like the other water-soluble vitamins, vitamin B6 could not reach toxic concentrations in the body.**

- **The report described neurological damage in people who had been taking more than 2 grams of vitamin B6 daily (20 times the current UL of 100 milligrams per day) for 2 months or more.**

Vitamin B6 Food Sources

- **Meats, fish, and poultry, potatoes and a few other vegetables, and fruits offer vitamin B6. As is true of most of the other vitamins, fruits and vegetables rank considerably higher when foods are judged by nutrient density (vitamin B6 per kcalorie).**

- **Several servings of vitamin B6–rich foods are needed to meet recommended intakes.**
- **Foods lose vitamin B6 when heated. Information is limited, but vitamin B6 bioavailability from plant-derived foods seems to be lower than from animal-derived foods.**
- **Fiber does not appear to interfere with vitamin B6 absorption.**

Folate

(folacin, folic acid or pteroylglutamic acid-PGA)

- **Its Primary coenzyme form, THF (tetrahydrofolate), serves as part of an enzyme complex that transfers 1-carbon compounds that arise during metabolism.**
- **Converts vitamin B12 to one of its coenzyme forms, synthesizes the DNA required for all rapidly growing cells, and regenerates the amino acid methionine from homocysteine.**

- **To activate folate, the methyl group must be removed by an enzyme that requires the help of vitamin B12. Without that help, folate becomes trapped inside cells in its methyl form, unavailable to support DNA synthesis and cell growth.**
- **The liver incorporates excess folate into bile that is then sent to the gallbladder and GI tract. Thus folate travels in the same enterohepatic circulation as bile.**

- **Because folate is actively secreted back into the GI tract with bile, it can be reabsorbed repeatedly. If the GI tract cells are damaged, then folate is lost. Such is the case in alcohol abuse; folate deficiency rapidly develops and, atypically, further damages the GI tract. Remember, folate is active in cell multiplication—and the cells lining the GI tract are among the most rapidly replaced cells in the body. When unable to make new cells, the GI tract deteriorates and not only loses folate, but fails to absorb other nutrients as well.**

Folate Recommendations

- **The bioavailability of folate ranges from 50 percent for foods to 100 percent for supplements taken on an empty stomach. These differences in bioavailability must be considered when establishing folate recommendations.**
- **The DRI committee gives naturally occurring folate from foods full credit.**

- **Synthetic folate from fortified foods and supplements is given extra credit because, on average, it is 1.7 times more available than naturally occurring food folate. Thus a person consuming 100 micrograms of folate from foods and 100 micrograms from a supplement receives 270 dietary folate equivalents.**
- **The need for folate rises considerably during pregnancy and whenever cells are multiplying, so the recommendations for pregnant women are considerably higher than for other adults.**

Folate and Neural Tube Defects

- **The brain and spinal cord develop from the neural tube, and defects in its orderly formation during the early weeks of pregnancy may result in various central nervous system disorders and death.**
- **Folate supplements taken 1 month before conception and continued throughout the first trimester of pregnancy can help prevent neural tube defects.**
- **For this reason, all women of childbearing age who are capable of becoming pregnant should consume 0.4 milligram (400 micrograms) of folate daily.**

- **Because half of the pregnancies each year are unplanned and because neural tube defects occur early in development before most women realize they are pregnant, the Food and Drug Administration (FDA) has mandated that grain products be fortified to deliver folate to the US population.**
- **Labels on fortified products may claim that "adequate intake of folate has been shown to reduce the risk of neural tube defects."**
- **Fortification has improved folate status in women of childbearing age and lowered the prevalence rate of neural tube defects.**

- **Some research suggests that folate may also prevent other congenital birth defects, such as cleft lip and cleft palate.**
- **Such findings strengthen recommendations for women to pay attention to their folate needs.**
- **Folate fortification raises safety concerns as well. Because high intakes of folate can mask a vitamin B12 deficiency, folate consumption should not exceed 1 milligram daily without close medical supervision.**

Folate and Heart Disease

- **The FDA's decision to fortify grain products with folate was strengthened by research suggesting a role for folate in protecting against heart disease.**
- **One of folate's key roles in the body is to break down the amino acid homocysteine. Without folate, homocysteine accumulates, which seems to enhance formation of blood clots and atherosclerotic lesions.**
- **Fortified foods and folate supplements raise blood folate and reduce blood homocysteine, but do not seem to reduce the risk of heart attacks, strokes, or death from cardiovascular causes.**

Folate and Cancer

- **Because the synthesis of DNA and the transfer of methyl groups depend on folate, its relationships with cancer are complex, depending on the type of cancer and the timing of folate supplementation.**
- **Some research suggests that sufficient folate may protect against the initiation of cancer, whereas other studies report that high intakes may enhance progression once cancer has begun.**

- **In general, foods containing folate probably reduce the risk of pancreatic cancer Limited evidence suggests folate may also reduce the risk of esophageal and colorectal cancer.**

Folate Deficiency

- **Folate deficiency impairs cell division and protein synthesis processes critical to growing tissues.**
- **In a folate deficiency, the replacement of red blood cells and GI tract cells falters.**
- **Two of the first symptoms of a folate deficiency are anemia and GI tract deterioration.**
- **The anemia of folate deficiency is known as macrocytic or megaloblastic anemia and is characterized by large, immature red blood cells.**

- **Without folate, DNA damage destroys many of the red blood cells as they attempt to divide and mature. The result is fewer, but larger, red blood cells that cannot carry oxygen or travel through the capillaries as efficiently as normal red blood cells.**
- **Primary folate deficiencies may develop from inadequate intake and have been reported in infants who were fed goat's milk, which is notoriously low in folate.**
- **Secondary folate deficiencies may result from impaired absorption or an unusual metabolic need for the vitamin. Metabolic needs increase in situations where cell multiplication must speed up, such as pregnancies involving twins and triplets; cancer; skin-destroying diseases such as chicken pox and measles; and burns, blood loss, GI tract damage, and the like.**

- **Of all the vitamins, folate appears to be most vulnerable to interactions with drugs, which can also lead to a secondary deficiency.**
- **Some medications, notably anticancer drugs, have a chemical structure similar to folate's structure and can displace the vitamin from enzymes and interfere with normal metabolism.**
- **Like all cells, cancer cells need the real vitamin to multiply—without it, they die. Unfortunately, anticancer drugs affect both cancerous cells and healthy cells, creating a folate deficiency for all cells.**

- **Aspirin and antacids also interfere with the body's folate status: aspirin inhibits the action of folate-requiring enzymes, and antacids limit the absorption of folate.**

Folate Toxicity

- **A UL has been established for folate from fortified foods or supplements.**
- **Commonly consumed amounts of folate from both natural sources and fortified foods appear to cause no harm. The small percentage of adults who also take high-dose folate supplements, however, can reach levels that are high enough to obscure a vitamin B12 deficiency and delay diagnosis of neurological damage.**

Folate Food Sources

- **Folate is especially abundant in legumes, fruits, and vegetables. The vitamin's name suggests the word foliage, and indeed, dark green, leafy vegetables are outstanding sources.**
- **With fortification, grain products also contribute folate. Meats and milk products are poor folate sources.**
- **Heat and oxidation during cooking and storage can destroy as much as half of the folate in foods.**

Vitamin B12

- **Vitamin B12 and folate are closely related: each depends on the other for activation. Recall that vitamin B12 removes a methyl group to activate the folate coenzyme. When folate gives up its methyl group, the vitamin B12 coenzyme becomes activated.**
- **The regeneration of the amino acid methionine and the synthesis of DNA and RNA depend on both folate and vitamin B12. In addition, without any help from folate, vitamin B12 maintains the sheath that surrounds and protects nerve fibers and promotes their normal growth. Bone cell activity and metabolism also depend on vitamin B12.**

- **The digestion and absorption of vitamin B12 depends on several steps. In the stomach, hydrochloric acid and the digestive enzyme pepsin release vitamin B12 from the proteins to which it is attached in foods.**
- **Then as vitamin B12 passes from the stomach to the small intestine, it binds with a stomach secretion called intrinsic factor. Bound together, intrinsic factor and vitamin B12 travel to the end of the small intestine, where receptors recognize the complex. Importantly, the receptors do not recognize vitamin B12 without intrinsic factor.**

- **The vitamin is gradually absorbed into the bloodstream as the intrinsic factor is degraded. Transport of vitamin B12 in the blood depends on specific binding proteins. Like folate, vitamin B12 enters the enterohepatic circulation—continuously being secreted into bile and delivered to the intestine where it is reabsorbed.**
- **Because most vitamin B12 is reabsorbed, healthy people rarely develop a deficiency even when their intake is minimal.**

Vitamin B12 Recommendations

- **The RDA for adults is only 2.4 micrograms of vitamin B12 a day. As tiny as this amount appears to the human eye, it contains billions of molecules of vitamin B12, enough to provide coenzymes for all the enzymes that need its help.**

Vitamin B12 Deficiency and Toxicity

- **Most vitamin B12 deficiencies reflect inadequate absorption, not poor intake. Inadequate absorption typically occurs for one of two reasons: a lack of hydrochloric acid or a lack of intrinsic factor. Without hydrochloric acid, the vitamin is not released from the dietary proteins and so is not available for binding with the intrinsic factor. Without the intrinsic factor, the vitamin cannot be absorbed.**

- **Vitamin B12 deficiency is common among the elderly. Many older adults develop atrophic gastritis, a condition that damages the cells of the stomach.**
- **Atrophic gastritis may also develop in response to iron deficiency or infection with Helicobacter pylori, the bacterium implicated in ulcer formation. Without healthy stomach cells, production of hydrochloric acid and intrinsic factor diminishes. Even with an adequate intake from foods, vitamin B12 status suffers. The vitamin B12 deficiency caused by atrophic gastritis and a lack of intrinsic factor is known as pernicious anemia.**

- **Because vitamin B12 is found primarily in foods derived from animals, people who follow a vegan diet may develop a vitamin B12 deficiency.**
- **It may take several years for people who stop eating animal-derived foods to develop deficiency symptoms because the body recycles much of its vitamin B12, reabsorbing it over and over again. Even when the body fails to absorb vitamin B12, deficiency may take up to 3 years to develop because the body conserves its supply.**

- **Because vitamin B12 is required to convert folate to its active form, one of the most obvious vitamin B12–deficiency symptoms is the anemia commonly seen in folate deficiency. This anemia is characterized by large, immature red blood cells, which indicate slow DNA synthesis and an inability to divide. When folate is trapped in its inactive (methyl folate) form due to vitamin B12 deficiency or is unavailable due to folate deficiency itself, DNA synthesis slows. First to be affected in a vitamin B12 or folate deficiency are the rapidly growing blood cells.**

- **Marginal vitamin B12 deficiency impairs cognition. Advanced neurological symptoms include a creeping paralysis that begins at the extremities and works inward and up the spine. Early detection and correction are necessary to prevent permanent nerve damage and paralysis. With sufficient folate in the diet, the neurological symptoms of vitamin B12 deficiency can develop without evidence of anemia. Such interactions between folate and vitamin B12 highlight some of the safety issues surrounding the use of supplements and the fortification of foods. No adverse effects have been reported for excess vitamin B12, and no UL has been set.**

Vitamin B12 Food Sources

- **Vitamin B12 is unique among the vitamins in being found almost exclusively in foods derived from animals. Its bioavailability is greatest from milk and fish.**
- **Anyone who eats reasonable amounts of animal derived foods is most likely to have an adequate intake, including vegetarians who use milk products or eggs. Vegans, who restrict all foods derived from animals, need a reliable source, such as vitamin B12–fortified soy milk or vitamin B12 supplements. Yeast grown on a vitamin B12–enriched medium and mixed with that medium provides some vitamin B12, but yeast itself does not contain active vitamin B12. Similarly, neither fermented soy products such as miso (a soybean paste) nor sea algae such as spirulina provide active vitamin B12.**

- **As mentioned earlier, the water-soluble vitamins are particularly vulnerable to losses in cooking. For most of these nutrients, microwave heating minimizes losses as well as, or better than, traditional cooking methods. Such is not the case for vitamin B12, however. Microwave heating inactivates vitamin B12.**
- **To preserve this vitamin, use the oven or stovetop instead of a microwave to cook meats and milk products (major sources of vitamin B12).**

Vitamin C

Vitamin C serves as a cofactor helping a specific enzyme perform its job, but in others, it acts as an antioxidant participating in more general ways.

Vitamin C as an Antioxidant

- **Vitamin C loses electrons easily, a characteristic that allow it to perform as an antioxidant.**
- **In the body, antioxidants defend against free radicals.**

- **A free radical is a molecule with one or more unpaired electrons, which makes it unstable and highly reactive.**
- **Antioxidants can neutralize free radicals by donating an electron or two. In doing so, antioxidants protect other substances from free radical damage.**
- **The recycling of vitamin C is key to limiting losses and maintaining a reserve of antioxidants in the body.**
- **Vitamin C is like a bodyguard for water-soluble substances; it stands ready to sacrifice its own life to save theirs.**

- **In the cells and body fluids, vitamin C protects tissues from the oxidative stress of free radicals and thus may play an important role in preventing diseases. In the intestines, vitamin C enhances iron absorption by protecting iron from oxidation.**

Vitamin C as a Cofactor in Collagen Formation

Vitamin C helps to form the fibrous structural protein of connective tissues known as collagen. Collagen serves as the matrix on which bones and teeth are formed. When a person is wounded, collagen glues the separated tissues together, forming scars. Cells are held together largely by collagen; this is especially important in the walls of the blood vessels, which must withstand the pressure of blood surging with each beat of the heart.

- **During the synthesis of collagen, each time a proline or lysine is added to the growing protein chain, an enzyme hydroxylates it (adds an OH group), making the amino acid hydroxyproline or hydroxylysine, respectively. These two special amino acids facilitate the binding together of collagen fibers to make strong, ropelike structures. The conversion of proline to hydroxyproline requires both vitamin C and iron. Iron works as a cofactor in the reaction, and vitamin C protects iron from oxidation, thereby allowing iron to perform its duty. Without vitamin C and iron, the hydroxylation step does not occur.**

Vitamin C As a Cofactor in Other Reactions

- **Vitamin C also serves as a cofactor in the synthesis of several other compounds.**
- **As in collagen formation, vitamin C helps in the hydroxylation of carnitine, a compound that transports fatty acids, especially long-chain fatty acids, across the inner membrane of mitochondria in cells.**
- **It also participates in the conversions of the amino acids tryptophan and tyrosine to the neurotransmitters serotonin and norepinephrine, respectively.**

- **Vitamin C also assists in the making of hormones, including thyroxin, which regulates the metabolic rate; when metabolism speeds up in times of extreme physical stress, the body's use of vitamin C increases.**

In Stress

- **Among the stresses known to increase vitamin C needs are infections; burns; extremely high or low temperatures; intakes of toxic heavy metals such as lead, mercury, and cadmium; the chronic use of certain medications, including aspirin, barbiturates, and oral contraceptives; and cigarette smoking.**

- **During stress, the adrenal glands—which contain more vitamin C than any other organ in the body—release vitamin C and hormones into the blood.**

- **When immune system cells are called into action, they use a great deal of oxygen and produce free radicals. In this case, free radicals are helpful. They act as ammunition in an "oxidative burst" that demolishes the offending viruses and bacteria and destroys the damaged cells. Vitamin C steps in as an antioxidant to control this oxidative activity.**

In the Prevention and Treatment of the Common Cold

- **Vitamin C has been a popular option for the prevention and treatment of the common cold for decades, but research supporting such claims has been conflicting and controversial.**
- **Some studies find no relationship between vitamin C and the occurrence of the common cold, whereas others report modest benefits—fewer colds, fewer days, and shorter duration of severe symptoms, especially for those exposed to physical and environmental stresses.**

- **A review of the research on vitamin C in the treatment and prevention of the common cold reveals a slight, but consistent reduction (of 8 percent) in the duration of the common cold in favor of those taking a daily dose of at least 200 milligrams of vitamin C.**
- **The question for consumers to consider is, “Is this enough to warrant routine daily supplementation?” Findings from one study show that consumers want their colds to be at least 25 percent less severe to justify the costs of taking vitamin C supplements regularly.**

- **Discoveries about how vitamin C works in the body provide possible links between the vitamin and the common cold. Anyone who has ever had a cold knows the discomfort of a runny or stuffed-up nose.**
- **Nasal congestion develops in response to elevated blood histamine, and people commonly take antihistamines for relief. Like an antihistamine, vitamin C comes to the rescue and deactivates histamine**

Vitamin C Recommendations

- **Vitamin C ranked at the top of dietary supplement sales. How much vitamin C does a person need? As is true of all the vitamins, recommendations are set generously above the minimum requirement to prevent deficiency disease and well below the toxicity level.**
- **The requirement—the amount needed to prevent the overt symptoms of scurvy— is only 10 milligrams daily. Consuming 10 milligrams a day does not saturate all the body tissues, however; higher intakes will increase the body's total vitamin C. At about 100 milligrams per day, 95 percent of the population reaches tissue saturation.**

- **Recommendations are slightly lower, based on the amounts needed to provide antioxidant protection. At about 200 milligrams, absorption reaches a maximum, and there is little, if any, increase in blood concentrations at higher doses.**
- **Excess vitamin C is readily excreted. As mentioned earlier, cigarette smoking increases the need for vitamin C.**
- **Cigarette smoke contains oxidants, which greedily deplete this potent antioxidant.**

- **Exposure to cigarette smoke, especially when accompanied by low dietary intakes of vitamin C, depletes the body's vitamin C in both active and passive smokers.**
- **People who chew tobacco also have low levels of vitamin C. Because people who smoke cigarettes regularly suffer significant oxidative stress, their requirement for vitamin C is increased an additional 35 milligrams; nonsmokers regularly exposed to cigarette smoke should also be sure to meet their RDA for vitamin C. Smokers are among those most likely to suffer vitamin C deficiency.**

Vitamin C Deficiency

- **Early signs of nutrient deficiencies can be difficult to recognize.**
- **Two of the most notable signs of a vitamin C deficiency reflect its role in maintaining the integrity of blood vessels. The gums bleed easily around the teeth, and capillaries under the skin break spontaneously, producing pinpoint hemorrhages.**

- **When vitamin C concentrations fall to about a fifth of optimal levels (this may take more than a month on a diet lacking vitamin C), scurvy symptoms begin to appear.**
- **Inadequate collagen synthesis causes further hemorrhaging.**
- **Muscles, including the heart muscle, degenerate. The skin becomes rough, brown, scaly, and dry.**
- **Wounds fail to heal because scar tissue will not form.**
- **Bone rebuilding falters; the ends of the long bones become softened, malformed, and painful, and fractures develop.**

- **The teeth become loose as the cartilage around them weakens. Anemia and infections are common. There are also characteristic psychological signs, including hysteria and depression. Sudden death is likely, caused by massive internal bleeding.**
- **Once diagnosed, scurvy is readily resolved by vitamin C. Moderate doses in the neighborhood of 100 milligrams per day are sufficient, curing the scurvy within about 5 days. Such an intake is easily achieved by including vitamin C–rich foods in the diet.**

Vitamin C Toxicity

- **The availability of vitamin C supplements and the publication of books recommending vitamin C to prevent colds and cancer have led many people to take large doses of vitamin C.**
- **The side effects of vitamin C supplementation such as gastrointestinal distress and diarrhea have been reported.**
- **Large amounts of vitamin C excreted in the urine obscure the results of tests used to detect glucose or ketones in the diagnosis of diabetes. In some instances, excess vitamin C gives a false positive result; in others, a false negative.**

- **People with kidney disease, a tendency toward gout, or a genetic abnormality that alters vitamin C's breakdown to its excretion products are prone to forming kidney stones if they take large doses of vitamin C.**
- **Vitamin C supplements may adversely affect people with iron overload. Vitamin C enhances iron absorption and releases iron from body stores; too much free iron causes the kind of cellular damage typical of free radicals. These adverse consequences illustrate how vitamin C can act as a prooxidant when quantities exceed the body's needs.**

Vitamin C Food Sources

- **Fruits and vegetables can easily provide a generous amount of vitamin C. A cup of orange juice at breakfast, a salad for lunch, and a stalk of broccoli and a potato for dinner alone provide more than 300 milligrams.**
- **The citrus fruits are justly famous for being rich in vitamin C, but that other fruits and vegetables are in the same league. A half cup of broccoli, bell pepper, or strawberries provides more than 50 milligrams of the vitamin.**

- **Because vitamin C is vulnerable to heat, raw fruits and vegetables usually have a higher nutrient density than their cooked counterparts. Similarly, because vitamin C is readily destroyed by oxygen, foods and juices should be stored properly and consumed within a week of opening.**
- **The potato is an important source of vitamin C, not because one potato by itself meets the daily need, but because potatoes are such a common staple that they make significant contributions.**

- **Grains, milk and milk products (except breast milk), and most protein foods are poor sources of vitamin C.**
- **Organ meats (liver, kidneys, and others) and raw meats contain some vitamin C, but most people don’t eat large quantities of these foods.**
- **Raw meats and fish contribute enough vitamin C to be significant sources.**

- **Because of vitamin C's antioxidant property, food manufacturers sometimes add a variation of vitamin C to some beverages and most cured meats, such as luncheon meats, to prevent oxidation and spoilage.**
- **This compound safely preserves these foods, but it does not have vitamin C activity in the body.**