

DIET AND EXERCISE

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Many chronic diseases result from unhealthful eating and a sedentary lifestyle. Poor nutrition and inadequate exercise substantially increase the risk of such maladies as coronary artery disease, hypertension, stroke, diabetes, obesity, osteoporosis, and certain cancers. The World Health Organization is attempting to signal a shift from the treatment of illness to the promotion of health. Its emphasis is on changing modifiable health risk factors such as smoking, unhealthy diets, and physical inactivity.¹ Dietary factors also contribute to cholelithiasis, hemorrhoids, hernias, constipation, irritable bowel syndrome, and diverticulosis. A rigorous program that combines a low-fat, high-fiber diet with daily exercise can produce dramatic improvement in cardiovascular risk factors in as little as 3 weeks' time.²

Diet

In the 20th century, the average American diet shifted from one based on fresh, minimally processed vegetable foods to one based on animal products and highly refined, processed foods. As a result, Americans now consume far more calories, fat, cholesterol, refined sugar, animal protein, sodium, and alcohol and far less fiber and starch than is healthful.

In the United States, 133.6 million (66%) adults are overweight (body mass index [BMI] ≥ 25 kg/m²), with 63.3 million (31.4%) considered to be obese (BMI ≥ 30 kg/m²).³ The consequences include a substantial decrease in life expectancy and an increase in morbidity similar in magnitude to the burden imposed by smoking.⁴

Obesity is a complex, multifactorial disorder, but an element common to all cases is a positive energy balance in which more calories are consumed than expended. During the obesity epidemic of the past four decades, portion size and caloric intake have increased,⁵ but exercise has not. Excess calories are stored in body fat; each pound of adipose tissue contains 3,500 calories. Weight loss is accomplished only by achieving a negative energy balance.

ENERGY

Genetic, metabolic, and behavioral variables make it difficult to predict an individual's caloric requirements with precision. However, physicians can provide estimates: sedentary adults require about 30 cal/kg/day to maintain body weight; moderately active adults require 35 cal/kg/day; and very active adults require 40 cal/kg/day. On average, therefore, a 70 kg (154 lb) person can expect to maintain body weight by consuming 2,100 to 2,800 calories daily.

Although any source of dietary energy, including carbohydrate, protein, and alcohol, can be converted in the body to fatty acids and cholesterol, the caloric value of foods varies considerably; for example, fat provides 9 cal/g and alcohol provides 7 cal/g, but protein and carbohydrates each provide only 4 cal/g. Patients with excess body fat should be encouraged to reduce their caloric intake by

reducing portion size and restricting the intake of calorie-dense foods. As an example, to lose 1 lb a week, patients must consume 500 fewer calories than they expend each day; in almost all cases, sustained weight loss requires both an energy-restricted diet and regular vigorous exercise.

FAT AND CHOLESTEROL

Structure

Most dietary lipids are triglycerides, in which three fatty acids are joined to one glycerol molecule. At the core of every fatty acid is a chain of carbon atoms with a methyl group at one end and a carboxyl group at the other [see Figure 1]. The biologic properties of fatty acids are determined by the presence or absence of double bonds between carbon atoms, the number and location of the double bonds, and the configuration of the molecules.

Most of the fatty acids in foods are composed of an even number of carbon atoms, generally in chains of 12 to 22 atoms. The number of double bonds between carbon atoms determines the saturation of fats. Fatty acids with no double bonds are fully saturated; they have no room for additional hydrogen atoms. Fatty acids with one double bond are monounsaturated, and those with two or more double bonds are polyunsaturated.

Fatty acids contain zero to six double bonds, where additional hydrogen atoms can be attached. The location of the double bonds is of great physiologic importance;

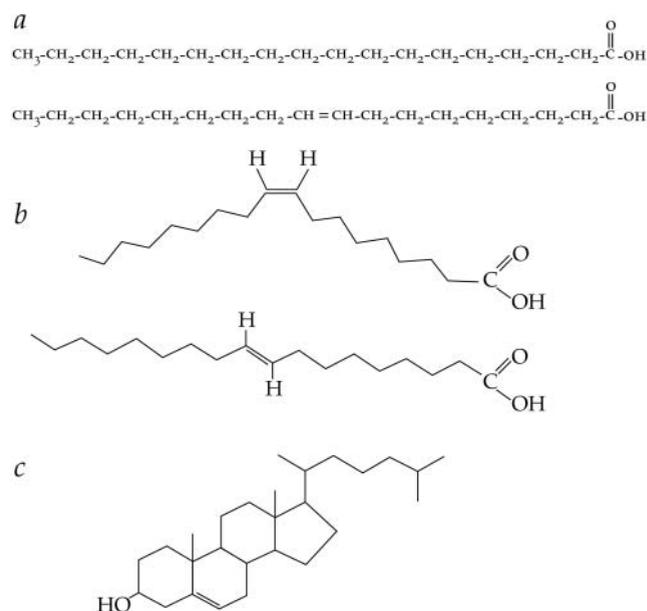


Figure 1 The structure of fat and cholesterol is shown. (a) Stearic acid (top) is a saturated fatty acid. Oleic acid (bottom) is a monounsaturated omega-9 fatty acid. (b) Oleic acid (top) displays a *cis* double bond. Elaidic acid (bottom) displays a *trans* double bond. (c) Cholesterol has a structure similar to that of fatty acids.

an unsaturated fatty acid's group (i.e., omega-3, omega-6, or omega-9) is determined by the position of the double bond closest to the methyl group. In omega-3 fatty acids, for example, three carbon atoms lie between the methyl end of the chain and the first double bond.

Most of the fatty acids in natural foods are in the curved, or *cis*, configuration. When hydrogen is added back to unsaturated fats during food manufacturing, however, the molecules assume a straightened, or *trans*, configuration [see Figure 1].

Cholesterol is a waxy, fatlike molecule that is present in the membranes of all animal cells but is absent from plant cells. Although cholesterol is a sterol rather than a true fat, its metabolism is intimately linked to the dietary intake of fatty acids.

Effects on Blood Lipid Levels and Cardiovascular Risk

Although all fats have the same caloric value (9 cal/g), their effects on human health vary greatly, largely because of their disparate effects on blood cholesterol levels. Saturated fats stimulate hepatic cholesterol production, thus increasing blood cholesterol levels. Of the four saturated fatty acids that predominate in the American diet, myristic acid (14 carbons) has the most potent hypercholesterolemic effect, followed by palmitic acid (16 carbons) and lauric acid (12 carbons). Stearic acid (18 carbons) has little effect on blood cholesterol levels. Evidence strongly suggests that the degree to which saturated fat and cholesterol intake increase the risk of coronary artery disease depends on their effects on blood cholesterol concentration.⁶

Unsaturated fatty acids are generally derived from vegetable and marine sources; they are often called oils rather than fats because they are liquid at room temperature. When monounsaturated or polyunsaturated fatty acids are substituted for saturated fats, blood cholesterol levels fall. Neither type of unsaturated fat, however, has a direct ability to lower low-density lipoprotein cholesterol (LDL-C) or raise high-density lipoprotein cholesterol (HDL-C) levels. Although monounsaturated and polyunsaturated fats have a similar, generally neutral, effect on blood cholesterol levels, monounsaturated fats are less susceptible to oxidation and may therefore be less atherogenic. Omega-3 polyunsaturated fatty acids in particular have been shown to have a cardioprotective effect.

Consumption of omega-3 fatty acids is inversely related to the incidence of death from coronary artery disease,⁷ atrial fibrillation,⁸ and strokes⁹ and may have plaque-stabilizing properties.¹⁰ In high doses, omega-3 fatty acids may reduce blood triglyceride levels,¹¹ but in dietary amounts, they have little effect on blood lipid levels. The role of omega-3 fatty acids is less clear on ventricular arrhythmias.¹² Diets high in α -linolenic acid appear to reduce the risk of coronary artery disease^{13,14} and stroke.

Like saturated fats, *trans*-fatty acids increase blood LDL-C levels; unlike saturated fats, *trans*-fatty acids reduce HDL-C levels, making *trans*-fatty acids even more detrimental.¹⁵ Diets high in *trans*-fatty acids have been associated with an increased risk of atherosclerosis and coronary events.⁶

Dietary cholesterol increases blood LDL-C levels but has a less potent hypercholesterolemic effect than saturated fat.⁶ Diets high in cholesterol are associated with an increased

risk of coronary artery disease independent of their effects on blood cholesterol levels,¹³ reinforcing the importance of reducing cholesterol intake.

Fat and Health

A high intake of saturated fat from animal sources appears to increase the risk of colon cancer,¹⁶ but a modest reduction in total dietary fat does not reduce the risk of colon cancer.¹⁷ A large multicenter study did not show an association between dietary fat and prostate cancer risk.¹⁸

Some dietary fat is essential. For example, omega-3 and omega-6 fatty acids cannot be synthesized endogenously and therefore must be obtained from food. Dietary fat is required for the absorption of fat-soluble vitamins. Lipids are essential components of cell membranes and steroid hormones; adipose tissue is the body's major energy depot, and it provides insulation against heat loss. As little as 15 to 25 g of dietary fat a day can provide essential physiologic functions.

Dietary Recommendations

The American Heart Association (AHA) dietary guidelines for healthy adults suggest that no more than 30% of calories should come from fat, with less than 10% coming from saturated fat and the remainder coming from unsaturated fat in vegetables, fish, legumes, and nuts.¹⁹ The AHA guidelines also specify consumption of less than 300 mg of cholesterol a day. Patients with atherosclerosis or diabetes and persons who are hyperlipidemic or obese should follow more stringent limits, such as a saturated fat intake of no more than 7% of daily calories, with a corresponding decrease in cholesterol consumption to less than 200 mg a day. In some persons, very low-fat diets providing 15 to 22% of calories from fat can reduce blood HDL levels and produce other adverse effects^{20,21}; however, in carefully monitored high-risk persons, diets with about 10% fat and virtually no cholesterol have been beneficial.²² Although reductions in total fat intake can help reduce body fat and serum cholesterol levels, the risk of coronary artery disease may depend more on the type of fat in the diet; saturated fats and *trans*-fatty acids are the most atherogenic, whereas monounsaturated and omega-3 fatty acids are the most desirable [see Table 1].^{6,19}

Food labels list the fat, saturated fat, *trans*-fatty acid, and cholesterol contents of packaged foods. Consumers should be advised to read them carefully and to be sure the portion sizes used for the computations are realistic.

CARBOHYDRATES

Carbohydrates are a vital source of energy for metabolic processes. They are also vital constituents of nucleic acids, glycoproteins, and cell membranes.

Plants are the principal dietary sources of carbohydrates. The only important carbohydrates that originate from animal sources are the lactose in milk and the glycogen in muscle and liver. Carbohydrate-rich foods contain varying amounts of simple and complex carbohydrates. Simple carbohydrates include monosaccharides such as glucose, fructose, and galactose and disaccharides such as sucrose (table sugar), maltose, and lactose. Complex carbohydrates include polysaccharides (e.g., starch and glycogen that can

Table 1 Recommended Daily Intake of Fat and Other Nutrients

Nutrient	Recommended Intake
Total fat	20–35% of total calories
Saturated fat*	< 7% of total calories
Polyunsaturated fat	≤ 10% of total calories
Monounsaturated fat	≤ 20% of total calories
Cholesterol	< 300 mg/day
Carbohydrate†	50–60% of total calories ≥ 25 g/day
Fiber	15% of total calories
Protein	—
Total calories‡	Balance energy intake and expenditure to maintain desirable body weight and prevent weight gain

Adapted from Krauss RM et al.¹⁹

**Trans*-fatty acids, which raise low-density lipoprotein (LDL) and lower high-density lipoprotein (HDL) cholesterol, should also be kept at low levels.

†Carbohydrates should be derived predominantly from foods rich in complex carbohydrates, including grains, especially whole grains, fruits, and vegetables. Simple sugars should contribute no more than 25% of total calories.

‡Daily energy expenditure should include at least moderate physical activity (consuming 200 kcal/day).

be digested into sugars by intestinal enzymes) and fiber (i.e., high-molecular-weight carbohydrates that cannot be split into sugars by human intestinal enzymes). Sugars, starches, and glycogen provide 4 cal/g; because fiber is indigestible, it has virtually no caloric value.

Carbohydrates contribute about 50% of the calories in the average American diet—half from sugar and half from complex carbohydrates. Because sugars are more rapidly absorbed, they have a higher glycemic index than starches. In addition to provoking higher insulin levels, carbohydrates with a high glycemic index appear to reduce HDL-C levels²³ and may increase the risk of coronary artery disease, diabetes, and obesity.^{24,25} Processed foods containing simple sugars are often calorie dense, whereas foods that are rich in complex carbohydrates provide vitamins, trace minerals, and other valuable nutrients. A healthful diet should provide 55 to 65% of calories from complex carbohydrates found in fresh fruits and vegetables, legumes, and whole grains.¹⁹

DIETARY FIBER

Dietary fiber is a heterogeneous mix of very long-chain branched carbohydrates that resist digestion by human intestinal enzymes because of the ways their monosaccharide components are linked to one another. Fiber is found only in plants, particularly in the bran of whole grains, in the stems and leaves of vegetables, and in fruits, seeds, and nuts. The two general categories of dietary fiber are soluble and insoluble.

Soluble fiber delays gastric emptying, which produces a sensation of satiety, and slows the absorption of digestible carbohydrates, which reduces insulin levels. Soluble fiber also lowers blood cholesterol levels, probably by inhibiting bile acid and nutrient absorption in the small intestine and by promoting bile acid sequestration by colonic bacteria.²⁶ Because soluble fiber is metabolized by these bacteria, it has

little effect on fecal bulk. In contrast, insoluble fiber increases the water content and bulk of feces and shortens intestinal transit time [see Table 2].

Diets that are high in fiber also tend to be low in fat. Such diets have been associated with a reduced risk of intestinal disorders, including constipation, irritable bowel syndrome, cholelithiasis, hemorrhoids, and diverticulosis. Although studies have suggested that a very high intake of fiber may substantially reduce the risk of colorectal cancer,²⁷ 13 cohort studies were evaluated, with more than 725,000 men and women followed for 6 to 10 years, with results indicating that high dietary fiber intake was not associated with a reduced risk of colorectal cancer.²⁸ Whole-grain consumption, however, was associated with a modest reduced risk.²⁹ Nevertheless, a dietary pattern that includes a high intake of fruits, vegetables, legumes, fish, poultry, and whole grains but little red meat, processed meats, sweets, or refined grains appears protective.³⁰ A high intake of fiber is associated with a reduced risk of diabetes³¹; in patients with diabetes, it is associated with improved glycemic control and decreased blood lipids.³² It is also associated with a reduced risk of obesity³³ and coronary artery disease^{34,35} and a lower all-cause mortality.³⁶ The Institute of Medicine recommends 38 g of fiber a day for men younger than 50 years and 30 g a day for older men; for women, the recommended intake of fiber is 25 g a day before age 50 and 21 g a day thereafter.³⁷

PROTEINS

Unlike reserves of fat (which is stored in large amounts as triglyceride in adipose tissue) and reserves of carbohydrate (which is stored in small amounts as glycogen in liver and muscle), there are no endogenous reserves of amino acids or protein; all proteins in the body are serving a structural or metabolic function. As a result, bodily function can be impaired if proteins are catabolized because of energy deficiency, wasting diseases, or dietary protein intake that is not sufficient to replace protein losses.

All proteins in human cells are continuously catabolized and resynthesized. In a healthy 70 kg adult, about 280 g of protein is degraded and replaced daily. In addition, about 30 g of protein is lost externally through the urine (urea), feces, and skin.

Table 2 Types of Dietary Fiber and Representative Food Sources

Fiber Type	Food Sources
Gums*	Oats, beans, legumes, guar
Pectin*	Apples, citrus fruits, soybeans, cauliflower, squash, cabbage, carrots, green beans, potatoes
Mucilage*	Psyllium
Hemicellulose**	Barley, wheat bran and whole grains, brussels sprouts, beet roots
Lignin†	Green beans, strawberries, peaches, pears, radishes
Cellulose†	Root vegetables, cabbage, wheat and corn, peas, beans, broccoli, peppers, apples

*Soluble fiber.

†Insoluble fiber.

In healthy adults, daily protein losses can be fully replaced by as little as 0.4 g/kg. Because not all dietary proteins are fully digestible, the recommended dietary allowance (RDA) of protein for healthy adults is 0.8 g/kg. People who exercise strenuously on a regular basis may benefit from extra protein to maintain muscle mass; a daily intake of about 1 g/kg has been recommended for athletes. Women who are pregnant or lactating require up to 30 g/day in addition to their basal requirements. To support growth, children should consume 2 g/kg/day.

A healthful diet should provide 10 to 15% of its calories from protein.¹⁹ For healthy, nonpregnant women, an intake of 44 to 50 g/day of protein is required; for men, an intake of 45 to 63 g/day of protein is needed. Although excessive protein intake has not been proved to be harmful, there are several potential disadvantages to a very high protein intake. The protein in foods derived from animals is often accompanied by large amounts of fat. In the body, excessive protein can be transaminated to carbohydrate, adding to the energy surplus responsible for obesity. When excess protein is eliminated from the body as urinary nitrogen, it is often accompanied by increased urinary calcium, perhaps increasing the risk of nephrolithiasis and osteoporosis. Because nitrogen is excreted in the urine, high dietary protein intake is associated with an increase in renal plasma flow and glomerular filtration rates and, eventually, with increased renal size. In some animal models, increased dietary protein is associated with accelerated renal aging; and in humans with kidney disease, high dietary protein intake is associated with more rapid disease progression.³⁸ On the other hand, high dietary protein intake appears linked to somewhat reduced blood pressure readings,³⁹ possibly because of increased urinary sodium losses; protein supplements may be beneficial for patients with acute or chronic illnesses.⁴⁰

The thousands of proteins in the human body are synthesized from just 21 amino acids. Most amino acids can be synthesized endogenously, but nine cannot. Not all dietary proteins contain all nine essential amino acids; in particular, vegetable proteins may be incomplete. However, by eating a varied diet with foods that contain a mix of proteins, even strict vegetarians can obtain all the amino acids they need. In fact, diets high in vegetable proteins are associated with a lower risk of coronary artery disease than diets high in animal proteins (e.g., red meats).⁴¹

VITAMIN AND MINERAL CONSUMPTION

Vitamins

Vitamins are either fat soluble or water soluble. Vitamins A, D, E, and K are fat soluble. They are found in fatty foods and are absorbed, transported, and stored with fat. Because excretion is minimal and storage in fat is abundant, deficiencies of fat-soluble vitamins are rare, but toxic amounts can accumulate if intake is excessive. Vitamin C and the B-complex group are water soluble; they are absorbed in the intestine, bound to transport proteins, and excreted in the urine. Because storage is minimal, water-soluble vitamins should be ingested regularly; toxicity is rare except in cases involving the ingestion of large doses of vitamin B₃ and B₆ [see Table 3].

Although there is great disparity between popular beliefs about vitamins and their known physiologic effects, new medical information may narrow the gap. It is clear that many persons in the United States, particularly the elderly and the poor, do not consume adequate amounts of vitamin-rich foods. Laboratory and animal experiments demonstrate that antioxidant vitamins can retard atherogenesis and suggest that antioxidants may lower the risk of carcinogenesis. Epidemiologic and observational studies have indicated an association between a low dietary intake or low plasma levels of antioxidants and an increased risk of atherosclerosis and certain cancers; however, randomized clinical trials have failed to demonstrate benefit from antioxidant supplements.^{42,43} Moreover, β -carotene supplements actually appear to increase the risk of lung cancer in smokers,⁴⁴ and hypervitaminosis A may increase the risk of fractures.⁴⁵ Similarly, studies have linked low levels of folic acid, vitamin B₆, and vitamin B₁₂ with elevated blood homocysteine levels and a heightened risk of coronary artery disease,⁴⁶ stroke, and dementia,⁴⁷ but early trials of folic acid supplements have not demonstrated benefit.^{48,49} It is clear that additional studies are required to clarify the impact of vitamins on health.

Women of childbearing age, the elderly, and people with suboptimal nutrition should take a single multivitamin tablet daily; others may benefit as well.⁵⁰ Strict vegetarians should take vitamin B₁₂ in the recommended daily amount (2–4 μ g); because many people older than 60 years have atrophic gastritis and cannot absorb B₁₂ bound to food protein, they may also benefit from supplementary B₁₂. Multivitamin supplements may also be necessary to avert vitamin D deficiencies, particularly in the elderly.⁵¹ A supplement that combines antioxidants with zinc can slow the progression of age-related macular degeneration.⁵² Use of so-called megadose vitamins should be discouraged. Expensive brand-name and so-called all-natural preparations are no more effective than reputable generic preparations. In any case, vitamin supplements should never be used as a substitute for a balanced, healthful diet that provides abundant amounts of vitamin-rich foods.

Minerals

Although minerals are chemically the simplest of nutrients, their roles in metabolism and health are complex. At least 16 minerals are essential for health [see Table 4]; 10 are classified as trace elements because only small amounts are required. Other minerals, such as boron, nickel, vanadium, and silicon, have been shown to be essential in various animal studies but have not been found to be necessary for humans. Many persons in the United States consume too little of some minerals (e.g., calcium and iron) or too much of others (e.g., sodium).

Sodium The body can conserve sodium so effectively that only small amounts are required in the diet. The Food and Nutrition Board of the National Academy of Science estimates that an intake of no more than 500 mg of sodium a day is needed for health; the average American diet contains more than 4,000 mg a day.

Population studies have demonstrated conclusively that a high sodium intake increases blood pressure, especially in

Table 3 The Vitamins

Vitamin	Functions	Deficiency Effects	Toxic Effects	Sources	RDA for Adults*
A (retinol, retinoic acid)	Vision, epithelial integrity; possible protection against epithelial cancers and atherosclerosis	Night blindness; increased susceptibility to infection	Teratogenicity, hepatotoxicity, cerebral edema, desquamation; yellowish skin discoloration by carotenoids; increased fracture risk	Liver, dairy products, eggs; dark-green and yellow-orange vegetables (carotenoids)	Men, 3,000 IU or 900 µg Women, 2,333 IU or 700 µg
B ₁ (thiamine)	Metabolism of carbohydrates, alcohol, and branched-chain amino acids	Beriberi, Wernicke-Korsakoff syndrome	None	Grains, legumes, nuts, poultry, meat	Men, 1.2 mg Women, 1.1 mg
B ₂ (riboflavin)	Cellular oxidation-reduction reactions	Stomatitis, dermatitis, anemia	None	Grains, dairy products, meat, eggs, dark-green vegetables	Men, 1.3 mg Women, 1.1 mg
B ₃ (niacin, nicotinic acid)	Oxidative metabolism; reduces LDL cholesterol; increases HDL cholesterol	Pellagra	Flushing, headaches, pruritus, hyperglycemia, hyperuricemia, hepatotoxicity	Meat, poultry, fish, grains, peanuts; synthesized from tryptophan in foods	Men, 16 mg Women, 14 mg
B ₆ (pyridoxine)	Amino acid metabolism and heme synthesis; neuronal excitability; reduces blood homocysteine levels	Anemia, cheilosis, dermatitis	Neurotoxicity	Meat, poultry, fish, grains, soybeans, bananas, nuts	Men 19–50 yr, 1.3 mg; men ≥50 yr, 1.7 mg Women 19–50 yr, 1.3 mg; women ≥50 yr, 1.5 mg
B ₁₂ (cobalamin)	DNA synthesis (with folate); myelin synthesis (without folate); reduces blood homocysteine levels	Megaloblastic anemia, neuropathies	None	Meat (especially liver), poultry, fish, dairy products	2–4 µg
Folic acid	DNA synthesis (with B ₁₂); reduces blood homocysteine levels	Megaloblastic anemia, birth defects	None	Vegetables, legumes, grains, fruit, poultry, meat	400 µg
Biotin	Metabolic processes	Rare	None	Many foods	30 µg
Pantothenic acid	Metabolic processes	Rare	None	Many foods	5 mg
C (ascorbic acid)	Collagen synthesis; possible protection against certain neoplasms	Scurvy	Nephrolithiasis, diarrhea	Fruits, green vegetables, potatoes, cereals	Men, 90 mg Women, 75 mg
D (calciferol)	Intestinal calcium absorption	Osteomalacia and rickets	Hypercalcemia	Fortified dairy products, fatty fish, egg yolks, liver	< 50 yr, 200 IU; 50–70 yr, 400 IU; > 70 yr, 600 IU
E (α-tocopherol)	Reduces peroxidation of fatty acids; possible protection against atherosclerosis	Rare	Antagonism of vitamin K, possible headaches	Vegetable oils, wheat germ, nuts, broccoli	15 mg
K	Synthesis of clotting factors VII, IX, X, and possibly V	Hemorrhagic diathesis	None	Leafy green vegetables (K ₁), intestinal bacteria (K ₂)	Men, 120 µg Women, 90 µg

HDL = high-density lipoprotein; IU = international units; LDL = low-density lipoprotein; RDA = recommended dietary allowance.
*RDAs during pregnancy and lactation may differ.

older people.⁵³ The Dietary Approaches to Stop Hypertension (DASH) trial demonstrated that reduction of sodium intake from high amounts to moderate amounts will result in lower blood pressures and that further reductions in sodium intake will produce additional benefits.⁵⁴ When combined with other elements of the DASH diet (i.e.,

increased consumption of fruits, vegetables, whole grains, and low-fat dairy products, along with decreased consumption of saturated fat and sugar), sodium restriction can lower systolic blood pressure by an average of 7.1 mm Hg in normotensive persons and 11.5 mm Hg in patients with hypertension. Hence, reductions in dietary sodium could

substantially reduce the risk of stroke and coronary artery disease. A high sodium intake also increases urinary calcium excretion, which in turn increases the risk of osteoporosis.

There is no RDA for sodium, and additional controlled clinical trials are needed to provide conclusive evidence that sodium restriction is beneficial to normotensive persons. Pending such information, the AHA recommends that daily consumption of sodium not exceed 2,400 mg.¹⁹ Dietary guidelines published by the US Department of Agriculture (USDA) recommend a 2,300 mg daily maximum intake of sodium⁵⁵; the Institute of Medicine proposes a limit of 1,500 mg of dietary sodium a day.⁵⁶ Patients with illnesses such as hypertension, congestive heart failure, cirrhosis, and nephrotic syndrome may benefit from substantially lower sodium intakes.

About 80% of dietary sodium comes from processed foods. Physicians should review these hidden sources of salt with patients who would benefit from sodium restriction.

Calcium A high intake of calcium, either from dairy products or supplements,⁵⁷ improves bone density and may provide protection from bone fracture⁵⁸; high-dose vitamin D may be effective in reducing fracture risk.⁵⁹ Dietary calcium intake is inversely related to blood pressure⁶⁰ and to the risk of stroke^{60,61}; calcium supplements, on the other hand, produce only small reductions in systolic blood pressure.⁶² Calcium supplements appear to reduce the risk of colorectal adenomas,⁶³ but high doses may increase the risk of prostate cancer.⁶⁴

At present, fewer than 50% of persons in the United States consume the RDA of calcium [see Table 4]. Persons who do not consume enough calcium from foods should consider a supplement such as calcium carbonate or calcium citrate. High-calcium diets do not increase the risk of

nephrolithiasis,⁶⁵ but prolonged overdoses of supplements may produce hypercalcemia (milk-alkali syndrome) or nephrolithiasis.

Iron Iron deficiency is the most common cause of anemia. In the United States, 9 to 11% of women of childbearing age are iron deficient, and 2 to 5% have iron deficiency anemia; only 1% of men are iron deficient. Routine administration of iron supplements is recommended only for infants and pregnant women⁶⁶; dietary sources should provide adequate amounts of iron for other healthy people. However, vegetarians who exclude all animal products from their diet may need almost twice as much dietary iron each day as nonvegetarians because of the lower intestinal absorption of the nonheme form of iron derived from plant foods.⁶⁷ Good sources of nonheme iron include chickpeas, spinach, molasses, figs, and apricots.

A high intake of iron is harmful for patients with hemochromatosis and for others at risk for iron overload. Studies have found no association between iron stores and mortality from cardiovascular disease and other causes.⁶⁸

Potassium Dietary potassium is inversely related to blood pressure and to stroke mortality in hypertensive men.⁶⁹ Although potassium supplements may assist in the treatment of hypertension,⁷⁰ current data do not justify the routine use of potassium supplements. Physicians should encourage a high dietary potassium intake in most individuals,^{19,54} but low-potassium diets may be necessary for patients with renal disease or other conditions that cause hyperkalemia. For most people, a diet rich in vegetables and fruits provides all of the potassium needed.

Selenium Selenium is a cofactor of the free radical scavenger enzyme glutathione peroxidase. Selenium levels have been inversely associated with mortality from prostate cancer⁷¹ and gastroesophageal malignancies.⁷² These data, however, do not yet support the routine use of selenium supplements, which can be toxic in high doses and may even increase the risk of total nonmelanoma skin cancer.⁷³ Selenium is present in many foods, including tomatoes, poultry, shellfish, garlic, meat, egg yolks, and grains grown in selenium-rich soil.

Chromium Chromium plays a role in glucose metabolism,⁷⁴ and low chromium levels are associated with an increased risk of coronary artery disease.⁷⁵ There is no scientific basis for the claims that chromium supplements contribute to weight loss or increased energy. Chromium supplements may be beneficial for persons with low HDL-C levels, but more study is needed. Dietary sources of chromium include brewer's yeast, whole grains, legumes, peanuts, and meats.

Magnesium Magnesium deficiency is common in diabetic patients, persons with alcoholism, patients who take diuretics, and hospitalized patients. Persons with hypomagnesemia may require magnesium supplements, but others can rely on foods such as green vegetables, whole grains,

Table 4 Essential Minerals and Trace Elements

Minerals and Elements	RDA/ESADDI for Healthy Individuals
Macrominerals	
Calcium	1,000 mg before age 50; 1,200 mg after age 50
Phosphorus	700 mg
Magnesium	Men, 350 mg; women, 280 mg
Potassium	1,700–5,100 mg
Trace elements	
Iron	Men and postmenopausal women, 8 mg; premenopausal women, 18 mg; pregnant women, 27 mg
Chromium	Men 19–50 yr, 35 µg; men ≥ 50 yr, 30 µg; women 19–50 yr, 25 µg; women ≥ 50 yr, 20 µg
Cobalt	Required in small amounts as a component of vitamin B ₁₂
Copper	900 µg
Fluoride	Men, 4 mg; women, 3 mg
Iodine	150 µg
Manganese	Men, 2.3 mg; women, 1.8 mg
Molybdenum	45 µg
Selenium	55 µg
Zinc	Men, 11 mg; women, 8 mg

ESADDI = estimated safe and adequate daily dietary intake; RDA = recommended dietary allowance.

bananas, apricots, legumes, nuts, soybeans, and seafood to provide magnesium.

WATER AND FOOD CONSUMPTION

Water

On average, adults consume about 2 L/day of water, with two thirds coming from beverages and the remainder coming from food. Healthy people have no need to track their water intake. Patients with conditions such as nephrolithiasis and urinary tract infections may benefit from consciously increasing their fluid intake; patients who are at risk for hyponatremia should restrict their water consumption.

Foods

Fruits and vegetables Fruits and vegetables provide many desirable nutrients, including complex carbohydrates, fiber, vitamins, and minerals. Deep-green and yellow-orange vegetables may be particularly beneficial because of their carotenoids, and citrus fruits may be valuable because of their vitamin C, soluble fiber, and potassium. Cruciferous vegetables, such as cabbage, may reduce the risk of certain cancers. Vegetables and fruits are low in sodium and calories; none contain cholesterol, and only coconut, palm oil, and cocoa butter contain saturated fat.

Findings of many case-control and cohort studies strongly suggest that the consumption of fruits and vegetables is inversely related to the risk of coronary artery disease,⁷⁶ stroke,⁷⁷ malignancies of the respiratory and digestive tracts,²⁹ chronic obstructive pulmonary disease,⁷⁸ and all-cause mortality⁷⁹; a meta-analysis of cohort studies supports these findings.⁸⁰ A dietary intervention trial demonstrated that a diet rich in vegetables, fruits, and low-fat dairy products can substantially reduce blood pressure.⁵⁴ The USDA dietary guidelines recommend eating two to four servings of fruit and three to five servings of vegetables a day; at present, fewer than half of men and women meet these standards, often those with the most need to (e.g., type 2 diabetics).⁸¹

Legumes Often neglected in the Western diet, legumes (beans, peas, and lentils) are rich in complex carbohydrates with low glycemic indices, iron, and B vitamins. Legumes are an excellent source of dietary fiber, including soluble fiber that can reduce blood cholesterol levels. Because of their high protein content, legumes are an excellent meat substitute. Soy protein can reduce blood cholesterol⁸² and blood pressure⁸³ levels, and soy intake is inversely related to the risk of prostate and breast cancers.

Legumes can increase intestinal gas, causing bloating, flatulence, and cramps. Distress can be minimized by use of the nonprescription α -galactosidase preparation Beano.

Grains The seed-bearing fruits of grains, called kernels, consist of three layers: the inner germ, which contains vitamins and polyunsaturated fats; the middle endosperm, which contains complex carbohydrates; and the outer bran, which contains dietary fiber. Because milling removes the bran and endosperm, whole grains are nutritionally superior to refined grain; whole-grain consumption is inversely related to the risk of diabetes,³¹ coronary artery disease,^{34,35}

all-cause mortality,³⁶ and possibly stroke.^{84,85} Whole-grain flour can be used to make cereals, baked goods, and even pasta. Whole grains such as brown rice, couscous, and yellow cornmeal (polenta) are easily prepared and healthful side dishes. Oats and barley contain soluble fiber that can lower blood cholesterol levels.

Meat and poultry Although meat is a source of protein, vitamins, and iron and other minerals, its high content of saturated fat, cholesterol, and calories makes it a potentially unhealthy food. Patients who eat meat should be encouraged to select lean cuts, trim away visible fat, and use cooking methods that remove, rather than add, fat. It is even more beneficial to reduce the amount of meat consumed by reducing portion size and frequency; a reasonable goal is to eat about 4 oz one to three times a week.

Poultry is a more healthful source of protein and other nutrients. Chicken and turkey are best, but the skin should be removed before cooking to reduce the fat content.

Dairy products and eggs To reduce the intake of saturated fat and cholesterol, nonfat or low-fat dairy products can be substituted for whole-milk products. The use of nondairy creamers, imitation cheese, margarine, and other products that contain *trans*-fatty acids in partially hydrogenated vegetable oils should be limited. The consumption of up to one egg a day does not appear to increase the risk of cardiovascular disease in healthy, nondiabetic people,⁸⁶ but additional egg yolk consumption should be limited. One egg yolk contains about two thirds of the total amount of cholesterol that is recommended for an entire day. Egg whites and egg substitutes are good alternatives to egg yolks.

Fish A 2007 trial that randomized 2,033 myocardial infarction survivors to usual care or usual care plus fish consumption found that an increase in fatty fish intake reduced 2-year all-cause mortality by 29%.⁸⁷ Fish consumption has also been associated with a reduced risk of primary cardiac arrest,⁸⁸ hypertension,¹⁵ and prostate cancer.⁸⁹ As little as 4 oz of fish twice a week may provide protection.⁹⁰ Fish should be baked, broiled, grilled, steamed, or poached rather than fried, and high-fat sauces should be avoided. Because of their higher content of omega-3 fatty acids, oily deep-water fish may be best. People who are reluctant to eat fish may benefit from fish oil supplements in the modest dose of about 1 g/day.⁹⁰

Cooking oils Canola oil contains an omega-3 fatty acid, α -linolenic acid. High serum levels of α -linolenic acid have been associated with a decreased risk of stroke, and consumption of canola oil is inversely related to the risk of myocardial infarction.¹³ Canola oil and olive oil have a high content of oxidation-resistant monounsaturated fatty acids. Olive oil may be a cardioprotective element in the Mediterranean diet. Although more study is needed, canola and olive oils appear to be the most beneficial oils for food preparation.

Nuts Nuts are high in monounsaturated and polyunsaturated fatty acids and fiber. Nut consumption appears to

be inversely related to the risk of coronary artery disease⁹¹ and diabetes.⁹²

Garlic Medical studies of garlic have shown mixed results. Some meta-analyses suggest that garlic extracts can improve blood cholesterol levels, but others do not.⁹³ The putative benefits of garlic on blood pressure and coagulation are even less clear.

Flavonoid-rich foods Flavonoids are polyphenolic antioxidants that are found in a variety of foods, including apples, onions, tea, and red wine. Flavonoids may protect against cancer development, but trials have yielded inconsistent results.⁹⁴

Alcohol Rarely regarded as a nutrient, alcohol should be considered when dietary recommendations are formulated. Containing 7 cal/g, alcohol is a calorie-dense food. Numerous studies demonstrate that low to moderate alcohol consumption substantially reduces the risk of coronary artery disease, peripheral vascular disease, and all-cause mortality.⁹⁵ The major mechanism of protection is alcohol's ability to increase HDL-C levels; favorable effects on blood coagulation mechanisms may also contribute. Protective doses of alcohol can be obtained from one to two drinks a day; 5 oz of wine, 12 oz of beer, or 1.5 oz of spirits is counted as one drink. Despite its antioxidant content, red wine is no more protective than other alcoholic beverages.⁹⁶

Caffeine Studies have failed to confirm putative links between caffeine and hypertension,⁹⁷ peptic ulcers, coronary artery disease, breast disease, or cancer. Caffeine can trigger migraines in sensitive individuals, and caffeine withdrawal can precipitate headaches or depression in habitual consumers. Caffeine can cause anxiety, insomnia, and gastroesophageal reflux. Brewed coffee can increase blood cholesterol levels, but filtered coffee does not. The effects of caffeine on pregnancy are not fully understood, but it is wise to discourage consumption.⁹⁸ Caffeine restriction does not reduce palpitations in patients with idiopathic premature ventricular contractions.⁹⁹

DIET AND HEALTH

Much remains to be learned about the complex relation between nutrition, health, and disease. Dietary preferences are no less complex and individual. Despite these uncertainties, a dietary pattern characterized by a high intake of vegetables, fruits, legumes, whole grains, fish, and poultry is associated with major health benefits for men¹⁰⁰ and women.¹⁰¹ Physicians have an important role in educating patients about healthful nutrition and in providing dietary guidelines [see Table 5].

Exercise

Numerous observational studies have demonstrated an inverse relation between the amount of habitual physical activity and the risk of many of the chronic illnesses that afflict people in industrialized societies.¹⁰² The protective effect of exercise is strongest against coronary artery disease but is also significant against hypertension, stroke, type 2

Table 5 Dietary Guidelines for Healthy People

Eat more vegetable products than animal products
Eat more fresh and homemade foods than processed foods
Less than 30% of calories should come from fat
Limit cholesterol to less than 300 mg a day
Eat at least 30 g of fiber a day
55–65% of calories should come from complex carbohydrates
10–15% of calories should come from protein
Limit sodium to less than 2,400 mg a day
Obtain 1,200–1,500 mg of calcium a day from food or supplement
Eat 6 or more servings of grain products a day
Eat 3–5 servings of vegetables and legumes a day
Eat 2–4 servings of fruit a day
Eat two 4 oz servings of fish a week
Eat no more than two 4 oz servings of red meat a week
Chicken and turkey should be eaten in moderation with skin removed
Eat no more than one egg yolk a day, including those used in cooking and baking
Use vegetable oils, preferably olive and canola oils, in moderation
Have no more than two alcoholic drinks a day
Adjust caloric intake and exercise level to maintain a desirable body weight
Avoid fad diets and extreme or unconventional nutrition schemes
Avoid untested nutritional supplements, including megavitamins, herbs, food extracts, and amino acids

(non-insulin-dependent) diabetes mellitus, obesity, anxiety, depression, osteoporosis, and cancers of the colon and breast. Despite these proven benefits, only 25% of adults in the United States exercise at recommended levels. Of all deaths in the United States, as many as 250,000 annually can be attributed to a sedentary lifestyle.¹⁰³

EXERCISE PHYSIOLOGY

The physiologic effects of exercise depend on the type of exercise, its intensity, its duration, and its frequency. Exercise is either isometric or isotonic. Isometric contraction of muscle is characterized by an increase in muscle tension without a significant change in fiber length. No external work is accomplished, but substantial energy is expended. Examples of isometric work include handgrip exercises, pushing or pulling against a fixed resistance, and holding a heavy weight. In contrast, isotonic work involves a shortening of muscle fibers with little increase in tension; examples include swimming, bicycling, and running. Most exercise includes both isometric elements and isotonic elements.

Isometric and isotonic exercises differ substantially in their physiologic effects. Isometric work increases total peripheral resistance; both systolic blood pressure and diastolic blood pressure rise substantially, with relatively little increase in stroke volume or cardiac output. Isotonic work lowers total peripheral resistance, but heart rate and cardiac output rise. Systolic blood pressure rises substantially, but diastolic pressure changes little, resulting in a small increase in mean arterial pressure. Isometric work places a pressure load on the heart, whereas isotonic work imposes a volume load.

Isometric exercise increases muscle strength and bulk, which is desirable for competitive athletes, for patients recovering from musculoskeletal injuries, and for individuals who wish to attenuate the loss of muscle mass and bone

strength that accompanies sedentary aging and certain chronic illnesses.¹⁰⁴ However, static exercises produce minimal cardiovascular conditioning, and the circulatory demands of intense isometric work can be hazardous to patients with heart disease. In contrast, dynamic exercises enhance endurance and can produce adaptive cardiovascular changes in healthy individuals and cardiac patients.

Cardiovascular Response to Dynamic Exercise

The acute circulatory response to maximal dynamic exercise is a dramatic rise in cardiac output, from about 5 to 20 L/min in healthy young men. The increased cardiac output results from a 300% increase in heart rate. This increased transport of oxygen is matched by a threefold increase in peripheral oxygen extraction. Total peripheral resistance falls, and blood is shunted away from nonworking muscles and the viscera toward exercising muscles and the coronary circulation, where blood flow increases fourfold.

The physiologic adaptations produced by repetitive dynamic exercise are known collectively as the training effect. The magnitude of the training effect depends on the intensity, duration, and frequency of exercise. Training requires rhythmic, repetitive use of large muscle groups for prolonged periods. Aerobic fitness can be developed and maintained in healthy adults with three to five exercise sessions a week. Each day's exercise should involve isotonic work at 60 to 90% of maximal heart rate for 20 to 60 minutes, either continuously or in increments of 10 minutes or longer.¹⁰⁵ Obviously, sedentary persons and patients with cardiopulmonary disease must initiate training at lower intensities and shorter durations and build up gradually. In addition, most of the health benefits of regular exercise can be attained by moderate exercise at intensities well below the aerobic intensity level¹⁰⁶; gardening and walking during golf are examples of activities that have major health benefits without producing major gains in aerobic fitness.

Perhaps the most obvious effect of aerobic training is resting bradycardia; heart rates of 40 to 50 beats/min are common in highly trained endurance athletes. The mechanisms responsible are not fully understood but probably involve increased vagal tone, decreased sympathetic activity, and increased stroke volume. The best overall measurement of the aerobic training effect and of physical fitness is the maximal oxygen uptake ($\dot{V}O_{2MAX}$).

Oxygen consumption relates directly to the amount of muscular work; maximal oxygen uptake therefore reflects maximal work capacity. Many factors determine an individual's $\dot{V}O_{2MAX}$, including age, gender, lean body mass, genetics, and, most important, the level of habitual aerobic exercise. Just 3 weeks of bed rest will cause a 20 to 25% decline in $\dot{V}O_{2MAX}$. It is no wonder that patients are debilitated after being confined to bed by illness or treatment regimens. In contrast, regular aerobic training lasting weeks or months will increase $\dot{V}O_{2MAX}$, typically by 30 to 40%.

Both central (cardiac) and peripheral (muscular) adaptations are involved in the aerobic training effect. In healthy individuals, training produces dramatic changes in cardiac structure. The dimensions of all cardiac chambers increase by up to 20%, and myocardial mass may increase as much as 70%.¹⁰⁷ Although increased coronary blood flow

and collateralization have not been demonstrated directly in humans, echocardiographic studies show that elite athletes have increased proximal coronary artery size, which is proportional to their increased left ventricular mass. Cardiac function is also enhanced by training; left ventricular contractility, stroke volume, and compliance¹⁰⁸ increase, and angiographic studies have demonstrated increased dilating capacity in the coronary arteries of endurance athletes. Exercise training also improves endothelial function in patients with coronary artery disease and in elderly persons¹⁰⁹; this improvement in endothelial function is achieved, in part, by an increase in nitric oxide production.¹¹⁰ In addition, exercise increases the number of circulating endothelial progenitor cells,¹¹¹ which appears to protect against cardiovascular events.¹¹²

In addition to these cardiac changes that allow enhanced O_2 delivery, exercise training improves peripheral O_2 extraction by enhancing O_2 extraction by the skeletal muscles themselves. This effect on skeletal muscle is specific for the muscles that have been trained; if only leg muscles are trained, the circulatory response to strenuous leg exercise will improve, but the response to vigorous arm exercise will not change.

Exercise training decreases the risk of hypertension. A meta-analysis of randomized controlled trials concluded that endurance training induced significant net reductions in resting and daytime ambulatory blood pressure; systemic vascular resistance also decreased.¹¹² With regular exercise, the benefit has been shown to be maintained for at least 2 years.¹¹³ Regular exercise can even reduce left ventricular hypertrophy and blood pressure in patients with severe hypertension. Regular exercise also lowers catecholamine levels, protecting against arrhythmias, and reduces myocardial oxygen demands.

Isotonic exercise reduces peripheral resistance and lowers blood pressure at rest and during exercise¹¹²; however, intense isometric exercise increases total peripheral resistance and acutely elevates blood pressure. Sustained hypertension is not a complication of resistance training, and moderate resistance training can even reduce resting blood pressure.¹¹⁴ Unsupervised isometric exercising should be avoided by patients with cardiovascular disease; with appropriate precautions, however, it can be safe for selected cardiac patients and can produce favorable effects on muscular function.¹¹⁵

Pulmonary Response

Except in people with intrinsic lung disease, the pulmonary diffusion capacity does not limit exercise. At heavy workloads, however, skeletal muscle oxygen demands exceed oxygen delivery. As a result, muscle metabolism becomes anaerobic; the lactic acid that accumulates is buffered by bicarbonate, so the pH remains nearly normal. The CO_2 that is liberated by the buffering reaction produces an increased ventilatory drive and tachypnea. Athletes know when they have crossed the anaerobic threshold by a markedly increased respiratory rate and a sensation of dyspnea. Habitual exercise does not improve pulmonary function in healthy people, but exercise training may be helpful in patients with chronic lung disease as a result of adaptations in muscles rather than in the lungs.

Musculoskeletal Response

Isotonic exercises increase muscle endurance. Training increases capillary density and can increase muscle mitochondria and oxidative capacity more than twofold. These changes account for the greater oxygen extraction that is an important element of the training effect. Isometric training builds muscle mass, which improves performance and may decrease the risk of injuries. Isometric exercises involving slow repetitions of work against high resistance produce fiber hypertrophy and strength but do not alter muscle enzyme content.

Exercise training affects tissues in addition to muscles. Of great importance, weight-bearing exercises increase bone mineral density, reducing the risk of osteoporosis. Repetitive performance of athletic tasks improves coordination and efficiency; changes in neuromuscular recruitment may be partially responsible. Tendon strength and bone density increase as a result of repetitive use. Joint wear and tear remains a concern, but as long as there is no trauma, habitual exercise probably does not produce degenerative joint disease.¹¹⁶ In fact, aerobic and resistance exercise may help reduce disability in patients with osteoarthritis and fibromyalgia.^{117,118}

Metabolic Effects

Skeletal muscle contains only very limited energy stores; preformed adenosine triphosphate (ATP) and creatine phosphate (CP) can supply less energy than that which is consumed in a 100-yard dash. Clearly, ATP and CP must be generated during exercise. Only three sources of fuel are available to skeletal muscle for this purpose: endogenous muscle glycogen, blood glucose, and free fatty acids (FFAs) derived either from muscle triglyceride or from adipose tissue. Normally, the body's skeletal muscle contains only 120 g of glycogen and the liver only 70 g. The 600 kcal of energy available from these two sources could sustain running for only 6 miles. The blood glucose provides only 40 kcal more. In contrast, the average person's 15,000 g of adipose tissue provides 100,000 kcal of energy—theoretically, enough to fuel a run from Boston to Atlanta.

At rest and during low-intensity exercise, both FFAs and muscle glycogen provide energy. As exercise begins, catecholamines stimulate adipose lipase, which cleaves triglyceride into glycerol and three FFA molecules [see Figure 2]. In muscle cells, FFAs are metabolized to acetyl coenzyme A (acetyl CoA); in the presence of oxygen, acetyl CoA undergoes oxidative metabolism by enzymes of the citric acid (Krebs) cycle in mitochondria.

As the intensity of exercise increases, the relative contribution of FFAs decreases and glycogen becomes more important; at maximum work, muscle depends entirely on glycogen. When oxygen is available, glycogen is metabolized in the cytoplasm to pyruvate, which then undergoes oxidation in the mitochondria via the citric acid cycle to water and CO₂. However, when the demands of muscle outstrip the availability of oxygen, energy can be generated only anaerobically via glycolysis. Anaerobic metabolism is much less efficient: from a gram of glycogen, anaerobic metabolism generates only 5% of the energy that aerobic metabolism generates. In addition, pyruvate cannot be

converted to acetyl CoA. Instead, pyruvate is reduced to lactate. Acidosis limits muscular performance, and buffering by the bicarbonate system generates CO₂, causing tachypnea.

Although the blood glucose itself constitutes only a modest caloric reserve, glucose turnover is greatly accelerated by exercise. During exercise, the liver releases glucose by both glycogenolysis and gluconeogenesis. Simultaneously, peripheral glucose uptake is enhanced. As a result of these metabolic events, blood glucose can account for 10 to 30% of exercising muscle's metabolic needs. The blood glucose level remains normal and may even rise during modest exertion. However, hypoglycemia can occur if hepatic glycogen stores are depleted and high-intensity exercise continues to consume blood glucose and muscle glycogen.

These changes in glucose metabolism are moderated by a number of hormonal alterations. Circulating catecholamines, growth hormone, cortisol, and glucagon levels rise. Insulin levels fall. All of these factors tend to elevate blood glucose levels. Glucose that is ingested during exercise will also tend to maintain blood glucose levels, but ingestion of glucose before exercise may actually raise insulin levels, thus impeding energy mobilization. Contrary to popular so-called instant-energy theories, preexercise meals should not contain concentrated sweets. Indeed, preexercise meals should be sparse, and people should probably ingest little other than water during the 2 hours before exercise.

Exercise increases the insulin sensitivity of muscle, thereby increasing glucose transport and muscle glycogen synthesis. Even moderate physical activity such as walking can help prevent the development of type 2 diabetes mellitus¹¹⁹ and the metabolic syndrome.¹²⁰ Because exercise improves glucose tolerance in diabetic patients, patients taking insulin may require special precautions to exercise safely [see Medical Complications of Exercise, *below*].

During exercise, the rate of protein synthesis is depressed. As a result, amino acids are available for anabolic processes, including hepatic gluconeogenesis. Amino acids also may directly provide a small fraction of the energy needed for muscle contraction. It is not clear whether athletes have higher nutritional protein requirements than sedentary persons; the ingestion of protein and amino acid supplements does not enhance athletic performance.

Regular exercise also alters body weight and body composition. Even if dietary caloric intake remains constant, regular exercise will produce weight loss and a reduction in central adiposity¹²¹; moderately intensive activities are beneficial if they are sustained.¹²² It takes 35 miles of walking or jogging to consume the calories present in 1 lb of adipose tissue. Intense exercise also stimulates both energy expenditure and lipid oxidation for up to 17 hours after exercise itself, thus further contributing to a reduction in body fat. Even as body fat declines, muscle mass increases; because muscle is denser than fat, net weight loss may be slight. Swimming appears to be less effective than land exercise for reducing body fat and increasing bone mineral content. Although weight loss is an important goal for people who are obese, regular physical activity will reduce mortality independent of weight loss.¹²³

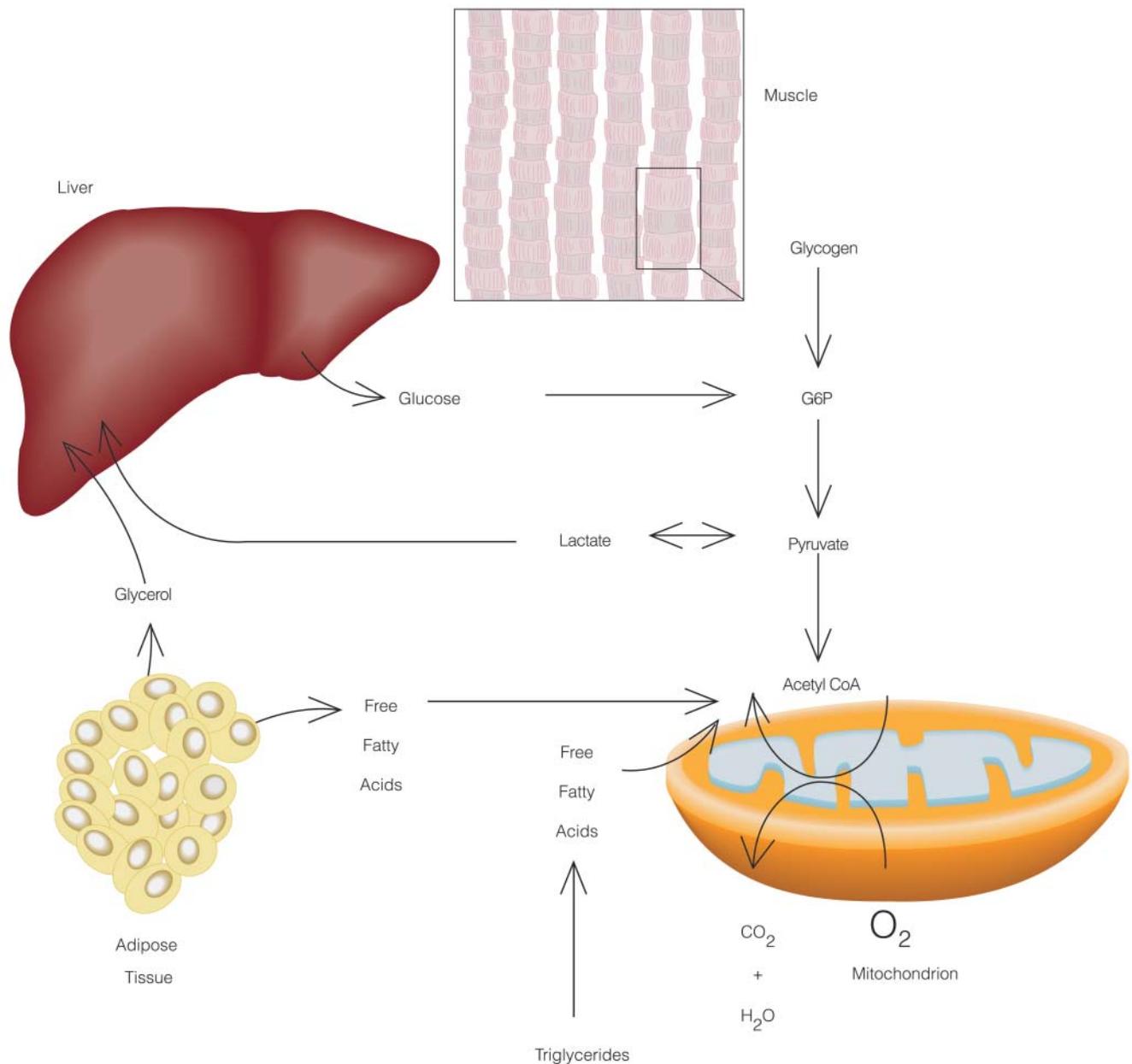


Figure 2 During exercise, catecholamine stimulation of adipose tissue rapidly mobilizes free fatty acids to achieve blood levels that are six times the normal level, which are far higher than the muscle can use. Glucose derived from the liver and muscle glycogen are initially phosphorylated to yield glucose-6-phosphate (G6P). The G6P, the free fatty acids from adipose tissue, and the muscle's own triglycerides are metabolized to acetyl coenzyme A (acetyl CoA). This compound then undergoes oxidative metabolism in the mitochondrial Krebs cycle (blue), thus providing energy for exercising muscle.

Effects on Blood Lipid Levels

Exercise increases serum levels of HDL-C, probably by increasing the formation of apo A-I, which is the major structural protein of HDL, and cellular lipids.¹²⁴ The amount of exercise appears to be the major determinant of the magnitude of the increase in HDL-C. As little as 5 to 10 miles of jogging a week will elevate HDL-C levels, which rise with increasing exercise in a dose-response fashion. Beyond about 35 miles a week, however, additional training does not produce a further increase in HDL-C levels¹²⁵; the mean increase in HDL-C is about 8%.⁶ Similar changes in HDL-C levels

have also been demonstrated in walkers, cross-country skiers, tennis players, bicyclists, and other endurance athletes. The effects of exercise are independent of other factors known to alter HDL-C levels, such as diet, body weight, smoking, and alcohol consumption. Exercise must be sustained to maintain high HDL-C levels.

The effects of exercise on HDL-C levels are observed consistently, but changes in the other blood lipid levels have varied. In general, exercise reduces chylomicron levels and produces a fall in triglyceride levels that averages 24%.⁶ Total cholesterol and LDL-C levels are less likely to decline

in the absence of weight loss. Heritable factors, in part, determine lipid profile responses to exercise.¹²⁶

Hematologic Effects

A mild decrease in hematocrit is commonly observed in endurance athletes. This so-called sports anemia is usually a pseudoanemia because red blood cell mass is normal but plasma volume is increased; decreased viscosity has also been observed. Exercise-related hemolysis or gastrointestinal blood loss may be an additional factor in some cases of anemia in athletes. No consistent long-term changes in polymorphonuclear leukocytes, lymphocytes, or immunoglobulins have been noted.

Hemostatic mechanisms are influenced by exercise. Endurance exercise acutely increases fibrinolytic activity, and repetitive exercise is associated with reduced fibrinogen levels. In contrast, intense exercise can activate platelets, perhaps contributing to a prothrombotic state that may contribute to exertion-induced cardiac events [see Medical Complications of Exercise, *below*]. The effects of exercise on platelet function require further study.

Effects on Vascular Inflammation

It has become clear that atherosclerosis is accompanied by vascular inflammation that contributes importantly to arterial damage and occlusive events. Elevated serum levels of C-reactive protein and other inflammatory markers predict cardiovascular risk in persons without known atherosclerosis and indicate an adverse prognosis in patients with the disease. Regular exercise reduces blood levels of C-reactive protein and other inflammatory markers.¹²⁷ Similar benefits have been documented in cardiac patients during exercise-based rehabilitation.¹²⁸

Effects on Body Fluids

During exercise, skeletal muscle generates a tremendous amount of heat. Sweating is necessary to dissipate this heat. During strenuous exercise in a warm environment, up to 2 L can be lost each hour. Because sweat is hypotonic, the serum sodium concentration rises. Even in the absence of systemic acidosis, serum potassium levels may rise because of an efflux of potassium from muscle cells, but potassium levels normalize within minutes after exertion ceases.

The decline in blood volume, together with a shift in blood flow from the kidneys to skeletal muscle, produces a sharp decline in urine volume during exercise. The rise in plasma osmolarity increases thirst. However, thirst lags behind volume requirements, and fluid intake is often inadequate during athletic events. Volume depletion impairs athletic performance and can contribute to renal dysfunction or heatstroke. Unfortunately, coaching lore often limits fluid intake for fear of cramps, when, in fact, athletes can tolerate large volumes of fluids during brief pauses in exercise. Although water is an excellent fluid replacement, excessive amounts during prolonged exercise can produce severe, even fatal, hyponatremia.¹²⁹ Athletes do not require supplemental potassium or salt, so popular glucose-sodium-potassium solutions make little sense physiologically.

Psychological Effects

Endurance exercise produces improvements in mood, self-esteem, and work behavior both in healthy people and

in patients undertaking cardiac rehabilitation; exercise training can help treat depression.¹³⁰ Several mechanisms have been suggested to explain the psychological effects of exercise. Purely psychological factors, such as distraction, may be involved. The serum levels of β -endorphin, monoamines, and other neuropeptides are affected by exercise in direct relation to the intensity and duration of exercise. Changes in endogenous opioid peptides may mediate the subjective effects of exercise (so-called runner's high).

EXERCISE AND THE ELDERLY

Many physiologic changes attributed to aging closely resemble those that result from inactivity.¹³¹ In both circumstances, bone calcium wastage occurs, and there are decreases in $\dot{V}O_{2MAX}$, cardiac output, red blood cell mass, glucose tolerance, and muscle mass; total peripheral resistance and systolic blood pressure are increased, as are body fat and serum cholesterol levels. Regular exercise appears to retard these age-related maladies. Exercise training improves left ventricular systolic function and increases stroke volume to maintain exercise cardiac output in healthy older people.^{108,132} The age-related decline in $\dot{V}O_{2MAX}$ has been found to be twice as great for sedentary men as for active men, and even low-intensity training can improve $\dot{V}O_{2MAX}$ in the elderly. Exercise training also helps blunt the age-related decline in peripheral vascular function experienced by sedentary people. Endurance training improves glucose tolerance and serum lipid levels in older men and women, and regular exercise appears to blunt the age-related decline in resting metabolic rate. Physical activity in the elderly is associated with increased functional status and decreased mortality. Exercise is safe in the elderly if simple precautions are observed [see Prescribing Exercise, *below*]. Walking programs increase aerobic capacity in persons 70 to 79 years of age, with few injuries; healthy elderly persons who are randomly assigned to aerobic exercise acquire fewer new cardiovascular disorders than control subjects. Appropriate resistance weight programs are not hemodynamically stressful in the elderly and produce increases in muscle strength, functional mobility, and walking endurance. Even frail nursing home residents (mean age, 87 years) responded to resistance training with an increase in muscle mass and strength, as well as improved gait velocity, stair-climbing power, and spontaneous activity. Although more studies are needed to clarify correlations between aging, inactivity, and exercise, enough information is available to warrant a recommendation of carefully planned exercise programs for the elderly.¹³³

EXERCISE AND LONGEVITY

Primary Prevention of Atherosclerosis

Exercise training can favorably modify many of the conditions associated with an increased risk of coronary artery disease, including hypercholesterolemia, elevated blood pressure, glucose intolerance, obesity, elevated levels of C-reactive protein, and the less firmly incriminated traits of hypertriglyceridemia, hyperinsulinemia, hyperfibrinogenemia, and psychological stress. Studies conducted in men, women, and children demonstrated a consistent inverse relation between physical fitness and body weight, percent body fat, systolic blood pressure, and serum levels of cholesterol, triglycerides, and glucose.¹³⁴

Is a sedentary way of life itself a risk factor independent of these other traits? Investigators at the Centers for Disease Control and Prevention (CDC) reviewed 43 methodologically sound studies of exercise and coronary artery disease.¹³⁵ Collectively, these studies showed that sedentary living increases coronary risk by 1.9 times. An independent meta-analysis derived the same relative risk.¹³⁶ The magnitude of this excess risk is similar to that conferred by other risk factors: hypertension, 2.1 times; hypercholesterolemia, 2.4 times; and cigarette smoking, 2.5 times.¹³⁵ Because sedentary living is at least two to three times more prevalent than any of these other risk factors, it can be argued that physical inactivity makes the most significant contribution to the epidemic of coronary artery disease in the United States. Maintaining a physically active way of life can be expected to reduce the risk of myocardial infarction by 35 to 70%. Even mild to moderate exercise that is started later in life is highly protective.¹³⁷

Although reductions in coronary artery disease account for the great majority of the improvements in survival conferred by exercise, other factors may play a role. Physical activity protects against stroke¹³⁸ and hip fracture.¹³⁹ Exercise also reduces the risk of colon cancer¹⁴⁰ and breast cancer.¹⁴¹ It may confer some protection against cancer of the reproductive organs in women and prostate cancer. Large studies have demonstrated that there is a graded, inverse association between activity and mortality.¹⁴²

Secondary Prevention of Ischemic Heart Disease

A growing body of evidence supports the role of exercise in the rehabilitation of patients after myocardial infarction and in the prevention of recurrent cardiac events.¹⁴³⁻¹⁴⁶ Certain benefits of supervised exercise programs have been clearly established, including physiologic and symptomatic improvements and the reduction of risk factors. Patients completing exercise programs demonstrate the training effect, including a lower heart rate at rest and both a lower heart rate and a lower systolic blood pressure at submaximal workloads. These changes reduce myocardial oxygen demands, thereby increasing the angina threshold. Significant improvements in maximal oxygen uptake and work capacity can also be demonstrated. Exercise training can improve walking distances in patients with claudication.¹⁴⁴ Exercise can be useful even for patients with severe ischemic left ventricular dysfunction and chronic congestive heart failure,¹⁴⁵ although extra precautions should be taken in these patients; cardiac exercise programs are safe. Unsupervised moderate exercise, such as walking or gardening, also appears to reduce mortality in older patients with coronary artery disease.¹⁴⁷

PRESCRIBING EXERCISE

Physicians can provide important incentives for their patients by educating them about the benefits, as well as the risks, of habitual exercise. Healthy, sedentary individuals are the largest group in need of such advice. In addition, physicians may be responsible for the medical screening of competitive athletes or for prescribing exercise for patients with chronic illnesses.

A careful history and physical examination are central to the medical evaluation of all potential exercisers. Particular attention should be given to a family history of coronary

disease, hypertension, stroke, or sudden death and to symptoms suggestive of cardiovascular disease. Cigarette smoking, sedentary living, hypertension, diabetes, and obesity all increase the risks of exercise and may indicate the need for further testing. Physical findings suggestive of pulmonary, cardiac, or peripheral vascular disease are obvious causes for concern. A musculoskeletal evaluation is also important.

The choice of screening tests for apparently healthy individuals is controversial. A complete blood count and urinalysis are reasonable in all cases. Determination of blood glucose, serum cholesterol, and creatinine levels may also be useful in screening for risk factors or occult disease. The Valsalva maneuver and the isometric handgrip may be useful additions to the workup.

Young adults who are free of risk factors, symptoms, and abnormal physical findings do not require further evaluation. It is not at all clear that more aggressive medical screening can prevent sudden cardiac death. Although echocardiography and electrocardiography might reveal asymptomatic hypertrophic cardiomyopathy in some patients, the infrequency of this problem makes routine screening impractical.

The role of exercise electrocardiography as a screening test before an individual begins an exercise program is controversial. The AHA no longer recommends routine exercise testing for asymptomatic individuals.¹⁰² A cohort study of 18,964 patients, without known cardiovascular disease who had a clinically normal resting electrocardiogram, showed that exercise testing showed only modest information for predicted mortality; in the follow-up over 10.7 years, 1,585 (8%) patients died.¹⁴⁸ Conversely, exercise testing has been shown to predict adverse cardiac outcome in high-risk individuals.¹⁴⁹ Even in elderly people, routine exercise testing before starting a moderate exercise program may not be necessary.¹³³

Despite its limitations as a screening test for silent coronary artery disease, exercise testing can be useful for detecting exercise-induced arrhythmias, establishing a maximal heart rate for the exercise prescription, and determining work capacity. Serial testing may help motivate a patient by demonstrating increased work capacity. Specialized tests such as pulmonary function tests and exercise ergometry, Holter or telemetric monitoring during exercise, and echocardiography may be very useful in the evaluation of patients who have known or suspected cardiovascular abnormalities.

Screened patients will fall into one of three groups:

1. Healthy persons who can exercise without supervision (Medical guidelines [see below] may still be helpful.)
2. Patients with ischemic heart disease or other significant cardiovascular abnormalities who should have medically supervised, graded exercise programs (If structured programs are not available, such patients should engage in milder forms of exercise, such as walking or bicycling, with appropriate precautions.)
3. Patients for whom physical exertion is contraindicated because of decompensated congestive heart failure, complex ventricular irritability, unstable angina, significant aortic valve disease, aortic aneurysm, uncontrolled diabetes, or uncontrolled seizure disorders

People can exercise in the course of daily life or in formal exercise programs. Although most physicians have recommended structured exercise, studies demonstrate that even modest levels of physical activity are beneficial.^{106,136,147} Walking and gardening are good examples¹⁵⁰; such activities are protective even if they are not started until midlife or late in life.¹⁴⁵ In one clinical trial, for example, relatively healthy middle-aged persons were shown to have less vascular stiffness after a prescribed regimen of walking.¹⁵¹ Compliance with walking is good,¹⁵² and lifestyle interventions appear to be as effective as formal exercise programs of similar intensity in improving cardiopulmonary fitness, blood pressure, and body composition.¹⁵³

People should be encouraged to exercise nearly every day. Formal, intense exercise is not necessary; even moderate exercise that consumes about 150 kcal/day or 1,000 kcal/wk is very beneficial to health. Warm-ups, stretches, and a graded increase in exercise intensity can help prevent musculoskeletal problems.¹⁰⁶

Whereas all people can benefit from moderate daily activity, additional benefit can be obtained from more intense exercise; people who consume about 2,000 kcal in exercise a week obtain the greatest reduction of cardiovascular risk and mortality¹⁴² [see Table 6]. On average, people can obtain optimal health benefits from about 30 minutes of aerobic exercise or 45 to 60 minutes of mild to moderate exercise a day.

Physicians who provide specific practical advice are most likely to motivate their patients to adopt better health habits, including diet and exercise [see Table 7].

The success of a structured fitness program depends on the frequency, duration, and intensity of exercise. At least three sessions a week are needed. An alternate-day schedule will help prevent muscle soreness, but as fitness improves, individuals should be encouraged to increase exercise sessions to five or even seven times a week. Each session

Table 6 Exercise Time Required to Consume 2,000 kcal

Activity	Time (hr)
Strolling	10
Bowling	8.5
Golf	8
Raking leaves	7
Doubles tennis	6
Brisk walking	5.5
Biking (leisurely)	5.5
Ballet	4.5
Singles tennis	4.5
Racquetball, squash	4
Biking (hard)	4
Jogging	4
Downhill skiing	4
Calisthenics, brisk aerobics	3.3
Running	3
Cross-country skiing	3

Table 7 Exercise Advice for Patients

- Get a medical checkup before beginning a formal exercise program
- Warm up before each exercise session and cool down afterward with 10 min of stretching and light calisthenics
- Start slowly and build up to 30 min of moderate to intense exercise or 45–60 min of mild to moderate exercise
- Begin with aerobic-type exercise and later add stretching exercises for flexibility and low-resistance weight training for strength
- Exercise daily if possible, and alternate harder workouts with easier ones
- Dress comfortably
- Use good equipment, especially good shoes
- Do not eat during the 2 hr before you exercise but drink plenty of water before, during, and after exercise, particularly in warmer weather
- Do not ignore aches and pains that may signify injury
- Do not exercise if you are feverish or ill
- Learn warning signals of heart disease, including chest pain or pressure, disproportionate shortness of breath, fatigue, sweating, erratic pulse, light-headedness, or even indigestion
- Consider getting instruction or joining a health club

consists of 15 to 60 minutes of activity. Untrained individuals may not be able to sustain even 15 minutes at first, but they should be encouraged to progress slowly as they improve. Each exercise session should be preceded by a 5- to 10-minute warm-up period and followed by a 5- to 10-minute cool-down period; stretching, gentle calisthenics, and walking are ideally suited for this purpose. These same exercises are excellent for a 5- to 10-minute cool-down period.

The intensity of exercise can best be judged by the target heart rate. A heart rate of 60 to 85% of maximum is considered optimal for aerobic training. If an exercise test has not been performed, a maximal heart rate can be calculated by subtracting the patient's age from 220. Unfit people should start at the lower end of the target heart rate range. Healthy people need not monitor pulse rate. Instead, they can adjust the intensity of effort to a talking pace: they are working hard but still able to talk to a companion without a sensation of dyspnea.

Many kinds of exercise can be used to attain fitness. Dynamic (i.e., isotonic or aerobic) exercises in which large muscle groups are used continuously in a rhythmic, repetitive fashion for prolonged periods are ideal. The energy requirements of various activities have been measured. An energy expenditure of 5 to 6 metabolic equivalents (METs) or more is desirable for aerobic training (1 MET is equal to the energy expenditure at rest or equivalent to approximately 3.5 mL O₂/kg body weight/min). Brisk walking, jogging, swimming, cross-country skiing, skating, bicycling, and vigorous singles racket sports all provide good conditioning. Sports that allow prolonged periods of inactivity, such as doubles tennis, golf, bowling, and baseball, are much less desirable for aerobic fitness but can still make important contributions to health. Activities requiring sudden bursts of intense isometric activity, such as weight lifting, provide little cardiovascular conditioning and are contraindicated for patients with hypertension or heart disease. Contact sports cannot be recommended for health.

Although physicians should encourage patients to choose the sports that appeal most to them, medical considerations may also be important. For example, swimming is particularly desirable for individuals who have various musculoskeletal problems, and it is also ideal for people who experience exercise-induced asthma (EIA). Walking and bicycling are ideal for older individuals or for anyone who is starting from a low level of fitness. Jogging can be recommended because it is convenient and because the participants can easily adjust intensity and duration upward as fitness develops. Most desirable of all is a balanced program containing a variety of activities that exercise different muscle groups. People who have several activities at their command find it easier to remain active despite constraints of climate, schedules, and minor injuries. Although moderate or aerobic exercise is most important for metabolic improvement and cardiovascular health, exercises for flexibility and strength should be part of a balanced fitness program.¹⁰⁶ Stretching exercises promote flexibility and help prevent injuries. A stretching routine should be performed at least two to three times a week, but it is best when incorporated in the warm-up and cool-down periods that should surround aerobic exercise. Low-resistance strength training is important to preserve muscle mass and power in the face of the aging process; two to three sessions a week are ideal.

COMPLICATIONS OF EXERCISE

Reducing Risk of Injury and Complications

Physicians can minimize injuries and medical complications associated with exercise by educating patients about potential problems. Physicians should stress the need for such safety devices as helmets for biking, eye guards for squash and racquetball, and elbow and knee pads for roller-skating. Diet, weight control, stress management, smoking cessation, and other preventive health measures should be discussed, as should the warning signs of cardiac disease and the precautions for exercising in cold or hot climates.

Medical Complications of Exercise

Exercise promotes health, but it can also have adverse consequences. In some cases, the physiologic adaptations to exercise produce changes that may be misinterpreted as pathologic; athlete's heart is one example. In other cases, however, exercise can precipitate clinically important problems.

The cardiac complications of exercise include ischemia, infarction, and sudden death, often caused by rupture of an atherosclerotic plaque. These dire events are infrequent and can be minimized by proper patient screening and instruction [see Prescribing Exercise, *above*]. Exercise-induced cardiac events are less common in people who exercise regularly than in sedentary individuals.¹⁵⁴ On balance, exercise is clearly beneficial for the heart.

The most common pulmonary complication of exercise is EIA, which usually responds well to treatment.¹⁵⁵ A much less common problem that can mimic hypersensitivity disorders is exercise-induced anaphylaxis.

The gastrointestinal response to exercise may produce reflux, diarrhea, or bleeding, which is usually occult and

transient. Women who exercise very strenuously may experience oligomenorrhea or amenorrhea; the menstrual dysfunction is reversible but may be accompanied by osteoporosis. With appropriate precautions, exercise is safe during pregnancy. Precautions are also in order for prevention of hypoglycemia in diabetic patients who exercise.

People who exercise regularly can experience increased plasma volume that produces hemodilution or pseudoanemia. True anemia is less common but may result from a shortening of the life span of red cells caused by vascular trauma or iron deficiency. Exercise can produce proteinuria or hematuria; both are benign but are indications for performing studies to rule out renal disease. In warm, humid weather, exercise can produce heat cramps, hyperthermia, or heatstroke, all of which are preventable.

Exercise does not appear to cause or accelerate osteoarthritis.¹¹⁶ Acute muscle injury, manifested by transient elevations of creatine phosphokinase levels, is common, but exertional rhabdomyolysis is rare. Extremely prolonged exercise can elevate troponin levels without other evidence of injury to cardiac muscle.¹⁵⁶ Musculoskeletal problems, however, are the most frequent side effects of exercise.¹⁵⁷ Overstress, overuse, or trauma is usually responsible. Poor technique, faulty equipment, or fatigue often contributes to injury. Soft tissue injuries such as sprains, strains, and tendinitis usually respond well to simple treatment regimens. The same is true of stress fractures. Primary care physicians can manage many of these problems, but more serious injuries may merit referral to a sports medicine facility.

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Figure 1 Marcia Kammerer.

Figure 2 Talar Agasyan.