CHAPTER 30

# Exercise Physiology

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## CHAPTER OUTLINE

- THE QUANTIFICATION OF EXERCISE
- CARDIOVASCULAR RESPONSES
- RESPIRATORY RESPONSES
- MUSCLE AND BONE RESPONSES
- GASTROINTESTINAL, METABOLIC, AND ENDOCRINE RESPONSES
- AGING, IMMUNE, AND PSYCHIATRIC RESPONSES

## KEY CONCEPTS

1. Exercise must be accurately defined before acute or chronic physiological responses can be predicted.
2. Maximal oxygen uptake predicts work performance and the physiological responses to exercise.
3. Substantial regional blood flow shifts occur during dynamic and isometric exercise.
4. Training affects both myocardial muscle and the coronary circulation.
5. The respiratory system responds predictably to increased $O_2$ consumption and $CO_2$ production with exercise.
6. In healthy individuals, muscle fatigue during exercise is linked to ADP accumulation.
7. Chronic physical activity enhances insulin sensitivity and glucose entry into cells.

Exercise, or physical activity, is a ubiquitous physiological state, so common in its many forms that true physiological "rest" is indeed rarely achieved. Defined ultimately in terms of skeletal muscle contraction, exercise involves every organ system in coordinated response to increased muscular energy demands.

## THE QUANTIFICATION OF EXERCISE

Exercise is as varied as it is ubiquitous. A single episode of exercise, or "acute" exercise, may provoke responses different from the adaptations seen when activity is chronic—that is, during **training**. The forms of exercise vary as well. The amount of muscle mass at work (one finger? one arm? both legs?), the intensity of the effort, its duration, and the type of muscle contraction (isometric, rhythmic) all influence the body's responses and adaptations.

These many aspects of exercise imply that its interaction with disease is multifaceted. There is no simple answer as to whether exercise promotes health. In fact, physical activity can be healthful, harmful, or irrelevant, depending on the patient, the disease, and the specific exercise in question.

### Measuring Maximal Oxygen Uptake Is the Most Common Method of Quantifying Dynamic Exercise

**Dynamic exercise** is defined as skeletal muscle contractions at changing lengths and with rhythmic episodes of relaxation. Fundamental to any discussion of dynamic exercise is a description of its intensity. Since dynamically exercising muscle primarily generates energy from oxidative metabolism, a traditional standard is to measure, by mouth, the oxygen uptake ($\dot{V}O_2$) of an exercising subject. This measurement is limited to dynamic exercise and usually to the steady state, when exercise intensity and oxygen consumption are stable and no net energy is provided from nonoxidative sources. Three implications of the original oxygen consumption measurements deserve mention. First, the centrality of oxygen usage to work output gave rise to the now-standard term "aerobic" exercise. Second, the apparent excess in oxygen consumption during the first minutes of recovery has been termed the **oxygen debt** (Fig. 30.1). The "excess" oxygen consumption of recovery results from a multitude of physiological processes and little usable information is obtained from its measurement. Third, and more

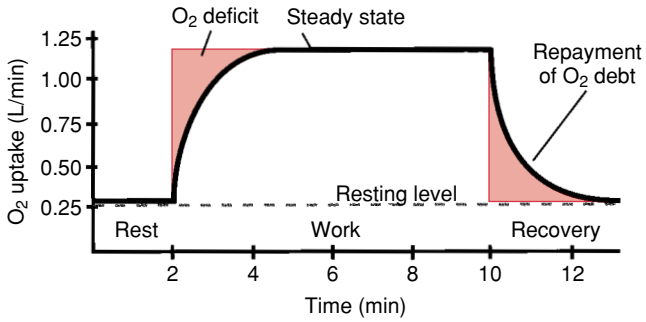


**FIGURE 30.1** **Oxygen uptake before, during, and after light steady-state exercise.**

useful, during dynamic exercise that uses a large muscle mass, each person has a **maximal oxygen uptake**, a ceiling up to 20 times basal consumption, that cannot be exceeded, although it can be increased by appropriate training. This maximal oxygen uptake is a useful but imperfect predictor of the ability to perform prolonged dynamic external work or, more specifically, of endurance athletic performance. Maximal oxygen uptake is decreased, all else being equal, by age, bed rest, or increased body fat.

Maximal oxygen uptake is also used to express relative work capacity. A world champion cross-country skier obviously has a greater capacity to consume oxygen than a novice. However, when both are exercising at intensities requiring two thirds of their respective maximal oxygen uptakes (the world champion is moving much faster in doing this, as a result of higher capacity), both become exhausted at roughly the same time and for the same physiological reasons (Fig. 30.2). In the discussion that follows, relative as well as absolute (expressed as L/min of oxygen uptake) work levels are used to explain physiological responses. The energy costs and relative demands of some familiar activities are listed in Table 30.1.

What causes oxygen uptake to reach a ceiling? Historically, many arguments claim primacy for either cardiac output (oxygen delivery) or muscle metabolic capacity (oxygen use) limitations. However, it may be that every link in the chain taking oxygen from the atmosphere to the mitochondrion reaches its capacity at about the same time. In practical terms, this means that any lung, heart, vascular, or musculoskeletal illness that reduces oxygen flow capacity will diminish a patient's functional capacity.

In **isometric exercise**, force is generated at constant muscle length and without rhythmic episodes of relaxation. Isometric work intensity is usually described as a percentage of the **maximal voluntary contraction** (MVC), the peak isometric force that can be briefly generated for that specific exercise. Analogous to work levels relative to maximal oxygen uptake, the ability to endure isometric effort, and many physiological responses to that effort, are predictable when the percentage of MVC among individuals is held constant.

## CARDIOVASCULAR RESPONSES

Increased energy expenditure with exercise demands more energy production. For prolonged work, this energy is supplied by the oxidation of foodstuff, with the oxygen carried to working muscles by the cardiovascular system.

### Blood Flow Is Preferentially Directed to Working Skeletal Muscle During Exercise

Local control of blood flow ensures that only working muscles with increased metabolic demands receive increased blood and oxygen delivery. If the legs alone are active, leg muscle blood flow should increase while arm muscle blood flow remains unchanged or is reduced. At rest, skeletal muscle receives only a small fraction of the cardiac output. In dynamic exercise, both total cardiac output and relative and absolute output directed to working skeletal muscle increase dramatically (Table 30.2).

Cardiovascular control during exercise involves systemic regulation (cardiovascular centers in the brain, with their autonomic nervous output to the heart and systemic resistance vessels) in tandem with local control. For millennia our ancestors successfully used exercise both to escape being eaten and to catch food; therefore, it is no surprise that cardiovascular control in exercise is complex and unique. It's as if a brain software program entitled "Exercise"

**TABLE 30.1** **Absolute and Relative Costs of Daily Activities**

| | | % Maximal Oxygen Uptake | |
|---|---|---|---|
| Activity | Energy Cost (kcal/min) | Sedentary 22-Year-Old | Sedentary 70-Year-Old |
| Sleeping | 1 | 6 | 8 |
| Sitting | 2 | 12 | 17 |
| Standing | 3 | 19 | 25 |
| Dressing, undressing | 3 | 19 | 25 |
| Walking (3 miles/hr) | 4 | 25 | 33 |
| Making a bed | 5 | 31 | 42 |
| Dancing | 7 | 44 | 58 |
| Gardening/shoveling | 8 | 50 | 67 |
| Climbing stairs | 11 | 69 | 92 |
| Crawl swimming (50 m/min) | 16 | 100 | |
| Running (8 miles/hr) | 16 | 100 | |

**TABLE 30.2 Blood Flow Distribution During Rest and Dynamic Exercise in an Athlete**

| | Rest | | Heavy Exercise | |
|---|---|---|---|---|
| Area | mL/min | % | mL/min | % |
| Splanchnic | 1,400 | 24 | 300 | 1 |
| Renal | 1,100 | 19 | 900 | 4 |
| Brain | 750 | 13 | 750 | 3 |
| Coronary | 250 | 4 | 1,000 | 4 |
| Skeletal muscle | 1,200 | 21 | 22,000 | 86 |
| Skin | 500 | 9 | 600 | 2 |
| Other | 600 | 10 | 100 | 0.5 |
| Total Cardiac Output | 5,800 | 100 | 25,650 | 100 |

were inserted into the brain as work begins. Initially, the motor cortex is activated: The total neural activity is roughly proportional to the muscle mass and its work intensity. This neural activity communicates with the cardiovascular control centers, reducing vagal tone on the heart (which raises heart rate) and resetting the arterial baroreceptors to a higher level. As work rate is increased further, lactic acid is formed in actively contracting muscles, which stimulates muscle afferent nerves to send information to the cardiovascular center that increases sympathetic outflow to the heart and systemic resistance vessels. However, despite this **muscle chemoreflex** activity, within these same working muscles, low $P_{O_2}$, increased nitric oxide, vasodilator prostanoids, and associated local vasoactive factors dilate arterioles despite rising sympathetic vasoconstrictor tone. Increased sympathetic drive does elevate heart rate and cardiac contractility, resulting in increased cardiac output; local factors in the coronary vessels mediate coronary vasodilation. Increased sympathetic vasoconstrictor tone in the renal and splanchnic vascular beds, and in inactive muscle, reduces blood flow to these tissues. Blood flow to these inactive regions can fall 75% if exercise is strenuous. Increased vascular resistance and decreased blood volume in these tissues helps maintain blood pressure during dynamic exercise. In contrast to blood flow reductions in the viscera and in inactive muscle, the brain autoregulates blood flow at constant levels independent of exercise. The skin remains vasoconstricted only if thermoregulatory demands are absent. Table 30.3 shows how a profound fall in systemic vascular resistance matches the enormous rise in cardiac output during dynamic exercise.

**TABLE 30.3 Cardiac Output, Mean Arterial Pressure, and Systemic Vascular Resistance Changes With Exercise**

| | Rest | Strenuous Dynamic Exercise |
|---|---|---|
| Cardiac output (L/min) | 6 | 21 |
| Mean arterial pressure (mm Hg) | 90 | 105 |
| Systemic vascular resistance (mm Hg · min/L) | 15 | 5 |

Dynamic exercise, at its most intense level, forces the body to choose between maximum muscle vascular dilation and defense of blood pressure. Blood pressure is, in fact, maintained. During strenuous exercise, sympathetic drive can begin to limit vasodilation in active muscle. When exercise is prolonged in the heat, increased skin blood flow and sweating-induced reduction in plasma volume both contribute to the risk of hyperthermia and hypotension (heat exhaustion). Although chronic exercise provides some heat acclimatization, even highly trained people are at risk for hyperthermia and hypotension if work is prolonged and water is withheld in demanding environmental conditions.

Isometric exercise causes a somewhat different cardiovascular response. Muscle blood flow increases relative to the resting condition, as does cardiac output, but the higher mean intramuscular pressure limits these flow increases much more than when exercise is rhythmic. Because the blood flow increase is blunted inside a statically contracting muscle, the fruits of hard work with too little oxygen appear quickly: a shift to anaerobic metabolism, the production of lactic acid, a rise in the ADP/ATP ratio, and fatigue. Maintaining just 50% of the MVC is agonizing after about 1 minute and usually cannot be continued after 2 minutes. A long-term sustainable level is only about 20% of maximum. These percentages are much less than the equivalent for dynamic work, as defined in terms of maximal oxygen uptake. Rhythmic exercise requiring 70% of the maximal oxygen uptake can be maintained in healthy individuals for about an hour, while work at 50% of the maximal oxygen uptake may be prolonged for several hours (see Fig. 30.2).

The reliance on anaerobic metabolism in isometric exercise triggers muscle ischemic chemoreflex responses that raise blood pressure more and cardiac output and heart rate

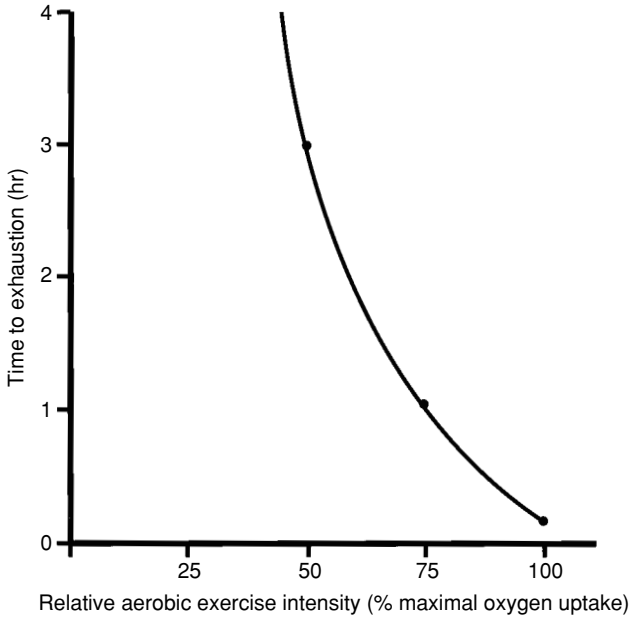


**FIGURE 30.2 Time to exhaustion during dynamic exercise.** Exhaustion is predictable on the basis of relative demand upon the maximal oxygen uptake.

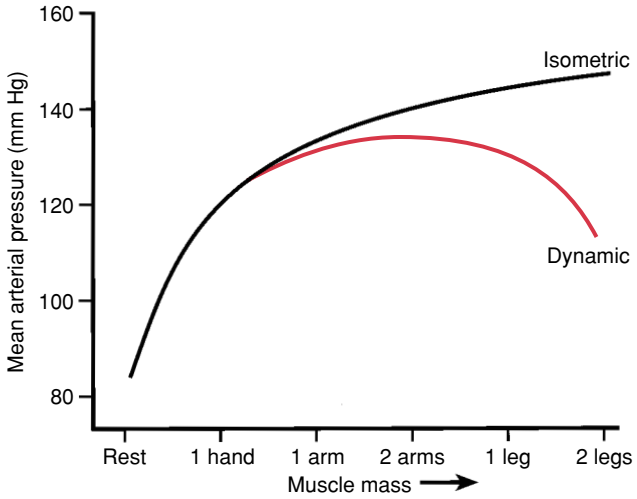


**FIGURE 30.3** **Effect of active muscle mass on mean arterial pressure during exercise.** The highest pressures during dynamic exercise occur when an intermediate muscle mass is involved; pressure continues to rise in isometric exercise as more muscle is added.

less than in dynamic work (Fig. 30.3). Oddly, for dynamic exercise, the elevation of blood pressure is most pronounced when a medium muscle mass is working (see Fig. 30.3). This response results from the combination of a small, dilated active muscle mass with powerful central sympathetic vasoconstrictor drive. Typically, the arms exemplify a medium muscle mass; shoveling snow is a good example of primarily arm and heavily isometric exercise. Shoveling snow can be risky for people in danger of stroke or heart attack because it substantially raises systemic arterial pressure. The elevated pressure places compromised cerebral arteries at risk and presents an ischemic or failing heart with a greatly increased afterload.

## Acute and Chronic Responses of the Heart and Blood Vessels to Exercise Differ

In acute dynamic exercise, vagal withdrawal and increases in sympathetic outflow elevate heart rate and contractility in proportion to exercise intensity (Table 30.4). Cardiac output is also aided in dynamic exercise by factors enhancing venous return. These include the "muscle pump," which compresses veins as muscles rhythmically contract, and the "respiratory pump," which increases breath-by-breath oscillations in intrathoracic pressure (see Chapter 18). The importance of these factors is clear in patients with heart transplants who lack extrinsic cardiac innervation. Stroke volume rises in cardiac transplant patients with increasing exercise intensity as a result of increased venous return that enhances cardiac preload. In addition, circulating epinephrine and norepinephrine from the adrenal medulla and norepinephrine from sympathetic nerve spillover augment heart rate and contractility.

Maximal dynamic exercise yields a maximal heart rate: further vagal blockade (e.g., via pharmacological means) cannot elevate heart rate further. Stroke volume, in contrast, reaches a plateau in moderate work and is unchanged as exercise reaches its maximum intensity (see Table 30.4). This plateau occurs in the face of ever-shortening filling time, testimony to the increasing effectiveness of the mechanisms that enhance venous return and those that promote cardiac contractility. Sympathetic stimulation decreases left ventricular volume and pressure at the onset of cardiac relaxation (as a result of increased ejection fraction), leading to more rapid ventricular filling early in diastole. This helps maintain stroke volume as diastole shortens. Even in untrained individuals, the ejection fraction (stroke volume as a percentage of end-diastolic volume) reaches 80% in strenuous exercise.

The increased blood pressure, heart rate, stroke volume, and cardiac contractility seen in exercise all increase myocardial oxygen demands. These demands are met by a linear increase in coronary blood flow during exercise that can reach a value 5 times the basal level. This increase in flow is driven by local, metabolically linked factors (nitric oxide, adenosine, and the activation of ATP-sensitive $K^+$ channels) acting on coronary resistance vessels in defiance of sympathetic vasoconstrictor tone. Coronary oxygen extraction, high at rest, increases further with exercise (up to 80% of delivered oxygen). In healthy people, there is no evidence of myocardial ischemia under any exercise condition, and there may be a coronary vasodilator reserve in even the most intense exercise (Clinical Focus Box 30.1).

Over longer periods of time, the heart adapts to exercise overload much as it does to high-demand pathological states: by increasing left ventricular volume when exercise requires high blood flow, and by left ventricular hypertrophy when exercise creates high systemic arterial pressure (high afterload). Consequently, the hearts of individuals adapted to prolonged, rhythmic exercise that involves relatively low arterial pressure exhibit large left ventricular

**TABLE 30.4** **Acute Cardiac Response to Graded Exercise in a 30-Year-Old Untrained Woman**

| Exercise Intensity | Oxygen Uptake (L/min) | Heart Rate (beats/min) | Stroke Volume (mL/beat) | Cardiac Output (L/min) |
|---|---|---|---|---|
| Rest | 0.25 | 72 | 70 | 5 |
| Walking | 1.0 | 110 | 90 | 10 |
| Jogging | 1.8 | 150 | 100 | 15 |
| Running fast | 2.5 | 190 | 100 | 19 |

## CLINICAL FOCUS BOX 30.1

### Stress Testing

To detect coronary artery disease, physicians often record an electrocardiogram (ECG), but at rest, many disease sufferers have a normal ECG. To increase demands on the heart and coronary circulation, an ECG is performed while the patient walks on a treadmill or rides a stationary bicycle. It is sometimes called a **stress test**.

Exercise increases the heart rate and the systemic arterial blood pressure. These changes increase cardiac work and the demand for coronary blood flow. In many patients, coronary blood flow is adequate at rest, but because of coronary arterial blockage, cannot rise sufficiently to meet the increased demands of exercise. During a stress test, specific ECG changes can indicate that cardiac muscle is not receiving sufficient blood flow and oxygen delivery.

As heart rate increases during exercise, the distance between any portion of the ECG (for example, the R wave) on the ECG becomes shorter (Fig. 30.A and 30.B). In patients suffering from ischemic heart disease, however, other changes occur. Most common is an abnormal depression between the S and T waves, known as ST segment depression (see Fig. 30.B). Depression of the ST segment arises from changes in cardiac muscle electrical activity secondary to lack of blood flow and oxygen delivery.

During the stress test, the ECG is continuously analyzed for changes while blood pressure and arterial blood oxygen saturation are monitored. At the start of the test, the exercise load is mild. The load is increased at regular intervals, and the test ends when the patient becomes exhausted, the heart rate safely reaches a maximum, significant pain occurs, or abnormal ECG changes are noted. With proper supervision, the stress test is a safe method for detecting coronary artery disease. Because the exercise load is gradually increased, the test can be stopped at the first sign of problems.

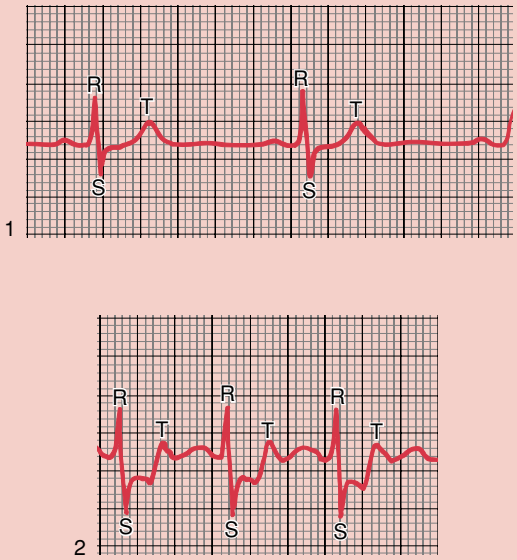


**FIGURE 30.A Effect of exercise on the electrocardiogram (ECG) in a patient with ischemic heart disease.** 1, The ECG is normal at rest. 2, During exercise, the interval between R waves is reduced, and the ECG segment between the S and T waves is depressed.

volumes with normal wall thickness, while wall thickness is increased at normal volume in those adapted to activities involving isometric contraction and greatly elevated arterial pressure, such as lifting weights.

The larger left ventricular volume in people chronically active in dynamic exercise leads directly to larger resting and exercise stroke volume. A simultaneous increase in vagal tone and decrease in β-adrenergic sensitivity enhance the resting and exercise bradycardia seen after training, so that in effect the trained heart operates further up the ascending limb of its length-tension relationship (see Fig. 10.3). Nonetheless, resting bradycardia is a poor index of endurance fitness because genetic factors explain a much larger proportion of the individual variation in resting heart rate than does training.

The effects of endurance training on coronary blood flow are partly mediated through changes in myocardial oxygen uptake. Since myocardial oxygen consumption is roughly proportional to the rate-pressure product (heart rate × mean arterial pressure), and since heart rate falls after training at any absolute exercise intensity, coronary flow at a fixed submaximal workload is reduced in parallel. The peak coronary blood flow is, however, increased by training, as are cardiac muscle capillary density and peak capillary exchange capacity. Training also improves endothelium-mediated regulation, responsiveness to adenosine, and control of intracellular free calcium ions within coronary vessels. Preserving endothelial vasodilator function may be the primary benefit of chronic physical activity on the coronary circulation.

## The Blood Lipid Profile Is Influenced by Exercise Training

Chronic, dynamic exercise is associated with increased circulating levels of high-density lipoproteins (HDLs) and reduced low-density lipoproteins (LDLs), such that the ratio of HDL to total cholesterol is increased. These changes in cholesterol fractions occur at any age if exercise is regular. Weight loss and increased insulin sensitivity, which typically accompany increased chronic physical activity in sedentary individuals, undoubtedly contribute to these changes in plasma lipoproteins. Nonetheless, in people with lipoprotein levels that place them at high risk for coronary heart disease, exercise appears to be an essential adjunct to dietary restriction and weight loss for lowering

LDL cholesterol levels. Because exercise acutely and chronically enhances fat metabolism and cellular metabolic capacities for β-oxidation of free fatty acids, it is not surprising that regular activity increases both muscle and adipose tissue lipoprotein lipase activity. Changes in lipoprotein lipase activity, in concert with increased lecithin-cholesterol acyltransferase activity and apo A-I synthesis, enhance the levels of circulating HDLs.

### Exercise Has a Role in Preventing and Recovering From Several Cardiovascular Diseases

Changes in the ratio of HDL to total cholesterol that take place with regular physical activity reduce the risk of atherogenesis and coronary artery disease in active people, as compared with those who are sedentary. A lack of exercise is now established as a risk factor for coronary heart disease similar in magnitude to hypercholesterolemia, hypertension, and smoking. A reduced risk grows out of the changes in lipid profiles noted above, reduced insulin requirements and increased insulin sensitivity, and reduced cardiac β-adrenergic responsiveness and increased vagal tone. When coronary ischemia does occur, increased vagal tone may reduce the risk of fibrillation.

Regular exercise often, but not always, reduces resting blood pressure. Why some people respond to chronic activity with a resting blood pressure decline and others do not remains unknown. Responders typically show diminished resting sympathetic tone, so that systemic vascular resistance falls. In obesity-linked hypertension, declining insulin secretion and increasing insulin sensitivity with exercise may explain the salutary effects of combining training with weight loss. Nonetheless, because some obese people who exercise and lose weight show no blood pressure changes, exercise remains adjunctive therapy for hypertension.

### Pregnancy Shares Many Cardiovascular Characteristics With the Trained State

The physiological demands and adaptations of pregnancy in some ways are similar to those of chronic exercise. Both of them increase blood volume, cardiac output, skin blood flow, and caloric expenditure. Exercise clearly has the potential to be deleterious to the fetus. Acutely, it increases body core temperature, causes splanchnic (hence, uterine and umbilical) vasoconstriction, and alters the endocrinological milieu; chronically, it increases caloric requirements. This last demand may be devastating if food shortages exist: the superimposed caloric demands of successful pregnancy and lactation are estimated at 80,000 kcal. Given adequate nutritional resources, however, there is little evidence of other damaging effects of maternal exercise on fetal development. The failure of exercise to harm well-nourished pregnant women may relate in part to the increased maternal and fetal mass and blood volume, which reduces specific heat loads, moderates vasoconstriction in the uterine and umbilical circulations, and diminishes the maternal exercise capacity.

At least in previously active women, even the most intense concurrent exercise regimen (unless associated with excessive weight loss) does not alter fertility, implantation, or embryogenesis, although the combined effects of exercise on insulin sensitivity and central obesity can restore ovulation in anovulatory obese women suffering from polycystic ovary disease.

Regular exercise may reduce the risk of spontaneous abortion of a chromosomally normal fetus. Continued exercise throughout pregnancy characteristically results in normal-term infants after relatively brief labor. These infants are usually normal in length and lean body mass but reduced in fat. The risk of large infant size for gestational age, increased in diabetic mothers, is reduced by maternal exercise through improved glucose tolerance. The incidence of umbilical cord entanglement, abnormal fetal heart rate during labor, stained amniotic fluid, and low fetal responsiveness scores may all be reduced in women who are active throughout pregnancy. Further, when examined 5 days after birth, newborns of exercising women perform better in their ability to orient to environmental stimuli and their ability to quiet themselves after sound and light stimuli than weight-matched children of nonexercising mothers.

## RESPIRATORY RESPONSES

Increased breathing is perhaps the single most obvious physiological response to acute dynamic exercise. Figure 30.4 shows that minute ventilation (the product of breathing frequency and tidal volume) initially rises linearly with work intensity and then supralinearly beyond that point. Ventilation of the lungs in exercise is linked to the twin goals of oxygen intake and carbon dioxide removal.

### Ventilation in Exercise Matches Metabolic Demands, but the Exact Control Mechanisms Is Unknown

Exercise increases oxygen consumption and carbon dioxide production by working muscles, and the pulmonary response is precisely calibrated to maintain homeostasis of these gases in arterial blood. In mild or moderate work, ar-


**FIGURE 30.4** **The dependence of minute ventilation on the intensity of dynamic exercise.** Ventilation rises linearly with intensity until exercise nears maximal levels.

terial $P_{O_2}$ (and, hence, oxygen content), $P_{CO_2}$, and pH all remain unchanged from resting levels (Table 30.5). The respiratory muscles accomplish this severalfold increase in ventilation primarily by increasing tidal volume, without provoking sensations of dyspnea.

More intense exercise presents the lungs with tougher challenges. Near the halfway point from rest to maximal dynamic work, lactic acid formed in working muscles begins to appear in the circulation. This point, which depends on the type of work involved and the person's training status, is called the **lactate threshold**. Lactate concentration gradually rises with work intensity, as more and more muscle fibers must rely on anaerobic metabolism. Almost fully dissociated, lactic acid causes metabolic acidosis. During exercise, healthy lungs respond to lactic acidosis by further increasing ventilation, lowering the arterial $P_{CO_2}$, and maintaining arterial blood pH at normal levels; it is the response to acidosis that spurs the supralinear ventilation rise seen in strenuous exercise (see Fig. 30.4). Through a range of exercise levels, the pH effects of lactic acid are fully compensated by the respiratory system; however, eventually in the hardest work—near-exhaustion—ventilatory compensation becomes only partial, and both pH and arterial $P_{CO_2}$ may fall well below resting values (see Table 30.5). Tidal volume continues to increase until pulmonary stretch receptors limit it, typically at or near half of vital capacity. Frequency increases at high tidal volume produce the remainder of the ventilatory volume increases.

Hyperventilation relative to carbon dioxide production in heavy exercise helps maintain arterial oxygenation. The blood returned to the lungs during exercise is more thoroughly depleted of oxygen because active muscles with high oxygen extraction receive most of the cardiac output. Because the pulmonary arterial $P_{O_2}$ is reduced in exercise, blood shunted past ventilated areas can profoundly depress systemic arterial oxygen content. Other than having a diminished oxygen content, pulmonary arterial blood flow (cardiac output) rises during exercise. In compensation, ventilation rises faster than cardiac output: The ventilation-perfusion ratio of the lung rises from near 1 at rest to greater than 4 with strenuous exercise (see Table 30.5). Healthy people maintain nearly constant arterial $P_{O_2}$ with acute exercise, although the alveolar-to-arterial $P_{O_2}$ gradient does rise. This increase shows that, despite the increase in the ventilation-perfusion ratio, areas of relative pulmonary underventilation and, possibly, some mild diffusion limitation exist even in highly trained, healthy individuals.

The ventilatory control mechanisms in exercise remain undefined. Where there are stimuli—such as in mixed venous blood, which is hypercapnic and hypoxic in proportion to exercise intensity—there are seemingly no receptors. Conversely, where there are receptors—the carotid bodies, the lung parenchyma or airways, the brainstem bathed by cerebrospinal fluid—no stimulus proportional to the exercise demand exists. Paradoxically, the central chemoreceptor is immersed in increasing alkalinity as exercise intensifies, a consequence of blood-brain barrier permeability to $CO_2$ but not hydrogen ions. Perhaps exercise respiratory control parallels cardiovascular control, with a central command proportional to muscle activity directly stimulating the respiratory center and feedback modulation from the lung, respiratory muscles, chest wall mechanoreceptors, and carotid body chemoreceptors.

## The Respiratory System Is Largely Unchanged by Training

The effects of training on the pulmonary system are minimal. Lung diffusing capacity, lung mechanics, and even lung volumes change little, if at all, with training. The widespread assumption that training improves vital capacity is false; even exercise designed specifically to increase inspiratory muscle strength elevates vital capacity by only 3%. The demands placed on respiratory muscles increase their endurance, an adaptation that may reduce the sensation of dyspnea in exercise. Nonetheless, the primary respiratory changes with training are secondary to lower lactate production that reduces ventilatory demands at previously heavy absolute work levels.

## In Lung Disease, Respiratory Limitations May Be Evidenced by Shortness of Breath or Decreased Oxygen Content of Arterial Blood

Any compromise of lung or chest wall function is much more apparent during exercise than at rest. One hallmark of lung disease is **dyspnea** (difficult or labored breathing) during exertion, when this exertion previously was unproblematic. Restrictive lung diseases limit tidal volume, reducing the ventilatory reserve volumes and exercise capacity. Obstructive lung diseases increase the work of breathing, exaggerating dyspnea and limiting work output. Lung diseases that compromise oxygen diffusion from alveolus to blood exaggerate exercise-induced widening of the alveolar-to-arterial $P_{O_2}$ gradient. This effect contributes to po-

**TABLE 30.5 Acute Respiratory Response to Graded Dynamic Exercise in a 30-Year-Old Untrained Woman**

| Ventilation Exercise Intensity | Ventilation-(L/min) | Alveolar $P_{O_2}$ Perfusion Ratio | Arterial $P_{O_2}$ (mm Hg) | Arterial $P_{CO_2}$ (mm Hg) | Arterial pH (mm Hg) | |
|---|---|---|---|---|---|---|
| Rest | 5 | 1 | 103 | 100 | 40 | 7.40 |
| Walking | 20 | 2 | 103 | 100 | 40 | 7.40 |
| Jogging | 45 | 3 | 106 | 100 | 36 | 7.40 |
| Running fast | 75 | 4 | 110 | 100 | 25 | 7.32 |

**CLINICAL FOCUS BOX 30.2**

**Exercise in Patients with Emphysema**

Normally, the respiratory system does not limit exercise tolerance. In healthy individuals, arterial blood saturation with oxygen, which averages 98% at rest, is maintained at or near 98% in even the most strenuous dynamic or isometric exercise. The healthy response includes the ability to augment ventilation more than cardiac output; the resulting rise in the ventilation-perfusion ratio counterbalances the falling oxygen content of mixed venous blood.

In patients with **emphysema**, ventilatory limitations to exercise occur long before ceilings are imposed by either skeletal muscle oxidative capacity or by the ability of the cardiovascular system to deliver oxygen to exercising muscle. These limitations are manifest during a stress test on the basis of three primary measurements. First, patients with ventilatory limitations typically cease exercise at relatively low heart rate, indicating that exhaustion is due to factors unrelated to cardiovascular limitations. Second, their primary complaint is usually shortness of breath, or dyspnea. In fact, patients with chronic obstructive pulmonary disease often first seek medical evaluation because of dyspnea experienced during such routine activities as climbing a flight of stairs. In healthy people, exhaustion is rarely associated solely with dyspnea. In emphysematous patients, exercise-induced dyspnea results, in part, from respiratory muscle fatigue exacerbated by diaphragmatic flattening brought on by loss of lung elastic recoil. Third, in emphysematous patients, arterial oxygen saturation will characteristically fall steeply and progressively with increasing exercise, sometimes reaching dangerously low levels. In emphysema, the inability to fully oxygenate blood at rest is compounded during exercise by increased pulmonary blood flow, and by increased exercise oxygen extraction that more fully desaturates blood returning to the lungs.

tentially dangerous systemic arterial hypoxia during exercise. The signs and symptoms of a respiratory limitation to exercise include exercise cessation with low maximal heart rate, oxygen desaturation of arterial blood, and severe shortness of breath (Clinical Focus Box 30.2). The prospects of training-based rehabilitation are modest, although locomotor muscle-based adaptations can reduce lactate production and ventilatory demands in exercise. Specific training of respiratory muscles to increase their strength and endurance is of minimal benefit to patients with compromised lung function.

Exercise causes bronchoconstriction in nearly every asthmatic patient and is the sole provocative agent for asthma in many people. In healthy individuals, catecholamine release from the adrenal medulla and sympathetic nerves dilates the airways during exercise. Sympathetic bronchodilation in people with asthma is outweighed by constrictor influences, among them heat loss from airways (cold, dry air is a potent bronchoconstrictor), release of inflammatory mediators, and increases in airway tissue osmolality. Leukotriene-receptor antagonists block exercise-induced symptoms in most people. The effects of exercise on airways are due to increased ventilation per se; the exercise is incidental. Individuals with exercise-induced bronchoconstriction are simply the most sensitive people along a continuum; for example, breathing high volumes of cold, dry air provokes at least mild bronchospasm in everyone.

## MUSCLE AND BONE RESPONSES

Events within exercising skeletal muscle are a primary factor in fatigue. These same events, when repeated during training, lead to adaptations that increase exercise capacity and retard fatigue during similar work. Skeletal muscle contraction also increases stresses placed on bone, leading to specific bone adaptations.

### Muscle Fatigue Is Independent of Lactic Acid

Although strenuous exercise can reduce intramuscular pH to values as low as 6.8 (arterial blood pH may fall to 7.2), there is little evidence that elevations in hydrogen ion concentration are the sole cause of fatigue. The best correlate of fatigue in healthy individuals is ADP accumulation in the face of normal or slightly reduced ATP, such that the ADP/ATP ratio is very high. Because the complete oxidation of glucose, glycogen, or free fatty acids to carbon dioxide and water is the major source of energy in prolonged work, people with defects in glycolysis or electron transport exhibit a reduced ability to sustain exercise.

These metabolic defects are distinct from another group of disorders exemplified by the various muscular dystrophies. In these illnesses, the loss of active muscle mass as a result of fat infiltration, cellular necrosis, or atrophy reduces exercise tolerance despite normal capacities (in healthy fibers) for ATP production. It is unclear whether fatigue in health ever occurs centrally (pain from fatigued muscle may feed back to the brain to lower motivation and, possibly, to reduce motor cortical output) or at the level of the motor neuron or the neuromuscular junction.

### Endurance Activity Enhances Muscle Oxidative Capacity

Within skeletal muscle, adaptations to training are specific to the form of muscle contraction. Increased activity with low loads results in increased oxidative metabolic capacity without hypertrophy; increased activity with high loads produces muscle hypertrophy. Increased activity without overload increases capillary and mitochondrial density, myoglobin concentration, and virtually the entire enzymatic machinery for energy production from oxygen (Table 30.6). Coordination of energy-producing and energy-utilizing systems in muscle ensures that even after atrophy the remaining contractile proteins are adequately

**TABLE 30.6 Effects of Training and Immobilization on the Human Biceps Brachii Muscle in a 22-Year-Old Woman**

| | After Strength Training | After 4 Months Immobilization | Sedentary | After Endurance Training |
|---|---|---|---|---|
| Total number of cells | 300,000 | 300,000 | 300,000 | 300,000 |
| Total cross-sectional area ($cm^2$) | 10 | 10 | 13 | 6 |
| Isometric strength (% control) | 100 | 100 | 200 | 60 |
| Fast-twitch fibers (% by number) | 50 | 50 | 50 | 50 |
| Fast-twitch fibers, average area ($\mu m^2 \times 10^2$) | 67 | 67 | 87 | 40 |
| Capillaries/fiber | 0.8 | 1.3 | 0.8 | 0.6 |
| Succinate dehydrogenase activity/unit area (% control) | 100 | 150 | 77 | 100 |

Modified from Gollnick PD, Saltin B. Skeletal muscle physiology. In: Teitz CC, ed. Scientific Foundations of Sports Medicine. Toronto: BC Decker, 1989;185–242.

supported metabolically. In fact, the easy fatigability of atrophied muscle is due to the requirement that more motor units be recruited for identical external force; the fatigability per unit cross-sectional area is normal. The magnitude of the skeletal muscle endurance training response is limited by factors outside the muscle, since cross-innervation or chronic stimulation of muscles in animals can produce adaptations 5 times larger than those created by the most intense and prolonged exercise.

Local adaptations of skeletal muscle to endurance activity reduce reliance on carbohydrate as a fuel and allow more metabolism of fat, prolonging endurance and decreasing lactic acid accumulation. Decreased circulating lactate, in turn, reduces the ventilatory demands of heavier work. Because metabolites accumulate less rapidly inside trained muscle, there is reduced chemosensory feedback to the central nervous system at any absolute workload. This reduces sympathetic outflow to the heart and blood vessels, reducing cardiac oxygen demands at a fixed exercise level.

## Muscle Hypertrophies in Response to Eccentric Contractions

Everyone knows it is easier to walk downhill than uphill, but the mechanisms underlying this commonplace phenomenon are complex. Muscle forces are identical in the two situations. However, moving the body uphill against gravity involves muscle shortening, or **concentric contractions**. In contrast, walking downhill primarily involves muscle tension development that resists muscle lengthening, or **eccentric contractions**. All routine forms of physical activity, in fact, involve combinations of concentric, eccentric, and isometric contractions. Because less ATP is required for force development during a contraction when external forces lengthen the muscle, the number of active motor units is reduced and energy demands are less for eccentric work. However, perhaps because the force per active motor unit is greater in eccentric exercise, eccentric contractions can readily cause muscle damage. These include weakness (apparent the first day), soreness and edema (delayed 1 to 3 days in peak magnitude), and elevated plasma levels of intramuscular enzymes (delayed 2 to 6 days). Histological evidence of damage may persist for 2 weeks. Damage is accompanied by an acute phase reaction that includes complement activation, increases in circulating cytokines, neutrophil mobilization, and increased monocyte cell adhesion capacity. Training adaptation to the eccentric components of exercise is efficient; soreness after a second episode is minimal if it occurs within two weeks of a first episode.

Eccentric contraction-induced muscle damage and its subsequent response may be the essential stimulus for muscle hypertrophy. While standard resistance exercise involves a mixture of contraction types, careful studies show that when one limb works purely concentrically and the other purely eccentrically at equivalent force, only the eccentric limb hypertrophies. The immediate changes in actin and myosin production that lead to hypertrophy are mediated at the posttranslational level; after a week of loading, mRNA for these proteins is altered. Although its precise role remains unclear, the activity of the 70-kDa S6 protein kinase is tightly linked with long-term changes in muscle mass. The cellular mechanisms for hypertrophy include the induction of insulin-like growth factor I, and upregulation of several members of the fibroblast growth factor family.

## Exercise Plays a Role in Calcium Homeostasis

Skeletal muscle contraction applies force to bone. Because the architecture of bone remodeling involves osteoblast and osteoclast activation in response to loading and unloading, physical activity is a major site-specific influence on bone mineral density and geometry. Repetitive physical activity can create excessive strain, leading to inefficiency in bone remodeling and stress fracture; however, extreme inactivity allows osteoclast dominance and bone loss.

The forces applied to bone during exercise are related both to the weight borne by the bone during activity and to the strength of the involved muscles. Consequently, bone strength and density appear to be closely related to applied gravitational forces and to muscle strength. This suggests that exercise programs to prevent or treat **osteoporosis** should emphasize weight-bearing activities and strength as well as endurance training. Adequate dietary calcium is essential for any exercise effect: weight-bearing activity enhances spinal bone mineral density in post-

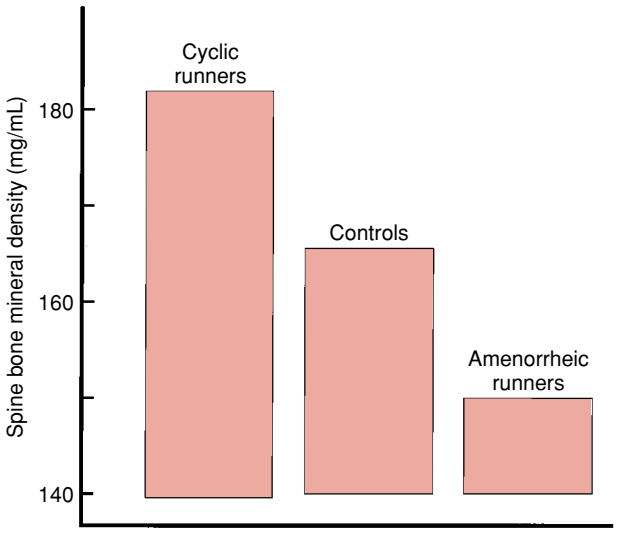


**FIGURE 30.5** **Exercise and bone density.** This graph shows spine bone density in young adult women who are nonathletes (controls), distance runners with regular menstrual cycles (cyclic runners), and distance runners with amenorrhea (amenorrheic runners). Differences from controls indicate the roles that exercise and estrogen play in determination of bone mineral density.

menopausal women only when calcium intakes exceed 1 g/day. Because exercise may also improve gait, balance, coordination, proprioception, and reaction time, even in older and frail persons, the risk of falls and osteoporosis are reduced by chronic activity. In fact, the incidence of hip fracture is reduced nearly 50% when older adults are involved in regular physical activity. However, even when activity is optimal, it is apparent that genetic contributions to bone mass are greater than exercise. Perhaps 75% of the population variance is genetic, and 25% is due to different levels of activity. In addition, the predominant contribution of estrogen to homeostasis of bone in young women is apparent when amenorrhea occurs secondary to chronic heavy exercise. These exceptionally active women are typically very thin and exhibit low levels of circulating estrogens, low trabecular bone mass, and a high fracture risk (Fig. 30.5).

Exercise also plays a role in the treatment of **osteoarthritis**. Controlled clinical trials find that appropriate, regular exercise decreases joint pain and degree of disability, although it fails to influence the requirement for anti-inflammatory drug treatment. In **rheumatoid arthritis**, exercise also increases muscle strength and functional capacity without increasing pain or medication requirements. Whether or not exercise alters disease progression in either rheumatoid arthritis or osteoarthritis is not known.

## GASTROINTESTINAL, METABOLIC, AND ENDOCRINE RESPONSES

The effects of exercise on gastrointestinal (GI) function remain poorly understood. However, chronic physical activity plays a major role in the control of obesity and type 2 diabetes mellitus.

### Exercise Can Modify the Rate of Gastric Emptying and Intestinal Absorption

Dynamic exercise must be strenuous (demanding more than 70% of the maximal oxygen uptake) to slow gastric emptying of liquids. Little is known of the neural, hormonal, or intrinsic smooth muscle basis for this effect. Although gastric acid secretion is unchanged by acute exercise of any intensity, nothing is known about the effects of exercise on other factors relevant to the development or healing of peptic ulcers. There is some evidence that strenuous postprandial dynamic exercise provokes gastroesophageal reflux by altering esophageal motility.

Chronic physical activity accelerates gastric emptying rates and small intestinal transit. These adaptive responses to chronically increased energy expenditure lead to more rapid processing of food and increased appetite. Animal models of hyperphagia show specific adaptations in the small bowel (increased mucosal surface area, height of microvilli, content of brush border enzymes and transporters) that lead to more rapid digestion and absorption; these same effects likely take place in humans rendered hyperphagic by regular physical activity.

Blood flow to the gut decreases in proportion to exercise intensity, as sympathetic vasoconstrictor tone rises. Water, electrolyte, and glucose absorption may be slowed in parallel, and acute diarrhea is common in endurance athletes during competition. However, these effects are transient, and malabsorption as a consequence of acute or chronic exercise does not occur in healthy people. While exercise may not improve symptoms or disease progression in inflammatory bowel disease, there is some evidence that repetitive dynamic exercise may reduce the risk for this illness.

Although exercise is often recommended as treatment for postsurgical ileus, uncomplicated constipation, or irritable bowel syndrome, little is known in these areas. However, chronic dynamic exercise does substantially decrease the risk for colon cancer, possibly via increases in food and fiber intake, with consequent acceleration of colonic transit.

### Chronic Exercise Increases Appetite Slightly Less Than Caloric Expenditure in Obese People

Obesity is common in sedentary societies. Obesity increases the risk for hypertension, heart disease, and diabetes and is characterized, at a descriptive level, as an excess of caloric intake over energy expenditure. Because exercise enhances energy expenditure, increasing physical activity is a mainstay of treatment for obesity.

The metabolic cost of exercise averages 100 kcal/mile walked. For exceptionally active people, exercise expenditure can exceed 3,000 kcal/day added to the basal energy expenditure, which for a 55-kg woman averages about 1,400 kcal/day. At high levels of activity, appetite and food intake match caloric expenditure (Fig. 30.6). The biological factors that allow this precise balance have never been defined. In obese people, modest increases in physical activity increase energy expenditure more than food intake, so progressive weight loss can be instituted if exercise can be regularized (see Fig. 30.6). This method of weight control is superior to dieting alone, since substantial caloric re-

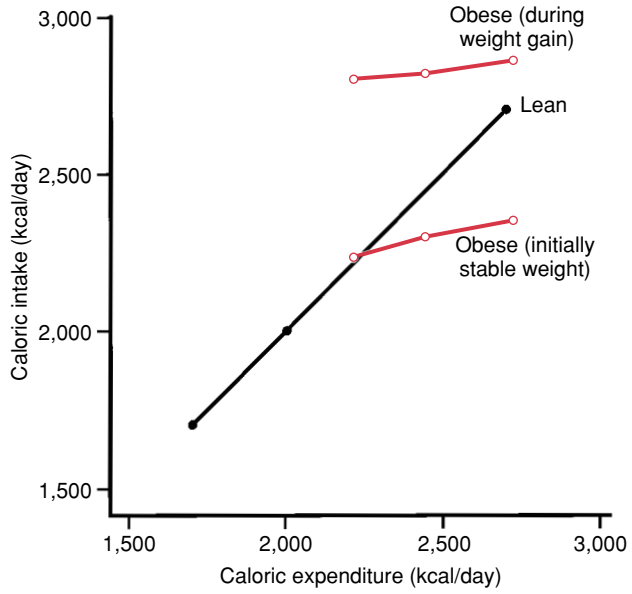


**FIGURE 30.6 Caloric intake as a function of exercise-induced increases in daily caloric expenditure.** For lean individuals, intake matches expenditure over a wide range. For obese individuals during periods of weight gain or periods of stable weight, increases in expenditure are not matched by increases in caloric intake. (Modified from Pi-Sunyer FX. Exercise effects on calorie intake. Annals NY Acad Sci 1987;499:94–103.)

striction (>500 kcal/day) results in both a lowered BMR and a substantial loss of fat-free body mass.

Exercise has other, subtler, positive effects on the energy balance equation as well. A single exercise episode may increase basal energy expenditure for several hours and may increase the thermal effect of feeding. The greatest practical problem remains compliance with even the most precise exercise "prescription"; patient dropout rates from even short-term programs typically exceed 50%.

## Acute and Chronic Exercise Increases Insulin Sensitivity, Insulin Receptor Density, and Glucose Transport into Muscle

Though skeletal muscle is omnivorous, its work intensity and duration, training status, inherent metabolic capacities, and substrate availability determine its energy sources. For very short-term exercise, stored phosphagens (ATP and creatine phosphate) are sufficient for crossbridge interaction between actin and myosin; even maximal efforts lasting 5 to 10 seconds require little or no glycolytic or oxidative energy production. When work to exhaustion is paced to be somewhat longer in duration, glycolysis is driven (particularly in fast glycolytic fibers) by high intramuscular ADP concentrations, and this form of anaerobic metabolism, with its by-product lactic acid, is the major energy source. The carbohydrate provided to glycolysis comes from stored, intramuscular glycogen or blood-borne glucose. Exhaustion from work in this intensity range (50 to 90% of the maximal oxygen uptake) is associated with carbohydrate depletion. Accordingly, factors that increase carbohydrate availability improve fatigue resistance. These include prior high dietary carbohydrate, cellular training adaptations that increase the enzymatic potential for fatty acid oxidation (thereby sparing carbohydrate stores), and oral carbohydrate intake during exercise. Frank hypoglycemia rarely occurs in healthy people during even the most prolonged or intense physical activity. When it does, it is usually in association with the depletion of muscle and hepatic stores and a failure to supplement carbohydrate orally.

Exercise suppresses insulin secretion by increasing sympathetic tone at the pancreatic islets. Despite acutely falling levels of circulating insulin, both non-insulin-dependent and insulin-dependent muscle glucose uptake increase during exercise. Exercise recruits glucose transporters from their intracellular storage sites to the plasma membrane of active skeletal muscle cells. Because exercise increases insulin sensitivity, patients with **type 1 diabetes** (insulin-dependent) require less insulin when activity increases. However, this positive result can be treacherous because exercise can accelerate hypoglycemia and increase the risk of insulin coma in these individuals. Chronic exercise, through its reduction of insulin requirements, up-regulates insulin receptors. This effect appears to be due less to training than simply to a repeated acute stimulus; the effect is full-blown after 2 to 3 days of regular physical activity and can be lost as quickly. Consequently, healthy active people show strikingly greater insulin sensitivity than do their sedentary counterparts (Fig. 30.7). In addition, up-

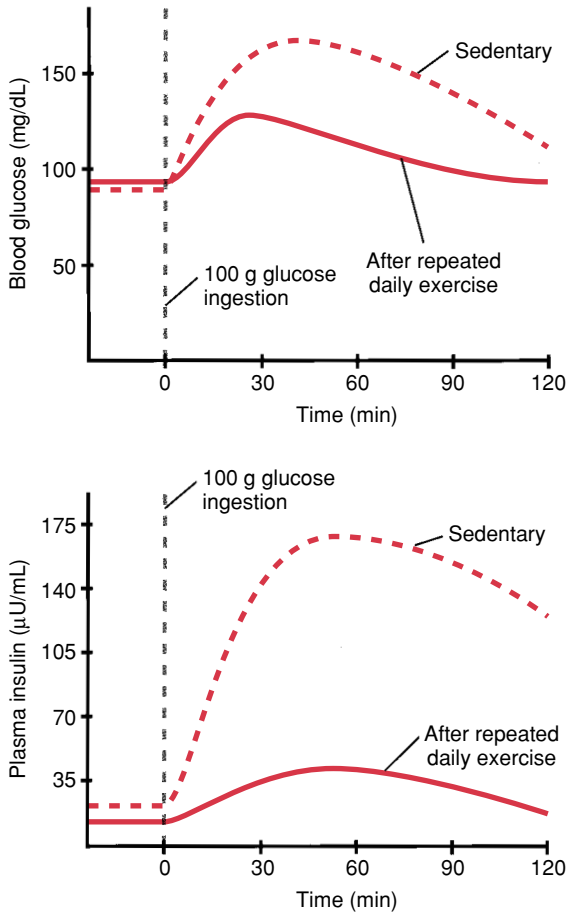


**FIGURE 30.7 Repeated daily exercise and the blood glucose and insulin response to glucose ingestion.** Both responses are blunted by repeated exercise, demonstrating increased insulin sensitivity.

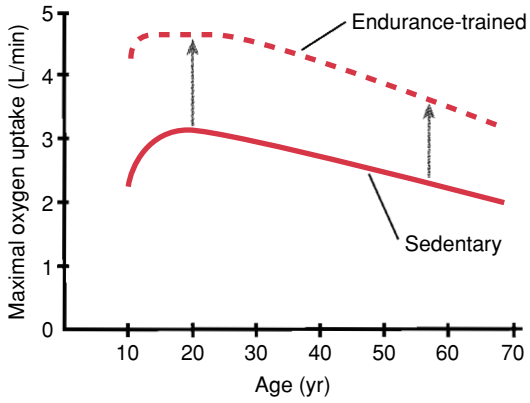


**FIGURE 30.8** **Maximal oxygen uptake, endurance training, and age.** Endurance-trained subjects possess greater maximal oxygen uptake than sedentary subjects, regardless of age.

regulation of insulin receptors and reduced insulin release after chronic exercise is ideal therapy in **type 2 diabetes** (non–insulin-dependent), a disease characterized by high insulin secretion and low receptor sensitivity. In persons with type 2 diabetes, a single episode of exercise results in substantial glucose transporter translocation to the plasma membrane in skeletal muscle.

## AGING, IMMUNE, AND PSYCHIATRIC RESPONSES

Maximal dynamic and isometric exercise capacities are lower at age 70 than at age 20. There is overwhelming evidence, however, that declines in strength and endurance with advancing age can be substantially mitigated by training. Changes in functional capacity, as well as protection against heart disease and diabetes, do increase longevity in active persons. However, it remains controversial if chronic exercise enhances lifespan, or if exercise boosts the immune system, prevents insomnia, or enhances mood.

### As People Age, the Effects of Exercise on Functional Capacity Are More Profound Than Their Effect on Longevity

The influence of exercise on strength and endurance at any age is dramatic. Although the ceiling for oxygen uptake during work gradually falls with age, the ability to train toward an age-appropriate ceiling is as intact at age 70 as it is at age 20 (Fig. 30.8). In fact, a highly active 70-year-old, otherwise healthy, will typically display an absolute exercise capacity greater than a sedentary 20-year-old. Aging affects all the links in the chain of oxygen transport and use, so aging-induced declines in lung elasticity, lung diffusing capacity, cardiac output, and muscle metabolic potential take place in concert. Consequently, the physiological mechanisms underlying fatigue are similar at all ages.

Regular dynamic exercise, compared with inactivity, increases longevity in rats and humans. In descriptive terms, the effects of exercise are modest; all-cause mortality is reduced, but only in amounts sufficient to increase longevity by 1 to 2 years. These facts leave open the possibility that exercise might alter biological aging. While physical activity increases cellular oxidative stress, it simultaneously increases antioxidant capacity. Food-restricted rats experience increased life span, and exhibit elevated spontaneous activity levels, but the role exercise may play in the apparent delay of aging in these animals remains unclear.

### Acute Exercise Transiently Alters Many Circulating Immune System Markers, but the Long-Term Effects of Training on Immune Function Are Unclear

In protein-calorie malnutrition, the catabolism of protein for energy lowers immunoglobulin levels and compromises the body's resistance to infection. Clearly, in this circumstance, exercise merely speeds the starvation process by increasing daily caloric expenditure and would be expected to diminish the immune response further. Nazi labor camps of the early 1940s became death camps, partly, by severe food restrictions and incessant demands for physical work—a combination guaranteed to cause starvation.

If nutrition is adequate, it is less clear whether adopting an active versus a sedentary lifestyle alters immune responsivity. In healthy people, an acute episode of exercise briefly increases blood leukocyte concentration and transiently enhances neutrophil production of microbicidal reactive oxygen species and natural killer cell activity. However, it remains unproven that regular exercise over time can lower the frequency or reduce the intensity of, for example, upper respiratory tract infections. In HIV-positive men and in men with AIDS and advanced muscle wasting, strength and endurance training yield normal gains. There is also incomplete evidence that training may slow progression to AIDS in HIV-positive men, with a corresponding increase in CD4 lymphocytes.

### Exercise May Help Relieve Depression, but Its Efficacy and Neurochemical Effects Are Uncertain

In healthy people, prolonged exercise increases subsequent deep sleep, defined as stages 3 and 4 of slow-wave sleep (see Chapter 7). This effect is apparently mediated entirely through the thermal effects of exercise, since equivalent passive heating produces the same result. Whether or not exercise can improve sleep in patients with insomnia is not known.

Clinical depression is characterized by sleep and appetite dysfunction and profound changes in mood. Whether acute or chronic exercise can help relieve depression remains unproven. The two most prominent biological theories of depression—the dysregulation of central monoamine activity and dysfunction of the hypothalamic-pituitary-adrenal axis—have received almost no study with regard to the impact of exercise.

Panic disorder patients, often characterized by agoraphobia, have reduced exercise capacity. Although sodium lactate infusion does provoke panic in these patients, the anxiety mediator appears to be hypernatremia, not lactate; even strenuous exercise with substantial lactic acidosis will not trigger panic attacks in these individuals.

## REVIEW QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered answer or completion that is BEST in each case.

1. In an effort to strengthen selected muscles after surgery and immobilization has led to muscle atrophy, isometric exercise is recommended. The intensity of isometric exercise is best quantified
   (A) Relative to the maximal oxygen uptake
   (B) As mild, moderate, or strenuous
   (C) As percentage of the maximum voluntary contraction
   (D) In terms of anaerobic metabolism
   (E) On the basis of the total muscle mass involved
2. Two people, one highly trained and one not, each exercising at 75% of the maximal oxygen uptake, become fatigued
   (A) For similar physiological reasons
   (B) Very slowly
   (C) At different times
   (D) While performing equally well for at least a short period of time
   (E) Despite much higher circulating lactic acid levels in the trained person
3. A patient completes a graded, dynamic exercise test on a treadmill while showing a modest rise (25%) in mean arterial blood pressure. In contrast, during the highest level of exercise at the end of the test, an indirect method shows that cardiac output has risen 300% from rest. These results indicate that during graded, dynamic exercise to exhaustion, systemic vascular resistance
   (A) Is constant
   (B) Rises slightly
   (C) Falls only if work is prolonged
   (D) Falls dramatically
   (E) Cannot be measured
4. A patient with inflammatory bowel disease and compromised kidney function asks if exercise will alter blood flow to either the gastrointestinal tract or to the kidneys. The answer is that vasoconstriction in both the renal and splanchnic vascular beds during exercise
   (A) Rarely occurs
   (B) Occurs only after prolonged training
   (C) Helps maintain arterial blood pressure
   (D) Allows renal and splanchnic flows to parallel cerebral blood flow
   (E) Will be balanced by local dilation in these vascular beds
5. A young, healthy, highly trained individual enters a marathon (40 km) run on a warm, humid day (32°C, 70% humidity). The best medical advice for this individual is to be concerned about the possibility for
   (A) Heat exhaustion
   (B) Coronary ischemia
   (C) Renal ischemia and anoxia
   (D) Hypertension
   (E) Gastric mucosal ischemia and increased risk for gastric ulceration
6. An individual with hypertension has been advised to increase physical activity. At the same time, this person has been counseled to avoid activities that substantially increase the systemic arterial blood pressure. In terms of dynamic exercise, this individual should avoid exercise that
   (A) Causes fatigue
   (B) Is prolonged
   (C) Uses untrained muscle groups
   (D) Is substituted for isometric exercise
   (E) Involves an intermediate muscle mass
7. In a patient with heart disease, a treadmill test involving graded dynamic exercise results in falling blood pressure at each exercise level. Eventually, faintness and dizziness cause termination of the test. These results arise from inadequate cardiac output during exercise because the baroreceptors, during exercise,
   (A) Reset blood pressure to a lower level
   (B) Are "turned off"
   (C) Are increased in sensitivity by training
   (D) Are decreased in sensitivity by training
   (E) Reset blood pressure to a higher level
8. A man with a family history of heart disease has both diabetes and hypertension. His total serum cholesterol is 270 mg/dL. In addition, his LDL cholesterol is elevated and his HDL cholesterol is reduced, compared with individuals with low cardiovascular disease risk. When exercise and diet are recommended, this individual asks what effect a long-term exercise program will have on the blood lipid profile. The answer is that exercise, over time, will
   (A) Have no independent effect on blood cholesterol levels
   (B) Elevate both HDL and LDL
   (C) Lower HDL and LDL, thereby lowering total cholesterol
   (D) Reduce risk of myocardial infarction despite elevated total cholesterol levels
   (E) Elevate HDL and lower LDL
9. A healthy individual, aged 60, completes a 500 m freestyle swim at an age-group competition. Breathing hard after the race, she explains that her increased ventilation is a normal response to heavy, dynamic exercise. Her increased ventilation results in
   (A) Clinically significant systemic arterial hypoxemia
   (B) Normal or reduced arterial $P_{CO_2}$
   (C) Respiratory alkalosis
   (D) Respiratory acidosis
   (E) Dizziness and decreased cerebral blood flow
10. A 33-year-old woman embarks on an extensive program of daily exercise, with both strenuous dynamic and isometric exercise included. After two years, her maximal voluntary contraction of many major muscle groups and her maximal oxygen uptake, are both increased 30%. Predictably, pulmonary function tests show
    (A) A 30% rise in vital capacity
    (B) No effect on lung elasticity, inspiratory or expiratory flow rates, or vital capacity
    (C) An increase in resting pulmonary diffusing capacity of 30 to 50%
    (D) A 25% increase in maximal forced expiratory flow rate
    (E) Decreases in residual volume and airways resistance at rest
11. In older adults at risk for falls, osteoporosis, and fractures, a program of weight-bearing exercise
    (A) Increases the risk of hip fracture
    (B) Decreases bone mineral density
    (C) Leaves gait, coordination, proprioception, and reaction time unaltered
    (D) Reduces the risk of osteoporosis, falls, and fractures
    (E) Is less valuable than dynamic exercise during water immersion
12. A 57-year-old woman, told that she is at risk for osteoporosis, starts an exercise class that emphasizes weight-bearing activities and development of muscle strength. She develops extensive muscle soreness after the first two sessions, indicating that the exercise that she performed
    (A) Involved isometric contractions
    (B) Produced muscle ischemia
    (C) Was actually most effective for increasing muscle endurance

*(continued)*

(D) Involved eccentric contractions
(E) Required at least 50% of the maximum voluntary contractile force

13. A high-school football player injures a knee early in the season. The knee requires immobilization for six weeks, after which time the athlete undergoes rehabilitation before joining the team. Immediately after rehabilitation begins, the individual notices that the flexors and extensors of the knee are much weaker than before the injury because during contraction at a fixed force
(A) Fewer motor units are involved
(B) There is a relative excess of contractile protein
(C) Muscle cells are small, so more cells are required to perform the same work
(D) Oxidative energy-producing systems are up-regulated
(E) Eccentric work is less, while concentric work is increased

14. A tenth-grade distance runner finishes in the top five of her statewide high school cross-country championships. Encouraged, she redoubles her training intensity, only to find that her menstrual periods cease for nearly a year. After finally visiting her doctor, her serum estrogen levels are found to be well below normal. In addition, it is predictable that this young woman will be found to have
(A) Dynamic exercise endurance less than an untrained person
(B) Weak leg muscles
(C) Normal body weight
(D) No risk for fractures as a result of her young age
(E) Low trabecular bone mass

15. A man with recently diagnosed type 2 diabetes asks for advice about exercise. His specific concern is the impact that an acute episode of exercise will have on his blood glucose levels and insulin requirements. He is correctly informed that during exercise, an important factor to consider is that
(A) Muscle glucose uptake decreases in patients with either type 1 or type 2 diabetes
(B) The pancreas will release increased amounts of both insulin and glucagon
(C) Muscle glucose uptake will increase only if endogenous or exogenous insulin levels rise
(D) Muscle glucose transporters will be translocated to the plasma membrane, increasing insulin-dependent and insulin-independent glucose uptake
(E) Insulin-independent glucose uptake is reduced in active muscles

16. A highly active woman is pregnant for the first time. She asks what benefits might ensue from continued physical activity during pregnancy. Which of the following is a predictable effect of chronic, dynamic exercise during pregnancy?
(A) Increased average gestational length
(B) Increased fetal weight at term
(C) Decreased risk of maternal gestational diabetes
(D) Increased risk of spontaneous abortion during the first trimester
(E) Decreased neonatal responsiveness scores

## SUGGESTED READING

Beck LH. Update in preventive medicine. Ann Intern Med 2001;134:128–135.
Berchtold MW, Brinkmeier H, Muntener M. Calcium ion in skeletal muscle: Its crucial role for muscle function, plasticity, and disease. Physiol Rev 2000;80:1215–1265.
Booth FW, Gordon SE, Carlson CJ, et al. Waging war on modern chronic diseases: Primary prevention through exercise biology. J Appl Physiol 2000;88:774–787.
Bray MS. Genomics, genes, and environmental interaction: the role of exercise. J Appl Physiol 2000;88:788–792.
Clapp JF 3rd. Exercise during pregnancy. A clinical update. Clin Sports Med 2000;19:273–286.
Fairfield WP, Treat M, Rosenthal DI, et al. Effects of testosterone and exercise on muscle leanness in eugonadal men with AIDS wasting. J Appl Physiol 2001;90:2166–2171.
Gielen S, Schuler G, Hambrecht R. Exercise training in coronary artery disease and coronary vasomotion. Circulation 2001;103:E1–E6.
Jones NL, Killian KJ. Exercise limitation in health and disease. N Engl J Med 2000;343:632–641.
Marcus R. Role of exercise in preventing and treating osteoporosis. Rheum Dis Clin North Am 2001;27:131–141.
Pedersen BK, Hoffman-Goetz L. Exercise and the immune system: regulation, integration, and adaptation. Physiol Rev 2000;80:1055–1081.
Peters HP, De Vries WR, Vanberge-Henegouwen GP, et al. Potential benefits and hazards of physical activity and exercise on the gastrointestinal tract. Gut 2001;48:435–439.
Ryder JW, Chibalin AV, Zierath JR. Intracellular mechanisms underlying increases in glucose uptake in response to insulin or exercise in skeletal muscle. Acta Physiol Scand 2001;171:249–257.

# CASE STUDIES FOR PART VIII • • •

## Case Study for Chapter 29

### *Heat Exhaustion with Dehydration*

A Michigan National Guard infantry unit was sent at the end of May to Louisiana for a field training exercise. Spring in Michigan was cool, but during the exercise in Louisiana, the temperature reached at least 30°C (86°F) every afternoon. At 3:30 PM on the second day of the exercise, a 70-kg infantryman became unsteady and, after a few more steps, sat on the ground. He told his comrades that he was dizzy and had a headache. When they urged him to drink from his canteen, he took a few swallows and said that he was sick in his stomach.

At the field aid station, he is observed to be sweating, his rectal temperature is 38.5°C, and his pulse is rapid. He appears dazed, and his answers to questions are coherent but slow. He cannot produce a urine sample. Blood samples are drawn, and an intravenous drip is started. The laboratory report shows serum [$Na^+$] of 156 mmol/L (normal range,135 to 145 mmol/L). Two liters of normal saline (0.9% NaCl) are infused over 45 minutes. Well before the end of the infusion, the patient is alert, his nausea disappears, and he asks for, and is given, water to drink. After the end of the infusion he is sent back to his unit with instructions to consume salt with dinner, drink at least three quarts of fluid before going to bed, and to return for follow-up in the morning.

***Questions***

**1.** What is the likely basis of the patient's nausea, which also contributes to his inability to produce a urine specimen?

2. If we assume that the patient's total body water was 36 L when he came for treatment, it can be shown that giving the patient 3 L of water without salt (by mouth and/or as an intravenous infusion of glucose in water) would reduce serum [$Na^+$] to 144 mmol/L. Such treatment would improve the patient's condition considerably. How might the medical officer argue the case for giving 2 L of normal saline?
3. What other (and relatively unusual) condition could produce the patient's symptoms? Did the medical officer rule this possibility out by appropriate means?

***Answers to Case Study Questions for Chapter 29***

1. The patient's nausea is probably a result of constriction of the splanchnic vascular beds, which is part of the homeostatic cardiovascular response that helps maintain cardiac output and blood pressure when central blood volume is reduced. Central blood volume, in turn, was reduced by the loss of body water and pooling of blood in the peripheral vascular beds. This homeostatic response also includes constriction of the renal vascular beds, which, in turn, contributes (along with the release of vasopressin and activation of the renin-angiotensin system) to scanty urine production.
2. Because the weather was cool back home, the patient probably was probably not acclimatized to heat and was not conserving salt in his sweat. He was probably secreting large amounts of sweat, and losing correspondingly large amounts of salt because of the weather and the activity involved in the exercise. If the patient returns to training the next morning without correcting the salt deficit, he is likely to have further difficulties in the heat. Even if the medical officer has guessed incorrectly about the patient's salt balance, a patient with normal renal function and adequate fluid intake should be able to excrete any excess salt resulting from the treatment.
3. Hyponatremia can produce symptoms similar to the patient's symptoms. However, the medical officer was able to exclude hyponatremia (although not necessarily some degree of salt deficit) on the basis of elevated serum [$Na^+$]. Giving a hyponatremic patient large volumes of fluid without an equivalent of salt (which would have been a reasonable alternative treatment for the patient in this example) would worsen the hyponatremia, perhaps to a dangerous degree.

***Reference***

Knochel JP. Clinical complications of body fluid and electrolyte balance. In: Buskirk ER, Puhl SM, eds. Body Fluid Balance: Exercise and Sport. Boca Raton, FL: CRC Press, 1996;297–317.

# Case Study for Chapter 30

## *A Patient With Dyspnea During Exercise*

A 56-year-old man complained of shortness of breath and chest pain when climbing stairs or mowing the lawn. He is subjected to a stress test, with noninvasive monitoring of heart rate, blood pressure, arterial blood oxygen saturation, and cardiac electrical activity. His resting heart rate is 73 beats/min; blood pressure, 118/75 mm Hg; arterial blood oxygen saturation, 96%; and the ECG, normal (Fig. 30.A, 1). After 3.5 minutes of increasingly intense exercise, the test is terminated because of the subject's severe dyspnea. His heart rate is 119 beats/min (his age and sex-adjusted predicted maximal heart rate is 168 beats/min), blood pressure is 146/76 mm Hg, arterial blood oxygen saturation is 88%, and the ECG is normal (Fig. 30.A, 2).

***Questions***

1. What are three lines of evidence for ventilatory limitation to this subject's exercise?
2. Why did arterial blood oxygen saturation fall during exercise?
3. Why did exhaustion occur before maximal heart rate was reached?
4. Why did the pulse pressure rise in exercise?
5. Why would endurance exercise training likely increase this individual's exercise capacity?

***Answers to Case Study Questions for Chapter 30***

1. Ventilatory limitation is evidenced by severe dyspnea as a primary symptom in exercise, falling arterial blood oxygenation, and exercise termination at relatively low heart rate.
2. Arterial blood oxygen saturation fell during exercise because increased cardiac output (increased pulmonary blood flow) and decreased pulmonary arterial blood oxygen content (a result of increased skeletal muscle oxygen extraction) increase demands for oxygenation in lungs with inadequate diffusing capacity.
3. Exhaustion occurred before a maximal heart rate was reached because lung disease creates severe dyspnea even in mild exercise.
4. The pulse pressure rose during exercise because sympathetic stimulation and enhanced venous return increase the stroke volume at constant arterial compliance.
5. Endurance exercise training would have little effect on any aspect of lung function. However, training would cause adaptations within exercising muscle that would increase muscle oxidative capacity and reduce lactic acid production. By reducing the ventilatory demands of exercise, these changes would increase exercise capacity in this individual.