CHAPTER

5

Introduction to Energy Transfer

CHAPTER OBJECTIVES

- Describe the first law of thermodynamics related to energy balance and work within biologic systems
- Define potential energy and kinetic energy and give examples of each
- Discuss the role of free energy in biologic work
- Give examples of exergonic and endergonic chemical reactions within the body and indicate their importance
- State the second law of thermodynamics and give a practical application of this law
- Discuss the role of coupled reactions in biologic processes
- Differentiate between photosynthesis and respiration and give the biologic significance of each
- Identify and give examples of the three forms of biologic work
- Describe how enzymes and coenzymes affect energy metabolism
- Differentiate between hydrolysis and condensation and explain their importance in physiologic function
- Discuss the role of redox chemical reactions in energy metabolism

The capacity to extract energy from the food macronutrients and continually transfer it at a high rate to the contractile elements of skeletal muscle determines one's capacity for swimming, running, or skiing long distances. Likewise, specific energy-transferring capacities that demand all-out, "explosive" power output for brief durations determine success in weightlifting, sprinting, jumping, and football line play. Although muscular activity represents the main frame of reference in this text, *all* forms of biologic work require power generated from the direct transfer of chemical energy.

The sections that follow introduce general concepts about bioenergetics that form the basis for understanding energy metabolism during physical activity.

ENERGY—THE CAPACITY FOR WORK

Unlike the physical properties of matter, one cannot define energy in concrete terms of size, shape, or mass. Rather the term *energy* reflects a dynamic state related to change; thus, energy emerges only when change occurs. Within this context, energy relates to the performance of work—as work increases so also does energy transfer and thus change. From a Newtonian (mechanical) perspective, work is the product of a given force acting through a given distance. In the body, cells more commonly accomplish chemical and electrical work than mechanical work. Because it is possible to exchange and convert energy from one form to another, we commonly express biologic work in mechanical units.

Bioenergetics refers to the flow and exchange of energy within a living system. The **first law of thermodynamics** describes a principle related to biologic work. Its basic tenet states that energy cannot be created or destroyed but transforms from one form to another without being depleted. In essence, this law describes the important **conservation of energy principle** that applies to both living and nonliving systems. In the body, chemical energy within the bonds of the macronutrients does not immediately dissipate as heat during energy metabolism; instead, a large portion remains as chemical energy, which the musculoskeletal system then changes into mechanical energy (and ultimately to heat energy). *The first law of thermodynamics dictates that the body does not produce, consume, or use up energy; instead it transforms it from one state into another as physiologic systems undergo continual change*.

INTEGRATIVE QUESTION

Based on the first law of thermodynamics, why is it imprecise to refer to energy "production" in the body?

Potential and Kinetic Energy

Potential energy *and* ***kinetic energy*** *constitute the total energy of a system.* FIGURE 5.1 shows potential energy as energy of position, similar to a boulder tottering atop a cliff or water

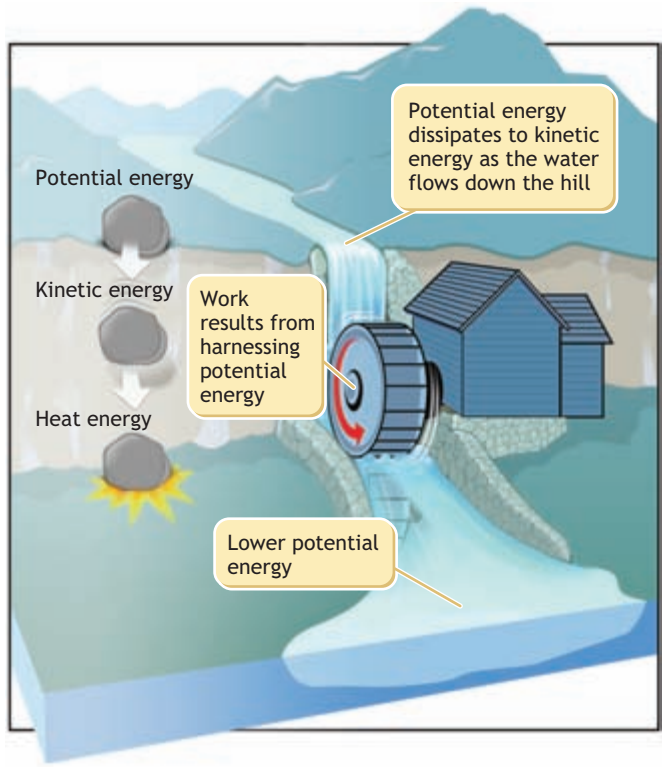


Figure 5.1 • High-grade potential energy capable of performing work degrades to a useless form of kinetic energy. In the example of falling water, the waterwheel harnesses potential energy to perform useful work. For the falling boulder, all of the potential energy dissipates to kinetic energy (heat) as the boulder crashes to the surface below.

before it flows downstream. In the example of flowing water, the energy change is proportional to the water's vertical drop—the greater the vertical drop, the greater the potential energy at the top. The waterwheel harnesses a portion of the energy from the falling water to produce useful work. In the case of the falling boulder, *all* potential energy transforms to kinetic energy and dissipates as unusable heat.

Other examples of potential energy include bound energy within the internal structure of a battery, a stick of dynamite, or a macronutrient before releasing its stored energy in metabolism. *Releasing potential energy transforms it into kinetic energy of motion*. In some cases, bound energy in one substance directly *transfers* to other substances to increase their potential energy. Energy transfers of this type provide the necessary energy for the body's chemical work of **biosynthesis**. In this process, specific building-block atoms of carbon, hydrogen, oxygen, and nitrogen become activated and join other atoms and molecules to synthesize important biologic compounds and tissues. Some newly created compounds provide structure as in bone or the lipid-containing plasma membrane that encloses each cell. Other synthesized compounds such as adenosine triphosphate (ATP) and phosphocreatine (PCr) serve the cell's energy requirements.

Energy-Releasing and Energy-Conserving Processes

The term **exergonic** describes any physical or chemical process that releases (frees) energy to its surroundings. Such reactions represent "downhill" processes because of a decline in free energy—"useful" energy for biologic work that encompasses all of the cell's energy-requiring, life-sustaining processes. Within a cell, where pressure and volume remain relatively stable, free energy (denoted by the symbol G to honor Willard Gibbs [1839–1903] whose research provided the foundation of biochemical thermodynamics) equals the potential energy within a molecule's chemical bonds (called *enthalpy,* or H) minus the energy unavailable because of randomness (S) times the absolute temperature (°C + 273). The equation $G = H - TS$ describes free energy quantitatively.

Chemical reactions that store or absorb energy are **endergonic**; these reactions represent "uphill" processes and proceed with an increase in free energy for biologic work. Exergonic processes sometimes link or *couple* with endergonic reactions to transfer some energy to the endergonic process. In the body, coupled reactions conserve in usable form a large portion of the chemical energy stored within the macronutrients.

FIGURE 5.2 illustrates the flow of energy in exergonic and endergonic chemical reactions. Changes in free energy occur when the bonds in the reactant molecules form new product molecules with different bonding. The equation that expresses these changes, under conditions of constant temperature, pressure, and volume, takes the following form:

$$\Delta G = \Delta H - T\Delta S$$

The symbol Δ designates change. The change in free energy represents a keystone of chemical reactions. In exergonic reactions, ΔG is negative; the products contain *less* free energy than the reactants, with the energy differential released as heat. For example, the union of hydrogen and oxygen to form water releases 68 kCal per mole (molecular weight of a substance in grams) of free energy in the following reaction:

$$H_2 + O \rightarrow H_2O - \Delta G\ 68\ \text{kCal} \cdot \text{mole}^{-1}$$

In the reverse endergonic reaction, ΔG remains positive because the product contains *more* free energy than the reactants. The infusion of 68 kCal of energy per mole of water causes the chemical bonds of the water molecule to split apart, freeing the original hydrogen and oxygen atoms. This "uphill" process of energy transfer provides the hydrogen and oxygen atoms with their original energy content to satisfy the principle of the first law of thermodynamics—*the conservation of energy*.

$$H_2 + O \leftarrow H_2O + \Delta G\ 68\ \text{kCal} \cdot \text{mole}^{-1}$$

Energy transfer in cells follows the same principles as those in the waterfall–waterwheel example. Carbohydrate, lipid, and protein macronutrients possess considerable potential energy within their chemical bonds. The formation of product substances progressively reduces the nutrient molecule's original potential energy with a corresponding increase in kinetic energy. Enzyme-regulated transfer systems harness or conserve a portion of this chemical energy in new compounds for use in biologic work. In essence, living cells serve as transducers with the capacity to extract and use chemical energy stored within a compound's atomic structure. Conversely, and equally important, cells also bond atoms and molecules together to raise them to a higher level of potential energy.

The transfer of potential energy in any spontaneous process always proceeds in a direction that *decreases* the capacity to perform work. The tendency of potential energy to degrade to kinetic energy of motion with a lower capacity for work (i.e., increased **entropy**) reflects the **second law of thermodynamics**. A flashlight battery provides a good illustration. The electrochemical energy stored within its cells slowly dissipates, even if the battery remains unused. The

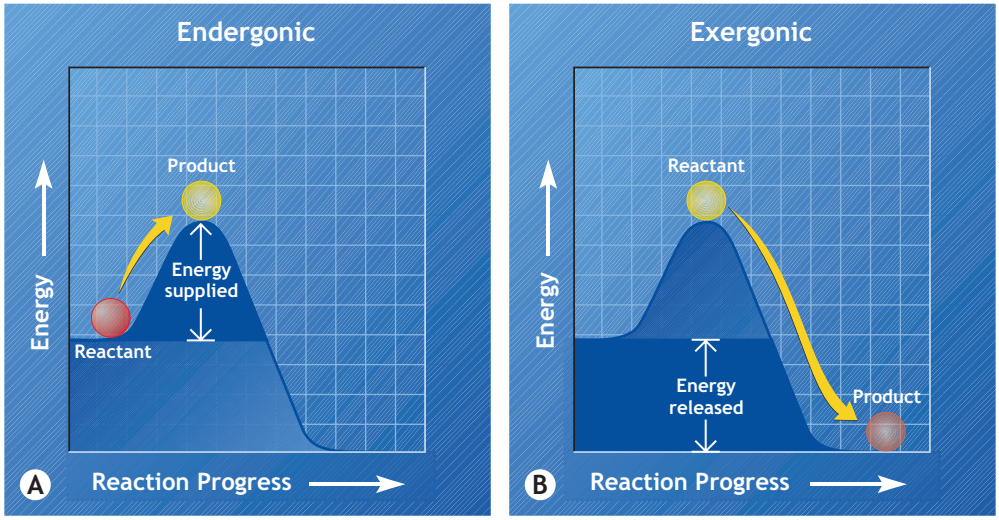


Figure 5.2 • Energy flow in chemical reactions. **A.** Energy supply prepares an endergonic reaction to proceed because the reaction's product contains *more* energy than the reactant. **B.** Exergonic reaction releases energy, resulting in *less* energy in the product than in the reactant.

energy from sunlight also continually degrades to heat energy when light strikes and becomes absorbed by a surface. Food and other chemicals represent excellent stores of potential energy, yet this energy continually decreases as the compounds decompose through normal oxidative processes. Energy, like water, always runs downhill so potential energy decreases. *Ultimately, all of the potential energy in a system degrades to the unusable form of kinetic or heat energy.*

INTERCONVERSIONS OF ENERGY

The total energy in an isolated system remains constant; a decrease in one form of energy matches an equivalent increase in another form. During energy conversions, a loss of potential energy from one source often produces a temporary increase in the potential energy of another source. In this way, nature harnesses vast quantities of potential energy for useful purposes. Even under such favorable conditions, the net flow of energy in the biologic world moves toward entropy, ultimately producing a *loss* of potential energy.

In 1877, Austrian physicist Ludwig Boltzmann (1844–1906) established the relationship between entropy and the statistical analysis of molecular motion. Entropy reflects the continual process of energy change. All chemical and physical processes proceed in a direction where total randomness or disorder *increases* and the energy available for work *decreases.* In coupled reactions during biosynthesis, part of a system may show a decrease in entropy while another part shows an increase. No way exists to circumvent the second law—the entire system always shows a net *increase* in

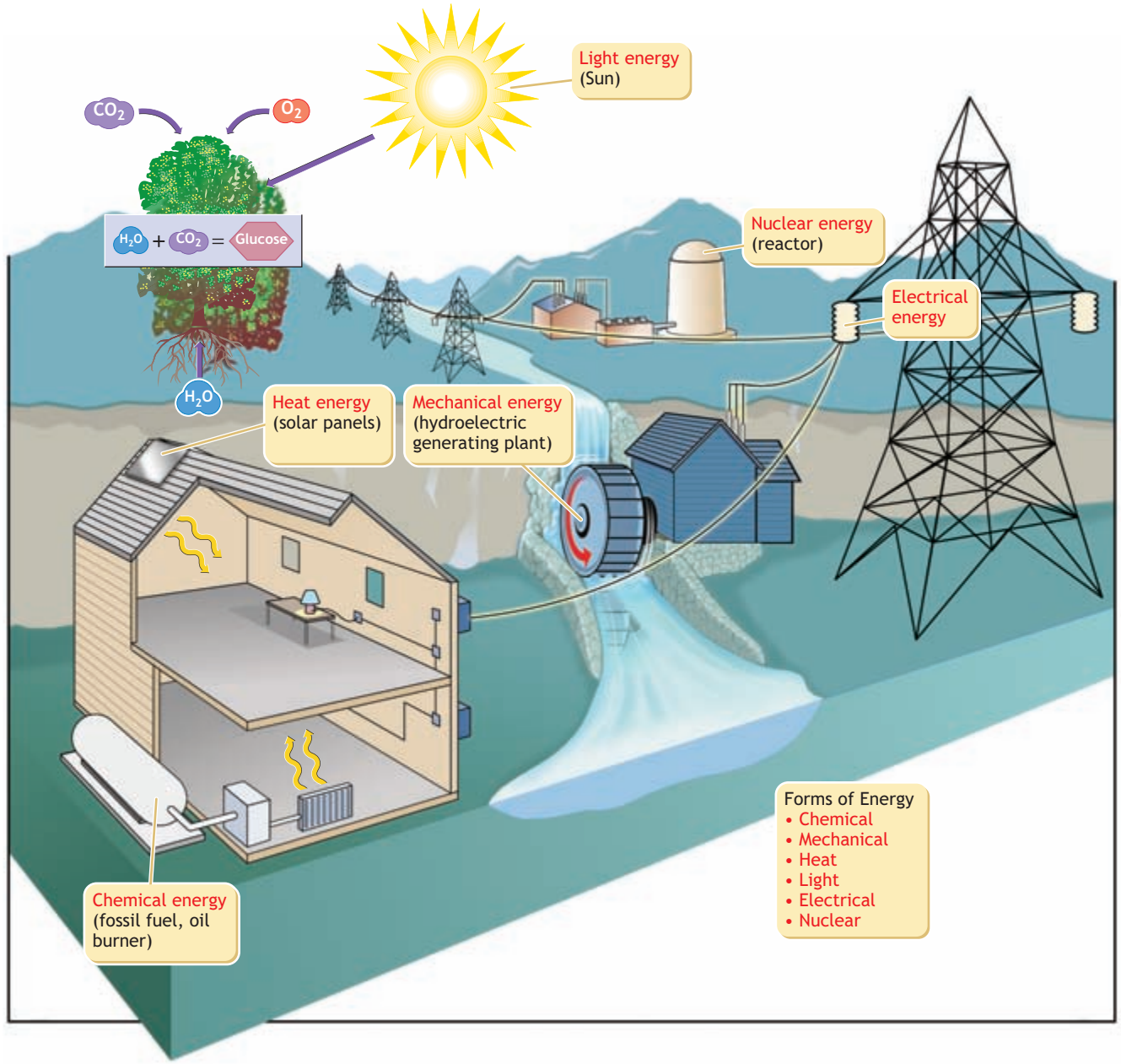


Figure 5.3 • Interconversions among six forms of energy.

entropy. In a more global sense, the biochemical reactions within the body's trillions of cells (as within the universe as a whole) "tilt" in the direction of spontaneity that favors disorder and randomness of an irreversible process (i.e., entropy) as originally theorized by Boltzmann.

Forms of Energy

FIGURE 5.3 shows energy categorized into one of six forms: chemical, mechanical, heat, light, electrical, and nuclear.

Examples of Energy Conversions

The conversion of energy from one form to another occurs readily in the inanimate and animate worlds. **Photosynthesis** and **respiration** represent the most fundamental examples of energy conversion in living cells.

Photosynthesis. In the sun, nuclear fusion releases part of the potential energy stored in the nucleus of the hydrogen atom. This energy, in the form of gamma radiation, then converts to radiant energy.

FIGURE 5.4 depicts the dynamics of photosynthesis, an endergonic process powered by energy from sunlight. The pigment chlorophyll, contained in large chloroplast organelles within the leaf's cells, absorbs radiant (solar) energy to synthesize glucose from carbon dioxide and water, while oxygen flows to the environment. The plant also converts carbohydrates to lipids and proteins for storage as a future reserve for energy and to sustain growth. Animals then ingest plant nutrients to serve their own energy and growth needs. *In essence, solar energy coupled with photosynthesis powers the animal world with food and oxygen.*

Respiration. FIGURE 5.5 shows the exergonic reactions of respiration, the reverse of photosynthesis, as the plant's stored energy is recovered for biologic work. In the presence of oxygen, the cells extract the chemical energy stored in the carbohydrate, lipid, and protein molecules. For glucose, respiration releases 689 kCal per mole (180 g) oxidized. *A portion of the energy released during cellular respiration is conserved in other chemical compounds for use in energy-requiring processes; the remaining energy flows to the environment as heat.*

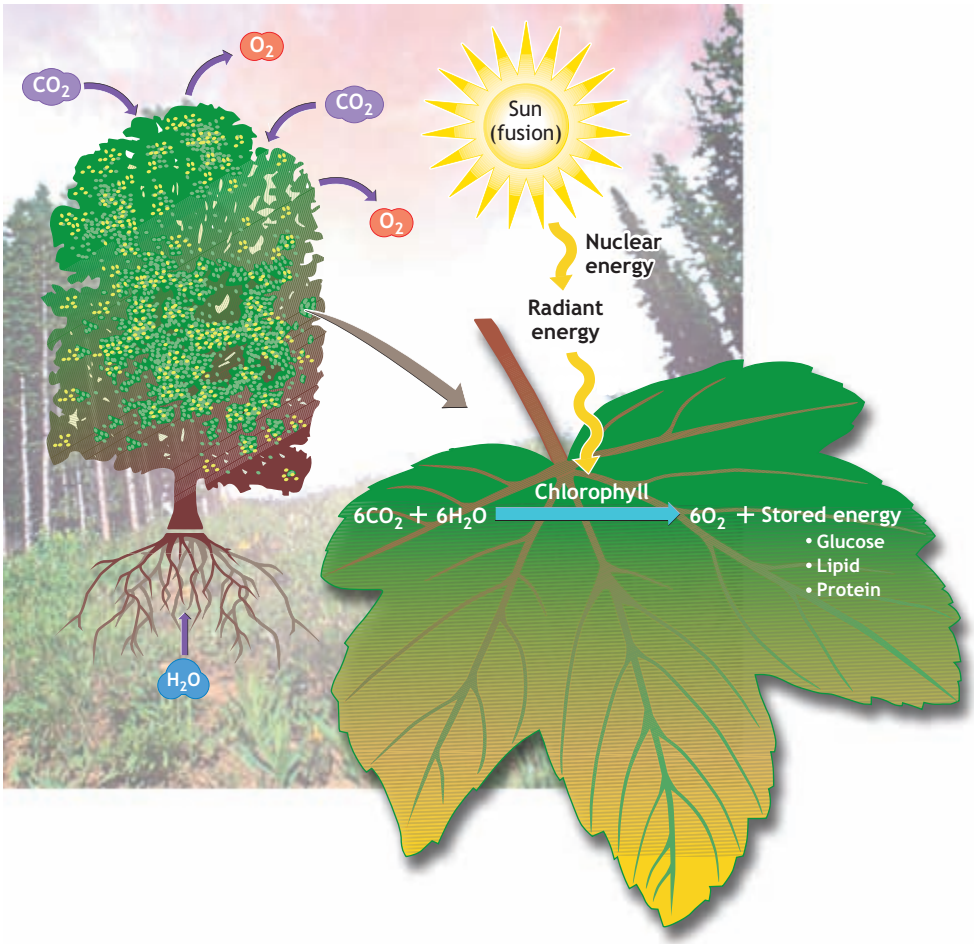


Figure 5.4 • The endergonic process of photosynthesis in plants, algae, and some bacteria serves as the mechanism to synthesize carbohydrates, lipids, and proteins. In this example, a glucose molecule forms when carbon dioxide binds with water with a positive free energy (useful energy) change ($+\Delta G$).

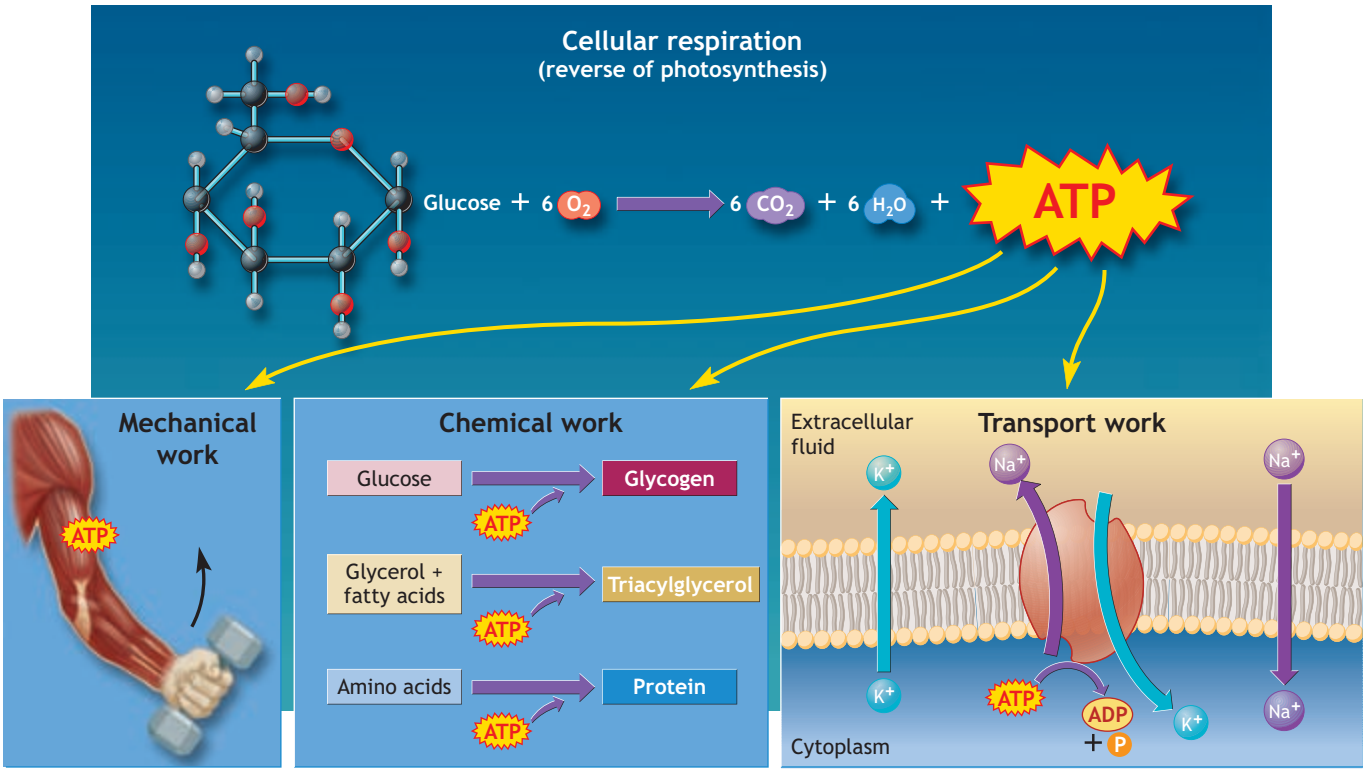


Figure 5.5 • The exergonic process of cellular respiration. Exergonic reactions, such as the burning of gasoline or the oxidation of glucose, release potential energy. This produces a negative standard free energy change (i.e., reduction in total energy available for work or $-\Delta G$). In this illustration, cellular respiration harvests the potential energy in food to form ATP. Subsequently, the energy in ATP powers all forms of biologic work.

INTEGRATIVE QUESTION

From the perspective of human bioenergetics, discuss the significance of a bumper sticker that reads: Have you thanked a green plant today?

BIOLOGIC WORK IN HUMANS

Figure 5.5 also illustrates that biologic work takes one of three forms:

1. **Mechanical work** of muscle contraction
2. **Chemical work** that synthesizes cellular molecules
3. **Transport work** that concentrates substances in the intracellular and extracellular fluids

Mechanical Work

Mechanical work generated by muscle contraction and subsequent movement provides the most obvious example of energy transformation. The molecular motors in a muscle fiber's protein filaments directly convert chemical energy into mechanical energy. This does not represent the body's only form of mechanical work. In the cell nucleus, contractile elements literally tug at chromosomes to facilitate cell division. Specialized structures (such as cilia) also perform mechanical work in many cells. "In a Practical Sense," see p. 125, shows the method for quantifying work (and power) for three common exercises.

Chemical Work

All cells perform chemical work for maintenance and growth. Continuous synthesis of cellular components takes place as other components break down. The muscle tissue synthesis that occurs in response to chronic overload in resistance training vividly illustrates chemical work.

Transport Work

The biologic work of concentrating substances in the body (transport work) progresses much less conspicuously than mechanical or chemical work. Cellular materials normally flow from an area of high concentration to one of lower concentration. This passive process of **diffusion** does not require energy. Under normal physiologic conditions, some chemicals require transport "uphill" from an area of lower to higher concentration. **Active transport** describes this energy-requiring process. Secretion and reabsorption in the kidney tubules rely on active transport mechanisms, as does neural tissue to establish the proper electrochemical gradients about its plasma membranes. These "quiet" forms of biologic work require a continual expenditure of stored chemical energy.

FACTORS THAT AFFECT THE RATE OF BIOENERGETICS

The upper limits of exercise intensity ultimately depend on the rate that cells extract, conserve, and transfer chemical energy in food nutrients to the contractile filaments of skeletal muscle. *The sustained pace of a marathon runner at close to 90% of aerobic capacity, or the sprinter's rapid speed in all-out exercise, directly reflects the body's capacity to transfer chemical energy to mechanical work.* Enzymes and coenzymes greatly alter the rate of energy release during chemical reactions.

fyi What Is in a Name?

Because of confusion in the naming of enzymes, the International Union of Biochemistry and Molecular Biology (www.chem.qmul.ac.uk/iubmb/) developed a systematic system that classified and named enzymes according to their specific functions. Each enzyme class has a general name as well as a recommended name. Except for older enzyme names such as renin, trypsin, and pepsin, the suffix *–ase* appends to the enzyme based on its mode of operation or substance with which it interacts.

The six classifications of enzymes are as follows:

1. **Oxidoreductases**—Catalyze oxidation-reduction reactions where the substrate oxidized is regarded as hydrogen or electron donor; includes dehydrogenases, oxidates, oxygenases, reductases, peroxidases, and hydroxylases. (Example = lactate dehydrogenase)
2. **Transferases**—Catalyze the transfer of a group (for example, the methyl group or a glycosyl group) from one compound (generally regarded as donor) to another compound (generally regarded as acceptor) and include kinases, transcarboxylases, and transaminases. (Example = hexokinase)
3. **Hydrolases**—Catalyze reactions that add water and include esterases, phosphatases, and peptidases. (Example = lipase)
4. **Lyases**—Catalyze reactions that cleave C–C, C–O, C–N, and other bonds by other means than by hydrolysis or oxidation. They differ from other enzymes in that two substrates are involved in one reaction direction, but only one in the other direction. Include synthases, deaminases, and decarboxylases. (Example = carbonic anhydrase)
5. **Isomerases**—Catalyze reactions that rearrange molecular structure and include isomerases and epimerases. These enzymes catalyze changes within one molecule. (Example = phosphoglycerate mutase)
6. **Ligases**—Catalyze bond formation between two substrate molecules with concomitant hydrolysis of the diphosphate bond in ATP or a similar triphosphate. (Example = pyruvate carboxylase)

Enzymes as Biologic Catalysts

Enzymes *are highly specific and large protein catalysts that accelerate the forward and reverse rates of chemical reactions without being consumed or changed in the reaction.* Enzymes only govern reactions that normally take place, but at a much slower rate. In a way, enzymes reduce required **activation energy**—the energy input to initiate a reaction—so its rate changes. Enzyme action takes place without altering equilibrium constants and total energy released (free energy change, or ΔG) in the reaction. FIGURE 5.6 contrasts the effectiveness of a catalyst in initiating a chemical reaction with initiation in the uncatalyzed state. The vertical axis represents energy required to activate each reaction; the

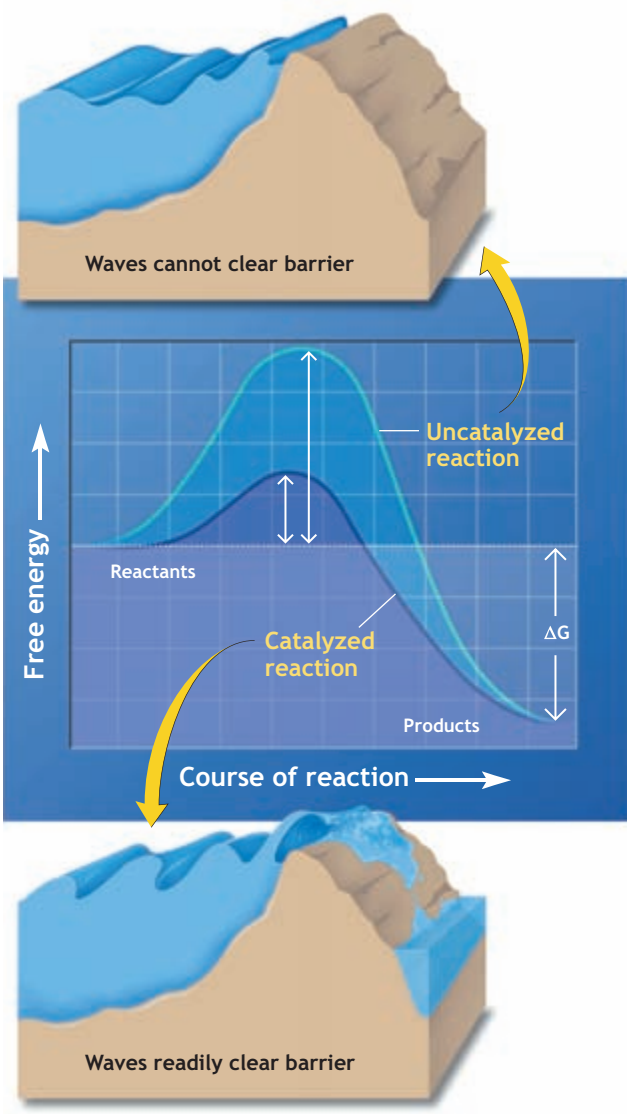


Figure 5.6 • The presence of a catalyst greatly reduces the activation energy to initiate a chemical reaction compared with the energy for an uncatalyzed reaction. For the uncatalyzed reaction to proceed, the reactant must have a higher free energy level than the product.

IN A PRACTICAL SENSE

Measurement of Work on a Treadmill, Cycle Ergometer, and Step Bench

An ergometer is an exercise apparatus that quantifies and standardizes physical exercise in terms of work and/or power output. The most common ergometers include treadmills, cycle and arm-crank ergometers, stair steppers, and rowers.

Work (W) represents application of force (F) through a distance (D):

$$W = F \times D$$

For example, for a body mass of 70 kg and vertical jump score of 0.5 m, work accomplished equals 35 kilogram-meters (70 kg × 0.5 m). The most common units of measurement to express work include kilogram-meters (kg-m), foot-pounds (ft-lb), joules (J), Newton-meters (Nm), and kilocalories (kCal).

Power (P) represents W performed per unit time (T):

$$P = F \times D \div T$$

CALCULATION OF TREADMILL WORK

Consider the treadmill as a moving conveyor belt with variable angle of incline and speed. Work performed on a treadmill equals the product of the weight (mass) of the person *(F)* and the vertical distance (*vert dist*) the person achieves walking or running up the incline. Vert dist equals the sine of the treadmill angle (theta, or θ) multiplied by the distance traveled (*D*) along the incline (treadmill speed × time).

$$W = \textit{body mass (force)} \times \textit{vertical distance}$$

EXAMPLE

For an angle θ of 8° (measured with an inclinometer or determined by knowing the percent grade of the treadmill), the sine of angle θ equals 0.1392 (see table). The *vert dist* represents treadmill speed multiplied by exercise duration multiplied by sine θ. For example, *vert dist* on the incline while walking at 5000 m · h^{-1} for 1 hour equals 696 m (5000 × 0.1392). If a person with a body mass of 50 kg walked on a treadmill at an incline of 8° (grade approximately 14%) for 60 minutes at 5000 m · h^{-1}, work accomplished computes as:

$$\begin{aligned} \boldsymbol{W = F \times \textit{vert dist}\ (\text{sine}\ \theta \times D)} \\ = 50\ \text{kg} \times (0.1392 \times 5000\ \text{m}) \\ = 34{,}800\ \text{kg-m} \end{aligned}$$

The value for power equals 34,800 kg-m ÷ 60 minutes, or 580 kg-m · min^{-1}.

CALCULATION OF CYCLE ERGOMETER WORK

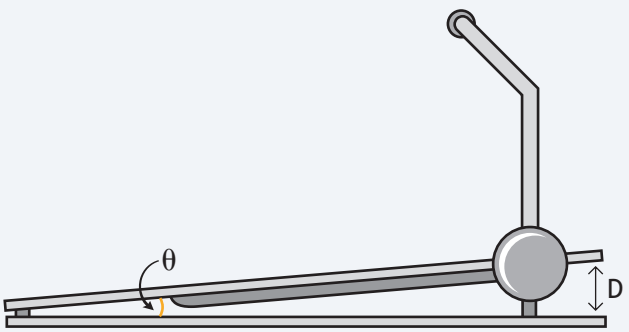
The mechanically braked cycle ergometer contains a flywheel with a belt around it connected by a small spring at one end and an adjustable tension lever at the other end. A pendulum balance indicates the resistance against the flywheel as it turns. Increasing the tension on the belt increases flywheel friction, which increases resistance to pedaling. The force (flywheel friction) represents braking load in kg or kilopounds (kp = force acting on 1-kg mass at the normal acceleration of gravity). The distance traveled equals number of pedal revolutions times flywheel circumference.

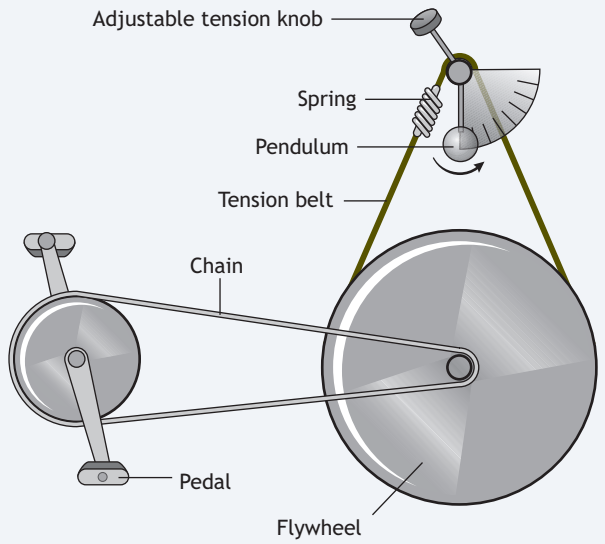
Angle (°)	Sine (θ)	Grade (%)
1	0.0175	1.75
2	0.0349	3.49
3	0.0523	5.23
4	0.0698	6.98
5	0.0872	8.72
6	0.1045	10.51
7	0.1219	12.28
8	0.1392	14.05
9	0.1564	15.84
10	0.1736	17.63
15	0.2588	26.80
20	0.3420	36.40

EXAMPLE

A person pedaling a bicycle ergometer with a 6-m flywheel circumference at 60 rpm for 1 minute covers a distance (D) of 360 m each minute (6 m × 60). If the frictional resistance on the flywheel equals 2.5 kg, total work computes as:

$$\begin{aligned} W &= F \times D \\ &= \text{frictional resistance} \times \text{distance traveled} \\ &= 2.5\ \text{kg} \times 360\ \text{m} \\ &= 900\ \text{kg-m} \end{aligned}$$





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IN A PRACTICAL SENSE

Continued

Power generated by the effort equals 900 kg-m in 1 minute or 900 kg-m · min^{-1} (900 kg-m ÷ 1 min).

CALCULATION OF WORK DURING BENCH STEPPING

Only the vertical (positive) work can be calculated in bench stepping. Distance (D) computes as bench height times the number of times the person steps; force (*F*) equals the person's body mass (kg).

EXAMPLE

If a 70-kg person steps on a bench 0.375-m high at a rate of 30 steps per minute for 10 minutes, total work computes as

$W = F \times D$
= body mass, kg × (vertical distance [m] × steps per min × 10 min)
= 70 kg × (0.375 m × 30 × 10)
= 7875 kg-m

Power generated during stepping equals 787 kg-m · min^{-1} (7875 kg-m ÷ 10 min).

horizontal axis plots the reaction's progress. Clearly, initiation (activation) of an uncatalyzed reaction requires considerably more energy than a catalyzed one. Without enzyme action, the complete digestion of a breakfast meal might take 50 years!

Enzymes possess the unique property of not being readily altered by reactions they affect. Consequently, enzyme turnover in the body remains relatively slow, and the specific enzymes are continually reused. A typical mitochondrion may contain up to 10 billion enzyme molecules, each carrying out millions of operations within a brief time. During all-out exercise, enzyme activity increases tremendously as energy demands rise about 100 times above the resting level. A single cell can contain thousands of different enzymes, each with a specific function that catalyzes a distinct cellular reaction. For example, glucose breakdown to carbon dioxide and water requires 19 different chemical reactions, each catalyzed by its own specific enzyme. Many enzymes operate outside the cell—in the bloodstream, digestive mixture, or intestinal fluids.

Reaction Rates

Enzymes do not all operate at the same rate; some operate slowly, others more rapidly. Consider the enzyme carbonic anhydrase, which catalyzes the hydration of carbon dioxide to form carbonic acid. Its maximum **turnover number**—number of moles of substrate that react to form product per mole of enzyme per unit time—is 800,000. In contrast, the turnover number is only 2 for tryptophan synthetase, which catalyzes the final step in tryptophan synthesis. Enzymes also act along small regions of substrate, each time working at a different rate than previously. Some enzymes delay initiating their work. The precursor digestive enzyme trypsinogen, manufactured by the pancreas in inactive form, serves as a good example. Trypsinogen enters the small intestine where upon activation by intestinal enzyme action it becomes the active enzyme trypsin, which digests complex proteins into simple amino acids. **Proteolytic action** describes this catabolic process. Without the delay in activity, trypsinogen would literally digest the pancreatic tissue that produced it.

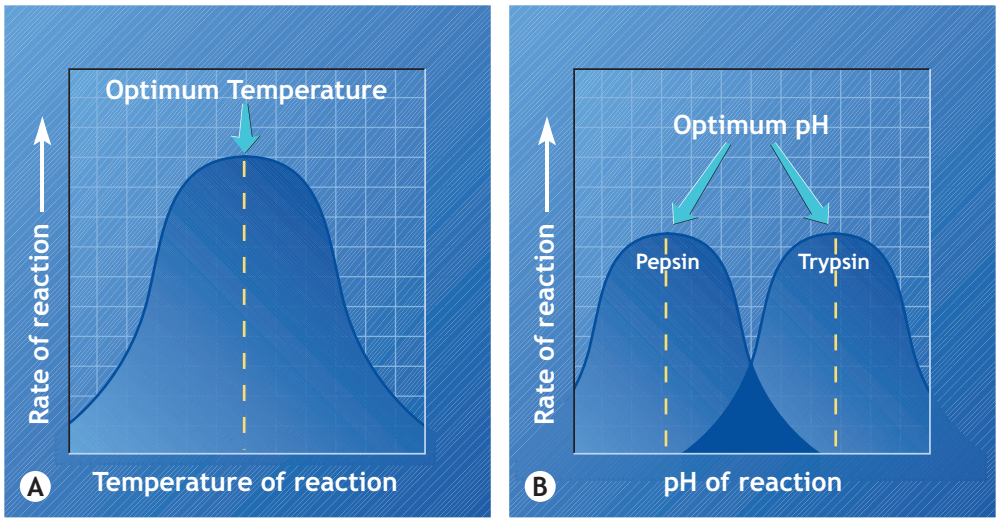


Figure 5.7 • Effects of (**A**) temperature and (**B**) pH on the enzyme action turnover rate.

FIGURE 5.7 shows that pH and temperature dramatically alter enzyme activity. For some enzymes, peak activity requires relatively high acidity, whereas others function optimally on the alkaline side of neutrality. Note that the two enzymes pepsin and trypsin exhibit different pH profiles that modify their activity rates and determine optimal function. Pepsin operates optimally at a pH between 2.4 and 2.6, whereas trypsin's optimum range approximates that of saliva and milk (6.2 to 6.6). This pH effect on enzyme dynamics takes place because changing a fluid's hydrogen ion concentration alters the balance between positively and negatively charged complexes in the enzyme's amino acids. Increases in temperature generally accelerate enzyme reactivity. As temperature rises above 40 to 50°C, the protein enzymes permanently denature and their activity ceases.

Mode of Action

Interaction with its specific substrate represents a unique characteristic of an enzyme's 3-dimensional globular protein structure. Interaction works like a key fitting a lock, as illustrated in FIGURE 5.8. The enzyme turns on when its **active site** (usually a groove, cleft, or cavity on the protein's surface) joins in a "perfect fit" with the substrate's active site. Upon forming an **enzyme–substrate complex**, the splitting of chemical bonds forms a new product with new bonds. This frees the enzyme to act on additional substrate. The example depicts the interaction sequence of the enzyme maltase as it disassembles (hydrolyzes) maltose into its component two glucose building blocks:

Step 1: The active site of the enzyme and substrate line up to achieve a perfect fit, forming an enzyme–substrate complex.

Step 2: The enzyme catalyzes (greatly speeds up) the chemical reaction with the substrate. Note that the hydrolysis reaction adds a water molecule.

Step 3: An end product forms (two glucose molecules), releasing the enzyme to act on another substrate.

First proposed in the early 1890s by the German chemist and Nobel laureate Emil Fischer (1852–1919), a "**lock-and-key mechanism**" describes the enzyme–substrate interaction. This process ensures that the correct enzyme "mates" with its specific substrate to perform a particular function. Once the enzyme and substrate join, a *conformational change* in enzyme shape takes place as it molds to the substrate. Even if an enzyme links with a substrate, unless the specific conformational change occurs in the enzyme's shape, it will not interact chemically with the substrate. A more contemporary hypothesis considers the lock and key more of an "induced fit" because of the required conformational characteristics of enzymes.

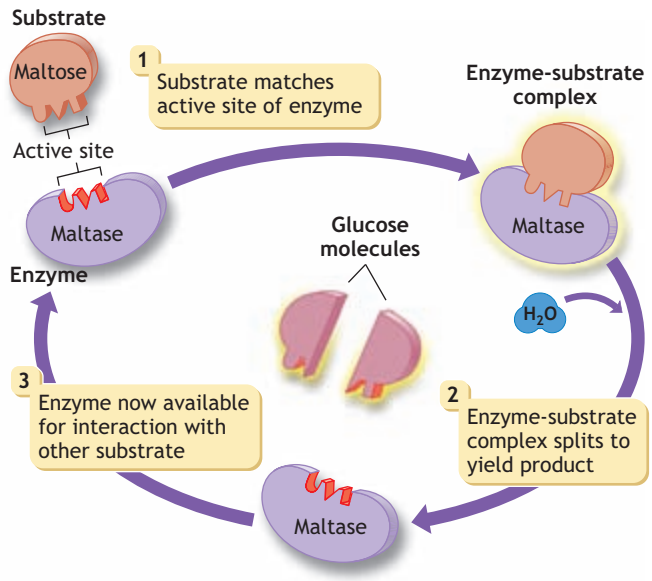


Figure 5.8 • Sequence of steps in the "lock-and-key mechanism" of an enzyme with its substrate. The example shows how two monosaccharide glucose molecules form when maltase interacts with its disaccharide substrate maltose.

The lock-and-key mechanism serves a protective function so only the correct enzyme activates a given substrate. Consider the enzyme hexokinase, which accelerates a chemical reaction by linking with a glucose molecule. When this occurs, a phosphate molecule transfers from ATP to a specific binding site on one of glucose's carbon atoms. Once the two binding sites join to form a glucose–hexokinase complex, the substrate begins its stepwise degradation (controlled by other specific enzymes) to form less complex molecules during energy metabolism.

Coenzymes

Some enzymes remain totally dormant unless activated by additional substances termed **coenzymes**. These nonprotein organic substances facilitate enzyme action by binding the substrate with its specific enzyme. Coenzymes then regenerate to assist in further similar reactions. The metallic ions iron and zinc play coenzyme roles, as do the B vitamins or their derivatives. Oxidation–reduction reactions use the B vitamins riboflavin and niacin, while other vitamins serve as transfer agents for groups of compounds in different metabolic processes (see Table 2.1).

Vitamins Serve As Coenzymes But Do Not Provide Energy

Some advertisements for vitamins imply that taking vitamin supplements provides immediate usable energy for exercise. This simply does not occur. Vitamins often serve as coenzymes to "make reactions go," but they contain *no* chemical energy for biologic work.

A coenzyme requires less specificity in its action than an enzyme because the coenzyme affects a number of different reactions. It either acts as a "cobinder" or serves as a temporary carrier of intermediary products in the reaction. For example, the coenzyme **nicotinamide adenine dinucleotide** (**NAD^+**) forms NADH in transporting hydrogen atoms and electrons released from food fragments during energy metabolism. The electrons then pass to other special transporter molecules in another series of chemical reactions that ultimately deliver the electrons to oxygen.

Enzyme Inhibition. A variety of substances inhibit enzyme activity to slow the rate of a reaction. **Competitive inhibitors** closely resemble the structure of the normal substrate for an enzyme. They bind to the enzyme's active site but the enzyme cannot change them. The inhibitor repetitively occupies the active site and blunts the enzyme's interaction with its substrate. **Noncompetitive inhibitors** do not resemble the enzyme's substrate and do not bind to its active site. Instead, they bind to the enzyme at a site other than the active site. This changes the enzyme's structure and ability to catalyze the reaction because of the presence of the bound inhibitor. Many drugs act as noncompetitive enzyme inhibitors.

HYDROLYSIS AND CONDENSATION: THE BASIS FOR DIGESTION AND SYNTHESIS

In general, hydrolysis reactions digest or break down complex molecules into simpler subunits; condensation reactions build larger molecules by bonding their subunits together.

Hydrolysis Reactions

Hydrolysis catabolizes carbohydrates, lipids, and proteins into simpler forms the body easily absorbs and assimilates. This basic decomposition process splits chemical bonds by adding H^+ and OH^- (constituents of water) to the reaction byproducts. Examples of hydrolytic reactions include digestion of starches and disaccharides to monosaccharides, proteins to amino acids, and lipids to their glycerol and fatty acid constituents. Specific enzymes catalyze each step of the breakdown process. For disaccharides, the enzymes are lactase (lactose), sucrase (sucrose), and maltase (maltose). The lipid enzymes (lipases) degrade the triacylglycerol molecule by adding water. This cleaves the fatty acids from their glycerol backbone. During protein digestion, protease enzymes accelerate amino acid release when the addition of water splits the peptide linkages. The following represents the general form for all hydrolysis reactions:

$$AB + HOH \rightarrow A\text{-}H + B\text{-}OH$$

Water added to the substance AB causes the chemical bond that joins AB to decompose to produce the breakdown products A-H (H refers to a hydrogen atom from water) and B-OH (OH refers to the hydroxyl group from water). FIGURE 5.9A illustrates the hydrolysis reaction for the disaccharide sucrose to its end-product molecules, glucose and fructose. The figure also shows the hydrolysis of a dipeptide (protein) into its two constituent amino acid units. Intestinal absorption occurs quickly following hydrolysis of the carbohydrate, lipid, and protein macronutrients.

Condensation Reactions

The reactions of hydrolysis can occur in the opposite direction as the compound AB synthesizes from A-H and B-OH. A water molecule also forms in this building process of **condensation** (also termed *dehydration synthesis*). The structural components of the nutrients bind together in condensation reactions to form more complex molecules and compounds. Figure 5.9B shows the condensation reactions for maltose synthesis from two glucose units and the synthesis of a more complex protein from two amino acid units. During protein synthesis, a hydroxyl removed from one amino acid and a hydrogen from the other amino acid join to create a water molecule. **Peptide bond** describes the new bond that forms for the

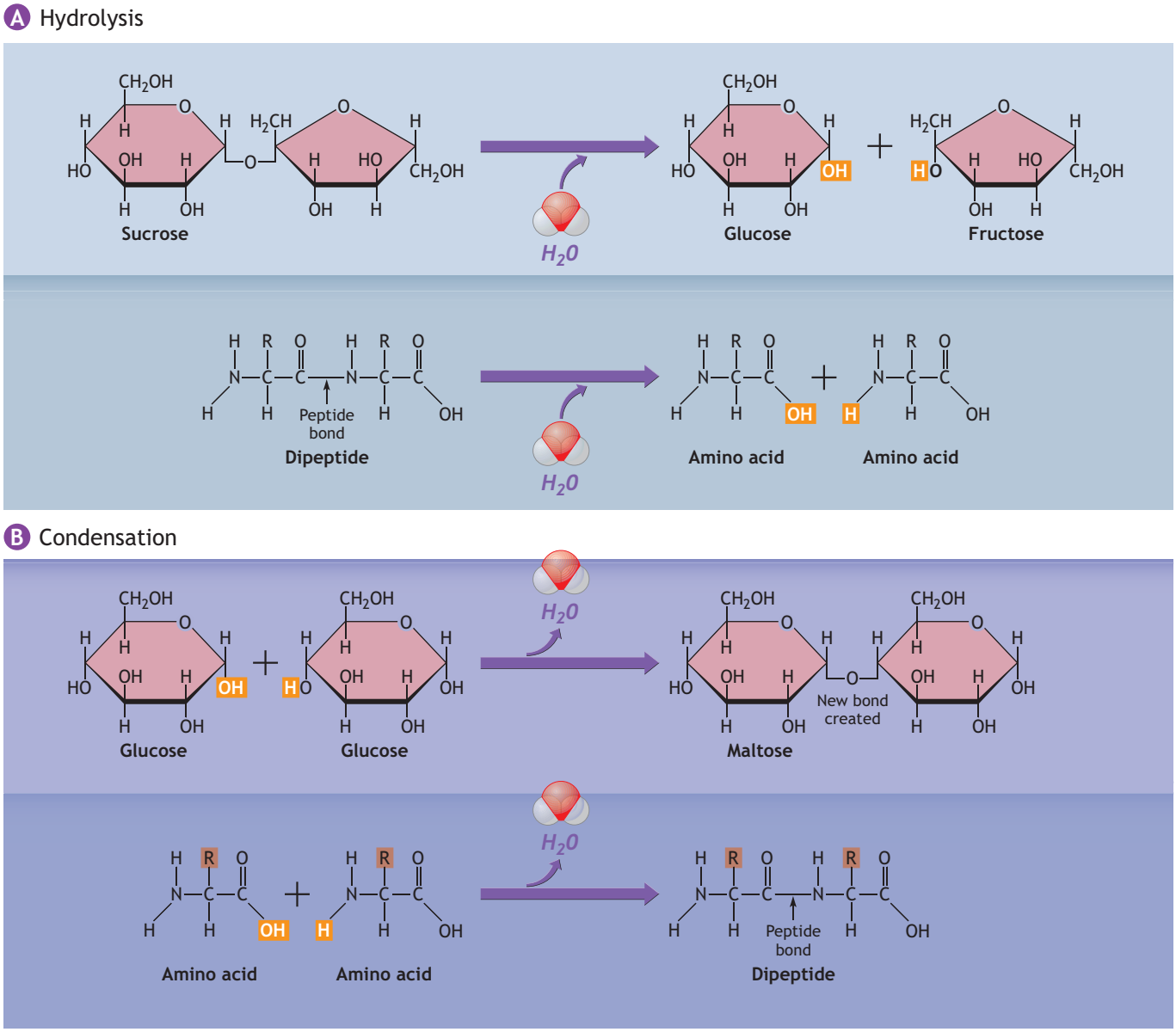


Figure 5.9 • **A.** Hydrolysis of the disaccharide sucrose to the end-product molecules glucose and fructose and the hydrolysis of a dipeptide (protein) into two amino acid constituents. **B.** A condensation chemical reaction for synthesizing maltose from two glucose units and creation of a protein dipeptide from two amino acid subunits. Note that the reactions in **B** illustrate the reverse of the hydrolysis reaction for the dipeptide. The symbol *R* represents the remainder of the molecule.

protein. Water also forms in the synthesis of more complex carbohydrates from simple sugars; for lipids, water forms when glycerol and fatty acid components combine to form a triacylglycerol molecule.

Oxidation and Reduction Reactions

Literally thousands of simultaneous chemical reactions occur in the body that involve the transfer of electrons from one substance to another. ***Oxidation*** *reactions transfer oxygen atoms, hydrogen atoms, or electrons.* A loss of electrons always occurs in oxidation reactions, with a corresponding net *gain* in valence. For example, removing hydrogen from a substance yields a net gain of valence electrons. ***Reduction*** *involves any process in which the atoms in an element gain electrons, with a corresponding net decrease in valence.*

The term **reducing agent** describes the substance that donates or loses electrons as it oxidizes. The substance being reduced or gaining electrons is called the electron acceptor, or **oxidizing agent**. Electron transfer requires both oxidizing and reducing agents. Oxidation and reduction reactions become characteristically **coupled**. Whenever oxidation occurs, the reverse reduction also takes place; when one substance loses electrons, the other substance gains them. The term **redox reaction** commonly describes a coupled oxidation–reduction reaction.

An excellent example of a redox reaction involves the transfer of electrons within the mitochondria. Here, special

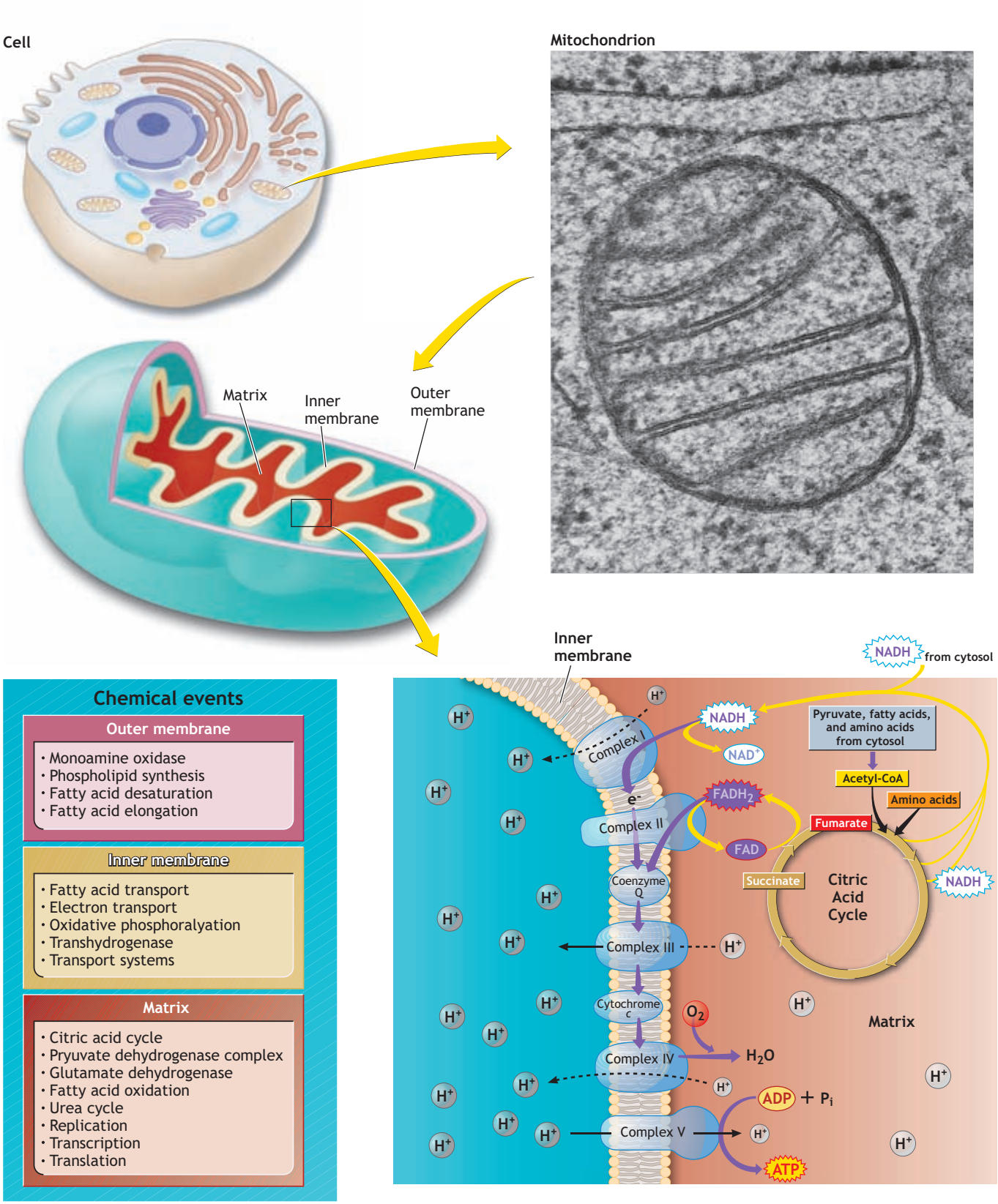


Figure 5.10 • The mitochondrion, its intramitochondrial structures, and primary chemical reactions. The inset table summarizes the different chemical events in relation to mitochondrial structures.

carrier molecules transfer oxidized hydrogen atoms and their removed electrons for delivery to oxygen, which becomes reduced. The carbohydrate, fat, and protein substrates provide a ready source of hydrogen atoms. Dehydrogenase (oxidase) enzymes speed up the redox reactions. Two hydrogen-accepting dehydrogenase coenzymes are the vitamin B–containing NAD^+ and flavin adenine dinucleotide (FAD). Transferring electrons from NADH and $FADH_2$ harnesses energy in the form of ATP.

Energy release in glucose oxidation occurs when electrons reposition (shift) as they move closer to oxygen atoms—their final destination. The close-up illustration of a mitochondrion in FIGURE 5.10 shows the various chemical events that take place on the outer and inner mitochondrial membranes and matrix. The inset table summarizes the mitochondrion's molecular reactions related to its structures. Most of the energy-generating "action," including the redox reactions, takes place within the mitochondrial matrix. The inner membrane is rich in protein (70%) and lipid (30%), two key macromolecules whose configurations encourage transfer of chemicals through membranes.

INTEGRATIVE QUESTION

What biologic benefit comes from the coupling of oxidation and reduction reactions?

The transport of electrons by specific carrier molecules constitutes the ***respiratory chain***. **Electron transport** represents the final common pathway in aerobic (oxidative) metabolism. For each pair of hydrogen atoms, two electrons flow down the chain and reduce one oxygen atom. The process ends when oxygen accepts two hydrogens and forms water. This coupled redox process constitutes hydrogen oxidation and subsequent oxygen reduction. Chemical energy trapped (conserved) during cellular oxidation–reduction forms ATP, the energy-rich molecule that powers all biologic work.

FIGURE 5.11 illustrates a redox reaction during vigorous physical activity. As exercise intensifies, hydrogen atoms are stripped from the carbohydrate substrate faster than their oxidation in the respiratory chain. To continue energy metabolism, a substance other than oxygen must "accept" the nonoxidized excess hydrogens. This occurs when a pyruvate molecule, an intermediate compound formed in the initial phase of carbohydrate catabolism, temporarily accepts a pair of hydrogens (electrons). A new compound, lactate (ionized lactic acid in the body), forms when reduced pyruvate accepts additional hydrogens. Fig. 5.11 illustrates that as more intense exercise produces a greater flow of excess hydrogens to pyruvate, lactate concentration rises rapidly within the blood and active muscle. During recovery, the excess hydrogens in lactate oxidize (electrons removed and passed to NAD^+) to re-form a pyruvate molecule. The enzyme lactate dehydrogenase (LDH) accelerates this reversal. Chapter 6 more fully discusses oxidation–reduction reactions in human energy metabolism.

Measuring Energy Release in Humans

The gain or loss of heat in a biologic system provides a simple way to determine the energy dynamics of any chemical process. In food catabolism within the body, a human calorimeter (see Fig. 8.1), similar to the bomb calorimeter

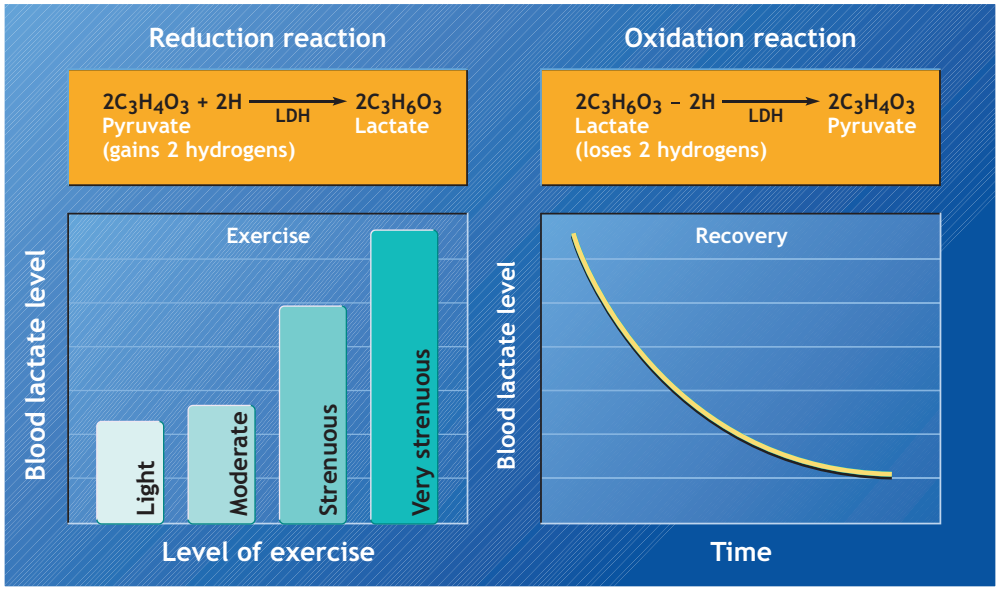


Figure 5.11 • Example of a redox (oxidation–reduction) reaction. During progressively more strenuous exercise when oxygen supply (or use) becomes inadequate, some pyruvate formed in energy metabolism gains two hydrogens (two electrons) and becomes *reduced* to a new compound, lactate. In recovery, when oxygen supply (or use) becomes adequate, lactate loses two hydrogens (two electrons) and *oxidizes* back to pyruvate. This example shows how a redox reaction continues energy metabolism, despite limited oxygen availability (or use) in relation to exercise energy demands.

FOCUS ON RESEARCH

Valid Determination of Oxygen Consumption

Wilmore JH, Costill DL. Adequacy of the Haldane transformation in the computation of exercise $\dot{V}O_2$ in man. J Appl Physiol 1973;35:85.

➤ Oxygen consumption using open-circuit spirometry represents a fundamental measurement in exercise physiology. This methodology assumes no nitrogen production or retention by the body, so the nitrogen volume remains equal in the inspired and expired air. Because of this intrinsic relationship, no need exists to collect and analyze both inspired and expired air volumes during measurement of oxygen consumption and carbon dioxide production. The following mathematical relationship, known as the *Haldane transformation,* exists between inspired and expired air volumes:

$$V_I = V_E \times F_{EN_2} \div F_{IN_2}$$

where V_I equals air volume inspired, V_E equals air volume expired, and F_{EN_2} and F_{IN_2} equal the fractional concentrations of nitrogen in the expired and inspired air. Because the fractional concentrations for inspired oxygen, carbon dioxide, and nitrogen are known, only V_E (or V_I) and the concentrations in expired air of CO_2 (F_{ECO_2}) and O_2 (F_{EO_2}) are required to calculate the oxygen consumed each minute ($\dot{V}O_2$):

$$\dot{V}O_2 = \dot{V}_E \times F_{EN_2}/F_{IN_2} \times F_{IO_2} - \dot{V}_E \times F_{EO_2}$$

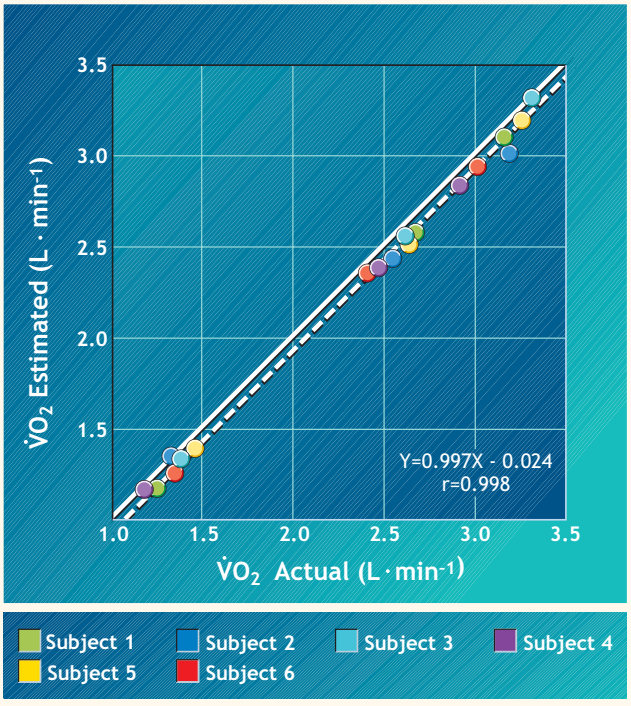
In this formula, F_{EN_2} usually equals $1.00 - (F_{EO_2} + F_{ECO_2})$.

The Wilmore and Costill study determined any nitrogen retention or production and how it influenced the accuracy of oxygen consumption computations using the traditional *Haldane transformation* during light-to-intense exercise. Six subjects completed treadmill exercise by walking on the level at 4 mph; a 5-minute jog followed at 6.0 mph, followed again by a 5-minute run at 7.5 mph. Oxygen consumption, continuously monitored using open-circuit spirometry, included measurement of inspired and expired ventilation volumes. Measurements also included barometric pressure, inspired and expired gas temperatures, relative humidity, and F_{EO_2}, F_{ECO_2}, F_{IO_2}, and F_{ICO_2}.

The figure shows $\dot{V}O_2$ calculated from the inspired and expired air volumes (actual) for all subjects compared with the values estimated from the *Haldane transformation.* The slope of the regression line deviates only 0.003 units from unity (the intercept equals nearly zero), demonstrating the closeness between the actual oxygen consumption and that predicted by the *Haldane transformation.* The largest difference between the 68 actual and estimated $\dot{V}O_2$ values was 230 mL, an error of 7.3%. The average difference of 0.8% for all subjects fell within the measurement error of the instruments. For the nitrogen data, a difference of 1.6% occurred between the minute volume of nitrogen inspired and expired for any subject at any exercise intensity; 11 of 17 subjects' work rates exhibited less than 1% difference. The largest difference, 1099 mL of $N_2 \cdot min^{-1}$, occurred during intense exercise (2.1% difference).

The major sources of variation in assessing $\dot{V}O_2$ included the measurement of ventilation volume, gas meter calibration, and determination of the inspired air's water vapor pressure (P_{H_2O}). Ventilation volume posed a problem because accuracy depended on the subject being "switched in" and "switched out" at the same phase of the tidal volume at the beginning and end of the collection period. This remains difficult (if not impossible) to achieve, so an inspired-to-expired volume differential nearly always occurs. Also, a 10 percentage point difference in inspired P_{H_2O} (e.g., from 50 to 60% relative humidity) produces more than a 100-mL difference between the inspired and expired N_2 volumes.

This study supported the continued use of the *Haldane transformation* to calculate exercise $\dot{V}O_2$. Although production and/or retention of N_2 can occur during exercise, it exerts little or no effect on the $\dot{V}O_2$ computation.



Actual versus estimated exercise oxygen consumption for six subjects. The *solid line* represents the line of identity, and the *dashed line* represents the regression line that predicts oxygen consumption estimated from the *Haldane transformation* (y axis) from the actual oxygen consumption (*x* axis). Note the slope of nearly 1.00 and intercept of 0. *Colored data points* indicate the same subjects measured under each condition.

described in Chapter 4 (Fig. 4.1), measures the energy change directly as heat (kCal) liberated from the chemical reactions.

The complete combustion of food takes place at the expense of molecular oxygen, so the heat generated in these exergonic reactions can be inferred readily from oxygen consumption measurements. Oxygen consumption measurement forms the basis of indirect calorimetry to determine the energy expended by humans during rest and diverse physical activities (see "Focus on Research," p. 132). Chapter 8 discusses how direct calorimetry and indirect calorimetry determine heat production (energy metabolism) in humans.

INTEGRATIVE QUESTION

Discuss the implications of the second law of thermodynamics for measuring energy expenditure.

Summary

1. Energy, defined as the ability to perform work, emerges only when a change takes place.
2. Energy exists in either potential or kinetic form. *Potential energy* refers to energy associated with a substance's structure or position; *kinetic energy* refers to energy of motion. Potential energy can be measured when it transforms into kinetic energy.
3. The six forms of energy are chemical, mechanical, heat, light, electrical, and nuclear. Each energy form can convert or transform to another form.
4. Exergonic energy reactions release energy to the surroundings. Endergonic energy reactions store, conserve, or increase free energy. All potential energy ultimately degrades into kinetic (heat) energy.
5. Living organisms temporarily conserve a portion of potential energy within the structure of new compounds, some of which power biologic work.
6. Entropy describes the tendency of potential energy to degrade to kinetic energy with a lower capacity for work.
7. Plants transfer the energy of sunlight to the potential energy bound within carbohydrates, lipids, and proteins through the endergonic process of photosynthesis.
8. Respiration, an exergonic process, releases stored energy in plants for coupling to other chemical compounds for biologic work.
9. Energy transfer in humans supports three forms of biologic work: chemical (biosynthesis of cellular molecules), mechanical (muscle contraction), or transport (transfer of substances among cells).
10. Enzymes represent highly specific protein catalysts that accelerate chemical reaction rates without being consumed or changed in the reaction.
11. Coenzymes consist of nonprotein organic substances that facilitate enzyme action by binding a substrate to its specific enzyme.
12. Hydrolysis (catabolism) of complex organic molecules performs critical functions in macronutrient digestion and energy metabolism. Condensation (anabolism) reactions synthesize complex biomolecules for tissue maintenance and growth.
13. The linking (coupling) of oxidation–reduction (redox) reactions enables oxidation (a substance loses electrons) to coincide with the reverse reaction of reduction (a substance gains electrons). Redox reactions provide the basis for the body's energy-transfer processes.
14. The transport of electrons by specific carrier molecules constitutes the respiratory chain. Electron transport represents the final common pathway in aerobic metabolism.

Suggested Readings are available online at http://thepoint.lww.com/mkk7e.

On the Internet

International Union of Biochemistry and Molecular Biology Recommendations on Biochemical and Organic Nomenclature, Symbols & Terminology
www.chem.qmul.ac.uk/iubmb/