A nephron in a human kidney (colorized SEM). Nephrons are the specialized tubules in kidneys that filter the blood to conserve nutrients and water, balance salts in the body, and concentrate wastes for excretion from the body.

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STUDY PLAN

46 Regulating the Internal Environment

WHY IT MATTERS

The crew of the World War II bomber *Lady Be Good* was assigned to fly a night mission to Naples, Italy, from a base on the North African coast on August 4, 1943. But trouble dogged the mission, forcing the crew to turn back before reaching their target. Navigational errors and a cloud layer led them to miss their home base and continue south over the hostile Sahara Desert. Some 440 miles from the coastline, with the fuel running out, the nine crew members parachuted from the aircraft. The bomber remained airborne for a few more minutes and then crashed, leaving its crew miles behind.

The eight men who survived began a northward trek with only half a canteen of water among them, in desert heat that reached 130°F during the day. In a testimony to the physiological mechanisms that conserve water and cool the body, they continued onward for eight days. But then, one by one, they succumbed as the merciless heat and dehydration exceeded their capacity to survive. Rescue teams searched the desert for weeks after their disappearance, but no trace was found of the crew or their airplane.

The fate of the *Lady Be Good* remained unknown until 1958, when an oil exploration team flying over the desert spotted the aircraft, sit-

ting largely intact in the desert sands. A 2-year search finally led to the remains of the crew, some of them more than a hundred miles north of the downed bomber. Diaries found among the scattered effects told the poignant story of the flight and the futile struggle against the dehydrating desert environment.

This story illustrates only too clearly the trials of animal life under changing environmental conditions. Water and required nutrients may become more or less abundant. Temperatures may rise or fall. Animals have evolved an astounding capacity to compensate for fluctuating external conditions and to maintain the internal environment of their bodies within the relatively narrow limits that cells can tolerate.

These limits, and the compensating mechanisms that maintain them, are the subjects of this chapter. First we examine **osmoregulation,** the regulation of water and ion balance, and the closely related topic of **excretion,** which helps maintain the body's water and ion balance while ridding the body of metabolic wastes. We then consider **thermoregulation,** the control of body temperature.

46.1 Introduction to Osmoregulation and Excretion

Living cells contain water, are surrounded by water, and constantly exchange water with their environment. For the simplest animals, the water of the external environment directly surrounds cells. For more complex animals, an aqueous extracellular fluid surrounds the cells, and is separated from the external environment by a body covering. In animals with a circulatory system, the extracellular fluid includes both the interstitial fluid immediately surrounding cells and the blood or other circulated fluid; these are commonly called body fluids.

In this section, we review the mechanisms cells use to exchange water and solutes with the surrounding fluid through *osmosis.* We also look at how animals harness osmosis to maintain *water balance,* the equilibrium in inward and outward flow of water.

Osmosis Is a Form of Passive Diffusion

In osmosis (see Section 6.3), water molecules move across a selectively permeable membrane from a region where they are more highly concentrated to a region where they are less highly concentrated. The difference in water concentration is produced by differing numbers of solute molecules or ions on the two sides of the membrane. The side of the membrane with a *lower* solute concentration has a *higher* concentration of water molecules, so water will move osmotically to the other side, where water concentration is *lower.*

Selective permeability is a key factor in osmosis because it helps maintain differences in solute concentration on either side of biological membranes. Proteins are among the most important solutes in establishing the conditions that produce osmosis.

The total solute concentration of a solution, called its **osmolarity,** is measured in *osmoles*—the number of solute molecules and ions (in moles)—per liter of solution. Because the

total solute concentration in the body fluids of most animals is less than 1 osmole, osmolarity is usually expressed in thousandths of an osmole, or *milliosmoles* (mOsm). As shown in **Figure 46.1,** the osmolarity of body fluids in humans and other mammals is about 300 mOsm/L; osmolarity in a flounder, a marine teleost (bony fish), is about 330 mOsm/L, and in a goldfish, a freshwater teleost, it is about 290 mOsm/L. By contrast, sharks and many marine invertebrates such as lobsters have osmolarities close to that of seawater, about 1000 mOsm/L, and freshwater invertebrates have an osmolarity of about 225 mOsm/L.

Considering solutions on either side of a selectively permeable membrane, a solution of higher osmolarity is said to be *hyperosmotic* to a solution of lower osmolarity, and a solution of lower osmolarity is said to be *hypoosmotic* to a solution of higher osmolarity. If the solutions on either side of a membrane have the same osmolarity, they are said to be *isoosmotic*. Water moves across the membrane between solutions that differ in osmolarity (see Figure 6.9), whereas when two solutions are isoosmotic, no net water movement occurs.

Animals Use Different Approaches to Keep Osmosis from Swelling or Shrinking Their Cells

Because even small differences in osmolarity can cause cells to swell or shrink, animals must keep their cellular and extracellular fluids isoosmotic. In some animals, called **osmoconformers**, the osmolarity of the cellular and extracellular solutions simply matches the osmolarity of the environment. Most marine invertebrates are osmoconformers. Other animals, called **osmoregulators**, use control mechanisms to keep the osmolarity of cellular and extracellular fluids the same, but at levels that may differ from the osmolarity of the surroundings. Most freshwater and terrestrial invertebrates, and almost all vertebrates, are osmoregulators.

For terrestrial animals, one of the greatest challenges to osmoregulation is the limited supply of water in the environment—if the crew of the *Lady Be Good* had had an adequate supply of water, for example, they could probably have reached safety at the North African coast even without food.

Excretion Is Closely Tied to Osmoregulation

Control over osmolarity is partly maintained by removing certain molecules and ions from cells and body fluids and releasing them into the environment; thus, excretion is closely related to osmoregulation. Animals excrete H^+ ions to keep the pH of body fluids near the neutral levels required by cells for survival. They also excrete toxic products of metabolism, such as nitrogenous (nitrogen-containing) compounds resulting from the breakdown of proteins and nucleic acids, and
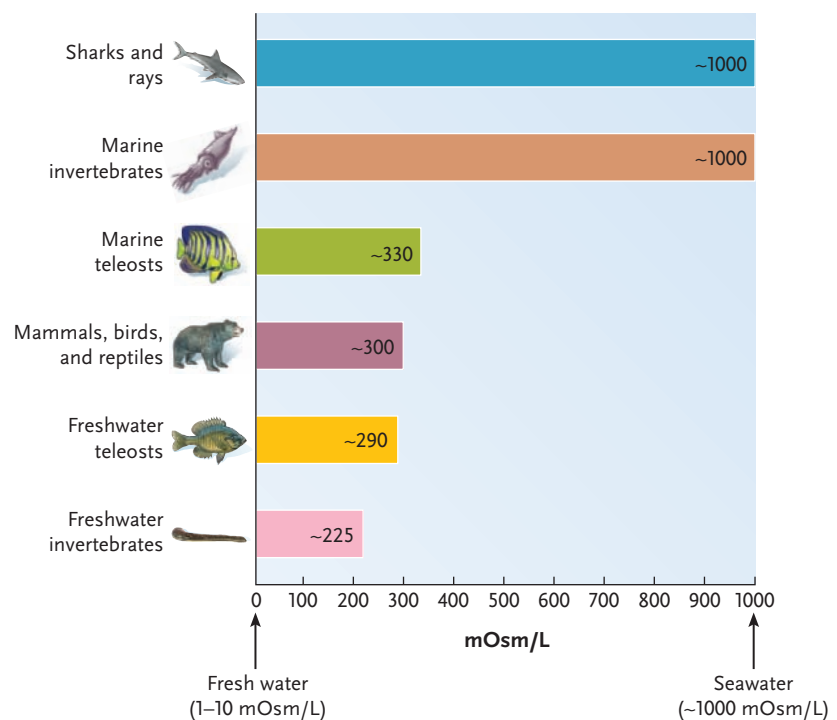
Figure 46.1
Osmolarity of body fluids in some animal groups.

breakdown products of poisons and toxins. Excretion of ions and metabolic products is accompanied by water excretion since water serves as a solvent for those molecules. Animals that take in large amounts of water may also excrete water to maintain osmolarity.

Microscopic Tubules Form the Basis of Excretion in Most Animals

Except in the simplest animals, minute tubular structures carry out osmoregulation and excretion **(Figure 46.2).** The tubules are immersed in body fluids at one end (called the *proximal end* of the tubules), and open directly or indirectly to the body exterior at the other end (called the *distal end* of the tubules). The tubules are formed from a **transport epithelium**—a layer of cells with specialized transport proteins in their plasma membranes. The transport proteins move specific molecules and ions into and out of the tubule by either active or passive transport, depending on the particular substance and its concentration gradient.

Typically, the tubules function in a four-step process:

• **Filtration.** Filtration is the nonselective movement of some water and a number of solutes—ions and small molecules, but not large molecules such as proteins—into the proximal end of the tubules through spaces between cells. In animals with an open circulatory system, the water and solutes come from body fluids, with movement into the tubules driven by the higher pressure of the body fluids compared with the fluid inside the tubule. In animals with a closed circulatory system, such

Proximal end of tubule

Filtration: Small molecules and ions from body fluids or blood nonselectively pass through narrow spaces between cells into the tubule.

Excretory tubule (formed from transport epithelium)

Reabsorption: Nutrient molecules, some ions and conserved water are returned to the body fluids or blood by transport epithelium.

Secretion: Excess ions and toxic breakdown products are transported selectively from the body fluids or blood into the tubule.

Distal end of tubule

Release: Urine (nitrogenous wastes, some ions, toxic breakdown products, excreted water) is released into the environment.

Figure 46.2

Common structures and operations of the tubules carrying out osmoregulation and excretion in animals. The tubules are typically formed from a single layer of cells with transport functions.
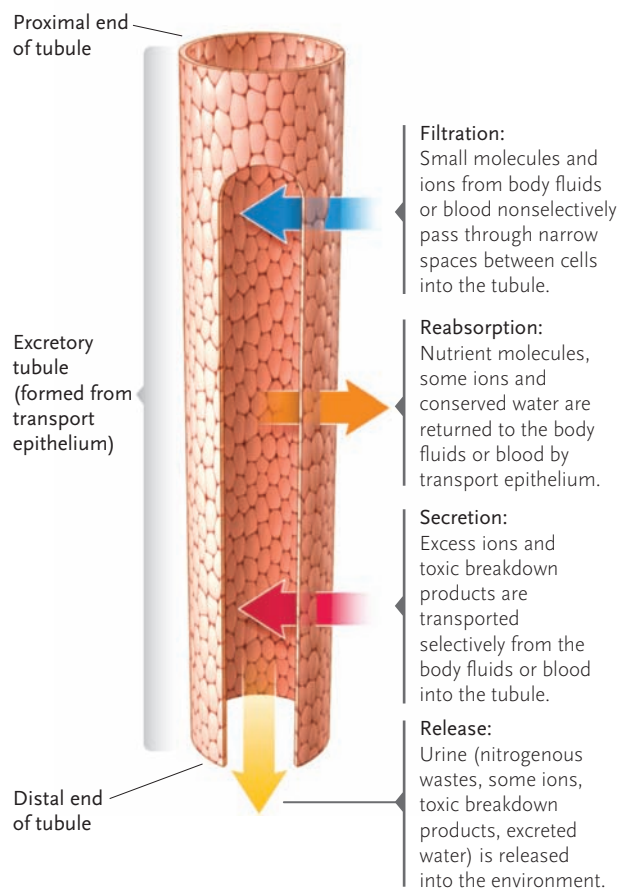
as humans, the water and solutes come from the blood in capillaries that surround the tubules, with the movement into the tubules driven by blood pressure. (Open and closed circulatory systems are described in Section 42.1.)

- **Reabsorption.** In reabsorption, some molecules (for example, glucose and amino acids) and ions are transported by the transport epithelium back into the body fluid (animals with open circulatory systems) or into the blood in capillaries surrounding the tubules (animals with closed circulatory systems) as the filtered solution moves through the excretory tubule.

- **Secretion.** Secretion is a selective process in which specific small molecules and ions are transported from the body fluids (animals with open circulatory systems) or blood (animals with closed circulatory systems) into the tubules. Secretion is the second and more important route for eliminating particular substances from the body fluid or blood, filtration being the first. The difference between the two processes is that filtration is nonselective whereas secretion is selective for substances transported. The same substances are transported into the tubule by secretion as in filtration; those sub-

stances are added, therefore, to substances already in the tubule as a result of filtration.

- **Release.** The fluid containing waste materials—urine—is released into the environment from the distal end of the tubule. In some animals the fluid is concentrated into a solid or semisolid form.

The tubules may number from hundreds to millions depending on the species. In combination, they expand the transport epithelium to a total surface area large enough to accomplish the osmoregulatory and excretory functions of the animal. In all vertebrates and many invertebrates, the excretory tubules are concentrated in specialized organs, the *kidneys,* which are discussed in later sections.

Animals Excrete Nitrogen Compounds as Metabolic Wastes

The metabolism of ingested food is a source of both energy and molecules for the biosynthetic activities of an animal. Importantly, metabolism of ingested food produces water—called *metabolic water*—that is used in chemical reactions and is involved in physiological processes such as the excretion of wastes.

The proteins, amino acids, and nucleic acids in food are broken down as part of digestion. The same molecules are broken down in body cells as a result of the normal processes of synthesis and replacement. The nitrogenous products of this breakdown are excreted by most animals as *ammonia, urea,* or *uric acid,* or a combination of these substances **(Figure 46.3).** The particular molecule or combination of molecules produced depends on a balance among toxicity, water conservation, and energy requirements.

Ammonia. Ammonia (NH_3) is the result of a series of biochemical steps beginning with the removal of amino groups ($—NH_3^+$) from amino acids as a part of protein breakdown. Ammonia is readily soluble in water, but it is also highly toxic. Therefore, ammonia must either be excreted or be converted to a nontoxic derivative. However, because of its toxicity, ammonia can be excreted from the body only in dilute solutions, making this path possible only in animals with a plentiful supply of water. Those animals include aquatic invertebrates, teleosts, and larval amphibians; ammonia is the primary nitrogenous waste for them. Terrestrial animals, and some aquatic animals, instead detoxify ammonia, converting it either into urea or uric acid.

Urea. All mammals, most amphibians, some reptiles, some marine fishes, and some terrestrial invertebrates combine ammonia with HCO_3^- and convert the product in a series of steps to *urea,* a soluble and relatively nontoxic substance. Although producing urea requires more energy than forming ammonia, excreting urea

instead of ammonia requires only about 10% as much water.

Uric Acid. Water is conserved further in some animals, including terrestrial invertebrates, reptiles, and birds, by the formation of uric acid instead of ammonia or urea. Uric acid is nontoxic, and so insoluble that it precipitates in water as a crystal. (The white substance in bird droppings is uric acid.) The embryos of reptiles and birds, which develop within leathery or hard-shelled eggs that are impermeable to liquids, also conserve water by forming uric acid, which is stored as a waste product.

Although making uric acid requires even more energy than urea, molecule for molecule it contains four times as much nitrogen as ammonia. And, because uric acid precipitates from water as a crystal, it can be excreted as a concentrated paste. These factors conserve about 99% of the water that would be required to excrete an equivalent amount of nitrogen as ammonia.

We have now covered the basics of osmoregulation and excretion. In the sections that follow, we look at the specifics of these processes in different animal groups, beginning with the invertebrates.

Figure 46.3

Nitrogenous wastes excreted by different animal groups. Although humans and other mammals primarily excrete urea, they also excrete small amounts of ammonia and uric acid.

STUDY BREAK

Define the terms osmosis, osmolarity, hypoosmotic, osmoregulator, and transport epithelium.

46.2 Osmoregulation and Excretion in Invertebrates

Both osmoconformers and osmoregulators occur among the invertebrates. Except for the simplest groups, most invertebrates, whether osmoconformers or osmoregulators, carry out excretion by specialized excretory tubules.

Most Marine Invertebrates Are Osmoconformers; All Freshwater and Terrestrial Invertebrates Are Osmoregulators

Most marine invertebrates are osmoconformers. All these animals release water, certain ions, and nitrogenous wastes—usually in the form of ammonia—directly from body cells to the surrounding seawater. The cells of these animals do not swell or shrink because the osmolarity of their intracellular and extracellular fluids and the surrounding seawater is the same, about 1000 mOsm/L. Therefore, they do not have to expend energy to maintain their osmolarity. However, osmoconformers do expend energy to keep some ions, such as Na^+, at lower concentrations inside cells than in the surroundings.

In contrast, all freshwater invertebrates are osmoregulators because their cells could not survive if their internal ion concentrations were reduced to freshwater levels. Terrestrial invertebrates are osmoregulators as well. These animals must expend energy to keep their internal fluids hyperosmotic to their surroundings. Although osmoregulation is energetically expensive, these invertebrates can live in more varied habitats than osmoconformers can.

The internal hyperosmoticity of freshwater osmoregulators such as flatworms and mussels causes water to move constantly from the surroundings into their bodies. This excess water must be excreted, at a considerable cost in energy, to maintain internal hyperosmoticity. These animals must also obtain the salts required to keep their body fluids hyperosmotic to fresh water. The salts are obtained from foods, and by actively transporting salt ions from the water into their bodies (even fresh water contains some dissolved salts). This active ion transport occurs through the skin or gills.

Among terrestrial osmoregulators are annelids (earthworms), arthropods (insects, spiders and mites, millipedes, and centipedes), and mollusks (land snails and slugs). Like their freshwater relatives, these invertebrates must obtain salts from their surroundings, usually in their foods. While they do not have to excrete water entering by osmosis, they must constantly replace water lost from their bodies by evaporation.

In Invertebrate Osmoregulators, Specialized Excretory Tubules Participate in Osmoregulation and Carry Out Excretion

Invertebrate osmoregulators typically use specialized tubules for carrying out excretion. Three common types of these specialized tubules that differ in which body fluids are processed and how are *protonephridia,* found in flatworms and larval mollusks; *metanephridia,* found in annelids and most adult mollusks; and *Malpighian tubules,* found in insects and other arthropods.

Protonephridia. The flatworm *Dugesia* provides an example of the simplest form of invertebrate excretory tubule, the **protonephridium** (*protos* = first; *nephros* = kidney). In *Dugesia,* two branching networks of protonephridia run the length of the body **(Figure 46.4).** The smallest branches of the tubule network end with a large cell containing a bundle of cilia that reach into the tubule and that beat to move fluid through the tubule. This cell is called a *flame cell* because the movement of its cilia resembles a flickering flame. The plasma membrane of the flame cell interdigitates with the plasma membrane of the tubular cell with which it connects. Hemolymph enters the tubule through the membranes in the area where the two membranes interdigitate. As the fluids pass through the protonephridia, some molecules and ions are reabsorbed and others, including nitrogenous wastes, are secreted into the tubules; the urine resulting from this filtration system is released through pores at the ends of the tubules where the tubules reach the body surface.

Figure 46.4
The protonephridia of the planarian *Dugesia,* showing a flame cell.
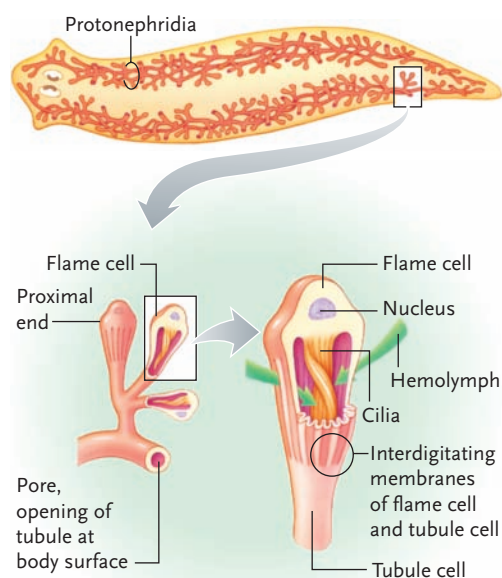
Metanephridia. The excretory tubule of most annelids and adult mollusks, the **metanephridium** (*meta* = between), has a funnel-like proximal end surrounded with cilia that admits hemolymph. Like protonephridia, metanephridia are filtration systems. As hemolymph moves through the tubule, some molecules and ions are reabsorbed, and other ions and nitrogenous wastes are secreted into the tubule and excreted from the body surface.

Figure 46.5 shows the arrangement of metanephridia in an earthworm. The proximal ends of a pair of metanephridia are located in each body segment, one on either side of the animal. Each tubule of the

Hemolymph enters through openings at proximal ends of metanephridia in each segment.

Urine is released through pore opening to exterior in a different segment.
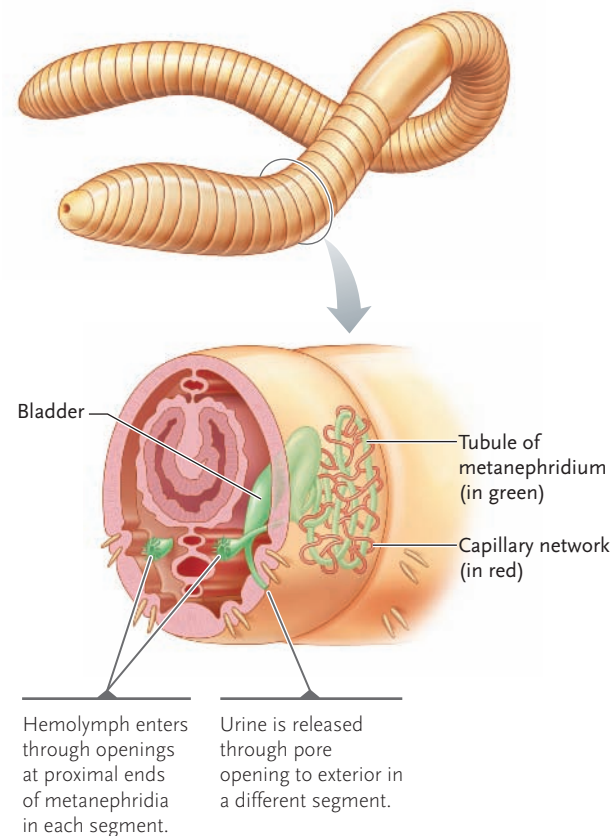
Figure 46.5
The metanephridium of an earthworm.

pair extends into the following segment, where it bends and folds into a convoluted arrangement surrounded by a network of blood vessels. Reabsorption and secretion take place in the convoluted section. Urine from the distal end of the tubule collects in a saclike storage organ, the *bladder,* from where it is released through a pore in the surface of the segment. Samples taken with a microneedle from various regions of a metanephridium show that the fluid entering the tubule contains all the smaller molecules and ions of the body fluid; as the fluid moves through the tubules, specific molecules and ions are removed by reabsorption and added by secretion.

Malpighian Tubules. The excretory tubule of insects, the **Malpighian tubule,** has a closed proximal end that is immersed in the hemolymph **(Figure 46.6).** The distal ends of the tubules empty into the gut. In contrast to protonephridia and metanephridia, Malpighian tubules do not filter body fluids; instead, they are excretory systems that use secretion to generate the fluid for release from the body. In particular, uric acid and several ions, including Na^+ and K^+, are actively secreted into the tubules. As the concentration of these substances rises, water moves osmotically from the hemolymph into the tubule. The fluid then passes into the

hindgut (intestine and rectum) of the insect as dilute urine. Cells in the hindgut wall actively reabsorb most of the Na$^+$ and K$^+$ back into the hemolymph; water follows by osmosis. The uric acid left in the gut precipitates into crystals, which mix with the undigested matter in the rectum and are released with the feces.

STUDY BREAK

Describe protonephridia, metanephridia, and Malpighian tubules. In which animal groups are each of these excretory tubules found?

46.3 Osmoregulation and Excretion in Mammals

In all vertebrates, specialized excretory tubules contribute to osmoregulation and carry out excretion. The excretory tubules, called **nephrons**, are located in a specialized organ, the kidney. We begin our survey of vertebrate osmoregulation and excretion with a description of the structure and function of the mammalian kidney.

The Kidneys and Ureters, the Bladder, and the Urethra Constitute the Urinary System

Mammals have a pair of kidneys, located on either side of the vertebral column at the back of the abdominal cavity **(Figure 46.7).** Internally, the mammalian kidney is divided into an outer **renal cortex** surrounding a central region, the **renal medulla.**

Body fluids are carried in blood through the **renal artery** to a kidney, where metabolic wastes and excess ions are moved into the nephrons and where urine is formed. The filtered blood is routed away from the kidney by the **renal vein.** The urine leaving individual nephrons is processed further in **collecting ducts** and then drains into a central cavity in the kidney called the **renal pelvis.**

From the renal pelvis, the urine flows through a tube called the **ureter** to the **urinary bladder,** a storage sac located outside the kidneys. Urine leaves the bladder through another tube, the **urethra,** which (in most mammals) opens to the outside. In human females, the opening of the urethra is just in front of the vagina; in males, the urethra opens at the tip of the penis. The two kidneys and ureters, the urinary bladder, and the urethra constitute the mammalian urinary system.

Two sphincter muscles control the flow of urine from the bladder to the urethra. In human infants, urination is an autonomic reflex triggered by stretch receptors in the bladder wall. When the bladder be-
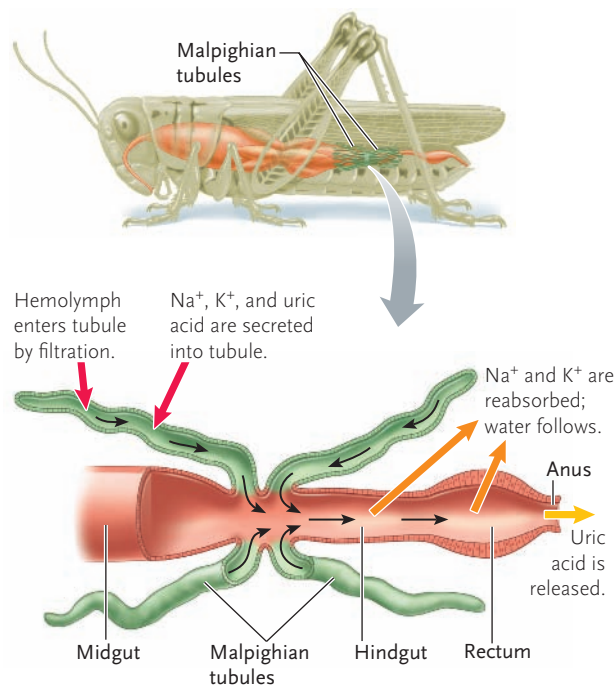
Figure 46.6
Excretion through Malpighian tubules in a grasshopper.

comes full, the sphincters relax, smooth muscles in the bladder wall contract, and the urine is forced to the exterior. At about the age of two years, children learn to override the autonomic reflex by consciously keeping the striated sphincter contracted until urination is convenient.

Mammalian Nephrons Are Differentiated into Regions with Specialized Functions

As in all mammals, human nephrons are differentiated into regions that perform successive steps in excretion. At its proximal end, a human nephron forms the **Bowman's capsule,** an infolded region that cups around a ball of blood capillaries called the **glomerulus (Figure 46.8).** The capsule and glomerulus are located in the renal cortex. Filtration takes place as body fluids are forced into Bowman's capsule from the capillaries of the glomerulus.

Following Bowman's capsule, the nephron forms a **proximal convoluted tubule** in the renal cortex, which descends into the renal medulla in a U-shaped bend called the **loop of Henle** and then ascends again to form a **distal convoluted tubule.** The distal tubule drains the urine into a collecting duct that leads to the renal pelvis. As many as eight nephrons may drain into a single collecting duct. The combined activities of the proximal convoluted tubule, the loop of Henle, the distal convoluted tubule, and the collecting duct convert the filtrate entering the nephron into urine.

Unlike most capillaries in the body, the capillaries in the glomerulus do not lead directly to venules. In-
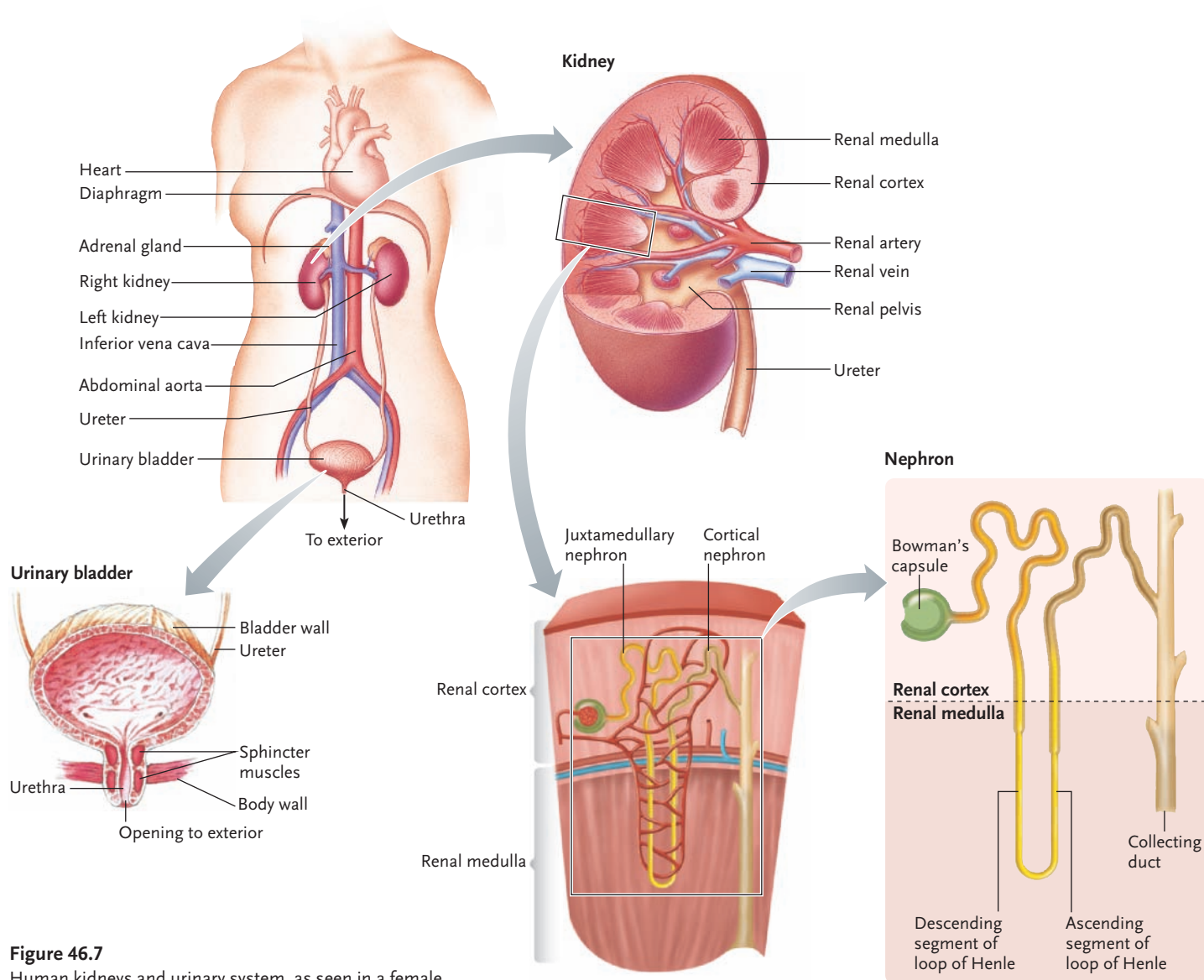
Figure 46.7
Human kidneys and urinary system, as seen in a female.

Kidney labels: Renal medulla, Renal cortex, Renal artery, Renal vein, Renal pelvis, Ureter

Body labels: Heart, Diaphragm, Adrenal gland, Right kidney, Left kidney, Inferior vena cava, Abdominal aorta, Ureter, Urinary bladder, Urethra, To exterior

Urinary bladder labels: Bladder wall, Ureter, Sphincter muscles, Urethra, Body wall, Opening to exterior

Juxtamedullary nephron, Cortical nephron, Renal cortex, Renal medulla

Nephron labels: Bowman's capsule, Renal cortex, Renal medulla, Collecting duct, Descending segment of loop of Henle, Ascending segment of loop of Henle

stead, they form another arteriole that branches into a second capillary network called the **peritubular capillaries**. These capillaries thread around the proximal and distal convoluted tubules and the loop of Henle. Molecules and ions that were reabsorbed during excretion are transferred between the nephron and the peritubular capillaries. However, because the capillaries and the tubules are not in physical contact due to the interstitial fluid between them, this transfer is not direct. Instead, the molecules or ions pass through the wall of the tubule, which is one cell layer thick; diffuse through the interstitial fluid; and then pass into the capillary through its wall, also one cell thick.

Each human kidney has more than a million nephrons. Of these, about 20% (the *juxtamedullary nephrons*) have long loops that descend deeply into the me-dulla of the kidney. The remaining 80% (the *cortical nephrons*) have shorter loops, most of which are located entirely in the cortex, and the remainder of which extend only partway into the medulla.

Mammalian Nephrons Interact with Surrounding Kidney Structures to Produce Hyperosmotic Urine

In mammals, urine is hyperosmotic to body fluids. All other vertebrates except for a few aquatic bird species produce urine that is hypoosmotic to body fluids, or is at best isoosmotic. Production of hyperosmotic urine is a water-conserving adaptation that is primarily a mammalian characteristic. The production of hyperosmotic urine involves the activities of the mammalian

Figure 46.8
A nephron and its blood circulation.

nephron itself and an interaction between nephrons and the highly ordered structure of the mammalian kidney. Three features underlie this interaction:
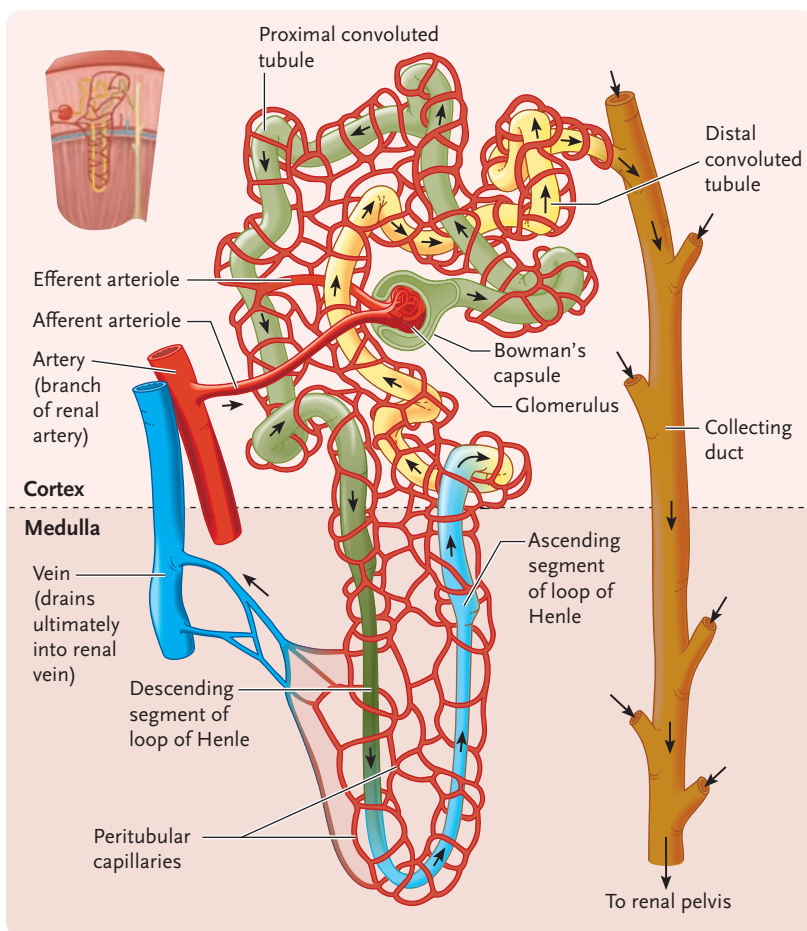
- The arrangement of the loop of Henle, which descends through the medulla and returns to the cortex again.
- Differences in the permeability of successive regions of the nephron, established by a specific group of membrane transport proteins in each region.
- A gradient in the concentration of molecules and ions in the interstitial fluid of the kidney, which increases gradually from the renal cortex to the deepest levels of the renal medulla.

These features interact to conserve nutrients and water, balance salts, and concentrate wastes for excretion from the body.

Researchers determined the transport activities of specific regions of nephrons by dissecting segments of nephrons out of an animal and experimentally manipulating them in vitro. They placed segments in different buffered solutions and passed solutions containing various components of filtrates through the segment. By labeling specific molecules or ions radioactively, the scientists followed the movements of molecules in the solution surrounding the nephron segment or in the filtrate.

Filtration in Bowman's Capsule Begins the Process of Excretion

The mechanisms of excretion (shown in **Figure 46.9** and summarized in **Table 46.1**) begin in Bowman's capsule. The endothelial cells of the glomerulus capillaries and the cells of the Bowman's capsule are separated by spaces just wide enough to admit water, ions, small nutrient molecules such as glucose and amino acids, and nitrogenous waste molecules, primarily urea. The higher pressure of the blood drives fluid containing these molecules and ions from the capillaries of the glomerulus into the capsule. A thin net of connective tissue between the capillary and Bowman's capsule epithelia contributes to the filtering process. Blood cells and plasma proteins are too large to pass and are retained inside the capillaries.

Two factors help maintain the pressure driving fluid into Bowman's capsule. First, the diameters of

Figure 46.9
The movement of ions, water, and other molecules to and from nephrons and collecting tubules in the human kidney. Nephrons in other mammals and in birds work in similar fashion. The numbers are osmolarity values in mOsm/L.
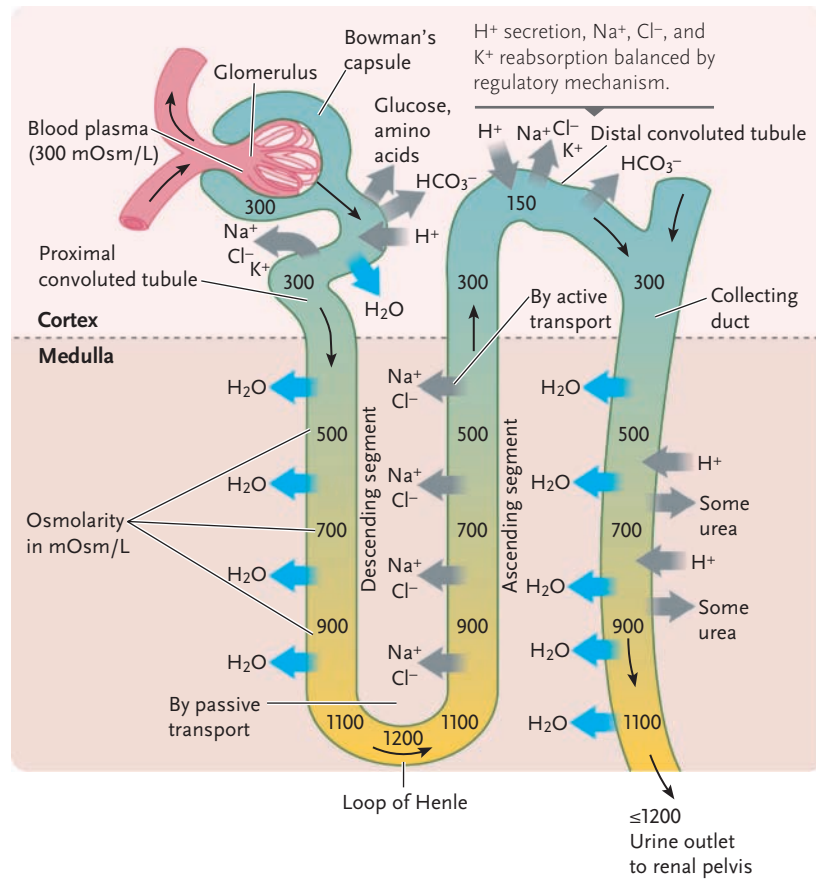
Table 46.1	Filtration, Reabsorption, and Secretion in Nephrons and Collecting Ducts			
Segment	**Location**	**Permeability and Movement**	**Osmolarity of Filtrate and Urine**	**Result of Passage**
Bowman's capsule	Cortex	Water, ions, small nutrients, and nitrogenous wastes move through spaces between epithelia	300 mOsm/L, same as surrounding interstitial fluid	Water and small substances, but not proteins, pass into nephron
Proximal convoluted tubule	Cortex	Na^+ and K^+ actively reabsorbed, Cl^- follows; water leaves through aquaporins; H^+ actively secreted; HCO_3^- reabsorbed into plasma of peritubular capillaries; glucose, amino acids, and other nutrients actively reabsorbed	300 mOsm/L	67% of ions, 65% of water, 50% of urea, and all nutrients return to interstitial fluid; pH maintained
Descending segment of loop of Henle	Cortex into medulla	Water leaves through aquaporins; no movement of ions or urea	From 300 mOsm/L at top to 1200 mOsm/L at bottom of loop	Additional water returned to interstitial fluid
Ascending segment of loop of Henle	Medulla into cortex	Na^+ and Cl^- actively transported out; no entry of water; no movement of urea	From 1200 mOsm/L at bottom to 150 mOsm/L at top of loop	Additional ions returned to interstitial fluid
Distal convoluted tubule	Cortex	K^+ and Na^+ secreted via active transport into urine; Na^+ and Cl^- reabsorbed; water moves into urine through aquaporins; HCO_3^- reabsorbed into plasma of peritubular capillaries	From 150 mOsm/L at beginning to 300 mOsm/L at junction with collecting duct	Ion balance, pH balance
Collecting ducts	Cortex through medulla, empties into renal pelvis	Water moves out via aquaporins; no movement of ions; some urea leaves at bottom of duct	From 300 mOsm/L to 1200 mOsm/L at junction with renal pelvis	More water and some urea returned to interstitial fluid; some H^+ added to urine

the arteriole delivering blood to the glomerulus (called the **afferent arteriole**) and the capillaries of the glomerulus itself are larger than that of arterioles and capillaries elsewhere in the body. The larger diameter maintains blood pressure by presenting less resistance to blood flow. Second, the diameter of the arteriole that receives blood from the glomerulus (called the **efferent arteriole**) is smaller than the diameter of the afferent arteriole, producing a damming effect that backs up the blood in the glomerulus and helps keep the pressure high.

In humans, Bowman's capsules collectively filter about 180 L (47.5 gallons) of fluid each day, from a daily total of 1400 L (369.5 gallons) of blood that pass through the kidneys. The human body contains only about 2.75 L of blood plasma, meaning that the kidneys filter a fluid volume equivalent to 65 times the volume of the blood plasma each day. On average, more than 99% of the filtrate, mostly water, is reabsorbed in the nephrons, leaving about 1.5 L to be excreted daily as urine.

Reabsorption and Secretion Take Place in the Remainder of the Nephron

The fluid filtered into Bowman's capsule contains water, other small molecules, and ions at essentially the same concentrations as the blood plasma. By the time the fluid reaches the distal end of the tubules and passes through the collecting ducts, reabsorption out of the tubules and secretion into them have markedly altered the concentrations of all components of the filtrate.

The Proximal Convoluted Tubule. Reabsorption of water, ions, and nutrients back into the interstitial fluid is the main function of the proximal convoluted tubule. Na^+/K^+ pumps in the epithelium of the proximal convoluted tubule move Na^+ and K^+ from the filtrate into the interstitial fluid surrounding the tubule (see Figure 46.9). The movement of positive charges sets up a voltage gradient that causes Cl^- ions to be reabsorbed from within the tubule with the positive ions. Specific active transport proteins reabsorb essentially all the glucose, amino acids, and other nutrient molecules from the filtrate into the interstitial fluid, making the filtrate hypoosmotic to the interstitial fluid surrounding the tubule. As a result, water moves from the tubule into the interstitial fluid by osmosis. The osmotic movement is aided by *aquaporins,* transport proteins that form passages for water molecules in the transport epithelium of the tubule cells. The nutrients and water that entered the interstitial fluid move into the capillaries of the peritubular network.

Some substances are also secreted into the tubule, however: primarily H^+ ions by active transport and the products of detoxified poisons by passive secretion (detoxification takes place in the liver). The secretion of H^+ ions into the filtrate helps balance the acidity constantly generated in the body by metabolic reactions. H^+ secretion is coupled with HCO_3^- reabsorption from the filtrate in the tubule to the plasma in the peritubular capillaries. Small amounts of ammonia are also secreted into the tubule.

In all, the proximal convoluted tubule reabsorbs about 67% of the Na^+, K^+, and Cl^- ions, 65% of the water, 50% of the urea, and essentially all the glucose, amino acids, and other nutrient molecules in the filtrate. The ions, nutrients, and water reabsorbed by the tubule are transported into the interstitial fluid, and then into capillaries of the peritubular network. Although half of the urea is reabsorbed, the constant flow of filtrate through the tubules keeps the concentration of nitrogenous wastes low in body fluids.

The proximal convoluted tubule has structural specializations that fit its function. The epithelial cells that make up its walls are carpeted on their inner surface by a brush border of microvilli. Like the brush border of epithelial cells in the small intestine (see Section 45.3), these microvilli greatly increase the surface area available for reabsorption and secretion.

The Descending Segment of the Loop of Henle. The filtrate leaving the proximal convoluted tubule enters the descending segment of the loop of Henle, where water is reabsorbed. As this tubule segment descends, it passes through regions of increasingly higher solute concentrations in the interstitial fluid of the medulla (see Figure 46.9). (The generation of this concentration gradient is described later.) As a result, more water moves out of the tubule by osmosis as the fluid travels through the descending segment.

The descending segment has aquaporins, which allow the rapid transport of water. The outward movement of water concentrates the molecules and ions inside the tubule, gradually increasing the osmolarity of the fluid to a peak of about 1200 mOsm/L at the bottom of the loop. This is the same as the osmolarity of the interstitial fluid at the bottom of the medulla.

The Ascending Segment of the Loop of Henle. The fluid then moves into the ascending segment of the loop of Henle, where Na^+ and Cl^- are reabsorbed into the interstitial fluid. As this segment ascends, it passes through regions of gradually lessening osmolarity in the interstitial fluid of the medulla. The ascending segment has membrane proteins that transport salt ions, but no aquaporins. Because water is trapped in the ascending segment, the osmolarity of the urine is reduced as salt ions, primarily Na^+ and Cl^-, move out of the tubule.

In the part of the ascending segment immediately following the loop, the ion concentrations in the tubule filtrate are still high enough to move Na^+ and Cl^- out of the tubule by passive transport. Toward the top of the segment, they are moved out by active transport.

An Ore Spells Relief for Osmotic Stress

Almost all cells respond to osmotic stress—osmotic imbalance with the surroundings—by adjusting the cytoplasmic concentration of small organic molecules called *osmolytes*. When cells are surrounded by a hyperosmotic solution, for example, osmolytes accumulate in the cytoplasm, raising its osmolarity to match that of the surroundings. The almost universal occurrence of osmolytes means that they must have appeared very early in the evolution of life.

In humans, cells in the renal medulla are regularly exposed to high solute concentrations in the interstitial fluid. These cells would quickly die from osmotic water loss if they were not protected by osmolytes. In these cells, as well as in many other types of mammalian cells, one of the primary osmolytes is *sorbitol,* made from glucose in a reaction catalyzed by the enzyme *aldose reductase.* In some unknown way, placing cells in a hyperosmotic medium activates the gene encoding and synthesizing aldose reductase in the cytoplasm.

Joan D. Ferraris and her colleagues at the National Institutes of Health in Bethesda, Maryland, were interested in the molecular steps leading to activation of the aldose reductase gene. To begin their research, the investigators extracted DNA from cells in the renal medulla of a rabbit, and cloned the DNA to increase its quantity. They then probed the DNA with a radioactive DNA segment that could pair with the DNA of aldose reductase genes previously isolated from humans and rats. The probe marked the rabbit version of the gene with radioactivity so that it could be separated from the sample.

The researchers were particularly interested in the promoter sequences controlling the gene, which might contain a region activating transcription in cells exposed to a hypertonic medium. To identify the region, they constructed a composite gene from a segment of the separated DNA containing the promoter and surrounding sequences attached to the coding portion of a gene for luciferase (the firefly enzyme, which catalyzes a cytoplasmic reaction emitting light). The composite gene was then increased in quantity by the polymerase chain reaction.

The composite gene was introduced into cultured renal medulla cells from the rabbit, which were then divided into two groups. One group was maintained in an isotonic medium; the other one was exposed to a medium made hypertonic by added NaCl. The cells exposed to the hypertonic solution glowed with light, showing that the luciferase gene had been turned on by having some part of the promoter segment derived from the aldose reductase gene.

The next step was to isolate the particular control sequence. To accomplish this, the researchers broke the promoter segment into fragments, attached them one at a time to the luciferase gene, and tested them by the same experimental procedure. Eventually, they identified the smallest fragment capable of activating the luciferase gene in cells placed in hypertonic medium; it proved to be the sequence CGGAAAATCAC, beginning 1105 base pairs in advance of the site where transcription begins. The investigators termed the activating sequence an *osmotic response element (ORE).*

Presumably, placing the renal medulla cells under osmotic stress triggers a series of reactions that culminates in synthesis or activation of a nuclear regulatory protein that binds the ORE, leading to activation of the aldose reductase gene. The next step in the investigation is to find the nuclear regulatory protein, and then work backwards one step at a time until the entire series of reactions leading from the first cell receptor to activation of the gene is traced out. If successful, the research will reveal an evolutionarily ancient mechanism that is critical to the survival of virtually all living cells.

Besides reducing the osmolarity of the filtrate in the ascending segment, the reabsorption of salt ions from the tubule into the interstitial fluid helps establish the concentration gradient of the medulla, high near the renal pelvis and low near the renal cortex. The energy required to transport NaCl from higher levels of the ascending segment makes the kidneys one of the major ATP-consuming organs of the body.

By the time the fluid reaches the cortex at the top of the ascending loop, its osmolarity has dropped to about 150 mOsm/L. During the travel of fluid around the entire loop of Henle, water, nutrients, and ions have been conserved and returned to body fluids, and the total volume of the filtrate in the nephron has been greatly reduced. Urea and other nitrogenous wastes have been concentrated in the filtrate. Little secretion occurs in either the descending or ascending segments of the loop of Henle.

The Distal Convoluted Tubule. The transport epithelium of the distal convoluted tubule removes additional water from the fluid in the tubule, and works to balance the salt and bicarbonate concentrations of the tubule fluid against body fluids. In response to hormones triggered by changes in the body's salt concentrations (described in Section 46.4), varying amounts of K^+ and H^+ ions are secreted into the fluid, and varying amounts of Na^+ and Cl^- ions are reabsorbed. Bicarbonate ions are reabsorbed from the filtrate as in the proximal tubule.

In total, more ions move outward than inward and, as a consequence, water moves out of the tubule by osmosis, through aquaporins in the distal tubule. The amounts of urea and other nitrogenous wastes remain the same. By the time the fluid—now urine—enters the collecting ducts at the end of the nephron, its osmolarity is about 300 mOsm/L.

The Collecting Ducts. The collecting ducts concentrate the urine. These ducts, which are permeable to water but not salt ions, descend downward from the cortex through the medulla of the kidney. As the ducts descend, they encounter the gradient of increasing solute concentration in the medulla. This increase makes water move osmotically out of the ducts and greatly increases the concentration of the urine, which can become as high as 1200 mOsm/L at the bottom of the medulla. Near the bottom of the medulla, the walls of the collecting ducts contain passive urea transporters that allow a portion of this nitrogenous waste to pass from the duct into the interstitial fluid. This urea adds significantly to the concentration gradient of solutes in the medulla.

In addition to these mechanisms, H^+ ions are actively secreted into the fluid by the same mechanism as in the proximal and distal convoluted tubules. The balance of the H^+ and bicarbonate ions established in the urine, interstitial fluid, and blood, achieved by secretion of H^+ into the urine by the nephrons and collecting ducts, is important for regulating the pH of blood and body fluids. The kidneys thus provide a safety valve if the acidity of body fluids rises beyond levels that can be controlled by the blood's buffer system (see Section 44.4).

At its maximum value of 1200 mOsm/L, reached when water conservation is at its maximum, the urine at the bottom of the collecting ducts is about four times more concentrated than body fluids. It can also be as low as 50 to 70 mOsm/L, when very dilute urine is produced in response to conditions such as excessive water intake.

The high osmolarity of the interstitial fluid toward the bottom of the medulla would damage the medulla cells if they were not protected against osmotic water loss. The protection comes from high concentrations of otherwise inert organic molecules called *osmolytes* in these cells. The osmolytes, primarily a sugar alcohol called *sorbitol,* raise the osmolarity of the cells to match that of the surrounding interstitial fluid. *Insights from the Molecular Revolution* describes research that identified the genetic controls leading to sorbitol production in kidney medulla cells and other cells subjected to osmotic stress.

Urine flows from the end of the collecting ducts into the renal pelvis, and then through the ureters into the urinary bladder where it is stored. From the bladder, urine exits through the urethra to the outside.

Terrestrial Mammals Have Additional Water-Conserving Adaptations

Terrestrial mammals have other adaptations that complement the water-conserving activities of the kidneys. One is the location of the lungs deep inside the body, which reduces water loss by evaporation during breathing (see Section 44.1). Another is a body covering of keratinized skin. Skin is so impermeable that it almost eliminates water loss by evaporation, except for the controlled loss through evaporation of sweat in mammals with sweat glands.

Among mammals, water-conserving adaptations reach their greatest efficiency in desert rodents such as the kangaroo rat **(Figure 46.10).** The proportion of nephrons with long loops extending deep into the kidney medulla of kangaroo rats is very high, allowing them to excrete urine that is 20 times more concentrated than body fluids. Further, most of the water in the feces is absorbed in the large intestine and rectum. Lacking sweat glands, kangaroo rats lose little water by evaporation from the body surface. Much of the moisture in their breath is condensed and recycled by specialized passages in the nasal cavities. They stay in burrows during daytime, and come out to feed only at night.

About 90% of the kangaroo rat's daily water supply is generated from oxidative reactions in its cells. (Humans, in contrast, can make up only about 12% of their daily water needs from this source.) The remaining

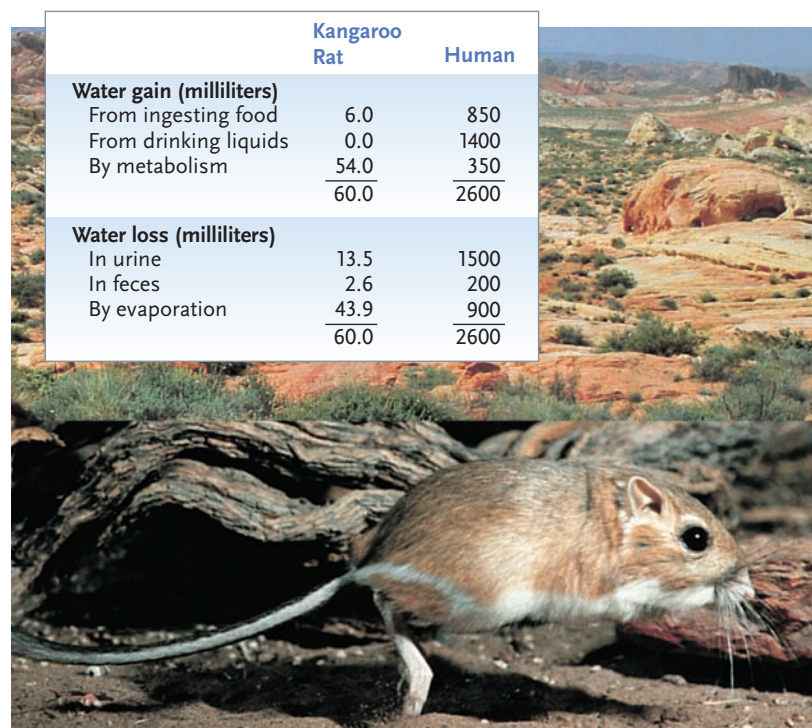|	Kangaroo Rat	Human
Water gain (milliliters)		
From ingesting food	6.0	850
From drinking liquids	0.0	1400
By metabolism	54.0	350
	60.0	2600
Water loss (milliliters)		
In urine	13.5	1500
In feces	2.6	200
By evaporation	43.9	900
	60.0	2600

Figure 46.10
A comparison of the sources of water for a human and a kangaroo rat (genus *Dipodymus*). Water conservation in the kangaroo rat is so efficient that the animal never has to drink water.

David Noble/FPG/Getty Images

Claude Steelman/Tom Stack & Associates

10% of the kangaroo rat's water comes from its food. These structural and behavioral adaptations are so effective that a kangaroo rat can survive in the desert without ever drinking water.

Marine mammals, including whales, seals, and manatees, eat foods that are high in salt content and never drink fresh water. They are able to survive the high salt intake because they produce urine that is more concentrated than seawater. As a result, they are easily able to excrete all the excess salt they ingest in their diet.

We now turn to the regulatory mechanisms that integrate kidney function with body functions as a whole.

STUDY BREAK

1. Describe the structure of a human nephron from the proximal end to the distal end.
2. The urine entering the collecting ducts at the end of the nephron has an osmolarity essentially the same as that of fluids in other parts of the body. How is the urine subsequently made more concentrated?

46.4 Regulation of Mammalian Kidney Function

Mammalian excretory functions are integrated into overall body functions by three primary control systems, which link kidney functions to blood pressure, to the osmolarity and pH of body fluids, and to the body's water balance. An *autoregulation system* located entirely within the kidney keeps glomerular filtration constant during relatively small variations in blood pressure, as when we move from sitting to standing. Two other systems involve hormonal controls that compensate for excessive loss of salt and body fluids and that adjust the rate of water uptake in the kidneys to compensate for excessive water intake or loss. These two hormonal systems regulate interactions between the kidneys and the rest of the body.

Autoregulation Involves Interactions between the Glomerulus and the Nephron

The autoregulation system responds almost instantly to keep the filtration rate constant during small variations in blood pressure. The system depends on signals from receptors in the **juxtaglomerular apparatus** (*juxta* = near) **(Figure 46.11),** which is located at a point where the distal convoluted tubule contacts the afferent arteriole carrying blood to the glomerulus. The receptors, located in the tubule wall, monitor the pressure and flow of fluid through the distal tubule. If a rise in blood pressure increases the filtration rate, the receptors release chemical signals that trigger constriction of the afferent arteriole. The constriction reduces blood flow through the glomerulus and lowers the filtration rate. A drop in filtration rate due to a fall in blood pressure has the opposite effect: signals from the receptors cause the arterioles to dilate, blood flow increases in the glomerulus, and the filtration rate rises.

The RAAS Responds to Na^+ by Triggering Na^+ Reabsorption

Major changes in blood volume and pressure occur when the body loses or gains Na^+ in excessive amounts. Excessive Na^+ loss may result from prolonged and heavy sweating, repeated vomiting, severe diarrhea, or insufficient Na^+ uptake in the diet. The Na^+ loss reduces the osmolarity of body fluids, which causes less water to be reabsorbed in the kidneys. The water loss reduces the volume of blood and interstitial fluid and causes the blood pressure to drop. Excessive Na^+ intake in salty foods may have the opposite effects. The body must compensate for significant changes in Na^+.

The **renin-angiotensin-aldosterone system (RAAS)** is the most important hormonal system involved in regulating Na^+ (see Figure 46.11). At normal body salt concentrations, the RAAS allows about 10 g of salt to be excreted in the urine each day. If excessive Na^+ is lost in the excreted salt, blood pressure and body fluid volume drop, and the glomerular filtration rate falls below levels that can be restored by the juxtaglomerular apparatus. In response, cells in the juxtaglomerular apparatus secrete the enzyme **renin** into the bloodstream. (The RAAS also is activated to promote renin secretion when blood pressure or blood volume decreases independently of Na^+ levels, as in the case of a hemorrhage.) Renin converts a blood protein into the peptide hormone **angiotensin.** Angiotensin quickly raises blood pressure by constricting arterioles in most parts of the body; it also stimulates the release of the steroid hormone **aldosterone** from the adrenal cortex. Aldosterone increases Na^+ reabsorption in the kidneys, which raises the osmolarity of body fluids. As a result, water moves from the tubules into the extracellular fluid, which conserves water. Angiotensin also stimulates secretion of **antidiuretic hormone (ADH)** by the posterior pituitary (antidiuretic means "against urine output"). ADH increases water absorption in the kidneys. And, angiotensin stimulates thirst so that more water will be brought into the body. Overall, the combined effects of angiotensin act to raise the blood pressure back to normal levels.

In the opposite situation, when salt intake is too high, both body fluid volume and blood pressure rise above normal levels. Under these conditions, renin secretion is inhibited and, as a result, angiotensin production and aldosterone secretion are not stimulated. The reduction in angiotensin lowers blood pressure by al-
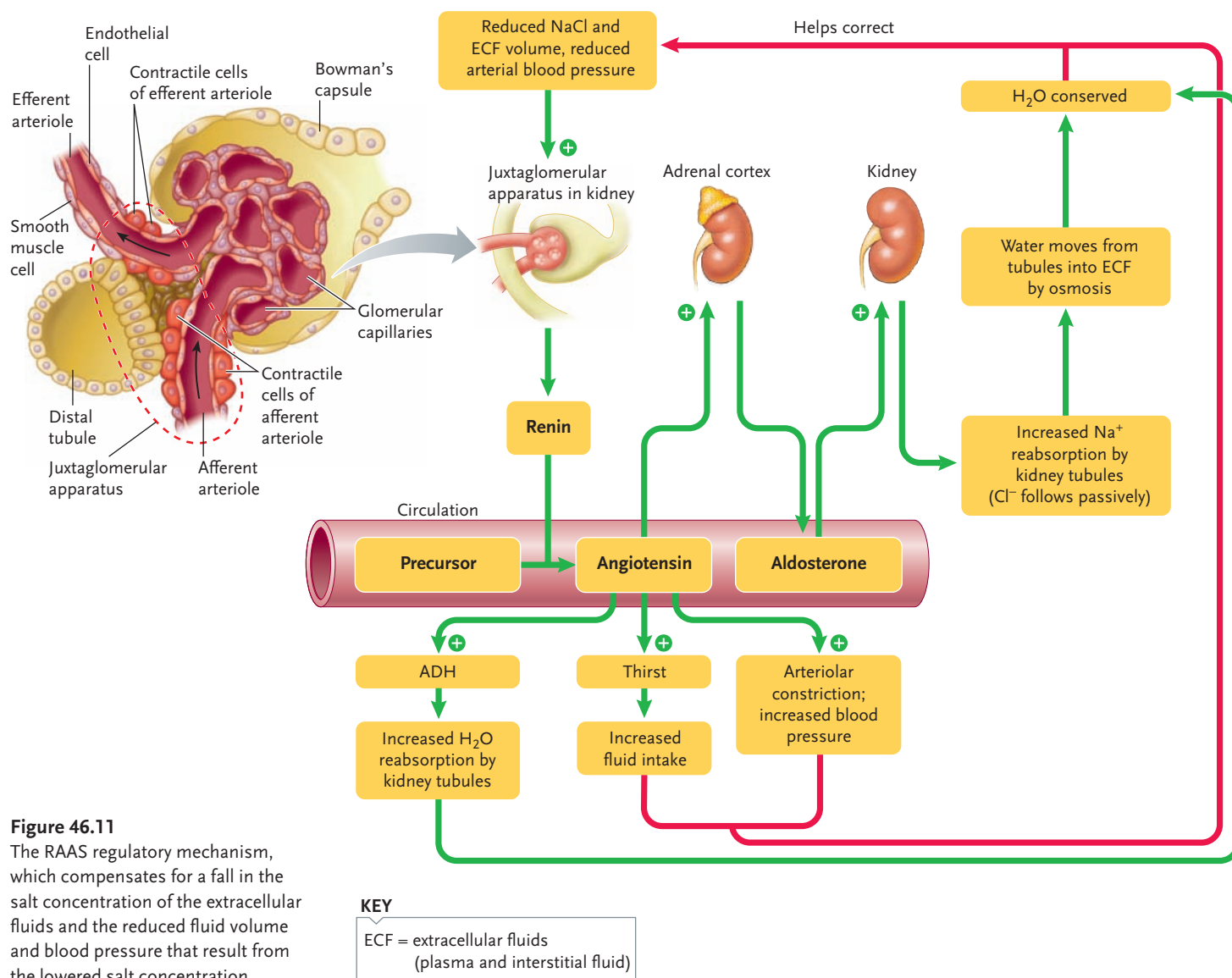
Figure 46.11
The RAAS regulatory mechanism, which compensates for a fall in the salt concentration of the extracellular fluids and the reduced fluid volume and blood pressure that result from the lowered salt concentration.

KEY

ECF = extracellular fluids (plasma and interstitial fluid)

lowing arterioles to dilate; the reduction in aldosterone increases Na^+ release in the urine by retarding the reabsorption of Na^+ and Cl^- from the kidney tubules.

As a backup to these controls, elevated blood pressure stimulates specialized cells in the heart to release **atrial natriuretic factor (ANF)**, a peptide hormone that also inhibits renin release. ANF also increases the filtration rate by dilating the arterioles that deliver blood to glomeruli and by inhibiting aldosterone release. As less Na^+ is reabsorbed and urine volume increases, both plasma volume and blood pressure fall to normal levels.

The ADH System Also Regulates Osmolarity and Water Balance

You have just learned that the ADH system is stimulated by angiotensin of the RAAS in response to an increase in Na^+. The ADH system regulates osmolarity and water balance—and, therefore, urinary output—by increasing water reabsorption in the kidneys without changing the usual excretion of salt. Independently of being stimulated by angiotensin, the ADH system is triggered by **osmoreceptors,** chemoreceptors in the hypothalamus that respond to changes in the osmolarity of the fluid surrounding them, which reflects the osmolarity generally of the body fluids **(Figure 46.12).**

When an animal becomes dehydrated, the osmolarity of its body fluids increases and its need for water conservation increases. In this situation, osmoreceptors detect the increase in concentration of salts and other dissolved substances in the extracellular fluid (see Figure 46.12, step 1). Signals from the osmoreceptors are routed to the brain stem, where they trigger thirst (step 2). The resulting increase in water ingestion helps compensate for water loss (step 3).

In addition, neurons of the hypothalamus stimulate the posterior pituitary to secrete ADH (step 4). ADH makes the otherwise impermeable distal convoluted tubules and collecting ducts permeable to water.
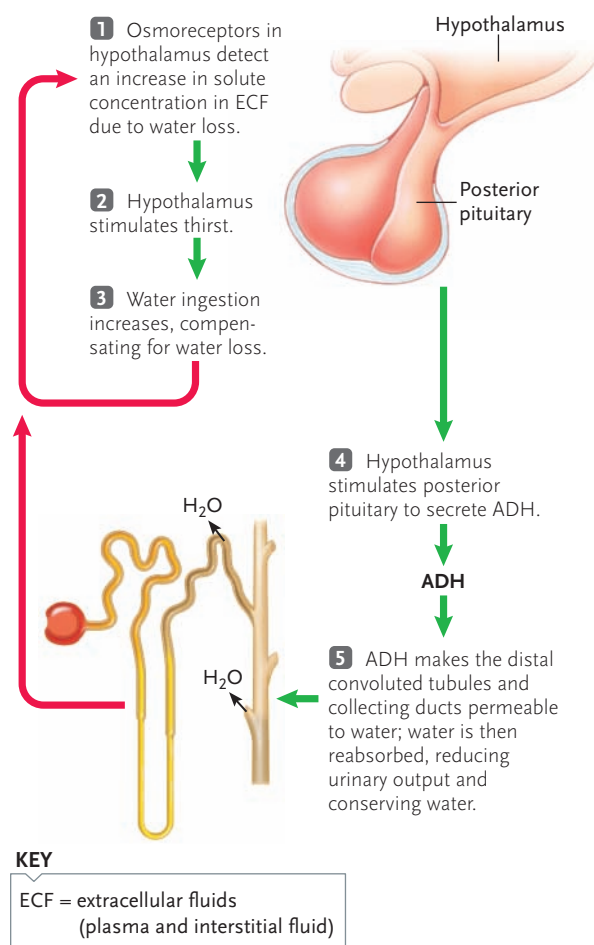
1 Osmoreceptors in hypothalamus detect an increase in solute concentration in ECF due to water loss.

2 Hypothalamus stimulates thirst.

3 Water ingestion increases, compensating for water loss.

Hypothalamus

Posterior pituitary

4 Hypothalamus stimulates posterior pituitary to secrete ADH.

H_2O

ADH

H_2O

5 ADH makes the distal convoluted tubules and collecting ducts permeable to water; water is then reabsorbed, reducing urinary output and conserving water.

KEY

ECF = extracellular fluids (plasma and interstitial fluid)

Figure 46.12
The ADH regulatory system, which stimulates water reabsorption to compensate for a loss in the fluid volume of the extracellular fluids due to excessive water loss from the body.

As a result, water is reabsorbed into those tubules and ducts so that urinary output is reduced and water is conserved (step 5).

By stimulating thirst and water reabsorption in the kidneys, the body's depleted stock of water is restored. The newly added water dilutes the solutes in the body fluids to normal concentrations.

In the opposite condition, when there is a water excess in extracellular fluids, the osmolarity of those fluids drops below normal levels. Here, there is no stimulation of the osmoreceptors in the hypothalamus. Consequently, there is no sensation of thirst, and no ADH release from the posterior pituitary. (In going from water deficiency to water excess, there is a gradual change in both of these parameters as the body adjusts to match its needs, meaning that the sensation of thirst decreases and ADH release is reduced as water in body fluids increases.) Without ADH, the distal convoluted tubules and collecting ducts again become impermeable to water. The animal excretes large volumes of dilute urine until the osmolarity of the extracellular fluids returns to normal. Alcohol also causes frequent urination by inhibiting ADH release.

Although the RAAS and ADH systems interact to regulate the body's water balance over a wide range of conditions, their regulatory mechanisms cannot compensate for water losses for more than a few days if water is unavailable. Dehydration becomes fatal when water loss amounts to about 12% of the normal fluid volume of the body.

Unlike mammals, most other vertebrates cannot conserve water by producing highly concentrated, hyperosmotic urine. In the next section, we consider some of the adaptations that nonmammalian vertebrates use to maintain the osmolarity of body fluids and water balance while excreting hypoosmotic urine.

Study Break

Outline the roles of the RAAS and ADH system in regulating mammalian kidney function.

46.5 Kidney Function in Nonmammalian Vertebrates

Among nonmammalian vertebrates, only a few species of aquatic birds produce urine that is hyperosmotic to body fluids. The particular adaptations that maintain osmolarity and water balance among these animals vary depending on whether retention of water or salts is the major issue.

Marine Fishes Conserve Water and Excrete Salts

Marine teleosts live in seawater, which is strongly hyperosmotic to their body fluids. As a result, they continually lose water to their environment by osmosis and must replace it by continual drinking. The kidneys of marine teleosts play little role in regulating salt in their body fluids because they cannot produce hyperosmotic urine that would both remove salt and conserve water. Instead, excess Na^+, K^+, and Cl^- ions are eliminated from the body by specialized cells in the gills, called *chloride cells,* which actively transport Cl^- into the surrounding seawater; the Na^+ and K^+ ions are also actively transported to maintain electrical neutrality **(Figure 46.13a).** Certain other ions in the ingested seawater, such as Ca^{2+} and Mg^{2+}, are removed by the kidneys in an isoosmotic urine. On balance, a marine teleost is able to retain most of the water it drinks and eliminate most of the salt, allowing its body fluids to remain hypoosmotic to the surrounding water with no need to secrete hyperosmotic urine. Nitrogenous wastes are released from the gills, primarily as ammonia, by simple diffusion. The kidneys play little role in nitrogenous-waste removal.

Sharks and rays have a different adaptation to seawater—the osmolarity of their body fluids is main-

tained close to that of seawater by retaining high levels of urea in body fluids, along with another nitrogenous waste, *trimethylamine oxide (TMAO)*. The match in osmolarity keeps sharks and rays from losing water to the surrounding sea by osmosis, and they do not have to drink seawater continually to maintain their water balance. Excess salts ingested with food are excreted in the kidney and by specialized secretory cells in a *rectal salt gland* located near the anal opening.

Freshwater Fishes and Amphibians Excrete Water and Conserve Salts

The body fluids of freshwater fishes and aquatic amphibians (no amphibians live in seawater) are hyperosmotic to the surrounding water, which usually ranges from about 1 to 10 mOsm/L. Water therefore moves osmotically into their tissues. Such animals rarely drink, and they excrete large volumes of dilute urine to get rid of excess water **(Figure 46.13b)**. In freshwater fishes, salt ions lost with the urine are replaced by salt in foods and by active transport of Na^+ and K^+ into the body by the gills; Cl^- follows to maintain electrical neutrality. Aquatic amphibians obtain salt in the diet and by active transport across the skin from the surrounding water. Nitrogenous wastes are excreted from the gills as ammonia in both freshwater fishes and aquatic amphibians.
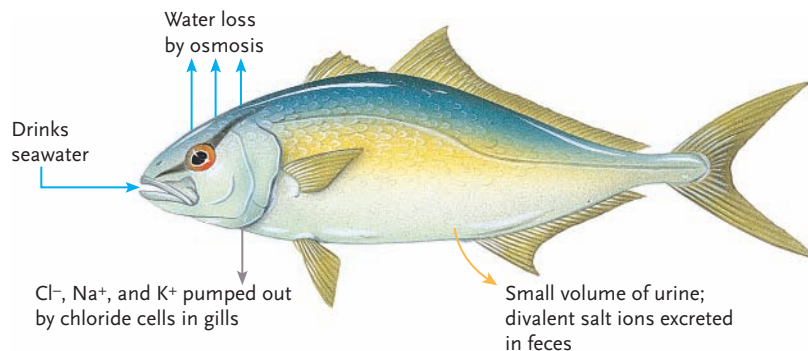
Terrestrial amphibians must conserve both water and salt, which is obtained primarily in foods. In these animals, the kidneys secrete salt into the urine, causing water to enter the urine by osmosis. In the bladder, the salt is reclaimed by active transport and returned to body fluids. The water remains in the bladder, making the urine very dilute; during times of drought, it is reabsorbed as a water source. Terrestrial amphibians also have behavioral adaptations that help minimize water loss, such as seeking shaded, moist environments and remaining inactive during the day.

Larval amphibians, which are completely aquatic, excrete nitrogenous wastes from their gills as ammonia. Adult amphibians excrete nitrogenous wastes through their kidneys as urea.

Reptiles and Birds Excrete Uric Acid to Conserve Water

Terrestrial reptiles conserve water by secreting nitrogenous wastes in the form of an almost water-free paste of uric acid crystals. Further water conservation occurs as the epithelial cells of the cloaca, the common exit for the digestive and excretory systems, absorb water from feces and urine before those wastes are excreted. Most birds conserve water by the same processes—they excrete nitrogenous wastes as uric acid and absorb water from the urine and feces in the cloaca. In reptiles, the scales covering the skin allow almost no water to escape through the body surface.

a. Marine teleosts

Water loss by osmosis

Drinks seawater

Cl^-, Na^+, and K^+ pumped out by chloride cells in gills

Small volume of urine; divalent salt ions excreted in feces

b. Freshwater teleosts

Water gain by osmosis

Drinks little or no water; some salts enter with food

Salts pumped in by cells in gills

Large volume of dilute urine
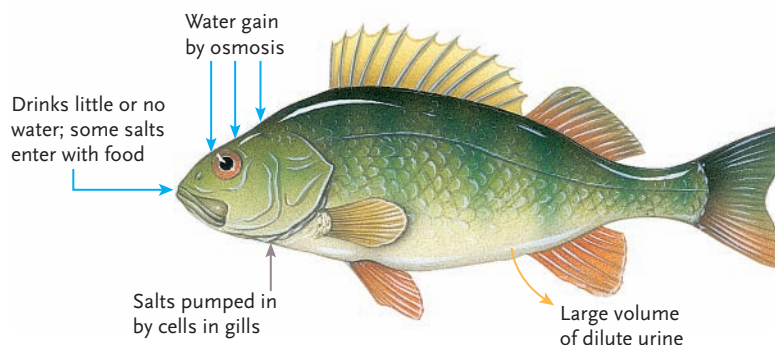
Figure 46.13
The mechanisms balancing the water and salt content of **(a)** marine teleosts and **(b)** freshwater teleosts.

Reptiles and birds that live in or around seawater, including reptiles such as crocodilians, sea snakes, and sea turtles and birds such as seagulls, penguins, and pelicans, take in large quantities of salt with their food and rarely or never drink fresh water. These animals typically excrete excess salt through specialized *salt glands* located in the head **(Figure 46.14),** which remove salts from the blood by active transport. The salts are secreted to the environment as a water solution in which salts are two to three times more concentrated

Salt glands in skull

Ducts leading to nostrils and beak

Droplets of concentrated salt solution

Figure 46.14
Salt glands in a bird living on a seacoast.

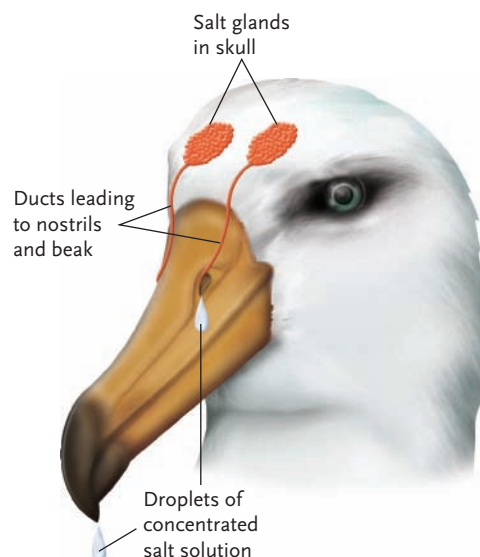than in body fluids. The secretion exits through the nostrils of birds and lizards, through the mouth of marine snakes, and as salty tears from the eye sockets of sea turtles and crocodilians. Neural and hormonal controls, essentially the same as those regulating osmolarity in mammals, control the rate of fluid secretion and its salt concentration.

The adaptations described in this section permit excretion of toxic wastes and allow animals to maintain the concentration of body fluids at levels that keep cells from swelling or shrinking. Animals also have mechanisms that address an equally vital challenge—maintaining their internal environment at temperatures that can be tolerated by body cells. We take up these processes in the next section.

STUDY BREAK

1. How do marine and freshwater teleosts differ in water, salt, and nitrogenous-waste regulation?
2. Reptiles and birds excrete nitrogenous wastes in the form of uric acid. Is there an advantage to doing this as opposed to the mammalian process of excreting nitrogenous wastes as urea?

46.6 Introduction to Thermoregulation

Environmental temperatures vary enormously across Earth's surface. However, animal cells can survive only within a temperature range from about 0°C to 45°C (32°F to 113°F). Not far below 0°C, the lipid bilayer of a biological membrane changes from a fluid to a frozen gel, which disrupts vital cell functions, and ice crystals dest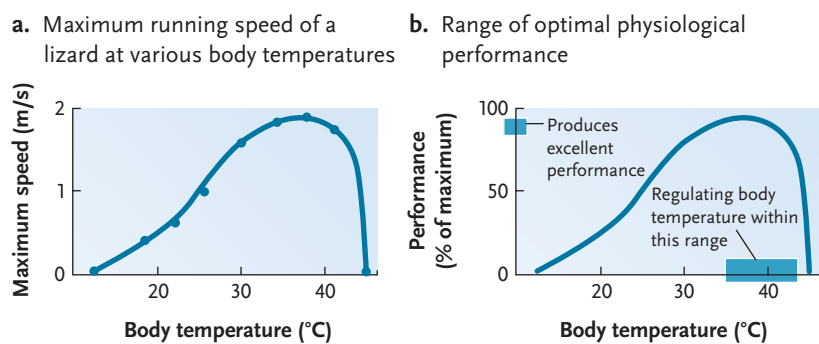roy the cell's organelles. At the other extreme, as temperatures approach 45°C, the kinetic motions of molecules become so great that most proteins and nucleic acids unfold from their functional form. Either condition leads quickly to cell death. Animals therefore usually maintain internal body temperatures somewhere within the 0°C to 45°C limits.

Temperature regulation—thermoregulation—is based on negative feedback pathways in which temperature receptors *(thermoreceptors)* detect changes from a temperature *set point*. Signals from the receptors trigger physiological and behavioral responses that return the temperature to the set point (thermoreceptors are discussed in Section 39.6; negative feedback mechanisms and set points are discussed in Section 36.4). All of the responses triggered by negative feedback mechanisms involve adjustments in the rate of heat-generating oxidative reactions within the body, coupled with adjustments in the rate of heat gain or loss at the body surface. The particular adaptations accomplishing these responses vary widely among species, however. And, while body temperature is closely regulated around a set point in all endotherms, the set point itself may vary over the course of a day and between seasons.

In this section, we describe the structures, mechanisms, and behavioral adaptations that enable animals to regulate their temperature.

Thermoregulation Allows Animals to Reach Optimal Physiological Performance

Within the 0°C to 45° range of tolerable temperatures, an animal's *organismal performance*—the rate and efficiency of its biochemical, physiological, and whole-body processes—varies greatly. For example, the speed at which the Middle Eastern lizard *Agama stellio* can sprint is low when the animal's body temperature is cold, rises smoothly with body temperature until it levels to a fairly broad plateau, and then drops off dramatically with further increases in body temperature **(Figure 46.15a).** Similar patterns of temperature dependence are observed for numerous other body functions **(Figure 46.15b).** The temperature range that provides good organismal performance varies from one species to another, however.

Animals that maintain body temperature within a fairly narrow optimal range can run quickly, digest food efficiently, and carry out necessary activities and processes rapidly and effectively (see Figure 46.15b). Besides keeping body temperatures within tolerable limits, thermoregulation allows animals to achieve this level of performance.

Animals Exchange Heat with Their Environments by Conduction, Convection, Radiation, and Evaporation

As part of thermoregulation, animals exchange heat with their environment. Virtually all heat exchange occurs at surfaces where the body meets the external en-

a. Maximum running speed of a lizard at various body temperatures

b. Range of optimal physiological performance

Produces excellent performance

Regulating body temperature within this range

Figure 46.15
Body temperature and organismal performance. **(a)** The maximum sprint speed of a lizard *(Agama stellio)* changes dramatically with body temperature. **(b)** An animal's other behavioral and physiological processes respond to temperature changes in similar ways. The advantage of regulating body temperature within the range indicated by the bar on the horizontal axis is a high level of organismal performance, indicated by the bar on the vertical axis.

vironment. As with all physical bodies, heat flows into animals if they are cooler than their surroundings and flows outward if they are warmer. This heat exchange occurs by four mechanisms: *conduction, convection, radiation,* and *evaporation* **(Figure 46.16).**

Conduction is the flow of heat between atoms or molecules in direct contact. An animal loses heat by conduction when it contacts a cooler object, and gains heat when it contacts an object that is warmer. **Convection** is the transfer of heat from a body to a fluid, such as air or water, that passes over its surface. The movement maximizes heat transfer by replacing fluid that has absorbed or released heat with fluid at the original temperature. **Radiation** is the transfer of heat energy as electromagnetic radiation. Any object warmer than absolute zero ($-273°C$) radiates heat; as the object's temperature rises, the amount of heat it loses as radiation increases as well. Animals also gain heat through radiation, particularly by absorbing radiation from the sun. **Evaporation** is heat transfer through the energy required to change a liquid to a gas. Evaporation of water from a surface is an efficient way to transfer heat; when the water in sweat evaporates from the body surface, the body cools down because heat is being transferred to the evaporated water in the surrounding air.

All animals gain or lose heat by a combination of these four mechanisms. A marathon runner or a bicycle racer struggling with the heat on a sunny summer day, for example, loses heat by the evaporation of sweat from the skin, by convection as air flows over the skin, and by outward infrared radiation. The runner gains heat from internal biochemical reactions (especially oxidations), by absorbing infrared and solar radiation, and by conduction as the feet contact the hot ground. To maintain a constant body temperature, the heat gained and lost through these pathways must balance.

Ectothermic and Endothermic Animals Rely on Different Heat Sources to Maintain Body Temperature

Different animals use one of two major strategies to balance heat gain and loss. Animals that obtain heat primarily from the external environment are known as **ectotherms** (*ecto* = outside); those obtaining most of their heat from internal physiological sources are called **endotherms** (*endo* = inside). All ectotherms generate at least some heat from internal reactions, however, and endotherms can obtain heat from the environment under some circumstances.

Virtually all invertebrates, fishes, amphibians, and reptiles are ectotherms. Although these animals are popularly described as cold-blooded, the body temperature of some, such as an active lizard, may be as high as or higher than ours on a sunny day. Ectotherms regulate body temperature by controlling the rate of heat exchange with the environment. Through behav-
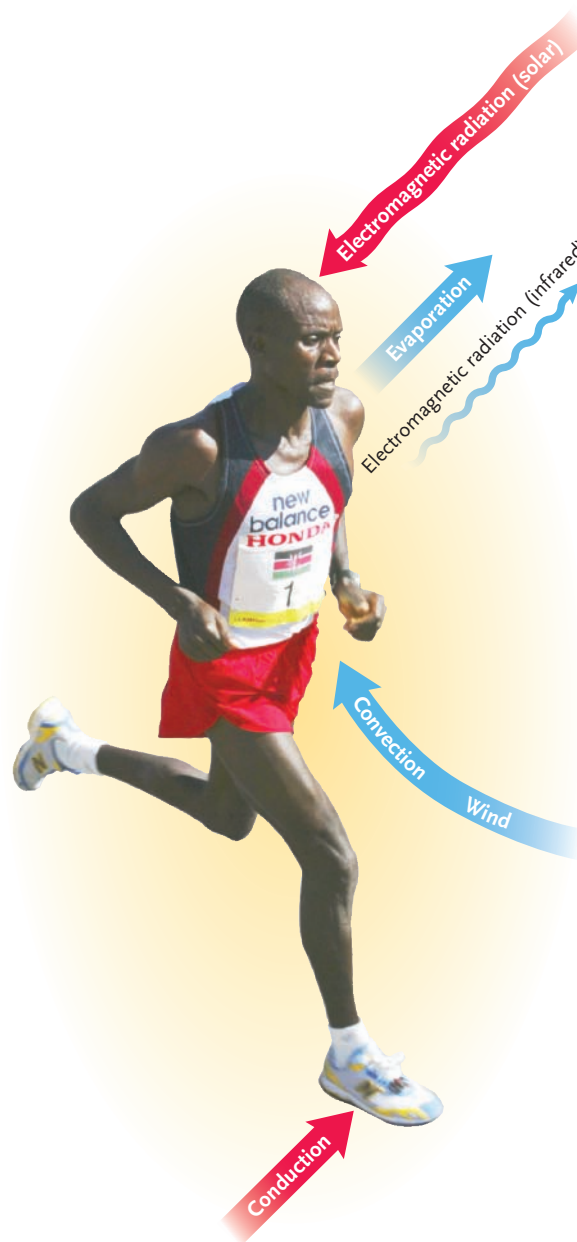
Figure 46.16
Heat flow to (in red) and from (in blue) a marathon runner on a hot, sunny day. Unlike conduction, convection, and evaporation, which take place through the kinetic movement of molecules, electromagnetic radiation is transmitted through space as waves of energy. (Photo: Rafael Winer/Corbis.)

ioral and physiological mechanisms, they adjust body temperature toward a level that allows optimal physiological performance. However, most ectotherms are unable to maintain optimal body temperature when the temperature of their surroundings departs too far from that optimum, particularly when environmental temperatures fall. As a result, the body temperatures of ectotherms fluctuate with environmental temperatures, and they typically are less active when it is cold. Nevertheless, ectotherms are highly successful, particularly in warm environments.

The endotherms—birds, mammals, some fishes, sea turtles, and some invertebrates—keep their bodies

at an optimal temperature by regulating two processes: (1) the amount of heat generated by internal oxidative reactions and (2) the amount of heat exchanged with the environment. Because endotherms use internal heat sources to maintain body temperature at optimal levels, they can remain active over a broader range of environmental temperatures than ectotherms, and they can inhabit a wider range of habitats. However, endotherms require a nearly constant supply of energy to maintain their body temperatures. And because that energy is provided by food, endotherms typically consume much more food than ectotherms of equivalent size.

The difference between ectotherms and endotherms is reflected in their metabolic responses to environmental temperature **(Figure 46.17)**. For example, the metabolic rate of a resting mouse *increases* steadily as the environmental temperature falls from 25°C to 10°C (77°F to 50°F). This increase reflects the fact that in order to maintain a constant body temperature in a colder environment, endotherms must process progressively more food and generate more heat to compensate for their increased rate of heat loss. In this respect, an endotherm can be likened to a house in winter. To maintain a constant internal temperature, the homeowner must burn more oil or gas on a cold day than on a warm day.

By contrast, the metabolic rate of a resting lizard typically *decreases* steadily over the same temperature range. Because ectotherms don't maintain a constant body temperature, their biochemical and physiological functions, including oxidative reactions, slow down as environmental and body temperatures decrease. Thus, an ectotherm consumes and uses less energy when it is cold than when it is warm. This difference between ectotherms and endotherms is so fundamental that even samples of living tissue extracted from an ectotherm consume energy more slowly than equivalent samples from an endotherm.

Ectothermy and endothermy represent different strategies for coping with the variations in environmental temperature that all animals encounter; neither strategy is inherently superior to the other. Endotherms can remain fully active over a wide temperature range. Cold weather does not prevent them from foraging, mating, or escaping from predators, but it does increase their energy and food needs—and, to satisfy their need for food, they may not have the option of staying curled up safely in a warm burrow. Ectotherms do not have the capacity to be active when environmental temperatures drop too low; they move sluggishly and are unable to capture food or escape from predators. However, because their metabolic rates are lower under such circumstances, so are their food needs, and they do not have to actively look for food and expose themselves to danger to the extent that endotherms do.

Having laid the ground rules of heat transfer and weighed the relative advantages and disadvantages of ectothermy and endothermy, we now begin a more detailed examination of how animals actually regulate their body temperatures within these overall strategies.
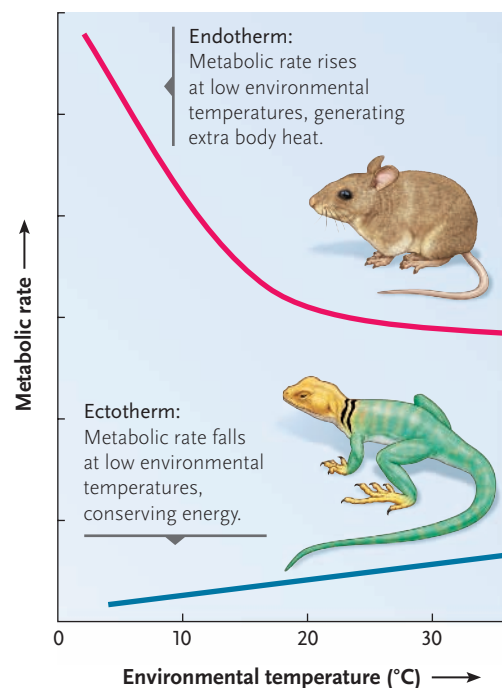
STUDY BREAK

Distinguish between ectothermy and endothermy. Give one advantage and one disadvantage for each form of thermoregulation.

46.7 Ectothermy

Ectotherms vary widely in their ability to regulate internal body temperatures. For example, most aquatic invertebrates have such limited ability to thermoregulate that their body temperatures closely match those of the surrounding environment. These species live in or seek warm or temperate environments, where temperatures fall within a range that produces optimal physiological performance. Ectotherms with a greater ability to thermoregulate may occupy more varied habitats.

Ectotherms Are Found in All Invertebrate Groups

Most aquatic invertebrates are limited thermoregulators whose body temperature closely follows the temperature of their surroundings. However, even among

Endotherm:
Metabolic rate rises at low environmental temperatures, generating extra body heat.

Ectotherm:
Metabolic rate falls at low environmental temperatures, conserving energy.

Metabolic rate ⟶

0   10   20   30

Environmental temperature (°C) ⟶

Figure 46.17
Metabolic responses of ectotherms and endotherms to cooling environmental temperatures. At any temperature, the metabolic rates of endotherms are always higher than those of endotherms of comparable size.

these animals, some use behavioral responses to regulate body temperature. For example, a South American intertidal mollusk, *Echinolittorina peruviana,* is longer than it is wide. Researchers have shown that this animal orients itself as a means of thermoregulation. On sunny, summer days, it faces the sun, offering a smaller surface area for the sun's rays. On overcast summer days, or during the winter, it orients itself with a lateral side—which has the larger surface area—toward the sun's rays.

Invertebrates living in terrestrial habitats regulate body temperatures more closely. Many also use behavioral responses, such as moving between shaded and sunny regions, to regulate body temperature. Some winged arthropods, including bees, moths, butterflies, and dragonflies, use a combination of behavioral and heat-generating physiological mechanisms for thermoregulation. For example, in cool weather, these animals warm up before taking flight by rapidly vibrating the large flight muscles in the thorax, in a mechanism similar to shivering in humans. The tobacco hawkmoth *(Manduca sexta)* vibrates its flight muscles until its thoracic temperature reaches about 36°C before flying. During flight, metabolic heat generated by the flight muscles sustains the elevated thoracic temperature, so much so that a flying sphinx moth produces more heat per gram of body weight than many mammals.

Most Fishes, Amphibians, and Reptiles Are Ectotherms

Vertebrate ectotherms—fishes, amphibians, and reptiles—also vary widely in their ability to thermoregulate. Most aquatic species have a more limited thermoregulatory capacity than that found among terrestrial species, particularly the reptiles. Some fishes, however, are highly capable thermoregulators.

Fishes. The body temperatures of most fishes remain within one or two degrees of their aquatic environment. However, many fishes use behavioral mechanisms to keep body temperatures at levels allowing good physiological performance. Freshwater species, for example, may use opportunities provided by the thermal stratification of lakes and ponds (see Figure 52.22). During hot summer days they remain in deep, cool water, moving to the shallows to feed only during early morning and late evening when air and water temperatures fall.

Amphibians and Reptiles. The body temperatures of most amphibians also closely match environmental temperatures. Some, such as the tadpoles of foothill yellow-legged frogs *(Rana boylii),* regulate their body temperature to some degree by changing their location in ponds and lakes to take advantage of temperature differences between deep and shallow water, or be-
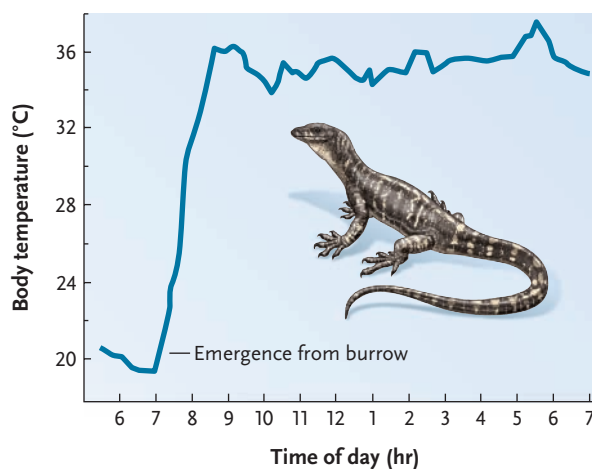

Figure 46.18
An example of excellent thermoregulation in ectotherms. The body temperature of the Australian lizard *Varanus varius* rises quickly after the animal emerges from its burrow and remains relatively stable throughout the day.

tween sunny and shaded regions. Some terrestrial amphibians bask in the sun to raise their body temperature, and seek shade to lower body temperature. However, basking can be dangerous to amphibians because they lose water rapidly through their permeable skin. One South American hylid frog *(Phyllomedusa sauvagei),* which often basks in sunlight, avoids this problem by coating itself with waterproofing lipids secreted by glands in its skin.

Thermoregulation is more pronounced among terrestrial reptiles. Some lizard species can maintain temperatures that are nearly as constant as those of endotherms **(Figure 46.18).** For small lizards, the most common behavioral thermoregulatory mechanism is shuttling between sunny (warmer) and shady (cooler) regions; in the deserts, lizards and other reptiles retreat into burrows during the hottest part of summer days. Some, such as the desert iguana *(Dipsosaurus dorsalis),* lose excess heat by *panting*—rapidly moving air in and out of the airways. The air movement increases heat loss by convection and by evaporation of water from the respiratory tract.

Lizards also frequently adjust their posture to foster heat exchange with the environment, and control the angle of their body relative to the rays of the sun. For example, horned lizards (genus *Phrynosoma*) often warm up by flattening themselves against warm, sunlit rocks to maximize their rate of heat gain by conduction from the rock and radiation from the sun. Snakes and lizards can often be found on large rocks and on roads on chilly nights, taking advantage of the heat retained by the stone or concrete. *Agama savignyi,* a lizard that lives in the Negev Desert in Israel, cools off at midday by climbing into shady bushes, moving away from the hot sand and catching a cooling breeze.

Researchers have demonstrated experimentally that several lizard species couple physiological re-

sponses to behavioral mechanisms of thermoregulation. For example, when a Galapagos marine iguana (*Amblyrhynchus cristatus;* see Figure 19.8c) is exposed to heat from infrared radiation, blood flow increases in the heated regions of the skin. The blood absorbs heat rapidly and carries it to critical organs in the core of the body. Conversely, when an area of skin is experimentally cooled, blood flow to it is restricted, thereby preventing the loss of heat to the external environment.

Ectotherms Can Compensate for Seasonal Variations in Environmental Temperature

Many ectotherms undergo physiological changes, called **thermal acclimatization,** in response to seasonal shifts in environmental temperature. These changes allow the animals to attain good physiological performance at both winter and summer temperatures.

For example, in the summer a bullhead catfish (*Ameiurus* species) can survive water temperatures as high as 36°C (97°F), but it cannot tolerate temperatures below 8°C (46°F). In the winter, however, the bullhead cannot survive water temperatures above 28°C (82°F), but can tolerate temperatures near 0°C (32°F). Scientists have hypothesized that the production of different versions of the same enzyme (perhaps encoded by different genes, or produced as a result of alternative splicing; see Section 16.3), each having optimal activity at cooler or warmer temperatures, underlies such acclimatization.

Another acclimatizing change involves the phospholipids of biological membranes (see *Focus on Research* in Chapter 6). For example, membrane phospholipids have higher proportions of double bonds in carp living in colder environments than in carp living in warmer environments. The higher proportion of double bonds makes it harder for the membrane to freeze. A higher proportion of cholesterol also protects membranes from freezing.

When seasonal temperatures fall below 0°C (32°F), some ectotherms add molecules to their body fluids that act as antifreeze molecules to depress their freezing point and retard ice crystal formation. For example, glycerol added to the cellular and extracellular fluids of a parasitic wasp (*Bracon* species) keeps the insect from freezing at temperatures as low as −45°C (−49°F). Similarly, antifreeze proteins allow fishes such as the winter flounder to remain active in seawater as cold as −1.8°C (29°F) (see *Insights from the Molecular Revolution* in Chapter 52).

Ectotherms thus primarily control body temperature by regulating heat exchange with the environment; internal-heat generating mechanisms contribute to the control mechanisms in some species, but are rarely the primary source of body heat. The opposite conditions occur among endotherms: although these animals also regulate heat exchange with the environment, their primary sources of body heat are internal.

STUDY BREAK

1. Describe two mechanisms an ectothermic animal can use to regulate its temperature.
2. What is thermal acclimatization?

46.8 Endothermy

Endotherms—mostly birds and mammals—have the most elaborate and extensive thermoregulatory adaptations of all animals. Highly specialized features of body structure interact with both physiological and behavioral mechanisms to keep the body temperature constant within a narrow range. Typically, the body temperatures of fully active individuals are held constant at levels between about 39° to 42°C (102° to 108°F) in birds, and 36° to 39°C (97° to 102°F) in mammals. These internal temperatures are maintained in the face of environmental temperatures that may range over much greater extremes, from as low as −42°C to as high as +48°C (−45°F to +120°F). Some highly specialized endotherms can even survive temperatures beyond these limits.

We begin by describing the basic feedback mechanisms that maintain body temperature, with primary emphasis on the human system. Later sections discuss variations in the responses of other mammals and of birds, and daily and seasonal variations in the temperature set point.

Information from Thermoreceptors Located in the Skin and Internal Structures Is Integrated in the Hypothalamus

Thermoreceptors are found in various locations in the human body, including the **integument** (skin; introduced in Chapter 36), spinal cord, and hypothalamus. Two types of thermoreceptors occur in human skin. One, called a *warm receptor,* sends signals to the hypothalamus as skin temperature rises above 30°C (86°F), and reaches maximum activity when the temperature rises to 40°C (104°F). The other type, the *cold receptor,* sends signals when skin temperature falls below about 35°C (95°F) and reaches maximum activity at 25°C (77°F). By contrast, the highly sensitive thermoreceptors in the hypothalamus send signals when the blood temperature shifts from the set point by as little as 0.01°C (0.02°F).

Signals from the thermoreceptors are integrated in the hypothalamus and other regions of the brain to bring about compensating physiological and behavioral responses **(Figure 46.19).** The responses keep body temperature close to the set point, which varies normally in humans between 35.5° and 37.7°C (96.0° to 99.9°F) for the head and trunk. The appendages typically vary more widely in temperature; in freezing

weather, for example, our arms, hands, legs, and feet are typically lower in temperature than the body core—and the ears and nose especially so.

The hypothalamus was identified as a major thermoreceptor and response integrator in mammals by experiments in which various regions of the brain were heated or cooled with a temperature probe. Within the brain, only the hypothalamus produced thermoregulatory responses such as shivering or panting. Later experiments revealed a similar response when regions of the spinal cord were cooled, indicating that thermoreceptors also occur in this location. The hypothalamus is also a major thermoreceptor and response integrator in fishes and reptiles. In birds, thermoreceptors in the spinal cord appear to be most significant in thermoregulation.

Responses When Core Temperature Falls below the Set Point. When thermoreceptors signal a fall in core temperature below the set point, the hypothalamus triggers compensating responses by sending signals through the autonomic nervous system. Among the immediate responses is constriction of the arterioles in the skin (vasoconstriction), which reduces the flow of blood to capillary networks in the skin. The reduced flow cuts down the amount of heat delivered to the skin and lost from the body surface. The reduction in flow is most pronounced in the skin covering the extremities, where blood flow may be reduced by as much as 99% when core temperature falls.

Another immediate response is contraction of the smooth muscles erecting the hair shafts in mammals and feather shafts in birds, which traps air in pockets over the skin, reducing convective heat loss. The response is minimally effective in humans because hair is sparse on most parts of the body—it produces the goose bumps we experience when the weather gets chilly. However, in mammals with fur coats or in birds, erection of the hair or feather shafts significantly increases the thickness of the insulating layer that covers the skin.

Immediate behavioral responses triggered by a reduction in skin temperature also help reduce heat loss from the body. Mammals may reduce heat loss by moving to a warmer locale, curling into a ball, or huddling together. We have all seen puppies huddled together to keep warm; birds such as penguins also keep warm by huddling. We humans may also put on more clothes or slip into a tub of hot water.

If these immediate responses do not return body temperature to the set point, the hypothalamus triggers further responses, most notably the rhythmic tremors of skeletal muscle we know as shivering. The heat released by the muscle contractions and the oxidative reactions powering them can raise the total heat production of the body substantially. At the same time, the hypothalamus triggers secretion of *epinephrine* (from the adrenal medulla) and *thyroid hormone* (see
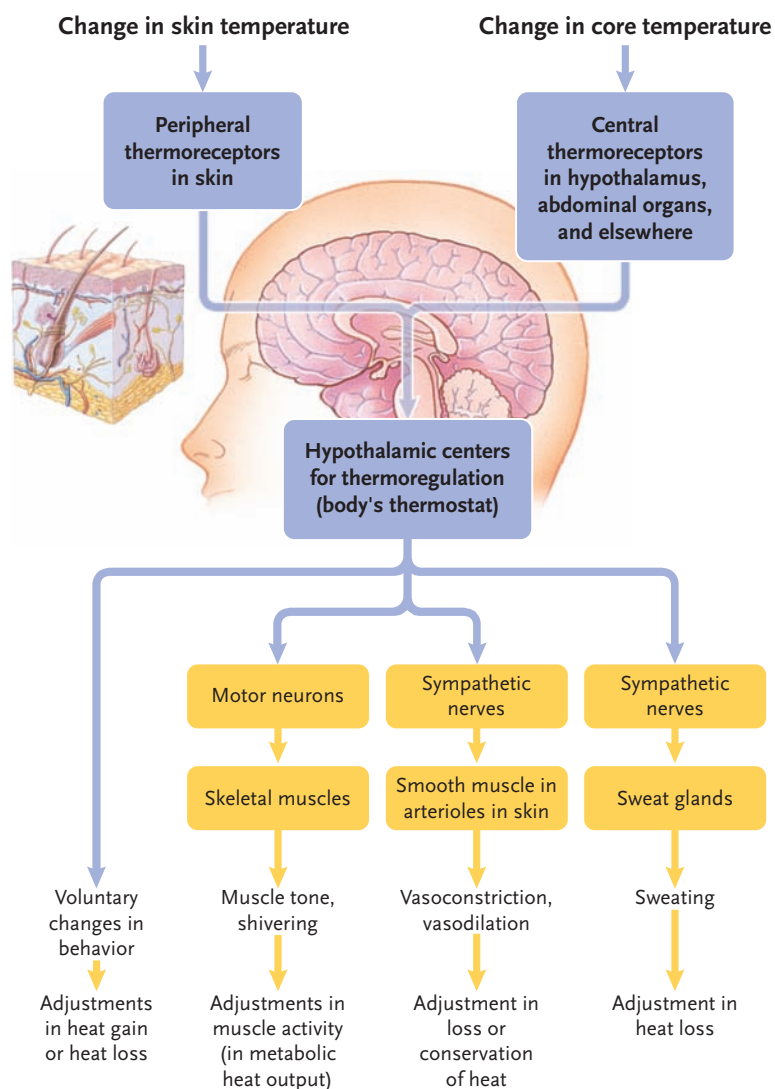
Change in skin temperature

Change in core temperature

Peripheral thermoreceptors in skin

Central thermoreceptors in hypothalamus, abdominal organs, and elsewhere

Hypothalamic centers for thermoregulation (body's thermostat)

Motor neurons	Sympathetic nerves	Sympathetic nerves
Skeletal muscles	Smooth muscle in arterioles in skin	Sweat glands

Voluntary changes in behavior

Muscle tone, shivering

Vasoconstriction, vasodilation

Sweating

Adjustments in heat gain or heat loss

Adjustments in muscle activity (in metabolic heat output)

Adjustment in loss or conservation of heat

Adjustment in heat loss

Figure 46.19
The physiological and behavioral responses of humans and other mammals to changes in skin and core temperature.

Section 40.4), both of which increase heat production by stimulating the oxidation of fats and other fuels. The generation of heat by oxidative mechanisms in nonmuscle tissue throughout the body is termed **nonshivering thermogenesis**.

In human newborn babies and many other mammals, the most intense heat generation by nonshivering thermogenesis takes place in a specialized **brown adipose tissue** (also called **brown fat**) that can produce heat rapidly. Heat is generated by a mechanism that uncouples electron transport from ATP production in mitochondria (see Section 8.4); the heat is transferred throughout the body by the blood. Animals that hibernate or are active in cold regions, as well as the young of many others, contain brown adipose tissue. In most mammals, brown adipose tissue is concentrated between the shoulders in the back and around the neck. In human newborn babies, this tissue accounts for about 5% of body weight. Typically the tissue shrinks as humans age, until it is absent or essentially so in most adults. However, if exposure to cold is ongoing, the tissue remains. For instance, some Japanese and

Korean divers who harvest shellfish in frigid waters, and male Finlanders who work outside during the year, have significant amounts of brown adipose tissue.

If none of these responses succeeds in raising body temperature to the set point, the result is **hypothermia,** a condition in which the core temperature falls below normal for a prolonged period. In humans, a drop in core temperature of only a few degrees affects brain function and leads to confusion; continued hypothermia can lead to coma and death.

Responses When Core Temperature Rises above the Set Point. When core temperature rises above the set point, the hypothalamus sends signals through the autonomic system that trigger responses lowering body temperature. As an immediate response, the signals relax smooth muscles of arterioles in the skin (vasodilation), increasing blood flow and with it, the heat lost from the body surface. In addition, in humans and other mammals with sweat glands, such as antelopes, cows, and horses, signals from the hypothalamus trigger the secretion of sweat, which absorbs heat as it evaporates from the surface of the skin.

Some endotherms, including dogs (which have sweat glands only on their feet) and many birds (which have no sweat glands), use panting as a major way to release heat. These physiological changes are reinforced by behavioral responses such as seeking shade or a cool burrow, plunging into cold water, wallowing in mud, or taking a cold drink. Elephants typically take up water in their trunk and spray it over their body to cool off in hot weather.

When the heat gain of the body is too great to be counteracted by these responses, **hyperthermia** results. An increase of only a few degrees above normal for a prolonged period is enough to disrupt vital biochemical reactions and damage brain cells. Most adult humans become unconscious if their body temperature reaches 41°C (106°F) and die if it goes above 43°C (110°F) for more than a few minutes.

The Skin Is Highly Adapted to Control Heat Transfer with the Environment
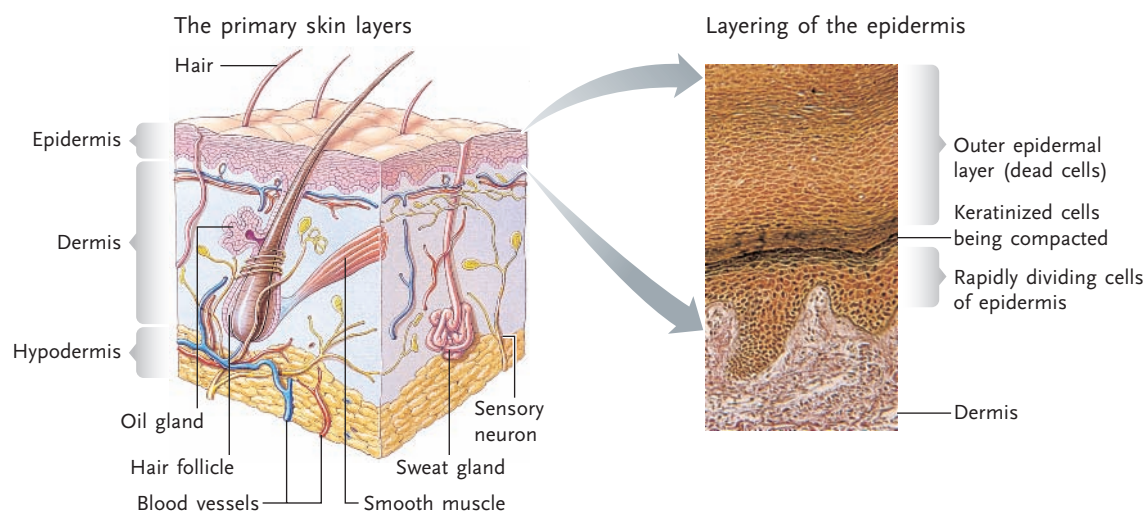
Besides its defensive role against infection described in Section 43.1, the skin of birds and mammals is an organ of heat transfer. The arterioles delivering blood to the capillary networks of the skin constrict or dilate to control blood flow and, with it, the amount of heat transferred from the body core to the surface.

The outermost living tissue of human skin, the **epidermis,** consists of cells that grow and divide rapidly **(Figure 46.20),** becoming packed with fibers of a highly insoluble protein, *keratin* (see Section 5.3). When fully formed, the epidermal cells die and become compacted into a tough, impermeable layer that limits water loss primarily to evaporation of the fluids secreted by the sweat glands.

The sweat glands and hair follicles are embedded in the layer below the epidermis. Called the **dermis,** it is packed with connective tissue fibers such as collagen, which resist compression, tearing, or puncture of the skin. The dermis also contains thermoreceptors and the dense networks of arterioles, capillaries, and venules that transfer heat between the skin and the environment.

The innermost layer of the skin, the **hypodermis,** contains larger blood vessels and additional reinforcing connective tissue. The hypodermis also contains an insulating layer of fatty tissue below the dermal capillary network, which ensures that heat flows between the body core and the surface primarily through the blood. The insulating layer is thickest in mammals that live in cold environments, such as whales, seals, walruses, and polar bears, in which it is known as *blubber.*

Figure 46.20
The structure of human skin.
(Micrograph: John D. Cunningham/Visuals Unlimited.)

The primary skin layers

Hair
Epidermis
Dermis
Hypodermis
Oil gland
Hair follicle
Blood vessels
Sweat gland
Smooth muscle
Sensory neuron

Layering of the epidermis

Outer epidermal layer (dead cells)
Keratinized cells being compacted
Rapidly dividing cells of epidermis
Dermis

a. Dissipating heat　　**b.** Conserving heat

Joe McDonald/Corbis

Fredrik Broman/Iconica/Getty Images, Inc.

Figure 46.21
Structural and behavioral adaptations controlling heat transfer at the body surface. **(a)** A jackrabbit *(Lepus californicus)* dissipating heat from its ears on a hot summer day. Notice the dilated blood vessels in its large ears. Both the large surface area of the ears and the extensive network of blood vessels promote the dissipation of heat by convection and radiation. **(b)** A husky *(Canis lupus familiaris)* conserving heat by curling up with the limbs under the body and the tail around the nose.

Many Birds and Mammals Have Additional Thermoregulatory Structures and Responses

The thermoregulatory mechanisms we have described to this point are common to many birds and mammals. Many species also have specialized responses that enhance thermoregulation. In hot weather, for example, many birds fly with their legs extended, so that heat flows from their legs into the passing air. Similarly, penguins expose featherless patches of skin under their wings to cool off on days when the weather is too warm. Jackrabbits **(Figure 46.21a)** and elephants dissipate heat from their large ears, which are richly supplied with blood vessels. In times of significant heat stress, kangaroos and rats spread saliva on their fur to increase heat loss by evaporation; some bats coat their fur with both saliva and urine.

Many mammals have an uneven distribution of fur that aids thermoregulation. In a dog, for example, the fur is thickest over the back and sides of the body and the tail, and thinnest under the legs and over the belly. In cold weather, dogs curl up, pull in their limbs, wrap their tail around the body, and bury their nose in the tail, so that only body surfaces insulated by thick fur are exposed to the air **(Figure 46.21b).** When the weather is hot, dogs spread their limbs, turn on their side or back, and expose the relatively bare skin of the belly, which acts as a heat radiator. These responses are combined with seeking sun or shade or a warm or cool surface to lie on.

In marine mammals such as whales and seals, heat loss is regulated by adjustments in the blood flow through the thick blubber layer to the skin. In cold water, blood flow is minimized by constriction of the vessels, making the skin temperature close to that of the surrounding water while the body temperature remains constant under the insulating blubber. In warmer water, blood flow to the skin increases, bypassing the blubber and allowing excess heat to be lost from the body surface.

In addition, heat loss in whales and seals is controlled by adjustments of the flow of blood to the flippers, which are not insulated by blubber and act as a heat radiator. When a whale generates excessive internal heat through the muscular activity of swimming, the flow of blood from the body core to the flippers increases. In contrast, when heat must be conserved to maintain core temperature at the set point, blood flow to the flippers is reduced.

As with ectotherms, many mammals also undergo thermal acclimatization to adjust to seasonal temperature change. That is, the development of a thick fur coat in winter, which is shed in summer, enables them to adapt to seasonal temperature changes. Note that the trigger for the coat changes in many cases is day length, rather than temperature; there is a general correlation with temperature and day length over the year. Some arctic and subarctic mammals develop a thicker layer of insulating fat in winter.

The Set Point Varies in Daily and Seasonal Rhythms in Many Birds and Mammals

The temperature set point in many birds and mammals varies in a regular cycle during the day. In some, the daily variations are relatively small and not obviously keyed to changes in environmental temperature. In others, larger variations are correlated with daily or seasonal temperature changes.

Humans are among the endotherms for which daily variations in the temperature set point are small. Normally, human core temperature varies from a minimum of about 35.5°C (95.9°F) in the morning to a maximum of about 37.7°C (99.9°F) in the evening. Women also show a monthly variation keyed to the menstrual cycle, with temperatures rising about 0.5°C (0.9°F) from the time of ovulation until menstruation begins. The physiological significance of these variations is unknown.

Camels undergo a daily variation of as much as 7°C (13°F) in set point temperature. During the day, a

camel's set point gradually resets upward, an adaptation that allows its body to absorb a large amount of heat. The heat absorption conserves water that would otherwise be lost by evaporation to keep the body at a lower set point. At night, when the desert is cooler, the thermostat resets again, allowing the body temperature to cool several degrees, releasing the excess heat absorbed during the day.

When the environmental temperature is cool, having a lowered temperature set point greatly reduces the energy required to maintain body temperature. In many animals, the lowered set point is accompanied by reductions in metabolic, nervous, and physical activity (including slower respiration and heartbeat), producing a sleeplike state known as **torpor.**

Entry into **daily torpor**—a period of inactivity keyed to variations in daily temperature—is typical of many small mammals and birds. These animals typically expend more energy per unit of body weight to keep warm than larger animals, because the ratio of body surface to volume increases as body size decreases. Hummingbirds, for example, feed actively during the daytime, when their set point is close to 40°C (104°F). During the cool of night, however, the set point drops to as low as 13°C (55°F), which allows the birds to conserve enough energy to survive overnight without feeding. Some nocturnal animals, including bats and small rodents such as the deer mouse, become torpid in cool locations during daylight hours when they do not actively feed. At night, their temperature set point rises and they become fully active **(Figure 46.22).**

Many animals enter a prolonged state of torpor tied to the seasons, triggered in most cases by a change in day length that signals the transition between summer and winter. The importance of day length has been demonstrated by laboratory experiments in which animals have been induced to enter seasonal torpor by changing the period of artificial light to match the winter or summer day length.
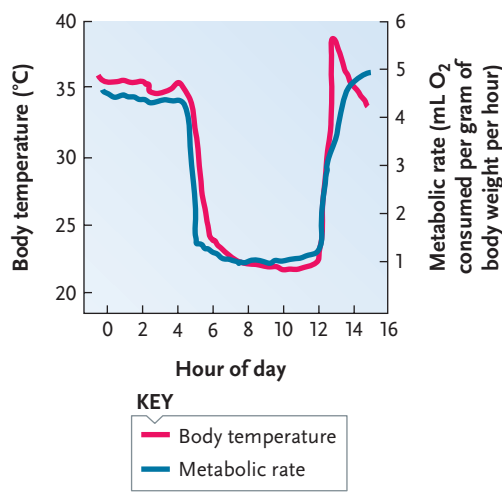
Extended torpor during winter, called **hibernation** (*hibernus* = relating to winter), greatly reduces metabolic expenditures when food is unobtainable. Typically, hibernators must store large quantities of fats to serve as energy reserves. The drop in body temperature during hibernation varies with the mammal. In some, such as hedgehogs, woodchucks, and squirrels, body temperature may fall by 20°C (36°F) or more. In certain hedgehogs, for example, body temperature falls from about 38°C (100°F) in the summer to as low as 5° to 6°C (41° to 43°F) during winter hibernation. Body temperature even drops to near 0°C in some small hibernating mammals and, in the Arctic ground squirrel, the body supercools (goes to a below-freezing, unfrozen state) during hibernation, with body temperature dropping to about -3°C. Some ectotherms, including amphibians and reptiles living in northern latitudes and even some insects, also become torpid during winter.

The depth of torpor differs among hibernating mammals. In bears, the core temperature drops only a few degrees. Although sluggish, hibernating bears will waken readily if disturbed. They also waken normally from time to time, as when females wake to give birth during the hibernating season.

Some mammals enter seasonal torpor during summer, called **estivation** (*aestivus* = relating to summer), when environmental temperatures are high and water is scarce. Some ground squirrels, for example, remain inactive in the cooler temperatures of their burrows during extreme summer heat. Many ectotherms, among them land snails, lungfishes, many toads and frogs, and some desert-living lizards, weather such climates by digging into the soil and entering a state of estivation that lasts throughout the hot dry season.

Some Animals Use a Form of Endothermy That Does Not Heat All of Their Cores

In contrast to birds and mammals, some animals exhibit a form of endothermy that does not heat all of their cores. For example, some cold-water marine teleosts (such as tunas and mackerels) and some sharks (such as the great white) use endothermy in their aerobic swimming muscles to maintain a body core temperature as much as 10° to 12°C warmer than their surroundings. These animals have in common the fact that they migrate over long distances, swimming continuously and, therefore, generating constant heat with the swimming muscles. That heat is insufficient to heat the entire body because too much heat is lost at the gill–water interface. These animals have evolved a *countercurrent heat exchanger* system between the swimming muscles and the gills to prevent most of the loss (countercurrent exchange is discussed in Section 44.2).

The system works as follows. Cold blood from the gills is first routed through arteries under the skin,

Figure 46.22
Cycle of daily torpor in a deer mouse *(Peromyscus maniculatus).*

KEY
— Body temperature
— Metabolic rate

Unanswered Questions

What is the maximum temperature for life?

As you've read, most nondormant animals cannot live above about 45°C. However, the actual limit remains controversial. Some desert ants, such as *Cataglyphis,* forage on hot Saharan sand with body temperatures exceeding 50°C! In laboratory studies, *Cataglyphis bicolor* remained active at a body temperature of 55°C for short periods. This tolerance for high temperatures may allow it to outcompete others scavengers during the heat of the day.

Most controversial are the alvinellid worms, small tube-building polychaetes that live at hydrothermal vents in the deep sea. Investigators on the submersible *Alvin* (for which the worms were named) found that temperatures in the tubes of *Alvinella* worms were routinely about 60°C, with occasional peaks over 80°C. But other scientists were skeptical, noting that accurate temperature measurements are difficult due to violent currents near the vents, which mix 300°C vent water with the near-freezing water nearby. (At the high pressures of the deep sea, water does not boil at 300°C.) Moreover, laboratory studies of alvinellid enzymes showed that they malfunction above 45°–50°C. To examine tolerance directly, Peter Girguis of Harvard and Raymond Lee of Washington State University placed *Paralvinella* worms (a species related to *Alvinella* and having enzymes with similar thermal limits) in special high-pressure chambers. The chambers have a regulated temperature gradient ranging from 20°C at one end to 61°C at the other. The worms were kept at their natural habitat pressure and observed for seven hours. The animals crawled about and settled around the area at 50°C, where they appeared to behave normally. One worm even survived 55°C water for 15 minutes. These behavioral studies (published in 2006) show that 50°C is *Paralvinella*'s preferred temperature and that it may tolerate higher temperatures briefly. However, the actual limit in nature for these and similar worms remains unknown. What sets the upper limit for animals and other eukaryotes is not known, but is suspected to be fundamental features of gene transcription, RNA processing, and/or translation that cannot be stabilized beyond a certain temperature.

What about limits for archaeans and bacteria? Hyperthermophilic ("high-heat-loving") microbes can be found in abundance at hydrothermal vents. Although none are known to live at the highest temperatures (up to 400°C), one species discovered in 2003 by Derek Lovley and Kazem Kashefi of the University of Massachusetts remained viable in the laboratory after 10 hours at 121°C, a temperature used in autoclaves for sterilizing medical equipment. But the actual upper limit for hyperthermophiles remains speculative. Understanding these aspects of cells is crucial to hypotheses about life's origins and possible life elsewhere in the universe.

How do proteins work in high urea and at high pressure?

You have just read that sharks and their relatives use urea and trimethylamine oxide (TMAO) as osmolytes. Organic osmolytes are often said to be *compatible;* that is, unlike inorganic ions such as Na^+ and Cl^-, they do not perturb proteins even at high concentrations. Thus, organic osmolytes can safely build up in an organism. However, urea is a clear exception. At the urea concentration typical of sharks (300–400 mM),

many proteins—including ones in sharks—are perturbed. Indeed, biochemists often use urea to unfold proteins. How, then, can the sharks function with such high urea concentration? In the 1970s, George Somero and I, then of Scripps Institution of Oceanography, found that TMAO is not simply compatible: it actually stabilizes proteins and can *counteract* urea's effect. In mixtures of TMAO and urea at shark levels, stabilizing and destabilizing effects cancel out. Thus, by using two waste products as osmolytes, sharks maintain water balance while not perturbing proteins.

This shark finding led Robert Balaban, Maurice Burg, and coworkers at the National Institutes of Health to realize that a balancing effect could explain how mammalian kidneys survive the high levels of salt and urea in the medulla (where urea can exceed 1 M). In fact, a study led by Serena Bagnasco, now at Johns Hopkins Hospital, found that kidney cells maintain osmotic balance with sorbitol, inositol, glycerophosphorylcholine (GPC), and betaine (and not with salts, as previously believed). Moreover, GPC and betaine are *methylamines,* which, like TMAO, can counteract urea's effects. How methylamines like TMAO actually stabilize proteins remains uncertain. Wayne Bolen and colleagues at the University of Texas Medical Branch at Galveston recently showed that the peptide backbone of proteins is in a sense repelled by solutions of TMAO, making proteins fold up to avoid contact. The physicochemical properties of TMAO responsible for this effect are under investigation.

Stabilizing osmolytes may also help deep-sea organisms cope with high pressure. Low TMAO levels have long been known in bony fish (it is the source of "fishy odor"), but as osmoregulators, all bony fish were thought to have osmotic pressures of 300–400 mOsm/L, with little need for osmolytes. Recently, I and my students at Whitman College found that the deeper a species lives, the more TMAO it has. Indeed, deep-sea species can have osmotic pressures of 600 mOsm/L or more due to TMAO. Why might this be? Laboratory studies showed that TMAO readily counteracts the destabilizing effects that pressure has on protein structure and function.

Such research may be medically useful. William Welch and colleagues at the University of California at San Francisco hypothesize that stabilizing osmolytes might "repair" disease-causing mutant proteins. For example, cystic fibrosis (CF) arises from a chloride channel protein that does not fold properly, leading to symptoms that include impaired production of sweat and digestive secretions. Marybeth Howard in Welch's laboratory and collaborators recently treated cultured CF cells with organic osmolytes, and the mutant protein indeed folded and worked properly. Whether osmolytes can be used in whole mammals is now being studied.

Paul H. Yancey holds the Carl E. Peterson Endowed Chair of Sciences at Whitman College in Walla Walla, Washington. His main research interests are in areas of animal physiology, especially water stress and osmoregulation. To learn more about his research, go to http://marcus.whitman.edu/~yancey/.

which is at the same temperature as the water. The blood enters the body core through small arteries that form the countercurrent heat exchanger along with small veins that bring warm blood from the swimming muscles in the core. Countercurrent exchange warms the arterial blood, which returns to the heart in veins and is then pumped around the body in arteries, including to the core and the gills. The overall result is that heat is retained within the muscles, so that the core body temperature can remain significantly higher than that of the surrounding water.

Review

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46.1 Introduction to Osmoregulation and Excretion

- Solute concentration is measured as osmolarity in milliosmoles per liter of solution (mOsm/L). A solution can be comparatively hyperosmotic, hypoosmotic, or isoosmotic to another solution. Water moving from a region of higher osmolarity to a region of lower osmolarity across a selectively permeable membrane is known as osmosis.

- Osmoregulators keep the osmolarity of body fluids different from that of the environment. Osmoconformers allow the osmolarity of their body fluids to match that of the environment.

- Molecules and ions must be removed from the body to keep cellular and extracellular fluids isoosmotic. In most animals, extracellular fluids are filtered through tubules formed from a transport epithelium and released to the exterior of the animal as urine (Figure 46.2).

- Nitrogenous wastes are excreted as ammonia, urea, or uric acid, or as a combination of these substances (Figure 46.3).

Animation: Diffusion, osmosis, and countercurrent systems

Animation: Water and solute balance

46.2 Osmoregulation and Excretion in Invertebrates

- Most marine invertebrates are osmoconformers. Because their body fluids are isoosmotic to seawater, they expend little or no energy on maintaining water balance.

- Freshwater and terrestrial invertebrates are osmoregulators, with body fluids that are hyperosmotic to their surroundings. They must expend energy to excrete water that moves into their cells by osmosis.

- The cells of the simplest marine invertebrates exchange water and solutes directly with the surrounding seawater. More complex invertebrates have specialized excretory tubules (Figures 46.4–46.6).

46.3 Osmoregulation and Excretion in Mammals

- In mammals and other vertebrates, excretory tubules are concentrated in the kidney.

- The mammalian excretory tubule, the nephron, has a proximal end at which filtration takes place, a middle region in which reabsorption and secretion occur, and a distal end that releases urine. A network of capillaries surrounding the nephron takes up ions and water and other molecules absorbed by the nephron. The urine leaving individual nephrons is processed further in collecting ducts and then pools in the renal pelvis. From there it flows through the ureter to the urinary bladder, and through the urethra to the exterior of the animal (Figures 46.7 and 46.8).

- At its proximal end, the nephron forms a cuplike Bowman's capsule around a ball of capillaries, the glomerulus. A filtrate consisting of water, other small molecules, and ions is forced from the glomerulus into Bowman's capsule, from which it travels through the nephron and drains into the collecting ducts and renal pelvis. The proximal convoluted tubule of the nephron secretes H^+ into the filtrate and reabsorbs Na^+, Cl^-, and K^+ along with water, HCO_3^-, and nutrients. In the descending segment of the loop of Henle, water is reabsorbed by osmosis. In the ascending segment of the loop, Na^+ and Cl^- are reabsorbed. In the distal convoluted tubule, the concentrations of H^+ and salts are balanced between the urine and the interstitial fluid surrounding the nephron. In the collecting ducts, additional H^+ is secreted into the urine and water is reabsorbed; some urea is also reabsorbed at the bottom of the ducts (Figure 46.9 and Table 46.1).

Animation: Human urinary system

Animation: Human kidney

Animation: Urine formation

Animation: Tubular reabsorption

46.4 Regulation of Mammalian Kidney Function

- The kidney's autoregulation system is activated by receptors in the juxtaglomerular apparatus. The receptors trigger constriction or dilation of the afferent arteriole to keep blood flow and filtration constant during small variations in blood pressure.

- When blood volume and blood pressure drop, the hormones of the renin-angiotensin-aldosterone system (RAAS) raise blood pressure by stimulating arteriole constriction and increasing NaCl reabsorption in the kidneys (Figure 46.11).

- ADH, which increases water reabsorption and stimulates thirst, is released from the pituitary when osmoreceptors detect an increase in the osmolarity of body fluids (Figure 46.12).

Animation: Structure of the glomerulus

46.5 Kidney Function in Nonmammalian Vertebrates

- Marine teleosts continually drink seawater to replace body water lost by osmosis to their hyperosmotic environment. Excess salts and nitrogenous wastes are excreted by the gills (Figure 46.13a).

- The body fluids of sharks and rays are isoosmotic with seawater. They do not lose water by osmosis, and do not drink seawater. Excess salts are excreted in the kidney and by a rectal salt gland.

- Body fluids of freshwater fishes and amphibians are hyperosmotic to their environment, and these animals must excrete the excess water that enters by osmosis. Body salts are obtained from food and, in fishes, through the gills (Figure 46.13b).

Nitrogenous wastes are excreted from the gills of fishes and larval amphibians as ammonia, and through the kidneys of adult amphibians as urea.

- Reptiles and birds conserve water by secreting nitrogenous wastes as uric acid and by absorbing water from urine and feces in the cloaca.

46.6 Introduction to Thermoregulation

- Animals must maintain body temperature at a level that provides optimal physiological performance. Heat flows between animals and their environment by conduction, convection, radiation, and evaporation (Figures 46.15 and 46.16).
- Ectothermic animals obtain heat energy primarily from the environment; endothermic animals obtain heat energy primarily from internal reactions (Figure 46.17).

  Animation: Endotherms and ectotherms

46.7 Ectothermy

- Ectotherms obtain heat energy externally and control body temperature primarily by physiological or behavioral methods of regulating heat exchange with the environment (Figure 46.18).
- Many animals undergo thermal acclimatization, a structural or metabolic change in the limits of tolerable temperatures as the environment alternates between warm and cool seasons.

46.8 Endothermy

- Endotherms obtain heat energy primarily from internal reactions and maintain body temperature over a narrow range by balancing internal heat production against heat loss from the body surface.
- Internal heat production is controlled by negative feedback pathways triggered by thermoreceptors. When deviations from the temperature set point occur, signals from the receptors bring about compensating responses such as changes in blood flow to the body surface, sweating or panting, and behavioral modifications (Figure 46.19).
- The skin of endotherms is water-impermeable, reducing heat lost by direct evaporation of body fluids. The blood vessels of the skin regulate heat loss by constricting or dilating. A layer of insulating fatty tissue under the vessels limits losses to the heat carried by the blood. The hair of mammals and feathers of birds also insulate the skin. Erection of the hair or feathers reduces heat loss by thickening the insulating layer (Figures 46.20 and 46.21).
- The temperature set point in many birds and mammals varies in daily and seasonal patterns. During cooler conditions, a lowered set point is accompanied by torpor (Figure 46.22).
- Some animals exhibit a form of endothermy in which part of their core is maintained at a temperature significantly higher than the surrounding environment.

  Animation: Human thermoregulation

Questions

Self-Test Questions

1. Which of the following statements about osmoregulation is true?
   a. In freshwater invertebrates, salts move out of the body into the water because the animal is hypoosmotic to the water.
   b. A marine teleost has to fight gaining water because it is isoosmotic to the sea.
   c. Most land animals are osmoconformers.
   d. Vertebrates are usually osmoregulators.
   e. Terrestrial animals can regulate their osmolarity without expending energy.

2. One role of tubules in excretion is to:
   a. absorb H^+ ions to buffer body fluids.
   b. transport proteins across transport epithelium.
   c. reabsorb glucose and amino acids.
   d. move toxic substances from the filtrate into the cells composing the transport tubules.
   e. filter by maintaining a lower pressure in the fluid outside the tubule than inside it.

3. Products of metabolism in humans, as in:
   a. terrestrial amphibians, can include urea, which requires more energy to produce than ammonia.
   b. birds and reptiles, can include uric acid, which is nontoxic and excreted as a paste.
   c. sharks, are primarily excreted as ammonia.
   d. hydra, must be isoosmotic with the water ingested.
   e. other mammals, cannot be water as water comes only from what they drink.

4. Filtration and/or excretion can be carried out by:
   a. ciliated metanephridia in insects.
   b. protonephridia containing flame cells in flatworms.
   c. a nephron and bladder in insects.
   d. Malpighian tubules on the segments of earthworms.
   e. the hindgut, which reabsorbs Na^+ and K^+ into the hemolymph of earthworms.

5. A mammalian nephron contains the:
   a. Bowman's capsule, which delivers the filtrate to the glomerulus.
   b. Bowman's capsule, which filters fluids, 99% of which will be excreted.
   c. proximal convoluted tubule, which moves Na^+ and K^+ into the filtrate of the interstitial fluids.
   d. proximal convoluted tubule, which reabsorbs K^+, Na^+, Cl^-, H_2O, and urea.
   e. proximal convoluted tubule, which lacks microvilli to ease fluid movement through it.

6. Which of the following correctly describes a part of kidney function?
   a. Collecting ducts dilute urine because they are permeable to salt but not water.
   b. In the ascending loop of Henle, Na^+ and Cl^- move into the tubules because the osmolarity of the filtrate is increased.
   c. The descending loop of Henle receives filtrate from the ascending loop.
   d. The distal convoluted tubule pumps water into the tubule by active transport.
   e. The renal pelvis receives urine from the collecting ducts and carries it to the ureters.

7. Which of the following is an example of autoregulation of kidney function?
   a. The RAAS regulates Na^+ by secreting renin when blood pressure or blood volume decreases.
   b. The ADH system regulates water balance by decreasing water reabsorption and increasing excretion of salt.

c. Receptors in the juxtaglomerular apparatus of the distal convoluted tubule detect drops in blood pressure and cause a higher filtration rate.
   d. ANF is released by the kidney to increase renin release.
   e. Angiotensin lowers blood pressure by constricting arterioles.

8. Deficient water levels in humans are prevented by:
   a. osmoreceptors on the hypothalamus that detect decreases in salt concentrations.
   b. the hypothalamus stimulating the posterior pituitary to secrete a hormone that allows the collecting ducts and distal convoluted tubules to be permeable to water.
   c. inhibiting ADH, which causes a rise in osmolarity of extracellular fluids.
   d. producing dilute urine.
   e. drinking alcohol, which stimulates aldosterone to raise the osmolarity of body fluids.

9. Which best exemplifies ectothermy?
   a. The metabolic rate increases as the temperature decreases.
   b. Body temperature remains constant when environmental temperatures change.
   c. Food demand increases when temperatures drop.
   d. Virtually all invertebrate groups are ectotherms.
   e. No vertebrate groups are ectotherms.

10. Unique to endotherms is:
   a. torpor.
   b. thermal acclimatization.
   c. a nonchanging body temperature.
   d. response to seasonal temperature changes.
   e. thermoregulation by a hypothalamus.

Questions for Discussion

1. A urinalysis reveals glucose, urea, hemoglobin, and sodium. Which of these substances are abnormal in urine, and why?

2. As a person ages, nephron tubules lose some of their ability to concentrate urine. What is the effect of this change?

3. Shivering increases air movement over the body surface. What effect does this air movement have on heat conservation in the shivering animal?

4. What heat transfer processes might account for the change in body temperature when a mammal's body temperature undergoes daily variations?

Experimental Analysis

Design experiments to demonstrate the role of fluid consumption in thermoregulation during endurance exercise.

Evolution Link

Humans produce urea as an excretion product, whereas reptiles and birds produce uric acid. Indeed, human kidneys are not as efficient as those of reptiles and birds. What does this mean in an evolutionary sense?

How Would You Vote?

Many companies use urine testing to screen for drug and alcohol use among prospective employees. Some people say this is an invasion of privacy. Do you think employers should be allowed to require a person to undergo urine testing before being hired? Go to www.thomsonedu.com/login to investigate both sides of the issue and then vote.