44

Osmoregulation and Excretion

OVERVIEW

A Balancing Act

With a wingspan that can reach 3.5 m, the largest of any living bird, a wandering albatross (*Diomedea exulans*) soaring over the ocean is hard to miss **(Figure 44.1)**. Yet the albatross commands attention for more than just its size. This massive bird remains at sea day and night throughout the year, returning to land only to reproduce. A human with only seawater to drink would die of dehydration, but faced with the same conditions, the albatross thrives.

For both albatross and human, maintaining the fluid environment of their cells, tissues, and organs requires keeping relative concentrations of water and solutes within fairly narrow limits. In addition, ions such as sodium and calcium must be maintained at concentrations that permit normal activity of muscles, neurons, and other body cells. Homeostasis thus requires **osmoregulation**, the general term for the processes by which animals control solute concentrations and balance water gain and loss.

A number of strategies for water and solute control have arisen during evolution, reflecting the varied and often severe osmoregulatory challenges presented by an animal's surroundings. The arid environment of a desert, for instance, can quickly deplete an animal of body water. Despite a quite different environment, albatrosses and other marine animals also face potential dehydration. The success of animals in an ocean environment depends critically on conserving water and, for marine birds and fishes, eliminating excess salts. In contrast, freshwater animals live in an environment that threatens to flood and dilute their body fluids. These organisms survive by conserving solutes and absorbing salts from their surroundings.

In safeguarding their internal fluid environment, animals must also deal with a hazardous metabolite produced by the dismantling of proteins and nucleic acids. Breakdown of *nitrogenous* (nitrogen-containing) molecules releases ammonia, a very toxic compound. Several different mechanisms have evolved for **excretion**, the process that rids the body of nitrogenous metabolites and other metabolic waste products. Because systems for excretion and osmoregulation are structurally and functionally linked in many animals, we will consider both of these processes in this chapter.

CONCEPT 44.1
Osmoregulation balances the uptake and loss of water and solutes

Just as thermoregulation depends on balancing heat loss and gain (see Chapter 40), regulating the chemical composition of body fluids depends on balancing the uptake and loss of water and solutes. This process of osmoregulation is based largely on the controlled movement of solutes between internal fluids and the external environment. Because solute movement results in the movement of water by osmosis, the net effect is to regulate both solutes and water.

Osmosis and Osmolarity

All animals—regardless of habitat or type of waste produced—face the same need to balance water uptake and loss. If water
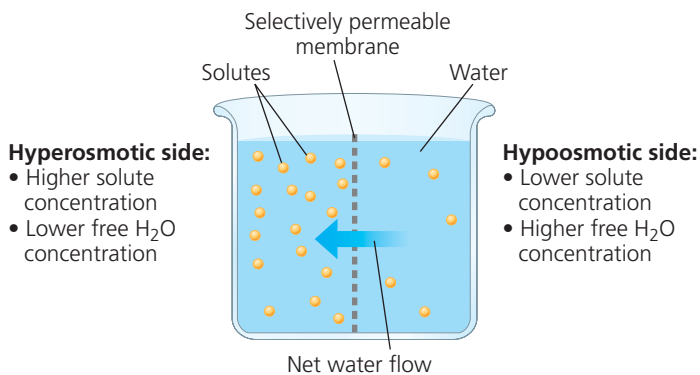
▲ **Figure 44.2 Solute concentration and osmosis.**
MAKE CONNECTIONS *Review types of membrane proteins and their functions in Concepts 7.1 and 7.2 (pp. 129–132). Which membrane proteins allow water, but not solutes, to diffuse across a lipid bilayer?*

Selectively permeable membrane
Solutes   Water

Hyperosmotic side:
• Higher solute concentration
• Lower free H_2O concentration

Hypoosmotic side:
• Lower solute concentration
• Higher free H_2O concentration

Net water flow

uptake is excessive, animal cells swell and burst; if water loss is substantial, they shrivel and die (see Figure 7.15).

Water enters and leaves cells by osmosis. Recall from Chapter 7 that osmosis, a special case of diffusion, is the movement of water across a selectively permeable membrane. It occurs whenever two solutions separated by the membrane differ in osmotic pressure, or **osmolarity** (total solute concentration expressed as molarity, that is, moles of solute per liter of solution). The unit of measurement for osmolarity used in this chapter is milliOsmoles per liter (mOsm/L). Seawater has an osmolarity of about 1,000 mOsm/L (equivalent to a total solute concentration of 1 *M*), while the osmolarity of human blood is about 300 mOsm/L.

If two solutions separated by a selectively permeable membrane have the same osmolarity, they are said to be *isoosmotic*. Water molecules continually cross the membrane, but under these conditions they do so at equal rates in both directions. Thus, there is no *net* movement of water by osmosis between isoosmotic solutions. When two solutions differ in osmolarity, the one with the greater concentration of solutes is said to be *hyperosmotic*, and the more dilute solution is said to be *hypoosmotic* **(Figure 44.2)**. Water flows by osmosis from a hypoosmotic solution to a hyperosmotic one.*

Osmotic Challenges

Given the chemical principles that govern osmotic flow, an animal can maintain water balance in two ways. One is to be an **osmoconformer**: to be isoosmotic with its surroundings. The second is to be an **osmoregulator**: to control internal osmolarity independent of that of its environment.

All osmoconformers are marine animals. Because an osmoconformer's internal osmolarity is the same as that of its environment, there is no tendency to gain or lose water.

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*In this chapter, we use the terms *isoosmotic, hypoosmotic,* and *hyperosmotic,* which refer specifically to osmolarity, instead of *isotonic, hypotonic,* and *hypertonic.* The latter set of terms applies to the response of animal cells—whether they swell or shrink—in solutions of known solute concentrations.

Many osmoconformers live in water that has a stable composition and hence have a constant internal osmolarity.

Osmoregulation enables animals to live in environments that are uninhabitable for osmoconformers, such as freshwater and terrestrial habitats. To survive in a hypoosmotic environment, an osmoregulator must discharge excess water. In a hyperosmotic environment, an osmoregulator must instead take in water to offset osmotic loss. Osmoregulation also allows many marine animals to maintain an internal osmolarity different from that of seawater.

Most animals, whether osmoconformers or osmoregulators, cannot tolerate substantial changes in external osmolarity and are said to be *stenohaline* (from the Greek *stenos*, narrow, and *halos*, salt). In contrast, *euryhaline* animals (from the Greek *eurys*, broad) can survive large fluctuations in external osmolarity. Euryhaline osmoconformers include many barnacles and mussels, which are continually covered and uncovered by ocean tides; examples of euryhaline osmoregulators are the striped bass and the various species of salmon.
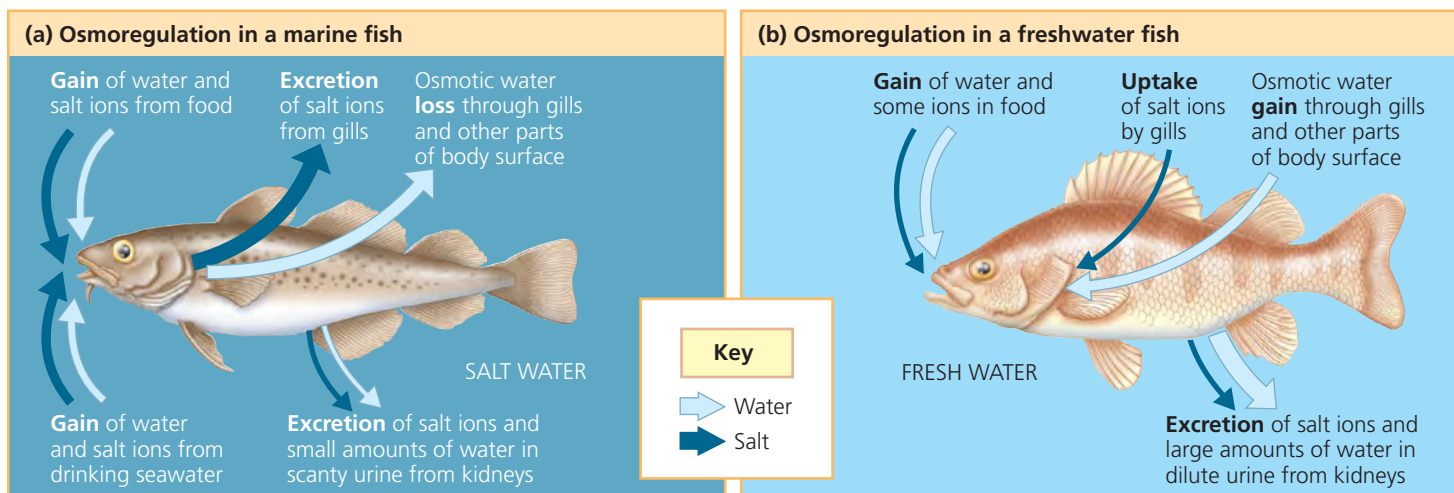
Next we'll examine some adaptations for osmoregulation that have evolved in marine, freshwater, and terrestrial animals.

Marine Animals

Most marine invertebrates are osmoconformers. Their osmolarity is the same as that of seawater. They therefore face no substantial challenges in water balance. However, because these animals differ considerably from seawater in the concentrations of *specific* solutes, they must actively transport these solutes to maintain homeostasis. For example, although the concentration of magnesium ions (Mg^{2+}) in seawater is 50 m*M* (millimolar, or 10^{-3} mol/L), homeostatic mechanisms in the Atlantic lobster (*Homarus americanus*) result in a Mg^{2+} concentration of less than 9 m*M* in this animal's hemolymph (circulatory fluid).

Many marine vertebrates and some marine invertebrates are osmoregulators. For most of these animals, the ocean is a strongly dehydrating environment. For example, marine fishes, such as the cod in **Figure 44.3a**, constantly lose water by osmosis. Such fishes balance the water loss by drinking large amounts of seawater. In ridding themselves of salts, they make use of both their gills and kidneys. In the gills, specialized *chloride cells* actively transport chloride ions (Cl^-) out and allow sodium ions (Na^+) to follow passively. In the kidneys, excess calcium, magnesium, and sulfate ions are excreted with the loss of only small amounts of water.

A distinct osmoregulatory strategy evolved in marine sharks and most other chondrichthyans (cartilaginous animals; see Chapter 34). Like "bony fishes" (as we'll refer collectively to ray-finned and lobe-finned fishes in this chapter), sharks have an internal salt concentration much lower than that of seawater. Thus, salt tends to diffuse into their bodies from the water, especially across their gills. Unlike bony fishes, however, marine sharks are not hypoosmotic to seawater. The explanation

(a) Osmoregulation in a marine fish

Gain of water and salt ions from food

Excretion of salt ions from gills

Osmotic water **loss** through gills and other parts of body surface

SALT WATER

Gain of water and salt ions from drinking seawater

Excretion of salt ions and small amounts of water in scanty urine from kidneys

(b) Osmoregulation in a freshwater fish

Gain of water and some ions in food

Uptake of salt ions by gills

Osmotic water **gain** through gills and other parts of body surface

FRESH WATER

Excretion of salt ions and large amounts of water in dilute urine from kidneys

Key
→ Water
→ Salt

▲ **Figure 44.3 Osmoregulation in marine and freshwater bony fishes: a comparison.**

is that shark tissue contains high concentrations of urea, a nitrogenous waste product of protein and nucleic acid metabolism (see Figure 44.8). A shark's body fluids also contain trimethylamine oxide (TMAO), an organic molecule that protects proteins from damage by urea. Together, the salts, urea, TMAO, and other compounds maintained in the body fluids of sharks result in an osmolarity very close to that of seawater. For this reason, sharks are often considered osmoconformers. However, because the solute concentration in their body fluids is actually somewhat higher than 1,000 mOsm/L, water slowly *enters* the shark's body by osmosis and in food (sharks do not drink). This small influx of water is disposed of in urine produced by the shark's kidneys. The urine also removes some of the salt that diffuses into the shark's body; the rest is lost in feces or is secreted from a specialized gland.

Freshwater Animals

The osmoregulatory problems of freshwater animals are the opposite of those of marine animals. The body fluids of freshwater animals must be hyperosmotic because animal cells cannot tolerate salt concentrations as low as that of lake or river water. Having internal fluids with an osmolarity higher than that of their surroundings, freshwater animals face the problem of gaining water by osmosis and losing salts by diffusion. Many freshwater animals, including bony fishes, solve the problem of water balance by drinking almost no water and excreting large amounts of very dilute urine. At the same time, salts lost by diffusion and in the urine are replenished by eating. Freshwater fishes, such as the perch in **Figure 44.3b**, also replenish salts by uptake across the gills. Chloride cells in the gills of the fish actively transport Cl^- into the body, and Na^+ follows.

Salmon and other euryhaline fishes that migrate between fresh water and seawater undergo dramatic changes in osmoregulatory status **(Figure 44.4)**. When living in rivers and streams, salmon osmoregulate like other freshwater fishes,


▲ **Figure 44.4 Sockeye salmon (*Oncorhynchus nerka*), euryhaline osmoregulators.**

producing large amounts of dilute urine and taking up salt from the dilute environment through their gills. When they migrate to the ocean, salmon acclimatize. They produce more of the steroid hormone cortisol, which increases the number and size of salt-secreting chloride cells. As a result of these and other physiological changes, salmon in salt water excrete excess salt from their gills and produce only small amounts of urine—just like bony fishes that spend their entire lives in salt water.

Animals That Live in Temporary Waters

Extreme dehydration, or *desiccation*, is fatal for most animals. However, a few aquatic invertebrates that live in temporary ponds and in films of water around soil particles can lose almost all their body water and survive. These animals enter a dormant state when their habitats dry up, an adaptation called **anhydrobiosis** ("life without water"). Among the
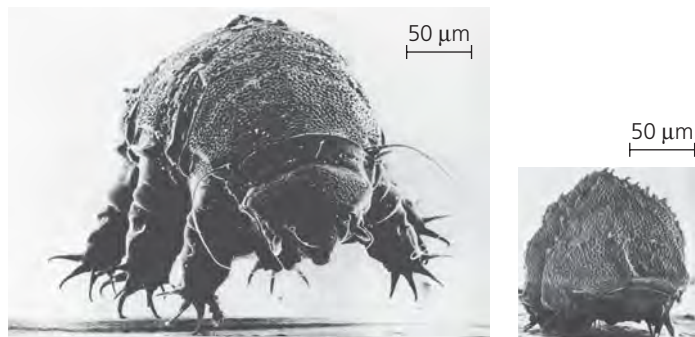
(a) Hydrated tardigrade

(b) Dehydrated tardigrade

▲ **Figure 44.5 Anhydrobiosis.** SEM images of tardigrades (water bears), which inhabit temporary ponds as well as droplets of water in soil and on moist plants.

▲ **Figure 44.6 Water balance in two terrestrial mammals.** Kangaroo rats, which live in the American Southwest, eat mostly dry seeds and do not drink water. A kangaroo rat gains water mainly from cellular metabolism and loses water mainly by evaporation during gas exchange. In contrast, a human gains water in food and drink and loses the largest fraction of it in urine.

most striking examples are the tardigrades, or water bears **(Figure 44.5)**. Less than 1 mm long, these tiny invertebrates are found in marine, freshwater, and moist terrestrial environments. In their active, hydrated state, they contain about 85% water by weight, but they can dehydrate to less than 2% water and survive in an inactive state, dry as dust, for a decade or more. Just add water, and within hours the rehydrated tardigrades are moving about and feeding.

Anhydrobiosis requires adaptations that keep cell membranes intact. Researchers are just beginning to learn how tardigrades survive drying out, but studies of anhydrobiotic roundworms (phylum Nematoda; see Chapter 33) show that desiccated individuals contain large amounts of sugars. In particular, a disaccharide called trehalose seems to protect the cells by replacing the water that is normally associated with proteins and membrane lipids. Many insects that survive freezing in the winter also use trehalose as a membrane protectant, as do some plants resistant to desiccation.
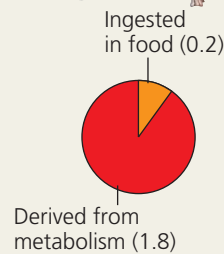
Land Animals

The threat of dehydration is a major regulatory problem for terrestrial plants and animals. Humans, for example, die if they lose as little as 12% of their body water (desert camels can withstand approximately twice that level of dehydration). Adaptations that reduce water loss are key to survival on land. Much as a waxy cuticle contributes to the success of land plants, the body coverings of most terrestrial animals help prevent dehydration. Examples are the waxy layers of insect exoskeletons, the shells of land snails, and the layers of dead, keratinized skin cells covering most terrestrial vertebrates, including humans. Many terrestrial animals, especially desert-dwellers, are nocturnal, which reduces evaporative water loss because of the lower temperature and higher humidity of night air.

Despite these and other adaptations, most terrestrial animals lose water through many routes: in urine and feces, across their skin, and from the surfaces of gas exchange organs. Land animals maintain water balance by drinking and
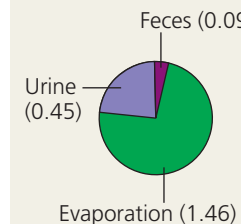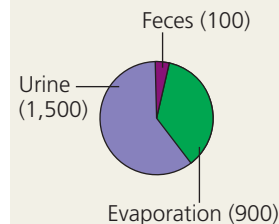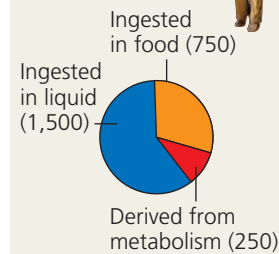
eating moist foods and by producing water metabolically through cellular respiration. A number of desert animals, including many insect-eating birds and other reptiles, are well enough adapted for minimizing water loss that they can survive for long periods of time without drinking. A noteworthy example is the kangaroo rat: It typically loses so little water that 90% is replaced by water it generates metabolically **(Figure 44.6)**; the remaining 10% comes from the small amount of water in its diet of seeds. During particularly hot periods, kangaroo rats supplement their diet with juicy insects, thereby maintaining their water balance.

Energetics of Osmoregulation

Maintaining an osmolarity difference between an animal's body and its external environment carries an energy cost. Because diffusion tends to equalize concentrations in a system, osmoregulators must expend energy to maintain the osmotic gradients that cause water to move in or out. They do so by using active transport to manipulate solute concentrations in their body fluids.

The energy cost of osmoregulation depends on how different an animal's osmolarity is from its surroundings, how easily water and solutes can move across the animal's surface, and how much work is required to pump solutes across the membrane. Osmoregulation accounts for 5% or more of the resting

metabolic rate of many freshwater and marine bony fishes. For brine shrimp, small crustaceans that live in extremely salty lakes, the gradient between internal and external osmolarity is very large, and the cost of osmoregulation is correspondingly high—as much as 30% of the resting metabolic rate.

The energy cost to an animal of maintaining water and salt balance is minimized by having body fluids that are adapted to the salinity of the animal's habitat. Thus, the body fluids of most animals that live in fresh water (which has an osmolarity of 0.5–15 mOsm/L) have lower solute concentrations than the body fluids of their closest relatives that live in seawater (1,000 mOsm/L). For instance, whereas marine molluscs have body fluids with solute concentrations of approximately 1,000 mOsm/L, some freshwater molluscs maintain the osmolarity of their body fluids at just 40 mOsm/L. In each case, minimizing the osmotic difference between body fluids and the surrounding environment decreases the energy the animal expends for osmoregulation.
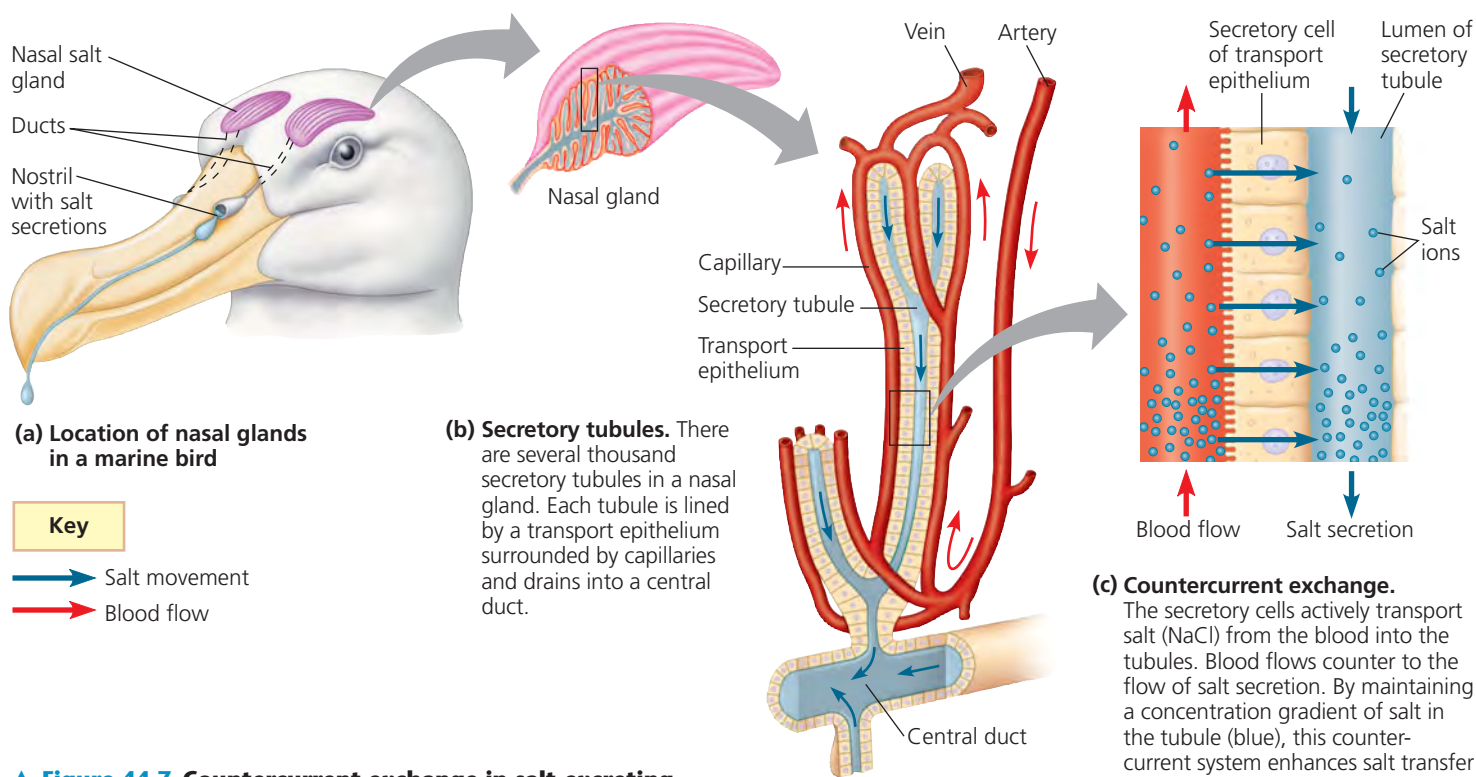
Transport Epithelia in Osmoregulation

The ultimate function of osmoregulation is to control solute concentrations in cells, but most animals do this indirectly by managing the solute content of an internal body fluid that bathes the cells. In insects and other animals with an open circulatory system, the fluid surrounding cells is hemolymph. In vertebrates and other animals with a closed circulatory system, the cells are bathed in an interstitial fluid that contains a mixture of solutes controlled indirectly by the blood. Maintaining the composition of such fluids depends on structures ranging from individual cells that regulate solute movement to complex organs such as the vertebrate kidney.

In most animals, osmoregulation and metabolic waste disposal rely on **transport epithelia**—one or more layers of epithelial cells specialized for moving particular solutes in controlled amounts in specific directions. Transport epithelia are typically arranged into complex tubular networks with extensive surface areas. Some transport epithelia face the outside environment directly, while others line channels connected to the outside by an opening on the body surface.

The transport epithelium that enables the albatross to survive on seawater remained undiscovered for many years. Some scientists suggested that marine birds do not actually drink water, asserting that although the birds take water into their mouths, they do not swallow. Questioning this idea, Knut Schmidt-Nielsen and colleagues at the Mount Desert Island Laboratory, in Maine, gave captive marine birds only seawater to drink. The researchers found that while very little salt appeared in the birds' urine, fluid dripping from the tip of their beaks was a concentrated solution of salt (NaCl). Where did this fluid come from? As Schmidt-Nielsen demonstrated, the salt solution was produced by a pair of structures called the nasal glands. Similar structures, called salt glands, eliminate excess salt from the bodies of sea turtles and marine iguanas.

As shown in **Figure 44.7**, the nasal gland removes excess NaCl (in the form of Na^+ and Cl^-) from the blood

(a) Location of nasal glands in a marine bird

Key
→ Salt movement
→ Blood flow

(b) Secretory tubules. There are several thousand secretory tubules in a nasal gland. Each tubule is lined by a transport epithelium surrounded by capillaries and drains into a central duct.

(c) Countercurrent exchange. The secretory cells actively transport salt (NaCl) from the blood into the tubules. Blood flows counter to the flow of salt secretion. By maintaining a concentration gradient of salt in the tubule (blue), this countercurrent system enhances salt transfer from the blood to the lumen of the tubule.

▲ **Figure 44.7 Countercurrent exchange in salt-excreting nasal glands.**

by countercurrent exchange. Recall from Chapter 40 that countercurrent exchange occurs between two fluids separated by one or more membranes and flowing in opposite directions. In the albatross's nasal gland, the net result is the secretion of fluid much saltier than the ocean. Thus, even though drinking seawater brings in a lot of salt, the bird achieves a net gain of water. By contrast, humans who drink a given volume of seawater must use a *greater* volume of water to excrete the salt load, with the result that they become dehydrated.

Transport epithelia that function in maintaining water balance also often function in disposal of metabolic wastes. We will see examples of this coordinated function in our upcoming consideration of earthworm and insect excretory systems as well as the vertebrate kidney.

CONCEPT CHECK 44.1

1. The movement of salt from the surrounding water to the blood of a freshwater fish requires the expenditure of energy in the form of ATP. Why?
2. Why aren't any freshwater animals osmoconformers?
3. **WHAT IF?** Researchers found that a camel standing in the sun required much more water when its fur was shaved off, although its body temperature remained the same. What can you conclude about the relationship between osmoregulation and the insulation provided by fur?

For suggested answers, see Appendix A.

CONCEPT 44.2

An animal's nitrogenous wastes reflect its phylogeny and habitat

Because most metabolic wastes must be dissolved in water to be excreted from the body, the type and quantity of an animal's waste products may have a large impact on its water balance. In this regard, some of the most significant waste products are the nitrogenous breakdown products of proteins and nucleic acids **(Figure 44.8)**. When proteins and nucleic acids are broken apart for energy or converted to carbohydrates or fats, enzymes remove nitrogen in the form of **ammonia** (NH_3). Ammonia is very toxic, in part because its ion, ammonium (NH_4^+), interferes with oxidative phosphorylation. Although some animals excrete ammonia directly, many species expend energy to convert it to less toxic compounds prior to excretion.

Forms of Nitrogenous Waste

Animals excrete nitrogenous wastes as ammonia, urea, or uric acid. These different forms vary significantly in their toxicity and the energy costs of producing them.
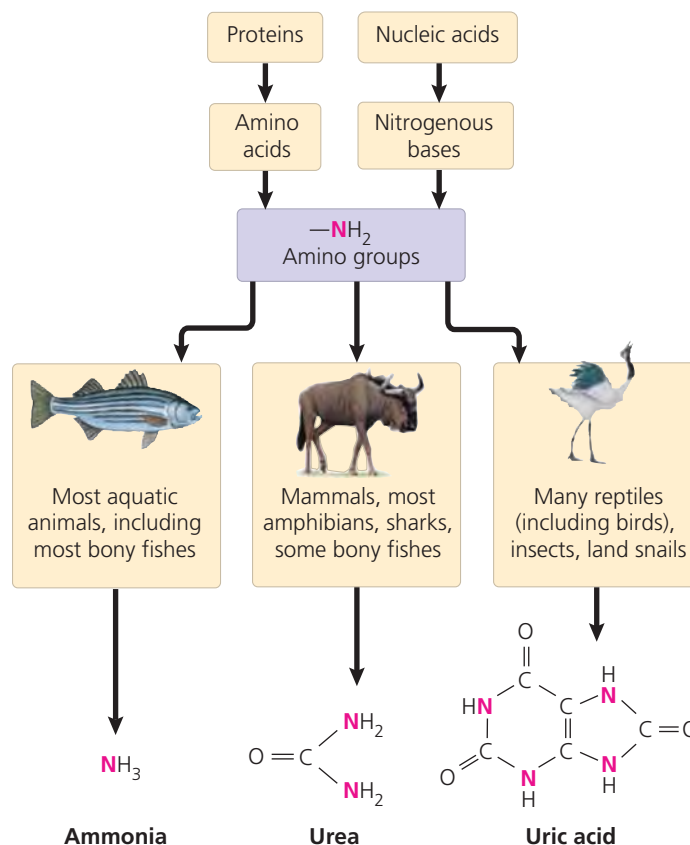
▲ **Figure 44.8 Forms of nitrogenous waste.**

Ammonia

Because ammonia can be tolerated only at very low concentrations, animals that excrete nitrogenous wastes as ammonia need access to lots of water. Therefore, ammonia excretion is most common in aquatic species. Being highly soluble, ammonia molecules easily pass through membranes and are readily lost by diffusion to the surrounding water. In many invertebrates, ammonia release occurs across the whole body surface. In fishes, most of the ammonia is lost as NH_4^+ across the epithelium of the gills; the kidneys excrete only minor amounts of nitrogenous waste.

Urea

Although ammonia excretion works well in many aquatic species, it is much less suitable for land animals. Ammonia is so toxic that it can be transported and excreted only in large volumes of very dilute solutions. As a result, most terrestrial animals and many marine species (principally those that tend to lose water to their environment by osmosis) simply do not have access to sufficient water to routinely excrete ammonia. Instead, mammals, most adult amphibians, sharks, and some marine bony fishes and turtles mainly excrete a different nitrogenous waste, **urea**. Produced in the vertebrate liver, urea is the product of a metabolic cycle that combines ammonia with carbon dioxide.

The main advantage of urea is its very low toxicity. Animals can transport urea in the circulatory system and store it safely at high concentrations. Furthermore, much less water is lost when a given quantity of nitrogen is excreted in a concentrated solution of urea rather than a dilute solution of ammonia.

The main disadvantage of urea is its energy cost: Animals must expend energy to produce urea from ammonia. From a bioenergetic standpoint, we would predict that animals that spend part of their lives in water and part on land would switch between excreting ammonia (thereby saving energy) and excreting urea (reducing excretory water loss). Indeed, many amphibians excrete mainly ammonia when they are aquatic tadpoles and switch largely to urea excretion when they become land-dwelling adults.

Uric Acid

Insects, land snails, and many reptiles, including birds, excrete **uric acid** as their primary nitrogenous waste. (Bird droppings, or *guano*, are a mixture of white uric acid and brown feces.) Uric acid is relatively nontoxic and does not readily dissolve in water. It therefore can be excreted as a semisolid paste with very little water loss. This is a great advantage for animals with little access to water, but there is a cost: Uric acid is even more energetically expensive to produce than urea, requiring considerable ATP for synthesis from ammonia.

Because uric acid releases nitrates to soil, bird guano can be used as fertilizer in agriculture. Before synthetic fertilizers were developed, this "waste" was so valued that nations fought wars over South American islands covered with piles of seabird guano as tall as 12-story buildings! Recently, interest in organic fertilizers has revived the commercial trade in guano **(Figure 44.9)**.

While not primarily uric acid producers, humans and some other animals generate a small amount of uric acid as a product of purine breakdown. Diseases that alter this process reflect the problems that can arise when a metabolic product is

▼ **Figure 44.9 Recycling nitrogenous waste.** Seabirds nesting on islands off Peru annually produce 12,000 tons of guano, which workers collect for sale as organic fertilizer.

insoluble. For example, a genetic defect in purine metabolism predisposes Dalmatian dogs to form uric acid stones in their bladder. In humans, adult males are particularly susceptible to *gout*, a painful joint inflammation caused by deposits of uric acid crystals. Meals containing purine-rich animal tissues can increase the inflammation. Some dinosaurs appear to have been similarly affected: Fossilized bones of *Tyrannosaurus rex* exhibit joint damage characteristic of gout.

The Influence of Evolution and Environment on Nitrogenous Wastes

EVOLUTION In general, the kind of nitrogenous wastes an animal excretes depends on both the species' evolutionary history (phylogeny) and its habitat, especially the availability of water. For example, terrestrial turtles (which often live in dry areas) excrete mainly uric acid, whereas aquatic turtles excrete both urea and ammonia. Another factor affecting the primary type of nitrogenous waste produced by a particular group of animals is the immediate environment of the animal egg. For example, soluble wastes can diffuse out of a shell-less amphibian egg or be carried away from a mammalian embryo by the mother's blood. However, the shelled eggs produced by birds and other reptiles (see Figure 34.25) are permeable to gases but not to liquids, which means that soluble nitrogenous wastes released by an embryo would be trapped within the egg and could accumulate to dangerous levels. (Although urea is much less harmful than ammonia, it is toxic at very high concentrations.) Using uric acid as a waste product conveys a selective advantage because it precipitates out of solution and can be stored within the egg as a harmless solid left behind when the animal hatches.

Regardless of the type of nitrogenous waste, the amount produced is coupled to the animal's energy budget. Endotherms, which use energy at high rates, eat more food and produce more nitrogenous waste than ectotherms. The amount of nitrogenous waste is also linked to diet. Predators, which derive much of their energy from protein, excrete more nitrogen than animals that rely mainly on lipids or carbohydrates as energy sources.

Having surveyed the forms of nitrogenous waste and their interrelationship with evolutionary lineage, habitat, and energy consumption, we will turn next to the processes and systems animals use to excrete these and other wastes.

CONCEPT CHECK 44.2

1. What advantage does uric acid offer as a nitrogenous waste in arid environments?
2. **WHAT IF?** Suppose a bird and a human both have gout. Why might reducing purine in their diets help the human much more than the bird?

For suggested answers, see Appendix A.

Diverse excretory systems are variations on a tubular theme

Whether an animal lives on land, in salt water, or in fresh water, water balance depends on the regulation of solute movement between internal fluids and the external environment. Much of this movement is handled by excretory systems. These systems are central to homeostasis because they dispose of metabolic wastes and control body fluid composition. Before we describe particular excretory systems, let's consider a generalized version of the process of excretion.

Excretory Processes

Animals across a wide range of species produce a fluid waste called urine through the basic steps shown in **Figure 44.10**. In the first step, body fluid (blood, coelomic fluid, or hemolymph) is brought in contact with the selectively permeable membrane of a transport epithelium. In most cases, hydrostatic pressure (blood pressure in many animals) drives a process of **filtration**. Cells, as well as proteins and other large molecules, cannot cross the epithelial membrane and
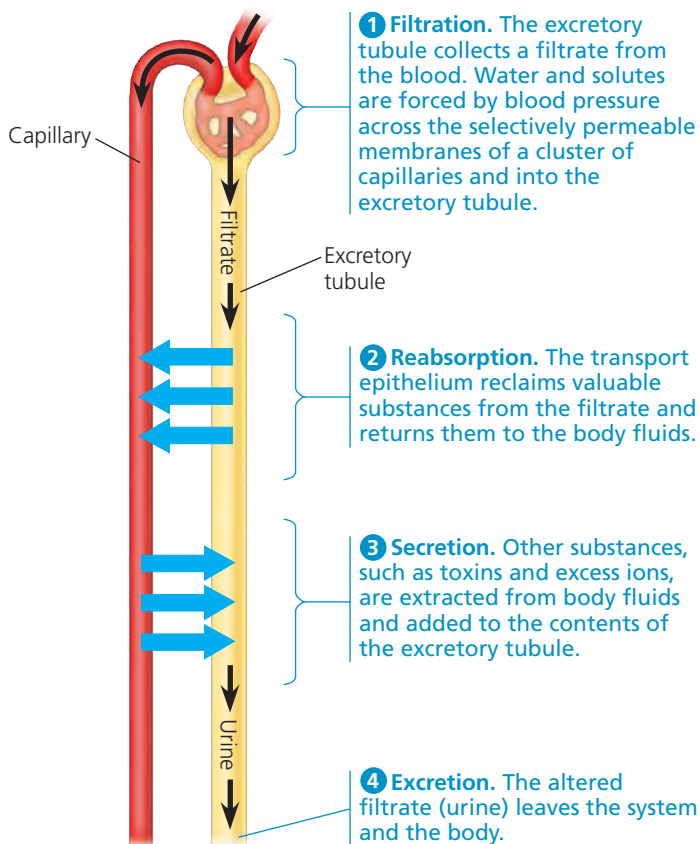
remain in the body fluid. In contrast, water and small solutes, such as salts, sugars, amino acids, and nitrogenous wastes, cross the membrane, forming a solution called the **filtrate**.

The filtrate is converted to a waste fluid by the specific transport of materials into or out of the filtrate. The process of selective **reabsorption** recovers useful molecules and water from the filtrate and returns them to the body fluids. Valuable solutes—including glucose, certain salts, vitamins, hormones, and amino acids—are reabsorbed by active transport. Nonessential solutes and wastes are left in the filtrate or are added to it by selective **secretion**, which also occurs by active transport. The pumping of various solutes adjusts the osmotic movement of water into or out of the filtrate. In the last step—excretion—the processed filtrate containing nitrogenous wastes is released from the body as urine.

Survey of Excretory Systems

The systems that perform the basic excretory functions vary widely among animal groups. However, they are generally built on a complex network of tubules that provide a large surface area for the exchange of water and solutes, including nitrogenous wastes. We'll examine the excretory systems of flatworms, earthworms, insects, and vertebrates as examples of evolutionary variations on tubule networks.

Protonephridia

Flatworms (phylum Platyhelminthes) have excretory systems called **protonephridia** (singular, *protonephridium*), which form a network of dead-end tubules **(Figure 44.11)**. The

1 Filtration. The excretory tubule collects a filtrate from the blood. Water and solutes are forced by blood pressure across the selectively permeable membranes of a cluster of capillaries and into the excretory tubule.

2 Reabsorption. The transport epithelium reclaims valuable substances from the filtrate and returns them to the body fluids.

3 Secretion. Other substances, such as toxins and excess ions, are extracted from body fluids and added to the contents of the excretory tubule.

4 Excretion. The altered filtrate (urine) leaves the system and the body.

▲ **Figure 44.10 Key steps of excretory system function: an overview.** Most excretory systems produce a filtrate by pressure-filtering body fluids and then modify the filtrate's contents. This diagram is modeled after the vertebrate excretory system.

▶ **Figure 44.11 Protonephridia: the flame bulb system of a planarian.** Protonephridia are branching internal tubules that function mainly in osmoregulation.
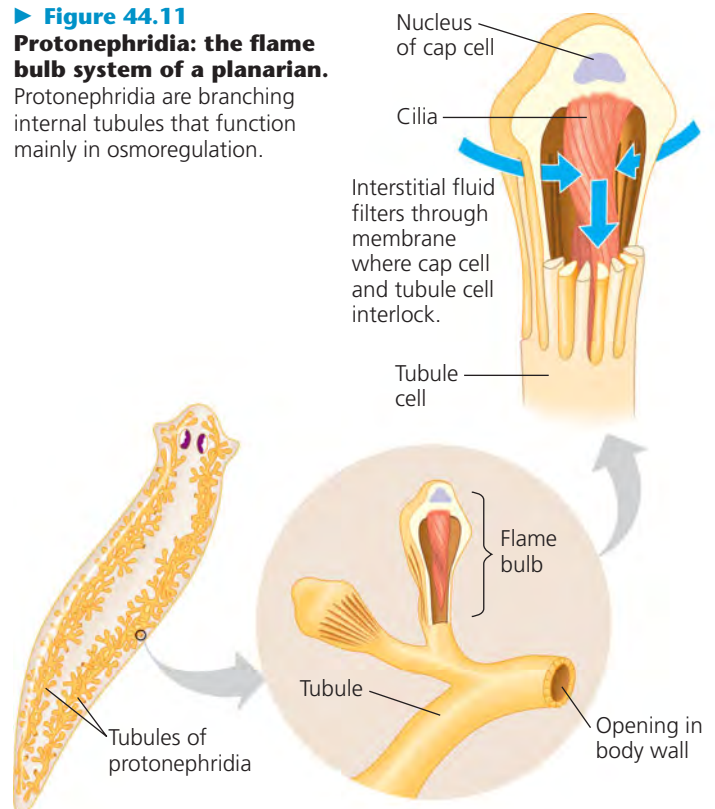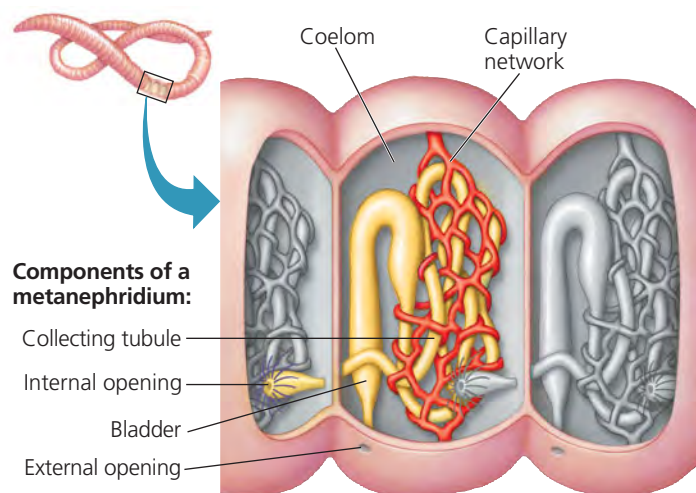
tubules, which are connected to external openings, branch throughout the flatworm body, which lacks a coelom or body cavity. Cellular units called flame bulbs cap the branches of each protonephridium. Consisting of a tubule cell and a cap cell, each flame bulb has a tuft of cilia projecting into the tubule. During filtration, the beating of the cilia draws water and solutes from the interstitial fluid through the flame bulb, releasing filtrate into the tubule network. (The moving cilia resemble a flickering flame, hence the name *flame bulb*.) The processed filtrate then moves outward through the tubules and empties as urine into the external environment. The urine excreted by freshwater flatworms has a low solute concentration, helping to balance the osmotic uptake of water from the environment.

Protonephridia are also found in rotifers, some annelids, mollusc larvae, and lancelets (see Figure 34.4). Among these animals, the function of the protonephridia varies. In the freshwater flatworms, protonephridia serve chiefly in osmoregulation. Most metabolic wastes diffuse out of the animal across the body surface or are excreted into the gastrovascular cavity and eliminated through the mouth (see Figure 33.10). However, in some parasitic flatworms, which are isoosmotic to the surrounding fluids of their host organisms, the main function of protonephridia is the disposal of nitrogenous wastes. Natural selection has thus adapted protonephridia to different tasks in different environments.

Metanephridia

Most annelids, such as earthworms, have **metanephridia** (singular, *metanephridium*), excretory organs that collect fluid directly from the coelom **(Figure 44.12)**. Each segment of a worm has a pair of metanephridia, which are immersed in coelomic fluid and enveloped by a capillary network. A ciliated funnel surrounds the internal opening. As the cilia beat, fluid is drawn into a collecting tubule, which includes a storage bladder that opens to the outside.

The metanephridia of an earthworm have both excretory and osmoregulatory functions. As urine moves along the tubule, the transport epithelium bordering the lumen reabsorbs most solutes and returns them to the blood in the capillaries. Nitrogenous wastes remain in the tubule and are excreted to the outside. Earthworms inhabit damp soil and usually experience a net uptake of water by osmosis through their skin. Their metanephridia balance the water influx by producing urine that is dilute (hypoosmotic to body fluids).

Malpighian Tubules

Insects and other terrestrial arthropods have organs called **Malpighian tubules** that remove nitrogenous wastes and that also function in osmoregulation **(Figure 44.13)**. The Malpighian tubules extend from dead-end tips immersed in hemolymph (circulatory fluid) to openings into the digestive tract. The filtration step common to other excretory systems is absent. Instead, the transport epithelium that lines the tubules secretes certain solutes, including nitrogenous wastes, from the hemolymph into the lumen of the tubule. Water follows the solutes into the tubule by osmosis, and the fluid then passes into the rectum. There, most solutes are pumped back into the hemolymph, and water reabsorption by osmosis follows. The nitrogenous wastes—mainly insoluble
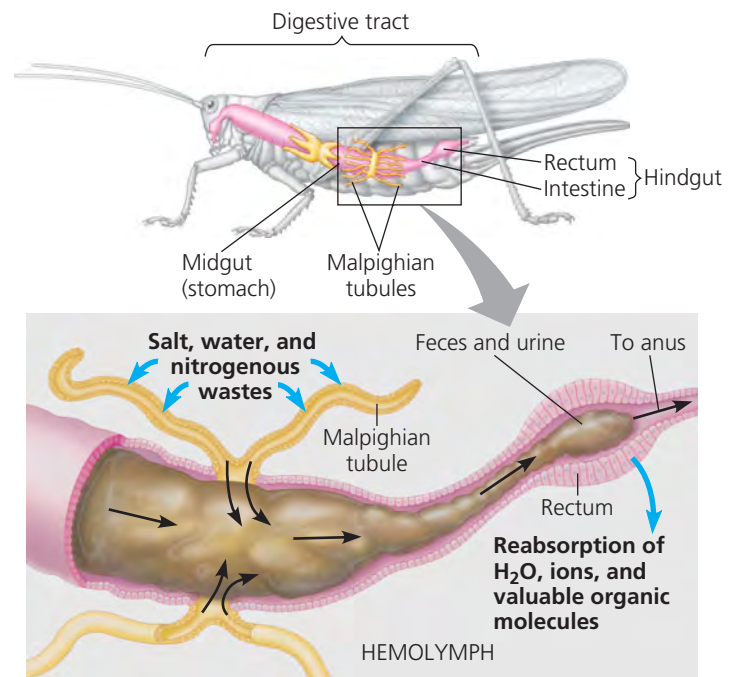

▲ **Figure 44.12 Metanephridia of an earthworm.** Each segment of the worm contains a pair of metanephridia, which collect coelomic fluid from the adjacent anterior segment. The region highlighted in yellow illustrates the organization of one metanephridium of a pair; the other would be behind it.

▲ **Figure 44.13 Malpighian tubules of insects.** Malpighian tubules are outpocketings of the digestive tract that remove nitrogenous wastes and function in osmoregulation.

Exploring the Mammalian Excretory System

Excretory Organs

Posterior vena cava
Renal artery and vein
Aorta
Kidney
Ureter
Urinary bladder
Urethra
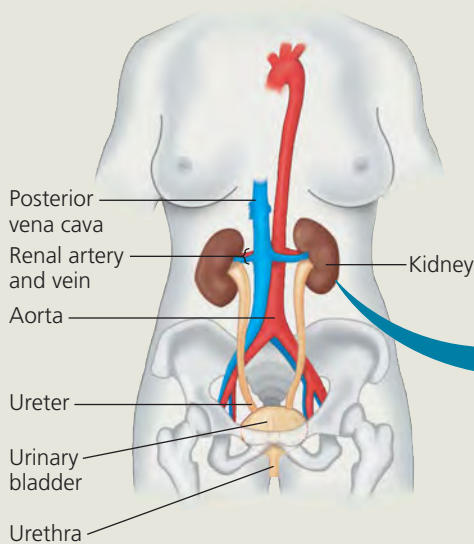
In humans, the excretory system consists of a pair of **kidneys**, bean-shaped organs about 10 cm in length, as well as organs for transporting and storing urine. Urine produced by each kidney exits through a duct called the **ureter**; the two ureters drain into a common sac called the **urinary bladder**. During urination, urine is expelled from the bladder through a tube called the **urethra**, which empties to the outside near the vagina in females and through the penis in males. Sphincter muscles near the junction of the urethra and bladder regulate urination.

Kidney Structure

Renal cortex
Renal medulla
Renal artery
Renal vein
Ureter
Renal pelvis
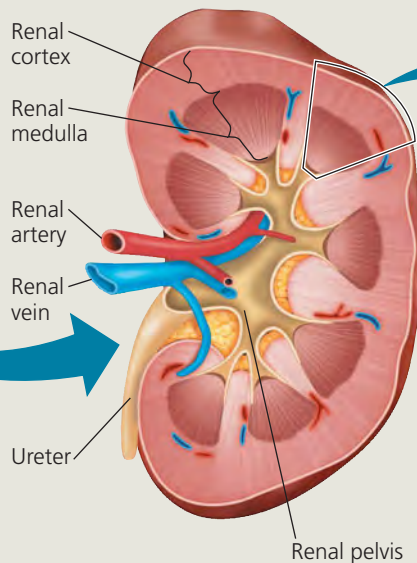
Each kidney has an outer **renal cortex** and an inner **renal medulla**. Both regions are supplied with blood by a renal artery and drained by a renal vein. Within the cortex and medulla lie tightly packed excretory tubules and associated blood vessels. The inner **renal pelvis** collects urine from the excretory tubules and passes it to the urinary bladder.

Nephron Types

Cortical nephron   Juxtamedullary nephron
Renal cortex
Renal medulla
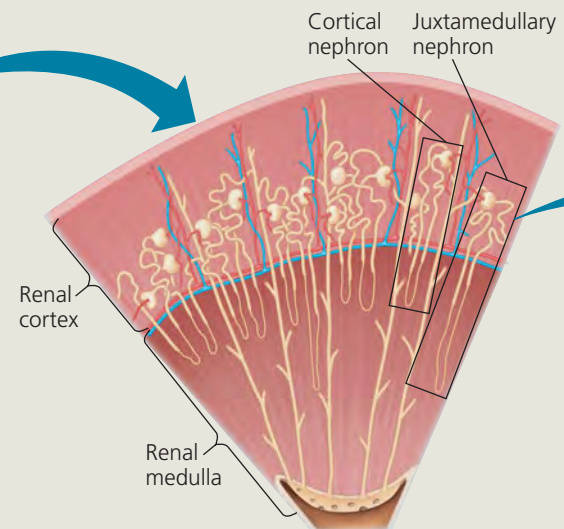
Weaving back and forth across the renal cortex and medulla are the **nephrons**, the functional units of the vertebrate kidney. Of the roughly 1 million nephrons in a human kidney, 85% are **cortical nephrons**, which reach only a short distance into the medulla. The remainder, the **juxtamedullary nephrons**, extend deep into the medulla. Juxtamedullary nephrons are essential for production of urine that is hyperosmotic to body fluids, a key adaptation for water conservation in mammals.

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uric acid—are eliminated as nearly dry matter along with the feces. Capable of conserving water very effectively, the insect excretory system is a key adaptation contributing to these animals' tremendous success on land.

Some terrestrial insects have an additional adaptation for water balance: The rectal end of their gut enables water uptake from the air. Although some species absorb water from air only when it is very humid, others, such as fleas (genus *Xenopsylla*), can capture water from the atmosphere when relative humidity is as low as 50%.
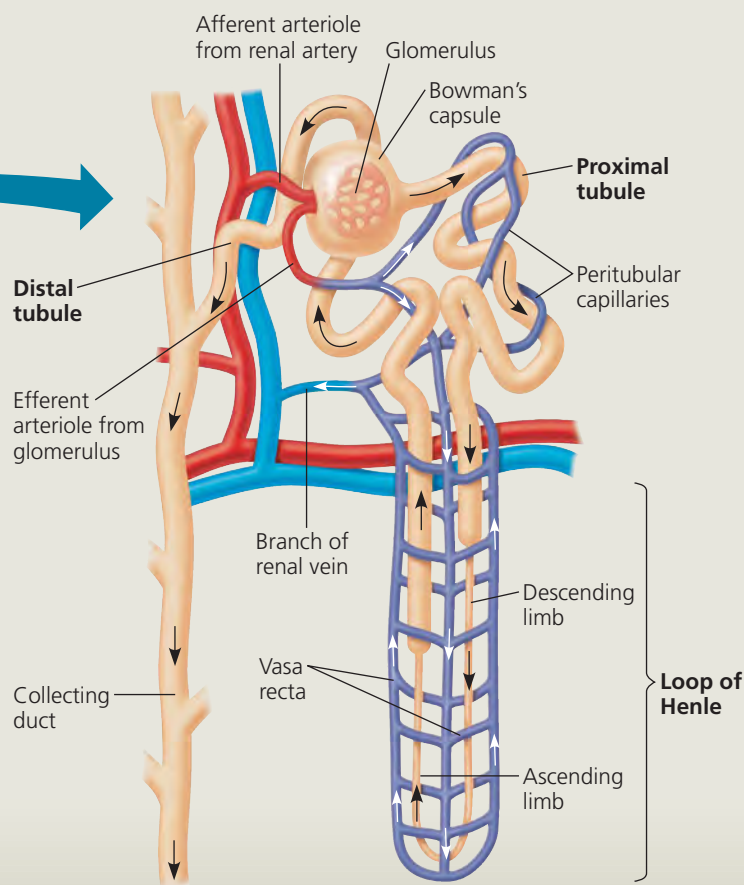
Kidneys

In vertebrates and some other chordates, a specialized organ called the kidney functions in both osmoregulation and excretion. Like the excretory organs of most animal phyla, kidneys consist of tubules. The numerous tubules of these compact organs are arranged in a highly organized manner and are closely associated with a network of capillaries. The vertebrate excretory system also includes ducts and other structures that carry urine from the tubules out of the kidney and, eventually, the body.

Vertebrate kidneys are typically nonsegmented. However, hagfishes, which are invertebrate chordates, have kidneys with segmentally arranged excretory tubules. This suggests that the excretory structures of vertebrate ancestors also may have been segmented.

Because kidney organization is integral to kidney function, we begin with **Figure 44.14**, an exploration of the anatomy of the mammalian kidney and associated structures. Familiarizing yourself with the terms and diagrams in this figure will provide you with a solid foundation for learning about filtrate processing in the kidney, our focus in the next concept.
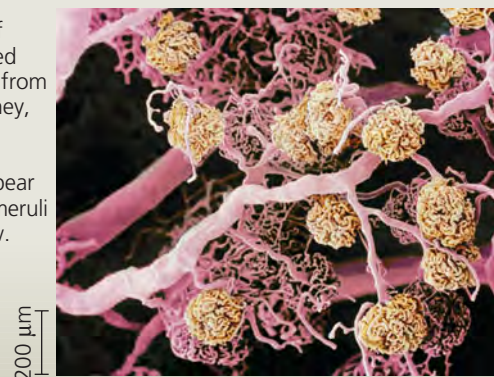
Nephron Organization

Afferent arteriole from renal artery

Glomerulus

Bowman's capsule

Proximal tubule

Peritubular capillaries

Distal tubule

Efferent arteriole from glomerulus

Branch of renal vein

Descending limb

Vasa recta

Loop of Henle

Collecting duct

Ascending limb

Each nephron consists of a single long tubule as well as a ball of capillaries called the **glomerulus**. The blind end of the tubule forms a cup-shaped swelling, called **Bowman's capsule**, which surrounds the glomerulus. Filtrate is formed when blood pressure forces fluid from the blood in the glomerulus into the lumen of Bowman's capsule. Processing occurs as the filtrate passes through three major regions of the nephron: the **proximal tubule**, the **loop of Henle** (a hairpin turn with a descending limb and an ascending limb), and the **distal tubule**. A **collecting duct** receives processed filtrate from many nephrons and transports it to the renal pelvis.

Each nephron is supplied with blood by an *afferent arteriole*, an offshoot of the renal artery that branches and forms the capillaries of the glomerulus. The capillaries converge as they leave the glomerulus, forming an *efferent arteriole*. Branches of this vessel form the **peritubular capillaries**, which surround the proximal and distal tubules. Other branches extend downward and form the **vasa recta**, hairpin-shaped capillaries that serve the renal medulla, including the long loop of Henle of juxtamedullary nephrons.

► In this SEM of densely packed blood vessels from a human kidney, arterioles and peritubular capillaries appear pink; the glomeruli appear yellow.

200 µm

CONCEPT 44.4

The nephron is organized for stepwise processing of blood filtrate

We'll continue our exploration of the nephron with a discussion of filtrate processing. We will then focus on how tubules, capillaries, and surrounding tissue function together.

The porous capillaries and specialized cells of Bowman's capsule are permeable to water and small solutes, but not blood cells or large molecules, such as plasma proteins. Thus, the filtrate produced in the capsule contains salts, glucose, amino acids, vitamins, nitrogenous wastes, and other small molecules. Because such molecules pass freely between glomerular capillaries and Bowman's capsule, the concentrations of these substances in the initial filtrate are the same as those in blood plasma.

From Blood Filtrate to Urine: *A Closer Look*

In this section, we will follow filtrate along its path in the nephron and collecting duct, examining how each region contributes to the stepwise processing of filtrate into urine. The circled numbers correspond to the numbers in **Figure 44.15**.

1 **Proximal tubule.** Reabsorption in the proximal tubule is critical for the recapture of ions, water, and valuable nutrients from the huge volume of initial filtrate. NaCl (salt) in the filtrate diffuses into the cells of the transport epithelium, where Na^+ is actively transported into the interstitial fluid. This transfer of positive charge out of the tubule drives the passive transport of Cl^-, as well as the movement of more Na^+ from the lumen into the cells of the tubule wall by facilitated diffusion and cotransport mechanisms (see Figures 7.17 and 7.21).

As salt moves from the filtrate to the interstitial fluid, water follows by osmosis. The salt and water then diffuse from the interstitial fluid into the peritubular capillaries. Glucose, amino acids, potassium ions (K^+), and other essential substances are also actively or passively transported from the filtrate to the interstitial fluid and then into the peritubular capillaries.

Processing of filtrate in the proximal tubule helps maintain a relatively constant pH in body fluids. Cells of the transport epithelium secrete H^+ into the lumen of the tubule but also synthesize and secrete ammonia, which acts as a buffer to trap H^+ in the form of ammonium ions (NH_4^+). The more acidic the filtrate, the more ammonia the cells produce and secrete, and a mammal's urine usually contains some ammonia from this source (even though most nitrogenous waste is excreted as urea). The proximal tubules also reabsorb about 90% of the buffer bicarbonate (HCO_3^-) from the filtrate, contributing further to pH balance in body fluids.

As the filtrate passes through the proximal tubule, materials to be excreted become concentrated. Many wastes leave the body fluids during the nonselective filtration process and remain in the filtrate while water and salts are reabsorbed. Urea, for example, is reabsorbed at a much lower rate than are salt and water. Some other toxic materials are actively secreted into filtrate from surrounding tissues. For example, drugs and toxins that have been processed in the liver pass from the peritubular capillaries into the interstitial fluid. These molecules then enter the proximal tubule, where they are actively secreted from the transport epithelium into the lumen.
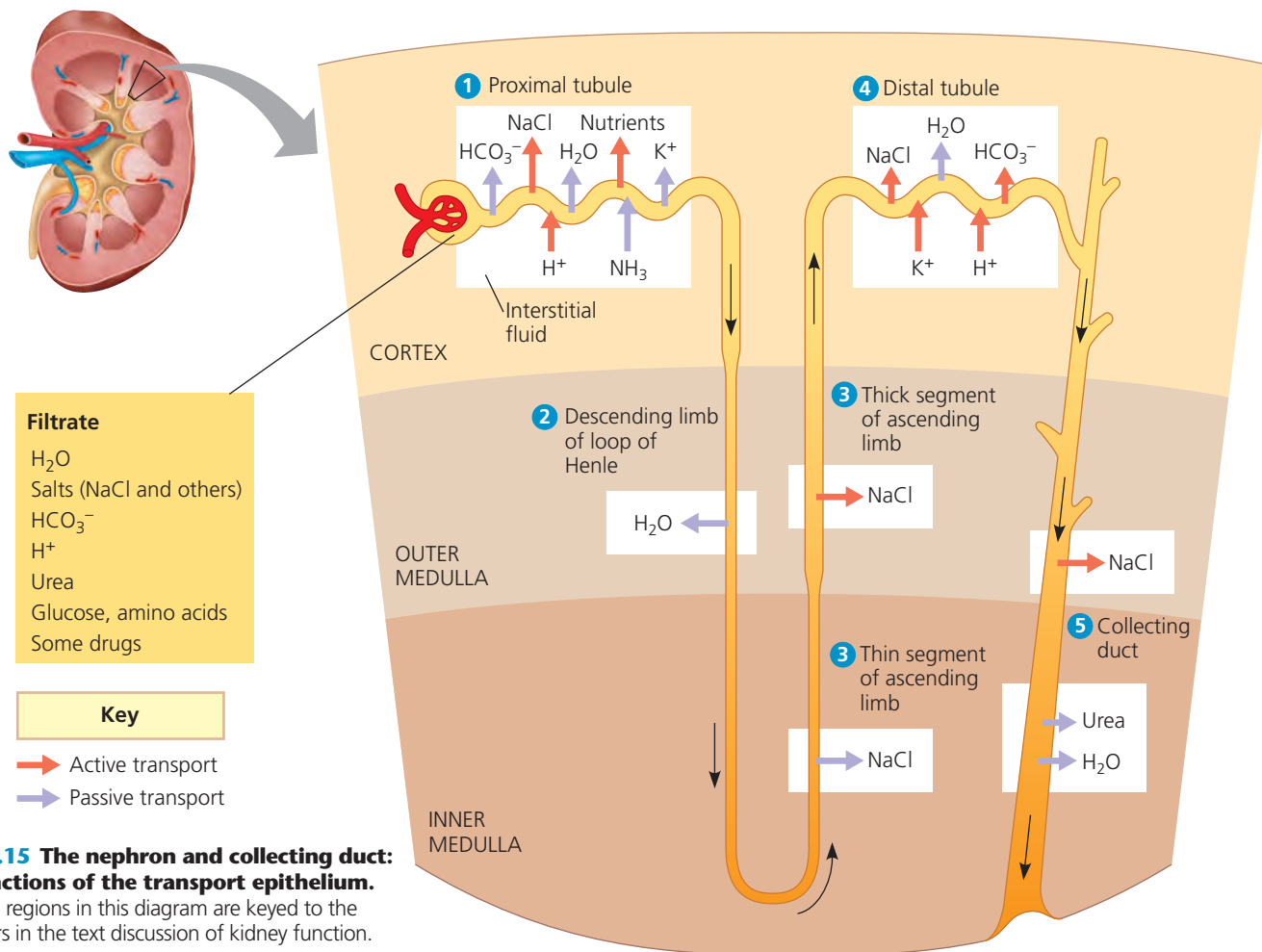
▲ **Figure 44.15 The nephron and collecting duct: regional functions of the transport epithelium.** The numbered regions in this diagram are keyed to the circled numbers in the text discussion of kidney function.

? *Some cells lining tubules in the kidney synthesize organic solutes to maintain normal cell volume. Where in the kidney would you find these cells? Explain.*

2 **Descending limb of the loop of Henle.** Reabsorption of water continues as the filtrate moves into the descending limb of the loop of Henle. Here numerous water channels formed by **aquaporin** proteins make the transport epithelium freely permeable to water. In contrast, there are almost no channels for salt and other small solutes, resulting in very low permeability for these substances.

For water to move out of the tubule by osmosis, the interstitial fluid bathing the tubule must be hyperosmotic to the filtrate. This condition is met along the entire length of the descending limb, because the osmolarity of the interstitial fluid increases progressively from the outer cortex to the inner medulla of the kidney. As a result, the filtrate loses water—and therefore its solute concentration increases—all along its journey down the descending limb.

3 **Ascending limb of the loop of Henle.** The filtrate reaches the tip of the loop and then travels within the ascending limb as it returns to the cortex. Unlike the descending limb, the ascending limb has a transport epithelium studded with ion channels, but not water channels. Indeed, this membrane is impermeable to water. Impermeability to water is very rare among biological membranes and is critical to the function of the ascending limb.

The ascending limb has two specialized regions: a thin segment near the loop tip and a thick segment adjacent to the distal tubule. As filtrate ascends in the thin segment, NaCl, which became concentrated in the descending limb, diffuses out of the permeable tubule into the interstitial fluid. This movement of NaCl out of the tubule helps maintain the osmolarity of the interstitial fluid in the medulla. In the thick segment of the ascending limb, the movement of NaCl out of the filtrate continues. Here, however, the epithelium actively transports NaCl into the interstitial fluid. As a result of losing salt but not water, the filtrate becomes progressively more dilute as it moves up to the cortex in the ascending limb of the loop.

4 **Distal tubule.** The distal tubule plays a key role in regulating the K^+ and NaCl concentration of body fluids. This regulation involves variation in the amount of K^+ secreted into the filtrate as well as the amount of NaCl reabsorbed from the filtrate. Like the proximal tubule, the distal tubule contributes to pH regulation by the controlled secretion of H^+ and reabsorption of HCO_3^-.

5 **Collecting duct.** The collecting duct carries the filtrate through the medulla to the renal pelvis. The transport epithelium of the nephron and collecting duct processes the filtrate, forming the urine. One of this epithelium's most important tasks is reabsorption of solutes and water. Under normal conditions, approximately 1,600 L of blood flows through a pair of human kidneys each day, about 300 times the total volume of blood in the body. From this

enormous traffic of blood, the nephrons and collecting ducts process about 180 L of initial filtrate. Of this, about 99% of the water and nearly all of the sugars, amino acids, vitamins, and other organic nutrients are reabsorbed into the blood, leaving only about 1.5 L of urine to be transported to the bladder.

As filtrate passes along the transport epithelium of the collecting duct, hormonal control of permeability and transport determines the extent to which the urine becomes concentrated.

When the kidneys are conserving water, aquaporin channels in the collecting duct allow water molecules to cross the epithelium. At the same time, the epithelium remains impermeable to salt and, in the renal cortex, to urea. As the collecting duct traverses the gradient of osmolarity in the kidney, the filtrate becomes increasingly concentrated, losing more and more water by osmosis to the hyperosmotic interstitial fluid. In the inner medulla, the duct becomes permeable to urea. Because of the high urea concentration in the filtrate at this point, some urea diffuses out of the duct and into the interstitial fluid. Along with NaCl, this urea contributes to the high osmolarity of the interstitial fluid in the medulla. The net result is urine that is hyperosmotic to the general body fluids.

In producing dilute rather than concentrated urine, the kidney actively reabsorbs salts without allowing water to follow by osmosis. At these times, the epithelium lacks water channels, and NaCl is actively transported out of filtrate. As we will see shortly, the state of the collecting duct epithelium is controlled by hormones that together maintain homeostasis for osmolarity, blood pressure, and blood volume.

Solute Gradients and Water Conservation

The mammalian kidney's ability to conserve water is a key terrestrial adaptation. In humans, the osmolarity of blood is about 300 mOsm/L, but the kidney can excrete urine up to four times as concentrated—about 1,200 mOsm/L. Some mammals can do even better: Australian hopping mice, small marsupials that live in dry desert regions, can produce urine with an osmolarity of 9,300 mOsm/L, 25 times as concentrated as the animal's blood.

In a mammalian kidney, the production of hyperosmotic urine is possible only because considerable energy is expended for the active transport of solutes against concentration gradients. The nephrons—particularly the loops of Henle—can be thought of as energy-consuming machines that produce an osmolarity gradient suitable for extracting water from the filtrate in the collecting duct. The two primary solutes affecting osmolarity are NaCl, which is deposited in the renal medulla by the loop of Henle, and urea, which passes across the epithelium of the collecting duct in the inner medulla.

The Two-Solute Model

To better understand the physiology of the mammalian kidney as a water-conserving organ, let's retrace the flow of filtrate through the excretory tubule. This time, let's focus on how the juxtamedullary nephrons maintain an osmolarity gradient in the tissues that surround the loop of Henle and how they use that gradient to excrete a hyperosmotic urine **(Figure 44.16)**. Filtrate passing from Bowman's capsule to the proximal tubule has an osmolarity of about 300 mOsm/L, the same as blood. A large amount of water *and* salt is reabsorbed from the filtrate as it flows through the proximal tubule in the renal cortex. As a result, the filtrate's volume decreases substantially, but its osmolarity remains about the same.

As the filtrate flows from cortex to medulla in the descending limb of the loop of Henle, water leaves the tubule by osmosis. Solutes, including NaCl, become more concentrated, increasing the osmolarity of the filtrate. The highest osmolarity (about 1,200 mOsm/L) occurs at the elbow of the loop of Henle. This maximizes the diffusion of salt out of the tubule as the filtrate rounds the curve and enters the ascending limb, which is permeable to salt but not to water. NaCl diffusing from the ascending limb helps maintain a high osmolarity in the interstitial fluid of the renal medulla.

Notice that the loop of Henle has several qualities of a countercurrent system, such as the mechanisms that maximize oxygen absorption by fish gills (see Figure 42.22) or reduce heat loss in endotherms (see Figure 40.12). In those cases, the countercurrent mechanisms involve passive movement along either an oxygen concentration gradient or a heat gradient. In contrast, the countercurrent system involving the loop of Henle expends energy to actively transport NaCl from the filtrate in the upper part of the ascending limb of the loop. Such countercurrent systems, which expend energy to create concentration gradients, are called **countercurrent multiplier systems**. The countercurrent multiplier system involving the loop of Henle maintains a high salt concentration in the interior of the kidney, enabling the kidney to form concentrated urine.

What prevents the capillaries of the vasa recta from dissipating the gradient by carrying away the high concentration of NaCl in the medulla's interstitial fluid? As shown in Figure 44.14, the descending and ascending vessels of the vasa recta carry blood in opposite directions through the kidney's osmolarity gradient. As the descending vessel conveys blood toward the inner medulla, water is lost from the blood and NaCl is gained by diffusion. These fluxes are reversed as blood flows back toward the cortex in the ascending vessel, with water reentering the blood and salt diffusing out. Thus,

▶ **Figure 44.16 How the human kidney concentrates urine: the two-solute model.** Two solutes contribute to the osmolarity of the interstitial fluid: NaCl (used as shorthand here to refer collectively to Na^+ and Cl^-) and urea. The loop of Henle maintains the interstitial gradient of NaCl, which increases continuously in concentration from the cortex to the inner medulla. Urea diffuses into the interstitial fluid of the medulla from the collecting duct (most of the urea in the filtrate remains in the collecting duct and is excreted). The filtrate makes three trips between the cortex and medulla: first down, then up, and then down again in the collecting duct. As the filtrate flows in the collecting duct past interstitial fluid of increasing osmolarity, more water moves out of the duct by osmosis. The loss of water concentrates the solutes, including urea, that will be excreted in the urine.

WHAT IF? *The drug furosemide blocks the cotransporters for Na^+ and Cl^- in the ascending limb of the loop of Henle. What effect would you expect this drug to have on urine volume?*

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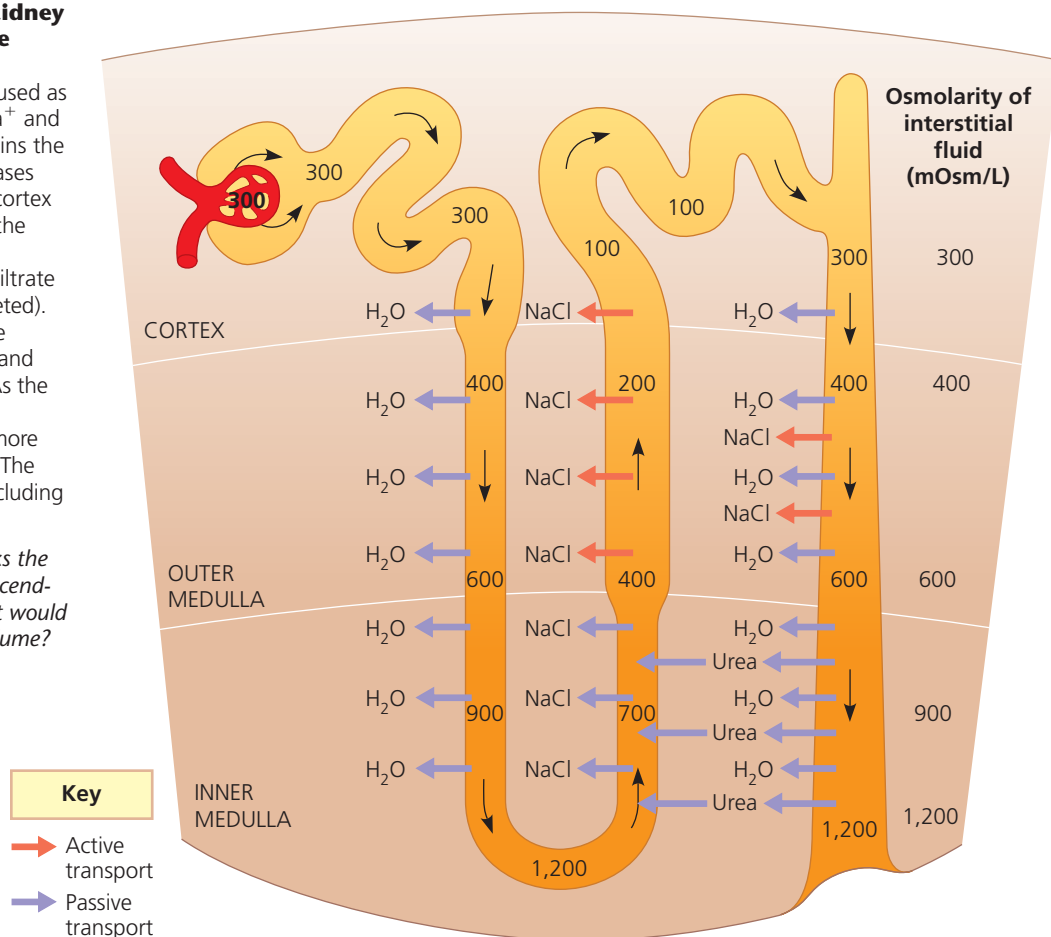
the vasa recta can supply the kidney with nutrients and other important substances carried by the blood without interfering with the osmolarity gradient in the inner and outer medulla.

The countercurrent-like characteristics of the loop of Henle and the vasa recta help to generate the steep osmotic gradient between the medulla and cortex. However, diffusion will eventually eliminate any osmotic gradient within animal tissue unless gradient formation is supported by an expenditure of energy. In the kidney, this expenditure largely occurs in the thick segment of the ascending limb of the loop of Henle, where NaCl is actively transported out of the tubule. Even with the benefits of countercurrent exchange, this process—along with other renal active transport systems—consumes considerable ATP. Thus, for its size, the kidney has one of the highest metabolic rates of any organ.

As a result of active transport of NaCl out of the thick segment of the ascending limb, the filtrate is actually hypoosmotic to body fluids by the time it reaches the distal tubule. Next the filtrate descends again toward the medulla, this time in the collecting duct, which is permeable to water but not to salt. Therefore, osmosis extracts water from the filtrate as it passes from cortex to medulla and encounters interstitial fluid of increasing osmolarity. This process concentrates salt, urea, and other solutes in the filtrate. Some urea passes out of the lower portion of the collecting duct and contributes to the high interstitial osmolarity of the inner medulla. (This urea is recycled by diffusion into the loop of Henle, but continual leakage from the collecting duct maintains a high interstitial urea concentration.) When the kidney concentrates urine maximally, the urine reaches 1,200 mOsm/L, the osmolarity of the interstitial fluid in the inner medulla. Although *isoosmotic* to the inner medulla's interstitial fluid, the urine is *hyperosmotic* to blood and interstitial fluid elsewhere in the body. This high osmolarity allows the solutes remaining in the urine to be excreted from the body with minimal water loss.

Adaptations of the Vertebrate Kidney to Diverse Environments

EVOLUTION Vertebrate animals occupy habitats ranging from rain forests to deserts and from some of the saltiest bodies of water to the nearly pure waters of high mountain lakes. Variations in nephron structure and function equip the kidneys of different vertebrates for osmoregulation in their various habitats. The adaptations of the vertebrate kidney are made apparent by comparing species that inhabit a wide range of environments or by comparing the responses of different vertebrate groups to similar environmental conditions.

Mammals

The juxtamedullary nephron, with its urine-concentrating features, is a key adaptation to terrestrial life, enabling mammals to get rid of salts and nitrogenous wastes without squandering

water. As we have seen, the remarkable ability of the mammalian kidney to produce hyperosmotic urine depends on the precise arrangement of the tubules and collecting ducts in the renal cortex and medulla. In this respect, the kidney is one of the clearest examples of how natural selection links the function of an organ to its structure.

Mammals that excrete the most hyperosmotic urine, such as Australian hopping mice, North American kangaroo rats, and other desert mammals, have loops of Henle that extend deep into the medulla. Long loops maintain steep osmotic gradients in the kidney, resulting in urine becoming very concentrated as it passes from cortex to medulla in the collecting ducts.

In contrast, beavers, muskrats, and other aquatic mammals that spend much of their time in fresh water and rarely face problems of dehydration have nephrons with relatively short loops, resulting in a much lower ability to concentrate urine. Terrestrial mammals living in moist conditions have loops of Henle of intermediate length and the capacity to produce urine intermediate in concentration to that produced by freshwater and desert mammals.

Birds and Other Reptiles

Most birds, including the albatross (see Figure 44.1) and the roadrunner **(Figure 44.17)**, live in environments that are dehydrating. Like mammals, birds have kidneys with juxtamedullary nephrons that specialize in conserving water. However, the nephrons of birds have loops of Henle that extend less far into the medulla than those of mammals. Thus, bird kidneys cannot concentrate urine to the high osmolarities achieved by mammalian kidneys. Although birds can produce hyperosmotic urine, their main water conservation adaptation is having uric acid as the nitrogen waste molecule. Since uric acid can be excreted as a paste, it reduces urine volume.

The kidneys of other reptiles, which have only cortical nephrons, produce urine that is isoosmotic or hypoosmotic to body fluids. However, the epithelium of the chamber from

▲ **Figure 44.17 The roadrunner (*Geococcyx californianus*), an animal well adapted to its dry environment.**

which urine and feces leave the body (the cloaca) helps conserve fluid by reabsorbing water from these wastes. Also like birds, most other reptiles excrete their nitrogenous wastes as uric acid.

Freshwater Fishes and Amphibians

Freshwater fishes are hyperosmotic to their surroundings, so they must excrete excess water continuously. In contrast to mammals and birds, freshwater fishes produce large volumes of very dilute urine. Their kidneys, which contain many nephrons, produce filtrate at a high rate. Freshwater fishes conserve salts by reabsorbing ions from the filtrate in their distal tubules, leaving water behind.

Amphibian kidneys function much like those of freshwater fishes. When in fresh water, the kidneys of frogs excrete dilute urine while the skin accumulates certain salts from the water by active transport. On land, where dehydration is the most pressing problem of osmoregulation, frogs conserve body fluid by reabsorbing water across the epithelium of the urinary bladder.

Marine Bony Fishes

The tissues of marine bony fishes gain excess salts from their surroundings and lose water. These environmental challenges are opposite to those faced by their freshwater relatives. Compared with freshwater fishes, marine fishes have fewer and smaller nephrons, and their nephrons lack a distal tubule. In addition, their kidneys have small glomeruli or lack glomeruli entirely. In keeping with these features, filtration rates are low and very little urine is excreted.

The main function of kidneys in marine bony fishes is to get rid of divalent ions (those with a charge of 2+ or 2−) such as calcium (Ca^{2+}), magnesium (Mg^{2+}), and sulfate (SO_4^{2-}). Marine fishes take in divalent ions by incessantly drinking seawater. They rid themselves of these ions by secreting them into the proximal tubules of the nephrons and excreting them in urine. Secretion by the gills maintains proper levels of monovalent ions (charge of 1+ or 1−) such as Na^+ and Cl^-.

CONCEPT CHECK 44.4

1. What do the number and length of nephrons in a fish's kidney indicate about the fish's habitat? How do they correlate with urine production?
2. Many medications make the epithelium of the collecting duct less permeable to water. How would taking such a drug affect kidney output?
3. **WHAT IF?** If blood pressure in the afferent arteriole leading to a glomerulus decreased, how would the rate of blood filtration within Bowman's capsule be affected? Explain.

For suggested answers, see Appendix A.

CONCEPT 44.5

Hormonal circuits link kidney function, water balance, and blood pressure

In mammals, both the volume and osmolarity of urine are adjusted according to an animal's water and salt balance and its rate of urea production. In situations of high salt intake and low water availability, a mammal can excrete urea and salt in small volumes of hyperosmotic urine with minimal water loss. If salt is scarce and fluid intake is high, the kidney can instead get rid of the excess water with little salt loss by producing large volumes of hypoosmotic urine. At such times, the urine can be as dilute as 70 mOsm/L, compared with an osmolarity of 300 mOsm/L for human blood.

The South American vampire bat shown in **Figure 44.18** illustrates the versatility of the mammalian kidney. Bats of this species feed at night on the blood of large birds and mammals. The bats use their sharp teeth to make a small incision in the prey's skin and then lap up blood from the wound (the prey animal is typically not seriously harmed). Anticoagulants in the bat's saliva prevent the blood from clotting. Because vampire bats often search for hours and fly long distances to locate a suitable victim, they benefit from consuming as much blood as possible when they do find prey—so much that after feeding, a bat could be too heavy to fly. However, the bat's kidneys offload much of the water absorbed from a blood meal by excreting large volumes of dilute urine as it feeds, up to 24% of body mass per hour. Having lost enough weight to take off, the bat can fly back to its roost in a cave or hollow tree, where it spends the day.

In the roost, the bat faces a different regulatory problem. Most of the nutrition it derives from blood comes in the form of protein. Digesting proteins generates large quantities of urea, but roosting bats lack access to the drinking water necessary to
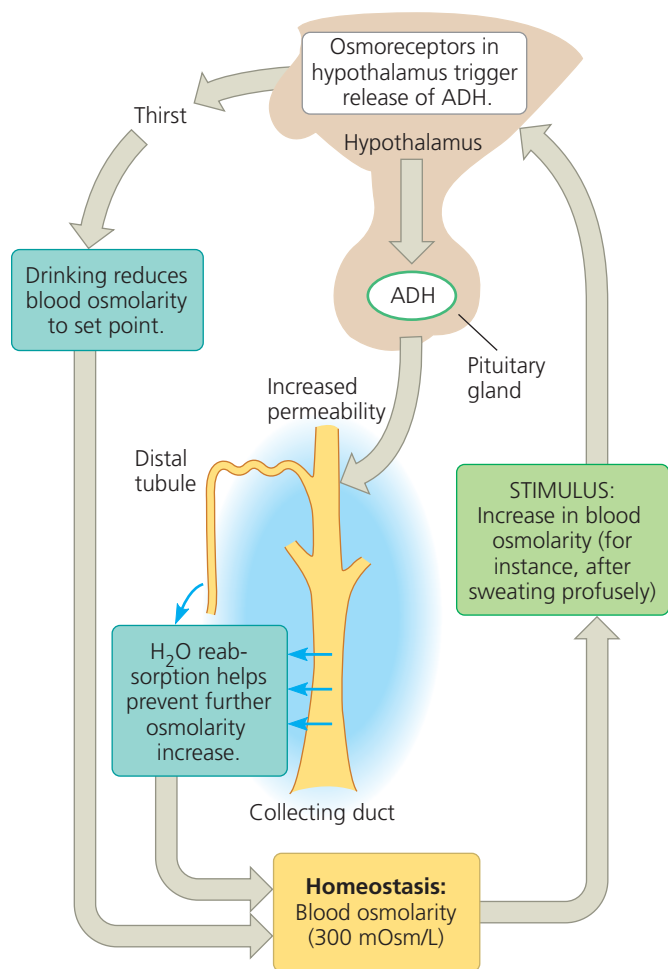

▲ **Figure 44.18 A vampire bat (*Desmodus rotundas*), a mammal with a unique excretory situation.**

dilute it. Instead, their kidneys shift to producing small quantities of highly concentrated urine (up to 4,600 mOsm/L), an adjustment that disposes of the urea load while conserving as much water as possible. The vampire bat's ability to alternate rapidly between producing large amounts of dilute urine and small amounts of very hyperosmotic urine is an essential part of its adaptation to an unusual food source.

Antidiuretic Hormone

A combination of nervous and hormonal controls manages the osmoregulatory function of the mammalian kidney. One key hormone in this regulatory circuitry is **antidiuretic hormone (ADH)**, also called *vasopressin*. ADH is produced in the hypothalamus of the brain and stored in the posterior pituitary gland, located just below the hypothalamus. Osmoreceptor cells in the hypothalamus monitor the osmolarity of blood and regulate release of ADH from the posterior pituitary.

To understand the role of ADH, let's consider what occurs when blood osmolarity rises, such as after eating salty food or losing water through sweating **(Figure 44.19)**. In response to an increase in osmolarity above the set point of 300 mOsm/L, more ADH is released into the bloodstream. When ADH reaches the kidney, its main targets are the collecting ducts. There, ADH brings about changes that make the epithelium more permeable to water. The resulting increase in water reabsorption concentrates urine, reduces urine volume, and lowers blood osmolarity back toward the set point. (Only the gain of additional water in food and drink can fully restore osmolarity to 300 mOsm/L.) As the osmolarity of the blood subsides, a negative-feedback mechanism reduces the activity of osmoreceptor cells in the hypothalamus, and ADH secretion is reduced (not shown in figure).

A reduction in blood osmolarity below the set point has the opposite set of effects. For example, intake of a large volume of water leads to a decrease in ADH secretion to a very low level. The resulting decrease in permeability of the collecting ducts reduces water reabsorption, resulting in discharge of large volumes of dilute urine. (Diuresis refers to increased urination, and ADH is called *anti*diuretic hormone because it opposes this state.)

ADH influences water uptake in the kidney's collecting ducts by regulating the water-selective channels formed by aquaporins. Binding of ADH to receptor molecules leads to a temporary increase in the number of aquaporin proteins in the membranes of collecting duct cells **(Figure 44.20)**. Additional channels recapture more water, reducing urine volume.

▲ **Figure 44.19 Regulation of fluid retention in the kidney by antidiuretic hormone (ADH).**
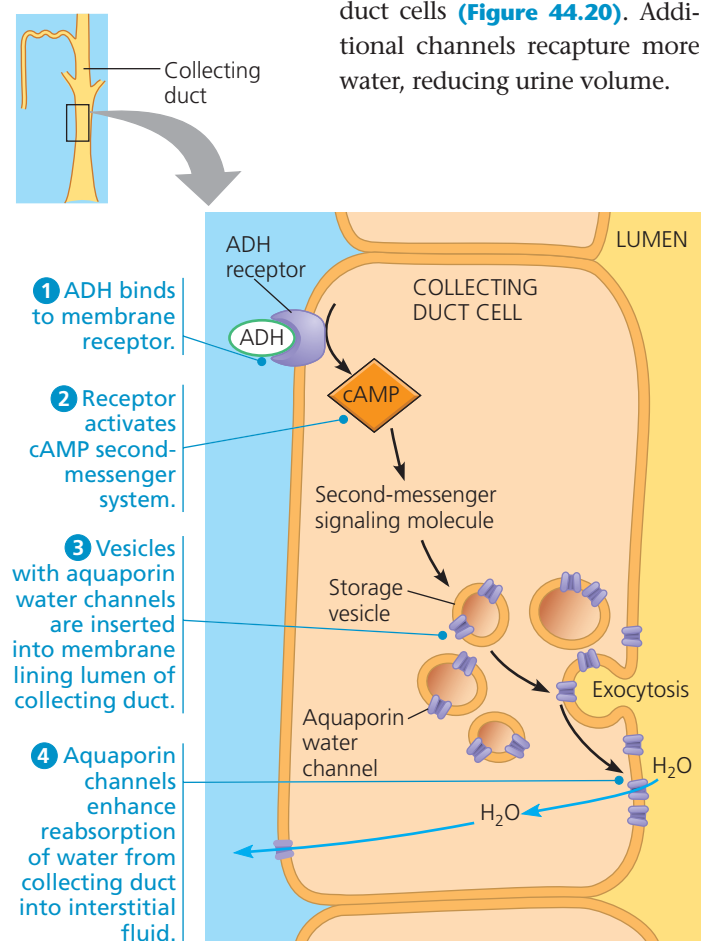
▲ **Figure 44.20 ADH response pathway in the collecting duct.**

Mutations that prevent ADH production or that inactivate the ADH receptor gene block the increase in channel number and thus the ADH response. The resulting disorder can cause severe dehydration and solute imbalance due to production of urine that is abnormally large in volume and very dilute. These symptoms give the condition its name: *diabetes insipidus* (from the Greek for "to pass through" and "having no flavor").

Researchers in the Netherlands wondered whether mutations in an aquaporin gene itself might also cause diabetes insipidus. Having found aquaporin gene mutations in a patient, they set out to determine whether the alterations led to nonfunctional water channels **(Figure 44.21)**.

Taken together with previous studies, the experiment described in Figure 44.21 demonstrated that a wide variety of genetic defects can disrupt ADH regulation of water balance in the body. Even in the absence of such genetic changes, certain substances can alter the regulation of osmolarity. For example, alcohol can disturb water balance by inhibiting ADH release, leading to excessive urinary water loss and dehydration (which may cause some of the symptoms of a hangover). Normally, blood osmolarity, ADH release, and water reabsorption in the kidney are all linked in a feedback loop that contributes to homeostasis.

The Renin-Angiotensin-Aldosterone System

A second regulatory mechanism that helps maintain homeostasis by acting on the kidney is the **renin-angiotensin-aldosterone system (RAAS)**. The RAAS involves the **juxtaglomerular apparatus (JGA)**, a specialized tissue consisting of cells of and around the afferent arteriole that supplies blood to the glomerulus **(Figure 44.22)**. When blood pressure or blood volume in the afferent arteriole drops (for instance, as a result of dehydration), the JGA releases the enzyme renin. Renin initiates a sequence of chemical reactions that cleave a plasma protein called angiotensinogen, ultimately yielding a peptide called **angiotensin II**.

Functioning as a hormone, angiotensin II raises blood pressure by constricting arterioles, which decreases blood flow to many capillaries, including those of the kidney. Angiotensin II also stimulates the adrenal glands to release a hormone called **aldosterone**. This hormone acts on the nephrons' distal tubules and collecting duct, making them reabsorb more Na^+ and water, thus increasing blood volume and pressure.

Because angiotensin II acts in several ways that increase blood pressure, drugs that block angiotensin II production are widely used to treat hypertension (chronic high blood pressure). Many of these drugs are specific inhibitors of angiotensin converting enzyme (ACE), which catalyzes the second step in the production of angiotensin II. As shown in Figure 44.21, renin released from the JGA acts on

▼ **Figure 44.21**

INQUIRY

Can aquaporin mutations cause diabetes insipidus?

EXPERIMENT Bernard van Oost and colleagues at the University of Nijmegen were studying a patient with diabetes insipidus but a normal ADH receptor gene. Sequencing of the patient's DNA revealed two different mutations, one in each copy of an aquaporin gene. To determine whether each mutation blocked channel formation, they studied the mutant proteins in a cell that could be manipulated and studied outside the body. The cell they chose was the frog oocyte, which can be collected in large numbers from an adult female and will express foreign genes. The researchers synthesized messenger RNA from clones of the wild-type and mutant aquaporin genes and injected the synthetic mRNA into oocytes. Within the oocytes, the cellular machinery translated the mRNA into aquaporin proteins. To determine if the mutant aquaporin proteins made functional water channels in the plasma membrane, the investigators transferred the oocytes from a 200-mOsm to a 10-mOsm solution. They then measured swelling by light microscopy and calculated the permeability of the oocytes to water.
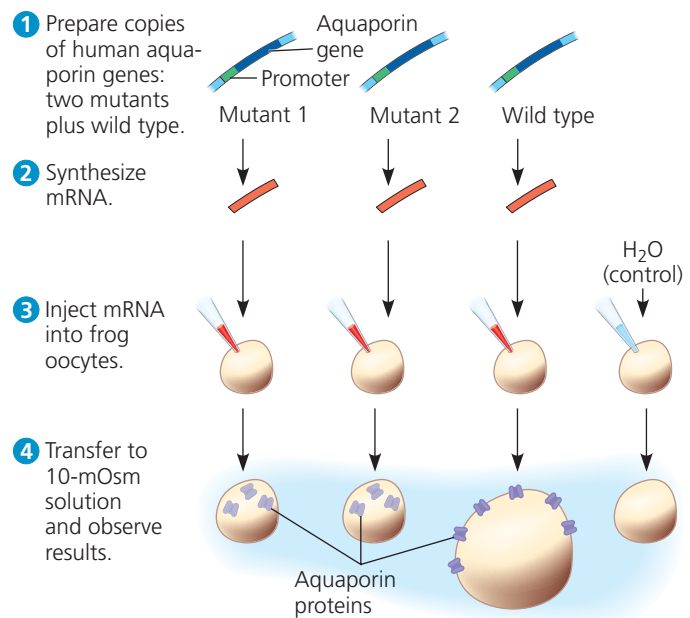

RESULTS

Injected RNA	Permeability (µm/sec)
Wild-type aquaporin	196
None	20
Aquaporin mutant 1	17
Aquaporin mutant 2	18

CONCLUSION Because each mutation inactivates aquaporin as a water channel, the patient's disorder can be attributed to these mutations.

SOURCE P. M. Deen, M. A. Verdijk, N. V. Knoers, B. Wieringa, L. A. Monnens, C. H. van Os, and B. A. van Oost, Requirement of human renal water channel aquaporin-2 for vasopressin-dependent concentration of urine, *Science* 264:92–95 (1994).

WHAT IF? If you measured ADH levels in patients with ADH receptor mutations and in patients with aquaporin mutations, what would you expect to find, compared with wild-type subjects?
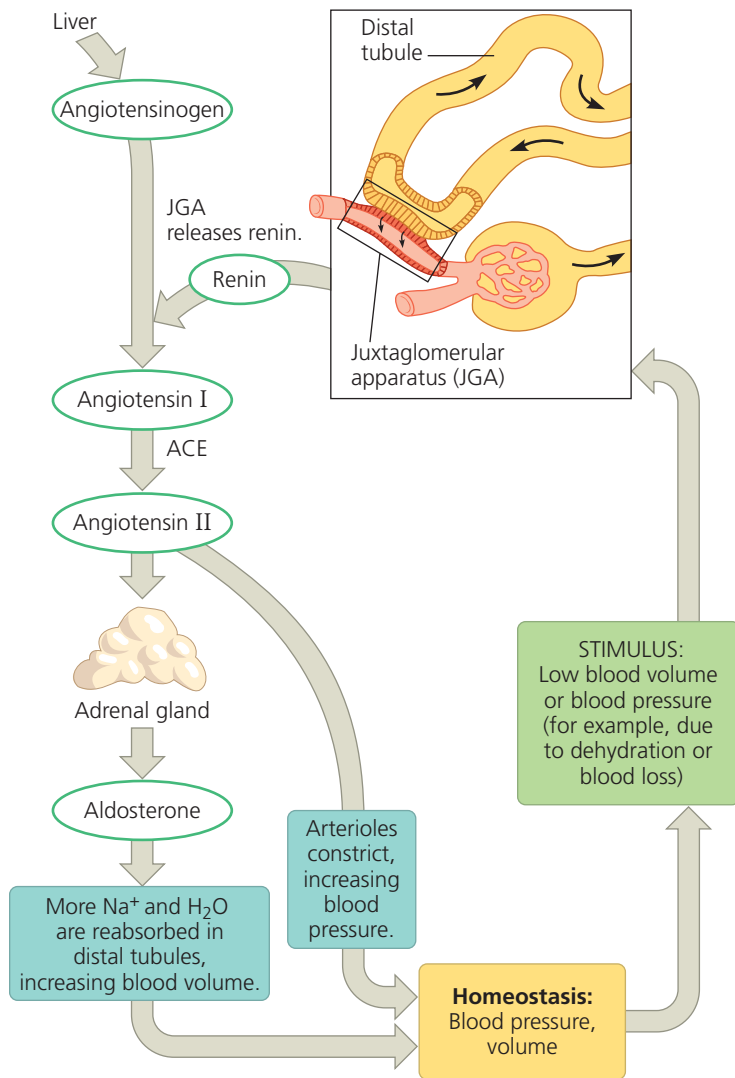
▲ **Figure 44.22 Regulation of blood volume and blood pressure by the renin-angiotensin-aldosterone system (RAAS).**

angiotensinogen (in the blood), forming angiotensin I. ACE in vascular endothelium, particularly in the lungs, then splits off two amino acids from angiotensin I, forming active angiotensin II. Blocking ACE activity with drugs prevents angiotensin II production and often lowers blood pressure into the normal range.

Homeostatic Regulation of the Kidney

The renin-angiotensin-aldosterone system operates as part of a complex feedback circuit that results in homeostasis. A drop in blood pressure and blood volume triggers renin release from the JGA. In turn, the rise in blood pressure and volume resulting from the various actions of angiotensin II and aldosterone reduces the release of renin.

The functions of ADH and the RAAS may seem to be redundant, but this is not the case. Both increase water reabsorption

in the kidney, but they counter different osmoregulatory problems. The release of ADH is a response to an increase in blood osmolarity, as when the body is dehydrated from excessive water loss or inadequate water intake. However, a situation that causes an excessive loss of both salt and body fluids—a major wound, for example, or severe diarrhea—will reduce blood volume *without* increasing osmolarity. This will not affect ADH release, but the RAAS will respond to the drop in blood volume and pressure by increasing water and Na^+ reabsorption. Thus, ADH and the RAAS are partners in homeostasis. ADH alone would lower blood Na^+ concentration by stimulating water reabsorption in the kidney, but the RAAS helps maintain the osmolarity of body fluids at the set point by stimulating Na^+ reabsorption.

Another hormone, **atrial natriuretic peptide (ANP)**, opposes the RAAS. The walls of the atria of the heart release ANP in response to an increase in blood volume and pressure. ANP inhibits the release of renin from the JGA, inhibits NaCl reabsorption by the collecting ducts, and reduces aldosterone release from the adrenal glands. These actions lower blood volume and pressure. Thus, ADH, the RAAS, and ANP provide an elaborate system of checks and balances that regulate the kidney's ability to control the osmolarity, salt concentration, volume, and pressure of blood. The precise regulatory role of ANP is an area of active research.

In all animals, certain of the intricate physiological machines we call organs work continuously in maintaining solute and water balance and excreting nitrogenous wastes. The details that we have reviewed in this chapter only hint at the great complexity of the neural and hormonal mechanisms involved in regulating these homeostatic processes.

CONCEPT CHECK 44.5

1. How does alcohol affect regulation of water balance in the body?
2. Why could it be dangerous to drink a very large amount of water in a short period of time?
3. **WHAT IF?** Conn's syndrome is a condition caused by tumors of the adrenal cortex that secrete high amounts of aldosterone in an unregulated manner. What would you expect to be the major symptom of this disorder?
4. **MAKE CONNECTIONS** Compare the activity of renin and ACE in the renin-angiotensin-aldosterone system with that of the protein kinases in a phosphorylation cascade, such as the one shown in Figure 11.10 (p. 215). How are the roles of these enzymes similar and different in the two regulated response pathways?
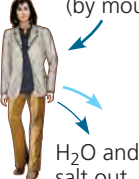
For suggested answers, see Appendix A.

SUMMARY OF KEY CONCEPTS

CONCEPT 44.1

Osmoregulation balances the uptake and loss of water and solutes (pp. 953–958)

- Cells balance water gain and loss through **osmoregulation**, a process based on the controlled movement of solutes between internal fluids and the external environment and on the movement of water, which follows by osmosis. **Osmoconformers** are isoosmotic with their marine environment and do not regulate their **osmolarity**. In contrast, **osmoregulators** control water uptake and loss in a hypoosmotic or hyperosmotic environment, respectively. Water-conserving excretory organs help terrestrial animals to avoid desiccation. Animals that live in temporary waters may be **anhydrobiotic** for one stage of life.

Animal	Inflow/Outflow	Urine
Freshwater fish. Lives in water less concentrated than body fluids; fish tends to gain water, lose salt	Does not drink water. Salt in (active transport by gills), H$_2$O in. Salt out	▶ Large volume of urine ▶ Urine is less concentrated than body fluids
Marine bony fish. Lives in water more concentrated than body fluids; fish tends to lose water, gain salt	Drinks water. Salt in, H$_2$O out. Salt out (active transport by gills)	▶ Small volume of urine ▶ Urine is slightly less concentrated than body fluids
Terrestrial vertebrate. Terrestrial environment; tends to lose body water to air	Drinks water. Salt in (by mouth). H$_2$O and salt out	▶ Moderate volume of urine ▶ Urine is more concentrated than body fluids

- **Transport epithelia** contain specialized epithelial cells that regulate the solute movements required for waste disposal and for tempering changes in body fluids.

> **?** *Under what environmental conditions does water move into a cell by osmosis?*

CONCEPT 44.2

An animal's nitrogenous wastes reflect its phylogeny and habitat (pp. 958–959)

- Protein and nucleic acid metabolism generates **ammonia**. Most aquatic animals excrete ammonia. Mammals and most adult amphibians convert ammonia to the less toxic **urea**, which is excreted with a minimal loss of water. Insects and many reptiles, including birds, convert ammonia to **uric acid**, a mostly insoluble waste excreted in a paste-like urine.
- The kind of nitrogenous waste excreted depends on an animal's evolutionary history and habitat. The amount of nitrogenous waste produced is coupled to the animal's energy budget and amount of dietary protein.

> **DRAW IT** *Construct a table summarizing the three major types of nitrogenous wastes and their relative toxicity, energy content, and associated water loss during excretion.*

CONCEPT 44.3

Diverse excretory systems are variations on a tubular theme (pp. 960–963)

- Most excretory systems carry out **filtration**, **reabsorption**, **secretion**, and **excretion**. The **protonephridia** of the flatworm flame bulb excrete a dilute **filtrate**. An earthworm has pairs of open-ended **metanephridia** in each segment that produce urine. In insects, **Malpighian tubules** function in osmoregulation and removal of nitrogenous wastes. **Kidneys** function in both excretion and osmoregulation in vertebrates.
- Excretory tubules (consisting of **nephrons** and **collecting ducts**) and blood vessels pack the mammalian kidney. Blood pressure forces fluid from blood in the **glomerulus** into the lumen of **Bowman's capsule**. Following reabsorption and secretion, filtrate flows into a collecting duct. The **ureter** conveys urine from the **renal pelvis** to the **urinary bladder**.

> **?** *Given that a typical excretory system selectively absorbs and secretes materials, what function does filtration serve?*

CONCEPT 44.4

The nephron is organized for stepwise processing of blood filtrate (pp. 963–968)

- Within the nephron, selective secretion and reabsorption in the **proximal tubule** alter filtrate volume and composition. The *descending limb* of the **loop of Henle** is permeable to water but not salt; water moves by osmosis into the interstitial fluid. The *ascending limb* is permeable to salt but not water; as the filtrate ascends, salt leaves by diffusion and by active transport. The **distal tubule** and collecting duct regulate K$^+$ and NaCl levels in body fluids. The collecting duct can respond to hormonal signals to reabsorb more water.
- In a mammalian kidney, a **countercurrent multiplier system** involving the loop of Henle maintains the gradient of salt concentration in the kidney interior. In response to hormonal signals, urine can be concentrated in the collecting duct. Urea, which leaves the collecting duct within the inner medulla, contributes to the osmotic gradient of the kidney.
- Natural selection has shaped the form and function of nephrons in various vertebrates to the osmoregulatory challenges of the animals' habitats. For example, desert mammals, which excrete

the most hyperosmotic urine, have loops of Henle that extend deep into the **renal medulla**, whereas mammals in moist habitats have shorter loops and excrete more dilute urine.

? *How do cortical and juxtamedullary nephrons differ with respect to reabsorbing nutrients and concentrating urine?*

CONCEPT 44.5

Hormonal circuits link kidney function, water balance, and blood pressure (pp. 968–971)

• The posterior pituitary gland releases **antidiuretic hormone (ADH)** when blood osmolarity rises above a set point, such as when water intake is inadequate. ADH increases permeability to water in collecting ducts through an increase in the number of epithelial water channels. When blood pressure or blood volume in the afferent arteriole drops, the **juxtaglomerular apparatus (JGA)** releases renin. **Angiotensin II** formed in response to **renin** constricts arterioles and triggers release of the hormone **aldosterone**, raising blood pressure and reducing the release of renin. This **renin-angiotensin-aldosterone system (RAAS)** has functions that overlap with those of ADH and are opposed by **atrial natriuretic peptide (ANP)**.

? *Why can only some patients with diabetes insipidus be treated effectively with ADH?*

TEST YOUR UNDERSTANDING

LEVEL 1: KNOWLEDGE/COMPREHENSION

1. *Unlike* an earthworm's metanephridia, a mammalian nephron
   a. is intimately associated with a capillary network.
   b. forms urine by changing fluid composition inside a tubule.
   c. functions in both osmoregulation and excretion.
   d. receives filtrate from blood instead of coelomic fluid.
   e. has a transport epithelium.

2. Which process in the nephron is *least* selective?
   a. filtration
   b. reabsorption
   c. active transport
   d. secretion
   e. salt pumping by the loop of Henle

3. Which of the following animals generally has the lowest volume of urine production?
   a. a vampire bat
   b. a salmon in fresh water
   c. a marine bony fish
   d. a freshwater bony fish
   e. a shark inhabiting freshwater Lake Nicaragua

LEVEL 2: APPLICATION/ANALYSIS

4. The high osmolarity of the renal medulla is maintained by all of the following *except*
   a. diffusion of salt from the thin segment of the ascending limb of the loop of Henle.
   b. active transport of salt from the upper region of the ascending limb.
   c. the spatial arrangement of juxtamedullary nephrons.
   d. diffusion of urea from the collecting duct.
   e. diffusion of salt from the descending limb of the loop of Henle.

5. Natural selection should favor the highest proportion of juxtamedullary nephrons in which of the following species?
   a. a river otter
   b. a mouse species living in a tropical rain forest
   c. a mouse species living in a temperate broadleaf forest
   d. a mouse species living in a desert
   e. a beaver

6. African lungfish, which are often found in small stagnant pools of fresh water, produce urea as a nitrogenous waste. What is the advantage of this adaptation?
   a. Urea takes less energy to synthesize than ammonia.
   b. Small stagnant pools do not provide enough water to dilute the toxic ammonia.
   c. The highly toxic urea makes the pool uninhabitable to potential competitors.
   d. Urea forms an insoluble precipitate.
   e. Urea makes lungfish tissue hypoosmotic to the pool.

LEVEL 3: SYNTHESIS/EVALUATION

7. **DRAW IT** Using Figure 44.3 as an example, sketch the exchange of salt (NaCl) and water between a shark and its marine environment.

8. **EVOLUTION CONNECTION**
   Merriam's kangaroo rats (*Dipodomys merriami*) live in North American habitats ranging from moist, cool woodlands to hot deserts. Assuming that natural selection has resulted in differences in water conservation between *D. merriami* populations, propose a hypothesis concerning the relative rates of evaporative water loss by populations that live in moist versus dry environments. Using a humidity sensor to detect evaporative water loss by kangaroo rats, how could you test your hypothesis?

9. **SCIENTIFIC INQUIRY**
   You are exploring kidney function in kangaroo rats. You measure urine volume and osmolarity, as well as the amount of chloride (Cl^-) and urea in the urine. If the water source provided to the animals were switched from tap water to a 2% NaCl solution, what change in urine osmolarity would you expect? How would you determine if this change was more likely due to a change in the excretion of Cl^- or urea?

10. **WRITE ABOUT A THEME**
    Structure and Function In a short essay (100–150 words), compare how membrane structures in the loop of Henle and collecting duct of the mammalian kidney enable water to be recovered from filtrate in the process of osmoregulation.

For selected answers, see Appendix A.

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1. MasteringBiology® Assignments

Make Connections Tutorial Kidney Function (Chapter 44) and Passive and Active Transport (Chapter 7)
Tutorial Kidney Structure and Function
Activities Structure of the Human Excretory System • The Mammalian Kidney • Nephron Function • Control of Water Reabsorption
Questions Student Misconceptions • Reading Quiz • Multiple Choice • End-of-Chapter

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