Chapter 44

Osmoregulation and Excretion

Lecture Outline

Overview: A Balancing Act

- The wandering albatross, *Diomedea exulans,* remains at sea all year long, drinking only seawater.
- **Homeostasis** requires osmoregulation, the general process by which animals control solute concentrations and balance water gain and loss.
- The physiological systems of animals operate within a fluid environment.
  - The relative concentrations of water and solutes must be maintained within narrow limits, despite variations in the animal's external environment.
  - Ions such as sodium and calcium must be maintained at concentrations that permit normal activity of muscles and neurons.
- Desert and marine animals face the possibility of dehydration and must conserve water.
- Freshwater animals are threatened with dilution of body fluids and must conserve solutes and absorb salts.
- Metabolism also creates the problem of disposing of hazardous metabolites from the breakdown of proteins and nucleic acids.
  - The breakdown of *nitrogenous* molecules releases ammonia, a very toxic compound.
- Several different strategies have evolved for **excretion**, the removal of nitrogen-containing waste products of metabolism.

Concept 44.1 Osmoregulation balances the uptake and loss of water and solutes.

- All animals face the same central problem of osmoregulation: Over time, the rates of water uptake and loss must balance.
  - Animal cells—which lack cell walls—swell and burst if there is a continuous net uptake of water, or shrivel and die if there is a substantial net loss of water.
- Water enters and leaves cells by osmosis, the movement of water across a selectively permeable membrane.
- Osmosis occurs whenever two solutions separated by a membrane differ in osmotic pressure, or **osmolarity** (moles of solute per liter of solution).
  - The unit of measurement of osmolarity is milliOsmoles per liter (mOsm/L).
  - The osmolarity of human blood is about 300 mOsm/L; seawater has an osmolarity of about 1,000 mOsm/L.

- If two solutions separated by a selectively permeable membrane have the same osmolarity, they are said to be *isoosmotic.*
  - There is no *net* movement of water by osmosis between isoosmotic solutions because water molecules cross the membrane at equal rates in both directions.
- When two solutions differ in osmolarity, the one with the higher concentration of solutes is referred to as *hyperosmotic*, and the more dilute solution is *hypoosmotic*.
  - Water flows by osmosis from a hypoosmotic solution to a hyperosmotic one.
- There are two basic solutions to the problem of balancing water gain and water loss.
- One solution—available only to marine animals—is to be isoosmotic to the surroundings as an **osmoconformer**.
  - Although they do not compensate for changes in external osmolarity, osmoconformers live in water that has a stable composition and they have a constant internal osmolarity.
- The second solution is to be an **osmoregulator,** an animal that expends energy to control its internal osmolarity because its body fluids are not isoosmotic with the outside environment.
- Osmoregulation enables animals to live in environments that are uninhabitable to osmoconformers, such as freshwater and terrestrial habitats.
  - It also enables many marine animals to maintain internal osmolarities different from that of seawater.
  - An osmoregulator must discharge excess water if it lives in a hypoosmotic environment or take in water to offset osmotic loss if it inhabits a hyperosmotic environment.
- Most animals, whether osmoconformers or osmoregulators, cannot tolerate substantial changes in external osmolarity and are said to be *stenohaline*.
- In contrast, *euryhaline* animals—which include some osmoregulators as well as osmoconformers—can survive large fluctuations in external osmolarity.
- Euryhaline osmoconformers include many barnacles and mussels, which are covered and uncovered by ocean tides.
  - Familiar euryhaline osmoregulators include striped bass and various species of salmon.
- Most marine invertebrates are osmoconformers.
  - Their osmolarity is the same as that of seawater.
- However, their concentrations of *specific* solutes differ considerably from those of seawater.
  - Thus, even an animal that conforms to the osmolarity of its surroundings does regulate its internal composition, actively transporting solutes to maintain homeostasis.
  - For example, although the concentration of magnesium ions (Mg^{2+}) in seawater is 50 *mM,* homeostatic mechanisms in the Atlantic lobster (*Homarus americanus*) result in a Mg^{2+}concentration of less than 9 *mM* in the hemolymph (circulatory fluid).
- Marine vertebrates and some marine invertebrates are osmoregulators.
  - For most of these animals, the ocean is a strongly dehydrating environment because it is much saltier than internal fluids, and water is lost from their bodies by osmosis.
- Marine bony fishes, such as cod, are hypoosmotic to seawater. They constantly lose water by osmosis and gain salt by diffusion and from the food they eat.
  - The fishes balance water loss by drinking seawater.
  - Specialized *chloride cells* in the gills actively transport chloride ions out, with sodium ions following passively.

- In the kidneys, excess calcium, magnesium, and sulfate ions are excreted with little loss of water.

- Marine sharks and most other chondrichthyans use a distinct osmoregulatory strategy.
  - Like bony fishes, sharks have an internal salt concentration lower than that of seawater.
  - Salts diffuse into the body from seawater, especially across the gills.
- Unlike bony fishes, marine sharks do not experience a continuous osmotic loss because high concentrations of urea and trimethylamine oxide (TMAO) in body fluids lead to an osmolarity slightly higher than that of seawater.
  - Consequently, water slowly *enters* the shark's body by osmosis and in food, and is removed in urine.
  - The urine also removes some of the salt that diffuses into the shark's body. The rest is lost in feces or excreted.
- In contrast to marine organisms, freshwater animals are constantly gaining water by osmosis and losing salts by diffusion.
  - This happens because the osmolarity of their internal fluids is much higher than that of their surroundings.
  - Many freshwater animals, including fish such as perch, maintain water balance by drinking no water and excreting large amounts of very dilute urine.
  - Salts are replenished in food and by active uptake of salts across the gills.
- Salmon and other euryhaline fishes that migrate between fresh water and seawater undergo dramatic and rapid changes in their osmoregulatory status.
  - When living in fresh water, salmon cease drinking and begin to produce lots of dilute urine, and their gills start taking up salt from the dilute environment—the same as fishes that spend their entire lives in fresh water.
  - While they migrate to the ocean, salmon undergo acclimatization.
  - They produce the steroid hormone cortisol, which increases the number and size of salt-secreting chloride cells. They excrete excess salt from their gills and produce very small amounts of urine—just like fishes that spend their entire lives in saltwater.
- Extreme dehydration or *desiccation* dooms most animals, but some aquatic invertebrates living in temporary ponds and films of water around soil particles can lose almost all their body water when their habitats dry up, surviving in a dormant state, called **anhydrobiosis**.
  - For example, tardigrades, or water bears, contain about 85% of their weight in water when hydrated but can dehydrate to less than 2% water and survive in an inactive state for a decade until revived by water.
- Anhydrobiotic animals require adaptations that keep their cell membranes intact.
- Although the mechanism that tardigrades use is still under investigation, researchers do know that anhydrobiotic nematodes contain large amounts of sugars, especially the disaccharide trehalose.
  - Trehalose protects cells by replacing water associated with membrane lipids and proteins.
  - Many insects that survive freezing in the winter also use trehalose as a membrane protectant.
- The threat of desiccation is perhaps the largest regulatory problem confronting terrestrial plants and animals.
  - Humans die if they lose about 12% of their body water, while camels can withstand twice that level of dehydration.

- Adaptations that reduce water loss are key to survival on land.
    - Most terrestrial animals have body coverings that help prevent dehydration.
    - Other adaptations include waxy layers in insect exoskeletons, the shells of land snails, and the multiple layers of dead, keratinized skin cells of most terrestrial vertebrates.
    - Being nocturnal also reduces evaporative water loss.
- Despite these adaptations, most terrestrial animals lose considerable water from surfaces of their gas exchange organs, in urine and feces, and across the skin.
    - Land animals balance their water budgets by drinking and eating moist foods and by using metabolic water produced through aerobic respiration.
- Some animals are so well adapted for minimizing water loss that they can survive in deserts without drinking.
    - For example, kangaroo rats lose so little water that they can recover 90% of the loss from metabolic water and gain the remaining 10% in their diet of seeds.
- Whenever animals maintain an osmolarity difference between the body and the external environment, osmoregulation has an energy cost.
    - Because diffusion tends to equalize concentrations in a system, osmoregulators must expend energy to maintain the osmotic gradients via active transport.
- The energy costs depend mainly 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 membrane transport work is required to pump solutes.
    - Osmoregulation accounts for nearly 5% of the resting metabolic rate of many marine and freshwater bony fishes.
    - Brine shrimp live in extremely salty lakes, with a very large gradient between internal and external osmolarity. The cost of osmoregulation is up to 30% of their resting metabolic rate.
- The energy cost to an animal of maintaining water and salt balance is minimized by a body fluid composition adapted to the salinity of the animal’s habitat.
- The body fluids of most freshwater animals have lower solute concentrations than their marine relatives.
    - For instance, whereas marine molluscs have body fluids with a solute concentration of approximately 1,000 mOsm/L, some freshwater mussels maintain the solute concentration of their body fluids at 40 mOsm/L.
- The ultimate function of osmoregulation is to control solute concentrations in cells, but most animals do this by managing the solute content of an internal body fluid that bathes the cells.
    - In animals with an open circulatory system, this fluid is hemolymph.
    - In vertebrates and other animals with a closed circulatory system, the cells are bathed in an interstitial fluid that is controlled through the composition of the blood.
- The maintenance of fluid composition depends on structures ranging from individual cells that regulate solute movement to complex organs such as the vertebrate kidney.
- In most animals, osmotic regulation and metabolic waste disposal rely on **transport epithelia** to move specific solutes in controlled amounts in specific directions.
    - In most animals, transport epithelia are arranged into complex tubular networks with extensive surface area.

- Some transport epithelia directly face the outside environment, while others line channels connected to the outside by an opening on the body surface.

- The salt-secreting nasal glands of some marine birds, such as the albatross, secrete an excretory fluid that is much more salty than the ocean.
  - The countercurrent system in these glands removes salt from the blood, allowing the birds to drink seawater during their months at sea.
- Transport epithelia in excretory organs often have the dual functions of maintaining water balance and disposing of metabolic wastes.

Concept 44.2 An animal's nitrogenous wastes reflect its phylogeny and habitat.

- Because most metabolic wastes must be dissolved in water when they are removed from the body, the type and quantity of waste products may have a large impact on water balance.
- The nitrogenous breakdown products of proteins and nucleic acids are among the most important wastes in terms of their effect on osmoregulation.
- During their breakdown, enzymes remove nitrogen in the form of **ammonia** (NH_3), a small and very toxic molecule.
  - Some animals excrete ammonia directly, but many species first convert ammonia to other compounds that are less toxic but more costly to produce.

Animals excrete nitrogenous wastes in different forms that vary in toxicity and energy cost.

- Animals that excrete nitrogenous wastes as ammonia need access to lots of water, so ammonia excretion is most common in aquatic species.
  - This is because ammonia is very soluble and can be tolerated at only very low concentrations.
  - Many invertebrates release ammonia across the whole body surface.
  - In fishes, most of the ammonia is lost as ammonium ions (NH_4^+) at the gill epithelium.
- Ammonia excretion is much less suitable for land animals.
  - Because ammonia is so toxic, it can be transported and excreted only in large volumes of very dilute solutions.
  - Most terrestrial animals and many marine organisms (which tend to lose water to their environment by osmosis) do not have access to sufficient water for ammonia excretion.
- Instead, mammals, most adult amphibians, sharks, and some marine bony fishes and turtles excrete mainly **urea**.
  - Urea is synthesized in the liver by combining ammonia with carbon dioxide and is excreted by the kidneys.
- The main advantage of urea is its low toxicity, so it can be transported in the circulatory system and stored safely at high concentrations.
  - Urea's low toxicity reduces the amount of water needed for nitrogen excretion when a concentrated solution of urea rather than a dilute solution of ammonia is released.
- The main disadvantage of urea is that animals must expend energy to produce it from ammonia.
- Many amphibians excrete mainly ammonia (saving energy) when they are aquatic tadpoles, and then switch to urea (reducing excretory water loss) as land-dwelling adults.

- Land snails, insects, birds, and many reptiles excrete **uric acid** as the main nitrogenous waste.
  - Bird droppings, or *guano*, are a mixture of white uric acid and brown feces.
- Like urea, uric acid is relatively nontoxic.
- Unlike either ammonia or urea, however, uric acid is largely insoluble in water and can be excreted as a semisolid paste with very little water loss.
- While saving more water than urea, uric acid is more energetically expensive to produce.
- Many animals produce a small amount of uric acid as a product of purine breakdown.
  - A genetic defect in purine metabolism predisposes Dalmatian dogs to form uric acid stones in the bladder.
  - Humans may develop *gout*, a painful inflammation of the joints caused by deposits of uric acid crystals.
  - Meals containing purine-rich animal tissues can increase the severity of the inflammation.
  - Some dinosaurs appear to have been similarly affected by consuming meat: Fossilized bones of the carnivore *Tyrannosaurus rex* exhibit joint damage characteristic of gout.
- Uric acid and urea represent different adaptations for excreting nitrogenous wastes with minimal water loss.
- Mode of reproduction appears to have been important in determining the type of nitrogenous wastes an animal excretes.
  - Soluble wastes can diffuse out of a shell-less amphibian egg or be carried away by the mother's blood in a mammalian embryo.
  - However, the shelled eggs of birds and reptiles are not permeable to liquids, which means that soluble nitrogenous wastes trapped within the egg could accumulate to dangerous levels.
  - Even urea is toxic at very high concentrations.
  - Uric acid precipitates out of solution and can be stored within the egg as a harmless solid left behind when the animal hatches.
- The type of nitrogenous waste reflects habitat as well as evolutionary lineage.
  - For example, terrestrial turtles (which often live in dry areas) excrete mainly uric acid, whereas aquatic turtles excrete both urea and ammonia.
- The amount of nitrogenous waste produced is coupled to the energy budget and depends on how much and what kind of food an animal eats.
  - Because they use energy at high rates, endotherms eat more food—and thus produce more nitrogenous wastes—per unit volume than ectotherms.
  - Carnivores (which derive much of their energy from dietary proteins) excrete more nitrogen than animals that obtain most of their energy from lipids or carbohydrates.

Concept 44.3 Diverse excretory systems are variations on a tubular theme.

- Although the problems of water balance on land or in salt water or fresh water are very different, the solutions all depend on the regulation of solute movements between internal fluids and the external environment.

- Much of this regulation is handled by excretory systems, which are central to homeostasis because they dispose of metabolic wastes and control body fluid composition by adjusting the rates of loss of particular solutes.

Most excretory systems produce urine by refining a filtrate derived from body fluids.

- Although excretory systems are diverse, nearly all produce urine in a process that involves several steps.
- First, body fluid (blood, coelomic fluid, or hemolymph) is collected.
- The initial fluid collection usually involves **filtration**, driven by hydrostatic pressure, through selectively permeable membranes consisting of a single layer of transport epithelium, driven by hydrostatic pressure.
- Water and small solutes, such as salts, sugars, amino acids, and nitrogenous wastes, form a solution called the **filtrate**.
- It is important to recover useful molecules from the filtrate and return them to the body fluids.
- Excretory systems specifically transport materials into or out of the filtrate in a process of selective **reabsorption**.
  - Valuable solutes—including glucose, certain salts, vitamins, hormones, and amino acids—are reabsorbed by active transport in excretory systems.
- Nonessential solutes and wastes are left in the filtrate or added to it by selective **secretion**, which also uses active transport.
  - The pumping of various solutes also adjusts the osmotic movement of water into or out of the filtrate.
- The processed filtrate containing nitrogenous wastes is excreted as urine.

The systems that perform basic excretory functions vary widely among animal groups.

- In all animals, excretory systems are built of a complex network of tubules that provide a large surface area for the exchange of water and solutes, including nitrogenous wastes.
- Flatworms have an excretory system called **protonephridia**, consisting of a branching network of dead-end tubules connected to external openings.
  - The openings are capped by a *flame bulb* with a tuft of cilia that draws water and solutes from the interstitial fluid, through the flame bulb, and into the tubule system.
- The urine in the tubules exits through openings into the external environment.
  - The excreted urine of freshwater flatworms is very dilute, helping to balance the osmotic uptake of water from the environment.
- Protonephridia are found in rotifers, some annelids, larval molluscs, and lancelets.
- In freshwater flatworms, the major function of the flame-bulb system is osmoregulation, whereas most metabolic wastes diffuse across the body surface or are excreted into the gastrovascular cavity.
- In some parasitic flatworms, however, protonephridia do dispose of nitrogenous wastes.
- **Metanephridia**, a tubular excretory system found in most annelids, consist of internal openings that collect body fluids from the coelom through a ciliated funnel.
  - Beating of the cilia draws fluid into a coiled collecting tubule, which includes a storage bladder that opens to the outside.
- An earthworm's metanephridia 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 dumped outside.
- Because earthworms experience a net uptake of water from damp soil, their metanephridia balance water influx by producing dilute urine.

- Insects and other terrestrial arthropods have organs called **Malpighian tubules** that remove nitrogenous wastes and also function in osmoregulation.
  - The tubules open into the digestive system and dead-end at tips that are immersed in the hemolymph.
  - The filtration step common to other excretory systems is absent.
- The transport epithelium lining 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, where most of the solutes are pumped back into the hemolymph.
  - Water again follows the solutes, and the nitrogenous wastes, primarily insoluble uric acid, are eliminated along with the feces.
- This system is highly effective in conserving water and is one of several key adaptations contributing to the tremendous success of insects on land.
- Some terrestrial insects have an additional adaptation for water balance: the rectal end of their gut enables water uptake from the air.
- The kidneys of vertebrates usually function in both osmoregulation and excretion.
- Like the excretory organs of most animal phyla, kidneys are built of tubules.
- The vertebrate excretory system includes a dense network of capillaries intimately associated with the tubules, along with ducts and other structures that carry urine out of the tubules and kidney and eventually out of the body.
- The kidneys of vertebrates are nonsegmented.
  - However, hagfishes, chordates that lack vertebrae, have kidneys with segmentally arranged excretory tubules.
  - This suggests that the excretory segments of vertebrate ancestors were segmented.

We'll take a closer look at the mammalian excretory system.

- Mammals have a pair of bean-shaped kidneys.
- Each kidney is supplied with blood by a **renal artery** and drained by a **renal vein**.
  - In humans, the kidneys account for less than 1% of body weight, but they receive about 25% of the blood exiting the heart.
- Urine exits each kidney through a duct called the **ureter,** and both ureters drain into a common **urinary bladder.**
- During urination, urine is expelled from the urinary bladder through a tube called the **urethra**, which empties to the outside near the vagina in females or through the penis in males.
  - Sphincter muscles near the junction of the urethra and the bladder control urination.
- The mammalian kidney has two distinct regions: an outer **renal cortex** and an inner **renal medulla.**

- Both regions are packed with microscopic excretory tubules, nephrons, and their associated blood vessels.
- Each **nephron** consists of a single long tubule and a ball of capillaries, called the **glomerulus**.
- The blind end of the tubule forms a cup-shaped swelling, called **Bowman's capsule**, that surrounds the glomerulus.
    - Each human kidney contains about a million nephrons, with a total tubule length of 80 km.
- Filtration occurs as blood pressure forces fluid from the blood in the glomerulus into the lumen of Bowman's capsule.
    - The porous capillaries, along with specialized capsule cells, are permeable to water and small solutes but not to blood cells or large molecules such as plasma proteins.
    - The filtrate in Bowman's capsule contains salt, glucose, amino acids, vitamins, nitrogenous wastes such as urea, and other small molecules.
    - Because filtration of small molecules is nonselective, the mixture mirrors the relative concentrations of solutes in blood plasma.
- From Bowman's capsule, the filtrate passes through three 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.**
- The distal tubule empties into a **collecting duct**, which receives processed filtrate from many nephrons.
- The many collecting ducts empty into the **renal pelvis**, which is drained by the ureter.
- In the human kidney, about 85% of the nephrons, the **cortical nephrons**, have reduced loops of Henle and are almost entirely confined to the renal cortex.
- The other 15%, the **juxtamedullary nephrons**, have well-developed loops that extend deeply into the renal medulla.
    - It is the juxtamedullary nephrons that enable mammals to produce urine that is hyperosmotic to body fluids, conserving water.
- The nephron and the collecting duct are lined by a transport epithelium that processes the filtrate to form the urine. Their most important task is to reabsorb solutes and water.
    - The nephrons and collecting ducts reabsorb nearly all of the sugar, vitamins, and other organic nutrients from the initial filtrate and about 99% of the water.
    - This reabsorption reduces 180 L of initial filtrate to about 1.5 L of urine to be voided.
- Each nephron is supplied with blood by an **afferent arteriole**, a branch of the renal artery that subdivides into the capillaries of the glomerulus.
- The capillaries converge as they leave the glomerulus, forming an **efferent arteriole.**
    - This vessel subdivides again into the **peritubular capillaries**, which surround the proximal and distal tubules.
    - Additional capillaries extend downward to form the **vasa recta**, a loop of capillaries that serves the loop of Henle.
- The tubules and capillaries are immersed in interstitial fluid, through which substances diffuse.

- Although the excretory tubules and their surrounding capillaries are closely associated, they do not exchange materials directly.
- The tubules and capillaries are immersed in interstitial fluid, through which various materials diffuse between the plasma in the capillaries and the filtrate within the nephron tubule.
- The vasa recta and the loop of Henle function together as part of a countercurrent system that enhances nephron efficiency.

Concept 44.4 The nephron is organized for stepwise processing of blood filtrate.

- 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 filtrate mirror those in blood plasma.
- As the filtrate moves through the nephron and collecting duct, each region contributes to the stepwise processing of filtrate into urine.

1. ***One of the most important functions of the proximal tubule is the reabsorption of ions, water, and valuable nutrients from the initial filtrate volume.***

- NaCl (salt) in the filtrate diffuses into the cells of the transport epithelium.
- The epithelial cells actively transport Na^+ into the interstitial fluid.
    - This transfer of positive charge drives the passive transport of Cl^- out of the tubule, as well as the movement of more Na^+ from the lumen into the tubule by facilitated diffusion and cotransport mechanisms.
- As salt moves from the filtrate to the interstitial fluid, water follows by osmosis.
- Salt and water diffuse into the peritubular capillaries.
- Glucose, amino acids, potassium ions, and other essential molecules are also actively or passively transported from the filtrate to the interstitial fluid, and then move 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^+ in the form of ammonium ions (NH_4^+).
    - The more acidic the filtrate, the more ammonia the cells secrete.
    - The proximal tubules also reabsorb about 90% of the buffer bicarbonate (HCO_3^-) from the filtrate.
- As the filtrate passes through the proximal tubule, materials to be excreted become concentrated.
    - Waste products such as urea remain in the filtrate, while water and salts leave.
- Some toxic materials are actively secreted into the filtrate from surrounding tissues.
    - Drugs that have been processed in the liver pass from the peritubular capillaries and into the interstitial fluid, where they are actively secreted into the lumen of the proximal tubule.

2. Reabsorption of water continues as the filtrate moves into the descending limb of the loop of Henle.

- The transport epithelium in the descending limb is freely permeable to water with water channels formed by the protein **aquaporin**, but it is not very permeable to salt and other small solutes.
  - For water to move out of the tubule by osmosis, the interstitial fluid bathing the tubule must be hyperosmotic to the filtrate.
- Because the osmolarity of the interstitial fluid becomes progressively greater from the outer cortex to the inner medulla, the filtrate moving within the descending loop of Henle continues to lose water.

3. In contrast to the descending limb, the transport epithelium of the ascending limb of the loop of Henle is permeable to salt, not water.

- Rare in biological membranes, the membrane in the ascending limb is impermeable to water.
  - Unlike the descending limb, the ascending limb has a transport epithelium studded with ion channels, but not water channels.
- 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 the thin segment of the ascending limb, NaCl diffuses out of the permeable tubule into the interstitial fluid, increasing the osmolarity of the medulla.
  - The active transport of salt from the filtrate into the interstitial fluid takes place in the thick segment of the ascending limb.
- By losing salt without giving up water, the filtrate becomes progressively more dilute as it moves up to the cortex in the ascending limb of the loop.

4. The distal tubule plays a key role in regulating the K^+ and NaCl concentrations of body fluids.

- This regulation involves variation in the amount of K^+ that is secreted into the filtrate and the amount of NaCl that is reabsorbed from the filtrate.
  - Like the proximal tubule, the distal tubule also contributes to pH regulation by the controlled secretion of H^+ and the reabsorption of bicarbonate (HCO_3^-).

5. 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, a volume about 300 times the total volume of blood in the body.
  - From this 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, while 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 as it loses 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.
- To produce dilute rather than concentrated urine, the kidney actively reabsorbs salts without allowing water to follow by osmosis.
    - Aquaporin molecules are removed from the epithelium, and NaCl is actively transported out of the filtrate.
- The collecting duct epithelium is controlled by hormones that maintain homeostasis for osmolarity, blood pressure, and blood volume.

The mammalian kidney's ability to conserve water is a key terrestrial adaptation.

- The osmolarity of human blood is about 300 mOsm/L, but the kidney can excrete urine up to four times as concentrated—about 1,200 mOsm/L.
    - At an extreme of water conservation, Australian hopping mice, which live in desert regions, can produce urine concentrated to 9,300 mOsm/L—25 times as concentrated as their body fluid.
- In a mammalian kidney, the maintenance of osmotic differences and the production of hyperosmotic urine are possible only because considerable energy is expended by the active transport of solutes against concentration gradients.
    - The nephrons—especially the loops of Henle—can be thought of tiny energy-consuming machines whose function is to produce a region of high osmolarity in the kidney, which can then extract water from the urine 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 juxtamedullary nephrons, which maintain an osmotic gradient in the kidney and use that gradient to excrete hyperosmotic urine, are the key to understanding the physiology of the mammalian kidney as a water-conserving organ.
    - Filtrate passing from Bowman's capsule to the proximal tubule has an osmolarity of about 300 mOsm/L.
    - As the filtrate flows through the proximal tubule in the renal cortex, large amounts of water *and* salt are reabsorbed.
    - The volume of the filtrate decreases substantially, but its osmolarity remains about the same.
- As the filtrate flows from the cortex to the medulla in the descending limb of the loop of Henle, water leaves the tubule by osmosis.
    - The osmolarity of the filtrate increases as solutes, including NaCl, become more concentrated.
    - The highest molarity (about 1,200 mOsm/L) occurs at the elbow of the loop of Henle.

- This increased osmolarity 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.
- Thus, the two limbs of the loop of Henle cooperate in generating the gradient of osmolarity in the interstitial fluid of the kidney.
- The loop of Henle has several qualities common to a countercurrent system.
  - 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.
- The vasa recta is also a countercurrent system, with descending and ascending vessels carrying 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 diffuses into it.
  - These fluxes are reversed as blood flows back toward the cortex in the ascending vessel.
  - Thus, the vasa recta can supply the kidney with nutrients and other important substances without interfering with the osmolarity gradient necessary to excrete a hyperosmotic urine.
- The countercurrent-like characteristics of the loop of Henle and the vasa recta maintain the steep osmotic gradient between the medulla and the cortex.
  - This gradient is initially created by the active transport of NaCl out of the thick segment of the ascending limb of the loop of Henle into the interstitial fluid.
- This active transport and other active transport systems in the kidney consume considerable ATP, requiring the kidney to have one of the highest relative metabolic rates of any organ.
- By the time the filtrate reaches the distal tubule, it is actually hypoosmotic to body fluids because of active transport of NaCl out of the thick segment of the ascending limb.
- As the filtrate descends again toward the medulla in the collecting duct, water is extracted by osmosis into the hyperosmotic interstitial fluids, but salts cannot diffuse in because the epithelium is impermeable to salt.
- This process concentrates salt, urea, and other solutes in the filtrate.
  - Some urea leaks out of the lower portion of the collecting duct, contributing to the high interstitial osmolarity of the inner medulla.
- Before leaving the kidney, the urine may reach the osmolarity of the interstitial fluid in the inner medulla, which can be as high as 1,200 mOsm/L.
  - 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 secreted from the body with minimal water loss.

Diverse adaptations of the vertebrate kidney have evolved in different environments.

- The juxtamedullary nephron is a key adaptation to terrestrial life, enabling mammals to get rid of salts and nitrogenous wastes without squandering water.
- The remarkable ability of the mammalian kidney to produce hyperosmotic urine is completely dependent on the precise arrangement of the tubules and collecting ducts in the renal cortex and medulla.
  - The kidney is one of the clearest examples of how the function of an organ is inseparably linked to its structure.
- Variations in nephron structure and function equip the kidneys of different vertebrates for osmoregulation in their various habitats.
  - Mammals that excrete the most hyperosmotic urine, such as hopping mice and other desert mammals, have exceptionally long loops of Henle that extend deep into the medulla. Long loops maintain steep osmotic gradients, resulting in very concentrated urine.
  - In contrast, aquatic mammals like beavers, which rarely face problems of dehydration, have nephrons with short loops, resulting in much less concentrated urine.
- Birds, like mammals, have kidneys with juxtamedullary nephrons that specialize in conserving water.
  - However, the nephrons of birds have much shorter loops of Henle than do mammalian nephrons, and bird kidneys cannot concentrate urine to the osmolarities achieved by mammalian kidneys.
  - The main water conservation adaptation of birds is the use of uric acid as the nitrogen excretion molecule.
- The kidneys of other reptiles, which have only cortical nephrons, produce urine that is, at most, isoosmotic to body fluids.
  - However, the epithelium of the cloaca helps conserve fluid by reabsorbing some of the water present in urine and feces.
  - Also, like birds, most other terrestrial reptiles excrete nitrogenous wastes as uric acid.
- In contrast to mammals and birds, a freshwater fish must excrete excess water because it is hyperosmotic to its surroundings.
  - Instead of conserving water, the nephrons produce a large volume of very dilute urine.
  - Freshwater fishes conserve salts by the reabsorption of ions from the filtrate in the distal tubule of the nephron.
- Amphibian kidneys function much like those of freshwater fishes.
  - When a frog is in fresh water, its skin accumulates certain salts from the water by active transport, and the kidneys excrete dilute urine.
  - On land, where dehydration is the most pressing problem, frogs conserve body fluid by reabsorbing water across the epithelium of the urinary bladder.
- Marine bony fishes, being hypoosmotic to their surroundings, have the opposite problem of their freshwater relatives.
  - Compared with freshwater fishes, marine fishes have fewer and smaller nephrons, which lack a distal tubule.
  - In many species, nephrons have small glomeruli or lack glomeruli altogether.
  - The kidneys of marine fishes have slow filtration rates, excrete very little urine, and function mainly to get rid of divalent ions such as Ca_2^+, Mg_2^+, and SO_4^{2-}, which the fish takes in by its incessant drinking of seawater.

- Marine fishes secrete these ions into the proximal tubules and excrete them with urine.
- The gills secrete monovalent ions such as Na^+ and Cl^-.

Concept 44.5 Hormonal circuits link kidney function, water balance, and blood pressure.

- One important aspect of the mammalian kidney is its ability to adjust both the volume and the osmolarity of urine, depending on the animal's water and salt balance and the rate of urea production.
  - With high salt intake and low water availability, a mammal can excrete urea and salt with minimal water loss in small volumes of hyperosmotic urine.
  - If salt is scarce and fluid intake is high, the kidney can get rid of excess water with little salt loss by producing large volumes of hypoosmotic urine (as dilute as 70 mOsm/L).
- The South American vampire bat, *Desmodus rotundas*, illustrates the flexibility of the mammalian kidney to adjust rapidly to contrasting osmoregulatory and excretory problems.
  - This species feeds on the blood of large birds and mammals by making an incision in the victim's skin and then lapping up blood from the wound.
- Because the bats fly long distances to locate suitable victims, they benefit from consuming as much blood as possible when they do find prey—so much that a bat is too heavy to fly after feeding.
  - The bat uses its kidneys to 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 water to fly, the bat returns to its roost in a cave or hollow tree.
- In the roost, the bat faces a very different regulatory problem.
  - Its food is mostly protein, which generates large quantities of urea, but roosting bats don't have access to drinking water.
  - Their kidneys shift to producing small quantities of highly concentrated urine (up to 4,600 mOsm/L), disposing 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.

A combination of nervous and hormonal controls manages the osmoregulatory function of the mammalian kidney.

- **Antidiuretic hormone (ADH)**, also called *vasopressin*, is important in regulation of water balance.
- ADH is produced in the hypothalamus of the brain and stored in and released from the pituitary gland, which lies just below the hypothalamus.
- Osmoreceptor cells in the hypothalamus monitor the osmolarity of the blood and regulate the release of ADH.
  - When blood osmolarity rises above a set point of 300 mOsm/L, more ADH is released into the bloodstream and reaches the kidney.
  - ADH induces the epithelium of the distal tubules and collecting ducts to become more permeable to water, amplifying water reabsorption.
  - This reabsorption concentrates urine, reduces urine volume, and lowers blood osmolarity back toward the set point.

- By negative feedback, the subsiding osmolarity of the blood reduces the activity of osmoreceptor cells in the hypothalamus, and less ADH is secreted.
    - ADH alone prevents further movements away from the set point, but only intake of additional water in food and drink can bring osmolarity back down to 300 mOsm/L.
- Conversely, if a large intake of water has reduced blood osmolarity below the set point, very little ADH is released.
- A low level of ADH decreases the permeability of the distal tubules and collecting ducts, so that water reabsorption is reduced, resulting in an increased discharge 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 through regulation of the water-selective channels formed by aquaporin proteins.
    - Binding of ADH to its receptor leads to a transient increase in the number of aquaporin molecules in the membranes of collecting duct cells, increasing water uptake and reducing urine volume.
- Mutations that prevent ADH production or that inactivate the human ADH receptor block the increase in the number of channels and thus the ADH response.
    - The resulting disorder, *diabetes insipidus*, causes severe dehydration and solute imbalance due to production of urine that is abnormally large in volume and dilute.
- A wide variety of genetic defects can disrupt ADH regulation of water balance in the body.
- Even in the absence of genetic changes, certain substances can alter the regulation of osmolarity.
    - For example, alcohol can disturb the water balance by inhibiting the release of ADH, 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.
- A second regulatory mechanism that helps maintain homeostasis is the **renin-angiotensin-aldosterone system (RAAS)**.
- The RAAS involves a specialized tissue called the **juxtaglomerular apparatus (JGA)**, located near the afferent arteriole that supplies blood to the glomerulus.
    - When blood pressure or blood volume in the afferent arteriole drops (for instance, due to blood loss or reduced salt intake), the JGA releases the enzyme renin.
    - Renin initiates chemical reactions that convert a plasma protein angiotensinogen to a peptide called **angiotensin II**.
- Acting as a hormone, angiotensin II increases blood pressure and blood volume.
    - Angiotensin II raises blood pressure by constricting arterioles, thus decreasing blood flow to many capillaries, including those of the kidney.
    - Angiotensin II also stimulates the adrenal glands to release a hormone called **aldosterone.**
    - Aldosterone acts on the distal tubules and collecting tube, increasing reabsorbtion of Na^+ and water, and thus increasing blood volume and pressure.
- Drugs that block angiotensin II 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 angiotensin II production.
- Renin released from the JGA cleaves a circulating substrate, angiotensinogen, to form angiotensin I.
- ACE present in vascular endothelium, particularly in the lungs, then cleaves two amino acids off from angiotensin I to form active angiotensin II.
- Blocking ACE activity with drugs prevents angiotensin II production, lowering blood pressure.

- The renin-angiotensin-aldosterone system (RAAS) is part of a complex feedback circuit that functions in homeostasis.
  - A drop in blood pressure triggers a release of renin from the JGA.
  - In turn, the rise in blood pressure and volume resulting from the various actions of angiotensin II and aldosterone reduce the release of renin.
- Although both ADH and the RAAS increase water reabsorption, they counter different osmoregulatory problems.
- The release of ADH is a response to an increase in the osmolarity of the blood, as when the body is dehydrated from excessive loss or inadequate intake of water.
  - However, a situation that causes excessive loss of salt and body fluids—an injury or severe diarrhea, for example—reduces blood volume *without* increasing osmolarity.
- The RAAS detects the fall in blood volume and pressure and responds by increasing water and Na^+ reabsorption.
- ADH and the RAAS are partners in homeostasis.
  - ADH alone would lower blood Na^+ concentration by stimulating water reabsorption in the kidney.
  - The RAAS helps maintain the osmolarity of body fluids by stimulating Na^+ reabsorption.
- Another hormone, **atrial natriuretic peptide (ANP)**, opposes the RAAS.
- The walls of the atria 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 pressure and volume.
- Thus, ADH, the RAAS, and ANP provide an elaborate system of checks and balances that regulates the kidney's ability to control the osmolarity, salt concentration, volume, and pressure of blood.